[3,3]-SIGMATROPIC REACTIONS IN THE ENAMINE SERIES*

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Thermal isomerization of 1-methyl-2-(3-butenylidene)pyrrolidine (*Ib*) afforded a mixture of *Ib* and 1,2-dimethyl-3-allyl-2-pyrroline (*IIIa*). Analogous reaction with 1-methyl-2-(3-butenyl)-2-piperidine (*IIa*) gave quantitatively 1,2-dimethyl-3-allyl-2-piperideine (*IVa*) by [3,3]-sigmatropic rearrangement.

The best studied reactions of enamines are reactions with electrophilic reagents and reactions of enamine salts with nucleophiles. Cycloaddition reactions of enamines represent a special category. On the otherhand, only a few rearrangements have been observed[1].

In one of our previous communications we studied the isomerization of quaternary salts of enamines in order to decide whether their alkylation at the β-carbon atom is a direct C-alkylation reaction or an N-alkylation followed by isomerization to the C-alkyl product[2]. The reaction can be classified as a [1,3]-sigmatropic rearrangement. This paper concerns [3,3]-sigmatropic reaction of the heterocyclic enamines *I* and *II* which contain a 1,5-hexadiene system. The best known example of such reaction is the Cope reaction[3] or the „aza-Cope" rearrangement of ammonium or iminium salts[4]. The starting compounds, *i.e.* 1-methyl-2-(3-butenyl)-2-pyrroline (*I*) and 1-methyl-2-(3-butenyl)-2-piperideine (*II*), were prepared by reaction of 3-butenylmagnesium bromide with the corresponding lactams[5].

The obtained unsaturated bases can exist in two tautomeric forms, differing in position of the double bond. Lukeš and coworkers[6] analyzed the IR-spectra of unsaturated bases containing five-membered ring and assigned the maxima at 1 632 cm^{-1} and 1 677 cm^{-1} to the endocyclic and exocyclic double bond, respectively. These authors proved that most of the tertiary bases, described in the literature as 1-methyl-2-alkyl-2-pyrrolines, are in fact 1-methyl-2-alkylidenepyrrolidines, except 1,2-dimethyl-2-pyrroline which has an endocyclic double bond. Analogous compounds with six-membered ring were studied by Červinka[7]. He found that in the region of C=C stretching vibrations 1-methyl-2-alkyl-2-piperideines have only one band at

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1 635 – 1 645 cm^{-1}. Since the position of double bond absorption maxima depends on the ring size, we can assume that the maximum at 1 635 – 1 645 cm^{-1} is due to the vibration of the double bond in the six-membered ring. Similar conclusions were derived also from the ^1H NMR spectra of these compounds[8].

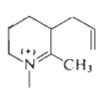
In accord with the literature[6,7], analysis of IR and ^1H NMR spectra has shown that in the five-membered ring series the tautomeric equilibrium mixture contains about 10% of 1-methyl-2-(3-butenyl)-2-pyrroline (*Ia*), the equilibrium being shifted to the

Ia *Ib*

IIa *IIb*

IIIa *IIIb*

IVa *IVb*



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side of *cis*- and *trans*-1-methyl-2-butenylidenepyrrolidine (*Ib*). On the contrary, in the six-membered ring series the compound *II* exists exclusively as 1-methyl-2-(3-butenyl)-2-piperideine (*IIa*), as indicated by the only band at 1 640 cm^{-1} in the IR spectrum.

The rearrangement of both bases *I* and *II* was performed by heating in a sealed ampoule at 220–245°C which was the optimal temperature, whereas at 280°C a profound degradation of the starting compounds took place. According to the spectral analysis, the isomerization mixture contained compounds *I* and *III*.

We prepared the expected isomerization product *III* by reaction of methylmagnesium iodide with 1-methyl-3-allyl-2-pyrrolidone which in turn was obtained by alkylation of 1-methyl-2-pyrrolidone. Infrared spectrum of the compound *III* exhibits bands at 1 638 cm^{-1} *I* (endocyclic double bond) and 1 674 cm^{-1} (exocyclic double bond) in the approximate integrated intensity ratio 2 : 1. Its ^{1}H NMR spectrum displays a singlet at 1·64 ppm which was assigned to the $C_{(2)}$ methyl protons of *IIIa*. In accord with the IR spectra, the ratio of the integrated intensity of the methyl signal to that of the olefinic proton signals shows that also the structure *IIIb* with an exocyclic double bond contributes to the compound *III*. The spectrum also has a singlet at 3·45 ppm which is obviously due to the exomethylene olefinic protons. A similar singlet of an exomethylene group was found by Booth and collaborators[9] in the spectrum of 3,3-diallyl-1-methyl-2-methylenepyrrolidine. The singlet at 2·46 ppm was ascribed to the N-methyl protons of the endo derivative, the weaker singlet at 2·64 ppm to the methyl protons of the exo derivative.

