ranging from 400 mg to 8 g of epoxide. The yield of benzocyclobutenol was generally in the 70–85% range.

In THF with the Order of Addition of $MgBr_2$ and *n*-BuLi Reversed. In these situations the $MgBr_2$ was added within 2–3 min after completion of the *n*-BuLi addition. The yield of benzocyclobutanol from *o*-bromostyrene oxide with this procedure was generally 65–75%.

(C) In Ether. When the reaction was carried out in ether the order of addition was *n*-BuLi followed by $MgBr_2$. In several experiments, *o*-bromostyrene oxide was converted to benzocyclobutenol in 60–70% yield via this method.

Benzocyclobutenol-*d*$_2$. *o*-Bromo-*β*,*β*-dideuteriostyrene (402 mg, 2 mmol) was reacted with 4 mmol of $MgBr_2$ and 2 mmol of *n*-BuLi in THF as outlined in procedure A. The yield of recrystallized (hexanes) benzocyclobutanol was 150 mg (62%). The NMR spectrum showed a ratio 2:1:1 for the *α* to *β*-cis to *β*-trans hydrogens.

Benzocyclobutenol from *o*-Iodostyrene Oxide. Iodo epoxide **2b** (1.3 g, 5.3 mmol) was dissolved in 30 mL of THF. $MgBr_2$ (10.8 mmol) was added and the solution cooled to −78 °C. The reaction mixture containing the suspended $MgBr_2$ was then treated with 5.8 mmol of *n*-BuLi, kept at −78 °C for 30 min, warmed to 0 °C, and worked up. Chromatography of the crude product gave 0.57 g (85%) of benzocyclobutenol, identical with the material obtained from **2a**.

4-Methoxybenzocyclobutenol. Iodostyrene oxide (**24**; 552 mg, 2.0 mmol) in 10 mL of anhydrous ether at −78 °C was treated first with 2.2 mmol of *n*-BuLi and then with 4 mmol of $MgBr_2$. The reaction mixture was warmed to room temperature and worked up, and the crude product was purified by silica gel chromatography (4:1 hexane–ethyl acetate). The yield of 4-methoxybenzocyclobutanol was 227 mg (76%): white needles; mp 39–42 °C; NMR δ 2.75 (1 H, OH), 2.94 (dd, J = 14.0, 1.0 Hz, 1 H), 3.50 (dd, J = 14.0, 4.5 Hz, 1 H), 3.76 (s, 3 H), 5.15 (dd, J = 4.5, 1 Hz, 1 H), 6.6–7.2 (m, 3 H); ^{13}C NMR δ 41.7, 55.4, 70.0, 108.9, 114.1, 123.6, 139.8, 143,4, 161.1; IR ($CHCl_3$) 3300–3600 cm^{-1} (br). Anal. Calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.71; H, 6.58.

Structure Elucidation. 4-Methoxybenzocyclobutenol was heated with 10 mL of ethanol and 1 mL of 50% NaOH solution for 2 h. Workup afforded an aldehyde (280 mg) which had NMR peaks at δ 2.63 (s, 3 H), 3.86 (s, 3 H), 6.73 (d, J = 2 Hz, 1 H), 6.80 (dd, J = 7, 2 Hz, 1 H), 7.73 (d, J = 7 Hz, 1 H), and 10.08 (s, 1 H). On air oxidation this aldehyde was converted in 4-methoxy-2-methylbenzoic acid, mp 175–177 °C (lit.[12] mp 175–177 °C).

4,5-(Methylenedioxy)benzocyclobutenol was prepared in 75% yield in ether as the reaction solvent: mp 118–120 °C; NMR δ 2.23 (1 H, OH), 2.83 (dd, J = 14.0, 1.0 Hz, 1 H), 3.41 (dd, J = 14.0, 4.5 Hz, 1 H), 5.10 (dd, J = 4.5, 1.0 Hz, 1 H), 5.87 (s, 2 H), 6.61 (s, 1 H), 6.71 (s, 1 H); IR ($CHCl_3$) 3200–3550 cm^{-1} (br); mass spectrum, m/e 164 ($M^{+\cdot}$). Anal. Calcd for $C_9H_8O_3$: C, 65.85; H, 4.91. Found: C, 65.49; H, 4.89.

1-Methylbenzocyclobutanol. This product was obtained in 35% and 34% isolated yields from *o*-bromo- and *o*-iodo-*trans*-*β*-methylstyrene oxide, respectively, by using THF as solvent and procedure B: mp 77–78 °C (lit.[7] mp 79–80 °C); ^{1}H NMR δ 1.63 (s, 3 H), 2.43 (1 H, OH), 3.15 (d, J = 14 Hz, 1 H), 3.32 (d, J = 14 Hz, 1 H), 7.0–7.3 (m, 4 H); ^{13}C NMR δ 25.6, 48.3, 78.2, 120.4, 124.0, 127.2, 129.3, 165.8; mass spectrum, m/e 134 ($M^{+\cdot}$).

1-Benzylbenzocyclobutanol. This product was obtained from 867 mg of 2-bromo-*trans*-*β*-benzylstyrene oxide by using THF as solvent (procedure B). The crude reaction product was separated by preparative TLC and gave, as the upper band, in 40% yield dibenzyl ketone (identified by comparison of its NMR and IR spectra with those of an authentic sample). The lower band was identified as the desired benzocyclobutenol: yield 40%; colorless oil; ^{1}H NMR 2.67 (1 H, OH), 3.17 (s, 2 H), 3.18 (d, J = 14 Hz, 1 H), 3.50 (d, J = 14 Hz, 1 H), 7.0–7.5 (m, 9 H); ^{13}C NMR δ 45.1, 46.8, 80.2 (nonaromatics); mass spectrum, m/e 210 ($M^{+\cdot}$).

