242. *Chalcones and Related Compounds. Part IV.* Addition of Hydrogen Cyanide to Chalcones.*

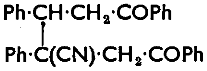
By W. Davey and D. J. Tivey.

The optimum preparative conditions for chalcones have been confirmed and some new chalcones prepared. Improvements have been effected in the addition of hydrogen cyanide to chalcones and in the hydrolysis of the resulting adducts. New lactones, pyridazinones, and diols have been prepared from these adducts.

Although sodium hydroxide is usually assumed to be the preferred reagent for the condensation of benzaldehydes with acetophenones, few attempts have been made to compare accurately the efficacy of various condensing agents. Comparative experiments have shown that sodium hydroxide and sodium methoxide are generally more effective than hydrogen chloride, phosphorus oxychloride, or boron trifluoride in the preparation of chalcone and of some twelve substituted chalcones. The experimental procedures and the results obtained are detailed later and the preparation of some new chalcones is described.

Treatment of chalcone with potassium cyanide and acetic acid yields 3-cyano-1 : 3-diphenylpropan-1-one (I) and a sparingly soluble product (II) by further addition.[1,2,3] Although some improvements in the yield of adduct (I) have been obtained [4,5] and the method extended to some other chalcones,[6] some workers [7,8] have recorded difficulties in the reaction or failure in some cases. Although Allan and Kimball's method [5] was found satisfactory for the addition of hydrogen cyanide to chalcone and to 4-methoxychalcone, it failed with 4′-methoxy-, 4 : 4′-dimethoxy-, and 4′-hydroxy-chalcone. Variations in reaction temperature and amounts of potassium cyanide and acetic acid had little effect

(I) $Ph{\cdot}CH(CN){\cdot}CH_2{\cdot}COPh$



$$\begin{array}{l} Ph{\cdot}CH{\cdot}CH_2{\cdot}COPh \\ \;\;\,| \\ Ph{\cdot}C(CN){\cdot}CH_2{\cdot}COPh \end{array}$$

(II)

---

* Part III, *J.*, 1957, 1017.

[1] Anschütz and Montfort, *Annalen*, 1895, **284**, 2.

[2] Rupe and Schneider, *Ber.*, 1895, **28**, 960.

[3] Hann and Lapworth, *J.*, 1904, **85**, 1355.

[4] Lapworth and Wechsler, *J.*, 1910, **97**, 39.

[5] Allan and Kimball, *Org. Synth.*, Coll. Vol. II, p. 498.

[6] Robertson and Stephen, *J.*, 1931, 863.

[7] Kohler and Leers, *J. Amer. Chem. Soc.*, 1934, **56**, 981.

[8] Mehta *et al.*, *J. Univ. Bombay*, 1942, **10**, 137; 1940, **9**, 156.

on yield, and addition of hydrochloric acid gave tars. Addition of hydrogen cyanide to chalcones in the presence of sulphuric acid and ethanol gave high yields of adducts free from secondary reaction products. Although the amount of acid was not critical, the best results were obtained when the acid and potassium cyanide were used in a molar ratio of 1 : 2. The required adducts were obtained from chalcone, 4′-methoxy-, 4 : 4′-dimethoxy-, 3 : 4 : 4′-trimethoxy-, and 2 : 4 : 4′-trimethoxy-chalcone.

Acid hydrolysis of the 3-cyano-1 : 3-diarylpropan-1-ones to the corresponding acids is difficult [1,3,9] and after such hydrolysis the 2 : 4-diaryl-4-oxobutanoic acids tended to separate as oils. Conversion of the cyano-ketones into methyl esters by boiling them with methanolic hydrogen chloride, followed by hydrolysis with dilute sodium hydroxide, gave the acids in good yield.

