Stereochemistry of Lithium Dialkylamide Induced 1,4-Eliminations Leading to Substituted Isobenzofurans

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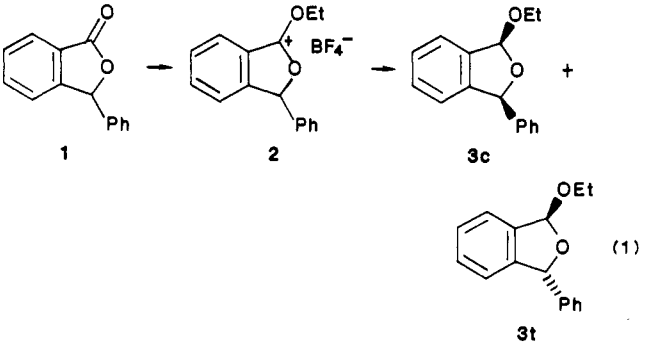
The O-ethylation of 3-methyl- and 3-phenylphthalide followed by borohydride reduction was used to prepare cis/trans mixtures of 1,3-dihydro-1-ethoxy-3-methyl(or phenyl)isobenzofuran. The cis isomer is formed preferentially, presumably due to steric interference of hydride attack by the 3-substituent. Equilibrium mixtures of the 1-methoxy analogues, formed by acid-catalyzed transacetalization in methanol, slightly favor the trans isomer. Stereochemical assignments were made on the basis of long range coupling constants and difference NOE spectra. The stereochemistry of lithium diisopropylamide induced 1,4-elimination was examined with mixtures of cis/trans isomers, and preference for syn elimination was found for both the 3-phenyl and 3-methyl acetals. However, both isomers of each substrate react to form the isobenzofurans, showing that a formal anti elimination pathway is also energetically accessible. The $LiNR_2$ reaction of the 3-phenyl acetal has been used to prepare 1-phenylisobenzofuran; although isolable, this material is very reactive, more closely resembling the unsubstituted parent than 1,3-diarylisobenzofurans in this regard. The base-induced (anti) elimination of the cis 3-methyl acetal is much slower than the reactions of the other substrates examined in this study, allowing recovery of pure cis isomer from incomplete reactions of cis/trans mixtures. When resubjected to base, however, this isomer also slowly formed 1-methylisobenzofuran. Lithiation of the unsubstituted furan site occurs with these isobenzofurans, as shown by quenching with trimethylsilyl chloride and further characterization of silylated derivatives. Reaction of the 3-methyl acetal in the presence of trimethylsilyl chloride with lithium tetramethylpiperidide causes trimethylsilylation of both the furan site and the methyl group. After cycloaddition, the bridgehead silyl group was selectively removed by treatment with a fluoride ion source. The *O*-ethyl-3-substituted-phthalidium tetrafluoroborate salts were converted to the diethyl orthoesters by addition to alkoxide solutions. The standard Meerwein procedure (NaOR in ROH) is suitable for the 3-methyl derivative, but preparation of the 3-phenyl orthoester requires the use of aprotic conditions. $LiNR_2$-induced eliminations were used to generate 1-alkoxy-3-methyl(or phenyl)isobenzofurans. Treatment of the 1-ethoxy-3-methylisobenzofuran with methanol gave, by preferred syn 1,4-addition, the *cis*-1-ethoxy-*trans*-1-methoxy orthoester. The opposite stereoisomer was prepared by similar syn 1,4-addition of ethanol to the 1-methoxyisobenzofuran analogue. The stereoisomerically enriched orthoesters synthesized in this manner were used to study the stereochemistry of the base-induced 1,4-elimination, which was found to occur with high syn selectivity.

The generality of $LiNR_2$-induced 1,4-elimination of 1-alkoxy-1,3-dihydroisobenzofurans to form the corresponding isobenzofurans is well-established.[1] The mechanistic details are, however, unknown. We have been particularly interested in determining the stereochemical preference (if any) involved in these eliminations. It has recently been demonstrated that 1,4-eliminations of two "allylic" ethers occur with high syn selectivity.[2] Although these reactions led to products of very different stability (naphthalene and a reactive intermediate *o*-xylylene, respectively), the substrates were both cyclohexyl derivatives, and it is possible that the stereochemistry in these cases is controlled by conformational effects of this ring system.[3] The reactions described in the present work demonstrate that syn elimination is also preferred in furanoid structures, suggesting that the result may be general.

We elected to work with 3-methyl- and 3-phenylphthalide derivatives in order to cover some range in substrate acidity. Acetals derived from the latter substrate offered the additional possibility of determining the properties of 1-phenylisobenzofuran, which has previously only been implicated as a reactive intermediate in a few reactions.[4]

Results and Discussion

A. Preparation and Stereochemical Assignment of the Acetals. Commercial *o*-benzoylbenzoic acid was converted to 3-phenylphthalide (**1**) in 92% yield, following a slightly modified procedure described by Newman.[5] *O*-Ethylation with diethoxycarbenium tetrafluoroborate[6] followed by $NaBH_4$ reduction in DMF[7] provided a mixture of cis (**3c**) and trans (**3t**) acetals, isolated by chromatography in 43% yield (eq 1). The ratio of **3c**/**3t** obtained



from this sequence was consistently 85/15 and unaffected by the isolation procedure. Presumably the preferential formation of **3c** reflects a modest steric interaction between

(1) (a) Naito, K.; Rickborn, B. *J. Org. Chem.* **1980**, *45*, 4061. (b) Makhlouf, M. A.; Rickborn, B. *Ibid.* **1981**, *46*, 2734. (c) Mir-Mohamad-Sadeghy, B.; Rickborn, B. *Ibid.* **1983**, *48*, 2237. (d) Cornejo, J.; Ghodsi, S.; Johnson, R. D.; Woodling, R.; Rickborn, B. *Ibid.* **1983**, *48*, 3869. (e) Crump, S. L.; Rickborn, B. *Ibid.* **1984**, *49*, 304. (f) Crump, S. L.; Netka, J.; Rickborn, B. *Ibid.* **1985**, *50*, 2746.

(2) Moss, R. J.; Rickborn, B. *J. Org. Chem.* **1986**, *51*, 1992.

(3) The possibility that syn elimination is exclusively caused by lithium counterion coordination to the alkoxy leaving group is cast into doubt by the observation that other counterions, including a quaternary ammonium, also lead to very high syn elimination selectivity.[2]

(4) (a) Faragher, R.; Gilchrist, T. L. *J. Chem. Soc., Perkin Trans. 1* **1976**, 336. (b) Hayakawa, K.; Yamaguchi, Y.; Kanematsu, K. *Tetrahedron Lett.* **1985**, *26*, 2689. (c) Rodrigo and co-workers have utilized substituted arylisobenzofurans as reactive intermediates in lignan syntheses; see: Weeratunga, G.; Rajapaksa, D.; Rodrigo, R. *J. Org. Chem.* **1985**, *50*, 5905 and references to earlier work cited there.

(5) Newman, M. S. *J. Org. Chem.* **1961**, *26*, 2630.

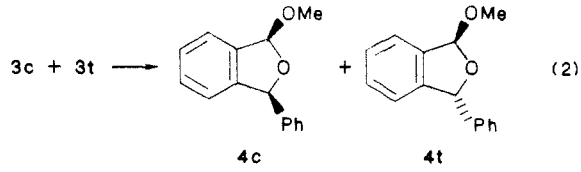
(6) Borch, R. F. *J. Org. Chem.* **1969**, *34*, 627.

(7) Moss, R. J.; Rickborn, B. *J. Org. Chem.* **1982**, *47*, 5391.

0022-3263/86/1951-3849$01.50/0

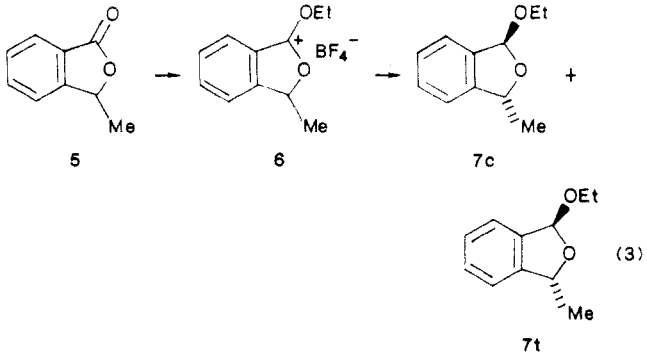
the hydride donor and the 3-phenyl substituent in substrate **2**.

Transacetalization was effected by brief treatment of **3c/3t** in methanol with catalytic trifluoroacetic acid (TFA), leading to an equilibrium mixture[8] of the methoxy derivatives **4c** and **4t** (96% yield). The trans isomer **4t** is very slightly favored, leading to a ratio **4c/4t** = 44/56.

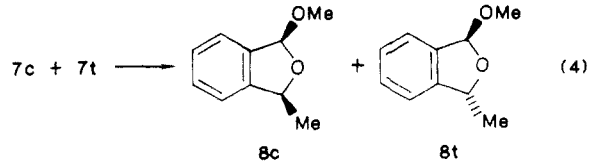


Assignment of stereochemistry was accomplished by ^{1}H NMR. The major isomer (**4t**) exhibited two doublets (J = 2 Hz) at 6.36 and 6.28 ppm, while the minor isomer (**4c**) showed two singlets at 6.23 and 6.12 ppm. The visible long range coupling (2 Hz) was assumed to be associated with the trans configuration of H-1 and H-3, based on Barfield and co-workers analysis[9] of analogous dihydrofurans and on studies of related phthalans done in our laboratory. This assignment was confirmed by a difference nuclear Overhauser enhancement (DNOE) experiment, which also served to distinguish between the acetal (H-1) and benzylic (H-3) protons for each isomer. Thus, simultaneous irradiation of both methoxy groups in a mixture of **4c/4t** gave the following: 6.12 (s, 0% NOE , H-3 of **4c**), 6.23 (s, 10% NOE, H-1 of **4c**), 6.28 (d, 3% NOE, H-3 of **4t**), and 6.36 ppm (d, 10% NOE, H-1 of **4t**).

The 3-methyl acetal was prepared in a similar manner. Reduction ($NaBH_4$) of *o*-acetylbenzoic acid gave 3-methylphthalide (**5**) in essentially quantitative yield.



