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A Convenient Preparation of Arylmaleic Anhydrides

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Arylmaleic anhydrides are often desirable as components in Diels-Alder reactions, both for synthetic purposes and as a convenient means of studying the influence of aryl substituents of varying electronic requirements on the rate of formation and stereochemistry of the adducts.[1-3] A particular point of interest is the finding[4] that phenylmaleic anhydride can serve as diene as well as dienophile.

Studies of this sort have been limited only by the difficulty of preparation of some members of this class, especially those containing alkoxy substituents. The practical methods of synthesis appear to be the following:

(a) Dehydrogenation of arylsuccinic anhydrides by bromine[5] or *N*-bromosuccinimide.[6] This is probably the method of choice for the phenyl[6] and *p*-nitrophenyl[1b] compounds, but cannot be used on aryl rings containing activating substituents because of ring bromination.[7] The Experimental section describes an attempt to dehydrogenate 3,4-methylenedioxyphenylsuccinic anhydride by bromine and *N*-bromosuccinimide, both of which apparently brominated the aromatic ring, since the halogen could not be removed from the product by boiling with lutidine.

(b) The Meerwein addition of diazonium salts to maleic acid and its derivatives.[8] This reaction is applicable to a variety of aryl substituents, but gives only low to moderate yields.

(c) Addition of hydrogen cyanide to the formyl derivative of an ethyl arylacetate, followed by hydrolysis and dehydration, gives arylmaleic anhydrides in 15–30% over-all yields.[2,3,9] Attempts to apply this method, in the present study, to the formyl and oxalyl derivatives of 3,4-dimethoxyphenylacetonitrile were unsuccessful.

Other methods, such as the Reformatsky reaction on ethyl phenylglyoxylate and the condensation of ethyl glyoxylate with ethyl arylacetates have been used in specific cases,[10] but do not appear to be of general utility.

As arylsuccinic acids are easily available in high yield by the addition of cyanide to the condensation products of aromatic aldehydes with cyanoacetic acid and its derivatives,[11] the dehydrogenation of these compounds with reagents other than positive halogen seemed worth pursuing. The well known ability of selenium dioxide to introduce a double bond in conjugation with 1,4-diketones[12] prompted an investigation of its application to the present problem.

It has been found that selenium dioxide in boiling acetic anhydride rapidly dehydrogenates arylsuccinic acids in high yield. The use of acetic anhydride as solvent makes it possible to use the free succinic acids as starting materials. Phenyl (IIa), *p*-methoxyphenyl- (IIb), and 3,4-methylenedioxyphenylmaleic anhydrides (IIc) were prepared in this way in yields of 86, 80, and 66%, respectively, from readily available acids (I). The first two anhydrides had properties in agreement with those described in the literature, while the third was identified by hydrogenation to the known succinic anhydride. 3,4-Methylenedioxyphenylmaleic anhydride (IIc) readily added butadiene to form the adduct III.

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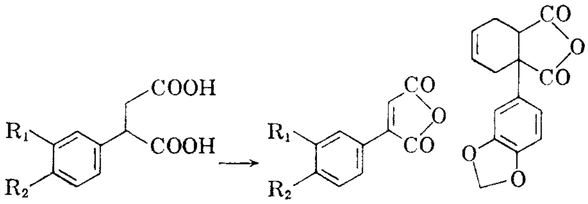

I II III

a. $R_1 = R_2 = H$
b. $R_1 = H; R_2 = CH_3O$
c. $R_1R_2 = —O—CH_2O—$

The aryl group appears to be essential to the success of the reaction, since under the same conditions, and even though selenium was deposited, only starting material could be recovered from the attempted dehydrogenation of succinic, ethylsuccinic, and 1,2-cyclohexanedicarboxylic anhydrides.[13]

EXPERIMENTAL

Melting points are uncorrected. Microanalyses were performed by Dr. W. C. Alford and his staff.

Phenylmaleic anhydride (IIa). A mixture of phenylsuccinic acid (4.9 g.), selenium dioxide (3.3 g.), and acetic anhydride (20 ml.) was refluxed for 3 hr., filtered hot through a sintered glass funnel, and the residue washed with a little ether. Concentration of the filtrate under reduced pressure and trituration of the residue with ether gave 3.8 g. (86%) of anhydride, m.p. 119–120.5° (lit.,[5] m.p., 119–119.5°). Recrystallization from benzene-hexane or sublimation *in vacuo* just below its melting point did not raise the melting point.

p-Methoxyphenylmaleic anhydride (IIb). A mixture of *p*-methoxyphenylsuccinic acid[11c,e] (33.5 g.), selenium dioxide (19 g.), and acetic anhydride (125 ml.) was refluxed for 30 min., then filtered hot through a sintered glass funnel; the residue was rinsed with a little chloroform. Concentration of the filtrate afforded a yellow solid, which was collected and washed with hexane and ether. The yield of crude anhydride was 24.5 g. (80%). Sublimation at 120–125° *in vacuo* and recrystallization from carbon tetrachloride gave light yellow crystals, m.p. 142.5–143.5° (lit.,[3,8e] m.p., 141.5–143.5°, 143–144°).

