OXIDATION OF AZACYCLOALKANES

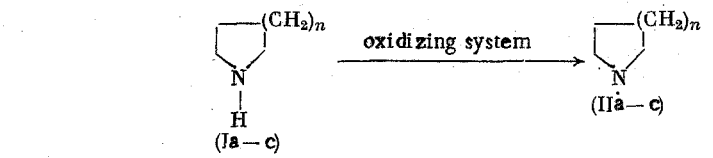
É. I. Troyanskii, V. A. Ioffe, and G. I. Nikishin

UDC 542.943.7:547.335.2:547.495.281.5

Recent studies of the free-radical reactions of organic amines have thrown considerable light on the kinetic and mechanistic aspects of these processes, established the structures of the N-centered aminium cation-radicals and aminyl radicals (and the α-aminoalkyl radicals isomeric with these), and led to the formulation of certain relationships between the reactivity and structure of these unstable species [1, 2].

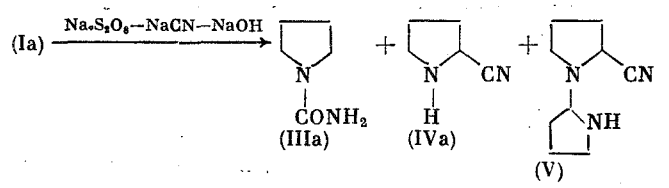
Much less attention has been devoted to investigations of the chemical reactions of organic amines, especially of the aliphatic and alicyclic series, in redox systems as a means of modifying functional groups and the carbon skeleton.

Continuing studies of the one-electron oxidation of primary and secondary aliphatic amines [3-6], we have examined the reaction of secondary amines, viz., the azacycloalkanes (Ia-c), and the cycloaminyl radicals (IIa-c) generated therefrom in the sodium peroxydisulfate–NaCN–NaOH, potassium ferricyanide–NaOH, and $Na_2S_2O_8$–$AgNO_3$–NaOH systems:

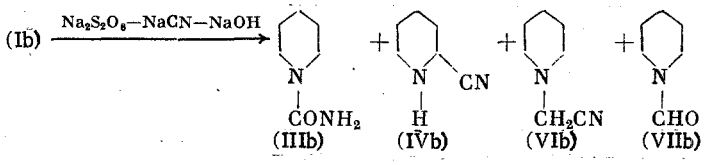


The $Na_2S_2O_8$–NaCN system constitutes a novel reagent, which permits the efficient oxidative N-cyanation of primary and secondary aliphatic amines. Several features relate the ability of these amines to undergo oxidative cyanation to their structures and the reaction conditions [5, 6].

On treatment with this system using equimolar amounts of the substrate, $Na_2S_2O_8$, and NaCN in water at 70-75°C, pyrrolidine (Ia) is converted into N,N-tetramethyleneurea (IIIa), 2-cyanopyrrolidine (IVa), and 2-cyano-1-(pyrrolidin-2-yl)pyrrolidine (V) in yields of 4, 10, and 4% on (Ia) taken, 85% conversion. Also isolated was 17% [calculated on (Ia) consumed] of resinous material with a mean molecular weight of 1100.



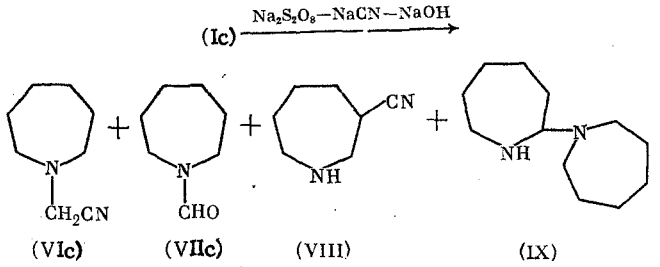
Under similar conditions, piperidine (Ib) gives N,N-pentamethyleneurea (IIIb), 2-cyanopiperidine (IVb), N-(cyanomethyl)piperidine (VIb), and N-formylpiperidine (VIIb) in yields of 3, 28, 11, and 2% on (Ib) taken, conversion 84%:



N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow.
Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 11, pp. 2537-2546, November, 1985. Original article submitted August 3, 1984.

0568-5230/85/3411-2351$09.50

Oxidation of perhydroazepine (Ic) affords N-(cyanomethyl)perhydroazepine (VIc), N-formylperhydroazepine (VIIb), 3-cyanoperhydroazepine (VIII), and 2-(perhydroazepino)perhydroazepine (IX) in yields of 10, 4, 10, and 6% on (Ic) taken, conversion 80%. Also isolated were two fractions of resinous material with mean molecular weights of 680 and 810, in yields of 12 and 18% [on (Ic) consumed].

