REACTIONS OF 3-IMIDAZOLINES WITH DIBORANE AND SODIUM BOROHYDRIDE

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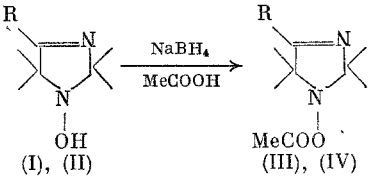
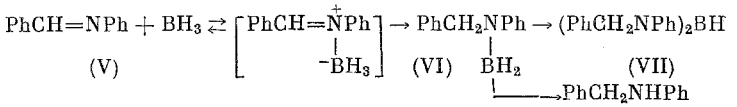
It has previously been shown [1, 2] that in 3-imidazolines it is possible to introduce various substituents at the alkyl group at position 4 because of the activating effect of the imino group. In our work we have studied the reaction of 3-imidazolines with nascent diborane and also the mode of activation of the C=N bond of the heterocycle towards addition of hydride ion with the aim of obtaining imidazolidine derivatives as precursors of nitroxyl radicals.

By analogy, with iminium salts [1] it might be expected that the protonated imino group could be reduced by $NaBH_4$. However, on treatment of 3-imidazolines (I and II) with $NaBH_4$ in the presence of acetic acid, the C=N bond was not reduced and only the products of O-acylation were produced.



R = Me (I), (III); Ph (II), (IV).

According to [3], benzalaniline (V) forms the adduct (VI) with diborane which is cleaved by methanol to N-benzylaniline. Upon standing, VI disproportionates to VII, treatment of which with methanol also gives N-benzylaniline.



Upon treatment of imidazoline (I) with nascent diborane there is formed VIII with elemental analytical data corresponding to the adduct of I with BH_3. Bands are observed in the infrared spectrum of VIII at 2285, 2300, and 2390 cm^{-1} characteristic of the B–H bond [3] and at 1665 cm^{-1} for νC=N. The shift in the C=N band when compared with the starting imidazoline (1645 cm^{-1} [4]) is the same as when going from 3-imidazoline derivatives to imidazolinium salts [1]. In the PMR spectrum of VIII ($CDCl_3$) there are observed signals at 1.25 (6H) and 1.44 (6H) ppm for the two gem-dimethyl groups, at 2.17 (3H, MeC=N) and 4.88 (1H, OH) ppm. The shift of the MeC=N signal to low field by 0.25 ppm [4] is analogous to that observed in going from imino compounds to their complexes with BF_3 [5]. On the basis of this data, compound VIII has been identified as 1-hydroxy-2,2,4,5,5-pentamethyl-3-imidazoline-3-borane. In analogous conditions adducts XI-XIII are obtained from II, IX, and X. Compounds VIII and XI-XIII are stable at ~20°C and do not have a tendency toward disproportionation.

Thus, reaction of cyclic imines (3-imidazoline derivatives) with diborane leads to formation of adducts in which the molecule of BH_3 is coordinated to the atom of N in the C=N group, but hydroboration is not found to occur in contrast to [3].

Treatment of adducts VIII and XI-XIII with MnO_2 leads to the formation of nitroxyl radicals XIV-XVII. Their monomer structure is indicated by the EPR spectrum in which there is a characteristic nitroxyl monoradical triplet with a hyperfine splitting constant of α_N = 14.0 Oersted. Compounds XIV-XVII are reducing agents and able to convert carbonyl compounds into alcohols. It should also be mentioned that compounds XIV and XV may be obtained by the action

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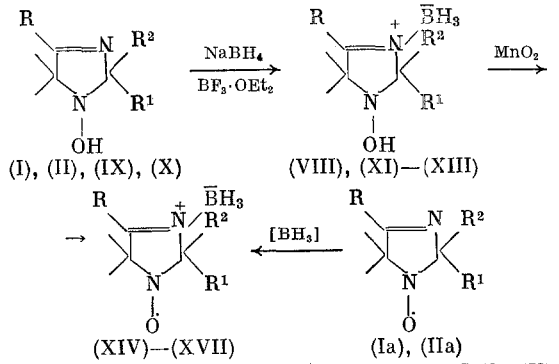
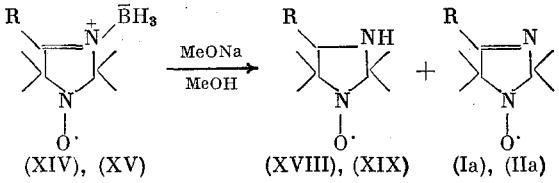


