Experimental Section

Laboratory-Scale Preparation of Diphosgene. Freshly distilled methyl chloroformate (1 L, 1223 g, 12.94 mol) was placed in a three-necked round-bottomed 3-L flask fitted with a gas inlet tube, an efficient reflux condenser,[9a] and a thermometer. The magnetically stirred solution was irradiated with an external UV flood lamp (Hanovia, 125 W) while dry chlorine[9b] was slowly introduced into the reaction mixture. After a brief induction period of up to 30 min, the decoloration of the yellow chlorine solution and the rising of the temperature both signify the starting of the exothermic chlorination reaction. The rate of addition of chlorine was gradually increased in order to maintain the reaction temperature in the range of 75–85 °C for approximately 35 h. Upon completion of the reaction,[9c] evident by the sharp drop in temperature, the mixture was carefully purged with dry nitrogen in order to remove unreacted chlorine, and then the product was distilled under reduced pressure [58 °C (69 mm)]. This procedure gave an 84% yield of diphosgene (1300 cm^3) containing trace amounts (<1%) of ClCOOCHCl$_2$. Further purification of the diphosgene can be achieved, if needed, by a repeated distillation using an efficient fractionating column.

Syntheses of Diisocyanoarenes. Preparation of 1,4-Diisocyanobenzene (Ib). Diphosgene (11.5 mL, 19 g 96 mmol) dissolved in dry dichloromethane (70 mL) was added dropwise, over a 2-h duration, into a boiling suspension consisting of *N*,-*N*′-diformyl-1,4-diaminobenzene (15 g, 91.5 mmol), triethylamine (70 mL) and dichloromethane (250 mL). After an additional 30 min of reflux, the reaction mixture was allowed to cool to ambient temperature before being washed with an aqueous 10% Na$_2$CO$_2$ solution (3 × 100 mL). The organic layer was dried over anhydrous MgSO$_4$ and then vacuum dried to afford a crude brown product. The crude material was purified on a neutral alumina oxide column, using dichloromethane–hexane (1:1, v/v) solvent mixture as an eluant. Recrystallization from the same solvent system gave 1,4-diisocyanobenzene (8.9 g) in 76% yield.

Essentially the same experimental procedure was also utilized for the preparation of 1,3-diisocyanobenzene (Ia), 4,4′-diisocyanobiphenyl (Ic), and 4,4′-diisocyanodiphenylmethane (Id). Data pertaining to the characterization of these compounds are furnished in Table I.

Acknowledgment. We are indebted to the KFA, NCRD, and the Minerva Foundation for partial financial support and to Dr. Hugo E. Gottlieb for assisting in the running of the ^{13}C NMR spectra.

Registry No. Ia, 626-17-5; Ib, 623-26-7; Ic, 1591-30-6; Id, 10466-37-2; IIa, 25227-79-6; IIb, 6262-22-2; IIc, 49645-23-0; IId, 52721-83-2; diphosgene, 503-38-8; methyl chloroformate, 79-22-1; chlorine, 7782-50-5.

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(9) (a) The top of the condenser should be connected to alkaline traps capable of absorbing the large volume of HCl gas which evolves during the reaction. (b) Chlorine used in this reaction was dried by passage through several gas-washing bottles containing concentrated H$_2$SO$_4$. (c) The progress of this reaction can coveniently be followed by ^{1}H NMR techniques. The chemical shifts (τ) of the precursors are ClCOOCH$_3$ (6.23), ClCOOCH$_2$Cl (4.43), and ClCOOHCl$_2$ (2.55).

Isobenzofuran: New Approaches from 1,3-Dihydro-1-methoxyisobenzofuran

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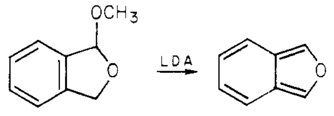
We have found that the strong base induced 1,4-elimination of allylic ethers is a general reaction,[2] and it was of interest to see if this method was capable of disrupting aromaticity. To this end, we chose first to examine the reactivity of 1,3-dihydro-1-methoxyisobenzofuran (**1**) and report here that **1** reacts readily with lithium diisopropylamide (LDA) to give reasonably stable solutions of isobenzofuran (**2**).

