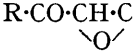
353. *Chalkones: Synthesis of Deoxybenzoins from Chalkones.*

By W. A. Hutchins, D. C. Motwani, K. D. Mudbhatkal, and T. S. Wheeler.

The possibility of conversion of chalkones into deoxybenzoins through the intermediate ketoethylene oxides and glycollic acids is found to depend on the nature of the substituent groups. Chalkones containing a naphthalene nucleus readily undergo condensation reactions, hitherto studied with the simpler benzene chalkones only.

Baker and Robinson (J., 1932, 1798) investigated the conversion of 2 : 4-dimethoxyphenyl styryl and 2 : 4-dimethoxyphenyl *p*-methoxystyryl ketones into deoxybenzoins through the intermediate keto-ethylene oxides and glycollic acids, $R{\cdot}CO{\cdot}CH{:}CHR' \longrightarrow$  $\underset{\diagdown O \diagup}{R{\cdot}CO{\cdot}CH{\cdot}CHR'}$ $\longrightarrow R{\cdot}C(OH)(CO_2H){\cdot}CH_2R' \longrightarrow R{\cdot}CO{\cdot}CH_2R'$, and stated that the yields were almost quantitative at every stage, and that the chain of reactions involved provided a general method for the synthesis of a large variety of deoxybenzoins. Widman (*Ber.*, 1916, **49**, 477) and Jörlander (*ibid.*, p. 2782; 1917, **50**, 406) had previously carried out the same series of reactions with the oxides of phenyl and *p*-anisyl styryl ketones respectively. The generality of the method was brought into question by Dodwadmath and Wheeler (*Proc. Indian Acad. Sci.*, 1935, **2**, 438), who found that the oxide of phenyl 6-nitro-3 : 4-methylenedioxystyryl ketone could not be converted into a glycollic acid.

The series of reactions has now been examined with the following six chalkones: phenyl *p*-methoxystyryl ketone (1), *m*-nitrophenyl *p*-methoxystyryl ketone (2), *p*-tolyl *p*-methoxystyryl ketone (3), 2 : 4 : 6-trimethoxyphenyl *p*-methoxystyryl ketone (4), β-*naphthyl* p-*methoxystyryl ketone* (5), and 2 : 4-dimethoxyphenyl 3 : 4-methylenedioxystyryl ketone (6). Of these chalkones, (2) did not yield an oxide, and the *oxide* from (5) could not be converted into a diketone or glycollic acid; also the oxide from (4) gave with alkali a very stable *diketone*, which, on prolonged heating with alkali, could not be further transformed into the glycollic acid. Murakami and Irie (*Proc. Imp. Acad. Tokyo*, 1934, **10**, 568) claim the synthesis of the glycollic acid, in an amorphous condition, from the oxide of (4). The remaining oxides underwent rearrangement to glycollic acids, and the further oxidation of such acids appears to be a general reaction. It is evident from these results that the possibility of conversion of chalkones into deoxybenzoins is not independent of the nature of the substituent groups.

The action of hydrazine hydrate, and of alcohols and acids, on some of the oxides has also been examined (cf. Dodwadmath and Wheeler, *loc. cit.*). Condensation reactions of some chalkones with deoxybenzoins (cf. Hill, J., 1935, 1115), *cyclo*hexanone (cf. Hill, *loc. cit.*), and ethyl acetoacetate (cf. Nadkarni, Warriar, and Wheeler, J., 1937, 1798) are also described. Chalkones of the naphthalene series, which have not hitherto been examined in this connection, undergo these reactions readily; on the other hand, the nitro-chalkone (2) is quite inert (cf. Dodwadmath and Wheeler, *loc. cit.*, p. 440).

EXPERIMENTAL.

Compounds are numbered for brevity in cross-reference. Recrystallisation was from alcohol unless another solvent is mentioned. The compounds are colourless unless otherwise stated.

