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A NOVEL HETEROCYCLIC SYSTEM—2,4-DIAZABICYCLO[1.1.0]BUTANE

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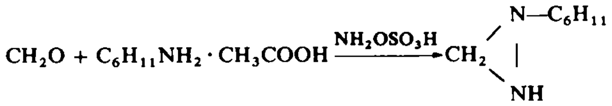
Abstract—A novel class of organic compounds are reported—2,4-diazabicyclo[1.1.0]butanes, formed by a previously unknown reaction between formaldehyde, a primary aliphatic amine, and hydroxylamine-O-sulphonic acid.

REACTION of formaldehyde and a primary aliphatic amine with aminating agents—chloramine or hydroxylamine-O-sulphonic acid—was first studied by Schmitz *et al.*[1,2]

Hexahydrotriazines are shown by the authors[2] to be the reaction products when chloroamine in ether solution is employed. When formaldehyde was reacted with cyclohexylamine acetate and hydroxylamine-O-sulphonic acid in H_2O, 1-cyclohexyldiaziridine was isolated in 4% yield only:[1]

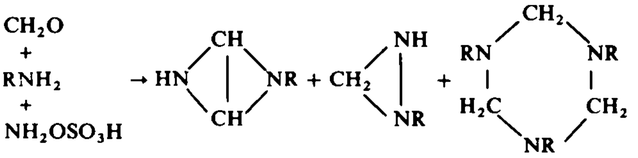


$$CH_2O + C_6H_{11}NH_2 \cdot CH_3COOH \xrightarrow{NH_2OSO_3H} CH_2\left<\begin{matrix} N{-}C_6H_{11} \\ | \\ NH \end{matrix}\right.$$

The composition of other reaction products in both cases was not examined.

In contrast to the above[1] we have reacted the amines instead of their acetates with hydroxylamine-O-sulphonic acid and formaldehyde; the medium remained basic within the limits pH 9·0 to 7·5 (potentiometric measurements).

In this way 2-alkyl-2,4-diazabicyclo[1.1.0]butanes (Ia–d) were obtained, and represent a new class of organic compound; along with them 1-alkyldiaziridines (IIa–d) and, as a rule, traces of hexahydrotriazines (IIIa, c) were produced (yield of IIIb was 7%).



I 22–33%

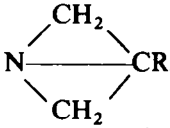
II 11–28%

III traces (7% of IIIb)

Ia, IIa, IIIa $R = iso\text{-}C_3H_7$
Ib, IIb, IIIb $R = n\text{-}C_4H_9$
Ic, IIc, IIIc $R = sec\text{-}C_4H_9$
Id, IId, IIId $R = t\text{-}C_4H_9$

2-Alkyl-2,4-diazabicyclo[1.1.0]butanes are colourless, mobile liquids, readily soluble in organic solvents and H_2O. They decompose rapidly in aqueous acid solution, but give hydrochlorides with gaseous HCl in dry C_6H_6. In aqueous alkaline solution they are quite stable and darken gradually in contact with solid alkali.

2-Alkyl-2,4-diazabicyclo[1.1.0]butanes, (Ia–d), may be regarded as heteroanalogues of bicyclo[1.1.0]butane.

Only one rigorously proved type of azaanalogue of bicyclo[1.1.0]butane, 1-azabicyclo[1.1.0]butane , (R = H, Me, Et, Ph), with a tertiary nitrogen atom, has been previously described.[3,4]

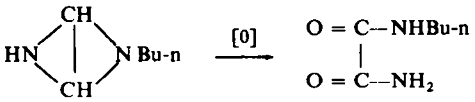
Other heterobicyclobutanes either were not rigorously proved,[5–9] or have been postulated only as intermediate compounds in some reactions.[10–11]

The formation of I indicates a previously unknown reaction course between formaldehyde, a primary aliphatic amine and hydroxylamin-O-sulphonic acid. This process is to be studied further in detail.

2-Alkyl-2,4-diazabicyclo[1.1.0]butanes were registered along with other reaction products (1-alkyldiaziridines, II, and hexahydrotriazines, III) by use of TLC and isolated by fractional distillation. 2-Alkyl-2,4-diazabicyclo[1.1.0]butanes, (Ia–d), R_f 0·62–0·71, gave yellow spots (as in the case of IIIa–c), whereas I-alkyldiaziridines, (IIa–d), R_f 0·53–0·64, gave white spots with a yellow rim when developed in iodine vapour.

The structure of 2-alkyl-2,4-diazabicyclo[1.1.0]butanes has been proven by chemical transformation, as well as by elemental analysis, cryscopy, mass-spectra, IR and NMR.

