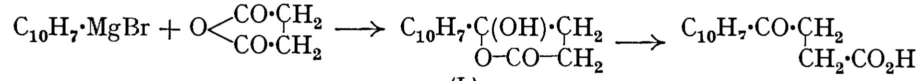
325. *The Reaction of Grignard Reagents with Some Succinic Anhydrides.*

By CHAIM WEIZMANN, (MRS.) OTTILIE BLUM-BERGMANN, and FELIX BERGMANN.

CERTAIN phenanthrene derivatives are of interest owing to their relation to the sterols, bile acids, and sexual hormones. Haworth (J., 1932, **1125**) developed a synthesis of such compounds by condensing naphthalene with succinic anhydride in the presence of aluminium chloride, but this led to the formation of both α- and β-naphthoylpropionic acids, which had to be separated. It was thought that succinic anhydride might react like phthalic anhydride (Weizmann and Pickles, P., 1904, **20**, 201; see also preceding paper) with α- or β-naphthylmagnesium bromide to give a homogeneous product:



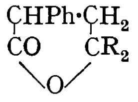
$$C_{10}H_7\cdot MgBr + O\begin{array}{l}\diagup CO\cdot CH_2\\ \diagdown CO\cdot CH_2\end{array} \longrightarrow \begin{array}{l}C_{10}H_7\cdot C(OH)\cdot CH_2\\ \qquad O-CO-CH_2\end{array} \longrightarrow \begin{array}{l}C_{10}H_7\cdot CO\cdot CH_2\\ \qquad\qquad CH_2\cdot CO_2H\end{array}$$

(I.)

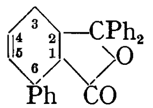
Succinic anhydride is known to react with Grignard compounds to give tetra-alkylbutanediols, but the further reaction of the primary product is easily prevented by addition of the Grignard solution to the ethereal suspension of succinic anhydride. β-(α-Naphthoyl)-propionic acid and the β-naphthoyl acid were isolated and identified.

In view of the facts reported in the foregoing paper it was of interest to determine whether the course of the reaction is affected by substituents. We accordingly used phenylsuccinic and 3-phenyl-1 : 2 : 3 : 6-tetrahydrophthalic anhydride, but in neither case could a crystalline keto-acid be isolated. The interaction between the former anhydride and phenyl- and α-naphthyl-magnesium bromide and between the latter one and phenylmagnesium bromide yielded respectively the *lactones* of *γ-hydroxy-αγγ-triphenyl-* (II;

(II.)



$$\begin{array}{c}CHPh\cdot CH_2\\ CO\qquad CR_2\\ \diagdown O \diagup\end{array}$$



(III.)

R = Ph) and *γ-hydroxy-α-phenyl-γγ-(α-naphthyl)-*n*-butyric acid* (II; R = $C_{10}H_7$) and *2-diphenylmethylol-6-phenyl-*1 : 2 : 3: *6-tetrahydrobenzoic acid* (III). Since the anhydrides are unsymmetrical, each pair of the above components could lead to two isomerides, although only one has been isolated in each case. For reasons of "steric hindrance," it seems more likely that, in the above reactions, exclusively the less substituted half of the molecules is attacked by the Grignard reagents, as in the case of Friedel–Crafts reactions with methylsuccinic anhydride (Oppenheim, *Ber.*, 1901, **34**, 4228; Haworth, J., 1932, 1125, 1784).

While the work described in this paper was proceeding, Komppa and Rohrmann (*Annalen*, 1934, **509**, 259) published results on a similar subject (see preceding paper).

EXPERIMENTAL.

A solution prepared from magnesium turnings (2·7 g.) and α-bromonaphthalene (22·8 g.) was added drop by drop to a boiling suspension of finely powdered succinic anhydride (10 g.) in anhydrous ether (200 c.c.). The white amorphous precipitate became spontaneously transformed into a yellow crystalline powder after a few minutes; the mixture was heated on the water-bath for 2 hrs., then decomposed with ice and dilute sulphuric acid, and the ethereal layer was extracted with dilute caustic soda solution, and the extract acidified; β-(α-naphthoyl)-propionic acid was precipitated as an oil, which was dissolved in ether, the ether evaporated, and the residue triturated with ethyl acetate; m. p. and mixed m. p. with a pure sample 133°; yield 2·5 g.

