Xanthine-derived N-heterocyclic carbenes and their metal complexes

A Dissertation submitted to

The University of Wuppertal

For the degree of

Doctor of science

In the Faculty of

Mathematics and Natural Sciences

By

Moloud Mokfi

2021

The PhD thesis can be quoted as follows:

urn:nbn:de:hbz:468-20210812-151557-8
[http://nbn-resolving.de/urn/resolver.pl?urn=urn%3Anbn%3Ade%3Ahbz%3A468-20210812-151557-8]

DOI: 10.25926/9qkx-mz67
[https://doi.org/10.25926/9qkx-mz67]

“Science knows no country because Knowledge belongs to Humanity and is the torch that illuminates the world.”

-Louis Pasteur

The present work was carried out from June 2017 to October 2020 at the Faculty of Mathematics and Natural Sciences of the University of Wuppertal under the guidance of Prof. Dr. Fabian Mohr.

Acknowledgment

I would like to thank my supervisor Prof. Dr. Fabian Mohr, for giving me this great chance to be a member of his research group, and for his consistent support and guidance during the running of this project.

I would also like to acknowledge the University of Wuppertal for a Ph.D. scholarship.

I'm also thankful to the Analytical Service of the Chemistry Department, for carrying out identification analyses and for their contributions to data collection. Furthermore, I would like to thank Prof. Christian W. Lehmann from The Max Planck Institut for Coal Research in Mülheim an der Ruhr, for the measurement of some X-ray crystallography analyses and for providing advice regarding the analysis. Thanks also to Dr. Björn Beele, for carrying out some NMR analyses and help with the interpretation of some NMR spectra.

I can't forget to thank Ms. Marion Litz, for help with the removal of bureaucratic hurdles and especially for help with learning the German Language, and also for friendly conversations.

Furthermore, I would like to say a special thank you to my colleagues especially to my best friend Darya. Schmidt for their energy, understanding, and help throughout my project. It truly has been a very good time for me throughout my study at the University of Wuppertal.

Finally, from the bottom of my heart, I would like to say a big thank you to my husband for all the unconditional support, patience, and encouragement and to my family in Iran, who set me off on the road to this goal a long time ago, and for supporting me during the compilation of this dissertation.

Contents

Figures

Schemes

Tables

Abbreviations

NHC……N-heterocyclic carbene

EtOTs……Ethyl p-toluenesulfonate

$(EtO)_2SO_2$……Diethyl sulfate

HRMS……High-resolution Mass Spectrometry

EA……Elemental Analysis

FT-IR……Fourier-transform infrared spectroscopy

dmba……Dimethylbenzylamine

$(MeO)_2SO_2$……Dimethyl sulfate

MeOTs……Methyl tosylate

$MeOSO_3$……Methyl sulfate

TsO^-……Tosylate

$[Me_3O]BF_4$……Trimethyloxonium tetrafluoroborate

PPh_3……Triphenylphosphine

PTA…… 1,3,5-Triaza-7-phosphaadamantane

$EtOSO_3^-$……Ethyl sulfate

TBAC……Tetrabutylammonium chloride

TBAI……Tetrabutylammonium iodide

DEA……Diethylamine

THF……Tetrahydrofuran

$NaBPh_4$……Sodium tetraphenylborate

$NaBF_4$……Sodium tetrafluoroborate

p-cymene……1-Isopropyl-4-methylbenzene

Cp*……1,2,3,4,5-Pentamethylcyclopentadienyl

Au(tht)Cl……Chloro(tetrahydrothiophene)gold(I)

cod……1,5-Cyclooctadiene

mL……milliliter

g……gram

mg……milligram

Eq……Equivalent

h……hour

RT……Room temperature

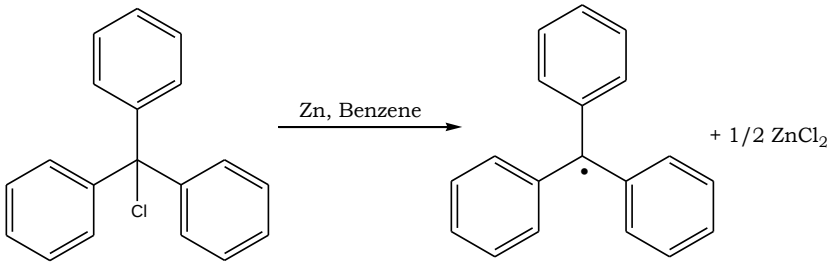
Abstract

In the present study, a series of N-heterocyclic carbene (NHC) precursors derived from theophylline, theobromine, and caffeine have been synthesized. In this regard, ethyl p-toluenesulfonate (EtOTs) and diethyl sulfate $(EtO)_2SO_2$ were used as a new generation of alkylating agents to afford the ethylation of the NHC precursors at the N^9 position. The structures of all products were evaluated and confirmed by NMR spectroscopy, high-resolution mass spectrometry (HRMS), and in some cases by elemental analysis (EA). Based on the experimental data, due to several advantages such as ease of use, high availability, low cost, and high alkylating power, $(EtO)_2SO_2$ can be preferred to EtOTs as the alkylating agent. In the next part, different NHC precursors of various anions (e.g. PF_6^-, BPh_4^-, BF_4^-, Cl^-, and I^-) were prepared by an ion-exchange reaction of the corresponding NHC precursors. The successful synthesis of the products was confirmed by NMR spectrometry, HRMS, and in some cases by EA. Moreover, regarding a great increase in biomedical applications of transition metal NHC complexes, it was decided to synthesize silver(I)-NHC complexes with general formulas of $[Ag(NHC)(NH_3)]^+$, $[Ag(NHC)(Phosphine)]^+$ (Phosphine: PPh_3, PTA), and [Ag(NHC)(X)] (X: Cl, I). Some other transition metal-NHC complexes of Ru(II), Rh(I), Rh(III), and Au(I) were prepared by following a transmetallation reaction from the corresponding [Ag(NHC)Cl] complexes. All synthesized complexes were characterized by NMR spectrometry, HRMS, EA analyses, and in some cases by single crystal X-ray diffraction. Finally, the formation of [Pd(NHC)(dmba)Cl] complex was examined by the reaction of [NHCH]Cl salts with $[Pd(dmba)Cl]_2$ dimer at 100 °C for 30-60 minutes.

1. Introduction

1.1. N-Heterocyclic carbenes

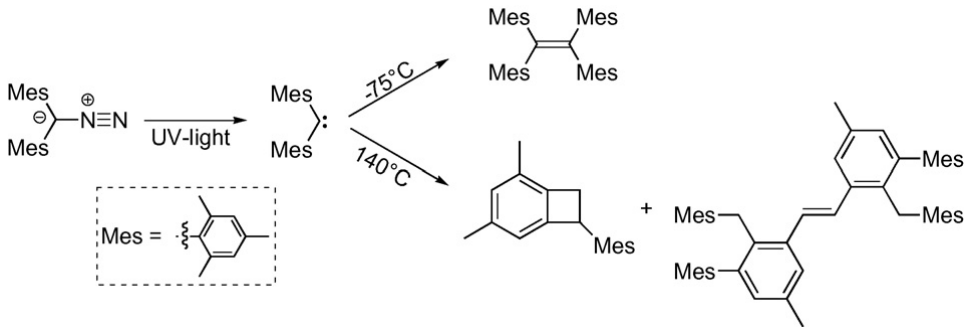
Carbenes, neutral compounds containing a divalent carbon atom with an electron sextet, have achieved considerable attention since 1855 when the first assumption of a carbene species was made by Geuther and Hermann [1]. They suggested the formation of a divalent carbon atom called dichlorocarbene as the reaction intermediate during the alkaline hydrolysis of chloroform. The same reaction intermediate was also suggested by Nef for the Reimer–Tiemann reaction and the transformation of pyrrol to chloropyridine in chloroform in 1897 [2]. However, the existence of free radicals was doubted at that time and most chemists were not convinced of the existence of free radicals. Finally, three years later, Gomberg was able to characterize triphenylchloromethylene as the first example of a free radical through elemental analysis and chemical reactivity (Scheme 1) [3]. This finding received increasing attention from the scientific community and it made carbenes the subject of an intensive research area.



Scheme 1. Synthesis of the first stable free radical.

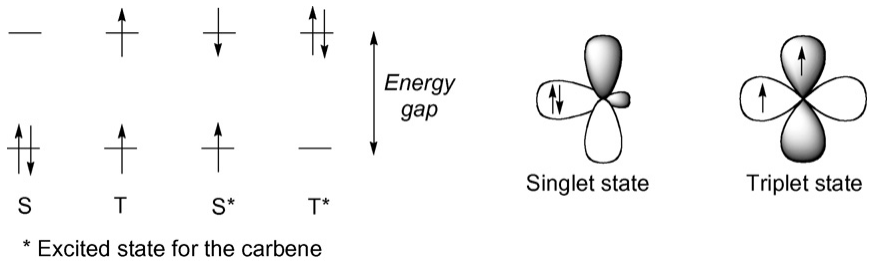
For a long time, a large proportion of researches contributed significantly to the recognition of carbenes and their use in organic chemistry as reaction intermediates. In this regard, Staudinger and Kupfer reported their success in the recognition of carbene radical intermediates by studying the formation of methylene derivatives [4] and diazomethane [5]. some other important contributions came several years later when the methylene carbene was introduced as a linear species with two generate p-orbitals leading to a triplet state [6-8]. In 1951, Lennard-Jones and Pople applied quantum mechanics to

determine the geometry and properties of small molecules [9]. They proposed two different ground states for the methylene carbene but couldn't determine which one was of the lowest energy. One of the ground states was suggested as a singlet state with triangular geometry containing three orbitals filled with paired electrons and an empty orbital. The other ground state they suggested was a triplet state with a linear geometry containing two orbitals filled with paired electrons and two orbitals filled with two unpaired electrons [9,10]. In the other research carried out in 1953, Duschenne and Burnelle confirmed that **:**CF_2 had a nonlinear symmetrical structure with a singlet ground state bearing an sp^2 hybridization, and nonbonding electrons occupied an orbital s character [11]. To accurately determine the ground state of carbenes, Zimmerman et al. tried to synthesize an isolable carbene on this presumption that steric protection would improve the stability of the carbene center. They attempted to synthesize an isolable carbene stabilized by bulky substituents (mesitylene) [12]. Although they couldn't isolate the carbene, the analysis of rearrangement products proposed a triplet ground state with an unexpectedly nonlinear geometry for the carbene center (Scheme 2).



Scheme 2. Synthesis of a triplet carbene and rearrangement products **(1)**.

In 1968, Hoffmann et al. could correctly determine the lowest splitting energy needed between both ground states to have methylene with a singlet state [13-15]. They also suggested that the π-overlap between the p-orbitals of the carbene and the α-substituents helps to favor the singlet state as the ground state (Scheme 3).



Scheme 3. Electronic states of a carbene **(1)**.

Throughout the 1970s and 1980s, a large number of theoretical works using quantum calculations were carried out to elucidate the electronic structures and the geometries of methylene moieties, for instance :CH_2, :CHF, :CHBr, :CF_2, and :CCl_2 [16-20]. Finally, in 1991, Arduengo et al. reported the successful synthesis of the first extraordinary stable, isolable, and storable carbene incorporated into an N-heterocyclic carbene (NHC) (Scheme 4) [21,22]. They tried to carefully analyze the reaction by the measurement of the amount of H_2 and NaCl formed as the by-products as well as the spectroscopic and X-ray analysis techniques (Figure 1) [22]. The obtained results confirmed the identity of NHC IAd as the first stable and storable carbene [21].

Scheme 4. Synthesis of the first stable NHC **(21)**.

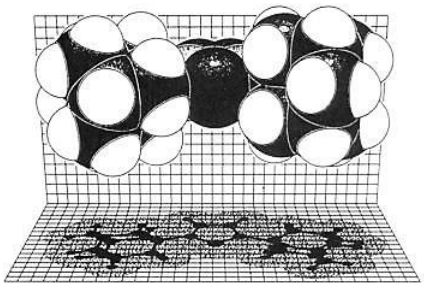
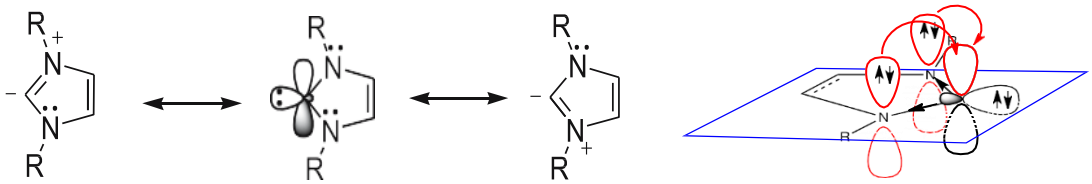


Figure 1. The X-ray structure of NHC IAd **(22)**.

The remarkable stability of the NHC IAd has been explained by two important factors including steric and electronic effects. First of all, the bulky adamantyl substituents cause the high steric shielding of the carbene carbon atom which increases the carbene lifetime. As a consequence, it was revealed that more sterically demanding substituents lead to the formation of more stable carbenes. As the second important factor, the orbital interaction of the empty p-orbital of the carbene carbon atom with the non-bonding electrons of the neighboring nitrogens delocalizes the lone pairs into the empty p-orbital which causes more stability of the carbene (Scheme 5) [21,23].



Scheme 5. Stabilization of NHCs by the electronic effect **(21,23)**.

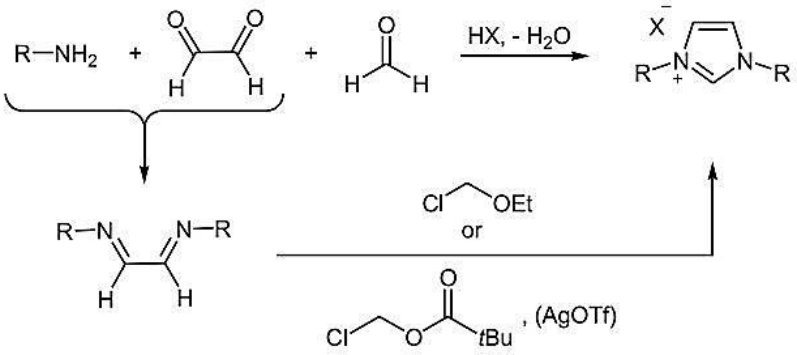
On the other hand, This orbital interaction can increase the electron density on the carbene carbon atom (Scheme 5), and therefore N-heterocyclic carbenes have been considered to be electron-rich compounds despite traditional carbenes which are regarded as electron-deficient compounds [21]. These significant findings have led to an increasing interest in the synthesis of various NHCs and their metal complexes [24-26].

In continuing theoretical and practical studies, some new attractive features of NHCs as ligands for transition metal complexes were reported. For instance, N-heterocyclic carbenes are very electron-rich ligands that act like typical σ-donor ligands such as amines, ether, and phosphines in organometallic chemistry [27-31]. It is also worth mentioning that the electronic properties of NHCs ligands can be altered by changing the nature of the azole ring. For example, the electron-donating power increases in the order benzimidazole < imidazole < imidazoline [32, 33]. Moreover, the Π-acceptor power of NHCs can be considered as another feature of NHCs that is still open to dispute. Based on the theoretical and experimental studies, this property can be influenced by different factors like the metal, the co-ligands, the substituents on the NHC, and the orientation of the NHC ligand relative to the metal [21,34-37]. So, NHC ligands can form stable transition metal complexes

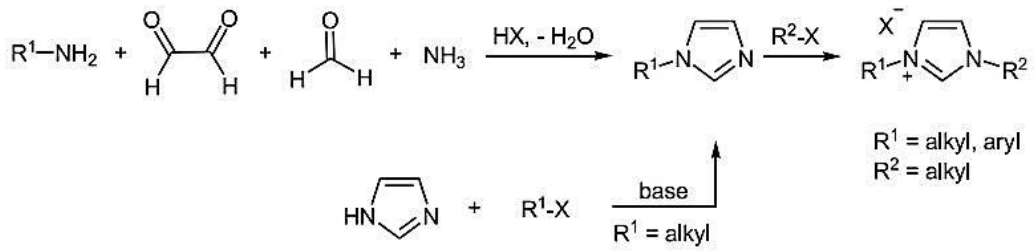
caused by their strong σ-donor and weak π-acceptor properties [38-41]. In the light of all features mentioned above, NHCs have become a very attractive group of ligands that can be prepared, functionalized, and coordinated in a fairly simple manner, and form stable transition metal complexes.

1.2. Synthesis of N-heterocyclic carbenes

In the following years, many research groups from all over the world have released their reports on the synthesis of NHC ligands, their metal complexes, and potential applications of NHC-metal complexes in different fields such as synthetic chemistry as carbene transfer agent [42,43], medicinal chemistry [44-48], and catalysis [49-52]. The scientific studies revealed that NHCs, also known as imidazole-2-ylidene, can be generally obtained through deprotonation of the corresponding azolium salts for example imidazolium [53], triazolium [54], pyrazolium [55], and benzimidazolium salts [56] aided by a suitable base. Among these NHC precursors, imidazolium, and benzimidazolium salts with pK_a of 21-24 have recently attracted significant interest [57,58]. According to recent researches, imidazolium salts can be prepared with two different procedures. Based on the first method, the N,Ń-substituted imidazolium ring can be built up through a multicomponent reaction [59]. This method provides an opportunity for the preparation of many symmetrical as well as unsymmetrical sterically demanding imidazolium salts (Scheme 6, Scheme 7) [21].



Scheme 6. Synthesis of symmetrical imidazolium salts **(21)**.



Scheme 7. Synthesis of unsymmetrical imidazolium salts **(21)**.

Moreover, imidazolium salts can also be synthesized by alkylation of existing imidazoles at nitrogen atoms using suitable electrophiles [29]. According to this procedure, unsymmetrical N,Ń-substituted imidazolium salts can be obtained through alkylation of monosubstituted imidazoles (Scheme 7) [29,60-66].

In the following years with the growing tendency for *Green Chemistry*, more studies have focused on using naturally occurring imidazoles as NHC precursors. In this sense, xanthine derivatives (Figure 2) with imidazole moiety have recently attracted more attention.

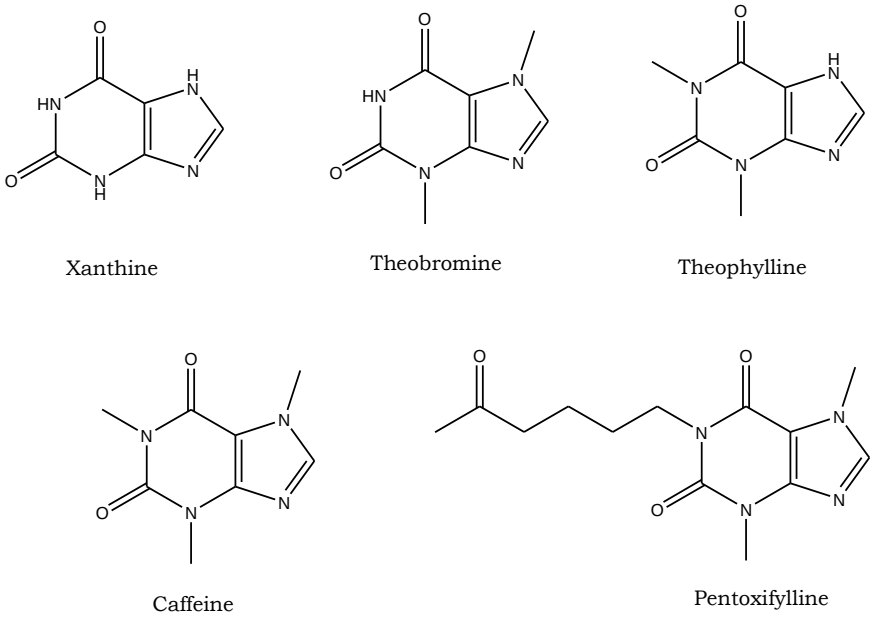
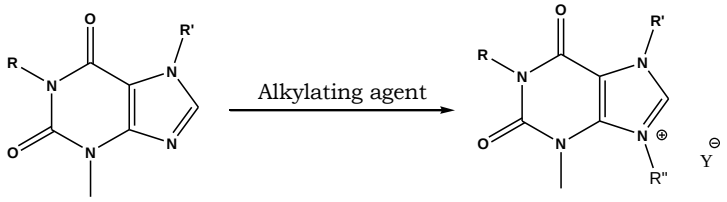


Figure 2. The molecular structures of some common xanthine derivatives.

These compounds are natural products that are often found in coffee, cacao, tea, and chocolate, so the low toxicity and high accessibility have made them the ideal potential NHC precursors. Moreover, biomedical studies of xanthine derivatives such as caffeine revealed

the fact that these compounds themselves have potential pharmaceutical properties that can be improved in combination with a metal center and form NHC-metal complexes with medical applications [67-69]. On the other hand, xanthine derivatives such as theophylline and theobromine can be functionalized before the synthesis of their corresponding imidazolium salts which can lead to the formation of very attractive systems for medical [70,71] and catalytic applications [72].

The synthesis of NHCs derived from xanthines generally starts with the alkylation of xanthine derivatives at the N^9 position to produce their corresponding imidazolium cations which are consequently subjected to the deprotonation reaction in the presence of a suitable base (Scheme 8). In this regard, there are many reports on the synthesis of different imidazolium salts using various alkylating agents such as trimethyloxonium tetrafluoroborate [70,73], iodoalkyl [69,71,74], dimethyl sulfate [68,75-77], or methyl tosylate [76].



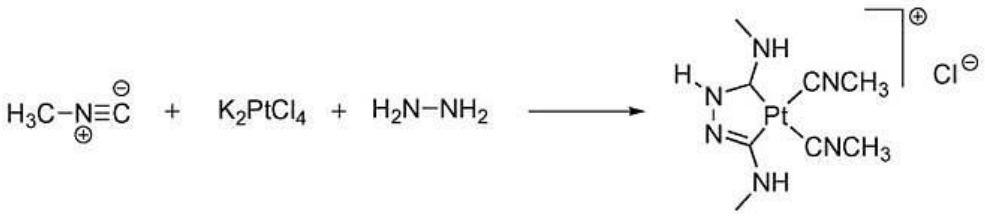
Scheme 8. The general synthesis procedure of imidazolium salts derived from xanthines.

Based on the scientific studies, although $[Me_3O]BF_4$ can be used in stoichiometric amounts and mild reaction conditions for the alkylation of xanthines, the high-price of $[Me_3O]BF_4$ reagent and the need for anhydrous conditions can be considered as significant drawbacks of this procedure. As an alternative to this reagent, Cannon and Youngs employed iodomethane for the alkylation of caffeine [69]. Even though this alkylating agent has highly been desirable for its low-price in comparison with $[Me_3O]BF_4$ the reaction conditions such as the need for a large excess of the alkylating agent, long reaction time, and high reaction temperature can be regarded as some disadvantages of this procedure [71,74,78]. On another attempt, Youngs and et al. employed dimethyl sulfate for the alkylation of caffeine and were able to obtain the desired product in 72% yield [77]. Due to the low price of

the reagent, short reaction time, and high reaction efficiency, dimethyl sulfate and similar alkylating agents such as diethyl sulfate, ethyl tosylate, and methyl tosylate have recently been investigated for the alkylation of xanthine derivatives and research in this area is still expanding [79,80].

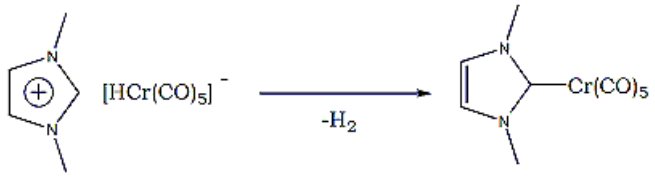
1.3. Synthesis and applications of NHC-metal complexes

In 1915 Chugaev reported the synthesis of a platinum complex of a non-cyclic N-stabilized carbene ligand which could be considered as the most significant contribution to the organometallic chemistry of NHC-metal complexes (Scheme 9) [81,82]. Unfortunately, cause of the lack of the required spectroscopic techniques they couldn't reveal the first synthesis of a metal-carbene complex. Several years later, in 1970, the structure of the synthesized complex was finally proposed by Rouschias and Shaw [83].



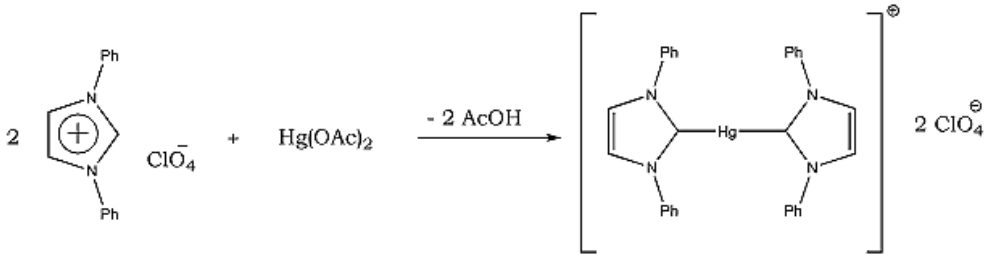
Scheme 9. Synthesis of the Chugaev's platinum complex **(1)**.

In 1968 the synthesis of the first transition metal-NHC complexes was reported by Öfele [84] and Wanzlick [85,86]. Öfele prepared the first $(NHC)Cr(CO)_5$ complex through the in situ deprotonation of the azolium cation by Brönstedt basic metallate anions upon heating (Scheme 10). In the following years, this procedure was used to prepare other NHC-metal complexes from benzimidazolium, pyrazolium, triazolium, and tetrazolium salts [87-89]. However, this synthesis procedure is limited by the availability of the suitable metallate precursor, which is governed by the nature and oxidation state of the metal center in the new complex as well as its ligand environment [90].



Scheme 10. The synthesis of the first NHC-metal complex by Öfele.

In another work, Wanzlick reported the successful synthesis of a mercury bis-NHC complex using a different procedure. Based on this method, the complex was obtained from the reaction between the azolium cation and mercury(II) acetate as the basic anion which can provide the desired ligand by the in situ deprotonation of the azolium cation (Scheme 11) [85,86].



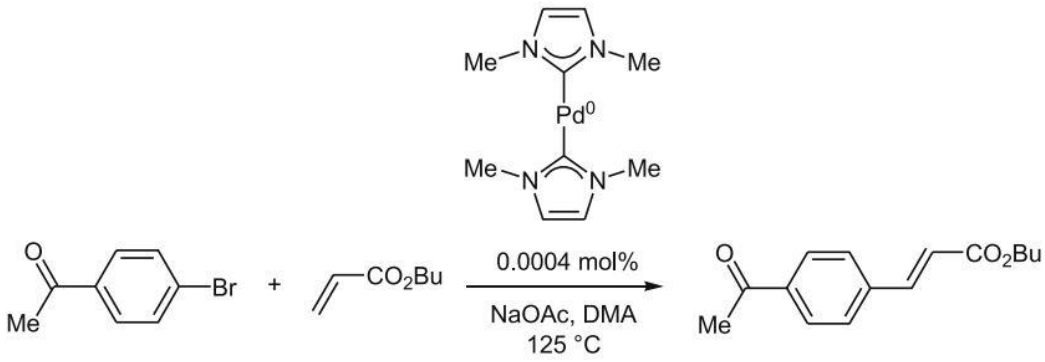
Scheme 11. The first Hg(II)-NHC complex synthesized by Wanzlick.

Two years after the isolation of the first free NHC by Arduengo [22], the synthesis of the first homoleptic silver(I)-NHC complex was reported in 1993 [91]. But due to difficulties in obtaining free carbenes, only a limited number of silver(I)-NHC complexes were synthesized using this procedure. Several years later, Lin et al. reported a facile synthesis of gold(I) and silver(I)-NHC complexes from the reaction of azolium salts with metal precursors under basic phase transfer catalysis (PTC) conditions [92,93].

Furthermore, silver(I)-NHC complexes were introduced as carbene transfer agents in transmetallation reactions to prepare different transition metal-NHC complexes [93]. This synthesis method has recently been established as a common method for the preparation of metal-NHC complexes with various transition metal centers such as Au(I) [94-101], Pd (II) [102-109], Pt(II) [110-112], Rh (I) [113-120], Rh (III) [121,122] Ru(II) [123-129], Ru (III) [125], Ru (IV) [130,131], Ir (I) [120,121,132-136], Ir (III) [121,137-139], Ni (II) [140,141], Cu (I) [142-144], Cu (II) [145-147]. In addition to silver(I)-NHC complexes Tungesten carbene complexes have also been reported as an effective carbene transfer reagents for the synthesis of Pt, Pd, Au, and Rh complexes [148].

Synthesis of various transition metal-NHC complexes has led to enormous researches on potential applications of these complexes in organometallic chemistry [149-152].

For the first time, in 1995, Herrmann et al. confirmed the catalytic activity of NHC transition metal complexes [153]. This work revealed that palladium-NHC complexes show high catalytic activity and a remarkably long lifetime which make them an excellent catalyst for several Heck reactions (Scheme 12). It was found that due to the strong σ–donor property of NHC ligands, they can produce stable metal-NHC complexes with high reactivity and relative selectivity for numerous chemical transformations [154-157].



Scheme 12. The first application of NHC-metal complexes as catalyts **(21)**.

Since this finding, metal-NHC complexes have extensively been studied in organocatalysis [158-160]. Further works demonstrated that silver(I)-NHC complexes can not only act as efficient catalysts for a wide range of organic transformations [145,161-163] but also show promise as antimicrobial or potential anti-cancer agents [164-167]. The antimicrobial properties of silver are known for centuries and the successful application of different silver compounds such as silver nitrate [168] and silver sulfadiazine [169] in wound treatment has been documented. However, the mechanism of the antimicrobial action of silver compounds is not completely understood. It is assumed that the efficacy of silver compounds as antimicrobial agents can be attributed to the slow release of silver cation over a long time to prevent reinfection [71,170]. In 2004 silver(I)-NHC complexes were first introduced as a novel class of antimicrobial agents (Figure 3) [171]. The results revealed that the alkanol N-functionalized silver-carbene complexes are soluble in aqueous media and they showed better bacteriostatic activity than silver nitrate, even at a much lower concentration. Moreover, it was also found that the counter ion can affect the water solubility of the silver(I)-NHC complexes for example

hydroxide as the counter ion can increase the water solubility of the complex.

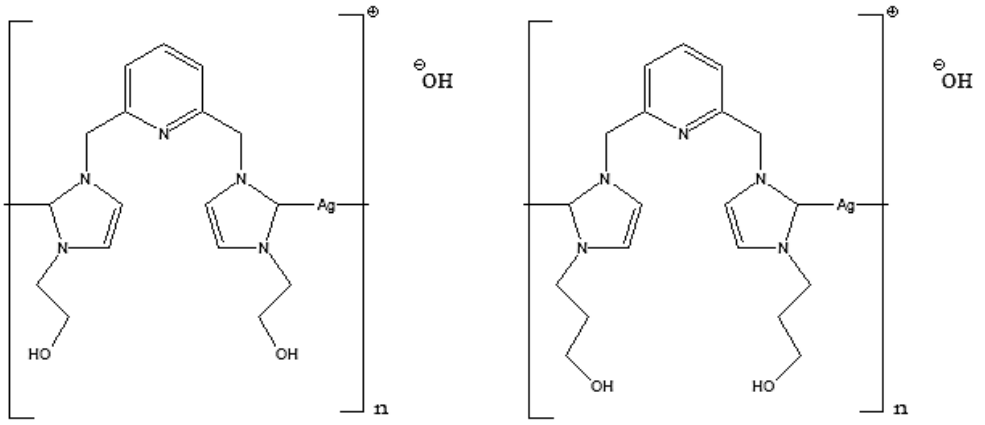


Figure 3. Some silver(I)-NHC complexes with antimicrobial activity.

In continuing studies, it was suggested that NHC ligands, as strong σ-donors, can form a stable silver-carbon bond that causes the slow release of silver cations which prevents reinfection [167,172,173]. On the other hand, several studies have revealed that silver(I)-NHC complexes can have a potential future in the treatment of cancer [174-176].

After the successful application of platinum-based drugs such as cisplatin in chemotherapy [177,178], severe side effects and the development of drug resistance have increased demand for new organometallic anticancer drugs. In this regard, silver with relatively low toxicity compared to platinum has received increasing attention in cancer chemotherapy. According to the organometallic studies, ligands as the delivery agent surrounding the silver can make significant effects on the character of silver(I) complexes such as toxicity. Thus xanthine derivatives as natural products with low toxicity have attracted significant attention. In addition to low toxicity and high availability, xanthine derivatives have themselves been used for their chemotherapeutic effects [179].

In 2006 Youngs et al reported the synthesis of silver(I)-NHC complex from caffeine, which was found to be active against resistant respiratory pathogens [69]. Three years later, the same group described the synthesis of a functionalized-theobromine by adding a hydroxyethyl group to the backbone of this ligand and confirmed that the silver(I) complex of this ligand can be effective against a variety of

cystic fibrosis relevant pathogens (Figure 4) [180]. Based on the obtained results, SCC8 by adding a hydroxyethyl group at the N^1 position shows a better water solubility compared to SCC1.

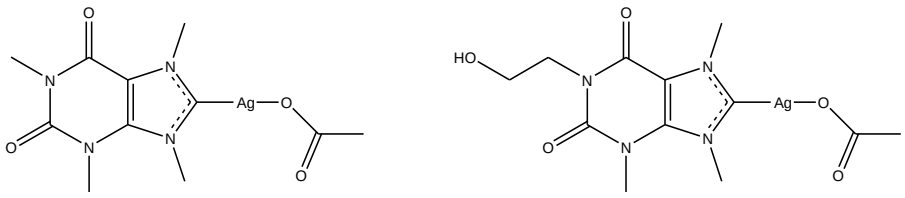


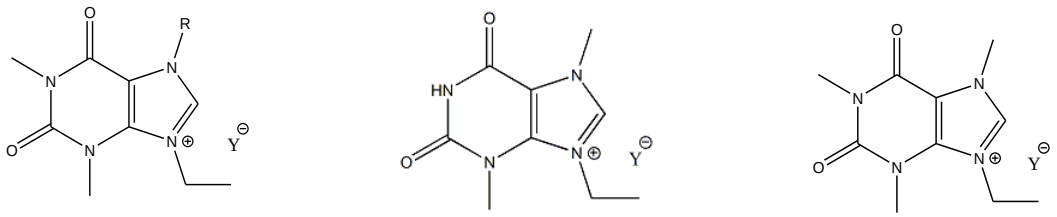
Figure 4. Theobromine derived silver(I)-NHC with antimicrobial efficacy.

As a consequence, the synthesis of metal complexes with functionalized NHCs has been considered one of the newest strategies to increase the effectiveness and bio-conjugation of metal-NHC complexes by adding biologically relevant groups to the backbone of the ligand [181-183].

In further works, the biological activity of caffeine-based NHC complexes of gold(I) as anticancer agents has been reported [70]. However, due to the more favorable toxicological profile of silver(I)-NHC complexes compared to gold(I)-NHC complexes they have recently been more evaluated for their anticancer and antimicrobial properties [184-189]. Here, it should be noted that synthesis and biological evaluation of transition metal-NHC complexes are still the subjects of intensive research.

2. Amis and objectives

Recently, N-heterocyclic carbenes (NHCs) and their metal complexes have attracted great interest and have widely been investigated due to their pharmaceutical properties. Therefore, in this contribution, we firstly decided to examine the synthesis of some new NHC precursors derived from theophylline, theobromine, and caffeine. These compounds contain an imidazolium ring which makes them an ideal choice for evaluation as potential precursors to NHCs. Moreover, they are widely found in foods and beverages, so high availability and low toxicity can be considered as their added benefits. In the present work, we examined the ethylation of the xanthine derivatives at the N^9 position utilizing ethyl p-toluenesulfonate (EtOTs) and diethyl sulfate $(EtO)_2SO_2$ as the new generation of alkylating agents under solvent-free conditions. As the result, the synthesis of a series of NHC precursors with the following structures is expected in (Figure 5).



R; H, Bn, BnCl

Y; TsO, $EtOSO_3$

Figure 5. The NHC precursors that are expected to be synthesized in this research.

The second aim of this project is to synthesize a family of heteroleptic silver(I)-NHC complexes, due to their biomedical properties such as antimicrobial and anticancer effects. In this context, it is worth noting that according to recent studies these complexes are generally prepared by a reaction of [NHCH]X salts (X: PF_6^-, BF_4^-, and halides) with silver(I) precursors. Thus, we should first test the formation of the NHC salts of various anions like PF_6^-, BF_4^-, BPh_4^-, Cl^-, and I^- by following an ion-exchange reaction between the [NHCH]Y salts (Y: TsO^- and $EtOSO_3^-$) and the proper anion precursor. Next, the silver(I)-NHC complexes with the general formulas of $[NHC\text{-}Ag\text{-}NH_3]^+$, $[NHC\text{-}Ag\text{-}Phosphine]^+$ (Phosphine: PPh_3 and PTA), and [NHC-Ag-Cl] would be synthesized from the newly synthesized NHC precursors.

To keep up with our objectives of the synthesis of different transition metal-NHC complexes, we examine the formation of $[RuCl_2(NHC)(p\text{-cymene})]$,

[$RhCl_2$(NHC)(Cp*)], [RhCl(NHC)(cod)], and [Au(NHC)Cl] complexes (Figure 6) by following a transmetallation reaction from [NHC-Ag-Cl].

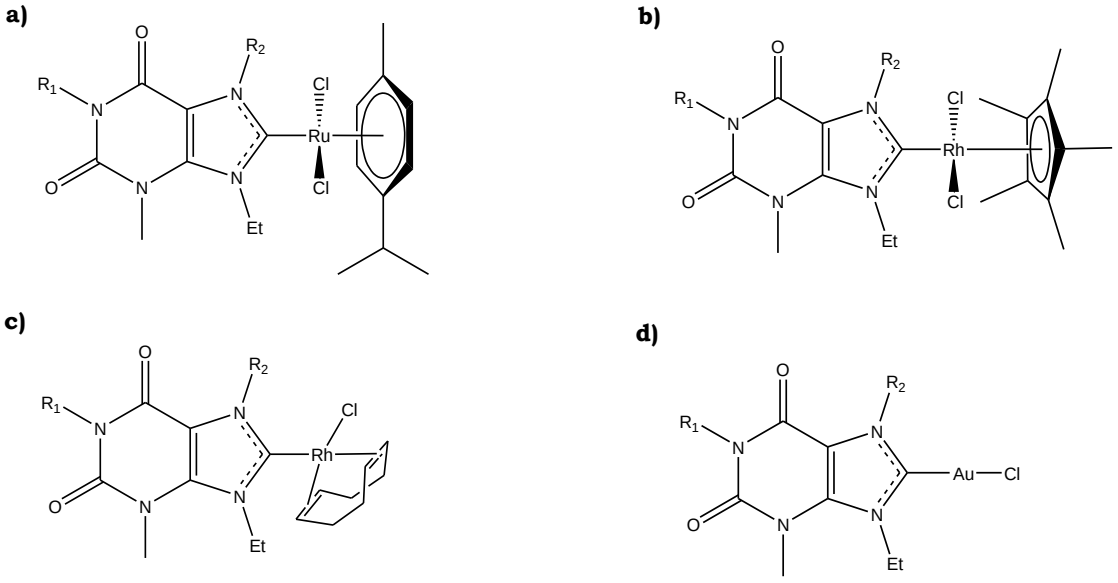


Figure 6. The expected transition metal-NHC complexes obtained from the transmetallation reactions. a) [$RuCl_2$(NHC)(p-cymene)], b) [$RhCl_2$(NHC)(Cp*)], c) [RhCl(NHC)(cod)], d) [Au(NHC)Cl].

Finally, we evaluate the synthesis of some Pd(II)-NHC complexes which can directly be synthesized from a reaction between [NHCH]Cl salts and the Pd(II) precursor in presence of a base. Two different Pd(II)-NHC complexes are proposed to be synthesized in this work (Figure 7).

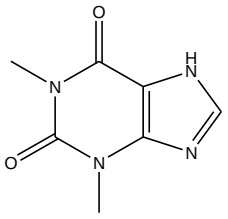
Figure 7. Some Pd(II)-NHC complexes that may hold interest for evaluation in this work .

3. Results and discussion

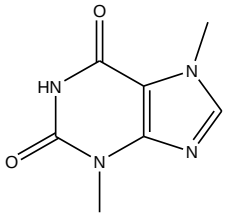
3.1. Synthesis of N-heterocyclic carbene ligands

3.1.1. Synthesis of xanthine-derivatives

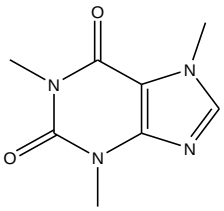
In this research, we firstly examined the formation of various substituted imidazolium salts from naturally occurring derivatives of xanthine (Figure 8). Taking into account that these derivatives contain an imidazole ring, they could be used as N-heterocyclic carbene precursors. Moreover, they are natural products that are naturally presented in coffee beans, tea leaves, and cocoa beans, so their low toxicity and high availability can be considered as distinct advantages of these compounds.



Theophylline



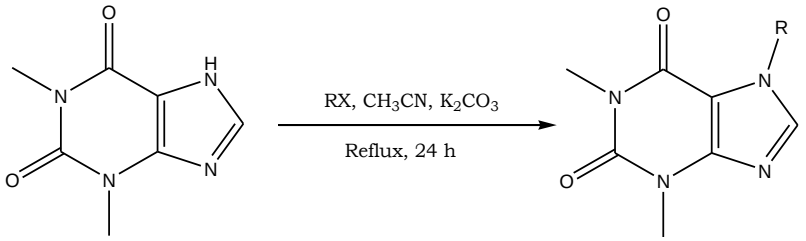
Theobromine



Caffeine

As the first set of experiments, two different derivatives of theophylline (**1a** and **2a**) were synthesized and characterized according to the reported procedure [71]. More details are shown in Table 1.