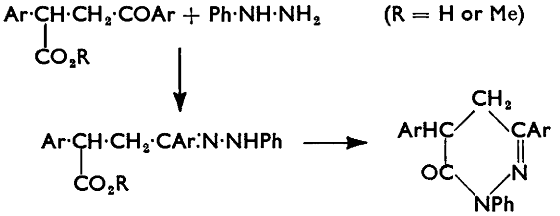
1 : 3-Diarylbutane-1 : 4-diols have not been previously prepared and it appeared that the reduction of esters of the 2 : 4-diaryl-4-oxobutanoic acids by lithium aluminium hydride should give such compounds:

$$\mathrm{MeO_2C{\cdot}CHAr{\cdot}CH_2{\cdot}COAr \longrightarrow HO{\cdot}CH_2{\cdot}CHAr{\cdot}CH_2{\cdot}CHAr{\cdot}OH}$$

The keto-esters and -acids already contain one asymmetric carbon atom and, on reduction of the keto-group, a second asymmetric carbon atom will be produced, giving rise to two stereoisomers (*threo* and *erythro*), each being a racemate. Reduction occurred readily to yield the diols as low-melting solids or oils. Since the keto-esters were sparingly soluble in ether, reduction was carried out either by ethereal lithium aluminium hydride in a Soxhlet apparatus with the keto-ester in the thimble, or by the addition of a benzene solution of the ester to ethereal lithium aluminium hydride.

Reduction of 4-oxo-2 : 4-diphenylbutanoic acid with sodium in ethanol gave 4-hydroxy-2 : 4-diphenylbutanoic lactone. It was thought possible that reduction by potassium borohydride, or catalytically, of esters of 4-oxo-2 : 4-diarylbutanoic acids would give the corresponding hydroxy-esters and avoid lactone formation but, in fact, potassium borohydride gave the lactone. Catalytic hydrogenation in presence of a Raney nickel W.7 catalyst was used to avoid lactonisation and a syrup having the correct analysis obtained. Since it was presumably a mixture of stereoisomers an attempt was made to separate it chromatographically but without success. Alkaline hydrolysis or vacuum-fractionation of the syrup gave the saturated lactone. Reduction of other keto-esters by potassium borohydride gave saturated lactones in good and reproducible yields.

The action of phenylhydrazine in γ-keto-acids yields tetrahydro-oxopyridazines,[1] and such compounds were readily obtained by treatment of 4-oxo-2 : 4-diarylbutanoic acids or their methyl esters, with phenylhydrazine in hot glacial acetic acid:



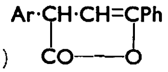
The infrared spectrum of a di-(p-methoxyphenyl)pyridazine derivative showed peaks at **1696** (amide-carbonyl group in a six-membered ring), **1514** (conjugated $\mathrm{C{:}N^-}$ attached to N), and at **1490** and **1601** cm.$^{-1}$, both characteristic of the aromatic systems. Such analysis confirms the above structure for such compounds.

The formation of butenolactones from diaryloxobutanoic acids has been described [1,3,4,6] and two isomeric forms have been reported. The low-melting form was assigned the structure (III) and the high-melting form the structure (IV). The insolubility of the

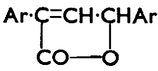
---

[9] Rupe and Gisiger, *Helv. Chim. Acta*, 1925, **8**, 338.

latter and the wide difference in m. p.s suggested that isomer (IV) might be a dimer and the problem was investigated in detail.


$$\begin{array}{l}\mathrm{Ar{\cdot}CH{\cdot}CH{=}CPh}\\ \quad\mathrm{CO{-\!-}O}\end{array}$$

(III)


$$\begin{array}{l}\mathrm{Ar{\cdot}C{=}CH{\cdot}CHAr'}\\ \quad\mathrm{CO{-\!-}O}\end{array}$$

(IV)

