413. *Studies in Relation to Biosynthesis. Part XXXII.**
Preparation, Spectra, and Hydrolysis of Poly-β-carbonyl Compounds.

By A. J. Birch, P. Fitton, D. C. C. Smith, D. E. Steere, and
A. R. Stelfox.

Ultraviolet spectra of mono- and di-anions of some linear tri-β-carbonyl compounds and of acetoacetic and 3,5-dioxohexanoic acid are reported and the course of decomposition of these compounds by alkali is described. A new approach to the preparation of poly-β-diketones by ozonolysis of dihydro-aromatic compounds is described, leading to a ketal of undecane-2,4,6,8,10-pentaone, the first reported derivative of a linear penta-β-ketone. A new explanation is offered for the " acidic " fission of β-keto-esters.

LINEAR poly-β-keto-acids, as their coenzyme-A esters, appear to be intermediates in the biosynthesis of many plant and mould products by the acetate–malonate (polyketide) route.[1] Normally they exist only as enzyme-bound complexes, but it may be possible to obtain them by biochemical techniques; for example, Wakil and Bressler[2] obtained evidence of the production in fatty acid synthesis of an unknown compound of this type. Such work is handicapped by lack of information on the spectra and chemical behaviour of these compounds, owing in part to the lack of methods for their synthesis.

The present work was aimed at the preparation of substances of types (I)—(IV), by ozonolysis of cyclohexa-1,4-dienes which has been shown[3] to lead to β-diketones. The highest members of this series so far described are diformylacetone (I; $n = 2$),[4] diacetylacetone (II; $n = 2$),[5] formylacetone (III; $n = 1$),[6] and 3,5-dioxohexanoic acid (IV; $n = 2$).[7]

$$(\text{I})\ \ H \cdot [CO \cdot CH_2]_n \cdot CHO \qquad\qquad Me \cdot [CO \cdot CH_2]_n \cdot COMe\ \ (\text{II})$$

$$(\text{III})\ \ Me \cdot [CO \cdot CH_2]_n \cdot CHO \qquad\qquad Me \cdot [CO \cdot CH_2]_n \cdot CO_2 H\ \ (\text{IV})$$

In order to characterise higher members of the series it was first necessary to study the ultraviolet spectra and hydrolysis into acetone and acetic acid of simpler members, about which surprisingly little information is available.

* Part XXXI, *J.*, 1962, 3586.

[1] Birch and Donovan, *Austral. J. Chem.*, 1953, **6**, 360; Lynen and Tada, *Angew. Chem.*, 1961, **73**, 513; Birch, *Proc. Chem. Soc.*, 1962, 3.
[2] Wakil and Bressler, *J. Biol. Chem.*, 1962, **237**, 687.
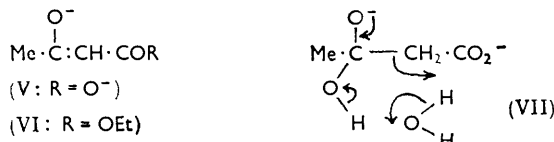[3] Birch, *J.*, 1944, 430.
[4] Willstätter and Pummerer, *Ber.*, 1905, **38**, 1461.
[5] Feist, *Annalen*, 1890, **257**, 253.
[6] Boileau, *Bull. Soc. chim. France*, 1954, 761.
[7] Witter and Stotz, *J. Biol. Chem.*, 1948, **176**, 485.

Solutions of sodium acetoacetate are reported to have no selective ultraviolet absorption,[8] which indicates that the anion probably exists in the keto-form. In more concentrated alkali, sodium acetoacetate shows a strong absorption band at 263 mμ ($E_{mol.}$ 28,800 in 10N-NaOH), which we attribute to the conjugated dianion (V) since the anion (VI) of ethyl acetoacetate has a similar band at 271 mμ (ε 30,000). It should be noted that the E value above is almost certainly lower than the true ε because of incomplete dissociation. Similarly, other β-keto-acids (values for the ester in parentheses) develop absorption properties in 10N-sodium hydroxide: 2-methylacetoacetic acid, $\lambda_{max.}$ 270 mμ, $E_{mol.}$ 2600 (281 mμ); 2-oxocyclohexanecarboxylic acid, $\lambda_{max.}$ 274 mμ, $E_{mol.}$ 7200 (284 mμ); 2-oxocyclopentanecarboxylic acid, $\lambda_{max.}$ 276 mμ, $E_{mol.}$ 5100 (288 mμ).

