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(Difluoroamino)methyl derivatives of urea, and difluoroamino-derivatives of imidazolidin-2-ones and 1,2-diamidoethanes were prepared from hydroxy- and alkoxy-derivatives by the action of difluorimide in the presence of strong acid.

WE have described the addition of difluorimide to aldehydes or ketones to give difluoroamino-alcohols,2,3 which condense with urea in the presence of dehydrating agents to form N-(difluoroamino)alkyl derivatives. We have now examined possible alternative routes to NN'bis[(difluoroamino)methyl]urea. A similar product, NN'-bis-(2,2,2-trinitroethyl)urea, is formed by the action of 2,2,2-trinitroethanol on urea 4 and also by the action of trichloronitromethane on NN'-bis-hydroxymethylurea.⁵ NN'-Bis-hydroxymethylurea (I), isolated from the reaction of urea with formaldehyde,⁶ is a possible intermediate in the reaction of urea with (difluoroamino)methanol in the presence of sulphuric acid. We treated the urea derivative (I), in the presence of sulphuric, chlorosulphonic, or fluorosulphonic acid, with difluorimide, and obtained NN'-bis[difluoroamino)methyl]urea (II) in >95% yield.

$$\begin{array}{c} \text{HO} \cdot \text{CH}_2 \cdot \text{NH} \cdot \text{CO} \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{OH} + 2\text{HNF}_2 \xrightarrow{\text{H}_2 \text{SO}_4} \\ (\text{I}) \\ \text{F}_2 \text{N} \cdot \text{CH}_2 \cdot \text{NH} \cdot \text{CO} \cdot \text{NH} \cdot \text{CH}_2 \cdot \text{NF}_2 + 2\text{H}_2 \text{O} \\ (\text{II}) \end{array}$$

Supporting evidence for the direct replacement of hydroxy- or alkoxy-groups (the latter are more stable to acid conditions) by difluorimide was obtained by the conversion of the cyclic urea derivatives 4,5-dihydroxyimidazolidin-2-one (III; $R^1 = R^2 = R^3 = H$) and its 4,5-dimethyl and 4,5-diethyl ethers (III; $R^1 = Me$ or Et, $R^2 = R^3 = H$) into 4,5-bis(difluoroamino)imidazolidin-2-one (IV; $R^4 = R^5 = H$), in ca. 80% yields. 4,5-Dimethoxy-1,3-bis(methoxymethyl)imidazolidin-2-one (III; $R^1 = Me$, $R^2 = R^3 = CH_2 OMe$) was con-

4,5-bis(difluoroamino)-1,3-bis[(difluoroverted into amino)methyl]imidazolidin-2-one (IV; $R^4 = R^5 =$ CH₂·NF₂) in 90% yield, and 1-hydroxymethyl-4,5-dimethoxy-3-(2,2,2-trinitroethyl)imidazolidin-2-one [III; $R^1 = Me$, $R^2 = CH_2 \cdot OH$, $R^3 = CH_3 \cdot C(NO_2)_3$] was converted into 4,5-bis(difluoroamino)-1-[(difluoroamino)methyl]-3-(2,2,2-trinitroethyl)imidazolidin-2-one [IV: $R^4 = CH_2 \cdot NF_2$, $R^5 = CH_2 \cdot C(NO_2)_3$ in 74% yield by the same technique.

The replacement of hydroxy-groups by difluoroaminogroups was extended to other linear compounds with a reactive centre similar to that of the urea derivatives, namely the HO·CH·NH·CO group. 1,2-Diformamidoethane-1,2-diol (V; R = H) and 1,2-bis(trifluoroacetamido)ethane-1,2-diol (V; $R = CF_3$), prepared by the

$$\begin{array}{c|c} R^{1}OCH \cdot NR^{2} & \longrightarrow & F_{2}N \cdot CH \cdot NR^{4} \\ \hline CO + 2HNF_{2} & \longrightarrow & F_{2}N \cdot CH \cdot NR^{4} \\ R^{1}OCH \cdot NR^{3} & & (III) \\ (III) & & (IV) \\ R^{1} = H, Me, \text{ or Et} \\ R^{2} = H, CH_{2} \cdot OMe, \text{ or } CH_{2} \cdot OH \\ R^{3} = H, CH_{2} \cdot OMe, \text{ or } CH_{2} \cdot C(NO_{2})_{3} \\ R^{4} = H \text{ or } CH_{2} \cdot NF_{2} \\ R^{5} = H \text{ or } CH_{2} \cdot NF_{2} \end{array}$$

addition of glyoxal to the appropriate amides, gave the corresponding 1,2-bis(difluoroamino)-1,2-diamidoethane derivatives.