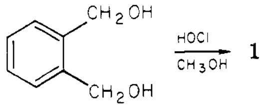


1 **2**

Other approaches to **2** have involved reverse Diels–Alder reactions;[3–5] of these only one[5,6] appears to be suitable for modest-scale preparations. The reaction reported here is the first ambient temperature synthesis and gives good yields (50–70%, not optimized) of **2** from a readily accessible starting material. The structure of **2** was confirmed by comparison with literature spectra and by reaction with maleic anhydride to give the previously reported Diels–Alder adducts.[7]

Solutions of **2** in benzene or ether are, in agreement with earlier reports, of moderate stability; 1.8% solutions had an approximate half-life of 6 days at room temperature. The reaction of **1** with LDA is quite rapid, and **2** appears to be stable toward further reaction with this base. Thus, holding the reaction mixture for 1 day at room temperature before quenching gave 80–90% of the yield of **2** found with quenching a few minutes after mixing, about the value anticipated from polymerization of **2** alone.

The starting material **1** was prepared by LiAlH$_4$ reduction of phthalide to phthalyl alcohol;[8] treatment of this diol in a two-phase system (pentane/methanol–sulfuric acid) with aqueous sodium hypochlorite solution (commercial laundry bleach) gave **1** in ca. 60% yield.



An alternative preparation of **1** has recently been reported by Tidwell and co-workers.[9]

Analysis of **1** by VPC at temperatures above 115 °C resulted in a minor shorter retention time peak that proved to be **2**. Also, distillation of **1** usually resulted in viscous pot residues. Refluxing a solution of **1** in toluene for 1 day caused loss of the material with formation of polymer. These observations suggested that **1** might be a convenient source of **2** by direct[10] elimination of methanol, and this was subjected to experimental test.

A solution of **1** with maleic anhydride in toluene was refluxed for 2 h. After evaporation of the solvent and washing of the resultant solid with chloroform, a quanti-

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[1] K.N. expresses his gratitude to Sanyo Chemical Industries, Ltd., of Japan for support during the course of this work.

[2] Unpublished work of B. Rickborn, B. H. Williams, K. Blonski, D. Svedberg, and T. Tuschka; portions of this work have been presented at the Pacific Conferences on Chemistry and Spectroscopy, San Diego, CA, Nov 1973, and Pasadena, CA, Oct 1979.

[3] R. N. Warrener, *J. Am. Chem. Soc.*, **93**, 2346 (1971).

[4] W. Wege, *Tetrahedron Lett.*, 2337 (1971).

[5] U. E. Wiersum and W. J. Mijs, *J. Chem. Soc., Chem. Commun.*, 347 (1972).

[6] A review of isobenzofuran chemistry has appeared recently: M. J. Haddadin, *Heterocycles*, **9**, 865 (1978).

[7] Wiersum and Mijs[5] reported that **2** and maleic anhydride gave an unseparated mixture of exo and endo adducts in quantitative yield.

[8] R. F. Nystrom and W. G. Brown, *J. Am. Chem. Soc.*, **69**, 1198 (1947).

[9] C. M. Rynard, C. Thankachan, and T. T. Tidwell, *J. Am. Chem. Soc.*, **101**, 1196 (1979).

[10] Whether these observations are associated with an uncatalyzed thermal elimination, or trace acid catalyzed reaction, has not been established.

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tative yield of Diels–Alder adducts of **2** was obtained. The reaction was also complete in refluxing benzene after 10 h. Similarly refluxing **1** with *N*-phenylmaleimide in toluene for 2 h gave adduct quantitatively.

These two facile and complementary routes (base-induced and direct) to isobenzofuran offer ready access to this reactive compound. Both methods can in principle be adapted to in situ formation of **2** with simultaneous formation of adducts. We are currently exploring these and related applications.

Experimental Section

1,3-Dihydro-1-methoxyisobenzofuran (1). A mixture of 2.0 g (0.015 mol) of *o*-phthalyldiol,[8] 80 mL of methanol, 3.4 mL of concentrated sulfuric acid, and 150 mL of pentane was vigorously stirred while 30 mL of 5.25% aqueous NaOCl (commercial laundry bleach) was added over a period of 8 h. After 24 h of additional stirring, the phases were separated, and the aqueous part was washed twice with small portions of pentane. The combined pentane solution was washed with aqueous bicarbonate and dried over potassium carbonate. Evaporation of the solvent gave an oil which was essentially pure **1**; vacuum distillation gave material with bp 32 °C (0.1 torr) in 65% yield. The spectral properties of **1** coincided with those reported by Tidwell.[9]

Isobenzofuran (2). To an ice-cooled solution of 1.43 g of diisopropylamine in 5 mL of benzene was added 6.7 mL of a 2.1 M hexane solution of *n*-butyllithium. The stirred LDA was allowed to warm to near room temperature, and then 0.8 g of **1** in 8 mL of benzene was added over a few minutes. After being stirred for an additional 5 min, the reaction mixture was quenched by adding an equal volume of aqueous NH_4Cl. The organic phase was separated and dried over sodium sulfate.

