pound was also prepared using dry petroleum ether or dry benzene as the reaction medium.

Anal. Calcd. for $C_{14}H_{12}NOCl$: Cl, 15.17. Found: (analysis by author) Cl, 14.85.

Some preparations gave products (usually pale yellow or off-white in color) that were obviously not pure, but these were found to be satisfactory for synthetic use. All of the reactions cited below were run with the solid cinnamoylpyridinium chloride and most of them were run also by adding the calculated amount of cinnamoyl chloride and pyridine to the other reactants. The yields were comparable by both procedures.

Cinnamic Anhydride.—To a solution of 2 ml. of water in 70 ml. of acetone was added 15 g. (0.06 mole) of cinnamoylpyridinium chloride. The mixture was stirred vigorously for five minutes and poured into 500 ml. of water containing 5 ml. of hydrochloric acid. The solid was filtered off, washed with 5% sodium bicarbonate and with water. The air-dried product was recrystallized from absolute ethanol, giving 6.0 g. (71%) of cinnamic anhydride, m.p. 135–136°. When the procedure of Wedekind[5] was followed, the yield of cinnamic anhydride was 13% (after recrystallization). The principal product whenever a large excess of water was used (as in the Wedekind procedure) was cinnamic acid.

Ethyl β-Cinnamoyloxycrotonate.—A mixture of 24.6 g. (0.1 mole) of cinamoylpyridinium chloride and 19.2 g. (0.1 mole) of ethyl benzoylacetate was warmed on the steam-bath for two hours and allowed to stand overnight. The crude mixture was washed with 5% hydrochloric acid, water, 5% sodium bicarbonate and water in that order. The solid remaining was recrystallized from absolute ethanol, giving 19 g. (59%) of ethyl β-cinnamoyloxycrotonate, m.p. 125.4–126.1°. The product gave no enolic tests.

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63. Found: C, 74.30; H, 5.39.

4-(*p*-Dimethylaminophenyl)-pyridine.—A mixture of 12.3 g. (0.05 mole) of cinnamoylpyridinium chloride, 4.0 g. (0.05 mole) of pyridine and 6.0 g. (0.05 mole) of dimethylaniline was heated on the steam-bath for eight hours. The mushy mixture was made acid with concentrated hydrochloric acid and steam distilled. The 150-ml. of steam distillate was extracted with ether, the ether evaporated and the residue treated with phenylhydrazine in ethanol,[10] giving *ca.* 0.1 g. of cinnamaldehyde phenylhydrazone, m.p. 167–168°. The residue from the distillation was filtered from a large mass of black tarry material and the filtrate was made alkaline. Steam distillation of the alkaline mixture yielded 3.0 g. (50%) of dimethylaniline. The residue in the distillation flask was filtered off and recrystallized three times from 9:1 ethanol:chloroform to give 3.5 g. (35%) of 4-(*p*-dimethylaminophenyl)-pyridine, m.p. 234–235°, as colorless, flat plates which colored quickly in air to a light yellow solid. This interesting substance had, as one might expect, indicator properties, being yellow in acidic (organic or inorganic) and colorless in neutral or alkaline solutions. It reacted (in chloroform solution) with acid halides to give brilliantly colored complexes, *e.g.*, a bright red with benzoyl chloride and a deeper red with cinnamoyl chloride, even in high dilutions.

Phenyl Cinnamate.—To 24.5 g. (0.1 mole) of cinnamoylpyridinium chloride was added 9.4 g. (0.1 mole) of phenol. A bright yellow color appeared immediately and slowly faded on standing. From this point two procedures were used: (a) 16.0 g. (0.2 moles) of pyridine was added and the mixture was heated for four hours on the steam-bath or (b) the mixture (without added pyridine) was allowed to stand at room temperature overnight. In each case the resultant mixture was poured into 500 ml. of water and stirred until the oily lower layer solidified. The solid was collected on the buchner funnel, washed with 10% hydrochloric acid, 5% sodium bicarbonate, 10% potassium hydroxide, and with water in that order, and recrystallized from 95% ethanol, giving 16–18.5 g. (73–83%) of phenyl cinnamate, m.p. 75–76°. This procedure compares favorably with respect to yields (reported 56–75%) and with respect to the manipulations required with that reported in reference 11.

