

In all of the above separation procedures, each step was tested for completeness by placing a small portion of the material in question on the phosphoric acid-impregnated paper and treating the spot with ferric chloride. When the mixture being tested was so strongly colored as to mask the color of iron complexes, a small portion of iso-octane was allowed to migrate through the spot, carrying with it any tropolone present and leaving behind the interfering substances.

**Chromatography.** The phosphoric acid procedure of Zavarin and Anderson<sup>1</sup> was used throughout most of the work. Some streaking tendency of the tropolones was still encountered, particularly in the case of nootkatin. Removal of the highly colored, phlobaphenic impurities from the tropolonic fractions seemed to be of utmost importance for control of streaking. Development of the chromatograms at a constant temperature near 21° was also helpful. The streaking was reduced when Whatman No. 3 was substituted for Whatman No. 1 paper.

As in the phosphoric acid procedure, the  $R_f$  values of nootkatin and hydroxytropolones T-11 and T-10 are rather close. The resolution was achieved by the dimethylsulfoxide procedure of Wachmeister and Wickberg,<sup>16</sup> using iso-octane as the developing solvent. This method completely separated the three compounds; in addition, nootkatin showed much less tendency to streak.

The 5% ferric chloride solution was mostly used as chromogenic agent. The tendency of the spots obtained to fade with time was overcome by neutralizing the phosphoric acid of the paper with gaseous ammonia. This treatment also regenerated the partially faded spots. The color of the spots was changed characteristically by this treatment.

Another chromagenic agent used was a solution of diazotized *o*-aminobiphenyl, prepared by dissolving 0.1 g. of *o*-aminobiphenyl in 0.3 ml. of 10% hydrochloric acid, treat-

ing the resulting mixture with 1 ml. of 10% sodium nitrite for 5 min. with stirring, decomposing the excess of nitrous acid with 0.5 g. of urea, and diluting the whole to 10 ml. The solution gave a characteristic purple color with  $\gamma$ -thujaplicin, and buff to pink colors with the other tropolones after the sprayed paper was treated with gaseous ammonia. The diazo compounds of the other amines tested, such as aniline, benzidine, *p*-nitroaniline, *p*-aminobenzoic acid, and sulfanilic acid, were much less stable to the treatment with ammonia, and produced background color which interfered with that of the formed azodyes.

For semiquantitative evaluation of the concentration of tropolones in wood, the intensities of the spots containing known amounts of substance were compared visually with the intensity of the spots from the extracts. Greater accuracy was considered unnecessary because of the natural variation of the tropolone content within the species.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

## Friedel-Crafts Reactions of Some Acylals

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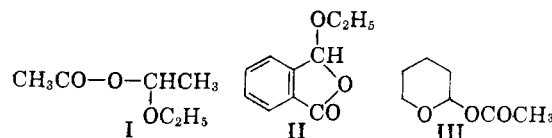
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1-Ethoxyethyl acetate (I) reacts with anisole to form *p*-methoxyacetophenone and 4,4'-vinylidenedianisole (IV) if sufficient aluminum chloride is present, or 4,4'-ethylidenedianisole with less aluminum chloride. The IV was formed also starting with *p*-(1-ethoxyethyl)anisole, anisole and aluminum chloride. The products from I, toluene and aluminum chloride were *p*-methylacetophenone, 1,1-di-*p*-tolylethane and some meta isomer of the latter. 3-Ethoxyphthalide, toluene and aluminum chloride yielded 3-*p*-tolylphthalide and an unidentified carboxylic acid. The reaction of tetrahydropyran-2-yl acetate, toluene, and aluminum chloride gave rise only to an intractable sirup.

A few acylals have been subjected to reactions under Friedel-Crafts conditions but these have all been of carbohydrate nature. Such a reaction is the conversion of glucose pentaacetate into tetraacetylglucosyl chloride<sup>1</sup> by means of aluminum chloride. Another reaction is the synthesis of aryl tetraacetylglucosides by fusing glucose pentaacetate with a phenol<sup>2</sup> in the presence of aluminum chloride (or zinc chloride). Finally, there is the glucosylation of benzene and other aromatic hydrocarbons by reaction with glucose pentaace-

tate or tetraacetylglucosyl chloride and aluminum chloride<sup>3</sup> or hydrogen fluoride.<sup>4</sup>

The purpose of the present investigation was to subject simpler acylals to Friedel-Crafts conditions, and for this purpose 1-ethoxyethyl acetate (I), 3-ethoxyphthalide (II), and tetrahydropyran-2-



(1) A. Kunz and C. S. Hudson, *J. Am. Chem. Soc.*, **48**, 1978 (1926).