3,4-Methylenedioxyphenylmaleic anhydride (IIc). A mixture of 3,4-methylenedioxyphenylsuccinic acid[11b] (36.3 g.), selenous acid (21 g.), and acetic anhydride (250 ml.) was refluxed for 19 hr., filtered hot through a sintered glass funnel, and the residue washed with several portions of hot acetic anhydride. The filtrate was cooled well in ice and the yellow solid collected and washed with ether. The weight of crude product was 22.1 g. (66%). It could be purified by recrystallization from xylene or by sublimation at 150–170° (0.01 mm.), affording yellow needles, m.p. 210–211.5°.

Anal. Calcd. for $C_{11}H_6O_5$: C, 60.56; H, 2.77. Found: C, 60.25; H, 2.97.

Hydrogenation of the anhydride over palladium-charcoal in ethyl acetate solution resulted in the uptake of 1 mole of hydrogen, and yielded 3,4-methylenedioxyphenylsuccinic anhydride, m.p. 97–98° (lit.,[11c] m.p. 96°). Its identity with an authentic sample was shown by a mixed melting point determination and comparison of infrared spectra.

1-(3,4-Methylenedioxyphenyl)cyclohex-4-ene-1,2-dicarboxylic anhydride (III). A pressure bomb was charged with 809 mg. of resublimed 3,4-methylenedioxyphenylmaleic anhydride, 15 ml. of liquefied butadiene, 30 ml. of xylene, a pinch of hydroquinone, and heated for 40 hr. at 135°. After cooling, the bomb was emptied and rinsed with acetone, and the combined contents evaporated to dryness. The residue crystallized on trituration with dry ether, and was filtered and washed with ether, giving 744 mg. of crude anhydride. Recrystallization from ether gave 593 mg. of colorless needles, m.p. 113–113.5°.

Anal. Calcd. for $C_{15}H_{12}O_5$: C, 66.17; H, 4.44. Found: C, 66.01; H, 4.53.

Ethyl [α-cyano(3,4-dimethoxyphenyl)]pyruvate. A mixture of 3,4-dimethoxyphenylacetonitrile (18 g.), ethyl oxalate (30 g.), and sodium hydride (5.2 g.) in 250 ml. of ether was treated with two drops of ethanol, then refluxed with stirring for 19 hr. Ethanol was added to destroy unchanged sodium hydride, followed by enough water to dissolve the salts. The layers were separated and the aqueous layer washed twice with ether. The aqueous solution was then acidified in the cold with ice cold hydrochloric acid, and the solid product collected and washed with water. Recrystallization from benzene gave 26.4 g. (94%) of pale yellow needles, m.p. 140–141°. The compound gave a deep green color with ethanolic ferric chloride; its infrared spectrum in chloroform showed that it exists completely in the enol form.

Anal. Calcd. for $C_{14}H_{15}NO_5$: C, 60.64; H, 5.45; N, 5.05. Found: C, 60.42; H, 5.50; N, 4.95.

The keto group of the pyruvate could not be reduced catalytically or with sodium borohydride, and the compound did not form a cyanohydrin when treated with aqueous hydrogen cyanide.

α-Cyano-3,4-dimethoxyphenylacetaldehyde. To a mixture of 3,4-dimethoxyphenylacetonitrile (18 g.), ethyl formate (17 g.), and sodium hydride (5.1 g.) in 250 ml. of dry ether was added 2 drops of ethanol, and the mixture gently refluxed with stirring for 16 hr. The reaction mixture was worked up as described above for the oxalate condensation, and afforded 17.5 g. of colorless product. Recrystallized twice from benzene-hexane, it melted at 116.5–118°. The infrared spectrum in chloroform showed that the molecule exists completely in the enol form.

Anal. Calcd. for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.48; H, 5.59; N, 6.82.

An attempt to form a cyanohydrin by treatment with potassium cyanide and 1:1 hydrochloric acid was unsuccessful.

Bromination of 3,4-methylenedioxyphenylsuccinic anhydride. (a) *With N-bromosuccinimide.* 3,4-Methylenedioxyphenylsuccinic anhydride (1.10 g.), *N*-bromosuccinimide (0.886 g.), and benzoyl peroxide (9.8 mg.) were refluxed in 15 ml. of carbon tetrachloride for 8 hr. The solvent was evaporated in a stream of nitrogen, and the residue boiled for 10 min. with dilute potassium carbonate solution, stirred with charcoal, and filtered. Acidification of the filtrate gave a bromo acid (0.973 g.), which melted at 223–224° after recrystallization from boiling water.

Anal. Calcd. for $C_{11}H_9O_6Br$: C, 41.67; H, 2.86; Br, 25.20. Found: C, 41.78; H, 2.97; Br, 25.10.

(b) *With bromine.* A solution of 3,4-methylenedioxyphenylsuccinic anhydride (2.20 g.) in 10 ml. of tetrachloroethane was heated on the steam bath and treated dropwise with an equimolar amount of bromine in the same solvent. The solution was heated for 16 hr. and evaporated in a stream of nitrogen. The residue crystallized on trituration with ether-benzene, and was collected and washed with ether; yield, 1.68 g. Hydrolysis with 5% sodium hydroxide gave the same bromo acid as in (a), m.p. 232–233°.