$$\text{Me·C:CH·COR} \quad (\overset{O^-}{\underset{}{}})$$

(V: R = O⁻)

(VI: R = OEt)

(VII)

By altering the concentration of sodium hydroxide the concentration of dianion was found to become appreciable in >~N-solution; such alteration also changes the ratio of acetone and acetic acid produced by hydrolysis at 100° (Table 1), and it may be significant that " acidic " fission is inappreciable in <N-solution. The times for 20% decomposition of sodium acetoacetate solutions at room temperature are: N, 70 hr.; 10N, 15 min. Possibly the differences both in the rate and in the direction of fission can be explained by intervention of the dianion at higher pH. Hydration of this ion (V) to (VII) and breakdown as indicated could occur. Repulsion between negatively charged groups may weaken the central C–C bond.

TABLE 1.

Amounts of acetone and acetic acid recovered when ethyl acetoacetate is hydrolysed to sodium acetoacetate in 1·7% aqueous sodium hydroxide at room temperature, then heated for 1 hr. at 100° with aqueous sodium hydroxide.

[NaOH] (N)	0·32	1·0	1·8	3·2	5·6	7·1	10·0
Acetone (%)	97	96	93·5	82	55	27	3
Acetic acid (%)	0	0	10	20	45	79	98

The crystalline salts of diacetylacetone (II; $n = 2$), *e.g.*, Na$_2$C$_7$H$_8$O$_3$,H$_2$O and BaC$_7$H$_8$O$_3$,4H$_2$O, probably contain the dianion (IX). In aqueous 0·01N-sodium hydroxide diacetylacetone has one absorption band, at $\lambda_{max.}$ 295 mμ (ε 20,700), the similarity of which to that of acetylacetone in alkali, $\lambda_{max.}$ 293 mμ (ε 23,600), suggests that it is due to the mono-anion (VIII). A similar spectrum has been recorded for the disodium salt dissolved in water,[9] and the dissociation constants of diacetylacetone determined by means of pH measurements are pK_{a1} 7·4, pK_{a2} 13·5.[10] In >N-alkali there is an absorption band at 342 mμ, which resembles that of the anion of glutaconaldehyde ($\lambda_{max.}$ 360 mμ; ε 40,000) and can be reasonably attributed to the dianion (IX).

(VIII) Me·C—CH—C·CH$_2$·COMe

(IX) Me·C—CH—C—CH—CMe

The extinction of this band could be estimated only by extrapolating specific absorption back to the time of mixing, since the intensity diminishes quite rapidly; times for 10% of decomposition at room temperature are: N, 50 min.; 2N, 24 min.; 3N, 13 min.; 5N, 6 min.; 8N, 3 min.; 10·5N, 2 min. If $E_{mol.}$ 35,000 (342 mμ) (in 10·5N-sodium hydroxide) is used as a minimum estimate of the extinction of the dianion, $E_{mol.}$ (342 mμ) attains half

[8] Kornberg, Ochoa, and Mehler, *J. Biol. Chem.*, 1948, **174**, 159.
[9] Schwarzenbach, Lutz, and Felder, *Helv. Chim. Acta*, 1944, **27**, 576.
[10] Schwarzenbach and Lutz, *Helv. Chim. Acta*, 1940, **23**, 1162.

this value in approximately ∼4N-alkali, indicating that pK_{a2} has a considerably higher value than estimated previously.[10]

The self-condensation of diacetylacetone in solutions of pH values near pK_{a1}, containing barium ions, has been described [11] and elucidated.[12] We find that the monoanion (VIII) is stable in solutions free from appreciable amounts of neutral triketone and dianion (IX); decomposition into acetic acid and acetylacetone would not affect the ultraviolet spectrum, but the amount of triketone present was determined independently by raising the pH of aliquot portions and determining the initial extinction due to the dianion (IX). The decomposition of diacetylacetone in concentrated alkali yields ultimately acetone and acetic acid. At lower concentrations of sodium hydroxide, the relative amount of acetone increases, as shown in Table 2.

TABLE 2.

Amounts of acetone and acetic acid recovered when diacetylacetone is cleaved by aqueous sodium hydroxide at room temperature for 2 days.

[NaOH] (N)	10	5	1
Acetone (mol.)	0·99	1·13	1·22
Acetic acid (mol.)	1·77	1·59	1·05

This parallels the behaviour of acetoacetic acid, which may therefore be an intermediate in the alkaline decomposition of diacetylacetone.

