Studies Dealing with the Cycloaddition/Ring Opening/Elimination Sequence of 2-Amino-Substituted Isobenzofurans†

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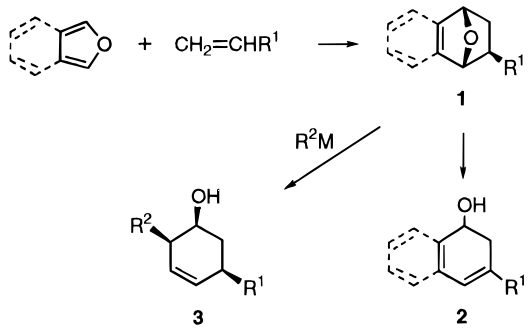
The α-thiocarbocation generated from the Pummerer reaction of an *o*-amido-substituted sulfoxide is intercepted by the adjacent amido carbonyl group to produce a 2-amino-substituted isobenzofuran as a transient intermediate. In the presence of an electron-deficient dienophile, the reactive isobenzofuran undergoes a Diels−Alder cycloaddition followed by ring opening to furnish a vinylogous *C*-acyliminium ion that readily aromatizes. The one-pot intramolecular cascade process only occurs either if the olefinic tether is activated by an ester or if a carbonyl group is located adjacent to the nitrogen atom of the 2-amino-substituted isobenzofuran. To examine the amine *vs* amide influence on the course of intramolecular cycloaddition, density functional theory (DFT) calculations have been carried out for both ground and transition states. The results strongly suggest that the amide-substituted isobenzofurans are destabilized by steric effects between the aromatic ring and the nitrogen-containing side chain. Raising of the ground-state amide energies thereby reduces the activation energy for internal cycloaddition and leads to Diels−Alder adducts more rapidly than for the corresponding amines. Amide tethers emerge as remote-site promoters of intramolecular cycloaddition for tandem processes yielding products with multiple fused rings.

The synthesis of polycyclic systems from readily available precursors with a minimum number of steps and with regio- and stereochemical control constitutes an important synthetic challenge.[1−3] In this regard, one of the most powerful ring-forming reactions currently used for this purpose is the Diels−Alder cycloaddition.[4,5] Furans[6] and isobenzofurans[7] have frequently been employed as dienes in the Diels−Alder reaction to afford substituted 7-oxabicyclo[2.2.1]heptanes (**1**) that serve as key intermediates in the synthesis of a variety of natural products.[8−15] The large number of selective transformations possible with the oxabicyclic system endow this nucleus with impressive versatility. A crucial synthetic transformation employing these intermediates (Scheme 1) involves the cleavage of the oxygen bridge to produce functionalized cyclohexene derivatives **2** or **3**. Many groups have developed different approaches including β-elimination of suitable derivatives,[16] treatment with strong acids,[17] reductive elimination of *endo* functionalities (R_1 = Cl or SO_2Ph),[18] fragmentation,[19] hydrolytic ring openings,[20] and alkylative bridge cleavage reactions.[21]

Scheme 1



Prompted by our recent work dealing with the Pummerer-promoted cyclization of *o*-amido-substituted sulfoxides,[22] we have become interested in the Diels−Alder reaction of 2-amino-5-(alkylthio)-substituted isobenzofurans. We envisioned that the resulting 7-oxabicyclo-

† This paper is dedicated to my good friend, Waldemar Adam, on the occasion of his 60th birthday.

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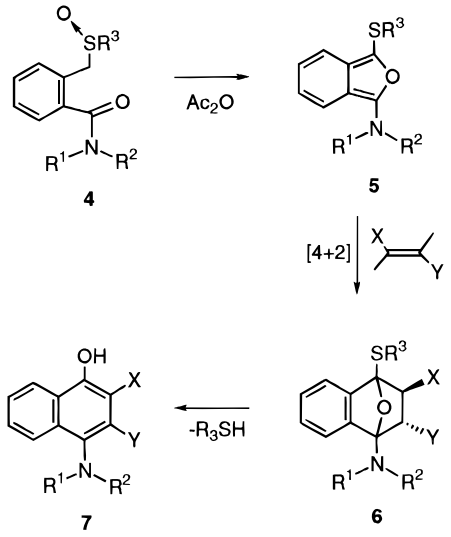
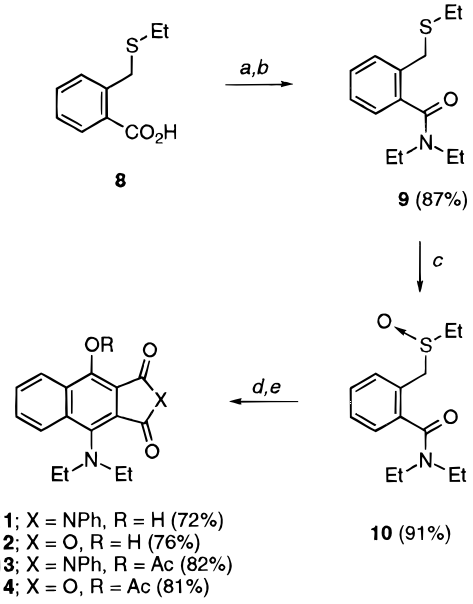
Scheme 2



Scheme 3[a]



[a] Reagents: (a) $SOCl_2$; (b) Et_2NH; (c) $NaIO_4$; (d) Ac_2O, *p*-TsOH; (e) *N*-phenylmaleimide or maleic anhydride.

[2.2.1]heptane system (*i.e.*, **6**) could be used for the synthesis of a variety of 1-hydroxy-4-aminonaphthalene derivatives (Scheme 2). These substituted naphthylamines are important starting materials for the preparation of heterocyclic compounds and pharmaceuticals.[23−25] Notable examples of biologically active molecules containing derivatized anilines in their structure include antibiotics,[26] analgesics,[27] and β-adrenergic blockers.[28] In this paper, we report a full account of our efforts in this field.

Results and Discussion

The required sulfoxide precursors necessary for the Pummerer-induced *cyclization−cycloaddition* sequence were easily obtained from 2-[(ethylthio)methyl]benzoic acid (**8**). This acid was available in large quantities and in high yield by the ring-opening reaction of phthalide with sodium ethylthiolate. Treatment of **8** with thionyl chloride at room temperature and subsequent reaction of the crude acid chloride with diethylamine in CH_2Cl_2 provided amide **9** in 87% overall yield. Sulfoxide **10** was obtained in 91% yield from the oxidation of sulfide **9** using sodium periodate.[29] It is well known that the classical Pummerer reaction can be initiated by a variety of electrophilic reagents (Pummerer promoters).[30] Acetic anhydride is by far the most commonly used promoter and is often utilized as the solvent at reflux temperature or in combination with other solvents or cocatalysts. The more electrophilic trifluoroacetic anhydride has also been employed, as it allows the reaction to proceed under very mild conditions.[30]

After some experimentation with a variety of Pummerer promoters, we found that the highest yield of product obtained from the cascade process utilized a mixture of acetic anhydride and a catalytic quantity of *p*-toluenesulfonic acid in refluxing toluene.[31] Treatment of sulfoxide **10** with either *N*-phenylmaleimide or maleic anhydride under these conditions led to the formation of the bright yellow amino-substituted naphthols **11** or **12** in 72 and 76% yield, respectively (Scheme 3). Slightly higher yields were obtained by using acetic anhydride as the solvent, although, under these conditions, the O-acetylated cycloadducts **13** and **14** were obtained. The formation of these naphthols is fully compatible with a *ring-opening/iminium ion/deprotonation* sequence (Scheme 4).

Interestingly, when a less reactive dienophile such as dimethyl maleate was employed, α-acetoxy sulfide **17** was the only product isolated from the reaction mixture. This same product was isolated in high yield when the Pummerer reaction was performed without using *p*-TsOH as a cocatalyst. Apparently, the initially generated thionium ion **15** is either captured internally by the adjacent carbonyl group[32] to give oxonium ion **16**, which subsequently deprotonates to produce the isobenzofuran intermediate **18**, or else it reacts with an external nucleophile (*i.e.*, AcO^-) to furnish the acetoxy sulfide **17** (Scheme 4). The presence of *p*-TsOH effectively drives the reaction in the desired direction (**15** → **18**) probably by assisting in the ejection of the acetoxy group (**17** → **15**). This interpretation is supported by a control experiment that showed that the treatment of **17** with *p*-TsOH in toluene in the presence of *N*-phenylmaleimide produced cycloadduct **11** in 61% yield. Once the 2-aminoisobenzofuran intermediate **18** is generated, it undergoes ready Diels−Alder reaction with any reactive dienophile present in solution.[33] Fragmentation of the initially formed oxa-bridged cycloadduct **19** produces the

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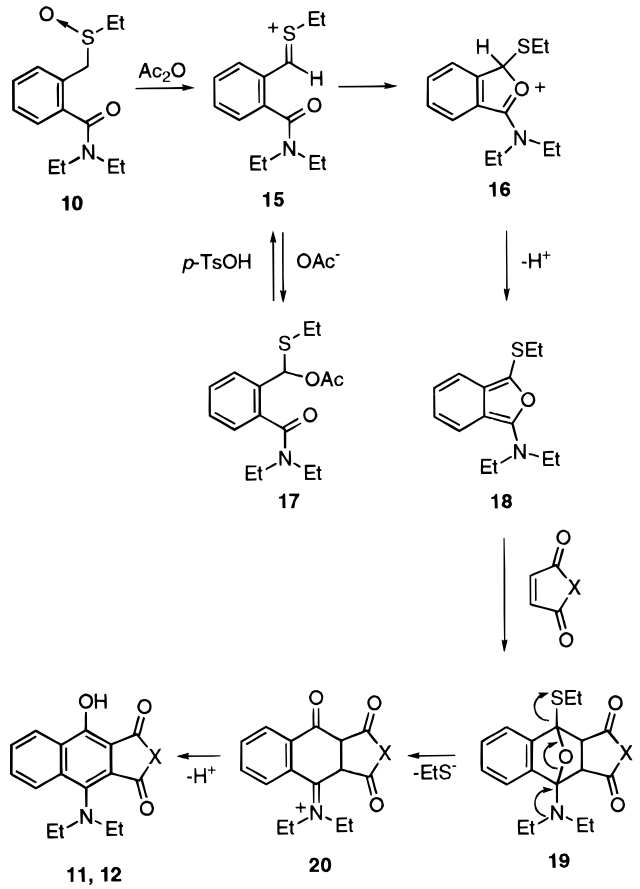
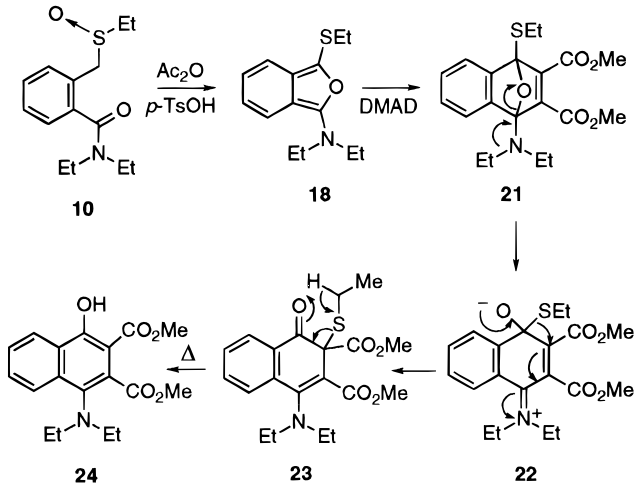
Scheme 4



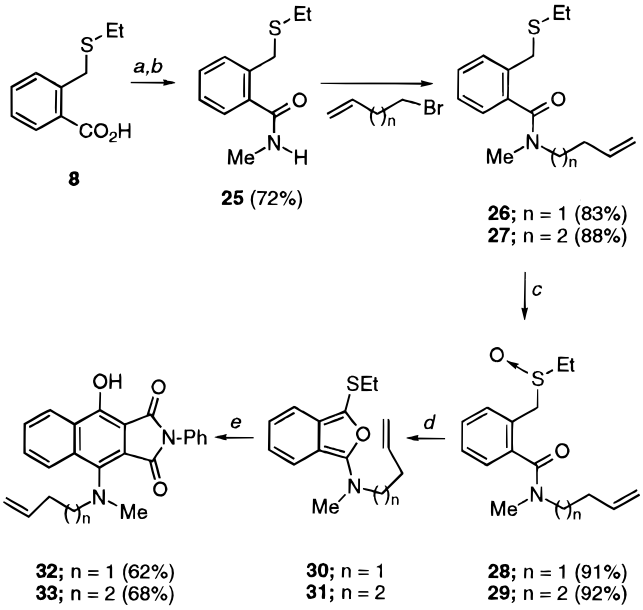
Scheme 5



exocyclic iminium species **20**, which undergoes a deprotonation followed by subsequent aromatization to furnish the amino-substituted naphthols **11** or **12**.