Treatment of 4-oxo-2 : 4-diphenylbutanoic acid with acetic anhydride gave a good yield of the low-melting form, with a small amount of the other. Heating the low-melting form in ethanol or acetic acid for long periods gave only small amounts of the other form, and prolonged heating of the keto-acid above its m. p. gave a small amount of high-melting lactone and much unchanged acid. The action of acetic anhydride on three other keto-acids gave high- and low-melting lactones, the former in very small yield. The low-melting lactones had m. p. *ca.* 100° and were soluble in most common solvents whilst the high-melting forms were extremely insoluble in solvents and had m. p. *ca.* 300°. Molecular-weight determinations by the Rast method confirmed the monomeric nature of the low-melting lactones and, although results were poor for the sparingly soluble high-melting forms, some evidence of their monomeric nature was obtained. Repeated analyses confirmed the formulæ for unsaturated lactones. Catalytic hydrogenation of the low-melting isomer gave $\alpha\gamma$-diphenylbutyric acid in high yield. The infrared spectra of both forms provided little evidence since, owing to the insolubility of the high-melting form, determinations were on Nujol mull and not on solutions. The high-melting lactone from 2 : 4-di-(*p*-methoxyphenyl)-4-oxobutanoic acid showed a band at 1763 cm.$^{-1}$ which is rather low for a carbonyl group in a five-membered ring lactone, but it is higher than the corresponding band for the low-melting isomer (1750 cm.$^{-1}$) and is slight evidence that the latter is 4-hydroxy-2 : 4-di-(*p*-methoxyphenyl)but-2-enoic lactone. The infrared spectra of the other lactones were even less conclusive, but, in spite of the wide differences in m. p. and solubility, there is no reason to suppose that the high-melting lactones are other than simple isomers of the low-melting forms.

EXPERIMENTAL

Preparation of Chalcones (see Table).—(*a*) This was Kohler and Chadwell's method,[10] the aldehyde and ketone in aqueous ethanol being condensed by sodium hydroxide.

(*b*) The benzaldehyde (1 mol.) and acetophenone (1 mol.) were mixed at 25° and, if either or both were solid, enough ethanol added to make the mixture homogeneous at 30°. 5N-Sodium hydroxide was then added in an amount 10% more than that required to make the mixture distinctly alkaline to " Brilliant Yellow." External cooling kept the mixture at 25—30° and water usually separated. Ethanol was added to make the mixture homogeneous and this procedure repeated as long as water was produced (½—5 hr.). At this stage crystallisation usually began and the product was filtered off and washed with water. Dilution of the filtrate and seeding gave more chalcone, which was filtered off and washed with water. The product was generally pure and one crystallisation gave the required chalcone.

(*c*) A mixture of the benzaldehyde (1 mol.) and acetophenone (1 mol.) in acetic anhydride (200 ml.) was saturated with hydrogen chloride at $\ngtr 30$°, kept at room temperature for 12 hr., then poured into dilute ammonia solution and ice. The separated oil was then steam-distilled and the residue recrystallised.

(*d*) To a mixture of benzaldehyde (1 mol.) and acetophenone (1 mol.), liquefied if necessary by addition of benzene, a few drops of phosphorus oxychloride were added at 30° and the whole was kept at room temperature for some hours. The product was washed with 2N-ammonia, then water, and, after removal of the benzene under reduced pressure, steam-distilled, and the residue recrystallised.

(*e*) The benzaldehyde (1 mol.) was treated with a 48% solution of boron trifluoride (1 mol.) in acetic acid at 25°, enough acid being added to dissolve the aldehyde. Acetophenone (1 mol.) was then slowly added, the temperature being kept at 25—30°. The mixture became red and

---

[10] Kohler and Chadwell, *Org. Synth.*, Coll. Vol. I, 2nd edn., p. 78.

after 12 hr. at room temperature was treated with excess of sodium acetate solution, then steam-distilled, and the product repeatedly recrystallised.

(*f*) The benzaldehyde (1 mol.) in dry methanol (200 ml.) was added at 30° to a solution of sodium methoxide (from 10 g. of sodium in 100 ml. of methanol), and the acetophenone (1 mol.) added. After some hours at room temperature the separated chalcone was filtered off and washed with water, and the filtrate diluted with water and set aside, more chalcone separating. The product was then recrystallised.

Chalcone.

	(*a*)	(*b*)	(*c*)	(*d*)	(*e*)	(*f*)
Yield (%)	89	76	50	48	53	71
Reaction time (hr.)	2	1	12	12	6	4
M. p. (no. of crystns. in parentheses)	52° (1)	55° (0)	53° (2)	52° (2)	52° (2)	52° (1)

Kohler and Chadwell [10] report m. p. 55° and 98% yield by method (*a*).

Substituted chalcones: yields (m. p.s in parentheses).

