56-0; (+)-(2R)-8, 91684-37-6; (-)-(2S)-8, 84276-31-3; (2R)-8 (benzoate), 91684-38-7; (±)-9, 88598-49-6; (-)-(2R)-9, 91684-39-8; (±)-11, 36667-75-1; (+)-(2R)-11, 54656-99-4; (-)-(2S)-11, 91684-33-2; (±)-12, 36667-73-9; (+)-(2R)-12, 91684-34-3; (-)-(2S)-12, 52079-66-0; (±)-13, 91586-53-7; (±)-13 (p-nitrobenzoate), 91586-54-8; (-)-(2S)-13, 91684-40-1; (±)-14, 5746-69-0; (±)-14 (p-nitrobenzoate), 91586-54-8; (+)-(2R)-14, 91684-35-4; (2R)-14 (p-nitrobenzoate), 91684-36-5; (-)-MTPA chloride, 39637-99-5; $ClCOCH_2Cl$, 79-04-9; (-)-menthyl N-aminocarbamate, 21391-40-2; phthalic anhydride, 85-44-9; p-nitrobenzoyl chloride, 122-04-3; p-bromobenzoyl chloride, 586-75-4.

Supplementary Material Available: Table III, atomic parameters for anisotropic and isotropic atoms of (-)-*cis,cis*-decahydro-2-naphthyl p-bromobenzoate (1 page). Ordering information is given on any current masthead page.

α-Methoxy-o-xylylene:† Formation by $LiNR_2$-Induced 1,4-Elimination of o-Tolualdehyde Dimethyl Acetal

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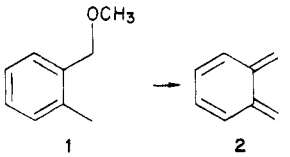
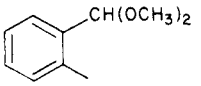
o-Tolualdehyde dimethyl acetal (3) undergoes 1,4-elimination on treatment with $LiNR_2$, generating α-methoxy-o-xylylene (6), as shown by trapping with various olefinic dienophiles. Norbornene gives two isomeric cycloadducts, one of which (trans) undergoes further elimination; the new o-xylylene formed in this step reacts with a second norbornene to form a symmetrical bis(norbornene) adduct. Similarly, the trans cycloadduct of 6 and norbornadiene undergo further elimination, yielding naphthalene by subsequent retro-Diels–Alder reaction. Cycloadducts of 6 with cyclopentene, isoprene, and 1-hexene are formed in moderate to low yields. The reaction with cyclopentene provides a single isomer (cis) which is resistant to further elimination. Isoprene and 1-hexene give complex mixtures of cycloadducts. Control reactions demonstrate that, in the absence of a reactive dienophile, 6 partitions between dimer formation and electrocyclic closure to α-methoxybenzocyclobutene (7); 7 undergoes rapid elimination with LDA to generate benzocyclobutadiene, as shown by trapping with 1,3-diphenylisobenzofuran. Thermal reactions of 7 with norbornene and cyclopentene give the same cycloadducts as formed in the base-induced reactions of 3, suggesting that these arise from the *E* isomer of 6.

The unique propensity of allylic ethers to undergo 1,4-elimination on treatment with lithium dialkylamides has been shown to extend to analogous benzylic ethers. These substrates experience disruption of benzene aromaticity in order to follow this pathway, and hence represent severe tests of the generality of this reaction. The preparation of isobenzofuran (moderately stable in solution) in this manner is quite straightforward,[1] and the procedure has been used to form some substituted derivatives.[2,3] A modification using alkyllithium reagents and catalytic $LiNR_2$ has recently been developed for these materials.[4] The finding that o-xylylene (2) is generated on similar treatment of methyl o-methylbenzyl ether (1) with $LiNR_2$ is particularly strong evidence for the general preference for 1,4-elimination.[5]



1 2

In this paper, results obtained with the analogous acetal 3 are presented. This work was undertaken with the goal



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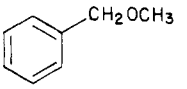
of determining whether the base-induced elimination would in fact occur with this substrate, and if so, to examine some properties of the methoxy-substituted o-xylylene, the stereochemistry of cycloadducts formed on reaction with dienophiles, and the potential of these cycloadducts for further elimination or other reactions.

Results and Discussion

Wittig ether rearrangement and α-elimination processes are the most obvious alternatives to 1,4-elimination in the systems examined in this work. Indeed, reexamination of the simple ether 4 with lithium tetramethylpiperidide



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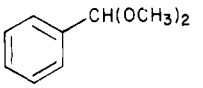

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(LTMP) in hexane showed that Wittig rearrangement occurs, leading to 1-phenylethanol (isolated in moderate yield); the reaction is, however, slower than the 1,4-elimination of the o-methylbenzyl ether 1. The dimethyl acetal of benzaldehyde (5) also reacts with this strong base, giving viscous and presumably polymeric material which has not been characterized. These observations show that α-proton abstraction pathways are likely alternatives for ethers and acetals where 1,4-elimination is either slow or precluded.

A competition kinetics experiment was carried out to explore this point. When an equimolar mixture of 3 and 5 was refluxed for 2.5 h in hexane containing 6 equiv of lithium diisopropylamide (LDA), all of 3 was consumed

† A more systematic name for α-methoxy-o-xylylene is 5-(methoxymethylene)-6-methylene-1,3-cyclohexadiene.

(1) Naito, K.; Rickborn, B. *J. Org. Chem.* **1980**, *45*, 4061.
(2) Makhlouf, M. A.; Rickborn, B. *J. Org. Chem.* **1981**, *46*, 2734.
(3) Cornejo, J.; Ghodsi, S.; Johnson, R. D.; Woodling, R.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 3869.
(4) Crump, S.; Rickborn, B. *J. Org. Chem.* **1984**, *49*, 304.
(5) Tuschka, T.; Naito, K.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 70.

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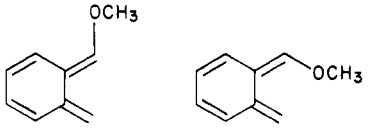
while ≥95% of **5** remained. This implies that attack at the o-methyl group is strongly favored over α-proton abstraction from the acetal carbon ($k(3)/k(5) \geq 20$) and is in keeping with 1,4-elimination being the more facile of the two pathways available to **3**.

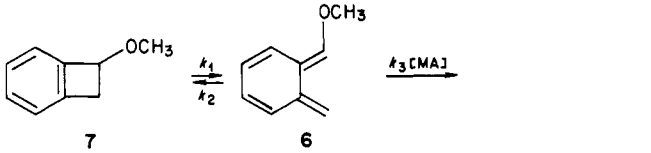
The acetal **3** is less reactive than the ether **1**, although the difference is not large. The ratio is $k(1)/k(3) = 4 \pm 1$ for reaction with both LDA and LTMP, as shown by direct determination of rate constants[6] and by a competition experiment. The bulkier base (LTMP) is more reactive than LDA by a factor of ca. 2–3 with the acetal **3**, similar to the effect observed[5] earlier for **1**. Several factors may enter into the (small) differences in rates between **1** and **3**, but the similarities in behavior of the two substrates suggest that identical mechanisms (1,4-elimination) are involved for both.