Table 1. The general synthesis procedure of the theophylline derivatives.



Sample	R	X	Yield (%)
1a	Bn	Br	97
2a	BnCl	Cl	67

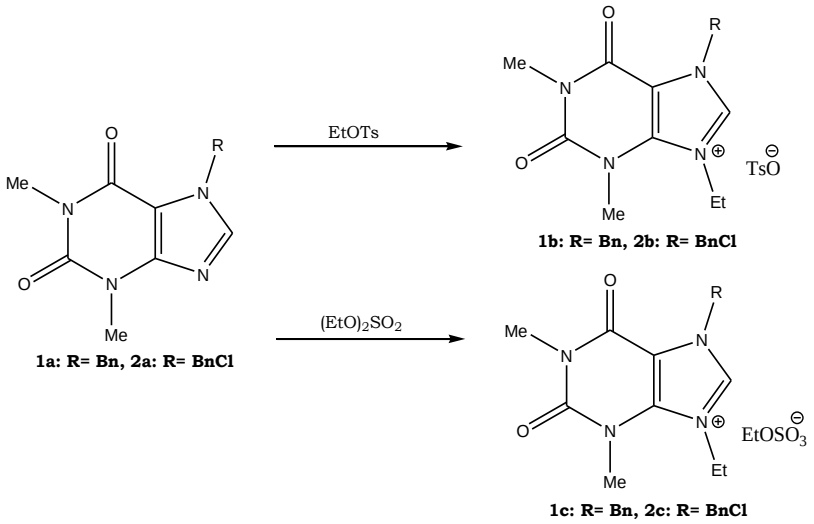
The ^{1}H and ^{13}C-NMR results, as well as the HRMS and EA, confirmed the successful synthesis of **1a** and **2a** compounds. For example, the most relevant change found in the ^{1}H and ^{13}C-NMR spectra was the appearance of the new resonance signals in the aromatic region (Table 2).

Table 2. The ^{1}H and ^{13}C-NMR results for **1a** and **2a** in $CDCl_3$.

Sample	^{1}H-NMR/δ (ppm)	^{13}C-NMR/δ (ppm)
1a	7.32-7.41	127-136
2a	7.25-7.37	129-135

3.1.2. Synthesis of imidazolium salts from xanthine-derivatives

Imidazolium salts are synthesized in most cases using alkyl halides as the alkylating agent [71,77,190]. However, this method suffers from some drawbacks, for instance, harsh reaction conditions, long reaction time, large amounts of expensive reagents or catalysts, and costly processing equipment [191]. Moreover, when the synthesized imidazolium halide salts are used for ion-exchange reactions (e.g., to prepare imidazolium hexafluorophosphate or tetrafluoroborate, etc.), the presence of halide contamination in the product can be mentioned as another disadvantage of utilizing this group of alkylating agents [192]. To overcome these drawbacks, we decided to use Alkyl sulfonates and dialkyl sulfates as the new generation of alkylating agents. So in the second part of this research, a family of imidazolium salts (**1b**, **1c**, **2b**, and **2c**) was prepared by ethylation of xanthine-derivatives with EtOTs and $(EtO)_2SO_2$ under solvent-free conditions (Scheme 13).



Scheme 13. The ethylation of xanthine-derivatives under solvent-free conditions.

The details of the optimized reaction conditions are reported in Table 3.

Table 3. The optimized ethylation reaction conditions of xanthine-derivatives.

Sample	Ethylating agent	Eq. ratio	T (°C)	Time (h)	Yield(%)
1b	EtOTs	3.6	150	2	87
2b	EtOTs	3.6	150	2	84
1c	$(EtO)_2SO_2$	2	130	2	87
2c	$(EtO)_2SO_2$	2	130	2	88

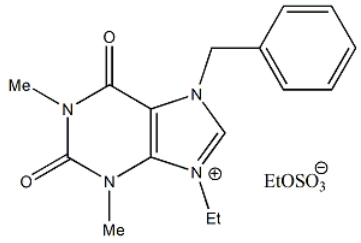
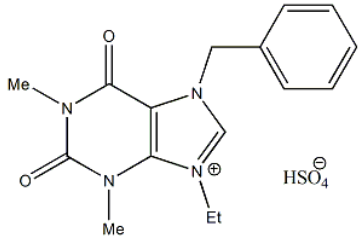
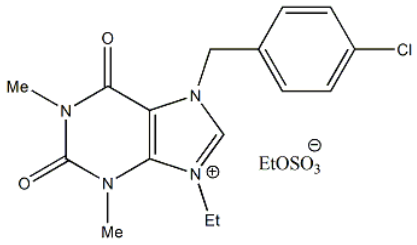
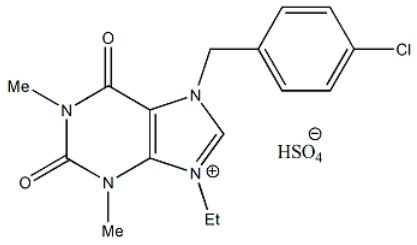
The product structures were characterized and confirmed by ^{1}H and ^{13}C-NMR spectroscopy, HRMS, and EA. In the ^{1}H-NMR spectra of the products, the resonance signals of the ethyl group were observed as a quartet for **-CH_2**CH_3 and a triplet for -CH_2**CH_3** at 5.65-5.75 and 1.50-1.55 ppm, respectively. Moreover, the imidazolium protons were characterized at 9-10 ppm that is consistent with the general acidic proton shift of imidazolium salts (δ: 8-10 ppm) [193]. Furthermore, in the ^{13}C-NMR spectra the imidazolium carbon (N-C-N), which later becomes the carbene centers, shows a chemical shift at 138-140 ppm. The HRMS also confirmed the formation of the expected products.

Based on the experiments, $(EtO)_2SO_2$ is preferred to EtOTs as the alkylating agent, due to its several desirable features, namely ease of use (diethyl sulfate is found as a liquid reagent, while EtOTs is a crystalline solid at room temperature), low cost, and high availability. Moreover, it needs to be noted that diethyl sulfate shows a higher alkylating power, so the expected products were synthesized using lower amounts of diethyl sulfate at a lower reaction temperature in comparison with using EtOTs as the alkylating agent.

Through the alkylation reaction with diethyl sulfate, it was found that diethyl sulfate can be decomposed to hydrogensulfate at temperatures above 130 °C to produce the xanthine-derivatives imidazolium hydrogensulfates as the product which shows higher water solubility than the same products with ethyl sulfate or tosylate as the counter-ion (Table 4). The ^{1}H and ^{13}C-NMR analyses are consistent with the expected structures. In ^{1}H-NMR spectra, signals of ethyl sulfate were disappeared, and instead, in some cases, a broad singlet signal was observed at 4-4.3 ppm that could be assigned to HSO_4^-. Also, the existence of

HSO_4^- as the counter-ion was approved by the mass spectrometry in the negative mode.

Table 4. The effect of reaction temperature on the product structure of alkylation reaction using diethyl sulfate as the alkylating agent.

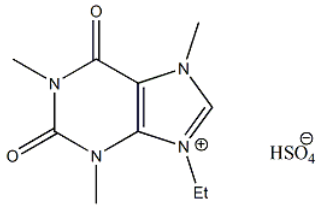
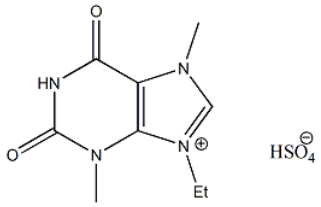
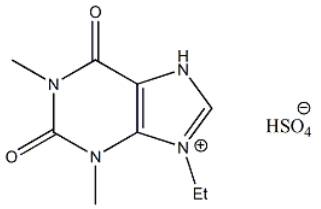
Sample	Structure	Eq. ratio	T(°C)	Time(min)	Yield(%)
1c		2	130	120	87
1d		2	150	180	76
2c		2	130	120	88
2d		2	150	150	83

* the optimized reaction conditions have been shown in the table.

As the final step, the generality of this procedure was examined by alkylation of other xanthine-derivatives (e.g. caffeine, theobromine, and theophylline). It is also worth noting that theobromine and theophylline as non-substituted xanthine-derivatives at N^1 and N^7 positions gave us the chance to evaluate the effect of the -NH group on

this alkylation method. More details are available in Table 5. The structures of the products were also established by ^{1}H and ^{13}C-NMR analyses and mass spectrometry in positive and negative modes. The results confirmed the formation of the imidazolium salts of HSO_4^- as the product.

Table 5. Evaluation of xanthine-derivative structure effect on the alkylation reaction using diethyl sulfate as the alkylating agent.

Sample	Structure	Eq. ratio	T (°C)	Time (min)	Yield(%)
3d		2	130	120	91
4d		2	160	95	65
5d		1.8	160	105	43

* the optimized reaction conditions have been shown in the table.

3.1.3. Ion-exchange reactions of the imidazolium salts

- **Synthesis of [NHCH]PF_6 salts**

The second goal of this project was the preparation of the imidazolium salts of various anions like PF_6^-, BPh_4^-, BF_4^-, and halides by ion-exchange reactions.

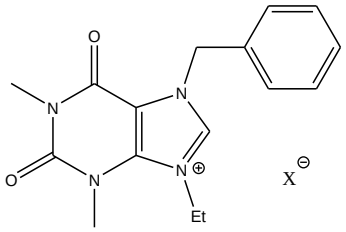
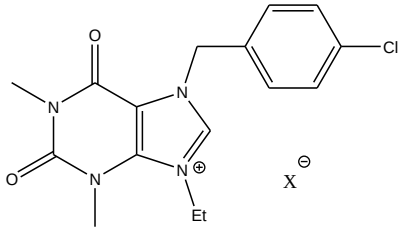
In this regard, first, the hydrophobic imidazolium hexafluorophosphates [NHCH]PF_6 were synthesized by the reaction of **1b-1d** and **2b-2d** with NH_4PF_6 in water as the solvent at room temperature. Due to the very low solubility of [NHCH]PF_6 in water, the product was obtained as a white

precipitate which was easily separated from the reaction mixture by simple filtration [77]. The structures of the products were proved by ^{1}H, ^{13}C, and ^{31}P-NMR spectroscopy, HRMS, and EA.

The disappearance of the resonance peaks of TsO^-, $EtOSO_3^-$, and HSO_4^- in ^{1}H and ^{13}C-NMR spectra and the appearance of PF_6^- signal as a heptate at -144 ppm in ^{31}P-NMR spectrum confirm the successful synthesis of the products as expected.

Quite interestingly, the experiments imply that in some cases the efficiency of the reaction increases in the sequence of counter-ion: HSO_4^->$EtOSO_3^-$>TsO^-, that it could be explained by the effect of counter-ion on the water solubility of the imidazolium salt. The $[NHCH]HSO_4$ with the higher water solubility shows more reactivity in the reaction which leads to the high yield for $[NHCH]PF_6$ as the product (Table 6).

Table 6. The effect of counter-ion on the efficiency of the ion-exchange reaction to prepare $[NHCH]PF_6$ salts.

Entry	Precursor	X^-	Yield(%)/$[NHCH]PF_6$
1		TsO	69
		$EtOSO_3$	74
		HSO_4	**89**
2		TsO	77
		$EtOSO_3$	74
		HSO_4	**79**

The performance of this procedure to provide other $[NHCH]PF_6$ salts with various cations, was evaluated by alternating $[NHCH]^+$ with the other ethylated xanthine-derivatives.

Based on the results obtained in this part of the research, ethylated caffeine and theobromine hydrogensulfates can be converted to corresponding PF_6^- salts, while after several additional attempts in different reaction conditions, it was found that the reaction of ethylated theophylline hydrogensulfate could not be successfully

carried out. The obtained product was characterized by ^{1}H, ^{13}C, and ^{31}P-NMR and mass spectrometry analyses.

The ^{31}P-NMR spectrum shows no PF_6^- signals for the product which reveals that HSO_4^- couldn't be replaced by PF_6^- successfully. But a strange change found in the ^{1}H-NMR spectrum was the appearance of a group of three peaks with an integral ratio of 1:1:1 at 6.68-7.32 ppm (Figure 9).

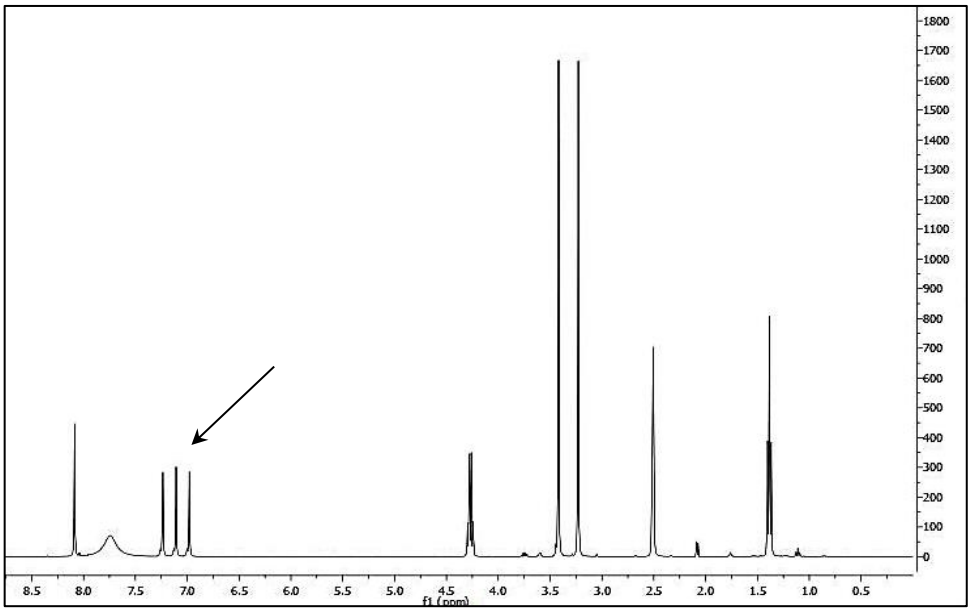


Figure 9. The ^{1}H-NMR spectrum of the product obtained from the ion-exchange reaction of ethylated theophylline with NH_4PF_6 (in DMSO, 400 MHz).

To get more information about this group of signals, different 2D NMR analyses (e.g. ^{1}H-^{13}C HSQC ($^{1}J_{CH}$), ^{1}H-^{13}C HMBC ($^{2,3}J_{CH}$), ^{1}H-^{1}H COSY) were carried out.

The HSQC analysis shows that this group of protons is bonded to a non-carbon atom and this finding was also proved by carrying out the ^{1}H-NMR analysis in different solvents with different polarities. This group of peaks disappears in a protic solvent like methanol which reveals that these protons exhibit hydrogen bondings and have to be attached to a heteroatom.

On the other hand, the HMBC spectrum confirms that there are no correlations between this group of protons and carbon atoms in the product. For more detail, the possible correlations between protons

were examined by the ^{1}H-^{1}H COSY analysis. Surprisingly, no correlations were found between this group of protons and other protons in the product structure (Figure 10).

Finally, we decided to do a mass spectrometry analysis in both positive and negative modes. Unfortunately, The mass spectrometry results couldn't be helpful to identify the product structure.

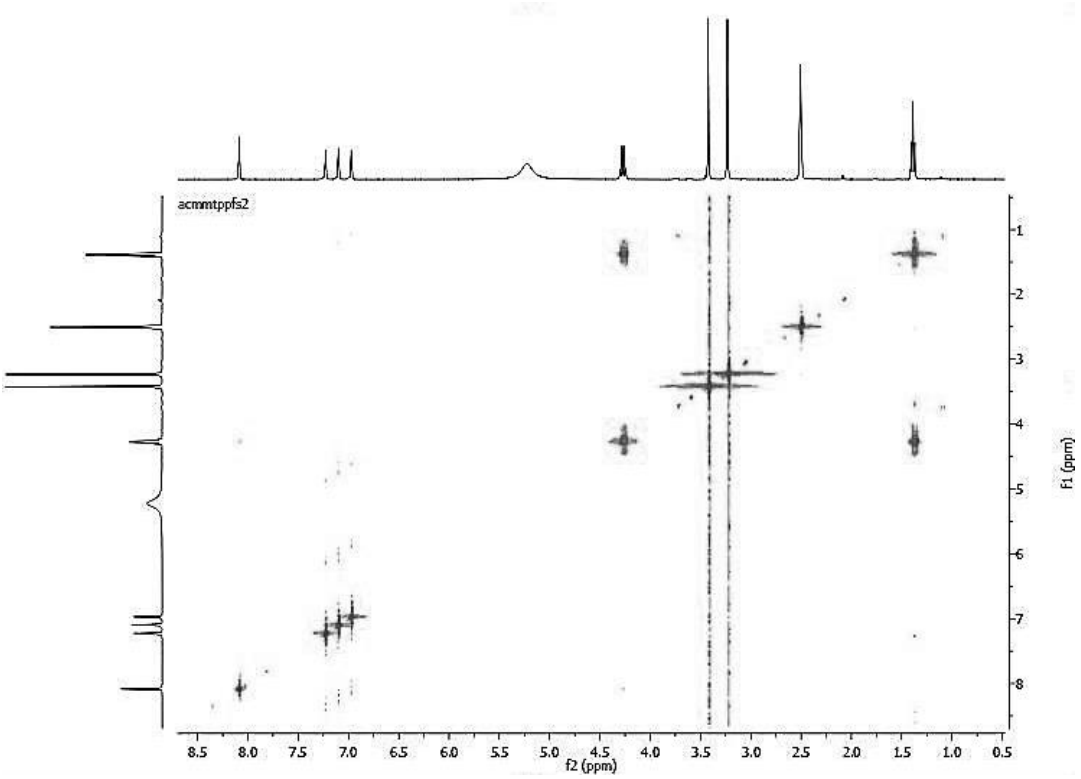


Figure 10. The ^{1}H-^{1}H COSY spectrum of the product obtained from the ion-exchange reaction of ethylated theophylline with NH_4PF_6 (in DMSO, 400 MHz).

- **Synthesis of [NHCH] BPh_4/BF_4 salts**

It should be noted that the ethylated xanthine-derivatives of various anions can also be obtained by alternating anions in [NHCH]X (X: TsO^-, $EtOSO_3^-$, HSO_4^-) with other anions. For example, in this work, [NHCH]BPh_4 was synthesized with the same method from the reaction of **1b-1d** and **2b-2d** with $NaBPh_4$ in water as the solvent. The products were fully characterized and confirmed by NMR spectroscopy and Mass spectrometry analyses.

We also examined the synthesis of [NHCH]BF_4 by the same method. According to the experiments, [NHCH]BF_4 can be obtained from the

reaction of [NHCH]HSO_4 (**1d, 2d**) with $NaBF_4$ in a mixture of methanol: H_2O (4:1) as the solvent. Based on the results, it should be considered that;

First, the [NHCH]HSO_4 can be converted to [NHCH]BF_4 in this route while for other ethylated xanthine-derivatives of TsO^- or $EtOSO_3^-$, the anion can't be successfully replaced by BF_4^-.

Second, the idea in this method is to utilize the solubility difference among [NHCH]HSO_4 and $NaBF_4$ as the starting materials and [NHCH]BF_4 and $NaHSO_4$ as the reaction products in the reaction solvent. Since they all show high solubility in water, it couldn't be an ideal choice as the solvent in this reaction. After several attempts, it was found that $NaBF_4$ and $NaHSO_4$ (as the by-product) are soluble in a mixture of methanol: H_2O (4:1), while [NHCH]HSO_4 and [NHCH]BF_4 (as the expected product) show low solubility in the solvent and the product is obtained as a white precipitate which can easily be isolated from the reaction mixture by a simple filteration method. But it should be noted that the amount of solvent in the reaction should be as small as possible. Because using a high amount of solvent could lead to an increase in the solubility of the substrate and the product which can cause low efficiency of the reaction.

Finally, the structures of the products (**1h** and **2h**) were confirmed by NMR and mass spectrometry in positive and negative modes. The ^{19}F-NMR spectrum shows two resonance peaks at -148.35 and -148.41 ppm for BF_4^- due to the two isotopes for boron (B-10 and B-11), respectively. Moreover, the mass spectrometry analysis, in negative mode, proved the successful replacement of HSO_4^- by BF_4^- (Table 7).

Table 7. The ^{19}F-NMR and mass spectrometry analyses of the synthesized [NHCH]BF_4.

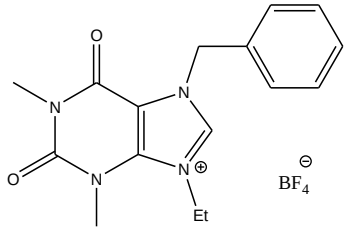
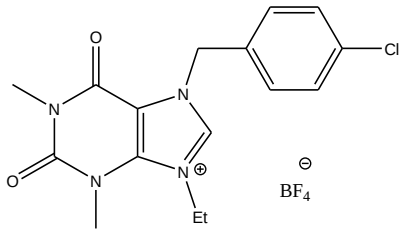
Sample	Structure	^{19}F-NMR/ δ (ppm)	Mass analysis (Negative mode) (m/z) %
1h		-148.35, -148.41	87

Table 7. The ^{19}F-NMR and mass spectrometry analyses of the synthesized [NHCH]BF_4.

Sample	Structure	^{19}F-NMR/ δ (ppm)	Mass analysis (Negative mode) (m/z) %
2h		-148.37, -148.42	87

- **Synthesis of [NHCH]Cl/I salts**

Keeping with our subject of exploring the synthesis of the ethylated xanthine-derivatives of various anions, it was decided to replace TsO^-, $EtOSO_3^-$, or HSO_4^- with chloride. As a common method, this could be carried out over an ion-exchange column by the anion exchange of [NHCH]X (X: TsO^-, $EtOSO_3^-$, HSO_4^-) with resin [194]. But some drawbacks to this method are that it needs costly equipment and expensive chemicals, mass transport takes longer than other methods, and a huge amount of solutions is required. So, this method is usually considered less desirable [195]. Another way to synthesize [NHCH]Cl salts from [NHCH]TsO could be a two-step ion-exchange reaction in ethanol [196]. Based on this method, first [NHCH]OH is obtained by the treatment of [NHCH]TsO with KOH in ethanol, and next the [NHCH]OH salt as the product would be converted to [NHCH]Y from its reaction with corresponding acids (HY). In the article, different acids like H_2SO_4 and HNO_3 were examined and we decided to synthesize [NHCH]Cl by using HCl as a new acid in the second step. Here it should be noted that the key point in this method is the formation of [NHCH]OH salt in the first step which acts as the intermediate for the synthesis of [NHCH]Cl in the next step. After several attempts, it was found that any [NHCH]OH couldn't be formed in the first step and unreacted starting materials were only obtained.

More studies revealed that [NHCH]Cl salts can also be synthesized from the reaction between corresponding [NHCH]PF_6 and TBAC in THF or acetone as the solvent [197]. Thus, it was decided to design a new two-step synthesis method of [NHCH]Cl salts from [NHCH]X (X: TsO^-, $EtOSO_3^-$, HSO_4^-). Based on this procedure, the [NHCH]PF_6 salt was first prepared as described before, and then it was treated with TBAC

in THF or acetone at room temperature for 2 h. Last, the product was obtained as a white precipitate which was isolated from the reaction mixture by a simple filteration method.

This method was examined with **1e-4e** as four different ethylated xanthine-derivatives (Table 8). All products were characterized and confirmed by NMR spectroscopy and HRMS. The ^{1}H-NMR spectrum represents a more deshielded imidazolium proton which confirmed the synthesis of the expected product. Taking into account that Chloride ion is smaller than PF_6^-, it exhibits a stronger coulombic interaction with an identical cation that can decrease the electron density around the imidazolium proton, so this proton shows a greater chemical shift. For example, **1f** shows a signal for imidazolium proton at 10.1 ppm. Additionally, the ^{35}Cl-NMR spectrum confirmed the formation of the expected product. For instance, the ^{35}Cl-NMR spectrum of **1f** shows the resonance peak for chloride ions at 69.39 ppm.

Table 8. Synthesis of [NHCH]Cl salts from the reaction between [NHCH]PF_6 and TBAC.

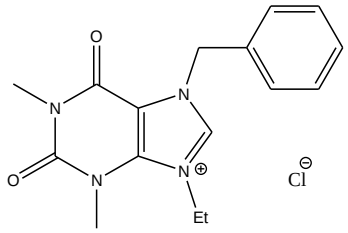
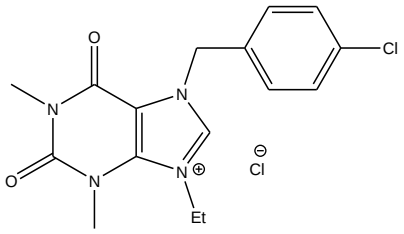
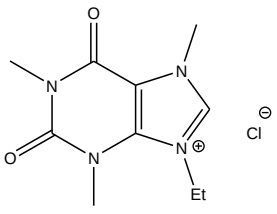
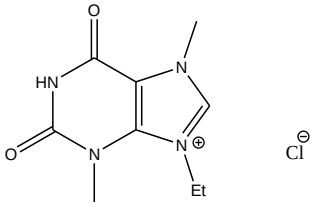
Sample	Structure	TBAC (Eq.)	Solvent	Yield(%)
1f		2	THF	85
2f		2	THF	75
3f		2	THF	97

Table 8. Synthesis of [NHCH]Cl salts from the reaction between [NHCH]PF_6 and TBAC.

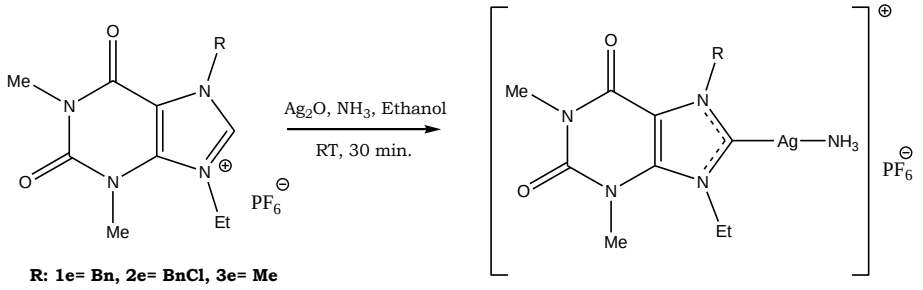
Sample	Structure	TBAC (Eq.)	Solvent	Yield(%)
4f		2	Acetone	97

This method was also evaluated for the synthesis of [NHCH]I salts. In this regard, [3,7-dimethyl-9-ethylxanthinium]I (**5f**) was obtained as a white precipitate from the reaction between [1,7-dimethyl-9-ethylxanthinium]PF_6 and TBAI in acetone at room temperature for 2 h. The product structure was characterized by NMR and mass spectrometry in positive and negative modes. Due to the disappearance of the PF_6^- signal in the ^{31}P-NMR spectrum, it was found that PF_6^- should be successfully replaced by I^- which was also proved by the mass spectrometry in the negative mode. But here it has to be pointed out that the product changes color to black after a while that could come out of the reduction of iodide (I^-) to iodine (I_2). Thus the product was analyzed by NMR and mass spectrometry before and after changing the color. In both situations, the ^{1}H-NMR spectra show two additional signals at ~ 3.34 and 3.85 ppm with an integral ratio of 1:1. Moreover, the ^{13}C-NMR spectra exhibit two groups of signals. Based on the NMR analysis and mass spectrometry in positive and negative modes, it implied that the product could contain a little amount of I_2 which could be responsible for changing the color of the product to black and I_3^- as a counter ion which leads to the appearance of an additional group of signals with the upfield chemical shift in the ^{1}H and ^{13}C-NMR spectra.

3.2. Synthesis of Ag(I)-NHC complexes

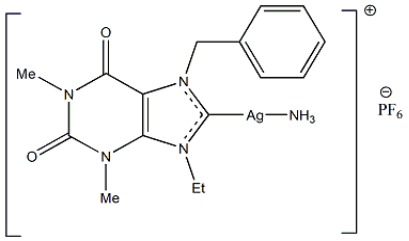
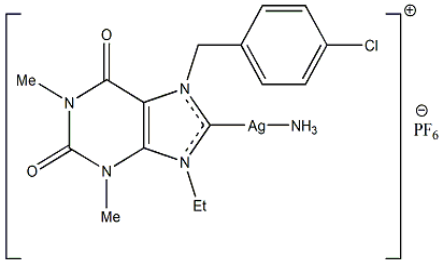
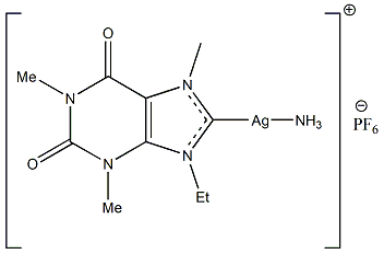
3.2.1. Synthesis of [Ag(NHC)(NH_3)]PF_6/BPh_4/BF_4 complexes

The first group of heteroleptic Ag(I)-NHC complexes with the general formula of [Ag(NHC)(NH_3)]PF_6 was synthesized from the reaction of the corresponding [NHCH]PF_6 with Ag_2O in the presence of NH_3 (Scheme 14) [198]. More details are presented in Table 9.



Scheme 14. Synthesis of [Ag(NHC)(NH_3)]PF_6 complexes

Table 9. The synthesized [Ag(NHC)(NH_3)]PF_6 complexes.

Sample	Structure	Yield(%)
1		78
2		77
3		68

The synthesized complexes were also fully characterized by NMR, FT-IR, HRMS analyses, and EA (due to a failure of the instrument, the purity of sample **3** wasn't examined by EA). The most relevant changes in the ^{1}H-NMR spectrum were the disappearance of the imidazolium proton at 9.30-9.60 ppm and the appearance of a new

signal at ~ 3 ppm with an integral of 3 which could be referred to NH_3 ligand. Furthermore, the appearance of the signal at 184-186 ppm in the ^{13}C-NMR which belonged to the ipso-carbon directly bonded to Ag, confirmed the successful synthesis of the expected product. In addition, the FT-IR spectrum exhibits two bands at high wavenumber (3300-3400 cm^{-1}) for NH_3 and a strong absorption at 833-835 cm^{-1} for PF_6^- as the counterion.

Crystals of complex **1** were of poor quality and the structure solution only confirmed the molecular connectivity but prevented a meaningful discussion of the geometrical parameters, while the single crystals of complexes **2** and **3** suitable for the X-ray diffraction analysis were obtained by slow diffusion of $CHCl_3$ into acetone solution. The molecular structures of complexes **2** and **3** in the solid state are shown in Figure 11.

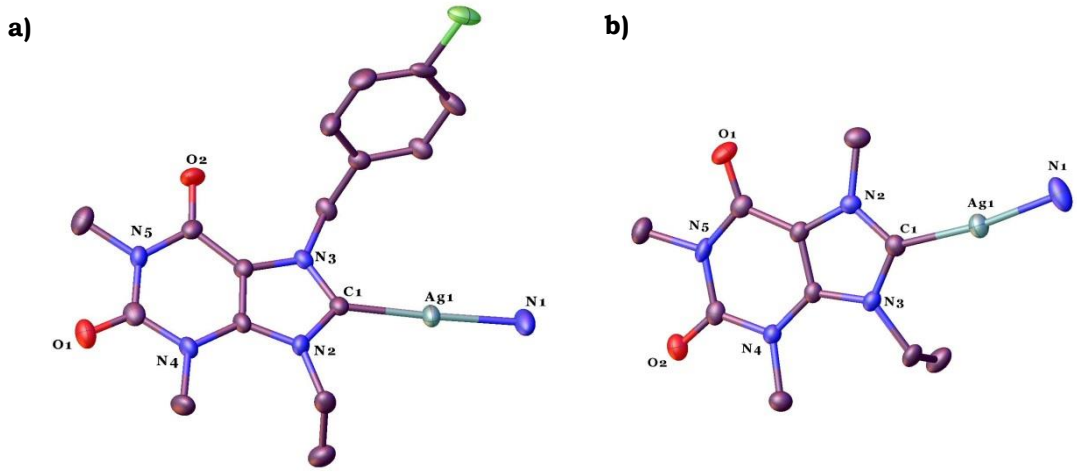


Figure 11. The molecular structures of the cationic part of $[Ag(NHC)(NH_3)]PF_6$ complexes in the solid state. Thermal ellipsoids are shown at the 50% probability level. Hydrogen atoms and PF_6^- anions have been omitted for more clarity. Selected interatomic distances [A°] and bond [°]: **a)** complex **2**: Ag1-N1= 2.110(5), Ag1-C1= 2.060(5) A°, C1-Ag1-N1= 176.4(2)° **b)** complex **3**: Ag1-N1= 2.119(3), Ag1-C1= 2.071(2) A°, C1-Ag1-N1= 172.96(2)°.

We also examined this procedure for the synthesis of [Ag(9-ethyl-1,7-dimethylxanthine-8-ylidene)$(NH_3)]PF_6$ from the corresponding $[NHCH]PF_6$ salt (**4e**) as an NHC precursor that isn't substituted at the N^1-position. After various attempts, we only obtained a dark brown residue as the product which was insoluble in common lab solvents. So, we weren't able to characterize and confirm the product structure.

Furthermore, it is worth noting that this procedure can also provide $[Ag(NHC)NH_3]^+$ complexes of other counterions. In this regard, $[Ag(NHC)NH_3]Y$ (Y: BPh_4^-, BF_4^-) complexes were prepared by the reaction of the

corresponding [NHCH]Y with Ag_2O in the presence of NH_3. All products were characterized by NMR, FT-IR, and HRMS techniques. It should be noted that due to the low solubility of [Ag(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(NH_3)]BPh_4 (**4**), we couldn't analyse this structure by HRMS. On the other hand, we weren't able to grow suitable single crystals from these two groups of Ag complexes for X-ray diffraction analysis.

Last, we decided to examine the formation of a new heteroleptic Ag complex having diethylamine (DEA) instead of NH_3 as the ligand. Thus, The [NHCH]PF_6 salt (**1e**, **2e**) was reacted with Ag_2O in the presence of DEA at room temperature for about 4h. The product was obtained as a gray precipitate which was filtered and washed with cold ethanol and diethyl ether, respectively, and dried at room temperature. Based on the proposed mechanism for this reaction [198], a heteroleptic $[Ag(NHC)(DEA)]^+$ complex was expected as the product, but the NMR and HRMS results confirmed the formation of a homoleptic $[Ag(NHC)_2]^+$ complex that it could be explained by the high degree of steric hindrance of DEA in comparison with NH_3 as the ligand. So it was proposed that DEA could act as the base to generate free NHC which is treated by Ag_2O in the next step to produce a homoleptic complex with the general formula of $[Ag(NHC)_2]PF_6$. But to overcome the steric hindrance of DEA, a larger amount of DEA was tested in the reaction. After several attempts, it was found that an increase in the amount of DEA can't change the product structure and the same homoleptic $[Ag(NHC)_2]PF_6$ complex is obtained as the product (Scheme 15). The X-ray crystallography analysis of the product also confirmed the formation of a silver(I)-NHC homoleptic complex with a linear geometry at the metal center as the product (Figure 12).

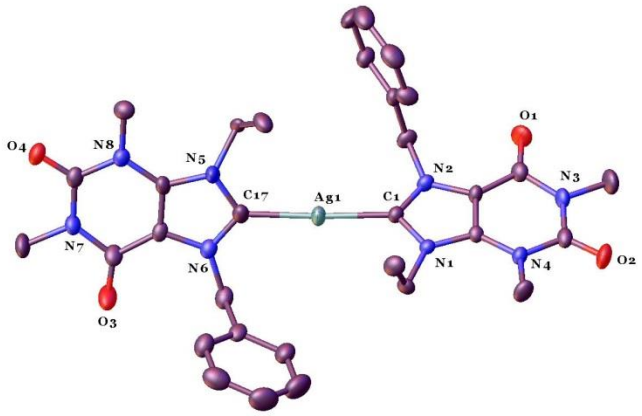
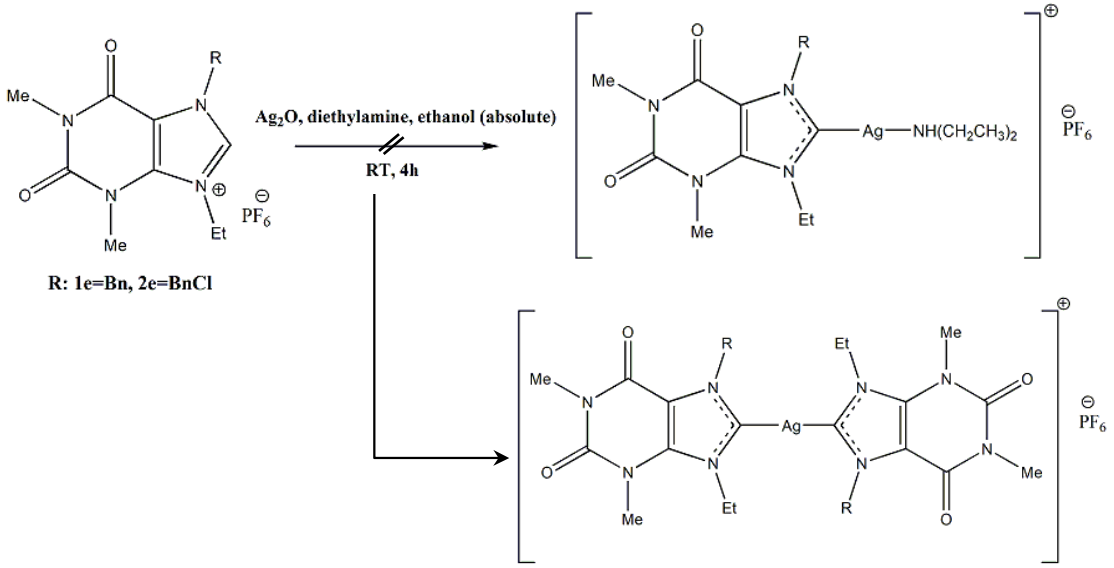


Figure 12. Molecular structure of the silver(I)-NHC homoleptic complex. NHC: 7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene.



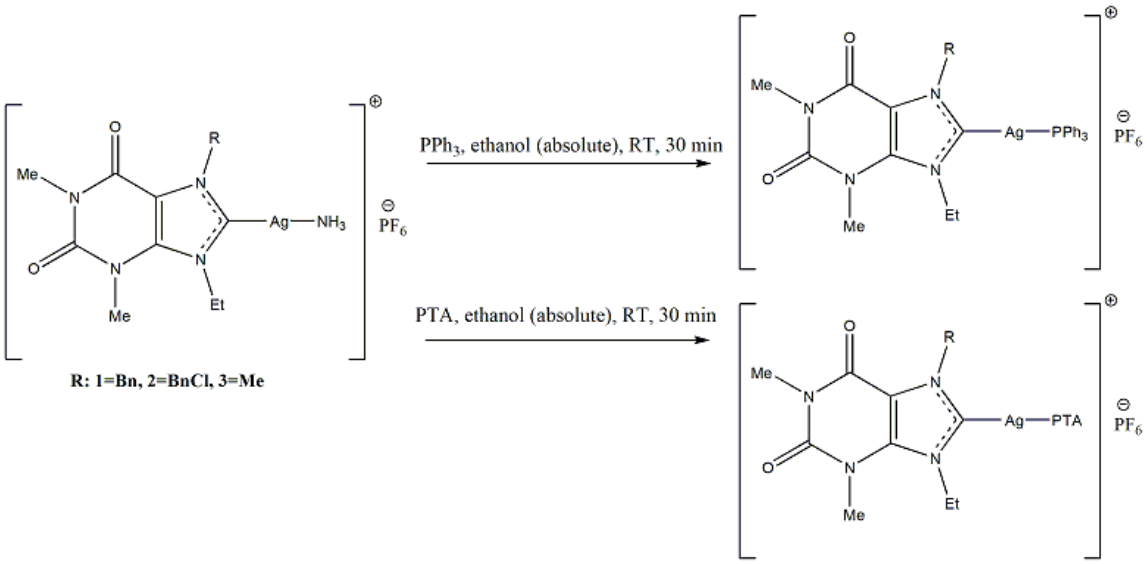
Scheme 15. The reaction between [NHCH]PF_6 (**1e** and **2e**) and Ag_2O in the presence of diethylamine instead of NH_3 as the ligand.

3.2.2. Synthesis of [Ag(NHC)(Phosphine)]PF_6 complexes

The second group of the heteroleptic Ag complexes with the general formula of [Ag(NHC)(Phosphine)]PF_6 was synthesized by following a ligand exchange procedure from the corresponding [Ag(NHC)(NH_3)]PF_6 complex (**1**, **2**, and **3**), by treatment with PPh_3 or PTA as the phosphine ligand in absolute ethanol (Scheme 16) [198].

The [Ag(NHC)(PPh_3)]PF_6 complexes as the first group of the synthesized complexes were characterized by NMR analysis and HRMS. The ^{1}H-NMR spectra display the resonance signals of PPh_3 in the aromatic region (7.20-7.55 ppm). Furthermore, for complexes **10** and **12**, the resonance signal of the carbene carbon atom bonded to the Ag metal center was detected as a doublet in the range of 182-187 ppm as the result of $^{2}J(^{13}C_{carb.}$-$^{31}P)$ coupling by the ^{13}C-NMR spectrometry.

