The Reaction between Formaldehyde and Ethyl α-Formylphenylacetate.

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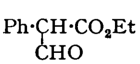
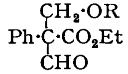
Re-examination has shown that the above reaction gives considerable amounts of 5-ethoxycarbonyl-4-hydroxy-5-phenyl-1 : 3-dioxan (IX; R = H).

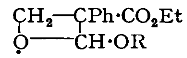
Investigation of the action of aqueous formaldehyde (35%) on ethyl α-formylphenylacetate (I) led Gault and Cogan (*Bull. Soc. chim.*, 1941, **8**, 140) to conclude that the product was substantially ethyl α-formyltropate (II; R = H) or the oxetan (III; R = H). They attributed the low carbon analyses to inadequate removal of moisture and the presence of some polyoxymethylenes, but based their structural conclusions mainly on the chemical behaviour of the product. Thus the product afforded a silver mirror in the cold, and gave a positive Schiff's test (aldehyde). It readily regenerated formaldehyde and ethyl α-formylphenylacetate, and gave a crystalline monoacetate which gave carbon and hydrogen analyses consistent with structure (II or III; R = Ac). In addition, hydrolysis with barium or sodium hydroxide afforded mixtures of tropic (IV), atropic (V), and phenylacetic acid.

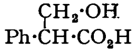

$Ph\cdot CH(CHO)\cdot CO_2Et$

(I)

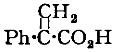

$Ph\cdot C(CH_2\cdot OR)(CHO)\cdot CO_2Et$

(II)

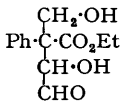

(III)


$Ph\cdot CH(CH_2\cdot OH)\cdot CO_2H$

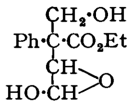
(IV)

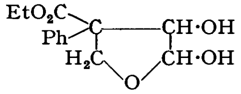

$Ph\cdot C(=CH_2)\cdot CO_2H$

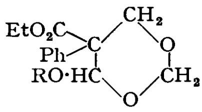
(V)

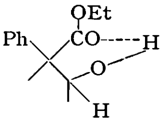

$Ph\cdot C(CH_2\cdot OH)(CO_2Et)\cdot CH(OH)\cdot CHO$

(VI)


(VII)


(VIII)


(IX)


(X)

In a reinvestigation in these laboratories the product afforded a crystalline fraction in yields of up to 50% (crude), analyses of which accorded with the empirical formula $C_{13}H_{16}O_5$, *i.e.*, (II; R = H) $+CH_2O$. This substance gave a silver mirror in the cold, readily lost formaldehyde at the melting point with reversion to (I), and afforded a crystalline monoacetate. Reduction could not be effected catalytically (palladium–charcoal or Adams catalyst) or with lithium aluminium hydride in tetrahydrofuran (reverse addition), and sodium borohydride gave boron complexes which could not be split. Hydrolysis with aqueous barium hydroxide gave tropic acid.

Structures (VI), (VII), and (VIII) were excluded by formation of only a monoacetate, because the resistance to reduction contraindicates an aldehyde group, and by infra-red spectral measurements. Structure (IX), however, accords with the facts. 4-Hydroxy-1 : 3-dioxans are known to arise by the action of aldehydes on aldols (Späth, Lorentz, and Freund, *Ber.*, 1944, **77**, 354; Späth, Lorentz, and Altman, *Ber.*, 1943, **76**, 513; Saunders and Murray, *J. Amer. Chem. Soc.*, 1944, **66**, 206) and to lose formaldehyde under mild conditions. The C–OH stretching frequency due to the hydroxyl group of ethyl tropate (cf. IV) (primary alcohol) appeared at 1040 cm.$^{-1}$ (see Table); the corresponding band in the new substance had been displaced to 1080 cm.$^{-1}$, which is compatible with a secondary hydroxyl group (Zeiss and Tsutsui, *ibid.*, 1953, **75**, 897). If, as this suggests, there is no primary alcoholic group present, the substance, m. p. 109°, must possess a cyclic structure. In the C=O stretching region in chloroform solutions the only band is that of the ester-carbonyl group at 1730 cm.$^{-1}$; there can thus be no free aldehyde group. It is interesting that in Nujol mull the ester-carbonyl frequency is displaced to 1715 cm.$^{-1}$; this might arise as a result of hydrogen bonding in the crystal lattice, which could be facilitated by a spatial arrangement such as (X). The wide hydroxyl band in the 3300-cm.$^{-1}$ region provides strong support for hydrogen bonding, which is further substantiated by the fact that ethyl α-formylphenylacetate and ethyl tropate have one large band at 1175 cm.$^{-1}$, whereas the new compound has three bands (1192, 1185, and 1164 cm.$^{-1}$). This type of resolution of the ester band has been attributed by Mazur and Spring (*J.*, 1954, 1224) to the presence of a relatively hindered ester group, such as might be present in our substance if there were hydrogen bonding with a neighbouring hydroxyl group.