Oxidation of 2-n-butyl-2,4-diazabicyclo[1.1.0]butane by $KMnO_4$ in an alkaline medium leads to N-butyloxamide a known compound, which unequivocally proves the presence of a C—C bond in the compound in question:



The structure of the N-butyloxamide thus obtained was confirmed by elemental analysis, IR and m.m.p. with an authentic sample, prepared by us by a known method.[12]

Hydrochlorides of I were obtained and characterized. IR spectra of all Ia–d contain absorption bands, specific to secondary amino group in the region of 3345 cm^{-1} (NH stretching vibrations) and of 875 and 760 cm^{-1} (NH in-plane and out-of-plane bending vibrations).

NMR spectra of I at room temperature have proton signals of the corresponding alkyl groups and a singlet at 3·50 ppm which we assigned to both methine groups of the 2,4-diazabicyclo[1.1.0]butane ring. Using 2-isopropyl-2,4-diazabicyclo[1.1.0]-butane, Ia, as an example it was shown that at $-42°$ this singlet splits into a doublet (3·56 and 3·66 ppm), and at 1·72 ppm there appears a broad triplet with the same coupling constant ($J = 8$ cps) and with half as great area. This picture holds to $-32·5°$, but at $-31°$ the doublet and triplet turn into broad singlets. Clearly, the doublet can be assigned to ring methine protons and the triplet—to the proton on nitrogen. The disturbance of the coupling between these two groups of protons above $-31°$ may be explained by increase of NH-group inversion rate similar to the phenomenon in aziridine rings.[13]

The mol. wt of Ia was found by mass spectra and determined cryoscopically in C_6H_6 to be, correspondingly, 98 and 99·6 (calc. 98).

The structure of 1-alkyldiaziridines was confirmed by IR spectra and by elemental analysis of their chloralhydrate derivatives.

EXPERIMENTAL

IR spectra of the compounds obtained were recorded with a UR-10 spectrometer. NMR spectra were taken by Varian DA-60-IL spectrometer.

2-Isopropyl-2,4-diazabicyclo[1.1.0]*butane* (Ia) *and 1-isopropyldiaziridine* (IIa). 33·5% aqueous formaldehyde soln (18·6 ml) was added to a soln of isoptopylamine (40·2 g; 57·5 ml; 0·675 mole) in H_2O (60 ml) at −5–0° and then 96·5% hydroxylamine-O-sulphonic acid (26·4 g; 0·225 mole) added. The mixture was kept at 0° for 1 hr and at ambient for 2 hr, extracted by ether, dried, evaporated, and the residue fractionated to give 2·18 g (11·3%) of IIa and 6·15 g (28·0%) of Ia. 1-Isopropyldiaziridine (IIa), b.p. 107–108°/760 mm, n_D^{23} 1·4218; IR: 3220 cm^{-1}. (Found: C, 55·78; H, 11·72. $C_4H_{10}N_2$ requires: C, 55·79; H, 11·62%). Chloralhydrate derivative, 1-isopropyl-2-(α-hydroxy-β-trichloroethyl) diaziridine, was prepared by adding chloralhydrate (1·06 g; 0·007 mole) to 0·3 g (0·0035 mole) of IIa in 1 ml of H_2O at room temperature. When chilled the product was filtered, 0·87 g (89%); m.p. 126–127° (from aq EtOH). (Found: C, 30·90; H, 4·73; Cl, 45·86. $C_6H_{11}N_2OCl_3$ requires: C, 30·83; H, 4·71; Cl; 45·61%). 2-Isopropyl-2,4-diazabicyclo-[1.1.0]butane (Ia), b.p. 63–63·5°/23 mm; n_D^{20} 1·4282; IR: 3345, 875, 760 cm^{-1}; NMR (CCl_4, room temperature), δ, 6H doublet at 0·817 and 1·08 (gem-dimethyl group), 1H multiplet at 2·99 (in isopropyl group), 2H singlet at 3·49 (ring methine protons); NMR ($CDCl_3$, at $-42°$), 6H doublet at 1·01 and 1·11 (gem-dimethyl group), 1H triplet at 1·72 (NH proton), 1H multiplet at 3·02 (isopropyl CH proton), 2H doublet at 3·56 and 3·66 (ring methine protons); mass spectrum, molecular ion 98·0 (calc. for $C_5H_{10}N_2$ 98·0). (Found: C, 61·32; H, 10·29; N, 28·69. $C_5H_{10}N_2$ requires: C, 61·22; H, 10·20; N, 28·55%). Chlorohydrate of Ia, m.p. 154–156° (decomp). (Found: C, 44·75; H, 8·36; N, 20·61. $C_5H_{11}N_2Cl$ requires: C, 44·61; H, 8·17; N, 20·82%).