The immediate product of such an elimination from **3** would be α-methoxy-o-xylylene (**6**), which can in principle

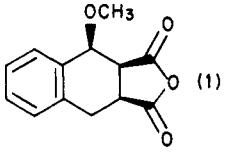


6-(*E*) **6-(*Z*)**

be formed in either the *E* or *Z* geometry. We will provide evidence supporting the formation of **6-(*E*)**, but ruling out the possible formation of **6-(*Z*)** is a difficult problem for which only indirect arguments can be made. A further interesting point concerns the possible electrocyclic closure of **6** to α-methoxybenzocyclobutene (**7**). Sammes and coworkers[7] have studied the reactions of optically active **7** in the presence of maleic anhydride (MA), as shown in eq 1. They concluded that the opening of **7**, k_1, was rate



7 **6**



(1)

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determining for the overall process, with the rate of adduct formation being identical with the rate of racemization in the absence of dienophile, hence $k_3(MA) > k_2 > k_1$. The methoxy substituent has a remarkable rate enhancing effect on the opening of **7**, as shown by comparison with the activation parameters determined by Roth's group for the parent benzocyclobutene.[8-10] Sammes also found that thermally generated **6** is reconverted to **7**, apparently without significant dimerization or polymerization, in the temperature range 80–130 °C (ca. 0.15 M **7** in C_6D_6 solutions were employed.) This is in marked contrast to the unsubstituted o-xylylene, which at 80 °C forms no detectable benzocyclobutene, as noted in our previous work[5] and implicit in the activation parameters for the reactions of this species found by Roth.[11,12] The activation parameters for electrocyclic closure of **6** to **7** are unknown, although Sammes' work allows limits for $\Delta H^{\ddagger}$ between 18 and 28 kcal/mol to be calculated.[13] The lower figure approaches the activation energy ($\Delta G^{\ddagger}$ at the temperature used) for the very fast dimerization of unsubstituted o-xylylene;[9] again, the corresponding activation parameters for dimerization of **6** are unknown, but this suggests that both closure and dimerization might be observed under our conditions. It should be noted, however, that the base-induced elimination of the acetal **3** is clearly the rate-controlling step, and barring unusual features, Sammes' observations would seem to require that **6** could not be formed in excess of a finite (steady state) concentration because of rapid conversion to **7**, and thus in the absence of reactive dienophiles, **7** or products of its further reaction should be observed.

To address this question **7** was prepared as described in the literature,[7] and it was established that this material was not observed (by VPC) in any of the base-induced reactions studied. The reason for this became apparent when **7** was treated with LDA under the usual reaction conditions. Elimination to benzocyclobutadiene occurred, as shown by in situ formation and trapping with 1,3-diphenylisobenzofuran.[14] Further, it was observed that this elimination is significantly faster than that of the acetal **3**, being complete within at most a few minutes at 80 °C.

A base-induced reaction of **3** was then carried out in the presence of 1,3-diphenylisobenzofuran (1.1 equiv), and the cycloadducts with benzocyclobutadiene were indeed formed, although in low yield (4%). This result is significant in demonstrating that some **6** does indeed cyclize to **7**. The yield of cycloadduct is not a valid measure of the extent of this process, since the benzocyclobutadiene should be consumed by both the isobenzofuran and the much more reactive **6**.

As noted below, in the absence of a good dienophile, several products are formed in the base-induced reaction of **3**. These include materials having the molecular formula of dimers of **6**; since **6** is generated efficiently as a reactive intermediate under these conditions (as shown by trapping with norbornene), it appears that these dimethoxy compounds must arise by direct dimerization of **6**. We conclude therefore that **6** partitions between dimer formation, and (irreversible) cyclization to **7**. Only the latter would be predicted from Sammes' results. Other than to note

(6) Tuschka, T. Ph.D. Dissertation, University of California, Santa Barbara, CA, 1980.[5]

(7) Arnold, B. J.; Sammes, P. G.; Wallace, T. W. *J. Chem. Soc., Perkin Trans. 1* **1974**, 409.

(8) Roth, W. R.; Biermann, M.; Dekker, H.; Jochems, R.; Mosselman, C.; Hermann, H. *Chem. Ber.* **1978**, *111*, 3892.

(9) Roth, W. R.; Scholz, B. P. *Chem. Ber.* **1981**, *114*, 3741.

(10) A similar very large effect has been observed for the cyclobutene–butadiene rearrangement; Kirmse, W.; Scheidt, F.; Vater, H. *J. Am. Chem. Soc.* **1978**, *100*, 3945. Professor Kirmse has kindly provided additional unpublished data on substituent effects of this reaction.

(11) A useful way to approach this question involves calculating the equilibrium concentration of o-xylylene from the ΔG° derived from Roth's parameters.[8,9] At 80 °C (the approximate temperature of refluxing hexane solutions used in our work), $K_{eq} \simeq 10^{-6}$, i.e., this would be the concentration of o-xylylene in equilibrium with 1 M benzocyclobutene if dimerization were artifically precluded. This value is ca. two or three orders of magnitude higher than the steady-state concentration of o-xylylene where dimerization would equal electrocyclic closure,[12] i.e., dimerization would be expected to dominate the overall reaction if opening of benzocyclobutene could be effected at this temperature. Note that Sammes' racemization results were obtained with ca. 0.15 M solutions of **7**.

(12) One may calculate from Roth's data,[8,9] at a typical operating temperature (80 °C) for the elimination of **1**, that the steady-state concentration of o-xylylene at which the rate of benzocyclobutene formation (first order) equals that of dimerization (second order) would be ca. 3×10^{-9} M. Since no benzocyclobutene is observed[5] in the base-induced reaction of **1**, the steady-state concentration of o-xylylene generated under these conditions must be higher than this value.

(13) The lower value is obtained by applying Roth's data for the unsubstituted system,[8,9] and Sammes' $\Delta H^{\ddagger}$ (31 kcal/mol) for the conversion of **7** to **6**; this value assumes that the effect of the methoxy group is expressed only in the transition state. The upper value is established by the fact that no **6** is visible in the NMR spectrum of **7**.

(14) Cava, M. P.; Hsu, A. C. *J. Am. Chem. Soc.* **1972**, *94*, 6641; a 3:2 exo:endo ratio was obtained (54% after recrystallization). We find a ratio of 55:45 (77% after chromatography).

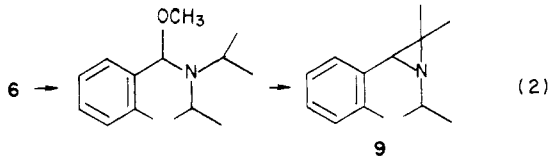
Table I. LDA-Induced Reactions of 3[a]

dienophile	cycloadduct,%
norbornene	74[b]
norbornadiene	62[b]
isoprene	48[c]
cyclopentene	40[b]
1-hexene	18[c]

[a] Conditions are given in the Experimental Section. [b] Distilled yield. [c] Yield based on VPC analysis with *n*-tridecane internal standard, corrected for differences in thermal conductivity.

the difference in reaction conditions, we have no explanation for this variation in outcome. The relative amount of cyclization to **7** cannot be directly determined from our results, since the dimer-like products also observed[15] (dimer minus one or two methanols) could arise by either further elimination reactions of dimers or by reactions of benzocyclobutadiene with **6**.

When **3** was added to a refluxing solution of 1.4 equiv of LDA in hexane and the progress of the reaction monitored by GC, ca. 85% of **3** was consumed, suggesting that further reactions of products might account for some consumption of base. In addition to a single more volatile compound (**9**), an incompletely separated mixture of at least eight components was found. Although individual structures for these materials have not been determined, GC/MS and other evidence[15] supports the "dimer" designation. The more volatile compound **9** which was observed in this reaction and others involving LDA and poor dienophiles in yields up to a maximum of 10%, proved to have unusual characteristics. It was extractable from the neutral organic residue by aqueous acid and recovered intact on neutralization, did not contain a methoxy group, and exhibited three sharp methyl singlets in ^{1}H NMR. The MS of **9** showed a parent ion of 203, corresponding



(2)

9

to the formula $C_{14}H_{21}N$. The aziridine structure shown in eq 2 is proposed for **9** Its formation implies that LDA/*i*-Pr_2NH adds regioselectively to **6** as indicated, although details of subsequent conversion to **9** are not known, and several pathways are possible. The addition of base to *o*-xylylene itself has precedent in our earlier work[5] and is known even for simpler butadienes.[16]

In the *o*-xylylene work it was found that amine addition could be avoided by using the bulky base LTMP. In the present study, no amine addition products were found when LTMP was employed, but preliminary trials with dienophiles present did not indicate any improvement in yield of cycloadduct when the bulkier base was used instead of LDA, and consequently most of our results were obtained with the simpler base.