(2) Edna Montgomery and N. K. Richtmyer, *J. Am. Chem. Soc.*, **64**, 690 (1942); C. D. Hurd and W. A. Bonner, *J. Org. Chem.*, **11**, 50 (1946).

(3) C. D. Hurd and W. A. Bonner, *J. Am. Chem. Soc.*, **67**, 1664, 1759, 1977 (1945).

(4) J. Heerema, G. Bollenback, and C. B. Linn, *J. Am. Chem. Soc.*, **80**, 5555 (1958).

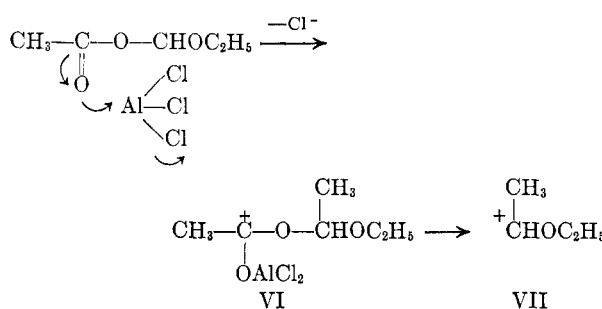
yl acetate (III) were selected. All three were studied with toluene and I was studied with anisole as well.

In the reaction of I with anisole, different results were obtained with differing ratios of reactants. At ratios of 1:1:3 for I : anisole : AlCl<sub>3</sub> the products were 4,4'-vinylidenedianisole (IV), *p*-methoxyacetophenone and considerable brown-black tar. At ratios of 1:2.7:1.5 (hence, more anisole and less aluminum chloride) the products were 4,4'-

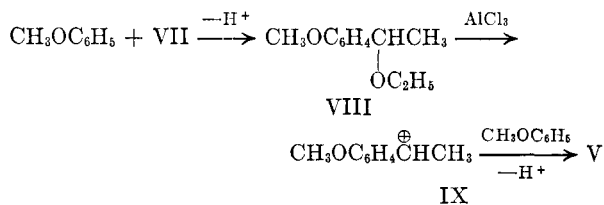


ethylidenedianisole (V), much less tar, and little or no IV or methoxyacetophenone. Anisole was recovered in both runs.

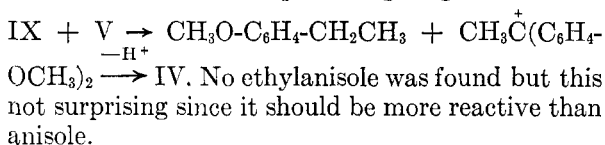
This evidence points to an initial attack of aluminum chloride at the carbonyl group of I:



With excess aluminum chloride part of carbonium ion VI appears to react with anisole to form *p*-methoxyacetophenone. VI, however, should rapidly decompose into an acetate and a new carbonium ion VII which is the precursor of V. These steps would apply. It is well known that aluminum



chloride sponsors hydrogen transfer reactions, hence carbonium IX may attack V if sufficient aluminum chloride is present giving rise to IV:



No ethylanisole was found but this not surprising since it should be more reactive than anisole.

To ascertain if *p*-(1-ethoxyethyl)anisole (VIII) was a reasonable intermediate, the compound was synthesized and placed in reaction with anisole and aluminum chloride. A fair yield of IV was obtained together with some polymeric material.

The polymeric product of the reaction may arise from any of several sources. It could have arisen by continued reaction of the carbonium intermediates with aromatic nuclei, or it could have resulted by

vinyl-type polymerizations of IV or of *p*-methoxystyrene formed from IX.

Analogies exist in the literature for the formation of IV. Gattermann<sup>5</sup> obtained it as a by-product in the reaction between acetyl chloride and anisole. Sisido and others<sup>6</sup> reported its formation from  $\alpha$ -chloro-*p*-methoxyacetophenone and anisole but their explanation for its formation seems obscure. Compound IV also has been reported<sup>7</sup> to be formed from V during reaction with phosphorus pentachloride.