Subst.	(*b*)	(*c*)	(*d*)	(*e*)	(*f*)
4-MeO [a]	76 (75)	50 (72)	47 (73)	52 (70)	61 (72)
4 : 4'-$(MeO)_2$ [b]	81 (100)	66 (99)	50 (100)	62 (97)	75 (98)
4-MeO-4'-Me [c]	55 (91)	—	—	—	48 (91)
3'-HO [d]	41 (124)	Tar	Tar	10 (123)	35 (123)
4 : 4'-Me_2 [e]	76 (126)	70 (124)	—	—	77 (126)
4-Me [f]	42 (94)	30 (95·5)	20 (96)	—	45 (95)
4-HO [g]	37 (180)	11 (182)	20 (179)	25 (179)	31 (182)
4'-MeO [h]	81 (106)	55 (105)	45 (104)	—	77 (108)
4-NO_2 [i]	60 (162)	80 (162)	42 (162)	35 (162)	57 (162)
3'-NO_2 [j]	75 (130)	25 (131)	10 (130)	—	Tar
4'-Me [k]	35 (75)	42 (75)	22 (72)	23 (72)	—

[a] Kohler and Conant, *J. Amer. Chem. Soc.*, 1917, **39**, 1709, used NaOH and gave m. p. 77°, 85% yield. [b] Straus, *Annalen*, 1910, **374**, 139 (NaOEt–EtOH), gives m. p. 101°, 84% yield. [c] Stobbe, *J. prakt. Chem.*, 1929, **123**, 241 (NaOEt–EtOH), gives m. p. 94°, 45% yield. [d] Kostanecki and Tambor, *Ber.*, 1899, **32**, 1924 (NaOH), give m. p. 126°, yield not stated. [e] Weygand, *Annalen*, 1926, **449**, 29 (NaOMe–MeOH), gives m. p. 127—128°, 82% yield. [f] Weygand, *Ber.*, 1927, **60**, 2431 (NaOH), gives m. p. 96·5°, yield not stated. [g] Sablich, *Ber.*, 1896, **29**, 236, gives m. p. 182, yield not stated. [h] Staudinger and Kon, *Annalen*, 1911, **384**, 123 (NaOH), give m. p. 106—107° and 83% yield. [i] Le Fèvre, Markham, and Pearson, *J.*, 1933, 344 (HCl), give m. p. 164°, 86% yield. [j] Le Fèvre, Markham, and Pearson (*loc. cit.*) (NaOMe–MeOH), give m. p. 131°, 33% yield. [k] Weygand, *Annalen*, 1926, **449**, 29 (NaOH), gives m. p. 75°, yield not stated.

2-*Chloro*-4'-*methylchalcone*.—To 2-chlorobenzaldehyde (14·1 g., 0·1 mole) and 4-methylacetophenone (13·4 g., 0·1 mole) in 96% ethanol (150 ml.) at 30°, 20% sodium hydroxide solution (5 ml.) was added. After 30 min. water separated and more ethanol was added to make the mixture homogeneous. This procedure was repeated during 1½ hr., crystallisation then beginning. Addition of water (15 ml.) and storage at 0° for 3 hr. gave 2-*chloro*-4'-*methylchalcone* (14·6 g., 57%), plates (from ethanol), m. p. 78° (Found: C, 74·9; H, 5·1; Cl, 13·9. $C_{16}H_{13}OCl$ requires C, 74·6; H, 4·9; Cl, 13·8%).

3-*Hydroxy*-4'-*methoxychalcone*.—*m*-Hydroxybenzaldehyde (12·2 g.) and 4-methoxyacetophenone (15·0 g.) were condensed in ethanol by method (*b*), to give 3-*hydroxy*-4'-*methoxychalcone* (18·8 g., 74%), needles (from ethanol), m. p. 160—161° (Found: C, 75·5; H, 5·5. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·6%).

3 : 4'-*Dimethylchalcone*.—*m*-Tolualdehyde (12·0 g.) with 4-methylacetophenone (13·4 g.) in ethanol by method (*b*) gave 3 : 4'-*dimethylchalcone* (8·5 g. 36%), as yellow plates (from methanol), m. p. 84° (Found: C, 86·1; H, 6·8. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%).

