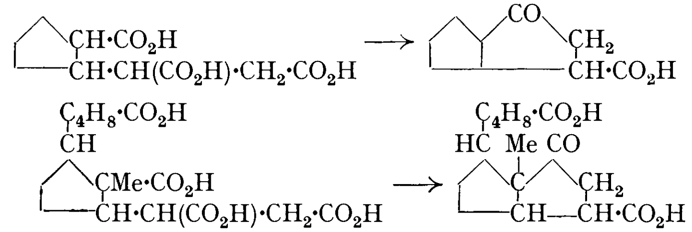
105. *Derivatives of* bicyclo[0 : 3 : 3]*Octane.*

By J. C. Bardhan and S. K. Banerji.

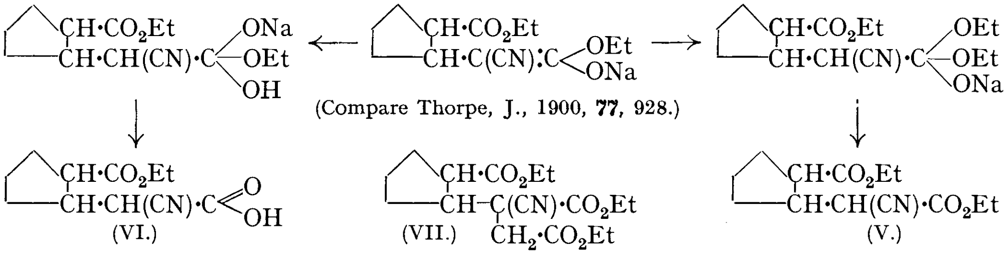
The chemistry of *bicyclo*[0 : 3 : 3]octane derivatives has been recently brought into prominence by the work of Wieland and his collaborators (*Z. physiol. Chem.*, 1924, **134**, 276; 1930, **191**, 69) on monocyclic fission products of bile acids. The parent member of this group was, however, first prepared by Schroeter (*Annalen*, 1922, **426**, 1) by a series of reactions the exact nature of which is little understood. More recently, Ruzicka, Borges de Almeida, and Brack (*Helv. Chim. Acta*, 1934, **17**, 183) and Linstead and co-workers (J., 1934, 935) have made a comprehensive study of the synthetical problem.

We have developed a new method of attack, the results of which are now recorded in view of Cook and Linstead's work (*loc. cit.*, p. 958).

It seemed to us probable that an acid of the structure (I) should on distillation in a vacuum furnish a *bicyclo*octane derivative (II), since Wieland and Vocke (*Z. physiol. Chem.*, 1928, **177**, 68) had shown that the analogously constituted tetrabasic acid (III) under the above conditions passed smoothly into the pyro-acid (IV).


(I.) (II.) (III.) (IV.)

A convenient method for the preparation of the acid (I) appeared to be the condensation of ethyl Δ^1-*cyclo*pentenecarboxylate with ethyl sodiocyanoacetate and treatment of the resulting sodio-derivative with ethyl bromoacetate. Repeating the condensation of ethyl sodiocyanoacetate with ethyl Δ^1-*cyclo*pentenecarboxylate according to Sircar (J., 1927, 1255; compare also Cook and Linstead, *loc. cit.*, p. 959), we obtained a considerably smaller yield of the cyano-ester (V) than that reported by them. The chief product of the con-

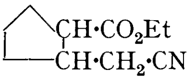

(Compare Thorpe, J., 1900, **77**, 928.)

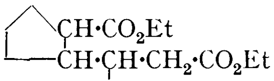
(VI.) (VII.) (V.)

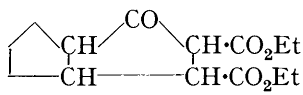
densation was the ethyl hydrogen ester (VI, not mentioned by those workers) the yield of which was a maximum after 12 hours' heating. The crude condensation product was treated directly with ethyl bromoacetate, and a good yield of the cyano-ester (VII) obtained. This ester on hydrolysis with sulphuric acid furnished the tribasic *acid* (I), distillation of which in a vacuum, however, did not give a satisfactory yield of the keto-acid (II).

