# 326. *The Reaction of Di-(2-cyanoethyl)amines with Ethyl Oxalate*

By A. H. Rees

Seven-membered nitrogen heterocycles are not obtained by the condensation of di(cyanoethyl)amines with ethyl oxalate. An alleged azatropolone has been shown to be a thiomaleimide derivative.

THE condensation of oxalic ester with di(cyanoethyl)amines (I; R = CN) to give heterocycles (II; R = CN) is a logical approach to azatropolones based on an analogous tropolone synthesis.[1] It had been reported [2] that for the amine (I; R = CN, R′ = tosyl) the condensation failed and that the amine (I; R = CN, R′ = H) gave the pyrroline derivative (III). This azatropolone route was also explored in these laboratories,[3] and the amines (I; R = CN and $CO_2Me$, R′ = $PhCH_2$) did not give the corresponding structure (II).

It therefore aroused our interest when the dinitrile (III) was claimed to have the structure (II; R = CN, R′ = H), and the derived diester the structure (II; R = $CO_2Me$, R′ = H).[4] This claim was based on the analogy that the acetamide (I; R = CN, R′ = COMe) gave, with ethyl oxalate, a product still containing the acetyl group and considered to be (II; R = CN, R′ = COMe). However, it was isolated as an ethanolate, which allows an alternative acyclic structure (IV).

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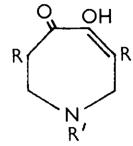
[1] J. W. Cook, J. D. Loudon, and D. K. V. Steel, *J.*, 1954, 530.
[2] J. D. Loudon and D. K. V. Steel, *J.*, 1954, 1163.
[3] A. H. Rees, Ph.D. Thesis, London, 1958.
[4] W. Treibs and A. Lange, *J. prakt. Chem.*, 1961, **14**, 208.

To settle this anomaly, the dinitrile (III or II; R = CN, R′ = H) was re-prepared. Its infrared spectrum had important similarities to that of 1-benzyl-4-cyano-3-hydroxy-2-oxo-3-pyrroline (V), a by-product from the condensation of the benzylamine (I; R = CN, R′ = $PhCH_2$), which contained monocyanoethylbenzylamine, with oxalic ester. The infrared spectrum of the *O*-methyl ether of the dinitrile had no band in the NH region,

$R'N(CH_2{\cdot}CH_2R)_2$

(I)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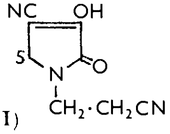
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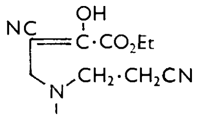
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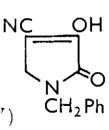
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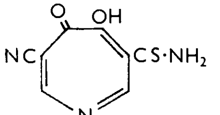
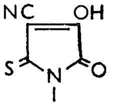
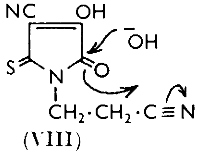
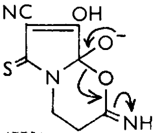
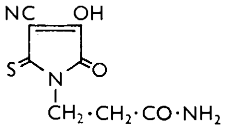
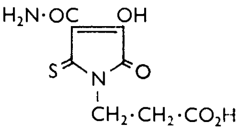

(VI)

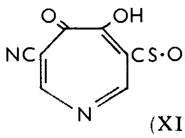

(VII)


(VIII)


(IX)


(X)


(XI)


(XII)

contrary to expectation if it were the enol ether of amine (II; R = CN, R′ = H). Finally, the n.m.r. spectrum of the dinitrile showed a two-proton singlet at 5·9 τ (5-methylene group), and two triplets centred at 7·1 and 6·2 τ, due, respectively, to the side-chain α- and β-methylenes.

These facts prove that the dinitrile has structure (III), and thus the structures given [4] for its derivatives have to be revised. In particular, sulphur dehydrogenation of the dinitrile in quinoline gave a product claimed to be the quinoline salt of the azatropolone (VI); this is in fact the thiomaleimide (VII). This is supported by the infrared spectrum of the quinoline salt which had imide bands at 5·6w and 5·75s μ, and two nitrile bands at 4·4 (αβ-unsaturated) and 4·5 μ. The quinoline salt, when split by cold alkali, gave a product which retained the imide bands though only one nitrile band (4·4) remained. An extra band at 6·0 is assigned to an amide carbonyl, and an internal mechanism is proposed for this easy nitrile hydrolysis [(VII) ⟶ (VIII), proton transfer, ⟶ (IX) ⟶ (X)]. The n.m.r. spectrum of the amide (X) showed the absence of the 5-methylene group, but the $A_2X_2$ system was retained, there being two triplets centred at 7·0 and 5·5 τ, respectively, for the side-chain α- and β-methylenes, the β-methylene being moved downfield by the sulphur atom from its position at 6·2 τ in the amide (III). The amide (X), which was hydrated, gave no ferric chloride colour and may be the compound described [4] as the thio-acid (XII) dihydrate.

