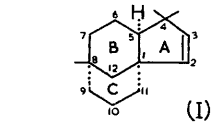
233. *An Alternative Synthesis of* (±)-*Clovene.*

By D. Becker and H. J. E. Loewenthal.

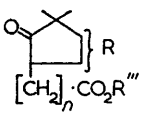
(±)-Clovan-3-one, which has previously been converted into (±)-clovene, has been synthesised in eight steps starting from methyl 2,2-dimethyl-3-oxocyclopentanecarboxylate.

The hydrocarbon clovene (I) [1] is one of a number of transformation products of caryophyllene the interesting bridged-ring structures of which have attracted the attention of a large number of workers.[1-7] Raphael, Parker, and their co-workers have recently reported a synthesis [8,9] of (±)-clovene; this started by construction of its bicyclo[3,3,1]-nonane system (rings B and C), followed by addition of the five-membered ring A.

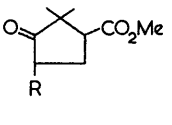
Our interest in this problem arose out of a current investigation into the general usefulness of the sequence [(II) ⟶ (III) ⟶ (IV)] which had been used with success in the synthesis of bicyclo[3,2,1]octane derivatives related to gibberellic acid [10,11] and which has since been shown to be applicable to the construction of other bridged-ring systems.[12]



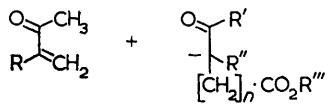
(I)



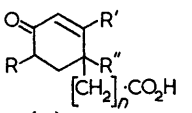
(V)



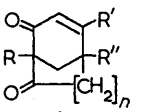
(VI)



(II)



(III)



(IV)

For a synthesis of clovene, compound (II) would have to be a cyclopentanone of the general structure (V), in which R is a functional group which is ultimately convertible into a cyclopentene double bond. Methyl 2,2-dimethyl-3-oxocyclopentanecarboxylate [13] (VI; R = H) appeared suitable as a starting point. Alkylation of this compound with methyl acrylate by way of its pyrrolidine enamine [14] gave the keto-diester (VI; R = $CH_2 \cdot CH_2 \cdot CO_2Me$). The latter reacted smoothly with isopropenyl methyl ketone in the presence of methanolic sodium methoxide to give, presumably *via* an aldol-δ-lactone intermediate, a non-crystalline half-ester, characterised by hydrolysis to a crystalline dicarboxylic acid (VII; R = R′ = H). It was clear from its subsequent reactions that the half-ester was the hoped-for compound (VII; R = Me, R′ = H) and not its alternative.

In clovene, the angular hydrogen atom at C_5 (clovane numering [3]) is *cis* to the three-carbon bridge.[1] While the above half-ester could be cyclised, though in poor yield, to the clovane derivative (VIII; R = Me), we were convinced that catalytic hydrogenation of the double bond in this tricyclic compound, if it took place at all, would proceed from the

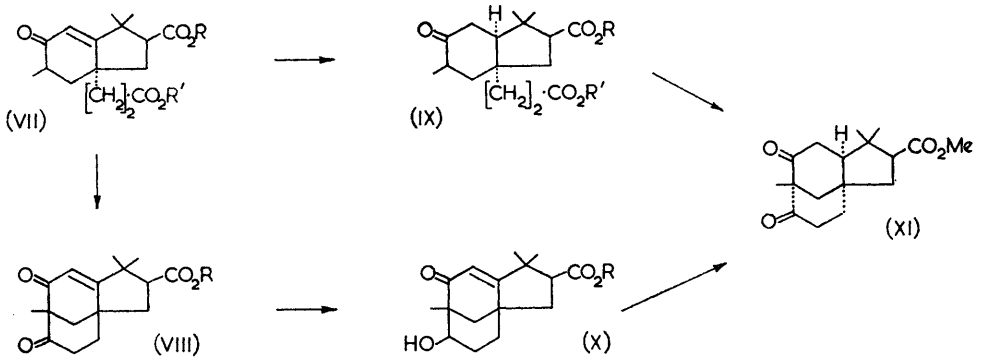
[1] Aebi, Barton, Burgstahler, and Lindsay, *J.*, 1954, 4660.
[2] Barton and Nickon, *J.*, 1954, 4665.
[3] Barton, Bruun, and Lindsey, *J.*, 1952, 2210.
[4] Lutz and Reid, *J.*, 1954, 2265.
[5] Eschenmoser and Gunthard, *Helv. Chim. Acta*, 1951, **34**, 2338.
[6] Clunie and Robertson, *J.*, 1961, 4382.
[7] Greenwood, Qurreshi, and Sutherland, *Proc. Chem. Soc.*, 1963, 373.
[8] Murray, Parker, Raphael, and Jhaveri, *Tetrahedron*, 1962, **18**, 55.
[9] Doyle, Maclean, Parker, and Raphael, *Proc. Chem. Soc.*, 1963, 239.
[10] Kos and Loewenthal, *J.*, 1963, 605.
[11] Loewenthal and Malhotra, *Proc. Chem. Soc.*, 1962, 230.
[12] Neuwirth, M.Sc. Thesis, Haifa, 1964.
[13] Gibson, Hariharan, and Simonsen, *J.*, 1927, 3009.
[14] Stork, Brizzolara, Landesman, Szmuszkovicz, and Terrell, *J. Amer. Chem. Soc.*, 1963, **85**, 207.

