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PLATINUM-PROMOTED CYCLIZATION REACTIONS OF AMINO-OLEFINS

I. THE CYCLIZATION OF 4-AMINOPENTENE AND RELATED COMPOUNDS *

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Summary

Olefinic amines of the type $CH_2=CH(CH_2)_nNHR$ undergo cyclization in acidic aqueous solution at 60°C in the presence of $PtCl_4^{2-}$. The $PtCl_4^{2-}$ is regenerated at the end of the cyclization so that the reaction may be considered as catalytic. Both pyrrolidines and piperidines may be formed although the former are favored.

Introduction

The reaction of coordinated olefins with nucleophiles to give species containing metal—carbon σ-bonds was first reported by Hofmann and von Narbutt in 1908 [1] although their essentially correct formulation for these compounds could be confirmed only 50 years later [2]. Since then a wide variety of olefin complexes have been reacted with a large number of nucleophiles and their products characterized [3]. Reactions of this type have also been extensively used to prepare various types of organic substances [4] including nitrogen heterocycles starting from amino-olefins, e.g., the cyclization reaction of *o*-allylaniline in the presence of $[PdCl_2(PhCN)_2]$ has been used to prepare 2-methylindole [5].

During the course of a study of the thermodynamics and kinetics of formation of platinum—olefin complexes it was observed [6] that $CH_2=CHCH_2CH_2CH_2NH_3^+Cl^-$, in the presence of $K_2[PtCl_4]$ gave a compound which was later

* Dedicated to Professor Ernst Otto Fischer on the occasion of his 60th birthday on November 10, 1978.

[7] identified as 2-methylpyrrolidine. This paper reports further details of this type of cyclization reaction.

Experimental

The visible/UV spectra were measured using a Varian/Techtron Spectrophotometer Model 635. The IR spectra were recorded either on a Perkin—Elmer 527 Grating or Beckman IR 4250 spectrophotometer. The NMR spectra were obtained either on a Perkin—Elmer R12B (^1H) or Bruker HX 90 FT (^1H and ^{13}C) NMR spectrometer. The mass spectra were obtained using a Hitachi—Perkin—Elmer RMU-6M spectrometer. The gas chromatographic studies were carried out using a Perkin—Elmer F11 gas chromatograph (length of column: 4.0 m, stationary phase: Polyglycol 4000-KOH). For the larger scale separations a Perkin—Elmer F21 preparative gas chromatograph was used (column length: 4.5 m; stationary phase: Polyglycol 4000/KOH). The combined gas chromatographic/mass spectrometric studies were carried out using a Perkin—Elmer 990 gas chromatograph Hitachi—Perkin—Elmer RMU-6L spectrometer (column length: 2.0 m; stationary phase: Polyglycol 4000-KOH). The microanalytical data were obtained by the Microanalytical Laboratory of the ETH Zurich.

The following organic compounds were prepared either as described in the appropriate reference or as indicated: but-3-enylamine (I) [8]; pent-4-enylamine (II) [9]; hex-3-enylamine (III) [10]; *N*-methylpent-4-enylamine (IV) [11] was prepared as described for I; *N*-n-propylpent-4-enylamine (V) [12]; *N*-iso-propylpent-4-enylamine (VI) [13]; *N,N*-dimethylpent-4-enylamine (VII) [14] was prepared as described for V; *N,N,N*-trimethylpent-4-enylammonium chloride (VIII) was prepared as described for the analogous allylammonium salt; 2-methylpyrrolidine (IX) [15]; 1,2-dimethylpyrrolidine (X) [16] was prepared by the amino-mercuration method described by Perie et al. [11]; 2-methyl-1-n-propylpyrrolidine (XI) [17] was prepared by the amino-mercuration method [11], as was 2-methyl-1-iso-propylpyrrolidine (XII) [11]; 1,1,2-trimethylpyrrolidinium iodide (XIII) [18], 1,1-dimethylpiperidinium iodide (XIV) [19] and 2-methylpiperidine (XV) [24].

Details concerning the preparation of these compounds, their purification, analytical, IR, NMR and MS data are reported elsewhere [20]. These data are in agreement with the above formulations and with published data.

The preparation of complexes of the type [$PtCl_3$(ligand H)] (ligand H = N-protonated amino-olefins, I—VIII) as well as the details of their characterization are reported elsewhere [20].