Reactions of 2-Bromo- and 2-Iodo-*trans*-stilbene Oxide. The bromo epoxide (1.1 g, 4 mmol) was dissolved in 20 mL of THF at −78 °C and reacted sequentially with 4 mmol of *n*-BuLi followed by 8 mmol of $MgBr_2$ solution. The reaction mixture was allowed to warm to room temperature and then worked up. The yield of isolated *trans*-stilbene oxide [NMR δ 3.87 (s, 2 H), 7.3 (s, 10 H)] was 543 mg (70%). A similar result was obtained when 2-iodo-*trans*-stilbene oxide was employed.

When the above reaction was carried out on 3 mmol of bromo epoxide in 30 mL of ether with 3 mmol of *t*-BuLi for the halogen–lithium exchange, deoxybenzoin (510 mg, 87%) was obtained after chromatography.

Acknowledgment. The continued financial assistance of NSERC (Canada) is gratefully acknowledged.

Registry No. **1**, 35447-99-5; **1**-*2,2*-d_2, 77287-55-9; *cis*-**1**-*1,2*-d_2, 77287-56-0; *trans*-**1**-*1,2*-d_2, 77287-57-1; **2a**, 71636-51-6; **2a**-*β*,*β*-d_2, 72525-55-4; **2b**, 72525-47-4; **7** (X = I; R = 5-OMe), 77287-58-2; **7** (X = I; R = H), 26260-02-6; **7** (X = Br; R = H), 6630-33-7; **7** (X = Br; R = 3,4-OCH_2O), 56008-63-0; **7** (X = R = H), 100-52-7; **8** (R = H) Cl^-, 3086-29-1; **8** (R = C_6H_4-*o*-Br) Br^-, 77287-59-3; **8** (R = H) I^-, 2181-42-2; **8** (R = Ph) Cl^-, 14182-14-0; **8** (R = C_6H_4-*o*-I) Br^-, 77287-60-6; **9** (X = Br; R = 3,4-OCH_2O; R^1 = H), 77287-61-7; *trans*-**9** (X = Br; R = H; R^1 = Me), 77287-62-8; *trans*-**9** (X = I; R = H; R^1 = Me), 77287-63-9; *trans*-**9** (X = Br; R = H; R^1 = CH_2Ph), 77287-64-0; **10a** (X = Br), 71095-28-8; *cis*-**11**, 77287-65-1; **12**, 72525-54-3; **13**, 19164-60-4; **15**, 77287-66-2; **16**, 102-04-5; **18**, 77287-67-3; *trans*-**19** (X = Br), 77287-68-4; *trans*-**19** (X = I), 77287-69-5; *trans*-**20**, 1439-07-2; **22**, 451-40-1; **24**, 72525-51-0; **25**, 72525-53-2; acetaldehyde, 75-07-0; 2-bromoacetophenone, 2142-69-0; 2-bromo-*cis*-*β*-methylstyrene, 31026-78-5; ethylidinetriphenylphosphorane, 1754-88-7; phenylacetaldehyde, 122-78-1; methyl *o*-methylbenzyl sulfide, 5925-79-1; 4-methoxy-2-methylbenzaldehyde, 52289-54-0; 4-methoxy-2-methylbenzoic acid, 6245-57-4; 4,5-(methylenedioxy)benzocyclobutenol, 77287-70-8.

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[12] P. Hill, W. F. Short, H. Stromberg, and A. E. Wiles, *J. Chem. Soc.*, 510 (1937).

1-Methoxyisobenzofuran: Formation from 1,3-Dihydro-1,1-dimethoxyisobenzofuran

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Received December 8, 1980

1-Methoxyisobenzofuran is formed by treatment of 1,3-dihydro-1,1-dimethoxyisobenzofuran with either a trace of acetic acid in refluxing toluene or with LDA at 70 °C. The requirements to obtain Diels–Alder adducts under both sets of conditions are examined, and various products are characterized.

We have recently reported the formation of isobenzofuran **2** from **1** using either strong base conditions (where solutions of **2** may be isolated) or in direct reaction with maleic anhydride, where **2** is implicated as a transient

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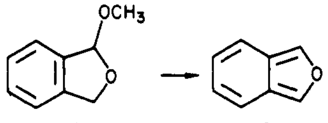
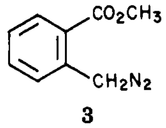
intermediate.[1]



1 2

It was of interest to extend these methods to substituted isobenzofurans (IBF). The 1-alkoxyisobenzofuran is an especially attractive goal since Diels–Alder adducts would contain the reactive ketal function. There is little earlier work on these materials. Hamaguchi and Ibata[2] have proposed the formation of 1-methoxyisobenzofuran (4)



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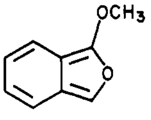

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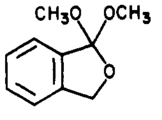
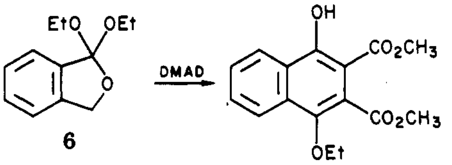


5

from the Cu-catalyzed decomposition of diazo ester 3; this suggestion was based on the products formed under varying reaction conditions. These authors also identified, by NMR, the previously unknown ortho ester 5 when the decomposition was carried out in the presence of methanol.

In work which is more directly related to part of that described here, MacLean and co-workers[3] have reported sealed-tube reactions of the ortho ester 6 ($CHCl_3$, 140–150 °C) with reactive dienophiles; 1-EtO-IBF was proposed as a transient intermediate. Although Diels–Alder adducts per se were not isolated, substituted naphthalenes and dihydronaphthalenes presumed to arise from the adducts were obtained, e.g., from dimethyl acetylenedicarboxylate (DMAD).