Moreover, in the ^{31}P-NMR spectra, the appearance of a singlet in the region of 3.90-5.90 ppm and a heptate at ~ -144.17 ppm is referred to Ag-PPh_3 and PF_6, proved the successful synthesis of the expected products. Additionally, the HRMS analyses confirmed the structures of the products (Table 10).



Scheme 16. The general synthesis method of [Ag(NHC)(Phosphine)]PF_6 complexes.

Table 10. The HRMS analysis of the synthesized [Ag(NHC)(Phosphine)]PF_6 complexes.

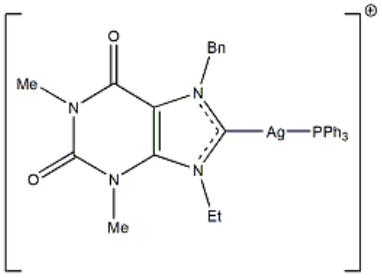
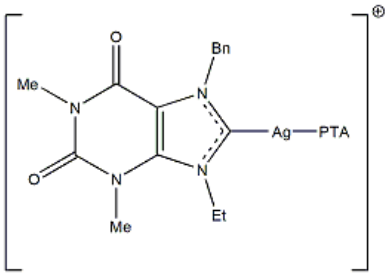
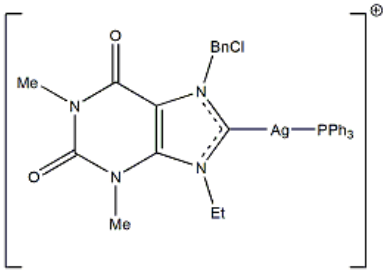
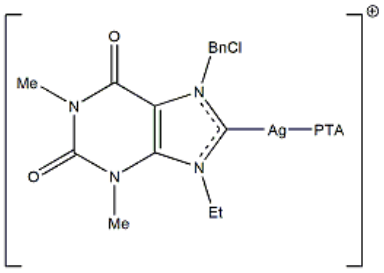
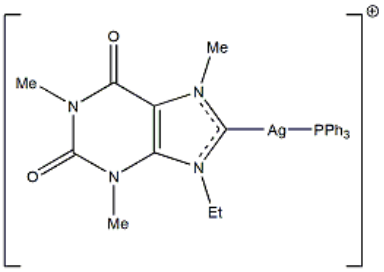
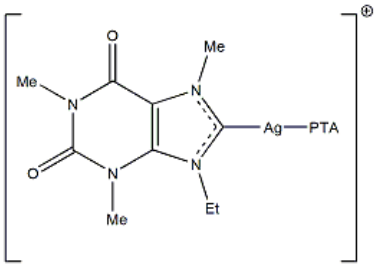
Sample	Structure	Mass analysis (Positive mode)/(m/z) %	
		Calc.	Found
10		667.1387	667.1626
11		562.1244	562.1265
12		701.0997	701.1158

Table 10. The HRMS analysis of the synthesized [Ag(NHC)(Phosphine)]PF_6 complexes.

Sample	Structure	Mass analysis (Positive mode)/(m/z) %	
		Calc.	Found
13		596.0854	596.1285
14		591.1074	591.1365
15		486.0931	486.1167

Unfortunately, we weren't able to study the product structure in the solid state by X-ray diffraction analysis. The X-ray diffraction analysis results showed a mixture of a bis-carbene complex of Ag and $Ag(PPh_3)_4$ as another crystal structure. It could be explained by the destruction of the product during the crystallization procedure.

In the same way, the [Ag(NHC)(PTA)]PF_6 complexes (**11**, **13**, and **15**) as the second group of phosphine complexes were prepared from the reaction between [Ag(NHC)(NH_3)]PF_6 and 1,3,5-triaza-7-phosphaadamantane (PTA) in PPh_3 place. The structures of the products were fully characterized and proved by ^{1}H, ^{13}C, and ^{31}P-NMR analyses and HRMS. The HRMS results are summarized in Table 10.

By the X-ray diffraction analysis, we were faced with the same problem. The analysis showed a bis-carbene complex of Ag.

3.2.3. Synthesis of [Ag(NHC)Cl] complexes

[Ag(NHC)Cl] complexes were prepared as the last group of heteroleptic silver complexes. Our inspiration for the synthesis of this type of silver complexes comes from the knowledge that [Ag(NHC)Cl] complexes are usually used in the synthesis of other metal-NHC complexes through transmetallation reactions [199,200]. The [Ag(NHC)Cl] complexes (**16**, **17**, and **18**) were synthesized by treatment of the corresponding [NHCH]Cl salt with Ag_2O in CH_2Cl_2 as the solvent [201-203]. This procedure generates an air-stable intermediate under mild reaction conditions and provides an easy way to synthesize a wide range of transition metal complexes, thus it is considered one of the most general synthesis methods of [Ag(NHC)Cl] complexes.

The synthesized complexes were fully characterized by NMR, HRMS, and EA (The purity of complexes **16** and **17** were examined by EA, but complex **18** wasn't evaluated by EA, due to a failure of the instrument).

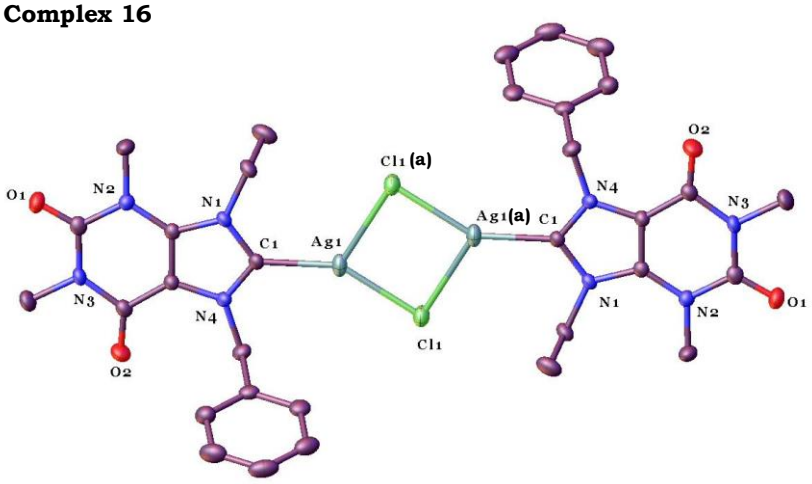
According to the ^{1}H and ^{13}C-NMR analyses of the synthesized complexes (**16**, **17**, and **18**), the disappearance of the imidazolium proton signal at 9-10 ppm in ^{1}H-NMR spectra, and the appearance of the new resonance peak referred to as the carbene carbon atom bonded to silver ($C_{Carb.}$-Ag) at 186-188 ppm in the ^{13}C-NMR proved the successful synthesis of the expected complexes. The HRMS analysis proved the structures of the products as well.

Finally, [3,7-dimethyl-9-ethylxanthinium]Cl (**4f**) was tested in the same reaction as an NHC proligand with non-substituted nitrogen at the N^1 position. Based on the synthesis method, compound **4f** was reacted with Ag_2O in CH_2Cl_2 as the solvent at room temperature for 4 h. After several attempts, it was determined that this reaction can't be carried out in CH_2Cl_2 successfully. It could come out from the presence of an –NH group in the proligand structure which reduces the solubility of the NHC proligand in CH_2Cl_2 as a polar aprotic solvent. So, it was decided to change the reaction solvent to acetonitrile and methanol but the obtained results revealed no success in the reaction.

The suitable crystals for X-ray diffraction studies were only obtained for complexes **16** and **17** by diffusion of diethyl ether into dichloromethane and chloroform into acetone solution, respectively (Figure 13). Complex **16** was detected as a dimeric structure containing an Ag_2Cl_2 core. The X-ray diffraction analysis of complex

17 displayed a trimeric structure with an Ag_3Cl_3 core. These structures are not unusual and the [Ag(NHC)Cl] complexes are widely known for their structural diversity [203]. The selected bond distances and angles are presented in Table 11 and Table 12.

a) Complex 16



b) Complex 17

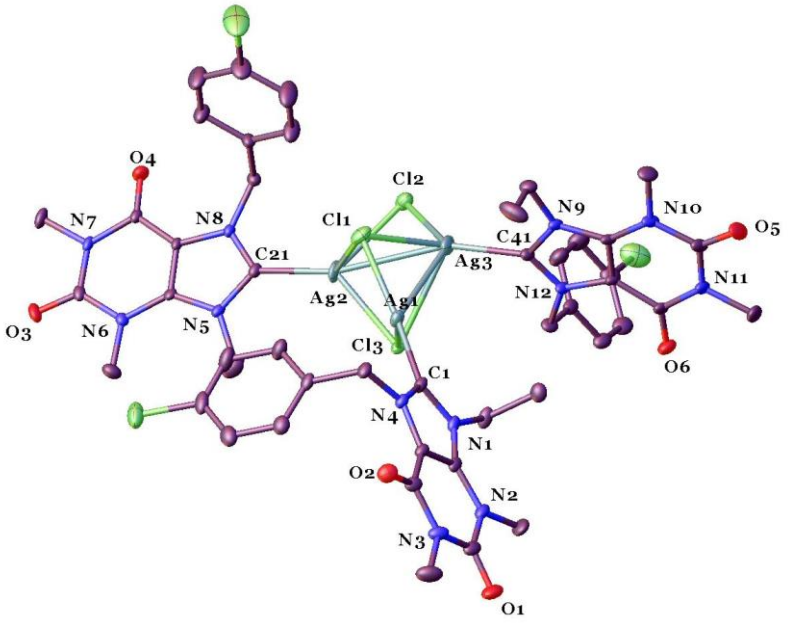


Figure 13. The molecular structures of complexes **16** and **17** in the solid state. Hydrogen atoms have been omitted for more clarity.

Table 11. Selected bond distances and angles for complex **16** with estimated standard deviations in parentheses.

Bond	Length (Å)	Bond	Angle (°)
C(1)-Ag(1)	2.102(2)	C(1)-Ag(1)-Cl(1)	149.50(7)
Ag(1)-Cl(1)	2.4412(7)	C(1)-Ag(1)-Cl(1)(a)	118.24(7)
Ag(1)-Cl(1)(a)	2.7212(7)	Cl(1)-Ag(1)-Cl(1)(a)	91.62(2)
		C(1)-Ag(1)-Cl(1)(a)	88.38(2)
		Ag(1)-Cl(1)-Ag(1)(a)	88.38(2)

Table 12. Selected bond distances and angles for complex **17** with estimated standard deviations in parentheses.

Bond	Length (Å)	Bond	Length (Å)
Ag(1)-Ag(3)	3.2112(4)	Ag(2)-Cl(1)	2.9008(7)
Ag(1)-Cl(3)	2.9295(6)	Ag(2)-C(21)	2.118(2)
Ag(1)-Cl(1)	2.3967(6)	Ag(3)-Cl(1)	2.7281(7)
Ag(1)-C(1)	2.104(2)	Ag(3)-Cl(2)	2.50947
Ag(2)-Ag(3)	3.1095(4)	Ag(3)-Cl(3)	2.9140(6)
Ag(2)-Cl(2)	2.6573(7)	Ag(3)-C(41)	2.110(2)
Bond	**Angle (°)**	**Bond**	**Angle (°)**
Cl(1)-Ag(1)-Ag(3)	55.972(17)	Cl(1)-Ag(1)-Cl(3)	86.936(18)
Cl(3)-Ag(1)-Ag(3)	56.434(12)	C(1)-Ag(1)-Ag(3)	136.89(6)
C(1)-Ag(1)-Cl(1)	163.62(6)	C(1)-Ag(1)-Cl(3)	108.73(6)
Cl(1)-Ag(2)-Ag(3)	53.854(15)	Cl(2)-Ag(2)-Ag(3)	50.851(15)
Cl(2)-Ag(2)-Cl(1)	87.36(2)	Cl(3)-Ag(2)-Ag(3)	61.040(13)
Cl(3)-Ag(2)-Cl(1)	84.808(17)	Cl(3)-Ag(2)-Cl(2)	98.819(19)
C(21)-Ag(2)-Ag(3)	166.70(6)	C(21)-Ag(2)-Cl(1)	119.74(6)
C(21)-Ag(2)-Cl(2)	121.01(7)	C(21)-Ag(2)-Cl(3)	132.08(6)
Ag(2)-Ag(3)-Ag(1)	75.915(8)	Cl(1)-Ag(3)-Ag(1)	46.727(14)
Cl(1)-Ag(3)-Ag(2)	59.162(15)	Cl(1)-Ag(3)-Cl(3)	81.470(19)
Cl(2)-Ag(3)-Ag(1)	130.035(17)	Cl(2)-Ag(3)-Ag(2)	55.209(16)

Table 12. Selected bond distances and angles for complex **17** with estimated standard deviations in parentheses.

Bond	Angle (°)	Bond	Angle (°)
Cl(2)-Ag(3)-Cl(1)	94.29(2)	Cl(2)-Ag(3)-Cl(3)	93.33(2)
Cl(3)-Ag(3)-Ag(1)	56.896(13)	Cl(3)-Ag(3)-Ag(2)	49.951(12)
C(41)-Ag(3)-Ag(1)	97.55(7)	C(41)-Ag(3)-Ag(2)	160.49(6)
C(41)-Ag(3)-Cl(1)	128.81(7)	C(41)-Ag(3)-Cl(2)	131.98(7)
C(41)-Ag(3)-Cl(3)	111.01(6)	Ag(1)-Cl(1)-Ag(2)	93.97(2)
Ag(1)-Cl(1)-Ag(3)	77.300(18)	Ag(3)-Cl(1)-Ag(2)	66.984(15)
Ag(3)-Cl(2)-Ag(2)	73.940(19)	Ag(2)-Cl(3)-Ag(1)	90.150(16)
Ag(2)-Cl(3)-Ag(3)	69.010(14)	Ag(3)-Cl(3)-Ag(1)	66.670(14)

3.2.4. Theophylline and theobromine as NHC-precursors

As previously mentioned, theophylline and theobromine were successfully ethylated at the N^9 position using $(EtO)_2SO_2$ as the alkylating agent under solvent-free conditions. In the next step, the synthesized imidazolium salts were subjected to an ion-exchange reaction to produce [NHCH]PF_6 salts which would be used to prepare various heteroleptic Ag(I)-NHC complexes.

According to the experimental results, in [1,3-dimethyl-9-ethyl xanthinium]HSO_4 (**5d**), hydrogensulfate can't be replaced by PF_6^-. So, it was decided to synthesize the homoleptic $[Ag(NHC)_2]^+$ complex which could be directly synthesized from compound **5d** [77]. In this regard, compound **5d** was dissolved in water and reacted with Ag_2O at room temperature for 2.5 h. Next, the reaction suspension was filtered through celite to give a clear solution and the solvent was removed under vacuum. But at the end of the work-up process, the product was obtained as a dark precipitate which showed very low solubility in common laboratory solvents, so we couldn't analyze the product.

On the other hand, [3,7-dimethyl-9-ethyl xanthinium]HSO_4 (**4d**) was successfully converted to the corresponding [NHCH]PF_6 salt (**4e**) through the same ion-exchange reaction. Then compound **4e** was evaluated as the NHC proligand to prepare $[Ag(NHC)NH_3]^+$ which could be subsequently used to produce [Ag(NHC)(Phosphine)]$^+$ complexes. But experimental studies implied that this reaction couldn't lead to the formation of the favorite product. On the second attempt,

compound **4e** was also tested in another reaction to prepare the corresponding $[Ag(NHC)_2]^+$ complex [77]. In this sense, compound **4e** was reacted with Ag_2O in DMSO at 60 °C for 2.5 h. Then the product was worked up as reported [77], but the final product was obtained as an insoluble precipitate which couldn't be characterized, due to its very low solubility in common laboratory solvents.

On the third attempt, [3,7-dimethyl-9-ethyl xanthinium]Cl (**4f**) was tested to prepare the corresponding [Ag(NHC)Cl] by following a reaction between compound (**4f**) and Ag_2O in different solvents like CH_2Cl_2, acetonitrile, and methanol. Unfortunately, all attempts were unsuccessful. Finally, [3,7-dimethyl-9-ethyl xanthinium]I (**5f**) was investigated in another reaction to obtain another heteroleptic Ag(I)-NHC complex with the general formula of [Ag(NHC)(OAC)] [204,205]. The synthesis of the silver complex started with the reaction between compound **5f** and silver acetate (in the molar ratio of 1:2) in methanol as the solvent. The reaction mixture was stirred at room temperature for 2.5 h. According to the results, this method didn't work as expected. At the end of the reaction, an insoluble solid phase was obtained which was filtered and the filtrate was dried but no precipitate was left as expected.
Finally, it was decided to continue on the project with other synthesized NHC-precursors.

3.3. Transmetallation reactions

3.3.1. Synthesis of $[RuCl_2(NHC)(p\text{-cymene})]$ complexes

$[RuCl_2(NHC)(p\text{-cymene})]$ complexes (**19**, **20**, and **21**) were synthesized via a transmetallation reaction from the corresponding Ag(NHC)Cl, by treatment with 0.5 Eq. of $[RuCl_2(p\text{-cymene})]_2$ in CH_2Cl_2 at room temperature for 24 h [202,203]. Finally, the product was obtained as an orange-brown precipitate which was fully characterized by NMR and HRMS techniques.

In the ^{1}H-NMR spectra of complexes **19** and **20**, aromatic proton signals of p-cymene ligand were observed as three broad multiplets in the range of 5.18-5.52 ppm whereas aromatic protons of p-cymene ligand for complex **21** were detected as two doublets in the range of 5.21-5.67 ppm. For all synthesized complexes (**19**, **20**, and **21**), the methyl group on the p-cymene ligand shows a singlet in the range of 2.04-2.19 ppm. Moreover, the methyl groups of isopropyl substitution on the p-cyemen ligand for complexes **19** and **20** were detected as two inequivalent methyl groups which show two doublets at ~1.30 and 1.20

ppm, while the ^{1}H-NMR spectrum of complex **21** shows a doublet at 1.35 ppm for the same methyl groups. Furthermore, complexes **19** and **20** show a broad singlet for –CH< at 2.75 ppm whereas the resonance signal of the same proton was found as a multiplet at 3.02 ppm for complex **21**.

By the ^{13}C-NMR spectroscopy, the resonance peak of the carbene carbon atom bonded to Ru as the metal center appears in the range of 186-189 ppm. In addition, the characteristic signals of the aromatic carbon atoms of the p-cymene ligand were observed in the range of 80-110 ppm. The methyl groups of the isopropyl on the p-cymene ligand were detected at 21-23 ppm and 18-19 ppm as two inequivalent carbon atoms. Last, the signal at 30-31 ppm was assigned to –CH< group. The HRMS analyses also confirmed the structures of the products as expected.

Suitable single crystals of complex **19** were grown by the vapor diffusion method from chloroform/n-Hexane (Figure 14). The X-ray diffraction analysis revealed the typical pseudo-octahedral piano-stool geometry around the Ru (II) metal center, with the η^6-p-cymene ligand occupying three sites, the remaining three sites being occupying by the two chlorides and an NHC ligand. Moreover, due to the π-acceptor property of NHC ligands, the bond length for Ru-$C_{carb.}$ was slightly shorter than that of the Ru-C_{arene} bond. The selected X-ray diffraction data are presented in Table 13.

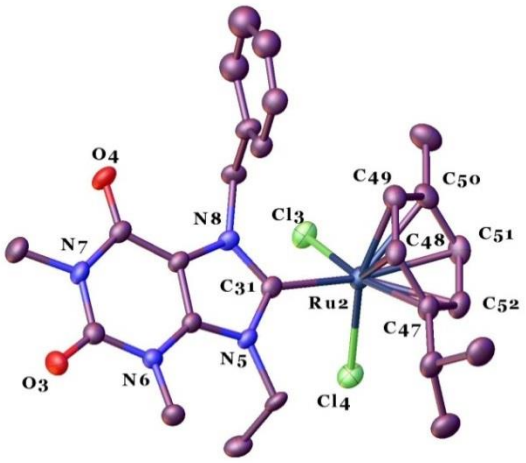


Figure 14. The molecular structure of complex **19** in the solid state. Hydrogen atoms have been omitted for more clarity.

Table 13. Selected bond distances and angles for complex **19** with estimated standard deviations in parentheses.

Bond	Length (Å)	Bond	Angle (°)
Ru(2)-Cl(3)	2.4201(10)	Cl(3)-Ru(2)-Cl(4)	82.67(3)
Ru(2)-Cl(4)	2.4240(10)	C(31)-Ru(2)-Cl(3)	87.34(10)
Ru(2)-C(31)	2.095(4)	C(31)-Ru(2)-Cl(4)	94.33(10)
N(5)-C(31)	1.383(5)	C(31)-Ru(2)-C(47)	104.47(14)
N(8)-C(31)	1.359(5)	C(31)-Ru(2)-C(48)	86.48(14)
Ru(2)-C(47)	2.220(4)	C(31)-Ru(2)-C(49)	97.86(15)
Ru(2)-C(48)	2.163(4)	C(31)-Ru(2)-C(50)	130.44(15)
Ru(2)-C(49)	2.203(4)	C(31)-Ru(2)-C(51)	163.76(14)
Ru(2)-C(50)	2.237(4)	C(31)-Ru(2)-C(52)	140.60(15)
Ru(2)-C(51)	2.246(4)	N(8)-C(31)-N(5)	105.2(3)
Ru(2)-C(52)	2.204(4)		

3.3.2. Synthesis of [$RhCl_2$(NHC)(Cp*)] complexes

The compounds with the general formula of [$RhCl_2$(NHC)(Cp*)] (**22**, **23**, and **24**) were synthesized by following a transmetallation route from the corresponding [Ag(NHC)Cl] complex using the synthesis method previously described [206, 207]. The products were fully characterized and confirmed by NMR and HRMS techniques.

The ^{1}H-NMR resonances for methyl groups on pentamethylcyclopentadiene (Cp*) ligand were found as a singlet with an integral of 15 at 1.50-1.70 ppm. In the ^{13}C-NMR spectra of complexes **22** and **23**, the metal-carbene carbon resonance was detected as a doublet at 183-184 ppm with the coupling constant of 53-55 MHz which is consistent with previously reported values for Rhodium-NHC complexes [208,209]. For all synthesized complexes, the aromatic carbon signals of the Cp* ligand were found as a doublet at 96-98 ppm with the coupling constant of 7-7.2 MHz resulting from $^{1}J_{C\text{-}Rh}$ coupling, and the methyl groups resonances were found in the range of 9.48-9.60 ppm. The HRMS data also proved the successful synthesis of the products as expected.

In addition to NMR and HRMS characterization methods, the structures of complexes **22** and **23** were also confirmed by X-ray diffraction analysis (Figure 15). The suitable single crystals were

grown by slow vapor diffusion of diethyl ether into a concentrated solution of dichloromethane. The selected X-ray data for complexes **22** and **23** are shown in Table 14. The X-ray diffraction analysis of complex **23** shows similar bond lengths but slightly different angles (Table 15).

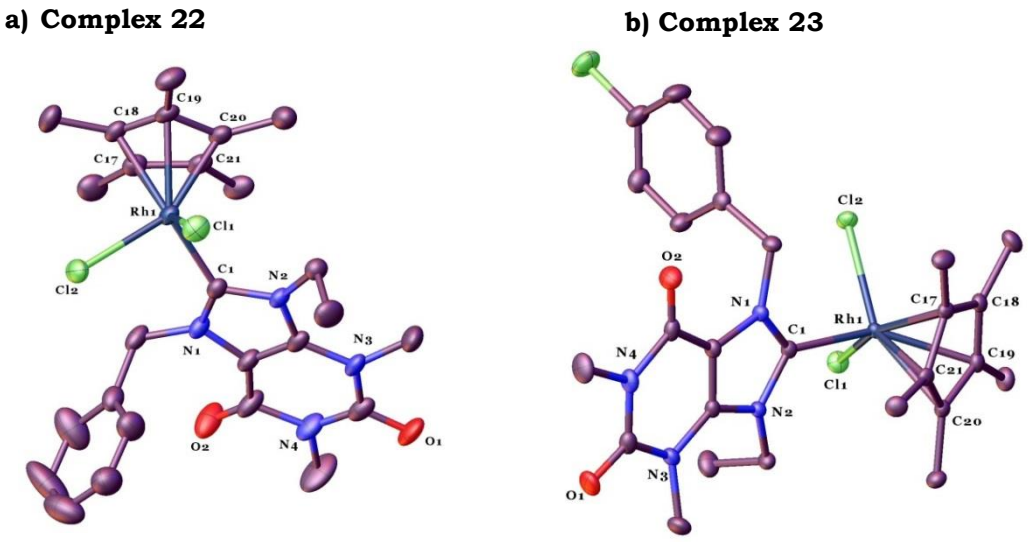


Figure 15. The molecular structure of complexes **22** and **23** in the solid state. Hydrogen atoms have been omitted for more clarity.

Table 14. Selected bond distances and angles for complex **22** with estimated standard deviations in parentheses.

Bond	Length (Å)	Bond	Length (Å)
Rh(1)-Cl(2)	2.4098 (7)	Rh(1)-C(19)	2.232(3)
Rh(1)-Cl(1)	2.4186(8)	Rh(1)-C(20)	2.149(3)
Rh(1)-C(1)	2.0551(3)	Rh(1)-C(21)	2.147(3)
Rh(1)-C(17)	2.139(3)	N(1)-C(1)	1.347(4)
Rh(1)-C(18)	2.235(2)	N(2)-C(1)	1.391(3
Bond	**Angle (°)**	**Bond**	**Angle (°)**
Cl(2)-Rh(1)-Cl(1)	87.16(3)	C(21)-Rh(1)-C(20)	38.65(11)
C(21)-Rh(1)-Cl(2)	133.30(9)	C(21)-Rh(1)-C(21)	38.85(11)
C(21)-Rh(1)-Cl(1)	138.72(9)	C(1)-Rh(1)-Cl(1)	96.19(8)
C(21)-Rh(1)-C(18)	63.78(10)	C(l)-Rh(1)-Cl(2)	95.56(8)
C(21)-Rh(1)-C(19)	63.83(10)		

Table 15. Selected angles for complex **23** with estimated standard deviations in parentheses.

Bond	Angle (°)	Bond	Angle (°)
Cl(2)-Rh(1)-Cl(1)	87.68(2)	C(21)-Rh(1)-C(20)	38.70(9)
C(21)-Rh(1)-Cl(2)	135.43(6)	C(17)-Rh(1)-C(21)	38.89(8)
C(21)-Rh(1)-Cl(1)	136.10(7)	C(1)-Rh(1)-Cl(1)	96.34(6)
C(21)-Rh(1)-C(18)	64.06(8)	C(l)-Rh(1)-Cl(2)	95.03(6)
C(21)-Rh(1)-C(19)	64.16(8)		

3.3.3. Synthesis of [RhCl(NHC)(cod)] complexes

In this part, we examined the formation of the complexes **25**, **26**, and **27** with the general formula of [RhCl(NHC)(cod)] as an example of common rhodium(I)-NHC complexes by following a classical transmetallation reaction from the corresponding [Ag(NHC)Cl] complex, by treatment with $[RhCl(cod)]_2$ in CH_2Cl_2 as the solvent at room temperature for 24 h [132,210,211]. The synthesized complexes were fully characterized using NMR and HRMS techniques.

In the ^{1}H-NMR spectra for complexes **25** and **26**, CH protons of 1,5-cyclooctadiene (cod) ligand were characterized as four inequivalent protons which exhibit their resonances in the range of 5.10-5.23 and 3.03-3.31 ppm. Moreover, CH_2 proton signals of cod ligand show a splitting pattern in the range of 1.70-2.52 ppm which is consistent with the previously recorded NMR spectra of [RhCl(NHC)(cod)] complexes [212].

For complexes **25** and **26**, the carbene carbon atom bonded to rhodium(I) shows a downfield chemical shift compared to the corresponding [Ag(NHC)Cl] complex by the ^{13}C-NMR spectroscopy. Furthermore, the olefinic carbon atoms of cod ligand were detected as four doublets at 100.08-100.90 and 69.84-69.67 ppm as a result of $^1J_{Rh\text{-}C}$ coupling. The CH_2 groups of cod ligand were also characterized as four signals with different chemical shifts in the range of 28.10-33.54 ppm which proves the existence of four non-equivalent carbon atoms.

The ^{1}H and ^{13}C-NMR spectra for complex **27** proved the product structure as expected but it should be noted that based on the ^{13}C-NMR spectrum, the product contains a little amount of unreacted $[RhCl(cod)]_2$. The resonance signals for $[RhCl(cod)]_2$ were observed as two doublets at 78.66 and 30.87 ppm. To overcome this problem, the

reaction was repeated with a lower amount of $[RhCl(cod)]_2$ (0.4 Eq.) which afforded the pure product but in yield of 30%. In another attempt, the reaction was carried out at room temperature for 48 h but the product still contained $[RhCl(cod)]_2$ impurities. So, it was concluded that this synthesis procedure can't be successful to produce complex **27** as a pure product.

Finally, we tried to grow suitable single crystals for X-ray diffraction analysis from the synthesized complexes. After several attempts, suitable single crystals of complex **26** were grown by slow diffusion of n-hexane into a dichloromethane solution (Figure 16). The crystallography data feature a typical square planar Rh-complex with the plane of the NHC ligand in an almost perpendicular arrangement to the coordination plane around the rhodium atom (Table 16).

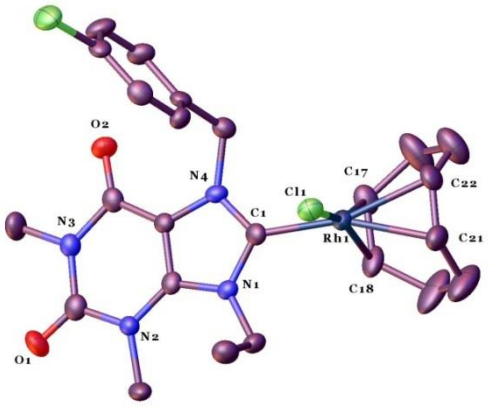


Figure 16. The molecular structure of complex **26** in the solid state. Hydrogen atoms have been omitted for more clarity.

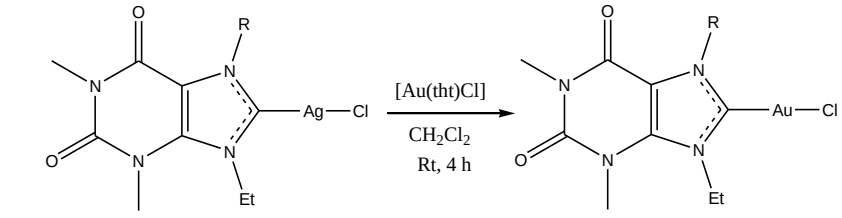
Table 16. Selected angles for complex **26** with estimated standard deviations in parentheses.

Bond	Angle (°)
C(1)-Rh(1)-Cl(1)	90.87(15)
C(1)-Rh(1)-C(17)	89.6(2)
C(1)-Rh(1)-C(18)	89.5(2)
C(1)-Rh(1)-C(21)	160.8(2)
C(1)-Rh(1)-C(22)	162.9(2)

Due to the Π-donating property of the Cl ligand, the rhodium atom as the metal center being made more electron-rich and it affords a strong coordination bond between the rhodium and the olefinic cod double bond trans to Cl ligand. The X-ray diffraction analysis recorded an average bond length of 2.106(6) and 2.107(6) Å for Rh-C(17) and Rh-C(18), respectively. On the other hand, the carbene as a Π-acceptor ligand decreases the electron density around the rhodium atom and the Rh-C bond to the cod ligand becomes significantly longer (2.213(6) Å) for the C(21)-C(22) double bond trans to the carbene ligand [213,214].

3.3.4. Synthesis of [Au(NHC)Cl] complexes

Complexes **28**, **29**, and **30** with the general formula of [Au(NHC)Cl] were synthesized as the last group of transition metal-NHC complexes obtained via a transmetallation reaction from the [Ag(NHC)Cl] complexes [202,203,215] (Scheme 17).



16: R= Bn, 17: R= BnCl, 18: R= Me **28: R= Bn, 29: R= BnCl, 30: R= Me**

Scheme 17. The synthesis procedure of the [Au(NHC)Cl] complexes.

The synthesized complexes were fully characterized by NMR and HRMS spectrometry analyses. The ^{1}H-NMR spectra show a similar pattern to those of the corresponding [Ag(NHC)Cl] complexes, whereas in the ^{13}C-NMR spectra, the carbene carbon atom bonded to the Au atom is shifted upfield from ~ 186 ppm for Ag-$C_{carb.}$ to ~ 177 ppm.

The molecular structures of complexes **28-30** were studied by X-ray diffraction analysis. In this regard, suitable single crystals of complexes **28** and **29** were obtained by the slow vapor diffusion method from acetone/diethyl ether (Figure 18) whereas single crystals of complex **30** were grown using the same method from CH_2Cl_2/diethyl ether (Figure 18).

While the silver-NHC complexes **16** and **17** were found to be dimeric and trimeric, respectively, the analogous gold(I) complexes (**28**, **29**) were monomeric with a linear geometry at gold(I) as the metal center [C(1)-Au(1)-Cl(1)= 177.70(11)°-179.41(10)°]. Moreover, the Au-$C_{carb.}$ bond lengths [C(1)-Au(1)= 1.976(4)-1.987(2) Å] in complexes **28** and **29** are shorter than the Ag-$C_{carb.}$ bond lengths [C(1)-Ag(1)= 2.102(2)-2.118(2) Å] in complexes **16** and **17**. This bond length difference arises from the smaller covalent radius of Au(I) [1.37 Å] compared to Ag(I) [1.46 Å] [202, 203].

The X-ray diffraction data of complex **30** confirmed the same crystal structure with a linear geometry at the gold(I) center [C(1)-Au(1)-Cl(1)= 176.45(10)°] and the bond distance of 1.996(4) Å for Au-$C_{Carb.}$ bond.

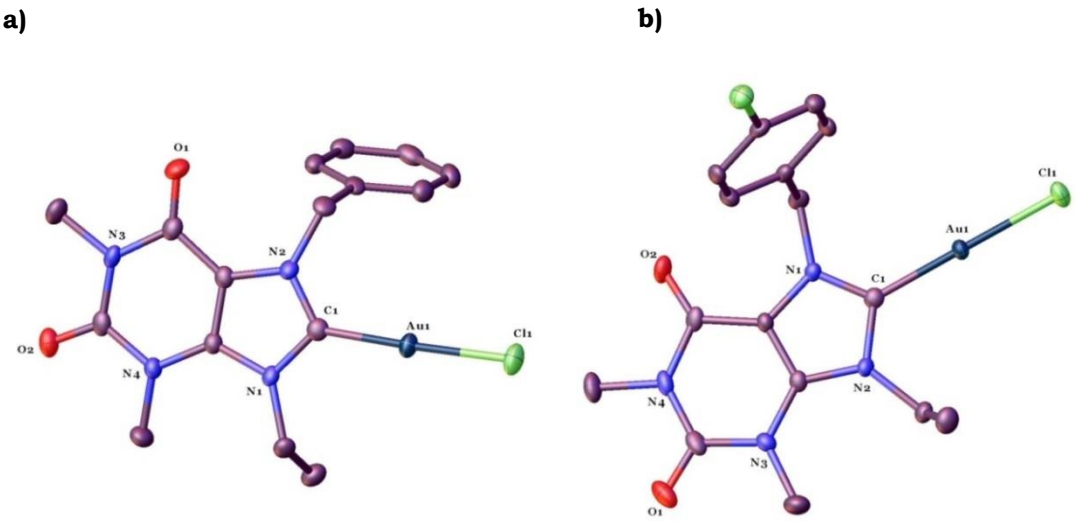


Figure 18. The molecular structures of complexes **28** and **29** in the solid state. Hydrogen atoms have been omitted for more clarity. Selected interatomic distances [A°] and bond [°]: **a)** complex **28**: Au1-C1= 1.976(4), Au1-Cl(1)= 2.2776(9) A°, C1-Au1-Cl(1)= 177.70(11)° **b)** complex **29**: Au1-C1= 1.978(2), Au1-Cl(1)= 2.2796(8) A°, C1-Au1-Cl(1)= 179.41(10)°.

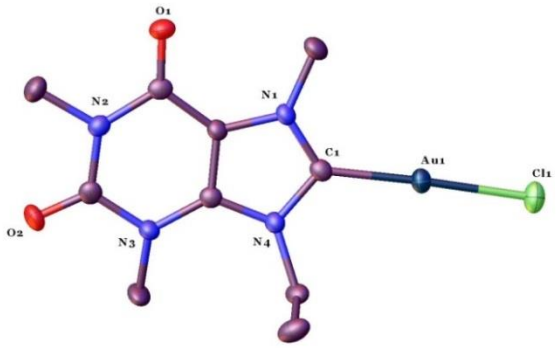
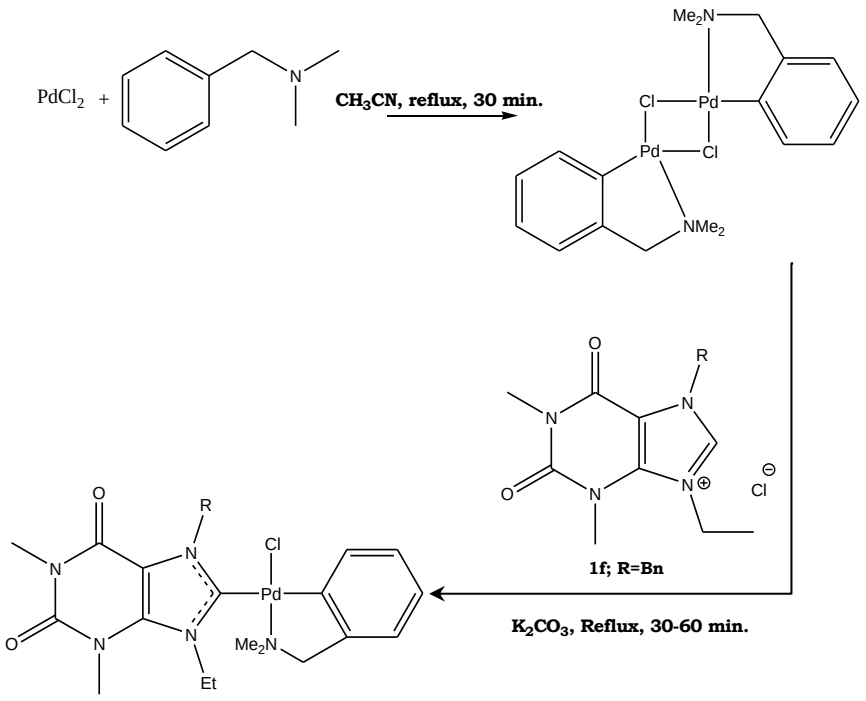


Figure 18. The molecular structure of complexe **30** in the solid state. Hydrogen atoms have been omitted for more clarity. Selected interatomic distances [A°] and bond [°]: Au1-C1= 1.996(4), Au1-Cl(1)= 2.2836(10) A°, C1-Au1-Cl(1)= 176.45(10)°.

3.4. Synthesis of Pd-NHC complexes

3.4.1. Synthesis of [Pd(NHC)(dmba)Cl] complexes

The last part of this project concerns the synthesis of Pd-NHC complexes which have recently attracted more attention due to their application in the field of organometallic chemistry and catalysis [216-218]. In this regard, the formation of [Pd(NHC)(dmba)Cl] complexes were examined using the previously reported procedure [219]. Based on the proposed mechanism, the $[Pd(dmba)Cl]_2$ dimer was firstly formed by heating $PdCl_2$ with N,N-dimethylbenzylamine (dmba) in acetonitrile under reflux for 30 minutes and it was sequentially reacted with the corresponding NHC precursor in the presence of K_2CO_3 (Scheme 18). Here it should be noted that no need for chromatography can be considered as one of the most important advantages of this procedure.



Scheme 18. The general synthesis procedure of [Pd(NHC)(dmba)Cl] complexes.

(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)Pd(dmba)Cl (**31**) as the first example of the Pd-NHC complexes was synthesized using the above mentioned method. First, a mixture of $PdCl_2$ and dmba (1:1.03 mmol) in acetonitrile was refluxed at 100 °C for about 30 minutes until $PdCl_2$ was completely dissolved and a clear, light yellow solution was formed. Then K_2CO_3 was added to the reaction mixture and it was

refluxed for a further 10 minutes. Finally, [7-benzyl-9-ethyl-1,3-dimethylxanthinium]Cl (**1f**) was taken into the reaction flask, and the reflux continued for 1 hour. It is worth noting that based upon the article, the reaction mixture should finally be refluxed for 30 minutes, however, after several attempts it was found that an increase in reaction time to 60 minutes can raise the reaction yield from 42% to 63%. Last, the product was worked up by following the noted procedure [219].

The prepared complex (**31**) was characterized by NMR spectrometry, HRMS, and X-ray diffraction analyses. The most important change found in ^{1}H and ^{13}C-NMR was the disappearance of imidazolium signals at 10.01 and 138.71 ppm, respectively, and the appearance of carbene carbon atom resonance at 182.74 ppm by the ^{13}C-NMR analysis which confirmed the formation of the Pd-carbene complex. Moreover, N,N-dimethylbenzylamine (dmba) ligand shows four resonance signals in the range of 6.03-7.02 ppm for aromatic protons by ^{1}H-NMR spectroscopy. The $>CH_2$ group of dmba ligand was also observed as two doublets at 4.03 and 3.87 ppm, and the $-N(CH_3)_2$ group was detected by a doublet for methyl groups at 2.86 ppm.