When dimethyl acetylenedicarboxylate is used as the trapping agent, the initially formed iminium ion **22** cannot undergo proton loss (Scheme 5). Instead, **22** rearranges by means of a 1,2-ethylthio shift to afford the tetralone derivative **23**. Here, best results were achieved by using xylene as the solvent and by employing a large excess of the dienophile. α-Acetoxy sulfide **17** was formed as a byproduct and was converted to tetralone **23** by further heating with DMAD in the presence of *p*-TsOH. Compound **23** was slowly converted to naphthol **24** in 65% yield upon further heating. This process presumably proceeds by elimination of thioacetaldehyde in a *hetero-retro-ene* fashion, for which there is ample precedence in the literature.[34]

Scheme 6[a]



[a] Reagents: (a) $SOCl_2$; (b) $MeNH_2$; (c) $NaIO_4$; (d) Ac_2O, *p*-TsOH; (e) *N*-phenylmaleimide.

In order to access synthetically more valuable targets, we focused our attention on an intramolecular variation of the *tandem-amido-Pummerer*−Diels−Alder *reaction sequence*. The requisite tethered amido sulfoxide precursors **28** and **29** were readily prepared from **8** by treatment with thionyl chloride followed by reaction with methylamine to furnish *N*-methylamide **25** in 72% yield (Scheme 6). Alkylation of **25** with butenyl or pentenyl bromide provided *N*-alkenylamides **26** and **27** in high yield. Oxidation with sodium periodate in methanol gave the desired sulfoxides **28** and **29**. Surprisingly, subjection of either sulfoxide to a variety of "*Pummerer*" reaction conditions failed to provide any product derived from an intramolecular cycloaddition.[4,5,35] Instead, α-acetoxy sulfides of type **17** were the only products formed. However, it was possible to trap the isobenzofuran intermediate (*i.e.*, **30** or **31**) with *N*-phenylmaleimide to furnish cycloadducts **32** and **33** in good yields. These results suggest that the unactivated olefinic tether present on the 2-amino isobenzofuran is not sufficiently reactive to participate in an intramolecular Diels−Alder reaction.

On the basis of FMO considerations,[36] we anticipated that activation of the C=C double bond with an electron-withdrawing group would promote the intramolecular [4 + 2]-cycloaddition.[35] The *p*-tolylsulfonyl functionality was first examined as an activating group since the requisite sulfoxide **34** could be readily prepared from the

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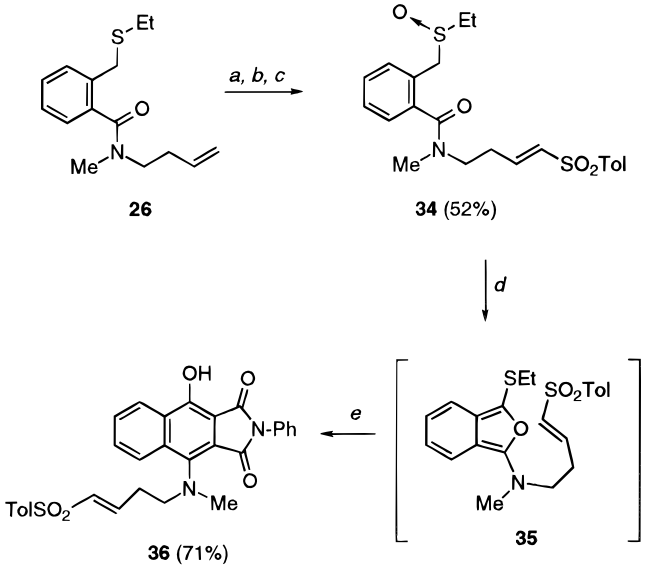
Scheme 7[a]

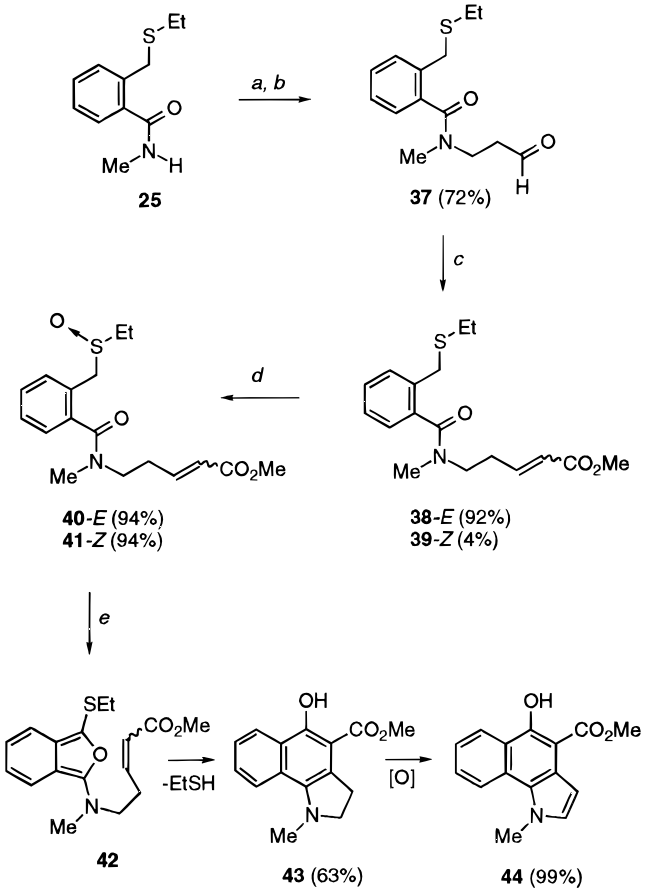


[a] Reagents: (a) $ToISO_2I/CuCl_2$; (b) Et_3N; (c) $NaIO_4$; (d) Ac_2O, *p*-TsOH; (e) *N*-phenylmaleimide.

alkenyl-tethered amide **26**. Copper-catalyzed addition of tosyl iodide to **26** followed by triethylamine-assisted dehydroiodination of the initially formed β-iodo sulfone[37] furnished the corresponding (*E*)-vinyl sulfone in 54% overall yield. Oxidation with sodium periodate provided the desired amido sulfoxide **34**. As was the case with the unactivated alkenyl group, no intramolecular cycloaddition was encountered when sulfoxide **34** was subjected to a variety of Pummerer conditions, even though the bimolecular trapping product **36** was formed in good yield when *N*-phenylmaleimide was present in the reaction mixture (Scheme 7).

The failure of isobenzofuran **35** to undergo intramolecular cycloaddition may be a consequence of unfavorable steric interactions in the transition state.[35] We reasoned that a sterically less demanding group might help overcome the potential problems associated with the bulky tosyl substituent. Consequently, the acrylic substituted esters **40** and **41** were synthesized in four steps from amide **25** as outlined in Scheme 8. Alkylation of **25** with 2-(2-bromoethyl)-1,3-dioxolane followed by hydrolysis of the cyclic acetal with oxalic acid provided aldehyde **37** in 72% yield. Wittig olefination using methyl (triphenylphosphorylidene)acetate afforded a mixture of (*E*)-**38** (94%) and (*Z*)-**39** (4%) esters that were separated by careful silica gel chromatography. Each isomer was independently oxidized to the corresponding sulfoxide (**40**-*E* and **41**-*Z*). Treatment of the individual sulfoxides using acetic anhydride/*p*-TsOH in refluxing xylene provided the same amino-substituted naphthol **43** in nearly identical yield (65%), suggesting that the relative orientation of the ester functionality in the isobenzofuran intermediate **42** is not a crucial factor for the intramolecular cycloaddition. Similar results were achieved using trifluoroacetic anhydride/triethylamine or trimethylsilyl trifluoromethanesulfonate/triethylamine as Pummerer promoters.[30] The hydroxy indoline ester **43** proved to be sensitive to air and was readily oxidized to benzo[g]indole **44**.

Scheme 8[a]



[a] Reagents: (a) $BrCH_2CH_2CH(OCH_2CH_2O)$; (b) oxalic acid; (c) $Ph_3P{=}CHCO_2Me$; (d) $NaIO_4$; (e) Ac_2O, *p*-TsOH.

We have also examined the Pummerer-induced reaction of sulfoxide **45** (Scheme 9). Slow addition of **45** to a refluxing mixture of xylene and acetic anhydride containing a catalytic amount of *p*-TsOH afforded a mixture of the *N*,*S*-ketal **49** (43%) as well as amino-substituted naphthol **50** (22%). Whereas **50** originates from the previously encountered *deprotonation/aromatization* sequence of the endocyclic iminium ion **48**, ketal **49** is formed by nucleophilic attack of ethylthiolate onto the *N*-acyliminium π-bond. Heating a pure sample of **49** in xylene at reflux in the presence of *p*-TsOH resulted in clean conversion to naphthol **50**. By increasing the amount of *p*-TsOH to 5 mol %, it was possible to isolate the O-acylated derivative **51** in a one-pot reaction from sulfoxide **45** in 59% overall yield.

Similar results were obtained when the dienophile tether was shortened by one methylene unit as illustrated in Scheme 10 for the conversion of sulfoxide **52** into benzo[g]indole **55**. High yields (75%) were achieved in the one-pot conversion of **52** into **55** by using 5 mol % of *p*-TsOH as cocatalyst for the tandem *cyclization−cycloaddition* sequence.

For comparison purposes, we have also investigated the chemistry of the closely related imido sulfoxide **57** where the carbonyl group has been switched from "*inside*" the tether to the "*outside*" position (Scheme 11). Sulfoxide **57** was prepared from acid **8** in three steps by conversion to the corresponding *N*-butenylamide **56**, followed by *N*-acetylation and subsequent oxidation with sodium periodate. Cycloadduct **60** was formed in 82%

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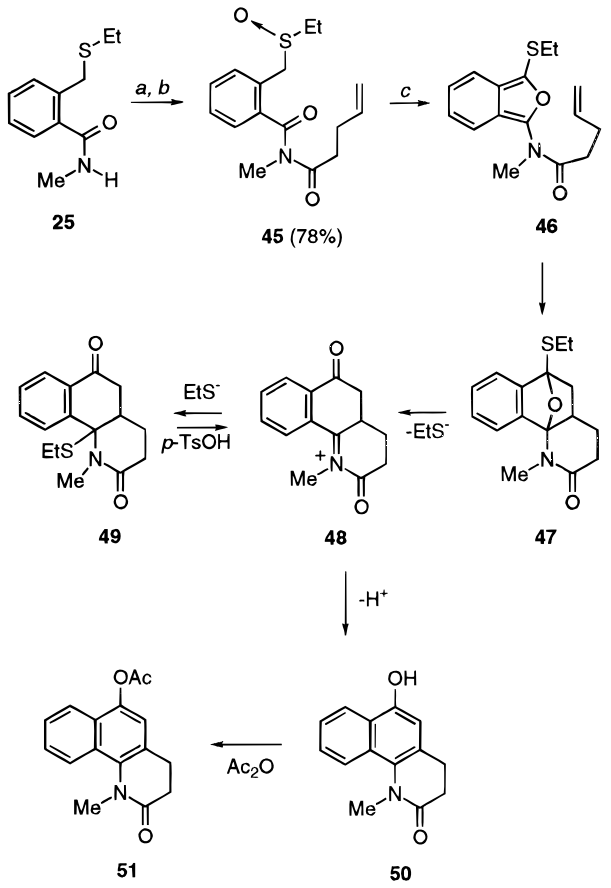
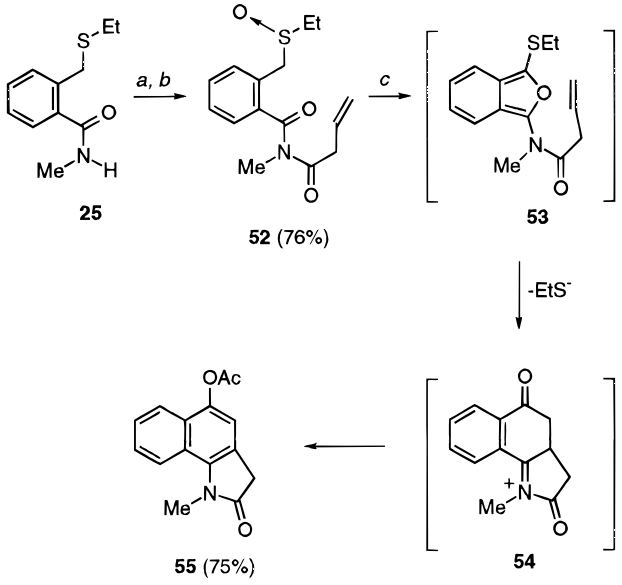
Scheme 9[a]



[a] Reagents: (a) pent-4-enoyl chloride; (b) $NaIO_4$; (c) Ac_2O, *p*-TsOH.