On distillation under reduced pressure the ethyl hydrogen ester (VI) passed smoothly into the cyano-ester (VIII), hydrolysis of which with concentrated hydrochloric acid gave *trans*-1-carboxy*cyclo*pentane-2-acetic acid, m. p. 66° (Linstead and Meade, *loc. cit.*, p. 946), also obtained from the ester (V) by hydrolysis with 65% sulphuric acid.

The acid (I) was converted by the alcohol vapour method into its triethyl ester (IX), which reacted with " molecular " sodium, giving a good yield of *ethyl* bicyclo[0 : 3 : 3]*octan*-1-*one*-2 : 3-*dicarboxylate* (X). This was readily converted by dilute hydrochloric acid into *bicyclo*[0 : 3 : 3]octan-1-one-3-carboxylic acid, which was characterised by the formation of the *semicarbazone*. The keto-acid regenerated therefrom could not be obtained in a solid state, probably owing to the formation of a mixture of *cis*- and *trans*- modifications. We wish to reserve this point and the conversion of the keto-acid into *bicyclo*[0 : 3 : 3]octane for a future communication.


(VIII.)


(IX.)


(X.)

EXPERIMENTAL.

Condensation of Ethyl Δ¹-cyclo*Pentenecarboxylate with Ethyl Sodiocyanoacetate.*—Ethyl Δ¹-*cyclo*pentenecarboxylate was prepared by the action of phosphoryl chloride on ethyl *cyclo*pentan-1-ol-1-carboxylate in dry benzene. 52 G. of the hydroxy-ester yielded 37 g. of the pure unsaturated ester, boiling constantly at 70°/4 mm. (bath 80—85°). The ester on hydrolysis gave Δ¹-*cyclo*pentenecarboxylic acid, m. p. 121°.

The following experiments on the addition of ethyl sodiocyanoacetate to ethyl Δ¹-*cyclo*pentenecarboxylate were made with a view to determine the exact conditions under which a maximum yield of the ethyl hydrogen ester (VI) could be obtained. The quantities employed were : 16·95 g. of ethyl cyanoacetate, 21·5 g. of the unsaturated ester, and 3·45 g. of sodium, dissolved in 56 c.c. of absolute alcohol. When the heating was finished, the condensation product was poured into water and separated into a neutral and an acid fraction in the usual way. The neutral fraction was finally distilled under reduced pressure to remove the unchanged ester.

Hours of heating	1	6	12	24
Ethyl ester (V.), g.	13	5	2	2·3
Ethyl hydrogen ester (VI), g.	9	21	24	24

Ethyl α-cyano-1-carbethoxy*cyclo*pentane-2-acetate (V) was obtained as a colourless oil, b. p. 162°/5 mm. (Found : C, 61·6; H, 7·7. Calc. : C, 61·7; H, 7·5%). Ethyl α-cyano-1-carbethoxy*cyclo*pentane-2-acetic acid (VI), which formed the main constituent of the acid fraction, decomposed on distillation under reduced pressure, giving 1-*carbethoxy*cyclo*pentane*-2-*acetonitrile* (VIII), a colourless oil, b. p. 128°/4 mm., 265°/757 mm. (Found : C, 66·3; H, 8·5. $C_{10}H_{15}O_2N$ requires C, 66·3; H, 8·3%).

The crude acid fraction (21 g.) containing the acid (VI) was heated with absolute alcohol (75 c.c.) and concentrated sulphuric acid (4·5 c.c.) at 110° in a current of alcohol vapour for 5 hours. The ester (V) obtained had b. p. 165°/6 mm. (yield, 21 g.). A portion of it, on hydrolysis with 65% sulphuric acid for 6 hours, gave a good yield of *trans*-1-carboxy*cyclo*pentane-2-acetic acid, m. p. 66°. We prefer this method, as the hydrochloric acid method used by previous workers requires a much longer time (30 hours) for completion.