(I), (II), (IX), (X) (VIII), (XI)—(XIII) (XIV)—(XVII) (Ia), (IIa)

$R = R^1 = R^2 = Me$ (I), (Ia), (VIII), (XIV); $R = R^1 = Me$, $R^2 = C_6H_{13}$ (X), (XIII), (XVII); $R = Me$, $R^1 + R^2 = (CH_2)_5$ (IX), (XII), (XVI); $R = Ph$, $R^1 = R^2 = Me$ (II), (IIa), (XI), (XV).

of diborane on radicals Ia and IIa, however, the reaction proceeds less readily in this case. This is probably connected with the lower basicity of the N atom in position 3 of the heterocycle in the paramagnetic imidazoline (compare [6]).

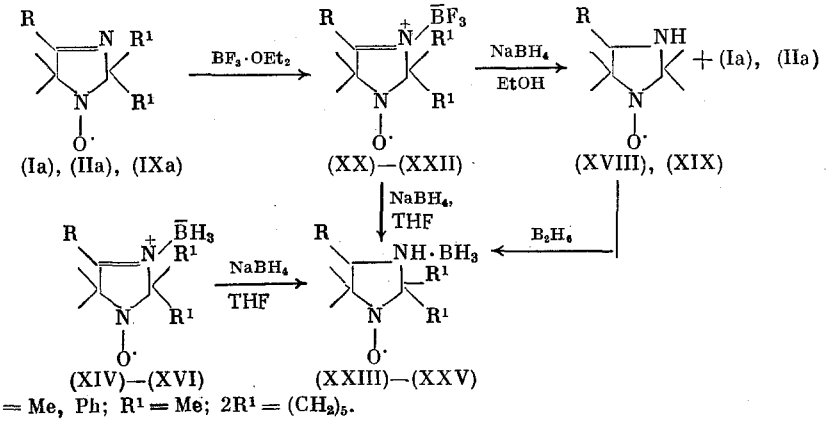
Workup of adducts XIV and XV with methanol in the presence of base leads to reduction of the C=N bond with the formation of imidazolidine derivatives 2,2,4,5,5-pentamethyl (XVIII) and 2,2,5,5-tetramethyl-4-phenylimidazolidin-1-oxyl (XIX). The reaction is accompanied by the splitting off of the BH_3 from the starting adduct to yield the imidazolines Ia and IIa. On carrying out the reaction in the absence of base the reduction of the C=N bond proceeds only to an insignificant degree.



(XIV), (XV) (XVIII), (XIX) (Ia), (IIa)

$R = Me$, Ph.

Another possible activation of the C=N bond in relation to the hydride ion is conversion to the BF_3 adduct. Compounds XX-XXII are formed by the action of BF_3•etherate on the corresponding imidazolinyloxyls. Coordination of BF_3 occurs at the N atom in position 3 of the heterocycle and not at the nitroxyl group as indicated by the triplet in the EPR spectrum (hyperfine splitting α_N = 14.5 Oersted) and the IR spectrum in which the C=N band (1680 cm^{-1} in XX) is the same as for iminium salts of analogous structure (1). Compounds XX-XXII are stable in nonaqueous media, however, they are rapidly hydrolyzed in the presence of traces of water with the formation of the starting imidazolinoxyls. By treating XX and XXI with $NaBH_4$ in ethanol, reduction of the C=N bond occurs with formation of the corresponding imidazolidine derivatives XVIII and XIX. The reaction is complicated by formation of significant quantities of the imidazolinoxyl hydrolysis products Ia and IIa. Upon treatment of XX-XXII with $NaBH_4$ in THF, hydrolysis products are not observed but borane adducts of the corresponding imidazolidines are formed (XXIII-XXV).

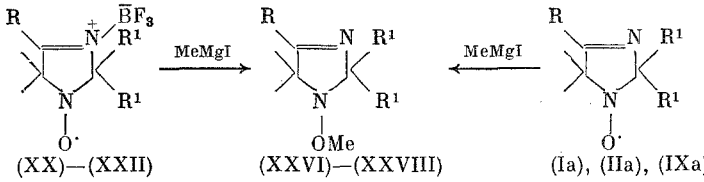


(Ia), (IIa), (IXa) (XX)—(XXII) (XVIII), (XIX) (XIV)—(XVI) (XXIII)—(XXV)

$R = Me$, Ph; $R^1 = Me$; $2R^1 = (CH_2)_5$.