The HRMS analysis also confirmed the successful synthesis of the product as expected (calculated for $C_{25}H_{30}ClN_5NaO_2Pd$ $[M+Na]^+$: 596.1022, found: 596.1034 m/z).

Furthermore, the single crystals of complex **31** were obtained by the slow vapor diffusion method from dichloromethane/n-hexane (Figure 19).

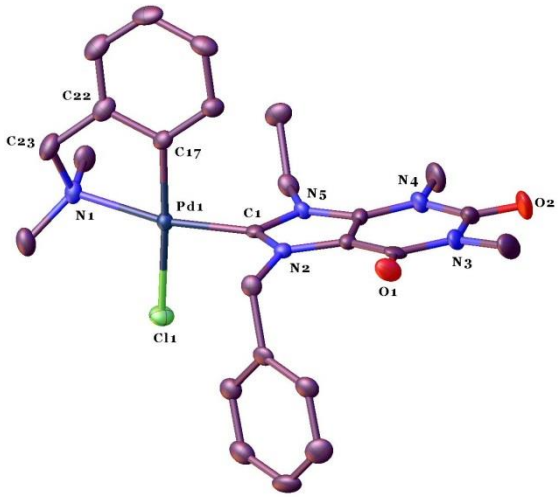


Figure 19. The molecular structure of complex **31** in the solid state. Hydrogen atoms have been omitted for more clarity.

The X-ray crystallography data proved a slightly distorted square-planar geometry at the Pd(II) center with the NHC positioned trans to N,N-dimethylbenzylamine ligand. The selected bond lengths and angels were shown in Table 17.

Table 17. Selected bond distances and angles for complex **31** with estimated standard deviations in parentheses.

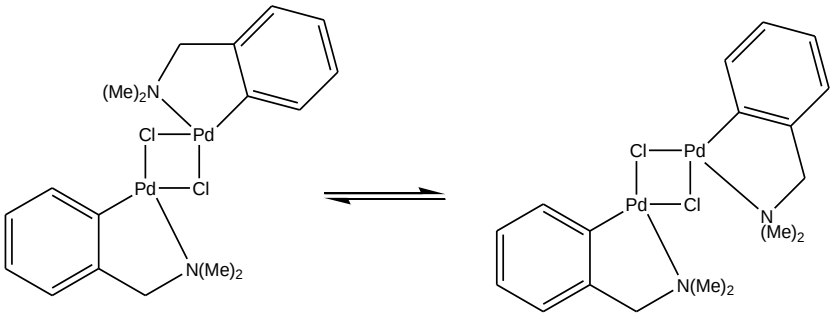
Bond	Length (Å)	Bond	Angle (°)
Pd(1)-C(1)	1.970(4)	C(1)-Pd(1)-Cl(1)	94.06(11)
Pd(1)-C(17)	2.006(4)	C(1)-Pd(1)-N(1)	168.45(13)
Pd(1)-N(1)	2.137(3)	C(1)-Pd(1)-C(17)	89.77(16)
Pd(1)-Cl(1)	2.4135(10)	N(1)-Pd(1)-Cl(1)	92.72(10)
		C(17)-Pd(1)-N(1)	83.08(15)

Here it must be noted that, although the formation of complex **31** was proved by NMR, HRMS, and X-ray diffraction analyses, the purity of the product is open to question. For example, in the ^{1}H-NMR spectrum, some additional signals were observed in the range of 7.30-7.50 ppm, and the corresponding carbon atom was detected at 128.49 ppm by the ^{13}C-NMR spectroscopy. Moreover, the HMBC and ^{1}H-^{1}H COSY analyses didn't display any correlation between this proton and other carbon atoms or other protons in the product structure. Furthermore, the ^{1}H and ^{13}C-NMR analyses of the product in DMSO-d_6 revealed the same pattern.

So, for further information on what these signals could belong to, we decided to firstly synthesize dimer $[Pd(Cl)(dmba)]_2$ that would be refluxed with the corresponding [NHCH]Cl salt in the presence of K_2CO_3 in the next step to produce the expected product.

To prepare the dimer, a mixture of $PdCl_2$ and dmba (in the optimized molar ratio of 1:1.05) in acetonitrile was refluxed at 100 °C until $PdCl_2$ was completely dissolved and a clear, bright yellow solution was obtained (in~ 30 minutes). After completion of the reaction, the volatile was evaporated in vacuo and the residue was washed with diethyl ether to get the final product as a yellow precipitate (Yield: 59%) [219]. The product structure was studied and confirmed by NMR analysis. In the ^{1}H-NMR spectrum, the resonances for methyl groups of -$N(CH_3)_2$ were observed at 2.87 and 2.90 ppm, and the methylene group (-**CH_2**($N(CH_3)_2$)-) was characterized as a singlet at 3.96 ppm. Moreover, aromatic protons of

dmba ligand showed some resonances in the aromatic region (6.90-7.30 ppm) as expected. By the ^{13}C-NMR spectroscopy, two sets of resonances with equal intensity were observed. It could come out of cis and trans isomers of the dimer which could presumably be converted to each other at ambient temperature slower than the NMR time scale (Scheme 19).



Trans Cis

Scheme 19. Trans to cis conversion of $[PdCl(dmba)]_2$.

By comparison the ^{1}H-NMR spectrum for $[PdCl(dmba)]_2$ with that for the synthesized Pd(II)-NHC complex, it was revealed that the same additional signals in the aromatic region are easily observable by the ^{1}H-NMR spectroscopy of the dimer, as well. So, it is assumed that these additional signals could result from some impurities in the dimer.

It seems to be necessary to purify the dimer before using it to synthesize the Pd(II)-NHC complex. Based on a proposed purification method [220] the dimer (47 mmol) should first be suspended in acetone followed by adding an excess amount of LiCl (150 mmol). Then the mixture is heated with vigorous stirring until the precipitate is completely dissolved. According to this procedure, with an excess amount of LiCl the salt $Li[Pd(dmba)Cl_2]$ is formed which is stable only in acetone in the absence of water. By adding some water the chloro-bridged dimer is immediately formed. Next, the yellow solution obtained is filtered over celite and the short column of celite is washed with acetone. The filtrate is poured into a beaker of water to afford $[PdCl(dmba)]_2$ as a yellow precipitate which is filtered and washed with water, methanol, and diethyl ether respectively. In this context, it is worth noting that the more quickly this process is performed better the yield of the reaction is obtained (maximum~ 30 minutes). Unfortunately, I didn't have enough time to evaluate this purification method but it will be worth trying that.

As another alternative suggestion, the dimer could be prepared using a different procedure [220]. Based on this method, lithium tetrachloropalladate(II) (Li_2PdCl_4) is firstly synthesized from the reaction between $PdCl_2$ and LiCl in the water at room temperature and in the next step, a solution of Li_2PdCl_4 in methanol is reacted with dmba in the presence of triethylamine (NEt_3) at room temperature. The final product is isolated as a yellow residue in the yield of 90%. But due to time constraints, I couldn't repeat this procedure and evaluate the reaction efficiency.

4. Conclusion and outlook

In this contribution, we have proposed a complete and optimized protocol for the synthesis of benzimidazolium salts in a good yield. In this regard, five different xanthine derivatives were ethylated at the N^9 nitrogen atom through heating the xanthine derivative with $(EtO)_2SO_2$ and EtOTs as two different alkylating agents in solvent-free conditions (Figure 20).

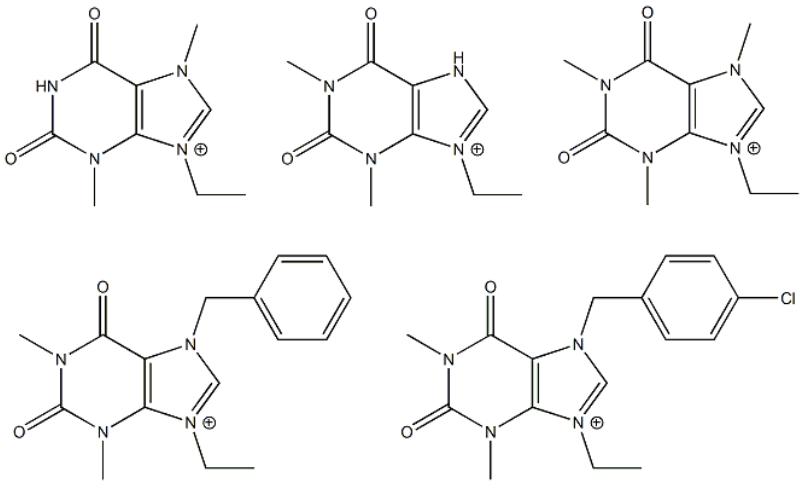


Figure 20. Different synthesized xanthinium salts.

In the next step, the obtained xanthinium salts were subjected to ion-exchange reactions to get different xanthinium salts of various counterions which are adopted to react with Ag_2O to obtain versatile coordinated silver(I)-NHCs. Furthermore, silver(I)-NHCs with the general formula of [Ag(NHC)Cl] were used as carbene transfer agents to produce the corresponding Ru(II), Rh(I), Rh(III), and Au(I)-NHC complexes.

In the last part of this work, a novel Pd(II)-NHC complex with the general formula of [(NHC)Pd(dmba)Cl] was synthesized and well characterized.

The obtained metal-NHC complexes might be further considered not only for their catalytic activity but also for possible biomedical applications in the field of anticancer treatment.

5. Experimental

5.1. General considerations

All the manipulations were carried out under ambient conditions without protection from air and moisture. All silver and gold reactions were performed with the exclusion of light. Some of the necessary reagents such as $[Ru(p\text{-cymene})Cl_2]_2$, $[Rh(Cp^*)Cl_2]_2$, $[Rh(cod)Cl]_2$ were synthesized in our laboratory while others were purchased from commercial suppliers and used without further purifications.

NMR spectrometry

The NMR spectra were recorded either on a Bruker Avance 400 MHz or Bruker Avance III 600 MHz spectrometer. Chemical shifts (δ) were given in ppm relative to tetramethylsilane [TMS] as an internal standard and the NMR peaks were labeled as singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m).

FT-IR spectroscopy

The FT-IR spectra were recorded using a Thermo Scientific Nicolet iS5 spectrometer with an iD7 Diamant ATR accessory in the range of 4000-400 cm^{-1}.

MS spectrometry

ESI-MS spectrometry analysis was performed on a Bruker Daltonics MicroTOF mass spectrometer in either positive or negative mode using acetonitrile or water as the solvent.

Elemental analysis

CHN analysis was carried out by a staff of the in-house elemental analysis facility using an Elementar Vario EL system.

X-ray Crystallography analysis

Some crystal data were collected using an Oxford Diffraction Gemini E Ultra Diffractometer [Mo-Kα (λ = 0.71073 Å)] equipped with an EOS CCD detector and a four-circle kappa goniometer at 150 K. Data integration, scaling, and empirical absorption correction were developed with the CrysAlis Pro (Oxford Diffraction Ltd., CrysAlis Pro

171.33.42, 2009). The structures were solved using direct methods and standard difference map techniques and refined by full-matrix least-squares procedures on F^2. The hydrogen atom sites were calculated from the geometry of the environment and at each Refinement cycle adjusted. All calculations were done with the Program Olex2(OlexSys Ltd. 2004-2018).

Some other crystals were measured by using a Bruker-AXS Kappa Mach3 APEX-II diffractometer with an ImS anode for generating the X-rays and an Incoatec Helios mirror as a monochromator at 100 K in Max Planck Institute for Coal Research in Mülheim. X-ray diffraction data were collected with APEX2 (Bruker AXS, 2005-2013). The data reduction and the absorption correction were carried out with SAINT Software (Bruker AXS, 2004) and SADABS (Bruker AXS, 2012), respectively. The structural solution was done using direct methods and refined using the least-squares method against F^2.

Moreover, there are some crystals, which were analyzed on an Enraf-Nonius KappaCCD system equipped with an FR591 Mo-rotating anode and an Oxford Cryosystems Cryostream 700. The data integration was carried out with EVAL-14.

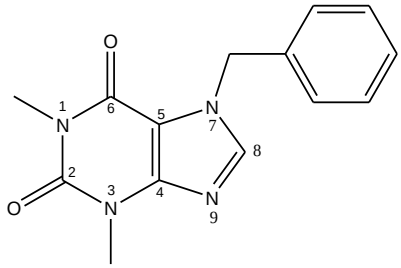
5.2. Synthesis of N-heterocyclic carbene ligands

5.2.1. Synthesis of xanthine-derivatives

Two different xanthine-derivatives were synthesized from the reaction between a solution of theophylline monohydrate (5.509 g, 27.8 mmol) in 80 ml acetonitrile with a benzyl halide-derivative (138.7 mmol) in the presence of potassium carbonate (4.25 g, 30.8 mmol) as a base. The reaction mixture was refluxed for 24 h. After completion of the reaction, the suspension was filtered and washed with acetonitrile. Finally, the filtrate was evaporated in vacuo to afford the product as a white precipitate which was washed several times with diethyl ether and dried at room temperature [71].

- **7-benzyl-1,3-dimethylxanthine (1a)**

To synthesize **1a**, theophylline monohydrate (5.509 g, 27.8 mmol) was reacted with benzyl bromide (16.5 mL, 138.7 mmol) as the benzyl halide. Yield: 7.3 g (97%).



^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.59 (s, 1H, C^8**H**), 7.32-7.41 (m, 5H, -C_6H_5), 5.52 (s, 2H, N^7-**CH_2**), 3.60 (s, 3H, N^3-**CH_3**), 3.42 (s, 3H, N^1-**CH_3**).

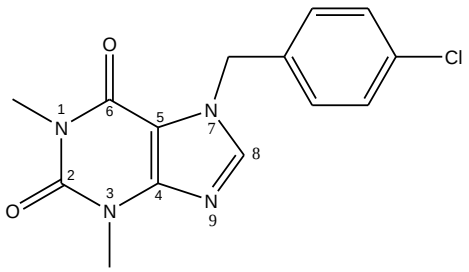
^{13}C-NMR (101 MHz, $CDCl_3$): δ [ppm] = 153.26 (C^6=O), 151.65 (C^2=O), 148.86 (C^4), 140.81 (C^8H), 135.32 (ipso-C, -C_6H_5), 129.08, 128.62, 127.95 (-C_6H_5), 106.99 (C^5), 50.28 (N^7-**CH_2**), 29.97 (N^3-**CH_3**), 27.83 (N^1-**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{14}H_{14}N_4O_2Na$ $[M+Na]^+$: 293.1009 Found: 293.1016.

Anal. Calcd for $C_{14}H_{14}N_4O_2$: C, 62.21; N, 20.73; H, 5.22. Found: C, 62.09; N, 20.45; H, 5.12.

- **7-p-chlorobenzyl-1,3-dimethylxanthine (2a)**

To prepare **2a**, theophylline monohydrate (5.509 g, 27.8 mmol) was reacted with 4-chlorobenzyl chloride (17.7 mL, 138.7 mmol) as the second benzyl halide. Yield: 5.50 g (67%).



^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.62 (s, 1H, C^8**H**), 7.25-7.37 (m, 4H, -C_6H_4Cl), 5.48 (s, 2H, N^7-**CH_2**), 3.60 (s, 3H, N^3-**CH_3**), 3.41 (s, 3H, N^1-**CH_3**).

^{13}C-NMR (101 MHz, $CDCl_3$): δ [ppm] = 155.20 (C^6=O), 151.58 (C^2=O), 148.84 (C^4), 140.62 (C^8H), 134.70 (ipso-C, -C_6H_4Cl), 133.85 (C-Cl),

129.30, (-C_6H_4Cl), 106.86 (C^5), 49.62 (N^7-**CH_2**), 29.81 (N^3-**CH_3**), 28.00 (N^1-**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{14}H_{13}ClN_4O_2Na$ $[M+Na]^+$: 327.0619 Found: 327.0625.

Anal. Calcd for $C_{14}H_{13}ClN_4O_2$: C, 55.18; N, 18.39; H, 4.30. Found: C, 55.24; N, 18.35; H, 4.19.

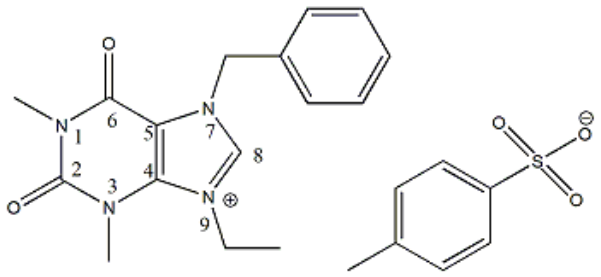
5.2.2. Synthesis of xanthine-derived salts

5.2.2.1. Xanthine-derived tosylate salts

A vial (4 mL) was charged with the xanthine-derivative (1 Eq.) and EtOTs (3.6 Eq.) and it was heated at 150 °C for 2 h. After cooling to room temperature, some excess amount of diethyl ether was added to the reaction vial to precipitate the product as a white solid. The product was washed several times with diethyl ether and dried at room temperature.

- **[7-benzyl-9-ethyl-1,3-dimethylxanthinium] TsO (1b)**

This compound was synthesized by the reaction between **1a** (0.1 g, 0.37 mmol) and EtOTs (0.267 g, 1.35 mmol, 3.6 Eq.). Yield: 0.151 g (87%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 9.63 (s, 1H, C^8**H**), 7.34-7.50 (m, 7H, -C_6H_5, CH_3(**C_6H_4**)SO_3^-), 7.10 (d, 2H, CH_3(**C_6H_4**)SO_3^-, J_{HH} = 8.4 Hz), 5.71 (s, 2H, N^7-**CH_2**), 4.59 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 3.71 (s, 3H, N^3-**CH_3**), 3.26 (s, 3H, N^1-**CH_3**), 2.29 (s, 3H, **CH_3**(C_6H_4)SO_3^-), 1.54 (t, 3H, -CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.06 (C^6=O), 150.27 (C^2=O), 145.68 (CH_3-**C**, CH_3(**C_6H_4**)SO_3^-), 139.51 (C^4), 138.51 (C^8H),

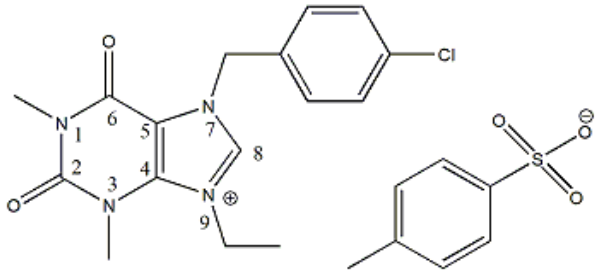
137.55 (**C**-SO_3^-, CH_3(**C_6H_4**)SO_3^-), 134.14 (ipso-C, -C_6H_5), 128.67, 128.04, 127.98, 127.47, 125.40 (-C_6H_5, CH_3(**C_6H_4**)SO_3^-), 107.09 (C^5), 51.21 (N^7-**CH_2**), 45.32 (N^9-**CH_2**), 31.66 (N^3-**CH_3**), 28.39 (N^1-**CH_3**), 20.72 (**CH_3**(C_6H_4)SO_3^-), 15.03 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{16}H_{19}N_4O_2$ $[M]^+$: 299.1503. Found: 299.1519.

Anal. Calcd for $C_{23}H_{26}N_4O_5S$: C, 58.71; N, 11.91; H, 5.57. Found: C, 59.03; N, 11.95; H, 5.59.

- **[7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthinium] TsO (2b)**

This compound was synthesized from a mixture of **2a** (0.1 g, 0.33 mmol) and ethyl p-toluenesulfonate (0.238 g, 1.19 mmol, 3.6 Eq.). Yield: 0.139 g (84%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 9.60 (s, 1H, C^8**H**), 7.44-7.49 (m, 6H, -C_6H_4Cl, CH_3(**C_6H_4**)SO_3^-), 7.09-7.12 (m, 2H, CH_3(**C_6H_4**)SO_3^-), 5.68 (s, 2H, N^7-**CH_2**), 4.58 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 3.71 (s, 3H, N^3-**CH_3**), 3.25 (s, 3H, N^1-**CH_3**), 2.29 (s, 3H, **CH_3**(C_6H_4)SO_3^-), 1.53 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.02 (C^6=O), 150.25 (C^2=O), 145.68 (CH_3-**C**, CH_3(**C_6H_4**)SO_3^-), 139.51 (C^4), 138.61 (C^8H), 137.54 (**C**-SO_3^-, CH_3(**C_6H_4**)SO_3^-), 133.43 (ipso-C, -C_6H_4Cl), 133.05 (C-Cl), 130.09, 128.72, 127.97, 125.39 (-C_6H_4Cl, CH_3(**C_6H_4**)SO_3^-), 107.06 (C^5), 50.57 (N^7-**CH_2**), 45.34 (N^9-**CH_2**), 31.66 (N^3-**CH_3**), 28.39 (N^1-**CH_3**), 20.71 (**CH_3**(C_6H_4)SO_3^-), 14.96 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{16}H_{18}ClN_4O_2$ $[M]^+$: 333.1113. Found: 333.1193.

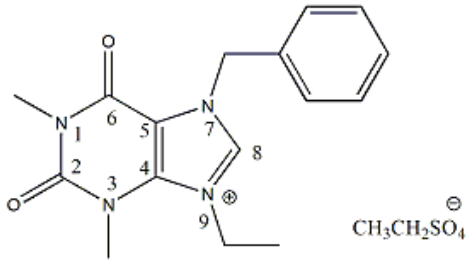
Anal. Calcd for $C_{23}H_{25}ClN_4O_5S$: C, 54.70; N, 11.09; H, 4.99. Found: C, 54.32; N, 10.76; H, 4.77.

5.2.2.2. Xanthine-derived ethyl sulfate salts

A mixture of the xanthine-derivative (1.0 mmol) and $(EtO)_2SO_2$ (2.0 mmol) was heated at 130 °C for 2 h. Then the reaction mixture was cooled down to room temperature and some excess amount of diethyl ether was added to the reaction flask to precipitate the product as a white solid. The product was washed with diethyl ether and was dried at room temperature.

- **[7-benzyl-9-ethyl-1,3-dimethylxanthinium] $EtOSO_3$ (1c)**

Compound **1c** was prepared by the reaction of **1a** (0.2 g, 0.74 mmol) and $(EtO)_2SO_2$ (194 µL, 1.48 mmol). Yield: 0.273 g (87%).



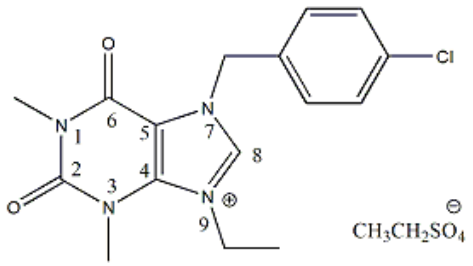
^{1}H-NMR (600 MHz, $CDCl_3$): δ [ppm] = 9.99 (s, 1H, C^8**H**), 7.62-7.66 (m, 2H, o-C_6H_5), 7.34-7.41 (m, 3H, -C_6H_5), 5.80 (s, 2H, N^7-**CH_2**), 4.76 (q, 2H, N^9-**CH_2**, J_{HH} = 7.3 Hz), 4.06 (q, 2H, CH_3**CH_2**SO_4^-, J_{HH} = 7.1 Hz), 3.85 (s, 3H, N^3-**CH_3**), 3.43 (s, 3H, N^1-**CH_3**), 1.68 (t, 3H, CH_2**CH_3**, J_{HH} = 7.3 Hz), 1.27 (t, 3H, **CH_3**$CH_2SO_4^-$, J_{HH} = 7.1 Hz).

^{13}C-NMR (151 MHz, DMSO-d_6): δ [ppm] = 153.08 (C^6=O), 150.29 (C^2=O), 139.55 (C^4), 138.54 (C^8H), 134.15 (ipso-C, -C_6H_5), 128.77, 128.66, 128.03 (-C_6H_5), 107.11 (C^5), 61.07 (CH_3**CH_2**SO_4^-), 51.20 (N^7-**CH_2**), 45.31 (N^9-**CH_2**), 31.67(N^3-**CH_3**), 28.39 (N^1-**CH_3**), 15.06 (-CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{16}H_{19}N_4O_2$ $[M]^+$: 299.1503. Found: 299.1565.

- **[7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthinium] $EtOSO_3$ (2c)**

To synthesize this product, **2a** (0.2 g, 0.65 mmol) was reacted with the diethyl sulfate (172 µL, 1.31 mmol). Yield: 0.264 g (88%).



^{1}H-NMR (600 MHz, $CDCl_3$): δ [ppm] = 10.06 (s, 1H, C^8**H**), 7.62 (d, 2H, *o*-C_6H_4Cl, J_{HH} = 8.4 Hz), 7.33-7.40 (m, 2H, *m*-C_6H_4Cl), 5.78 (s, 2H, N^7-**CH_2**), 4.74 (q, 2H, N^9-**CH_2**, J_{HH} = 7.3 Hz), 4.03 (q, 2H, CH_3**CH_2**SO_4^-, J_{HH} = 7.1 Hz), 3.85 (s, 3H, N^3-**CH_3**), 3.43 (s, 3H, N^1-**CH_3**), 1.68 (t, 3H, CH_2**CH_3**, J_{HH} = 7.3 Hz), 1.27 (t, 3H, **CH_3**$CH_2SO_4^-$, J_{HH} = 7.1 Hz).

^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.06 (C^6=O), 150.29 (C^2=O), 139.56 (C^4), 138.61 (C^8H), 133.44 (ipso-C, -C_6H_4Cl), 133.05 (C-Cl), 130.09 (*o*-C_6H_4Cl), 128.73 (*m*-C_6H_5Cl), 107.10 (C^5), 61.09 (CH_3**CH_2**SO_4^-), 50.58 (N^7-**CH_2**), 45.34 (N^9-**CH_2**), 31.68 (N^3-**CH_3**), 28.40 (N^1-**CH_3**), 15.07 (-CH_2**CH_3**), 14.99 (**CH_3**$CH_2SO_4^-$).

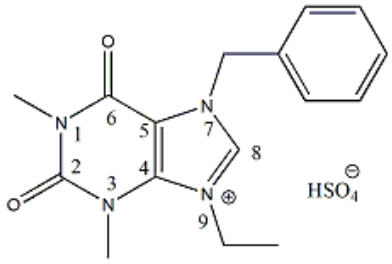
ESI-HRMS (m/z): Calcd for $C_{16}H_{18}ClN_4O_2$ $[M]^+$: 333.1113. Found: 333.1175.

5.2.2.3. Xanthine-derived hydrogensulfate salts

In this part, the same procedure was used as described above for the synthesis of derived-xanthinium ethyl sulfates. More details are available as follows:

- **[7-benzyl-9-ethyl-1,3-dimethylxanthinium] HSO_4 (1d)**

A mixture of **1a** (0.2 g, 0.65 mmol) and $(EtO)_2SO_2$ (194 µL, 1.48 mmol) was taken into a 4 mL vial and heated at 150 °C for 3 h. Last, the reaction mixture was cooled down to room temperature and then some excess amount of acetone was added to the reaction flask to precipitate the product as a white residue which was washed with acetone several times and dried at room temperature. Yield: 0.222 g (76%).



^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] = 9.65 (s, 1H, C^{8}**H**), 7.34-7.49 (m, 5H, -C$_6$H$_5$), 5.71 (s, 2H, N^{7}-**CH$_2$**), 4.60 (q, 2H, N^{9}-**CH$_2$**, J_{HH} = 7.2 Hz), 4.00 (broad s, HSO$_4^-$), 3.72 (s, 3H, N^{3}-**CH$_3$**), 3.26 (s, 3H, N^{1}-**CH$_3$**), 1.54 (t, 3H, CH$_2$**CH$_3$**, J_{HH} = 7.2 Hz).

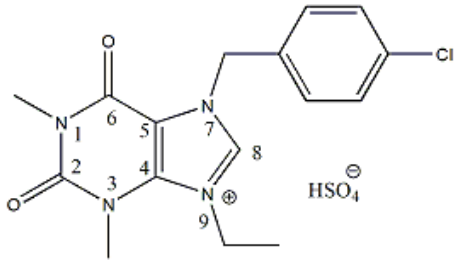
^{13}C-NMR (101 MHz, DMSO-d$_6$): δ [ppm] = 153.08 (C^{6}=O), 150.29 (C^{2}=O), 139.54 (C^{4}), 138.55 (C^{8}H), 134.15 (ipso-C, -C$_6$H$_5$), 128.76, 128.64, 128.03 (-C$_6$H$_5$), 107.10 (C^{5}), 51.19 (N^{7}-**CH$_2$**), 45.31 (N^{9}-**CH$_2$**), 31.66 (N^{3}-**CH$_3$**), 28.38 (N^{1}-**CH$_3$**), 15.05 (CH$_2$**CH$_3$**).

ESI-MS (m/z): 299 [M]$^+$, 96.96 [HSO$_4$]$^-$.

Anal. Calcd for C$_{16}$H$_{20}$N$_4$O$_6$S: C, 48.48; N, 14.13; H, 5.09. Found: C, 48.29; N, 13.92; H, 5.08.

- **[7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthinium] HSO$_4$ (2d)**

2d was synthesized by the analogous method to that for **1d**. A mixture of **2a** (0.20 g, 0.66 mmol) and (EtO)$_2$SO$_2$ (172 µL, 1.31 mmol) (in a 4 mL vial) was stirred at 150 °C for 2.5 h. Yield: 0.24 g (83%).



^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] = 9.62 (s, 1H, C^{8}**H**), 7.46-7.53 (m, 4H, -C$_6$H$_4$Cl), 5.70 (s, 2H, N^{7}-**CH$_2$**), 4.59 (q, 2H, N^{9}-**CH$_2$**, J_{HH} = 7.2 Hz), 4.28 (broad s, HSO$_4^-$), 3.72 (s, 3H, N^{3}-**CH$_3$**), 3.25 (s, 3H, N^{1}-**CH$_3$**), 1.54 (t, 3H, CH$_2$**CH$_3$**, J_{HH} = 7.2 Hz).

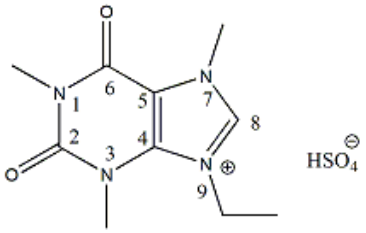
^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.05 (C^6=O), 150.28 (C^2=O), 139.56 (C^4), 138.65 (C^8H), 133.40 (ipso-C, -C_6H_4Cl), 133.07 (C-Cl), 130.10 (*o*-C_6H_4Cl), 128.70 (*m*-C_6H_4Cl), 107.08 (C^5), 50.55 (N^7-**CH_2**), 45.33 (N^9-**CH_2**), 31.66 (N^3-**CH_3**), 28.37 (N^1-**CH_3**), 14.97 (CH_2**CH_3**).

ESI-MS (m/z): 333 $[M]^+$, 96.96 $[HSO_4]^-$.

Anal. Calcd for $C_{16}H_{19}ClN_4O_6S$: C, 44.60; N, 13.00; H, 4.44. Found: C, 44.35; N, 12.82; H, 4.32.

- **[1,3,7-trimethyl-9-ethylxanthinium] HSO_4 (3d)**

Caffeine (0.2874 g, 1.480 mmol) and $(EtO)_2SO_2$ (388 µL, 2.955 mmol) were reacted together at 130°C for 2 h. The reaction mixture was cooled down to room temperature and some excess amount of acetone: toluene (3:7) was added to the reaction mixture and it was kept overnight. Finally, the crystalline product was obtained, which was filtered and washed with a little amount of acetone and dried under vacuum. Yield: 0.4335 g (91%).



^{1}H-NMR (600 MHz, DMSO-d_6): δ [ppm] = 9.42 (s, 1H, C^8**H**), 4.58 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 4.07 (s, 3H, N^7-**CH_3**), 3.73 (s, 3H, N^3-**CH_3**), 3.28 (s, 3H, N^1-**CH_3**), 1.53 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

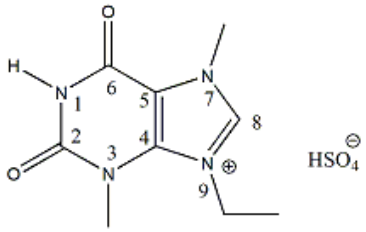
^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.31 (C^6=O), 150.34 (C^2=O), 138.87 (C^4), 138.76 (C^8H), 107.87 (C^5), 44.97 (N^9-**CH_2**), 35.61 (N^7-**CH_3**), 31.58 (N^3-**CH_3**), 28.31 (N^1-**CH_3**), 15.06 (CH_2**CH_3**).

ESI-MS (m/z): 223 $[M]^+$, 96.96 $[HSO_4]^-$.

- **[3,7-dimethyl-9-ethylxanthinium] HSO_4 (4d)**

A mixture of theobromine (0.4 g, 2.220 mmol) and $(EtO)_2SO_2$ (580 µL, 4.417 mmol) was taken into a 10 mL vial and heated at 160°C for 1:35

h. After cooling down to room temperature, some excess amount of acetone was added to the reaction flask to precipitate the product. The mixture was kept for 3-4 h until the product changes from sticky stuff to a fine white residue. Then it was filtered and washed with acetone several times and dried under vacuum. Yield: 0.4445 g (65%).



^{1}H-NMR (600 MHz, DMSO-d_6): δ [ppm] = 12.10 (s, 1H, N^{1}**H**), 9.34 (s, 1H, C^{8}**H**), 4.53 (q, 2H, N^{9}-**CH$_2$**, J_{HH} = 7.2 Hz), 4.02 (s, 3H, N^{7}-**CH$_3$**), 3.63 (s, 3H, N^{3}-**CH$_3$**), 1.50 (t, 3H, CH$_2$**CH$_3$**, J_{HH} = 7.2 Hz).

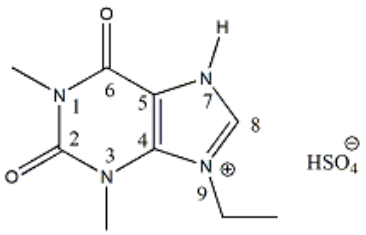
^{13}C-NMR (151 MHz, DMSO-d_6): δ [ppm] = 153.56 (C^{6}=O), 150.02 (C^{2}=O), 140.22 (C^{4}), 138.51 (C^{8}H), 108.32 (C^{5}), 44.75 (N^{9}-**CH$_2$**), 35.38 (N^{7}-**CH$_3$**), 30.37 (N^{3}-**CH$_3$**), 14.97 (CH$_2$**CH$_3$**).

ESI-MS (m/z): 209 $[M]^+$, 96.96 $[HSO_4]^-$.

Anal. Calcd for $C_9H_{14}N_4O_6S$: C, 35.29; N, 18.29; H, 4.61. Found: C, 34.85; N, 18.03; H, 4.64.

- **[1,3-dimethyl-9-ethylxanthinium] HSO$_4$ (5d)**

Theophylline (0.3 g, 1.665 mmol) was reacted with $(EtO)_2SO_2$ (396 µL, 3.016 mmol) at 160°C for 1:45. The reaction mixture was cooled down to room temperature and then some excess amount of acetone was added to the reaction flask to precipitate the product as a white solid which was washed with acetone several times and last with diethyl ether. The product was finally dried at room temperature. Yield: 0.2193 g (43%).



^{1}H-NMR (600 MHz, DMSO-d_6): δ [ppm] = 8.23 (broad s, N^{7}**H**), 8.10 (s, 1H, C^{8}**H**), 4.27 (q, 2H, N^{9}-**CH$_2$**, J_{HH} = 7.2 Hz), 3.42 (s, 3H, N^{3}-**CH$_3$**), 3.23 (s, 3H, N^{1}-**CH$_3$**), 1.39 (t, 3H, CH$_2$**CH$_3$**, J_{HH} = 7.2 Hz).

^{13}C-NMR (151 MHz, DMSO-d_6): δ [ppm] = 154.25 (C^6=O), 151.02 (C^2=O), 148.40 (C^4), 141.83 (C^8H), 105.84 (C^5), 41.49 (N^9-**CH_2**), 29.39 (N^3-**CH_3**), 27.54 (N^1-**CH_3**), 16.28 (CH_2**CH_3**).

ESI-MS (m/z): 209 $[M]^+$, 96.96 $[HSO_4]^-$.

5.2.2.4. Xanthine-derived hexafluorophosphate salts

[NHCH]PF_6 was prepared by an ion-exchange reaction between [NHCH]X (X: TsO^-, $EtOSO_3^-$, HSO_4^-) and NH_4PF_6 in water or ethanol as the solvent. The reaction mixture was stirred at room temperature for an indicated amount of time. Last, the reaction mixture was filtered and the residue was washed with water or ethanol and diethyl ether, respectively, and dried at room temperature [77].

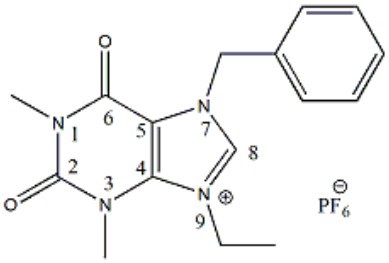
- **[7-benzyl-9-ethyl-1,3-dimethylxanthinium] PF_6 (1e)**

Compound **1e** was synthesized using the method as described above from three different substrates **(1b)**, **(1c)**, and **(1d)**.

1b (0.5 g, 1.063 mmol) was dispersed in 20 mL water. Then NH_4PF_6 (0.2 g, 1.227 mmol, 1.154 Eq.) was added to the reaction mixture. The mixture was stirred at room temperature for 30 minutes. Yield: 0.325 g (69%).

1c (0.1 g, 0.236 mmol) was dissolved in 10 mL water. Then NH_4PF_6 (0.0403 g, 0.247 mmol, 1.05 Eq.) was added to the reaction mixture. The mixture was stirred at room temperature for 20 minutes. Yield: 0.077 g (74%).

1d (0.29 g, 0.740 mmol) was dissolved in 20 mL water. Then NH_4PF_6 (0.127 g, 0.777 mmol, 1.05 Eq.) was added to the reaction mixture. The mixture was stirred at room temperature for 20 minutes. Yield: 0.294 g (89%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 9.60 (s, 1H, C^8**H**), 7.32-7.49 (m, 5H, -C_6H_5), 5.71 (s, 2H, N^7-**CH_2**), 4.59 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2

Hz), 3.72 (s, 3H, N^3-**CH_3**), 3.27 (s, 3H, N^1-**CH_3**), 1.54 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.07 (C^6=O), 150.28 (C^2=O), 139.51 (C^4), 138.48 (C^8H), 134.11 (ipso-C, -C_6H_5), 128.78, 128.68, 128.00 (-C_6H_5), 107.11 (C^5), 51.22 (N^7-**CH_2**), 45.30 (N^9-**CH_2**), 31.66 (N^3-**CH_3**), 28.39 (N^1-**CH_3**), 15.07 (CH_2**CH_3**).

^{31}P-NMR (162 MHz, DMSO-d_6): δ [ppm] = -144.19 (hept, PF_6, J_{P-F} = 711 Hz).

ESI-HRMS (m/z): Calcd for $C_{16}H_{19}N_4O_2$ $[M]^+$: 299.1503. Found: 299.1510.

Anal. Calcd for $C_{16}H_{19}F_6N_4O_2P$: C, 43.25; N, 12.61; H, 4.31. Found: C, 43.24; N, 12.64; H, 4.64.

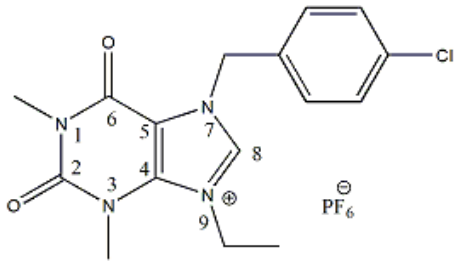
- **[7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthinium] PF_6 (2e)**

Compound **2e** was synthesized from three different derived-xanthinium salts as described below;

2b (0.3 g, 0.594 mmol) was dispersed in 20 mL water. Then NH_4PF_6 (0.1 g, 0.613 mmol, 1.03 Eq.) was added to the reaction mixture. The mixture was stirred at room temperature for 60 minutes. Yield: 0.219g (77%).

2c (0.1 g, 0.218 mmol) was dissolved in 15 mL water. Then NH_4PF_6 (0.0373 g, 0.229 mmol, 1.05 Eq.) was added to the reaction mixture. The mixture was stirred at room temperature for 20 minutes. Yield: 0.077 g (74%).

2d (0.283 g, 0.657 mmol) was dissolved in 20 mL water. Then NH_4PF_6 (0.112 g, 0.690 mmol, 1.05 Eq.) was added to the reaction mixture. The mixture was stirred at room temperature for 20 minutes. Yield: 0.248 g (79%).



^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] = 9.57 (s, 1H, C^{8}**H**), 7.44-7.54 (m, 4H, -C$_6$H$_4$Cl), 5.70 (s, 2H, N^{7}-**CH$_2$**), 4.59 (q, 2H, N^{9}-**CH$_2$**, J_{HH} = 7.2 Hz), 3.72 (s, 3H, N^{3}-**CH$_3$**), 3.26 (s, 3H, N^{1}-**CH$_3$**), 1.54 (t, 3H, CH$_2$**CH$_3$**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, DMSO-d$_6$): δ [ppm] = 153.04 (C^{6}=O), 150.27 (C^{2}=O), 139.52 (C^{4}), 138.58 (C^{8}H), 133.46 (ipso-C, -C$_6$H$_4$Cl), 133.01 (C-Cl), 130.07, 128.74 (-C$_6$H$_4$Cl), 107.09 (C^{5}), 50.59 (N^{7}-**CH$_2$**), 45.32 (N^{9}-**CH$_2$**), 31.67 (N^{3}-**CH$_3$**), 28.40 (N^{1}-**CH$_3$**), 15.00 (CH$_2$**CH$_3$**).