*Action of Ethyl Bromoacetate on the Sodio-derivative of Ethyl α-Cyano-1-carbethoxy*cyclo*pentane-2-acetate.*—The condensation of ethyl Δ¹-*cyclo*pentenecarboxylate with ethyl sodiocyanoacetate was brought about as described in the third experiment (12 hours' heating) above. The product was cooled in ice, treated with ethyl bromoacetate (17 c.c.) and, the vigour of the reaction having abated, heated on a steam-bath until neutral. The whole was then cooled and poured into a large volume of water, and the heavy oil was collected in ether, washed with water, dried, recovered, and fractionated under reduced pressure, *ethyl α-cyano-1-carbethoxy-*

cyclo*pentane*-2-*succinate* (VII) being obtained as a colourless, somewhat viscous oil (40 g.), b. p. 207°/5 mm. (Found: C, 60·5; H, 7·5. $C_{17}H_{25}O_6N$ requires C, 60·2; H, 7·4%).

The ester (VII) (60 g.) was heated with concentrated sulphuric acid (65 c.c.) and water (80 c.c.) under reflux for 15 hours, the alcohol formed being allowed to escape. On cooling, 1-*carboxy*cyclo*pentane*-2-*succinic acid* (I) separated, for the most part in a crystalline state; it was washed with as little water as possible and recrystallised from hot water, separating in well-formed prisms, m. p. 202° [Found: C, 52·2; H, 6·2; equiv., by titration, 77·0. $C_{10}H_{14}O_6$ (tribasic) requires C, 52·2; H, 6·1%; equiv., 76·7]. It is sparingly soluble in cold water and almost insoluble in ether, benzene, and light petroleum.

Ethyl 1-*carbethoxy*cyclo*pentane*-2-*succinate* (IX) was obtained in an almost quantitative yield from the acid (I) by the alcohol vapour method: in a typical experiment the acid (26 g.), alcohol (50 c.c.), and sulphuric acid (5 c.c.) gave 32 g. of the ester, b. p. 172°/4 mm. (Found: C, 61·4; H, 8·4. $C_{16}H_{26}O_6$ requires C, 61·1; H, 8·3%). The ester readily dissolved when boiled for a short time with concentrated hydrochloric acid; the solution, on cooling, deposited the acid, m. p. 202°, in a pure state.

Sodium-condensation of Ethyl 1-*Carbethoxy*cyclo*pentane*-2-*succinate*.—The ester (10 g.) was dissolved in benzene (25 c.c.) and heated with "molecular" sodium (1·5 g.) on the steam-bath for 3 hours. The product was cooled in ice and treated with dilute sulphuric acid. The benzene layer was removed, washed successively with water, sodium carbonate solution, and water, dried, and distilled, *ethyl* bicyclo[0 : 3 : 3]*octan*-1-*one*-2 : 3-*dicarboxylate* (X) being obtained as a colourless oil (6 g.), b. p. 166°/6 mm. (Found: C, 62·8; H, 7·6. $C_{14}H_{20}O_5$ requires C, 62·7; H, 7·5%). Its alcoholic solution gives a reddish-violet coloration with aqueous ferric chloride.

The keto-ester (X) (10 g.) was heated under reflux with hydrochloric acid (30 c.c.; *d* 1·19) and water (80 c.c.) for 3 hours. From the cooled solution, saturated with ammonium sulphate, ether extracted an oil, which was heated with semicarbazide hydrochloride (5 g.), sodium acetate (6 g.), and water (10 c.c.) on the steam-bath, enough alcohol being then added to make a clear solution. After a short time, the *semicarbazone* separated as a sandy powder; purified from absolute alcohol, it had m. p. 210° (Found: C, 53·1; H, 6·7; N, 18·7. $C_{10}H_{15}O_3N_3$ requires C, 53·3; H, 6·7; N, 18·7%). The *bicyclo*[0 : 3 : 3]octan-1-one-3-carboxylic acid regenerated from the semicarbazone by means of dilute hydrochloric acid in the usual way was a gum, which partly crystallised in a vacuum desiccator after several weeks. Owing to the small amount available, it could not be further investigated.

One of us (S. K. B.) thanks the Senatus of the Scottish Church College for the facilities afforded for carrying out this research.

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[*Received, October 23rd*, 1934.]