unhindered direction opposite to the three-carbon bridge to give a *trans*-junction (the eventual course of its hydrogenation is dealt with below).

On the other hand the half-ester (VII; R = Me, R′ = H) is an indanone of a type the hydrogenation of which has in all known previous cases given a *cis*-perhydroindanone, in spite of all attempts to obtain a *trans*-junction.[15-17] This compound was therefore hydrogenated, and the crude product was treated with naphthalene-2-sulphonic acid in boiling toluene, in the hope that electrophilic cyclisation would also take place in the present case of a *saturated* keto-acid, and that this cyclisation would proceed towards the more highly substituted 5-position rather than C_7 (indane numbering).

The product from these operations was a crystalline diketo-ester (XI), obtained in 40% overall yield, and examination of its n.m.r. spectrum showed that cyclisation had indeed taken place in the desired direction. It exhibited three unsplit *C*-methyl peaks at 0·94, 1·20, and at 1·28 p.p.m.; the last peak clearly corresponds to the methyl group adjacent to the two carbonyl groups.

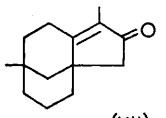
We now return to the stereochemistry of this compound. Catalytic hydrogenation of the unsaturated diketo-ester (VIII; R = Me), as well as of the corresponding acid [itself obtained by BF_3-catalysed cyclisation of the dicarboxylic acid (VII; R = R′ = H)], over Adams catalyst ceased after uptake of one mol. of hydrogen. From the spectra of the

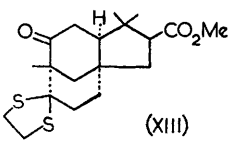


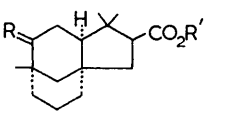
products (X; R = Me) and (X; R = H), respectively, it was clear that only the 9-keto-group had been reduced to hydroxyl. The acid (X; R = H) was now reduced with lithium in liquid ammonia and the product, after esterification, oxidised with chromic oxide in pyridine. The resulting diketo-ester was found to be identical with compound (XI) obtained by way of the *cis*-perhydroindane (IX; R = Me, R′ = H). If one accepts the views of Barton and Robinson,[18] this means that the desired *cis*-stereochemistry is also the most stable one for the clovane system, even though proton approach in the above reduction must be from a hindered direction. Alternatively, if more recently formulated views apply,[19] then (from inspection of scale models) it is clear that maximum orbital overlap of the intermediate C_5-carbanion with the incipient enolate double bond in ring B, together with nearly eclipsed conformation of bonds C_5—C_4 and C_1—C_2, do indeed lead to the produced stereochemistry. However, the final result is a boat conformation for ring B and this is at variance with recent results on the shape of simple bicyclo[3,3,1]nonanes.[20] Raphael, Parker, and their co-workers have obtained the same stereochemistry in their lithium–ammonia reduction of the unsaturated ketone (XII);[9] here it is difficult to judge

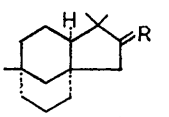
[15] Boyce and Whitehurst, *J.*, 1960, 4547.
[16] Dauben, McFarland, and Rogan, *J. Org. Chem.*, 1961, **26**, 297.
[17] Chaykovsky and Ireland, *J. Org. Chem.*, 1963, **28**, 748.
[18] Barton and Robinson, *J.*, 1954, 3045.
[19] Stork and Darling, *J. Amer. Chem. Soc.*, 1964, **86**, 1761.
[20] Brown, Eglinton, Martin, Parker, and Sim, *Proc. Chem. Soc.*, 1964, 57.

which configuration of the bridgehead carbanion would show maximum overlap with the cyclopentene enolate double bond.