2 : 4'-*Dimethylchalcone*.—*o*-Tolualdehyde (12·0 g.) with 4-methylacetophenone (13·4 g.) in ethanol by method (*b*) gave 2 : 4'-*dimethylchalcone* (7·1 g., 30%), yellow plates (from ethanol), m. p. 38—40° (Found: C, 86·8; H, 6·7. $C_{17}H_{16}O$ requires C, 86·4; H, 6·8%).

2-*Chloro*-4'-*methoxy*-*chalcone*.—*o*-Chlorobenzaldehyde (14·1 g.) with 4-methoxyacetophenone (15·0 g.) in ethanol by method (*b*) gave 2-*chloro*-4'-*methoxychalcone* (15·3 g., 64%), white plates (from ethanol), m. p. 89—90° (Found: C, 70·0; H, 4·8. $C_{16}H_{13}O_2Cl$ requires C, 70·4; H, 4·8%).

Addition of Hydrogen Cyanide.—(1) By the method of Allan and Kimball [5] hydrogen cyanide was added to chalcone and to 4-methoxychalcone.

(2) Kohler and Leers's method [7] gave a low yield of the hydrogen cyanide adduct of 4′-methoxychalcone and the reaction failed with 4 : 4′-dimethoxychalcone.

(3) 7N-Sulphuric acid (50 ml.) was slowly added to a cooled and stirred solution of chalcone (41·6 g.) in ethanol (700 ml.), the mixture was heated to 50°, and potassium cyanide solution (50 g. in 80 ml. of water) was slowly added. The mixture was refluxed for 5 min., then diluted with water (200 ml.), and set aside at room temperature for 12 hr. The precipitated solid was filtered off and extracted with boiling ethanol (3 × 100 ml.). The product from the extract, when recrystallised from ethanol, gave 3-cyano-1 : 3-diphenylpropan-1-one (35 g. 74%), white needles, m. p. and mixed m. p. 126° (Found: C, 81·4; H, 5·7. Calc. for $C_{16}H_{13}ON$: C, 81·7; H, 5·5%).

By this method the following adducts were obtained: 3-cyano-1-*p*-methoxyphenyl-3-phenylpropan-1-one, white needles (86%), m. p. 65° (Kohler and Leers [7] give m. p. 65°); 3-*cyano*-1 : 3-*di*-p-*methoxyphenylpropan*-1-*one*, white needles (from ethanol) (66%, m. p. 113—114° (Found: C, 73·5; H, 6·0; N, 5·0. $C_{18}H_{17}O_3N$ requires C, 73·2; H, 5·8; N, 4·7%); 3-*cyano*-3-p-*hydroxyphenyl*-1-*phenylpropan*-1-*one* (from ethanol) (68%), m. p. 173° (Found: C, 76·5; H, 4·9; N, 5·3. $C_{16}H_{13}O_2N$ requires C, 76·5; H, 5·2; N, 5·6%); 3-*cyano*-3-(2 : 4-*di-methoxyphenyl*)-1-p-*methoxyphenylpropan*-1-*one*, colourless needles (83%), m. p. 125—126° (Found: 69·8; H, 5·4; N, 4·0. $C_{19}H_{19}O_4N$ requires C, 70·2; H, 5·8; N, 4·3%); 3-*cyano*-3-(3 : 4-*dimethoxyphenyl*)-1-p-*methoxyphenylpropan*-1-*one*, needles (79%), m. p. 105° (Found: C, 69·8; H, 5·3; N, 4·1. $C_{19}H_{19}O_4N$ requires C, 70·2; H, 5·8; N, 4·3%).

Preparation of Methyl Esters from Hydrogen Cyanide Adducts.—A suspension of 3-cyano-1 : 3-diphenylpropan-1-one (23·5 g.) in methanol (200 ml.) was saturated with dry hydrogen chloride at 25°, refluxed for 1½ hr., about half of the methanol distilled off, and water (200 ml.) added. After being kept overnight at room temperature the product was filtered off and recrystallised from methanol, to yield *methyl* 4-*oxo*-2 : 4 *diphenylbutanoate*, needles, (24 g.), m. p. 103° (Found: C, 75·8; H, 5·7. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%).