In the reaction of I (1 part) with toluene (1.15 parts) instead of anisole in the presence of aluminum chloride (1 part) the products included unused toluene, a polymeric residue, and a distillable material which was fractionated. Each fraction was separated further by chromatography over silica gel. In this way were separated light yellow *p*-methylacetophenone and colorless 1,1-di-*p*-tolylethane which was admixed with some of its meta isomer. Distillation would not be expected to separate such isomers since reported<sup>8</sup> boiling points of 1,1- or 1,2-di-*p*-(or *m*-)-tolylethanes are all in the range 293–298°. Chromatography separated the colorless ditolylethane from other unidentified yellow cuts, but apparently it was incapable of separating the *m*- from the *p*-isomer. These yellow cuts may have been acetyl derivatives of the ditolylethane but the matter was not pursued in view of the difficulty in obtaining pure samples.

Pure 1,1-di-*p*-tolylethane was synthesized. Its principal infrared absorption peaks were at these places ( $\mu$ ): 3.30, 3.37, 3.46, 5.42, 5.50, 6.06, 6.19, 6.59, 6.70, 6.85, 7.28, 7.50, 7.78, 8.20, 8.85, 9.10, 9.75, 10.2, 10.6, 12.2, 12.85, 13.55, 14.22 (very weak). The ditolylethane obtained *via* I contained most of these bands, but the one at 14.22  $\mu$  was strong; also the substance showed a strong band at 12.68  $\mu$  that was absent in the pure para sample. These two bands are regarded as indicative of meta substitution.<sup>9</sup> The two bands at 12.22, 13.55  $\mu$  were a little weaker in the reaction product than in the pure para hydrocarbon and these are believed to represent para substitution.

A mechanism like that offered above for anisole would readily account for the *p*-methylacetophenone and 1,1-di-*p*-tolylethane (or 4,4'-ethylideneditoluene). Isomerization of the latter in part to the *m*-isomer would be analogous to the con-

(5) L. Gattermann, *Ber.*, **22**, 1132 (1889).

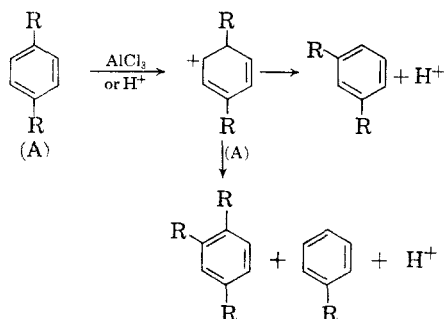
(6) K. Sisido and others, *J. Am. Chem. Soc.*, **79**, 3592 (1957).

(7) A. I. Lunjak, *J. Russ. Phys. Chem. Soc.*, **36**, 301 (1904).

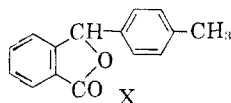
(8) G. Egloff, "Physical Constants of Hydrocarbons," Vol. 3, Reinhold Publishing Co., New York, N. Y., 1946, p. 362.

(9) R. Williams, S. Hastings, and J. Anderson, Jr., *Anal. Chem.*, **24**, 1911 (1952); W. Kaye and M. Otis, *Anal. Chem.*, **20**, 1006 (1948); C. Young, R. DuVall, and N. Wright, *Anal. Chem.*, **23**, 709 (1951).

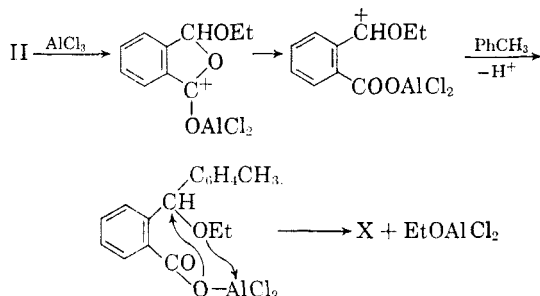
version of *p*- into *m*-xylene by aluminum chloride, which is explained<sup>10</sup> by a carbonium intermediate:



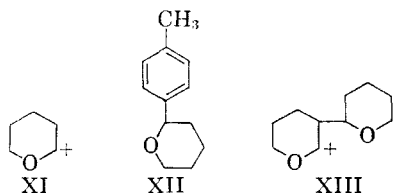
The reaction of II, toluene, and aluminum chloride, using molar ratios of 1 : 1.75 : 1, gave rise to 3-*p*-tolylphthalide (X) and an oily carboxylic acid



that was not identified. To form X, again one may assume initial attack of the aluminum chloride at the acylal carbonyl:



Treatment of acylal (III) with toluene and aluminum chloride yielded only polymeric products in an exothermic reaction. The carbonium ion (XI) which is probably formed as an intermediate may have reacted with toluene yielding XII and substances derivable from it, but it may have changed into dihydropyran and reacted with the latter to produce XIII in the first stage of a polymerization sequence. In the present work, III was



synthesized by acetylation of tetrahydropyran-2-ol (2,3,4-trideoxypentose), as well as by the older

(10) K. L. Nelson and H. C. Brown in "The Chemistry of Petroleum Hydrocarbons," Vol. 3, Reinhold Publishing Co., New York, N. Y., 1955, p. 527.

method involving addition of acetic acid to dihydropyran.<sup>11</sup>

#### EXPERIMENTAL

**Synthesis of reagents.** 1-Ethoxyethyl acetate (I), b.p. 27–28° at 17 mm., was prepared from ethanol, paraldehyde, hydrogen chloride and sodium acetate.<sup>12</sup> 3-Ethoxyphthalide (II), m.p. 65–66°, was prepared<sup>13</sup> by refluxing a mixture of ethanol and phthalaldehydic acid. Tetrahydropyran-2-yl acetate (III), b.p. 55–56° at 2 mm.,  $n_D^{20}$  1.4369, was made as in the literature<sup>11</sup> by adding acetic acid to dihydropyran, but it was made also by acetylation of tetrahydropyran-2-ol, as follows.

Pyridine (28 g.) was added little by little into a mixture of 54 g. of tetrahydropyran-2-ol and 86.5 g. of acetic anhydride with occasional shaking of the mixture. Heat was evolved as pyridine was added gradually. After all of the pyridine was added this mixture was heated on a steam bath for 15 min. On cooling, 80 cc. of ether was added and the solution was washed with three 50-cc. portions of water after which it was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated on a steam bath. Distillation of the residue yielded 35 g. boiling below 53° (2 mm.) and 42 g. 53–58° (2 mm.). The second fraction was redistilled: 33 g., b.p. 55–56° at 2 mm.,  $n_D^{20}$  1.4369.

The following compounds, needed for characterizations, were synthesized following established directions: *p*-(1-ethoxyethyl)-anisole,<sup>14</sup> b.p. 117–118° at 21 mm.,  $n_D^{20}$  1.4982; 1,1-di-*p*-tolylethane, b.p. 127° (1 mm.); 2-*p*-tolylbenzoic acid,<sup>15</sup> m.p. 140–141°; 3-*p*-tolylphthalide,<sup>17</sup> m.p. 132–133°.

**4,4'-Vinylidenedianisole.** This was prepared by gradual addition of aluminum chloride (76 g.) to an ice-cooled stirred mixture of anisole (62 g.), acetyl chloride (45 g.), and carbon disulfide (100 cc.) followed by refluxing for 1.5 hr. till hydrogen chloride was no longer evolved. After evaporation of the solvent, 13.6 g. of crystalline IV separated from the residue; m.p., after crystallization from ethyl acetate, 143–144°. This compares with the reported<sup>5</sup> m.p. of 140°. Processing the remainder of the products by vacuum distillation yielded 39.2 g. of *p*-methoxyacetophenone, b.p. 115–116° (4 mm.).

***p*-Methoxyacetophenone 2,4-dinitrophenylhydrazone.** This hydrazone was made in the usual way from the above ketone. It was recrystallized from ethyl acetate; m.p. 226–227°. This compares with a reported value<sup>18</sup> of 220°.

*Anal.* Calcd. for  $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_5$ : C, 54.5; H, 4.24. Found: C, 54.2; H, 4.16.

**Reaction of 1-ethoxyethyl acetate and anisole.** Excess of aluminum chloride. To an ice-cooled solution of anisole (122 g.) in carbon disulfide (300 cc.) was added aluminum chloride (452 g.) little by little. The mixture was cooled to –3°, stirred, and 1-ethoxyethyl acetate (150 g.) was gradually added during 4.5 hr., keeping the temperature below 5°. An increase in temperature followed each addition. Hydrogen chloride gas was noticeably evolved. After addition was completed the mixture was left stirring without cooling for 30 min., then was refluxed for 1.5 hr. The color turned from brown-red to brown-black. It was then cooled

(11) Bremner and Jones, Brit. patent 606,764; *Chem. Abstr.*, **43**, 1442 (1949).

(12) C. D. Hurd and F. O. Green, *J. Am. Chem. Soc.*, **63**, 2201 (1941).

(13) D. Wheeler, D. Young, and D. Erley, *J. Org. Chem.*, **22**, 547 (1957).

(14) R. Quelet, *Compt. rend.*, **199**, 483 (1934).

