



Water-soluble arene ruthenium complexes: From serendipity to catalysis and drug design

Georg Süss-Fink*

Institut de Chimie, Université de Neuchâtel, CH-2000 Neuchâtel, Switzerland

ARTICLE INFO

Article history:

Received 30 April 2013

Received in revised form

12 July 2013

Accepted 15 July 2013

Dedicated to Françoise Hardy, iconic figure of style and melancholy, whose art paralleled the development of the chemistry described here, in gratitude and admiration on the occasion of her 70th birthday

Keywords:

Water-soluble organometallics

Arene ligands

Ruthenium

Half-sandwich complexes

Catalysis

Anticancer activity

ABSTRACT

Shortly after the discovery of benzene ruthenium dichloride and some controversy about its polymeric or dimeric nature in the 1960s, the hydrolysis of this material in water to give a mixture of benzene ruthenium aqua complexes was discovered. However, it took a long time until this reaction and the hydrolysis of other arene analogs were used as an entry to the synthesis of water-soluble arene ruthenium complexes. These complexes are able to activate molecular hydrogen in aqueous solution and allow the design of arene ruthenium bioconjugates. They can serve as catalysts or catalyst precursors for hydrogenation and transfer hydrogenation reactions in water and they are at present one of the most promising classes of metal complexes to replace cisplatin in future cancer therapy, due to their inherent cytotoxicity and their good cellular uptake, conditioned by well balanced lipophilic and hydrophilic properties.

© 2013 Elsevier B.V. All rights reserved.

1. Introduction

Arene ruthenium complexes are children of the 1960s: during his PhD project in the laboratory of Professor Günter Winkhaus at the University of Mainz, Hellmut Singer reacted ruthenium trichloride hydrate with 1,3-cyclohexadiene in dry ethanol and obtained after gentle warming (35 °C, 5 h) a brownish precipitate, which was isolated by decantation, washed with methanol and dried in high vacuum. The elemental analysis of this material, obtained in 75% yield, suggested the composition $[(C_6H_6)RuCl_2]$, in accordance with the IR and 1H NMR data. A polymeric structure was assumed for this compound, $[(C_6H_6)RuCl_2]_x$, on grounds of the unsaturated character of the $(\eta^6-C_6H_6)RuCl_2$ fragment (a 16 electron species) and of the low solubility of the compound (Fig. 1). Winkhaus and Singer published this reaction (in German) in one of the first volumes of this journal [1]. The dehydrogenation of 1,3-cyclohexadiene to benzene in this reaction was also discussed in this paper and explained by a simultaneous reduction of the

formally trivalent metal to ruthenium(II); despite the modest claims and the erroneous assumption of a polymeric structure, this paper remains a milestone of organometallic chemistry (Fig. 2).

From the same reaction, but under slightly modified conditions (90% aqueous ethanol, 45 °C, 3 h), Zelonka and Baird obtained a red solid, which they believed to be different from Winkhaus' polymeric form and for which they proposed the molecular formula $[(C_6H_6)RuCl_2]_2$ with η^6 -coordinated benzene ligands on the basis of a detailed analysis of the infrared spectrum in 1972 (Fig. 1) [2,3]. This dimeric molecule containing two terminals and two bridging chloro ligands in accordance with the 18 electron rule is present in the solid state, but the compound dissolves in coordinating solvents such as acetonitrile (L) to give monomeric complexes of the type $[(C_6H_6)RuCl_2(L)]$ [2–4]. These findings were confirmed by Bennett and Smith, who also showed that Baird's red dimer $[(C_6H_6)RuCl_2]_2$ was identical with Winkhaus' original material considered to be polymeric [5]. They also synthesized a large number of derivatives $[(arene)RuCl_2]_2$ and $[(arene)RuCl_2(L)]$ [5] and showed the more soluble *p*-cymene derivative $[(p-MeC_6H_4Pr^i)RuCl_2]_2$ to be dimeric in chloroform solution by osmometry [6].

While the molecular structures of various derivatives $[(arene)RuCl_2]_2$ (arene being hexamethylbenzene [7], trindane [8],

* Tel.: +41 (0) 32 718 24 05; fax: +41 (0) 32 718 25 11.

E-mail address: georg.suess-fink@unine.ch.

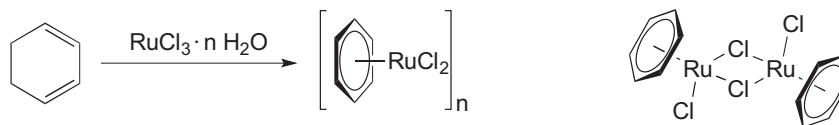


Fig. 1. Synthesis of benzene ruthenium dichloride considered to be a polymer [1], until its dimeric nature, $[(C_6H_6)RuCl_2]_2$, was established [2–5].

ethylbenzoate [9], 1,2,3,4-tetrahydronaphthalene [10], *o*-toluene methylcarboxylate [11], hexaethylbenzene [12], indane [13] and *p*-cymene [14] have been solved by X-ray structure analysis during the following years, the molecular structure of the parent benzene complex $[(C_6H_6)RuCl_2]_2$ was only confirmed in 2005 by a single-crystal X-ray analysis of the chloroform disolvate [15].

The molecule has indeed the expected dimeric structure; the two halves of the molecule are related by a crystallographic inversion center (Fig. 3). The two benzene rings are planar and the distance between the benzene centroid and the ruthenium atom is 1.646 Å. The bridging Ru–Cl distances are 2.4495(11) and 2.4580(9) Å and the terminal Ru–Cl distance is 2.3911(9) Å. The Ru···Ru distance is 3.7099(8) Å, there is no metal–metal bond in accordance with the electron count of 36 and the noble gas rule [15].