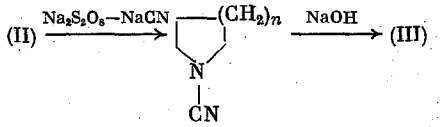


Control experiments showed that on heating the highly volatile and extremely water-soluble compounds (Ia-c) with equimolar amounts of NaCN and NaOH in the absence of the oxidant $Na_2S_2O_8$, 30% of (Ia), 55% of (Ib), and 75% of (Ic) were recovered from the reaction mixture, and compounds (III)-(IX) were not formed.

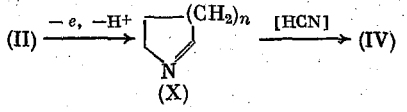
These results show that all these amines undergo oxidative N-cyanation to give ureas (IIIa, b) from amines (Ia, b); C-cyanation of the heterocyclic ring to give (IV) and (V) from (Ia) or (IVb) and (VIII) from (Ib) and (Ic), respectively, and in the case of the azacycloalkanes (Ib, c) N-cyanomethylation and N-formylation also occurred to give (VIb, c) and (VIIb, c).

We believe that the composition of the reaction products is in accordance with the intermediate generation by one-electron oxidation of (Ia-c) of the nitrogen-centered cycloaminyl radicals (IIa-c). Three principal types of reaction are displayed by these radicals.

1) Oxidative N-cyanation to give cyanamides, which undergo further hydrolysis to ureas (III) (this reaction has been the subject of close examination [5, 6]):

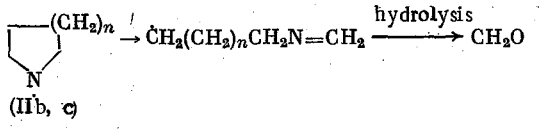


2) Oxidative deprotonation to Δ^1-azacycloalkenes (X), which are then hydrocyanated under the reaction conditions to give (IV):

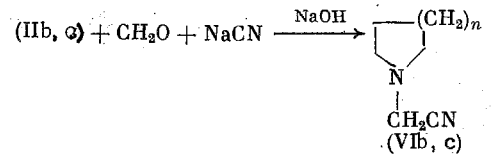


In this case (Xa) is also the most likely precursor of (V), which is apparently formed by nucleophilic addition of (IVa) to (Xa). Similar nucleophilic addition of (Ic) to (Xc) gives the N–C dimer (IX).

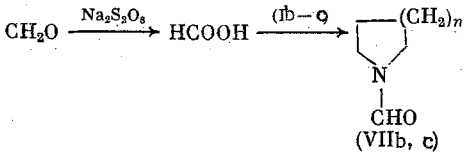
3) β-Fragmentation of (IIb, c) with opening of the ring, followed by hydrolysis to formaldehyde:



Subsequent Strecker cyanomethylation or formylation of the original (Ib, c) affords the N-cyanomethyl derivatives (VIb, c):

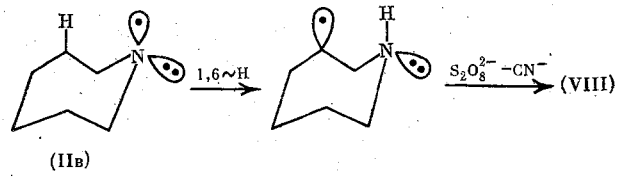


and N-formyl derivatives (VIIb, c):



A separate experiment showed that (Ib, c) underwent cyanomethylation on treatment with CH_2O and NaCN in the presence of base.

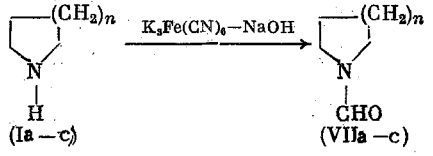
The conformational features of the aminyl radical (IIc) appear to favor its isomerization with 1,6-migration of hydrogen to the perhydroazepin-3-yl radical, which on subsequent oxidative cyanation gives (VIII).



It follows from the product ratios that the principal course of the reaction of cyclic aminyl radicals in the $Na_2S_2O_8$—NaCN—NaOH system is oxidative deprotonation to the intermediate Δ^1-azacycloalkenes (X). The extent of β-fragmentation with ring opening in (II) is somewhat greater in (IIc) than (IIb), but such behavior is not characteristic of (IIa). In contrast to alkyl- and dialkylamines, azacycloalkanes (I) undergo oxidative cyanation to only a small extent, the yields of ureas (III) decreasing as the amounts of the competing β-fragmentation products increase. In all likelihood, it is β-fragmentation with ring opening which is responsible for the marked differences in the chemical behavior of the cycloaminyl radicals (II) and their acyclic analogs, dialkylaminyl radicals [5].