$$(\text{HO·CH·NH·CO·R})_2 + 2\text{HNF}_2 \longrightarrow \\ (V) \qquad (F_2 N \cdot \dot{\text{CH·NH·CO·R}})_2 + 2\text{ROH} \\ (VI) \qquad (VI) \\ R = \text{H or } CF_3$$

The ¹⁹F n.m.r. spectrum of 4,5-bis(difluoroamino)imidazolidin-2-one in acetone showed a doublet centred at -31.6 p.p.m. (J 18 Hz, NF₂·CH). The ¹H n.m.r. spectrum of the compound in acetone showed a triplet centred at $\tau 4.39$ (J 18 Hz, CH·NF₂) and a broad peak at τ 2.12 (NH). The ¹⁹F n.m.r. spectrum of 4,5-bis-(difluoroamino)-1,3-bis[(difluoroamino)methyl]imidazolidin-2-one in carbon tetrachloride showed signals at -30.5 (d, J 18 Hz, NF₂·CH) and -43.2 (t, J 24 Hz, NF2·CH2) p.p.m. (ratio 1:1); its ¹H n.m.r. spectrum (carbon tetrachloride) was complex, showing fifteen peaks in the region $\tau 4.15 - 5.72$.

4,5-Bis(difluoroamino)-1-(difluoroamino)methyl-19F 3-(2,2,2-trinitroethyl)imidazolidin-2-one showed n.m.r. signals (deuteriochloroform) at -28.8 (d, J 21 Hz, 5-NF₂), -31.0 (d, J 21 Hz, 4-NF₂), and -43.6 (t, J 24 Hz, NF₂·CH₂) p.p.m. (ratio 1 : 1 : 1). The ¹H n.m.r. spectrum (deuteriochloroform) was complex, showing sixteen peaks in the region $\tau 4.03 - 5.68$.

EXPERIMENTAL

Molecular weights were determined ebullioscopically for solutions in acetone. Liquid products were purified until they gave a single peak on a Griffin and George D6 gas chromatograph (20% Embaphase silicone oil on Celite). I.r. spectra were determined with Perkin-Elmer Infracord

¹ Part II, A. H. Dinwoodie, J. A. Gibson, and J. B. Parker, preceding paper. ² Part I, A. C. Currie, A. H. Dinwoodie, G. Fort, J. A. Gibson,

J. Grigor, J. B. Parker, and J. Peters, J. Chem. Soc. (C), 1970, 1104.

³ J. P. Freeman, W. H. Graham, C. O. Parker, J. Amer. Chem. Soc., 1968, 90, 121.
⁴ R. Schenck and G. Wetterholm, B.P. 729,469/1955.
⁵ P. O. Tawney, U.S.P. 3,097,239/1963.
⁶ G. Walter, B.P. 284,272/1928.

137 or 337 spectrophotometers. N.m.r. spectra were determined with a Perkin-Elmer R10 instrument at $33\cdot5^{\circ}$ and at 60 or $56\cdot458$ Hz far ¹H and ¹⁹F, respectively, with tetramethylsilane or trichlorofluoromethane as internal standard.

CAUTION. The compounds described are explosive, and should be handled with care.

Difluorimide Apparatus and General Method.—Aqueous difluorourea 7 (5%; 200 ml.) and sulphuric acid (2N; 100 ml.) were placed in a flask fitted with a nitrogen inlet and an outlet leading through drying tubes containing phosphorus pentoxide and sodium fluoride to a cold-finger condenser (-80°). A receiver with a small tap-funnel attached was placed below the cold-finger condenser, and the upper exit from the condenser was fitted with a device to prevent air re-entering the apparatus.

