

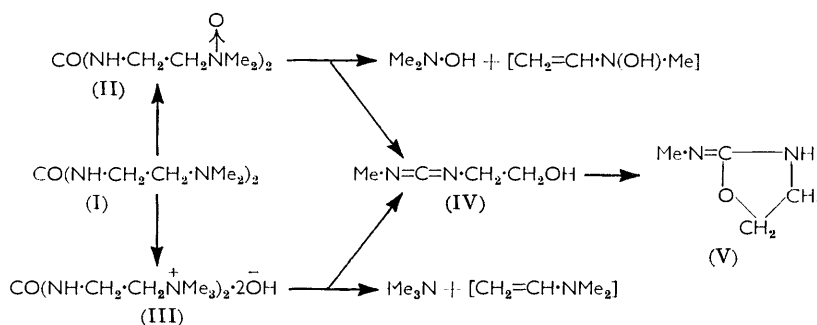
735. *Some Symmetrical Disubstituted Ureas*

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Some urea derivatives of the type $\text{CO}(\text{NH}\cdot\text{CH}_2\cdot\text{CH}_2\text{X})_2$ have been prepared, and the elimination of HX studied. When X is $-\text{NMe}_2\text{OH}^-$ or $-(\text{N}\rightarrow\text{O})\text{Me}_2$ the initial product on pyrolysis is methyl-2-hydroxyethylcarbodi-imide. Five-membered ring compounds are formed when X is $-\text{Cl}$ or $-\text{OH}$.

As potential precursors for the synthesis of divinylureas a number of compounds $\text{CO}(\text{NH}\cdot\text{CH}_2\cdot\text{CH}_2\text{X})_2$ have been prepared, and standard elimination procedures applied to them. The reaction between urea and 2-(dimethylamino)ethylamine gave *NN'*-bis-(2-dimethylaminoethyl)urea (I), which was the starting point for the Cope reaction of *N*-oxides and the Hofmann exhaustive methylation method. Careful treatment of the ditertiary amine (I) with hydrogen peroxide solution converted it into the di-*N*-oxide (II), isolated initially as a colourless viscous syrup, but crystallising as the trihydrate and characterised as its picrate. The ditertiary amine (I) gave the corresponding diquaternary ammonium iodide readily which by ion-exchange gave the hydroxide (III) in solution; evaporation gave a colourless syrup which evolved trimethylamine.

Both the di-*N*-oxide (II) and the diquaternary ammonium hydroxide (III) were pyrolysed at about 160° under nitrogen, and at low pressures, in an apparatus with a very short-path distillation head. Each main distillate was pale yellow, viscous, and unsaturated to permanganate and bromine solutions. The two distillates were identical from their infrared spectra, showing the very strong, distinctive absorption at 2130 cm^{-1} of a carbodi-imide.¹ This band disappeared if the product was kept in a closed vessel for several days, or more rapidly when warmed. Vacuum sublimation of the viscous distillate gave crystals which, from analytical and spectral data, appeared to be 2-methylimino-oxazolidine (V). The known hydriodide² of (V) was prepared, *via* 2-imino-oxazolidine and methyl iodide, and the free base from it had an infrared spectrum identical to that of the crystalline sublimate. Support for the structure of (V) is its ready hydrolysis to oxaxolid-2-one (VII). The obvious precursor of 2-methylimino-oxazolidine (V) is therefore methyl-2-hydroxyethylcarbodi-imide (IV), which would undergo an intramolecular reaction as expected for an alcohol and a carbodi-imide group. A few analogous cases are recorded,³ *e.g.*, allyl-2-hydroxyethylcarbodi-imide exists as 2-allylimino-oxazolidine.



The other products from the pyrolyses of the di-*N*-oxide (II) and the diquaternary ammonium hydroxide (III) were collected in cold traps in series with the main receiver. The contents from the di-*N*-oxide (II) were treated with dilute hydrochloric acid, and

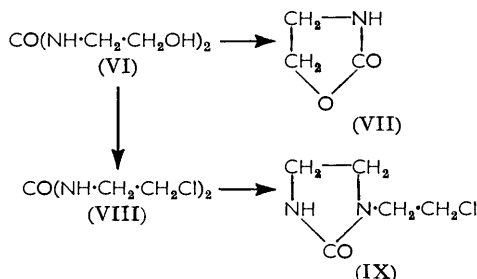
¹ G. D. Meakins and R. J. Moss, *J.*, 1957, 993.

² E. Fromm, R. Kapeller, L. Pirk, A. Hahn, and Th. Leipert, *Annalen*, 1926, 447, 271.