Another possible intermediate in the alkaline decomposition of poly-β-ketones is 3,5-di-oxohexanoic acid (IV; $n = 2$). It shows an absorption band at 295 mμ (ε 18,000) in alkali of concentration 0·01—10N; such a spectrum could be due to the monoanion or the dianion, or to decarboxylation giving acetylacetone, as all would have a similar chromophore. Decomposition in 10N-sodium hydroxide yields acetic acid (1·09 mol.) and acetone (0·93 mol.), in contrast to that of acetoacetic acid, which yields only a trace of acetone under these conditions.

Formylacetone in 0·1N-sodium hydroxide has an absorption band at 282 mμ (ε 17,700); the intensity falls, times for 10% decomposition at room temperature being: 0·1N, 120 min.; N, 12 min. The decomposition into acetone is therefore faster than for acetyl-acetone. 4-Pyrone, on dissolution in alkali, suffers ring-opening to yield diformylacetone.[4] This solution exhibits a strong absorption band at 337 mμ which corresponds approximately with that of the dianion (IX) and is therefore attributable to the dianion of diformyl-acetone. Like the dianion (IX) this was unstable: the times for 50% decomposition at room temperature were: 3·05N, 40 min., 5·1N, 16·5 min.; 8·2N, 5·5 min. The molecular extinction of the dianion of diformylacetone was calculated, by extrapolation to the time of mixing, to be 42,700. In contrast to diacetylacetone, no absorption due to a mono-anion was detected initially, even in solutions as weakly alkaline as 0·01N-sodium hydroxide: this demonstrates the greater acidity of diformylacetone.

A second stage in this study was the synthesis of dihydro-aromatic compounds which might give poly-β-carbonyl compounds on ozonolysis. One approach to substances of type (I) is suggested by the existence of 1,4,5,8-tetrahydronaphthalene (X). We have extended this series by reducing anthracene with sodium and ethanol in liquid ammonia to 1,4,5,8,9,10-hexahydroanthracene (XI). Another approach could be from derivatives of 4,7-dihydroindan-2-one, and compounds of this type (XII—XIV) have therefore been synthesised. Indan-2-one was converted into a ketal (XV), which was easily reducible to the dihydro-compound (XII). Exceptional ease of reduction of indane by a metal–ammonia system, as compared with that of o-xylene, has been reported,[13] and without assistance from this effect the analogous reduction of the tri- and tetra-substituted aromatic system in the ketals (XVI) and (XVII) would probably be impracticable.

[11] Collie and Myers, *J.*, 1893, 122.
[12] Birch, Cameron, and Rickards, *J.*, 1960, 4395.
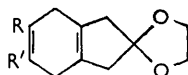[13] Krapcho and Bothner-By, *J. Amer. Chem. Soc.*, 1959, **81**, 3658.

2-Methylnaphthalene was reduced with sodium in isopropyl alcohol to a mixture of dihydro-compounds. Hückel *et al.*[14] prepared a mercuric acetate adduct from the mixture produced in this way and formulated it as the adduct of 1,4-dihydro-2-methylnaphthalene
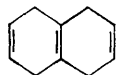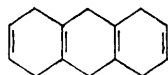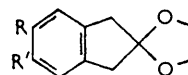

(X)   (XI)   (XII: R = R' = H)   (XV: R = R' = H)
(XIII: R = Me, R' = H)   (XVI: R = Me, R' = H)
(XIV: R = R' = Me)   (XVII: R = R' = Me)

(XVIII). We have found the mixture to contain 5,8-dihydro-2-methylnaphthalene (XX), since ozonisation followed by oxidation with alkaline hydrogen peroxide afforded 4-methyl-1,2-phenylenediacetic acid (XXII). Esterification, cyclisation with sodium, hydrolysis, and decarboxylation then gave 5-methylindan-2-one. This gave the ketal (XVI) which was reduced to the dihydro-compound (XIII).
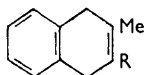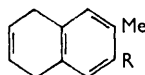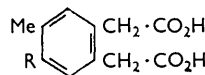

(XVIII: R = H)   (XX: R = H)   (XXII: R = H)
(XIX: R = Me)   (XXI: R = Me)   (XXIII: R = Me)

