STUDIES IN THE CHEMISTRY OF CHALCONES AND CHALCONE-OXIDES.

I. Phenyl-(3'-4'-Methylene-dioxy-styryl)-ketone.

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The marked reactivity of chalcones and chalcone-oxides makes it of interest to examine how far this reactivity is affected by the presence of other groups in the nuclei. A comparative study has now been made of the reactivities of phenyl-(3'-4'-methylene-dioxy-styryl)-ketone (I; \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)) which contains an electron source (methylene-dioxy-group) and of phenyl-(3'-4'-methylene-dioxy-6-nitro-styryl)-ketone (I; \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_4\text{NO}_2 \)) which contains an electron sink (nitro group) in addition to the electron source.

\[
\begin{align*}
R_1 &= \text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \quad \text{or} \quad \text{CH}_2\text{O}_2\text{C}_6\text{H}_4\text{NO}_2 \quad \text{or} \quad \text{C}_6\text{H}_5 \\
R_2 &= \text{CH}_2\text{O}_2\text{C}_6\text{H}_2 =. \quad R' = \text{CH}_3 \text{ or } \text{C}_2\text{H}_5.
\end{align*}
\]

\[
\begin{align*}
\text{R}_2\text{Br} - \text{CH} & \text{(OR')} - \text{CHBr} - \text{COPh} \\
\text{R}_2\text{Br} - \text{CH} & \text{Br} - \text{CHBr} - \text{COPh} \xrightarrow{\text{KI (acetone)}} \text{R}_2\text{Br} - \text{CH} = \text{CH} - \text{CO} - \text{Ph} \\
\text{R}_2\text{Br} - \text{CH} & \text{Cl} - \text{CHCl} - \text{CO} - \text{Ph} \xrightarrow{\text{Br}_2} \text{R}_2\text{Br} - \text{CHBr} - \text{CHBr} - \text{COPh} \xrightarrow{\text{R'OH}} \text{R}_2\text{CH} & \text{(OR')} - \text{CHBr} - \text{COPh}
\end{align*}
\]

\[
\begin{align*}
\text{R}_2\text{Cl} - \text{CHCl} - \text{CHCl} - \text{CO} - \text{Ph} \rightarrow \text{R}_1\text{CH} & \text{CH}_2\text{CH}_2 - \text{CH(OH)Ph} \\
\text{R}_1\text{CH} & \text{(CN)} - \text{CH}_2 - \text{CO} - \text{Ph} \xrightarrow{\text{Hydrolysis}} \text{R}_2\text{CH} & \text{(COOH)} - \text{CH}_2 - \text{CO} - \text{Ph}
\end{align*}
\]

\[
\begin{align*}
\text{R}_2\text{Br} - \text{CH} & \text{(OR')} - \text{CHBr} - \text{COPh} \\
\text{R}_2\text{Br} - \text{CH} & \text{Br} - \text{CHBr} - \text{COPh} \xrightarrow{\text{KI (acetone)}} \text{R}_2\text{Br} - \text{CH} = \text{CH} - \text{CO} - \text{Ph} \\
\text{R}_2\text{Br} - \text{CH} & \text{Cl} - \text{CHCl} - \text{CO} - \text{Ph} \xrightarrow{\text{Br}_2} \text{R}_2\text{Br} - \text{CHBr} - \text{CHBr} - \text{COPh} \xrightarrow{\text{R'OH}} \text{R}_2\text{CH} & \text{(OR')} - \text{CHBr} - \text{COPh}
\end{align*}
\]

shows the reaction proceeds with \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)

\[
\begin{align*}
\text{R}_2\text{Br} - \text{CH} & \text{(OR')} - \text{CHBr} - \text{COPh} \\
\text{R}_2\text{Br} - \text{CH} & \text{Br} - \text{CHBr} - \text{COPh} \xrightarrow{\text{KI (acetone)}} \text{R}_2\text{Br} - \text{CH} = \text{CH} - \text{CO} - \text{Ph} \\
\text{R}_2\text{Br} - \text{CH} & \text{Cl} - \text{CHCl} - \text{CO} - \text{Ph} \xrightarrow{\text{Br}_2} \text{R}_2\text{Br} - \text{CHBr} - \text{CHBr} - \text{COPh} \xrightarrow{\text{R'OH}} \text{R}_2\text{CH} & \text{(OR')} - \text{CHBr} - \text{COPh}
\end{align*}
\]

Fig. I.
Phenyl-(3·4-methylene-dioxy-styryl)-ketone (I; \( R_1 = CH_2OOC_6H_5 \))—see Fig. 1) with bromine (1 mol.) yielded \( \alpha \)-benzoyl-\( \beta \)-(3·4-methylene-dioxy-phenyl)-\( \alpha \)-\( \beta \)-dibromo-ethane (II; \( R_1 = CH_2OOC_6H_5 \))\(^1\) which with boiling ethyl or methyl alcohol gave respectively \( \alpha \)-benzoyl-\( \alpha \)-bromo-\( \beta \)-ethoxy-\( \beta \)-(3·4-methylene-dioxy-phenyl)-ethane (V; \( R' = Et \)) and \( \alpha \)-benzoyl-\( \alpha \)-bromo-\( \beta \)-methoxy-\( \beta \)-(3·4-methylene-dioxy-phenyl)-ethane (V; \( R' = Me \)). The labile nature of one of the bromine atoms in compounds of the type (II) has been already observed by Pond and Shoffstall\(^2\) with \( \alpha \)-benzoyl-\( \beta \)-(\( \beta \)-methoxy-phenyl)-\( \alpha \)-\( \beta \)-dibromo-ethane (II; \( R_1 = CH_2OOC_6H_5 \)) which contains a methoxy-group in the nucleus. These authors assumed that the bromine atom in the \( \alpha \)-position to the keto-group was replaced by the alkyl group, because the elimination of alcohol by heating the alkoxy-compound (V; \( R_1 = CH_2OOC_6H_5 \), \( R' = Me \)) gave a mono-bromo-anisylidene-acetophenone identical with the compound obtained by the action of sodium ethoxide on the dibromo-compound (II; \( R_1 = CH_2OOC_6H_5 \)). Following Wislicenus,\(^3\) they supposed that this bromine was in the \( \beta \)-position to the keto-group. Dufraisse and his collaborators,\(^4\) however, have shown that the bromine in mono-bromo-chalcones obtained by the action of sodium alcoholate on the chalcone dibromides of the type (II) is in the \( \alpha \)-position and hence the formula now given to (V) is to be preferred. Further support is given to the formula now adopted by the consideration that the nucleus containing the activating group may be expected to influence the nearer bromine atom.*