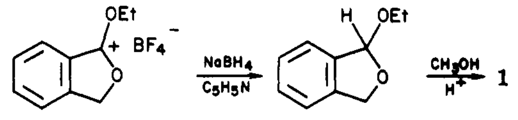


6

Results and Discussion

We chose to focus on 1,3-dihydro-1,1-dimethoxyisobenzofuran (5) as a starting material since the methoxy group offered prospective facile analysis of product formation by NMR. An attempt to methylate phthalide by using trimethyloxonium fluoborate failed,[4] precluding formation of 5 by a route directly analogous to Meerwein's synthesis[5] of the diethyl ortho ester 6. An alternative and satisfactory synthesis of 5 was developed by using the literature method to 6 and then transorthoesterifying in methanol with a trace of weak acid.

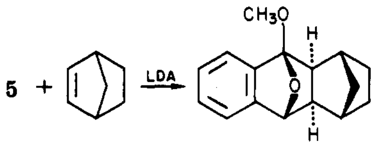
Since it was of interest to determine differences in reactivity of 1-methoxyisobenzofuran (4) and unsubstituted IBF (2), we also devised an alternative procedure to 1 via the ethyl analogue 8. Treatment of the Meerwein salt 7 with $NaBH_4$ in ethanol gave a mixture of 8 and 6. To avoid this competing solvolysis, the use of dimethoxyethane as solvent was tried, but this led to exclusive formation of phthalan, presumably by diborane reduction of 8. The use of pyridine as a solvent avoided this overreduction; relatively unreactive pyridine–borane complex is known to form under these conditions.[6] Although yields of 8 are modest with this procedure, its simplicity makes it a preferred route. The acetal 8 can be used directly to form IBF or converted to 1 by treatment with methanol and acid catalyst.



7 8

(a) Strong Base Induced Reactions. Attempts were made to form solutions of 1-methoxyisobenzofuran (4) by treatment of 5 with lithium diisopropylamide (LDA), but these led only to formation of tarry residues. However, slow inverse addition of LDA to a solution of 5 and excess norbornene in hexane gave crude product in good yield.

The NMR spectrum of this material indicated that it was a mixture of exo,exo isomer 9 and endo,exo isomer; the latter proved to be impossible to isolate because of facile hydrolysis, but its presence is strongly supported by the appearance of two sharp peaks in the aromatic region (9 has only one), by an apparent benzylic doublet (one leg falling under the benzylic singlet of 9), and most conclusively by a pair of doublets at 0.11 and −1.45 ppm (see the discussion of product 11 below). Hydrolysis of the endo,exo isomer occurred on all chromatography attempts. The difference in reactivity between 9 and the endo,exo isomer has some parallel in the work of Wittig and Reuther.[7] Compound 9 was easily obtained in pure form by column chromatography provided care was taken to maintain neutral or mildly basic conditions. The exo,exo structure of 9 is based on the absence of significant coupling of the benzylic protons and the known propensity of norbornene to undergo cycloadditions exclusively at the exo face.[8]



9

In order to examine the question of cycloaddition selectivity under analogous conditions, we also examined the base-induced reaction of the acetal 8 with norbornene. Two isomeric Diels–Alder adducts were cleanly separated by silica gel chromatography, giving a ratio of 10/11 of 2/1, in an overall 44% yield. The major isomer 10 was iden-

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[1] K. Naito and B. Rickborn, *J. Org. Chem.*, **45**, 406 (1980). An exhaustive review of IBF chemistry has recently appeared: W. Friedrichsen, *Adv. Heterocycl. Chem.*, **26**, 135–24 (1980).

[2] M. Hamaguchi and T. Ibata, *Chem. Lett.*, 287 (1976). The ortho ester 5 was identified by NMR of a mixture, without purification.

[3] L. Contreras, C. E. Slemon, and D. B. MacLean, *Tetrahedron Lett.*, 4237 (1978). Full papers on this work have recently appeared: L. Contreras and D. B. MacLean, *Can. J. Chem.* **58**, 2573, 2580 (1980). For related work on IBF via an acetal, see B. A. Keay, D. K. W. Lee, and R. Rodrigo, *Tetrahedron Lett.*, 3663 (1980).

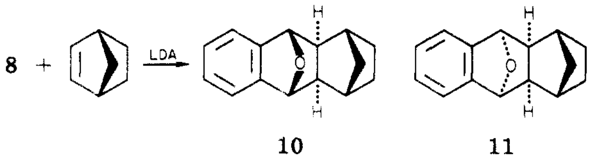
[4] Very few lactones (and apparently no esters) have been alkylated by using Meerwein's procedure.[5] The successful instances may reflect solubility differences more than intrinsic reactivity. See also H. Perst, "Oxonium Ions in Organic Chemistry", Verlag Chemie/Academic Press, Weinheim/Bergstr., Germany, 1971.

[5] H. Meerwein, P. Borner, O. Fuchs, H. J. Sasse, H. Schrodt, and J. Spille, *Chem. Ber.*, **89**, 2060 (1956).

[6] M. R. Johnson and B. Rickborn, *Org. Synth.*, **51**, 11 (1971).

[7] G. Wittig and W. Reuther, *Justus Liebigs Ann. Chem.*, **761**, 20–4 (1972). Two isomers were obtained in the Diels–Alder reaction of 1,4-dihydro-1,4-oxanaphthalene with *N*-methylisoindole. The exo,exo isomer failed to react with methyl iodide.

[8] For a recent discussion of the reactivity of norbornene in cycloadditions see R. Huisgen, P. H. J. Ooms, M. Mingin, and N. L. Allinger, *J. Am. Chem. Soc.*, **102**, 3951 (1980); we have also found that *o*-xylylene adds exclusively to the exo face of norbornene (unpublished work with T. Tuschka).