Compounds XXII-XXV are formed by $NaBH_4$ treatment of XIV-XVI under analogous conditions. The structure of these compounds is confirmed by their formation from diborane and the corresponding imidazolidines. The BH_3 molecule in these compounds coordinates at the N atom in position 3 as shown by the EPR spectrum. Thus XXIII shows a triplet with α_N = 15.7 Oersted.

It might be expected that significant polarization of the C=N bond in the borofluorides XX-XXII would lead to easy addition of methylmagnesium iodide as happens in the case of imidazolinium salts [1]. However, treatment of XX-XXII with excess methylmagnesium iodide does not lead to products of addition, but to the corresponding 1-methoxy-3-imidazolines (XXVI-XXVIII)



(XX)—(XXII) (XXVI)—(XXVIII) (Ia), (IIa), (IXa)

$R = R^1 = Me$ (XX), (Ia), (XXVI); $R = Ph$, $R^1 = Me$ (IIa), (XXI), (XXVII); $R = Me$, $2R^1 = (CH_2)_5$ (XXII), (IXa), (XXVIII).

It should also be mentioned that the action of methylmagnesium iodide on imidazolin-1-oxyls (Ia, IIa, IXa) with subsequent oxidation of the reaction mixture by MnO_2 gives the corresponding 1-methoxy derivatives along with starting compounds in approximately equal quantities.

EXPERIMENTAL

IR spectra were recorded on a UR-20 instrument in KBr (concentration 0.25%) and in CCl_4 (concentration 5%). PMR spectra were measured on a Varian A56-60A instrument for 7-10% solutions. Elemental analytical data, melting points and yields of the synthesized compounds are given in Table 1.

1-Acetoxy-2,2,4,5,5-pentamethyl-3-imidazoline (III). Acetic acid (5 ml) was added dropwise to a solution of imidazoline I (1 g) and $NaBH_4$ (1.4 g) in dioxan (45 ml) with stirring, cooling to 0°C, and the mixture allowed to stand for 24 h at ~20°C. The solution was diluted with water, extracted with $CHCl_3$, the extract washed with 5% $NaHCO_3$, and dried ($MgSO_4$). The solution was then evaporated, triturated with hexane, and the solid filtered off. PMR spectrum: (CCl_4, δ, ppm): 1.32s (6H, Me_2C), 1.47s (6H, Me_2C), 1.99s (3H, MeCO), 2.18s (3H, MeC=N).

1-Acetoxy-2,2,5,5-tetramethyl-4-phenyl-3-imidazoline (IV). Obtained analogously from II. PMR spectrum (CCl_4, δ, ppm): 1.32s (6H, Me_2C), 1.47s (6H, Me_2C), 1.99s (3H, MeCO), 7.4m (5H, Ph).

1-Hydroxy-2,2,4,5,5-pentamethyl-3-imidazoline-3-borane (VIII). BF_3 etherate (1.1 ml) was added dropwise to a solution of imidazoline (I, 1 g) and $NaBH_4$ (0.25 g) in dry THF with stirring and cooling to 0°C. Stirring was continued for 1 h at ~20°C, the solution evaporated, diluted with water, and extracted with ether. The extract was dried with $MgSO_4$, evaporated, the residue washed with hexane, and the precipitated compound VIII filtered off. Mol. wt.: found (ebullioscopic in $CHCl_3$) 172; calculated 170.

1-Hydroxy-2,2,5,5-tetramethyl-4-phenyl-3-imidazoline-3-borane (XI). Obtained analogously from imidazoline II. PMR spectrum ($CDCl_3$, δ, ppm): 1.30s (6H, Me_2C), 1.62s (6H, Me_2C), 4.78s (1H, OH), 7.2m (5H, Ph).

1-Hydroxy-4,5,5-trimethyl-2-spirocyclohexan-3-imidazoline-3-borane (XII) and 1-hydroxy-2-hexyl-2,4,5,5-tetramethyl-3-imidazoline-3-borane (XIII) were obtained analogously from IX and X.

2,2,4,5,5-Pentamethyl-3-imidazoline-1-oxyl-3-borane (XIV). A solution of VIII (0.2 g) in dry ether (10 ml) was stirred with MnO_2 (1 g) for 1 h at ~20°C. Excess oxidant was filtered off and the solvent evaporated to give XIV.