(I; \( R_1 = CH_2OOC_6H_5 \)) with bromine (2 mols.) gave \( \alpha \)-benzoyl-\( \beta \)-(3·4-methylene-dioxy-6-bromo-phenyl)-\( \alpha \)-\( \beta \)-dibromo-ethane (III; \( R_2 = CH_2OOC_6H_5 \)) which with the corresponding alcohols yielded respectively \( \alpha \)-benzoyl-\( \alpha \)-bromo-\( \beta \)-ethoxy-\( \beta \)-(3·4-methylene-dioxy-6-bromo-phenyl)-ethane (VI; \( R' = Et \)) and \( \alpha \)-benzoyl-\( \alpha \)-bromo-\( \beta \)-methoxy-\( \beta \)-(3·4-methylene-dioxy-6-bromo-phenyl)-ethane (VI; \( R' = Me \)). Heated with potassium iodide (2 mols.) in acetone both (II) and (III; \( R_2 = CH_2OOC_6H_5 \)) reformed the corresponding chalcones (I) and (IV; \( R_2 = CH_2OOC_6H_5 \)). The constitution of (IV) as phenyl-(3·4-methylene-dioxy-6-bromo-styryl)-ketone and hence of (III) is proved by the synthesis of (IV;

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\(^1\) Bauer and Werner, *Ber.*, 1922, 55, 2497.

\(^2\) J.A.C.S., 1900, 22, 658; cf. Werner, *Ber.*, 1906, 39, 35, who describes Pond and Shoffstall's compounds without reference to their work, and assumes that the bromine atom in the \( \beta \)-position to the keto-group is replaced; see also Golschmidt, 1906, 39, 651; Bauer and Vogel, *J.pr. Chem.*, 1913, 88, 329; Angeli, *Atti R.Acad.Lincei*, 1924, (v), 33, 109; for similar work on alkoxyacinnamic acid dibromides see Hoering, *Ber.*, 1907, 40, 2174.

\(^3\) Ann., 1899, 308, 219.

\(^4\) Comm. rend., 1920, 171, 1062; 1921, 173, 985; 1922, 174, 1631.

* Motwan in this laboratory has recently shown that a methoxy-group in the other nucleus does not enhance the reactivity of the bromine atoms.
R₂=CH₂O₂C₆H₅=), from 6-bromo-piperonal and acetophenone. (I) with chlorine (1 mol. and 2 mols.) formed respectively, α-benzoyl-β-(3,4-methylene-dioxo-phenyl)-α-β-dichloro-ethane (VII) and α-benzoyl-β-(3,4-methylene-dioxo-6-chloro-phenyl)-α-β-dichloro-ethane (IX; R₂=CH₂O₂C₆H₅=). The constitution of (IX) was deduced by analogy with (III). (VII) which was isolated only in the form of paste yielded with ethyl alcohol, α-benzoyl-α-chloro-β-ethoxy-β-(3,4-methylene-dioxo-phenyl)-ethane (VIII).

The dibromide (II; R₁=CH₂O₂C₆H₅—) with potassium cyanide gave α-(3,4-methylene-dioxo-phenyl)-β-benzoyl-propio-nitride (X; R₁=CH₂O₂C₆H₅—) which on hydrolysis formed α-(3,4-methylene-dioxo-phenyl)-β-benzoyl-propionic acid (XI; R₁=CH₂O₂C₆H₅—). The formulae of (X) and (XI) were confirmed by the fact that benzylidene-acetophenone-dibromide (II; R₁=C₆H₅—) with potassium cyanide gave α-phenyl-β-benzoyl-propio-nitride (X; R₁=C₆H₅—) which has been synthesised previously from phenyl-styryl-ketone and hydrogen cyanide by Hann and Lapworth. This nitrile on hydrolysis gave α-phenyl-β-benzoyl-propionic acid (XI; R₁=C₆H₅—) which has also been previously prepared.

Phenyl-(3,4-methylene-dioxo-6-nitro-styryl)-ketone (I; R₁=CH₂O₂C₆H₅—) with bromine (1 mol.) gave α-benzoyl-β-(3,4-methylene-dioxo-6-nitro-phenyl)-α-β-dibromo-ethane (II; R₁=CH₂O₂C₆H₂NO₂—), which did not react further with bromine or with alcohol but was converted into (I; R₁=CH₂O₂C₆H₂NO₂—) by the action of potassium iodide in acetone. By the action of chlorine (1 mol.) on (I; R₁=CH₂O₂C₆H₂NO₂—), α-benzoyl-β-(3,4-methylene-dioxo-6-nitro-phenyl)-α-β-dichloro-ethane (VII; R₁=CH₂O₂C₆H₂NO₂—) was obtained.