Chalkones.—The following chalkones were prepared from the acetophenone and aldehyde components in presence of alcoholic alkali (Sorge, *Ber.*, 1902, **35**, 1065): phenyl *p*-methoxystyryl ketone (1) (Pond and Shoffstall, *J. Amer. Chem. Soc.*, 1900, **22**, 666); *m*-nitrophenyl *p*-methoxystyryl ketone (2) (Dilthey, Neuhaus, and Schommer, *J. pr. Chem.*, 1929, **123**, 235); *p*-tolyl *p*-methoxystyryl ketone (3) (Petrov, *Ber.*, 1930, **63**, 901); 2 : 4 : 6-trimethoxyphenyl *p*-methoxystyryl ketone (4) (Bargellini, *Gazzetta*, 1914, **44**, ii, 424); β-*naphthyl* p-*methoxystyryl ketone* (5), m. p. (alcohol–acetone) 95—97° (Found: C, 83·3; H, 5·6. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·6%), and 2 : 4-dimethoxyphenyl 3 : 4-methylenedioxystyryl ketone (6) (Perkin and Weizmann, J., 1906, **89**, 1653). All the chalkones are yellow.

1 : 3-*Diphenyl*-5-p-*anisyl*-4 : 5-*dihydropyrazole* (3·5 g.) separated from a mixture of (1) (5 g.), phenylhydrazine (2·5 g.), and acetic acid (30 c.c.) which had been heated at 100° for 20 minutes and cooled. Recrystallised from alcohol–acetone, it formed yellow needles, m. p. 125—126° (Found: N, 8·6. $C_{22}H_{20}ON_2$ requires N, 8·5%). It dissolved in sulphuric acid to a light green solution and gave Knorr's pyrazoline reaction; also it formed an unstable nitroso-derivative with potassium nitrite and acetic acid; it is, therefore, a pyrazoline and not a hydrazone (see Auwers and Voss, *Ber.*, 1909, **42**, 4417; Widman, *ibid.*, 1916, **49**, 2781).

Oxides of the Chalkones.—A hot solution of (3) (20 g.) in alcohol (150 c.c.) and acetone (50 c.c.) was cooled to 40° and treated with hydrogen peroxide (30%; 20 c.c.) and 4N-sodium hydroxide (15 c.c.). The resulting precipitate (increased by dilution) of p-*tolyl* αβ-*epoxy*-β-p-*anisylethyl ketone* (20 g.) (7) separated from alcohol–acetone in needles, m. p. 109—110° (Found: C, 75·9; H, 6·0. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%).

The following oxides were with minor modifications similarly prepared from (1), (4), (5), and (6) respectively (cf. Weitz and Scheffer, *Ber.*, 1921, **54**, 2327; Baker and Robinson, J., 1932, 1798; Dodwadmath and Wheeler, *Proc. Indian Acad. Sci.*, 1935, **2**, 438): phenyl αβ-epoxy-β-*p*-anisylethyl ketone (8) (Weitz and Scheffer, *loc. cit.*, p. 2339); 2 : 4 : 6-trimethoxyphenyl αβ-epoxy-β-*p*-anisylethyl ketone (9) [prepared by Murakami and Irie (*Proc. Imp. Acad. Tokyo*, 1934, **10**, 568) from *p*-anisaldehyde and ω-chloro-2 : 4 : 6-trimethoxyacetophenone], m. p. (alcohol–acetone) 118—120° (Found: C, 66·0; H, 5·8. Calc. for $C_{19}H_{20}O_6$: C, 66·3; H, 5·8%); β-*naphthyl* αβ-*epoxy*-β-p-*anisylethyl ketone* (10), m. p. (alcohol–acetone) 131° (Found: C, 79·1; H, 5·4. $C_{20}H_{16}O_3$ requires C, 78·9; H, 5·3%); and 2 : 4-*dimethoxyphenyl* αβ-*epoxy*-β-3 : 4-*methylenedioxystyryl ketone* (11), m. p. (alcohol–acetone) 143° (Found: C, 66·0; H, 5·0. $C_{18}H_{16}O_6$ requires C, 65·8; H, 4·9%). (2) did not react with hydrogen peroxide, nor could the oxide be prepared by the condensation of ω-bromo-*m*-nitroacetophenone and anisaldehyde in presence of sodium ethoxide by the method of Widman (*Ber.*, 1916, **49**, 477). Jörlander (*Ber.*, 1917, **50**, 1457) also failed to obtain oxides with chalkones derived from nitroacetophenones.