The organic solvents employed were purified by standard procedures. Boiling, melting and decomposition points are uncorrected. The aqueous solutions described below were prepared using deionized water, sodium chloride ("pro analysi", Merck), 1 *N* hydrochloric acid (Titrisol, Merck) and $K_2[PtCl_4]$ (Johnson—Matthey) which had been recrystallized from 0.1 *N* hydrochloric acid prior to use.

The solutions used in the cyclization studies contained either 10^{-3} *M* $K_2[PtCl_4]$ and 10^{-3} *M* amino-olefin (Reacting system 1) or 10^{-3} *M* [$PtCl_3^-$(amino-olefin H^+)] (Reacting system 2). Each reacting system was studied in the three following media: *Medium 1:* 0.1 *M* HCl, 1.9 *M* NaCl; *Medium 2:* 0.01 *M* HCl, 1.99 *M*

NaCl; *Medium 3:* 0.01 *M* HCl, 0.09 *M* NaCl.

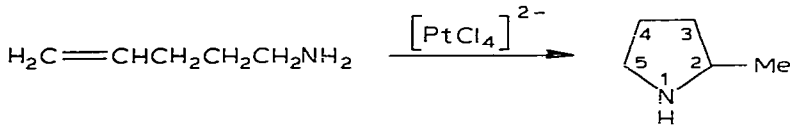
The cyclization reactions were carried out at 60 ± 2°C using a thermostatted bath. The course of the reaction was followed spectrophotometrically. Probes taken from the reaction vessel were cooled to room temperature, before measuring their visible/UV spectra. In selected cases the spectral changes occurring during the reaction were followed over the whole visible/UV region. It was also established that a reliable indication of the completion of the reaction could be obtained by following the changes in absorbance at 295 nm. The reaction was considered as having gone to completion when the value of ϵ_{295} remained constant over a period of two to three days. In most cases this value corresponded to that of $\epsilon_{295}\{[PtCl_4]^{2-}\} = 25$.

The following standard procedure was used for the identification of the organic products of the cyclization reactions: 2 l of one of the solutions obtained as described above was evaporated to dryness on a rotary evaporator. The residue was dried under high vacuum for ca. 12 h and extracted with $CHCl_3$ in a Soxhlet apparatus for ca. 12 h. The extract, after evaporation of the solvent, was dissolved in D_2O and its ^1H and ^{13}C NMR spectra recorded. The values of the parameters obtained were compared with those of the same compounds prepared by independent methods as described above. These solutions were then cooled to 0°C, neutralized with solid NaOH and extracted with ether. The extracts were then analysed by gas chromatography. The identification of the products was done either by combined gas chromatography/mass spectrometry or by comparing retention times of the unknown compound with those of the independently synthesized possible reaction products. When mixtures of compounds were obtained, their relative proportions were also determined by gas chromatography.

The overall yields of products formed were determined by carrying out the standard procedure described above on 1 liter of solution, and then dissolving the organic residue in 1.5 ml D_2O, adding 11.5 mg DSS * and integrating the ^1H NMR spectrum of this solution.

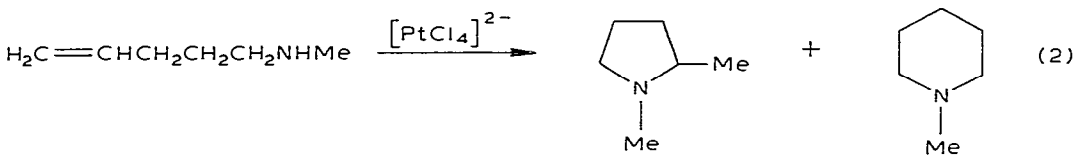
Results

Molecules of the type $CH_2{=}CH(CH_2)_nNH_2$, where n = 3 or 4, cyclize in the presence of $[PtCl_4]^{2-}$ to give five- or six-membered nitrogen heterocycles res-respectively, e.g.,



(1)

N-Substituted amino-olefins, however, give a mixture of five- and six-membered heterocycles, e.g.,



(2)

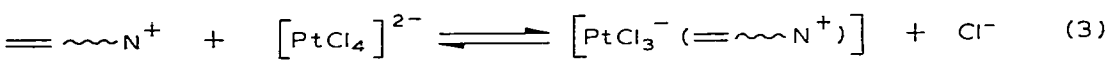
* DSS = 2,2-dimethyl-2-sila-5-pentanesodium sulfalene.