2-n-Butyl-2,4-diazabicyclo[1.1.0]*butane* (Ib), *1-n-butyldiaziridine* (IIb), *and 1,3,5-tributyl-1,3,5-hexahydrotriazine* (IIIb). From n-butylamine (131·4 g; 1·8 mole) in H_2O (200 ml), 33·5% aqueous formaldehyde soln (49·6 ml) and 96·3% hydroxylamine-O-sulphonic acid (70·4 g; 0·6 mole) was obtained similarly 9·1 g (15%) of IIb, 19·3 g (29%) of Ib and 4·75 g (7%) of IIIb. 1-n-Butyldiaziridine (IIb), b.p. 54°/23 mm; IR: 3225 cm^{-1}. In view of purification difficulties IIb was analyzed in form of chloralhydrate derivative. 1-n-Butyl-2-(α-hydroxy-β-trichloroethyl) diaziridine, m.p. 76–77° (from aq EtOH). (Found: C, 34·10; H, 5·22; Cl, 42·91. $C_3H_{13}N_2OCl_3$ requires: C, 33·93; H, 5·25; Cl, 43·33%). 2-n-Butyl-2,4-diazabicyclo[1.1.0]butane (Ib), b.p. 94–96°/15 mm; n_D^{20} 1·4346; IR: 3350, 875, 740 cm^{-1}. NMR (CCl_4, room temperature), δ, 3H triplet at 0·91 (Me group), 4H multiplet at 1·43 (two methylene groups), 2H triplet at 2·63 (methylene group at N), 2H singlet at 3·49 (ring methine protons). Chlorohydrate of IIb, m.p. 98·5–99°. (Found: C, 48·20; H, 8·95; Cl, 23·88. $C_6H_{13}N_2Cl$ requires: C, 48·48; H, 8·75; Cl, 23·90%). IIIb, b.p. 155°/20 mm (lit.[13] b.p. 146–149°/12 mm).

2-sec-Butyl-2,4-diazabicyclo[1.1.0]*butane* (Ic) *and 1-sec-butyldiaziridine* (IIc). From sec butylamine (32·15 g; 0·45 mole) in H_2O (60 ml), 33·5% aqueous formaldehyde soln (12·5 ml) and 93·5% hydroxylamine-O-sulphonic acid (18·2 g; 0·15 mole) was obtained 4·24 g (28%) of IIc and 5·5 g (33%) of Ic. 1-sec-Butyldiaziridine (IIc) b.p. 134–135°, 760 mm; n_D^{20} 1·4334; IR: 3220 cm^{-1}. In view of purification difficulties IIc was analyzed in the form of chloralhydrate derivative. 1-sec-Butyl-2-(α-hydroxy-β-trichloroethyl) diaziridine, m.p. 93–94° (from aq EtOH). (Found: C, 33·85; H, 5·51; Cl, 42·87. $C_7H_{13}N_2OCl_3$ requires: C, 33·93; H, 5·25; Cl, 43·33%). 2-sec-Butyl-2,4-diazabicyclo[1.1.0]butane (Ic), b.p. 90–91°/20 mm; n_D^{20} 1·4352; IR: 3350, 875, 760 cm^{-1}. (Found: C, 64·05; H, 10·69; N, 25·13. $C_6H_{12}N_2$ requires: C, 64·28; H, 10·72; N, 25·00%). Chlorohydrate of Ic, m.p. 161–162°. (Found: C, 48·21; H, 8·73; Cl, 23·82. $C_6H_{13}N_2Cl$ requires: C, 48·48; H, 8·75; Cl, 23·90%).

2-tert-Butyl-2,4-diazabicyclo[1.1.0]*butane* (Id) *and 1-t-butyldiaziridine* (IId). From 10·95 g (0·15 mole) of t-*n*-butylamine (10·95 g; 0·15 mole) in H_2O (40 ml), 33·5% aqueous formaldehyde soln (4·17 ml), and 93·5%

hydroxylamine-O-sulphonic acid (6·05 g; 0·05 mole) was obtained 0·6 g (12%) of IId and 1·22 g (22%) of Id. 1-t-Butyldiaziridine (IId), b.p. 30–31°/18 mm (lit.[2] b.p. 31–35°/17 mm), n_D^{20} 1·4310; IR: 3220 cm^{-1}. IId was analyzed in the form of chloralhydrate derivative. 2-t-Butyl-2,4-diazabicyclo[1.1.0]butane (Id), b.p. 87–88°/21 mm; n_D^{20} 1·4348; IR: 3350, 870, 750 cm^{-1}. Chlorohydrate of Id sublimes at 213° without melting. (Found: C, 48·38; H, 8·86; Cl, 23·86. $C_6H_{13}N_2Cl_3$ requires: C, 48·48; H, 8·75; Cl, 23·90%).

Oxidation of 2-n-butyl-2,4-diazabicyclo[1.1.0]*butane* (Ib). Potassium permanganate (5·92 g) in H_2O (70 ml) was added to Ib (3·15 g) at 5–7° with stirring. After 3 hr stirring was stopped and mix left at room temperature overnight. MnO_2 was filtered off and the aqueous soln extracted with ether, dried and evaporated to give N-butyloxamide (0·75 g), m.p. 198° (from H_2O) (lit.[12] m.p. 198–199°). IR: 3400, 3330, 1650, 1560 cm^{-1}. (Found: C, 50·14; H, 8·55; N, 19·62. $C_6H_{12}N_2O_2$ requires: C, 49·98; H, 8·39; N, 19·43%).

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