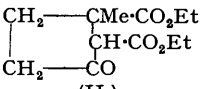
190. *The Course of Cyclisation in the Formation of Alicyclic Rings. Part I. Effect of Alkyl Groups on the Cyclisation of Esters of Polycarboxylic Acids.*

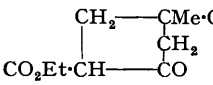
By R. N. CHAKRAVARTI.

The Dieckmann condensation of a simple or substituted β-alkyl-adipic or -pimelic ester leads to a ketonic ester in which the reactive methylene group nearer to the alkyl radical remains unaffected by preference when there is an alternative way of ring formation.

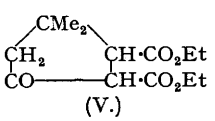
A DIFFICULTY often experienced in the synthesis of hydroaromatic ring systems is the determination of the structure of the ketonic esters obtained by the sodium condensation of esters of unsymmetrical polycarboxylic acids having two reactive methylene groups. A well-known example of this type is afforded by the sodium condensation of ethyl 2-methylbutane-1 : 2 : 4-tricarboxylate (I), which, on the basis of certain oxidative degradations, was found to lead to the keto-ester (II) (Baker, *J.*, 1931, 1548; cf. Banerjee, *J. Indian Chem. Soc.*, 1940, **17**, 423). More critical examination, however, revealed that the product of the condensation should be represented as ethyl 4-methyl*cyclo*pentanone-2 : 4-dicarboxylate (III) (Chakravarti, *J. Indian Chem. Soc.*, 1943, **20**, 173, 189, 243, 247, 399), and not (II) as was found by Baker (*loc. cit.*).

$CO_2Et\cdot CH_2\cdot CH_2\cdot CMe(CO_2Et)\cdot \overset{*}{C}H_2\cdot CO_2Et$ (I.)

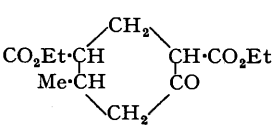

(II.)


(III.)

The cyclisation of the analogously constituted ethyl 2 : 2-dimethylbutane-1 : 3 : 4-tricarboxylate (IV) led to the keto-ester (V) (Perkin and Thorpe, *J.*, 1906, **89**, 781). Also, only (VII) was isolated in the cyclisation of ethyl 2-methylpentane-1 : 3 : 5-tricarboxylate (VI) (Chakravarti, *J. Indian Chem. Soc.*, 1944, **21**, 322).*


(V.)

$CO_2Et\cdot \overset{*}{C}H_2\cdot CMe_2\cdot CH(CO_2Et)\cdot CH_2\cdot CO_2Et$ (IV.)


(VII.)

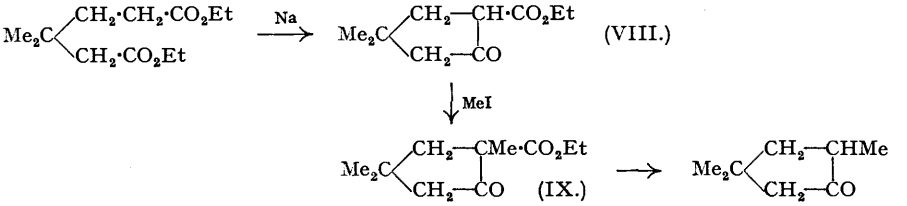
(VI.) $CO_2Et\cdot \overset{*}{C}H_2\cdot CHMe\cdot CH(CO_2Et)\cdot CH_2\cdot CH_2\cdot CO_2Et$

The above results definitely lead one to believe that the methyl groups in (I), (IV), and (VI) exert some steric influence on the reactive methylene groups marked (*), which accounts for

* Since this paper was communicated, another interesting case has been discussed elsewhere (Chakravarti, *Experientia*, 1947, **3**, 149).

their lesser reactivity. This effect may be due to the positive character of the alkyl group, and if this be true it can be concluded that the positive character of a methyl group is much more pronounced than the negative character of a carbethoxyl group (cf. the first example cited above).

