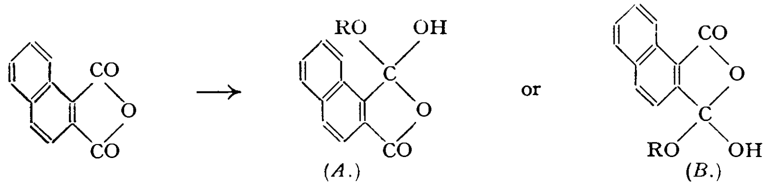
229. *The Action of Alcohol on Phthalic Anhydrides.*

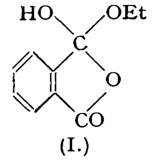
By YEHUDA HIRSHBERG, DAVID LAVIE, and ERNST D. BERGMANN.

By an analysis of the ultra-violet absorption spectra of the substances concerned and of related compounds of unambiguous structure, it is shown that phthalic anhydride, hemipinic anhydride, and naphthalenedicarboxylic anhydrides react with alcohols first by addition to the double bond of one of the CO groups. The hemiacetal-like substances thus formed isomerise gradually to the corresponding monoesters. 4 : 5-Dimethoxyphthalic anhydride forms the monoester almost instantaneously.

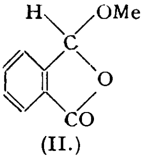
HIRSHBERG AND JONES (*Canad. J. Res.*, 1949, *B*, **27**, 437) have observed that the ultra-violet absorption spectra of naphthalene-1 : 2- and -2 : 3-dicarboxylic anhydride in alcoholic solution undergo a slow change, until eventually a stationary state is reached which differs significantly from the spectra of the same substances in non-alcoholic solvents. The change could be ascribed to a formation of hemi-esters and, indeed, Siegel and Moran (*J. Amer. Chem. Soc.*, 1947, **69**, 1457) have reported that this reaction is instantaneous. However, the validity of Siegel and Moran's interpretation has been refuted by Anderson and Kenyon (*ibid.*, 1948, **70**, 3952) and by Lavine and Herkness (*ibid.*, p. 3951). Hirshberg and Jones have already suggested an alternative explanation of the effect, *viz.*, the addition of alcohol to one of the carbonyl groups, in a manner known for aldehydes and ketones :



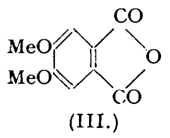
(*A*.) (*B*.)



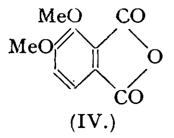
(I.)



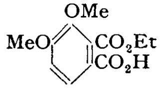
(II.)



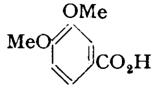
(III.)



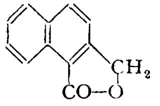
(IV.)



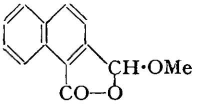
(V.)



(VI.)



(VII.)

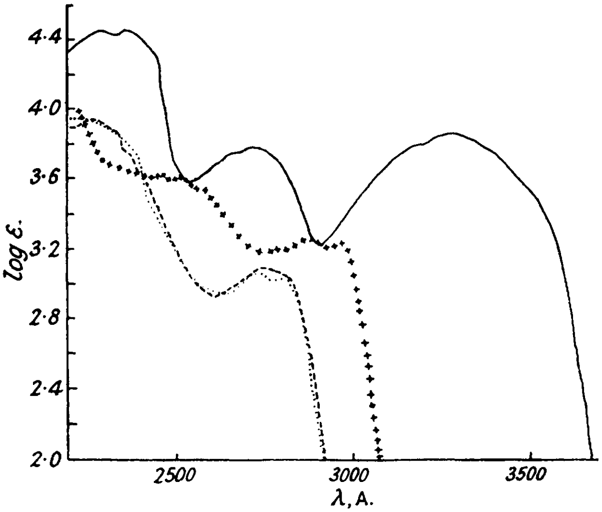


(VIII.)