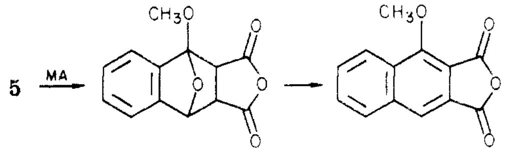


10 11

tified as exo,exo on the basis of the negligible coupling of the benzylic protons. The minor isomer **11** has the endo,exo structure shown; it exhibits the same kind of AA′BB′ pattern of the benzylic protons as observed in the endo adduct of **2** with maleic anhydride (MA).[1] Compelling evidence for this structure is the strong shielding experienced by the norbornyl methylene protons, which appear at 0.11 and −1.56 ppm as doublets with $J = 11$ Hz, further broadened, for the anti and syn protons, respectively.[9]

Since we were unable to isolate solutions of **4** under conditions where reasonably stable dilute solutions of **2** were obtained, we conclude that **4** is significantly more reactive than **2** in self-condensation or polymerization. The formation of Diels–Alder adduct **9** shows that **4** is formed as a transient intermediate in the strong base conditions. Although only the single isomer **9** could be isolated in this reaction, the crude product contained significant amounts of both exo,exo and endo,exo material; i.e., the reactions of **4** and **2** exhibit similar low endo/exo cycloaddition selectivity.

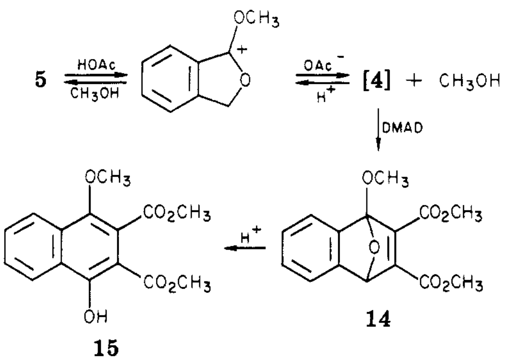
(b) Acid-Catalyzed Reactions. The reaction of acetal **1** with MA proceeds without added catalyst upon heating.[1] Ortho ester **5** behaves analogously; when a solution of **5** and MA in toluene is refluxed, aliquots withdrawn in the first few hours indicate the formation of intermediates, identified as *exo*- and *endo*-**12** by NMR, which subsequently undergo opening and elimination to form the known[10] **13** in good yield. An attempt was made to stop the reaction at **12** by using refluxing benzene as the solvent, but even at this lower temperature the rate of conversion of **12** to **13** competes with that of the initial reaction.

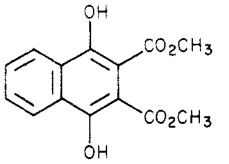


12 13

The reaction of **5** with DMAD was examined in detail. Unlike the reaction with MA, no loss of starting materials was detected in refluxing toluene for several days. When a trace of glacial acetic acid was added, however, the reaction was complete within 72 h. Interestingly, the use of trifluoroacetic acid or methanesulfonic acid in place of acetic acid failed to catalyze the reaction. This suggests that the conjugate base plays an important role in the generation of **4** from **5** (presumably trace amounts of maleic acid in the MA sequence function in the same manner). A mechanistic scheme that accommodates these and other observations discussed below is illustrated in Scheme I. In this instance it was possible to slow the conversion by using benzene (28 h) to obtain crude **14** containing very little **15**. Efforts to purify this material by chromatography were unsuccessful, because of hydrolysis on the columns used. The known[11] product **16** was obtained in this manner. The structure **14** thus rests on its NMR spectrum, three equal area methoxy peaks and a characteristic benzylic proton absorption. Conversion to **15** in the higher boiling solvent occurs cleanly.

Scheme I





16

The base-induced reaction demonstrated that **4** gives a Diels–Alder adduct with the poorer dienophile norbornene. It was therefore of interest to see if this cycloaddition would occur under the acid-catalyzed conditions. Six days of reflux in toluene containing a trace of AcOH and excess norbornene failed to give observable reaction. In the hope of driving the equilibria shown in Scheme I to the right, another attempt was made with norbornene, AcOH, and sufficient acetic anhydride to trap the methanol liberated in this process. While the latter goal was apparently achieved, no evidence of Diels–Alder reaction was observed. Instead, the NMR spectra of the crude product and chromatographed fractions indicated some loss of methoxy protons and addition of an acetoxy group (singlet at 2.0 ppm). It appears that the activation energy for Diels–Alder reaction with norbornene is significantly higher than those for readdition of methanol or reaction with acetic acid; even though the latter processes are presumed to be reversible, the concentration of free **4** must be insufficient to give measurable cycloaddition with poor dienophiles under these conditions. Presumably this situation could be altered by using a different trapping agent for methanol—one that does not itself add to the IBF or intermediate carbonium ion—or by carrying out the reactions at higher temperatures. Further work along these lines is planned, since the acid-catalyzed procedure offers some obvious advantages over the base-induced method, in particular allowing greater variation in dienophile functionality.

Other reactive dienophiles have also been employed. Dimethyl fumarate reacts more rapidly than dimethyl maleate,[12] the latter so sluggishly that the major product observed is the naphthalene derivative **18**. The fumarate reaction was halted at the ketal stage, and while the product **17** has not been fully characterized, its NMR

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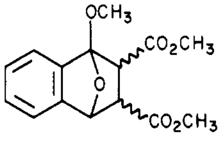
(9) Unpublished work of Professor D. H. Aue and A. J. Kos: A. J. Kos, Ph.D. Dissertation, University of California, Santa Barbara, 1978. Identification of the higher field proton as syn to the aromatic ring is based on analogy with examples found in this reference, where different substitution patterns allowed unambigous assignment.

(10) B. Sket, M. Zupan, and A. Pollak, *J. Heterocycl. Chem.*, 13(3), 671 (1976). We thank Professor Zupan for sending us comparison spectra for **13**. See also Z. Horii, T. Katagi, Y. Tamura, and T. Tanaka, *Chem. Pharm. Bull.*, 10, 887 (1962).

(11) C. W. Bird, C. K. Wong, D. Y. Wong, and F. L. Koh, *Tetrahedron*, 32, 269 (1976).