(I; R₁=CH₂O₂C₆H₅—) condensed readily with ethyl-acetoacetate to yield ethyl-2-(3′,4′-methylene-dioxo-phenyl)-4-phenyl-Δ⁴-cyclohexene-6-one-1-carboxylate (XII; R₁=CH₂O₂C₆H₅—). The nitrochalcone (I; R₁=CH₂O₂C₆H₅—) did not react. (I; R₁=CH₂O₂C₆H₅—) was reduced by hydrogen in presence of palladium, to give α-phenyl-γ-(3,4-methylene-dioxo-phenyl)-propylalcohol (XIII; R₁=CH₂O₂C₆H₃—) (m.p. 95—96°). The saturated ketone, i.e., dihydropiperonal-acetophenone (m.p. 39—40°) was not obtained. The nitrochalcone (I; R₁=CH₂O₂C₆H₂NO₂—) could not be reduced.

(I; R₁=CH₂O₂C₆H₅—; see Fig. 2) with hydrazine hydrate gave 3-phenyl-5-(3′,4′-methylene-dioxo-phenyl)-pyrazoline (XIV; R₁=CH₂O₂C₆H₅—)
which was unstable, but formed a stable hydrochloride, picrate and acetyl derivative. The substance did not give Knorr's pyrazoline colour reaction, i.e., a trace dissolved in conc. sulphuric acid gave no colour with a drop of ferric chloride or sodium nitrite solution. This points to it being a hydrazone. On the other hand unlike hydrazones, it gave no ammonia on reduction with sodium amalgam, and formed a hydrochloride. The evidence is conflicting; as it seemed definitely basic, the more probable assumption is that it is a pyrazoline.

With phenyl-hydrazine (I; \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_3^- \)) gave 1-3-diphenyl-5-(3',4'-methylene-dioxy-phenyl)-pyrazoline (XV; \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_3^- \)) which answered Knorr's pyrazoline's tests and gave a nitroso-derivative. With hydrogen peroxide (6%) (I; \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_3^- \)) gave the *oxide* of phenyl-(3,4-
methylene-dioxy-styryl)-ketone (XVI; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \))
which yielded a hydrazone (XVII; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)) with hydrazine hydrate. (XVII) is taken
to be a hydrazone and not a hydroxy-pyrazoline,\(^{11}\) because it does not form a nitroso-derivative. With sodium ethylate or acetic anhydride, (XVII) gave 3-
phenyl-5-(3',4'-methylene-dioxy-phenyl)-pyrazole (XVIII; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)).

When a suspension of the oxide (XVI; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)) in methyl
alcohol was treated with a little conc. sulphuric acid, the oxide ring ruptured
with the formation of \( \alpha \)-benzoyl-\( \alpha \)-hydroxy-\( \beta \)-methoxy-\( \beta \)-(3,4-methylene-dioxy-
phenyl)-ethane (XIX; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \); \( \text{R}'=\text{Me} \)). Ethyl alcohol reacted
similarly giving \( \alpha \)-benzoyl-\( \alpha \)-hydroxy-\( \beta \)-ethoxy-\( \beta \)-(3,4-methylene-dioxy-
phenyl)-ethane (XIX; \( \text{R}'=\text{Et} \)). (XIX; \( \text{R}'=\text{Me} \)) when boiled with sodium acetate
and acetic acid, for two hours, or with aqueous-alcoholic sodium hydroxide
for a few minutes, gave phenyl-(3,4-methylene-dioxy-benzyl)diketone (XX;
\( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)), the constitution of which as an \( \alpha \)-diketone was
confirmed by the formation of a quinoxaline with \( \sigma \)-phenylene-diamine.
The formation of the \( \alpha \)-diketone also establishes the structure of (XIX;
\( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \); \( \text{R}'=\text{Me} \) and \( \text{Et} \)). The diketone was also obtained
by boiling an alcoholic solution of (XVI; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)) with aq. sodium
hydroxide for 30 seconds. The diketone gave a colour reaction with alcoholic
ferric chloride showing that the enol form is present in the solution. (XVI;
\( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)) on prolonged heating with sodium hydroxide gave phenyl-
(3,4-methylene-dioxy-benzyl)-glycolic acid (XXI; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)). This
acid was readily oxidised by potassium dichromate in acetic acid to phenyl-

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\text{R}_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2
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11 See Widman, \textit{Bcr.}, 1916, 49, 2781.
(3·4-methylene-dioxy-benzyl)-ketone (XXII; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)) which has been previously prepared by Tiffeneau and Lévy\(^\text{12}\) by the distillation of the oxide of (3·4-methylene-dioxy-styryl)-benzene. This oxidation proves the structure of the acid (XXI). (XVI; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)) did not give a definite product with HCl.

(I; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2 \)); see Fig. 3) with hydrogen peroxide (6%) gave the oxide of phenyl-(3·4-methylene-dioxy-6-nitro-styryl)-ketone (XVI; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2 \)) which, however, was better prepared (quantitative yield) by the method of Widman and Almström\(^\text{13}\) from 6-nitro piperonal and \( \omega \)-bromo-acetophenone. (XVI; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2 \)) unlike (XVI; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)) did not react with ethyl or methyl alcohols or with NaOH, but with hydrogen chloride in acetic acid gave phenyl-\( \beta \)-chloro-\( \alpha \)-hydroxy-\( \beta \)-(3·4-methylene-dioxy-6-nitro-phenyl)-ethyl-ketone (XXIII; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2 \)), in which the position of chlorine atom was determined by the results of Widman.\(^\text{14}\) (I; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_2\text{NO}_2 \)) with hydrazine hydrate in acetic acid gave the acetyl derivative of the hydrazone of phenyl-(3·4-methylene-dioxy-6-nitro-styryl)-ketone (XXIV; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2 \)). Analysis of the product showed that it was an acetyl derivative of the hydrazone or pyrazoline. It is difficult to decide in this case between the alternative formulae, since the acetyl group may mask the various tests. Auwers and Voss,\(^\text{15}\) however, have shown that the nitro-group stabilises the hydrazone form and it has been found (see later) that the phenyl-hydrazone of the chalcone now under discussion is stable.