(XII)


(XIII)


(XIV)


(XV)

Treatment of the diketo-ester (XI) with an excess of ethanedithiol in the presence of the boron trifluoride–ether complex gave in high yield a monothioketal which we believe to have structure (XIII). Its hydrogenolysis with Raney nickel in dioxan, followed by oxidation of the partly-formed hydroxy-ester (XIV; R = H or OH), led to the keto-ester (XIV; R = :O, R′ = Me). Huang-Minlon reduction of the latter compound gave a mixture of C_3-epimers of the carboxylic acid (XIV; R = H_2, R′ = H). The latter mixture could also be obtained, though in somewhat lower yield, by direct " double " Huang-Minlon reduction of the monothioketal (XIII).[21,22] Separation of a single epimer of this acid in good yield proved to be tedious. Hence, one pure epimer and also the mixture were separately esterified and treated with an excess of phenylmagnesium bromide. Dehydration of the resulting diphenylcarbinols gave in both cases the same crystalline diphenylethylene (XV; R = :CPh_2). Oxidation of the latter with ruthenium dioxide–sodium metaperiodate in acetone [23] gave the expected mixture of benzophenone and of the desired (±)-clovan-3-one (XV; R = :O) which were conveniently separated by preparative gas–liquid chromatography. The infrared spectrum of the latter ketone was identical in all respects with that prepared by Raphael, Parker, and their co-workers.[9] Since the latter group have converted it, in two further steps, to (±)-clovene, the above work constitutes a further synthesis of this caryophyllene rearrangement product.

P.m.r. spectra of clovane derivatives (in p.p.m. units downfield from tetramethylsilane).

Compound	C_8-methyl	C_4-methyls	C_3-ester methyl
(VIII; R = Me)	1·52	1·18, 1·24	3·86
(XI)	1·28	0·94, 1·20	3·82
(XIII)	1·33	0·88, 1·21	3·82
(XIV; R = :O, R′ = Me)	1·17	0·82, 0·99	3·74
(XIV; R = H_2, R′ = Me)	1·15	0·73, 0·88	3·69
Clovene (I) [24]	1·08	0·88, 0·97	
Clovane [24]	1·00	0·89	

Experimental

Unless otherwise stated, ultraviolet spectra were measured for methanol solutions and infrared spectra for chloroform solutions. Nuclear magnetic resonance spectra were determined in deuterochloroform solution on a Varian DP-60 spectrometer operating at 60 Mc./sec. with tetramethylsilane as internal reference. Gas–liquid chromatograms (g.l.c.) were run on a Wilkens Aerograph A-90-P2 instrument, with helium as carrier gas.

Methyl 5-(2-Methoxycarbonylethyl)-2,2-dimethyl-3-oxocyclopentanecarboxylate (VI; R = CH_2·CH_2·CO_2Me).—Methyl 2,2-dimethyl-3-oxocyclopentanecarboxylate (VI; R = H) was prepared by the original procedure [13] as partly modified by Stork and Clarke.[25] It had b. p. 70—75°/0·1 mm. and showed a single g.l.c. peak (Silicone SE-20 on Chromosorb W at 180°, flow rate 40 ml./min., retention time 3·4 min.).

This keto-ester (20 g.) was heated under reflux in benzene (50 ml.) with pyrrolidine (17 ml.) until azeotropic separation of water ceased (12 hr.); reflux was then continued for another

[21] Georgian, Harrison, and Gubitsch, *J. Amer. Chem. Soc.*, 1959, **81**, 5835.
[22] Corey, Ohno, Mitra, and Vatakencherry, *J. Amer. Chem. Soc.*, 1964, **86**, 481.
[23] Becker and Pappo, *Bull. Res. Council Israel*, 1956, **5A**, 300.
[24] Personal communication from Dr. Parker.
[25] Stork and Clarke, *J. Amer. Chem. Soc.*, 1961, **83**, 3123.