Preparation of Diketones.—2 : 4 : 6-*Trimethoxyphenyl* 4-*methoxybenzyl diketone* (6 g.) separated from a solution of (9) (7 g.) in alcohol (70 c.c.), which had been heated under reflux for 4 hours with sodium hydroxide (3·5 c.c.) in water (14 c.c.), diluted, and acidified with dilute hydrochloric acid after filtration; it crystallised from acetone in pale yellow needles, m. p. 144—145° (Found: C, 66·2; H, 6·0. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8%). The diketones obtained from (7) and (11) by similar treatment, for ½ minute only, with boiling aqueous alcoholic sodium hydroxide, decomposed on keeping. Phenyl 4-methoxybenzyl diketone (12) was similarly obtained from (8), or by the action of aqueous-alcoholic sodium hydroxide on the methoxy-compound (19) (see below. Cf. Baker and Robinson, *loc. cit.*, p. 1802). (12) had previously been prepared by Malkin and Robinson (J., 1925, **127**, 374) by the action of hydrogen bromide in acetic acid on phenyl β : 4-dimethoxystyryl ketone. (10) yielded neither a diketone nor a glycollic acid on treatment with alcoholic alkali; the paste obtained could not be purified. 2-p-*Tolyl*-3-p-*methoxybenzylquinoxaline*, m. p. 113—115° (Found: N, 8·2. $C_{23}H_{20}ON_2$ requires N, 8·2%), was prepared from the corresponding unstable diketone from (7) by heating for 1 minute in alcoholic solution with *o*-phenylenediamine.

Preparation of Glycollic Acids from the Oxides.—An alcoholic solution of (7) (10 g. in 150 c.c.) was boiled under reflux with aqueous sodium hydroxide (30%; 15 c.c.) for 4 hours, diluted after cooling, and acidified to precipitate p-*tolyl*-p-*methoxybenzylglycollic acid* (13) (9·5 g.), m. p. 153° (Found: C, 71·1; H, 6·3. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%). 2 : 4-*Dimethoxyphenyl*-3 : 4-*methylenedioxybenzylglycollic acid* (14), m. p. 181° (Found: C, 62·4; H, 5·2. $C_{18}H_{18}O_7$ requires C, 62·5; H, 5·2%), and phenyl-4-methoxybenzylglycollic acid (15) [previously obtained by Malkin and Robinson, *loc. cit.*, by the action of alkali on (12)], were similarly prepared from (11) and (8) respectively. (14), when heated above the m. p. until effervescence had ceased or with acetic acid for 4 hours, lost the elements of water to yield 3 : 4-*methylenedioxy*-α-2′ : 4′-*dimethoxyphenylcinnamic acid*, m. p. 176—177° (Found: C, 65·9; H, 5·0. $C_{18}H_{16}O_6$ requires C, 65·8; H, 4·9%). Malkin and Robinson (*loc. cit.*) observed a similar transformation into cinnamic acid with phenylbenzylglycollic acid (cf., Jörlander, *Ber.*, 1917, **50**, 413).

Preparation of Deoxybenzoins.—A solution of (13) (5 g.) in acetic acid was treated with a solution of potassium chromate or dichromate (3 g.) which had been made with the minimum quantity of water and diluted with acetic acid. After 2 minutes, p-*tolyl* p-*methoxybenzyl ketone* (16), m. p. (alcohol–acetone) 101—103°, was precipitated by dilution (Found: C, 79·7; H, 6·6. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%). (15), when treated similarly, gave phenyl *p*-methoxybenzyl ketone (17), previously prepared by Orékhov and Tiffeneau (*Bull. Soc. chim.*, 1925, **37**, 1410) from *s*-phenyl-*p*-anisylglycol.