Scheme 10[a]



[a] Reagents: (a) but-3-enoyl chloride; (b) $NaIO_4$; (c) Ac_2O, *p*-TsOH.

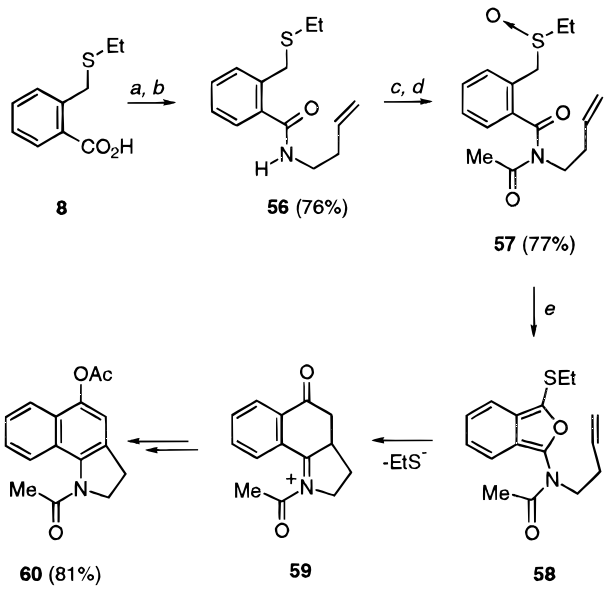
when **57** was subjected to the standard Pummerer conditions.

The Amine vs Amide Conundrum

The intramolecular cycloaddition behavior of incipient isobenzofurans in response to the presence of a C=O group is striking. Five and six ring precursors **53** and **46**, respectively, deliver cyclized products bearing a carbonyl within the newly formed rings in good to excellent yields. Externalization of the C=O as in **58** likewise leads to facile internal cyclization. Removal of the C=O functionality, however (**30**, **31**), suppresses intramolecular cycloaddition in favor of bimolecular attack by acetic acid (*e.g.*, **10**→**17**). The amine−amide effect is not limited to isobenzofurans. In a previous study of the intramolecular cycloaddition of incipient carbonyl ylide dipoles and tethered alkenyl π-bonds, a similar phenomenon was observed.[39] Intermediates with carbonyl groups in the tether provided cycloaddition products. Those lacking the C=O failed to cyclize. Since FMO theory was unable to predict the result in these cases, full-scale *ab initio* transition-state optimizations were carried out. The reactivity discrepancy was traced to steric effects in the transition states leading to the intervention of low energy boat conformations.

To probe the forces responsible for intramolecular ring formation in the present series, we have carried out similar calculations for the isobenzofurans. The characteristics of the reaction were explored within the five-membered ring series (**30**, **53**, and **58**), while the SEt group was modeled as SH. The structures in question are **61**−**63** and **64**†−**66**†. For a discussion of preliminary calculations leading to choices of molecular structures for subsequent *ab initio* refinement, see the Experimental Section. Final optimized geometries were obtained with the density functional theory (DFT)[40] B3LYP/3-21G* basis set, while energies were taken at the B3LYP/6-31G* level (*i.e.*, B3LYP/6-31G*// B3LYP/3−21G*). A similar approach has been successfully applied to a number of cycloaddition reactions.[41]

Scheme 11[a]



[a] Reagents: (a) $SOCl_2$; (b) but-3-enylamine; (c) MeCOCl; (d) $NaIO_4$; (e) Ac_2O, *p*-TsOH.

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(41) Wiest, O.; Black, K. A.; Houk, K. N. *J. Am. Chem. Soc.* **1994**, *116*, 10336.

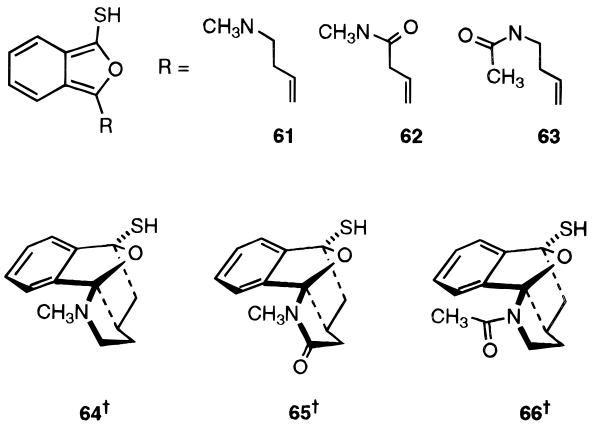
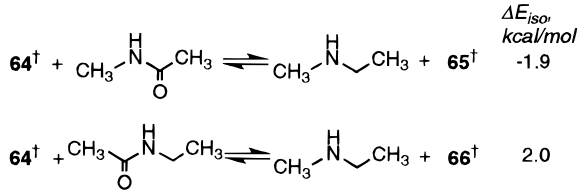


Table 1 lists the energies for various optimized structures including ground-state (gs) and transition-state (ts) conformations. The energy differences between ground and transition states for the amine (**61**, **64**†), the internal carbonyl (**62**, **65**†), and the external carbonyl (**63**, **66**†) are in qualitative agreement with experiment, $\Delta E^{\dagger} = 21.1$, 18.9, and 13.7 kcal/mol, respectively. That is, the amine structure experiences the greatest energy barrier; the amides, 2.2 (**66**†) and 7.4 (**65**†) kcal/mol lower. Figure 1 depicts the three transition states. The conformer of **66**† with an *all-trans* alkyl moiety is lowest (ΔE [**66a**† − **66b**†] = −4.0 kcal/mol). The new bonds forming within the pericycles are calculated to differ by no more than 0.09−0.15 Å. This is relatively symmetric by comparison with the transition states for intramolecular cyclization of carbonyl ylides with similar tethers ($\Delta r = 0.29-0.30$ Å).[39] All of the activiation complexes in Figure 1 reveal that the fused five-membered azacycle exists in an envelope conformation. Furthermore, the latter is disposed such that there is no conjugation between nitrogen and the aromatic π-system. The nitrogen lone-electron pairs are essentially coplanar with the isobenzofuran bicycle.

3-D graphics inspection and analysis of atom−atom distances for transition states **64**†−**66**† reveals no structural features that suggest fundamental stability differences as was the case for the carbonyl ylides. To examine this point further, the structures of methylethylamine, *N*-methylacetamide, and *N*-ethylacetamide were optimized with the B3LYP/3-21G* protocol in their *all-trans* conformations and subjected to single-point B3LYP/6-31G* energy evaluations. These unstrained structures were then combined with the transition states in the following isodesmic[42] reactions.



The amine transition state **64**† is calculated to be slightly less stable than the C=O internal amide structure **65**† and slightly more stable than the corresponding C=O external polycycle **66**†. In view of the calculated cycloaddition barrier height for the amine, the diminutive ΔE_{iso} values suggest that transition-state structure is not the source of the apparent increase in rate for the amides.

(42) Hehre, W. J.; Radom, L.; Schleyer, P. v.R.; Pople, J. A. *ab initio Molecular Orbital Theory*; John Wiley and Sons: New York, 1986.

Table 1. DFT Energies (au)[a] for Optimized Low Energy Conformations of Ground States 61−63 and Transition States 64†−66† Δ*E*(ts−gs), kcal/mol

	energies			
compd	3-21G*[a]	Δ*E*(ts−gs)[c]	6-31G*[b]	Δ*E*(ts−gs)[c]
61	−1027.194 46		−1032.514 34	
64†	−1027.168 95	16.0	−1032.480 67	21.1
62a	−1100.813 56		−1106.549 05	
62b	−1100.811 16		−1106.527 27	
65†	−1100.798 53	9.4	−1100.811 16	13.7
63a	−1139.918 70		−1145.867 73	
63b	−1139.916 97		−1145.859 90	
66a†	−1139.897 60	17.2	−1145.837 62	18.9
66b†	−1139.891 26		−1145.831 46	
67	−871.060 53		−875.526 88	
68	−871.058 78		−875.527 30	
69	−871.048 37		−875.521 75	
MeNHCOMe	−247.158 29		−248.522 14	
MeNHEt	−173.526 70		−174.478 60	
MeCONHEt	−286.262 93		−287.838 69	

[a] 3-21G* = B3LYP/3-21G*//B3LYP/3-21G*. [b] 6-31G* = B3LYP/6-31G*//B3LYP/3-21G*. [c] Difference between the lowest ground state and transition state, respectively.

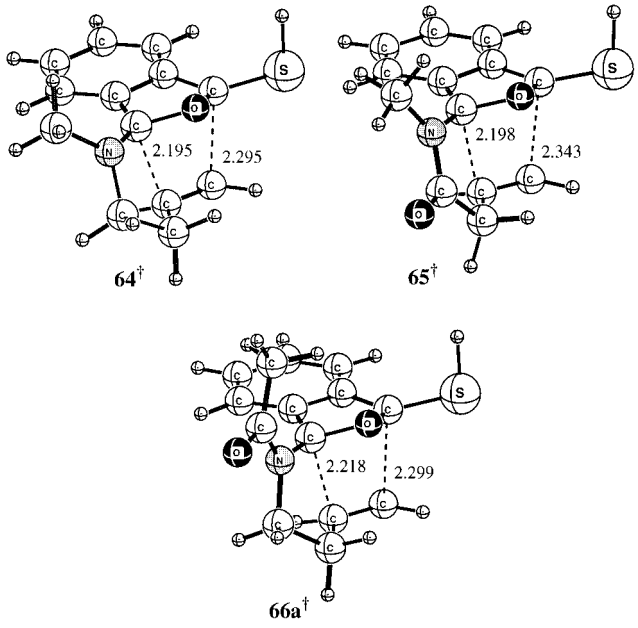


Figure 1. B3LYP/3-21G*-optimized transition states for isobenzofuran intramolecular cycloaddition. Ring closure bond lengths shown with dotted lines; Å.

A similar pair of isodesmic reactions has been applied to the lowest energy conformations of the ground state isobenzofurans. These comparisons imply that the amine-substituted furan is considerably more stable than the amide analogs. Examination of the optimized ground-state isobenzofurans (Figure 2) provides insight as to why.

In the absence of mediating factors, it can be safely assumed that the nitrogen atom of the side chains in **61**−**63** prefers to be conjugated to the aromatic π-system. Thus, the nitrogen atom in amine **61** is predicted by optimization to be planar, although it sustains a nonbonded H- - -H contact of 2.27 Å. The latter is just under the sum of the van der Waals radii (2.40 Å).[43] Several attempts to optimize to a nonconjugated local minimum by starting with pyramidal nitrogen, and a conformation similar to **62a** consistently yielded planar **61**. Resonance

(43) Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441.