The yield of **2** in some runs was determined by VPC, using a tetramethylbenzene internal standard on an SE-30 column at 107 °C, conditions where no decomposition of **1** occurred. A sample for NMR analysis was also obtained by preparative VPC under these conditions, giving a spectrum identical with that reported by Warrener.[3] Yields were also determined by adding maleic anhydride to portions of the solutions of **2**; after standing at room temperature for a short time the solvents were removed in vacuo, and the crystalline products were washed with small volumes of cold chloroform. The resultant solids consisted only of Diels–Alder adducts (exo/endo ca. 1:1), as shown by NMR. Yields ranged from 60–69%.

The use of ether in place of benzene as solvent gave a somewhat lower yield (47%).

Allowing longer reaction time with LDA did not materially affect the yield, taking into account the inherent instability of **2**. A benzene–hexane solution of **2** (1.8%) kept at room temperature lost over 60% of **2** after 8 days; a portion of the same solution kept at −20 °C retained over 70% of the original **2** over this same time period. The addition of hydroquinone had little if any stabilizing influence on **2**.

Reaction of 1 with Maleic Anhydride. A mixture of 0.32 g of **1** and 0.50 g (2.3 equiv) of maleic anhydride in 20 mL of toluene was refluxed for 2 h, after which the solvent was removed by rotary evaporation. The crystalline residue was washed with small amounts of cold chloroform to remove the excess maleic anhydride, giving Diels–Alder adducts in essentially pure form (exo/endo = 4/5) and quantitative yield. Fair separation of the isomers was accomplished by dissolving 0.1-g samples in 3 mL of benzene and seeding with the visibly different crystals; on cooling overnight, material related to the seed formed on the walls of the test tubes. The exo product, with assignment based on the absence of bridgehead proton coupling, had mp ca. 212 °C. The endo isomer melted at 172 °C.

A similar reaction of **1** in refluxing benzene followed by NMR showed incomplete loss of **1** after 4 h; no further **1** was seen after 10 h.

N-Phenylmaleimide was also used in refluxing toluene, giving a quantitative yield of exo/endo (5:12) product after 2 h.

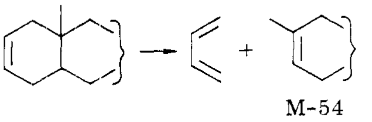
Registry No. 1, 67536-29-2; 2, 270-75-7; *o*-phthalyldiol, 612-14-6; maleic anhydride, 108-31-6.

Communications

Mass Spectra of Androstane-7,17-diones

Summary: Steroids with the 7,17-dione structure (**1**) undergo an unusual fragmentation process yielding an intense peak in the mass spectrum at M − 47 (M − CH_3O_2) regardless of the ring A substitution pattern.

Sir: During the period of rapid advances in the development of organic mass spectrometry, a report appeared[1] which stated that 5α-androst-2-ene-7,17-dione (**1**) was the sole exception to the rule that cyclohexenes would undergo the retro-Diels–Alder reaction[2] which can lead to a peak at M − 54 (loss of butadiene). This is shown in eq 1 for a typical Δ^2 steroid. It was noted that the bicyclic analogue **2** behaved normally as did 5α-androst-2-en-17-one.[3] These facts have been restated in publications dealing with mass spectrometry to this date.[4] The simplest explanation of the data would be that the compound thought to be the Δ^2-olefin was in fact some other compound, perhaps the Δ^3-olefin. (In this case, the retro-Diels–Alder reaction can occur but no fragmentation would be observed. The fragment ion would have the same mass as the parent ion.) Apparently, the sample used for this measurement[1] was obtained from a group of Czech chemists as their report[5]



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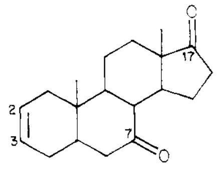
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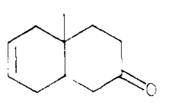
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(2) Budzikiewicz, H.; Brauman, J.; Djerassi, C. *Tetrahedron* **1965**, *21*, 1855.

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