The ^{1}H NMR spectrum of thermal isomerization products contained several signals ascribable to the base *III*. The most characteristic was the singlet at 1·64 ppm which is absent in the spectrum of the starting pyrrolidine and which can be ascribed to the $C_{(2)}$ methyl protons. The spectrum further contained signals of both the N-methyl groups at 2·46 and 2·64 ppm and a singlet at 2·57 due to the unrearranged product.

The incomplete isomerization in the five-membered series can be explained by dominant population of the tautomer *IIb* with the exocyclic double bond. This is in accord with the fact that in a concerted thermal isomerization a double bond shift, combined with the [1,3]-sigmatropic shift of the hydrogen, represents a prohibited reaction.

On the other hand, the exclusive presence of the endocyclic double bond in the piperidine derivative *II* favours the rearrangement. Since in the expected rearrangement product a similar tautomeric equilibrium between the endocyclic and exocyclic forms *IVa* and *IVb* can exist, we converted the isomerization products into their perchlorates. Both the tautomeric bases afford the same perchlorate *V* which simplifies the analysis. Rearrangement of the compound *II* afforded almost quantitatively the isomeric base *IV*. Although the melting points of the perchlorates of the starting and resulting compound were almost the same (104°C and 105°C), their

mixture showed a considerable depression in the melting point (a 1 : 1 mixture melted at 69°C). The ^{1}H NMR spectrum of perchlorate of the isomerization product exhibits a new singlet at 2·48 ppm which can be ascribed to the methyl at $C_{(2)}$. Because of simplicity of the spectra it was possible to assign also other signals to the corresponding carbon atoms. The results are summarized in Table I.

The attempted photoisomerization of compound *I* afforded only the starting compound. According to the Woodward–Hoffmann rules,we can predict that a thermal [3,3]-sigmatropic isomerization will be an allowed reaction (suprafacial or antarafacial) for both fragments. The photochemical reaction, however, will be prohibited since the transition state geometry is unfavourable (suprafacial for one fragment and antarafacial for the other, so that one of the fragments should be in the excited state). Our results confirm this assumption.

EXPERIMENTAL

The melting points and boiling points are uncorrected. ^{1}H NMR spectra were taken on Varian XL-100 and 200 instruments, IR spectra on a Perkin–Elmer 325 spectrometer and mass spectra

TABLE I

Signal assignments for the ^{1}H NMR spectra of perchlorates of *II* and *IV*

Chemical shift	Multiplicity	*J*, Hz	Assignment
	Perchlorate of *II*		
1·88	m	20	3-CH_2, 4-CH_2
2·46	m	11	10-CH_2
2·86	t	8	5-CH_2 + 7-CH_2
3·55	s	—	1-CH_3
3·80	t	6	2-CH_2
5·16	m	10	8-CH_2
5·90	m	23	9-CH
	Perchlorate of *IV*		
1·88	m	20	3-CH_2 + 4-CH_2
2·48	s	—	7-CH_3
2·85	m	20	5-CH + 8-CH_2
3·53	s	—	1-CH_3
3·78	t	5	2-CH_2
5·17	m	11	10-CH_2
5·86	m	23	9-CH

on an AEI-MS 902 instrument. Analytical samples were dried *in vacuo* (oil pump) at room temperature for 8 h.

1-Methyl-2-(3-butenylidene)pyrrolidine (*Ib*)

A solution of 3-butenyl bromide[10] (b.p. 97·5–98·5°C; 27 g; 0·2 mol) in ether (100 ml) was added dropwise during 2 h to magnesium (6 g; 247 mmol), activated with iodine vapours. After refluxing for 2 h, a solution of 1-methyl-2-piperidone (10 g; 100 mmol) in ether (20 ml) was added dropwise, the mixture was boiled for 4 h, set aside for 12 h at room temperature and poured on ice. Barium hydroxide octahydrate (80 g) was added and the base steam-distilled and neutralized with 0·4M-$HClO_4$, yielding 8·4 g (35·3H) of the perchlorate, m.p. 93–96°C, which was crystallized three times from ethanol. For $C_9H_{16}ClNO_4$ (237·7) calculated: 45·48% C, 6·79% H, 5·89% N; found: 45·51% C, 6·91% H, 5·91% N. ^{1}H NMR spectrum (100 MHz, C^2HCl_3, δ, ppm): 2·39 m, 2·84 m, 3·24 t, J = 16 Hz, 3·49 s, 4·26 t, J = 16 Hz, 5·13 m, J = 18 Hz, 5·83 m. The perchlorate was treated with aqueous sodium hydroxide, the base taken up into ether and dried over potassium hydroxide; b.p. 60–61°C/2·0 kPa. ^{1}H NMR spectrum (200 MHz, $C_6^2H_6$, δ, ppm): 1·50 m, 2·27 t, 2·42 s, 2·72 t, 2·86 m, 4·07; 5·14 m, 5·99 m; ^{1}H NMR spectrum (100 Hz, C^2HCl_3, δ, ppm): 1·82 m, 2·44 t, 2·57 s, 3·00 t, 5·82 m, 4·95 m. The mother liquors afforded 1-methyl-2-,2-bis(3-butenyl)pyrrolidine, isolated as its picrate, m.p. 96–99°C. For $C_{19}H_{26}N_4O_7$ (422·4) calculated: 54·02% C, 6·20% H, 13·26% N; found: 54·05% C, 6·49% H, 13·37% N.