Heating the crude bromoanhydride to reflux with 2,6-lutidine for 16 hr. failed to remove the halogen atom, and the bromo acid was recovered.

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[13] These experiments were performed by Mr. David Gordon.

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Reaction of Triphenyltin Hydride with Some Organic Halides and Amines

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The ability of triphenyltin hydride to convert organic halides and amines to the corresponding hydrocarbon and triphenyltin halide and hexaphenylditin, respectively, is a relatively new development in organotin chemistry.[1,2] In connection with a study of the stereochemistry of these reactions currently being carried out in these laboratories, it was necessary to see if triphenyltin hydride would satisfactorily react with *dl-α*-phenethyl chloride and *dl-α*-methylbenzylamine. It was also considered of interest to study the reaction of triphenyltin hydride with benzyl chloride and benzylamine.

The experimental procedure employed was similar to that reported for the reaction of triphenyltin hydride with allyl bromide and allylamine.[3] The reaction of triphenyltin hydride with benzyl chloride gave triphenyltin chloride (65.6%) and toluene (25.5%). With *dl-α*-phenethyl chloride there was obtained triphenyltin chloride (68.4%) and ethylbenzene (79.4%).

The reaction of triphenyltin hydride with benzylamine in the molar ratio of 2:1 gave hexaphenylditin (75.8%), toluene, and ammonia. With *dl-α*-methylbenzylamine there was obtained hexaphenylditin (52.7%) and ammonia.

The liquid products were isolated by distillation of the reaction mixture and were identified by the fact that their infrared spectra were superimposable upon those of authentic samples. No attempt was made to separate quantitatively the liquid product from the solid. In the case of benzylamine the mixture was distilled only until enough of the liquid was obtained for an infrared spectral determination. In the case of *dl-α*-methylbenzylamine, ethylbenzene was probably formed, but it was not isolated. In this reaction an amount of unchanged *dl-α*-methylbenzylamine was isolated which was consistent with the yield of hexaphenylditin. The solids were isolated as quantitatively as possible and were identified by the fact that admixture with authentic samples did not depress the melting points.

In each of the above reactions a small quantity of tetraphenyltin was isolated. This compound may have been formed from unchanged triphenyltin hydride during processing of the reaction mixture. It is reported that triphenyltin hydride is decomposed by air and by exposure to light with separation of tetraphenyltin.[4]

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. All the reactions were carried out in a nitrogen atmosphere.[5]

Reaction of triphenyltin hydride with benzyl chloride. Triphenyltin hydride[4] (30.0 g., 0.0854 mole) was added to a dry 50-ml. flask fitted with a Claisen head, thermometer, and condenser. Freshly distilled benzyl chloride (10.8 g., 0.0854 mole), b.p. 176°, was added in one portion, and the system was evacuated. The reaction mixture was placed under 1 atm. of nitrogen and then was heated with occasional shaking at 80° ± 5° for 4 hr. After 4 hr. a colorless crystalline material was evident in the reaction mixture.

The mixture was distilled at atmospheric pressure (pot temperature to 140°). The distillation was stopped when the residue began to turn brown. There was obtained 2.0 g. (25.5%) of toluene, b.p. 109–110°, infrared spectrum superimposable upon that of an authentic sample of toluene.

The brown residue was refluxed with two 25-ml. portions of diethyl ether, and the cloudy solution was filtered. The ether-insoluble material, m.p. 223–225°, weighed 1.5 g. Admixture with an authentic sample of tetraphenyltin did not depress the melting point. There was no metallic tin mixed with the product.

The ether solution was evaporated to dryness, and the crude product was recrystallized from ethanol. There was obtained 21.6 g. (65.6%) of triphenyltin chloride, m.p. 105–106°, melting point undepressed on admixture with an authentic sample of triphenyltin chloride.

Reaction of triphenyltin hydride with dl-α-phenethyl chloride. Triphenyltin hydride[4] (30.0 g., 0.0854 mole) was placed in a dry, 50-ml. flask equipped with a Claisen head, thermometer, and condenser. *dl-α*-Phenethyl chloride[6] (12.0 g., 0.0854 mole), b.p. 77–78° (17.5 mm.) [lit.[6,7] b.p. 78–82° (17 mm.), 74–75° (14 mm.)] was added in one portion, and the system was evacuated. The reaction mixture was placed under 1 atm. of nitrogen and heated to 80° ± 5°. After 1 hr. the temperature suddenly rose from 80° to 140°. The temperature rise was accompanied by heavy refluxing. The mixture was cooled to 40°, and when it failed to solidify, it was heated to 80° ± 5°. The mixture was maintained at this temperature, with occasional shaking, for 7 hr.

The mixture was distilled (pot temperature to 140°). The colorless distillate, b.p. 128° to 133°, weighed 7.2 g., and was redistilled. The fraction boiling at 131° to 133° was collected. The infrared spectrum of this material was superimposable upon that of an authentic sample of ethylbenzene, b.p. 134–136°.

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