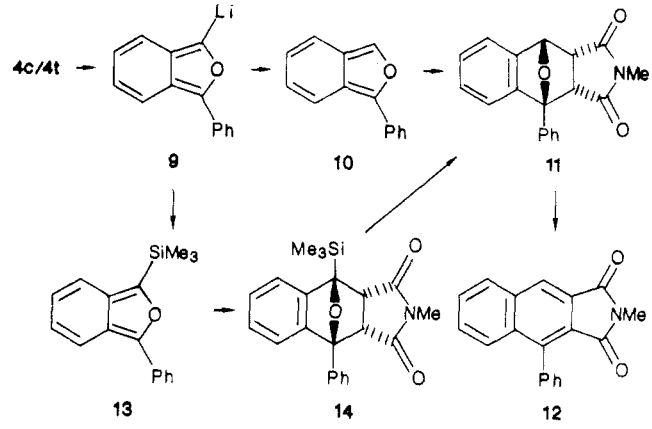
O-Ethylation and reduction afforded 68% of **7c/7t** in a ratio of 78/22. Conversion of **7c/7t** to the equilibrium mixture of **8c/8t** (ratio 42/58) was accomplished as described above. Stereochemical assignments for these



materials are based on the observed coupling constant (J = 2 Hz) for the presumed trans isomer, with the other (cis) isomer giving rise to an acetal proton singlet.

No appreciable separation of the acetal isomers was observed on chromatography or simple vacuum distillation. Further reactions were carried out with (known) mixtures of these materials.

Scheme I



B. Acetal Eliminations. Isobenzofuran itself is more acidic than dialkylamines,[1e] and it is reasonable to assume that this is also true of 1-substituted derivatives. This introduces a complication in attempts to carry out elimination reactions on acetal precursors with a limited amount of $LiNR_2$. Alkyllithiums (e.g., methyl- or *n*-butyllithium), although much stronger bases (by thermodynamic definition), are relatively unreactive in 1,4-eliminations to form isobenzofuran,[1e] and 1-lithioisobenzofuran probably resembles RLi in this respect. Consideration of these factors led us to conclude that somewhat greater control of reaction conditions could be maintained through the use of $LiNR_2$ as a catalyst, with RLi as the measured base. In this way the isobenzofuran is rapidly lithiated as it is formed, and the R_2NH is reconverted to $LiNR_2$, maintaining a constant concentration of this reactive species. This method was used for most of the elimination reactions described in this paper.

The elimination reactions of the 3-phenyl acetal (**4c/4t** = 44/56) and other steps used to characterize products are outlined in Scheme I. When **4** was treated with 0.1 equiv of diisopropylamine (DIPA) and 2.5 equiv of MeLi, the solution changed color from an initial pale yellow to red over 0.25 h, accompanied by some precipitation. Direct ^{1}H NMR examination of this ethereal solution showed a broad absorption at 6.5–8.05 ppm, attributed to 1-lithio-3-phenylisobenzofuran (**9**). The addition of *tert*-butyl alcohol at this stage served to quench excess MeLi and to convert **9** to 1-phenylisobenzofuran (**10**).

Very little is known about the properties (stability, reactivity) of **10**, in marked contrast to isobenzofuran itself (isolable cold, moderately stable in solution but polymerizes if stored neat at ambient temp), and the 1,3-diarylisobenzofurans (at least moderate shelf stability; the long known diphenyl parent is an article of commerce). As noted previously, **10** has not previously been isolated, although its existence as a reactive intermediate has been demonstrated.[4] In order to address this issue, various experiments were carried out on solutions of **10** prepared as described above.

(a) Direct examination of the ethereal solution ^{1}H NMR spectrum again showed a broad absorption at 6.5–8.0 ppm (much like **9**), but with an additional singlet at 8.15 pm, attributed to H-3 of **10**.

(b) Addition of this quenched crude reaction mixture to a solution of *N*-methylmaleimide (NMM) led to the

(8) This ratio remained unchanged on longer treatment and was reproducible; essentially identical cis/trans ratios of the homologous acetals were obtained when the procedure was carried out in ethanol or isopropanol in place of methanol.

(9) Barfield, M.; Spear, R. J.; Sternhill, S. *J. Am. Chem. Soc.* **1975**, *97*, 5160. While both trans and cis 1,3-couplings may be observable, Barfield has concluded that the trans J will always have the larger magnitude; this generalization holds for the several phthalans that have been examined in our laboratory.

isolation by chromatography of a single (endo) cycloadduct **11** in 68% yield. This structure was confirmed by dehydration to the known[10] material **12** (92%).

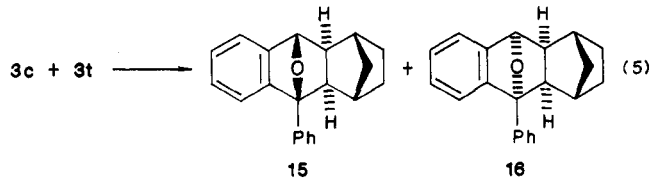
(c) When ethereal solutions of **10** were washed with saturated aqueous NaCl solution to remove strong bases (which interfere with the NMM cycloaddition step), diminished yields (30–36%) of cycloadduct **11** resulted. This suggests that **10**, even in solution, has limited stability toward water, or more probably, air.

(d) It is possible to isolate neat **10** as a red oil (the origin of the color is unclear) by either vacuum evaporation of the solvent or better by passing the crude mixture, under N_2, through a short silica gel column, followed by evaporation under a stream of N_2. This procedure gave 82% of material which by NMR (in benzene-d_6) and MS was identified as ca. 90% pure **10**. Samples of this neat **10** on standing (0.5–1 h) changed from red oils to yellow solids; the NMR spectra of the latter contained broad absorptions in the aromatic region, suggesting possible oligomerization.

It appears that **10** resembles the parent unsubstituted isobenzofuran in its limited stability; the nature of its decomposition products have not been elucidated, although it appears that a small amount of *o*-benzoylbenzaldehyde is formed along with apparent polymeric material.

The intermediacy of the lithiated isobenzofuran **9** in these experiments was demonstrated by treating the basic solution containing this material with Me_3SiCl, which effected the formation of 1-phenyl-3-(trimethylsilyl)isobenzofuran (**13**). Addition of the solution containing **13** to NMM gave the cycloadduct **14** (70%); examination of the NMR spectrum of the crude product indicated that the cycloaddition gave one isomer, with high selectivity. This was shown to be the endo isomer by fluoride-induced protio-desilylation, which gave the previously characterized (doublet for bridgehead proton) **11**. In a separate experiment, the cycloadduct (not pictured) of **13** with dimethyl acetylenedicarboxylate was prepared, in 55% yield. It also proved possible to isolate **13**, which as anticipated based on our experience with unsubstituted and 1,3-bis(trimethylsilyl)isobenzofuran,[1f] appeared to be somewhat more stable than **10**.

These observations show, for the first time, that monoarylisobenzofurans can be prepared in solution at useful concentration levels, and that these (basic to neutral) solutions have at least modest stability if protected from air. Adducts of **10** and norbornene have also been prepared by generation of **10** in a refluxing hexane solution of the olefin and acetal (eq 5). Slow (syringe pump) addition of base



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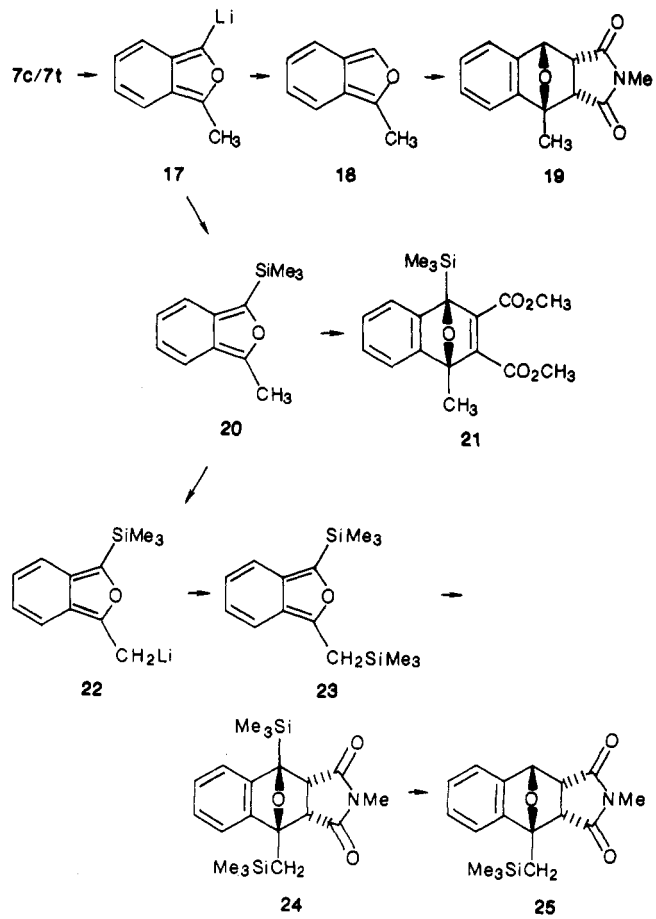
is needed to obtain even moderate yields, since the cycloaddition is slow,[1b] and lithiated isobenzofurans have been shown to be unsuitable in other Diels–Alder applications.[1f]

The relative reactivity of **4c** vs. **4t** proved to be similar, i.e., both isomers appeared to be quite reactive toward strong base. Some indication that syn elimination (from **4t**) occurs more readily than anti elimination (from **4c**) was obtained by examination of mixtures of the acetals recovered from reactions with limited amounts of base. The

Scheme II



preferential loss of **4t** vs. **4c** was also detected by NMR examination of ethereal solutions of **4c**/**4t** (initially 44/56) treated with increments of MeLi (catalytic LDA). The acetal (C-1) and benzylic (C-3) protons were sufficiently downfield from solvent absorptions to be measured, and these were integrated vs. Ph_3CH used as an internal standard. This competition kinetics approach gave k_{4t}/k_{4c} ratios of 1.6–2.1 for individual points. Further, the yields of cycloadducts (e.g., 68% of **11**) formed when nearly equal mixtures of **4c**/**4t** were employed shows clearly that pathways exist for both syn and anti elimination, with both leading to **10**. Thus syn elimination is favored for the 3-phenyl acetal, but by a very modest factor.

Unlike 1-phenylisobenzofuran, 1-methylisobenzofuran has previously been prepared in solution, by both a retro-Diels–Alder route[11] and by methylation of 1-lithioisobenzofuran.[1e] It appears to be similar in stability to the unsubstituted material, although more sensitive to acidic conditions, as one might expect. The base-induced reactions of acetals which we have used in the present study to form this material are outlined in Scheme II. This chemistry closely parallels that already described for the 3-phenyl acetals with some interesting differences which are discussed below.