1,2-Dimethyl-3-allyl-2-pyrroline (*IIIa*)

Methyl iodide (38·5 g; 270 mmol) in ether (100 ml) was added dropwise to magnesium turnings (6·6 g; 270 mmol) and the mixture was boiled for 1 h and cooled. A solution of 3-allyl-1-methyl-2-pyrrolidone (12·2 g; 90 mmol; b.p. 108–110°C/2·0 kPa; prepared from 1-methyl-2-pyrrolidone and allyl bromide in the presence of sodium amide) in ether (45 ml) was added. The mixture was set aside for 3 days at room temperature, decomposed by pouring on ice (150 g) and after addition of $Ba(OH)_2$. 8 H_2O (80 g) the base was steam-distilled. The distillate was titrated with 1M-$HClO_4$, taken down and the perchlorate (8·0 g; 34%) crystallized three times from ethanol, m.p. 109 to 111°C. For $C_9H_{16}ClNO_4$ (237·7) calculated: 45·58% C, 6·79% H, 5·89% N; found: 45·23% C, 6·63% H, 6·01% N. The base was liberated from the perchlorate with aqueous sodium hydroxide, extracted with ether and dried over solid potassium hydroxide. After evaporation of ether the base was distilled, b.p. 60–62°C/2·0 kPa. For $C_9H_{15}N$ (137·2) calculated: 78·77% C, 11·02% H, 10·21% N; found: 78·63% C, 10·79% H, 10·58% N. ^{1}H NMR spectrum (200 MHz, C^2HCl_3, δ, ppm): 1·64 s, 2·26 t, J = 16 Hz, 2·46 s, 2·64 s, 2·75 d, J = 6 Hz, 2·9 t, J = 18 Hz, 3·45 s, 5·01 m, 5·75 m. IR spectrum (CCl_4): 1 638 cm^{-1}, 1 674 cm^{-1}.

Thermal Isomerization of *Ib*

The base *Ib* (0·25 g) was heated in a sealed ampoule to 220°C for 6 h and the product was distilled; b.p. 60–62°C/2 kPa. ^{1}H NMR spectrum (100 MHz, C^2HCl_3, δ, ppm): 1·64 s, 2·46 s, 2·67 s, 2·63 s, 5·01 m, 5·76 m.

1-Methyl-2-(3-butenyl)-2-piperideine (*IIa*)

A solution of 1-methyl-2-piperidone (13·3 g) in ether (30 ml) was added to a boiling solution of Grignard reagent prepared from magnesium (8 g) and 3-butenyl bromide (36 g) in ether (130 ml). After boiling for 4 h the mixture was set aside at room temperature for 14 h, decomposed with ice (160 g) and treated with $Ba(OH)_2$. 8 H_2O (107 g). The base was steam-distilled and neutralized

with 4M-$HClO_4$. Evaporation and crystallization from ethanol gave 9 g (30%) of the perchlorate, m.p. 105·5°C. For $C_{10}H_{18}ClNO_4$ (251·7) calculated: 47·71H C, 7·16% H, 5·57% N; found: 47·73% C, 7·43% H, 5·77% N. The base was liberated from the perchlorate with aqueous sodium hydroxide, taken up into ether and dried with solid potassium hydroxide. The solvent was evaporated and the product distilled, b.p. 66·5°C/1·3 kPa.

1,2-Dimethyl-3-allyl-2-piperideine *IVa*)

The base *IIa* (0·8 g) was heated in a sealed ampoule to 240—250°C for 4·5 h. The product was distilled (b.p. 64·5°C/1·3 kPa), neutralized with 1M-$HClO_4$ and the perchlorate crystallized from ethanol; m.p. 105°C. For $C_{10}H_{18}ClNO_4$ (251·5) calculated: 47·71% C, 7·16% H, 5·57% N; found: 47·32% C, 7·56% H, 5·49% N.

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