³ E. Schmidt, F. Hitzler, E. Lahde, R. Herbeck, and M. Pezzati, *Ber.*, 1938, 71B, 1933; E. Schmidt and W. Striewsky, *ibid.*, 1941, 74B, 1285.

dimethylhydroxylamine hydrochloride and acetaldehyde were isolated. Similarly, from the diquaternary ammonium hydroxide (III), trimethylamine hydrochloride and acetaldehyde were obtained. Dimethylhydroxylamine and trimethylamine are normal products of these reactions. In both pyrolyses the cold-trap contents were highly unsaturated before acidification and we suggest that methylvinylhydroxylamine and dimethylvinylamine are formed, in the Cope and Hofmann reaction, respectively, and that both would be hydrolysed readily with dilute acid to acetaldehyde. A feasible mechanism has been suggested⁴ for the above degradation of the diquaternary ammonium hydroxide (III). A similar one can be given for the di-*N*-oxide (II).

As an alternative approach to the synthesis of divinylureas the dehydration of *NN'*-bis-(2-hydroxyethyl)urea (VI) was attempted, with phosphoric oxide and alumina under a variety of conditions. With phosphoric oxide the vigorous, exothermic reaction gave a black, intractable mixture, the only identifiable product being oxazolid-2-one (VII). With alumina the mixture remained white but the product, which sublimed, was again oxazolid-2-one (VII). Obtaining this product means that a molecule of ethanolamine



has been eliminated. The corresponding dichloro-compound (VIII) was prepared from the diol (VI) so that dehydrochlorinations could be investigated. Similar compounds with a tertiary nitrogen atom, *e.g.*, *N*-(2-chloroethyl)pyrrolidone,⁵ have been used to obtain the corresponding *N*-vinyl compounds. In this case, with the "acidic" hydrogen atom on nitrogen, treatment with bases led to dehydrochlorination with cyclisation to give *N*-(2-chloroethyl)-*NN'*-ethyleneurea (IX).

EXPERIMENTAL

NN'-Bis-(2-dimethylaminoethyl)urea (I).—Urea (20 g.) was heated under reflux with 2-(dimethylamino)ethylamine (70 g.). The reaction was complete after 12 hr. Distillation *in vacuo* gave a colourless liquid (53 g.), b. p. 144°/0.5 mm., n_D^{21} 1.4882, which solidified on standing to white crystals, m. p. 19° (Found: N, 27.9. Calc. for C₉H₂₂N₄O: N, 27.7%).

Di-N-oxide (II).—Hydrogen peroxide (9M, 33.3 g.) was added during 30 min. to a solution of *NN'*-bis-(2-dimethylaminoethyl)urea (I; 10.1 g.) cooled in ice. The mixture was allowed to warm to room temperature and kept for 20 hr., by which time phenolphthalein paper could no longer detect the basic starting material (I). The excess of peroxide was removed by stirring with manganese dioxide (0.5 g.) during 20 hr. The mixture was filtered and evaporated at 40° *in vacuo* to a colourless syrup. Crystallisation from ethanol-ether gave the *di-N-oxide trihydrate* as white crystals (8 g.), m. p. 125° (decomp.) (Found: C, 37.5; H, 10.05; N, 19.4. C₉H₂₂N₄O₃·3H₂O requires C, 37.55; H, 9.8; N, 19.45%). A solution in methanol was used to prepare the *picrate* m. p. 138° (Found: N, 20.65. C₁₅H₃₁N₇O₁₀ requires N, 20.25%).

Diquaternary Ammonium Iodide and Hydroxide (III).—*NN'*-Bis(2-dimethylaminoethyl)urea (I; 20.2 g.) in ethanol (95%, 500 ml.) was treated with methyl iodide (28.4 g.) dropwise during 30 min. at 40°. The white precipitate formed on cooling crystallised from ethanol (95%) as colourless needles of the *diquaternary ammonium iodide* (42 g.), m. p. 252—254° (sealed tube)

⁴ A. Crawshaw and A. N. Mason, *Chem. and Ind.*, 1964, 365.

⁵ B. Puetzer, L. Katz, and L. Horwitz, *J. Amer. Chem. Soc.*, 1952, **74**, 4959.

(Found: C, 27.3; H, 5.8; I, 52.35. $C_{11}H_{28}I_2N_4O$ requires C, 27.1; H, 5.8; I, 52.3%). Conversion into the hydroxide (III) was achieved in two ways: (i) The iodide (10 g.) was dissolved in water (150 ml.) and stirred vigorously with silver oxide (50 g.) until the solution no longer contained iodide ions. The mixture was filtered through hardened filter paper and concentrated under reduced pressure to give the hydroxide (III) as a colourless syrup. (ii) A dilute solution of the iodide (10 g.) was allowed to percolate slowly through a column of Amberlite resin (IRA 400; 200 g.) and the iodide-free eluate was evaporated under reduced pressure to afford the same colourless syrup.