12 hr. in such a way that condensed liquid returned to the reaction mixture *via* a bed of molecular sieves (type 4A). The reaction mixture was then concentrated at 100°/0·1 mm. and the residue, the infrared spectum of which showed a band at 6·15 μ (enamine double bond), was dissolved in dry dioxan (50 ml.). Methyl acrylate (25 ml.) was then added and the solution was refluxed under nitrogen for 24 hr., after which water (10 ml.) was added and reflux continued for 5·5 hr. The solution was then concentrated *in vacuo* and the residue was taken up in ether–benzene. The organic layer was washed with dilute hydrochloric acid, water, 5% aqueous sodium hydroxide, again with water, dried ($MgSO_4$), and the solvents removed. The residue was fractionated *in vacuo*, giving (*a*) a forerun (11·0 g.) of unchanged starting ester, followed by (*b*) the *keto-diester* (14·0 g.), b. p. 130°/0·5 mm. (Found: C, 61·1; H, 7·85. $C_{13}H_{20}O_5$ requires C, 60·9; H, 7·85%), $\lambda_{max.}$ 5·75—5·80 μ, which showed a single g.l.c. peak (Silicone SE-30 on Chromosorb W at 210°, flow rate 42·8 ml./min., retention time 10 min.). It failed to give a ketonic derivative, presumably owing to steric hindrance.

An attempt was made to prepare this compound *via* Michael addition of methyl acrylate to dimethyl 4,4-dimethyl-5-oxocyclopentane-1,3-dicarboxylate.[25] However, g.l.c. studies showed that decarboxylation of the resulting adduct was incomplete even after prolonged acid hydrolysis.

Reaction of the Keto-diester (VI; R = $CH_2{\cdot}CH_2{\cdot}CO_2Me$) *with Isopropenyl Methyl Ketone.*—The keto-diester (10·2 g.) was added to a solution of sodium (2·3 g.) in methanol (80 ml.) at 0° under nitrogen, followed by dropwise addition of isopropenyl methyl ketone (6·0 ml.). The reaction mixture was allowed to reach room temperature overnight, after which it was acidified with dilute hydrochloric acid. The oil obtained after removal of methanol and addition of water was taken up in ether–benzene, and the organic layer was extracted with 10% aqueous potassium hydrogen carbonate. Acidification of the extracts and isolation with chloroform gave the *half-ester* (VII; R = Me, R′ = H), $\lambda_{max.}$ 5·73—5·80 and 5·98 μ (10·0 g.), which could not be crystallised and which was used without further purification.

Hydrolysis of this product (9·6 g.) in methanol (120 ml.) and 10% aqueous potassium hydroxide (120 ml.) at 40—50° under nitrogen for 2 hr., followed by removal of methanol *in vacuo*, acidification, and isolation with chloroform gave an oil which crystallised on trituration with ether to give 2-*carboxy*-β-(3a,4,5,6-*tetrahydro*-1,1,5-*trimethylindan*-6-*oxo*-3a-*yl*)-*propionic acid* (VII; R = R′ = H) (3·0 g.), m. p. 228° (decomp.) after recrystallisation from ethyl acetate–methylcyclohexane (Found: C, 65·4; H, 7·55. $C_{16}H_{22}O_5$ requires C, 65·3; H, 7·55%), $\lambda_{max.}$ 243 mμ (ε 12,400).

Hydrogenation of the latter acid in acetic acid in the presence of palladium on carbon (10%) gave cis-2-*carboxy*-β-(3a,4,5,6,7,7a-*hexahydro*-1,1,5-*trimethylindan*-3a-*yl*-6-*oxo*)*propionic acid* (IX; R = R′ = H), m. p. 166—167° (from chloroform–isopropyl ether) (Found: C, 64·65; H, 8·4. $C_{16}H_{24}O_5$ requires C, 64·85; H, 8·15%).

