507. *The Action of Organo-lithium Compounds on Some Esters and Anhydrides of Dicarboxylic Acids.*

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The action of organo-lithium compounds on a number of esters and anhydrides of dicarboxylic acids which do not easily react with organomagnesium compounds has been investigated. Phenyl-lithium reacts satisfactorily with ethyl mesoxalate, methylmalonate, and ethylmalonate, and phthalic anhydride, but not with succinic anhydride, thus demonstrating the superiority of organo-lithium compounds over the usual Grignard reagent. Some glycols not readily prepared by other methods have been synthesised.

Despite the fact that organomagnesium halides react readily with numerous compounds containing more than one carbonyl group (giving as final products *sec.*- and *tert.*-glycols), cases are known where one or more of the carbonyl groups fail to react. Thus, whereas Valeur (*Compt. rend.*, 1901, **132**, 833) found that ethyl oxalate and methylmagnesium iodide readily gave 2 : 3-dimethylbutane-2 : 3-diol, Lamaire (*Bull. Acad. Roy. Belg.*, 1909, 83) failed to obtain the corresponding pentamethyl glycerol by use of ethyl mesoxalate. A similar study of the action of ethylmagnesium bromide gave a mixture of four products, one of which appeared to be 3 : 5-diethyl-3 : 5-dihydroxyheptan-4-one. Lamaire attributed the failure of the medial carbonyl group to react, to the influence of the adjacent groups.

In marked contrast phenyl-lithium (5 mols.) reacts easily and satisfactorily with ethyl mesoxalate (1 mol.), and pentaphenyl glycerol is obtained on hydrolysis.

Organo-metallic derivatives do not as a rule readily give glycols from malonic ester (or its substituted derivatives). According to Dilthey and Last (*Ber.*, 1909, **42**, 2639) the reaction does not proceed to completion, but gives the intermediate hydroxy-ketone : *e.g.*, phenylmagnesium bromide gave β-hydroxy-ββ-diphenylpropiophenone from ethyl malonate. Wittig and Obermann (*Ber.*, 1934, **67**, 2053) obtained from the intermediate compound the desired glycol, *viz.*, 1 : 1 : 3 : 3-tetraphenylpropane-1 : 3-diol by the use of phenyl-lithium at −80°. The action of Grignard reagents on substituted derivatives of ethyl malonate has been studied by Kalischiev (*J. Russ. Phys. Chem. Soc.*, 1914, **46**, 427), who concluded that the reaction $CR'R''(CO_2Et)_2 + 4MgR'''X$ proceeds to completion only when R′, R″, and R‴ are methyl. This work has now been extended to derivatives of malonic ester of the type $Alk{\cdot}CH(CO_2Et)_2$. The reactions were conducted at −80°. Ethyl methylmalonate (1 mol.) reacts with phenyl-lithium (4 mols.) to give in small yield 2-methyl-1 : 1 : 2 : 3 : 3-pentaphenylpropane-1 : 3-diol, the hydrogen atom attached to the medial carbon atom being replaced by a phenyl group. On the other hand, ethyl ethylmalonate does not react to completion; it gave a large yield of the intermediate β-hydroxy-αββ-triphenylpropiophenone (in this case the alkyl group, and not the hydrogen atom, was replaced by phenyl).

In general, anhydrides of dicarboxylic acids do not readily react with organometallic compounds. Thus Houben and Hann (*Ber.*, 1908, **41**, 1580) found that succinic acid did not react readily with a Grignard reagent. These workers found that succinic anhydride (1 mol.) and phenylmagnesium bromide (6 mols.) in boiling toluene react abnormally, giving in poor yield 1 : 1 : 4 : 4-tetraphenylbutane-1 : 4-diol, *i.e.*, the product normally given by succinic ester. We have found that succinic anhydride and phenyl-lithium in ether or dioxan at −80° fail to give a glycol; the reaction afforded a small yield of diphenyl, and a large amount of a thick viscous oil.

The nature of the reaction between phthalic anhydride and a Grignard reagent is controversial. Bauer (*Ber.*, 1904, **37**, 135) obtained dialkylphthalides by use of alkylmagnesium bromides, and claims to have obtained diphenylphthalide (m. p. 115°) but he did not identify this compound by analysis. On the other hand, Howell (*J. Amer. Chem. Soc.*, 1920, **42**, 2533) claims to have obtained 5-hydroxy-2 : 2 : 5-triphenylbenzofuran by the action of phenylmagnesium bromide. Wittig and Leo (*Ber.*, 1931, **64**, 2395) state phenyl-lithium and phthalic anhydride afford only a resinous compound and triphenylcarbinol. It has now been found that phenyl-lithium gives diphenylphthalide (m. p. 115°). It appears that only one of the CO groups of the anhydride behaves as a true carbonyl group. As phthalic anhydride is sparingly soluble in ether, anhydrous dioxan was used as a solvent. As in the case of succinic anhydride, a large amount of viscous by-product was obtained. This oil has been repeatedly noticed by other workers (cf. Howell, Houben *et al.*, *locc. cit.*), and all efforts to crystallise the compound in its presence fail. However, when the mixture is distilled under reduced pressure, the phthalide distils and may be obtained as a white crystalline compound on recrystallisation from alcohol.