The β-fragmentation of cyclic alkoxyl [7, 8] and oxacycloalkyl radicals [9] with cleavage of the hydrocarbon or heterocyclic ring has been examined in detail, but no such investigations have previously been carried out into cyclic aminyl radicals. There has only been a report of the oxidation of 1,4-diazabicyclo[2.2.2]octane to piperazine on treatment with ClO_2, followed by extensive oxidation during the course of the reaction to give ammonia and formaldehyde [10].

β-Fragmentation of the cycloaminyl radicals (IIa-c) also occurs in other oxidative systems. For example, treatment of the azacycloalkanes (Ia-c) with $K_3Fe(CN)_6$ in the presence of base, taking equimolar amounts of substrate, oxidant, and sodium hydroxide at 70-75°C gives the N-formyl derivatives (VIIa-c) (Table 1):



The formaldehyde formed by β-fragmentation of the cycloaminyl radicals (IIa-c) followed by hydrolysis as described above is oxidized under the reaction conditions to formic acid, which then acylates the original (Ia-c).

TABLE 1. Oxidation of Azacycloalkanes (Ia-c) in the $K_3Fe(CN)_6$–NaOH System [70-75°C, 7 h, 100 mmoles amine (I)]

Azacycloalkane	Ratio (I):$K_3Fe(CN)_6$			
	1:1		1:2	
	amount of recovered (I), %	yield of (VII) on (I) consumed, %	amount of recovered (I), %	yield of (VII) on (I) consumed, %
(Ia)	35	8	27	8
(Ib)	57	3	37	4
(Ic)	48	5	37	7

*100 mmoles $K_3Fe(CN)_6 \cdot 3H_2O$, 100 moles NaOH, 120 ml water.
†200 moles $K_3Fe(CN)_6 \cdot 3H_2O$, 200 mmoles NaOH, 220 ml water.

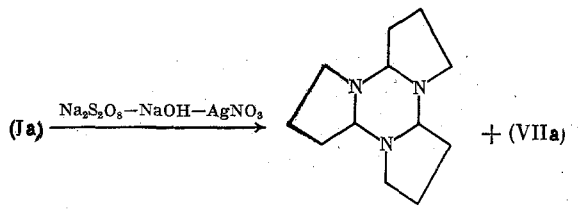
The formation of (VII) directly from (I) and formaldehyde by oxidative formylation is unlikely, since reaction of (Ib) with formaldehyde in the presence of $K_3Fe(CN)_6$ in the presence of base gives mainly the products of the Strecker reaction, viz., N-cyanomethylpiperidine (VIb) (40%) and N-(hydroxymethyl)piperidine (XI) (30%), (VIIb) being obtained as a by-product only (10%).

According to the stoichiometry of the reaction, the formation of 1 mole of the N-formyl derivative (VIIa-c) requires at least 2 moles of the oxidant, $K_3Fe(CN)_6$. In fact, when two equivalents of $K_3Fe(CN)_6$ are used in the oxidation of (Ia-c), the amounts of recovered amines (Ia-c) are reduced (Table 1).

The considerable differences between the yields of (VIIa-c) and the amounts of (Ia-c) consumed appear to be due, in the absence of any other identifiable products, to incomplete extraction of unreacted substrate, as shown above, these substrates being miscible with water in all proportions [11, 12], and to the instability of (VII) under the reaction conditions. On heating with sodium hydroxide, (VIIc) obtained by direct synthesis is hydrolyzed to the extent of 17% to (Ic), 78% of the (VIIc) being recovered unchanged from the reaction mixture. In basic solution, in the presence of $K_3Fe(CN)_6$, the N-formyl derivatives are highly labile, and the conversion of (VIIb) is 75% (see the Experimental section).

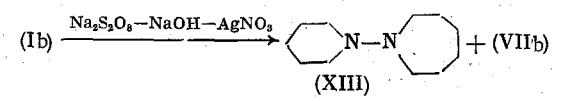
Oxidative cleavage of (Ia-c) to give (VIIa-c) is also brought about by $Na_2S_2O_8$ in basic media in the presence of catalytic amounts of $AgNO_3$. It has previously been shown that in the presence of this system, (Ia) is converted into a trimer of 1-pyrroline, viz., perhydrotris(pyrrolo[1,2-a]:[1,2-c][1,2-e])-1,3,5-triazine (XII) [13], and (Ib) affords 1,1'-bipiperidine (XIII) together with trace amounts (<2%) of 2,3,4,5-tetrahydropyridine [14].