Typically, the ethyl acetal isomers **7c**/**7t** (78/22) upon treatment with base afforded only modest yields of cycloadduct, along with recovered starting material which proved to be essentially pure **7c**. This provided a clear illustration of substantially faster syn elimination (from **7t**) than anti elimination (from **7c**). By controlling the

(10) Rigaudy, J.; Perlat, M. C.; Simon, D.; Cuong, N. K. *Bull. Soc. Chim. Fr.* **1976**, *3–4*, 493.

(11) (a) Wiersum, U. E.; Mijs, W. J. *J. Chem. Soc., Chem. Commun.* **1972**, 347. (b) Chacko, E.; Sardella, D. J.; Bornstein, J. *Tetrahedron Lett.* **1976**, 2507.

amount of base and/or reaction time, pure **7c** could be obtained in moderate yield and isolated by vacuum distillation. Although syn elimination is very strongly favored, when pure **7c** obtained in this manner was resubjected to the elimination conditions followed by addition to a dienophile solution, a cycloadduct of 1-methylisobenzofuran (**18**) was obtained, showing that for this substrate (like the phenyl analogue) an anti elimination pathway is accessible. It is evident that k_{syn}/k_{anti} is much larger for the 3-methyl acetal than the 3-phenyl analogue, perhaps reflecting the greater acidity of the 3-phenyl derivative and signaling greater carbanionic character in the transition state for the latter.

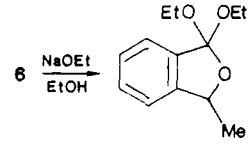
Except for the large rate difference for elimination of **7c** and **7t**, these reactions proceeded as expected in the presence of MeLi (cat. LDA) to form 1-lithio-3-methylisobenzofuran (**17**); quenching of this intermediate with a proton source gave 1-methylisobenzofuran (**18**), as shown by formation of the cycloadduct **19** (again, endo isomer was formed nearly exclusively). Quenching of solutions containing **17** by Me_3SiCl gave 1-methyl-3-(trimethylsilyl)-isobenzofuran (**20**), characterized by cycloadduct formation with dimethyl acetylenedicarboxylate, giving **21** (Scheme II).

We have recently shown[12] that it is possible to take advantage of the compatibility of Me_3SiCl and lithium tetramethylpiperidide (LTMP), as demonstrated by Martin,[13] to effect the trimethylsilylation of some very weak acids. Interestingly, when this approach was used with **7c**/**7t** the sequence of reactions leading to intermediate **23** (Scheme II) took place. Thus elimination gave **18** as in the catalyzed reaction (note that no intermediate carbanion is trapped to give silylated acetal); this was in turn rapidly lithiated to **17**, followed by rapid silylation to generate the previously described **20**. The pK_a of **20** is probably similar to typical benzylic materials, i.e., insufficiently acidic for $LiNR_2$ to generate a significant equilibrium concentration of the anion (organolithium **22**). However, if a small concentration is formed and bled off by reaction with Me_3SiCl, this equilibrium can be quite effectively "shifted" to the right by the formation of the bis-trimethylsilylated isobenzofuran **23**. Evidence for the formation of this material was obtained by isolation and characterization of the cycloadduct **24**. Interestingly, when **24** was subjected to fluoride-induced protio-desilylation (which presumably generates a carbanion intermediate), only the bridgehead trimethylsilyl group was removed, to give **25**. We interpret this to indicate that the acidity of the methyl group in **20** is lost when cycloadduct is formed, since the "benzylic" resonance stabilization available for the carbanion at the isobenzofuran stage is no longer present. Conversely, the bridgehead positions of benzoxabicyclo[2.2.1]heptenes are notably acidic,[12] and protio-desilylation occurs quite readily with many such derivatives.[1f]

C. Preparation and Reactions of Orthoesters. MacLean and his co-workers first reported[14] that the orthoester derivatives of phthalide could serve as precursors for 1-alkoxyisobenzofurans, where these species were generated as reactive intermediates in an acid-catalyzed process. Work in this laboratory extended this use, by showing that base-induced 1,4-eliminations could also be employed to form these intermediates.[1b] More recently we have developed conditions which allow the isolation (in solution) of these unusual and very acid-sensitive "ketene acetals", in the process learning a good deal about the interrelationship of these materials with the orthoesters.[15] In particular, the use of MeOD with 1-ethoxyisobenzofuran gave the unsymmetrical (methyl, ethyl) orthoester containing one D/mol, showing that protonation was rate-determining and irreversible. We speculated at the time that this 1,4-addition might occur with syn selectivity, based on a proposed mechanism involving slow proton (deuteron) transfer from ROH to generate an ion pair which could collapse preferentially in a suprafacial manner. Not surprisingly, the stereoisomers differing by cis/trans-3-*d* substitution in the 1-ethoxy-1-methoxy orthoester were not distinguishable by NMR, and so this interesting point remained unanswered until the present work. As described in greater detail below, current results not only establish this anticipated syn 1,4-addition preference but also allow the construction of orthoesters which can be used to distinguish syn from anti 1,4-elimination.

The Meerwein orthoester synthesis involves the addition of a dialkoxycarbenium tetrafluoborate to a solution of NaOR in ROH solvent; it is often an excellent procedure, as exemplified by the prototype literature conversion of *O*-ethylphthalidium salt to 1,1-diethoxy-1,3-dihydroisobenzofuran.[16] The reaction cannot however be used to prepare "mixed" orthoesters, at least in certain cases; we have recently shown, for example, that the major product of adding *O*-ethylphthalidium tetrafluoroborate to NaOMe (excess) in MeOH is the solvent-incorporated product, the 1,1-dimethyl orthoester.[15] This result was shown to be due to limitations of bulk diffusion (mixing), and the problem could be circumvented by avoiding a protic solvent. Thus, the addition of *O*-ethylphthalidium salt to LiOMe in acetonitrile was successfully employed to prepare the mixed orthoester 1-ethoxy-1-methoxy-1,3-dihydroisobenzofuran.[15]

An interesting difference emerged when the standard Meerwein procedure was used in an effort to extend this procedure to the 3-substituted-phthalidium salts. The *O*-ethyl-3-methylphthalidium salt **6** reacted in the normal manner to furnish the diethyl orthoester **26** (eq 6).



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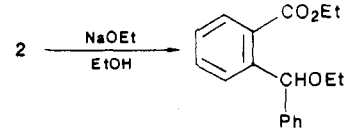
However, under the same conditions, the *O*-ethyl-3-phenyl analogue **2** gave almost exclusively the ether–ester derivative **27** (eq 7). This unexpected result can be attributed



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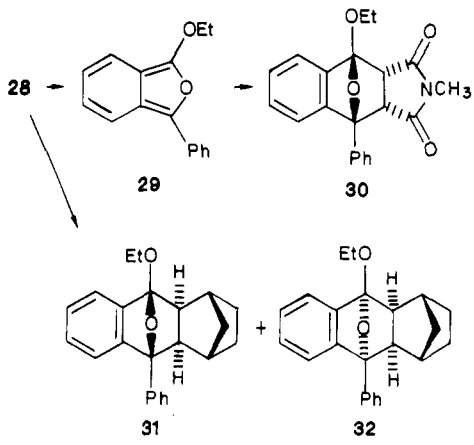
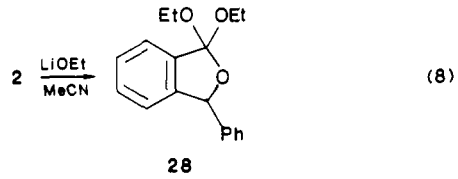
to *relatively* greater preference for attack by nucleophile at the 3-position when this site carries a cation-stabilizing phenyl group, although the mechanism discussed above for solvent incorporation in orthoester formation would

(12) Mirsadeghi, S.; Rickborn, B. *J. Org. Chem.* **1986**, *51*, 986.
(13) Krizan, T. D.; Martin, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 6155. Taylor, S. L.; Lee, D. Y.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4156.
(14) Contreras, L.; Slemon, C. E.; MacLean, D. B. *Tetrahedron Lett.* **1978**, 4237.
(15) Mir-Mohamad-Sadeghy, B.; Rickborn, B. *J. Org. Chem.* **1984**, *49*, 1477.
(16) Meerwein, H.; Borner, P.; Fuchs, O.; Sasse, H. J.; Schrodt, H.; Spille, J. *Chem. Ber.* **1956**, *89*, 2060.

Scheme III



allow this outcome even if the *absolute* rate of attack at the 1-position remained greater for the phenyl-substituted case. Reasoning along these lines led us to examine the reaction of **2** added to LiOEt in acetonitrile, and indeed this proved a useful way to prepare the desired orthoester **28** (eq 8).



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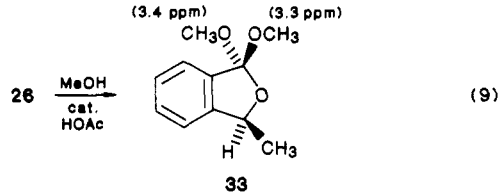
Only a few experiments were carried out with **28**, and these are outlined in Scheme III. Syringe pump addition of LDA to a refluxing hexane solution of **28** and norbornene gave a 40% combined yield of the cycloadducts **31** and **32**, establishing that **29** can be generated (as a reactive intermediate) by base-induced 1,4-elimination. That **29** also has at least modest stability in basic solution was shown by treatment of **28** with MeLi/catalytic LDA (room temperature). Addition of the resulting solution to NMM gave cycloadduct **30** (single isomer, presumably endo) in 38% yield.

In order to carry out a stereochemical study of orthoester 1,4-eliminations, means of distinguishing between the two alkoxy groups and identifying the stereochemistry of the starting material was needed. The first indication that this might be feasible came when the dimethoxy orthoester **33**, prepared as indicated in eq 9, was found to exhibit two well

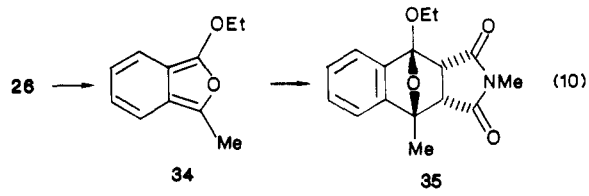


(9)

separated methoxy singlets by NMR in benzene-d_6 solvent. Difference NOE measurements were carried out; irradiation of the downfield methoxy peak (3.4 ppm) caused a 2.5% NOE of the benzylic proton, while irradiation of the upfield methoxy (3.3 ppm) gave no enhancement. On this basis the assignments for cis and trans methoxy groups were made as shown for structure **33**.