Main infra-red absorption peaks (*cm.*$^{-1}$). (*In Nujol, except where stated.*)

	OH	CO			Ester		OH	
(IX; R = H)	*ca.* 3300	1715	—	1265	1192	—	1080	998
	—	—	—	1245	1185	—	—	980
	—	—	—	—	1164	1135	—	925
	—	—	—	—	—	—	—	902
	—	1730 (in $CHCl_3$)		—	—	—	—	—
(I)	—	1717	1400	1275	1175	1155	—	1020
	—	(1653 enol)	1380	—		—	—	—
	—	—	1340	—	—	—	—	—
Ethyl tropate (cf. IV)	—	1727	1595	1260	1175	—	1040	1025
	—	—	1490	—	—	—	—	—
	—	—	1453	—	—	—	—	—
	—	—	1380	—	—	—	—	—
	—	—	1346	—	—	—	—	—
Tetrahydro-3 : 4-dihydroxy-2 : 5-dimethoxyfuran	—	—	—	—	—	1130	1098	1020
	—	—	—	—	—	—	—	990
	—	—	—	—	—	—	—	980
	—	—	—	—	—	—	—	953
	—	—	—	—	—	—	—	940

Attempts to isolate a pure, oily product, free from the dioxan, were abandoned in view of the continued deposition of crystalline material.

EXPERIMENTAL

5-*Ethoxycarbonyl*-4-*hydroxy*-5-*phenyl*-1 : 3-*dioxan* (IX; R = H).—Ethyl α-formylphenylacetate (40·4 g.) in benzene (120 c.c.) was treated with formaldehyde solution (48 g.; 36—40%) and anhydrous potassium carbonate (1·2 g.) in water (2 c.c.). Benzene was omitted by Gault and Cogan in this preparation, but the course of the reaction was the same in both cases. The mixture was left overnight, and the benzene layer then separated, washed with a little water, and dried (Na_2SO_4). After removal of the solvent at 20—30° under reduced pressure, the residual oil partly crystallized. The crystals (20 g.; m. p. 89—90°) were collected and dried in a vacuum-desiccator (P_2O_5). These dissolved almost completely in dry ether. The solution was filtered and treated with light petroleum (b. p. 40—60°). The precipitated *dioxan* was recrystallized from the same solvent mixture, being obtained as colourless scales, m. p. 109° (Found: C, 61·9; H, 6·4. $C_{13}H_{16}O_5$ requires C, 61·9; H, 6·35%), insoluble in cold water and melting in hot water. It was soluble in ethanol, ether, sparingly soluble in benzene, insoluble in light petroleum. It gave no colour with ferric chloride solution, but reduced ammoniacal silver nitrate solution at room temperature, and Fehling's solution on warming. After having been boiled in aqueous alcohol for a few minutes, the product yielded a violet colour with ferric chloride, identical with that given by ethyl α-formylphenylacetate under analogous conditions. The solid, when heated at, or above, its m. p. evolved formaldehyde; the residual oil gave a violet colour with ferric chloride solution and was identified as ethyl α-formylphenylacetate, b. p. 95—96°/2 mm., n_D^{20} 1·5170.

The dioxan (0·1 g.) was dissolved in a solution of dimedone (0·3 g.) in magnesium-dried ethanol (4 c.c.). No crystallization occurred during several days. The clear solution was then diluted with water. The crystals which appeared overnight were the formaldehyde–dimedone complex, m. p. and mixed m. p. 188—189°.

Alkaline Hydrolysis.—The dioxan (IX; R = H) (2·5 g.) was stirred with barium hydroxide octahydrate (4 g) in water (10 c.c.), formaldehyde being liberated in a few minutes. After 2·5 hr. the solid was filtered off, suspended in water (3 c.c.), and acidified (Congo-red) The precipitated tropic acid, recrystallized from water, had m. p. and mixed m. p. 116—117° (0·79 g.).

Acetylation.—The dioxan (2·5 g.) was kept in dry pyridine (18 c.c.) with acetic anhydride (3 c.c.) for 15 hr. at 20°. The mixture was poured into ice-water, and the crude *acetate*, which slowly crystallized (2·3 g.), was recrystallized from light petroleum (b. p. 40—60°), affording colourless prisms, m. p. 76—77° (Found: C, 61·0; H, 6·0. $C_{15}H_{18}O_6$ requires C, 61·1; H, 6·1%).

The acetate (0·3 g.) was recovered unchanged after being kept in a solution of dimedone (0·4 g.) in magnesium-dried ethanol (4 c.c.) for several days.

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