By a parallel series of reactions, 2,3-dimethylnaphthalene was converted into the ketal (XVII) and thence into the dihydro-compound (XIV). The initial reduction of 2,3-dimethylnaphthalene with sodium and isopropyl alcohol gave a crystalline product, m. p. 55—58°. In view of its subsequent ozonolysis to yield 4,5-dimethyl-1,2-phenylene-diacetic acid (XXIII), this product clearly contains 5,8-dihydro-2,3-dimethylnaphthalene (XXI). To permit estimation of the relative amounts of this and of 1,4-dihydro-2,3-dimethylnaphthalene (XIX) in the reduction product, the latter compound was synthesised. 4a,5,8,8a-Tetrahydro-6,7-dimethyl-1,4-naphthaquinone (XXIV) was reduced to the diol (XXV) by aluminium isopropoxide, then dehydrated with phosphorus oxychloride,
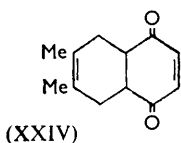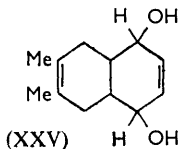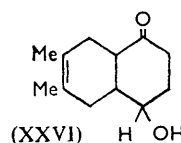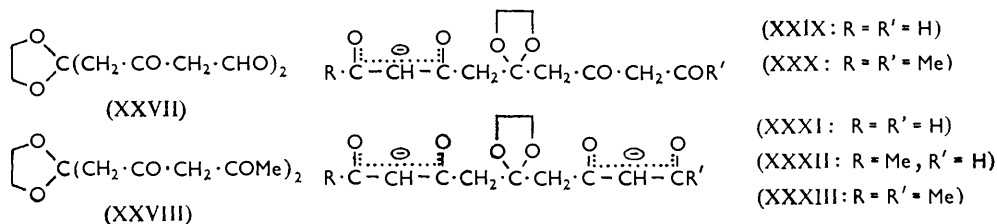

(XXIV)   (XXV)   (XXVI)

affording 1,4-dihydro-2,3-dimethylnaphthalene. Reduction of the diketone (XXIV) with lithium aluminium hydride afforded none of the diol (XXV), but instead a 95% yield of the hydroxy-ketone (XXVI). Other unsaturated 1,4-diketones have been reported to give analogous products with lithium aluminium hydride.[15] Comparison of the infrared spectra of 1,4-dihydro-2,3-dimethylnaphthalene and of the reduction product of 2,3-dimethylnaphthalene revealed that the latter contains approximately equal amounts of the two dihydro-compounds (XIX) and (XXI).

The last stage in the present study, ozonolysis to yield poly-β-carbonyl compounds, was carried out in methanol below 0°. The ozonide of the ketal (XII) was hydrogenated to yield the tetraketone (XXVII), isolated as a colourless oil that gave a red colour with ferric chloride and darkened within a few minutes of isolation. Its ultraviolet spectrum showed a complex changing pattern: the substance is clearly unstable. Direct hydrolysis of the ozonide with 0·1N-sodium hydroxide gave a simple ultraviolet spectrum with a single

[14] Hückel, Cramer, and Läufer, *Annalen*, 1960, **630**, 89.
[15] Lutz and Gillespie, *J. Amer. Chem. Soc.*, 1950, **72**, 2002; Boyland and Manson, *J.*, 1951, 1837.

strong band at 280 mμ [$E_{mol.}$ 10,000, calculated on the weight of ketal used], falling in intensity by 50% in an hour. This is reminiscent of formylacetone (I: $n = 1$) and is therefore as expected for the spectrum of the monoanion (XXIX) or the dianion (XXXI).

$$C(CH_2 \cdot CO \cdot CH_2 \cdot CHO)_2 \quad (XXVII)$$

$$R \cdot C = CH - C \cdot CH_2 \cdot C \cdot CH_2 \cdot CO \cdot CH_2 \cdot COR'$$

(XXIX : R = R' = H)
(XXX : R = R' = Me)

$$C(CH_2 \cdot CO \cdot CH_2 \cdot COMe)_2 \quad (XXVIII)$$

$$R \cdot C = CH - C \cdot CH_2 \cdot C \cdot CH_2 \cdot C = CH - CR'$$

(XXXI : R = R' = H)
(XXXII : R = Me, R' = H)
(XXXIII : R = R' = Me)

A similar hydrolysis of the ozonide from the ketal (XIII) gave an ultraviolet spectrum with a single broad maximum at 290 mμ, possibly due to the dianion (XXXII).

Ozonisation and hydrogenation converted the ketal (XIV) into the tetraketone (XXVIII). This proved more stable than the diformyl compound (XXVII). Direct hydrolysis of the ozonide with sodium hydroxide solutions yielded solutions with a single absorption band at 294 mμ. This was sharpest when the hydrolysis was carried out in 0·1N-sodium hydroxide; the intensity first increased, then decreased again, and was more intense, though broader, in more concentrated alkali.