(12) R. Huisgen, R. Grashey, and J. Sauer in "Cycloaddition Reactions of Alkenes", "The Chemistry of Alkenes", S. Patai, Ed., Interscience, New York, 1964, p920.



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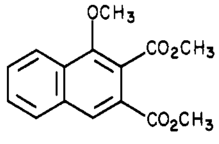
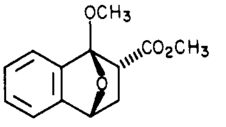


18

shows six methoxy singlets attributable to endo and exo addition; the ratios suggest about 4/1 selectivity, of unspecified geometry. The small amount of ketal seen in the maleate reaction exhibits slightly different chemical shifts in the benzylic region, implying no crossover between maleate and fumarate. The diester **18** was characterized by alternative synthesis from the anhydride **13**.

The question of regioselectivity was examined by using methyl acrylate and α-chloroacrylonitrile. The ester reaction was slow and led to a mixture of ketal and various hydrolysis and aromatized products which were incompletely separated by chromatography. One fraction solidified and on recrystallization gave ketal, the NMR of which is best accomodated by structure **19**; the highest field signal resembles a doublet of triplets, a reasonable pattern for the *exo*-methylene proton (large geminal and syn coupling and smaller coupling to the benzylic proton). A small amount of hydrolysis product **20** was also isolated, with structure assigned by spectral means, in particular the characteristic low-field hydrogen bonded enol absorption. The naphthalene derivative **21** exhibited only two methoxy signals in its NMR, but this proved deceptively simple. Saponification of combined chromatography fractions which differed only in the aromatic region gave a mixture of acids (1-methoxy- and 4-methoxy-2-naphthoic), showing that, in fact, the reaction was not totally regioselective. Finally, stripping the chromatography column with methanol gave a substantial amount of material tentatively identified as **22**.



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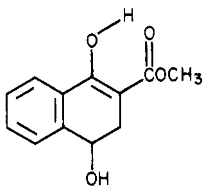

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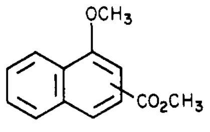

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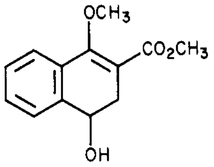
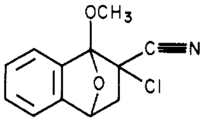


22

The reaction between ortho ester and α-chloroacrylonitrile was much cleaner, giving a high yield of exo and endo ketal products **23** as the only observable products.



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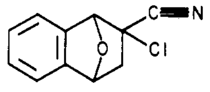
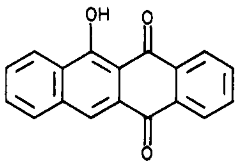


24

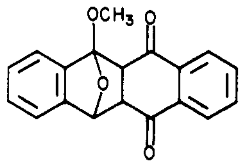
The more rapidly eluted isomer was obtained as a slightly impure viscous liquid, characterized by NMR to establish its regiochemistry. The second isomer was obtained as a sharp-melting solid that has been fully characterized except for some uncertainty remaining as to its designation as having the cyano group exo. This assignment is based on its NMR; the downfield methylene proton is a doublet of doublets (geminal and benzylic coupling), while the higher field proton occurs as a simple doublet (geminal coupling). Dihedral angle arguments indicate that bridgehead coupling should be greater with the exo than with the endo proton.

The acetal **8** gives **24** in analogous fashion. Here also one solid isomer was isolated in pure form and the other characterized only by NMR.

The reaction of the ortho ester **5** with 1,4-naphthoquinone occurs readily in refluxing toluene. When the mixture cooled orange crystals (10%) precipitated which proved to be the known[13] hydroxyquinone **25**. In addition, 40% of a yellow solid was obtained by column chromatography. The sharp melting point and certain features of its NMR spectrum suggest that this material is a single isomer (exo or endo) of the ketal structure **26**. This assignment is supported by the position of the benzylic proton (6.3 ppm), which occurs as an apparent triplet. A corresponding apparent doublet due to the two protons adjacent to the carbonyl groups occurs at unusually low field (4.3 ppm). The IR spectrum of **26** is devoid of absorption in the hydroxyl region (no conversion to hydroquinone tautomer) but exhibits another unusual feature in the carbonyl stretching frequency (1724 cm^{-1}). The coupling in the NMR would seem best fit by the endo structure for **26**, and models suggest that distortion of the dione ring may result in noncoplanarity of the aromatic ring with the adjacent carbonyl groups, which might account for the unusually high IR frequency observed. It is difficult to reach any other structural assignment given overall spectral features.



25



26

In addition to these products, the reaction with naphthoquinone gave on chromatography very dark blue material which has not been characterized.

In summary, ortho esters derived from phthalide offer convenient access to 1-alkoxyisobenzofuran, either through strong base induced 1,4-elimination or by carboxylic acid catalyzed reaction. This reactive intermediate can be trapped with dienophiles, leading to ketals or derived aromatic products. The Diels–Alder reactions are regioselective, a feature which can in principle be used to control the placement of more remote substituents. These and related applications are being explored currently.

Experimental Section

Melting points were taken on a Mel-Temp apparatus in open capillary tubes and are uncorrected. ^{1}H NMR spectra were obtained on a Varian T-60 and are reported in parts per million from Me$_4$Si. IR spectra were recorded on a Perkin-Elmer 283 instrument. Elemental analyses were carried out by Galbraith Laboratories. All reactions were done under nitrogen.