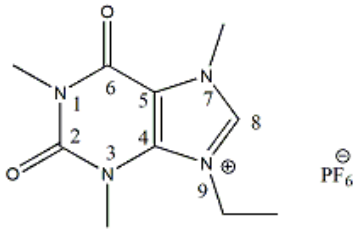
^{31}P-NMR (162 MHz, DMSO-d$_6$): δ [ppm] = -144.20 (hept, PF$_6$, $J_{P\text{-}F}$ = 711 Hz).

ESI-HRMS (m/z): Calcd for C$_{16}$H$_{18}$ClN$_4$O$_2$ [M]$^{+}$: 333.1113. Found: 333.1118.

Anal. Calcd for C$_{16}$H$_{18}$ClF$_6$N$_4$O$_2$P: C, 40.14; N, 11.70; H, 3.79. Found: C, 40.72; N, 12.02; H, 3.32.

- **[1,3,7-trimethyl-9-ethylxanthinium] PF$_6$ (3e)**

Compound **3d** (0.4325 g, 1.412 mmol) was dissolved in 5 mL water and reacted with NH$_4$PF$_6$ (0.4403 g, 2.701 mmol) at room temperature for 1 h. Yield: 0.382 g (77%).



^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] = 9.34 (s, 1H, C^{8}**H**), 4.56 (q, 2H, N^{9}-**CH$_2$**, J_{HH} = 7.2 Hz), 4.05 (d, 3H, N^{7}-**CH$_3$**, J_{HH} = 0.6 Hz), 3.71 (s, 3H, N^{3}-**CH$_3$**), 3.27 (s, 3H, N^{1}-**CH$_3$**), 1.50 (t, 3H, CH$_2$**CH$_3$**, J_{HH} = 7.2 Hz).

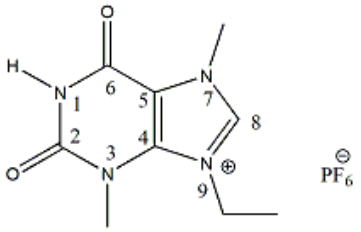
^{13}C-NMR (101 MHz, DMSO-d$_6$): δ [ppm] = 153.31 (C^{6}=O), 150.33 (C^{2}=O), 138.85 (C^{4}), 138.69 (C^{8}H), 107.88 (C^{5}), 44.98 (N^{9}-**CH$_2$**), 35.63 (N^{7}-**CH$_3$**), 31.57 (N^{3}-**CH$_3$**), 28.32 (N^{1}-**CH$_3$**), 15.09 (CH$_2$**CH$_3$**).

^{31}P-NMR (162 MHz, DMSO-d$_6$): δ [ppm] = -144.21 (hept, PF$_6$, $J_{P\text{-}F}$ = 711 Hz).

ESI-MS (m/z): 223 $[M]^+$, 144 $[PF_6]^-$.

- **[3,7-dimethyl-9-ethylxanthinium] PF_6 (4e)**

NH_4PF_6 (0.106 g, 0.650 mmol) was added into the mixture of **4d** (0.2 g, 0.653 mmol) in ethanol and it was stirred at room temperature for 1 h. The product was filtered and washed with ethanol and diethyl ether, respectively. Yield: 0.1387 g (63%).



^{1}H-NMR (600 MHz, DMSO-d_6): δ [ppm] = 12.15 (s, 1H, N^1**H**), 9.32 (s, 1H, C^8**H**), 4.55 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 4.04 (s, 3H, N^7-**CH_3**), 3.65 (s, 3H, N^3-**CH_3**), 1.51 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.64 (C^6=O), 150.11 (C^2=O), 140.29 (C^4), 138.53 (C^8H), 108.42 (C^5), 44.84 (N^9-**CH_2**), 35.52 (N^7-**CH_3**), 30.47 (N^3-**CH_3**), 15.12 (CH_2**CH_3**).
^{31}P-NMR (162 MHz, DMSO-d_6): δ [ppm] = -144.13 (hept, PF_6, J_{P-F} = 711Hz).

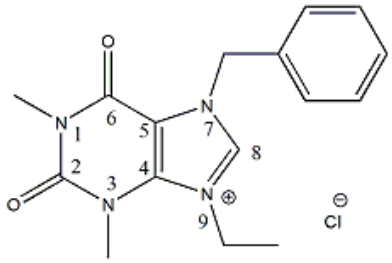
ESI-MS (m/z): 209 $[M]^+$, 144 $[PF_6]^-$.

5.2.2.5. Xanthine-derived chloride salts

[NHCH]Cl was synthesized from [NHCH]PF_6 by an ion-exchange reaction. Based on this synthesis method [NHCH]PF_6 (1.0 mmol) was suspended in THF or acetone and reacted with a solution of TBAC (2.0 mmol). The reaction mixture was stirred at room temperature for 2 h. Finally, the reaction mixture was filtered and the residue was washed with a little amount of THF and diethyl ether and dried at room temperature [197].

- **[7-benzyl-9-ethyl-1,3-dimethylxanthinium] Cl (1f)**

1e (0.2416 g, 0.544 mmol) was suspended in 3 mL THF and reacted with a solution of TBAC (0.304 g, 1.094 mmol) in 2.5 mL THF. Yield: 0.1548 g (85%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 10.01 (s, 1H, C^{8}**H**), 7.32-7.54 (m, 5H, -C_6H_5), 5.74 (s, 2H, N^{7}-**CH_2**), 4.62 (q, 2H, N^{9}-**CH_2**, J_{HH} = 7.2 Hz), 3.72 (s, 3H, N^{3}-**CH_3**), 3.26 (s, 3H, N^{1}-**CH_3**), 1.55 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

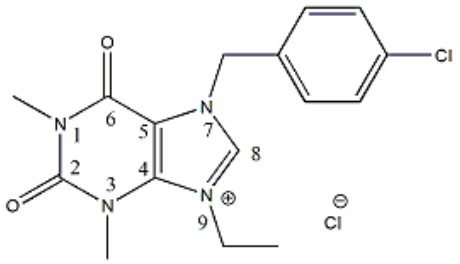
^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.08 (C^{6}=O), 150.29 (C^{2}=O), 139.53 (C^{4}), 138.71 (C^{8}H), 134.22 (ipso-C,-C_6H_5), 128.74, 128.64, 128.09 (-C_6H_5), 107.03 (C^{5}), 51.10 (N^{7}-**CH_2**), 45.30 (N^{9}-**CH_2**), 31.69 (N^{3}-**CH_3**), 28.39(N^{1}-**CH_3**), 15.09 (CH_2**CH_3**).

^{35}Cl-NMR (54 MHz, DMSO-d_6): δ [ppm] = 69.4 (s, Cl^-).

ESI-HRMS (m/z): Calcd for $C_{16}H_{19}N_4O_2$ $[M]^+$: 299.1503. Found: 299.1561.

- **[7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthinium] Cl (2f)**

2e (0.2604 g, 0.544 mmol) was suspended in 8 mL THF and reacted with a solution of TBAC (0.304 g, 1.094 mmol) in 3 mL THF. Yield: 0.152 g (75%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 10.01 (s, 1H, C^{8}**H**), 7.47-7.55 (m, 4H, -C_6H_4Cl), 5.73 (s, 2H, N^{7}-**CH_2**), 4.61 (q, 2H, N^{9}-**CH_2**, J_{HH} = 7.2 Hz), 3.72 (s, 3H, N^{3}-**CH_3**), 3.26 (s, 3H, N^{1}-**CH_3**), 1.55 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

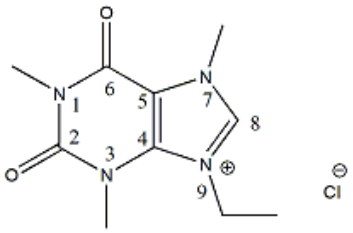
^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.05 (C^6=O), 150.27 (C^2=O), 139.53 (C^4), 138.81 (C^8H), 133.42 (ipso-**C**, -C_6H_4Cl), 133.14 (C-Cl), 130.17 (*o*-C_6H_4Cl), 128.69 (*m*-C_6H_4Cl), 107.00 (C^5), 50.44 (N^7-**CH_2**), 45.33 (N^9-**CH_2**), 31.70 (N^3-**CH_3**), 28.39(N^1-**CH_3**), 15.01 (CH_2**CH_3**).

^{35}Cl-NMR (54 MHz, DMSO-d_6): δ [ppm] = 69.4 (s, Cl^-).

ESI-HRMS (m/z): Calcd for $C_{16}H_{18}ClN_4O_2$ $[M]^+$: 333.1113. Found: 333.1035.

- **[1,3,7-trimethyl-9-ethylxanthinium] Cl (3f)**

3e (0.2 g, 0.543 mmol) was suspended in 3 mL THF and reacted with a solution of TBAC (0.304 g, 1.094 mmol) in 2.5 mL THF. Yield: 0.136 g (97%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 9.58 (s, 1H, C^8**H**), 4.58 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 4.07 (d, 3H, N^7-**CH_3**, J_{HH} = 0.6 Hz), 3.72 (s, 3H, N^3-**CH_3**), 3.28 (s, 3H, N^1-**CH_3**), 1.51 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

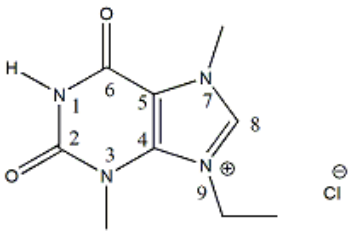
^{13}C-NMR (151 MHz, DMSO-d_6): δ [ppm] = 153.32 (C^6=O), 150.34 (C^2=O), 138.92 (C^4), 138.85 (C^8H), 107.82 (C^5), 44.97 (N^9-**CH_2**), 35.59 (N^7-**CH_2**), 31.61 (N^3-**CH_3**), 28.31 (N^1-**CH_3**), 15.12 (CH_2**CH_3**).

^{35}Cl-NMR (39 MHz, DMSO-d_6): δ [ppm] = 35.16 (s, Cl^-).

ESI-HRMS (m/z): Calcd for $C_{10}H_{15}N_4O_2$ $[M]^+$: 223.1190. Found: 223.1191.

- **[3,7-dimethyl-9-ethylxanthinium] Cl (4f)**

4e (0.120 g, 0.340 mmol) in 4 mL acetone was reacted with a solution of TBAC (0.190 g, 0.684 mmol) in 3 mL acetone. The product was obtained as a white precipitate which was washed with a little amount of acetone and diethyl ether, respectively. Yield: 0.0811 g (97%).



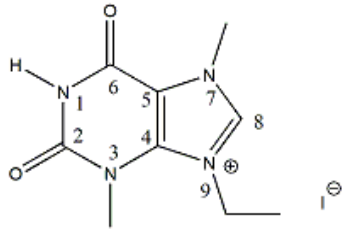
^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 12.11 (s, 1H, N^{1}**H**), 9.59 (s, 1H, C^{8}H), 4.55 (q, 2H, N^{9}-**CH$_2$**, J_{HH} = 7.2 Hz), 4.03 (s, 3H, N^{7}-**CH$_3$**), 3.63 (s, 3H, N^{3}-**CH$_3$**), 1.50 (t, 3H, CH$_2$**CH$_3$**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.64 (C^{6}═O), 150.10 (C^{2}═O), 140.29 (C^{4}), 138.69 (C^{8}H), 108.37 (C^{5}), 44.84 (N^{9}-**CH$_2$**), 35.47 (N^{7}-**CH$_3$**), 30.49 (N^{3}-**CH$_3$**), 15.14 (CH$_2$**CH$_3$**).

ESI-HRMS (m/z): Calcd for $C_9H_{13}N_4O_2$ [M]$^{+}$: 209.1033. Found: 209.1040.

- **[3,7-dimethyl-9-ethylxanthinium] I (5f)**

For more chance of working with 3,7-dimethyl-9-ethylxanthinium salts, [NHCH]I was synthesized through the same ion-exchange reaction between **4e** (0.120 g, 0.339 mmol) and TBAI (0.253 g, 0.684 mmol) in acetone as solvent at room temperature for 2 h. Finally, the reaction mixture was filtered and the residue was washed with acetone carefully to obtain the product as an off-white precipitate. Yield: 0.0655 g (58%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 9.34 (s, 1H, C^{8}**H**), 7.97 (d, 1H, N^{1}**H**, J_{HH} = 0.5 Hz), 4.55 (q, 2H, N^{9}-**CH$_2$**, J_{HH} = 7.2 Hz), 4.03 (s, 3H, N^{7}-**CH$_3$**), 3.65 (s, 3H, N^{3}-**CH$_3$**), 1.51 (t, 3H, CH$_2$**CH$_3$**, J_{HH} = 7.2 Hz).

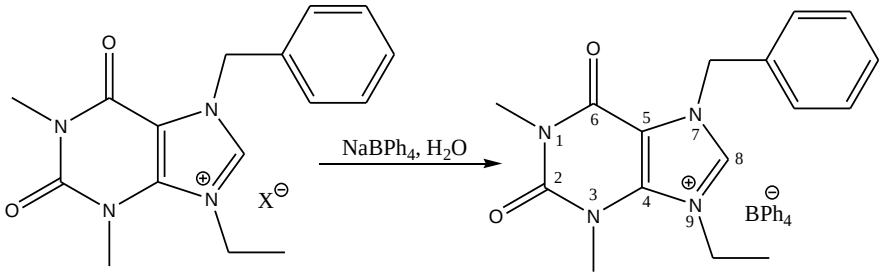
^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.64 (C^{6}═O), 150.10 (C^{2}═O), 140.29 (C^{4}), 138.51 (C^{8}H), 108.42 (C^{5}), 44.87 (N^{9}-**CH$_2$**), 35.52 (N^{7}-**CH$_3$**), 30.54 (N^{3}-**CH$_3$**), 15.10 (CH$_2$**CH$_3$**).

ESI-MS (m/z): 209 [M]$^{+}$, 126.9050 [I]$^{-}$.

5.2.2.6. Xanthine-derived tetraphenylborate salts

This product was prepared from three different substrates by the same method. According to this procedure, 1.05 Eq. of $NaBPh_4$ was added to a mixture of [NHCH]X (X: TsO^-, $EtOSO_3^-$, HSO_4^-) (1 Eq.) in water. The mixture was stirred at room temperature for about 30 minutes. Last, the white solid residue was isolated as the product, washed with water and diethyl ether, respectively, and dried at room temperature [190].

- **[7-benzyl-9-ethyl-1,3-dimethylxanthinium] BPh_4 (1g)**



X: TsO^- **(1b)**, $CH_3CH_2SO_4^-$ **(1c)**, HSO_4^- **(1d)**

$NaBPh_4$ (0.076 g, 0.222 mmol, 1.05 Eq.) was added to a mixture of **1b** (0.10 g, 0.212 mmol) in water (15 mL). Yield: 0.0835 g (63%).

$NaBPh_4$ (0.0846 g, 0.247 mmol, 1.05 Eq.) was added to a mixture of **1c** (0.1 g, 0.235 mmol) in water (15 mL). Yield: 0.115 g (77%).

$NaBPh_4$ (0.266 g, 0.777 mmol, 1.05 Eq.) was added to a mixture of **1d** (0.293 g, 0.739 mmol) in water (20 mL). Yield: 0.338 g (74%).

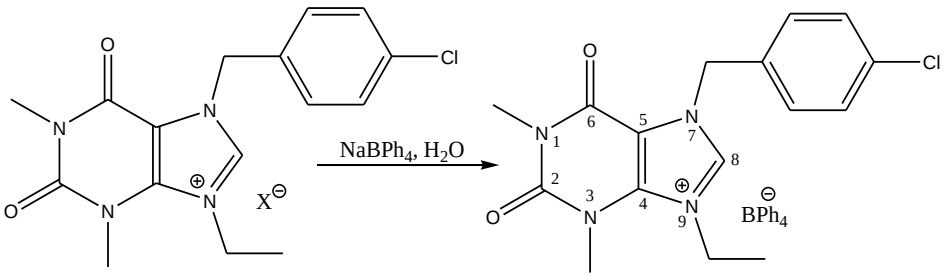
^{1}H-NMR (600 MHz, DMSO-d_6): δ [ppm] = 9.60 (s, 1H, C^8**H**), 7.37-7.48 (m, 5H, -C_6H_5), 7.17-7.22 (m, 8H, *o*-CH, BPh_4), 6.94 (t, 8H, *m*-CH, BPh_4, J_{HH} = 7.4 Hz), 6.80 (t, 4H, *p*-CH, BPh_4, J_{HH} = 7.2 Hz), 5.72 (s, 2H, N^7-**CH_2**), 4.58 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 3.71 (s, 3H, N^3-**CH_3**), 3.28 (s, 3H, N^1-**CH_3**), 1.54 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (151 MHz, DMSO-d_6): δ [ppm] = 163.81-162.83 (q, **C**-B, $J_{C\text{-}B}$ = 49 Hz), 153.08 (C^6=O), 150.28 (C^2=O), 139.51 (C^4), 138.47 (C^8H), 135.49 (*o*-C_6H_5, BPh_4), 134.11 (ipso-C, -C_6H_5), 128.79, 128.70, 128.02 (-C_6H_5), 125.22 (*m*-C_6H_5, BPh_4), 121.45 (*p*-C_6H_5, BPh_4), 107.11 (C^5), 51.23 (N^7-**CH_2**), 45.30 (N^9-**CH_2**), 31.67 (N^3-**CH_3**), 28.41 (N^1-**CH_3**), 15.08 (CH_2**CH_3**).

^{11}B-NMR (193 MHz, DMSO-d$_6$): δ [ppm] = -6.67.

ESI-HRMS (m/z): Calcd for $C_{40}H_{39}BN_4O_2Na$ $[M+Na]^+$: 641.3065. Found: 641.3046.

- **[7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthinium] BPh$_4$ (2g)**



X: TsO^- **(2b)**, $CH_3CH_2SO_4^-$ **(2c)**, HSO_4^- **(2d)**

$NaBPh_4$ (0.071 g, 0.207 mmol, 1.05 Eq.) was added to a mixture of **2b** (0.10 g, 0.198 mmol) in water (15 mL) (0.0935 g, 72%).
$NaBPh_4$ (0.0783 g, 0.229 mmol, 1.05 Eq.) was added to a mixture of **2c** (0.1 g, 0.218 mmol) in water (15 mL) (0.118 g, 83%).

$NaBPh_4$ (0.236 g, 0.690 mmol, 1.05 Eq.) was added to a mixture of **2d** (0.283 g, 0.657 mmol) in water (20 mL) (0.381 g, 89%).

^{1}H-NMR (600 MHz, DMSO-d$_6$): δ [ppm] = 9.56 (s, 1H, C^8**H**), 7.46-7.51 (m, 4H, -C_6H_4Cl), 7.18 (d, 8H, *o*-CH, BPh_4, J_{HH} = 1.2 Hz), 6.92 (t, 8H, *m*-CH, BPh_4, J_{HH} = 7.2 Hz), 6.79 (t, 4H, *p*-CH, BPh_4, J_{HH} = 7.2 Hz), 5.68 (s, 2H, N^7-**CH_2**), 4.56 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 3.70 (s, 3H, N^3-**CH_3**), 3.26 (s, 3H, N^1-**CH_3**), 1.52 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, DMSO-d$_6$): δ [ppm] = 164.10-162.48 (q, **C**-B, $J_{C\text{-}B}$ = 49.3 Hz), 153.03 (C^6=O), 150.26 (C^2=O), 139.50 (C^4), 138.56 (C^{8}H), 135.47 (m, *o*-C_6H_5, BPh_4), 133.46 (ipso-C, -C_6H_4Cl), 133.03 (C-Cl), 130.07, 128.73 (-C_6H_4Cl), 125.20, 121.42 (-C_6H_5, BPh_4), 107.08 (C^5), 50.58 (N^7-CH_2), 45.30 (N^9-**CH_2**), 31.66 (N^3-**CH_3**), 28.39 (N^1-**CH_3**), 15.00 (CH_2**CH_3**).

^{11}B-NMR (193 MHz, DMSO-d$_6$): δ [ppm] = -6.67.

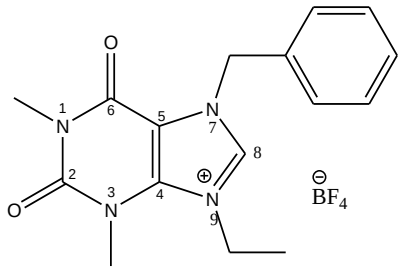
ESI-HRMS (m/z): Calcd for $C_{16}H_{18}ClN_4O_2$ $[M]^+$: 333.1113. Found: 333.1210.

5.2.2.7. Xanthine-derived tetrafluoroborate

[NHCH]HSO_4 (1.0 mmol) was dissolved in a certain amount of methanol:H_2O (4:1) and reacted with $NaBF_4$ (2.0 mmol) at room temperature for 30 minutes. After the reaction reached completion, the white precipitate was separated as the product and washed with a little amount of THF and diethyl ether, respectively, and dried at room temperature [191,192].

- **[7-benzyl-9-ethyl-1,3-dimethylxanthinium] BF_4 (1h)**

1d (0.1g, 0.252 mmol) was dissolved in 10 mL methanol:H_2O (4:1) and reacted with $NaBF_4$ (0.0582 g, 0.530 mmol). Yield: 0.0850 g (87%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 9.59 (s, 1H, C^8**H**), 7.35-7.47 (m, 5H, -C_6H_5), 5.71 (s, 2H, N^7-**CH_2**), 4.58 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 3.71 (s, 3H, N^3-**CH_3**), 3.26 (s, 3H, N^1-**CH_3**), 1.53 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

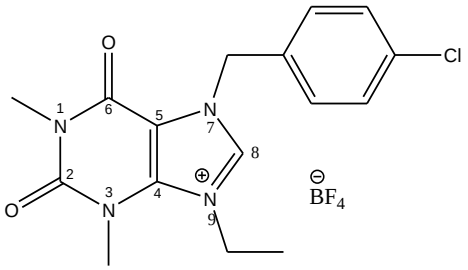
^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.06 (C^6=O), 150.27 (C^2=O), 139.51 (C^4), 138.47 (C^8H), 134.10 (ipso-C, -C_6H_5), 128.77, 128.67, 127.99 (-C_6H_5), 107.11 (C^5), 51.21 (N^7-**CH_2**), 45.29 (N^9-**CH_2**), 31.66 (N^3-**CH_3**), 28.39 (N^1-**CH_3**), 15.06 (CH_2**CH_3**).

^{19}F-NMR (376 MHz, DMSO-d_6): δ [ppm] = -148.35, -148.41.

ESI-MS (m/z): 299 $[M]^+$, 87 $[BF_4]^-$.

- **[7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthinium] BF_4 (2h)**

2d (0.1g, 0.232 mmol) was dissolved in 5 mL methanol: H_2O (4:1) and reacted with $NaBF_4$ (0.0534 g, 0.486 mmol). Yield: 0.0690 g (71%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 9.56 (s, 1H, C^{8}**H**), 7.45-7.52 (m, 4H, -C_6H_4Cl), 5.69 (s, 2H, N^{7}-**CH_2**), 4.58 (q, 2H, N^{9}-**CH_2**, J_{HH} = 7.2 Hz), 3.71 (s, 3H, N^{3}-**CH_3**), 3.25 (s, 3H, N^{1}-**CH_3**), 1.53 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.03 (C^{6}=O), 150.26 (C^{2}=O), 139.52 (C^{4}), 138.57 (C^{8}H), 133.45 (ipso-C, -C_6H_4Cl), 133.00 (C-Cl), 130.07, 128.73 (-C_6H_4Cl), 107.09 (C^{5}), 50.58 (N^{7}-**CH_2**), 45.31 (N^{9}-**CH_2**), 31.67 (N^{3}-**CH_3**), 28.39 (N^{1}-**CH_3**), 15.00 (CH_2**CH_3**).

^{19}F-NMR (376 MHz, DMSO-d_6): δ [ppm] = -148.37, -148.42.

ESI-MS (m/z): 333 $[M]^+$, 87 $[BF_4]^-$.

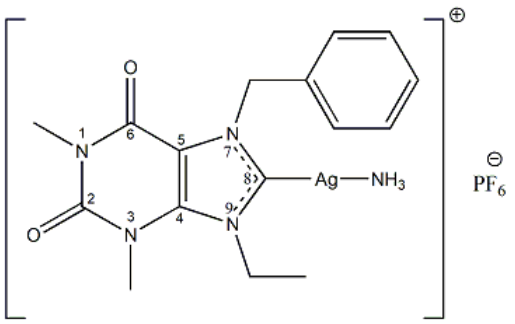
5.3. Synthesis of silver(I)-NHC complexes

5.3.1. Synthesis of [Ag(NHC)NH_3] PF_6/BPh_4/BF_4 complexes

[NHCH]X (X: PF_6^-, BPh_4^-, BF_4^-) (1.0 mmol) was suspended in ethanol and Ag_2O (0.5 mmol), followed by aqueous ammonia was added to the mixture. The reaction mixture was stirred at room temperature for 30 minutes to 4 hours. Then the reaction mixture was filtered and the product was obtained as an off-white residue which was finally washed with cold ethanol and diethyl ether, respectively, and dried at room temperature [198].

- **[Ag(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(NH_3)] PF_6 (1)**

1e (0.111 g, 0.25 mmol) was suspended in 2 mL ethanol. Ag_2O (0.029 g, 0.125 mmol) followed by aqueous ammonia (170 µL, 16.54 mol/L, 2.6 mmol) was added to the mixture. Yield: 0.1105 g (78%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 7.25-7.40 (m, 5H, -C_6H_5), 5.72 (s, 2H, N^7-**CH_2**), 4.59 (broad q, 2H, N^9-**CH_2**), 3.72 (s, 3H, N^3-**CH_3**), 3.50 (s, 3H, Ag-NH_3), 3.24 (s, 3H, N^1-**CH_3**), 1.42 (broad t, 3H, CH_2**CH_3**).

^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 185.27 (C^8-Ag), 152.93 (C^6=O), 150.57 (C^2=O), 140.26 (C^4), 136.56 (ipso-C, -C_6H_5), 128.58, 127.88, 127.27 (-C_6H_5), 108.28 (C^5), 52.86 (N^7-**CH_2**), 46.32 (N^9-**CH_2**), 31.35 (N^3-**CH_3**), 28.15 (N^1-**CH_3**), 17.21 (CH_2**CH_3**).

FT-IR analysis: the IR spectrum exhibits a strong PF_6 absorption at 833 cm^{-1} and two peaks at 3300-3400 cm^{-1} which can be referred to the coordinated ammonia.

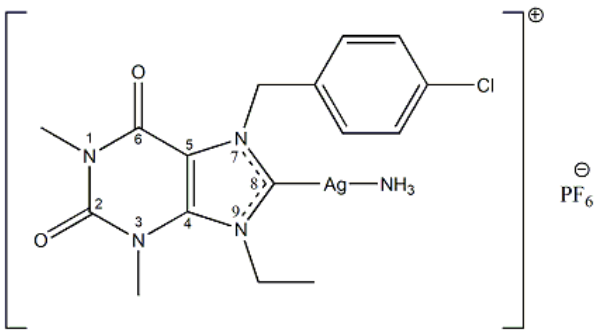
^{31}P-NMR (162 MHz, DMSO-d_6): δ [ppm] = -144.19 (hept, PF_6, $J_{P\text{-}F}$ = 711 Hz).

ESI-HRMS (m/z): Calcd for $C_{16}H_{21}AgN_5NaO_2$ $[M+Na]^+$: 446.0717. Found: 446.0686.

Anal. Calcd for $C_{16}H_{21}AgF_6N_5O_2P$: C, 33.82; N, 12.33; H, 3.73. Found: C, 33.57; N, 12.03; H, 3.22.

- **[Ag(7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(NH_3)] PF_6 (2)**

This complex was synthesized by the same method as mentioned above from the reaction between a suspension of **2e** (0.119 g, 0.25 mmol) in 2 mL ethanol and Ag_2O (0.029 g, 0.125 mmol) in the presence of ammonia (170 µL, 16.54 mol/L, 2.6 mmol). Yield: 0.1163 g (77%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 7.28-7.45 (m, 4H, -C_6H_4Cl), 5.71 (s, 2H, N^7-**CH_2**), 4.60 (q, 2H, N^9-**CH_2**, J_{HH} = 7.0 Hz), 3.72 (s, 3H, N^3-**CH_3**), 3.23 (s, 3H, N^1-**CH_3**), 3.03 (s, 3H, Ag-NH_3), 1.43 (t, 3H, CH_2**CH_3**, J_{HH} = 7.0 Hz).

^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 152.92 (C^6=O), 150.60 (C^2=O), 140.34 (C^4), 135.63 (ipso-C, -C_6H_4Cl), 132.60 (C-Cl), 129.10 (*o*-C_6H_4Cl), 128.56 (*m*-C_6H_4Cl), 108.22 (C^5), 52.02 (N^7-**CH_2**), 46.35 (N^9-**CH_2**), 31.39 (N^3-**CH_3**), 28.20 (N^1-**CH_3**), 17.26 (CH_2**CH_3**). Carbene carbon missing.

FT-IR analysis: the IR spectrum shows a strong PF_6 absorption at 834.51 cm^{-1} and two peaks at 3300-3400 cm^{-1} which can be referred to the coordinated ammonia.

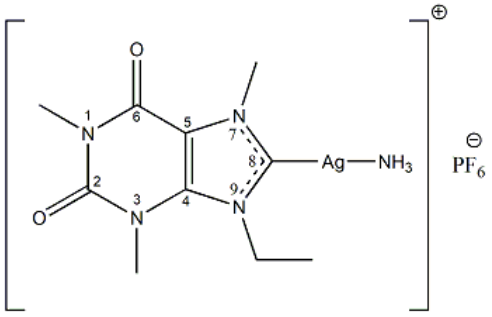
^{31}P-NMR (162 MHz, DMSO-d_6): δ [ppm] = -144.19 (hept, PF_6, $J_{P\text{-}F}$ = 711 Hz).

ESI-HRMS (m/z): Calcd for $C_{16}H_{20}AgClN_5NaO_2$ $[M+Na]^+$: 480.0327. Found: 480.0328.

Anal. Calcd for $C_{16}H_{20}AgClF_6N_5O_2P$: C, 31.83; N, 11.60; H, 3.51. Found: C, 32.28; N, 11.55; H, 3.56.

- **[Ag(1,3,7-trimethyl-9-ethylxanthine-8-ylidene)(NH_3)] PF_6 (3)**

A suspension of **3e** (0.0920 g, 0.25 mmol) in 2 mL ethanol was reacted with Ag_2O (0.029 g, 0.125 mmol) followed by aqueous ammonia (163 µL, 16.54 mol/L, 2.7 mmol). Yield: 0.0840 g (68%).



^{1}H-NMR (600 MHz, DMSO-d_6): δ [ppm] = 4.60 (q, 2H, N^9-**CH_2**, J_{HH} = 7.0 Hz), 4.08 (s, 3H, N^7-**CH_3**), 3.72 (s, 3H, N^3-**CH_3**), 3.26 (s, 3H, N^1-**CH_3**), 3.06 (broad s, Ag-NH_3), 1.46 (t, 3H, CH_2**CH_3**, J_{HH} = 7.0 Hz).

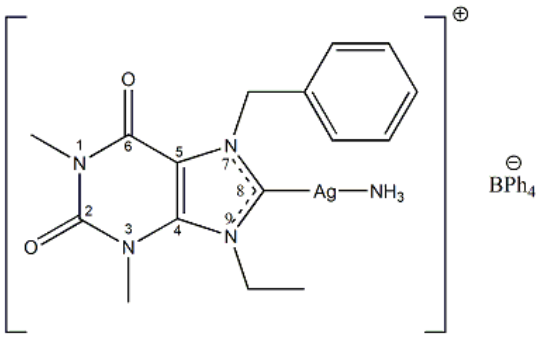
^{13}C-NMR (151 MHz, DMSO-d_6): δ [ppm] = 153.21 (C^6=O), 150.68 (C^2=O), 139.83 (C^4), 108.88 (C^5), 46.04 (N^9-**CH_2**), 38.01 (N^7-**CH_3**), 31.34 (N^3-**CH_3**), 28.17 (N^1-**CH_3**), 17.38 (CH_2**CH_3**). Carbene carbon missing.

FT-IR analysis: the IR spectrum exhibits a strong PF_6 absorption at 833 cm^{-1} and two absorbing peaks at 3300-3400 cm^{-1} which can be referred to the coordinated ammonia.

ESI-HRMS (m/z): Calcd for $C_{10}H_{18}AgN_5O_2$ $[M+H]^+$: 347.0506. Found: 347.0275.

- **[Ag(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(NH_3)] BPh_4 (4)**

1g (0.0773 g, 0.125 mmol) was suspended in 2 mL ethanol and reacted with Ag_2O (0.0145 g, 0.0626 mmol) followed by aqueous ammonia (98 µL, 16.54 mol/L, 1.62 mmol). The reaction mixture was stirred at room temperature for **4 h** and the product was isolated by the same method as already mentioned. Yield: 0.0615 g (66%).



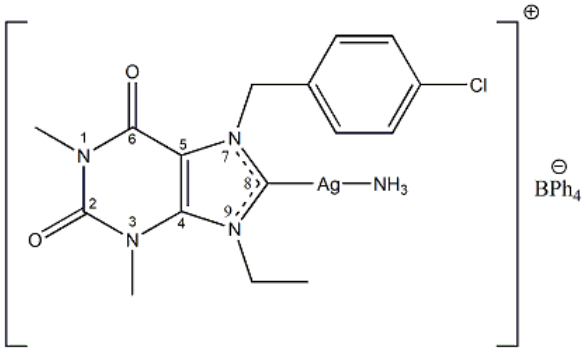
^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] = 7.27-7.37 (m, 5H, -C$_6$H$_5$), 7.14-7.21 (m, 8H, *o*-C$_6$H$_5$, BPh$_4$), 6.92 (t, 8H, *m*-C$_6$H$_5$, BPh$_4$, J_{HH} = 7.2 Hz), 6.79 (t, 4H, *p*-C$_6$H$_5$, BPh$_4$, J_{HH} = 7.2 Hz), 5.71 (s, 2H, N^7-**CH$_2$**), 4.57 (q, 2H, N^9-**CH$_2$**, J_{HH} = 7.1 Hz), 3.70 (s, 3H, N^3-**CH$_3$**), 3.23 (s, 3H, N^1-**CH$_3$**), 3.09 (broad s, Ag-NH$_3$), 1.42 (t, 3H, CH$_2$**CH$_3$**, J_{HH} = 7.1 Hz).

^{13}C-NMR (101 MHz, DMSO-d$_6$): δ [ppm] = 163.30 (q, **C**-B, $J_{C\text{-}B}$ = 49.2 Hz), 152.94 (C^6=O), 150.60 (C^2=O), 140.30 (C^4), 136.62 (ipso-C, -C$_6$H$_5$), 135.46 (d, *o*-C$_6$H$_5$, BPh$_4$, $J_{C\text{-}B}$ = 1.3 Hz), 128.61, 127.91, 127.31 (-C$_6$H$_5$), 125.22 (dd, *m*-C$_6$H$_5$, BPh$_4$, $J_{C\text{-}B}$ = 5.5, 2.7 Hz), 121.44 (p-C$_6$H$_5$, BPh$_4$), 108.27 (C^5), 52.90 (N^7-**CH$_2$**), 46.32 (N^9-**CH$_2$**), 31.38 (N^3-**CH$_3$**), 28.20 (N^1-**CH$_3$**), 17.26 (CH$_2$**CH$_3$**). Carbene carbon missing.

FT-IR analysis: the IR spectrum exhibits two absorption peaks at 3300-3400 cm^{-1} which can be referred to the coordinated ammonia.

- **(7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(NH$_3$)] BPh$_4$ (5)**

2g (0.0815 g, 0.125 mmol) was suspended in 2 mL ethanol and reacted with Ag$_2$O (0.0145 g, 0.0625 mmol), followed by aqueous ammonia (98 µL, 16.54 mol/L, 1.62 mmol). The reaction mixture was stirred at room temperature for **2 h**. Yield: 0.097 g (73%).



^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] = 7.30-7.43 (m, 4H, -C$_6$H$_4$Cl), 7.18 (m, 8H, *o*-C$_6$H$_5$, BPh$_4$), 6.92 (t, 8H, *m*-C$_6$H$_5$, BPh$_4$, J_{HH} = 7.2 Hz), 6.79 (t, 4H, *p*-C$_6$H$_5$, BPh$_4$, J_{HH} = 7.2 Hz), 5.70 (s, 2H, N^7-**CH$_2$**), 4.58 (q, 2H, N^9-**CH$_2$**, J_{HH} = 7.1 Hz), 3.71 (s, 3H, N^3-**CH$_3$**), 3.22 (s, 3H, N^1-**CH$_3$**), 2.92 (broad, Ag-NH$_3$), 1.42 (t, 3H, CH$_2$**CH$_3$**, J_{HH} = 7.1 Hz).

^{13}C-NMR (151 MHz, DMSO-d$_6$): δ [ppm] = 163.33 (q, **C**-B, $J_{C\text{-}B}$ = 49.4 Hz), 152.95 (C^6=O), 150.63 (C^2=O), 140.36 (C^4), 135.50 (m, *o*-C$_6$H$_5$, BPh$_4$), 133.20 (ipso-C, -C$_6$H$_4$Cl), 132.63 (C-Cl), 128.59, 128.29 (-C$_6$H$_4$Cl), 125.25 (dd, *m*-C$_6$H$_5$, BPh$_4$, $J_{C\text{-}B}$ = 5.4, 2.7 Hz), 121.47 (p-C$_6$H$_5$,

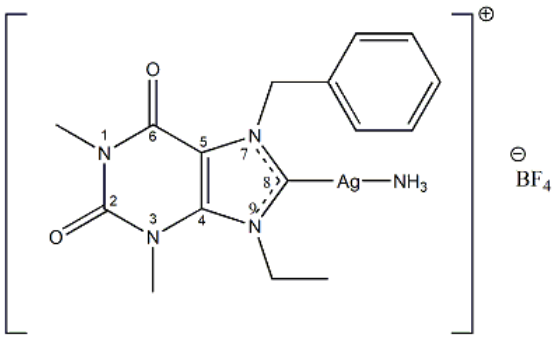
BPh_4), 108.25 (C^5), 52.29 (N^7-**CH_2**), 46.38 (N^9-**CH_2**), 31.42 (N^3-**CH_3**), 28.23 (N^1-**CH_3**), 17.29 (CH_2**CH_3**). Carbene carbon missing.

FT-IR analysis: the IR spectrum exhibits two absorption peaks at 3300-3400 cm^{-1} which can be referred to the coordinated ammonia.

ESI-HRMS (m/z): Calcd for $C_{16}H_{17}AgClN_4O_2$ $[M\text{-}NH_3]^+$: 441.01. Found: 441.0155.

- **[Ag(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(NH_3)] BF_4 (6)**

1h (0.0643 g, 0.166 mmol) was suspended in 2 mL ethanol and reacted with Ag_2O (0.0193 g, 0.0833 mmol) followed by aqueous ammonia (108 µL, 16.54 mol/L, 1.79 mmol) at room temperature for 30 minutes. Yield: 0.0655 g (77%).



^{1}H-NMR (600 MHz, DMSO-d_6): δ [ppm] = 7.25-7.39 (m, 5H, -C_6H_5), 5.71 (s, 2H, N^7-**CH_2**), 4.58 (broad q, 2H, N^9-**CH_2**), 3.71 (s, 3H, N^3-**CH_3**), 3.23 (s, 3H, N^1-**CH_3**), 3.04 (s, 3H, Ag-NH_3), 1.42 (broad t, 3H, CH_2**CH_3**).

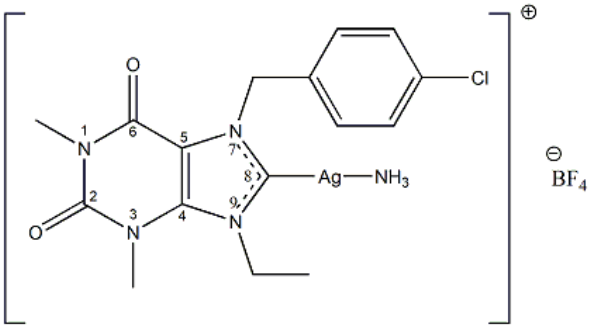
^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 152.94 (C^6=O), 150.60 (C^2=O), 140.29 (C^4), 136.61 (ipso-C, -C_6H_5), 128.61, 127.91, 127.29 (-C_6H_5), 108.27 (C^5), 52.90 (N^7-**CH_2**), 46.33 (N^9-**CH_2**), 31.38 (N^3-**CH_3**), 28.20 (N^1-**CH_3**), 17.27 (CH_2**CH_3**). Carbene carbon missing.

FT-IR analysis: the IR spectrum exhibits two absorption peaks at 3300-3400 cm^{-1} which can be referred to the coordinated ammonia.