(I; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_2\text{NO}_2 \)) with phenyl-hydrazine in hot acetic acid gave the phenyl-hydrazone of phenyl-(3·4-methylene-dioxy-6-nitro-styryl)-ketone (XXV; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2 \)) which did not give Knorr's pyrazoline colour reaction and dissolved slowly in conc. sulphuric acid with the formation of colour. When boiled with acetic acid, it yielded 1·3-diphenyl-5-(3′·4′-methylene-dioxy-6′-nitro-phenyl)-pyrazole (XXVI; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2 \)) which answered the pyrazoline colour tests. (XXVI) was converted by silver nitrate into 1·3-diphenyl-5-(3′·4′-methylene-dioxy-6′-nitro-phenyl)-pyrazole (XXVII; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2 \)) which was also obtained by the action of phenyl-hydrazine on (XVI; \( R_1=\text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2 \)).

A study of the experimental results indicates that the nitro-group removes the enhanced activity which the presence of a nuclear alkoxy group

\(^{12}\) Compt. rend., 1930, 190, 1510.
\(^{13}\) Ann., 1913, 408, 105.
\(^{14}\) Ber., 1916, 49, 477; cf. Jörlander, Ber., 1916, 49, 2783; 1917, 50, 1457; Bodforss, Ber., 1916, 4′, 2795, and Baker and Robinson, loc. cit.
\(^{15}\) Ber., 1909, 42, 4414.
confers on one of the bromine atoms in the chalcone dibromide; and further it reduces the reactivity of the oxide towards ethyl or methyl alcohols and alkali, but not towards HCl.

Experimental.

1. a-Benzoyl-β-(3,4-methylene-dioxy-phenyl)-α-β-dibromo-ethane (II; \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)) was prepared by the action of bromine (1 mol.) on (I; \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)).\(^1\) (Found : Br, 39·0; \( \text{C}_{15}\text{H}_{13}\text{O}_7\text{Br} \) requires Br, 38·8%)

2. a-Benzoyl-a-bromo-β-ethoxy-β-(3,4-methylene-dioxy-phenyl)-ethane (V; \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \); \( R' = \text{Et} \)).—The preceding dibromide was boiled with ethyl alcohol for fifteen minutes; on cooling the solution, white prisms separated, m.p. 143–44\(^\circ\). (Found : Br, 21·1; \( \text{C}_{18}\text{H}_{17}\text{O}_4\text{Br} \) requires Br, 21·2%)

3. a-Benzoyl-a-bromo-β-methoxy-β-(3,4-methylene-dioxy-phenyl)-ethane (V; \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \); \( R' = \text{Me} \)).—Prepared as in (2); crystallised from methyl alcohol in prismatic needles m.p. 115–16\(^\circ\). (Found : Br, 22·1; \( \text{C}_{17}\text{H}_{13}\text{O}_4\text{Br} \) requires Br, 22·0%)

4. a-Benzoyl-β-(3,4-methylene-dioxy-6-bromo-phenyl)-α-β-dibromo-ethane (III; \( R_2 = \text{CH}_2\text{O}_2\text{Br} \)).—Bromine (32 g.) in gl. acetic acid (50 c.c.) was added slowly to (I; \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)) (25 g.) in hot acetic acid (150 c.c.), and the mixture was heated at 100\(^\circ\) for 30 minutes, when (III; \( R_2 = \text{CH}_2\text{O}_2\text{Br} \)) separated in the form of crystalline needles (yield, 30 g.). It recrystallised from benzene-petroleum ether in white needles. m.p. 174–75\(^\circ\). (Found : Br, 49·3; \( \text{C}_{16}\text{H}_{11}\text{O}_5\text{Br} \) requires Br, 48·9%). It formed (IV; \( R_2 = \text{CH}_2\text{O}_2\text{Br} \)) when treated with potassium iodide as described in (7).

5. a-Benzoyl-a-bromo-β-ethoxy-β-(3,4-methylene-dioxy-6-bromo-phenyl)-ethane (VI; \( R_2 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \); \( R' = \text{Et} \)).—Prepared as in (2); it crystallised from ethyl alcohol in white needles, m.p. 126–27\(^\circ\). (Found : Br, 34·8; \( \text{C}_{15}\text{H}_{14}\text{O}_4\text{Br} \) requires Br, 35·1%)

6. a-Benzoyl-a-bromo-β-methoxy-β-(3,4-methylene-dioxy-6-bromo-phenyl)-ethane (VI; \( R_2 = \text{CH}_2\text{O}_2\text{Br} \); \( R' = \text{Me} \)) was prepared as in (2); it recrystallised from methyl alcohol in colourless prisms, m.p. 131–32\(^\circ\). (Found : Br, 36·3; \( \text{C}_{17}\text{H}_{13}\text{O}_4\text{Br} \) requires Br, 36·2%)

7. Phenyl-(3,4-methylene-dioxy-6-bromo-styryl)-ketone (IV; \( R_2 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)).—(III; \( R_2 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5 \)) (6 g.) in hot acetone was heated at 90–100\(^\circ\) with potassium iodide dissolved in a small quantity of water and acetone, when iodine was liberated. The product separating on cooling recrystallised from alcohol-acetone in white needles, m.p. 146–47\(^\circ\). The substance turns pink on exposure for a few days. (Found : Br, 24·3; \( \text{C}_{16}\text{H}_{11}\text{O}_3\text{Br} \) requires

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\(^1\) cf. Bauer and Werner, loc. cit.
Br, 24.2%). It was also formed when a mixture of 6-bromo piperonal (4.6 g.), alcohol (100 c.c.), acetophenone (2.4 g.) and sodium hydroxide solution (10% 2 c.c.) was heated at 80-100° for 15 minutes.