The increase in extinction caused by alkali, without a shift in the position of the absorption band, is consistent with the replacement of the monoanion (XXX) by the dianion (XXXIII) with rising pH. The reason for the spontaneously increasing extinction observed immediately after the ozonide has been mixed with alkali is not clear, but the subsequent fall on storage has been shown to be accompanied by cleavage of the penta-β-ketone ketal to acetone and acetate. Each mole of the ketal (XIV) yielded, after ozonisation and hydrolysis in 10N-sodium hydroxide, 2·26 mol. of acetic acid and 1·07 mol. of acetone. These amounts are about what one would predict from the observed cleavage products of simpler substances in concentrated alkali (see Table 3).

TABLE 3.

Possible products of alkaline cleavage of undecane-2,4,6,8,10-pentaone, if initial breakage of the chain is random and is followed by cleavage of the initial products similar to that found for diacetylacetone, 3,5-dioxohexanoic acid, and acetoacetic acid. (The experimental yields of acetic acid and acetone from these compounds in 10N-sodium hydroxide are used.)

Initial products	Predicted yields (mol.) of ultimate products	
	Acetone	Acetate
Acetone + 3,5,7,9-tetraoxo-octanoic acid	2·03 *	1·98 *
Acetylacetone + 3,5-dioxohexanoic acid	1·93	2·09
Diacetylacetone + acetoacetic acid	1·02	3·73
Nonane-2,4,6,8-tetraone + acetic acid	1·93 †	1·09 †
Average	1·73	2·22

* Calc. by assuming that 3,5,7,9-tetraoxo-octanoic acid yields acetone (1 mol.), carbon dioxide and acetoacetic acid (1 mol.). † Calc. by assuming that nonane-2,4,6,8-tetraone yields acetone (1 mol.) and dioxohexanoic acid (1 mol.).

Attempts to prepare crystalline derivatives from the pentaketone or its ketal (XXVIII) failed. Attempts to cyclise it by the aldol reaction gave amorphous mixtures, shown by paper chromatography to be complex. Apart from intermolecular condensations, the possibilities of alicyclic, phenolic, and pyrone ring formation by a linear penta-β-ketone are numerous.

EXPERIMENTAL

Acetone was determined, unless otherwise stated, by Folin's method [16] and acetic acid was titrated with 0·01N-sodium hydroxide after steam-distillation from solutions acidified with phosphoric acid.

Ultraviolet Measurements with Sodium Acetoacetate.—Ethyl acetoacetate was dissolved in 1·7% sodium hydroxide solution and kept at 5° for 24 hr. The amount of acetone produced by decarboxylation was estimated colorimetrically by Korenman's method [17] to be 1·8%. Aliquot parts of the solution were diluted with aqueous sodium hydroxide of various strengths for spectroscopic measurements, and molar extinction values were calculated from the weight of ethyl acetoacetate originally taken, with a small correction for decarboxylation (see Table 4).

TABLE 4.

[NaOH] (N)	0·01	0·02	0·10	0·20	1·0	5·0	10·0
$\lambda_{max.}$ (mμ)	272	269	267	265	264	263	263
$E_{mol.}$	55	66	159	282	2000	17,800	28,800

Ultraviolet Measurements with Diacetylacetone.—Diacetylacetone was dissolved in 0·1N-sodium hydroxide and aliquot parts were made up with aqueous sodium hydroxide to various strengths. The solutions showed two absorption bands ($\lambda_{max.}$ 293 and 342 mμ). Extinctions at 342 mμ were plotted at measured intervals, and the extinctions at first mixing determined by extrapolation. Results are in Table 5.

TABLE 5.

[NaOH] (N)	0·98	1·96	2·99	4·11	4·95	8·03	10·46
E_{342} at first mixing (c 5·8 mg./l.)	0·21	0·47	0·62	0·91	1·05	1·37	1·43

1,4,5,8,9,10-Hexahydroanthracene (XI).—Anthracene (1 g.) was dissolved in tetrahydrofuran (150 c.c.) and ethanol (20 g.). This mixture was added to liquid ammonia (250 c.c.), and the vigorously stirred suspension of anthracene was reduced with sodium (2·6 g.). The ammonia was replaced by water (200 c.c.), and the product isolated with ether. Removal of solvent afforded a colourless solid (0·95 g.) which recrystallised from light petroleum (b. p. 40—60°), giving *1,4,5,8,9,10-hexahydroanthracene* (0·45 g.), m. p. 141—144° (Found: C, 91·2; H, 8·6. $C_{14}H_{16}$ requires C, 91·3; H, 8·7%).