2. Arene ruthenium aqua complexes

By the time when this compound was discovered, organometallic chemists were trained to work with rigorous exclusion of air and water in thoroughly dried organic solvents, since organometallic compounds and water were thought to be antagonists [16]. Indeed, organometallics are in general either hydrophobic or water-sensitive, but the credo of their incompatibility with water was so prevalent that for organometallic reactions anhydrous conditions have become a general feature of laboratory techniques in this field, considered to be an absolute must [17,18].

The overcoming of this inveterate prejudice in the case of arene ruthenium complexes is the merit of Professor Michael Baird from Queen's University in Kingston, who unintentionally pioneered the chemistry of arene ruthenium aqua complexes. In an attempt to study the properties of benzene ruthenium dichloride dimer, Zelonka and Baird treated this brownish red solid with water and observed complete dissolution, with decomposition though,

however, the organometallic benzene ruthenium unit stayed intact [2]. When they dissolved $[(C_6H_6)RuCl_2]_2$ in D_2O , they observed two 1H NMR signals for coordinated benzene, which they tentatively attributed to the cationic complexes $[(C_6H_6)RuCl(D_2O)_2]^+$ ($\delta = 5.93$ ppm) and $[(C_6H_6)Ru(D_2O)_3]^{2+}$ ($\delta = 6.03$ ppm) [3]. This important finding did not find much attention, since these arene ruthenium aqua complexes could not be isolated.

Professor Martin Bennett from the Australian National University in Canberra questioned Baird's assignment of the 1H NMR signals in D_2O : Bennett and Smith had observed the formation of a dinuclear cation $[(C_6H_6)_2Ru_2Cl_3]^+$ from the reaction of $[(C_6H_6)RuCl_2]_2$ with hot water; this chloro-bridged species was isolated and fully characterized as the hexafluorophosphate salt ($\delta = 6.04$ ppm). Therefore, Bennett believed that the signal observed by Baird at $\delta = 6.03$ ppm was rather due to $[(C_6H_6)_2Ru_2Cl_3]^+$ [5]. Professor Anthony Stephenson from the University of Edinburgh, however, attributed this signal to the neutral mono-aqua complex $[(C_6H_6)RuCl_2(D_2O)]$, given that his group had studied the dissolution of Bennett's salt $[(C_6H_6)_2Ru_2Cl_3][PF_6]$ in D_2O and observed two 1H NMR signals for coordinated benzene, which was interpreted by the bridge-opening splitting of the dinuclear cation $[(C_6H_6)_2Ru_2Cl_3]^+$ with D_2O to give the aqua complexes $[(C_6H_6)RuCl(D_2O)_2]^+$ and $[(C_6H_6)RuCl_2(D_2O)]$, which show almost identical 1H NMR resonances as those observed by Baird for the reaction of $[(C_6H_6)RuCl_2]_2$ with D_2O [19].

In contrast to these early NMR observations with two signals for coordinated benzene in a D_2O solution of $[(C_6H_6)RuCl_2]_2$ [3,5,19] (Fig. 4), we observed in 1994 the three expected signals, which we assigned to the three aqua complexes $[(C_6H_6)RuCl_2(D_2O)]$ ($\delta_H = 5.89$ ppm, $\delta_C = 84.3$ ppm), $[(C_6H_6)RuCl(D_2O)_2]^+$ ($\delta_H = 5.97$ ppm, $\delta_C = 83.3$ ppm) and $[(C_6H_6)Ru(D_2O)_3]^{2+}$ ($\delta_H = 6.06$ ppm, $\delta_C = 82.4$ ppm), the signal intensity being 8:28:5 in the 1H NMR spectrum [20].

RUTHEN(II)-KOMPLEXE MIT ZWEIZÄHNIGEM CYCLOHEPTATRIEN UND BENZOL

G. WINKHAUS UND H. SINGER

Institut für Anorganische Chemie und Kernchemie der Universität Mainz (Deutschland)

(Eingegangen den 28. Juni 1966)

Die Umsetzung von $RuCl_3 \cdot xH_2O$ mit 1,3-Cyclohexadien, C_6H_8 , in Äthanol ergab eine polymere, braune, in Benzol und Chloroform unlösliche, in DMSO lösliche Verbindung der Zusammensetzung $[Ru(C_6H_6)Cl_2]_x$ (II).

Das bandenarme IR-Spektrum von (II) (KBr-Preßling) ist den Spektren bekannter Übergangsmetall-Benzol-Komplexe ähnlich und unterscheidet sich stark

von den bandenreicheren Spektren bekannter 1,3-Cyclohexadien-Metall-Komplexe. Charakteristisch sind vor allem die C–H-Valenzschwingungsbanden bei 3045 und 2913 cm^{-1} (Dibenzolchrom⁶ 3037 und 2907 cm^{-1}).

Im 1H -KMR-Spektrum von (II) in DMSO- d_6 tritt nur eine verbreiterte, nicht aufgelöste Bande bei $\tau = 3.96$ (60 MHz; TMS als Standard) auf, die der Resonanz nahezu gleichwertiger Protonen des C_6H_6 -Liganden zuzuordnen ist. {Freies Benzol in DMSO (15 Vol. %) $\tau = 2.52$; $C_6H_6RuC_6H_8$ ⁷ in CCl_4 , C_6H_6 -Protonen $\tau = 5.00$.

Fig. 2. Excerpt of the landmark paper by Winkhaus and Singer on benzene ruthenium dichloride in Volume 7 of the Journal of Organometallic Chemistry (1967).

Download English Version:

<https://daneshyari.com/en/article/1324259>

Download Persian Version:

<https://daneshyari.com/article/1324259>

[Daneshyari.com](https://daneshyari.com)