A Facile and Efficient Synthesis of Thieno[2,3-*c*]furans and Furo[3,4-*b*]indoles via a Pummerer-Induced Cyclization Reaction†

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The α-thiocarbocation generated from the Pummerer reaction of an *o*-heteroaroyl-substituted sulfoxide is intercepted by the adjacent keto group to produce an α-thio-substituted heteroaromatic isobenzofuran. In the presence of a suitable dienophile, the reactive *o*-xylylene undergoes a Diels−Alder cycloaddition followed by an acid-catalyzed ring-opening and aromatization to give heteroaromatic naphthalene derivatives. This one-pot procedure occurs smoothly with electron-deficient dienophiles. The tandem Pummerer cyclization−cycloaddition sequence also occurs intramolecularly using unactivated alkenyl tethers of variable length. With acetylenic dienophiles, the primary cycloadducts undergo *in situ* ring-opening to produce hydroxynaphthalene derivatives. In the absence of a dienophile, it was possible to prepare 4-(ethylthio)-6-phenylthieno[2,3-*c*]furan and 1-ethyl-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole. Various synthetic approaches were used for the preparation of the requisite thiophene- and indole-derived sulfoxide precursors. The facility of the tandem Pummerer−Diels−Alder reaction was very dependent on the experimental conditions used to promote the reaction. The best results were achieved by employing a mixture of acetic anhydride and toluene which contained a catalytic quantity of *p*-toluenesulfonic acid. The presence of the acid effectively drives the reaction in the desired direction by preventing formation of the acetoxy sulfide, which corresponds to the normal Pummerer product.

o-Quinodimethanes are highly reactive diene components that have been extensively utilized for the assembly of a variety of polycyclic aromatic compounds.[1] Heterocyclic analogs of *o*-xylylene are of considerable interest for their potential in organic synthesis. Recently, there has been an increasing number of reports on the generation and reactivity of various heterocyclic *o*-xylylenes containing one, two, or three heteroatoms.[2−17] Isobenzofurans **1** correspond to one of the more interesting members of the *o*-quinodimethane family of dienes and have been the focus of considerable interest in both the synthetic and theoretical communities.[18,19] As highly reactive heteroaromatic *o*-xylylenes, they readily participate in inter- and intramolecular 4+2-cycloaddition reactions.[18,19] Further synthetic manipulation of the initially formed oxo-bridged cycloadduct usually provides an easy entry into naphthalene derivatives and related polycyclic aromatic ring systems. In many instances, the reactive isobenzofuran derivative is generated in the presence of a suitable dienophile. By comparison, heteroaromatic isobenzofuran analogs, in particular five-membered heteroaromatic derivatives, have not been extensively studied and only a few examples of synthetically useful Diels−Alder reactions of such species are known.[20−27] Most notable among the heteroaromatic isobenzofurans (**2**) reported in recent years are the furo[3,4-*b*]furans,[20] thieno[2,3-*c*]furans,[21,22] furo[3,4-*d*]isoxazoles,[23] and furo-

† This paper is dedicated to Professor Philip E. Eaton on the occasion of his 60th birthday.

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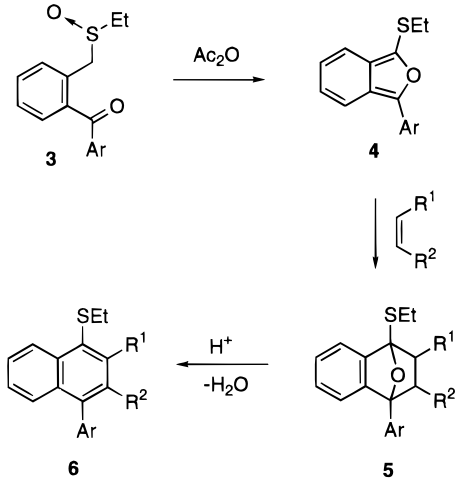
1 **2**; X = O, S, N

[3,4-*b*]indoles.[24−27] These 10π-systems are isoelectronic with the pentalene dianion and have been of some theoretical interest.[20] MO calculations on these heteroisobenzofurans indicate that they possess little or no aromatic character, and this is reflected in their high chemical reactivity.[20] Over the years, most of the studies reported in the literature for these systems center on their use as dienes in inter- and intramolecular Diels−Alder reactions.[20−27] Such cycloaddition processes allow for a rapid entry into complex polyheterocyclic rings and makes these compounds potentially useful for natural product synthesis.

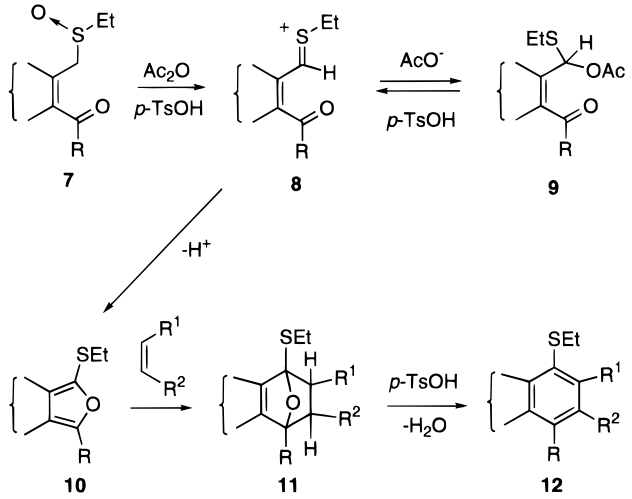
The vast majority of 2,3-methylene heteroaromatics have been prepared by flash vacuum pyrolysis or by 1,4-elimination from suitable precursors. One limitation of these methods is that the precursors are sometimes not easily available. Recently, we reported on the Pummerer-induced cyclization of keto sulfoxides[28] as a method to prepare thio-substituted isobenzofurans of type **4**. The



α-thiocarbocation generated from the Pummerer reaction of an *o*-benzoyl substituted sulfoxide is intercepted by the adjacent keto group to produce isobenzofuran **4** as a transient intermediate which undergoes a subsequent Diels−Alder cycloaddition with an added dienophile. The resulting cycloadduct **5** can be readily converted to representatives of several types of arylnaphthalene lignans.[29] In a continuation of our studies in this general area, we now report on an extension of the tandem Pummerer−Diels−Alder sequence for the synthesis of several thieno[2,3-*c*]furans and furo[3,4-*b*]indoles. The results of these studies are described herein.