From the corresponding adducts the following esters were prepared by this method: *methyl* 4-*oxo*-4-p-*methoxyphenyl*-2-*phenylbutanoate*, plates (91%), m. p. 96° (Kohler and Leers [7] give m. p. 97°); *methyl* 2 : 4-*di*-p-*methoxyphenyl*-4-*oxobutanoate*, needles (from methanol; 85% yield), m. p. 96—97° (Found: C, 69·1; H, 6·2. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·1%); *methyl* 2-p-*hydroxyphenyl*-4-*oxo*-4-*phenylbutanoate*, needles (83%), m. p. 143—144° (Found: C, 71·6; H, 5·5. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6%); *methyl* 2-(2 : 4-*dimethoxyphenyl*)-4-p-*methoxyphenyl*-4-*oxobutanoate*, needles (from ethanol; 83%), m. p. 128—129° (Found: C, 66·8; H, 6·3. $C_{20}H_{22}O_6$ requires C, 67·0; H, 6·1%); *methyl* 2-(3 : 4-*dimethoxyphenyl*)-4-p-*methoxyphenyl*-4-*oxobutanoate*, needles (from methanol; 73%), m. p. 74—75° (Found: C, 67·2; H, 6·3. $C_{20}H_{22}O_6$ requires C, 67·0; H, 6·1%).

Hydrolysis of Methyl Esters.—Methyl 4-oxo-2 : 4-diphenylbutanoate (26·8 g.) was refluxed for 2 hr. with ethanol (100 ml.) and 2N-sodium hydroxide (100 ml.). Excess of 2N-hydrochloric acid (120 ml.) was added and the mixture set aside overnight at room temperature. The precipitated acid was filtered off and recrystallised from ethanol, to give 4-oxo-2 : 4-diphenylbutanoic acid, needles (23 g., 80%), m. p. and mixed m. p. 152°. The following acids (all needles) were obtained by the same method: 4-*p*-methoxyphenyl-4-oxo-2-phenylbutanoic acid (93%), m. p. 139—140° (Kohler and Leers [7] give m. p. 141°); 2 : 4-*di*-p-*methoxyphenyl*-4-*oxobutanoic acid* (from ethanol; 91%), m. p. 163—164° (Found: C, 68·5; H, 5·9. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·9%); 2-p-*hydroxyphenyl*-4-*oxo*-4-*phenylbutanoic acid* (from methanol; 83%), m. p. 143—144° (Found: C, 69·8; H, 5·0. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%); 2-(2 : 4-*dimethoxyphenyl*)-4-p-*methoxyphenyl*-4-*oxobutanoic acid* (from ethanol; 80%), m. p. 127—128° (Found: C, 66·1; H, 5·4. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%); 2-(3 : 4-*dimethoxy-phenyl*)-4-(p-*methoxyphenyl*)-4-*oxobutanoic acid* as colourless needles from ethanol, yield 80%, m. p. 179—180° (Found: C, 66·1; H, 5·7. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%).

Preparation of Unsaturated Lactones.—4-Oxo-2 : 4-diphenylbutanoic acid (12·7 g.) was refluxed for 3 hr. in acetic anhydride (25 ml.), cooled, poured into cold water, and set aside for 1 hr. The solid was filtered off. The crude product (10 g.) was dissolved in boiling ethanol (50 ml.), filtered hot and, on cooling, gave colourless needles (2·6 g.), m. p. 199°. Dilution of the filtrate with water (15 ml.) gave a solid which was filtered off and dried (6·1 g,; m. p. 91°). The higher-melting product was twice crystallised from ethanol, to yield 4-hydroxy-2 : 4-diphenylbut-2-enoic lactone (1·7 g.; m. p. 283—285°), whilst the lower-melting material, after two crystallisations from ethanol, gave 4-hydroxy-2 : 4-diphenylbut-3-enoic lactone, as colourless needles (3·7 g.; m. p. 107—108°). Anschutz and Montfort [1] give m. p. 109° and 288°. It was found that the reflux time with acetic anhydride was critical, excessive refluxing yielding intractable gums. Examples of pairs of isomeric *lactones* (all colourless needles) with reflux times are given in the Table.