(±)-7,9-*Dioxoclov*-5-*ene*-3-*carboxylic Acid* (VIII; R = H), *and its Methyl Ester* (VIII; R = Me).—(*a*) The dicarboxylic acid (VII; R = R′ = H) (305 mg.) was dissolved in acetic acid (1·0 ml.) and acetic anhydride (0·2 ml.), and the solution was treated at room temperature with the boron trifluoride–ether complex (0·5 ml.). After being warmed at 100° for 15 min. the solution was left at room temperature overnight. Ice was added and the product extracted with chloroform. The extract was washed with water and dried ($MgSO_4$), and the solvent removed. Two crystallisations of the residue from chloroform–isopropyl ether gave the pure *diketo-acid* (151 mg.), m. p. 216—216·5° (Found: C, 69·4; H, 7·25. $C_{16}H_{20}O_4$ requires C, 69·55; H, 7·3%), $\lambda_{max.}$ 206 (ε 4300) and 243·5 mμ (8900).

Treatment with ethereal diazomethane gave the *methyl ester*, m. p. 138—138·5° (from methylene chloride–hexane) (Found: C, 70·45; H, 7·5. $C_{17}H_{22}O_4$ requires C, 70·3; H, 7·65%), $\lambda_{max.}$ 5·75 and 5·97 μ.

(*b*) The crude half-ester (VII; R = Me, R′ = H) (2·30 g.), dissolved in acetic acid (10 ml.) and acetic anhydride (1·0 ml.), was treated at room temperature with the boron trifluoride–ether complex (2·5 ml.). After 12 hr. water was added and the product taken up in ether. The extract was washed with 5% aqueous sodium carbonate, then with water, and dried ($MgSO_4$), and the ether removed. After chromatography of the residue on Florisil (40 g.), followed by recrystallisation from methanol at −10°, there was obtained the above methyl ester (0·5 g.), identical (mixed m. p. and i.r. spectrum) with the product as obtained under (*a*).

Hydrogenation of the acid (VIII; R = H) (437 mg.) in methanol in the presence of Adams catalyst (prereduced; 50 mg.) ceased (2 hr.) after uptake of 0·95 mol. equiv. hydrogen. The resulting (±)-9-*hydroxy*-7-*oxoclov*-5-*ene*-3-*carboxylic acid* (X; R = H) had m. p. 221—221·5°

(398 mg.) (from ethyl acetate–methylcyclohexane) (Found: C, 69·0; H, 7·9. $C_{16}H_{22}O_4$ requires C, 69·05; H, 7·95%).

Similar hydrogenation of the methyl ester (VIII; R = Me) gave the *methyl ester* of the foregoing acid (X; R = Me), m. p. 115·5—116° (from hexane) (Found: C, 69·9; H, 8·2. $C_{17}H_{24}O_4$ requires C, 69·85; H, 8·25%); $\lambda_{max.}$ 244 mμ (ε 10,000); 2·70, 5·75, and 6·02 μ.

Methyl (±)-7,9-*Dioxoclovane*-3-*carboxylate* (XI).—(*a*) The crude half-ester (VII; R = Me, R′ = H) (10·6 g.) was hydrogenated in acetic acid in the presence of palladium on carbon (30%, 1·5 g.) until hydrogen uptake (470 ml.) ceased (2 hr.). The residue obtained after filtration and removal of acetic acid at 100°/0·1 mm. was refluxed in toluene (200 ml.) with naphthalene-2-sulphonic acid (500 mg.) for 12 hr. with azeotropic removal of water. After being cooled the solution was washed with 5% aqueous sodium carbonate, and then with water and dried ($MgSO_4$). Removal of solvent and cystallisation of the residue from methylene chloride–isopropyl ether gave the *diketo-ester* (4·0 g.), m. p. 156·5—157° (Found: C, 70·7; H, 8·4. $C_{17}H_{24}O_4$ requires C, 69·85; H, 8·25%), $\lambda_{max.}$ 5·75 and 5·85 μ. A further quantity could be obtained by chromatography of the mother-liquors on Florisil.