ESI-MS (m/z): Calcd for $C_{16}H_{21}AgN_5O_2$ $[M\text{-}NH_3]^+$: 405.05. Found: 405.0522, $[M+H]^+$: 425.0628. Found: 425.07, $[M+Na^+]^+$: 446.07. Found: 446.0787.

- **[Ag(7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(NH_3)] BF_4 (7)**

2h (0.0525 g, 0.125 mmol) was suspended in 2 mL ethanol and reacted with Ag_2O (0.0145 g, 0.0626 mmol) followed by aqueous ammonia (82 µL, 16.54 mol/L, 1.36 mmol) at room temperature for 30 minutes. Yield: 0.0450 g (66%).



^{1}H-NMR (600 MHz, DMSO-d_6): δ [ppm] = 7.35-7.44 (m, 4H, -C_6H_4Cl), 5.70 (s, 2H, N^7-**CH_2**), 4.59 (q, 2H, N^9-**CH_2**, J_{HH} = 7.1 Hz), 3.71 (s, 3H, N^3-**CH_3**), 3.22 (s, 3H, N^1-**CH_3**), 2.99 (s, 3H, Ag-NH_3), 1.43 (t, 3H, CH_2**CH_3**, J_{HH} = 7.1 Hz).

^{13}C-NMR (151 MHz, DMSO-d_6): δ [ppm] = 152.96 (C^6=O), 150.61 (C^2=O), 140.33 (C^4), 136.62 (ipso-C, -C_6H_4Cl), 128.63, 128.57, 127.98 (-C_6H_4Cl), 108.28 (C^5), 52.89 (N^7-**CH_2**), 46.35 (N^9-**CH_2**), 31.39 (N^3-**CH_3**), 28.21 (N^1-**CH_3**), 17.28 (CH_2**CH_3**). Carbene carbon missing.

FT-IR analysis: the IR spectrum exhibits two absorption peaks at 3300-3400 cm^{-1} which can be referred to the coordinated ammonia.

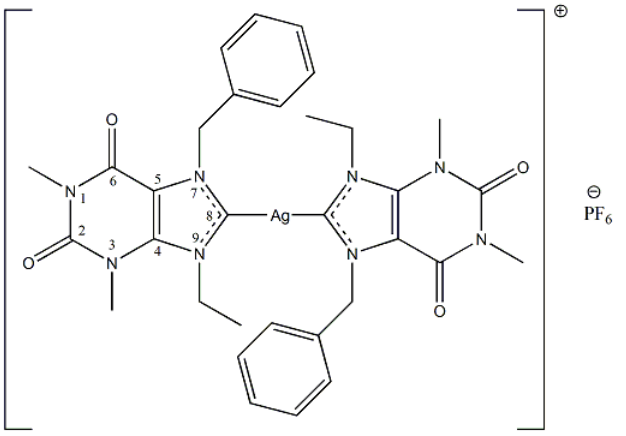
ESI-MS (m/z): Calcd for $C_{16}H_{17}AgClN_4O_2$ $[M\text{-}NH_3]^+$: 441.01 Found: 441.0104, $[M+H]^+$: 459.04. Found: 459.0203, $[M+Na^+]^+$: 482.03. Found: 482.0373.

5.3.2. Synthesis of $[Ag(NHC)_2]$ PF_6 complexes

A suspension of [NHCH]PF_6 (1.0 mmol) in absolute ethanol was reacted with Ag_2O (0.5 mmol) in the presence of diethylamine. The reaction mixture was stirred at room temperature for 4 h. Last, the product was obtained as a white precipitate which was washed with cold ethanol and diethyl ether, respectively, and dried at room temperature [198].

- **[Ag(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)$_2$] PF_6 (8)**

1e (0.0555 g, 0.125 mmol) was suspended in 2 mL absolute ethanol and reacted with Ag_2O (0.0145 g, 0.0626 mmol) followed by aqueous diethylamine (65 µL, 0.627 mmol). Yield: 0.0425 g (80%).



^{1}H-NMR (600 MHz, DMSO-d_6): δ [ppm] = 7.25-7.33 (m, 10H, -C_6H_5), 5.74 (s, 4H, N^7-**CH_2**), 4.56 (q, 4H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 3.73 (s, 6H, N^3-**CH_3**), 3.25 (s, 6H, N^1-**CH_3**), 1.39 (t, 6H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

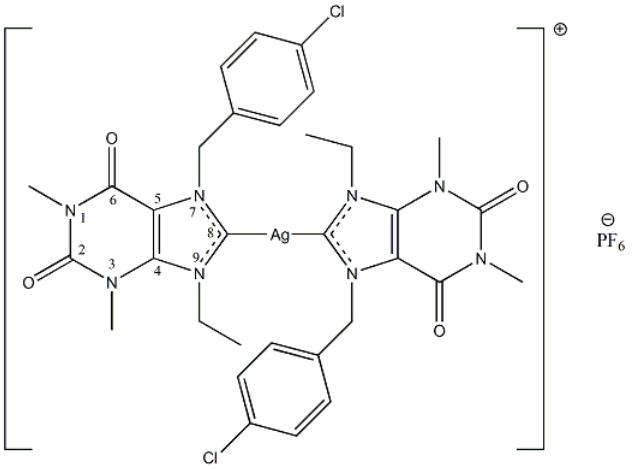
^{13}C-NMR (151 MHz, DMSO-d_6): δ [ppm] = 186.92, 185.56 (d, C^8-Ag, $J_{C\text{-}Ag}$ = 192, 214 Hz), 152.98 (C^6=O), 150.61 (C^2=O), 140.23 (C^4), 136.59 (ipso-C, -C_6H_5), 128.61, 127.88, 127.00 (-C_6H_5), 108.34 (C^5), 52.69 (N^7-**CH_2**), 46.35 (N^9-**CH_2**), 31.38 (N^3-**CH_3**), 28.19 (N^1-**CH_3**), 17.26 (CH_2**CH_3**).

^{31}P-NMR (162 MHz, Acetone-d_6): δ [ppm] = -144.27 (hept, PF_6, $J_{P\text{-}F}$ = 707 Hz).

ESI-HRMS (m/z): Calcd for $C_{32}H_{36}AgN_8O_4$ $[M]^+$: 703.1905. Found: 703.1906.

- **[Ag(7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)$_2$] PF_6 (9)**

2e (0.0598 g, 0.125 mmol) was suspended in 2 mL absolute ethanol and reacted with Ag_2O (0.0145 g, 0.0625 mmol) followed by aqueous diethylamine (65 µL, 0.627 mmol). Yield: 0.0400 g (72%).



^{1}H-NMR (400 MHz, Acetone-d_6): δ [ppm] = 7.30-7.43 (m, 8H, -C_6H_4Cl), 5.83 (s, 4H, N^7-**CH_2**), 4.79 (q, 4H, N^9-**CH_2**, J_{HH} = 7.3 Hz), 3.88 (s, 6H, N^3-**CH_3**), 3.30 (s, 6H, N^1-**CH_3**), 1.60 (t, 6H, CH_2**CH_3**, J_{HH} = 7.3 Hz).

^{13}C-NMR (101 MHz, Acetone-d_6): δ [ppm] = 154.96 (C^6=O), 152.47 (C^2=O), 142.06 (C^4), 137.19 (ipso-C, -C_6H_4Cl), 135.15 (C-Cl), 130.77 (*o*-C_6H_4Cl), 130.41 (*m*-C_6H_4Cl), 110.44 (C^5), 54.25 (N^7-**CH_2**), 48.63 (N^9-**CH_2**), 32.77 (N^3-**CH_3**), 29.36 (N^1-**CH_3**), 18.76 (CH_2**CH_3**).

^{31}P-NMR (162 MHz, Acetone-d_6): δ [ppm] = -144.27 (hept, PF_6, $J_{P\text{-}F}$ = 707 Hz).

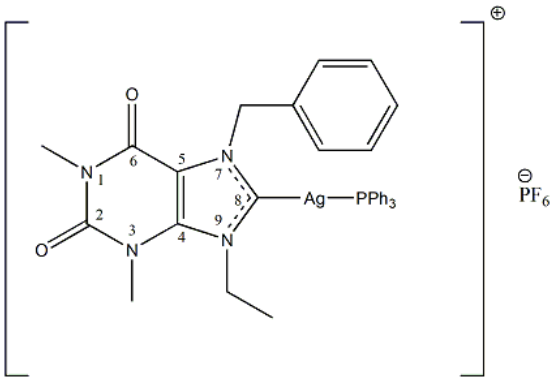
ESI-HRMS (m/z): Calcd for $C_{32}H_{34}AgCl_2N_8O_4$ $[M]^+$: 771.1126. Found: 771.1103.

5.3.3. Synthesis of [Ag(NHC)(Phosphine)] PF_6 complexes

[Ag(NHC)(NH_3)]PF_6 (1.0 mmol) was suspended in absolute ethanol and the reaction mixture was treated in an ultrasound bath for 5 minutes. Then the phosphine (0.95 mmol) was added and the mixture was treated with ultrasounds for a further 10 minutes. Finally, the reaction mixture was stirred at room temperature for 30 min. The product was isolated as a white solid phase which was washed with ethanol and diethyl ether, respectively, and dried at room temperature [198].

- **[Ag(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(PPh_3)] PF_6 (10)**

A suspension of complex **1** (0.05 g, 0.088 mmol) in 2 mL absolute ethanol was reacted with the PPh_3 (0.022 g, 0.084 mmol). Yield: 0.0716 g (57%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 7.45-7.52 (m, 3H, *p*-C_6H_5, PPh_3), 7.39 (m, 5H, -C_6H_5), 7.22-7.33 (m, 12 H, *o*- and *m*-C_6H_5, PPh_3), 5.73 (s, 2H, N^7-**CH_2**), 4.56 (broad q, 2H, N^9-**CH_2**), 3.72 (s, 3H, N^3-**CH_3**), 3.23 (s, 3H, N^1-**CH_3**), 1.37 (broad t, 3H, CH_2**CH_3**).

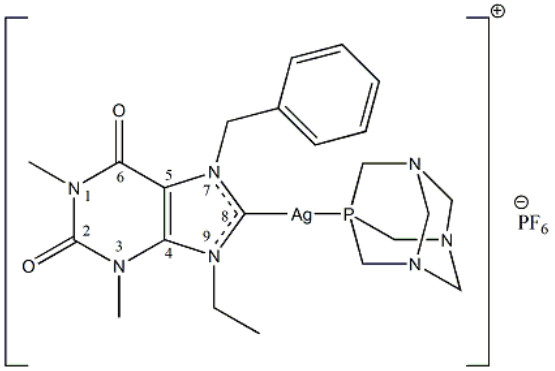
^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 185.20, 187.0 (C^8-Ag), 152.97 (C^6=O), 150.61 (C^2=O), 136.50 (ipso-C, -C_6H_5), 133.30 (d, *m*-C_6H_5, PPh_3, $J^3_{C\text{-}P}$ = 17.0 Hz), 132.44 (P-**C**,-PPh_3), 130.33 (*p*-C_6H_5, PPh_3), 129.00 (d, *o*-C_6H_5, PPh_3, $J^2_{C\text{-}P}$ = 9.0 Hz), 128.60, 127.87, 126.99 (-C_6H_5), 108.20 (C^5), 52.68 (N^7-**CH_2**), 46.72 (N^9-**CH_2**), 31.39 (N^3-**CH_3**), 28.20 (N^1-**CH_3**), 17.27 (CH_2**CH_3**).

^{31}P-NMR (162 MHz, DMSO-d_6): δ [ppm] = 5.81 (s, Ag-PPh_3), -144.18 (hept, PF_6, $J_{P\text{-}F}$ = 711 Hz).

ESI-HRMS (m/z): Calcd for $C_{34}H_{33}AgN_4O_2P$ $[M]^+$: 667.1387. Found: 667.1626.

- **[Ag(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(PTA)] PF_6 (11)**

Complex **1** (0.025 g, 0.0440 mmol) was reacted with PTA (0.0066 g, 0.0420 mmol) in absolute ethanol as the solvent. Yield: 0.0230 g (80%).



^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] = 7.20-7.46 (m, 5H, -C$_6$H$_5$), 5.72 (s, 2H, N^7-**CH$_2$**), 4.56 (d, 5H, 2H (N^9-**CH$_2$**), 3H, PTA (N**CH$_2$**N), J_{HH}= 12.6 Hz), 4.42 (d, 3H, PTA (N**CH$_2$**N), J_{HH}= 12.6 Hz), 4.16 (d, 6H, PTA (P**CH$_2$**N), $J_{P\text{-}H}$ = 3.6 Hz), 3.71 (s, 3H, N^3-**CH$_3$**), 3.23 (s, 3H, N^1-**CH$_3$**), 1.38 (broad t, 3H, CH$_2$**CH$_3$**).

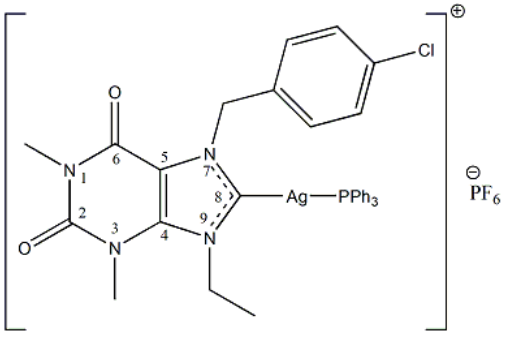
^{13}C-NMR (101 MHz, DMSO-d$_6$): δ [ppm] = 185.10, 187.9 (C^8-Ag), 152.98 (C^6=O), 150.61 (C^2=O), 128.62, 127.89, 127.04 (-C$_6$H$_5$), 72.09 (d, N**CH$_2$**N, PTA, $J^3_{P\text{-}C}$ = 5.90 Hz), 53.05 (N^7-**CH$_2$**), 50.16 (d, P**CH$_2$**N, PTA, $J_{P\text{-}C}$ = 2.20 Hz), 46.68 (N^9-**CH$_2$**), 31.38 (N^3-**CH$_3$**), 28.20 (N^1-**CH$_3$**), 17.27 (CH$_2$**CH$_3$**).

^{31}P-NMR (162 MHz, DMSO-d$_6$): δ [ppm] = -86 (s, Ag-PTA), -144.17 (hept, PF$_6$, $J_{P\text{-}F}$ = 711 Hz).

ESI-HRMS (m/z): Calcd for $C_{22}H_{30}AgN_7O_2P$ $[M]^+$: 562.1244. Found: 562.1265.

- **[Ag(7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(PPh$_3$)] PF$_6$ (12)**

A suspension of complex **2** (0.05 g, 0.083 mmol) in 2 mL absolute ethanol was reacted with PPh$_3$ (0.021 g, 0.079 mmol). Yield: 0.0703 g (67%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 7.49 (dd, 3H, *p*-C_6H_5, PPh_3, J_{HH} = 10.6, 4.1 Hz), 7.40 (dd, 6 H, -C_6H_4Cl and -PPh_3, J_{HH} = 7.5, 6.2 Hz), 7.21-7.36 (m, 10 H, -C_6H_5, PPh_3), 5.72 (s, 2H, N^7-**CH_2**), 4.58 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 3.72 (s, 3H, N^3-**CH_3**), 3.22 (s, 3H, N^1-**CH_3**), 1.39 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

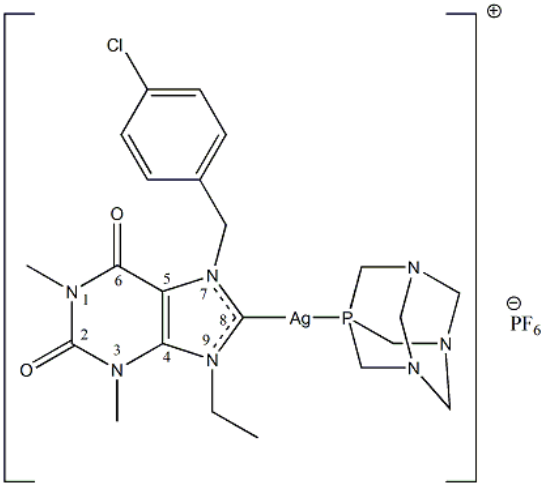
^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 183.27, 182.02 (C^8-Ag), 152.93 (C^6=O), 150.61 (C^2=O), 135.58 (ipso-**C**, -C_6H_4Cl), 133.32 (d, *m*-C_6H_5, PPh_3, $J^3_{C\text{-}P}$ = 16.7 Hz), 132.12 (P-**C**, -PPh_3), 131.93 (C-Cl), 130.45 (*p*-C_6H_5, PPh_3), 129.02 (d, *o*-C_6H_5, PPh_3, $J^2_{C\text{-}P}$ = 9.2 Hz), 128.76, 128.51 (-C_6H_4Cl), 111.33 (C^5), 52.09 (N^7-**CH_2**), 46.07 (N^9-**CH_2**), 31.40 (N^3-**CH_3**), 28.19 (N^1-**CH_3**), 17.26 (CH_2**CH_3**).

^{31}P-NMR (162 MHz, DMSO-d_6): δ [ppm] = 6.86 (s, Ag-PPh_3), -144.18 (hept, PF_6, $J_{P\text{-}F}$ = 711 Hz).

ESI-HRMS (m/z): Calcd for $C_{34}H_{32}AgClN_4O_2P$ $[M]^+$: 701.0997. Found: 701.1158.

- **[Ag(7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(PTA)] PF_6 (13)**

complex **2** (0.03 g, 0.050 mmol) was reacted with PTA (0.0074 g, 0.047 mmol) in absolute ethanol as the solvent. Yield: 0.037 g (69%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 7.22-7.40 (m, 4H, -C_6H_4Cl), 5.70 (s, 2H, N^7-**CH_2**), 4.56 (d, 5H, 2H of N^9-**CH_2**, 3H, PTA (N**CH_2**N), J_{HH} = 12.6 Hz), 4.43 (d, 3H, PTA (N**CH_2**N), $J_{H\text{-}H}$= 12.6 Hz), 4.18 (d, 6H, PTA (P**CH_2**N), $J^2_{P\text{-}H}$ = 3.5 Hz), 3.72 (s, 3H, N^3-**CH_3**), 3.22 (s, 3H, N^1-**CH_3**), 1.40 (t, 3H, CH_2**CH_3**, J_{HH}= 7.1 Hz).

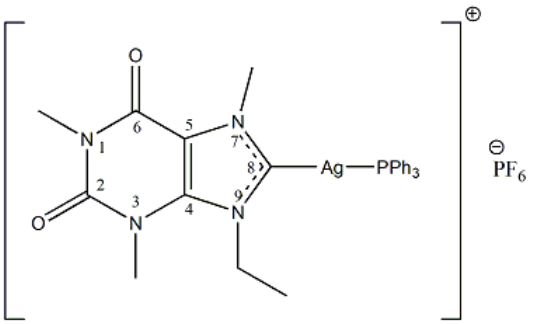
^{13}C-NMR (101 MHz, DMSO-d$_6$): δ [ppm] = 152.94 (C^6=O), 150.61 (C^2=O), 132.58 (C-Cl), 128.54 (-C$_6$H$_4$Cl), 93.56 (C^5), 72.08 (d, N**CH$_2$**N, PTA, $J^3_{P\text{-}C}$ = 5.90 Hz), 52.07 (N^7-**CH$_2$**), 50.03 (d, P**CH$_2$**N, PTA, $J_{P\text{-}C}$ = 3.20 Hz), 45.45 (N^9-**CH$_2$**), 31.39 (N^3-**CH$_3$**), 28.19 (N^1-**CH$_3$**), 17.27 (CH$_2$**CH$_3$**). Carbene carbon missing.

^{31}P-NMR (162 MHz, DMSO-d$_6$): δ [ppm] = -85.88 (s, Ag-PTA), -144.15 (hept, PF$_6$, $J_{P\text{-}F}$ = 711 Hz).

ESI-HRMS (m/z): Calcd for $C_{22}H_{29}AgClN_7O_2P$ $[M]^+$: 596.0854. Found: 596.1285.

- **[Ag(1,3,7-trimethyl-9-ethylxanthine-8-ylidene)(PPh$_3$)] PF$_6$ (14)**

A suspension of complex **3** (0.0433 g, 0.088 mmol) in 5 mL absolute ethanol was reacted with PPh$_3$ (0.022 g, 0.083 mmol). Yield: 0.0515 g (79%).



^{1}H-NMR (400 MHz, DMSO-d$_6$): δ [ppm] = 7.43-7.50 (m, 3H, *p*-C$_6$H$_5$, PPh$_3$), 7.37 (t, 6H, *m*-C$_6$H$_5$, PPh$_3$, J_{HH} = 6.8 Hz), 7.25 (t, 6H, *o*-C$_6$H$_5$, PPh$_3$, J_{HH} = 8.5 Hz), 4.63 (broad q, 2H, N^9-**CH$_2$**), 4.11 (s, 3H, N^7-**CH$_3$**), 3.73 (s, 3H, N^3-**CH$_3$**), 3.27 (s, 3H, N^1-**CH$_3$**), 1.49 (broad t, 3H, CH$_2$**CH$_3$**).

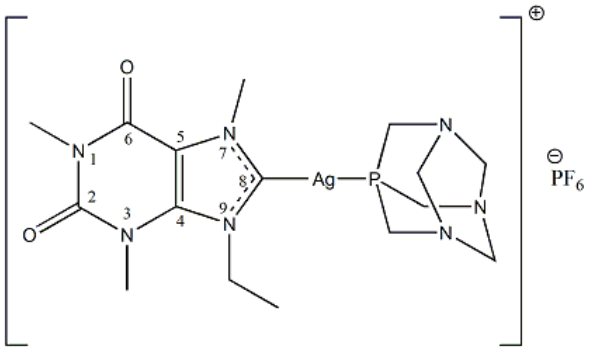
^{13}C-NMR (101 MHz, DMSO-d$_6$): δ [ppm] = 153.22 (C^6=O), 150.68 (C^2=O), 133.25 (d, *m*-C$_6$H$_5$, PPh$_3$, $J^3_{C\text{-}P}$ = 17.2 Hz), 130.11 (*p*-C$_6$H$_5$, PPh$_3$), 129.94 (d, *o*-C$_6$H$_5$, PPh$_3$, $J^2_{C\text{-}P}$ = 8.6 Hz), 46.04 (N^7-**CH$_3$**), 37.96 (N^9-**CH$_2$**), 31.35 (N^3-**CH$_3$**), 28.17 (N^1-**CH$_3$**), 17.42 (CH$_2$**CH$_3$**). Carbene carbon missing.

^{31}P-NMR (162 MHz, DMSO-d$_6$): δ [ppm] = 3.96 (s, Ag-PPh$_3$), -144.16 (hept, PF$_6$, $J_{P\text{-}F}$ = 711 Hz).

ESI-HRMS (m/z): Calcd for $C_{28}H_{29}AgN_4O_2P$ $[M]^+$: 591.1074. Found: 591.1365.

- **[Ag(1,3,7-trimethyl-9-ethylxanthine-8-ylidene)(PTA)] PF_6 (15)**

Complex **15** was synthesized from a reaction between complex **3** (0.0216 g, 0.0440 mmol) and PTA (0.0066 g, 0.0420 mmol). Yield: 0.0185 g (67%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ [ppm] = 4.60-4.65 (m, 1H, PTA (N**CH$_2$**N)), 4.57 (d, 3H, PTA (N**CH$_2$**N), J_{HH} = 12.8 Hz), 4.43 (d, 3H, PTA (N**CH$_2$**N), J_{HH} = 12.8 Hz), 4.18 (d, 5H, PTA (P**CH$_2$**N), $J_{P\text{-}H}$ = 3.8 Hz), 4.12-4.08 (broad s, 2H, N^9-**CH$_2$**), 3.73 (s, 3H, N^7-**CH$_3$**), 3.29 (s, 3H, N^3-**CH$_3$**), 3.26 (s, 3H, N^1-**CH$_3$**), 1.47 (broad t, 3H, CH$_2$**CH$_3$**, J_{HH}= 6.2 Hz).

^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 153.26 (C^6=O), 150.78 (C^2=O), 139.87 (C^4), 108.91 (C^5), 72.11 (d, N**CH$_2$**N, PTA, $J^3_{P\text{-}C}$ = 5.90 Hz), 50.10 (d, P**CH$_2$**N, PTA, $J_{P\text{-}C}$ = 2.0 Hz), 45.99 (N^7-**CH$_2$**), 37.95 (N^9-**CH$_2$**), 31.35 (N^3-**CH$_3$**), 28.16 (N^1-**CH$_3$**), 17.41 (CH$_2$**CH$_3$**). Carbene carbon missing.
^{31}P-NMR (162 MHz, DMSO-d_6): δ [ppm] = -86.20 (s, Ag-PTA), -144.19 (hept, PF_6, $J_{P\text{-}F}$ = 711 Hz).

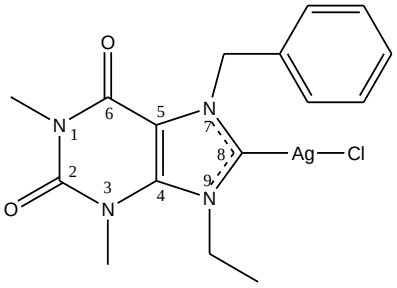
ESI-HRMS (m/z): Calcd for $C_{16}H_{26}AgN_7O_2P$ $[M]^+$: 486.0931. Found: 486.1167.

5.3.4. Synthesis of (NHC)AgCl complexes

[NHCH]Cl (1.0 mmol) was dissolved in an indicated amount of CH_2Cl_2 or acetone as the solvent and reacted with Ag_2O (0.50 mmol) at room temperature for 4 h. Next, the reaction mixture was filtered through celite and the filtrate was concentrated to 3 mL by rotary evaporator. Finally, the excess amount of diethyl ether was added to precipitate the product as a white solid phase. It was filtered and washed with diethyl ether and dried at room temperature [201-203].

- **(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)AgCl (16)**

1f (0.05 g, 0.149 mmol) was reacted with Ag_2O (0.0174 g, 0.0751 mmol) in 7.5 mL CH_2Cl_2. Yield: 0.0445 g (67%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ[ppm] = 7.26-7.39 (m, 5H, -C_6H_5), 5.70 (s, 2H, N^7-**CH_2**), 4.58 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 3.71 (s, 3H, N^3-**CH_3**), 3.23 (s, 3H, N^1-**CH_3**), 1.44 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

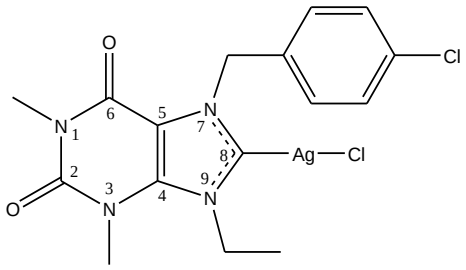
^{13}C-NMR (101 MHz, DMSO-d_6): δ[ppm] = 185.77 (C^8-Ag), 152.96 (C^6=O), 150.59 (C^2=O), 140.23 (C^4), 136.55 (ipso-C, -C_6H_5), 128.59, 127.92, 127.39 (-C_6H_5), 108.15 (C^5), 52.88 (N^7-**CH_2**), 46.40 (N^9-**CH_2**), 31.38 (N^3-**CH_3**), 28.19 (N^1-**CH_3**), 17.25 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{16}H_{18}AgClN_4NaO_2$ $[M+Na]^+$: 463.0061. Found: 463.0077.

Anal. Calcd for $C_{16}H_{18}AgClN_4O_2$: C, 43.51; N, 12.69; H, 4.11. Found: C, 43.36; N, 12.35; H, 3.95.

- **(7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)AgCl (17)**

2f (0.0554 g, 0.140 mmol) was reacted with Ag_2O (0.0174 g, 0.0751 mmol) in 7.5 mL CH_2Cl_2. Yield: 0.0475 g (66%).



^{1}H-NMR (400 MHz, Acetone-d_6): δ[ppm] = 7.51-7.58 (m, 2H, *m*-C_6H_4Cl), 7.34-7.36 (m, 2H, *o*-C_6H_4Cl), 5.81 (s, 2H, N^7-**CH_2**), 4.78 (q, 2H, N^9-**CH_2**,

J_{HH} = 7.2 Hz), 3.89 (s, 3H, N^3-**CH_3**), 3.31 (s, 3H, N^1-**CH_3**), 1.59 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

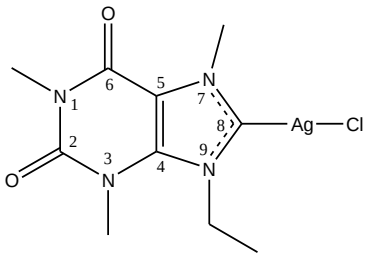
^{13}C-NMR (101 MHz, Acetone-d_6): δ[ppm] = 187.60 (C^8-Ag), 154.87 (C^6=O), 152.35 (C^2=O), 142.24 (C^4), 137.22 (ipso-C, -C_6H_4Cl), 135.10 (C-Cl), 131.48, 130.23 (-C_6H_4Cl), 110.12 (C^5), 54.39 (N^7-**CH_2**), 48.48 (N^9-**CH_2**), 32.78 (N^3-**CH_3**), 29.36 (N^1-**CH_3**), 18.61 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{16}H_{17}AgCl_2N_4NaO_2$ $[M+Na]^+$: 496.9672. Found: 496.9661.

Anal. Calcd for $C_{16}H_{18}AgCl_2F_6N_4O_2P$: C, 40.36; N, 11.77; H, 3.60. Found: C, 39.88; N, 11.47; H, 3.41.

- **(1,3,7-trimethyl-9-ethylxanthine-8-ylidene)AgCl (18)**

Based on the same method, compound **3f** (0.0387 g, 0.150 mmol) was reacted with Ag_2O (0.0174 g, 0.0751 mmol) in 4 mL CH_2Cl_2. Yield: 0.0285 g (52%).



^{1}H-NMR (400 MHz, DMSO-d_6): δ[ppm] = 4.56 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 4.04 (s, 3H, N^7-**CH_3**), 3.70 (s, 3H, N^3-**CH_3**), 3.24 (s, 3H, N^1-**CH_3**), 1.44 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, DMSO-d_6): δ [ppm] = 185.25 (C^8-Ag), 153.18 (C^6=O), 150.66 (C^2=O), 139.77 (C^4), 108.79 (C^5), 46.09 (N^7-**CH_3**), 37.99 (N^9-**CH_2**), 31.33 (N^3-**CH_3**), 28.14 (N^1-**CH_3**), 17.30 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{10}H_{15}N_4O_2$ $[M-AgCl]^+$: 223.1190. Found: 223.1218.

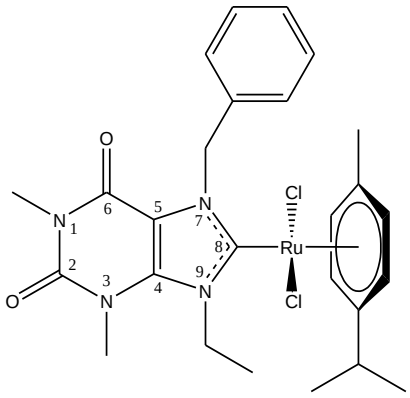
5.4. Transmetallation reactions

5.4.1. Synthesis of [$RuCl_2$(NHC)(p-cymene)]

This group of Ru-complexes was synthesized by following a transmetallation reaction from the silver complex, by the reaction between [Ag(NHC)Cl] (1.0 mmol) and [$RuCl_2$(p-cymene)]$_2$ (0.5 mmol) in CH_2Cl_2 at room temperature for 24 h. Finally, the resulting orange-brown solution was filtered through celite and the solvent was removed under vacuum to obtain the product as an orange-brown precipitate which was washed with diethyl ether and dried at room temperature [202,203].

- **(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(p-cymene)$RuCl_2$ (19)**

complex **16** (0.0438 g, 0.099 mmol) was treated with [$RuCl_2$(p-cymene)]$_2$ (0.0294 g, 0.048 mmol) in 6 mL CH_2Cl_2. Yield: 0.0431 g (72%).



^{1}H-NMR (400 MHz, $CDCl_3$, 223K): δ [ppm] = 7.30-7.48 (m, 3H, -C_6H_5), 6.89 (m, 2H, *o*-C_6H_5), 6.31 (d, 1H, N^7-**CH_2**, J_{HH} = 17 Hz), 5.96 (d, 1H, N^7-**CH_2**, J_{HH} = 17 Hz), 5.51, 5.27, 5.19 (broad m, 4H, *p*-CH_3C_6**H_4**$CH(CH_3)_2$), 5.42 (broad q, 1H, N^9-**CH_2**), 4.44 (broad q, 1H, N^9-**CH_2**), 3.78 (s, 3H, N^3-**CH_3**), 3.29 (s, 3H, N^1-**CH_3**), 2.74 (broad s, 1H, *p*-$CH_3C_6H_4$**CH**$(CH_3)_2$), 2.04 (s, 3H, *p*-**CH_3**$C_6H_4CH(CH_3)_2$), 1.52 (m, 3H, -CH_2**CH_3**), 1.30 (d, 3H, *p*-$CH_3C_6H_4CH$**$(CH_3)_2$**, J_{HH} = 4.9 Hz), 1.19 (d, 3H, *p*-$CH_3C_6H_4CH$**$(CH_3)_2$**, J_{HH} = 6.3 Hz).

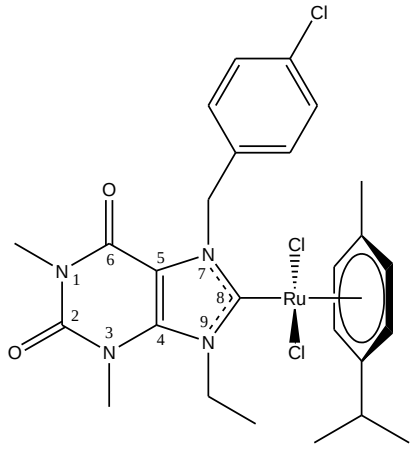
^{13}C-NMR (101 MHz, $CDCl_3$, 223K): δ [ppm] = 189.37 (C^8-Ru), 151.52 (C^6=O), 150.87 (C^2=O), 140.88 (C^4), 138.58 (ipso-C, -C_6H_5), 129.19, 127.38, 123.50 (-C_6H_5), 111.12 (C^5), 107.77 ($(CH_3)_2$CH-**C**, *p*-CH_3**C_6H_4**$CH(CH_3)_2$), 94.64 (CH_3-**C**, *p*-CH_3**C_6H_4**$CH(CH_3)_2$), 86.37, 86.12, 83.42, 82.78 (*p*-CH_3**C_6H_4**$CH(CH_3)_2$), 53.69 (N^7-**CH_2**), 47.18 (N^9-**CH_2**),

32.57 (N^3-**CH_3**), 30.48 (*p*-$CH_3C_6H_4$**CH**$(CH_3)_2$), 28.67 (N^1-**CH_3**), 22.57, 22.32 (*p*-$CH_3C_6H_4CH$**$(CH_3)_2$**), 18.01 (*p*-**CH_3**$C_6H_4CH(CH_3)_2$), 17.70 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{26}H_{32}ClN_4O_2Ru$ $[M\text{-}Cl]^+$: 569.1255. Found: 569.1257.

- **(7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)(p-cymene)$RuCl_2$(20)**

complex **17** (0.0471 g, 0.107 mmol) was reacted with $[RuCl_2(p\text{-cymene})]_2$ (0.0294, 0.048 mmol) in 6 mL CH_2Cl_2. Yield: 0.0495 g (76%).

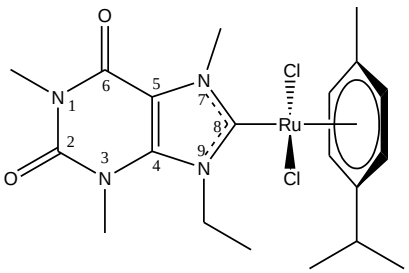


^{1}H-NMR (400 MHz, $CDCl_3$, 223K): δ [ppm] = 7.35-7.44 (d, 2H, *o*-C_6H_4Cl, J_{HH} = 7.5 Hz), 6.86 (m, 2H, *m*-C_6H_4Cl), 6.30 (d, 1H, N^7-**CH_2**, J_{HH} = 17.2 Hz), 5.87 (d, 1H, N^7-**CH_2**, J_{HH} = 17.2 Hz), 5.51, 5.30, 5.25 (broad m, 4H, *p*-CH_3C_6**H_4**$CH(CH_3)_2$), 5.42 (broad q, 1H, N^9-**CH_2**), 4.45 (broad q, 1H, N^9-**CH_2**), 3.78 (s, 3H, N^3-**CH_3**), 3.29 (s, 3H, N^1-**CH_3**), 2.76 (broad s, 1H, *p*-$CH_3C_6H_4$**CH**$(CH_3)_2$), 2.05 (s, 3H, *p*-**CH_3**$C_6H_4CH(CH_3)_2$), 1.52 (m, 3H, -CH_2**CH_3**), 1.30 (d, 3H, *p*-$CH_3C_6H_4CH$**$(CH_3)_2$**, J_{HH} = 4.3 Hz), 1.22 (d, 3H, *p*-$CH_3C_6H_4CH$**$(CH_3)_2$**, J_{HH} = 5.7 Hz).
^{13}C-NMR (101 MHz, $CDCl_3$, 223K): δ [ppm] = 189.52 (C^8-Ru), 151.48 (C^6=O), 150.78 (C^2=O), 140.97 (C^4), 137.18 (ipso-C, -C_6H_4Cl), 132.82, 129.38, 125.03 (-C_6H_4Cl), 110.90 (C^5), 108.04 ($(CH_3)_2CH$-**C**, *p*-CH_3**C_6H_4**$CH(CH_3)_2$), 94.68 (CH_3-**C**, *p*-CH_3**C_6H_4**$CH(CH_3)_2$), 86.37, 86.06, 83.26, 83.04 (*p*-CH_3**C_6H_4**$CH(CH_3)_2$), 53.41 (N^7-**CH_2**), 47.23 (N^9-**CH_2**), 32.55 (N^3-**CH_3**), 30.58 (*p*-$CH_3C_6H_4$**CH**$(CH_3)_2$), 28.69 (N^1-**CH_3**), 22.46 (*p*-$CH_3C_6H_4CH$**$(CH_3)_2$**), 18.09 (*p*-**CH_3**$C_6H_4CH(CH_3)_2$), 17.76 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{26}H_{31}Cl_2N_4O_2Ru$ $[M\text{-}Cl]^+$: 603.0863. Found: 603.0874.

- **(1,3,7-trimethyl-9-ethylxanthine-8-ylidene)(p-cymene)$RuCl_2$ (21)**

complex **18** (0.0362 g, 0.099 mmol) was reacted with $[RuCl_2(p\text{-cymene})]_2$ (0.0294, 0.048 mmol) in 6 mL CH_2Cl_2. Yield: 0.0420 g (80%).



^{1}H-NMR (600 MHz, $CDCl_3$): δ [ppm] = 5.47-5.66 (broad d, 2H, *p*-CH_3C_6**H_4**$CH(CH_3)_2$)), 5.26 (d, 2H, *p*-CH_3C_6**H_4**$CH(CH_3)_2$, J_{HH} = 6.1 Hz), 4.50-4.67 (broad s, 2H, N^9-**CH_2**), 4.36 (s, 3H, N^7-**CH_3**), 3.77 (s, 3H, N^3-**CH_3**), 3.42 (s, 3H, N^1-**CH_3**), 3.02 (m, 1H, *p*-$CH_3C_6H_4$**CH**$(CH_3)_2$, 2.18 (s, 3H, *p*-**CH_3**$C_6H_4CH(CH_3)_2$), 1.41 (t, 3H, -CH_2**CH_3**, J_{HH} = 7.3 Hz), 1.35 (d, 6H, *p*-$CH_3C_6H_4$CH**$(CH_3)_2$**, J_{HH} = 6.9 Hz).

^{13}C-NMR (151 MHz, $CDCl_3$): δ [ppm] = 186.12 (C^8-Ru), 152.80 (C^6=O), 151.17 (C^2=O), 140.76 (C^4), 111.85 (C^5), 109.36 ($(CH_3)_2$CH-**C**, *p*-CH_3**C_6H_4**$CH(CH_3)_2$), 99.08 (CH_3-**C**, *p*-CH_3**C_6H_4**$CH(CH_3)_2$), 86.22, 83.03, 81.27, 80.52 (*p*-CH_3**C_6H_4**$CH(CH_3)_2$), 46.70 (N^9-**CH_2**), 39.66 (N^7-**CH_3**), 32.51 (N^3-**CH_3**), 30.89 (*p*-$CH_3C_6H_4$**CH**$(CH_3)_2$), 28.58 (N^1-**CH_3**), 23.23, 22.11 (*p*-$CH_3C_6H_4CH$**$(CH_3)_2$**), 18.93 (*p*-**CH_3**$C_6H_4CH(CH_3)_2$), 17.36 (CH_2**CH_3**).

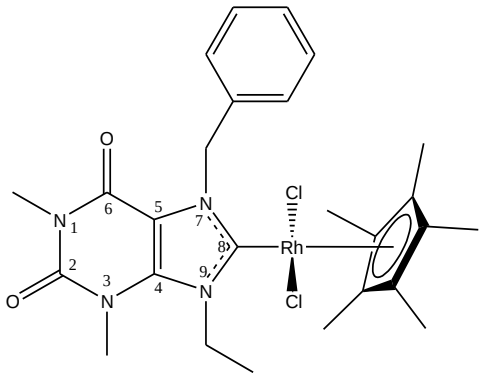
ESI-HRMS (m/z): Calcd for $C_{20}H_{28}ClN_4O_2Ru$ $[M\text{-}Cl]^+$: 493.0941. Found: 493.0947.