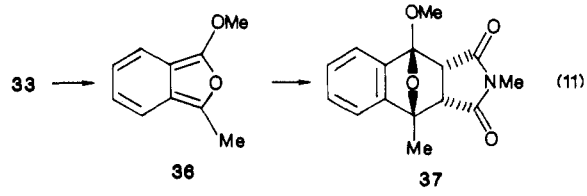
These assignments are important for establishing absolute stereochemical results for the 1,4-eliminations and 1,4-additions discussed below. Absent this information, we can conclude that both processes must occur (preferentially) by the same stereomode, i.e., both anti or both syn, because of the identity relationships established in the two-step sequences ($A \rightarrow B \rightarrow A$). Given these assignments, and the assumption that mixed methyl, ethyl orthoesters will exhibit the same *relative* shifts for the methoxy groups, it can be concluded that both processes occur with syn selectivity, as discussed in detail below.

The reaction of diethyl orthoester **26** with base (MeLi, catalytic LDA) was monitored by direct NMR examination of the ethereal solution. An approximate AA'BB' pattern characteristic of many 1,3-disubstituted isobenzofurans signaled the formation of 1-ethoxy-3-methylisobenzofuran (**34**). Addition of the liquid phase (separated by filtration or decanting away from the presumed LiOEt precipitate generated in the elimination) to a solution of NMM gave the cycloadduct **35** (60%).



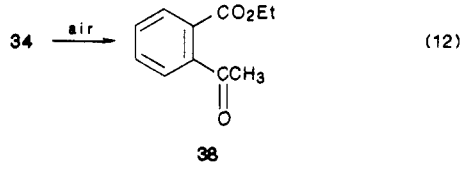
(10)

Analogous treatment of the dimethyl orthoester **33** gave a solution of 1-methoxy-3-methylisobenzofuran (**36**), which was in turn used to prepare the NMM cycloadduct **37**, in 57% yield (eq 11).



(11)

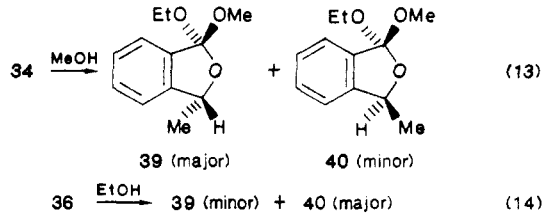
These reactions established the feasibility of forming the isobenzofurans **34** and **36** and also showed that solutions of these materials have at least moderate stability. Attention was turned to reactions with alcohols in order to form mixed orthoesters. Although rates have not been determined, qualitative observations indicate that addition of alcohols to these materials is slower that the analogous reaction of the parent 1-alkoxyisobenzofuran;[15] slower (rate-determining) proton transfer to tertiary vs. secondary carbon is presumably responsible for this difference. Interestingly, if the mixtures of **34** or **36** with alcohol added were subjected to an aqueous brine (exposure to air) workup after a short time, the major material formed was keto ester, as illustrated in eq 12 for the reaction of **34**. This oxidation process is noteworthy since classical



(12)

methods to approach such structures often result in ring-closed phthalan derivatives (as illustrated by the substituted phthalides formed in the present study). The structure of **38** is based on various spectral features (NMR, IR, MS) outlined in the Experimental Section. A high yield of **38** can be obtained by omitting the alcohol treatment and proceeding directly to the workup.

Longer reaction times did lead to the formation of mixed orthoesters, as illustrated in eq 13 and 14. The major product of the reaction of methanol of **34** was assigned structure **39** on the basis of its methoxy singlet appearing at 3.4 ppm (cf. **33**, eq 9). As expected, analogous addition of ethanol to **36** gave the opposite stereoisomer **40** as the



major product (methoxy singlet at 3.3 ppm). Thus we conclude that the addition of alcohols to isobenzofurans (under these conditions) occurs with significant syn selectivity. The ratios of **39/40** formed under different conditions or isolation procedures are listed in Table I. Chromatography led to poor recovery and some apparent isomer interconversion, and similar loss of stereointegrity was observed when the mixed orthoesters were stored at room temperature for extended periods. It is therefore important to use these materials shortly after preparation and of course to avoid acidic conditions in workup and handling. The intrinsic stereoselectivity of the addition reactions may in fact be higher than indicated by the data in Table I, because of this epimeric instability.

These mixed orthoesters were sufficiently enriched in one epimer (or the other) to be useful for examination of the stereochemistry of the base-induced 1,4-elimination. The limitations on quantitative conclusions are those of the analytical method involved (NMR). It was important to establish that the diethoxy or dimethoxy orthoester was fully consumed in the initial step to form **34** or **36**, respectively, and that the amount reformed (from LiOR) on addition of alcohol (R'OH) was minimized. The first condition was satisfied by NMR monitoring of the reaction to assure loss of starting material. For the latter, the reaction has an internal control which proved quite effective. As already noted, the addition involves rate-determining proton transfer, i.e., the rate is pH-dependent. The reactions are therefore quite slow when R'OH is first added to the ethereal mixtures, and the rates do not become appreciable until the pH is lowered by dilution as more R'OH is added; this also coincides with the development of a large ratio of R'OH/ROH. Typically the reactions were carried out with 20–30 equiv of R'OH per LiOR generated in the elimination. Integration of methyl vs. ethyl signals in the mixed orthoester products showed that, within measurement limits, these contained no measurable **26** (or **33**). Note that to the extent that these requirements were not fully met, the final product outcome might suggest higher syn selectivity than actually involved for the mixed orthoester.

Various mixtures of **39/40** were subjected to basic 1,4-elimination conditions to regenerate the 1-alkoxy-3-methylisobenzofurans; these were in turn added to NMM solutions, and the cycloadduct products were analyzed for the relative amounts of **35** and **37**, derived from the 1-ethoxy- and 1-methoxy-3-methylisobenzofurans, respectively. These ratios are also displayed in Table I. In each instance the ratio of **35/37** is, within measurement accuracy, the same as the ratio of **39/40**, showing that these 1,4-eliminations from orthoesters occur with high syn selectivity.

A few attempts were made to examine analogous ROH additions to 1-alkoxy-3-phenylisobenzofuran; these did not give easily decipherable products, perhaps because proton transfer to the doubly benzylic 3-position is strongly retarded.

In conclusion, the results of this study indicate that $LiNR_2$-induced eliminations of both acetal and orthoester precursors to isobenzofurans occur with syn selectivity. For the orthoesters, syn and anti elimination pathways are both in principle available within each molecule, and no evidence of incursion of anti elimination is detected. The acetals provide a more sensitive test of the accessibility of the anti elimination pathway, and this mode of reaction has been detected for both the phenyl- and methyl-substituted cis isomers. For the 3-methyl acetal, anti elimination appears to have a much higher activation energy than syn elimination, whereas the 3-phenyl acetal exhibits only slight syn selectivity. These results extend the limited number of 1,4-elimination stereochemical studies to molecules of different geometry than previously examined and also demonstrate that previously unexplored isobenzofurans can be prepared by the base-induced procedure. The properties and perspective synthetic utility of these materials, particularly the 1-alkoxyisobenzofurans, merit further study.

Table I. Stereochemistry of 1,4-Addition and 1,4-Elimination Reactions

34(or 36) → 39/40 → 35/37

run	1-RO-3-MeIBF	R'OH	time (h)[a]	39/40 (yield)[b]	35/37 (yield)[c]
1	**34** (from **26**)	MeOH	5.0	90/10 (97%)	not detmd
2	**34** (from **26**)	MeOH	0.5	95/5 (89%)	95/5 (35%)
3	**34** (from **26**)	MeOH	*d*	80/20 (29%)	85/15 (52%)[f]
4	**36** (from **33**)	EtOH	1.0	0/100 (81%)	0/100 (20%)
5	**36** (from **33**)	EtOH	24	4/96 (76%)[e]	4/96 (49%)

[a] Time of treatment with indicated R'OH prior to workup and isolation of mixed orthoester. [b] The yield is based on weight of crude sample, with the ratio determined by 300-MHz NMR (assignment of methoxy singlets as described in the text). In runs 2 and 4, the mixed orthoester was contaminated by the keto ester **38**. Distillation did not significantly improve the level of purity, and so crude product was used for the elimination step. [c] The ratios were determined by NMR integration of the methoxy singlet and -OCH_2CH_3 multiplet for the respective cycloadducts. Yields were determined after chromatography, which did not alter the ratio of these products. [d] This sample was obtained by basic alumina chromatography of the product from run 2. Some material is lost, but the change in ratio is considered to be caused by epimerization rather than selective loss of the major isomer. [e] Simple vacuum distillation of this sample gave recovered material of ratio **39/40** = 3/97, unchanged from the starting mixture (39% yield). [f] The yield in this instance refers to crude material, which was essentially pure by NMR analysis.

Experimental Section

All reactions were carried out at room temperature in oven-dried glassware under N_2, except where noted. ^1H NMR spectra were obtained at 300 MHz in $CDCl_3$ unless otherwise stated. The *o*-benzoyl- and *o*-acetylbenzoic acids were used as obtained from the Aldrich Chemical Co. Ether and CH_2Cl_2 were purified by distillation from $LiAlH_4$, while THF was distilled from sodium benzophenone ketyl. Hexane, dimethylformamide (DMF), Me_3SiCl, diisopropylamine (DIPA), and tetramethylpiperidine (TMP) were all distilled from CaH_2 and stored under N_2 if not used immediately. *N*-Methylmaleimide (NMM) was prepared and purified as described by Mehta et al.[17] *N*-Phenylmaleimide (NPM) was commercial material purified by recrystallization from benzene/hexanes. Spectra were recorded on the following instruments: NMR (Nicolet NT-300 or Varian EM-360A); IR (PE 282 or Infracord); MS (VG ZAB-2F or VG 70-250); and mp (Mel-temp, open capillary, uncorrected). Combustion analyses were performed by Galbraith Laboratories, Knoxville, TN.

(17) Mehta, N. B.; Phillips, A. P.; Fu, F.; Brooks, R. E. *J. Org. Chem.* **1960**, *25*, 1012.

3-Phenyl-1(3*H*)-isobenzofuranone (1). To a 0.5-L, round-bottomed flask equipped with a magnetic stirrer were added 50.0 g (0.22 mol) of *o*-benzoylbenzoic acid and 16.0 g (0.285 mol) of KOH in 220 mL of water. $NaBH_4$ (7.0 g, 0.185 mol) was added in several portions over a period of 0.25 h, and the mixture was stirred for 12 h. It was then acidified (concentrated HCl) to pH ca. 0 and extracted with CH_2Cl_2 (3 × 50 mL). The organic phase was washed with 10% Na_2CO_3 and brine, dried over $MgSO_4$, and rotary evaporated to give crude solid 1. Recrystallization from methanol afforded 42.8 g (92%) of pure 1, mp 118–118.5 °C (lit.[5] mp 114–115 °C): IR ($CHCl_3$) 1770 cm^{-1}; ^1H NMR δ 6.40 (s, 1 H), 7.25–7.40 (m, 6 H), 7.50–7.70 (m, 2 H), 7.96 (d, 1 H, J = 8 Hz).