The reactions of **3** with LDA in the presence of large excesses of various olefins showed that **6** behaves analogously to **2** in its ability to discriminate between better and poorer dienophiles. The cycloadduct yield results are displayed in Table I. The efficiency of adduct formation,

(15) In order of increasing retention times (GC), ^{1}H NMR evidence suggested the formation of a small amount (in mixture with other material) of dibenzo[*a*,*e*]cyclooctatetraene (dimer minus two methanols), while GC/MS indicated at least two proucts with parent ions of 236 (dimer minus methanol), and at least four products with parent ions of 268 (dimers).

(16) Imai, N.; Narito, T.; Tsuruta, T. *Tetrahedron Lett.* **1971**, 3517.

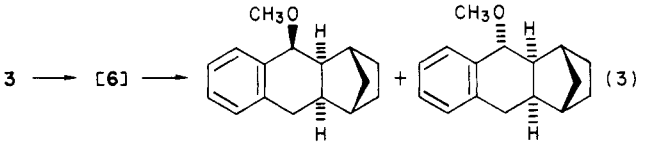
Table II. $LiNR_2$-Induced Reactions of 3 with Norbornene[a]

base (equiv)	time,[b] h	yield (10 + 11)[c]	10/11
LDA (1.4)	31[d]	95	46/54
(1.6)	2.5	84	48/52
(2.7)	69[d]	77	54/46
(2.9)	2.3	78	50/50
LTMP (1.3)	1.0	65	48/52
(2.8)	0.25	33	43/57
(3.1)	0.5	45	73/27
(3.1)	1.0	43	61/39
(2.8)	16	21	100/0

[a] Unless otherwise specificed, reactions were carried out in refluxing hexane, with ca. 30 equiv of norbornene. [b] At least 90% of **3** was consumed in the time shown. [c] Yields and ratios were determined by VPC at the time cited. [d] These reactions were carried out at 23 °C.

norbornene > norbornadiene > isoprene > cyclopentene > 1-hexene, follows the pattern observed in reactions of the benzyl ether **1**. When the better dienophiles were used, insoluble and/or nonvolatile (GC) material accounted for the remainder of the material balance, while the "dimers" of **6** mentioned above became significant only when the poorer dienophiles were employed (ca. 10% and 20%, respectively, with cyclopentene and 1-hexene.) Aziridine **9** was not observed in reactions of, e.g., norbornene, while a peak of this retention time was seen (4%) when 1-hexene was used. As also demonstrated for reactions of **1**, slow addition (syringe pump) of **3** to refluxing mixtures of base and olefin in hexane had no significant effect on the outcome, when allowance was made for further reaction of the initially formed cycloadducts as discussed below. These features again attest to the similarities in the reactions of **1** and **3**, with 1,4-elimination being the preferred but rate-determining step in the overall process.

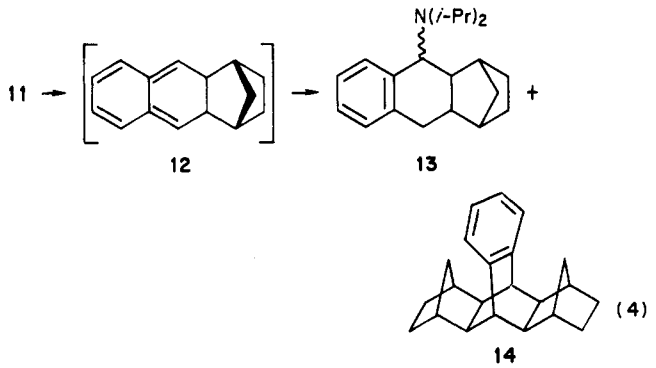
Reaction of 3 and Norbornene. The $LiNR_2$-induced elimination of **3** in the presence of excess norbornene leads to two primary cycloadducts, **10** and **11**, in good combined yield. Evidence for the stereochemical assignments is presented below. The formation of **10** and **11** constitutes the most direct proof that 1,4-elimination of **3** is the preferred mode of reaction, and that **6** is formed as an intermediate (eq 3). The yields of **10** and **11** are affected



(3)

10 11

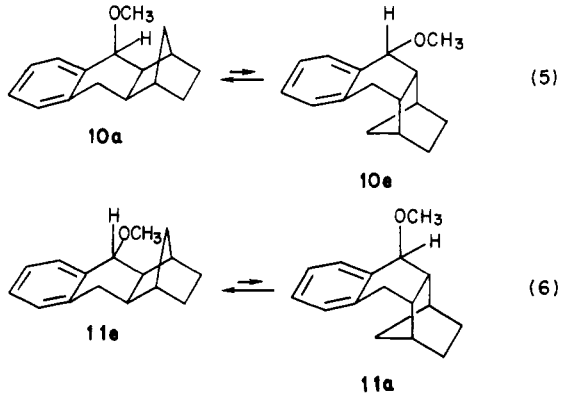
by the base used, its concentration, and reaction times as shown in Table II. It should be noted that the two isomers are initially formed in essentially equal amounts, but the ratio of the two and the total yield change in a manner consistent with further reaction of **11** with base. Further, the loss of **11** is associated with the formation of new products. When an isolated sample of pure **11** was subjected to the reaction conditions (3 equiv of LDA, excess norbornene in refluxing hexane), it was approximately 50% consumed in 24 h. Isomerization to **10** did not occur. Product analysis strongly supports the conclusion that **11** undergoes 1,4-elimination to give **12** as a reactive intermediate, which in turn adds either *i*-Pr_2NH to give **13** (GC/MS, P − H ion at 296, corresponding to a parent of $C_{21}H_{31}N$) or norbornene to give the interesting cycloadduct **14** (eq 4). Due to symmetry, **14** exhibits only eight peaks in proton decoupled ^{13}C NMR; it was formed in ca. 10% yield and isolated as a sharp melting crystalline solid. No evidence for the presence of isomeric bis(cycloadducts) was



obtained, implying that the addition of norbornene to **12** is stereoselective.

The stereochemical features of the primary cycloadducts **10** and **11** were established by alternative syntheses as outlined in Scheme I. The base-induced reaction of 1,3-dihydro-1,1-dimethoxyisobenzofuran with norbornene has been shown to give cycloadducts **15** and **16**, with stereochemistry clearly demonstrated by ^{1}H NMR characteristics.[2] After separation, these were converted via hydrolysis, Wolff–Kishner reduction, and Williamson ether reactions to **10** and **11**, respectively, shown to be identical with the materials derived from **3**.

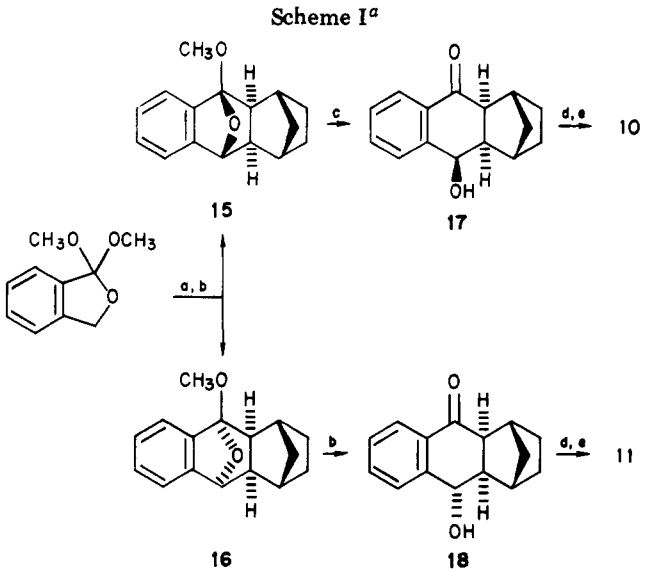
It is clear that **11** is considerably more reactive than **10** toward base. This is especially apparent in the LTMP reactions shown in Table II. The origin of this difference is of interest, since it may reflect stereochemical requirements of the 1,4-elimination process. Models show that two conformers may be considered for **10** and **11**, as depicted (eq. 5 and 6; enantiomer inversion is used to simplify



the drawings). NMR evidence supports the view that the equilibria strongly favor conformers **10a** and **11e**, based on analysis of chemical shifts and coupling constants for the methoxy and C*H*OCH$_3$ protons (see Table III), and the absence of significant upfield shifts of the syn bridge methylene protons anticipated for major contributions from **10e** and **11a**. Of course, one cannot conclude that the elimination of **11** occurs via the more stable conformer **11e**. Assuming that both conformations are accessible to both **10** and **11**, however, it appears that steric effects associated with the norbornyl system play a major role in determining the relative rates of elimination.