1,3-Dihydro-1,1-dimethoxyisobenzofuran (5). A mixture of 5.0 g of **6**,[5] 40 mL of anhydrous methanol, and 5 drops (ca. 25 mg) of glacial acetic acid was stirred at room temperature for 1 h. The mixture was then poured into 50 mL of 5% aqueous carbonate solution and extracted five times with small volumes of CH$_2$Cl$_2$. The combined organic phase was dried over K$_2$CO$_3$,

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(13) R. E. Winkler, *Helv. Chem. Acta*, **50**, 2497 (1967). This author reports a melting point of 310 °C for **25** after repeated recrystallization. D. H. R. Barton, J. H. Bateson, S. C. Datta, and B. D. Magnus, *J. Chem. Soc., Perkin Trans. 1*, 503 (1976). These authors obtained material with a melting point of 268–270 °C.

evaporated, and distilled [bp 115 °C (13 torr)]. Yields ranged from 65% to 93% in several runs: ^{1}H NMR (CCl_4) δ 7.1–7.4 (m, 4, aromatic), 4.98 (s, 2, benzylic), 3.2 (s, 6, OCH_3). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.56; H, 6.74.

1,3-Dihydro-1-ethoxyisobenzofuran (8). Phthalide was ethylated according to Meerwein's procedure.[5] This salt (25 g) was added rapidly in small batches to an ice-cooled, well-stirred mixture of 5.0 g of $NaBH_4$ in 80 mL of pyridine. The mixture was then taken up in water and extracted four times with pentane. The organic phase was washed several times with small amounts of 5% HCl and once with bicarbonate solution and then dried over K_2CO_3. Vacuum distillation gave 4.7 g (29%) of **8**, bp 57–60 °C (0.1 torr). The yields ranged from 20–40% in repeated runs and were generally lower when the acid-washing step was omitted: ^{1}H NMR (CCl_4) δ 7.2 (m, fairly sharp, 4, aromatic), 6.05 (d, CHOEt, J = 2.0 Hz), 5.25 and 5.05 (dd, 1, B part of AB q of $ArCH_2$, J = 2.0 Hz), 4.98 and 4.78 (d, 1, A part of AB q), 3.64 (m, approx dq, 2, OCH_2CH_3, J = 7 Hz), 1.18 (t, 3, J = 7 Hz). Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.38. Found: C, 72.97; H, 7.48.

Base-Induced Reaction of 8 and Norbornene. LDA solutions were prepared in hexane under N_2 in a mechanically stirred flask by adding 4 mL of 1.6 M *n*-BuLi to diisopropylamine (0.80 mL, 0.60 g). After the mixture was stirred for 15 min at room temperature, additional hexane (5 mL) was added to give a clear, nearly colorless solution. This was drawn into a syringe and added slowly (syringe pump) to a mixture of **8** (0.50 g), 5.0 g of norbornene, and 1.5 mL of hexane heated to approximately 70 °C. The base was added at a rate of 2.5 mL/h. The total addition and reaction time was 4.5 h. Water (10 mL) was added, and the mixture extracted five times with ether. The organic phase was dried over K_2CO_3 and vacuum evaporated to remove most of the norbornene. The residue was chromatographed on silica gel (20 g) by using a graded elution from pentane to neat CH_2Cl_2; the products were obtained at nearly a 1:1 solvent ratio.

The exo,exo isomer **10** had the following: mp 96–97 °C; 190 mg (67% of the total yield of 44%); ^{1}H NMR (CCl_4) δ 7.0 (narrow m, 4, aromatic), 4.98 (s, 2, benzylic), 0.8–2.4 (m, 10, norbornyl). Anal. Calcd for $C_{15}H_{16}O$: C, 84.87; H, 7.60. Found: C, 84.98; H, 7.60.

The endo,exo isomer **11** had the following: yield 93 mg; mp 124–125 °C; ^{1}H NMR (CCl_4) δ 7.0 (sharp s, 4, aromatic), 5.02 (m, $W_{1/2}$ = 7 Hz, 2, benzylic), 0.85–2.0 (m, 8, norbornyl), 0.11 (d, J = 11 Hz, 1, anti proton of norbornyl bridging CH_2), –1.56 (d, J = 11 Hz, 1, syn proton). Anal. Found: C, 85.00; H, 7.66.

LDA-Induced Reaction of 5 with Norbornene. The reaction was carried out as described above with 0.50 g of **5** and quenching of the reaction as soon as syringe pump delivery was completed. The crude yields in several runs were high. The ^{1}H NMR spectrum of the crude product showed the presence of both exo,exo, and endo,exo isomers, in roughly equal amounts. The endo,exo isomer was confirmed only by NMR, exhibiting broadened doublets at 0.11 and –1.45 ppm (J = 11 Hz). All attempts to isolate this isomer failed; even triethylamine-treated solvent on Florisil caused apparent hydrolysis.

The exo,exo isomer **9** was obtained by chromatography on neutral alumina (or better by using Florisil) with pentane/CH_2Cl_2 (80–20) containing a trace of triethylamine. The isolated yield was 127 mg (19%): mp 59–61 °C; ^{1}H NMR (CCl_4) δ 7.1 (s, 4, aromatic), 4.97 (s, 1, benzylic), 3.52 (s, 3, OCH_3), 2.58 (m, 1, norbornyl bridgehead), 2.37 (m, 1, norbornyl bridgehead), 0.76–1.6 (m, 8, norbornyl). Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.50; H, 7.54.

Stripping the chromatography column with CH_2Cl_2 containing 1–2% methanol gave material lacking a methoxy singlet in the NMR and exhibiting hydroxyl and carbonyl absorption in the IR, suggesting hydrolysis of the ketal function.

Reaction of 5 with MA. A mixture of 0.50 g of **5** and 0.27 g (1 equiv) of MA in 5 mL of toluene was refluxed for 24 h. Vacuum evaporation of the solvent gave 0.60 g (94%) of crude solid product. Recrystallization from toluene gave **13**:[10] mp 195–197 °C; 75% yield. This material exhibits an unusually low-field methoxy group in its ^{1}H NMR spectrum (4.48 ppm).