Results and Discussion

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 reagent 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 since it allows the reaction to proceed under very mild conditions in the presence of basic (*e.g.* pyridine, triethylamine) or Lewis acid catalysts (*e.g.* $SnCl_4$). Another very useful promoter is trimethylsilyl trifluoromethanesulfonate (TMSOTf) since this reagent permits the reaction to be carried out at temperatures well below 0 °C. The latter two reagents are frequently used if attack by the nucleophilic "*counterion*" on the Pummerer intermediate is to be avoided.[30] In our earlier studies, we have successfully employed neat acetic anhydride as the Pummerer promoter since we found it to be highly effective for inducing the Pummerer reaction in the isobenzofuran system. However, when thiophene- or indolo-derived sulfoxides (*vide infra*) were used, the desired cycloadducts were obtained in much lower yield (10−20%), with the major product in most cases being acetoxy sulfides of type **9**.[30] It became evident, therefore, that a modified triggering protocol had to be developed in order to achieve acceptable yields of the desired heterocyclic cycloadducts. After considerable experimentation with a variety of Pummerer promoters and cocatalysts, we found that the highest yield of cycloaddition that could be obtained from the cascade process utilized a mixture of toluene and acetic anhydride which also contained a catalytic quantity of *p*-toluenesulfonic acid (*p*-TsOH).[31] These conditions, whereby the sulfoxide is



slowly added to a refluxing mixture of toluene, acetic anhydride (10 equiv), *p*-TsOH (catalyst), and the appropriate dienophile (2−3 equiv) gave consistently the best results (>80% yields), both for inter- and intramolecular cycloaddition reactions (*vide infra*). It should be noted that when *p*-TsOH was used alone, the tandem cascade process did not occur.[30] Other standard Pummerer promoters such as trifluoroacetic anhydride or TMSOTf were also ineffective and afforded in most cases

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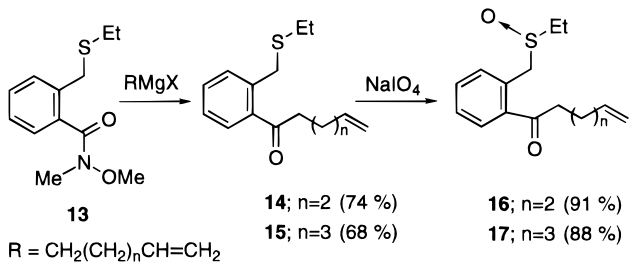
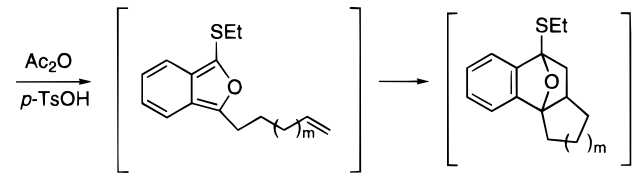
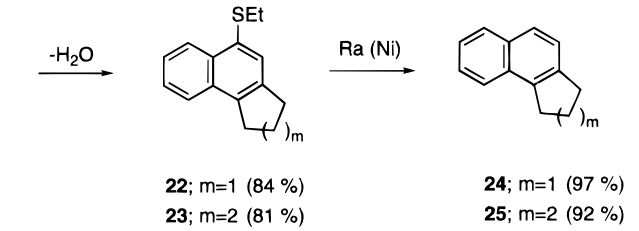
only the classical Pummerer products of type **9**. The presence of *p*-TsOH as a cocatalyst dramatically accelerated the rate in which sulfoxides of type **7** undergo the Pummerer transformation (**7** → **8**) as compared to reactions carried out without any *p*-TsOH. The initially formed thionium ion **8** can either be captured internally by the adjacent carbonyl group[32] to give, after proton loss, the isobenzofuran intermediate **10** or it can react in the traditional sense with an external nucleophile (*i.e.*, AcO^-) to furnish the acetoxy sulfide **9**. The presence of *p*-TsOH effectively drives the reaction in the desired direction (**8** → **10**) either by preventing the formation of the acetoxy sulfide **9** or by assisting the ejection of the acetoxy group (**9** → **8**), should **9** be formed. Indeed, control experiments with the thiophene-derived acetoxy sulfides of type **9** support the latter suggestion (*vide infra*). The presence of *p*-TsOH also promotes the conversion of the primary cycloadduct **11** into the aromatized product **12**, thereby adding another step to this series of cascade reactions.

In order to establish the feasibility of an intramolecular Diels–Alder cycloaddition in the α-thio isobenzofuran series, we first prepared sulfoxides **16** and **17** which contain an alkenyl tether attached to the keto group. Weinreb's amide **13**[33] was treated with the appropriate

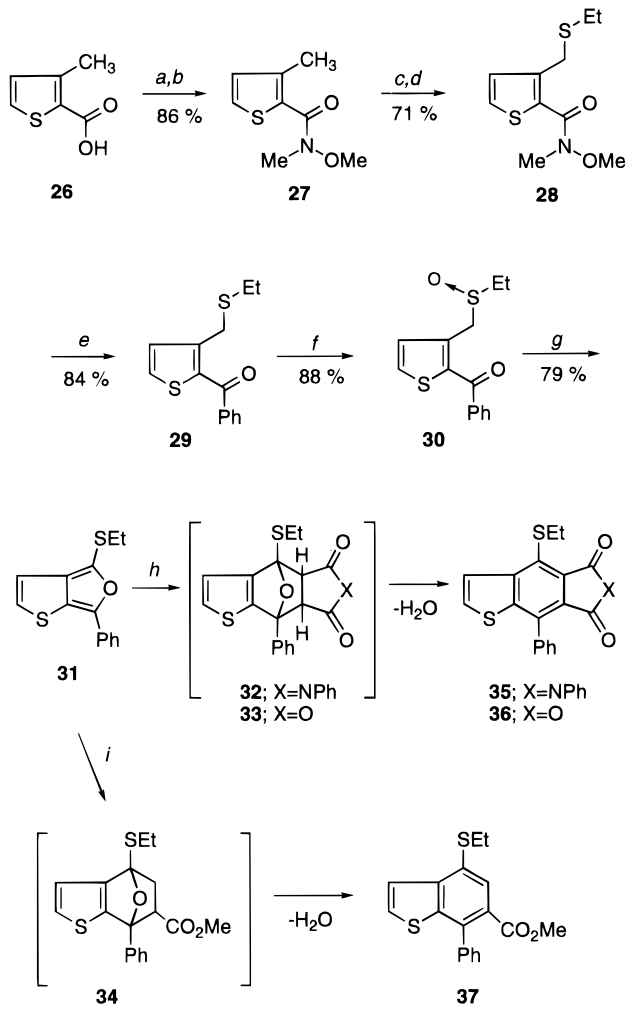






Grignard reagent to give the corresponding acetophenone-derived sulfides **14** and **15**, which were subsequently oxidized with sodium periodate[34] in methanol to produce sulfoxides **16** and **17** in good overall yield. Although both sulfoxides **16** and **17** bear an unactivated alkenyl tether, they smoothly underwent the intramolecular tandem Pummerer–Diels–Alder transformation when subjected to the acetic anhydride/*p*-TsOH conditions. It should be noted that bimolecular Diels–Alder reactions of α-thioisobenzofurans with unactivated π-systems (*e.g.* cyclohexene) only proceed in low yield or not at all.[28] The high yielding intramolecular Diels–Alder cycloaddition reaction of **18** and **19** is certainly related to entropic factors which place the tethered double bond in close proximity to the diene system. The products isolated correspond to the thionaphthalene derivatives **22** and **23**. Structures **22** and **23** were established by spectroscopic methods and this was further confirmed by desulfurization with Raney-Ni to give cyclopenta[a]-naphthalene **24**[35] and tetrahydrophenanthrene **25**,[36] respectively.

Scheme 1[a]



[a] Reagents: (a) $SOCl_2$, (b) MeNHOMe, (c) NBS, (d) EtSH, (e) PhMgBr, (f) $NaIO_4$/MeOH, (g) Ac_2O/*p*-TsOH, (h) *N*-phenylmaleimide or maleic anhydride/catalytic *p*-TsOH, (i) methyl acrylate.