8. \( \text{a-Benzoyl-\( \alpha \)-chlo-ro-\( \beta \)-\text{ethoxy-\( \beta \)-\( \text{(3.4-methylene-dioxy-phenyl) -ethane} \))} \) (VIII; \( R_1=\text{C}_2\text{H}_5 \text{O}_2\text{C}_6\text{H}_5 \)).—An attempt to prepare a dichloro-compound (VII; \( R_1=\text{CH}_2\text{O} \text{C}_6\text{H}_5 \)) similar to (II; \( R_1=\text{CH}_2\text{O} \text{C}_6\text{H}_5 \)) by passing dry chlorine (1 mol.) into an acetic acid solution of (I; \( R_1=\text{CH}_2\text{O} \text{C}_6\text{H}_5 \)) (1 mol.) resulted in a pasty mass which could not be re-cry stallised from any of the usual inert solvents. It recrystallised from ethyl alcohol (charcoal) in prismatic needles, m.p. 118-19°. (Found: Cl, 10.8; C\(_{18}\)H\(_{10}\)O\(_4\)Cl requires Cl, 10.7%). Methyl alcohol did not give a crystalline product.

9. \( \text{a-Benzoyl-\( \beta \)-\( \text{(3.4-methylene-dioxy-6-chloro-phenyl) -\beta -dichloro-ethane} \))} \) (IX; \( R_2=\text{CH}_2\text{O} \text{C}_6\text{H}_5 \)).—An acetic acid solution of (I; \( R_1=\text{CH}_2\text{O} \text{C}_6\text{H}_5 \)) was treated with chlorine and kept over-night, when crystals separated; a further yield was obtained on diluting with water. The product recrystallised from benzene-petroleum ether in colourless crystals, m.p. 127-28°. (Found: Cl, 29.3; C\(_{18}\)H\(_{11}\)O\(_3\)Cl requires Cl, 29.7%).

10. \( \text{a-\( \text{(3.4-Methylene-dioxy-phenyl)-\beta -benzoyl-propio-nitrile} \)) \) (X; \( R_1=\text{CH}_2\text{O} \text{C}_6\text{H}_5 \)).—A mixture of (II; \( R_1=\text{CH}_2\text{O} \text{C}_6\text{H}_5 \)) (20 g.), potassium cyanide (10 g.) and alcohol (100 c.c. methyl or ethyl) was heated under reflux for three hours at 100°, and kept at 0° for 24 hours, when the precipitate formed was filtered and washed with water and with alcohol (yield, 8 g.). It recrystallised from alcohol (charcoal) in white plates, m.p. 132-33°. (Found: \( * \) N, 5.1; C\(_{17}\)H\(_{12}\)O\(_2\)N requires N, 5.0%).

11. \( \text{a-\( \text{(3.4-Methylene-dioxy-phenyl)-\beta -benzoyl-propionic acid} \)) \) (XI; \( R_1=\text{CH}_2\text{O} \text{C}_6\text{H}_5 \)).—A mixture of the preceding nitrile (5 g.) aq. sodium hydroxide (10%; 50 c.c.) and alcohol (25 c.c.) was heated at 100° for 8 hours and filtered. The filtrate was acidified with dil. hydrochloric acid and the acid (4.2 g.) separating was recrystallised from benzene; prismatic crystals m.p. 143-44°. (Found: \( \dagger \) C, 68.7; H, 4.6; equiv. 294; C\(_{17}\)H\(_{14}\)O\(_2\) requires C, 68.5; H, 4.7%; equiv. 298).

12. \( \text{a-Phenyl-\( \beta -benzoyl-propio-nitrile} \)) (X; \( R_1=\text{C}_6\text{H}_5 \)).—a-Benzoyl-\( \beta \)-phenyl-\( \alpha \)-dibromo-ethane (II; \( R_1=\text{C}_6\text{H}_5 \)) treated as in (10) gave (X; \( R_1=\text{C}_6\text{H}_5 \)) m.p. 126-27°. (Found: \( * \dagger \) N, 6.1; C, 81.7; H, 5.5; C\(_{16}\)H\(_{14}\)ON requires N, 6.0; C, 81.5; H, 5.5%). Mixed m.p. with an authentic specimen prepared by the action of hydrogen cyanide on benzylidene-acetophenone\( ^{17} \) showed no depression.

\( ^{17} \) Hann and Lapworth, \textit{loc. cit.}
13. a-Phenyl-β-benzoyl-propionic acid (XI; $R_1 = \text{C}_6\text{H}_5$).—The preceding nitrile was hydrolysed as in (11); m.p. 152–53°. (Found: $\text{C}$, 75·6; $\text{H}$, 5·4; $\text{C}_{16}\text{H}_{14}\text{O}_3$ requires $\text{C}$, 75·6; $\text{H}$, 5·5%). This acid was obtained (m.p. 152–53°) by Hann and Lapworth\textsuperscript{18} by hydrolysing the nitrile (X; $R_1 = \text{C}_6\text{H}_5$) with conc. sulphuric acid.

14. a-Benzyl-β-(3·4-methylene-dioxy-6-nitro-phenyl)-α-dibromo-ethane (II; $R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2$) prepared as in (1) from phenyl-(3·4-methylene-dioxy-6-nitro-styryl)-ketone (I; $R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2$) crystallised from benzene-toluene in pale yellow needles, m.p. 174–75°. (Found: $\text{Br}$, 35·3; $\text{C}_{16}\text{H}_{11}\text{O}_6\text{NBr}_2$ requires $\text{Br}$, 35·0%). With potassium iodide as in (7) it reformed the chalcone (I; $R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2$).