2,6-Dimethylphenyl Cinnamate.—To 24.5 g. (0.1 mole) of cinnamoylpyridinium chloride was added 12.2 g. (0.1 mole) of 2,6-dimethylphenol (DPI 1772). A bright yellow-orange color appeared briefly then disappeared. To the mixture was added 8.0 ml. of pyridine and it was allowed to stand overnight. The reaction mixture was worked up as described for phenyl cinnamate (above), giving 19 g. (76%) of 2,6-dimethylphenyl cinnamate, m.p. 91–92°.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 81.39; H, 6.32.

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Reactions of 1,3-Diphenylisobenzofuran with Acetylenic Dienophiles

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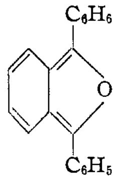
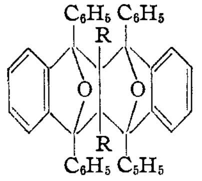
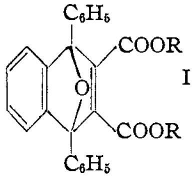
Although additions of 1,3-diphenylisobenzofuran (I) to a number of ethylenic dienophiles have been reported,[1–4] the literature does not seem to contain any examples of reactions of this interesting substance with acetylenic dienophiles. In connection with a separate study, we have had occasion to carry out such reactions. The preparation and properties of the adducts and their derivatives are reported here.

The reaction of I with acetylenedicarboxylic acid (II) produced the bis-adduct (III) in near-quantitative yield. Even in the presence of a large excess of II, only III could be isolated, albeit in smaller yield.


I


III, R = COOH

Diene addition of I to ethyl acetylenedicarboxylate afforded a 1:1 adduct (IVa) in excellent yield. The ester (IVa) was readily reduced to the corresponding dihydro adduct (V). Saponification of IVa yielded the very unstable unsaturated acid IVb, isolated only as the monohydrate. This acid suffers partial retrograde diene addition in alkaline solution and consequently, the saponification of the ester (IVa) yielded a small quantity of I, identified as the autoxidation product, *o*-dibenzoylbenzene. Pyrolysis of IVb at the melting point (140°) resulted in virtually quantitative conversion to the bis-adduct (III), presumably by retrograde diene addition and recombination of the addends. The facile dissociation of V and especially of IVb


IV a, R = C_2H_5
b, R = H

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(10) E. H. Huntress and S. P. Mulliken, "Identification of Pure Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1941, p. 72.

(11) *Org. Syntheses*, **20**, 77 (1940).

(1) R. Weiss, A. Abeles and E. Knapp, *Monatsh.*, **61**, 162 (1932).

(2) E. de B. Barnett, *J. Chem. Soc.*, 1326 (1935).

(3) C. Dufraisse and R. Priou, *Bull. soc. chim.*, [5] **5**, 502 (1938).

(4) A. Etienne and A. Spire, *Compt. rend.*, **230**, 2030 (1950).

parallels the previously reported[2,3] behavior of other adducts of I.

Experimental[5]

Reaction of 1,3-Diphenylisobenzofuran with Acetylenedicarboxylic Acid.—A solution of 0.61 g. of I[6,7] and 0.30 g. of II in 5 cc. of benzene and 5 cc. of ether was heated at reflux for 5 minutes. The ether was allowed to distil out of the reaction mixture and the residual solution was boiled an additional 55 minutes. After this time, the characteristic blue-green fluorescence of the isobenzofuran was no longer visible, even in ultraviolet light. The solution was concentrated by distillation and treated with a little carbon tetrachloride. The bis-adduct (III) crystallized as tiny, white prisms, m.p. 195.5–198.5°. The yield was 0.74 g. (quantitative). The analytical sample, recrystallized from benzene–carbon tetrachloride, had m.p. 203.5–204°.