Pyrolysis of the Di-N-oxide (II) and the Diquaternary Ammonium Hydroxide (III). The small still had a very short head between flask and receiver. The first receiver was water-cooled and was followed by two cooled to -70° . The temperature was raised slowly (at 0.2 mm. under nitrogen) and at 160° a pale yellow viscous syrup distilled in each case. Typically, 10 g. of the hydroxide (III) gave 2.3 g. of this distillate. The pyrolysis of (II) and (III) produced syrups with identical infrared spectra, with strong absorption bands at 2130 ($N=C=N$) and 3250 cm^{-1} (OH). The syrup rapidly decolourised solutions of potassium permanganate and bromine, in the cold. Sublimation of the syrup at 75° and 0.2 mm., followed by crystallisation from ethanol-ether, afforded 2-methylimino-oxazolidine (V) as white plates, m. p. $113-114^\circ$ (Found: C, 47.55; H, 8.0; N, 27.8. $C_4H_8N_2O$ requires C, 48.05; H, 8.05; N, 28.0%), ν_{max} . 1080 (C-O-C), 1665 (C=N), and 3230 cm^{-1} (NH). 2-Methylimino-oxazolidine hydriodide, prepared from 2-imino-oxazolidine and methyl iodide,² was treated with sodium carbonate solution to obtain the free base. Crystallisation from ethanol-ether gave 2-methylimino-oxazolidine having an identical infrared spectrum to that of (V).

Further pyrolysis products were isolated from the cold traps by treating the contents with dilute hydrochloric acid and then the resultant mixture as follows:

From the Di-N-oxide (II) Pyrolysis.—(a) A portion was evaporated *in vacuo* and the residue crystallised from ethanol-ether to give dimethylhydroxylamine hydrochloride as hygroscopic white needles, m. p. 108° (sealed capillary) (lit.,⁶ $106.5-109^\circ$) (Found: C, 24.9; H, 8.4. Calc. for C_2H_8ClNO : C, 24.6; H, 8.3%). (b) A portion was mixed with a solution of 2,4-dinitrophenylhydrazine in concentrated hydrochloric acid. The orange precipitate was purified by elution in benzene through alumina (Spence Type O) and crystallised from methanol as acetaldehyde 2,4-dinitrophenylhydrazone, m. p. $161-162^\circ$, with infrared spectrum identical to that of an authentic sample.

From the Diquaternary Ammonium Hydroxide (III) Pyrolysis.—(a) Saturated aqueous picric acid was added to a portion of the solution. The precipitate crystallised from benzene to give trimethylamine picrate, m. p. and mixed m. p. 215° . (b) A further portion was treated as previously described to afford acetaldehyde 2,4-dinitrophenylhydrazone, m. p. $162-163^\circ$.

Reaction of NN'-Bis-(2-hydroxyethyl)urea (VI)⁷ with Dehydrating Agents.—(a) The urea (VI; 1.5 g.) was heated with alumina (Spence Type O; 6 g.) in a small sublimation apparatus. At 180° a white sublimate collected which on crystallisation from ether afforded oxazolid-2-one (0.5 g.), m. p. $87-88^\circ$. (b) Using phosphoric oxide in a similar way also gave oxazolid-2-one, m. p. 88° .

NN'-Bis-(2-chloroethyl)urea (VIII).—Thionyl chloride (65 g.) was added dropwise during $1\frac{1}{2}$ hr. to NN'-bis-(2-hydroxyethyl)urea (VI; 37 g.) cooled in ice and protected from moisture. The mixture was allowed to warm to room temperature, then heated at 100° for 2 hr. The brown paste was treated with water (20 ml.) and crystallised from isopropyl alcohol to give NN'-bis-(2-chloroethyl)urea (VIII) as white crystals (39 g.), m. p. 123° (Found: C, 32.45; H, 5.1; Cl, 37.8; N, 14.85. $C_5H_{10}Cl_2N_2O$ requires C, 32.45; H, 5.45; Cl, 37.45; N, 15.15%).

N-(2-Chloroethyl)-NN'-ethyleneurea (IX).—(a) Triethylamine (40 ml.) was added dropwise during 30 min. to a refluxing solution of the dichloro-compound (VIII; 15 g.) in dioxan (125 ml.). The mixture was heated for a further 2 hr., cooled, and the precipitated triethylamine hydrochloride (13 g.) removed. The filtrate, on evaporation, gave a yellow solid which was extracted with hot benzene and the combined extracts treated with light petroleum (b. p. $60-80^\circ$). Further recrystallisation from the same solvents gave white needles of N-(2-chloroethyl)-NN'-ethyleneurea (IX; 4 g.), m. p. 86° (Found: Cl, 23.5; N, 18.55. $C_5H_9ClN_2O$ requires Cl, 23.85; N, 18.85%). (b) An aqueous solution of (VIII) (9.25 g. in 200 ml.) was treated with sodium hydrogen carbonate (30 g.) and the mixture stirred for 20 hr. After evaporation to dryness *in*

⁶ A. C. Cope, T. T. Foster, and P. H. Towle, *J. Amer. Chem. Soc.*, 1949, **71**, 3929.

⁷ For preparation see W. Froese, H. G. Trieschmann, and G. Wenner, G.P. 890,340.

vacuo, the residue was extracted with isopropyl alcohol to give the ethyleneurea (IX; 5.2 g.), m. p. 86°.

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