The compound (0.5 g.) to be treated with difluorimide was placed in the receiver, an inert diluent such as dichloromethane (10 ml.) was added in many cases, and the whole apparatus was flushed with nitrogen for 30 min. Difluorimide (*ca.* 4 g., 75 mmoles) was then generated by heating the flask containing the acidified aqueous difluorourea in a water-bath at 90—100° and was trapped in the receiver. The receiver rapidly cooled to -23° . Sulphuric (96—98%), chlorosulphonic, or fluorosulphonic acid (3 ml.) was then added dropwise, and difluorimide generation was continued for a further 1—4 hr.

The excess of difluorimide was removed by allowing the condenser to warm to $15-20^{\circ}$ and flushing the apparatus with nitrogen; the difluorimide was either destroyed by bubbling the gas stream into acidified aqueous potassium iodide solution, or vented into an efficient fume cupboard. The mixture remaining was poured into an excess of icewater, and the difluoroamino-substituted compound was obtained either by filtration of the diluted mixture, or by extraction with dichloromethane and diethyl ether.

NN-Bis-hydroxymethylurea, with difluorimide in the presence of sulphuric, fluorosulphonic, or chlorosulphonic

⁷ V. Grakauskas, Abstracts of the 140th Meeting of the American Chemical Society, Sept. 1961, p. 23M; B.P. 960,126/1964.

acid, gave NN-bis[(difluoroamino)methyl]urea (95–98%), m.p. 162° (decomp.) (from chloroform) (lit.,² 162°) (Found: C, 18.7; H, 3.1; F, 39.6; N, 29.2. Calc. for $C_3H_6F_4N_4O$: C, 18.9; H, 3.2: F, 40.0: N, 29.5%).

4,5-Dihydroxyimidazolidin-2-one gave 4,5-bis(difluoroamino)imidazolidin-2-one (78%), m.p. 172—173° (from benzene) (lit.,² 172—173°) (Found: C, 19·4; H, 1·9; F, 39·9; N, 29·8. Calc. for $C_3H_4F_4N_4O$: C, 19·2; H, 2·1; F, 40·4; N, 29·8%).

4,5-Dimethoxyimidazolidin-2-one gave 4,5-bis(difluoroamino)imidazolidin-2-one (78%), m.p. 172—173°. 4,5-Diethoxyimidazolidin-2-one gave 4,5-bis(difluoroamino)imidazolidin-2-one (84%), m.p. 172—173°.

4,5-Dimethoxy-1,3-bis(methoxymethyl)imidazolidin-2-one gave 4,5-bis(difluoroamino)-1,3-bis[(difluoroamino)-methyl]imidazolidin-2-one as a liquid (90%), b.p. 60°/9·3 mm. (Found: C, 18·9; H, 2·0; F, 47·3; N, 26·6%; M, 324. $C_5H_6F_8N_6O$ requires C, 18·9; H, 1·9; F, 47·8; N, 26·4; M, 318).

1-Hydroxymethyl-4,5-dimethoxy-3-(2,2,2-trinitroethyl)imidazolidin-2-one gave 4,5-bis(difluoroamino)-1-(difluoroamino)methyl-3-(2,2,2-trinitroethyl)imidazolidin-2-one (74%), m.p. 86—87° (from carbon tetrachloride) (Found: C, 17.5; H, 1.4; F, 27.1; N, 26.9. $C_6H_6F_6N_8O_7$ requires C, 17.3; H, 1.4; F, 27.4; N, 26.9%). The 1-methoxymethyl derivative gave the same product in 32% yield.

1,2-Diformamidoethane-1,2-diol gave 1,2-bis(difluoroamino)-1,2-diformamidoethane (50%), m.p. 184—185° (from propan-2-ol) (Found: C, 21·9; H, 2·9; F, 35·2; N, 25·4. Calc. for $C_4H_6F_4N_4O_2$: C, 22·0; H, 2·8; F, 34·9; N, 25·7%).

1,2-Bis(trifluoroacetamido)ethane-1,2-diol⁸ gave 1,2-bis-(difluoroamino)-1,2-bis(trifluoroacetamido)ethane (72%), m.p. 183—186° (Found: C, 20·1; H, 1·3; F, 53·9; N, 15·5%; M, 356. C₆H₄F₁₀N₄O₂ requires C, 20·3; H, 1·1; F, 53·7; N, 15·8%; M, 354).

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⁸ A. C. Currie, A. H. Dinwoodie, G. Fort, and J. M. C. Thompson, *J. Chem. Soc.* (C), 1967, 491.