We next turned our attention to the thiophene analogs (Scheme 1). Thiophene-2-carboxylic acid **26** was converted to the Weinreb amide **27** following standard procedures.[33] The (ethylthio)methyl functionality was then introduced by NBS bromination and subsequent displacement of bromide with ethanethiol.[37] The resulting sulfide **28** was treated with phenylmagnesium bro-

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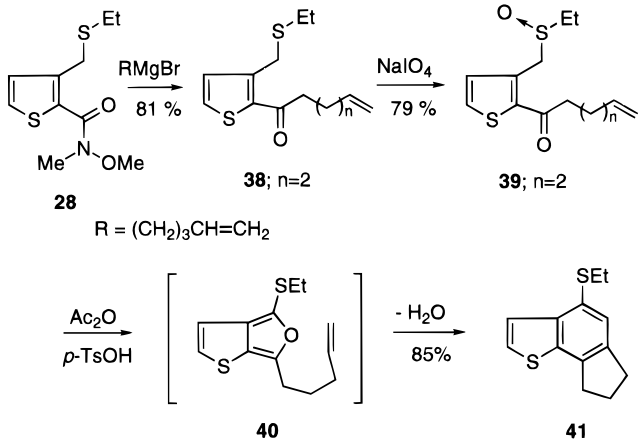
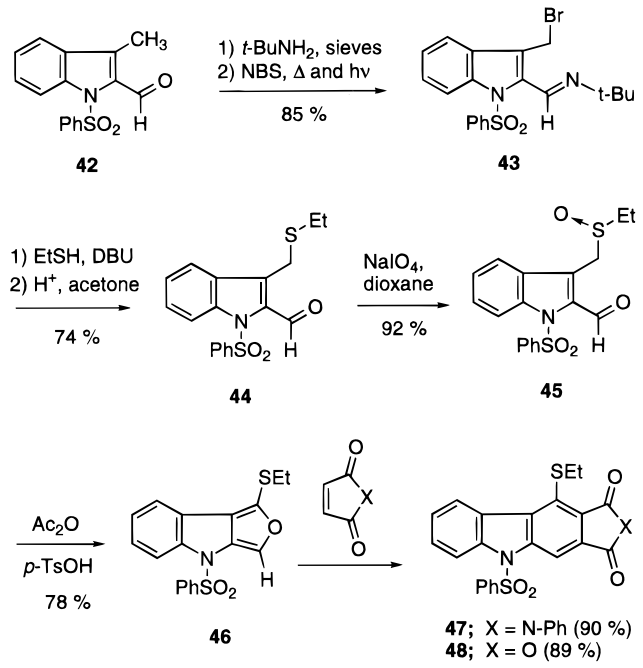
mide to produce ketone **29**, which in turn was oxidized with sodium periodate to give sulfoxide **30**. Treatment of **30** with *N*-phenylmaleimide or maleic anhydride under the tandem Pummerer−Diels−Alder conditions provided benzo[*b*]thiophene derivatives **35** and **36** in excellent yield. The initially formed primary cycloadducts **32** and **33** could not be isolated or observed. However, when the reaction was carried out in the absence of a dienophile, we were able to isolate thieno[2,3-*c*]furan **31** in 79% yield. This isobenzofuran analog proved to be surprisingly stable, and to the best of our knowledge corresponds to the second example of a stable thieno[2,3-*c*]furan reported in the literature.[21] As expected, **31** cleanly afforded thienoisoindole **35** (80%) when treated with *N*-phenylmaleimide in toluene in the presence of catalytic amounts of *p*-TsOH at room temperature. It should be noted that thienofuran **31** also underwent the Diels−Alder reaction when the less reactive methyl acrylate was used as the dienophile. Thus, treatment of **31** with methyl acrylate in the presence of scandium(III) trifluoromethanesulfonate [$Sc(OTf)_3$][38] for 2 days gave rise to benzo[*b*]thiophene **37** in 78% yield. This reaction also proceeded in the absence of $Sc(OTf)_3$ but in much lower yield. Analysis of the crude reaction mixture by ^{1}H-NMR failed to reveal the presence of the alternate regioisomer. The position of the ester group in **37** was determined by NOE experiments, which showed a significant enhancement of the signal for H_5 upon irradiation of the CH_3 and CH_2 multiplets of the adjacent ethylthio group. The ethylthio group plays a significant role in terms of influencing the regiochemistry of the Diels−Alder reaction, since the corresponding diphenyl derivative (*i.e.*, 4,6-diphenylthieno[2,3-*c*]furan) showed no regioselectivity, producing a 1:1 mixture of regioisomeric cycloadducts when treated with methyl acrylate.[21] The formation of adduct **37** as a single regioisomer is consistent with FMO theory. The most favorable interaction is between the HOMO of the thieno[2,3-*c*]furan and the LUMO of methyl propiolate. The atomic coefficient at the ethylthio-substituted position in the furan ring is larger than at the phenyl position in the HOMO and this nicely accommodates the high regioselectivity encountered.

As was mentioned above, the use of the toluene/acetic anhydride/*p*-TsOH reaction medium is critical for the success of the reaction. Subjection of sulfoxide **30** to standard Pummerer conditions (*i.e.*, refluxing acetic anhydride) led to a mixture of thienofuran **31** (23%) and to an acetoxy sulfide (64%). This acetoxy sulfide could be converted back to **31** by treatment with *p*-TsOH in toluene, and then trapped with *N*-phenylmaleimide to ultimately give cycloadduct **35**.

The intramolecular variation of the tandem Pummerer−Diels−Alder sequence also occurred in the thiophene series.[21b,c] The tethered sulfoxide **39** was prepared by reaction of Weinreb's amide **28** with pentenylmagnesium bromide followed by oxidation of the resulting sulfide with sodium periodate. Subjection of **39** to the acetic anhydride/*p*-TsOH conditions led to indeno[4,5-*b*]thiophene **41** in 85% yield. Here, the intramolecular Diels−Alder sequence of **39** to **41** provides an easy entry into this polycyclic ring system which is far superior to the previously reported multistep preparation of related indeno[4,5-*b*]thiophenes.[39]



Since furo[3,4-*b*]indoles have recently been employed as intermediates in the synthesis of some naturally occurring carbazole derivatives (*e.g.*, ellipticine[24] and murrayaquinone A[25]), we decided to explore the potential of the tandem Pummerer−Diels−Alder strategy toward the synthesis of several substituted carbazoles. The required sulfoxide **45** was prepared in the standard manner as outlined below. The readily available *N*-



(phenylsulfonyl)indole-2-carbaldehyde **42**[40] was first protected as an imine by treating it with *tert*-butylamine. The resulting imine was subsequently brominated with NBS to give bromomethyl derivative **43**. Nucleophilic displacement of the bromide by ethanethiol followed by acidic hydrolysis of the imine produced aldehyde **44**. Oxidation of the sulfide in the usual manner gave sulfoxide **45** in 58% overall yield (five steps).

Treatment of **45** with either *N*-phenylmaleimide or maleic anhydride utilizing the Pummerer−Diels−Alder conditions afforded the fused carbazoles **47** and **48** in excellent yield. When the reaction was carried out in the absence of a dienophile, it was possible to isolate furo-

(38) For a review on the use of $Sc(OTf)_3$ as catalyst in Diels−Alder reactions, see: Kobayashi, S. *Synlett* **1994**, 689.

