

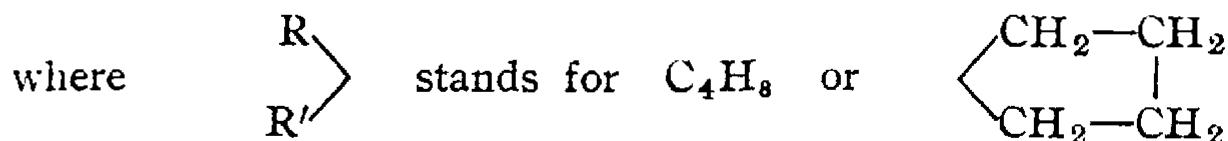
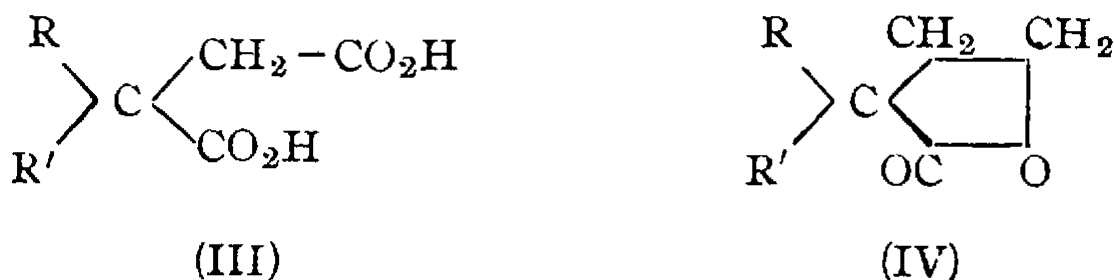
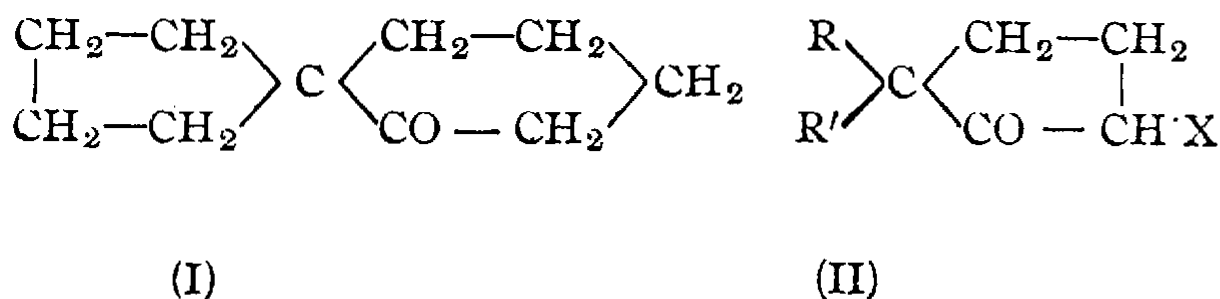
CHEMISTRY OF SPIRO-COMPOUNDS. PART II. SYNTHESIS OF CYCLOPENTANE-SPIRO- CYCLOPENTANONE.

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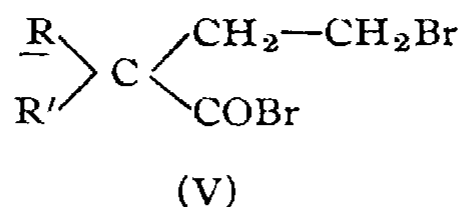
cyclopentane-spirocyclopentanone has been synthesised from *cyclopentane-1-carboxy-1-butyric acid*, which has been synthesised in a way which leaves no doubt regarding its configuration. The lactone obtained by the reduction of the anhydride of *cyclopentane-1-carboxy-1-acetic acid* yields a bromo-ester which by the action of sodium malonic ester and subsequent hydrolysis gives *cyclopentane-1-carboxy-1-butyric acid*. This acid has been converted into the spiro-ketone both by Dieckmann condensation of its ester, followed by hydrolysis, as also by its pyrolytic decomposition in presence of baryta.

cyclopentane-spiro-cyclopentanone (II, X=H) was prepared by Qudrat-i-Khuda and Ray (*J. Indian Chem. Soc.*, 1939, **16**, 518) from *cyclopentane-spiro-cyclohexanone* (I) through its product of oxidation, *viz.*, *cyclopentane-1-carboxy-1-butyric acid* (VII). The constitution of this ketone has been finally settled by an independent synthesis described in this paper.