(15) O. Kamm, editor, "Organic Syntheses," Vol. 4, John Wiley and Sons, New York, N. Y., 1925, p. 23.

(16) H. Limpricht, *Ann.*, **299**, 300 (1898).

(17) H. Limpricht, *Ann.*, **314**, 251 (1901).

(18) F. Wild, "Characterisation of Organic Compounds," Cambridge University Press, 1947, p. 141.

and poured into about 1 kg. of ice containing 350 cc. of concentrated hydrochloric acid. The oily product which separated was extracted with 500 cc. of ether. The extract was washed once with water, once with 5% sodium carbonate solution, and then again with water. Then, the ethereal solution was dried over sodium sulfate and evaporated, leaving 140 g. of brown-black oil from which fine leaflet crystals came out on standing. About 20 cc. of 95% alcohol was added to assist in the filtration of the crystals. The crystalline mass was washed with a small amount of alcohol; yield 13 g., m.p. 133–136°. It was recrystallized from ethyl acetate three times and it then melted at 143–144°. Analysis showed this to be 4,4'-vinylidenedianisole (IV). The compound showed no hydroxyl or carbonyl bands in the infrared. Its mixed m.p. with authentic IV was 143–144°.

*Anal.* Calcd. for  $C_{16}H_{16}O_2$ : C, 80.00; H, 6.66; mol. wt. 240. Found: C, 79.82; H, 6.57; mol. wt. (Rast) 236.

The filtrate, from which the crystals were separated, was evaporated and distilled under 1 mm. of mercury. A fraction boiling at 50–85° (30 g.) was obtained, leaving 78 g. of brown-black tar. The 30 g., on redistillation, yielded 21 g. at 50–80° (25 mm.), 2 g. at 80–90° (25 mm.), 4 g. at 70–95° (1 mm.). The dinitrophenylhydrazine test was positive for the last fraction. The 2,4-dinitrophenylhydrazone thus obtained was recrystallized from ethyl acetate, m.p. 226–227°; mixed m.p. with an authentic sample, 226–227°.

*Lesser quantity of aluminum chloride.* 1-Ethoxyethyl acetate (51 g.) was added slowly during 2 hr. into a cooled (2–6°), stirred solution of anisole (110 g.) in carbon disulfide (150 cc.) in the presence of aluminum chloride (77 g.). The reaction mixture gradually turned red with each addition of the acylal. The mixture was stirred at room temperature for 30 min., then was refluxed for 1.5 hr. The reaction product was processed as in the first run. A light brown colored residue (104 g.), obtained by evaporation of the red solution, was distilled: 71 g., at 62–64° (30–33 mm.), 2.1 g. up to 173° (2 mm.), 14 g. at 173–178° (2 mm.), and 6 g. of residue. The 14-g. fraction solidified on cooling and was recrystallized from 95% alcohol, m.p. 71–72°. It was 4,4'-ethylidenedianisole, the m.p. of which is given<sup>19</sup> as 70–72°.

*Anal.* Calcd. for  $C_{16}H_{18}O_2$ : C, 79.4; H, 7.45. Found: C, 79.34; H, 7.38.

*Reaction of anisole and p-(1-ethoxyethyl)anisole.* A solution of *p*-(1-ethoxyethyl)anisole (12 g.) in carbon disulfide was added slowly during 1 hr. into a cooled (3–8°), stirred mixture of anisole (10 g.) and aluminum chloride (19 g.). The mixture turned deep red in color. After the addition the mixture was stirred at room temperature for 1.5 hr. and then was refluxed for 3 hr. This red mixture was treated as in the former experiment.

After evaporation of the ethereal solution, crystals (5 g.) separated from the residue, m.p. 136–137°. The filtrate was distilled. Two g. were collected at 150–160° (0.5 mm.), leaving 7 g. of a light brown colored residue. The 2-g. fraction solidified on cooling, m.p. 137–138°. Therefore, 7 g. of this crude crystalline product was obtained. It was recrystallized from ethyl acetate, and then melted at 143–144°. It did not depress the melting point of an authentic sample of 4,4'-vinylidenedianisole, made above. Also, its infrared spectrum corresponded with that of the authentic sample.