***cis*/*trans*-1,3-Dihydro-1-ethoxy-3-phenylisobenzofuran (3c + 3t).** To a solution of 18.7 mmol of diethoxycarbenium tetrafluoroborate[6] in 8.0 mL of CH_2Cl_2 was added 2.96 g (14.1 mmol) of 1. After being stirred for 45 h, this solution was added dropwise (0.5 h) to a well-stirred ice-cooled solution of $NaBH_4$ (0.90 g, 24 mmol) and pyridine (1.7 g, 22 mmol) in 20 mL of DMF. After 0.3 h, 50 mL of brine was added, and the aqueous phase extracted with hexanes (3 × 15 mL). The organic phase was washed with water and brine, dried over K_2CO_3, and rotary evaporated to give 3.09 g of a yellow oil. This material was triturated with 3 × 10 mL of hexanes (1 is relatively insoluble, and recovered at this stage). The soluble portion was evaporated and chromatographed on neutral alumina (5% ether/hexanes) to afford 1.45 g (43%) of pure acetal as a mixture of isomers, 85% **3c** and 15% **3t** (by NMR), mp 50.5–53.5 °C: MS calcd for P – H, 239.1070, found, 239.1074. Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.64; H, 6.90.

3c: ^1H NMR δ 1.29 (t, 3 H, J = 7 Hz), 3.70–3.81 (m, 1 H), 3.86–4.03 (m, 1 H), 6.09 (s, 1 H), 6.30 (s, 1 H), 7.02 (d, 1 H, J = 7 Hz), 7.2–7.5 (m, 8 H).

3t: ^1H NMR: the spectrum of this isomer is very similar to that of **3c**, except for new absorptions at δ 6.29 (d, 1 H, J = 2 Hz) and 6.44 (d, 1 H, J = 2 Hz), replacing the singlets of the cis isomer.

***cis*/*trans*-1,3-Dihydro-1-methoxy-3-phenylisobenzofuran (4c + 4t).** A mixture of 554 mg (2.30 mmol) of **3c/3t** = 85/15 and 0.5 mmol of trifluoroacetic acid (TFA) in 30 mL of methanol was stirred for 1 h, made basic by the addition of 2 mL of 10% Na_2CO_3, taken up in water, and extracted with CH_2Cl_2. The usual washing, drying (K_2CO_3), and rotary evaporation gave 503 mg (96%) of a colorless oil, a mixture of **4c/4t** = 44/56 (by NMR): MS calcd for P–H, 225.0915, found 225.0925.

4c: ^1H NMR δ 3.59 (s, 3 H), 6.12 (s, 1 H), 6.23 (s, 1 H), 7.0–7.1 (m, 1 H), 7.2–7.45 (m, 8 H).

4t: ^1H NMR δ 3.54 (s, 3 H), 6.28 (d, 1 H, J = 2 Hz), 6.36 (d, 1 H, J = 2 Hz), 7.0–7.1 (m, 1 H), 7.2–7.45 (m, 8 H).

3-Methyl-1(3*H*)-isobenzofuranone (5). The procedure used to make 1 was employed, with 10.0 g (61 mmol) of *o*-acetylbenzoic acid, 4.0 g (71 mmol) of KOH, and 50 mL of water treated with 2.0 g (53 mmol) of $NaBH_4$. Workup as before gave an oil; pure **5** (8.93 g, 98%) was obtained by distillation, bp 75–78 °C (0.2 torr); lit.[18] bp 282–286 °C: ^1H NMR δ 1.64 (d, 3 H, J = 7 Hz), 5.57 (q, 1 H, J = 7 Hz), 7.45 (d, 1 H, J = 8 Hz), 7.53 (t, 1 H, J = 8 Hz), 7.69 (t, 1 H, J = 8 Hz), 7.89 (d, 1 H, J = 8 Hz).

***cis*/*trans*-1,3-Dihydro-1-ethoxy-3-methylisobenzofuran (7c + 7t).** The O-ethylation of **5** (1.99 g, 13.5 mmol) with diethoxycarbenium tetrafluoroborate (17.5 mmol) was done in CH_2Cl_2 for 28 h. This solution was then added dropwise (cannula) to a mixture of 720 mg (19 mmol) of $NaBH_4$ and 1.5 mL of pyridine in 12 mL of DMF, at 0 °C. After being stirred for 0.3 h, 50 mL of saturated brine was added, and the mixture was extracted with hexanes (3 × 10 mL). The combined hexane phase was washed with water (3×) and brine, dried over K_2CO_3, and rotary evaporated to give a viscous yellow oil. Short path distillation gave 1.64 g (68%) of pure **7c/7t** (ratio 78/22) as an oil, bp 57–57.5 °C (0.07 torr): MS calcd for P–H 177.0945, found 177.0930.

7c: ^1H NMR δ 1.26 (t, 3 H, J = 7 Hz), 1.54 (d, 3 H, J = 6 Hz), 3.6–3.85 (m, 2 H), 5.26 (q, 1 H, J = 6 Hz), 6.18 (s, 1 H), 7.15–7.2 (m, 1 H), 7.28–7.4 (m, 3 H).

7t: ^1H NMR δ 1.26 (t, 3 H, J = 7 Hz), 1.49 (d, 3 H, J = 6 Hz), 3.6–3.85 (m, 2 H), 5.44 (dq, 1 H, J = 6 and 2 Hz), 6.21 (d, 1 H, J = 2 Hz), 7.15–7.2 (m, 1 H), 7.28–7.4 (m, 3 H).

***cis*/*trans*-1,3-Dihydro-1-methoxy-3-methylisobenzofuran (8c + 8t).** A sample of **7c/7t** (78/22), 102 mg (0.57 mmol), was taken up in 10 mL of methanol and a drop of TFA was added. After 0.5 h the mixture was quenched by addition of base and the product isolated as described above; 90 mg (96%) of **8c/8t** in a ratio of 42/58 was obtained as an oil. Longer reaction times (up to 28 h) did not alter this ratio, indicating that it represents the equilibrium position.

8c: ^1H NMR δ 1.54 (d, 3 H, J = 7 Hz), 3.43 (s, 3 H), 5.27 (q, 1 H, J = 7 Hz), 6.12 (s, 1 H), 7.16–7.4 (m, 4 H).

8t: ^1H NMR δ 1.50 (d, 3 H, J = 7 Hz), 3.50 (s, 3 H), 5.44 (dq, 1 H, J = 7 and 2 Hz), 6.14 (d, 1 H, J = 2 Hz), 7.16–7.4 (m, 4 H).

1-Phenylisobenzofuran (10). A mixture of **4c/4t** (214 mg, 0.94 mmol, 44/56 ratio), 0.1 mmol of DIPA, and 1 mL of ether was treated with 4.45 mL (2.36 mmol) of MeLi (0.5 M in ether). The solution immediately became deep red and heterogeneous. After 0.3 h an aliquot was removed for NMR analysis (60 MHz, ether solvent also used as the internal standard, with the chemical shift taken as that for ether in $CDCl_3$): δ 6.5–8.05 (br m); this spectrum, which differed in gross structure and detail from the spectrum of **4c/4t** and **10** (see below), is that of 1-lithio-3-phenylisobenzofuran (**9**).

The addition of 0.15 mL (1.6 mmol) of *tert*-butyl alcohol to this solution of **9** caused the formation of **10** (the solution remained red): ^1H NMR (ether, 60 MHz), δ 6.8–8.05 (m, 10-11 H in various runs), 8.15 (s, 1 H, furan proton). There were no extraneous peaks between 5.5 and 10.5 ppm. The excess integrated value of the aromatic m (theory being 9:1) is indicative of the fairly high level of purity (ca. 90%) of these samples.

(a) A solution prepared in this manner was filtered through a few centimeters of silica gel, under N_2, with ether solvent. The first 20 mL of pale pink solution was evaporated under N_2 to give 117 mg (82% in this particular run) of a red oil. The NMR of this material in $CDCl_3$ solvent contained a singlet at 8.00 ppm, overlapping the remaining aromatic multiplet. The neat red oil was exposed to air for 3 h, which caused the red color to disappear and the formation of a pale yellow solid. The NMR of this material, which by TLC contained at least four components, exhibited two very small singlets at 5.0 and 10.1 ppm and a large broad featureless band at 6.0–8.0 ppm. An attempt to isolate by chromatography and identify the components of this mixture was unsuccessful.

(b) A sample of the red oil prepared as above and maintained under N_2 had MS (m/z) 210 (P + 16, 53), 194 (P, 100), 181 (42), 166 (12), 164 (75), 105 (23), and several other sizeable peaks below m/z 100; MS calcd for $C_{14}H_{10}O$ 194.0731, found 194.0722; ^1H NMR (300 MHz, benzene-d_6) δ 6.65–6.75 (m, 1 H), 6.90–7.25 (m, 6 H), 7.56 (s, 1 H), 7.80–7.85 (m, 2 H).

Addition of NMM to the NMR tube caused immediate formation of cycloadduct.

***endo*-4,9-Epoxy-2-methyl-4-phenyl-3a,4,9,9a-tetrahydro-1*H*-benz[*f*]isoindole-1,3(2*H*)-dione (11).** A solution of **10** prepared as described above from 234 mg (1.00 mmol) of **4c/4t** (44/56) was added to 174 mg (1.6 mmol) of NMM in ether. After 1 h the mixture was filtered to remove insoluble material and rotary evaporated to yield 215 mg (68%) of essentially pure **11**, mp after recrystallization from hexane, 200–202 °C: ^1H NMR δ 2.34 (s, 3 H), 3.85 (d, 1 H, J = 8 Hz), 3.98 (dd, 1 H, J = 8 and 6 Hz), 5.82 (d, 1 H, J = 6 Hz), 6.91 (d, 1 H, J = 7 Hz), 7.13–7.25 (m, 2 H), 7.31 (d, 1 H, J = 7 Hz), 7.4–7.54 (m, 3 H), 7.89–7.93 (m, 2 H) [the sizeable coupling (6 Hz) of the bridgehead proton identifies this as the endo isomer; no indication of exo isomer was seen in the spectra of crude product mixtures]; MS (CI, methane flow gas), calcd for P + H 306.1130, found 306.1118. Anal. Calcd for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.94. Found: C, 74.42; H, 5.20.