Action of Hydrazine Hydrate on the Oxides.—4-*Hydroxy*-5-p-*anisyl*-3-p-*tolyl*-4 : 5-*dihydropyrazole* (18), m. p. 168° (Found: C, 72·5; H, 6·3; N, 9·8. $C_{17}H_{18}O_2N_2$ requires C, 72·3; H, 6·4; N, 9·9%), separated from an alcoholic solution of (7) (10 g.) and hydrazine hydrate (10 g.) which had been heated under reflux for 5 minutes and cooled. An unstable nitroso-derivative, which gave Liebermann's nitroso-reaction, separated from an acetic acid solution of (18) on treatment with aqueous sodium nitrite. 4-*Hydroxy*-3-(2′ : 4′-*dimethoxyphenyl*)-5-(3′ : 4′-*methylenedioxyphenyl*)-4 : 5-*dihydropyrazole*, m. p. 151° (Found: N, 8·2. $C_{18}H_{18}O_5N_2$ requires N, 8·2%), was prepared in the same manner as (18) from (11) and had properties similar to those of (18). 4-*Acetoxy*-1-*acetyl*-3-*phenyl*-5-p-*anisyl*-4 : 5-*dihydropyrazole*, m. p. 125—126° (Found: N, 7·9. $C_{20}H_{20}O_4N_2$ requires N, 7·9%), separated as an oil, which afterwards solidified, from a solution of 4-hydroxy-3-phenyl-5-*p*-anisyl-4 : 5-dihydropyrazole [prepared from (8) by Freudenberg and Stoll, *Annalen*, 1924, **440**, 38] in acetic anhydride which had been boiled for 5 minutes and poured into water. (10) yielded on treatment with alcoholic hydrazine hydrate an unstable compound which gave Knorr's pyrazoline test when freshly prepared. The crystalline compound obtained by heating (9) with hydrazine hydrate in acetic acid did not give Knorr's test and was not further examined.

Preparation of Pyrazoles from Pyrazolines.—5-p-*Anisyl*-3-p-*tolylpyrazole*, m. p. 170° (Found: C, 77·1; H, 6·0; N, 10·5. $C_{17}H_{16}ON_2$ requires C, 77·2; H, 6·1; N, 10·6%), separated on dilution of an alcoholic solution of (18) (5 g.) and sodium ethoxide (0·5 g. of sodium) which had been boiled under reflux for 1½ hours. 5-p-*Anisyl*-3-β-*naphthylpyrazole*, m. p. 232° (Found: N, 9·4. $C_{20}H_{16}ON_2$ requires N, 9·3%), was similarly prepared from the unstable hydroxypyrazoline derived from (10).

Actions of Alcohols on the Oxides.—The solution formed by shaking a suspension of (8) (2 g.) in methyl alcohol (10 c.c.) with a mixture of methyl alcohol (5 c.c.) and sulphuric acid (3 c.c.) was heated at 40° for 3 hours, diluted slightly, and kept at 0° for some days, until *phenyl* α-*hydroxy*-β-*methoxy*-β-p-*anisylethyl ketone* (19), m. p. 87—89° (Found: C, 71·0; H, 6·2. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%), which first separated as an oil, solidified. 2 : 4-*Dimethoxyphenyl* α-*hydroxy*-β-*methoxy*-β-3 : 4-*methylenedioxyphenylethyl ketone*, m. p. (methyl alcohol) 200° (Found: C, 63·2; H, 5·6. $C_{19}H_{20}O_7$ requires C, 63·3; H, 5·6%), and 2 : 4-*dimethoxyphenyl* α-*hydroxy*-β-*ethoxy*-β-3 : 4-*methylenedioxyphenylethyl ketone*, m. p. 172° (Found: C, 64·2; H, 5·9. $C_{20}H_{22}O_7$ requires C, 64·1; H, 5·9%), were similarly prepared from (11), methyl and ethyl alcohol respectively being used.

