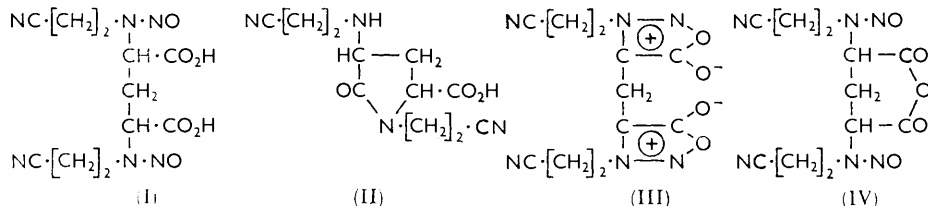


396. *Cyclodehydration of $\alpha\alpha'$ -Di-(N-2-cyanoethyl-N-nitrosoamino)-glutaric Acid.*

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WHETHER the cyclodehydration of the *N*-nitroso-derivatives of $\alpha\alpha'$ -iminodicarboxylic acids gives a sydnone or a cyclic six-membered anhydride may depend on relatively minor effects.^{1,2} A further example has now been examined, namely, $\alpha\alpha'$ -di-(*N*-2-cyanoethyl-*N*-nitrosoamino)glutaric acid (I).



In hot aqueous solution $\alpha\alpha'$ -di-(*N*-2-cyanoethylamino)glutaric acid³ was converted into another zwitterionic compound which is probably the pyrrolidone acid (II). Nitrosation of the biscyanoethyl-acid gave a mixture of diastereoisomeric nitroso-derivatives (I), one of which (α) was a solid, while the other (β) did not crystallise.

Treatment of the mixed nitroso-acids (I) with acetic anhydride at room temperature gave 3,3'-di-(2-cyanoethyl)-4,4'-methylenedisynnone (III). This result may be compared with the preferential formation of a glutamic anhydride rather than a sydnone from *N*-2-cyanoethyl-*N*-nitroso-*L*-glutamic acid under the same conditions.² However, when the individual α - and β -forms were treated with acetic anhydride, the anhydride (IV) was formed predominantly, with varying amounts of sydnone (III). The anhydride probably occurred in diastereoisomeric forms but this could not be confirmed; it was converted into the sydnone when warmed with acetic anhydride or stored in the solid state.

¹ Stewart, *Chem. and Ind.*, 1961, 1411.

² Stewart, *ibid.*, 1963, 701.

³ McKinney, Uhing, Setzkorn, and Cowan, *J. Amer. Chem. Soc.*, 1950, **72**, 2599; Hellmann, Lingens, and Polz, *Chem. Ber.*, 1956, **89**, 2433.

The exclusive production of sydnone (III) from the mixed nitroso-acids (I) is possibly due to the initial coexistence of both isomers of the anhydride (IV) in the reaction mixture with resultant inhibition of the crystallisation of either form, so that the slower formation of sydnone⁴ can proceed to the point where the latter separates.

The sydnone ultraviolet-absorption maximum occurred at a longer wavelength (303 m μ) than the corresponding value for 3-2'-cyanoethylsydnone (292 m μ), suggesting electronic interaction between the sydnone rings across the methylene bridge,⁵ in accord with polarographic evidence for 3,3'-ethylenedisynone.⁶

Experimental.— $\alpha\alpha'$ -Di-(N-2'-cyanoethylamino)glutaric acid. A solution of $\alpha\alpha'$ -diaminoglutaric acid⁷ (530 mg.) and sodium hydroxide (260 mg.) in water (1.5 ml.) was shaken with acrylonitrile (0.44 ml.) for several hours, kept overnight at room temperature, and acidified with concentrated hydrochloric acid (0.59 ml.). On cautious addition of a little acetone the cyanoethyl-acid separated as a granular solid which, when washed with acetone (yield, 727 mg., 83%), had m. p. 225—227° (decomp.), ν_{\max} . (in KBr) 2260 (CN), 1640 (sh, NH₂⁺), and 1580 cm.⁻¹ (CO₂⁻) (Found: C, 49.1; H, 6.6; N, 20.7. C₁₁H₁₆N₄O₄ requires C, 49.3; H, 6.0; N, 20.9%).