(*b*) The acid (X; R = H) (250 mg.) was suspended in liquid ammonia (50 ml.). With stirring, lithium was added in small pieces at −60° during 1·5 hr. until a blue colour persisted for more than 15 min.; this was then discharged by addition of ammonium chloride. Removal of ammonia, addition of water, acidification, and extraction with chloroform gave a solid which was esterified with ethereal diazomethane. The resulting methyl ester (237 mg.), $\lambda_{max.}$ 2·70, 5·72, and 5·85 μ, was dissolved in pyridine (2 ml.) and chromic oxide (220 mg.) was added cautiously with agitation. After 12 hr. at room temperature ether was added, the suspension was filtered and the filtrate was washed with dilute hydrochloric acid containing ferrous sulphate, with water, then with 5% aqueous sodium carbonate, again with water, dried ($MgSO_4$), and the ether removed. Crystallisation of the residue from isopropyl ether gave the diketo-ester (120 mg.), m. p. 155·5—156° undepressed by admixture with the product as obtained under (*a*) and showing an identical infrared spectrum.

Methyl (±)-9,9-*Ethylenedithio*-7-*oxoclovane*-3-*carboxylate* (XIII).—A suspension of the above diketo-ester (3·5 g.) in ethanedithiol (5 ml.) was treated with the boron trifluoride–ether complex (5 ml.). The solid at first dissolved; this was followed shortly by separation of the product. After 6 hr. at room temperature the mixture was taken up in chloroform, the organic layer was washed several times with cold 10% aqueous sodium hydroxide, then with water, dried ($MgSO_4$), and the chloroform removed. Crystallisation of the residue from chloroform–methanol gave the *thioketal* (3·7 g.), m. p. 214° (Found: C, 62·0; H, 7·75; S, 17·35. $C_{19}H_{28}O_3S_2$ requires C, 61·95; H, 7·65; S, 17·35%).

Methyl (±)-7-*Oxoclovane*-3-*carboxylate* (XIV; R = O, R′ = Me).—The above monothioketal (3·0 g.), dissolved in dioxan (25 ml.), was refluxed with stirring with Raney nickel (W2, 10 teaspoons) for 12 hr. The suspension was then filtered and the nickel washed with dioxan. The combined filtrate and washings were concentrated *in vacuo*. Two crystallisations of the residue from hexane gave the *keto-ester* (0·72 g.), m. p. 122° (Found: C, 73·3; H, 9·3. $C_{17}H_{26}O_3$ requires C, 73·35; H, 9·4%), $\lambda_{max.}$ 5·75 and 5·85 μ. The mother-liquors from this compound were concentrated, and the residue, which showed an hydroxyl band in the infrared, was oxidised in acetone with 8N-chromic acid in aqueous sulphuric acid.[26] The neutral residue obtained after the customary working-up, after crystallisation from hexane, gave a further 1·43 g. of the above keto-ester. The 2,4-*dinitrophenylhydrazone*, orange leaflets from chloroform–methanol, had m. p. 182—183° (decomp.) (Found: C, 60·35; H, 6·7. $C_{23}H_{30}N_4O_6$ requires C, 60·25; H, 6·6%).

Hydrolysis of the above ester with boiling 5% methanolic potassium hydroxide afforded the *acid* (XIV; R = :O, R′ = H), m. p. 182—183·5° (from chloroform–hexane) (Found: C, 72·8; H, 8·95. $C_{16}H_{24}O_3$ requires C, 72·7; H, 9·15%).

(±)-*Clovane*-3-*carboxylic Acid* (XIV; R = H_2, R′ = H).—(*a*) The above keto-ester (0·9 g.) was refluxed in dihydroxymethyl ether (10 ml.) with potassium hydroxide (1·2 g.) and hydrazine (64% in water, 2·1 ml.) for 4 hr., after which the mixture was distilled until the temperature reached 220°. It was then kept at this temperature for 2 hr. under nitrogen. The suspension obtained after cooling, dilution with water, acidification, and saturation with ammonium sulphate was continuously extracted with chloroform for 12 hr. The extract was washed with water

[26] Djerassi, Engle, and Bowers, *J. Org. Chem.*, 1956, **21**, 1547.

and then extracted with 5% aqueous potassium hydroxide. Acidification and isolation with chloroform gave an oil (0·93 g.) which was treated with an excess of ethereal diazomethane. The resulting *methyl ester* (XIV; R = H_2, R′ = Me) distilled at 120° (bath)/0·1 mm. (400 mg.) (Found: C, 77·1; H, 10·7. $C_{17}H_{28}O_2$ requires C, 77·2; H, 10·65%). This ester gave a single g.l.c. peak (Silicone SE-30 on Chromosorb W at 200°, flow rate 38 ml./min., retention time 16·4 min.). However, hydrolysis with boiling 10% methanolic potassium hydroxide gave a crude product, crystallisation of which from hexane gave only *ca.* 40% of one pure *epimer* of the acid, which after sublimation at 120°/0·1 mm. had m. p. 171—173° (Found: C, 76·7; H, 10·35. $C_{16}H_{26}O_2$ requires C, 76·75; H, 10·45%).