When the quinoline salt of the thiomaleimide (VII) was split with hot alkali,[4] the product had an infrared spectrum showing no nitrile bands, but an extra carbonyl band appeared. The imide system was retained, and structure (XI) is proposed for this compound. It gave a reddish colour with ferric chloride thought to be due to the carboxyl group.

## EXPERIMENTAL

NN-*Di-(2-cyanoethyl)benzylamine* (I; R = CN, R′ = $PhCH_2$).—Benzylamine (100 ml.) and acrylonitrile (100 g., 2 moles) were heated for 20 hr. on a water-bath. Distillation gave monocyanoethylbenzylamine [5] (91%), b. p. 131°/1 mm., $n_D^{20}$ 1·5335. The *hydrochloride* had m. p.

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[5] J. A. King and F. H. McMillan, *J. Amer. Chem. Soc.*, 1946, **68**, 1468.

210° (from aqueous ethanol) (Found: N, 14·3; Cl$^-$, 18·2. $C_{10}H_{13}ClN_2$ requires N, 14·2; Cl$^-$, 18·0%).

The monocyano-amine was then heated for 6 days at 90° in a sealed flask with excess of acrylonitrile and a pinch of copper sulphate catalyst. Fractionation gave biscyanoethylamine[6] (45%), b. p. 180°/0·4 mm., $n_D^{20}$ 1·531 (Found: N, 19·7. Calc. for $C_{13}H_{15}N_3$: N, 19·7%).

Lower-boiling fractions were combined and re-heated, to provide more tertiary amine which was characterised as its *methiodide*, m. p. 132° (from ethanol) (Found: N, 11·8; I$^-$, 36·0. $C_{14}H_{18}IN_3$ requires N, 11·8; I$^-$, 35·8%).

In an attempt at making a picrolonate, a very poor yield was obtained, m. p. 228° (decomp.) (from ethanol), identical (m. p. and mixed m. p.) with *monocyanoethylbenzylamine picrolonate* prepared from pure secondary amine (Found: N, 19·9. $C_{20}H_{20}N_6O_5$ requires N, 19·8%).

There were signs of decomposition of the tertiary amine during fractionation, so quick re-distillation is recommended.

NN-*Di-(2-methoxycarbonylethyl)benzylamine* (I; R = $CO_2Me$, R′ = $PhCH_2$).—The dinitrile (I; R = CN, R′ = $PhCH_2$) (60 g.) gave, with methanolic hydrogen chloride (600 ml.), the diester (40 g.), b. p. 139°/0·2 mm., $n_D^{20}$ 1·501 (Found: C, 64·0; H, 7·4; N, 5·0. $C_{15}H_{21}NO_4$ requires C, 64·5; H, 7·6; N, 5·0%). The *picrolonate* had m. p. 160° (from ethanol) (Found: N, 13·0. $C_{25}H_{29}N_5O_9$ requires N, 12·9%). The *methiodide* had m. p. 133° (Found: N, 3·3; I$^-$, 30·4. $C_{16}H_{21}INO_4$ requires N, 3·3; I$^-$, 30·4%). An attempted acyloin condensation of the diester failed.[7]

*Condensation of Cyanoethylbenzylamine with Ethyl Oxalate.*—Essentially the method of Loudon and Steel[2] gave a sodio-derivative which was acidified, giving an oil which became solid on addition of ether. The product, the *pyrroline* (V), m. p. 190° (from ethanol), gave a red ferric chloride colour attributed to the dihydroxypyrrole form (Found: C, 67·2; H, 4·8; N, 12·9. $C_{12}H_{10}N_2O_2$ requires C, 67·3; H, 4·7; N, 13·1%).

4-*Cyano*-1-2′-*cyanoethyl*-3-*methoxy*-2-*oxo*-3-*pyrroline*.—Equimolar aqueous solutions of the dinitrile (III) sodium salt[4] and silver nitrate were mixed, and the silver salt collected and dried then treated with methyl iodide in methanol. The methyl ether had m. p. 161° (from methanol) (lit.,[2] 160—162°) (Found: OMe, 16·8. Calc. for $C_9H_9N_3O_2$: OMe, 16·2%).

*Alkali Splitting of the Thiomaleimide* (VII) *Salt.*—The quinoline salt (0·5 g.)[4] was dissolved in 5N-sodium hydroxide (0·6 ml.) and extracted with ether. Hydrochloric acid (2N) was added to pH 6, and the precipitate washed with water and recrystallised from propanol. At a second recrystallisation, water had to be added to improve the solubility. The *amide* (X), yellow-green needles, had m. p. 253—254° (decomp.) and turned orange on drying. The analyses of thio-acid (XII) dihydrate and the amide (X) monohydrate differ significantly only in nitrogen content (Found: N/S, 1·32. $C_8H_4N_2O_3S,2H_2O$ requires N/S, 0·87. $C_8H_7N_3O_3S,H_2O$ requires N/S, 1·23).

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[6] A. E. Frost and A. E. Martell, *J. Org. Chem.*, 1950, **15**, 51.

[7] N. J. Leonard *et al.*, *J. Amer. Chem. Soc.*, 1954, **76**, 630, 5708.