2,2,5,5-Tetramethyl-4-phenyl- (XV), 4,5,5-trimethyl-2-spirocyclo hexan- (XVI) and 2-hexyl-2,4,5,5-tetramethyl-3-imidazoline-1-oxyl-3-borane (XVII). Obtained analogously from XI-XIII. Compound XVII was purified chromatographically on a silica gel column with a mixture of ether and hexane (1:3) as eluent.

TABLE 1. Constants for Synthesized Compounds

Compound	Yield, %	mp, °C, (solvent)*	Found/calculated, % C	H	N	Empirical formula	IR spectrum, ν, cm^{-1} (KBr)
(III)	60	71–72 (A)	55,1 / 55,4	9,3 / 9,3	13,1 / 13,0	$C_{10}H_{18}N_2O_2 \cdot H_2O$	1665 (C=N), 1785 (C=O)
(IV)	50	96–97 (A)	65,5 / 65,9	8,1 / 7,9	10,2 / 10,1	$C_{15}H_{20}N_2O_2 \cdot H_2O$	1665 (C=N), 1785 (C=O)
(VIII)	70	130–132 (B)	56,5 / 56,5	11,2 / 11,2	16,8 / 16,5	$C_8H_{16}N_2O \cdot BH_3$	1665 (C=N), 3580 (OH), ($CHCl_3$)
(XI)	45	115–117 (C)	66,9 / 67,2	9,0 / 9,0	11,5 / 11,6	$C_{13}H_{18}N_2O \cdot BH_3$	1620 (C=N), 2285, 2350, 2390 (BH), 3580 (OH), ($CHCl_3$)
(XII)	75	127–128 (B)	62,5 / 62,8	11,0 / 11,0	13,3 / 13,3	$C_{11}H_{20}N_2O \cdot BH_3$	1665 (C=N), 2285, 2330, 2390(BH), 3480 ($CHCl_3$)
(XIV)	90	113–115 (B)	56,7 / 56,9	10,3 / 10,6	17,0 / 16,7	$C_8H_{15}N_2O \cdot BH_3$	1650 (C=N), 2280, 2360, 2390 (BH)
(XV)	90	99–101 (A)	67,8 / 67,6	8,7 / 8,7	12,3 / 12,1	$C_{13}H_{17}N_2O \cdot BH_3$	1635 (C=N)
(XVI)	80	93–95 (A)	62,9 / 63,2	10,4 / 10,5	13,3 / 13,4	$C_{11}H_{19}N_2O \cdot BH_3$	1645 (C=N), 2350, 2380, 2420 (BH)
(XVII)	60	Oil	65,1 / 65,3	11,4 / 11,7	11,5 / 11,7	$C_{13}H_{25}N_2O \cdot BH_3$	1660 (C=N), 2280, 2410 (BH)
(XVIII)	70	Oil	61,0 / 61,2	11,1 / 10,8	17,6 / 17,8	$C_8H_{17}N_2O$	
(XIX)	60	76–78 (A)	71,5 / 71,3	8,7 / 8,7	12,8 / 12,8	$C_{13}H_{19}N_2O$	3300(NH)
(XX)†	75	120–122	43,0 / 43,1	6,5 / 6,7	12,4 / 12,6	$C_8H_{15}N_2O \cdot BF_3$	1680 (C=N)
(XXI)†	85	134–136	54,2 / 54,8	5,8 / 6,0	9,7 / 9,8	$C_{13}H_{17}N_2O \cdot BF_3$	1630 (C=N)
(XXII)†	90	120–122	50,3 / 50,6	7,0 / 7,3	10,4 / 10,7	$C_{11}H_{19}N_2O \cdot BF_3$	1680 (C=N)
(XXIII)	60	100–101 (D)	55,8 / 56,2	11,5 / 11,7	16,0 / 16,4	$C_8H_{17}N_2O \cdot BH_3$	2295, 2350, 2405 (BH) 3190 (NH)
(XXIV)	40	108–109 (C)	67,0 / 67,0	9,7 / 9,4	12,1 / 12,1	$C_{13}H_{19}N_2O \cdot BH_3$	2300, 2350, 2405 (BH) 3190 (NH)
(XXV)	30	102–104 (A)	62,7 / 62,6	11,5 / 11,4	13,6 / 13,3	$C_{11}H_{21}N_2O \cdot BH_3$	2295, 2390, 2415 (BH) 3165 (NH)
(XXVIII)	45	Oil (E)	68,9 / 68,6	10,6 / 10,5	13,2 / 13,3	$C_{12}H_{22}N_2O$	1665 (C=N)

*Solvent for crystallization: A, n-C_6H_{14}; B, $MeCO_2Et$; C, C_6H_6; D, CCl_4; E, purified by distillation.
†Found/Calculated for F, % 26.1/25.6 (XX), 21.0/20.2 (XXI), 22.4/21.9 (XXII).