*Reaction between 1-ethoxyethyl acetate, toluene, and aluminum chloride.* The acylal (120 g.) was added slowly during 2.5 hr. into a cooled (4–8°) stirred solution of toluene (96 g.) in carbon disulfide (270 cc.) in the presence of aluminum chloride (120 g.). Some hydrogen chloride gas evolution was observed. The reaction mixture turned brown colored gradually with each addition. Then the reaction mixture was stirred at room temperature for 1 hr. and refluxed for

1.5 hr. The reaction product was treated as in the former experiment. From the residue, after evaporation of solvent was obtained toluene (47 g.) and a brown oil (50 g.) which was fractionated at 1 mm.: (temp., g.) 40–60, 3.6; 60–100, 15.2; 100–135, 12.8; 135–170, 7.6; residue 9.0.

These fractions were chromatographed through a column (1.1 × 92 cm.) containing silica gel (Davison, 60–200 mesh). Although several cuts were obtained from the first and fourth fractions they were not identified. Generally, they were orange or yellow. One third of the 15.2-g. fraction, mixed with 5 cc. of *n*-pentane, was put on top of the column and absolute alcohol was the developing solvent. After collecting two cuts of colorless eluent six cuts were taken containing in all 3.4 cc. of light yellow liquid that was shown to be *p*-methylacetophenone. The latter was characterized by carbonyl band in the infrared spectrum and by 2,4-dinitrophenylhydrazone which was deep red, m.p. 256–257° (lit. 260°), and was analyzed: C, 57.7; H, 4.35 (calcd. for  $C_{15}H_{14}N_4O_4$ : C, 57.3; H, 4.46).

Similarly, 5 cc. of the 12.8-g. fraction (mixed with 5 cc. of pentane) was chromatographed using alcohol. The first three cuts contained 0.2, 1.3, and 0.3 cc. or 1.8 cc. of colorless liquid, and four cuts of yellow to brown material amounting to 1.2 cc. Since all of the first three cuts gave similar infrared spectra they were combined and distilled. The fraction collected at 112–120° (1.0 mm.) was 1.5 cc.

*Anal.* Calcd. for  $C_{16}H_{18}$ : C, 91.4; H, 8.6. Found: C, 91.13; H, 9.03.

*Reaction between toluene, 3-ethoxyphthalide, and aluminum chloride.* Nine g. of toluene and 7.5 g. of aluminum chloride were placed in a flask, cooled by an ice bath. A solution of 10 g. of 3-ethoxyphthalide in 70 cc. of carbon disulfide was added slowly into the flask, stirring well. No appreciable heat was evolved during the addition. Addition took 40 min., after which the reaction mixture was refluxed for 6 hr. The reaction product was processed as outlined above. The extraction ether and carbon disulfide solution was washed twice with 10% sodium carbonate solution. This alkaline solution was acidified with 5% hydrochloric acid. The oil which separated was extracted with ether and the ether solution was dried over sodium sulfate. After evaporation of solvent, 4.5 g. of oil remained.

The ether solution that had been washed with sodium carbonate solution was washed with water and dried over sodium sulfate. This solution was evaporated on the steam bath, leaving about 6 g. of oil. This residue was distilled under diminished pressure and 2.5 g. of toluene was recovered, leaving 2.4 g. of residue. The latter was distilled at 0.5 mm.: 1.5 g. of 3-ethoxyphthalide at 90–110° for it solidified on cooling and melted at 64–65°, and 0.7 g. at 110–140°. To the latter was added a little alcohol which promoted crystallization, yield 0.4 g. of white needles. After recrystallization from methanol its m.p. and mixed m.p. (with authentic sample) were 132–133°. That it was 3-*p*-tolylphthalide was confirmed by analysis: C, 80.65; H, 5.40 (calcd. for  $C_{15}H_{12}O_2$ : C, 80.40; H, 5.35).

*Reaction between tetrahydropyran-2-yl acetate, toluene, and aluminum chloride.* Into an ice-cooled mixture of 9 g. of toluene, 20 cc. of carbon disulfide, and 6 g. of aluminum chloride was added during 30 min. a mixture of 6.4 g. of tetrahydropyran-2-yl acetate in 10 cc. of carbon disulfide. Some hydrogen chloride was liberated. Then the mixture was stirred at 20° for 1.5 hr., followed by refluxing for 2 hr. The reaction product was a sirup.

*Acknowledgment.* The microanalyses were performed by Miss Hilda Beck. During this investigation one of us (T. I.) was on leave of absence from and was supported in part by Takamine Research Laboratory, Sankyo Co., Ltd., Shinagawa-ku, Tokyo, Japan.

(19) C. Price and G. Mueller, *J. Am. Chem. Soc.*, **66**, 634 (1944).