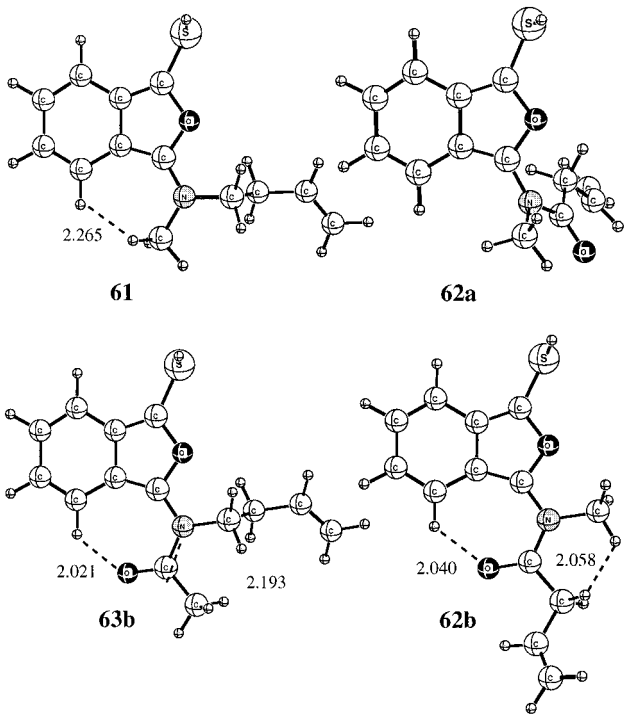
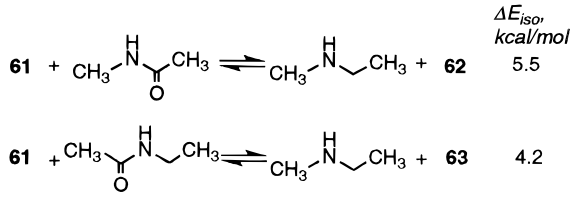


Figure 2. B3LYP/3-21G*-optimized isobenzofuran ground states. Close nonbonded atom−atom contacts are indicated; Å.



effects manifestly outweigh opposing van der Waals interactions.

For the amide system, the preference for planarity was tested by optimizing conformations of the *N*-methylacetamide derivative of mercaptofuran, **67**−**69** (Figure 3). Unconjugated *trans*-**67** with a side-chain twist of 56° is isoenergetic with planar *cis*-**68** in spite of the short nonbonded contacts in the latter (ΔE = 0.3 kcal/mol; B3LYP/6-31G*; Table 1). Resonance and steric effects exactly balance. A third conformer corresponding to the ring-nitrogen rotamer of **68** optimized to the nonplanar species **69**, 3.2 kcal/mol above **67**. Its moderately elevated energy results from the side-chain *cis*-alkyl amide orientation. Quite clearly, the planarizing effect of conjugation can be attenuated in different ways by adverse in-plane interactions between the furan ring and the coupled amide fragment.

Three conformations were optimized for the precursor to amide **65**†. The lowest, **62a** (Figure 2), has the side chain in an *all-trans* conformation and nearly perpendicular to the bicyclic ring. A second planar conformer with a *cis*-dialkyl conformation around the NCO functionality, **62b**, tolerates very short 1,7 H- - -O and 1,6 H- - -H nonbonded contacts of 2.040 and 2.058 Å, respectively. The latter distances arise as a consequence of the amide's drive for planarity. At the B3LYP/6-31G* level of theory, the conformer is 4.2 kcal/mol higher in energy than **62a**. This instability results from an imbalance between steric congestion (van der Waal sums: H- - -O 2.72 and H- - -H 2.40 Å)[43] and conjugation. A third

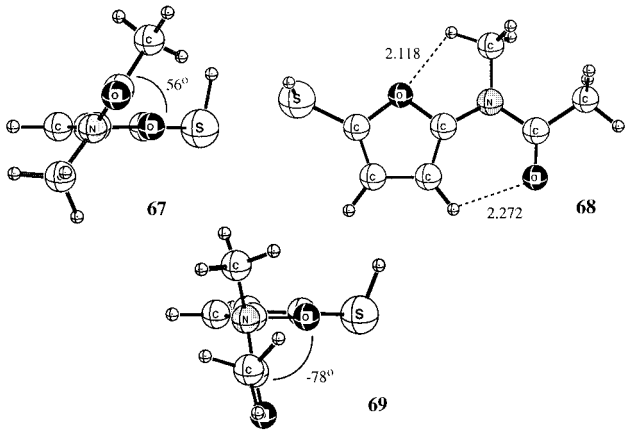


Figure 3. B3LYP/3-21G*-optimized *N*-methylacetamide-substituted mercaptofuran ground states; cis (**67**) and trans (**68**, **69**) amide isomer conformations, respectively. Close nonbonded atom−atom contacts are indicated; Å.

nonplanar conformation likewise falls 4.3 kcal/mol above **62a**. The lowest energy conformation found for isobenzofuran **63a**, the precursor to external amide **66**†, is an *all-trans* species predicted to resemble the nonplanar form **62a**. The crowded conjugated planar form **63b** (r(H- - -X) = 2.021 (O) and 2.193 (H) Å) is found 4.9 kcal/mol higher in energy. Again, conjugative stabilization is overtaken by steric effects.

The results described in this section reveal that utilization of an amide tether raises the energy of the intermediate isobenzofuran ground states and thereby reduces the intramolecular Diels−Alder activation barrier relative to the corresponding amine.

The outcome is not exclusive, however, since certain dienophile-activating substitutents (*e.g.*, CO_2Me, **42**) can override it, while others (*e.g.*, SO_2Tol, **36**) cannot. Similarly, even though the aminoisobenzofurans **30** and **31** do not ring-form with unactivated internal dienophiles, hotter external substrates such as *N*-phenylmaleimide are able to readily mount the Diels−Alder barrier (*e.g.*, **32**, **33**).

Conclusion

In conclusion, the results presented herein demonstrate the potential of the *tandem-amido-Pummerer−Diels−Alder reaction sequence* as an efficient protocol for generating vinylogous *C*-acyliminium ions. The cascade sequence allows for ready access to a number of highly functionalized amino-substituted naphthols and can be utilized in both a bimolecular and a intramolecular fashion. The novelty of the method lies in the unprecedented manner in which *C*- and *N*-acyliminium ion intermediates are produced.

Incorporation of a C=O group α to nitrogen either internal or external to the tether promotes intramolecular cycloaddition, whereas an amine-only tether reacts only sluggishly, if at all. The amine versus amide substitution pattern may be general in its overall reactivity consequence, since the same result has been observed for intramolecular dipolar cycloaddition of carbonyl ylide intermediates.[39] Surprisingly, while amide incorporation influences the latter chemistry by lowering transition-state energies, the presently investigated isobenzofurans experience an amide perturbation that raises the energies of the ground states. Both effects serve to shorten the path between a ground state and the corresponding

transition state and, thus, reduce the activation barrier. The outcome is clearly of synthetic advantage as it offers the opportunity to accelerate intramolecular cycloaddition by steric adjustment of ground-state and transition-state energies either separately or simultaneously. To our knowledge, an example of the latter phenomenon has yet to be discerned.

The two examples underscore the unexpected complexity of intramolecular cycloaddition processes that create several fused rings in a single step and simultaneously induce steric effects remote from the reacting centers. For such situations, the application of FMO theory or any other mechanistic procedure that focuses only on the pericycle MO's or the accompanying nascent bonds is likely to give misleading results. Other examples of this phenomenon are under active investigation. We are currently exploring the possibility of intercepting these highly electrophilic species with additional nucleophilic tethers incorporated on the backbone of these molecules and the use of this method for the synthesis of the erythrina family of alkaloids.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in flame-dried glassware under an atmosphere of dry argon. Solutions were evaporated under reduced pressure with a rotary evaporator, and the residue was chromatographed on a silica gel column using an ethyl acetate−hexane mixture as the eluent unless specified otherwise. All NMR spectra were determined in $CDCl_3$ at 300 MHz for ^{1}H-NMR and 75 MHz for ^{13}C-NMR.

***N,N*-Diethyl-2-[(ethylthio)methyl]benzamide (9).** To a stirred suspension containing 4.9 g (25 mmol) of 2-[(ethylthio)-methyl]benzoic acid (**8**)[38] in 50 mL of dry benzene was added 6.0 g (50 mmol) of thionyl chloride. After being stirred at rt for 1 h, the solution was concentrated under reduced pressure. The crude acid chloride was dissolved in 20 mL of dry CH_2-Cl_2, and the solution was added dropwise to a solution of 8.7 g (120 mmol) of diethylamine in 50 mL of dry CH_2Cl_2 at 0 °C under argon. After being stirred at rt for 2 h, the mixture was washed successively with 5% HCl, a saturated Na_2CO_3 solution, and brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The remaining oil was purified by flash silica gel chromatography to give 5.5 g (87%) of amide **9** as a colorless oil: IR (neat) 1629, 1430, 1287 cm^{-1}; ^{1}H-NMR δ 1.09 (t, 3H, J = 7.5 Hz), 1.23 (t, 3H, J = 7.5 Hz), 1.27 (t, 3H, J = 7.5 Hz), 2.47 (q, 2H, J = 7.5 Hz), 3.13 (q, 2H, J = 7.5 Hz), 3.33 (brs, 2H), 3.55 (brs, 2H), 7.16−7.39 (m, 4H); ^{13}C-NMR δ 12.5, 13.8, 14.4, 25.9, 33.0, 38.5, 43.2, 125.7, 126.7, 128.6, 130.1, 135.4, 137.0, 170.3; HRMS calcd for $C_{14}H_{21}$-NOS 251.1345, found 251.1339.

***N,N*-Diethyl-2-[(ethylsulfinyl)methyl]benzamide (10).** To a solution containing 2.5 g (10 mmol) of amide **9** in 50 mL of methanol was added 2.25 g (10.5 mmol) of sodium periodate at 0 °C. Water was added to the mixture until the solution began to turn cloudy (*ca.* 5−10 mL). After the solution was stirred for 5 h at rt, water and CH_2Cl_2 were added, the aqueous layer was extracted with CH_2Cl_2, and the combined organic fractions were washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by flash silica gel chromatography to give 2.4 g (91%) of sulfoxide **10** as a colorless oil: IR (neat) 1627, 1432, 1053 cm^{-1}; ^{1}H-NMR δ 1.10 (t, 3H, J = 7.5 Hz), 1.26 (t, 3H, J = 7.5 Hz), 1.33 (t, 3H, J = 7.5 Hz), 2.68−2.86 (m, 2H), 3.16−3.20 (m, 2H), 3.60 (brs, 2H), 3.92 and 4.10 (brs, 2H), 7.10−7.40 (m, 4H); ^{13}C-NMR δ 6.4, 12.3, 13.5, 38.6, 43.0, 45.2, 55.0, 125.7, 127.6, 127.7, 128.8, 131.2, 137.0, 169.3; HRMS (FAB) calcd for $C_{14}H_{22}NO_2S$ (M + H) 268.1371, found 268.1373.

General Procedure for the Tandem Pummerer Cyclization Diels−Alder Cycloaddition Sequence. A mixture containing 10 mL of the appropriate solvent (toluene, xylene, or acetic anhydride), 0.5 mL of acetic anhydride, 2.0 mmol of the dienophile, and a catalytic amount of *p*-toluenesulfonic acid (*ca.* 1 mg) was heated at reflux under argon. To this mixture was added dropwise a 0.5 mmol solution of the appropriate sulfoxide in 3 mL of solvent *via* syringe over a 20 min period. After the addition was complete, the solution was heated at reflux for an additional 20 min until no sulfoxide was detected by TLC. The mixture was concentrated under reduced pressure, and the crude residue was purified by flash silica gel chromatography.

4-(Diethylamino)-9-hydroxy-2-phenylbenzo[*f*]isoindole-1,3-dione (11) was obtained from 130 mg (0.5 mmol) of sulfoxide **10** and 170 mg (1 mmol) of *N*-phenylmaleimide (toluene) in 72% yield as a bright yellow solid: mp 146−147 °C; IR (KBr) 3380, 1744, 1694, 1372 cm^{-1}; ^{1}H-NMR δ 1.05 (t, 6H, J = 7.5 Hz), 3.46 (q, 4H, J = 7.5 Hz), 7.38−7.55 (m, 5H), 7.68−7.74 (m, 2H), 8.37 (dd, 1H, J = 6.0, 2.5 Hz), 8.61 (dd, 1H, J = 6.0, 2.5 Hz), 9.02 (s, 1H); ^{13}C-NMR δ 14.0, 48.1, 106.4, 119.1, 123.8, 126.4, 127.7, 128.0, 128.7, 128.8, 129.0, 129.6, 131.7, 138.7, 143.2, 151.2, 165.3, 169.7. Anal. Calcd for $C_{22}H_{20}N_2O_3$: C, 73.32; H, 5.59; N, 7.77. Found: C, 73.18; H, 5.58; N, 7.65.