TABLE 1

SUMMARY OF THE PLATINUM-PROMOTED CYCLIZATION REACTIONS

Starting material		Medium	Reaction time (days)	Product(s)	Overall yield (%)	Ratio of products
I	$CH_2=CHCH_2CH_2NH_2$	1	>180	no cyclization		
II	$CH_2=CHCH_2CH_2CH_2NH_2$	1	17			
		2	7	$HN\overline{CH_2CH_2CH_2CHCH_3}$ (IX)	67	
		3	4			
III	$CH_2=CHCH_2CH_2CH_2CH_2NH_2$	1	180			
		2	45	$HN\overline{CH_2CH_2CH_2CH_2CHCH_3}$ (XV)	79	
		3	30			
IV	$CH_2=CHCH_2CH_2CH_2NHCH_3$	2	7	$CH_3N\overline{CH_2CH_2CH_2CHCH_3}$ (X) $CH_3N\overline{CH_2CH_2CH_2CH_2CH_2}$	87	88 12
V	$CH_2=CHCH_2CH_2CH_2NHC_3H_7$-n	2	8	n-$C_3H_7N\overline{CH_2CH_2CH_2CHCH_3}$ (XI) n-$C_3H_7N\overline{CH_2CH_2CH_2CH_2CH_2}$	83	81 19
VI	$CH_2=CHCH_2CH_2CH_2NHC_3H_7$-iso	2	19	iso-$C_3H_7N\overline{CH_2CH_2CH_2CHCH_3}$ (XII) iso-$C_3H_7N\overline{CH_2CH_2CH_2CH_2CH_2}$	75	69 31
VII	$CH_2=CHCH_2CH_2CH_2N(CH_3)_2$	2	27	$(CH_3)_2N\overline{CH_2CH_2CH_2CHCH_3}^+$ (XIII) $(CH_3)_2N\overline{CH_2CH_2CH_2CH_2CH_2}^+$ (XIV)	not det.	50 50
VIII	$CH_2=CHCH_2CH_2CH_2N(CH_3)_3^+Cl^-$	1	>180	no cyclization		

This type of reaction does not occur when $CH_2{=}CHCH_2CH_2NH_2$ or $CH_2{=}CHCH_2CH_2CH_2NMe_3^+$ are used. In these cases, if sufficient chloride and acid are present, no further changes occur once equilibria of the type shown in eq. 3



(3)

have been established.

The amino-olefins used, the products obtained and the reaction conditions and times employed are summarized in Table 1.

As can be seen from Table 1, the speed of the cyclization reaction is strongly dependent on the total chloride concentration. Furthermore, the presence of some additional chloride ion and of an acidic medium are required to prevent the separation of metallic platinum.

The data given in Table 1 also show that: (1) the cyclization reaction is slowed down by the presence of bulky substituents on the nitrogen atom; (2) the relative amount of six-membered heterocycles increases with the bulk of the *N*-substituent.

This reaction can be carried out in a cyclic manner, i.e., further addition of amino-olefin to a solution in which a cyclization reaction has gone to completion, starts a new reaction cycle. Up to three such cycles have been carried out.