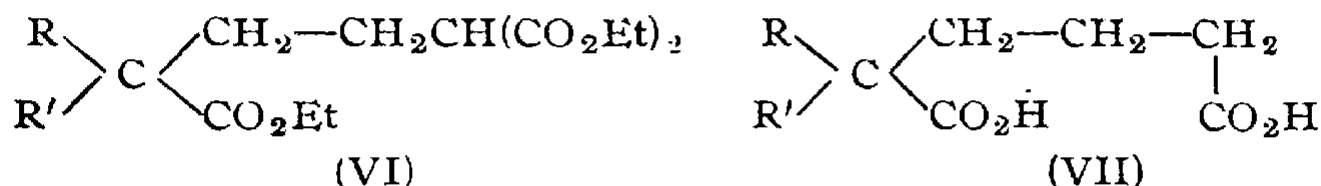
When the anhydride of *cyclopentane-1-carboxy-1-acetic acid* (III) is reduced by alcohol and sodium, it is converted into the lactone (IV).



The lactone ring is opened up with phosphorus pentabromide when a bromo-acid bromide (V) is obtained, which is converted into the bromo ester by the action of alcohol.



The bromo-ester reacting with sodio malonic ester, furnishes the tri-carbethoxy compound (VI). On hydrolysis, this tricarbethoxy compound is converted into *cyclopentane-1-carboxy-1-butyric acid* (VII) which is found to be identical with the acid obtained previously (*J. Indian Chem. Soc.*, 1939, 16, 518.)



The adipic acid (VII) gives the corresponding ester which after Dieckmann condensation yields the keto-ester (II, X = CO₂Et), which is hydrolysed to the ketone (II, X = H). *cyclopentane-spiro-cyclopentanone* could also be obtained by the dry distillation of the *cyclopentane-adipic acid* (VII) in presence of barium hydroxide.

E X P E R I M E N T A L.

Anhydride of cyclopentane-1-carboxy-1-acetic acid was prepared by heating the mixture of the acid (100 g.), acetic anhydride (75 c. c.) and acetyl chloride (15 c. c.). It was then distilled under reduced pressure when the anhydride boiled at 174°/38 mm., yield 80 g. It was kept in a vacuum desiccator for 2 days over fused calcium chloride and caustic potash.

Reduction of the Anhydride.—A solution of the anhydride (40 g.) in absolute alcohol (250 c. c.) was quickly dropped on the sodium kept in a 2-litre flask from a dropping funnel by a Y-tube, the other end of the Y-tube being connected to an inverted reflux condenser ending in a calcium chloride guard tube. The temperature of the bath was maintained at 80-90° during the addition of alcohol. When the solution of the anhydride had been added, absolute alcohol (350 c.c.) was poured on and the temperature of the bath was then raised to 130° and kept there for 1 hour more, when the whole of the sodium went into solution. It was then cooled and water (250 c.c.) was added and the alcohol was removed by distilling in a current of steam. The solution was then acidified by hydrochloric acid, cooled and extracted by ether, the ethereal layer was washed with sodium bicarbonate solution, water and dried. The solvent was removed and the product distilled at 154°/40 mm. (Found : C, 68.4 ; H, 8.5. C₈H₁₂O₂

requires C, 68.5; H, 8.5 per cent). It had $d_4^{30.1}$, 1.0751; n_D , 1.46345. Found: $[R_L]_D$, 35.9 (calc. 36.3). The yield of the lactone was 80 g. from 120 g. of the anhydride. From the bicarbonate extract about 35 g. of succinic acid could be recovered after the treatment of this whole amount of the anhydride.

Preparation of Ethyl cyclopentane-1-bromoethyl-1-carboxylate.—Phosphorus pentabromide (270 g.) was added to the above lactone (80 g.) and the mixture heated on a water-bath for 2 hours. The product was then cooled in ice and slowly poured into well cooled absolute alcohol (200 c.c.) and shaken, care being taken to avoid any moisture. It was then left at the ordinary temperature overnight, poured into crushed ice and the separated oil was taken in ether and washed thoroughly with a solution of sodium bicarbonate and water and dried. It was finally distilled at $118^\circ/5$ mm., yield 62 g. (Found: Br, 32.1. $C_{10}H_{17}O_2Br$ requires Br, 32.6 per cent). It had $d_4^{30.1}$, 1.2481; n_D , 1.46816. Found: $[R_L]_D$, 55.46 (calc: 55.48).

