

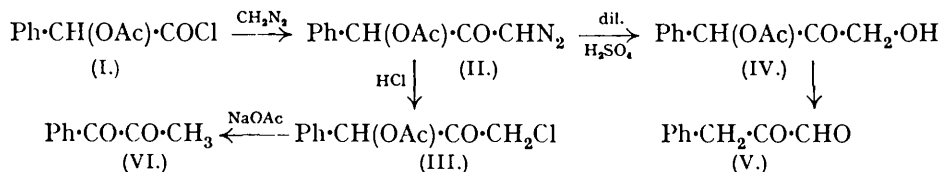
401. *The Acylation of Diazomethane. Part II. The Reaction of Diazomethane with O-Acetylmandelyl Chloride and Some Transformations of the Product.*

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The properties of the diazomethyl ketone from *O*-acetylmandelyl chloride and diazomethane are studied in relation to the use of compounds of this type as intermediates in the preparation of α -phenylglycerol derivatives from substituted mandelic acids. The diazo-ketone and hydrogen chloride give the related *chloro-ketone*, and this is changed either by keeping or by heating with methyl-alcoholic sodium acetate into acetylbenzoyl. Benzylglyoxal is formed when the diazo-ketone reacts with dilute sulphuric acid.

THE interest which is attached to arylglycerols as possible intermediates in phytochemical changes (cf. Robinson, *Nature*, 1936, **137**, 172) suggested an attempt to prepare compounds of this type from diazomethyl ketones, since these are readily accessible from the related

carboxylic acids (Bradley and Robinson, J., 1928, 1310, 1545; Bradley and Schwarzenbach, *ibid.*, p. 2904, now regarded as Part I). *O*-Acetylmandelyl chloride (I), added to ethereal diazomethane (at least two molecular proportions), gave an oily diazomethyl ketone (II), which with dry hydrogen chloride afforded the *chloro-ketone* (III). The diazomethyl ketone did not react easily with acetic acid, but dilute sulphuric acid decomposed it, forming a product which reduced Fehling's solution in the cold. The only crystalline compound isolated from the reaction product was benzylglyoxal, m. p. 119—120° (V) (Dakin and Dudley, *J. Biol. Chem.*, 1914, 18, 42, state m. p. 120—122°, softening at 115°), further characterised by the preparation of a *dioxime*, m. p. 163°. Apparently the glyoxal derivative is formed by hydrolysis of *O*-acetylphenyldihydroxyacetone (IV) and rearrangement of the product. The result recalls the dehydration of dihydroxyacetone to methylglyoxal in acid solution (Pinkus, *Ber.*, 1898, 31, 36). No compound which reduced Fehling's solution could be obtained when the chloro-ketone was heated with water alone or in presence of magnesium carbonate. Heating with methyl-alcoholic sodium acetate gave, not the expected acetoxy-ketone, but acetylbenzoyl (VI), a dioxime of which was compared directly with an authentic specimen prepared by the method of Borsche (*Ber.*, 1907, 40, 737). Except when carefully purified, samples of the chloro-ketone decomposed on keeping with liberation of hydrogen chloride and formation of acetylbenzoyl.



EXPERIMENTAL.

Chloromethyl α -Acetoxybenzyl Ketone (III).—A solution of diazomethane (8.8 g.) in ether (1100 c.c.) was added in a thin stream to a well-stirred solution of freshly prepared acetylmandelyl chloride (35.5 g.) in dry ether (100 c.c.). Nitrogen was liberated. After keeping overnight, dry hydrogen chloride was admitted until no further evolution of nitrogen occurred and the solution had become almost colourless. It was washed with water, sodium bicarbonate solution, and finally with dilute acetic acid. After drying and removal of the solvent under reduced pressure the residue solidified to a white crystalline mass (36.5 g.). Recrystallisation from light petroleum gave colourless prisms, m. p. 57° (Found: C, 58.2; H, 4.9; Cl, 15.6. $\text{C}_{11}\text{H}_{11}\text{O}_3\text{Cl}$ requires C, 58.3; H, 4.9; Cl, 15.7%). The *chloro-ketone* reduced Fehling's solution in the cold.