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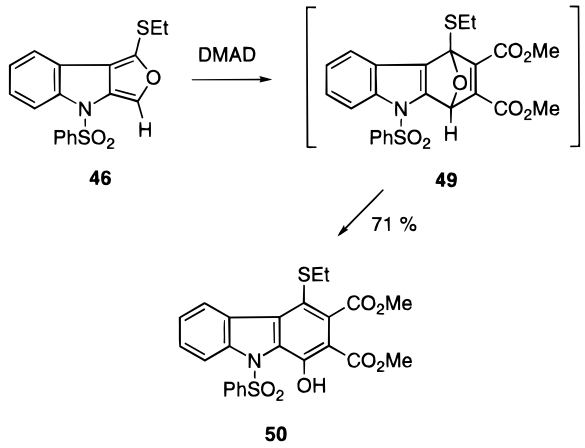
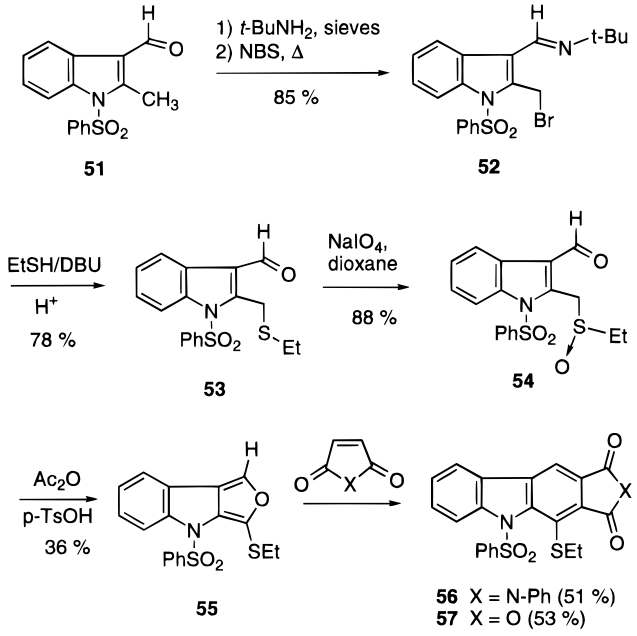
[3,4-*b*]indole **46** in 78% yield. Although **46** is not as stable as thienofuran **31**, it could be obtained in a high state of purity by rapid workup and chromatographic purification of the reaction mixture. However, if kept at room temperature, significant decomposition of **46** occurred within days. As expected, a pure sample of furoindole **46** readily reacts with *N*-phenylmaleimide in the presence of *p*-TsOH to give pyrrolocarbazole **47**.

Addition of dimethyl acetylenedicarboxylate (DMAD) to furoindole **46** afforded carbazole diester **50** in 67% yield. Here, the *in situ* ring-opening of the oxobridge in



intermediate **49** occurs even in the absence of an acidic catalyst. Presumably, the ring-opening reaction is assisted by the lone pair of electrons on the neighboring sulfur atom. This assumption is supported by the fact that some related oxo-bridged cycloadducts, where the ethylthio group is replaced by a phenyl group, are quite stable.[24]

In an extension of these studies, we have also investigated the reaction of the regioisomeric indolosulfoxide **54**. The synthesis of **54** exactly parallels the preparation



of **45** as described above. In this case, the overall yield of sulfoxide **54** starting from indole **51**[41] was 58%. Interestingly, with this regioisomer, the yields of cycloadducts **56** and **57** were significantly lower (*ca.* 50%) as compared to cycloadducts **47** and **48**. Evidently, the formation of furoindole **55** (36% yield from **54**) is not as efficient as in the case of the isomeric furoindole **46**, although the reasons for this are not fully understood at the moment.

In conclusion, we have demonstrated that the tandem Pummerer−Diels−Alder reaction sequence can be used to efficiently synthesize a variety of polyheterocyclic ring systems. The key intermediates in these cascade processes are α-thioisobenzofurans, which in some cases can be isolated and independently reacted with an appropriate dienophile to give 4+2-cycloadducts. We found it to be most convenient to carry out these reactions in an all-tandem fashion. Our results clearly indicate that the tandem-cascade process is a powerful method for the construction of complex heteroaromatic *o*-quinodimethanes. This area of research is currently being pursued in more detail in our laboratories.

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 nitrogen. 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.

1-(2-((Ethylthio)methyl)phenyl)hex-5-en-1-one (14). To a stirred solution containing 2.39 g (10 mmol) of amide **13**[33] in 30 mL of dry THF was added dropwise *via* transfer syringe a solution of pent-4-en-1-ylmagnesium bromide [prepared from 4.47 g (30 mmol) of 5-bromo-1-pentene and 0.77 g (32 mmol) of Mg in 30 mL of dry THF] at 0 °C under argon. After stirring at rt for 4 h, the mixture was poured into 5% HCl/ice−water and extracted with ether. The combined organic layer was washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The resulting oil was purified by flash silica gel chromatography to give 1.83 g (74%) of sulfide **14** as a colorless oil: IR (neat) 2925, 1687, 1438, 1232, 990, and 755 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.19 (t, 3H, J = 7.5 Hz), 1.84 (quint, 2H, J = 7.2 Hz), 2.15 (q, 2H, J = 7.2 Hz), 2.42 (q, 2H, J = 7.5 Hz), 2.92 (t, 2H, J = 7.2 Hz), 3.98 (s, 2H), 5.01 (m, 2H), 5.79 (m, 1H), 7.26−7.39 (m, 3H), and 7.56 (d, 1H, J = 7.2 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.4, 23.0, 25.8, 33.0, 33.5, 40.9, 115.1, 126.7, 128.2, 130.5, 130.9, 138.0, 138.3, 138.6, and 204.7; MS *m/e* 248 (M^+), 219, 186, 151, 145, 131, 119 (base), and 91; HRMS (EI) calcd for $C_{15}H_{20}OS$ 248.1235, found 248.1240.

1-(2-((Ethylthio)methyl)phenyl)hept-6-en-1-one (15) was prepared by a similar method starting from 2.39 g (10 mmol) amide **13**[33] and 6-bromo-1-hexene in 68% yield: IR (neat) 2926, 1685, 1439, 1221, and 904 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.20 (t, 3H, J = 7.5 Hz), 1.50 (m, 2H), 1.74 (m, 2H), 2.10 (q, 2H, J = 7.2 Hz), 2.43 (q, 2H, J = 7.5 Hz), 2.92 (t, 2H, J = 7.5 Hz), 3.98 (s, 2H), 4.98 (m, 2H), 5.81 (m, 1H), 7.27−7.39 (m, 3H), and 7.57 (d, 1H, J = 7.4 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.5, 23.6, 25.9, 28.4, 33.5, 33.6, 41.6, 114.5, 126.8, 128.2, 130.5, 131.0, 138.4, 138.5, 138.7, and 204.9; MS *m/e* 262 (M^+), 233, 179, 151, 131, 119 (base), and 91; HRMS (EI) calcd for $C_{16}H_{22}OS$ 262.1391, found 262.1383.