4-(Diethylamino)-9-hydroxynaphtho[2,3-*c*]furan-1,3-dione (12) was obtained from 130 mg (0.5 mmol) of sulfoxide **10** and 100 mg (1 mmol) of maleic anhydride (toluene) in 76% yield as a bright yellow solid: mp 174−175 °C; IR (KBr) 3428, 1802, 1794, 1751, 1307 cm^{-1}; ^{1}H-NMR δ 1.06 (t, 6H, J = 7.5 Hz), 3.47 (q, 4H, J = 7.5 Hz), 7.72−7.78 (m, 2 H), 8.40 (d, 1 H, J = 7.5 Hz), 8.52 (d, 1 H, J = 7.5 Hz); ^{13}C-NMR δ 14.3, 47.8, 105.5, 120.6, 125.1, 127.2, 129.1, 130.5, 131.9, 138.8, 140.9, 156.0, 162.5, 163.4. Anal. Calcd for $C_{16}H_{15}NO_4$: C, 67.36; H, 5.30; N, 4.91. Found: C, 67.23; H, 5.36; N, 4.85.

9-Acetoxy-4-(diethylamino)-2-phenylbenzo[*f*]isoindole-1,3-dione (13) was obtained from 130 mg (0.5 mmol) of sulfoxide **10** and 170 mg (1 mmol) of *N*-phenylmaleimide (acetic anhydride) in 82% yield as a pale yellow solid: mp 139−140 °C; IR (neat) 1776, 1757, 1711, 1386, 1260 cm^{-1}; ^{1}H-NMR δ 1.09 (t, 6H, J = 7.5 Hz), 2.54 (s, 3H), 3.53 (q, 4H, J = 7.5 Hz), 7.34−7.51 (m, 5H), 7.65−7.70 (m, 2H), 8.10−8.13 (m, 1H), 8.56−8.58 (m, 1H); ^{13}C-NMR δ 14.0, 20.6, 48.0, 117.2, 119.7, 123.2, 126.6, 127.5, 127.9, 128.8, 129.0, 129.4, 131.5, 131.6, 137.9, 140.9, 147.4, 164.7, 165.0, 168.7. Anal. Calcd for $C_{24}H_{22}N_2O_4$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.88; H, 5.76; N, 6.74.

9-Acetoxy-4-(diethylamino)naphtho[2,3-*c*]furan-1,3-dione (14) was obtained from 130 mg (0.5 mmol) of sulfoxide **10** and 100 mg (1 mmol) of maleic anhydride (acetic anhydride) in 81% yield as a yellow solid: mp 81−82 °C; IR (neat) 1825, 1776, 1387, 1226, 1179 cm^{-1}; ^{1}H-NMR δ 1.12 (t, 6H, J = 7.5 Hz), 2.57 (s, 3H), 3.59 (q, 4H, J = 7.5 Hz), 7.75−7.80 (m, 2H), 8.13−8.17 (m, 1H), and 8.48−8.50 (m, 1H); ^{13}C-NMR δ 13.8, 20.6, 48.1, 116.5, 116.9, 123.8, 127.8, 129.9, 130.4, 132.1, 137.4, 141.8, 149.7, 160.0, 168.3. Anal. Calcd for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.23; N, 4.27. Found: C, 65.93; H, 5.30; N, 4.16.

Acetic acid [2-(diethylcarbamoyl)phenyl](ethylthio)-methyl Ester (17) was obtained from 130 mg (0.5 mmol) of sulfoxide **10** (toluene) in 65% yield as a colorless oil: IR (neat) 1738, 1628, 1429, 1218 cm^{-1}; ^{1}H-NMR δ 1.08−1.13 (m, 3H), 1.24−1.32 (m, 6H), 2.13 (s, 3H), 2.51−2.79 (m, 2H), 3.10−3.17 (m, 2H), 3.40 and 3.80 (2 m, 2H), 6.92 (s, 1H), 7.21 (dd, 1H, J = 7.5, 1.2 Hz), 7.32 (ddd, 1H, J = 7.5, 7.5, 1.2 Hz), 7.39 (ddd, 1H, J = 7.5, 7.5, 1.2 Hz), 7.61 (dd, 1H, J = 7.5, 1.2 Hz); ^{13}C-NMR δ 12.5, 13.7, 14.5, 21.0, 25.9, 38.7, 43.0, 125.7, 126.7, 128.1, 128.8, 134.6, 134.8, 169.1, 169.4; HRMS (FAB) calcd for $C_{16}H_{23}NO_3SLi$ (M + Li) 316.1559, found 316.1544.

A 60 mg (0.2 mmol) sample of ester **17** in 1 mL of toluene was added dropwise to a mixture of 5 mL of toluene and 170 mg (1 mmol) of *N*-phenylmaleimide containing a catalytic amount of *p*-toluenesulfonic acid. After the addition was complete, the solution was heated at reflux for an additional 20 min. The mixture was concentrated under reduced pressure and the crude reside purified by flash silica gel chromatography to give 45 mg (61%) of cycloadduct **11**, which was identical in all respects to a sample obtained directly from sulfoxide **10**.

Dimethyl 4-(diethylamino)-2-(ethylthio)-1-oxo-1,2-dihydronaphthalene-2,3-dicarboxylate (23) and Dimethyl 1-(diethylamino)-4-hydroxynaphthalene-2,3-dicarboxylate (24) were obtained from 130 mg (0.5 mmol) of sulfoxide **10** and 360 mg (2.5 mmol) of DMAD (xylene). The crude mixture was purified by flash silica gel chromatography to give 7 mg (4%) of naphthol **24**, 70 mg (36%) of tetralone **23**, and 80 mg (50%) of ester **17**. Treatment of a sample of pure ester **17** with 5 equiv of DMAD in xylene (trace *p*-TsOH) at reflux for 20 min provided an additional amount of tetralone **23** (54% overall yield). Prolonged heating (2 h) of tetralone **23** at reflux in xylene led to a 65% isolated yield of naphthol **24**. Tetralone **23** exhibited the following spectral properties: IR (neat) 1752, 1732, 1721, 1684 cm^{-1}; ^{1}H-NMR δ 1.05 (t, 3H, J = 7.5 Hz), 1.14 (t, 6H, J = 7.5 Hz), 2.31−2.44 (m, 1H), 2.82−2.94 (m, 1H), 3.04−3.33 (m, 4H), 3.78 (s, 3H), 3.79 (s, 3H), 7.51 (ddd, 1H, J = 7.0, 7.0, 1.0 Hz), 7.66 (ddd, J = 7.0, 7.0, 1.0 Hz), 7.76 (dd, 1H, J = 7.0, 1.0 Hz), 8.01 (dd, J = 7.0, 1.0 Hz); ^{13}C-NMR δ 13.2, 13.3, 25.6, 46.4, 51.8, 53.1, 65.5, 115.7, 126.9, 127.5, 130.2, 130.9, 133.9, 136.9, 151.0, 166.3, 168.9, 188.4; HRMS (FAB) calcd for $C_{20}H_{26}NO_5S$ (M + H) 392.1532, found 392.1544.

Naphthol **24** exhibited the following properties: mp 115−116 °C; IR (KBr) 1735, 1655, 1433, 1335, 1221 cm^{-1}; ^{1}H-NMR δ 1.00 (t, 6H, J = 7.5 Hz), 3.14−3.30 (m, 4H), 3.91 (s, 3H), 3.95 (s, 3H), 7.49−7.62 (m, 2H), 7.96 (d, 1H, J = 8 Hz), 8.48 (d, 1H, J = 8 Hz), 12.37 (s, 1H); ^{13}C-NMR δ 14.6, 49.2, 51.8, 52.7, 102.0, 124.7, 124.9, 126.1, 126.3, 129.5, 131.5, 136.5, 136.6, 159.9, 169.3, 170.2. Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.52; N, 4.23. Found: C, 65.14; H, 6.32; N, 4.23.

***N*-Methyl-2-[(ethylthio)methyl]benzamide (25).** To a stirred suspension containing 4.9 g (25 mmol) of 2-[(ethylthio)-methyl]benzoic acid (**8**) in 50 mL of dry benzene was added 6.0 g (50 mmol) of thionyl chloride. After being stirred at rt for 1 h, the solution was concentrated under reduced pressure. The resulting crude acid chloride was added dropwise to an ice-cooled mixture of 20 mL of methylamine (40% aqueous solution) and 15 mL of dioxane. The clear solution was stirred at rt for 1 h and was then poured onto 200 g of ice−water to give 3.8 g (72%) of amide **25**: mp 74−75 °C; IR (KBr) 3288, 1630, 1545, 1403, 1317 cm^{-1}; ^{1}H-NMR δ 1.27 (t, 3H, J = 7.5 Hz), 2.53 (q, 2H, J = 7.5 Hz), 3.00 (d, 3H, J = 5.0 Hz), 3.90 (s, 2H), 6.60 (brs, 1H), 7.26−7.50 (m, 4H); ^{13}C-NMR δ 14.5, 26.0, 26.5, 33.6, 127.2, 128.2, 129.8, 130.6, 135.6, 136.4, 167.0. Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69. Found: C, 63.19; H, 7.19; N, 6.74.

***N*-But-3-enyl-*N*-methyl-2-[(ethylthio)methyl]benzamide (26).** A mixture of 2.09 g (10 mmol) of amide **25**, 480 mg (12 mmol) of NaH (60% dispersion in mineral oil), and 40 mL of toluene was heated at 60−70 °C for 1 h until the evolution of hydrogen gas ceased. After the addition of 2.0 g (15 mmol) of 4-bromo-1-butene, the mixture was heated at reflux for 4 h until all the starting material was consumed. After being cooled to rt, the mixture was poured onto 200 g of ice−water, and the organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash silica gel chromatography to give 2.3 g (88%) of amide **26** as a colorless oil that appeared as a mixture of two rotamers in solution: IR (neat) 1635, 1397, 1065, 911, 769 cm^{-1}; ^{1}H-NMR δ 1.12 (t, 3H, J = 7.5 Hz), 2.11 and 2.37 (m, 4H), 2.73 and 2.99 (s, 3H), 3.55 and 3.71 (m, 4H), 4.89−5.11 (m, 2H), 5.51 and 5.80 (m, 1H), 7.04−7.31 (m, 4H); ^{13}C-NMR δ 14.3, 25.7, 25.8, 31.3, 32.1, 32.5, 32.9, 33.0, 37.3, 46.2, 50.6, 116.6, 117.2, 126.2, 126.3, 126.6, 126.7, 128.5, 128.6, 130.0, 134.2, 135.3, 135.5, 136.4, 136.7, 170.6, 170.9; *m/z* 263 (M^+), 234, 203, 202, 188, 179, 151, 149 (base); HRMS calcd for $C_{15}H_{21}NOS$ 263.1344, found 263.1340.

***N*-But-3-enyl-*N*-methyl-2-[(ethylsulfinyl)methyl]benzamide (28).** A 2.6 g (10 mmol) sample of sulfide **26** was oxidized using conditions similar to those described for **10** to give sulfoxide **28** (91%) as a colorless oil that appears as a mixture of two rotamers in solution: IR (neat) 1627, 1444, 1400, 1050 cm^{-1}; ^{1}H-NMR δ 1.34 (t, 3H, J = 7.5 Hz), 2.28 and 2.45 (dt, 2H, J = 7.0, 7.0 Hz), 2.62−2.79 (m, 2H), 2.87 and 3.09 (s, 3H), 3.22 and 3.63 (t, 2H, J = 7.0 Hz), 3.94 (d, 1H, J = 13.0 Hz), 4.12 (d, 1H, J = 13.0 Hz), 4.99−5.21 (m, 2H), 5.56 and 5.93 (m, 1H), 7.22−7.46 (m, 4H); ^{13}C-NMR δ 6.7, 31.5, 32.4, 32.6, 37.4, 45.4, 45.5, 46.4, 50.7, 55.2, 55.4, 117.0, 117.6, 126.7, 126.8, 127.9, 128.0, 128.2, 129.3, 129.4, 131.5, 131.6, 134.0, 135.2, 136.8, 137.2, 170.1, 170.3; HRMS (FAB) calcd for $C_{15}H_{22}NO_2S$ (M + H) 280.1371, found 280.1375.