Indane-2-spiro-2'-dioxolan (XV).—Indan-2-one (5 g.), ethylene glycol (12 g.), and toluene-*p*-sulphonic acid (1 g.) were refluxed in benzene under a water separator until no more water was produced. The product was extracted with ether, washed with sodium carbonate solution, freed from ether, and distilled, giving the *ketal* (4·52 g.), b. p. 66—69°/0·01 mm. (Found: C, 74·7; H, 6·8. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·9%).

4,7-Dihydroindane-2-spiro-2'-dioxolan (XII).—The ketal (XV) (11 g.) and methanol (35 g.) were dissolved in liquid ammonia (400 c.c.). Sodium (8 g.) was added in small pieces. When this had dissolved, the ammonia was replaced by water. The solution was saturated with ammonium sulphate and extracted with ether. The extract gave, on removal of the ether, a viscous oil which on distillation afforded the *dihydro-ketal* (8·83 g.), b. p. 72—75°/0·01 mm., m. p. 43—44° (from ether–light petroleum) (Found: C, 73·9; H, 7·9. $C_{11}H_{14}O_2$ requires C, 74·1; H, 7·9%).

Ozonolysis of the Ketal (XII).—This compound (1 g.) in methanol (10 c.c.) was treated with ozonised oxygen at 0° until the increase in weight was 0·65 g. The solution was shaken with hydrogen and palladium–charcoal until the rapid uptake of hydrogen was complete. The catalyst was filtered off, and most of the methanol removed *in vacuo*, leaving a colourless oil (1·35 g.) containing the tetraketone (XXVII) (Found: C, 56·2; H, 7·0. Calc. for $C_{11}H_{14}O_6$: C, 54·6; H, 5·8%). It immediately changed colour, through yellow to red; with aqueous ferric chloride it gave an intense claret colour.

Ozonolysis of 1,4-Dihydronaphthalene.—1,4-Dihydronaphthalene [18] (4 g.) in methanol (25 c.c.) was treated with ozonised oxygen at 0°. Hydrogen peroxide (100-vol.; 100 c.c.) was then added, followed immediately by cold saturated sodium carbonate solution (100 c.c.).

[16] Folin, *J. Biol. Chem.*, 1907, **3**, 177.
[17] Korenman, *J. Appl. Chem. (U.S.S.R.)*, 1933, **6**, 1002.
[18] Hansky, U.S.P. 2,473,997/1949.

This mixture was extracted next morning with ether. The aqueous layer was acidified with sulphuric acid and again extracted with ether. This second extract gave, on evaporation, a sticky solid (5·9 g.); recrystallisation from water afforded *o*-phenylenediacetic acid (2·13 g.), m. p. 144—146°.

Reduction of 2,3-Dimethylnaphthalene.—2,3-Dimethylnaphthalene (66 g.) and sodium (39 g.) were heated to 140°, with stirring, to produce small droplets of sodium. The mixture was allowed to cool to 70° with stirring, then diluted with benzene (200 c.c.). The temperature was raised to 90°, and isopropyl alcohol added at a rate sufficient to maintain steady refluxing until all the sodium had dissolved. The mixture was poured into cold water (1 l.) and concentrated hydrochloric acid (200 c.c.). The benzene layer was separated, the aqueous layer was extracted with benzene, and the combined benzene solutions were washed with sodium carbonate solution and evaporated. Distillation of the residue afforded mixed dihydro-2,3-dimethyl-naphthalenes (62 g.), b. p. 140—142°/20 mm., m. p. 55—58°.

Reduction of 2-Methylnaphthalene.—2-Methylnaphthalene (36 g.) was reduced with sodium (23 g.) as in the previous experiment, giving mixed dihydro-2-methylnaphthalenes (32 g.), b. p. 112—116°/20 mm., having a weak absorption band at 319 mμ corresponding to 7% of unreduced material.

4,5-Dimethyl-1,2-phenylenediacetic Acid (XXIII).—Mixed dihydro-2,3-dimethylnaphth-alenes (2·5 g.) in methanol (100 c.c.) were ozonised at 0°. Fractionation of the product, as described above for the ozonolysis of 1,4-dihydronaphthalene, followed by recrystallisation from ether–light petroleum, afforded 4,5-*dimethyl*-1,2-*phenylenediacetic acid* (1·0 g.), m. p. 219—220° (Found: C, 64·6; H, 6·3. $C_{12}H_{14}O_4$ requires C, 64·9; H, 6·3%).