1-(2-((Ethylsulfinyl)methyl)phenyl)hex-5-en-1-one (16). To a solution containing 2.08 g (8.4 mmol) of sulfide **14** in 50 mL of methanol was added 1.93 g (9 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 stirring for 5 h at rt, water and CH_2Cl_2 were added to the reaction mixture. The aqueous layer was extracted with CH_2Cl_2, and the combined organic layer was washed with water, dried, and concentrated under reduced pressure. The crude sulfoxide was purified by flash silica gel chromatography to give 2.02 g (91%) of sulfoxide

(41) Rubiralta, M.; Diez, A.; Vila, C.; Troin, Y.; Miguel, D. *Heterocycles* **1991**, *32*, 1341.

16 as a pale yellow oil: IR (neat) 2932, 1680, 1445, 1225, 1040, 1018, and 762 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.26 (t, 3H, J = 7.5 Hz), 1.71 (quint, 2H, J = 7.2 Hz), 2.03 (q, 2H, J = 7.2 Hz), 2.57−2.77 (m, 2H), 2.87 (m, 2H), 3.84 (d, 1H, J = 12.3 Hz), 4.52 (d, 1H, J = 12.3 Hz), 4.91 (m, 2H), 5.71 (m, 1H), 7.29−7.41 (m, 3H), and 7.72 (d, 1H, J = 6.9 Hz); ^{13}C-NMR ($CDCl_3$) δ 6.4, 22.8, 32.6, 39.7, 45.1, 56.4, 114.9, 127.9, 129.1, 130.8, 131.5, 132.8, 136.8, 137.5, and 203.2.

1-(2-((Ethylsulfinyl)methyl)phenyl)hept-6-en-1-one (17). A 2.20 g (8.4 mmol) sample of sulfide **15** was oxidized in a manner similar to that described above using sulfide **14** and sodium periodate/methanol to give **17** (88%) as a pale yellow oil: IR (neat) 2931, 1680, 1443, 1221, 1041, 1017, and 904 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.36 (t, 3H, J = 7.5 Hz), 1.44 (m, 2H), 2.07 (m, 2H), 2.76 (m, 2H), 2.97 (t, 2H, J = 7.5 Hz), 3.88 (d, 1H, J = 12.0 Hz), 4.64 (d, 1H, J = 12.0 Hz), 4.98 (m, 2H), 5.76 (m, 1H), 7.37−7.51 (m, 3H), and 7.82 (d, 1H, J = 7.4 Hz); ^{13}C-NMR ($CDCl_3$) δ 6.4, 23.4, 28.0, 33.2, 40.4, 45.1, 56.6, 114.3, 127.9, 129.2, 131.0, 131.6, 132.8, 136.8, 138.0, and 203.3; HRMS (EI) calcd for $C_{16}H_{22}O_2S$ 278.1341, found 278.1331.

General Procedure for the Tandem Pummerer−Diels−Alder Reaction Sequence. A mixture of dry toluene (10 mL), acetic anhydride (0.5 mL), and the appropriate dienophile (1 mmol) containing a catalytic amount of *p*-toluenesulfonic acid (*ca*. 1 mg) was heated at reflux under argon. To this mixture was added dropwise a solution of the appropriate sulfoxide (0.5 mmol) in dry toluene (5 mL) *via* syringe over a 20 min period. For the intramolecular cycloadditions, the addition was carried out over a 1 h interval using 25 mL of solvent. After the addition was complete, the solution was heated at reflux for an additional 20 min until no more sulfoxide was detected by TLC. The mixture was evaporated to dryness and the crude residue was purified by flash silica gel chromatography or by recrystallization.

5-(Ethylthio)-2,3-dihydro-1*H*-cyclopenta[*a*]naphthalene (22) was obtained from 132 mg (0.5 mmol) sulfoxide **16** in 84% yield as a colorless oil: IR (neat) 2926, 1582, 1440, 1367, and 751 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.27 (t, 3H, J = 7.5 Hz), 2.20 (quint, 2H, J = 7.2 Hz), 2.93 (q, 2H, J = 7.5 Hz), 3.06 (t, 2H, J = 7.2 Hz), 3.20 (t, 2H, J = 7.2 Hz), 7.44 (m, 2H), 7.56 (s, 1H), 7.76 (m, 1H), and 8.44 (m, 1H); ^{13}C-NMR ($CDCl_3$) δ 14.5, 24.3, 29.0, 31.1, 33.7, 124.9, 125.0, 126.0, 126.8, 130.9, 131.4, 132.2, 139.1, and 140.7; MS *m*/*e* 228 (M^+, base), 199, 165, and 152; HRMS (EI) calcd for $C_{15}H_{16}S$ 228.0973, found 228.0983.

9-(Ethylthio)-1,2,3,4-tetrahydrophenanthrene (23) was obtained from 139 mg (0.5 mmol) of sulfoxide **17** in 81% yield as a colorless oil: IR (neat) 2925, 1584, 1445, 1370, and 751 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.39 (t, 3H, J = 7.5 Hz), 1.90−2.00 (m, 4H), 2.95 (t, 2H, J = 6 Hz), 3.02 (q, 2H, J = 7.5 Hz), 3.13 (t, 2H, J = 6 Hz), 7.43 (s, 1H), 7.59 (m, 2H), 8.02 (m, 1H), and 8.54 (m, 1H); ^{13}C-NMR ($CDCl_3$) δ 14.5, 22.8, 23.1, 25.5, 28.7, 30.3, 123.2, 125.0, 126.0, 125.9, 130.3, 131.1, 131.4, 131.8, 133.1, and 134.1; MS *m*/*e* 242 (M^+, base), 213, 181, and 165; HRMS (EI) calcd for $C_{16}H_{18}S$ 242.1129, found 242.1130.

2,3-Dihydro-1*H*-cyclopenta[*a*]naphthalene (24). A mixture of 228 mg (1 mmol) of **22**, 25 mL of ethanol, 5 mL of water, and 1 mL of Raney-Ni (50% slurry in water) was heated at reflux for 48 h. After the sulfide had been consumed, the mixture was filtered, and the catalyst was washed with warm ethanol. The clear solution was concentrated under reduced pressure and the residue was purified by flash silica gel chromatography to give the known[35] cyclopenta[a]naphthalene **24** (92%) as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 2.13 (quint, 2H, J = 7.4 Hz), 3.02 (t, 2H, J = 7.4 Hz), 3.15 (t, 2H, J = 7.4 Hz), 7.30−7.43 (m, 3H), 7.60 (d, 1H, J = 8.3 Hz), 7.71 (d, 1H, J = 8.1 Hz), and 7.77 (d, 1H, J = 7.9 Hz); ^{13}C-NMR ($CDCl_3$) δ 24.5, 31.0, 33.7, 123.2, 124.2, 125.7, 126.6, 128.3, 130.4, 132.5, 139.3, and 140.8; MS *m*/*e* 168 (M^+, base), 167, 165, 152, and 115.