1-Hydroxy-4-methoxy-2,3-bis(methoxycarbonyl)naphthalene (15). A mixture of 0.50 g of **5**, 0.40 g (10% excess) of DMAD, and 3 drops of glacial acetic acid in 5 mL of toluene was refluxed for 3 days. The progress of the reaction was monitored by NMR, which showed the formation of the ketal intermediate and slower conversion to **15**. The mixture was vacuum evaporated, and on being allowed to stand deposited crystals. Recrystallization from petroleum ether gave 338 mg (42%) of **15**: mp 84–85 °C; ^{1}H NMR (CCl_4) δ 11.84 (s, 1, OH), 7.45–8.6 (m, 4, aromatic), 3.86, 3.89, and 3.94 (3 s, 3 H each, OCH_3 groups). Anal. Calcd for $C_{15}H_{14}O_6$: C, 62.07; H, 4.86. Found: C, 62.15; H, 4.98.

Identical reaction mixtures in which the acetic acid was replaced by trifluoroacetic acid and methanesulfonic acid (3 drops each, respectively) showed no loss of starting material by NMR after 3 days. Addition of 3 drops of acetic acid to the mixture containing trifluoroacetic acid caused a reaction as described above, without a significant change in rate.

Use of otherwise identical conditions but with refluxing benzene as solvent gave, after 28 h, crude product in high yield which consisted mainly of the Diels–Alder intermediate **14**. Attempts to isolate this product by silica gel chromatography were unsuccessful; the hydrolysis product **16**[11] (mp 114–115 °C) was obtained in this way. The ^{1}H NMR of the crude ketal **14** exhibited a narrow multiplet centered at 7.25 (4, aromatic) ppm, a singlet benzylic proton at 5.70 ppm, and three equal-area methoxy singlets at 3.85, 3.82, and 3.79 ppm.

Reaction of 5 with Dimethyl Maleate. A mixture of 0.50 g of **5**, 0.40 g of dimethyl maleate, and 3 drops of glacial acetic acid in 5 mL of toluene was refluxed for 6 days; the reaction was still incomplete at this time. Chromatography on 20 g of silica gel afforded a small amount (27 mg) of ketal, characterized by NMR only (benzylic proton at 5.62 ppm and methoxy peaks 3.5–3.7 ppm), and 80 mg of 1-methoxy-2,3-bis(methoxycarbonyl)naphthalene (**18**): ^{1}H NMR (CCl_4) δ 7.35–8.25 (m, 5, aromatic), 3.98 (s, 3, OCH_3), 3.90 (s, 6, 2 OCH_3). Treatment of anhydride **13** with refluxing methanol containing a few drops of sulfuric acid gave diester identical with **18**.

Reaction of 5 with Dimethyl Fumarate. Refluxing for 30 h in benzene solvent was sufficient for complete reaction, giving after chromatography on silica gel 0.417 g (55%) of ketal products. The ^{1}H NMR of this material indicated that it was a mixture of isomers (ca. 85/15) and was not significantly separated by chromotography. The aromatic region showed a multiplet centered at 7.2 ppm, while the benzylic proton appeared as a singlet at 5.35 ppm, broadened at the base. The methoxy region exhibited three equal-area major singlets at 3.75, 3.60, and 3.46 ppm and three minor singlets (again all equal area) at 3.72, 3.52, and 3.42 ppm. This ketal mixture is a viscous liquid that has not been further characterized.

Reaction of 5 with α-Chloroacrylonitrile. Refluxing 0.50 g of **5** with 0.24 g of α-chloroacrylonitrile in toluene for 48 h gave crude adduct on vacuum evaporation of the solvent in quantitative yield. Rapid chromatography on silica gel with CH_2Cl_2 solvent gave partial separation of isomers; repetition with 1:1 pentane/CH_2Cl_2 gave 144 mg of a viscous liquid: ^{1}H NMR (CCl_4) δ 7.2–7.5 (br m, 4, aromatic), 5.30 (d, J = 5.5 Hz, benzylic), 3.66 (s, 3, OCH_3), 2.88 (dd, J = 13 and 5.5 Hz, 1 H, methylene), 2.43 (d, J = 13 Hz, 1 H methylene). The later-eluted isomer (163 mg) solidified on evaporation of the solvent: mp 104–106 °C; ^{1}H NMR (CCl_4) δ 7.2–7.5 (m, 4, aromatic), 5.35 (d, J = 5.5 Hz, benzylic), 3.68 (s, 3, OCH_3), 3.36 (dd, J = 13 and 5.5 Hz, 1 H, methylene), and 1.97 (d, J = 13 Hz, 1 H methylene). Anal. Calcd for $C_{12}H_{10}ClNO_2$: C, 61.16; H, 4.28. Found: C, 61.32; H, 4.37.

The solid isomer is presumed to have the *exo*-cyano (*endo*-chloro) structure on the basis of the chemical shifts of the methylene protons.

In other runs with these materials, it was found that the solid isomer crystallized from the evaporated crude product on being allowed to stand for several days. Hexane was a suitable solvent for recrystallization.

Reaction of 8 with α-Chloroacrylonitrile. Refluxing for 8 h in toluene was sufficient to cause acid-catalyzed reaction between **8** (0.51 g) and α-chloroacrylonitrile (0.27 g), giving adduct **24** in an overall 73% yield. Silica gel chromatography (graded elution, pentane through CH_2Cl_2) gave a small amount of nearly pure liquid isomer: ^{1}H NMR (CCl_4) δ 7.3 (m, 4, aromatic), 5.45 (d, J = 5 Hz, 1 H, and overlapping s, 1 H, benzylic protons), 2.68 (dd, J = 14 and 5 Hz, 1 H methylene), 2.28 (d, J = 14 Hz, 1 H, methylene). This was followed by a major amount of the product as a mixture of the two isomers and finally the presumed *exo*-

cyano isomer: mp 57–60 °C; ^{1}H NMR (CCl_4) δ 7.3 (m, 4, aromatic), 5.45 (d, J = 5 Hz, 1 H, and overlapping s, 1 H, benzylic), 3.00 (dd, J = 14 and 5 Hz, 1 H, methylene), 1.74 (d, J = 14 Hz, 1 methylene). Anal. Calcd for $C_{11}H_8ClNO$: C, 64.25; H, 3.92. Found: C, 64.33; H, 4.05.