The acid dissolved in boiling water; addition of ethanol precipitated (probably) 4-2'-cyanoethylamino-5-oxopyrrolidine-2-carboxylic acid (II). Recrystallised from aqueous ethanol, this had m. p. 234—236° (decomp.), ν_{\max} . (in KBr) 2260 (CN), 1710 (γ -lactam), 1645 (NH₂⁺), and 1590 cm.⁻¹ (-CO₂⁻) (Found: C, 52.2; H, 6.3; N, 22.0. C₁₁H₁₄N₄O₃ requires C, 52.8; H, 5.6; N, 22.4%).

3,3'-Di-(2-cyanoethyl)-4,4'-methylenedisynone (III). An ice-cold solution of $\alpha\alpha'$ -di-(N-2-cyanoethylamino)glutaric acid (300 mg.) and concentrated hydrochloric acid (0.3 ml.) in water (0.6 ml.) was treated with an aqueous solution of sodium nitrite (170 mg.). After 30 min. a little urea was added and the mixture was extracted with ethyl acetate. Evaporation of the dried extract gave an oil which was treated with acetic anhydride (1.5 ml.) at room temperature. The sydnone (III) began to separate after some hours, and the infrared spectrum of the first material to appear was identical with that of the pure compound. After 2 days the mixture was diluted with ether and the sydnone collected [200 mg., 62% overall; m. p. 200—201° (decomp.)]. It formed colourless leaflets (from acetic acid-ethanol), m. p. 206—207° (decomp.), ν_{\max} . (in KBr) 2260 (CN) and 1750 cm.⁻¹ (sydnone CO), λ_{\max} . (in 80% aq. EtOH) 303 m μ (ϵ 10,100); it always gave a very faint Liebermann reaction (Found: C, 45.6; H, 3.6; N, 28.8. C₁₁H₁₆N₄O₄ requires C, 45.5; H, 3.5; N, 29.0%).

For comparison the ultraviolet spectrum of 3-2'-cyanoethylsydnone⁷ was determined [λ_{\max} . 292 m μ (ϵ 4000)].

The crude nitroso-product partly crystallised and treatment with ethyl acetate gave the solid acid (α) in 20—30% yield. Recrystallised from ethanol-light petroleum, this had m. p. 148—149° (decomp.) (Found: C, 40.2; H, 4.3. C₁₁H₁₄N₄O₄ requires C, 40.5; H, 4.3%). Removal of the ethyl acetate *in vacuo* left the β -acid as an oil, ν_{\max} . (film) 2260 (CN) and 1730 cm.⁻¹ (CO₂H), giving a strong Liebermann reaction.

Treatment of the α - or β -acid with acetic anhydride at room temperature gave a precipitate of $\alpha\alpha'$ -di-(N-2-cyanoethyl-N-nitrosoamino)glutaric anhydride (IV) contaminated with varying amounts of the sydnone (III). The sydnone content was assessed by using the infrared peaks at 1750 and 780 cm.⁻¹. The m. p. of the purest specimen obtained was 129—130° (decomp.), and ν_{\max} . (in KBr) were 2260 (CN), 1820, 1785 (CO-O-CO), and 1390 cm.⁻¹ (NO). The anhydride gave a strong Liebermann reaction, and when warmed with acetic anhydride was converted into the sydnone (III). This conversion had also occurred to some extent in the solid state after several weeks at room temperature.

The author is indebted to the Mathilda and Terence Kennedy Trust for a Research Fellowship.

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[Received, November 12th, 1962.]

⁴ Baker, Ollis, and Poole, *J.*, 1950, 1542.

⁵ Stewart, *J. Org. Chem.*, 1962, **27**, 3374.

⁶ Zuman, *Coll. Czech. Chem. Comm.*, 1960, **25**, 3252.

⁷ Stewart, *J. Org. Chem.*, 1962, **27**, 687.