1,2,3,4-Tetrahydrophenanthrene (25) was prepared in an analogous fashion by treating 242 mg (1 mmol) of **23** with Raney-Ni to give the known tetrahydrophenanthrene **25** (92%) as a white solid: mp 32−34 °C (lit.[36] mp 34−35 °C); ^{1}H-NMR ($CDCl_3$) δ 1.85 (m, 2H), 1.94 (m, 2H), 2.88 (t, 2H, J = 6 Hz), 3.08 (t, 2H, J = 6 Hz), 7.17 (d, 1H, J = 8.4 Hz), 7.37−7.48 (m, 2H), 7.58 (d, 1H, J = 8.4 Hz), 7.76 (d, 1H, J = 8.4 Hz), and 7.93 (d, 1H, J = 8.4 Hz); ^{13}C-NMR ($CDCl_3$) δ 22.9, 23.2, 25.7, 30.4, 122.7, 124.6, 125.6, 125.7, 128.2, 128.3, 131.5, 132.0, 132.5, and 134.3; MS *m*/*e* 182 (M^+, base), 165, 154, and 141.

***N*-Methoxy-*N*-methyl-3-methylthiophene-2-carboxamide (27).** To a mixture containing 14.2 g (0.1 mol) of acid **26** and 200 mL of dry benzene was added 23.8 g (0.2 mol) of thionyl chloride. The mixture was stirred for 24 h at 50 °C. After the reaction was complete, the solvent and excess reagent were removed under reduced pressure and the crude acid chloride was dried under vacuum. The crude compound was dissolved in 400 mL of dry CH_2Cl_2, and 10.72 g (0.11 mol) of *N*,*O*-dimethylhydroxylamine hydrochloride was added. The mixture was stirred under argon at 0 °C while 18.2 g (0.23 mol) of pyridine was added dropwise *via* syringe. Stirring was continued for 2 h at rt, and then the mixture was washed with brine and extracted with ether. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to give 15.9 g (86%) of **27** as a colorless oil which was used without further purification in the next step: IR (neat) 1631, 1413, 1355, 1200, and 977 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 2.55 (s, 3H), 3.33 (s, 3H), 3.71 (s, 3H), 6.90 (d, 1H, J = 5.0 Hz), and 7.37 (d, 1H, J = 5.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 16.8, 33.1, 61.5, 124.8, 128.9, 130.7, 146.2, and 164.0; MS *m*/*e* 185 (M^+), 125 (base), 97, 69, 53, and 45; HRMS (EI) calcd for $C_8H_{11}NO_2S$ 185.0511, found 185.0512.

***N*-Methoxy-*N*-methyl-3-((ethylthio)methyl)thiophene-2-carboxamide (28).** A mixture containing 9.25 g (50 mmol) of amide **27**, 9.79 g (55 mmol) of *N*-bromosuccinimide, 200 mg of benzoyl peroxide, and 200 mL of carbon tetrachloride was heated at reflux under argon for 1 h. The mixture was cooled to rt and was filtered from the precipitated succinimide. Evaporation of the solvent under reduced pressure left the crude bromomethyl intermediate as a clear oil: ^{1}H-NMR ($CDCl_3$) δ 3.37 (s, 3H), 3.72 (s, 3H), 4.98 (s, 2H), 7.18 (d, 1H, J = 5.0 Hz), and 7.45 (d, 1H, J = 5.0 Hz). This material was used in the next step without further purification.

To a solution containing 3.10 g (50 mmol) of ethanethiol in 200 mL of dry benzene was added dropwise 7.60 g (50 mmol) of DBU. After stirring at 25 °C for 20 min, a solution of the above bromomethyl derivative in 70 mL of dry benzene was added dropwise within 30 min. After stirring for 2 h at rt, the precipitated hydrobromide salt was filtered, and the remaining solution was concentrated under reduced pressure to leave behind an oil which was purified by flash silica gel chromatography to give 8.70 g (71%) of **28** as a colorless oil: IR (neat) 1626, 1519, 1452, 1418, and 1360 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.23 (t, 3H, J = 7.5 Hz), 2.52 (q, 2H, J = 7.5 Hz), 3.34 (s, 3H), 3.70 (s, 3H), 4.18 (s, 2H), 7.14 (d, 1H, J = 5.0 Hz), and 7.41 (d, 1H, J = 5.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.3, 25.59, 29.4, 32.9, 61.3, 125.6, 129.0, 129.5, 146.7, and 163.1; MS *m*/*e* 245 (M^+), 214, 185, 157 (base), 153, 125, 96, 70, and 45; HRMS (EI) calcd for $C_{10}H_{15}NO_2S_2$ 245.0544, found 245.0539.

2-Benzoyl-3-((ethylthio)methyl)thiophene (29). To a solution containing 2.45 g (10 mmol) of amide **28** in 30 mL of dry THF was added dropwise *via* syringe a solution of phenylmagnesium Grignard (25 mmol, 25 mL of 1*M* THF solution) at 0 °C under argon. After stirring for 2 h at 0 °C, the mixture was poured into 5% HCl/ice and was extracted with ether. The combined organic layer was washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to give 2.20 g (84%) of sulfide **29** as a colorless oil: IR (neat) 1632, 1402, 1269, and 692 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.19 (t, 3H, J = 7.5 Hz), 2.47 (q, 2H, J = 7.5 Hz), 4.07 (s, 2H), 7.25 (d, 1H, J = 5.0 Hz), 7.42−7.55 (m, 4H), and 7.83 (dd, 2H, J = 7.8 and 1.2 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.4, 25.8, 29.3, 128.0, 129.0, 130.8, 131.1, 132.2, 135.1, 139.5, 146.7, and 189.0; MS *m*/*e* 262 (M^+), 233, 216, 202, 201 (base), 200, 199, 183, 171, 105, and 77; HRMS (EI) calcd for $C_{14}H_{14}OS_2$ 262.0486, found 262.0484.

2-Benzoyl-3-((ethylsulfinyl)methyl)thiophene (30). A 262 mg (1 mmol) sample of sulfide **29** was oxidized in a manner similar to that described with **14** using sodium periodate as the oxidant to give **30** (88%) as a white solid: mp 86−87 °C; IR (KBr) 1633, 1401, 1273, 1047, 1019, and 693 cm^{-1}; ^{1}H-NMR

($CDCl_3$) δ 1.36 (t, 3H, J = 7.5 Hz), 2.76 (m, 2H), 4.29 (d, 1H, J = 12.8 Hz), 4.63 (d, 1H, J = 12.8 Hz), 7.33 (d, 1H, J = 5.0 Hz), 7.49 (dd, 2H, J = 7.8 and 7.8Hz), 7.60 (dd, 1H, J = 7.8 and 7.8 Hz), 7.62 (d, 1H, J = 5.0 Hz), and 7.85 (dd, 2H, J = 7.8 and 1.2 Hz); ^{13}C-NMR ($CDCl_3$) δ 6.7, 45.2, 51.6, 128.2, 129.0, 131.6, 132.0, 132.5, 136.2, 138.3, 139.3, and 188.9. Anal. Calcd for $C_{14}H_{14}O_2S_2$: C, 60.40; H, 5.07. Found: C, 60.34; H, 5.07.

4-(Ethylthio)-6,8-diphenylthieno[2,3-*f*]isoindole-5,7-dione (35) was prepared from 139 mg (0.5 mmol) of sulfoxide **30** and 173 mg (1 mmol) of *N*-phenyl maleimide in 91% yield as a pale yellow solid: mp 144−145 °C; IR (KBr) 1755, 1710, 1500, 1373, 1118, 759, and 693 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.29 (t, 3H, J = 7.5 Hz), 3.25 (q, 2H, J = 7.5 Hz), 7.34−7.59 (m, 10H), 7.75 (d, 1H, J = 5.0 Hz), and 8.07 (d, 1H, J = 5.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 15.2, 30.9, 123.5, 126.0, 126.7, 127.8, 128.3, 128.5, 128.8, 129.0, 130.4, 131.7, 132.3, 134.6, 136.0, 146.3, 147.5, 165.8, and 165.9. Anal. Calcd for $C_{24}H_{17}NO_2S_2$: C, 69.37; H, 4.12; N, 3.37. Found: C, 69.25; H, 4.15; N, 3.36.