The ethyl mesoxalate used for this work was prepared by the oxidation of ethyl malonate. The action of selenium oxide (Muller, *Ber.*, 1933, **66**, 1668) proved unsatisfactory, whereas an excellent yield was obtained by use of nitrogen oxides (Bouveault and Wohl, *Compt. rend.*, 1903, **137**, 196).

EXPERIMENTAL.

Certain analyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.

Reaction of Ethyl Mesoxalate with Phenyl-lithium.—Metallic lithium (4 g.) in a three-necked flask fitted with a mechanical stirrer, reflux condenser, dropping funnel, nitrogen gas inlet, and mercury trap, was covered with anhydrous ether (100 c.c.). Bromobenzene (45 g.) was added and the reaction allowed to proceed for 30 minutes. The solution was allowed to cool, then ethyl mesoxalate (10 g.) in anhydrous ether (100 c.c.) was added slowly. A vigorous reaction ensued, and on its completion the flask was heated gently for 30 minutes. After cooling the product was hydrolysed by ice–water (100 g.). The ethereal layer was separated and the aqueous layer extracted with ether. Ether was removed from the combined ethereal fractions, finally under reduced pressure. The brown semi-solid viscous residue was dissolved in methyl alcohol. Pentaphenyl glycerol was obtained as a white crystalline product after a number of recrystallisations, and had m. p. 163° (yield, 5 g.) (Found : C, 83·2; H, 5·9. Calc. for $C_{33}H_{28}O_3$: C, 83·9; H, 5·9%). It was identified further by the following reaction. The product formed from it (0·3 g.) by acetyl chloride and dimethylaniline in the cold during 5 minutes was treated with a solution of hydroxylamine and the mixture made alkaline with alcoholic potassium hydroxide, heated, and cooled. A reddish-wine colour was produced on acidification and addition of ferric chloride solution.

Reaction of Ethyl Methylmalonate and Ethylmalonate with Phenyl-lithium.—Bromobenzene (62·8 g.), covered with ether (100 c.c.), was treated with lithium (5·6 g.) under nitrogen. On completion of the reaction, an additional 100 c.c. of ether were added, and the solution allowed to cool. The reaction vessel was immersed in a bath containing light petroleum to which solid carbon dioxide was added until the temperature had attained *ca.* −80°. Ethyl methylmalonate (Conrad, *Annalen*, 1870, **204**, 134) (17·4 g.) in ether (100 c.c.) was added gradually. A vigorous reaction ensued, controlled by further addition of solid carbon dioxide to the bath. The product was hydrolysed by ice-water, the ethereal layer separated, and the ether removed by distillation, finally under reduced pressure. The residue was dissolved in alcohol and decolorised with animal charcoal. Repeated crystallisation gave 2-methyl-1 : 1 : 2 : 3 : 3-pentaphenylpropane-1 : 3-diol (2·5 g.), m. p. 155—157° (Found : C, 87·0; H, 6·2. Calc. for $C_{34}H_{30}O_2$: C, 86·8; H, 6·4%).

Reaction of ethyl ethylmalonate (18·8 g. in 100 c.c. of ether) was much less vigorous. The residue obtained after hydrolysis, etc., on purification as above gave β-hydroxy-αββ-triphenylpropiophenone, m. p. 156·5° (10·0 g.) (Found : C, 85·8; H, 5·9. Calc. for $C_{23}H_{22}O_2$: C, 85·4; H, 5·6%).

Reaction of Succinic Anhydride and Phthalic Anhydride with Phenyl-lithium.—A suspension of succinic anhydride (20 g.) in ether (250 c.c.) was added gradually to a warm solution of phenyl-lithium, with gentle heating, and then refluxed for 3 hours. The cooled mixture was then hydrolysed with ice–water (100 c.c.). The ethereal layer was separated and the aqueous layer extracted with ether. The combined extracts were freed from ether, and the brown residue heated under reduced pressure. Crude diphenyl sublimed at 105°/8 mm. It was dissolved in alcohol and was purified by recrystallisation (leaflets, m. p. 67°) (Found : C, 93·1; H, 6·7. Calc. for $C_{12}H_{10}$: C, 93·5; H, 6·5%).

The experiment was repeated with a solution of succinic anhydride (20 g.) in dioxan (150 c.c.) at room temperature and at −80°. In both experiments the only product obtained was a small yield of diphenyl.

Similar experiments were conducted with (*a*) a suspension of phthalic anhydride (20 g.) in ether (300 c.c.) and (*b*) a solution of phthalic anhydride (20 g.) in dioxan (150 c.c.), with gentle heating, and the reactions were completed at the b. p. during 3 hours. The ethereal suspension gave only an unworkable yellowish viscid oil. In contrast, after distillation, at 200°/4 mm., of the hydrolysis product from the dioxan solution a greenish-yellow fluorescent gum was obtained, which readily crystallised from alcohol, to give αα-diphenylphthalide, m. p. 115° (5·0 g.) (Found: C, 82·9; H, 5·15. Calc. for $C_{20}H_{14}O_2$: C, 83·9; H, 4·9%). The m. p. was undepressed when the product was mixed with a specimen prepared by Copisarow's method (*J.*, 1917, **111**, 18).

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