***N*-Methyl-*N*-pent-4-enyl-2-[(ethylsulfinyl)methyl]-benzamide (29).** A sample of *N*-methyl-*N*-pent-4-enyl-2-[(ethylthio)methyl]benzamide (**27**) was obtained from 2.1 g (10 mmol) of amide **25** and 2.2 g (15 mmol) of 5-bromo-1-pentene in 84% yield as a colorless oil as a mixture of two rotamers: ^{1}H-NMR δ 1.21 (t, 3H, J = 7.5 Hz), 1.55−1.83 (m, 2H), 1.92 and 2.18 (dt, 2H, J = 7.0, 7.0 Hz), 2.46 (q, 2H, J = 7.5 Hz), 2.82 and 3.09 (s, 3H), 3.50−3.96 (m, 4H), 4.85−5.12 (m, 2H), 5.58−5.71 and 5.82−5.95 (m, 1H), 7.13−7.41 (m, 4H); ^{13}C-NMR δ 14.8, 26.3, 26.5, 27.1, 32.0, 33.1, 33.4, 34.1, 37.4, 46.3, 52.6, 115.3, 115.6, 126.6, 126.7, 126.9, 127.0, 128.5, 128.6, 130.5, 130.6, 135.8, 135.9, 136.4, 137.1, 137.9, 138.1, 171.1, 171.4; HRMS calcd for $C_{16}H_{23}NOS$ 277.1500, found 277.1498.

A 2.8 g (10 mmol) sample of sulfide **27** was oxidized in the standard manner to give sulfoxide **29** (92%) as a colorless oil that appears as a mixture of two rotamers in solution: ^{1}H-NMR δ 1.34 (t, 3H, J = 7.5 Hz), 1.55−1.81 (m, 2H), 1.88 and 2.15 (dt, 2H, J = 7.0, 7.0 Hz), 2.61−2.83 (m, 2H), 2.88 and 3.08 (s, 3H), 3.23 and 3.58 (t, 2H, J = 7.0 Hz), 3.95 (d, 1H, J = 13.0 Hz), 4.13 (d, 1H, J = 13.0 Hz), 4.88−5.12 (m, 2H), 5.56−5.71 and 5.79−5.91 (m, 1H), 7.21−7.45 (4H); HRMS (FAB) calcd for $C_{16}H_{24}NO_2S$ (M + H) 294.1528, found 294.1526.

4-(*N*-But-3-enyl-*N*-methylamino)-9-hydroxy-2-phenylbenzo[*f*]isoindole-1,3-dione (32) was obtained from 140 mg (0.5 mmol) of sulfoxide **28** and 170 mg (1 mmol) of *N*-phenylmaleimide (toluene) in 62% yield as a bright yellow solid: mp 73−74 °C; IR (KBr) 3376, 1743, 1689, 1381, 905, 730 cm^{-1}; ^{1}H-NMR δ 2.34 (dt, 2H, J = 7.0, 7.0 Hz), 3.06 (s, 3H), 3.47 (t, 2H, J = 7.0 Hz), 4.94−5.06 (m, 2H), 5.74−5.83 (m, 1H), 7.38−7.75 (m, 7H), 8.36−8.40 (m, 1H), 8.54−8.57 (m, 1H), 8.99 (s, 1H); ^{13}C-NMR δ 33.2, 41.2, 55.9, 106.2, 115.8, 117.9, 123.8, 126.4, 127.2, 127.9, 128.6, 128.8, 128.9, 129.5, 131.6, 136.5, 137.1, 144.3, 151.0, 165.2, 169.5. Anal. Calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52. Found: C, 74.12; H, 5.43; N, 7.47.

4-(*N*-Methyl-*N*-pent-4-enylamino)-9-hydroxy-2-phenylbenzo[*f*]isoindole-1,3-dione (33) was obtained from 150 mg (0.5 mmol) of sulfoxide **29** and 170 mg (1 mmol) of *N*-phenylmaleimide (toluene) in 68% yield as a bright yellow solid: mp 68−69 °C; IR (KBr) 3382, 1743, 1689, 1375, 1002, 760 cm^{-1}; ^{1}H-NMR δ 1.62−1.72 (m, 2H), 2.07 (dt, 2H, J = 7.0, 7.0 Hz), 3.05 (s, 3H), 3.40 (t, 2H, J = 7.0 Hz), 4.88−4.96 (m, 2H), 5.70−5.81 (m, 1H), 7.39−7.76 (m, 7H), 8.37−8.41 (m, 1H), 8.53−8.56 (m, 1H), 9.00 (s, 1H); ^{13}C-NMR δ 27.9, 31.3, 41.6, 55.8, 106.3, 114.6, 117.8, 123.9, 126.5, 127.2, 128.0, 128.7, 128.9, 129.0, 129.6, 131.7, 137.3, 138.4, 144.7, 151.1, 165.3, 169.7. Anal. Calcd for $C_{24}H_{22}N_2O_3$: C, 74.59; H, 5.74; N, 7.25. Found: C, 74.32; H, 5.81; N, 7.19.

***N*-Methyl-*N*-[4-(*p*-toluenesulfonyl)but-3(*E*)-enyl]-2-[(ethylsulfinyl)methyl]benzamide (34).** A mixture of 1.2 g (4.5 mmol) of sulfide **26**, 1.3 g (4.7 mmol) of *p*-toluenesulfonyl iodide, 30 mg (0.22 mmol) of cupric chloride, 30 mg (0.22 mmol) of triethylamine hydrochloride, and 3 mL of dry acetonitrile was stirred at rt under argon in the dark for 90 min. The solvent was removed under reduced pressure, and the crude mixture was dissolved in CH_2Cl_2, washed with brine, dried over Na_2SO_4, filtered through a short column of silica gel, and concentrated under reduced pressure. The resulting residue was dissolved in 5 mL of benzene and treated with 500 mg (5 mmol) of triethylamine. After being stirred for 10 min at rt, the mixture was diluted with ether and washed sucessively with 5% aqueous HCl and water. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to afford a dark oil that was purified by flash silica gel chromatography to give 1.29 g (54%) of pure *N*-methyl-*N*-[4-(*p*-toluenesulfonyl)but-3(*E*)-enyl]-2-[(ethylthio)methyl]benzamide as a colorless oil that exists as a mixture of two rotamers in solution: IR (neat) 1627, 1595, 1397, 1312, 1141 cm^{-1}; ^{1}H-NMR δ 1.17−1.23 (m, 3H), 2.37−2.47 (m, 6H), 2.61−2.68 (m, 1H), 2.80−3.12 (m, 3H), 3.63−3.78 (m, 4H), 6.29−6.52 (m, 1H), 6.69−7.37 (m, 7H), 7.70−7.83 (m, 2H); ^{13}C-NMR δ 14.3, 21.4,

25.5, 28.9, 32.8, 37.6, 45.3, 125.9−144.3, 170.9; HRMS (FAB) calcd for $C_{22}H_{27}NO_3S_2Li$ (M + Li) 424.1592, found 424.1596.

A 4.2 g (10 mmol) sample of the above sulfide was oxidized in the standard manner to give **34** (96%) as colorless oil that exists as a mixture of two rotamers in solution: IR (neat) 1627, 1595, 1397, 1312, 1141, 1045 cm^{-1}; ^{1}H-NMR δ 1.33 (t, 3H, J = 7.5 Hz), 2.43 and 2.45 (s, 3H), 2.59−2.82 (m, 4H), 2.87 and 2.95 (s, 3H), 3.33 and 3.67 (m, 2H), 3.97 (d, 1H, J = 13.0 Hz), 4.07 (d, 1H, J = 13 Hz), 6.25−6.52 (m, 1H), 6.68−7.04 (m, 1H), 7.08−7.83 (m, 8H); ^{13}C-NMR δ 6.6, 21.4, 28.9, 37.6, 45.3, 45.4, 54.8, 126.4−144.4, 170.3; HRMS (FAB) calcd for $C_{22}H_{28}NO_4S_2$ (M + H): 434.1460, found 434.1468.

4-Hydroxy-9-[4-(*p*-toluenesulfonyl)but-3(*E*)-enyl]methylamino]-2-phenylbenzo[*f*]isoindolo-1,3-dione (36) was obtained from 220 mg (0.5 mmol) of sulfoxide **34** and 430 mg (2.5 mmol) of *N*-phenylmaleimide (xylene) in 71% yield as a bright yellow solid: mp 151−152 °C; IR (KBr) 3373, 1746, 1687, 1382, 1137 cm^{-1}; ^{1}H-NMR δ 2.41 (s, 3H), 2.48 (ddt, 2H, J = 6.5, 6.5, 1.2 Hz), 3.01 (s, 3H), 3.60 (t, 2H, J = 6.5 Hz), 6.25−6.30 (m, 1H), 6.94 (dt, 1H, J = 15.0, 6.5 Hz), 7.42−7.73 (m, 11H), 8.38−8.46 (m, 2H), 8.98 (s, 1H); ^{13}C-NMR δ 21.4, 30.7, 41.5, 54.2, 106.1, 118.5, 123.9, 126.4, 126.8, 127.4, 128.0, 128.8, 128.9, 129.6, 130.0, 131.5, 131.6, 136.8, 137.3, 143.1, 144.0, 144.3, 155.4, 165.3, 169.4. Anal. Calcd for $C_{30}H_{26}N_2O_5S$: C, 68.42; H, 4.98; N, 5.32. Found: C, 68.08; H, 5.00; N, 5.25.

2-[(Ethylthio)methyl]-*N*-methyl-*N*-(3-oxopropyl)benzamide (37). A mixture of 2.1 g (10 mmol) of amide **25**, 480 mg (12 mmol) of NaH (60% dispersion in mineral oil), and 40 mL of toluene was heated at 60−70 °C for 1 h until the evolution of hydrogen gas had ceased. After the addition of 2.7 g (15 mmol) of 2-(2-bromoethyl)-1,3-dioxolane, the mixture was heated at reflux for 4 h until all the starting material was consumed. After being cooled to rt, the mixture was poured onto 200 g of ice−water. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash silica gel chromatography to give 2.5 g (79%) of *N*-(2-1,3-dioxolan-2-ylethyl)-2-[(ethylthio)methyl]-*N*-methylbenzamide as a colorless oil that consisted of a mixture of two rotamers in solution: IR (neat) 1633, 1597, 1396, 1134, 1062, 1031 cm^{-1}; ^{1}H-NMR δ 1.21 (t, 3H, J = 7.5 Hz), 1.92−2.11 (m, 2H), 2.44 (q, 2H, J = 7.5 Hz), 2.84 and 3.09 (s, 3H), 3.59−4.02 (m, 8H), 4.73 and 5.03 (t, 1H, J = 5.0 Hz), 7.10−7.39 (m, 4H); ^{13}C-NMR δ 14.3, 25.7, 31.0, 32.1, 32.8, 32.9, 34.0, 37.3, 42.5, 46.3, 64.6, 64.7, 64.8, 66.7, 70.0, 101.9, 102.1, 102.7, 125.9, 126.2, 126.7, 128.4, 128.6, 129.6, 130.0, 130.4, 135.5, 135.6, 136.6, 170.5, 170.8; MS calcd for $C_{16}H_{23}NO_3S$ 309.1399, found 309.1395.