Reaction of 5 with Methyl Acrylate. After a 5-day reflux of a mixture of 0.50 g of **5** and 0.358 g of methyl acrylate with 2 drops of glacial acetic acid in toluene, rotary evaporation and chromatography yielded 127 mg (20%) of **19**: mp 111–112 °C (after recrystallization from hexane); ^{1}H NMR (CCl_4) δ 7.2 (narrow m, 4, aromatic), 5.22 (d, J = 5.5 Hz, benzylic H), 3.66 (s, 3, OCH_3), 3.50 (s, 3, OCH_3) 2.4–2.9 (m, 2, one methylene and $CHCO_2CH_3$), 1.35–1.85 (m, 1 H, other methylene). Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 6.02. Found: C, 66.34; H, 5.96.

Further elution gave 65 mg (11%) of a mixture of 1-methoxy-2-(methoxycarbonyl)naphthalene and 4-methoxy-2-(methoxycarbonyl)naphthalene. Saponification of this liquid (several fractions) gave a mixture of acids (two nearly equal OCH_3 peaks in the NMR) with a melting point of 110–145 °C; 1-methoxy-2-naphthoic acid has a melting point of 127–128 °C,[14] and 4-methoxy-2-naphthoic acid has a melting point of 202–202.5 °C.[15] One chromatography fraction of the ester had an NMR spectrum superimposable (complex aromatic multiplet) with that of a sample of 4-methoxy-2-(methoxycarbonyl)naphthalene prepared by an alternative route. This was followed by very slow moving enol (39 mg obtained over several collection flasks). Identification of this material rests mainly on the presence in its NMR spectrum of a sharp singlet at 12.4 ppm, a reasonable shift for hydrogen bonded enol. The spectrum also exhibited a triplet at 4.7 ppm (CHOH), a methoxy singlet at 3.8 ppm, and a doublet at 2.7 ppm (AA′X pattern, AA′ portion due to CH_2).

Further elution of the column with methanol gave 240 mg of material tentatively assigned structure **22**.

Reaction of 5 with 1,4-Naphthoquinone. A solution of 0.50 g of **5** and 0.44 g of 1,4-naphthoquinone in 5 mL of toluene containing 3 drops of acetic acid was refluxed for 29 h. When the mixture cooled, a yellow-orange solid precipitated; this material (87 mg) was collected and recrystallized from toluene to give **25**:[13] mp 303–305 °C; IR (KBr) 3430, 1670, 1620, 1580, 1540, 1280 (s) cm^{-1}; UV (EtOH) 284 and 468 nm (EtOH + NaOH), 260, 512; mass spectrum, m/e 274.062 (calcd 274.063).

The solvent was removed from the filtered solution by rotary evaporation, and the residue was chromatographed on 20 g of silica gel with CH_2Cl_2 as solvent, giving 390 mg (40%) of **26**, contaminated with a small amount of phthalide. Recrystallization from aqueous methanol gave yellow crystals: mp 103–105 °C; IR (CCl_4) 1724, 1663, 1263, 1080 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.25–7.3 (br m, 8, aromatic), 6.28 (apparent t, J = 1.9 Hz, benzylic H), 4.28 (apparent d, J = 1.9 Hz, 2, adjacent to carbonyls), 3.78 (s, 3, OCH_3). Anal. Calcd for $C_{19}H_{14}O_4$: C, 74.50; H, 4.61. Found: C, 74.46; H, 4.73.

Elution with methanol gave very slow moving and slightly soluble dark blue material (200–300 mg) which was not further characterized.

Acknowledgment. This work was supported in part by a grant from the University of California Cancer Research Coordination Committee. M.A.M. thanks the University of El-Fatah, Tripoli, for financial support during the course of this study. We are also grateful for the skillful assistance of Cuc K. Huynh in certain aspects of this work, particularly the preparation of **8**. Discussions with Professor D. H. Aue were helpful in assigning NMR features of the norbornene derivatives.

Registry No. **5**, 59567-96-3; **6**, 70103-17-2; **7**, 487-97-8; **8**, 75802-19-6; *endo,exo*-**9**, 77341-76-5; *exo,exo*-**9**, 77399-11-2; *exo,exo*-**10**, 77341-77-6; *endo,exo*-**11**, 77399-12-3; *endo*-**12**, 77341-78-7; *exo*-**12**, 77399-13-4; **13**, 60678-31-1; **14**, 77341-79-8; **15**, 77341-80-1; **16**, 59279-02-6; **17**, 77357-31-4; **18**, 77341-81-2; *endo*-**19**, 77341-82-3; **22**, 77341-83-4; *endo*-**23**, 77341-84-5; *exo*-**23**, 77399-14-5; *endo*-**24**, 77341-85-6; *exo*-**24**, 77399-15-6; **25**, 6336-86-3; *endo*-**26**, 77341-86-7; norbornene, 498-66-8; maleic anhydride, 108-31-6; dimethyl acetylenedicarbonylate, 762-42-5; dimethyl maleate, 624-48-6; dimethyl fumarate, 624-49-7; α-chloroacrylonitrile, 920-37-6; methyl acrylate, 96-33-3; 1-methoxy-2-(methoxycarbonyl)naphthalene, 6039-59-4; 4-methoxy-2-(methoxycarbonyl)naphthalene, 33295-47-5; 1-methoxy-2-naphthoic acid, 883-21-6; 4-methoxy-2-naphthoic acid, 5773-93-3; 1,4-naphthoquinone, 130-15-4.

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