When a mixture of α-methoxybenzocyclobutene (**7**) and norbornene (5 M) in hexane was refluxed (9 days for complete conversion), a quantitative yield of **10** and **11** was obtained, in a ratio of 40:60. Sammes[7] has provided evidence that **6** formed in this manner has the *E* geometry, and this is also expected from studies[10] of cyclobutene–butadiene rearrangements. Since the same ratio of norbornene adducts is obtained when **6** is formed via base-induced elimination of **3**, it is tempting to suggest that the latter reaction also forms **6**-(*E*) as the only (trappable) isomer. However, since the adduct ratio from the elusive **6**-(*Z*) is unknown, unambiguous exclusion of this isomer is not possible.

Scheme I[a]



[a] (a) norbornene, LDA, refluxing hexane, (b) silica gel chromatography affords **15**, while **16** is hydrolyzed directly to **18** on the column, as reported earlier,[2] (c) dilute aqueous H_2SO_4, THF, (d) modified Wolff-Kishner reduction (see Experimental Section), (e) modified Williamson ether synthesis (see Experimental Section).

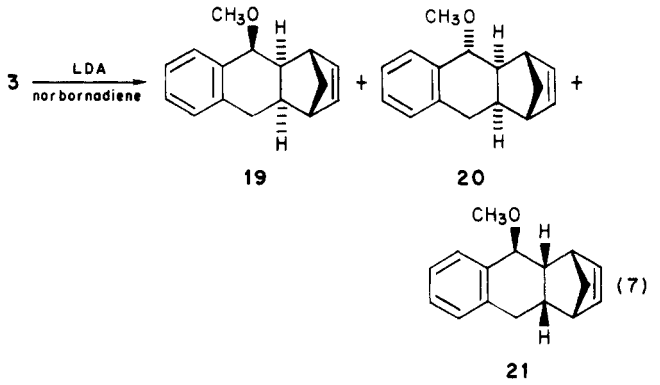
Table III. ^{1}H NMR Characteristics of Cycloadducts[a]

compd	methoxy	C*H*OCH$_3$	ortho aromatic H[b]
10	3.22	4.33 (d, 5)	
11	3.78	3.99 (d, 10)	7.48 (d, 9)
19	3.12	4.27 (d, 5)	
20	3.64	4.00 (d, 9.8)	7.39 (d, 9)
21	3.58	3.89 (d, 10)	7.33 (d, 9)
23	3.44	4.24 (d, 5.5)	7.38 (d, 7)
24	3.37	4.08 (d, 2.7)	
25	3.47	4.79 (dd, 10, 6)	7.50 (d, 8)
26	3.41	4.28 (t, 3)[c]	
27	3.46	3.84 (s)	
28	3.40	3.74 (s)	
29	3.34	4.26 (d, 2.5)	
30	3.35	4.50 (d, 7.5)	
31	3.44	4.33 (t, 3)[c]	
32	3.48	4.56 (dd, 9.9, 5.7)	7.50 (dd, 6.8, 2)

[a] Complete data are given in the Experimental Section. All spectra were recorded at 300 MHz, except for **26** (60 MHz); ppm from Me$_4$Si are shown, with multiplicities and coupling constants in parentheses. [b] The aromatic proton ortho to the CHOCH$_3$ function is deshielded and distinguished from the remaining protons in the compounds where entries are listed. This feature has diagnostic value, indicative of a (pseudo)equatorial methoxy group. [c] t is an apparent triplet.

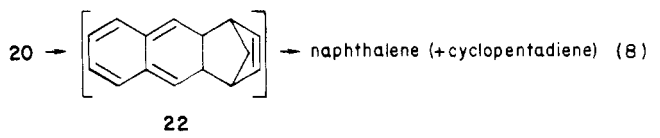
Reaction of 3 and Norbornadiene. Three primary cycloadducts were detected in the reaction involving norbornadiene as the dienophile (eq 7). These are formed in a ratio **19**:**20**:**21** of approximately 9:6.5:1. The cis exo isomer **19** was isolated in pure form by preparative VPC; its NMR characteristics (Table III) are in accord with the structure shown, and this was confirmed by catalytic reduction of the double bond to give **10**. Compounds **20** and **21** were collected together, and the structural assignments are based largely on NMR features; the cis endo assignment of **21** is tentative and based in part on previous observations[17] that norbornadiene tends to give small

(17) De Michelli, C.; Gandolfi, R.; Oberti, R. *J. Org. Chem.* **1980**, *45*, 1209.



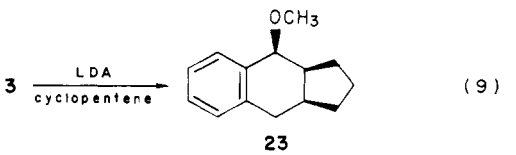
amounts of endo face cycloadducts.

High base concentrations and longer reaction times resulted in diminished yields and changes in the ratio of primary cycloadducts. When monitored by VPC, it was found that **20** diminished over time, while **19** appeared to be unaffected (the amount of **21** was too small to reach any conclusions about its stability). This behavior is analogous to that exhibited by the norbornene adducts, i.e., the trans isomer is clearly the more reactive of the pair. That the loss of **20** is also due to 1,4-elimination is supported by the appearance of naphthalene, believed to arise from intermediate **22** by facile retro-Diels–Alder reaction (eq 8). A



control reaction with isolated **20** (containing traces of **21**) established that this is the source of naphthalene. When the reaction of **3** and norbornadiene was carried out with LTMP in refluxing hexane for 0.75 h, **19** and **20** was observed in a ratio of 70/30 (39% yield), along with 11% of naphthalene. A similar starting material mixture heated for 4 h led to the nearly complete consumption of **20**, with **19** being formed in 40% yield, accompanied by 14% of naphthalene. It is difficult from the data available to extrapolate to the initial ratio of **19**/**20**, but it appears that, as with norbornene, there is little preference for formation of either product.

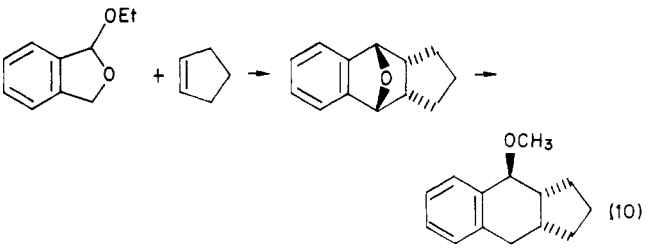
Reaction of 3 with Cyclopentene. In contrast to the results obtained with norbornene and norbornadiene, cyclopentene afforded only a single cycloadduct **23**, which is assigned the cis structure shown (eq 9) on the basis of



its spectral characteristics (Table III) and other evidence discussed below. Several attempts were made (lower temperature, base concentration, and reaction times) to detect the trans isomer, but all were fruitless. It appears that either **23** is the exclusive cycloadduct formed, or the trans isomer is much more reactive toward base and consumed before it can be detected. The product **23** is stable to base as shown by subjecting isolated samples to LTMP (3 equiv, 45 °C) and LDA (2 equiv, 96 h, 70 °C); in both cases **23** is completely unaffected, as judged by VPC analysis using an internal standard. This stability parallels that observed for the cis cycloadducts of norbornene and norbornadiene, but is perhaps more surprising for **23** since it should be more flexible conformationally than the bicyclic olefin derivatives.