Indeed, there are certain reactions in which the carbonyl group of phthalic anhydride exhibits a reactivity resembling that of aldehydes, *e.g.*, condensation with acetic anhydride or phenylacetic acid (Gabriel, *Ber.*, 1881, **14**, 919; 1884, **17**, 2521; 1885, **18**, 3470; Michael and Gabriel, *Ber.*, 1877, **10**, 391 ; Gabriel and Michael, *ibid.*, p. 1552 ; 1878, **11**, 1007, 1017).

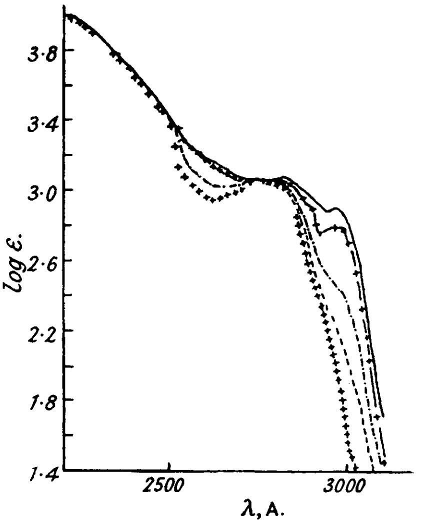
It appeared worth while to study the effect in a few simpler cases. Phthalic anhydride shows, immediately after dissolution, a different spectrum in dioxan and ethyl alcohol (Fig. 1); subsequently, the spectrum of the alcoholic solution slowly undergoes some very minor changes (Fig. 2) which do not cause any shift in the location or intensity of the absorption maximum at 2750 A. In view of the fact that Anderson and Kenyon (*loc. cit.*) have isolated only unchanged phthalic anhydride from its alcoholic solution after one hour (at room temperature), it may be assumed that phthalic anhydride forms a " hemiacetal " (I) of the above type which gradually isomerizes to the monoester. This assumption is supported by the observation that 3-methoxyphthalide (II) has—in both alcohol and dioxan—a spectrum which closely resembles that of phthalic anhydride in alcohol (Fig. 3). It is likely that the difference in

FIG. 1.



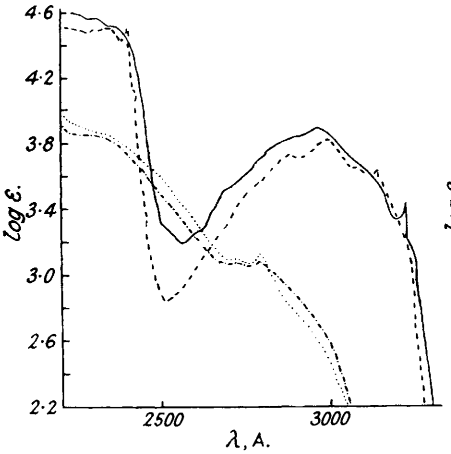
Phthalic anhydride in dioxan (+ + +) *and ethyl alcohol* (. . . .). *Ethyl phthalate in ethyl alcohol* (– – – –). *Hemipinic anhydride* (IV) *in* isooctane (———).

FIG. 2.



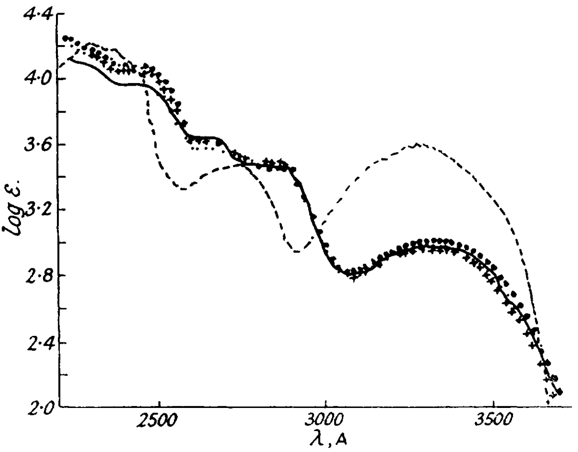
Alcoholic solution of phthalic anhydride: ——— *fresh*, — + — + *after* 80 *mins.*, — · — · *after* 3 *hrs.*, — — — *after* 5 *hrs.*, + + + *after* 24 *hrs.*