Ethyl cyclopentane-1-carbethoxy-1- α -carbethoxy-butyrate (VI).—The above bromo-ester (55 g.) was allowed to drop on to sodiomalonic ester (prepared from 32 g. of malonic ester using 4.6 g. of sodium), taken in a three-necked flask provided with a mercury-seal stirrer, under stirring at the ordinary temperature and was left overnight. Next day it was heated on a water-bath for 3-4 hours, and then the alcohol was removed. The cold mass was diluted with water and acidified with hydrochloric acid and the precipitated oil was taken up in ether and the ethereal solution washed with sodium bicarbonate and water and finally dried. The residue after removal of the solvent boiled at $154^\circ/6$ mm. and consisted of the ester (VI). (Found: C, 62.09; H, 8.48. $C_{17}H_{28}O_6$ requires C, 62.19; H, 8.5 per cent). It had $d_4^{31.1}$, 1.05401; n_D , 1.44486. Found: $[R_L]_D$, 82.7 (calc. 83.1).

cyclopentane-1-carboxy-1-butyric Acid (VII).—The above tricarboxylic ester (25 g.) was hydrolysed with concentrated hydrochloric acid (100 c.c.) by heating on a sand bath for 14-16 hours. A thick oily residue remained which was taken up in ether and washed completely with a solution of sodium carbonate. The sodium carbonate extract was acidified and extracted again with ether. After removal of the solvent the acid solidified in a vacuum desiccator and crystallised from ether-petroleum mixture, m. p. 92° . [Found: C, 59.85; H, 8.0; M.W. (by titration), 200.1. $C_{10}H_{16}O_4$ requires C, 60.0; H, 8.0 per cent. M.W., 200]. The *di-anilide* of the acid was obtained from aniline and the acid chloride, prepared by the action of thionyl chloride on the free acid. It crystallised from dilute alcohol, m. p. 163° . (Found: C, 75.5; H, 7.4. $C_{22}H_{26}O_2N_2$ requires C, 75.1; H, 7.4 per cent).

Ethyl cyclopentane-1-carbethoxy-1-butyrate.—*cyclopentane-1-carboxy-1-butyric acid* (45 g.) was dissolved in absolute alcohol (200 c.c.) and the solution saturated with dry hydrogen chloride. It was then left overnight and next it was heated for 4 hours. After usual methods of purification, the ester was obtained as a mobile liquid which boiled at $140^{\circ}/6$ mm., yield 35 g. (Found : C, 65.8 ; H, 9.2. $C_{14}H_{24}O_4$ requires C, 65.6 ; H, 9.4 per cent). It had $d_4^{32.1}$, 1.0170 ; n_D , 1.44910. Found : $[R_L]_D$, 67.67 (calc 67.96).

Ethyl cyclopentane-spiro-cyclopentane-2-one-3-carboxylate (II, X=CO₂Et) was obtained by the action of metallic sodium dissolved in alcohol on *ethyl cyclopentane-1-carbethoxy-1-butyrate*. The mixture was left in ice for $\frac{1}{2}$ hour and was then heated on a water-bath for 6 hours. The mass was then cooled and the keto-ester isolated in the usual way. It was distilled at $135^{\circ}/9$ mm. (Found : C, 68.2 ; H, 8.8. $C_{12}H_{18}O_3$ requires C, 68.6 ; H, 8.6 per cent). It had $d_4^{33.8}$, 1.03301 ; n_D , 1.45111. Found : $[R_L]_D$, 54.75 (calc. 54.88).

cyclopentane-spiro-cyclopentane-2-one (II, X=H). (Method I)—*Ethyl cyclopentane-spiro-cyclopentane-2-one-3-carboxylate* (10 g.) was heated on a sand-bath for 4 hours with hydrochloric acid (10%, 50 c.c.). It was then cooled and extracted with ether, the ethereal extract washed with a solution of sodium bicarbonate and water and finally dried over fused magnesium sulphate. The solvent was then removed and the spiro-ketone distilled at $115^{\circ}/30$ mm. It gave a semicarbazone, m.p. 215° . (Found : C, 61.5 ; H, 8.7. $C_{10}H_{17}ON_3$ requires C, 61.5 ; H, 8.7 per cent). The ketone regenerated from the semicarbazone boiled at $115^{\circ}/30$ mm. (Found : C, 78.09 ; H, 10.09. $C_9H_{14}O$ requires C, 78.26 ; H, 10.14 per cent). It had $d_4^{30.1}$, 0.9790 ; n_D , 1.46603. Found : $[R_L]_D$, 39.1 (calc. 39.4).

(Method II). A mixture of *cyclopentane-1-carboxy-1-butyric acid* (7 g.), and baryta (1 g.) and iron powder (1 g.) was heated in a 100 c.c. Jena distilling flask at first at 150° for 3 hours and then at 290° – 340° for 2 hours when a liquid product distilled over. It was taken up in ether and the ethereal solution purified by usual means. The residual ketone was converted into its semicarbazone, m.p. 215° (mixed m.p.).