The thermal reaction of α-methoxybenzocyclobutene and cyclopentene was of particular interest, since both cis and trans isomers of **23** should be stable in the absence of base. This reaction was carried out with excess cyclopentene in refluxing hexane (58 °C) for approximately one half-life (27 days), and also to completion in a sealed tube at 130 °C (cyclopentene solvent, 4 h). VPC analysis showed, in addition to cycloadduct, three peaks (each constituting $\leq 1\%$) which corresponded in retention times to dimers of **6**. The yields of cycloadduct suggest that the rate-determining step is the ring opening of **7** to **6**-(***E***), i.e., cyclopentene (excess) is an efficient trapping agent under these conditions.

Very interestingly, this reaction also gives only the single cycloadduct **23**, identical with that formed in the base-induced reaction of **3**, as shown by VPC, preparative collection, and comparison of spectra. This very high specificity was not anticipated, and its origins remain unknown. The failure of the thermal reaction of **7** to provide any of the other stereoisomer for comparison left uncertainty as to the cis designation of **23** and made a stereochemically unambiguous synthesis especially desirable. This was accomplished for the trans isomer as outlined in eq 10. A procedure developed earlier[18] was



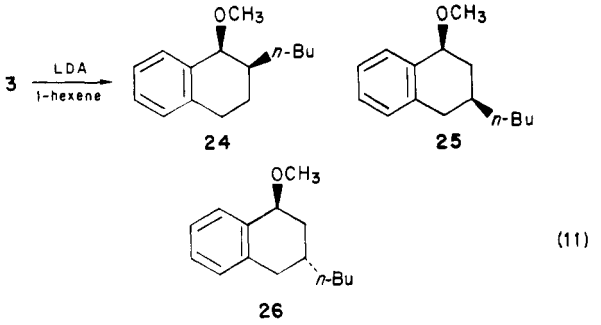
used to generate isobenzofuran in a sealed tube (160 °C) with cyclopentene as solvent. As Jones and Kneen have reported,[19] only the endo cycloadduct is formed in this reaction; the stereochemistry of this material is firmly established by the NMR coupling observed between the bridgehead and ring fusion protons. We were pleased to find that the reagent[20] obtained on mixing LiAlH(*O*-*tert*-butyl)$_3$ and triethylborane in tetrahydropyran solvent cleanly reduced the 1,4-epoxy function to give the benzyl alcohol, which was in turn converted to the methyl ether by treatment, in HMPA solvent, with *n*-butyllithium followed by methyl iodide.

The trans methoxy isomer formed as shown in eq 10 has many distinct NMR features which clearly distinguish it from **23** arising from the base-induced and thermal reactions utilizing **3** and **7**, respectively, and thus this synthesis provides strong evidence for the cis stereochemistry of **23**.

Reaction of 3 with 1-Hexene. The use of 1-hexene offered the opportunity to examine the regiochemical preference in cycloaddition of a simple olefin to **6**. However, in the best case the overall yield of this reaction was

(18) Mir-Mohamad-Sadeghy, B.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 2237.
(19) Jones, D. W.; Kneen, G. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1647.
(20) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1979**, *44*, 3678.

low, and the possibility of selective loss of some products cannot be excluded. With LDA, the cycloadducts **24**, **25**, and **26** were formed in a ratio of 5.2:3:1 (eq 11). Stereo-

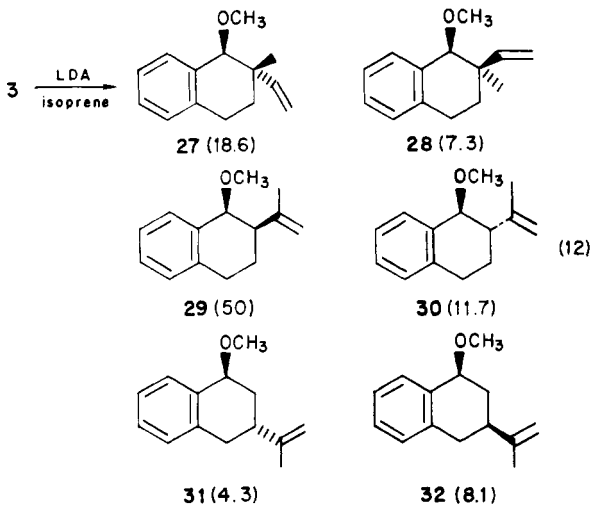


(11)

chemical assignments are based on the multiplicity and coupling constants of the benzylic methine protons (Table III), assuming that the predominant conformer in each compound is the half-chair form with the *n*-butyl group preferring the equatorial position. To the extent that this mixture of isomers represents the true selectivity of the cycloaddition reaction, it appears that cis products are favored over trans, while there is little preference for "ortho" over "meta" addition.

Reaction of 3 with Isoprene. There are eight possible primary cycloadducts from the reaction of **3** with isoprene. In our earlier work, it was found that the unsubstituted *o*-xylylene exhibited substantial selectivity (>9/1) for cycloaddition at the least substituted double bond of isoprene.[5] We also noted that Kametani had reported that the cycloaddition of α-cyano-*o*-xylylene (generated by heating α-cyanobenzocyclobutene, 180 °C) with isoprene was essentially devoid of such selectivity.[21] It is not clear whether these different outcomes are associated with the presence of the cyano group or variation in temperature.

The LDA-induced reaction of **3** and isoprene gave a complex mixture of cycloadducts which could not be completely separated by preparative VPC. Evidence was obtained for the formation of six isomers, in overall yield of 48%. These are given in order of retention time in eq 12, where the numbers in parentheses are the relative



(12)

percentages normalized to 100%, as determined by a combination of VPC and NMR analysis. Preparative collection gave four fractions. The first was a mixture of **27** and **28**. While these clearly have the gross structures shown (based on the number of vinyl protons and the singlet C*H*OCH$_3$ absorption), the stereochemical designations are less certain and may be inverted. The major isomer of the pair has the more deshielded methyl singlet and the more shielded vinyl protons. We attribute the shift differences as mainly due to aromatic ring current effects, with the quasi-axial methoxy conformer being preferred (for steric reasons) in both isomers.

The second fraction consisted of isomers **29** and **30**, identified by examination of the C*H*OCH$_3$ NMR signal, which appears as a doublet for both, but with J = 2.5 and 7.5 Hz, respectively.

Compounds **31** and **32** were collected separately. The C*H*OCH$_3$ signal of **31** was an apparent triplet (J = 3 Hz), while that of **32** was a doublet of doublets (J = 9.9, 5.7 Hz). The latter is interpreted as indicative of a preferred half-chair conformation with both substituents occupying equatorial sites.

The preference for cycloaddition at the less-substituted double bond of isoprene is not as pronounced for **6** as for *o*-xylylene **2**, although still favored by ca. 3/1. Ortho-substituted products are preferred over meta by a factor of ca. 7/1, while cis/trans ratios (perhaps reflecting endo/exo cycloaddition selectivity) are small (ca. 2–3/1) and not easily interpreted.

Conclusions

The formation of α-methoxy-*o*-xylylene **6** on treatment of the acetal **3** with LiNR$_2$ provides another striking example of the preference for 1,4-elimination of *o*-methylbenzyl ethers. The subsequent 1,4-elimination of some cycloadducts further demonstrates the generality of this reaction, while suggesting that the process has interesting stereochemical requirements. The data do not allow an unambiguous conclusion about the formation of **6**-(***E***) vs. **6**-(***Z***). The two primary cycloadducts of **6** and norbornene could be formed exclusively from **6**-(***E***) by endo and exo (exo face of norbornene) addition of the olefin, or from both isomers of **6**. The first of these possibilities has precedent in the reaction of norbornene with isobenzofuran, which gives a mixture of exo,exo and endo,exo products.[2,18] Further, the reaction of isobenzofuran with cyclopentene (and other simple cyclic olefins)[18,19] occurs with high endo selectivity. Addition of cyclopentene to **6**-(***E***) (electrocyclic opening of **7**) similarly leads exclusively to cis **23**, and this is the only cycloadduct found in the base-induced reaction of **3** with this olefin. The yield of **23** in the latter process leaves room for doubt about the possible formation and facile further reaction of **6**-(***Z***), which might be expected, by analogy with the reactions of isobenzofuran and **6**-(***E***), to lead to trans cycloadduct. All attempts to detect this material or its subsequent reaction products have failed to produce evidence for the formation of **6**-(***Z***). Also, the similarity in yields of cycloadducts with various olefins including cyclopentene from **6** and the parent *o*-xylylene[5] may suggest that no significant amount of **6**-(***Z***) is formed. Thus, our results are accomodated by formation of **6**-(***E***) alone, but do not conclusively rule out the formation of **6**-(***Z***).