Anal. Calcd. for $C_{24}H_{16}O_5$ (1:1 adduct): C, 74.99; H, 4.20. Calcd. for $C_{44}H_{30}O_6$ (bis-adduct): C, 80.72; H, 4.62. Found: C, 80.82, 80.54; H, 4.88, 5.00.

When the reaction was carried out under similar conditions using a 9:1 ratio of II to I, only III was isolated. The yield was 50%.

Reaction of 1,3-Diphenylisobenzofuran with Ethyl Acetylenedicarboxylate.—A solution of 0.54 g. of I and 0.34 g. of ethyl acetylenedicarboxylate in 4 cc. of benzene was heated at reflux for 105 minutes. The solvent was evaporated and the residue crystallized from benzene–ethanol to yield 0.74 g. (84%) of IVa, m.p. 139–140°. Recrystallization from benzene–ethanol raised the melting point to 143.0–143.5°. The substance instantaneously decolorized potassium permanganate in acetone at room temperature.

Anal. Calcd. for $C_{28}H_{24}O_6$: C, 76.35; H, 5.49. Found: C, 75.98; H, 5.18.

Catalytic Reduction of IVa.—A solution of 0.60 g. of IVa in 20.cc. of ethyl acetate was added to a suspension of Adams catalyst (previously generated from 0.05 g. of platinic oxide) in 10 cc. of ethyl acetate. The reaction mixture was stirred in hydrogen at one atmosphere pressure. The theoretical quantity of gas was absorbed in 38 minutes, whereupon the catalyst was filtered off and the filtrate evaporated to a thick oil which exhibited an intense blue-green fluorescence. The oil crystallized readily upon trituration and the product was recrystallized from ethanol to yield 0.40 g. of the dihydroester as white, rhombohedral tablets, m.p. 131.5–133°. After several recrystallizations from ethanol, the m.p. remained constant at 137.5–138°. A mixed m.p. with IVa was depressed to 106–120°. The dihydroester apparently suffers retrograde diene addition upon fusion, for the melt of the pure substance shows the characteristic blue-green fluorescence of I.

Anal. Calcd. for $C_{28}H_{26}O_5$: C, 76.00; H, 5.92. Found: C, 76.26; H, 6.07.

Saponification of IVa.—A mixture of 0.64 g. of IVa and 0.64 g. of potassium hydroxide in 10 cc. of ethanol was heated at reflux. The reaction mixture immediately turned bright-yellow and became strongly fluorescent. After 2.5 hours, the mixture was diluted with water and extracted with several portions of chloroform until the chloroform layer was no longer fluorescent. The chloroform solution was washed with water, dried over sodium sulfate and evaporated. The residue was recrystallized from benzene-Skellysolve B to give 0.03 g. of crude *o*-dibenzoylbenzene, m.p. 140–147° alone or mixed with an authentic sample.[6]

The original alkaline solution was acidified with concentrated hydrochloric acid and extracted with ether. The ether extract, after having been washed with water and dried over sodium sulfate, was evaporated to a thick, pale-yellow oil which crystallized readily from benzene–Skellysolve B as 0.30 g. (54%) of IVb, m.p. 134.5–135° with decomposition. Recrystallization from a mixture of ethyl acetate, benzene and Skellysolve B afforded pure-white rosettes of sharply-defined, transparent staves. The acid decomposed sharply at 139° with violent frothing when heated slowly from room temperature. When the substance was inserted into a bath preheated to 140.5° and the temperature was raised very slowly (1° per minute), decomposition occurred at 144.5–145°.

The acid was readily soluble in neutral ethanol. When this colorless solution was treated with a few drops of 10% sodium hydroxide, it immediately turned yellow and showed a blue-green fluorescence.