5.4.2. Synthesis of $[RhCl_2(NHC)(Cp^*)]$

A mixture of [Ag(NHC)Cl] (1.0 mmol) and $[Cp^*RhCl_2]_2$ (0.5 mmol) in CH_2Cl_2 as the solvent was stirred at room temperature for 24 h. The resulting red-brown solution was filtered through celite and the solvent was removed under vacuum and the product was obtained as an orange-brown precipitate. Last, the product was washed with diethyl ether and dried at room temperature [206,207].

- **Cp*Rh(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)Cl_2 (22)**

complex **16** (0.0177 g, 0.0400 mmol) was reacted with $[Cp^*RhCl_2]_2$ (0.0124, 0.0200 mmol) in 3 mL CH_2Cl_2. Yield: 0.0130 g (53%).



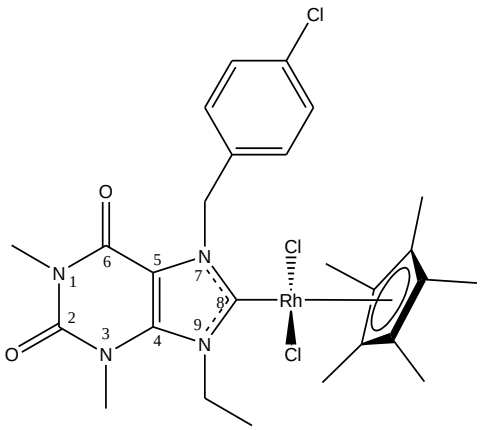
^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.26-7.32 (m, 2H, *m*-C_6H_5), 7.23 (t, 1H, *p*-C_6H_5, J_{HH} = 7.3 Hz), 6.89 (m, 2H, *o*-C_6H_5), 6.39 (d, 1H, N^7-**CH_2**, J_{HH} = 16.5 Hz), 5.98 (d, 1H, N^7-**CH_2**, J_{HH} = 16.5 Hz), 5.25, 4.73 (broad s, 2H, N^9-**CH_2**), 3.79 (s, 3H, N^3-**CH_3**), 3.24 (s, 3H, N^1-**CH_3**), 1.54 (s, 15H, Cp*), 1.49 (t, 3H, CH_2**CH_3**, J_{HH} = 7.3 Hz).

^{13}C-NMR (151 MHz, $CDCl_3$): δ [ppm] = 183.71 (d, C^8-Rh, $J_{C\text{-}Rh}$ = 54.5 Hz), 151.73 (C^6=O), 151.27 (C^2=O), 141.13 (C^4), 138.58 (ipso-C, -C_6H_5), 128.56, 127.12, 124.67 (-C_6H_5), 111.72 (C^5), 97.21 (d, **C**-CH_3, Cp*, $J_{Rh\text{-}C}$ = 7.2 Hz), 54.78 (N^7-**CH_2**), 47.10 (N^9-**CH_2**), 32.50 (N^3-**CH_3**), 28.60 (N^1-**CH_3**), 17.66 (CH_2**CH_3**), 9.49 (-C**CH_3**, Cp*).

ESI-HRMS (m/z): Calcd for $C_{26}H_{33}Cl_2N_4NaO_2Rh$ $[M+Na]^+$: 629.0928. Found: 629.0930.

- **Cp*Rh(7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)Cl_2 (23)**

complex **17** (0.0190 g, 0.0399 mmol) was reacted with $[Cp^*RhCl_2]_2$ (0.0124 g, 0.0200 mmol) in 3 mL CH_2Cl_2. Yield: 0.0140 g (55%).



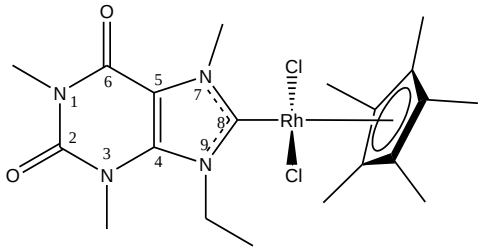
^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.24-7.28 (m, 2H, *o*-C_6H_4Cl), 6.92 (d, 2H, *m*-C_6H_4Cl, J_{HH} =7.8 Hz), 6.21, 6.05 (broad s, 2H, N^7-**CH_2**), 5,19, 4.84 (broad s, 2H, N^9-**CH_2**), 3.79 (s, 3H, N^3-**CH_3**), 3.25 (s, 3H, N^1-**CH_3**), 1.56 (s, 15H, Cp*), 1.49 (t, 3H,CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, $CDCl_3$): δ [ppm] = 183.60 (d, C^8-Rh, $J_{C\text{-}Rh}$ = 53.3 Hz), 151.76 (C^6=O), 151.20 (C^2=O), 141.34 (C^4), 136.90 (ipso-C, -C_6H_4Cl), 132.93 (C-Cl), 128.65, 126.64 (-C_6H_4Cl), 111.52 (C^5), 97.24 (d, **C**-CH_3, Cp*, $J_{Rh\text{-}C}$ = 7.1 Hz), 54.35 (N^7-**CH_2**), 47.00 (N^9-**CH_2**), 32.51 (N^3-**CH_3**), 28.64 (N^1-**CH_3**), 17.77 (CH_2**CH_3**), 9.52 (-C**CH_3**, Cp*).

ESI-HRMS (m/z): Calcd for $C_{26}H_{32}Cl_2N_4O_2Rh$ $[M\text{-}Cl]^+$: 605.0952. Found: 605.0957.

- **Cp* Rh(1,3,7-trimethyl-9-ethylxanthine-8-ylidene)Cl_2 (24)**

Complex **18** (0.0322 g, 0.0881 mmol) was reacted with $[Cp^*RhCl_2]_2$ (0.0248, 0.0400 mmol) in 6 mL CH_2Cl_2. Yield: 0.0355 g (76%).



^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 4.73-5.09 (broad d, 2H, N^9-**CH_2**), 4.33 (s, 3H, N^7-**CH_3**), 3.75 (s, 3H, N^3-**CH_3**), 3.39 (s, 3H, N^1-**CH_3**), 1.66 (s, 15H, Cp*), 1.39 (t, 3H,CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (151 MHz, $CDCl_3$): δ [ppm] = 152.94 (C^6=O), 151.20 (C^2=O), 140.92 (C^4), 112.06 (C^5), 96.98 (d, **C**-CH_3, Cp*, $J_{Rh\text{-}C}$ = 7.0 Hz), 46.41 (N^7-**CH_3**), 39.14 (N^9-**CH_2**), 32.54 (N^3-**CH_3**), 28.61 (N^1-**CH_3**), 17.55 (CH_2**CH_3**), 9.55 (-C**CH_3**, Cp*). Carbene carbon missing.

ESI-HRMS (m/z): Calcd for $C_{20}H_{29}N_4O_2Rh$ $[M\text{-}2Cl]^+$: 459.1300. Found: 459.1330.

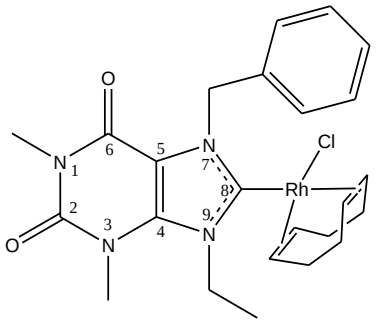
5.4.3. Synthesis of [RhCl(NHC)(cod)]

[Ag(NHC)Cl] (1.0 mmol) was reacted with $[RhCl(cod)]_2$ (0.45-0.5 Equiv.) in CH_2Cl_2 at room temperature for 24 h. The final yellow solution was filtered through celite and the solvent was removed under vacuum.

The product was obtained as a yellow precipitate which was washed with diethyl ether and dried at room temperature [210,211,132].

- **(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)Rh(cod)Cl (25)**

Complex **16** (0.0352 g, 0.0797 mmol) was reacted with $[RhCl(cod)]_2$ (0.0196 g, 0.0397 mmol) in 3 mL CH_2Cl_2. Yield: 0.0210 g (48%).



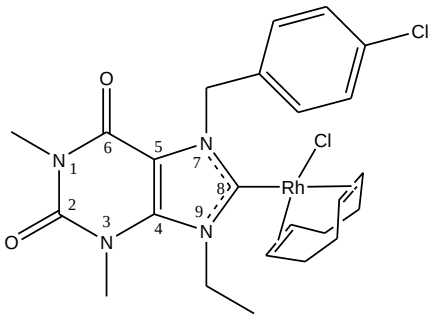
^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.44 (d, 2H, *o*-C_6H_5, J_{HH} = 7.3 Hz), 7.33 (t, 2H, *m*-C_6H_5, J_{HH} = 7.3 Hz), 7.23-7.29 (m, 1H, *p*-C_6H_5), 6.25, 6.10 (d, 2H, N^7-**CH_2**, J_{HH} = 14.8 Hz), 5.42-5.53 (m, 1H, N^9-**CH_2**), 5.16-5.23 (m, 1H, **CH**-cod), 5.07-5.15 (m, 1H, **CH**-cod), 4.99-5.07 (m, 1H, N^9-**CH_2**), 3.78 (s, 3H, N^3-**CH_3**), 3.31 (m, 3H, N^1-**CH_3**, 1H, **CH**-cod), 3.03 (m, 1H, **CH**-cod), 2.25-2.52 (m, 3H, **CH_2**-cod), 2.83-1.10 (m, 4H, **CH_2**-cod), 1.71- 1.76 (m, 1H, **CH_2**-cod), 1.69 (t, 3H,CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, $CDCl_3$): δ [ppm] = 193.49 (C^8-Rh), 152.14 (C^6=O), 150.81 (C^2=O), 140.08 (C^4), 136.92 (ipso-C, -C_6H_5), 128.50, 127.66, 127.32 (-C_6H_5), 109.00 (C^5), 100.89, 100.12 (d, **CH**, cod, J_{Rh-C} = 6.8 Hz), 69.84, 69.67 (d, **CH**, cod, J_{Rh-C} = 14.3 Hz), 53.71 (N^7-**CH_2**), 46.33 (N^9-**CH_2**), 33.53 (**CH_2**, cod), 31.89 (N^3-**CH_3**), 31.59, 28.55, 28.11 (**CH_2**, cod), 29.25 (N^1-**CH_3**), 17.67 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{24}H_{30}N_4O_2Rh$ $[M-Cl]^+$: 509.1418. Found: 509.1409.

- **(7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)Rh(cod)Cl (26)**

Complex **17** (0.0635 g, 0.1334 mmol) was reacted with $[RhCl(cod)]_2$ (0.0329 g, 0.0604 mmol) in 3 mL CH_2Cl_2. Yield: 0.0520 g (72%).



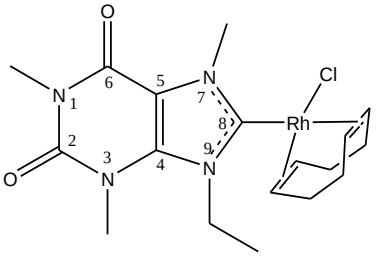
^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.47 (d, 2H, *o*-C_6H_4Cl, J_{HH} = 8.4 Hz), 7.29 (m, 2H, *m*-C_6H_4Cl), 6.26, 5.99 (d, 2H, N^7-**CH_2**, J_{HH} = 14.7 Hz), 5.44 (m, 1H, N^9-**CH_2**), 5.10-5.23 (m, 2H, **CH**-cod), 5.06 (m, 1H, N^9-**CH_2**), 3.78 (s, 3H, N^3-**CH_3**), 3.30 (m, 3H, N^1-**CH_3**, 1H, **CH**-cod), 3.08 (m, 1H, **CH**-cod), 2.28-2.52 (m, 3H, **CH_2**-cod), 2.16 (m, 1H, **CH_2**-cod), 1.75-2.08 (m, 4H, **CH_2**-cod), 1.69 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, $CDCl_3$): δ [ppm] = 193.28 (d, C^8-Rh, $J_{Rh\text{-}C}$ = 52.9 Hz), 152.12 (C^6=O), 150.74 (C^2=O), 140.23 (C^4), 135.15 (ipso-C, -C_6H_4Cl), 133.66 (C-Cl), 129.13, 128.65 (-C_6H_4Cl), 109.94 (C^5), 101.08, 100.54 (d, **CH**, cod, $J_{Rh\text{-}C}$ = 6.7 Hz), 69.86, 69.66 (d, **CH**, cod, $J_{Rh\text{-}C}$ = 13.8 Hz), 53.19 (N^7-**CH_2**), 46.35 (N^9-**CH_2**), 33.41, 33.06 (**CH_2**, cod), 31.58 (N^3-**CH_3**), 29.22 (**CH_2**, cod), 28.55 (N^1-**CH_3**), 28.19 (**CH_2**, cod), 16.89 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{24}H_{29}ClN_4O_2Rh$ $[M\text{-}Cl]^+$: 543.10. Found: 543.1097.

- **(1,3,7-trimethyl-9-ethylxanthine-8-ylidene)Rh(cod)Cl (27)**

Complex **18** (0.0291 g, 0.0796 mmol) was created with $[RhCl(cod)]_2$ (0.0196 g, 0.0360 mmol) in 3 mL CH_2Cl_2. Yield: 0.0370 g (99%).



^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 5.40-5.31 (m, 1H, N^9-**CH_2**), 5.09 (dd, 2H, **CH**, cod, J_{HH} = 21.0, 5.3 Hz), 4.90 (dq, 1H, N^9-**CH_2**, J_{HH} = 14.2, 7.0 Hz), 4.39 (s, 3H, N^7-**CH_3**), 3.76 (s, 3H, N^3-**CH_3**), 3.48-3.39 (m, 2H,

CH, cod), 3.35 (s, 3H, N^1-**CH_3**), 2.53-2.37 (m, 4H, **CH_2**, cod), 2.01 (d, 4H, **CH_2**, cod, J_{HH} = 9.5 Hz), 1.61 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (151 MHz, $CDCl_3$): δ [ppm] = 191.11 (C^8-Rh), 152.81 (C^6=O), 150.79 (C^2=O), 139.61 (C^4), 110.51 (C^5), 100.59, 100.30 (d, **CH**, cod, J_{Rh-C} = 6.2, 6.3 Hz), 69.62, 68.88 (broad s, **CH**, cod), 46.04 (N^9-**CH_2**), 37.42 (N^7-**CH_3**), 32.79 (**CH_2**, cod, J_{Rh-C} = 5.6 Hz), 31.48 (N^3-**CH_3**), 28.81 (N^1-**CH_3**), 28.72, 28.45, 28.00 (**CH_2**, cod), 16.93 (CH_2**CH_3**). Two signals at 78.66 and 30.87 ppm are assigned to the remains of $[RhCl(cod)]_2$.

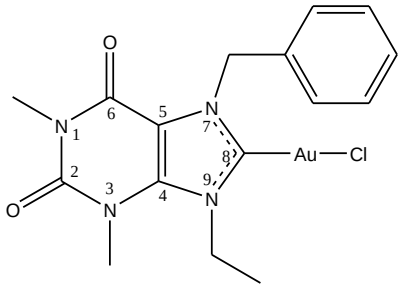
ESI-HRMS (m/z): Calcd for $C_{18}H_{25}N_4O_2Rh$ $[M-Cl]^+$: 433.11. Found: 433.1149.

5.4.4. Synthesis of [Au(NHC)Cl]

[Ag(NHC)Cl] (1.0 mmol) was reacted with [Au(tht)Cl] (1.0 mmol) in CH_2Cl_2 at room temperature for 4 h. The resulting solution was filtered through celite and the solvent was removed under vacuum. The product was obtained as a white precipitate which was washed with diethyl ether and dried at room temperature [202,203,215].

- **(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)AuCl (28)**

Complex **16** (0.0442 g, 0.100 mmol) was reacted with [Au(tht)Cl] (0.0320 g, 0.0998 mmol) in 5 mL CH_2Cl_2. Yield: 0.0340 g (64%).



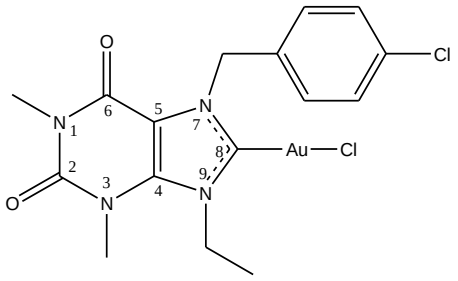
^{1}H-NMR (600 MHz, $CDCl_3$): δ [ppm] = 7.62 (d, 2H, *o*-C_6H_5, J_{HH} = 6.7 Hz), 7.27-7.36 (m, 3H, m-C_6H_5, p-C_6H_5), 5.78 (s, 2H, N^7-**CH_2**), 4.70 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 3.79 (s, 3H, N^3-**CH_3**), 3.38 (s, 3H, N^1-**CH_3**), 1.58 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (151 MHz, $CDCl_3$): δ [ppm] = 176.79 (C^8-Au), 152.93 (C^6=O), 150.63 (C^2=O), 139.33 (C^4), 134.87 (ipso-C, -C_6H_5), 128.84, 128.73, 128.59 (-C_6H_5), 108.16 (C^5), 53.68 (N^7-**CH_2**), 46.71 (N^9-**CH_2**), 31.68 (N^3-**CH_3**), 28.84 (N^1-**CH_3**), 17.33 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{16}H_{18}AuClN_4NaO_2$ $[M+Na]^+$: 553.0676. Found: 553.0792.

- **(7-p-chlorobenzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)AuCl (29)**

Complex **17** (0.0476 g, 0.100 mmol) was reacted with [Au(tht)Cl] (0.0320 g, 0.0998 mmol) in 5 mL CH_2Cl_2. Yield: 0.0420 g (74%).



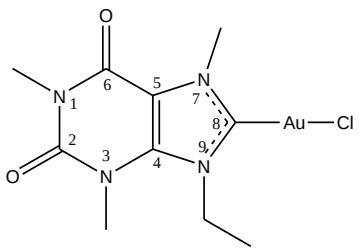
^{1}H-NMR (600 MHz, $CDCl_3$): δ [ppm] = 7.58 (d, 2H, *o*-C_6H_4Cl, J_{HH} = 8.4 Hz), 7.28-7.31 (m, 2H, *m*-C_6H_4Cl), 5.74 (s, 2H, N^7-**CH_2**), 4.69 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 3.79 (s, 3H, N^3-**CH_3**), 3.38 (s, 3H, N^1-**CH_3**), 1.58 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (151 MHz, $CDCl_3$): δ [ppm] = 176.79 (C^8-Au), 152.96 (C^6=O), 150.57 (C^2=O), 139.40 (C^4), 134.78 (ipso-C, -C_6H_4Cl), 133.29 (C-Cl), 130.10, 129.04 (-C_6H_4Cl), 108.04 (C^5), 52.96 (N^7-**CH_2**), 46.77 (N^9-**CH_2**), 31.70 (N^3-**CH_3**), 28.86 (N^1-**CH_3**), 17.33 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{16}H_{17}AuCl_2N_4NaO_2$ $[M+Na]^+$: 587.0286. Found: 587.0291.

- **(1,3,7-trimethyl-9-ethylxanthine-8-ylidene)AuCl (30)**

Complex **18** (0.0365 g, 0.0988 mmol) was reacted with [Au(tht)Cl] (0.0320 g, 0.0998 mmol) in 5 mL CH_2Cl_2. Yield: 0.0295 g (55%).



^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 4.71 (q, 2H, N^9-**CH_2**, J_{HH} = 7.2 Hz), 4.17 (s, 3H, N^7-**CH_3**), 3.83 (s, 3H, N^3-**CH_3**), 3.43 (s, 3H, N^1-**CH_3**), 1.60 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, $CDCl_3$): δ [ppm] = 177.33 (C^8-Au), 153.28 (C^6=O), 150.71 (C^2=O), 113.18 (C^5), 46.47 (N^7-**CH_3**), 37.98 (N^9-**CH_2**), 31.65 (N^3-**CH_3**), 28.76 (N^1-**CH_3**), 17.36 (CH_2**CH_3**).

ESI-HRMS (m/z): Calcd for $C_{10}H_{14}AuClN_4NaO_2$ $[M+Na]^+$: 477.0363. Found: 477.0366.

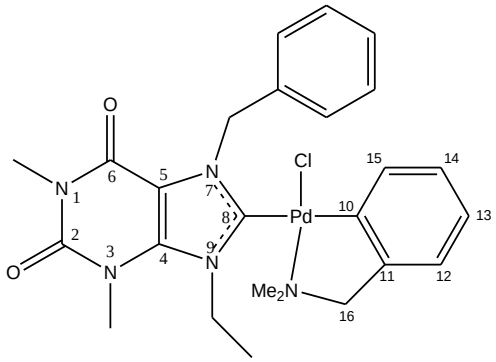
5.5. Synthesis of Pd-Complexes

5.5.1. Synthesis of [(NHC)Pd(dmba)Cl]

- **(7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)Pd(dmba)Cl (31)**

As the last part of this work, the preparation of Pd(II)-NHC complexes with the general formula of [(NHC)Pd(dmba)Cl] was evaluated. In this regard, (7-benzyl-9-ethyl-1,3-dimethylxanthine-8-ylidene)Pd(dmba)Cl (**31**), as the first example of the Pd(II)-NHC complexes, was synthesized using the synthesis procedure as follows:

On the first attempt, complex **31** was synthesized via a one-pot reaction. Based on this synthetic procedure, a two-necked flask was charged with $PdCl_2$ (0.0161g, 0.091 mmol), CH_3CN (370 µL; HPLC grade), and dmba (14 µL, 0.0942 mmol). One of the necks was equipped with a reflux condenser and the other was close with a glass stopper. The mixture was refluxed at 100 °C for 30 minutes until a clear, yellow solution was formed and $PdCl_2$ was completely dissolved. Then K_2CO_3 (0.0314 g, 0.227 mmol) was added to the reaction mixture, and the mixture was stirred for 5-10 minutes until the solution changed color to bright canary yellow. Next, compound **1f** (0.0320 g, 0.0956 mmol) was added in one portion, and the reaction continued for a further 1 h. Last, after cooling to room temperature, the reaction mixture was diluted with CH_2Cl_2 and filtered through celite, and the solvent was removed under vacuum to obtain the final product as a light yellow precipitate, Yield: 0.0347 g (63%) [219].



^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.70-7.75 (m, 2H, -C_6H_5), 7.18-7.28 (m, 3H, -C_6H_5), 7.02 (d, 1H, C^{12}**H**, J_{HH} = 6.4 Hz), 6.96 (td, 1H, -C^{13}**H**, J_{HH} = 7.3, 1.1 Hz), 6.70 (td, 1H, -C^{14}**H**, J_{HH} = 7.4, 1.1 Hz), 6.03 (dt, 2H, N^{7}-**CH_2**, -C^{15}**H**, J_{HH} = 12.8, 6.4 Hz), 5.87 (d, 1H, N^{7}-**CH_2**, J_{HH} = 14.3 Hz), 5.35 (dq, 1H, N^{9}-**CH_2**, J_{HH} = 14.6, 7.3 Hz), 4.87 (dq, 1H, N^{9}-**CH_2**, J_{HH} = 14.5, 7.2 Hz), 4.03, 3.87 (d, 2H, -C^{16}**H_2**, J_{HH} = 14.0, 14.1 Hz), 3.83 (s, 3H, N^{3}-**CH_3**), 3.39 (s, 3H, N^{1}-**CH_3**), 2.86 (d, 6H, -N**$(CH_3)_2$**, J_{HH} = 5.2 Hz), 1.65 (t, 3H, CH_2**CH_3**, J_{HH} = 7.3 Hz).

^{13}C-NMR (101 MHz, $CDCl_3$): δ [ppm] = 182.74 (C^{8}-Pd), 152.59 (C^{6}=O), 150.75 (C^{2}=O), 148.52, 148.12 (C^{10}, C^{11}), 139.88 (C^{4}), 135.72 (C^{15}), 129.01, 128.25, 127.94 (-C_6H_5), 125.77 (C^{13}), 124.17 (C^{14}), 122.37 (C^{12}), 109.52 (C^{5}), 72.36 (C^{16}), 54.23 (N^{7}-**CH_2**), 50.75, 50.21 (-N**$(CH_3)_2$**), 46.52 (N^{9}-**CH_2**), 31.63 (N^{3}-**CH_3**), 28.67 (N^{1}-**CH_3**), 16.54 (CH_2**CH_3**).

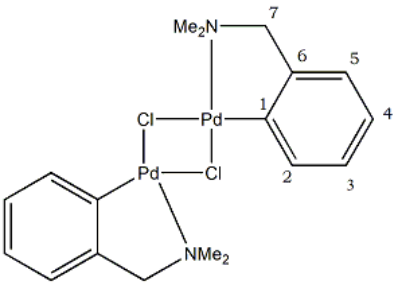
ESI-HRMS (m/z): Calcd for $C_{25}H_{30}ClN_5NaO_2Pd$ $[M+Na]^+$: 596.1022. Found: 596.1034.

In another attempt, complex **31** was synthesized using a multi-step reaction. First, the Pd(II) dimer -$[Pd(dmba)Cl]_2$- was synthesized and in the next step, it was reacted with [7-benzyl-9-ethyl-1,3-dimethylxanthinium] Cl (**1f**) in the presence of K_2CO_3 as a base to obtain the corresponding Pd(II)-NHC complex. More details are available as mentioned below.

- **Synthesis of $[Pd(dmba)Cl]_2$ dimer**

A mixture of $PdCl_2$ (0.0161 g, 0.091 mmol) and dmba (14 µL, 0.0942 mmol) in CH_3CN (185 µL; HPLC grade) was refluxed at 100 °C for 30 minutes until $PdCl_2$ was completely dissolved and a yellow, clear solution was obtained. Next, the solvent was evaporated in a vacuum to get the final product as a yellow fine precipitate which was washed

with diethyl ether and dried at room temperature, Yield: 0.01 g (40%) [219].

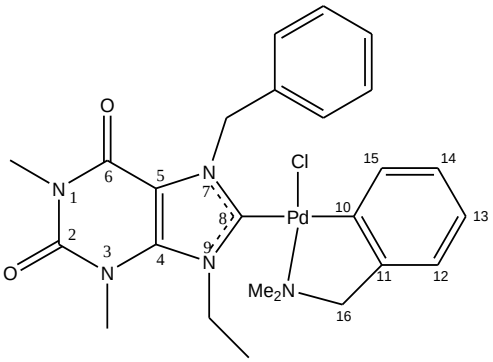


^{1}H-NMR (600 MHz, $CDCl_3$): δ [ppm] = 7.14-7.24 (dd, 1H, -C^{4}**H**, *J*= 27.6, 8.0 Hz), 7.00 (t, 1H, -C^{5}**H**, J_{HH} = 7.0 Hz), 6.90 (t, -C^{2}**H**, -C^{3}**H**, J_{HH} = 6.7 Hz), 3.96 (2H, -C^{7}**H$_2$**), 2.90, 2.87 (6H, -N**(CH$_3$)$_2$**).

^{13}C-NMR (151 MHz, $CDCl_3$): δ [ppm] = 146.93, 146.81 (C^{6}), 143.07, 142.94 (C^{1}), 133.47, 132.95 (C^{4}), 125.19, 121.49 (d, 2H, C^{2}, C^{3}, *J*= 8.2, 3.6 Hz), 124.73 (C^{5}), 73.35, 73.20 (-C^{7}**H$_2$**), 52.89, 52.61 (-N**(CH$_3$)$_2$**).

- **Synthesis of [(NHC)Pd(dmba)Cl] (31)**

In the second step, a mixture of compound **1f** (10 mg, 0.0299 mmol) and the synthesized $[Pd(dmba)Cl]_2$ (8.3 mg, 0.0150 mmol) was refluxed in the presence of K_2CO_3 (9.8 mg, 0.0710 mmol) at 100 °C for 1 h. Next, after cooling to room temperature, the reaction mixture was diluted with CH_2Cl_2 and filtered through celite, and the solvent was removed under vacuum to obtain the final product as a light yellow precipitate, Yield: 0.0110 g (64%) [219].



^{1}H-NMR (400 MHz, $CDCl_3$): δ [ppm] = 7.73 (d, 2H, -C_6H_5, J_{HH} = 6.7 Hz), 7.27-7.18 (m, 3H, -C_6H_5), 7.02 (d, 1H, C^{12}**H**, J_{HH} = 6.7 Hz), 6.96 (t, 1H, -C^{13}**H**, J_{HH} = 7.3), 6.70 (t, 1H, -C^{14}**H**, J_{HH} = 6.9 Hz), 6.04 (m, 2H,

N^7-**CH_2**, -C^{15}**H**), 5.87 (d, 1H, N^7-**CH_2**, J_{HH} = 14.3 Hz), 5.35 (dq, 1H, N^9-**CH_2**, J_{HH} = 14.6, 7.6 Hz), 4.87 (dq, 1H, N^9-**CH_2**, J_{HH} = 14.5, 7.2 Hz), 4.04, 3.87 (d, 2H, -C^{16}**H_2**, J_{HH} = 14.1 Hz), 3.83 (s, 3H, N^3-**CH_3**), 3.40 (s, 3H, N^1-**CH_3**), 2.86 (d, 6H, -N**$(CH_3)_2$**, J_{HH} = 5.1 Hz), 1.65 (t, 3H, CH_2**CH_3**, J_{HH} = 7.2 Hz).

^{13}C-NMR (101 MHz, $CDCl_3$): δ [ppm] = 182.76 (C^8-Pd), 152.61 (C^6=O), 150.77 (C^2=O), 148.53, 148.13 (C^{10}, C^{11}), 139.89 (C^4), 135.74 (C^{15}), 129.02, 128.26, 127.96 (-C_6H_5), 125.78 (C^{13}), 124.18 (C^{14}), 122.39 (C^{12}), 109.54 (C^5), 72.38 (C^{16}), 54.24 (N^7-**CH_2**), 50.76, 50.22 (-N**$(CH_3)_2$**), 46.53 (N^9-**CH_2**), 31.64 (N^3-**CH_3**), 28.68 (N^1-CH_3), 16.55 (CH_2**CH_3**).

References:

1. *"Carbenes: Synthesis, properties, and organometallic chemistry".* P. de Frémont, N. Marion, S. P. Nolan, Coord. Chem. Rev., 253 (2009), 862-892.

2. *"Ueber das zweiwerthige Kohlenstoffatom. (Vierte Abhandlung.) Die Chemie des Methylens".* J. U. Nef, Justus Liebig's Annalen Der Chemie, 298 (1897), 202-374.

3. *"An instance of trivalent carbon: triphenylmethyl".* M. Gomberg, J. Am. Chem. Soc., 22 (1900), 757-771.

4. *"Versuche zur Darstellung von Methylenderivaten".* H. Staudinger, O. Kupfer, Ber. Dtsch. Chem. Ges., 44 (1911), 2194-2197.

5. *"Über Reaktionen des Methylens. III. Diazomethan".* H. Staudinger, O. Kupfer, Ber. Dtsch. Chem. Ges., 45 (1912), 501-509.

6. *"The Interpretation of Band Spectra Part III. Electron Quantum Numbers and States of Molecules and Their Atoms".* R. S. Mulliken, Rev. Mod. Phys., 4 (1932), 1-86.

7. "*Molecular spectra and molecular –structure, spectra of diatomic molecules".* G. Herzberg, and K. P. Huber, D. van Nostrand Co., 1950.

8. *"Carbene Chemistry".* W. Kimse, New York & London: Academic Press, 1964.

9. *"A survey of the principles determining the structure and properties of molecules, part 1.—the factors responsible for molecular shape and bond energies".* J. Lennard-Jones, J. A. Pople, Discus. Faraday. Soc., 10 (1951), 9-18.

10. *"466. The electronic orbitals, shapes, and spectra of polyatomic molecules. Part I. AH2 molecules".* A. D. Walsh, J. Chem. Soc., (1953), 2260-2266.

11. *"Ground and Excited Electronic States and Molecular Vibrations of Some Polyatomic Molecules".* J. Duchesne, L. Burnelle, J. Chem. Phys., 21 (1953) 2005-2008.

12. *"A Study of Hindered Divalent Carbon Species and Diazo Compounds".* H. E. Zimmerman, D. H. Paskovich, J. Am. Chem. Soc., 86 (1964), 2149-2160.

13. *"Trimethylene and the addition of methylene to ethylene".* R. Hoffmann, J. Am. Chem. Soc., 6 (1968), 1475-1485.

14. *"The electronic structure of methylenes".* R. Hoffmann, G. D. Zeiss, G. W. Van Dine, J. Am. Chem. Soc., 90 (1968), 1485–1499.

15. *"Stabilizing a singlet methylene".* R. Hoffmann, R. Gleiter, J. Am. Chem. Soc., 90 (1968), 5457-5460.

16. *"Structure and energetics of simple carbenes methylene, fluoromethylene, chloromethylene, bromomethylene, difluoromethylene, and dichloromethylene".* C. W. Bauschlider, H. F. Schaefer III, P. S. Bagus, J. Am. Chem. Soc., 99 (1977), 7106-7110.

17. *"Multiplicity of the ground state and magnitude of the T1-S0 gap in substituted carbenes".* N. C. Baird, K. F. Taylor, J. Am. Chem. Soc., 100 (1978), 1333-1338.

18. *"A theoretical determination of the electron affinity of methylene".* D. Feller, L. E. McMurchie, W. T. Borden, E. R. Davidson, J. Chem. Phys., 77 (1982), 6134-6143.

19. *"Comprehensive theoretical study of isomers and rearrangement barriers of even-electron polyatomic molecules HmABHn (A, B = carbon, nitrogen, oxygen, and fluorine)".* J. A. Pople, K. Raghavachari, M. J. Frisch, et al., J. Am. Chem. Soc., 105 (1983), 6389-6399.

20. *"The potential surface and stretching frequencies of X̃3 B1 methylene (CH_2)determined from an experiment using the Morse oscillator rigid bender internal dynamics Hamiltonian".* P. Jensen, P. R. Bunker. J. Chem. Phys., 89 (1988), 1327-1332.

21. *"N-Heterocyclic Carbenes in Catalysis—An Introduction".* F. Glorius, Top Organomet Chem., 21 (2007), 1-20.

22. *"A stable crystalline carbene".* A. J. Arduengo III, R. L. Harlow, and M. Kline, J. Am. Chem. Soc., 113 (1991), 361-363.

23. *"Advances in the Knowledge of N-Heterocyclic Carbenes Properties. The Backing of the Electrochemical Investigation".* M. Feroci, I. Chiarotto, and A. Inesi, Catalysts, 6 (2016), 178-200.

24. *"Stable Singlet Carbenes—Plentiful and Versatile".* W. Kirmse, Angew Chem Int Ed, 43 (2004), 1767-1769.

25. *"Stable Carbenes".* D. Bourissou, O. Guerret, F. P. Gabbai, G. Bertrand, Chem Rev., 100 (2000), 39-92.

26. *"Heterocyclic Carbenes".* F. E. Hahn, Angew Chem Int Ed., 45 (2006), 1348-1352.

27. *"N-heterocyclic carbene complexes of palladium and rhodium: cis/trans-isomers".* W. A. Herrmann, J. Fischer, K. Öfele, G. R. J. Artus, J. Organomet., 530 (1997), 259-262.

28. *"Nickel(II) Complexes of N-Heterocyclic Carbenes".* W. A. Herrmann, G. Gerstberger, M. Spiegler, Organometallics, 16 (1997), 2209-2212.

29. *"Functionalized imidazoline-2-ylidene complexes of rhodium and palladium"*. W. A. Herrmann, L. J. Gooßen, M. Spiegler, J. Organomet. Chem., 547 (1997), 357-366.

30. *"Convenient syntheses of novel ruthenium catalysts bearing N-heterocyclic carbenes"*. W. Baratta, W. A. Herrmann, P. Rigo, J. Schwarz, J. Organomet., 593-594 (2000), 489-493.

31. *"New Ruthenium(II) Complexes Bearing N-Heterocyclic Carbenes"*. W. Baratta, E. Herdtweck, W. A. Herrmann, et al., Organometallics, 21 (2002), 2101-2106.

32. *"NHC ligands versus cyclopentadienyls and phosphines as spectator ligands in organometallic catalysis"*. R. H. Crabtree, J Organomet Chem., 690 (2005), 5451-5457.

33. *"Computed Ligand Electronic Parameters from Quantum Chemistry and Their Relation to Tolman Parameters, Lever Parameters, and Hammett Constants"*. L. Perrin, E. Clot, O. Eisenstein, et al., Inorg Chem., 40 (2001), 5806-5811.

34. *"N-Heterocyclic Carbene Functionalized Iridium Phsophinidene Complex Cp*(NHC)Ir=PMes*. Comparison of Phosphinidene, Imido, and Carbene Complexes"*. A. T. Termaten, M. Schakel, A. W. Ehlers., Chem., 9 (2003), 3577-3582.

35. *"Density Functional Study of N-Heterocyclic and Diamino Carbene Complexes: Comparison with Phosphines"*. M. T. Lee, C. H. Hu, Organometallics., 23 (2004), 976-983.

36. *"Dioxygen Activation by a Low-Valent Cobalt Complex Employing a Flexible Tripodal N-Heterocyclic Carbene Ligand"*. X. L. Hu, I. Castro-Rodriguez, K. Meyer, J. Am. Chem. Soc., 126 (2004), 13464-13473.

37. *"Steric and electronic effects in the bonding of N-heterocyclic ligands to transition metals"*. L. Cavallo, A. Correa, C. Costabile, H. Jacobsen, J Organomet Chem., 690 (2005), 5407-5413.

38. *"Stability and Reactivity of N-Heterocyclic Carbene Complexes"*. C. M. Crudden, D. P. Allen, Coord. Chem. Rev., 248 (2004), 2247-2273.

39. *"Stereoelectronic Parameters Associated with N-Heterocyclic Carbene (NHC) Ligands: A quest for Understanding"*. S. Díez-Gonzalez, S. P. Nolan, Coord. Chem. Rev., 251 (2007), 874-883.

40. *"Understanding the M-(NHC) (NHC = N-Heterocyclic Carbene)"*. H. Jacobsen, A. Correa, A. Poater, et al., Bond. Coord. Chem. Rev., 253 (2009), 687-703.

41. *"Quantifying and Understanding the Electronic Properties of N-Heterocyclic Carbenes"*. D. J. Nelson, S. P. Nolan, Chem. Soc. Rev., 42 (2013), 6723-6753.

42. *"Ag(I) N-Heterocyclic Carbene Complexes: Synthesis, Structure, and Application"*. J. C. Garrison, W. J. Youngs, Chem. Rev., 105 (2005), 3978-4008.

43. *"Preparation and application of N-heterocyclic carbene complexes of Ag(I)"*. I. J. B. Lin, C. S. Vasam, Coord. Chem. Rev., 251 (2007), 642-670.

44. *"Cytotoxicity and biodistribution studies of luminescent Au(I) and Ag(I) N-heterocyclic carbenes. Searching for new biological targets"*. R. Visbal, V. Fernández-Moreira, I. Marzo, et al., Dalton Trans, 45 (2016), 15026-15033.

45. *"Silver(I)-N-heterocyclic carbene complexes of nitrile-functionalized imidazole-2-ylidene ligands as anticancer agents"*. R. A. Haque, S. Budagumpi, H. Z. Zulikha, et al., Inorg. Chem. Commun., 44 (2014), 128-133.

46. *"Metallkomplexe mit N-heterocyclischen Carbenliganden: Entwicklungsmöglichkeiten für metallhaltige Krebsmedikamente"*. F. Cisnetti, A. Gautier, Angew. Chem., 125 (2013), 12194-12196.

47. *"Enhanced cytotoxicity of silver complexes bearing bidentate N-heterocyclic carbene ligands"*. D. C. F. Monteiro, R. M. Phillips, B. D. Crossley, et al., Dalto Trans, 41 (2012), 3720-3725.

48. *"Metal N-heterocyclic carbene complexes as potential antitumor metallodrugs"*. R. Gust, W. Liu, Chem. Soc. Rev., 42 (2012), 755-773.

49. *"Silver-catalyzed carboxylation"*. T. Yamada, K. Sekine, Chem. Soc. Rev., 45 (2016), 4524-4532.

50. *"Silver-catalysed reactions of alkynes: recent advances"*. G. Fang, X. Bi, Chem. Soc. Rev., 44 (2015), 8124-8173.

51. *"Cooperative dual palladium/silver catalyst for direct difluoromethylation of aryl bromides and iodides"*. Y. Gu, X. Leng, Q. Shen, Nature Commun., 5 (2014), 1-7.

52. *"Silver-Catalyzed Csp−H and Csp−Si Bond Transformations and Related Processes"*. Y. Yamamoto, Chem. Rev., 108 (2008), 3199-3222.

53. *"Expedient syntheses of the N-heterocyclic carbene precursor imidazolium salts IPr·HCl, IMes·HCl, and IXy·HCl"*. L. Hintermann, Beilstein J. Org. Chem., 3 (2007),

54. *"An Efficient Synthesis of Achiral and Chiral 1,2,4-Triazolium Salts: Bench Stable Precursors for N-Heterocyclic Carbenes"*. M. S. Kerr, J. R. de Alaniz, T. Rovis, J. Org. Chem., 70 (2005), 5725-5728.

55. *"Palladium(II) Pyrazolin-4-ylidenes: Remote N-Heterocyclic Carbene Complexes and Their Catalytic Application in Aqueous Suzuki-Miyaura*

Coupling". Y. Han, H. V. Huynh, and G. K. Tan, Organometallics., 26 (2007), 6581-6585.