We are currently examining the reaction of the ortho ester analogue of **3** with LiNR$_2$.

Experimental Section

General experimental and analytical procedures were identical with those reported earlier.[5] High field ^{1}H NMR spectra were recorded on a Nicolet NT-300 (partially funded by the NSF), and MS data were obtained by Dr. Hugh Webb on a VG Micromass ZAB-2F instrument. Analytical VPC data were obtained on (A) 3 m × 3.2 mm 20% SE-30 column, FI detector, with *n*-tridecane as the internal standard. Preparative collections were done on (B) 2 m × 6.4 mm 10% Apiezon N, (C) 6 m × 6.4 mm 8% SE-30,

(21) Kametani, T.; Hirai, Y.; Shiratori, Y.; Fukumoto, K.; Satoh, F. *J. Am. Chem. Soc.* **1978**, *100*, 554.

(D) 2 m × 6.4 mm 15% Carbowax 6 M, and (E) 3 m × 6.4 mm 8% SE-30 columns, TC detection. The amines were distilled from CaH_2 and stored under N_2. Olefins (except for norbornene, which was used as received) were distilled from CaH_2 immediately before use. THF was distilled as needed from sodium benzophenone ketyl, and commercial *n*-butyllithium in hexane was employed. The acetal **3** was prepared (84%) by tosic acid catalyzed reaction of *o*-tolualdehyde with trimethyl orthoformate in methanol. It had bp 59–61.5 °C (2 torr) and NMR features identical with those in the literature.[22] Solutions of $LiNR_2$ were prepared by dropwise addition of the amine to *n*-butyllithium in hexane at 0 °C. The olefin was added in large excess (30–40 equiv) and the mixture brought to reflux, at which point **3** dissolved in a few milliliters of hexane was added. The total volume of solution was typically 50 mL for reactions involving ca. 1 g of **3**.

Base-Induced Reactions of 3. (a) Without Added Dienophile. A mixture of **3** (967 mg) and 3.1 equiv of LDA was refluxed for 3 h, cooled, quenched with water, and taken up in ether. The organic phase was extracted with dilute HCl, washed with brine, and dried over K_2CO_3. Solvent evaporation and short path vacuum distillation (10^{-3} torr) gave 210 mg of viscous liquid. GC/MS showed parent ions, in order of increasing retention time, of 204, 236 (two major peaks), and 268 (three major peaks). Two components were isolated by a combination of preparative VPC (E) and TLC (silica gel), which corresponded to the peaks of 204 and one of those of 236 *m/z*. The former was shown to be dibenzo[*a*,*e*]1,3,5,7-cyclooctatetraene by mp 105–106 °C (lit.[23] mp 106.8-108.1 °C) and ^1H NMR spectrum, which was identical with the literature description.[24] The second component, mp 111.5–112.5 °C, corresponded to a dimer of **6** minus methanol (MS calcd for $C_{17}H_{16}O$ 236.1201, found 236.1227) but has not been more fully characterized.

The acidic aqueous phase was made basic and extracted with several portions of ether. After the usual workup the residue was subjected to preparative VPC (E) followed by preparative TLC, to give liquid compound **9**: ^1H NMR (300 MHz) δ 0.84 (s, 3 H), 1.20 (two overlapping d, apparent t, 6 H, *J* = 6.4 Hz), 1.46 (s, 3 H), 2.27 (s, 3 H), 2.29 (s, 1 H), 2.40 (septet, 1 H, *J* = 6.4 Hz), 7.12 (m, 3 H), and 7.42 ppm (m, 1 H); MS calcd for $C_{14}H_{21}N$ 203.1674, found 203.1699.

(b) With Norbornene. A mixture of **10** and **11** (74%) and **14** (5%) was obtained by high vacuum short path distillation of the residue from a reaction of 1.45 g of **3** and 1.6 equiv of LDA, 3 h reflux. Further separation was accomplished by preparative VPC (D); **10** and **11** are liquids.

10: ^1H NMR[25] δ 1.13 (d, 1 H, syn methano bridge, *J* = 9.7 Hz), 1.26 (m, 2 H, endo ethano bridge), 1.65 (m, 2 H, exo ethano bridge), 1.90 (br s, 3 H, anti methano bridge and ring fusion), 2.11 (br s, 1 H, distal bridgehead), 2.47 (br s, 1 H, proximal bridgehead), 2.68 (m, 2 H, benzylic), 3.22 (s, 3 H, methoxy), 4.33 (d, 1 H, C*H*OCH$_3$, *J* = 5 Hz), and 7.24 ppm (m, 4 H); MS calcd for $C_{16}H_{20}O$ 228.1514, found 228.1517. Anal. Calcd: C, 84.16; H, 8.83. Found: C, 84.1; H, 8.72.

11: ^1H NMR[25] δ 1.37 (m, 3 H, syn methano bridge and endo ethano bridge), 1.72 (m, 4 H, anti methano bridge, proximal ring fusion, and exo ethano bridge), 1.86 (m, 1 H, distal ring fusion), 2.23 (br s, 1 H, distal bridgehead), 2.38 (dd, apparent t, 1 H, cis benzylic, *J* = 14, 12 Hz), 2.59 (br s, 1 H, proximal bridgehead), 2.85 (dd, 1 H, trans benzylic, *J* = 14, 6 Hz), 3.77 (s, 3 H, methoxy), 3.99 (d, 1 H, C*H*OCH$_3$, *J* = 9.7 Hz), 7.3 (m, 3 H), and 7.48 ppm (m, 1 H). Anal. Found: C, 84.32; H, 8.92.

14: mp 127–128 °C after recrystallization from aqueous methanol; ^1H NMR δ −0.37 (dt, 2 H, syn methano bridge, *J* = 10.2, 2.2 Hz), 0.26 (br d, 2 H, anti methano bridge, *J* = 10.2 Hz), 1.13 (m, 4 H, exo ethano bridge), 1.33 (m, 4 H, endo ethano bridge), 1.84 (m, 8 H, ring fusion and norbornyl bridgehead), 2.94 (s, 2 H, benzylic bridgehead), 6.99 (m, 2 H), and 7.17 ppm (m, 2 H); ^{13}C NMR δ 31.39, 33.63, 40.53, 43.17, 49.29, 124.87, 126.12, and 141.32 ppm; MS calcd for $C_{22}H_{26}$ 290.2033, found 290.2035.

(c) With Norbornadiene. VPC analysis of the residue obtained from 3 h of reflux of 975 mg of **3** with 1.5 equiv of LDA showed 5% unreacted **3**, 6% of naphthalene, and three less volatile components. Short path vacuum distillation (105 °C bath, 0.002 torr) gave a fraction (62%) consisting of **19**, **20**, and **21** in a ratio of 9.2:6.5:1. Preparative VPC (D) afforded **19** and a mixture of **20** plus **21**.

19: ^1H NMR δ 1.34 (br d, 1 H, syn methano bridge, *J* = 8.4 Hz), 1.79 (m, 2 H, ring fusion), 1.98 (br d, 1 H, anti methano bridge, *J* = 8.4 Hz), 2.56 (br s, 1 H, distal bridgehead), 2.67 (m, 2 H, benzylic), 2.83 (br s, 1 H, proximal bridgehead), 3.12 (s, 3 H, methoxy) 4.27 (d, 1 H, C*H*OCH$_3$, *J* = 5.1 Hz), 6.17 (m, 2 H, olefinic), and 7.13 (m, 4 H); MS calcd for $C_{16}H_{18}O$ 226.1357, found 226.1356.