2 : 4-*Diaryl*-4-*hydroxybut*-2- (IV) *and* -3-*enoic lactones* (III).

Reflux (hr.)	2-Ar	4-Ar′		M. p.	Found (%)		Formula	Required (%)	
					C	H		C	H
2	Ph	*p*-MeO·C_6H_4	(IV)	250—260° *	76·5	5·2	$C_{17}H_{14}O_3$	76·7	5·3
			(III)	92	76·4	5·5			
1·5	*p*-MeO·C_6H_4	*p*-MeO·C_6H_4	(IV)	255—260 *	72·5	5·1	$C_{18}H_{16}O_4$	73·0	5·4
			(III)	106—107	73·2	5·1			
1	*p*-HO·C_6H_4	Ph	(IV)	282—284 *	75·8	4·7	$C_{16}H_{12}O_3$	76·2	4·8
			(III)	131—132	75·9	4·6			

* With decomp.

Effect of Heat on 4-*Oxo*-2 : 4-*diphenylbutanoic Acid*.—The acid (5 g.) was heated to 165° for 2 hr., cooled, and dissolved in boiling ethanol (30 ml.); the mixture was filtered and the filtrate allowed to crystallise. The crystals (0·5 g.) had m. p. 270—280°, and on recrystallisation from ethanol gave 4-hydroxy-2 : 4-diphenylbut-2-enoic lactone (0·2 g.; m. p. 282—284°). The filtrate on concentration yielded, after two recrystallisations from ethanol, 4-hydroxy-2 : 4-diphenylbut-3-enoic lactone (3·7 g.), m. p. 107—108° (*M*, 229. Calc.: *M*, 236).

Hydrogenation of 4-*Hydroxy*-2 : 4-*diphenylbut*-3-*enoic Lactone*.—The lactone (2 g.) was hydrogenated in ethanol (25 ml.) in presence of 10% palladised charcoal (0·5 g.), rapid hydrogen uptake (2 mol.) occurring. After filtration and dilution with water, the resulting oil was extracted with 2N-sodium carbonate (3 × 20 ml.), and the carbonate solution extracted with ether (2 × 20 ml.) and acidified with hydrochloric acid. The resulting oil was extracted with ether (2 × 20 ml.), the ether removed under reduced pressure, and the product crystallised from light petroleum (b. p. 40—60°), to give $\alpha\gamma$-diphenylbutyric acid (1·5 g., 60%), m. p. 73—74° (Found: C, 80·3; H, 6·8. Calc. for $C_{16}H_{16}O_2$: C, 80·0; H, 6·7%). Bergmann [11] gives m. p. 75°. An attempt to hydrogenate the high-melting lactone was not successful owing to insolubility of the compound.

Preparation of Saturated Lactones.—(*a*) Methyl 4-oxo-2 : 4-diphenylbutanoate (5 g.) in ethanol (50 ml.) was added slowly to a stirred solution of potassium borohydride (2 g.) in water (5 ml.) and ethanol (95 ml.) and kept at room temperature for 5 hr., then evaporated to one-fifth of its volume and acidified with hydrochloric acid. The resulting green viscous syrup was taken up in benzene and the benzene distilled off, to give an oil which solidified after 4 days. Recrystallisation from ethanol gave 4-hydroxy-2 : 4-diphenylbutanoic lactone as needles (3·5 g., 80%), m. p. 102°. Anschütz and Montford [1] give m. p. 103—104°.

(*b*) Methyl 4-oxo-2 : 4-diphenylbutanoate (4 g.) in ethanol (50 ml.) was shaken with Raney nickel W. 7(1 g.) and hydrogen until 1 mol. (337 ml.) was absorbed. After filtration and evaporation the syrup (4 g.) was distilled under reduced pressure (b. p. 190—200°/2 mm.) to give the lactone (2·8 g., 85%), m. p. 96°, rising to 102° on crystallisation from light petroleum (b. p. 40—60°). This was identical with that obtained as in (*a*).