We have found that on oxidation with one equivalent of $Na_2S_2O_8$, two equivalents of sodium hydroxide, and 0.5 mole% of silver nitrate at 0°C, (Ia) gave, in addition to 48% of (XII), 4% of (VIIa):



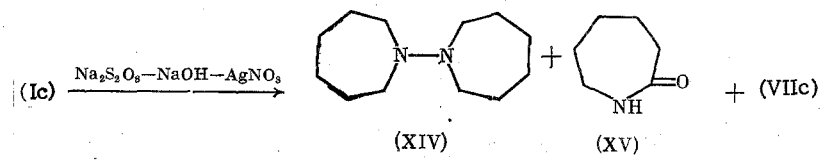
(XII)

and (Ib) afforded 50% of (XIII) and 4% of (VIIb):



(XIII)

Under similar conditions, oxidation of (Ic) gave N,N'-bis(perhydroazepine) (XIV), caprolactam (XV), and N-formylperhydroazepine (VIIc) in yields of 16, 20, and 9% on (Ic) taken, conversion 85%, together with resinous material [15% by weight on (Ic) taken]:



(XIV) (XV)

Most likely, (XIV) and (XIII) are formed by the Ag^+-ion catalyzed dimerization of the cyclic aminyl radicals (IIc) and (IIb). The ability of Ag^+ ions to induce dimerization of alkyl radicals is well known [15].

The lactam (XV) is evidently formed by oxidation of the perhydrazepin-2-yl radical, which is isomeric with the radical (IIc) (cf. [16]).

Hence, oxidative fragmentation with cleavage of the heterocyclic ring is a characteristic region of the cycloaminyl radicals (II) in redox systems.

The structures of (IIIa, b), (VIb, c), (VIIa-c), and (XV) were confirmed by comparison with authentic specimens and by their spectra. The structures of (IVa, b), (V), (VIII), (IX), (XI), (XIII), and (XIV) were established by their spectral data. The absence amongst the region products of N,N-hexamethyleneurea (IIIc) was shown by the use of an authentic sample. The presence of a cyano group at C^3 in (VIII) was shown by the presence in the PMR spectrum (250 MHz) of a doublet of doublets at 2.55 ppm, and the absence of a signal for NHCN in the region 2.90-4.10 ppm. The spectral properties of (XII) were similar to those described in [13].

EXPERIMENTAL

GLC analyses were carried out on an LKhM-8MD chromatograph with a flame ionization detector in a stream of nitrogen; stainless steel columns: 300 × 0.4 cm with 10% Carbowax 20M, 3% Na_3PO_4, and 0.5% NaOH in Celite-545 (52-60 mesh); 300 × 0.4 cm with 2% DS-550 on Chromosorb G (60-80 mesh) treated with Me_2SiCl_2; and 300 × 0.3 cm with 5% PEGS on Chromosorb P-AW (120-140 mesh) treated with Me_2SiCl_2. PMR spectra of solutions in $CDCl_3$ or $(CD_3)_2SO$ were obtained on Varian DA-60LL (60 MHz), Tesla BS-497 (100 MHz), and Bruker WM-250 (250 MHz) spectrometers, using TMS as the internal standard. ^{13}C NMR spectra of solutions in $CDCl_3$ were obtained on a Bruker WM-250 (62.5 MHz) spectrometer, and mass spectra on a Varian MAT CH-6, with direct introduction of the sample into the ion source and an ionizing-electron energy of 70 eV. GC—MS analyses were carried out on a Varian MAT CH111 instrument with a chromatograph sample inlet, using an ionizing-electron energy of 80 eV. IR spectra were recorded on Specord 75-IR and UR-20 instruments in chloroform or KBr disks. Molecular masses were measured on an EP-75 precision ebulliograph (Special Design Bureau, Institute of Organic Chemistry).

The oxidant $Na_2S_2O_8$ was chemically pure grade, and the $K_3Fe(CN)_6$ was pure for analysis; NaOH and NaCN (chemically pure grade) and $AgNO_3$ (pure for analysis) were used without further purification. The amines (Ia-c) were purified by distillation at atmospheric pressure under argon. Organic solvents (pure grade) were used without further purification, and the water was once-distilled.