FIG. 3.



a-*Methoxyphthalide* (II) *in dioxan* (. . . .) *and ethyl alcohol* (— · — ·). *Naphthalide* (VII) *in* isooctane (———). *Methoxynaphthalide* (VIII) *in* isooctane.

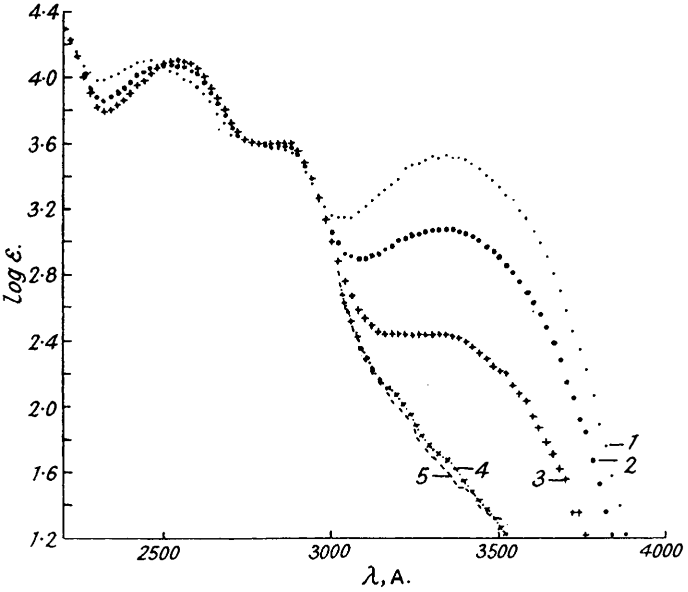
FIG. 4.



Metahemipinic anhydride (III) *in* isooctane (– – – –) *and ethyl alcohol* (——— *fresh*; •••• *after* 2 *hrs.*; + + + + *after* 24 *hrs.*; . . . . *after* 20 *days*).

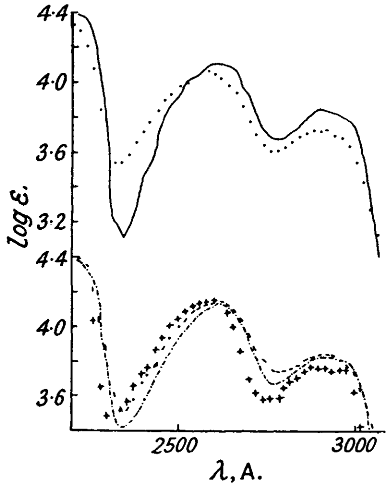
structure between (I) and (II), *viz.*, the absence of a hydroxyl group at the saturated α-carbon atom in (II), would not have a far-reaching influence on the spectrum. Further, any ester of phthalic acid, as the absorbing system is not very different from that of phthalic anhydride, should show approximately the same ultra-violet absorption curve. As Fig. 1 shows, for ethyl phthalate, this is, indeed, the case.

FIG. 5.



Hemipinic anhydride (IV) *in alcohol* : 1, *fresh* ; 2, *after* 90 *mins.* ; 3, *after* 4 *hrs.* ; 4, *after* 24 *hrs.* ; 5, *after* 71 *hrs.*

FIG. 6.



Upper part : 3 : 4-*dimethoxybenzoic acid* (VI) *in dioxan* (————) *and ethyl alcohol* (. . . .).
Lower part : *its methyl ester in dioxan* (— · — ·), iso*octane* (+ + + +), *and ethyl alcohol* (- - - -).