15. a-Benzyl-β-(3·4-methylene-dioxy-6-nitro-phenyl)-α-dichloro-ethane (VII; $R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5\text{NO}_2$) (3 g.) in acetic acid (50 c.c.) was treated with chlorine (0·7 g.) and diluted with water. The pasty product was kept in contact with sodium bicarbonate solution until it solidified. It recrystallised from benzene-petroleum ether (charcoal) in pale yellow crystals, m.p. 151–52°. (Found: $\text{Cl}$, 19·4; $\text{C}_{16}\text{H}_{11}\text{O}_6\text{NCl}_2$ requires $\text{Cl}$, 19·3%).

16. Ethyl-2-(3·4'-methylene-dioxy-phenyl)-4-phenyl-Δ\textsuperscript{4}-cyclo-hexene-6-one-1-carboxylate (XII; $R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5$).—A mixture of sodium ethylate (0·8 g. Na in 25 c.c. abs. alcohol), aceto-acetic ester (8 g.), (I; $R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5$) (10 g.) and alcohol (100 c.c.) was heated under reflux at 80–90° for three hours. The product (13 g.) recrystallised from alcohol-acetone in white needles, m.p. 151–52°. (Found: $\text{C}$, 72·3; $\text{H}$, 5·5; $\text{C}_{22}\text{H}_{20}\text{O}_5$ requires $\text{C}$, 72·5; $\text{H}$, 5·5%).

17. a-Phenyl-γ-(3·4-methylene-dioxy-phenyl)-propyl-alcohol (XIII; $R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5$).—(I; $R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5$) (5 g.) was dissolved in ethyl alcohol (250 c.c.) at 60–65° and the air in the flask containing the solution was expelled by pure hydrogen, after which palladous chloride solution (15 c.c. of 1%) and gum arabic (15 c.c. of 1% solution) were added. The flask was then connected to the hydrogen generator and vigorously shaken. It was difficult to observe the absorption of hydrogen, but after some time the yellow colour disappeared and a colourless solution was obtained. The suspended catalyst coagulated when the reduction was complete. The greater part of the alcohol was removed by distillation and the separated mass was recrystallised from dil. alcohol (yield: 4·5 g.; m.p. 95–96°. (Found: $\text{C}$, 75·1; $\text{H}$, 6·2; $\text{C}_{16}\text{H}_{14}\text{O}_3$ requires $\text{C}$, 75·0; $\text{H}$, 6·2%).

18. 3-Phenyl-5-(3·4'-methylene-dioxy-phenyl)pyrazoline (XIV; $R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5$).—A solution of (I; $R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_5$) (2 g.) in alcohol (20 c.c.)

\textsuperscript{18} Lec. cit.
after being heated with 50 per cent. hydrazine hydrate (2 c.c.) at 80°
deposited white needles on cooling. These decomposed on drying. The
following derivatives were prepared and analysed.

_Hydrochloride_—pinkish brown crystalline needles; m.p. 197–98° (Found:
Cl, 12.1; C_{16}H_{13}O_{2}N_{2}Cl requires Cl, 11.7%).

_Picrate_—recrystallised from alcohol in shining yellow plates; m.p.
185–86°. (Found: * N, 14.3; C_{22}H_{10}O_{9}N_{6} requires N, 14.1%).

_Acetyl derivative_—recrystallised from alcohol in white needles; m.p.
153–54°. (Found: N, 9.3; C_{11}H_{16}O_{3}N_{2} requires N, 9.1%). A trace of the
pyrazoline dissolved rather slowly in conc. sulphuric acid and the solution
did not give a colour with ferric chloride or sodium nitrite solution. When
it was reduced by 2.5% sodium amalgam, no odour of ammonia could be
detected.

19. _1-3-Diphenyl-5-(3′-4′-methylene-dioxy-phenyl)-pyrazoline_ (XV; R_{1} =
CH_{2}O_{2}C_{6}H_{5}−).—A mixture of (I; R_{1}=CH_{2}O_{2}C_{6}H_{5}−) (5 g.) in hot acetic
acid (50 c.c.) and phenyl-hydrazine (2.5 g.) after being heated at 90–100°
for fifteen minutes deposited on cooling white clusters which were recrystal-
lised from alcohol (yield, 5 g.); m.p. 129–30°. (Found: * N, 8.2; C, 77.1;
H, 5.5; C_{22}H_{18}O_{7}N_{2} requires N, 8.2; C, 77.1; H, 5.3%). The product
gave a fluorescent sky-blue colour in chloroform or benzene and was easily
soluble in conc. sulphuric acid. The solution gave an intense blue colour
with a drop of ferric chloride or sodium nitrite solution. It did not change
on boiling with acetic acid. It gave a nitroso-derivative which decomposed
when dry.

20. _Oxide of phenyl-(3′4-methylene-dioxy-styril)-ketone_ (XVI; R_{1} =
CH_{2}O_{2}C_{6}H_{5}−).—A solution of (I; R_{1}=CH_{2}O_{2}C_{6}H_{5}−) (20 g.) in a warm
mixture of methyl alcohol or rect. spirit (250 c.c.) and acetone (150 c.c.)
was cooled to 40° and to the suspension were quickly added hydrogen peroxide
(120 c.c. of 20 vol. concentration, i.e., 6%) and 10 per cent. aq. sodium
hydroxide (20 c.c.). The whole was shaken for about 15 minutes, when the
partly separated chalcone dissolved. The rise in temperature was controlled
by cooling under the tap. On cooling a needle-shaped crystalline product
separated. A further yield was obtained on diluting the filtrate. The precipitate (18.5 g.) recrystallised from alcohol-acetone in white prismatic
needles, m.p. 99–100°. (Found: † C, 71.7; H, 4.4; C_{10}H_{12}O_{4} requires
C, 71.6; H, 4.5%).