Oxidation of Azacycloalkanes (Ia-c) in the $Na_2S_2O_8$—NaCN—NaOH System. To a mixture of 100 mmoles of the amine (I), 100 mmoles of NaCN, and 100 mmoles of NaOH in 50 ml of water at 70°C was added over 1.5 h with vigorous stirring a solution of 100 mmoles of $Na_2S_2O_8$ in 50 ml of water. Stirring was continued for 3 h at the same temperature, then the mixture was cooled.

In the oxidation of pyrrolidine (Ia), the mixture was extracted with 3 × 100 ml of ether, followed by 3 × 100 ml of chloroform. The extracts were dried and evaporated (they were not combined). GLC and PMR showed the presence in the ether extract of 15 mmoles (15%) of unreacted (Ia), 10 mmoles (10%) of 2-cyanopyrrolidine (IVa), and 2 mmoles (4%) of 2-cyano-1-(pyrrolidin-2-yl)pyrrolidine (V). Evaporation of the chloroform extract gave 4 mmoles (4%) of N,N-tetramethylurea (IIIa) and 17% (by weight) of resinous material (mol. wt. 1100).

The reaction mixture from the oxidation of piperidine (Ib) was extracted with 3 × 100 ml of ether, and the extract dried and evaporated. GLC and PMR of the residue showed the presence of 16 mmoles (16%) of unreacted (Ib), 5.5 mmoles (11%) of N-cyanomethylpiperidine (VIb), 28 mmoles (28%) of 2-cyanopiperidine (IVb), and 1 mmole (2%) of 1-formylpiperidine (VIIb). Following evaporation, 1.5 mmoles (3%) of N,N-pentamethyleneurea (IIIb) was obtained. In the oxidation of perhydroazapine (Ic), the mixture was extracted with 3 × 100 ml of ether followed by 3 × 100 ml of chloroform. The extracts were dried and evaporated (they were not combined). The ether extract contained 20 mmoles (20%) of unreacted (Ic), 5 mmoles (10%) of N-cyanomethylperhydroazepine (VIc), 2 mmoles (4%) of N-formylperhydroazepine (VIIc), 10 mmoles (10%) of

TABLE 2. Physicochemical Characteristics of Reaction Products from Azacycloalkanes

Compound	mp, °C, or bp, °C (p, mm Hg)	IR spectrum, ν, cm^{-1}	PMR spectrum, δ, ppm	Mass spectrum, m/z (rel. intensity, %)
N,N-Tetramethyleneurea (IIIa)	218	3500, 3400, 3350, 3210, 1670, 1655, 1580	1,65 m (4H), 3,40 m (4H), 5,30 br.s (2H)	114(60), 86(72), 70(100), 56(25), 55(30), 44(90), 43(95), 42(50), 41(71)
N,N-Pentamethyleneurea (IIIb)	105	3400, 3200, 1660, 1600, 1500	1,55 m (6H), 3,30 m (4H), 5,30 br.s (2H)	128(55), 113(34), 100(5), 99(19), 84(100), 70(62), 57(77), 56(69), 55(44), 44(83), 43(65), 42(50), 41(65)
N,N-Hexamethyleneurea (IIIc)	122	3450, 3200 1665, 1610, 1500	1,55 m (8H), 3,35 m (4H), 5,30 br.s (2H)	142 M$^+$
2-Cyanopyrrolidine (IVa)		2230	1,80 m(3H), 2,10 m 2H), 3,10 m(2H), (2H), 4,05 d.d (1H)	96 M$^+$
2-Cyanopiperidine (IVb)*		2225	1,55 m (4H), 1,80 m (2H), 2,00 br.s (1H), 2,80 m (2H), 3,95 d.d (1H)	110 M$^+$
2-Cyano-1-pyrrolidin-2-yl)-pyrrolidine (V)		2230	1,55 m(8H), 1,80m (4H), 2,00 b.s (1H), 3,40m (1H), 4,05 d.d (1H)	166 [M+1]$^+$, 165 M$^+$
N-Cyanomethylpiperidine (VIb)*	85–87(12)	2205	1,50 m (6H), 2,40 m (4H), 3,40 s (2H)	124(21), 123(100), 113(47), 112(14), 98(57), 96(33), 85(34), 84(88), 83(44), 82(38), 57(58), 56(93), 55(60)
N-Cyanomethylperhydroazepine (VIc)	75–76(6)	2210	1,50m (8H), 2,45 m (4H), 3,45 s (2H)	138(31), 137(26), 112(100), 109(63), 98(74), 96(56), 84(58), 83(79), 82(68), 70(74), 69(79)
N-Formylpyrrolidine (VIIa)	87–89(16)	1665	1,80m (4H), 3,45 m (4H), 8,05 s (1H)	99(90), 71(75), 70(37), 44(35), 43(100), 42(55), 41(37)
N-Formylpiperidine (VIIb)	110–111(20)	1670	1,60 m (6H), 3,30 m (4H), 8,05 s(1H)	113(100), 112(46), 98(42), 84(75), 79(38), 56(83), 55(50), 52(33), 42(71), 41(50)
N-Formylperhydroazepine (VIIc)	127–130(25)	1675	1,55 m(8H), 3,40 m (4H), 8,05 s (1H)	127(87), 112(100), 99(16), 98(48), 84(45), 71(39), 70(52), 56(74), 55(42)
3-Cyanoperhydroazepine (VIII)		2225	1,45 m (7H), 2,40 m (2H), 2,55 d.d. (2H), 2,70 m (1H)	124(45), 123(100), 109(2), 96(38), 83(72), 82(26), 69(8), 68(10) 67(10), 56(8), 55(7)
2-(perhydroazepino)perhydroazepine (IX)			1,50m (17H), 2,40m (6H), 3,15m (1H)	196(45), 181(4), 167(10), 153(15), 140(26), 139(46), 127(20), 125(24), 113(86), 98(70), 70(100), 69(90), 68(80)
N-(Hydroxymethyl)piperidine (XI)			1,50m (6H), 1,60m (4H), 4,20 s (2H), 4,70 s (1H)	
1-Pyrroline trimer (XII)			1,9 m (12H), 2,4 m (3H), 3,1m (6H) (as in [13])	