2-Methyl-4-phenyl-1*H*-benz[*f*]isoindole-1,3(2*H*)-dione (12). A solution of 52.5 mg (0.17 mmol) of **11** and 0.1 mL of methanesulfonic acid in 2 mL of benzene was refluxed for 8 h, when TLC indicated consumption of **11**. The mixture was taken up in CH_2Cl_2, washed with brine, dried over K_2CO_3, and rotary evaporated to give 45.5 mg (92%) of ca. 90% pure **12**. Recrystallization from CH_2Cl_2 gave pure **12** with mp 267–269 °C (lit.[10] mp 259–260 °C): ^1H NMR δ 3.15 (s, 3 H), 7.37–7.43 (m, 2 H), 7.53–7.72 (m, 5 H), 7.80 (d, 1 H, J = 8 Hz), 8.09 (d, 1 H, J = 8 Hz), 8.37 (s, 1 H).

(18) Meth-Cohn, O.; Suschitzky, H.; Sutton, M. E. *J. Chem. Soc. C* **1968**, 1722.

1-Phenyl-3-(trimethylsilyl)isobenzofuran (13). This material, prepared by treating a solution of **9** (from 460 mg of **4c/4t**) with Me_3SiCl (2.5 equiv), was characterized indirectly by the cycloadducts described below and directly by ^1H NMR (ether solution, 60 MHz): δ 6.90–7.20 (m, 2 H), 7.30–7.75 (m, 4 H), 7.83–8.20 (m, 3 H). No change in the spectrum was observed when the solution was washed with brine and dried over K_2CO_3.

In another reaction, **13** was prepared in the same manner (without washing) from 202 mg (89 mmol) of **4c/4t** and filtered under N_2 through 3 g of silica gel (30 mL of ether collected). This was evaporated under a stream of N_2 to yield 226 mg (95%) of a red oil, which by NMR was >80% **13**: ^1H NMR (60 MHz, benzene-d_6) δ 0.37 (s, 9 H), 6.70–8.05 (m, 9 H). Addition of NMM to this sample tube resulted in immediate formation of **14**.

***endo*-4,9-Epoxy-2-methyl-4-phenyl-3a,4,9,9a-tetrahydro-9-(trimethylsilyl)-1*H*-benz[*f*]isoindole-1,3(2*H*)-dione (14).** The etheral solution of **13** described above was added to a solution of NMM (220 mg, 2.0 mmol) in 1 mL of ether. The homogenenous solution was stirred overnight and then rotary evaporated to give 714 mg of crude product. Chromatography (silica gel, graded elution hexanes to ether) afforded 494 mg (70%) of pure **14**, mp 133.5–135 °C (from methanol): ^1H NMR δ 0.41 (s, 9 H), 2.31 (s, 3 H), 3.79 (d, 1 H, J = 8 Hz), 3.83 (d, 1 H, J = 8 Hz), 6.86 (d, 1 H, J = 7 Hz), 7.05–7.26 (m, 3 H), 7.40–7.52 (m, 3 H), 7.91 (d, 2 H, J = 7 Hz); MS calcd 377.1448, found 377.1475. Anal. Calcd for $C_{22}H_{23}NO_3Si$: C, 70.00; H, 6.14. Found: C, 69.88; H, 6.45.

Fluoride-Induced Conversion of 14 to 11. A solution of 185 mg (0.49 mmol) of **14** in 5 mL of THF was treated with 0.55 mL of 1 M tetra-*n*-butylammonium fluoride in THF (0.55 mmol). After being stirred for 1 h, the mixture was poured into brine and extracted with ether. The organic phase was washed (water, brine), dried (Na_2SO_4), and evaporated to yield 129 mg (86%) of **11**, pure by NMR analysis.

2,3-Bis(methoxycarbonyl)-1,4-dihydro-1,4-epoxy-1-phenyl-4-(trimethylsilyl)naphthalene. A solution of brine-washed **13** prepared as described above from 704 mg (2.93 mmol) of **3c/3t** (85/15) was added to an ether solution of 0.43 mL (3.5 mmol) of dimethyl acetylenedicarboxylate (DMAD). After stirring for 16 h, the volatiles were evaporated to give 1.24 g of crude material which was chromatographed on neutral alumina to give 662 mg (55%) of pure cycloadduct as a colorless oil: ^1H NMR δ 0.40 (s, 9 H), 3.71 (s, 3 H), 3.78 (s, 3 H), 7.05–7.13 (m, 2 H), 7.40–7.52 (m, 5 H), 7.69 (d, 2 H, J = 7 Hz); MS calcd for $C_{23}H_{24}O_5Si$ 408.1393, found 408.1401.

In Situ LTMP/Me_3SiCl Reaction of 4c/4t. A solution of LTMP (2.32 mmol) in 7 mL of THF at 0 °C was treated with 0.34 mL (2.67 mmol) of Me_3SiCl, followed by 202 mg (0.89 mmol) of **4c/4t**. The ice bath was removed after a few minutes and after 0.5 h examination of an aliquot by NMR indicated that the reaction was nearly complete. The mixture was washed with brine, dried over K_2CO_3, and added to 106 mg (0.95 mmol) of NMM in a small amount of THF. After being stirred overnight, the solvent was evaporated in vacuo, and the residue was chromatographed (silica gel, hexanes to ether) to afford 218 mg (65%) of pure **14**; 24 mg (12%) of **4c/4t** was also recovered.

9,10-Epoxy-1,4-methano-1,2,3,4,4a,9,9a,10-octahydro-9-phenylanthracene (15 and 16). A solution of norbornene in hexane (5.15 mL of 5 M, 26 mmol) and 310 mg (1.3 mmol) of **3c/3t** (85/15) in 25 mL of hexane was brought to reflux, and, using a syringe pump, 4.7 mmol of LDA in 8.6 mL of hexane was added over a period of 5 h. One hour after the addition was complete, heating was discontinued, water was added, and the layers were separated. The aqueous phase was extracted with CH_2Cl_2, and the combined organic phase was washed with water and brine, dried over K_2CO_3, and rotary evaporated to give 377 mg of crude product. Column chromatography (neutral alumina, hexanes to ether) gave a pure sample of exo, exo cycloadduct **15**, 156 mg (42%), and essentially pure endo,exo **16**, 16 mg (4%).

15: mp 129–130 °C (after recrystallization from hexanes); ^1H NMR δ 0.79 (d, 1 H, J = 9 Hz), 0.98–1.12 (m, 2 H), 1.35–1.50 (m, 2 H), 1.82 (d, 1 H, J = 7 Hz), 1.99 (s, 1 H), 2.02 (d, 1 H, J = 7 Hz), 2.32 (d, 1 H, J = 9 Hz), 2.43 (s, 1 H), 5.36 (s, 1 H), 6.98–7.57 (m, 9 H); MS calcd 288.1512, found 288.1528. Anal. Calcd for $C_{21}H_{20}O$: C, 87.46; H, 6.99. Found: C, 88.00; H, 7.04.

16: mp 97–105 °C (off column); ^1H NMR δ −1.10 (d, 1 H, J = 11 Hz), 0.29 (d, 1 H, J = 11 Hz), 1.03–1.50 (m, 4 H), 1.90 (s, 1 H), 2.12 (s, 1 H), 2.45 (d, 1 H, J = 9 Hz), 2.57 (dd, 1 H, J = 9 and 5 Hz), 5.34 (d, 1 H, J = 5 Hz), 6.80–7.70 (m, 9 H); MS found, 288.1512.

***endo*-2,4-Dimethyl-4,9-epoxy-3a,4,9,9a-tetrahydro-1*H*-benz[*f*]isoindole-1,3(2*H*)-dione (19).** The general procedure used with the 3-phenyl acetal was employed for the methyl analogue. Thus treatment of 374 mg (2.10 mmol) of **7c/7t** (42/58) and 0.2 mmol of DIPA in 2 mL of ether with 6.2 mL (5.3 mmol) of MeLi in ether (1.2 M) gave a dark red solution. After being stirred for 12 h the solution was washed with brine, and dried (K_2CO_3), and an aliquot was examined by NMR; a small singlet at 7.93 ppm (ether solvent) signaled the formation of some 1-methylisobenzofuran (**18**). This orange solution was decanted into a solution of 203 mg (1.83 mmol) of NMM dissolved in ca. 1 mL of ether. After 8 h, the usual workup and silica gel chromatography gave 115 mg (22%) of **19**, mp 137.5–138.5 °C (after recrystallization from hexane): ^1H NMR δ 2.02 (s, 3 H), 2.42 (s, 3 H), 3.32 (d, 1 H, J = 8 Hz), 3.83 (dd, 1 H, J = 8 and 6 Hz), 5.61 (d, 1 H, J = 6 Hz), 7.14–7.27 (m, 4 H). Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.13; H, 5.39. Found: C, 69.19; H, 5.54.

Isolation of 7c. A 688-mg (3.86 mmol) sample of **7c/7t** (78/22) in 2.5 mL of ether was treated with 0.37 mmol of DIPA and 3.7 mmol (2.65 mL of 1.4 M solution in ether) of MeLi, for 0.3 h. The mixture was washed with brine, dried over K_2CO_3, and rotary evaporated to give 580 mg of a yellow oil. Distillation through a short path apparatus yielded 226 mg (42% based on the **7c** present in the starting mixture) of pure **7c** (NMR given above).

2,3-Bis(methoxycarbonyl)-1,4-epoxy-1-methyl-4-(trimethylsilyl)naphthalene (21). A sample of **8c/8t** (42/58) in 1 mL of ether was treated with 0.1 mmol of DIPA and 2.4 mmol of MeLi, with stirring for 0.25 h. Me_3SiCl (0.30 mL, 2.4 mmol) was then added, and after 5 min the mixture was washed with cold brine and dried in the usual way. This solution was added to a mixture of DMAD (0.14 mL, 1.16 mmol) in 2 mL of ether. Rotary evaporation after 6 h gave 371 mg of crude product. Chromatography (neutral alumina) gave 25 mg (31%) of recovered unreacted **8c** and 89 mg (22%) of **21**: ^1H NMR δ 0.30 (s, 9 H), 1.96 (s, 3 H), 3.74 (s, 3 H), 3.75 (s, 3 H), 6.97–7.10 (m, 2 H), 7.25–7.32 (m, 2 H); MS/CI calcd for P + H 347.1315, found 347.1336.