Action of Fatty Acids on the Oxides.—p-*Tolyl* α-*hydroxy*-β-*acetoxy*-β-p-*anisylethyl ketone*,

m. p. 103—105° (Found : C, 69·8; H, 6·1. $C_{19}H_{20}O_5$ requires C, 69·4; H, 6·1%), separated as a paste from a solution of (7) in acetic acid which had been boiled under reflux for ½ hour, kept for 2 hours, and then diluted. 2 : 4-*Dimethoxyphenyl* α-*hydroxy*-β-*formoxy*-β-3 : 4-*methylenedioxyphenylethyl ketone*, m. p. (acetic acid) 212° (Found : C, 60·3; H, 4·9. $C_{19}H_{18}O_8$ requires C, 60·8; H, 4·8%), was similarly prepared from (11) and formic acid.

Condensation of Chalkones with Deoxybenzoins.—1 : 5-*Diketo*-1 : 5-*diphenyl*-2 : 3-*di*-p-*anisylpentane* (3 g.) separated as a paste, which solidified after it had been boiled with alcohol, from a mixture of (1) (3 g.), (17) (3 g.), and alcohol (30 c.c.) in which sodium (0·25 g.) had been dissolved; it crystallised from alcohol–acetone in needles, m. p. 165—166° (Found : C, 80·2; H, 6·2. $C_{31}H_{28}O_4$ requires C, 80·0; H, 6·0%).

The following were similarly prepared and crystallised from alcohol–acetone : 1 : 5-*diketo*-5-*phenyl*-2 : 3-*di*-p-*anisyl*-1-p-*tolylpentane* [from (1) and (16)], m. p. 146—147° (Found : C, 80·1; H, 6·3. $C_{32}H_{30}O_4$ requires C, 80·3; H, 6·3%); 1 : 5-*diketo*-1 : 2-*diphenyl*-3-p-*anisyl*-5-p-*tolylpentane* [from (3) and deoxybenzoin], m. p. 152—153° (Found : C, 82·8; H, 6·3. $C_{31}H_{28}O_3$ requires C, 83·0; H, 6·2%); 1 : 5-*diketo*-2 : 3-*di*-p-*anisyl*-1 : 5-*di*-p-*tolylpentane* [from (3) and (16)], m. p. 150—151° (Found : C, 80·4; H, 6·3. $C_{33}H_{32}O_4$ requires C, 80·5; H, 6·5%); and 1 : 5-*diketo*-3-*phenyl*-5-o-*hydroxyphenyl*-2-p-*anisyl*-1-p-*tolylpentane* [from *o*-hydroxyphenyl styryl ketone and (16)], m. p. 167—168° (Found : C, 80·1; H, 6·0. $C_{31}H_{28}O_4$ requires C, 80·0; H, 6·0%); the alcoholic solution gave a brown coloration with ferric chloride.

2-Methoxy-1-acetonaphthone (Noller and Adams, *J. Amer. Chem. Soc.*, 1924, **46**, 1892) condensed with benzaldehyde in aqueous alcoholic alkali (Sorge, *loc. cit.*) to give 2-*methoxy*-1-*naphthyl styryl ketone* (20), which separated from alcohol–acetone in yellow needles, m. p. 140—142° (Found : C, 83·0; H, 5·7. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·6%). 1 : 5-*Diketo*-3-*phenyl*-2-p-*anisyl*-1-p-*tolyl*-5-(2'-*methoxy*-1'-*naphthyl*)*pentane* [from (20) and (16)] (Found : C, 81·5; H, 6·0. $C_{36}H_{32}O_4$ requires C, 81·8; H, 6·1%) had m. p. 156—157° after recrystallisation from alcohol–acetone.