56. *"Syntheses, Characterizations, and a Preliminary Comparative Cytotoxicity Study of Gold(I) and Gold(III) Complexes Bearing Benzimidazole- and Pyrazole-Derived N-Heterocyclic Carbenes"*. H. Sivaram, J. Tan, and H. V. Huynh, Organometallics., 31 (2012), 5875-5883.

57. *"Formation and Stability of N-Heterocyclic Carbenes in Water: The Carbon Acid pKa of Imidazolium Cations in Aqueous Solution"*. T. L. Amyes, S. T. Diver, J. P. Richard, et al., J. Am. Chem. Soc., 126 (2004), 4366-4374.

58. *"Proton Affinities of N-Heterocyclic Carbene Super Bases"*. H. Chen, D. R. Justes, and R. G. Cooks, Org. Lett., 7 (2005), 3949-3952.

59. *"Nickel-Catalyzed Cross-Coupling of Aryl Chlorides with Aryl Grignard Reagents"*. V. P. W. Böhm, T. Weskamp, C. W. K. Gstöttmayr, W. A. Herrmann, Angew. Chem. Int. Ed., 39 (2000), 1602-1604.

60. *"Triaryl phosphine-functionalized N-heterocyclic carbene ligands for Heck reaction"*. A. E. Wang, J. H. Xie, L. X. Wang, Q. L. Zhou, Tetrahedron., 61 (2005), 259-266.

61. *"Optically Active Iridium Imidazole-2-ylidene-oxazoline Complexes: Preparation and Use in Asymmetric Hydrogenation of Arylalkenes"*. M. C. Perry, X. Cui, M. T. Powell, et al., J. Am. Chem. Soc., 125 (2003), 113-123.

62. *"Direct Coupling of Oxazolines and N-Heterocyclic Carbenes: A Modular Approach to a New Class of C−N Donor Ligands for Homogeneous Catalysis"*. V. César, S. Bellemin-Laponnaz, L. H. Gade, Organometallics., 21 (2002), 5204-5208.

63. *"Palladium Complexes with Tridentate Pincer Bis-Carbene Ligands as Efficient Catalysts for C−C Coupling"*. J. A. Loch, M. Albrecht, E. Peris, et al., Organometallics., 21 (2002), 700-706.

64. *"Highly Efficient Heck Reactions of Aryl Bromides with n-Butyl Acrylate Mediated by a Palladium/Phosphine−Imidazolium Salt System"*. C. Yang, H. M. Lee, S. P. Nolan, Org. Lett., 3 (2001), 1511-1514.

65. *"Dicationic chelating N-heterocyclic carbene complexes of palladium: new catalysts for the copolymerization of C_2H_4 and CO"*. M. G. Gardiner, W. A. Herrmann, C. P. Reisinger, et al., J. Organomet. Chem., 572 (1999), 239-247.

66. *"Chiral Oxazoline/Imidazoline-2-ylidene Complexes"*. W. A. Herrmann, L. J. Gooßen, M. Spiegler, Organometallics., 17 (1998), 2162-2168.

67. *"Caffeine analogs: biomedical impact"*. J. W. Daly, Cell. Mol. Life Sci., 64 (2007), 2153-2169.

68. *"Reactions of 8, 9-Dihydroxanthines with Acetylenic Compounds. Formation of Heteropropellanes".* M. Hori, T. Kataoka, H. Shimizu, et al., Chem. Pharm. Bull., 33 (1985), 3681-3688.

69. *"Synthesis from Caffeine of a Mixed N-Heterocyclic Carbene−Silver Acetate Complex Active against Resistant Respiratory Pathogens".* A. Kascatan-Nebioglu, A. Melaiye, K. Hindi, et al., J. Med. Chem., 49 (2006), 6811-6818.

70. *"Caffeine-Based Gold(I) N-Heterocyclic Carbenes as Possible Anticancer Agents: Synthesis and Biological Properties".* B. Bertrand, L. Stefan, M. Pirrotta, et al., Inorg. Chem., 53 (2014), 2296-2303.

71. *Synthesis and anticancer activity of silver(I)–N-heterocyclic carbene complexes derived from the natural xanthine products caffeine, theophylline, and theobromine.* H. A. Mohamed, B. R. M. Lake, T. Laing, et al., Dalton Trans., 44 (2015), 7563-7569.

72. *"Synthesis of PS-supported NHC-Pd Catalyst Derived from Theobromine and its Applications in Suzuki-Miyaura Reaction".* F. T. Luo, H. K. Lo, J. Chin. Chem. Soc., 59 (2012), 394-398.

73. *"Purine-based carbenes at rhodium and iridium".* J. Schütz, W. A. Hermann, J. Organomet. Chem., 689 (2004), 2995-2999.

74. *"Short synthesis of bis-NHC-Pd catalyst derived from caffeine and its applications to Suzuki, Heck, and Sonogashira reactions in aqueous solution.".* F. T. Luo, H. K. Lo, J. Organomet. Chem., 696 (2011), 1262-1265.

75. *"Synthesen in der Purinreihe, XV1) Synthesen von Xanthinium- und Guaninium-betainen".* H. Bredereck, O. Christmann, W. Koser, et al., Chem. Ber., 95 (1962), 1812-1819.

76. *"Synthesen in der Purinreihe, XVI1) Über die Darstellung von 5-Alkyl- bzw. 5-Arylsulfonylamino-4-amino-uracilen, 4-Amino-5alkylamino-uracilen und 4-Amino-5-[pyridino-methylenamino]-uracil-chloriden".* H. Bredereck, U. Gotsmann, Chem. Ber., 95 (1962), 1902-1909.

77. *"Synthesis and Structural Characterization of N-Heterocyclic Carbene Complexes of Silver(I) and Rhodium(I) from Caffeine".* A. Kascatan-Nebioglu, M. J. Panzner, J. C. Garrison, et al., Organometallics, 23 (2004), 1928-1931.

78. *" New synthesis of caffeine methiodide and its homolog".* E. I. Ivanov, G. D. Kalayanov, et al., Chem. Heterocycl. Compd., 25 (1989), 1318.

79. *"Physical Properties of Pure 1-Ethyl-3-methylimidazolium Ethylsulfate and Its Binary Mixtures with ethanol and Water at several Temperatures".* E. Gomez, B. Gonzales, N. Calvar, et al., J. Chem. Eng. Data., 51 (2006), 2096-2102.

80. *"Xanthine based N-heterocyclic carbene (NHC) complexes".* H. Valdés, D. Canseco-González, J. M. Germán-Acacio, and D. Morales-Morales, J. Organomet. Chem., 867 (2018), 51-54.

81. *"Reaction of K_2PtCl_4 with isonitriles and hydrazine".* L. Chugaev, M. Skanavy-Grigorizeva, J. Russ. Chem. Soc., 47 (1915), 776.

82. *"Über Die Hydrazin-Carbylamin-Komplexe des Platins".* L. Chugaev, M. Skanavy-Grigorizeva, A. Posniak, Z. Anorg. Allg. Chem., 148 (1925), 37-42.

83. *"A revised structure for Chugaev's salt $[PtC_8H_{15}N_6]_xCl_x$".* G. Rouschias, B. L. Shaw, J. Chem. Soc. D: Chem. Commun., 183 (1970).

84. *"1,3-Dimethyl-4-imidazolinyliden-(2)-pentacarbonylchrom ein neuer übergangsmetall-carben-komplex".* K. Öfele, J. Organomet. Chem., 12 (1968), P42-P43.

85. *"Direct Synthesis of a Mercury Salt-Carbene Complex".* H. W. Wanzlick, H. J. Schönherr, Angew. Chem. Int. Ed. Engl., 7 (1968), 141-142.

86. *"Direkt-Synthese eines Quecksilbersalz-Carben-Komplexes".* H. W. Wanzlick, H. J. Schönherr, Angew. Chem., 80 (1968), 154-154.

87. *"(1.4-Dimethyl-tetrazolium)-carbonylferrate, Ausgangsprodukte für (1.4-Dimethyl-tetrazolinyliden)- und Bis(methylamino)carben-Komplexe".* K. Öfele, C. G. Kreiter, Chem. Ber., 105 (1972), 529-540.

88. *"Nucleophile cyclische Carbene als Komplexliganden an Übergangsmetallen".* K. Öfele, Angew. Chem., 81 (1969), 936-936.

89. *"Isomerisierungsreaktionen von cis- und trans-Dicarben-Komplexen des Typs $M(CO)_4L_2$ (M = Cr, Mo, W).".* K. Öfele, E. Roos, M. Herberhold, Z. Naturforsch. Teil B., 31 (1976), 1070-1077.

90. *"N-Heterocyclic carbenes: state of the art in transition-metal-complex synthesis".* T. Weskamp, V. P. W. Böhm, W. A. Herrmann, J. Organomet. Chem., 600 (2000), 12-22.

91. *"Homoleptic carbene-silver (I) and carbene-copper (I) complexes".* A. J. Arduengo, H. R. V. Dias, J. C. Calabrese, and F. Davidson, Organometallics., 12 (1993), 3405-3409.

92. *"A Facile Synthesis of Unusual Liquid-Crystalline Gold(I) Dicarbene Compounds".* K. M. Lee, C. K. Lee, I. J. B. Lin, Angew. Chem. Int. Ed., 36 (1997), 1850-1852.

93. *"Facile Synthesis of Silver(I)−Carbene Complexes. Useful Carbene Transfer Agents".* H. M. J. Wang, I. J. B. Lin, Organometallics, 17 (1998), 972-975.

94. *"Synthesis, Structure, and Spectroscopic Properties of Gold(I)−Carbene Complexes".* H. M. J. Wang, C. Y. L. Chen, I. J. B. Lin, Organometallics, 18 (1999), 1216-1223.

95. *"Gold(I) N-Heterocyclic Carbene and Carbazolate Complexes".* H. M. J. Wang, C. S. Vasam, T. Y. R. Tsai, et al, Organometallics, 24 (2005), 486-493.

96. *"Inorganic−Organic Hybrid Lamella of Di- and Tetranuclear Silver−Carbene Complexes".* C. K. Lee, K. M. Lee, I. J. B. Lin, Organometallics., 21 (2002), 10-12.

97. *"Synthesis of the First Gold(I) Carbene Complex with a Gold-Oxygen Bond — First Catalytic Application of Gold(I) Complexes Bearing N-Heterocyclic Carbenes".* S. K. Schneider, W. A. Herrmann, E. Z. Herdtweck, Anorg. Allg. Chem., 629 (2003), 2363-2370.

98. *"Synthetic, structural and spectroscopic studies of (pseudo)halo(1,3-di-tert-butylimidazol-2-ylidine)gold complexes".* M. V. Baker, P. J. Barnard, S. K. Brayshaw, et al., Dalton Trans., (2005), 37-43.

99. *"Mono-, Di-, and Trinuclear Luminescent Silver(I) and Gold(I) N-Heterocyclic Carbene Complexes Derived from the Picolyl-Substituted Methylimidazolium Salt: 1-Methyl-3-(2-pyridinylmethyl)-1H-imidazolium Tetrafluoroborate".* V. J. Catalano, A. L. Moore, Inorg. Chem., 44 (2005), 6558-6566.

100. *"Luminescent coordination polymers with extended Au(I)–Ag(I) interactions supported by a pyridyl-substituted NHC ligand".* V. J. Catalano, A. O. Etogo, J. Organomet. Chem., 690 (2005) 6041-6050.

101. *"Group 11 Metal Complexes of N-Heterocyclic Carbene Ligands: Nature of the Metal-Carbene Bond".* X. Hu, I. Castro-Rodriguez, K. Olsen, and K. Meyer, Organometallics, 23 (2004), 755-764.

102. *"Thermally Stable Mesomorphic Palladium(II)−Carbene Complexes".* C. K. Lee, J. C. C. Chen, K. M. Lee, et al., Chem. Mater., 11 (1999), 1237-1242.

103. *"Synthesis and crystal structure of trans-[$PdCl_2(EtMeIm)_2$] (EtMeIm = N-ethyl-N'-methylimidazol-2-ylidene)".* D. C. Li, D. J. Liu, J. Chem. Crystallogr., 33 (2003), 989-991.

104. *"Donor-Functionalized Heterocyclic Carbene Complexes of Palladium(II): Efficient Catalysts for C−C Coupling Reactions".* D. S. McGuinness, K. J. Cavell, Organometallics, 19 (2000), 741-748.

105. *"Methyl-palladium(II) complexes of pyridine-bridged bis(nucleophilic heterocyclic carbene) ligands: Substituent effects on structure, stability, and catalytic performance".* D. J. Nielsen, K. J. Cavell, B. W. Skelton, and A. H. White, Inorg. Chim. Acta., 359 (2006), 1855-1869.

106. *"A Trinuclear Silver(I) Functionalized N-Heterocyclic Carbene Complex and Its Use in Transmetalation: Structure and Catalytic Activity for Olefin*

Polymerization". X. Wang, S. Liu, L. H. Weng, and G.-X. Jin, Organometallics. , 25 (2006), 3565-3569.

107. *"Synthesis of New Chiral N-Heterocyclic Carbene−Imine Ligands and Their Application to an Asymmetric Allylic Alkylation Reaction".* L. G. Bonnet, R. E. Douthwaite, B. M. Kariuki, Organometallics., 22 (2003), 4187-4189.

108. *"Synthesis of chiral imino- and amino-imidazolium salts and of chelating amino-N-heterocyclic carbene palladium(II) complexes".* A. Flahaut, J. P. Baltaze, S. Roland, P. Mangeney, J.Organomet. Chem., 691 (2006), 3498-3508.

109. *"Anellated N-Heterocyclic Carbenes: 1,3-Dineopentylnaphtho[2,3-d]imidazol-2-ylidene: Synthesis, KOH Addition Product, Transition-Metal Complexes, and Anellation Effects".* S. Saravanakumar, A. I. Oprea, M. K. Kindermann, et al., Chem. Eur. J., 12 (2006), 3143-3154.

110. *"Coordination Chemistry of a Modular N,C-Chelating Oxazole-Carbene Ligand and Its Applications in Hydrosilylation Catalysis".* M. Poyatos, A. Maisse-Francois, S. Bellemin-Laponnaz, L. H. Gade, Organometallics., 25 (2006), 2634-2641.

111. *"Synthesis and characterization of palladium(II) complexes with a novel chelating iminocarbene ligand".* M. Froseth, A. Dhindsa, H. Roise, and M. Tilset, Dalton Trans., (2003), 4516-4524.

112. *"Hydrido(methyl)carbene Complex of Platinum(IV)".* E. M. Prokopchuk, R. J. Puddephatt, Organometallics., 22 (2003), 563-566.

113. *"A Stable Crystalline Imino-N-Heterocyclic Carbene Ligand and Its Corresponding Palladium(II) and Rhodium(I) Complexes".* S. Dastgir, K. S. Coleman, A. R. Cowley, M. L. H. Green, Organometallics., 25 (2006), 300-306.

114. *"Silver(I) complex of a new imino-N-heterocyclic carbene and ligand transfer to palladium(II) and rhodium(I)".* K. S. Coleman, H. T. Chamberlayne, S. Turberville, et al., Dalton Trans., 29 (2003), 2917-2922.

115. *"Formation of N-Heterocyclic Complexes of Rhodium and Palladium from a Pincer Silver(I) Carbene Complex".* R. S. Simons, P. Custer, C. A. Tessier, W. J. Youngs, Organometallics., 22 (2003), 1979-1982.

116. *"Formation of chiral ionic liquids and imidazole-2-ylidene metal complexes from the proteinogenic amino acid l-histidine".* F. Hannig, G. Kehr, R. Frohlich, and G. Erker, J. Organomet. Chem., 690 (2005), 5959-5972.

117. *"1,3-Dialkyl- and 1,3-Diaryl-3,4,5,6-tetrahydropyrimidin-2-ylidene Rhodium(I) and Palladium(II) Complexes: Synthesis, Structure, and Reactivity".* M. Mayr, K. Wurst, K. Ongania, and M. R. Buchmeiser, Chem. Eur. J., 10 (2004), 1256-1266.

118. *"Reactivity Differences in the Syntheses of Chelating N-Heterocyclic Carbene Complexes of Rhodium Are Ascribed to Ligand Anisotropy".* J. A. Mata, A. R. Chianese, J. R. Miecznikowski, et al., Organometallics., 23 (2004), 1253-1263.

119. *"Hydrogen bonding ligand functionality and catalytic selectivity in the homogeneous hydrosilylation of enones with rhodium complexes".* G. Rivera, R. H. Crabtree, J. Mol. Catal. A: Chem., 222 (2004), 59-73.

120. *"Imidazo[1,5-a]pyridine: A Versatile Architecture for Stable N-Heterocyclic Carbenes".* M. Alcarazo, S. J. Roseblade, A. R. Cowley, et al, J. Am. Chem. Soc., 127 (2005), 3290-3291.

121. *"Coordination Versatility of Pyridine-Functionalized N-Heterocyclic Carbenes: A Detailed Study of the Different Activation Procedures. Characterization of New Rh and Ir Compounds and Study of Their Catalytic Activity".* E. Mas-Marza, M. Sanau, E. Peris, Inorg. Chem., 44 (2005), 9961-9967.

122. *"The Potential Use of Rhodium N-Heterocyclic Carbene Complexes as Radiopharmaceuticals: The Transfer of a Carbene from Ag(I) to $RhCl_3 \cdot 3H_2O$".* C. A. Quezada, J. C. Garrison, M. J. Panzner, et al., Organometallics, 23 (2004), 4846-4848.

123. *"Development of Building Blocks for the Synthesis of N-Heterocyclic Carbene Ligands".* G. Xu, S. R. Gilbertson, Org. Lett., 7 (2005), 4605-4608.

124. *"Synthesis and Catalytic Properties of New Water-Soluble Ruthenium(II)−N-Heterocyclic Carbene Complexes".* P. Csabai, F. Joo, Organometallics., 23 (2004), 5640-5643.

125. *"Di- and Trivalent Ruthenium Complexes of Chelating, Anionic N-Heterocyclic Carbenes".* P. L. Arnold, A. C. S. carisbrick, Organometallics., 23 (2004), 2519-2521.

126. *"Chemistry of the PCNHCP Ligand: Silver and Ruthenium Complexes, Facial/Meridional Coordination, and Catalytic Transfer Hydrogenation".* P. L. Chiu, H. M. Lee, Organometallics., 24 (2005), 1692-1702.

127. *"Synthesis of Imidazolium-Tethered Ruthenium(II)-Arene Complexes and Their Application in Biphasic Catalysis".* T. J. Geldbach, G. Laurenczy, R. Scopelliti, and P. J. Dyson, Organometallics., 25 (2006), 733-742.

128. *"Synthesis and Characterization of Organometallic Ionic Liquids and a Heterometallic Carbene Complex Containing the Chromium Tricarbonyl Fragment".* M. E. Moret, A. B. Chaplin, A. K. Lawrence, et al., Organometallics., 24 (2005), 4039-4048.

129. *"Synthesis and structural chemistry of arene-ruthenium half-sandwich complexes bearing an oxazolinyl–carbene ligand".* M. Poyatos, A. Maisse-

Francois, S. Bellemin-Laponnaz, et al., J. Organomet. Chem., 691 (2006), 2713-2720.

130. *"A Readily Available Chiral Ag-Based N-Heterocyclic Carbene Complex for Use in Efficient and Highly Enantioselective Ru-Catalyzed Olefin Metathesis and Cu-catalyzed Allylic Alkylation Reactions".* J. J. Van Veldhuizen, J. E. Campbell, R. E. Giudici, and A. H. Hoveyda, J. Am. Chem. Soc., 127 (2005), 6877-6882.

131. *"A Recyclable Chiral Ru Catalyst for Enantioselective Olefin Metathesis. Efficient Catalytic Asymmetric Ring-Opening/Cross Metathesis in Air".* J. J. VanVeldhuizen, S. B. Garber, et al., J. Am. Chem. Soc., 124 (2002), 4954-4955.

132. *"Rhodium and Iridium Complexes of N-Heterocyclic Carbenes via Transmetalation: Structure and Dynamics".* A. R. Chianese, X. Li, M. C. Janzen, et al., Organometallics., 22 (2003), 1663-1667.

133. *"Carbene Complexes of Rhodium and Iridium from Tripodal N-Heterocyclic Carbene Ligands: Synthesis and Catalytic Properties".* E. Mas-Marza, M. Poyatos, et al., Inorg. Chem., 43 (2004), 2213-2219.

134. *"Group 9 complexes of an N-heterocycle carbene bearing a pentafluorobenzyl substituent: attempted dehydrofluorinative coupling of cyclopentadienyl and N-heterocycle carbene ligands".* S. McGrandle, G. C. Saunders, J. Fluor. Chem., 126 (2005), 449-453.

135. *"Abnormal C5-Bound N-Heterocyclic Carbenes: Extremely Strong Electron Donor Ligands and Their Iridium(I) and Iridium(III) Complexes".* A. R. Chianese, A. Kovacevic, B. M. Zeglis, et al., Organometallics., 23 (2004), 2461-2468.

136. *"C−H Oxidative Addition of Bisimidazolium Salts to Iridium and Rhodium Complexes, and N-Heterocyclic Carbene Generation. A Combined Experimental and Theoretical Study".* M. Viciano, M. Poyatos, M. Sanau, et al., Organometallics., 25 (2006), 1120-1134.

137. *"Highly Stable Cp*−Ir(III) Complexes with N-Heterocyclic Carbene Ligands as C−H Activation Catalysts for the Deuteration of Organic Molecules".* R. Corberan, M. Sanau, E. Peris, J. Am. Chem. Soc., 128 (2006), 3974-3979.

138. *"Aliphatic and Aromatic Intramolecular C−H Activation on Cp*Ir(NHC) Complexes".* R. Corberan, M. Sanau, E. Peris, Organometallics., 25 (2006), 4002-4008.

139. *"Blue and near-UV phosphorescence from iridium complexes with cyclometalated pyrazolyl or N-heterocyclic carbene ligands".* T. Sajoto, P. I. Djurovich, A. Tamayo, et al., Inorg. Chem., 44 (2005), 7992-8003.

140. *"Preparation, Structure, and Olefin Polymerization Behavior of Functionalized Nickel(II) N-Heterocyclic Carbene Complexes".* X. Wang, S. Liu, G. X. Jin, Organometallics., 23 (2004), 6002-6007.

141. *"Picoline and pyridine functionalized chelate N-heterocyclic carbene complexes of nickel: synthesis and structural studies".* S. Winston, N. Stylianides, A. A. D. Tulloch, et al., Polyhedron., 23 (2004), 2813-2820.

142. *"Chelating alkoxy-N-heterocyclic carbene complexes of silver and copper electronic supplementary information (ESI) available: spectroscopic data for 1–3, cyclic voltammetry.".* P. L. Arnold, A. C. Scarisbrick, A. J. Blake, and C. Wilson, Chem. Commun., (2001), 2340-2341.

143. *"Synthesis and crystal structure of metal (M = Ag, Cu) crown ether with N-heterocyclic carbene linkage".* X. J. Wan, F. B. Xu, Q. S. Li, Inorg. Chem. Commun., 8 (2005), 1053-1055.

144. *"Copper Complexes of Nitrogen-Anchored Tripodal N-Heterocyclic Carbene Ligands".* X. Hu, I. Castro-Rodriguez, and K. Meyer, J. Am. Chem. Soc., 125 (2003), 12237-12245.

145. *"Enantioselective conjugate addition of diethylzinc using catalytic silver(I) diaminocarbenes and Cu(OTf)$_2$".* J. Pytkowicz, S. Roland, and P. Mangeney, Tetrahedron: Asymmetry., 12 (2001), 2087-2089.

146. *"Enantioselective copper-catalyzed 1,4-conjugate addition reactions using chiral N-heterocyclic carbenes".* C. L. Winn, F. Guillen, J. Pytkowicz, et al., J. Organomet. Chem., 690 (2005), 5672-5695.

147. *"Asymmetric Synthesis with N-Heterocyclic Carbenes. Application to the Copper-Catalyzed Conjugate Addition".* A. Alexakis, C.L. Winn, F. Guillen, et al., Adv. Syn. Catal., 345 (2003), 345-348.

148. *"Metal Ion Mediated Transfer and Cleavage of Diaminocarbene Ligands".* R. Z. Ku, J. C. Huang, et al., Organometallics., 18 (1999), 2145-2154.

149. *"Nucleophilic Carbenes in Asymmetric Organocatalysis".* D. Enders, T. Balensiefer, Acc. Chem. Res., 37 (2004), 534-541.

150. *"Catalyzed Reactions of Acyl Anion Equivalents".* J. S. Johnson, Angew. Chem. Int. Ed., 43 (2004), 1326-1328.

151. *"New Developments in the Asymmetric Stetter Reaction".* M. Christmann, Angew. Chem. Int. Ed., 44 (2005), 2632-2634.

152. *"Extending Mechanistic Routes in Heterazolium Catalysis–Promising Concepts for Versatile Synthetic Methods".* K. Zeitler, Angew. Chem. Int. Ed., 44 (2005), 7506-7510.

153. *"Metal Complexes of N-Heterocyclic Carbenes—A New Structural Principle for Catalysts in Homogeneous Catalysis".* W. A. Herrmann, M. Elison, J. Fischer, et al., Angew. Chem. Int. Ed., 34 (1995), 2371-2374.

154. *"N-heterocyclic carbenes: novel ruthenium–alkylidene complexes".* T. Weskamp, F. J. Kohl, W. A. Herrmann, J. Organomet. Chem., 582 (1999), 362-365.

155. *"N-Heterocyclic Carbenes: A New Concept in Organometallic Catalysis".* W. A. Herrmann, Angew. Chem. Int. Ed., 41 (2002), 1290-1309.

156. *"Chiral N-heterocyclic carbene-transition metal complexes in asymmetric catalysis".* M. C. Perry, K. Burgess, Tetrahedron: Asymmetry., 14 (2003), 951-961.

157. *"Preparation of Metal−Imidazolidin-2-ylidene Complexes by Oxidative Addition".* A. Fürstner, G. Seidel, D. Kremzow, and C. W. Lehmann., Organometallics., 22 (2003), 907-909.

158. *"NHC–Ru complexes—Friendly catalytic tools for manifold chemical transformations".* V. Dragutan, I. Dragutan, L. Delaude, and A. Demonceau, Coord. Chem. Rev., 251 (2007), 765-794.

159. *"Well-Defined N-Heterocyclic Carbenes−Palladium(II) Precatalysts for Cross-Coupling Reactions".* S. P. Nolan, N. Marion, Acc. Chem. Res., 41 (2008), 1440-1449.

160. *"Mono-, Bi- and Tridentate N-Heterocyclic Carbene Ligands for the Preparation of Transition-Metal-Based Homogeneous Catalysts".* R. Corberán, E. Mas-Marzá, E. Peris, Eur. J. Inorg. Chem., 2009 (2009), 1700-1716.

161. *"Unprecedented use of silver(I) N-heterocyclic carbene complexes for the catalytic preparation of 1,2-bis(boronate) esters".* J. Ramírez, R. Corberán, M. Sanaú, et al., Chem. Commun., (2005), 3056-3058.

162. *"Silver(I)−Carbene Complexes/Ionic Liquids: Novel N-Heterocyclic Carbene Delivery Agents for Organocatalytic Transformations".* A. C. Sentman, S. Csihony, et al., J. Org. Chem., 70 (2005), 2391-2393.

163. *"N-Heterocyclic Carbenes in Late Transition Metal Catalysis".* S. Díez-González, N. Marion, and S. P. Nolan, Chem. Rev., 109 (2009), 3612-3676.

164. *"Nanoparticle encapsulated silver carbene complexes and their antimicrobial and anticancer properties: A perspective".* W. J. Youngs, A. R. Knapp, P. O. Wagers, and C. A. Tessier, Dalton Trans., 41 (2012), 327-336.

165. *"Beyond catalysis: N-heterocyclic carbene complexes as components for medicinal, luminescent, and functional materials applications".* L. Mercs, M. Albrecht, Chem. Soc., 39 (2010), 1903-1912.

166. *"Metal-NHC complexes: a survey of anti-cancer properties".* M. L. Teyssot, A. S. Jarrousse, and M. Manin, Dalton Trans., (2009), 6894-6902.

167. *"The Medicinal Applications of Imidazolium Carbene–Metal Complexes".* K. M. Hindi, M. J. Panzner, C. A. Tessier, et al., Chem. Rev., 109 (2009), 3859-3884.

168. *"Treatment of Large Human Burns With 0.5% Silver Nitrate Solution".* C. A. Moyer, L. Brentano, D. L. Gravens, et al., Arch. Surg., 90 (1965), 812-867.

169. *"Silver Sulfadiazine—A New Topical Therapy for Pseudomonas in Burns".* C. L. Fox, Arch. Surg., 96 (1968), 184-188.

170. *"Benzotriazole functionalized N-heterocyclic carbene-silver(I) complexes: Synthesis, cytotoxicity, antimicrobial, DNA binding, and molecular docking studies".* G. Onar, M. O. Karatas, S. Balcioglu, et al., Polyhedron., 153 (2018), 31-40.

171. *"Formation of Water-Soluble Pincer Silver(I)−Carbene Complexes: A Novel Antimicrobial Agent".* A. Melaiye, R. S. Simons, A. Milsted, et al., J. Med. Chem., 47 (2004), 973-977.

172. *"N-Heterocyclic carbene–silver complexes: A new class of antibiotics".* A. Kascatan-Nebioglu, M. J. Panzner, C. A. Tessier, et al., Coord. Chem. Rev., 251 (2007), 884-895.

173. *"Recent Developments in the Medicinal Applications of Silver-NHC Complexes and Imidazolium Salts".* N. A. Johnson, M. R. Southerland, W. J. Youngs, et al., Molecules., 22 (2017), 1263-1282.

174. *"A Fluorescent Silver(I) Carbene Complex with Anticancer Properties: Synthesis, Characterization, and Biological Studies".* M. G. Fabbrini, D. Cirri, A. Pratesi, et al., ChemMedChem., 14 (2019), 182-188.

175. *"Unsymmetrically substituted benzimidazolium based Silver(I)-N-heterocyclic carbene complexes: Synthesis, characterization and in vitro anticancer study against human breast cancer and colon cancer".* "A. Habib, M. Nazari, M. A. Iqbal, et al., J. Saudi. Chem. Soc., 23 (2019), 795-808.

176. *"Silver(I) N-Heterocyclic Carbene Complexes Derived from Clotrimazole: Antiproliferative Activity and Interaction with an Artificial Membrane-Based Biosensor".* H. A. Mohamed, S. Shepherd, N. William, et al., Organometallics., 39 (2020), 1318-1331.

177. *"Inhibition of cell division in Escherichia coli by electrolysis products from a platinum electrode".* B. Rosenber, L. Vancamp, and T. Krigas, Nature., 205 (1965), 698-699.

178. *"Platinum compounds: a new class of potent antitumor agents".* B. Rosenberg, L. Vancamp, J. E. Trosko, and V. H. Mansour, Nature., 223 (1969), 385-386.

179. *"Caffeine analogs: biomedical impact".* J. W. Daly, Cell. Mol. Life. Sci., 64 (2007), 2153-2169.

180. *"A theobromine derived silver N-heterocyclic carbene: synthesis, characterization, and antimicrobial efficacy studies on cystic fibrosis relevant pathogens.".* M. J. Panzer, K. M. Hindi, B. D. Wright, et al., Dalton.Trans., (2009), 7308-7313.

181. *"N-heterocyclic carbenes (NHC) with 1,2,4-oxadiazole-substituents related to natural products: Synthesis, structure, and potential antitumor activity of some corresponding gold(I) and silver(I) complexes.".* C. V. Maftei, E. Fodor, P. G. Jones, et al., Eur. J. Med. Chem., 101 (2015), 431-441.

182. *"N-heterocyclic carbene gold(I) and silver(I) complexes bearing functional groups for bio-conjugation".* M. E. Garner, W. Niu, X. Chen, et al., Dalton. Trans., 44 (2015), 1914-1923.

183. *"Synthesis, characterization and antimicrobial activities of novel silver(I) complexes with coumarin substituted N-heterocyclic carbene ligands.".* M. O. Karatas, B. Olgundeniz, S. Gunal, et al., Bioorg. Med. Chem., 24 (2016), 643-650.

184. *"Preclinical anti-cancer activity and multiple mechanisms of action of a cationic silver complex bearing N-heterocyclic carbene ligands.".* S. J. Allison, M. Sadiq, E. Baronov, et al., Cancer Lett.,403 (2017), 98-107.

185. *"Anticancer and Antimicrobial Metallopharmaceutical Agents Based on Palladium, Gold, and Silver N-Heterocyclic Carbene Complexes.".* S. Ray, R. Mohan, J. K. Singh, et al., J.Am. Chem. Soc., 129 (2007), 15042-15053.

186. *"Synthesis and biological studies of silver N-heterocyclic carbene complexes derived from 4,5-diarylimidazole.".* W. Liu, K. Bensdorf, A. Hagenbach, et al., Eur. J. Med. Chem., 46 (2011), 5927-5934.

187. *"Synthesis, structures, and antimalarial activities of some silver(I), gold(I) and gold(III) complexes involving N-heterocyclic carbene ligands.".* C. Hemmert, A. Fabie, A. Fabre, et al., Eur. J. Med. Chem., 60 (2013), 64-75.

188. *"4-Alkylated Silver–N-Heterocyclic Carbene (NHC) Complexes with Cytotoxic Effects in Leukemia Cells.".* A. H. Sandtoru, C. Leitch, S. L. Bedringaas, et al., ChemMedChem., 10 (2015), 1522-1527.

189. *"Novel benzimidazole-2-ylidene carbene precursors and their silver(I) complexes: Potential antimicrobial agents.".* M. Kaloglu, N. Kaloglu, I. Ozdemir, et al., Bioorg. Med. Chem., 24 (2016), 3649-3656.

190. *"The synthesis and thermolysis of imidazole quaternary salts".* B. K. M. Chan, N. Chang, M. R. Grimmett, et al., Aust. J. Chem., 30 (1977), 2005-2013.

191. *"Synthesis and Characterization of Imidazolium Salts Bearing Fluorinated Anions".* H. Ibrahim, N. A. Koorbanally, D. Ramjugernath, et al., Int. J. Inorg. chem., 638 (2012), 2304-2309.

192. *"Influence of chloride, water, and organic solvents on the physical properties of ionic liquids".* K. R. Seddon, A. Stark, and M. J. Torres, Pure. Appl. Chem., 72 (2000), 2275-2287.

193. *"N-Heterocyclische Carbene".* W. A. Herrmann, C. Köcher, Angewandte Chemie., 109 (1997), 2256-2282.

194. *"New chiral imidazolium ionic liquids from isomannide".* A. Pereira, M. D. R. Gomes, et al., Carbohydr. Res., 346 (2011), 197-202.

195. *"Tetrahexylammonium benzoate, a liquid salt at 25.degree., a solvent for kinetics or electrochemistry".* C. Gardner. Swain, A. Ohno, D. K. Roe, et al., J. Am. Chem. Soc., 89 (1967), 2648-2649.

196. *"An efficient and green approach to prepare hydrophilic imidazolium ionic liquids free of halide and its effect on oxygen reduction reaction of Pt/C catalyst".* J. Gao, J. Liu, W. Liu, et al., Int. J. Hydrog. Energy., 37 (2012), 13167-13177.

197. *"Luminescent iridium(iii) complexes of N-heterocyclic carbene ligands prepared using the 'click reaction'".* R. E. Karmis, S. Carrara, A. A. Baxter, et al., Dalton Trans., 48 (2019), 9998-10010.

198. *"Access to silver-NHC complexes from soluble silver species in aqueous or ethanolic ammonia".* C. Gibard, K. Fauché, R. Guillot, et al., J. Organomet. Chem., 840 (2017), 70-74.

199. *"Simple and efficient synthesis of [MCl(NHC)] (M = Au, Ag) complexes".* R. Visbal, A. Laguna, and M. C. Gimeno, Chem. Commun., 49 (2013), 5642-5644.

200. *"$AgOC(CF_3)_3$: an alternative and efficient reagent for preparing transition".* T. K. Maishal, J. M. Basset, M. Boualleg, et al., Dalton Trans., (2009), 6956-6959.

201. *"Synthesis, structural characterization and properties of new N-heterocyclic carbene Ag(I) complexes".* R. Kishore, S. K. Das, J. Mol. Struct., 1053 (2013), 38-47.

202. *"Highly Convenient Regioselective Intermolecular Hydroamination of Alkynes Yielding Ketimines Catalyzed by Gold(I) Complexes of 1,2,4-triazole Based N-heterocyclic Carbenes".* C. Dash, M. M. Shaikh, R. J. Butcher, and P. Ghosh, Inorg. Chem., 49 (2010), 4972-4983.

203. *"Anticancer and Antimicrobial Metallopharmaceutical Agents Based on Palladium, Gold, and Silver N-Heterocyclic Carbene Complexes".* S. Ray, R. Mohan, J. K. Singh, et al., J. Am. Chem. Soc., 129 (2007), 15042-15053.

204. *"Synthesis from Caffeine of a Mixed N-Heterocyclic Carbene-Silver Acetate Complex Active".* A. Kascatan-Nebioglu, A. Melaiye, K. Hindi, et al., J. Med. Chem., 49 (2006), 6811-6818.

205. *"Synthesis, Stability, and Antimicrobial Studies of Electronically Tuned Silver Acetate".* K. M. Hindi, T. J. Siciliano, S. Durmus, et al., J. Med. Chem., 51 (2008), 1577-1583.

206. *"Organometallic peptide NHC complexes of Cp∗Rh(III) and arene Ru(II) moieties from l-thiazolylalanine".* J. Lemke, N. Metzler-Nolte, J. Organomet. Chem., 696 (2011), 1018-1022.

207. *"Designing effective homogeneous catalysis for glycerol valorization: selective synthesis of a value-added aldehyde from 1,3-propanediol via hydrogen transfer catalysed by a highly recyclable, fluorinated Cp*Ir(NHC) catalyst".* Y. Ma, Y. M. Wang, P. J. Morgan, et al., Catal. Today., 307 (2018), 248-259.

208. *"Synthesis of binuclear iridium(III) and rhodium(III) complexes bearing methylnaphthalene-linked N-heterocyclic carbenes, and application to intramolecular hydroamination".* K. Ogata, T. Nagaya, and S. I. Fukuzawa, J. Organomet. Chem., 695 (2010), 1675-1681.

209. *"Irreversible cleavage of a carbene–rhodium bond in Rh-N-heterocyclic carbene complexes: implications for catalysis".* D. P. Allen, C. M. Crudden, L. A. Calhoun, and R. Wang, J. Organomet. Chem., 689 (2004), 3203–3209.

210. *"A new rhodium(I) NHC complex inhibits TrxR: In vitro cytotoxicity and in vivo hepatocellular carcinoma suppression".* R. Fan, M. Bian, L. Hu, et al., Eur. J. Med. Chem., 183 (2019), 111721-111735.

211. *"A multi-target caffeine derived rhodium(i) N-heterocyclic carbene complex: evaluation of the mechanism of action".* J. J. Zhang, J. K. Muenzner, M. A. Abu el Maaty, et al., Dalton Trans., 45 (2016), 13161-13168.

212. *"Rhodium(I) N-Heterocyclic Carbene Bioorganometallics as in Vitro Antiproliferative Agents with Distinct Effects on Cellular Signaling".* L. Oehninger, S. Spreckelmeyer, P. Holenya, et al., J. Med. Chem., 58 (2015), 9591−9600.

213. *"An N-Heterocyclic carbene with a sulfonamide group embedded within the heterocyclic backbone".* M. Jonek, A. Makhloufi, and C. Ganter, J. Organomet. Chem., 838 (2017), 37-41.

214. *"Synthesis and reactivity of (Benz)imidazol-2-ylidenes with exocyclic N-acyl or N-sulfonyl groups".* M. Jonek, A. Makhloufi, P. Rech, et al., J. Organomet. Chem., 750 (2014), 140-149.

215. *"Synthesis and characterization of silver and gold NHC complexes: Crystal structures and mass spectral studies".* P. Kumar, I. Cisarova, J. Organomet. Chem.,735 (2013), 32-37.

216. *"Palladium N-heterocyclic carbene complexes for the MizorokieHeck reaction: An appraisal.* K. R. Balinge, P. R. Bhagat, C. R. Chimie, 20 (2017), 1-32.

217. *"Heterocyclic Carbene Metal-catalyzed Csp^2-Csp^2 and Csp-Csp^2 Couplings Using Nonmetallic Substrates.* M. Yus, I. M. Pastor, Chem. Lett., 42 (2013), 94-108.

218. *"N-heterocycle carbene (NHC)-ligated cyclopalladated N, N-dimethylbenzylamine: a highly active, practical, and versatile catalyst for the Heck–Mizoroki reaction".* G. R. Peh, E. A. B. Kantchev, C. Zhang and J. Y. Ying, Org. Biomol. Chem., 7 (2009), 2110-2119.

219. *"Practical Heck–Mizoroki Coupling Protocol for Challenging Substrates Mediated by an N-Heterocyclic Carbene-Ligated Palladacycle".* E. A. B. Kantchev, G. R. Peh, C. Zhang, and J. Y. Ying, Org. Lett., 10 (2008), 3949-3952.

220. Michel Pfeffer, Anil B. Goel. "Cyclopalladated compounds". [book auth.] Herbert Kaesz. *Inorganic Synthesis, Volume 26.* s.l. : Wiley-Interscience, 1989.