4-Methyl-1,2-phenylenediacetic Acid (XXII).—Mixed dihydro-2-methylnaphthalenes (2·5 g.), when oxidised as above, afforded 4-*methyl*-1,2-*phenylenediacetic acid* (0·7 g.), m. p. 170—172° (Found: C, 63·8; H, 5·7. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%).

Dimethyl 4,5-Dimethyl-1,2-phenylenediacetate.—4,5-Dimethyl-1,2-phenylenediacetic acid (9·5 g.) and methanol (200 c.c.) containing sulphuric acid (0·25 c.c.) were refluxed for 4 hr., then neutralised with sodium carbonate solution. The product was isolated with ether, and distilled, giving *dimethyl* 4,5-*dimethyl*-1,2-*phenylenediacetate* (9·6 g.), b. p. 122—126°/0·05 mm., m. p. 39—41° (Found: C, 66·9; H, 7·1. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·3%).

Dimethyl 4-Methyl-1,2-phenylenediacetate.—4-Methyl-1,2-phenylenediacetic acid (5 g.), esterified as above, gave *dimethyl* 4-*methyl*-1,2-*phenylenediacetate* (5·6 g.), b. p. 100°/0·01 mm. (Found: C, 66·8; H, 7·0. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%).

5,6-Dimethylindan-2-one.—Dimethyl 4,5-dimethyl-1,2-phenylenediacetate (4·5 g.) was added, with stirring, to a suspension of sodium powder (1 g.) in toluene (100 c.c.). The mixture was then refluxed for 2 hr., allowed to cool, and mixed with ice–water (500 c.c.). The aqueous layer was separated, acidified with sulphuric acid, and steam-distilled, giving 5,6-*dimethylindan*-2-*one* (2·3 g.) as needles, m. p. 97—99° (Found: C, 82·1; H, 7·5. $C_{11}H_{12}O$ requires C, 82·5; H, 7·5%).

5-Methylindan-2-one.—Dimethyl 4-methyl-1,2-phenylenediacetate (4·5 g.), treated as above, afforded 5-*methylindan*-2-*one* (2·3 g.), m. p. 54—55° (Found: C, 81·7; H, 7·1. $C_{10}H_{10}O$ requires C, 82·2; H, 6·9%).

5,6-Dimethylindane-2-spiro-2′-dioxolan (XVII).—5,6-Dimethylindan-2-one (1 g.) was ketalised as described above for indan-2-one; the *product* (0·83 g.) had b. p. 118—124°/0·1 mm., m. p. 90—92° (Found: C, 75·8; H, 7·7. $C_{13}H_{16}O_2$ requires C, 76·4; H, 7·9%).

5-Methylindan-2-one (1 g.) similarly gave its *ketal* (XVI) (1 g.), b. p. 110°/0·1 mm., m. p. 25° (Found: C, 75·2; H, 7·5. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%).

4,7-Dihydro-5,6-dimethylindane-2-spiro-2′-dioxolan (XIV).—Attempts to reduce the ketal (XVII) by the method used for the unsubstituted analogue gave only starting material.

The following procedure, involving a large excess of lithium, was therefore used. The ketal (XVII) (0·13 g.) in tetrahydrofuran (10 c.c.) was added to liquid ammonia (200 c.c.). Lithium (0·8 g.) was added, followed by methanol (10 c.c.) dropwise with stirring. Finally more lithium (0·8 g.) was added gradually in small pieces. When all the lithium had reacted, the ammonia was replaced by water; the solution was saturated with ammonium sulphate, and extracted with ether. The extract was dried ($MgSO_4$), and evaporated, leaving a crystalline residue (0·12 g.), calculated from its extinction at 280 mμ to contain 7% of unreduced material. Recrystallisation from ether–light petroleum afforded the *ketal* (XIV) (0·062 g.), needles, m. p. 92—94° (Found: C, 75·2; H, 8·6. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·8%).

4,7-Dihydro-5-methylindane-2-spiro-2'-dioxolan (XIII).—The ketal (XVI) (0·13 g.) was reduced as described above, affording a *product* (XIII) (0·11 g.), m. p. 76° (Found: C, 74·5; H, 8·4. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·4%).