In the present instance, while devising a suitable method for the synthesis of 4 : 4-dimethyl-*cyclo*pentanone-2-acetic acid required in connection with another work, it became necessary to investigate the action of sodium on ethyl ββ-dimethyladipate. For this purpose, the product of the sodium condensation was heated with excess of methyl iodide and the resulting methylated keto-ester hydrolysed with dilute aqueous alkali to give a neutral ketone, b. p. 160°. It gave a crystalline semicarbazone, m. p. 168°, which proved to be identical with that of 2 : 4 : 4-trimethyl*cyclo*pentanone (Wallach, *Annalen*, 1918, **414**, 331; Qudrat-i-Khuda, *Nature*, 1933, **132**, 210; Dey and Linstead, *J.*, 1935, 1063). No evidence of the presence, in the hydrolysed product, of the isomeric ketone, 2 : 3 : 3-trimethyl*cyclo*pentanone (von Kregten, *Rec. Trav. chim.*, **36**, 78; Noyes, *Ber.*, 1899, **32**, 2291), b. p. 167—169° (semicarbazone, m. p. 222°), could be detected, thus indicating that in this cyclisation the keto-ester (VIII) is the only product.



The result obtained above confirms the view already postulated that the reactivity of a methylene group is reduced considerably by its closer proximity to a methyl group (or any other alkyl group). Thus the action of sodium on the ester of a substituted β-alkyl-adipic or -pimelic acid (having two alternatives for cyclisation) may be expected to lead to a ketonic ester in which the reactive methylene group, nearer to the alkyl radical, remains unaffected by preference. The other isomer in such a case, if produced at all, can only be in much smaller amount. This view is also in line with the results obtained by the cyclisation of ethyl β-methyl-adipate (Dieckmann and Groeneveld, *Ber.*, 1900, **33**, 595) and -pimelate (Einhorn and Klages, *ibid.*, 1901, **34**, 3793).

Experimental.

ββ-Dimethyladipic acid, required for this work, was prepared by the improved method of Rydon (*J.*, 1936, 594; 1937, 1341).

Ethyl 2 : 4 : 4-*Trimethyl*cyclo*pentanone-2-carboxylate* (IX).—Ethyl ββ-dimethyladipate (20 g.) was heated on the water-bath with a fine suspension of sodium (3·9 g.) in anhydrous benzene (50 c.c.) The heating was continued for about 6 hours till the whole of the sodium had passed into solution. The product was then cooled in ice, treated with excess of methyl iodide (20 c.c.), and kept overnight. The methylation was completed by heating the reaction mixture on the water-bath for 5—6 hours. The product at this stage should not give any coloration with alcoholic ferric chloride. Sufficient water was added to dissolve the sodium iodide, and the benzene layer was separated. It was washed thoroughly with water and dried ($CaCl_2$), and the solvent evaporated. The residual liquid on distillation under reduced pressure gave the *ester* as a colourless mobile oil (12 g.) with a characteristic odour, b. p. 88°/4 mm. (Found : C, 66·5; H, 9·1. $C_{11}H_{18}O_3$ requires C, 66·7; H, 9·1%).

2 : 4 : 4-*Trimethyl*cyclo*pentanone*.—The above ketonic ester (11·5 g.) was heated on a sand-bath for 6 hours with a solution of potassium hydroxide (12 g.) in water (150 c.c.). When cold, the product was taken up in ether, washed well with water, and dried (Na_2SO_4), and the ether removed. The liquid remaining was then distilled; with the exception of a little high boiling residue, it came over constantly at 160°, as a colourless liquid (6·8 g.) with a peppermint-like smell (Found: C, 75·9; H, 11·2. Calc. for $C_8H_{14}O$: C, 76·2; H, 11·1%). With semicarbazide acetate in aqueous alcohol it readily gave a semicarbazone, which crystallised from spirit in colourless shining laminæ, m. p. 168°, undepressed in admixture with an authentic specimen of the semicarbazone of 2 : 4 : 4-trimethyl*cyclo*pentanone (Found : C, 59·2; H, 9·4. Calc. for $C_9H_{17}ON_3$: C, 59·0; H, 9·3%).

Further work with 4 : 4-dimethyl*cyclo*pentanone-2-acetic acid is in progress.

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