4,9-Epoxy-2-methyl-3a,4,9,9a-tetrahydro-4-(trimethylsilyl)-9-[(trimethylsilyl)methyl]-1*H*-benz[*f*]isoindole-1,3-(2*H*)-dione (24). A mixture of 271 mg (1.52 mmol) of **8c/8t** (42/58) and 0.58 mL (4.6 mmol) of Me_3SiCl in 5 mL of THF at 0 °C was treated with 3.96 mmol of LTMP in 5 mL of THF, with stirring for 1 h (ice bath). The mixture was poured into 25 mL of brine, and the organic phase was separated, dried, and added to a flask containing 180 mg (1.62 mmol) of NMM. After 20 h the solvent was removed by rotary evaporation and the residue chromatographed (silica gel, hexanes to ether) to afford 67 mg (25%) of unreacted **8c** and 144 mg (30%) of solid **24**, mp (after recrystallization from aqueous methanol) 115–117 °C: ^1H NMR (CH_2Cl_2 used as internal reference) δ 0.01 (s, 9 H), 0.34 (s, 9 H), 1.71 (d, 1 H, J = 15 Hz), 1.89 (d, 1 H, J = 15 Hz), 2.19 (s, 3 H), 3.27 (d, 1 H, J = 8 Hz), 3.60 (d, 1 H, J = 8 Hz), 7.08–7.18 (m, 4 H); MS calcd for $C_{20}H_{29}NO_3Si_2$ 387.1686, found 387.1711.

4,9-Epoxy-2-methyl-3a,4,9,9a-tetrahydro-4-[(trimethylsilyl)methyl]-1*H*-benz[*f*]isoindole-1,3(2*H*)-dione (25). The reaction of 20 mg (0.052 mmol) of **24** with 0.11 mmol of tetrabutylammonium fluoride in 0.5 mL of THF for 0.5 h gave a fluorescent green solution. It was taken up in ether, washed and dried in the usual manner, rotary evaporated, and chromatographed on silica gel to give 9 mg (67%) of **25** contaminated with a small amount of **24**. Compound **25**: ^1H NMR δ 0.03 (s, 9 H), 1.72 (d, 1 H, J = 15 Hz), 1.93 (d, 1 H, J = 15 Hz), 2.22 (s, 3 H), 3.32 (d, 1 H, J = 8 Hz), 3.78 (dd, 1 H, J = 8 and 6 Hz), 5.61 (d, 1 H, J = 6 Hz), 7.1–7.25 (m, 4 H); MS calcd for P − CH_3 300.1025, found 300.1046.

1,1-Diethoxy-1,3-dihydro-3-methylisobenzofuran (26). A solution of NaOEt was prepared by addition of 2.0 g (87 mmol) of Na to 30 mL of EtOH, with stirring under N_2. To this was added gradually by cannula a solution of **6** prepared, as described above, from 19.9 mmol of **5**. After being stirred for 0.3 h, the mixture was taken up in 150 mL of water and extracted with CH_2Cl_2. The organic phase was washed with brine, dried over K_2CO_3, and rotary evaporated. The residue was short-path

distilled to yield 3.38 g (76%) of pure **26**: bp 57.5–58.6 °C (0.07 torr); ^{1}H NMR δ 1.18 (t, 3 H, J = 7 Hz), 1.20 (t, 3 H, J = 7 Hz), 1.53 (d, 3 H, J = 6 Hz), 3.30–3.75 (m, 4 H), 5.30 (q, 1 H, J = 6 Hz), 7.15–7.50 (m, 4 H); MS calcd for P – H 221.1177, found 221.1180. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.25; H, 8.16. Found: C, 70.04; H, 8.30.

Ethyl 2-(1-Ethoxybenzyl)benzoate (27). Similar treatment of **2** (addition to excess NaOEt, with analogous workup) gave, in several trials, mostly compound **27**, sometimes containing small amounts of **28**. Ether-ester **27**: ^{1}H NMR (60 MHz) δ 1.23 (t, 3 H, J = 7 Hz), 1.33 (t, 3 H, J = 7 Hz), 3.52 (q, 2 H, J = 7 Hz), 4.32 (q, 2 H, J = 7 Hz), 6.35 (s, 1 H), 7.15–7.90 (m, 9 H); IR ($CHCl_3$) 1720 cm^{-1}; MS/CI calcd for P + H 285.1491, found 285.1482.

1,1-Diethoxy-1,3-dihydro-3-phenylisobenzofuran (28). A solution of **2** (prepared from 8.69 mmol of **1**) was added dropwise to a solution of 26 mmol of LiOEt (freshly prepared from n-butyllithium and ethanol followed by removal of excess alcohol in vacuo) in acetonitrile (30 mL). After being stirred for 0.25 h, the mixture was taken up in 20 mL of CH_2Cl_2 and washed with water (2 × 20 mL). Drying (K_2CO_3) and rotary evaporation gave a semisolid, 2.15 g. This was triturated with hexanes (3 × 20 mL), and the combined hydrocarbon phase was evaporated to a yellow oil, 1.70 g (69%) of crude **28**. Chromatography on basic alumina using as solvent 2% ether in hexanes containing ca. 0.5% Et_3N afforded 946 mg (47%) of pure **28** as an oil: ^{1}H NMR δ 1.22 (t, 6 H, J = 7 Hz), 3.40–3.90 (m, 4 H), 6.12 (s, 1 H), 7.03 (d, 1 H, J = 7 Hz), 7.10–7.55 (m, 8 H); MS/CI calcd for P – OEt 239.1072, found 239.1071. Anal. Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: 76.16; H, 7.18.

4,9-Epoxy-4-ethoxy-2-methyl-9-phenyl-3a,4,9,9a-tetrahydro-1*H*-benz[*f*]isoindole-1,3(2*H*)-dione (30). A mixture of 523 mg (1.84 mmol) of **28** and 0.18 mmol of DIPA in 1 mL of ether was treated with 2.32 mmol of MeLi (1.95 mL of 1.2 M solution in ether), with stirring for 2 h. Direct examination of this ethereal solution by NMR showed a broad absorption (6.5–7.8 ppm) attributed to the isobenzofuran **29**. The mixture was cooled in an ice bath and the liquid phase transferred to another flask containing NMM (207 mg, 1.86 mmol) in 5 mL of ether. After 2 h, this mixture was washed with brine, dried, and rotary evaporated to give 448 mg of crude product. A portion (418 mg) was chromatographed (silica gel, hexanes to ether) to afford 230 mg (38%) of pure **30**, mp (hexane) 178–179.5 °C; ^{1}H NMR δ 1.44 (t, 3 H, J = 7 Hz), 2.33 (s, 3 H), 3.81 (d, 1 H, J = 8 Hz), 4.01 (d, 1 H, J = 8 Hz), 4.02–4.15 (m, 2 H), 6.93 (d, 1 H, J = 7 Hz), 7.17–7.53 (m, 6 H), 7.88–7.95 (m, 2 H); MS/CI calcd for P + H 350.1392, found 350.1428. Anal. Calcd for $C_{21}H_{19}NO_4$: C, 72.19; H, 5.48. Found: C, 72.11; H, 5.53.

9,10-Epoxy-9-ethoxy-1,4-methano-1,2,3,4,4a,9,9a,10-octahydro-10-phenylanthracenes (31 and 32). A solution of norbornene (56 mmol, 11.2 mL of a 5 M solution in hexane), 797 mg (2.80 mmol) of **28**, and 40 mL of hexane was brought to reflux, and then 11.2 mmol of LDA in 13.6 mL of hexane was added via syringe pump over a period of 6 h. Refluxing was continued an additional 2 h, after which the solution was cooled and washed with brine. The organic phase was rotary evaporated to give 953 mg of crude material which by column chromatography (basic alumina, hexanes, CH_2Cl_2 with ca. 0.5% of Et_3N) afforded 251 mg (27%) of exo,exo **31**, mp 92–94 °C: ^{1}H NMR δ 0.70–1.50 (m, 8 H), 190 (d, 1 H, J = 7 Hz), 1.97 (s, 1 H), 2.10 (d, 1 H, J = 7 Hz), 2.41 (d, 1 H, J = 9 Hz), 2.70 (s, 1 H), 3.96 (q, 2 H, J = 7 Hz), 7.00–7.65 (m, 9 H); MS/CI calcd for P + H 333.1852, found 333.1851.

Also collected was 125 mg (13%) of exo,endo **32** (oil): ^{1}H NMR δ –1.17 (d, 1 H, J = 10 Hz), 0.27 (d, 1 H, J = 10 Hz), 0.80–1.50 (m, 7 H), 1.99 (s, 1 H), 2.09 (s, 1 H), 2.49 (d, 1 H, J = 9 Hz), 2.67 (d, 1 H, J = 9 Hz), 3.99 (q, 2 H, J = 7 Hz), 6.85–7.60 (m, 9 H); MS calcd for $C_{23}H_{24}O_2$ 332.1777, found 332.1772.

The isomer **32** was quite sensitive to hydrolysis, and in another run hydrolysis occurred on attempted column chromatography to give product which exhibited: IR ($CHCl_3$) 1680, 3620 cm^{-1}; MS, m/z 304 (parent).

1,3-Dihydro-1,1-dimethoxy-3-methylisobenzofuran (33). A sample of **26** (296 mg, 1.33 mmol) was taken up in 15 mL of methanol and ca. 0.1 mL of glacial acetic acid was added. After stirring for 2 h, 2 mL of 10% aqueous K_2CO_3 was added, and the mixture was taken up in 100 mL of water. This was extracted with CH_2Cl_2 (5 × 5 mL), and the combined organic phase was washed with brine, dried, and evaporated to give 248 mg (96%) of essentially pure **33**: ^{1}H NMR δ 1.55 (d, 3 H, J = 7 Hz), 3.29 (s, 3 H), 3.32 (s, 3 H), 5.32 (q, 1 H, J = 7 Hz), 7.18–7.23 (m, 1 H), 7.35–7.46 (m, 3 H); in benzene-d_6 solvent δ 1.31 (d, 3 H, J = 7 Hz), 3.30 (s, 3 H), 3.39 (s, 3 H), 5.09 (q, 1 H, J = 7 Hz), 6.75–6.80 (d, 1 H, J = 7 Hz), 7.00–7.13 (m, 2 H), 7.41–7.45 (d, 1 H, J = 7 Hz). The greater separation of the methoxy singlets in the latter solvent was useful for DNOE experiments, which gave the results described in the text. Compound **33** was further characterized by MS: calcd for P – H 193.0864, found 193.0840.