Freshly-purified samples of the acid were pure-white in the solid state. The crystals became yellow in about two hours when dried at 1 mm. at room temperature. The dried material showed essentially the same melting point characteristics as the freshly-recrystallized substance.

Anal. Calcd. for $C_{24}H_{16}O_5 \cdot H_2O$: C, 71.63; H, 4.51. Found (after drying at 56° and 1 mm. for 2 hours, then at room temperature for 48 hours over phosphorus pentoxide): C, 71.34; H, 4.10. Found (after drying at 56° and 1 mm. for 24 hours, then at room temperature for 1 week over phosphorus pentoxide): C, 71.47; H, 4.70.

Pyrolysis of IVb.—Eighteen-hundredths of a gram of finely-powdered IVb was carefully heated to its melting point in a slow current of nitrogen. The exit gases were passed into baryta. At 140° the solid frothed vigorously and a sudden surge of gas produced a voluminous precipitate in the baryta solution. The melt was kept at 140–143° for 15 minutes and then allowed to cool. The yellow-brown glassy residue was dissolved in ether and extracted with potassium carbonate solution. The aqueous layer was freed of a small quantity of insoluble material by filtration and then acidified with concentrated hydrochloric acid. The precipitated solid, after drying at the pump, weighed 0.12 g. Recrystallization from benzene–Skellysolve B afforded glittering, short needles or prisms, m.p. 204–205°, alone or mixed with a sample of III prepared by diene addition.

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[5] Melting points are corrected. The microanalyses are by Mr. Joseph Pirie of this Laboratory and by Dr. Adalbert Elek, Elek Microanalytical Laboratory.

[6] R. Adams and M. H. Gold, THIS JOURNAL, **62**, 56 (1940).

[7] The preparation of I by the procedure of reference 6 was found to be superior to that of A. Guyot and J. Catel, *Bull. soc. chim.*, **35**, 1124 (1906). Compare E. Bergmann, *J. Chem. Soc.*, 1147 (1938).

Preparation of *p*-Acetaminobenzaldehyde Thiosemicarbazone

BY A. DAS AND S. L. MUKHERJEE

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Domagk, *et al.*,[1] reported the activity of thiosemicarbazones against tuberculosis. Of the two most effective thiosemicarbazones, *p*-acetaminobenzaldehyde thiosemicarbazone known commercially as TB/I and the *p*-ethylsulfonyl derivative known as TB/III, the former has found more popularity with the medical profession. This compound has been synthesized in a variety of ways[2,3,4] by using thiosemicarbazide in all cases. In still another method[5a] hydrazinium thiocyanate has reacted with aromatic aldehydes to give appropriate thiosemicarbazones. Almost simultaneously the preparation of acetone thiosemicarbazone by using hydrazinium thiocyanate with acetone has been reported by Sunner.[5b]

Following the well-known extension of Wöhler's synthesis as applied in the above two methods[5a,5b] as well as in the preparation of thiosemicarbazide[6]

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[1] Domagk, *et al.*, *Naturwissenschaften*, **33**, 315 (1946).

[2] Domagk (to I. G. Farbenindustrie), *German Patent Appli.*, **176**, 219 (1943); *Ind. Eng. Chem.*, **42**,1868 (1950).

[3] "Manufacture of thiosemicarbazone derivative of acetylamino or amino substituted aromatic aldehyde," Indian Patent 43,527 dated 22nd July 1950.

[4] Wilheim, *Acta Univ. Szeged, Chem. Phys.*, **3**, 54 (1950); *C. A.*, **46**, 2521 (1952).

[5] (a) Puetzer, *et al.*, THIS JOURNAL, **73**, 2958 (1951); (b) Sunner, *C. A.*, **45**, 5486 (1951).

[6] Freund and Wischewiansky, *Ber.*, **26**, 2877 (1893).