The NMR spectrum of the mixture of **20** and **21** allowed the following assignments. **20**: δ 3.65 (s, methoxy), 4.00 (d, C*H*OCH$_3$, *J* = 9.8 Hz). **21**: δ 3.58 (s, methoxy), and 3.89 ppm (d, C*H*OCH$_3$, *J* = 10 Hz). MS (for the mixture) found 226.1379.

(d) With Cyclopentene. After 7 h of refluxing and the usual workup, the reaction of **3** and 1.5 equiv of LDA afforded 37% of liquid cycloadduct, bp 72 °C (0.1 torr). Preparative VPC (E) gave an analytically pure sample of **23**: ^1H NMR[21] δ 0.86–1.88 (six separate m, 6 H), 2.46 (m, 1 H, distal ring fusion), 2.54 (dd, 1 H, trans benzylic, *J* = 14.2, 4.4 Hz), 2.66 (m, 1 H, proximal ring fusion), 2.69 (dd, 1 H, cis benzylic, *J* = 14.2, 6.1 Hz), 3.44 (s, 3 H, methoxy), 4.24 (d, 1 H, C*H*OCH$_3$, *J* = 5.5 Hz), 7.19 (m, 3 H), and 7.38 (br m, 1 H); MS calcd for $C_{14}H_{18}O$ 202.1358, found 202.1349. Anal. Calcd: C, 83.12; H, 8.97. Found: C, 83.3; H, 8.97.

(e) With 1-Hexene. VPC analysis (A) after 3 h of reflux with 3 equiv of LDA indicated the formation of aziridine **9** (4%), cycloadducts (overall 18%), and dimeric products (overall 12%). The cycloadducts were separated by preparative VPC.

24: ^1H NMR δ 0.92 (m, 3 H), 1.36 (m, 6 H), 1.50–1.95 (m, 3 H), 2.75 (ddd, 1 H, trans benzylic, *J* = 17.2, 9.1, 8.3 Hz), 2.91 (ddd, 1 H, cis benzylic, *J* = 17.2, 6.2, 3.9 Hz), 3.37 (s, 3 H, methoxy), 4.08 (d, 1 H, C*H*OCH$_3$, *J* = 2.7), and 7.2 ppm (m, 4 H); MS (CI, ethane) calcd for $C_{14}H_{19}$ (P − methoxy) 187.1487, found 187.1486.

25: ^1H NMR δ 0.92 (m, 3 H), 1.41 (m, 7 H), 1.76 (m, 1 H), 2.31 (m, 1 H), 2.46 (dd, 1 H, cis benzylic, *J* = 16.2, 11.4 Hz), 2.80 (ddd, 1 H, trans benzylic, *J* = 16.2, 4.7, 1.1 Hz, the latter due to long range coupling), 3.47 (s, 3 H, methoxy), 4.49 (dd, 1 H, C*H*OCH$_3$, *J* = 10.2, 5.7 Hz), 7.12 (m, 3 H), and 7.49 ppm (m, 1 H); MS-CI found 187.1492.

26: ^1H NMR δ 0.9 (m, 3 H), 1.4 (m, 6 H), 1.7–2.6 (m, 3 H), 2.7–3.1 (m, 2 H, benzylic), 3.41 (s, 3 H, methoxy), 4.28 (apparent t, 1 H, C*H*OCH$_3$, *J* = 3 Hz), and 7.2 ppm (m, 4 H); GC/MS 217 (P − 1), 129 (base).

(f) With Isoprene. This reaction involved 3.1 equiv of LDA and 6 h of reflux. VPC analysis (A) showed **9** (4%) and 48% of cycloadducts, with only traces of dimeric products. The ratios of cycloadducts are given in the text.

27: ^1H NMR δ 1.16 (s, 3 H, allylic methyl), 1.66 (ddd, 1 H, trans methylene, *J* = 13.4, 7.5, 5.4 Hz), 1.95 (ddd, 1 H, cis methylene, *J* = 13.4, 8.2, 7.3 Hz), 2.80 (m, 2 H, benzylic), 3.46 (s, 3 H, methoxy), 3.84 (s, 1 H, C*H*OCH$_3$), 4.93 (dd, 1 H, trans vinyl, *J* = 10.9, 1.2 Hz), 4.99 (dd, 1 H, cis vinyl, *J* = 17.6, 1.2 Hz), 5.79 (dd, 1 H, vinyl, *J* = 17.6, 10.9 Hz), and 7.2 ppm (m, 4 H).

28: ^1H NMR δ 0.98 (s, 3 H, allylic methyl), 1.6 (m, 1 H), 2.15 (m, 1 H), 2.9 (m, 2 H, benzylic), 3.40 (s, 3 H, methoxy), 3.74 (s, 1 H, C*H*OCH$_3$), 5.06 (dd, 1 H, trans vinyl, *J* = 10.8, 1.4 Hz), 5.09 (dd, 1 H, cis vinyl, *J* = 17.7, 1.4 Hz), 6.11 (dd, 1 H, vinyl, *J* = 17.7, 10.8 Hz), and 7.2 ppm (m, 4 H); MS-CI (mixture of **27** andf **28**) calcd for $C_{14}H_{19}O$ (P + H) 203.1435, found 203.1446.

Compounds **29** and **30** were collected together; the partial assignments given below are based on the relative amounts of the two isomers.

29: ^1H NMR δ 1.88 (m, 1 H, methylene), 1.89 (s, 3 H, vinylic methyl), 2.12 (m, 1 H, methylene), 2.80 (m, 2 H, benzylic), 2.99 (ddd, 1 H, allylic, *J* = 17.4, 6.5, 2.5 Hz), 3.34 (s, 3 H, methoxy), 4.26 (d, 1 H, C*H*OCH$_3$, *J* = 2.5 Hz), 4.88 (br s, 1 H, vinyl), 4.94 (br s, 1 H, vinyl), and 7.2 ppm (m, 4 H).

30: ^1H NMR δ 1.82 (s, vinylic methyl), 3.35 (s, methoxy), 4.50 (d, C*H*OCH$_3$, *J* = 7.5 Hz), 4.70 (br s, vinyl), and 4.83 (br s, vinyl); MS-CI (mixture of **29** and **30**) found 203.1456.

(22) Bruck, D.; Rabinovitz, M. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1656.
(23) Fieser, L. F.; Pechet, M. M. *J. Am. Chem. Soc.* **1946**, *68*, 2577.
(24) Wong, H. N. C.; Sondheimer, F. *Tetrahedron* **1981**, *37* (*Supplement 9*), 99.
(25) Assignments made using COSY-2D NMR,[26] 300 MHz.
(26) Bax, A.; Freeman, R. *J. Magn. Reson.* **1981**, *42*, 164.

31: ^{1}H NMR δ 1.83 (s, 3 H, vinylic methyl), 2.1–2.4 (m, 2 H), 2.55–2.75 (m, 2 H), 2.95 (dd, 1 H, benzylic, J = 16.3, 2.5 Hz), 2.45 (s, 3 H, methoxy), 4.33 (apparent t, 1 H, C*H*OCH$_3$, J = 3 Hz), 4.18 (br s, 2 H, vinyl), and 7.2 ppm (m, 4 H); MS-CI found 203.1424 (P + H).

32: ^{1}H NMR δ 1.82 (s, 3 H, vinylic methyl), 2.4 (m, 3 H, includes allylic), 2.78 (m, 2 H, benzylic), 3.48 (s, 3 H, methoxy), 4.56 (dd, 1 H, C*H*OCH$_3$, J = 9.9, 5.7 Hz), 4.82 (m, 2 H, vinyl), 7.1 (m, 3 H), and 7.50 ppm (m, 1 H); MS-CI calcd for $C_{13}H_{15}$ (P − methoxy) 171.1174, found 171.1178.