4-(Ethylthio)-8-phenylthieno[2,3-*f*]isobenzofuran-5,7-dione (36) was prepared from 139 mg (0.5 mmol) of sulfoxide **30** and 98 mg (1 mmol) of maleic anhydride in 89% yield as a pale yellow solid: mp 166−167 °C; IR (KBr) 1830, 1773, 1340, 1216, 1135, and 916 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.30 (t, 3H, J = 7.5 Hz), 3.26 (q, 2H, J = 7.5 Hz), 7.58 (s, 5H), 7.90 (d, 1H, J = 5.0 Hz), and 8.09 (d, 1H, J = 7.5 Hz); ^{13}C-NMR ($CDCl_3$) δ 15.2, 30.8, 122.5, 125.9, 127.7, 128.7, 129.0, 132.7, 133.5, 134.3, 137.6, 147.5, 148.4, 161.4, and 161.5. Anal. Calcd for $C_{18}H_{12}O_3S_2$: C, 63.51; H, 3.55. Found: C, 63.58; H, 3.64.

General Procedure for the Preparation of Heterocyclic Isobenzofurans 31, 46, and 55. A mixture containing dry toluene (10 mL), acetic anhydride (0.5 mL), and a catalytic amount of *p*-toluenesulfonic acid (*ca*. 1 mg) was heated at reflux under argon. A solution of the appropriate sulfoxide (0.5 mmol) in dry toluene (5 mL) was added dropwise *via* syringe over a 20 min interval. After the addition was complete, the solution was heated at reflux for an additional 10−15 min. The mixture was concentrated *in vacuo* to *ca*. 20% of its original volume. The resulting toluene solution was placed on a flash silica gel column and eluted first with hexane, followed by a 6:1 hexane/ethyl acetate mixture. Using this method the following compounds were prepared.

4-(Ethylthio)-6-phenylthieno[2,3-*c*]furan (31) was obtained from 139 mg (0.5 mmol) of sulfoxide **30** as a colorless oil in 79% yield: IR (neat) 1597, 1481, 1447, 1253, 977, and 760 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.30 (t, 3H, J = 7.5 Hz), 2.84 (q, 2H, J = 7.5 Hz), 6.85 (d, 1H, J = 5.0 Hz), 7.11 (d, 1H, J = 5.0 Hz), 7.24 (dd, 1H, J = 7.6 and 7.6 Hz), 7.43 (dd, 2H, J = 7.6 and 7.6 Hz), and 7.63 (dd, 2H, J = 7.6 and 1.2 Hz); ^{13}C-NMR ($CDCl_3$) δ 15.5, 31.3, 115.2, 122.6, 123.6, 126.9, 128.8, 129.8, 132.7, 133.3, 142.2, and 145.1; MS *m*/*e* 260 (M$^+$), 231 (base), 203, 199, and 77; HRMS (EI) calcd for $C_{14}H_{12}OS_2$ 260.0330, found 260.0326.

Methyl 4-(ethylthio)-7-phenylbenzo[*b*]thiophene-6-carboxylate (37). A mixture containing 66 mg (0.25 mmol) of **31**, 215 mg (2.5 mmol) of methyl acrylate, 12 mg (0.025 mmol) of $Sc(OTf)_3$, and 10 mL of dry THF was stirred under argon at 25 °C for 2 days. Evaporation of the solvent under reduced pressure followed by silica gel chromatography gave 64 mg (78%) of cycloadduct **37** as a pale yellow oil: IR (neat) 1718, 1432, 1248, and 1127 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.39 (t, 3H, J = 7.5 Hz), 3.10 (q, 2H, J = 7.5 Hz), 3.63 (s, 3H), 7.39−7.48 (m, 5H), 7.62 (m, 2H), and 7.90 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 14.4, 27.9, 52.0, 123.1, 125.8, 126.2, 128.0, 128.3, 128.4, 130.8, 136.2, 139.6, 141.6, 142.4, and 168.0; MS *m*/*e* 328 (M$^+$, base), 299, 267, 240, 208, 196, 162, and 112; HRMS (EI) calcd for $C_{18}H_{16}O_2S_2$ 328.0592, found 328.0583.

Generation and Cycloaddition of the Normal Pummerer Product Derived from Thiophene Sulfoxide 30. A solution of 100 mg (0.36 mmol) of sulfoxide **30** in 10 mL of acetic anhydride was heated at reflux under argon for 1 h. The mixture was evaporated to dryness and the resulting oil was dissolved in CH_2Cl_2. The solution was washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and concentrated under reduced pressure. The remaining oil was immediately purified by flash silica gel chromatography to give 22 mg (23%) of thienofuran **31** (fraction 1) and 73 mg (64%) of acetic acid [[2-(2-benzoylthiophene-3-yl)ethyl]thio]methyl ester (cf. **9**) (fraction 2) as a yellow oil. The latter was 90% pure: IR (neat) 1743, 1640, 1518, 1410, and 1260 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.28 (t, 3H, J = 7.5 Hz), 2.08 (s, 3H), 2.68−2.86 (m, 2H), 7.36 (d, 1H, J = 5.1 Hz), 7.43−7.59 (m, 4H), 7.61 (s, 1H), and 7.85 (d, 2H, J = 8.1 Hz). Prolonged standing at room temperature led to decomposition, and consequently, the product was used without further purification in the next step.

A mixture of 5 mL of dry toluene and 76 mg (0.44 mmol) of *N*-phenylmaleimide containing a catalytic amount of *p*-toluenesulfonic acid was heated at reflux under argon. A solution containing 73 mg (0.22 mmol) of the above acetoxy sulfide in 2 mL of dry toluene was added dropwise *via* syringe within 20 min. After the addition was complete, the solution was heated at reflux for an additional 5 min. The mixture was evaporated to dryness and the resulting oil was purified by flash silica gel chromatography to give 54 mg (60%) of pure **35**, identical in all respects with the material obtained in the tandem reaction described above.

1-(3-((Ethylthio)methyl)thiophene-2-yl)hex-5-en-1-one (38). To a solution containing 2.45 g (10 mmol) of amide **28** in 30 mL of dry THF was added dropwise *via* syringe a solution of pent-4-en-1-ylmagnesium bromide [prepared from 4.47 g (30 mmol) of 5-bromo-1-pentene and 0.77 g (32 mmol) of Mg in 30 mL of dry THF] at 0 °C under argon. After stirring for 2 h at 0 °C, the mixture was poured into 5% HCl/ice water and was extracted with ether. The combined organic layer was washed with water, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography to give 2.06 g (81%) of sulfide **38** as a colorless oil: IR (neat) 2924, 1665, 1519, 1408, 1234, and 909 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.23 (t, 3H, J = 7.5 Hz), 1.86 (m, 2H), 2.14 (m, 2H), 2.50 (q, 2H, J = 7.5 Hz), 2.87 (t, 2H, J = 7.4 Hz), 4.18 (s, 2H), 5.04 (m, 2H), 5.81 (m, 1H), 7.19 (d, 1H, J = 5.0 Hz), and 7.41 (d, 1H, J = 5.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.6, 23.5, 25.9, 29.4, 33.0, 41.2, 115.2, 129.2, 131.7, 135.7, 137.9, 146.2, and 193.6; MS *m*/*e* 254 (M$^+$), 194, 165, 157, 151, 140, 125 (base), 97, and 41; HRMS (EI) calcd for $C_{13}H_{18}OS_2$ 254.0799, found 254.0802.