By method (*a*) were obtained 4-*hydroxy*-4-p-*methoxyphenyl*-2-*phenylbutanoic lactone* plates (from ethanol) (62%), m. p. 77° (Found: C, 76·4; H, 5·9. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%), and 4-*hydroxy*-2 : 4-*di*-p-*methoxyphenylbutanoic lactone*, needles (from ethanol) (90%), m. p. 136—137° (Found: C, 73·2; H, 6·2. $C_{18}H_{18}O_4$ requires C, 72·4; H, 6·0%).

Reduction of Methyl 4-*Oxo*-2 : 4-*diphenylbutanoates to Diols*.—Methyl 4-oxo-2 : 4-diphenylbutanoate (5 g.) was extracted from the thimble of a Soxhlet apparatus into ethereal lithium aluminium hydride (1·5 g. in 150 ml. of ether). The mixture was refluxed for a further 2 hr., then excess of hydride was destroyed by the addition of ethyl acetate. 2N-Sulphuric acid (100 ml.) was added, and the ether layer washed with water and evaporated. The resulting syrup solidified under light petroleum (b. p. 40—60°) at 0° in 7 days and 1 : 3-*diphenylbutane*-1 : 4-*diol* (3 g., 66%) was obtained as plates, m. p. 92° (Found: C, 78·9; H, 7·6. $C_{16}H_{18}O_2$ requires C, 79·3; H, 7·5%). By this method were prepared:

1-p-*Methoxyphenyl*-3-*phenyl*-, cubes (33%), m. p. 48—50° (Found: C, 75·1; H, 7·6. $C_{17}H_{20}O_3$ requires C, 75·0; H, 7·4%), 1 : 3-*di*-p-*methoxyphenyl*-, needles (81%), m. p. 80—90°

---

[11] Bergmann, *J. Amer. Chem. Soc.*, 1942, **64**, 557.

(Found: C, 71·2; H, 7·1. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3%), and 3-p-*hydroxyphenyl*-1-*phenylbutane*-1 : 4-*diol*, a gum (Found: C, 73·9; H, 6·8. $C_{16}H_{18}O_3$ requires C, 74·4; H, 7·0%).

Preparation of Tetrahydro-oxopyridazines.—Methyl 4-oxo-2 : 4-diphenylbutanoate (20 g.) and phenylhydrazine (6·6 g.) in acetic acid (170 ml.) were heated on a steam-bath for 15 min. The solution was then cooled, diluted with water (100 ml.), and filtered. Recrystallisation of the crystalline residue from ethanol gave 1 : 4 : 5 : 6-tetrahydro-6-oxo-1 : 3 : 5-triphenylpyridazine as plates (18 g., 75%), m. p. 121—123°; Hann and Lapworth [3] gave m. p. 123°. By the same method, or by the use of the acid in place of the methyl ester, were prepared 1 : 4 : 5 : 6-*tetrahydro*-3-p-*methoxyphenyl*-6-*oxo*-1 : 5-*diphenylpyridazine*, plates (85%), m. p. 94—95° (Found: C, 77·2; H, 5·4; N, 7·7. $C_{23}H_{20}O_2N_2$ requires C, 77·5; H, 5·6; N, 7·9%), and 1 : 4 : 5 : 6-*tetrahydro*-3 : 5-*di*-p-*methoxyphenyl*-5-*oxo*-1-*phenylpyridazine*, needles (56%), m. p. 123° (Found: C, 74·6; H, 5·7; N, 7·3. $C_{26}H_{22}O_3N_2$ requires C, 74·6; H, 5·7; N, 7·3%).

Infrared Spectra.—4-Hydroxy-2 : 4-di-*p*-methoxyphenylbutenoic lactones had bands as follows: m. p. 106°, 1750 (C:O in 5-membered lactone), 1591 (Ph, conjugated), 1612 and 1514 (aromatic); m. p. 260°, 1763 (C:O in 5-membered lactone), 1579 (Ph, conjugated), 1615 and 1514 cm.$^{-1}$ (aromatic).

We are grateful to Miss E. M. Tanner, Parke Davis & Co., Hounslow, Middlesex, for determinations of the infrared spectra and for suggestions on their interpretation.

THE POLYTECHNIC, 309 REGENT ST., LONDON, W.1. [*Received, November* 6*th*, 1957.]