Alternative Synthesis of 10. A mixture of 4.0 g of ketal **15**[2] and 0.9 mL of 5% aqueous H_2SO_4 in 100 mL of THF was stirred for 5 min at ambient temperature and then made basic with saturated aqueous $NaHCO_3$. Most of the THF was removed by rotary evaporation, and the residue was taken up in ether, washed with brine, and dried over K_2CO_3. The waxy residue obtained by evaporation was recrystallized from CCl_4 to give keto alcohol **17** (2.96 g, 78%): mp 107–108.5 °C; ^{1}H NMR δ 0.9–1.9 (m, 7 H), 2.15 (s, 1 H, adjacent to carbonyl), 2.23 (d, 1 H, hydroxyl, J = 5 Hz), 2.58 (m, 2 H, bridgehead), 4.97 (apparent t, 1 H, C*H*OH, J = 5 Hz), and 7.4 ppm (m, 4 H); MS calcd for $C_{15}H_{16}O_2$ 228.1149, found 228.1161; IR ($CDCl_3$) 3600, 3470, 1668 cm^{-1}.

Wolff–Kishner reduction in refluxing diethylene glycol, 6 h, gave 96% of crude product, which proved to be largely (85%) the desired material, contaminated with ca. 15% of the epimeric alcohol. Since **17** was pure, this partial epimerization occurred in the reduction step, and caused us to use a lower boiling solvent in the alternative preparation of **11** (see below). The mixture of alcohols was methylated (NaH, CH_3I, THF, 46 h ambient), and the isomeric ethers separated by preparative VPC (E). The shorter retention time major product was identical with **10** obtained from the reaction of **3** and norbornene.

Alternative Synthesis of 11. Hydroxy ketone **18**[2] (IR 1678 cm^{-1}), 41 mg, was reduced in refluxing ethylene glycol (7 h) and gave 32 mg (81%) of pure alcohol, mp 158–159 °C. Attempted conversion to the methyl ether as above gave only partial reaction. The mixture of alcohol and ether was taken up in hexamethylphosphoric triamide, titrated with n-butyllithium (red end point), and treated with excess CH_3I. After 1 h, the mixture was taken up in water, extracted with pentane, dried, and evaporated to give essentially pure **11** in high yield; a sample collected by preparative VPC (E) was identical with **11** formed in the base-induced reaction of **3** and norbornene.

α-Methoxy-α,α′-dihydrobenzocyclobutene (7). The procedure of Sammes et al.[7] was followed with minor modification; methanolysis of the intermediate acetate was accomplished with Dowex 50W-X4 resin.

Thermal Reactions of 7. (a) With Norbornene. A mixture of **7** (134 mg) and 20 mL of a 5 M solution of norbornene in hexane was refluxed for 9 days and then vacuum evaporated to give **10** and **11** (VPC, NMR) in a ratio of 40/60, 95% combined yield, along with 5% of unreacted **7**.

(b) With Cyclopentene. A heavy-walled glass sealed tube containing 300 mg of **7** and 10 mL of cyclopentene was heated at 130 ± 5 °C for 19 h. After cooling and opening, the excess olefin was evaporated to give nearly pure **23** (VPC, NMR) along with ≤1% each of three apparently dimeric products (VPC). Control tubes indicated no additional products.

(c) With Norbornadiene. A mixture of **7** and the diene in toluene was refluxed for 7 h, giving 93% conversion to a mixture of **19**, **20**, and **21** in the ratio 46%/48%/6% (VPC, NMR).

LDA-Induced Reaction of 7 with 1,3-Diphenylisobenzofuran. To a refluxing solution of 1.0 mmol of 1,3-diphenylisobenzofuran and 2.0 mmol of LDA in 20 mL of hexane was added 1.0 mmol of **7**. The mixture became cloudy upon addition, indicating rapid reaction. After 0.5 h, the flask was cooled, water was added, and the combined organic phase from ether extraction was dried and evaporated. The ^{1}H NMR spectrum of this crude material indicated the presence of exo and endo cycloadducts[14] in approximately equal amounts. Column chromatography (silica gel, Skelly solv/CH_2Cl_2, 80/20) gave 77% of a mixture of the two isomers in ca. 1:1 ratio. the exo isomer (48.5 mg), mp 200.5–202.5 °C (lit.[14] mp 200–202 °C), was isolated by recrystallization from hexane–benzene.

Reaction of 3, LDA, and 1,3-Diphenylisobenzofuran. The acetal **3** (420 mg, 2.5 mmol) in 5 mL of hexane was added to a refluxing mixture of 2.6 mmol of 1,3-diphenylisobenzofuran and 7.5 mmol of LDA in 20 mL of hexane. After 4 h the usual workup gave a residue which was chromatographed to give 39.8 mg (4.3%) of an approximately equal mixture of the exo and endo cycloadducts of benzocyclobutadiene with 1,3-diphenylisobenzofuran, identical with the material described in the preceding experiment.

Cycloadduct of Isobenzofuran with Cyclopentene. A heavy-walled sealed tube containing 1.5 g (9.1 mmol) of 1-ethoxy-1,3-dihydroisobenzofuran,[18] 1.0 mmol of mesitoic acid, and 10 mL of cyclopentene was heated at 160 ± 5 °C for 50 h. The ^{1}H NMR spectrum of the crude material obtained by evaporation indicated 16% of unreacted acetal and 83% of the desired endo cycloadduct.[19] Recrystallization from petroleum ether gave 813 mg (48%) of material with mp 78–81 °C (lit.[19] 80–82 °C).

1β-Methoxy-2α,3α-propano-1,2,3,4-tetrahydronaphthalene. To an ice-cooled mixture of 186 mg (1.0 mmol) of the endo cyclopenteneisobenzofuran adduct and 4.0 mmol of LiAlH(O-t-Bu)$_3$ in 4 mL of tetrahydropyran (THP) was added 4.0 mL of commercial 1 M triethylborane in THP. The ice bath was removed, and stirring was continued for 2.5 h. After cooling again, the mixture was quenched by addition of 1 mL of 3 N NaOH followed by 1.5 mL of 30% H_2O_2. The solution was filtered to remove solids, and the THP was vacuum evaporated. The residue was taken up in ether, washed with water and brine, dried over K_2CO_3, and evaporated to give 177 mg of colorless solid. Silica gel chromatography (80/20 Skellysolv, acetate) gave a fraction, 95 mg (51%), of pure alcohol: mp 157–158 °C; ^{1}H NMR (300 MHz) δ 1.1–2.1 (four m, 6 H, propano bridge protons), 1.72 (s, OH), 2.16 (apparent pentet, 1 H, proximal ring fusion), 2.36 (dd over m, J = 17, 8.4 Hz, 2 H, α-benzylic and distal ring fusion), 2.97 (dd, 1 H, J = 17, 9.6 Hz, β-benzylic), 4.43 (d, 1 H, J = 7.5 Hz, C*H*OH), 7.1–7.35 (m, 3 H, aromatic), and 7.41 (br d, 1 H, ortho aromatic, J = 6.6 Hz); MS calcd for $C_{13}H_{15}O$ (P − H) 187.1122, found 187.1117.

To 60 mg of this material in 6 mL of HMPA cooled in an ice bath, n-butyllithium in hexane was added dropwise until the solution turned deep orange. Excess (0.2 mL) methyl iodide was added, and after a few minutes the mixture was taken up in water, extracted with Skellysolv, dried, and evaporated to give an oil. Preparative TLC (9/1 Skellysolv/ethyl acetate) afforded 35 mg (57%) of the methyl ether (trans isomer of **23**) as a colorless liquid: ^{1}H NMR (300 MHz) δ 0.996 (m, 2 H), 1.36 (m, 1 H), 1.47 (m, 1 H), 1.87 (m, 2 H), 2.37 (dd, 1 H, J = 14, 3.7 Hz, α-benzylic), 2.48 (m, 2 H, ring fusion), 3.06 (dd, 1 H, J = 14, 5.5 Hz, β-benzylic), 3.27 (s, 3 H, methoxy), 3.99 (d, J = 3.6 Hz, C*H*OCH$_3$), and 7.2 ppm (m, 4 H); MS calcd for $C_{14}H_{17}O$ (P − H) 201.1278, found 201.1300.

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