In the case also of metahemipinic (4 : 5-dimethoxyphthalic) anhydride (III), the fresh solution in alcohol shows a marked difference from that in *iso*octane. However, during twenty days, no further change takes place in the spectrum (Fig. 4). This could be interpreted to mean that the monoester is formed almost instantaneously and, indeed, working-up of an alcoholic solution after only a short time yields the ethyl hydrogen ester of m. p. 127° (Rossin, *Monatsh.*, 1891, **12**, 489). The nature of this product has also been established by titration (at 0°) and determination of the saponification number.

On the other hand, hemipinic anhydride (IV) shows the same behaviour as phthalic anhydride, only in a more pronounced manner. The initial difference between its solutions in *iso*octane and ethyl alcohol is greater (Fig. 1), and in the subsequent slow change in the spectrum of the alcoholic solution (Fig. 5) the maximum at 3280 A. disappears completely. It is not unlikely that the ester group of the product (V) (Wegscheider, *Monatsh.*, 1895, **16**, 141; Kahn, *Ber.*, 1903, **36**, 2533) is so completely hindered that it does not contribute to the absorbing system. The ester (V) should, therefore, have a spectrum similar to that of 3 : 4-dimethoxybenzoic acid (VI), and its methyl ester, and this is the case, as Fig. 6 shows (compare the spectrum of vanillic acid, Pearl, *J. Amer. Chem. Soc.*, 1948, **71**, 2331).

In order to complete Hirshberg and Jones's studies in the naphthalene-1 : 2-dicarboxylic anhydride series, the naphthalide (VII) and its methoxy-derivative (VIII) were prepared. The spectrum of the latter (Fig. 3) [which, of course, is substantially identical with that of (VII)] has definite similarity to that of an alcoholic solution of naphthalene-1 : 2-dicarboxylic anhydride, especially if one takes into account that (VII) is analogous to (*B*), whilst the anhydride may, at least partly, also add alcohol to form an adduct of type (*A*).

For the preparation of (VII), the following method was used: 2-methylnaphthalene-1-carboxylic acid was prepared according to Mayer and Sieglitz (*Ber.*, 1922, **55**, 1851) and Shoesmith and Rubli (*J.*, 1927, 3102), and its methyl ester was brominated in the 2-methyl group by means of *N*-bromosuccinimide (Newman and Kosak, *J. Org. Chem.*, 1949, **14**, 375; Buu-Hoï, *Annalen*, 1944, **556**, 1; Schmid and Karrer, *Helv. Chim. Acta*, 1946, **29**, 573). At 150°, the bromo-compound lost methyl bromide (Mayer, Schaefer, and Rosenbach, *Chem. Zentr.*, 1929, II, 3009) and gave (VII). As a model experiment with phthalide showed, the methylene group in (VII) can be brominated with *N*-bromosuccinimide; in the product, the bromine atom was replaced by methoxyl, on heating with methanol.

EXPERIMENTAL.

3-*Methoxyphthalide* (II).—Phthalide was brominated at 140°, according to Racine (*Annalen*, 1887, **239**, 79); the same 3-bromophthalide was obtained in excellent yield when phthalide (2·0 g.) was refluxed with *N*-bromosuccinimide (3·0 g.) in carbon tetrachloride (30 c.c.) for 2 hours and the filtered solution concentrated. From methyl*cyclo*hexane, leaflets, m. p. 81°, were obtained.

3-Bromophthalide (15 g.) was refluxed for 6 hours with five times its weight of methanol. The product which remained after removal of the solvent was purified by distillation *in vacuo* and had b. p. 149—151°/20 mm, m. p. 44° (yield, 9 g., 79%) (Racine, *loc. cit.*).