2 : 3 : 6-*Triphenyl*-4-p-*anisylpyridine*, m. p. (alcohol–chloroform) 188—189° (Found : C, 86·8; H, 5·7; N, 3·7. $C_{30}H_{23}ON$ requires C, 87·1; H, 5·6; N, 3·4%), separated from an alcoholic solution of 1 : 5-diketo-1 : 2 : 5-triphenyl-3-*p*-anisylpentane [from (1) and deoxybenzoin; see Dilthey *et al.*, *J. pr. Chem.*, 1934, **141**, 331] which had been heated at 140—145° in a sealed tube with an equal weight of hydroxylamine hydrochloride for 5 hours (cf. Knoevenagel, *Annalen*, 1894, **281**, 25).

Condensation of Chalkones with cyclo*Hexanone.*—2-(β-*Benzoyl*-α-p-*anisylethyl*)cyclo*hexanone* (10 g.) (Found : C, 78·7; H, 7·3. $C_{22}H_{24}O_3$ requires C, 78·6; H, 7·1%) separated when a mixture of (1) (10 g.), *cyclo*hexanone (20 c.c.), alcohol (150 c.c.), and aqueous sodium hydroxide (30 g.; 50%) which had been prepared at 40° and kept for 3 hours was poured into water (1 l.); it had m. p. 140—141° after crystallisation from alcohol–acetone. 2-(β-p-*Toluoyl*-α-p-*anisylethyl*)cyclo*hexanone*, m. p. 133—134° (Found : C, 78·8; H, 7·6. $C_{23}H_{26}O_3$ requires C, 78·8; H, 7·4%), 2-(β-*naphthoyl*-α-*phenylethyl*)cyclo*hexanone*, m. p. 155—156° (Found : C, 84·0; H, 6·9. $C_{25}H_{24}O_2$ requires C, 84·3; H, 6·7%), and 2-(β-*naphthoyl*-α-p-*anisylethyl*)cyclo*hexanone*, m. p. 128—130° (Found : C, 80·9; H, 6·7. $C_{26}H_{26}O_3$ requires C, 80·8; H, 6·7%), were similarly prepared from (3), β-*naphthyl styryl ketone* [(21); m. p. 105—107°, prepared from the components in alkali solution (Found : C, 88·5; H, 5·7. $C_{19}H_{14}O$ requires C, 88·4; H, 5·4%) (Shenoi, private communication)], and (5) respectively.

Condensation of Chalkones with Ethyl Acetoacetate.—*Ethyl* 6-*phenyl*-4-β-*naphthyl*-Δ^3-cyclo*hexen*-2-*one*-1-*carboxylate*, m. p. 174—175° (Found : C, 81·2; H, 6·0. $C_{25}H_{22}O_3$ requires C, 81·1; H, 5·9%), separated from an alcoholic solution of (21) (2·5 g.), ethyl acetoacetate (2·5 g.), and sodium ethoxide (0·3 g. of sodium) which had been heated under reflux for 30 minutes and cooled. *Ethyl* 6-p-*anisyl*-4-β-*naphthyl*-Δ^3-cyclo*hexen*-2-*one*-1-*carboxylate*, m. p. (alcohol–acetone) 145—147° (Found : C, 78·1; H, 5·8. $C_{26}H_{24}O_4$ requires C, 78·0; H, 6·0%), and *ethyl* 6-*phenyl*-4-(1'-*hydroxy*-2'-*naphthyl*)-Δ^3-cyclo*hexen*-2-*one*-1-*carboxylate*, m. p. (alcohol–acetone) 165—167° (Found : C, 77·1; H, 5·8. $C_{25}H_{22}O_4$ requires C, 77·7; H, 5·7%), were similarly prepared from (5) and 1-hydroxy-2-naphthyl styryl ketone (Kostanecki, *Ber.*, 1898, **31**, 706).

ROYAL INSTITUTE OF SCIENCE, BOMBAY.

[*Received, October 7th,* 1938.]