TABLE 2 (Continued)

N,N'-Bipiperidine (XII)	100–105(15)		1,45 m (12H), 2,60 m (8H)	168(94), 139(40), 126(97), 125(76), 113(45), 112(25), 111(38), 99(71), 84(100), 83(97)
N,N'-Bis(perhydroazepine (XIV)			1,50 m (16H), 2,65m (6H)	196(25), 181(2), 167(10), 153(10), 140(26), 139(46), 138(40), 124(35), 112(46), 98(70), 70(100)
Caprolactam (XV)		3300, 3220, 3075, 1660	1,90m (6H), 2,40 m (2H), 3,15m (2H) 7,90 m(1H)	113(47), 85(32), 84(35), 67(8), 56(55), 55(81), 42(45), 30(100) (as in [17])

*^{13}C NMR spectra (δ, ppm): (VIb); 22.6 (C^4), 24.9 (C^3 and C^5), 52.8 (C^2 and C^6), 45.9 (C–CN): 114.6 (CN); (IVb): 21.2 (C^5), 25.0 (C^4), 28.8 (C^3), 43.1 (C^6), 46.4 (C^2), 119.7 (CN).

3-cyanoperhydroazepine (VIII), and 3 mmoles (6%) of 2-(perhydroazepine)perhydroazepine (IX). The evaporated chloroform extract was dissolved in a 1:1 mixture of ether and chloroform. Evaporation of this solution gave 12% (by weight) of resinous products (mol. wt. 680). The insoluble residue was dissolved in chloroform, and the solution evaporated to give 18% (by weight) of resinous products (mol. wt. 810).

The physicochemical properties of the reaction products are given in Table 2.

Behavior of Azacycloalkanes (Ia-c) in the NaCN–NaOH System. (control experiment). A mixture of 100 mmoles of the amine (Ia-c), 100 mmoles of NaOH, and 100 mmoles of NaCN in 100 ml of water was stirred vigorously for 4 h at 70°C. The mixture was then cooled, extracted with ether, and the extract dried and evaporated. GLC was used to determine the amounts of (Ia-c) recovered (30, 55, and 75%, respectively).

Oxidation of Azacycloalkanes (Ia-c) in the $K_3Fe(CN)_6$–NaOH System. To a mixture of 100 mmoles of the amine (Ia-c) and a solution of 100 mmoles of NaOH in 20 ml of water was added with vigorous stirring at 70°C a solution 100 (or 200) mmoles of $K_3Fe(CN)_6 \cdot 3H_2O$ in 100 (or 200) ml of water over a period of 2 h. Stirring was continued at the same temperature for a further 5 h, then the mixture was cooled and extracted with 4 × 100 ml of ether. The ether extract was dried over $MgSO_4$ and evaporated. The residue was analyzed by GLC, and the oxidation product [N-formyl derivatives (VIIa-c)] isolated by distillation. The compositions of the reaction mixtures are given in Table 1, and the properties and spectral data for (VIIa-c) in Table 2.