Reduction of 4a,5,8,8a-*Tetrahydro*-6,7-*dimethyl*-1,4-*naphthaquinone* (XXIV).—(a) *With lithium aluminium hydride.* 4a,5,8,8a-Tetrahydro-6,7-dimethyl-1,4-naphthaquinone, m. p. 118°, was made by the general method described by Butz and Rytina.[19] This compound (2 g.), dissolved in ether (100 c.c.), was added to a suspension of lithium aluminium hydride in ether and stirred for 30 min. The excess of hydride was decomposed with methanol, the resulting precipitate filtered off, and the solution evaporated. The residue recrystallised from water, giving 1,2,3,4,4a,5,8,8a-*octahydro*-4-*hydroxy*-6,7-*dimethyl*-1-*oxonaphthalene* (XXVI) (1·9 g.), m. p. 119—120° (Found: C, 74·1; H, 9·6. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%). (b) *With aluminium isopropoxide.* 4a,5,8,8a-Tetrahydro-6,7-dimethyl-1,4-naphthaquinone (1 g.) and aluminium isopropoxide (5 g.) in isopropyl alcohol (100 c.c.) were heated under nitrogen so that slow distillation of isopropyl alcohol and acetone occurred. When the distillate no longer contained acetone, the mixture was cooled, evaporated *in vacuo*, hydrolysed with water (50 c.c.), and extracted with ether. Evaporation of the ether left a solid which on recrystallisation from ethyl acetate–light petroleum afforded 1,4,4a,5,8,8a-*hexahydro*-6,7-*dimethylnaphthalene*-1,4-*diol* (XXV) (1·0 g.) m. p. 195—196° (Found: C, 74·7; H, 9·3. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3%).

Comparison of 1,4-*Dihydro*-2,3-*dimethylnaphthalene with the Reduction Product of* 2,3-*Dimethylnaphthalene.*—1,4,4a,5,8,8a-Hexahydro-6,7-dimethylnaphthalene-1,4-diol (76 mg.), pyridine (10 c.c.), and phosphorus oxychloride (1 c.c.) were refluxed for $\frac{1}{2}$ hr. The mixture was poured on ice and extracted with ether. The extract was washed with dilute hydrochloric acid and water, then evaporated, leaving a solid residue (54 mg.). This was purified by sublimation at 80°/0·01 mm., giving colourless crystals, m. p. 50°. Its solution in carbon disulphide showed prominent infrared absorption bands at 735 and 1370 cm.$^{-1}$. The reduction product of 2,3-dimethylnaphthalene, described above, showed absorption bands at 735, 860, and 1370 cm.$^{-1}$; the two common bands were only about half as intense as in the spectrum of the synthetic isomer.

Alkaline Hydrolysis of the Ozonide from the Ketal (XIV).—(a) *Ultraviolet measurements.* The ketal (6 mg.) was ozonised in methanol (10 c.c.) at 0°. The resulting solution was mixed with 0·1N-sodium hydroxide (20 c.c.), and aliquot parts (5 c.c.) were immediately made up to 50 c.c. with aqueous sodium hydroxide so as to give 2N-, 4N-, 6N-, 9N-, and 11N-alkali. All these solutions showed an absorption maximum at 294 mμ, and extinction values at this wavelength were recorded at intervals. In each solution the extinctions rose initially, the maximum values being reached in times from 20 (11N) to 50 min. (2N); later the extinction decreased exponentially. By extrapolating the values of log E obtained during the period of falling extinction, back to the time of mixing, initial extinction values were found to be: 0·29 (2N); 0·32 (4N); 0·42 (6N); 0·51 (9N); 0·70 (11N).

(b) *Cleavage to acetone and acetic acid.* The ketal (50 mg.) was ozonised in methanol (50 c.c.), cooled with solid carbon dioxide. The solution was then removed from the cooling-bath and diluted with a solution of sodium hydroxide (60 g.) in water (100 c.c.). The mixture was immediately extracted with ether to remove non-acidic material, then kept at room temperature for 2 days. Analyses then indicated the formation of acetone (15 mg.) and acetic acid (33 mg.).

2,2-*Di*-(2,4-*dioxopentyl*)*dioxolan.*—The ketal (XIV) (20 mg.) was ozonised in methanol (20 c.c.), cooled with solid carbon dioxide. The solution was warmed to room temperature and immediately hydrogenated in presence of palladium–charcoal. The catalyst was filtered off and the solution evaporated *in vacuo*, leaving the *tetraketone* as a colourless gum (Found: C, 58·3; H, 6·8. $C_{13}H_{18}O_6$ requires C, 57·8; H, 6·7%).

THE UNIVERSITY, MANCHESTER, 13.   [*Received, October* 31*st*, 1962.]

[19] Butz and Rytina, *Organic Reactions*, 1949, **5**, 160.