21. _Hydrazone of the oxide of phenyl-(3′4-methylene-dioxy-styril)-ketone_
(XVII; R_{1}=CH_{2}O_{2}C_{6}H_{5}−).—The preceding oxide (2 g.) in alcohol (20 c.c.)
was boiled with 50 per cent. hydrazine-hydrate (2 c.c.) for five minutes. The
white crystals (1·6 g.) which separated on cooling were recrystallised from alcohol, m.p. 173–74°. (Found: N, 10·0; C₁₉H₂₄O₅N₅ requires N, 10·0%). Potassium nitrite in acetic acid did not react with the compound.

22. 3-Phenyl-5-(3′,4′-methylenedioxy-phenyl)-pyrazole (XVIII; R₁ = CH₃O₂C₆H₅—).—A solution of the preceding hydrazone (XVII; R₁ = CH₃O₂C₆H₅—) (2 g.) in alcohol was boiled with sodium ethoxide (0·5 g. sodium in 5 c.c. abs. alcohol), and cooled, when crystalline needles (1·5 g.), m.p. 194–95°, separated and were recrystallised from alcohol. The same product was obtained when the hydrazone was boiled with acetic anhydride. (Found: N, 10·8; C₁₆H₁₅O₂N₃ requires N, 10·6%).

23. α-Benzoyl-a-hydroxy-β-methoxy-β-(3·4-methylenedioxy-phenyl)-ethane (XIX; R₁ = CH₃O₂C₆H₅—; R′ = Me).—To a suspension of the oxide (XVI; R₁ = CH₃O₂C₆H₅—) (4 g.) in methyl alcohol (20 c.c.) was added a mixture of methyl alcohol (20 c.c.) and conc. sulphuric acid (5 c.c.); and the whole was shaken and warmed to 40°, when it formed a pale yellow solution. On keeping in the refrigerator colourless needles separated. They were washed with water and finally with alcohol (yield 2·5 g.); m.p. 117–18°. (Found: C, 67·7; H, 5·4; C₁₇H₁₄O₅ requires C, 68·0; H, 5·3%).

24. α-Benzoyl-a-hydroxy-β-ethoxy-β-(3·4-methylenedioxy-phenyl)-ethane (XIX; R₁ = CH₃O₂C₆H₅—; R′ = Et).—Prepared similarly to 21; the product did not separate until the solution was diluted, when it formed a paste containing crystals. It recrystallised from alcohol (charcoal) in small colourless prisms, m.p. 98–94°. (Found: C, 69·2; H, 5·9; C₁₈H₁₅O₅ requires C, 68·8; H, 5·7%).

25. Phenyl-(3·4-methylenedioxy-benzyl)-diketone (XX; R₁ = CH₃O₂C₆H₅—).—The methoxy-compound (XIX; R₁ = CH₃O₂C₆H₅—) (0·6 g.) was heated with sodium acetate (1 g.) in acetic acid (8 c.c.) for two hours at 100°; the product precipitated by addition of water crystallised from alcohol in yellow needles, m.p. 114–15°.

The same product was obtained when the methoxy-compound was boiled in alcoholic solution for 2–3 minutes with a few drops of aq. sodium hydroxide; the orange solution was diluted with dilute hydrochloric acid and the precipitate recrystallised from alcohol. (Found: C, 71·3; H, 4·4; C₁₉H₁₂O₄ requires C, 71·7; H, 4·5%).

The diketone was, however, best prepared by boiling the alcoholic solution of the oxide (XVI; R₁ = CH₃O₂C₆H₅—) with aq. sodium hydroxide for 30 seconds. The red solution was diluted with dilute hydrochloric acid, and the product crystallised from alcohol in yellow needles. The substance turns
pasty after a fortnight, unless kept in a sealed tube. It gives a purple colour with alcoholic ferric chloride.

26. 2-Phenyl-3-(3'-4'-methylenedioxy-benzyl)-quinoxaline.—The preceding diketone (0.7 g.) in alcohol (10 c.c.) was boiled with o-phenylene-diamine (0.3 g.) for five minutes. The product that separated on cooling recrystallised from alcohol in white needles (yield, 0.8 g.), m.p. 137-38°. (Found: N, 8.2; C_{22}H_{18}O_{2}N_{4} requires N, 8.2%).

27. Phenyl-(3,4-methylenedioxy-benzyl)-glycollic-acid (XXI; R_1 = CH_{3}O_{2}C_{6}H_{3}—).—The oxide (XVI; R_1 = CH_{3}O_{2}C_{6}H_{3}—) (10 g.) in alcohol (75 c.c.) was boiled under reflux for four hours with sodium hydroxide (5 g.) in water (15 c.c.) and the solution was diluted with water and filtered. The filtrate was acidified with dilute hydrochloric acid and the precipitate recrystallised from dilute alcohol; white needles, m.p. 149-50° (Yield, 6.2 g.). (Found: † C, 67.0; H, 5.2%; equiv. 290; C_{16}H_{14}O_{5} requires C, 67.1; H, 4.9%; equiv. 286).

28. Phenyl-(3,4-methylenedioxy-benzyl)-ketone (XXII; R_1 = CH_{3}O_{2}C_{6}H_{3}—).—The preceding acid (5 g.) in warm acetic acid was treated with potassium dichromate (3 g.) dissolved in the minimum quantity of water and then diluted with acetic acid. After one minute, the solution was diluted with water and the light green ppt. was filtered and extracted with acetone. The extract after removal of the solvent gave a paste which solidified after keeping at 0° for two days. It recrystallised from pet. ether in small colourless needles; m.p. 70-71° (yield, 2 g.).