Reaction of Piperidine (Ib) with Formaldehyde and the $K_3Fe(CN)_6$–NaOH System. a) To a mixture of 100 mmoles of (Ib), a solution of 100 mmoles of NaOH in 20 ml of water, and 100 mmoles of 40% formaldehyde was added with vigorous stirring at 70°C a solution of 100 mmoles of $K_3Fe(CN)_6 \cdot 3H_2O$ over a period of 2 h. The mixture was stirred for a further 5 h at this temperature, then cooled and extracted with ether. The extract was dried and evaporated. GLC of the residue showed the presence of 10 mmoles (10%) of N-formylpiperidine (VIIb), 40 mmoles (40%) of N-cyanomethylpiperidine (VIb), and 30 mmoles of N-(hydroxymethyl)piperidine (XI).

b) To a mixture of 100 mmoles of (Ib) and a solution of 100 mmoles of NaOH in 20 ml of water was added with vigorous stirring at 70°C over 2 h simultaneously from two dropping funnels 100 mmoles of 40% formaldehyde and a solution of 100 mmoles of $K_3Fe(CN)_6 \cdot 2H_2O$ in 100 ml of water. The mixture was stirred for a further 5 h at this temperature, then cooled and extracted with ether, and the extract dried and evaporated. GLC of the residue showed the presence of 90 mmoles (90%) of N-cyanomethylpiperidine (VIb) and 5 mmoles (5%) of N-formylpiperidine (VIIb).

Behavior of N-Formylperhydroazepine (VIIc) in Alkali. A mixture of 50 mmoles of (VIIc) and 50 mmoles of NaOH in 50 ml of water was stirred for 7 h at 70°C, cooled, and extracted with 4 × 50 ml of ether. GLC of the evaporated extract showed the presence of 39 mmoles (78%) of unreacted (VIIc) and 8.5 mmoles (17%) of perhydroazepine (Ic).

Behavior of N-Formylpiperidine (VIIb) in the $K_3Fe(CN)_6$—NaOH System. To a mixture of 50 mmoles of N-formylpiperidine (VIIb) and a solution of 50 mmoles of NaOH in 10 ml of water was added over 2 h with vigorous stirring at 70°C a solution of 50 mmoles of $K_3Fe(CN)_6 \cdot 3H_2O$ in 50 ml of water. The mixture was stirred for a further 5 h at this temperature, cooled, and extracted with 4 × 50 ml of ether. The extract was dried over $MgSO_4$ and evaporated. GLC of the residue showed the presence of 12.5 mmoles (25%) of unreacted (VIIb).

Oxidation of Azacycloalkanes (Ia-c) in the $Na_2S_2O_8$—NaOH—$AgNO_3$ System. To a mixture of 100 mmoles of the amine (Ia-c), 200 mmoles of NaOH, and 0.5 mmole of $AgNO_3$ in 100 ml of water was added at 0°C with vigorous stirring 100 mmoles of $Na_2S_2O_8$ in 75 ml of water, at such a rate that the temperature did not exceed 5°C. The mixture was then stirred for a further 2.5 h at 0°C, and warmed to ~20°C.

The reaction mixture from the oxidation of (Ia) was extracted with 3 × 100 ml of dichloromethane, and the extract dried and evaporated in the cold under reduced pressure, GLC of the residue showed the presence of 16 mmoles (48%) of the tripyrroline (XII) and 2 mmoles (4%) of N-formylpyrrolidine (VIIa).

The reaction mixture from the oxidation of (Ib) was saturated with NaCl and extracted with 3 × 100 ml of ether, and the extract dried and evaporated. GLC of the residue showed the presence of 30 mmoles (60%) of N,N'-bipiperidine (XIII) and 2 mmoles (4%) of N-formylpiperidine (VIIb). Distillation gave 25 mmoles (50%) of (XIII).

The reaction mixture from the oxidation of (Ic) was extracted with 3 × 100 ml of dichloromethane, and the extract dried, saturated with gaseous HCl, and washed with water. The organic layer was separated, dried, and evaporated. GLC of the residue showed the presence of 4.5 mmoles (9%) of (VIIc). The aqueous layer was basified with NaOH and extracted with ether to give 1.5 g of resinous products. The ether extract was dried and evaporated. According to GLC and PMR, the residue contained 14 mmoles (14%) of unreacted (Ic) and 8 mmoles (16%) of N,N'-bis(perhydroazepine) (XIV). The aqueous layer, after extraction with ether, was further extracted with dichloromethane, and the extract dried and evaporated to give 20 mmoles (20%) of caprolactam (XV).