Acetylbenzoyl (VI).—A solution of the chloro-ketone (9.2 g.) in methyl alcohol (50 c.c.) was added to anhydrous sodium acetate (12 g.) and glacial acetic acid (2.4 c.c.) in methyl alcohol (100 c.c.). After 3 hours' boiling, the precipitated sodium chloride was removed; no further precipitation occurred when the solution was boiled 2 hours longer. Most of the alcohol was distilled off, and the residue dissolved in ether and water. The ethereal solution, washed with aqueous sodium bicarbonate and dried, gave on evaporation of the solvent a yellow oil (10 g.), from which benzoic acid separated on keeping. A portion of the oil (0.5 g.) was warmed with sodium acetate (1 g.) and hydroxylamine hydrochloride (1 g.) in aqueous alcoholic solution at 45° during 6 hours and then at 80° for 12 hours longer. Water then precipitated a white crystalline derivative (0.3 g.), m. p. 236—237° after recrystallisation from alcohol (Found: C, 60.3; H, 5.6; N, 15.9. Calc. for $\text{C}_9\text{H}_9\text{O}_2\text{N}_2$: C, 60.7; H, 5.6; N, 15.7%). A red nickel complex was precipitated when an alcoholic solution of the derivative was added to aqueous nickel sulphate containing a little ammonia. No depression of m. p. was observed when the compound was mixed with a sample of acetylbenzoyldioxime, m. p. 235—236°, prepared by Borsche's method (*loc. cit.*).

When the chloro-ketone (1 g.) was heated with water (10 c.c.) and magnesium carbonate (0.5 g.) at 100° during 24 hours, a reddish oil was obtained which did not reduce Fehling's solution. Estimation of the extent to which hydrolysis had proceeded gave the following results: Found in solution: HCl, 0.12 g.; $\text{CH}_3\cdot\text{CO}_2\text{H}$, 0.24 g. Calc. for complete hydrolysis: HCl, 0.16 g.; $\text{CH}_3\cdot\text{CO}_2\text{H}$, 0.265 g.

Spontaneous Decomposition of the Chloro-ketone.—Hydrogen chloride was liberated and a

brown oil with reducing properties was obtained when a sample of the chloro-ketone (m. p. 55—56°) was kept during 12 months in a closed tube. Treatment of a portion of the oil (1.5 g.) with sodium acetate and hydroxylamine hydrochloride gave almost pure acetylbenzoyldioxime (1.75 g., m. p. 232°). Recrystallisation of the dioxime from dilute alcohol gave flat slender prisms, m. p. 236—237°, not depressed after mixing with an authentic specimen prepared by the method of Borsche (*loc. cit.*).

Benzylglyoxal (V).—*O*-Acetylmandelyl chloride (17.5 g.) ("Organic Syntheses," 4, 1), dissolved in dry ether (100 c.c.), was added through a capillary tube during 2 hours to a stirred, ice-cold solution of diazomethane (9.2 g.) in ether (850 c.c.). Nitrogen was evolved freely. After keeping overnight a portion of the solution was evaporated in a current of air; a yellow oil remained which could not be obtained crystalline. The remainder of the solution was concentrated by the same means to 500 c.c., and then shaken with a mixture of concentrated sulphuric acid (25 g.) and water (60 c.c.). Evolution of nitrogen occurred, greatly facilitated by the addition of porous tile. After a few hours, reaction had ceased and the ethereal solution had become only pale yellow, whilst the colour of the aqueous layer had become deep yellow.

The ethereal layer was separated, washed with sodium bicarbonate solution and water, and dried (sodium sulphate). When the solvent was allowed to evaporate, a viscous yellow oil remained. A portion (2 g.) was dissolved in alcohol, and alcoholic 2 : 4-dinitrophenylhydrazine added until a precipitate no longer formed. The hydrazone was boiled out with glacial acetic acid (25 c.c.), and the undissolved material crystallised from the same solvent. Slender orange-red prisms were obtained (Found : C, 54.6; H, 3.6. Calc. for $C_{13}H_{10}O_4N_4$: C, 54.5; H, 3.6%), m. p. 234°, not depressed by benzaldehyde-2 : 4-dinitrophenylhydrazone (m. p. 235°).

The aqueous acid layer was diluted with an equal volume of water. After 4—5 weeks long colourless needles and a little reddish-brown oil had separated from solution; the crystals were collected, m. p. 113—115°. After an equal time a further crop of crystals, m. p. 112—115°, was obtained. The total yield was 1.5 g. Repeated crystallisation from benzene gave pure benzylglyoxal, m. p. 119—120° (Found : C, 72.7; H, 5.4. Calc. for $C_9H_8O_2$: C, 72.9; H, 5.4%).

Benzylglyoxime.—0.1 G. of the compound, m. p. 119—120°, dissolved in alcohol (2 c.c.), was warmed at 45° during 12 hours and then at 80° during 6 hours with a concentrated aqueous solution of sodium acetate (0.1 g.) and hydroxylamine hydrochloride (0.1 g.) Water was then added, and the crystalline *product* recrystallised from aqueous alcohol; glistening white leaflets (0.07 g.) were obtained, m. p. 163° (Found : C, 60.7; H, 5.6; N, 15.5. $C_9H_{10}O_2N_2$ requires C, 60.7; H, 5.6; N, 15.7%).

Attempts to prepare α -phenylglycerol by reducing either the ether-soluble oil or the water-soluble product were unsuccessful.

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