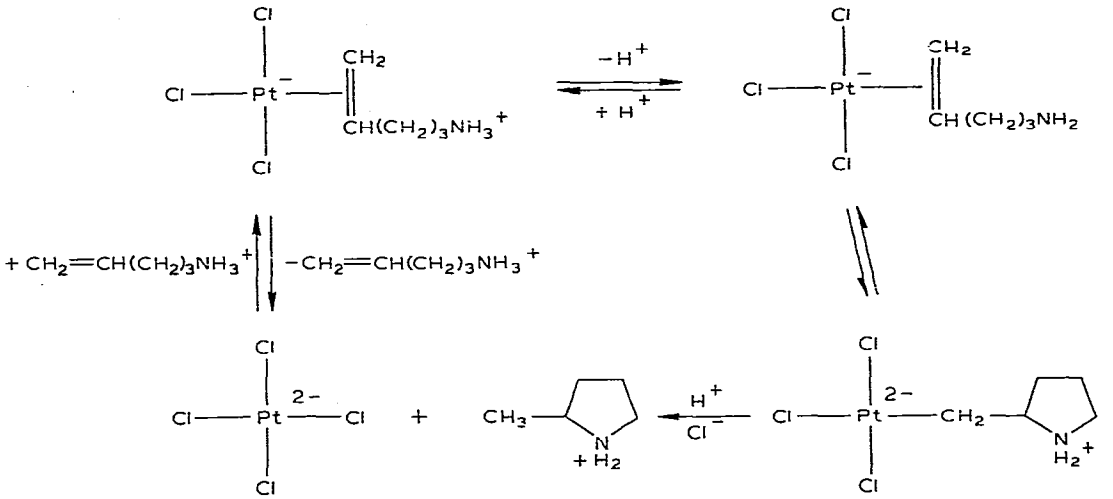
When the cyclization reaction was carried out in the presence of an excess of $CH_2{=}CH(CH_2)_3NH_2$, e.g., with $[PtCl_4]^{2-}$: amino-olefin ratios of 1/10 in Medium 1 or of 1/5 in Medium 3, the normal product, 2-methylpyrrolidine (IX) was accompanied by two by-products, A and B. The three products were found in the ratios 90/4/6 and 42/19/39 respectively. Gaschromatographic separation of the above mixtures and subsequent identification of the by-products by ^1H, ^{13}C NMR and MS spectroscopy showed A and B to be the *cis*- and *trans*-pent-3-enylammonium chlorides respectively. These assignments were confirmed by independent synthesis of the two amino olefins and by comparing their NMR spectra with those of the two by-products. Solutions containing these olefins in Media 1 to 3 show a typical UV absorbance indicating the presence of olefin complexes, i.e., these amino-olefins, after their formation, give rise to equilibria of type 3 without undergoing further reaction.

Discussion

The mechanism of the cyclization reaction is given in Scheme 1. All the postulated steps are well-documented [3], the novel feature being the formation of $[PtCl_4]^{2-}$ at the end of a cycle thus making this reaction potentially catalytic. While several cycles can be conducted, the slow to very slow rates of the cyclization reaction, as carried out at present, do not allow its synthetic exploitation as it would not represent a significant improvement over existing stoichiometric processes.

It is interesting to note that 5- and 6-membered heterocycles are obtained from the $CH_2{=}CH(CH_2)_3NHR$ derivatives in the presence of $[PtCl_4]^{2-}$ whereas only the pyrrolidine was found by Perie et al. [11] using $HgCl_2$ as reagent. As the formation of six-membered rings has not been observed in the latter case and since we found the size of the group R to be an important factor

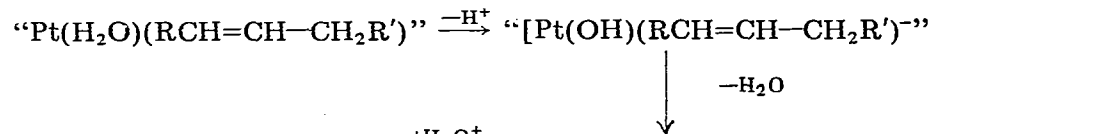
SCHEME 1



one could suppose that steric effects may play a more important role in the platinum series than in the analogous mercury complexes. It should be pointed out here, however, that the formation of six-membered rings has also been reported by Perie et al. [11] in the case of amino-olefins containing C-substituents either at the double bond or in α-position to the nitrogen atom. Our studies of the cyclization reactions of amino-olefins of this type will be reported in a later publication.

Finally, it is worthy of note that but-3-enyl amine does cyclize in the presence of mercuric salts giving pyrrolidine [11] while this reaction is not observed in the presence of $[PtCl_4]^{2-}$.

The double bond migration observed is not caused by the presence of acid as it does not occur in the absence of the metal. This reaction, however, is of frequent occurrence in organometallic chemistry [21]. A number of possible mechanisms have been postulated involving the formation of σ-alkyl [22], π-allyl [22], or carbene [23] intermediates. Our observation that the most extensive double bond migration occurs in the presence of an excess of amine and at low chloride concentration suggests that π-allyl intermediates may be involved according to:



Studies designed to extend the scope of this reaction are currently underway.

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