The ureas (IIIa-c) were synthesized directly from the amines (Ia-c) by reaction with urea [18].

Synthesis of N-Cyanomethylpiperidine (VIb) and N-Cyanomethylperhydroazepine (VIc). To a mixture of 100 mmoles of NaCN in 30 ml of water was added with stirring over 1 h at 25°C 100 mmoles of 40% formaldehyde. The mixture was stirred for 2 h at 50°C, cooled, extracted with 3 × 100 ml of ether, the extract dried, evaporated, and distilled to give (VIb, c). Yields 85-90%.

The direct synthesis of the N-formylazacycloalkanes (VIIa-c) was effected by reacting the amines (Ia-c) with formic acid as described in [19].

CONCLUSIONS

1. The azacycloalkanes $HNCH_2(CH_2)_nCH_2CH_2$ (n = 1-3), on treatment with the $Na_2S_2O_8$—NaCN—NaOH system, undergo the competing reactions of N-cyanation to give the ureas, C-cyanation to give 2-cyanoazacycloalkanes, and β-fragmentation to give N-cyanomethyl- and N-formylazacycloalkanes. The relative proportions of these three competing reactions depend on the size of the ring.

2. Oxidative β-fragmentation of azacycloalkanes also occurs in the $K_3Fe(CN)_6$—NaOH and $Na_2S_2O_8$—$AgNO_3$—NaOH systems.

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HYDROHALOGENATION OF 1-VINYLPYRAZOLES

L. A. Es'kova, V. K. Voronov,
E. S. Domnina, and G. G. Skvortsova*

UDC 542.944.5:547.772

In relation to structure, the reaction of hydrogen halides with vinylazoles having several concurrent nucleophilic centers occurs in different directions. Vinyl derivatives of imidazoles and triazoles form hydrohalides with an ionic type of bond, $NH^+...Hal^-$ [1, 2]. 1-Vinyl-2-(vinyloxymethylimidazole adds HCl at the double bond of the O-vinyl group and at the N^3 atom with retention of the N-vinyl group [3]. Unlike in the case of 1-vinylimidazoles, in relation to temperature the addition of hydrogen halides to 1-vinylindazole occurs at the N^2 atom or at the double bond of the vinyl group [4]. Polymeric charge-transfer complexes are formed in hydrohalogenation of N-vinylindole [5].

In the present paper, we investigated hydrohalogenation of a series of vinylpyrazoles in relation to their structure and the nature of the hydrogen halide. For this purpose, we used 1-vinylpyrazole (I), 4-bromo-1-vinylpyrazole (II), 3-methyl-1-vinylpyrazole (III), 5-methyl-1-vinylpyrazole (IV), 3,5-dimethyl-1-vinylpyrazole (V), and 4-nitro-3,5-dimethyl-1-vinylpyrazole (VI). Reactions with HCl and HBr were carried out in CCl_4 or ether at different temperatures.

Between −15 and 0°C, vinyl derivatives of all the investigated pyrazoles formed only the corresponding hydrohalides, white hygroscopic crystals. The hydrohalides of the less basic vinylpyrazoles (I), (II), and (VI) decomposed rapidly. The characteristics of the isolated salts are given in Table 1. The IR spectra of these compounds contained wide absorption bands with a maximum in the range of 2540-2700 cm^{-1}, which were due to stretching vibrations of the ammonium cation $\rangle NH^+$ [6]. Spectroscopic manifestation of donor–acceptor interaction of 1-vinyl- and 1-ethylpyrazoles with HCl (IR and UV spectra) was considered by us previously [6].

In the PMR spectra of the 1-vinylpyrazole hydrohalides (Table 2), there was a weak-field shift of signals of the protons of the ring (especially H^3) and the vinyl group. The values of constants $^2J_{AB}$ decreased significantly. These data indicate that donor–acceptor interaction between the N^2 atom and hydrogen halides led to significant change of the electronic state in the entire vinylpyrazole molecule. For methyl-substituted vinylpyrazoles the changes of the spectral parameters were more significant than for (I) and (II), which could be a consequence of strengthening of $n-\sigma$ interaction with increasing basicity.

*Deceased.

Irkutsk Institute of Organic Chemistry, Siberian Branch, Academy of Sciences of the USSR.
Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 11, pp. 2546-2549, November, 1985. Original article submitted June 18, 1984.

0568-5230/85/3411-2359$09.50