Methoxynaphthalide (3-*Methoxy*-6 : 7-*benzophthalide*) (VIII).—2-*Methylnaphthalene*-1-*carboxylic acid.* A solution of 1-bromo-2-methylnaphthalene (100 g.; b. p. 168—170°/25 mm.) in anhydrous ether (300 c.c.) was added during 15 minutes to magnesium turnings (13 g.) in ether (100 c.c.) containing methyl iodide (*ca.* 2 c.c.). A vigorous reaction set in. The mixture was refluxed for 8 hours (in a few runs the complex which separated was dissolved by the addition of benzene), and the solution poured on solid carbon dioxide (160 g.). When the gas evolution subsided, the product was decomposed with ice-water (350 g.) and concentrated hydrochloric acid (40 c.c.). The ethereal layer was washed with water and extracted with 10% sodium carbonate solution, until no more acid was precipitated on acidification. The combined sodium carbonate solutions were filtered and acidified with dilute hydrochloric acid. 2-Methylnaphthalene-1-carboxylic acid separated as an oil which crystallized on storage. Recrystallization from acetic acid gave white prisms, m. p. 126—127° (41 g., 36%). Some unchanged 1-bromo-2-methylnaphthalene could be recovered from the ethereal layer.

The acid chloride was prepared in quantitative yield, by refluxing the acid for 3 hours with an excess of thionyl chloride, as a yellow oil, b. p. 178—181°/27 mm. Refluxing with methanol then gave the methyl ester, b. p. 149—155°/6 mm., which separated as an oil and was washed with water and sodium carbonate solution and extracted with chloroform.

Methyl 2-*bromomethylnaphthalene*-1-*carboxylate.* The preceding ester (8 g.) was refluxed for 4 hours with *N*-bromosuccinimide (7·8 g.) in carbon tetrachloride (40 c.c.) in presence of some benzoyl peroxide. After cooling, the succinimide was filtered off and the filtrate evaporated to dryness, leaving a brown oil which could not be induced to crystallize. At 150°, it decomposed with evolution of methyl bromide and gave the 2-*hydroxymethylnaphthalene*-1-*carboxylic lactone* (*naphthalide*) (VII). This crystallized on cooling. From glacial acetic acid (charcoal), it formed white leaflets, m. p. 157° (5 g.) (Found: C, 78·3; H, 4·2. $C_{12}H_8O_2$ requires C, 78·3; H, 4·3%).

The 3-*bromonaphthalide.* The naphthalide (VII) (1·8 g.) was refluxed for 4 hours with *N*-bromosuccinimide (2 g.) in carbon tetrachloride (20 c.c.). The succinimide was filtered off, the solvent evaporated, and the residual *bromo*-compound (2·7 g.) recrystallized from light petroleum–benzene as needles, m. p. 140° (Found: Br, 30·6. $C_{12}H_7O_2Br$ requires Br, 30·4%).

The 3-*methoxynaphthalide* (VIII). The bromo-lactone (0·5 g.) was refluxed for 3 hours in 10 c.c. of anhydrous methanol. After removal of the methanol, an oily residue of *methoxynaphthalide* remained, which crystallized on storage. From light petroleum–benzene it formed white needles, m. p. 79—80° (yield, quantitative) (Found: C, 72·8; H, 4·9. $C_{13}H_{10}O_3$ requires C, 72·9; H, 4·7%).

Phthalic, hemipinic, and metahemipinic anhydrides were commercial samples, which were recrystallized from benzene, xylene, and butyl acetate, respectively; they then had m. p. 127°, 169°, and 175°, respectively. Ethyl phthalate, purified by distillation, had b. p. 156°/10 mm. 3 : 4-Dimethoxybenzoic acid, prepared by oxidation of veratraldehyde with permanganate (Edwards, Perkin, and Stoyle, *J.*, 1925, **127**, 198) and crystallised from *iso*propanol, had m. p. 181°. Treatment with an excess of ethereal diazomethane gave methyl 3 : 4-dimethoxybenzoate (from methyl*cyclo*hexane), m. p. 62° (Tiemann, *Ber.*, 1875, **8**, 1123).

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