The substance has previously been prepared (m.p. 71-72°) by Tiffeneau and Lévy\(^\text{10}\) by the distillation of the oxide of (3,4-methylenedioxy-styryl)-benzene.

29. Oxide of phenyl-(3,4-methylenedioxy-6-nitro-styryl)-ketone (XVI; R_1 = CH_{3}O_{2}C_{6}H_{4}NO_{2}—).—Prepared as in (20) from (I; R_1 = CH_{3}O_{2}C_{6}H_{4}NO_{2}—) but the present mixture was shaken for a longer time with slight warming at intervals, and only acetone was used as the solvent. It was difficult to obtain the oxide pure, owing to the insolubility of both the chalcone and its oxide, and it was preferably prepared by the gradual addition at 0° of an alcoholic solution of sodium alcohoholate (3 g. Na in 50 c.c. alcohol) to a mixture of α-bromo-acetophenone (20 g.), 6-nitro-piperonal (20 g.) and alcohol (200 c.c.). The oxide (27 g.) separated and was recrystallised from acetone; pale yellow needles, m.p. 159-60°. (Found*: N, 4.7; C_{16}H_{11}O_{2}N requires N, 4.5%).

\(^{10}\) Compt. rend., 1930, 190, 1510.
30. *Phenyl-β-chloro-a-hydroxy-β-(3,4-methylene-dioxy-6-nitro-phenyl)-ethy1-ketone* (XXIII; $R_1 = CH_2O_2C_6H_4NO_2$).—The red solution obtained by passing dry hydrogen chloride into a suspension of the preceding oxide in acetic acid cooled in water, was diluted with water after saturation (10 minutes). The precipitated chlorohydric recrystallised from benzene-pet. ether (charcoal) in pale yellow crystals; m.p. 183–84°. (Found: Cl, 10.5; $C_{16}H_{15}O_4NCl$ requires Cl, 10.2%).

Similar treatment of (XVI; $R_1 = CH_4O_2C_6H_4$) with hydrogen chloride gave a pasty substance which was not investigated further.

31. *Acetyl derivative of the hydrazone of phenyl-(3,4-methylene-dioxy-6-nitro-styryl)-ketone* (XXIV; $R_1 = CH_2O_2C_6H_4NO_2$).—A solution of (I; $R_1 = CH_2O_2C_6H_4NO_2$) (2 g.) in acetic acid (25 c.c.) was heated at 100° with 50 per cent. hydrazine hydrate (3 c.c.) for ten minutes. The ppt. separating on cooling (2 g.) crystallised from acetone in white needles, m.p. 244–25°. (Found: † C, 60.9; H, 4.2; $C_{19}H_{14}O_2N_4$ requires C, 61.1; H, 4.3%). A solution of the substance in conc. sulphuric acid does not give a colour either with ferric chloride or sodium nitrite solution.

32. *Phenyl-hydrazone of phenyl-(3,4-methylene-dioxy-6-nitro-styryl)-ketone* (XXV; $R_1 = CH_2O_2C_6H_4NO_2$). A mixture of (I; $R_1 = CH_2O_2C_6H_4NO_2$) (5 g.) in acetic acid (50 c.c.) and phenyl-hydrazone (2 g.) was heated at 100° for ten minutes. The red ppt. (6.6 g.) obtained on addition of dil. hydrochloric acid recrystallised from alcohol-acetone in red needles, m.p. 159–60°. (Found: * N, 11.1; $C_{22}H_{19}O_2N_4$ requires N, 10.9%). The substance dissolved slowly in concentrated sulphuric acid with the formation of colour; and the resulting solution did not give a colour with ferric chloride.

33. 1,3-Diphenyl-5-(3′,4′-methy1ene-dioxy-6′-nitro-phenyl)-pyrazoline (XXVI; $R_1 = CH_2O_2C_6H_4NO_2$).—The preceding phenyl-hydrazone was boiled for an hour with acetic acid. The orange-yellow ppt. obtained on cooling the solution was recrystallised from benzene-petroleum ether, m.p. 203–204°. (Found: N, 11.1; $C_{22}H_{19}O_2N_4$ requires N, 10.9%). It dissolved at once in conc. sulphuric acid and gave Knorr’s pyrazoline reaction.

34. 1,3-Diphenyl-5-(3′,4′-methylene-dioxy-6′-nitro-phenyl)-pyrazole (XXVII; $R_1 = CH_2O_2C_6H_4NO_2$).—The preceding pyrazoline (0.5 g.) in alcohol (20 c.c.) was heated under reflux for one hour with silver nitrate (1 g.) in water (2–3 c.c.) and the liquid filtered from separated silver and undissolved matter. The filtrate on dilution with water gave a precipitate which crystallised from acetone-alcohol in yellow needles, m.p. 163–64°. (Found: * N, 10.8; C, 68.6; H, 4.0; $C_{22}H_{13}O_2N_3$ requires N, 10.9; C, 68.5; H, 3.9%).
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It was better prepared by treating the oxide (XVI; \( R_1 = \text{CH}_2\text{O}_2\text{C}_6\text{H}_4\text{NO}_2^- \)) in hot acetic acid, with phenyl-hydrazine. The resulting pale yellow solution was poured into dil. hydrochloric acid and the pale yellow ppt. recrystallised from acetone-alcohol in yellow needles, m.p. 163–64°.

Note.—Micro-analyses of the compounds marked (*) were carried out by Dr. J. N. Ray of Lahore, and those marked (†) were made in Germany by Dr. Fischer and by Dr. Schöfler.