β-(β-Naphthoyl)propionic acid (4 g.), similarly prepared, was recrystallised from glacial acetic acid, and had m. p. and mixed m. p. 170°. The ethereal layer contained naphthalene and some di-β-naphthyl, which was purified by recrystallisation from butyl alcohol, affording leaflets exhibiting a remarkable blue fluorescence; m. p. 184—185° (lit., 187—188°, 180—181°, 181°).

Phenylsuccinic anhydride was prepared from the acid ("Organic Syntheses," Coll. Vol. I, p. 440) by reaction with 3 times its weight of boiling acetyl chloride; after 6 hrs., the excess of acetyl chloride was distilled off, and the residue fractionated; b. p. 203°/34 mm. (yield 80%). 3-Phenyl-1 : 2 : 3 : 6-tetrahydrophthalic anhydride, obtained according to Diels and Alder (*Ber.*, 1929, **62**, 2081) from maleic anhydride (12·5 g.; Master and Ahmann, *J. Amer. Chem. Soc.*, 1928, **50**, 145) and *cis*-1-phenylbutadiene (17 g.; Muskat and Herrman, *ibid.*, 1931, **53**, 252) in benzene (20 c.c.) on the water-bath (15 mins.), crystallised from toluene (50 c.c.) in needles (14·5 g.), m. p. 120°.

A solution prepared from magnesium (1·25 g.) and bromobenzene (5·5 c.c.) was added to phenylsuccinic anhydride (8·7 g.) in ether (15 c.c.), and the reaction mixture worked up as before. The product lactonised, and after trituration with methyl alcohol was obtained from 80% acetic acid as needles (1·2 g.), m. p. 162° (Found : C, 84·0, 84·3; H, 5·0, 5·9. $C_{22}H_{18}O_2$ requires C, 84·0; H, 5·7%). A second crop (1·0 g.) of the *lactone* (II; R = Ph) was isolated from the ethereal layer after the extraction.

The reaction product from phenylsuccinic anhydride (17·6 g.), magnesium (2·5 g.), and α-bromonaphthalene (21 g.) was separated into a neutral and an acid part. The former crystallised on treatment with methyl alcohol, and the *lactone* (II; R = $C_{10}H_7$) separated from amyl alcohol or from propyl alcohol–acetone in clusters of needles, m. p. 211° (Found : C, 86·8; H, 5·4. $C_{30}H_{22}O_2$ requires C, 87·0; H, 5·3%). The latter was a brown syrup, which would not crystallise; it was reduced with amalgamated zinc wool and concentrated hydrochloric acid, but the reduction product, too, was an oil, which was purified by repeated distillation in a vacuum, b. p. 265—270°/1·4 mm.

The mother-liquor of the crude syrup, on standing, gave crystals (2 g.) of phenylsuccinic acid, m. p. 166° (Found : C, 61·5; H, 5·2. Calc. for $C_{10}H_{10}O_4$: C, 61·8; H, 5·1%).

The acid products of the interaction between phenylmagnesium bromide (0·85 g. magnesium; 3·5 c.c. bromobenzene) and 3-phenyl-1 : 2 : 3 : 6-tetrahydrophthalic anhydride (7·6 g.) were amorphous and could not be purified, even after treatment with amalgamated zinc. The neutral product, the *lactone* (III), when recrystallised from propyl alcohol–acetone, formed needles, m. p. 227° (Found : C, 85·2; H, 6·0. $C_{26}H_{22}O_2$ requires C, 85·2; H, 6·0%).

THE DANIEL SIEFF RESEARCH INSTITUTE, REHOVOTH, PALESTINE. [*Received, March 6th*, 1935.]