A mixture containing 1.6 g (5 mmol) of the protected aldehyde, 50 mL of ethanol, 80 mL of H_2O, and 15 g of oxalic acid was heated at reflux for 20 h. After removal of most of the ethanol under reduced pressure, the mixture was extracted with CH_2Cl_2. The organic layer was washed with a saturated aqueous $NaHCO_3$ solution, dried over K_2CO_3, and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to give 1.22 g (92%) of aldehyde **37** as a colorless oil that consisted of a mixture of two rotamers in solution: IR (neat) 1718, 1627, 1397, 1060, 767 cm^{-1}; ^{1}H-NMR δ 1.22 (t, 3H, J = 7.5 Hz), 2.43 (q, 2H, J = 7.5 Hz), 2.70−2.92 (m, 2H), 2.88 and 4.07 (s, 3H), 3.47−3.90 (m, 4H), 7.14−7.34 (m, 4H), 9.70 and 9.90 (s, 1H); ^{13}C-NMR δ 14.4, 25.7, 33.0, 37.9, 41.4, 41.6, 126.5, 126.8, 128.8, 130.3, 135.9, 136.1, 171.1, 200.7; HRMS calcd for $C_{14}H_{19}NO_2S$ 265.1137, found 265.1131.

5-[2-[(Ethylthio)methyl]benzoyl]methylamino]pent-2-enoic Acid Methyl Ester (38, 39). To a solution of 1.1 g (4 mmol) of aldehyde **37** in 50 mL of CH_2Cl_2 was added 1.5 g (4.5 mmol) of methyl (triphenylphosphoranylidene)acetate at 0 °C. After the mixture was stirred for 2 h at rt, the solvent was removed under reduced pressure and the remaining residue was purified by flash silica gel chromatography to give 50 mg (4%) of **39**-*Z* and 1.21 g (94%) of **38**-*E* as colorless oils. Compound **38**-*E* consisted of a mixture of two rotamers in solution that exhibited the following spectral data: IR (neat) 1723, 1632, 1434, 1269, 1194 cm^{-1}; ^{1}H-NMR δ 1.21 (t, 3H, J = 7.5 Hz), 2.44 (q, 2H, J = 7.5 Hz), 2.59−2.67 and 3.21−3.29 (m, 2H), 2.84 and 3.10 (s, 3H), 3.62−3.79 (m, 4H), 3.72 and 3.74 (s, 3H), 5.80 and 5.97 (d, 1H, J = 16.0 Hz), 6.74 and 7.03 (dt, 1H, J = 16.0, 7.0 Hz), 7.13−7.36 (m, 4H); ^{13}C-NMR δ 14.0, 25.3, 25.5, 30.6, 31.8, 32.6, 37.1, 45.3, 49.5, 51.0, 122.4, 122.7, 125.9, 126.0, 126.4, 128.3, 128.5, 129.8, 135.3, 135.5, 135.9, 136.1, 144.1, 145.3, 165.8, 166.1, 170.4, 170.6; *m/z* 321 (M^+) 261, 202, 188, 179, 149 (base), 119, 90; HRMS calcd for $C_{17}H_{23}NO_3S$ 321.1399, found 321.1394.

Isomer **39**-*Z* showed the following properties: ^{1}H-NMR δ 1.22, (t, 3H, J = 7.5 Hz), 2.44 (q, 2H, J = 7.5 Hz), 2.87 and 3.13 (s, 3H), 2.93−3.29 (m, 2H), 3.71 and 3.73 (s, 3H), 3.69−3.85 (m, 4H), 5.84 and 5.92 (d, 1H, J = 12.0 Hz), 6.03 and 6.41 (dt, 1H, J = 12.0, 7.0 Hz), 7.11−7.40 (m, 4H).

5-[2-[(Ethylsulfinyl)methyl]benzoyl]methylamino]pent-2-enoic Acid Methyl Ester (40, 41). A 970 mg (3 mmol) sample of sulfide **38**-*E* was oxidized in the standard manner to give sulfoxide **40**-*E* (94%) as a colorless oil that exists as a mixture of two rotamers in solution: IR (neat) 1718, 1632, 1440, 1402, 1269, 1039 cm^{-1}; ^{1}H-NMR δ 1.34 (t, 3H, J = 7.5 Hz), 2.44 and 2.61 (dt, 2H, J = 7.0, 7.0 Hz), 2.63−2.80 (m, 2H), 2.90 and 3.09 (s, 3H), 3.32 and 3.68 (t, 2H, J = 7.0 Hz), 3.72 and 3.75 (s, 3H), 3.95 (d, 1H, J = 13.0 Hz), 4.10 (d, 1H, J = 13.0 Hz), 5.80 and 5.97 (d, 1H, J = 16.0 Hz), 6.71 and 7.00 (dt, 1H, J = 16.0, 7.0 Hz), 7.21−7.47 (m, 4H); ^{13}C-NMR δ 6.5, 6.6, 29.6, 30.7, 32.1, 37.4, 45.3, 45.6, 49.7, 51.3, 53.3, 54.8, 54.9, 122.7, 123.2, 126.4, 126.5, 127.8, 128.2, 129.2, 129.3, 131.4, 131.5, 136.4, 136.7, 143.9, 145.2, 165.9, 166.2, 170.0, 170.2; HRMS (FAB) calcd for $C_{17}H_{24}NO_4S$ (M + H) 338.1426, found 338.1437.

A sample of sulfoxide **41**-*Z* was obtained in analogous fashion in 94% yield: ^{1}H-NMR δ 1.33 (t, 3H, J = 7.5 Hz), 2.62−2.81 (m, 2H), 2.91 and 3.13 (s, 3H), 2.94−3.09 (m, 2H), 3.25−3.34 and 3.62−3.79 (m, 2H), 3.73 and 3.70 (s, 3H), 3.95 and 4.10 (d, 2H, J = 13.0 Hz), 5.83 and 5.92 (d, 1H, J = 12.0 Hz), 6.02 and 6.38 (dt, 1H, J = 12.0, 7.0 Hz), 7.21−7.47 (m, 4H).

Methyl 5-Hydroxy-1-methyl-2,3-dihydro-1*H*-benzo[*g*]-indole-4-carboxylate (43) was obtained from 170 mg (0.5 mmol) of sulfoxide **40**-*E* (25 mL of xylene) in 64% yield as a bright yellow solid: mp 91−92 °C; IR (KBr) 1654, 1627, 1445, 1354, 1236 cm^{-1}; ^{1}H-NMR δ 2.93 (s, 3H), 3.37−3.54 (m, 4H), 3.98 (s, 3H), 7.46 (t, 1H, J = 8.0 Hz), 7.60 (t, 1H, J = 8.0 Hz), 7.95 (d, 1H, J = 8.0 Hz), 8.41 (d, 1H, J = 8.0 Hz), 12.07 (s, 1H); ^{13}C-NMR δ 31.9, 43.9, 52.0, 56.5, 103.5, 122.3, 124.8, 124.9, 125.0, 126.8, 127.5, 129.3, 140.3, 158.5, 171.9. Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; C, 5.88; N, 5.44. Found: C, 69.75; H, 5.98; N, 5.37.

Methyl 5-Hydroxy-1-methyl-1*H*-benzo[*g*]indole-4-carboxylate (44). To a solution containing 25 mg (0.1 mmol) of indoline **43** in 2 mL of CH_2Cl_2 was added 50 mg of silica gel. The solvent was allowed to evaporate upon standing, and the resulting solid was kept in the open air for 1 week. After the oxidation was complete, indole **44** was extracted with CH_2Cl_2 and purified by flash silica gel chromatography to give 25 mg (100%) of **44** as a colorless solid: mp 129−130 °C; IR (KBr) 1644, 1618, 1441, 1340, 1239 cm^{-1}; ^{1}H-NMR δ 4.06 (s, 3H), 4.15 (s, 3 H), 6.90 (d, 1H, J = 3.0 Hz), 7.96 (d, 1 H, J = 3.0 Hz), 7.42 (t, 1H, J = 8.0 Hz), 7.60 (t, 1H, J = 8.0 Hz), 8.27 (d, 1H, J = 8.0 Hz), 8.52 (d, 1H, J = 8.0 Hz), 12.39 (s, 1H); ^{13}C-NMR δ 38.6, 52.0, 99.6, 103.1, 120.0, 121.4, 122.8, 123.1, 124.4, 125.2, 126.7, 129.1, 129.3, 157.7, 172.9. Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.57; H, 5.13; N, 5.49. Found: C, 70.57; H, 5.16; N, 5.47.

2-[(Ethylsulfinyl)methyl]-*N*-methyl-*N*-pent-4-enoylbenzamide (45). A mixture containing 1.1 g (5 mmol) of amide **25**, 890 mg (7.5 mmol) of pent-4-enoyl chloride, 4.0 g of powdered molecular sieves (4 Å), and 30 mL of CH_2Cl_2 was stirred for 24 h at rt. The reaction mixture was filtered through a pad of silica gel, the solvent was evaporated under reduced pressure, and the resulting crude oil was purified by flash silica gel chromatography to give 1.19 g (82%) of 2-[(ethylthio)methyl]-*N*-methyl-*N*-pent-4-enoylbenzamide as a colorless oil: IR (neat) 1691, 1659, 1317, 1210, 1050 cm^{-1}; ^{1}H-NMR δ 1.21 (t, 3H, J = 7.5 Hz), 2.37−2.47 (m, 4H), 2.90 (t, 2H, J = 7.0 Hz), 3.10 (s, 3H), 3.89 (s, 2H), 4.97−5.12 (m, 2H), 5.78−5.91 (m, 1H), 7.24−7.38 (m, 4H); ^{13}C-NMR δ 14.0, 25.4, 28.6, 32.7, 33.6, 37.4, 114.9, 126.8, 126.9, 129.9, 130.1, 135.4,

136.8, 137.1, 172.9, 175.6; HRMS (FAB) calcd for $C_{16}H_{22}NO_2S$ (M + H) 292.1371, found 292.1371.

A 1.16 g (4 mmol) sample of the above sulfide was oxidized in the standard manner to give sulfoxide **45** (95%) as a colorless oil: IR (neat) 1680, 1659, 1322, 1210, 1044 cm^{-1}; ^{1}H-NMR δ 1.35 (t, 3H, J = 7.5 Hz), 2.43 (dt, 2H, J = 7.0, 7.0 Hz), 2.65−2.78 (m, 2H), 2.86 (t, 2H, J = 7.0 Hz), 3.10 (s, 3H), 4.08 (d, 1H, 13.0 Hz), 4.25 (d, 1H, J = 13.0 Hz), 4.98−5.09 (m, 2H), 5.72−5.89 (m, 1H), 7.29−7.53 (m, 4H); ^{13}C-NMR δ 6.5, 28.7, 33.9, 37.1, 45.1, 54.1, 115.1, 127.3, 127.9, 129.7, 130.8, 132.2, 135.9, 136.7, 172.8, 175.5; HRMS (FAB) calcd for $C_{16}H_{22}NO_3S$ (M + H) 308.1322, found 308.1324.

6-Hydroxy-3,4-dihydro-1*H*-1-methylbenzo[*h*]quinoline-2,6-dione (50) and 10b-(ethylthio)-1-methyl-1,3,4,4a,5,10b-hexahydrobenzo[*h*]quinoline-2,6-dione (49) were obtained from 150 mg (0.5 mmol) of sulfoxide **45** (xylene) as a 1:2 mixture. The crude mixture was purified by flash silica gel chromatography to give 25 mg (22%) of naphthol **50** and 63 mg (43%) of *N*,*S*-ketal **49**. Heating a pure sample of ketal **49** in xylene at reflux for 30 min in the presence of a catalytic amount of *p*-TsOH provided naphthol **50** in 98% yield. Naphthol **50** exhibited the following properties: mp 189−190 °C; IR (KBr) 3150, 1639, 1626, 1385, 1248, 1196 cm^{-1}; ^{1}H-NMR δ 2.68 (t, 2H, J = 7.5 Hz), 2.92 (t, 2H, J = 7.5 Hz), 3.56 (s, 3H), 6.77 (s, 1H), 7.44−7.54 (m, 2H), 7.83 (dd, 1H, J = 8.0, 1.0 Hz), 8.26 (dd, 1H, J = 8.0, 1.0 Hz); ^{13}C-NMR δ 26.7, 32.9, 37.9, 108.1, 122.8, 122.9, 124.4, 124.5, 126.3, 126.6, 128.0, 130.8, 149.4, 174.3. Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.91; H, 5.81; N, 6.05.