2,2,4,5,5-Pentamethyl-3-imidazoline-1-oxyl borofluoride (XX). To a solution of Ia (1 g) in 50 ml dry ether was added dropwise with stirring BF_3 etherate (2 ml). The precipitated solid adduct (XX) was filtered off, washed with dry ether, and dried..

2,2,5,5-Tetramethyl-4-phenyl- (XXI) and 4,5,5-trimethyl-2-spirocyclohexan-3-imidazoline-1-oxyl (XXII) borofluorides. Prepared analogously from IIa and XIa.

2,2,4,5,5-Pentamethylimidazolidine-1-oxyl (XVIII) a) A solution of XIV (1.4 g) and MeONa (0.7 g) in dry MeOH (40 ml) was allowed to stand for 12 h at ~20°C and evaporated. Compound XVIII was separated chromatographically on a silica gel column using $CHCl_3$ as the eluent.

b) Compound XX (1 g) was added portionwise to a solution of $NaBH_4$ (0.25 g) in dry ethanol (15 ml) with stirring and cooling to 0°. After 30 min the solution was evaporated and XVIII was obtained by column chromatography on silica gel with $CHCl_3$ eluent.

Imidazolidine XIX was obtained analogously from borofluoride XXI.

2,2,4,5,5-Pentamethylimidazolidine-1-oxyl-3-borane (XXIII). A solution of XIV (0.23 g) in dry THF was stirred with $NaBH_4$ (0.2 g) for 1 h at ~20°C, evaporated, the resulting residue diluted with water, and extracted with $CHCl_3$. The extract was dried with $MgSO_4$, the solution evaporated, the residue washed with hexane, and compound XXIII filtered off.

Analogously from XV and XVI were obtained 2,2,5,5-tetramethyl-4-phenyl-(XXIV) and 4,5,5-trimethyl-2-spirocyclohexanimidazolidine-1-oxyl-3-borane (XXV). Compounds XXIII-XXV could also be obtained starting from borofluorides XX-XXII.

2,2,4,5,5-Pentamethyl-1-methoxy-3-imidazoline (XXVI). Compound XX (1 g) was added portionwise with stirring to a solution of methylmagnesium iodide (obtained from 0.52 g Mg and 2 ml of MeI in 30 ml of dry ether). After stirring for 2 h it was diluted with 20 ml water and the organic layer separated. The aqueous layer was extracted with ether. The ether extracts were dried ($MgSO_4$), evaporated, and XXVI [7] purified by silica gel chromatography using a mixture of ether and hexane (1:1). Yield: 0.35 g (46%).

Analogously from borofluorides XXI and XXII were obtained the methoxy derivative (XXVII) [7] with yield 35% and 4,5,5-trimethyl-1-methoxy-2-spirocyclohexan-3-imidazoline (XXVIII).

CONCLUSIONS

3-Imidazoline derivatives, when treated with $NaBH_4$ in the presence of BF_3 etherate, form adducts with borane, oxidation of which yields stable nitroxyl radicals. On treatment with methanol in the presence of base, the paramagnetic adducts are reduced to the corresponding imidazolidinoxyl derivatives.

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CONVERSION OF 3-IMIDAZOLINE-3-OXIDE NITROXYL RADICALS INTO NITRONYLNITROXYL RADICALS

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Continuing the studies of the effect of the pH of the medium on the EPR spectra of nitroxyl radicals (NR) containing acid-base functional groups at a distance of 2-3 σ-bonds from the radical center [1-4], we have examined the EPR spectra of NR (I) and (II), which contain OH groups in the 2-position of the heterocycle (formula, following page, below figure)

It is assumed that deprotonation of the OH group is accompanied by changes in the hfc constant a_N^1 and the g-factor, as for example, in the case of the radical (III) [5], as well as in radicals containing other groups [2-4]. At pH values ≥12, however, the EPR spectra of aqueous solutions of radicals (I) and (II) undergo irreversible changes from a triplet to a more complex multiplet, similar to the spectra of nitronylnitroxyl radicals (NNR) (Figs. 1

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