2,4-Dimethyl-4,9-epoxy-9-ethoxy-3a,4,9,9a-tetrahydro-1*H*-benz[*f*]isoindole-1,3(2*H*)-dione (35). A solution of 1-ethoxy-3-methylisobenzofuran (**34**) was generated by treatment of 308 mg (1.39 mmol) of **26** with catalytic DIPA and 1.73 mmol of MeLi in ether (total volume ca. 3.5 mL). Direct examination of this solution after 0.5 h showed ^{1}H NMR (60 MHz, ether): δ 6.40–6.80 (m, 2 H), 7.00–7.30 (m, 2 H), attributed to **34**. This was added to a solution of 156 mg of NMM in 1 mL of ether. Rotary evaporation after 7 h gave 459 mg of crude product, which upon being chromatographed (silica gel, hexanes to ether) afforded 240 mg (60%) of pure **35**, mp 145.5–147.5 °C (hexane): ^{1}H NMR δ 1.38 (t, 3 H, J = 7 Hz), 2.00 (s, 3 H), 2.25 (s, 3 H), 3.49 (d, 1 H, J = 8 Hz), 3.67 (d, 1 H, J = 8 Hz), 3.85–4.08 (m, 2 H), 7.15–7.20 (m, 1 H), 7.25–7.30 (m, 3 H); MS calcd 287.1158, found 287.1185. Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96. Found: C, 66.48; H, 6.01.

2,4-Dimethyl-4,9-epoxy-9-methoxy-3a,4,9,9a-tetrahydro-1*H*-benz[*f*]isoindole-1,3(2*H*)-dione (37). Analogous treatment of 172 mg (0.89 mmol) of **33** gave a solution of 1-methoxy-3-methylisobenzofuran (**36**); this was added to NMM to give 138 mg (57%) of pure (after chromatography) **37**, mp 145–146 °C: ^{1}H NMR δ 2.01 (s, 3 H), 2.25 (s, 3 H), 3.51 (d, 1 H, J = 9 Hz), 3.67 (d, 1 H, J = 9 Hz), 3.69 (s, 3 H), 7.17–7.21 (m, 1 H), 7.26–7.32 (m, 3 H); MS/CI calcd for P + H 274.1079, found 274.1070.

Reactions of Alkoxyisobenzofurans with Alcohols. (a) 34 with Methanol (Formation of 39). A solution of **34** was prepared as described above, starting with 852 mg (3.83 mmol) of **26**. Methanol (3.0 mL, 74 mmol) was added, and after being stirred for 0.5 h, the mixture was added to brine, the layers were separated, and the aqueous phase was extracted with hexanes (2 × 20 mL). The combined organic phase was dried over K_2CO_3 and rotary evaporated to yield 708 mg of a viscous yellow oil. The ^{1}H NMR spectrum of this material, in benzene-d_6, showed methoxy singlets at 3.3 and 3.4 ppm in a ratio of 5/95 (taken as the ratio of **40/39**). A portion (314 mg) of this material was chromatographed on basic alumina (hexanes with ca. 0.5% Et_3N), yielding 101 mg (29%) of **40/39** in a ratio of 20/80; these results suggest that the orthoesters are easily epimerized on chromatography.

39: ^{1}H NMR (benzene-d_6) δ 1.16 (t, 3 H, J = 7 Hz), 1.32 (d, 3 H, J = 6 Hz), 3.40 (s, 3 H), 3.55 (dq, 1 H, J = 9 and 7 Hz), 3.80 (dq, 1 H, J = 9 and 7 Hz), 5.09 (q, 1 H, J = 6 Hz), 6.79 (d, 1 H, J = 7 Hz), 7.01–7.13 (m, 2 H), 7.45 (d, 1 H, J = 7 Hz); MS calcd for P – H 207.1022, found 207.1001.

A major product formed in this and other short-time alcoholysis reactions appears to be a keto ester, in this instance ethyl 2-acetylbenzoate (**38**); IR (neat) 1700, 1750 cm^{-1}; ^{1}H NMR (60 MHz) δ 1.40 (t, 3 H, J = 7 Hz), 2.57 (s, 3 H), 4.39 (q, 2 H, J = 7 Hz), 7.30–8.00 (m, 4 H); MS, m/z 191 (P – H), 177 (P – Me), 149 (P – acetyl), 147 (P – OEt).

When the contact time for alcohol addition was increased to 5 h prior to the extraction procedure, no **38** was detected. The mechanism of formation of this interesting oxidation product is not known.

(b) 36 with EtOH (Formation of 40). A solution of **36** was generated in the usual way from 246 mg (1.27 mmol) of **33**. EtOH (2.0 mL, 34 mmol) was added and the mixture stirred for 24 h. Workup as above gave 200 mg (76%) of an oil, judged (NMR) to be mainly **40/39** in a ratio of 96/4. Short-path vacuum distillation of a portion (72 mg) of this material gave 37 mg (39%) of **40/39** in unchanged (97/3) ratio.

40: ^{1}H NMR (benzene-d_6) δ 1.18 (t, 3 H, J = 7 Hz), 1.32 (d, 3 H, J = 6 Hz), 3.30 (s, 3 H), 3.72 (dq, 1 H, J = 9 and 7 Hz), 3.90 (dq, 1 H, J = 9 and 7 Hz), 5.10 (q, 1 H, J = 6 Hz), 6.77 (dd, 1

H, J = 6 and 2 Hz), 7.02-7.10 (m, 2 H), 7.45 (dd, 1 H, J = 6 and 2 Hz).

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Registry No. **1**, 5398-11-8; **2**, 103934-98-1; **3c**, 103958-93-6; **3t**, 103934-75-4; **4c**, 103934-76-5; **4t**, 103934-77-6; **5**, 3453-64-3; **6**, 103934-94-7; **7c**, 103934-78-7; **7t**, 103934-79-8; **8c**, 103934-80-1; **8t**, 103934-81-2; **9**, 103934-82-3; **10**, 103934-83-4; **11**, 103934-84-5; **12**, 60231-30-3; **13**, 103934-85-6; **14**, 103934-86-7; **15**, 103934-88-9; **16**, 104011-62-3; **18**, 61200-10-0; **19**, 103934-89-0; **21**, 103934-90-3; **21** (1-phenyl), 103934-87-8; **24**, 103934-91-4; **25**, 103934-92-5; **26**, 103934-95-8; **27**, 103934-96-9; **28**, 103934-99-2; **29**, 103935-00-8; **30**, 103935-01-9; **31**, 103935-02-0; **32**, 104011-63-4; **33**, 103935-03-1; **34**, 103935-04-2; **35**, 103935-05-3; **36**, 103935-06-4; **37**, 103935-07-5; **38**, 103935-10-0; **38** (acid), 577-56-0; **39**, 103935-09-7; **40**, 103935-08-6; NMM, 930-88-1; DMAD, 762-42-5; 2-$PhCOC_6H_4CO_2H$, 85-52-9; norbornene, 498-66-8.

Photolysis of Dimethylcarbamoyl Azide in the Presence of a Cyclic Aminimide

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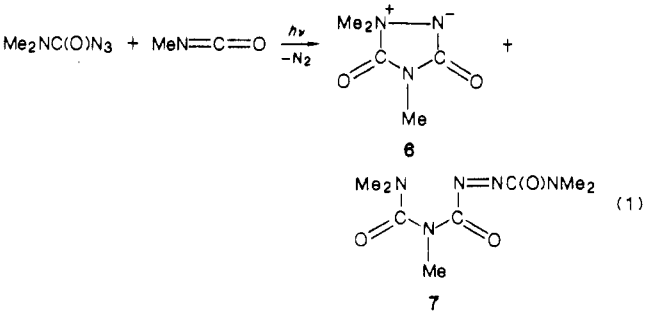
Dimethylcarbamoyl azide has been photolyzed in the presence of methyl isocyanate to produce the cyclic aminimide 1,1,4-trimethyl-1,2,4-triazolidine-3,5-dione 1,2-ylide (**6**) and the azo compound *N*-(dimethylcarbamoyl)-*N*,*N*',*N*'-trimethylazodicarboxamide (**7**). The azo compound **7** arises from a photolytic reaction between dimethylcarbamoyl azide and aminimide **6**. Mechanistic studies support a reaction path involving intermolecular-assisted loss of nitrogen from the azide as a result of interaction with aminimide **6**.

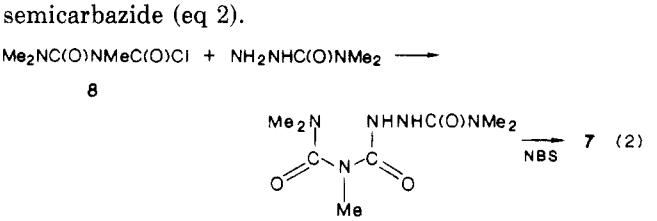
The photolysis of carbamoyl azides (**1**) provides a potential source of the intermediates shown in Scheme I.

Certain photoexcited carbamoyl azides (**2**) are known to give singlet (**3**) and triplet (**4**) nitrene intermediates as well as amino isocyanates (**5**) via a Curtius-type rearrangement. Arylalkylcarbamoyl azides give nitrene products,[1] dialkylcarbamoyl azides provide a source of amino isocyanates,[2] while diaryl derivatives apparently give both nitrene and amino isocyanate intermediates.[3] While there has been considerable work done with nitrene and amino isocyanate intermediates,[4] excited-state carbamoyl azides (**2**) have received little attention.[3] We wish to report the first example of intermolecular-assisted loss of nitrogen from a carbamoyl azide in the photoreaction of dimethylcarbamoyl azide with a cyclic aminimide, 1,1,4-trimethyl-1,2,4-triazolidine-3,5-dione 1,2-ylide (**6**).

As part of a study of the photolysis of carbamoyl azides in the presence of heterocumulenes,[5] dimethylcarbamoyl azide was photolyzed in the presence of methyl isocyanate in dichloromethane at −5 °C, producing the aminimide **6** (44%) and the azo compound **7** (40%) (eq 1).



Under these photolytic conditions, dimethylcarbamoyl azide is known to undergo loss of nitrogen with rearrangement to dimethylamino isocyanate.[2] In the presence of organic isocyanates, amino isocyanates produce cyclic aminimides such as **6** via cycloaddition reactions.[6,7] In contrast to the formation of aminimide **6**, the production of azo compound **7** was unexpected. Its structure was determined from instrumental analysis (^{1}H NMR, ^{13}C NMR, ^{15}N NMR, IR, MS), base-catalyzed hydrolysis to give trimethylurea, and an independent synthesis from 2,4,4-trimethylallophanoyl chloride (**8**) and 4,4-dimethylsemicarbazide (eq 2).



The structure of azo compound **7** suggests that it might arise from a reaction of dimethylcarbamoyl azide and aminimide **6**. Indeed, photolysis of dimethylcarbamoyl azide

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