(*b*) The monothioketal (XIII) (1·11 g.) was refluxed in diethylene glycol (12 ml.) with potassium hydroxide (1·5 g.) and hydrazine (64% in water; 2·8 ml.) and the reaction mixture was worked up, as described under (*a*). The acidic portion from this reaction (711 mg.) showed the same properties as the product described above, and gave a corresponding yield of the above crystalline epimer.

Substitution of anhydrous hydrazine for the hydrate in the above reactions gave mostly neutral product in low yield, which from its infrared spectrum appeared to be a hydrazide.

3-Diphenylmethylene-(±)-clovane (XV; R = :CPh_2).—The above crystalline epimer of the acid (XIV; R = H_2, R′ = H) was esterified with diazomethane. The resulting ester (366 mg.) was added in benzene (10 ml.) to a solution of phenylmagnesium bromide, prepared from bromobenzene (1·4 ml.) and magnesium (220 mg.) in ether (10 ml.). The resulting solution was distilled until the temperature reached 80° and was then heated under reflux for 10 hr. It was then decomposed with aqueous ammonium chloride and steam was passed through the resulting suspension for 3 hr. After being cooled the oil was extracted with methylene chloride, the extract was dried ($MgSO_4$), and the solvent removed. The residue, which still had a smell of biphenyl, was refluxed with acetic anhydride (10 ml.) for 12 hr., after which the anhydride was removed at 100°/0·1 mm. The residue was chromatographed in pentane on alumina (Merck, basic; 40 g.). The product, eluted with hexane and hexane–methylene chloride, was still contaminated with biphenyl. Repeated chromatography gave the pure *olefin*, which after crystallisation from ether–methanol had m. p. 110—110·5° (200 mg.). The anlytical sample was prepared by sublimation at 100°/0·05 mm. (Found: C, 90·5; H, 9·05. $C_{28}H_{34}$ requires C, 90·75; H, 9·25%).

The mother-liquors of the crystalline epimer of the acid (XIV; R = H_2, R′ = H) (1·30 g.) were esterified, and the resulting ester treated as described above, affording finally the olefin (305 mg.), identical in all respects with the above product.

(±)-Clovan-3-one (XV; R = :O).—The above olefin (100 mg.) was dissolved in pure acetone (8 ml.), and ruthenium dioxide (10 mg.) and 5% aqueous sodium metaperiodate (0·5 ml.) were added. With stirring sodium metaperiodate (0·3 g.) was added during 4 hr., after which isopropyl alcohol (2 ml.) was added and stirring continued for 15 min. The suspension was filtered and the solid washed with ether. The combined filtrate and washings were concentrated *in vacuo* and the residue taken up in hexane. The hexane solution was washed with 5% aqueous sodium hydroxide, then with water, dried ($MgSO_4$), and the hexane removed. The residue (91 mg.) on g.l.c. (Silicone SE-30 on Celite at 190°, flow rate 100 ml./min.) showed two peaks of equal area with retention tims of 15 and 16·5 min.; the former peak corresponded to that shown by authentic benzophenone. Complete preparative separation was effected on a column of neopentyl glycol succinate on Celite (1 : 4 w/w, 300 cm. by $\frac{3}{8}$ in., at 200°, flow rate 133 ml./min.); here the retention times were 42 min. for benzophenone, and 22·5 min. for the *ketone*, which was once redistilled at 90° (bath)/0·1 mm. Its infrared spectrum (liquid film), kindly measured for comparison by Dr. W. Parker, was identical in all respects with that of (±)-clovan-3-one synthesised by Raphael, Parker, and their co-workers.[9]

Part of this work was supported by the Petroleum Research Fund administered by the American Chemical Society; and thanks are expressed to the donors of this fund.

CHEMISTRY DEPARTMENT, ISRAEL INSTITUTE OF TECHNOLOGY,
HAIFA, ISRAEL.

[*Received, June 1st,* 1964.]