Ketal **49** exhibited the following properties: mp 115−116 °C; IR (KBr) 1682, 1646, 1592, 1350, 985 cm^{-1}; ^{1}H-NMR δ 1.23 (t, 3H, J = 7.5 Hz), 1.64−1.74 (m, 1H), 2.21−2.29 (m, 1H), 2.38−2.81 (m, 6H), 3.25−3.28 (m, 1H), 3.31 (s, 3H), 7.45 (t, 1H, J = 8.0 Hz), 7.62 (t, 1H, J = 8.0 Hz), 7.70 (d, 1H, J = 8.0 Hz), 8.03 (d, 1H, J = 8.0 Hz); ^{13}C-NMR δ 13.2, 23.3, 41.6, 24.8, 29.9, 32.9, 38.2, 41.4, 74.4, 127.7, 128.0, 129.0, 131.2, 133.8, 141.6, 170.6, 195.2. Anal. Calcd for $C_{16}H_{19}NO_2S$: C, 66.41; H, 6.62; N, 4.84. Found: C, 66.53; H, 6.66; N, 4.80.

6-Acetoxy-3,4-dihydro-1-methylbenzo[*h*]quinolin-2-one (51) was obtained from 150 mg (0.5 mmol) of sulfoxide **45** as described above. Instead of working up the reaction mixture after all the sulfoxide had been consumed, an additional 5 mg of *p*-TsOH was added to the reaction mixture and was subsequently heated at reflux for an additional 15 min. After concentration under reduced pressure, the crude product was purified by flash silica gel chromatography to give 80 mg (59%) of cycloadduct **51** as a colorless solid: mp 145−146 °C; IR (KBr) 1749, 1670, 1387, 1181 cm^{-1}; ^{1}H-NMR δ 2.41 (s, 3H), 2.65 (t, 2H, J = 7.5 Hz), 2.93 (t, 2H, J = 7.5 Hz), 3.52 (s, 3H), 7.10 (s, 1H), 7.46−7.49 (m, 2H), 7.84−7.90 (m, 2H); ^{13}C-NMR δ 20.7, 26.2, 32.4, 37.6, 117.5, 121.6, 123.4, 125.6, 125.9, 126.1, 126.6, 126.8, 135.9, 142.8, 169.3, 173.3. Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.42; H, 5.65; N, 5.13.

***N*-But-3-enoyl-2-[(ethylsulfinyl)methyl]-*N*-methylbenzamide (52).** A mixture of 1.1 g (5 mmol) of amide **25**, 780 mg (7.5 mmol) of but-3-enoyl chloride, 4.0 g of powdered molecular sieves (4 Å), and 30 mL of CH_2Cl_2 was stirred for 24 h at rt. The reaction mixture was filtered through a pad of silica gel, the solvent was evaporated under reduced pressure, and the crude oil was purified by flash silica gel chromatography to give 1.12 g (81%) of *N*-but-3-enoyl-2-[(ethylthio)methyl]-*N*-methylbenzamide as a colorless oil: IR (neat) 1691, 1659, 1418, 1317, 1210, 1050 cm^{-1}; ^{1}H-NMR δ 1.21 (t, 3H, J = 7.5 Hz), 2.41 (q, 2H, J = 7.5 Hz), 3.09 (s, 3H), 3.63 (d, 2H, J = 7.0 Hz), 3.89 (s, 2H), 5.11−5.19 (m, 2H), 5.98−6.12 (m, 1H) 7.27−7.39 (m, 4H); ^{13}C-NMR δ 13.9, 25.5, 32.7, 33.8, 42.7, 117.9, 126.7, 126.8, 126.9, 130.5, 130.8, 135.2, 137.1, 173.0, 174.3; HRMS calcd for $C_{15}H_{19}NO_2S$ 277.1137, found 277.1129.

A 1.1 g (4 mmol) sample of the above sulfide was oxidized in the standard manner to afford sulfoxide **52** (94%) as a colorless oil: IR (neat) 1691, 1685, 1656, 1317, 1210, 1050 cm^{-1}; ^{1}H-NMR δ 1.34 (t, 3H, J = 7.5 Hz), 2.65−2.81 (m, 2H), 3.17 (s, 3H), 3.58 (d, 2H, J = 7.0 Hz), 4.09 (d, 1H, J = 13.0 Hz), 4.27 (d, 1H, J = 13.0 Hz), 5.11−5.19 (m, 2H), 5.96−6.05 (m, 1H), 7.36−7.53 (m, 4H); ^{13}C-NMR δ 6.5, 34.2, 42.5, 45.2, 54.0, 118.2, 127.4, 128.0, 129.8, 130.6, 130.9, 132.3, 135.7, 172.8, 174.2; HRMS (FAB) calcd for $C_{15}H_{20}NO_3S$ (M + H) 294.1164, found 294.1167.

5-Acetoxy-1-methyl-2,3-dihydro-1*H*-benzo[g]indole-2-one (55) was obtained from 150 mg (0.5 mmol) of sulfoxide **52** (xylene, 5 mg of *p*-TsOH) in 75% yield as a colorless solid: mp 164−165 °C; IR (KBr) 1756, 1700, 1462, 1202 cm^{-1}; ^{1}H-NMR δ 2.42 (s, 3H), 3.51 (s, 2H), 3.63 (s, 3H), 7.08 (s, 1H), 7.36−7.45 (m, 2H), 7.82 (dd, 1H, J = 8.0, 1.0 Hz), 8.24 (dd, 1H, J = 8.0, 1.0 Hz); ^{13}C-NMR δ 20.7, 30.2, 36.0, 114.7, 119.2, 121.1, 121.3, 121.9, 125.6, 125.9, 126.6, 137.6, 141.5, 169.5, 175.8. Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.47; H, 5.16; N, 5.46.

***N*-But-3-enyl-2-[(ethylthio)methyl]benzamide (56).** To a stirred suspension containing of 4.9 g (25 mmol) of 2-[(ethylthio)methyl]benzoic acid (**8**)[38] in 50 mL of dry benzene was added 6.0 g (50 mmol) of thionyl chloride. After being stirred at rt for 1 h, the solution was concentrated under reduced pressure. The crude acid chloride was dissolved in 20 mL of dry CH_2Cl_2, and this was added dropwise to a solution containing 5.3 g (75 mmol) of but-3-enylamine in 50 mL of dry CH_2Cl_2 at 0 °C under argon. After being stirred at rt for 2 h, the mixture was washed successively with 5% HCl, a saturated $NaHCO_3$ solution, and brine. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to give 4.7 g (76%) of amide **56** as a colorless solid: mp 48−49 °C; IR (KBr) 3291, 1637, 1537, 1317, 701 cm^{-1}; ^{1}H-NMR δ 1.26 (t, 3H, J = 7.5 Hz), 2.39 (dt, 2H, J = 7.0, 7.0 Hz), 2.52 (q, 2H, J = 7.0 Hz), 3.54 (dt, 2H, J = 7.0, 7.0 Hz), 3.92 (s, 2H), 5.09−5.19 (m, 2H), 5.78−5.91 (m, 1H), 6.53 (brs, 1H), 7.25−7.49 (m, 4H); ^{13}C-NMR δ 14.3, 25.8, 33.5, 33.6, 38.9, 117.0, 127.0, 128.1, 129.6, 130.4, 135.2, 135.7, 136.4, 169.2. Anal. Calcd for $C_{14}H_{19}NOS$: C, 67.43; H, 7.68; N, 5.62. Found: C, 67.51; H, 7.75; N, 5.61.

***N*-Acetyl-*N*-but-3-enyl-2-[(ethylsulfinyl)methyl]benzamide (57).** A mixture containing 1.3 g (5 mmol) of amide **56**, 590 mg (7.5 mmol) of acetyl chloride, 4.0 g of powdered molecular sieves (4 Å), and 30 mL of CH_2Cl_2 was stirred for 24 h at rt. The reaction mixture was filtered through a pad of silica gel, the solvent was removed under reduced pressure, and the resulting crude oil was purified by flash silica gel chromatography to give 1.2 g (81%) of *N*-acetyl-*N*-but-3-enyl-2-[(ethylthio)methyl]benzamide as a colorless oil: IR (neat) 1696, 1654, 1440, 1345, 1262, 1215 cm^{-1}; ^{1}H-NMR δ 1.22 (t, 3H, J = 7.5 Hz), 2.18 (s, 3H), 2.36−2.47 (m, 4H), 3.80 (t, 2H, J = 7.0 Hz), 3.92 (s, 2H), 4.99−5.07 (m, 2H), 5.68−5.77 (m, 1H), 7.29−7.44 (m, 4H); ^{13}C-NMR δ 14.2, 25.8, 26.7, 33.0, 33.1, 44.9, 117.0, 126.9, 130.5, 130.8, 134.8, 135.5, 137.3, 173.2, 173.3; HRMS (FAB) calcd for $C_{16}H_{21}NO_2SLi$ (M + Li) 298.1453, found 298.1441.

A 1.2 g (4 mmol) sample of the above sulfide was oxidized in the standard manner to give sulfoxide **57** in 95% yield as a colorless oil: IR (neat) 1691, 1649, 1440, 1351, 1047 cm^{-1}; ^{1}H-NMR δ 1.37 (t, 3H, J = 7.5 Hz), 2.18 (s, 3H), 2.39 (dt, 2H, J = 7.0, 7.0 Hz), 2.68−2.86 (m, 2H), 3.83 (t, 2H, J = 7.0 Hz), 4.05 (d, 1H, J = 13.0 Hz), 4.26 (d, 1H, J = 13.0 Hz), 5.02−5.10 (m, 2H), 5.63−5.82 (m, 1H), 7.38−7.52 (m, 4H); ^{13}C-NMR δ 6.7, 26.7, 33.1, 45.1, 45.8, 55.2, 117.4, 128.1, 128.2, 130.5, 131.4, 132.5, 134.6, 135.9, 173.0, 173.3; HRMS (FAB) calcd for $C_{16}H_{22}NO_3S$ 308.1320, found 308.1311.

5-Acetoxy-1-acetyl-2,3-dihydro-1*H*-benzo[*g*]indole (60) was obtained from 150 mg (0.5 mmol) of sulfoxide **57** (xylene, 5 mg of *p*-TsOH) in 81% yield as a colorless solid: mp 141−142 °C; IR (KBr) 1760, 1656, 1622, 1592, 1400, 1326, 1217 cm^{-1}; ^{1}H-NMR δ 2.34 (brs, 3H), 2.46 (s, 3H), 3.20 (t, 2H, J = 7.0 Hz), 4.29 (brs, 2H), 7.19 (s, 1H), 7.42−7.55 (m, 2H), 7.80−7.91 (m, 2H); ^{13}C-NMR δ 20.8, 24.0, 30.2, 51.8, 115.0, 121.2, 125.0, 125.5, 125.6, 125.7, 125.8, 130.9, 136.4, 144.4, 169.3. Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.20; H, 5.70; N, 5.23.

Computational Procedures. Preliminary optimizations of **61**−**63** and **64**†−**66**† were carried out with MM3* in

Macromodel, v.4.5,[44] to identify the lower energy conformations of the nitrogen-containing substituent. *All-trans* starting geometries for **61**−**63** consistently reorganized to other forms in the force-field framework. The lowest energy for each was subsequently optimized by the DFT procedure B3LYP/3-21G* (B3LYP = Becke3LYP) encapsulated in Gaussian-94.[45] In addition, each of the structures was graphically converted to an *all-trans* conformer. These too were subjected to DFT optimization. Transition states **64**†−**66**† were modeled by constraining the newly formed pericyclic bonds to 2.2−2.5 Å and optimized with MM3*. A variety of ring conformations and *N*-methyl orientations were explored. In each case, one force-field conformer proved considerably lower in energy than the rest. Each was subsequently DFT optimized, as were both *N*-$COCH_3$ rotameric forms of **66**†. To construct the isodesmic reactions, *N*-methylacetamide, *N*-ethylacetamide, and methylethylamine were optimized with DFT in the *all-trans* conformations. Finally, all DFT-optimized structures were re-evaluated for energy by a single-point 6-31G* calculation using Gaussian-94: B3LYP/6-31G*//B3LYP/3-21G*. The resulting relative energies have been used throughout the computational discussion.

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Supporting Information Available: ^{1}H-NMR and ^{13}C-NMR spectra for new compounds lacking analyses (21 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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