1-(3-((Ethylsulfinyl)methyl)thiophene-2-yl)hex-5-en-1-one (39). A 254 mg (1 mmol) sample of sulfide **38** was oxidized in a manner similar to that described for sulfide **14** using sodium periodate/methanol to give **39** (79%) as a pale yellow oil: IR (neat) 2933, 1660, 1514, 1410, and 1051 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.35 (t, 3H, J = 7.5 Hz), 1.83 (m, 2H), 2.14 (m, 2H), 2.71 (m, 2H), 2.89 (t, 2H, J = 7.2 Hz), 4.30 (d, 1H, J = 12.3 Hz), 4.65 (d, 1H, J = 12.3 Hz), 5.02 (m, 2H), 5.81 (m, 1H), 7.22 (d, 1H, J = 5.0 Hz), and 7.52 (d, 1H, J = 5.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 6.5, 23.2, 32.7, 40.8, 45.0, 51.4, 45.2, 129.6, 132.3, 136.5, 137.0, 137.3, and 193.5; HRMS (FAB) calcd for $C_{13}H_{18}LiO_2S_2$ 277.0908, found 277.0909 (M + Li)$^+$.

4-(Ethylthio)-7,8-dihydro-6*H*-indeno[4,5-*b*]thiophene (41) was obtained from 135 mg (0.5 mmol) of sulfoxide **39** as a colorless solid in 85% yield: mp 35−36 °C; IR (KBr) 1582, 1439, 1365, and 847 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.28 (t, 3H J = 7.5 Hz), 2.20 (m, 2H), 2.94 (q, 2H, J = 7.5 Hz), 3.04 (m, 4H), 7.31 (s, 1H), 7.37 (d, 1H, J = 5.0 Hz), and 7.60 (d, 1H, J = 5.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.7, 25.0, 29.0, 32.2, 33.2, 123.7, 125.1, 128.3, 136.1, 139.4, and 140.7; MS *m*/*e* 234 (M$^+$, base), 205, and 171. Anal. Calcd for $C_{13}H_{14}S_2$: C, 66.62; H, 6.02. Found: C, 66.60, H, 6.03.

3-((Ethylthio)methyl)-1-(phenylsulfonyl)-1*H*-indole-2-carbaldehyde (44). To a solution containing 8.97 g (30 mmol) of aldehyde **42**[40] and 7.30 g (100 mmol) of distilled *tert*-butylamine in 100 mL of dry CH_2Cl_2 was added 6 g of molecular sieves (4 Å, activated). The mixture was heated at reflux for 4 h, and then additional sieves were added to the reaction mixture. After heating for an additional 12 h, the resulting mixture was filtered, and the solvent was removed under reduced pressure to give 10.3 g (97%) of the corresponding imine: mp 142−143 °C; IR (KBr) 2960, 1632, 1445, 1362, 1218, and 1174 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.39 (s, 9H), 2.36 (s, 3H), 7.20−7.43 (m, 6H), 7.64 (m, 2H), 8.14 (m, 1H), and 8.74 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 9.9, 29.6, 58.5, 115.0, 119.9, 123.1, 123.9, 125.9, 126.5, 128.9, 131.9, 132.7, 133.5, 136.3, 137.5,

and 149.6. This compound was used directly in the next step without further purification.

A mixture of 3.54 g (10 mmol) of the above imine, 1.96 g (11 mmol) of *N*-bromosuccinimide, 100 mg of benzoyl peroxide, and 120 mL of carbon tetrachloride was heated at 65−70 °C (bath temperature) with irradiation (150 W lamp) under argon. The reaction was stopped immediately after all the NBS had been consumed and succinimide was floating on the surface (*ca.* 30 min) by rapid immersion of the reaction flask in an ice bath. After filtration, the solvent was removed under reduced pressure and the residue was crystallized to give 3.8 g (88%) of the bromomethyl imine **43**: mp 109−110 °C; IR (KBr) 2966, 1627, 1445, 1373, and 1174 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.40 (s, 9H), 4.94 (s, 2H), 7.31−7.68 (m, 8H), 8.16 (m, 1H), and 8.77 (s, 1H). This compound was used immediately in the next step without further purification.

To a solution containing 310 mg (5 mmol) of ethanethiol in 50 mL of dry benzene was added dropwise 760 mg (5 mmol) of DBU. After stirring at rt for 20 min, a filtered solution containing 2.16 g (5 mmol) of imine **43** in 25 mL of dry benzene was added dropwise. The mixture was stirred for 2 h at rt and the precipitated hydrobromide salt was filtered and the remaining solution was concentrated under reduced pressure. The crude imine was dissolved in 20 mL of acetone and hydrolyzed by the addition of 20 mL of 2 N HCl. After stirring at rt for 30 min, the acetone was removed under reduced pressure, and the resulting solid was filtered to give 1.33 g (74%) of aldehyde **44** as a colorless solid: mp 113−114 °C; IR (KBr) 1677, 1547, 1365, and 1178 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.13 (t, 3H, J = 7.5 Hz), 2.29 (q, 2H, J = 7.5 Hz), 4.13 (s, 2H), 7.34−7.73 (m, 8H), 8.24 (m, 1H), and 10.60 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 14.4, 24.4, 25.5, 115.9, 122.2, 124.9, 126.6, 129.1, 132.5, 132.9, 134.2, 136.7, 137.7, 140.4, and 184.8. Anal. Calcd for $C_{18}H_{17}NO_3S_2$ C, 60.15; H, 4.77; N, 3.90. Found: C, 60.21; H, 4.80; N, 3.87.

3-((Ethylsulfinyl)methyl)-1-(phenylsulfonyl)-1*H*-indole-2-carbaldehyde (45). To a solution containing 718 mg (2 mmol) of sulfide **44** in 15 mL of dioxane was added a solution of 470 mg (2.2 mmol) of sodium periodate in 5 mL of water. After the mixture was stirred for 24 h at rt, water and CH_2Cl_2 were added. The aqueous phase was extracted with CH_2Cl_2 and the combined organic layer was washed with water and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure and the crude sulfoxide was purified by flash silica gel chromatography to give 700 mg (92%) of pure **45** as a white solid: mp 119−120 °C; IR (KBr) 1672, 1544, 1373, and 1179 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.28 (t, 3H, J = 7.5 Hz), 2.57 (m, 2H), 4.31 (d, 1H, J = 12.9 Hz), 4.54 (d, 1H, J = 12.9 Hz), 7.36−7.77 (m, 8H), 8.22 (m, 1H), and 10.64 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 6.8, 45.2, 48.0, 115.3, 122.7, 124.6, 125.3, 126.4, 129.2, 129.4, 129.7, 133.5, 134.4, 136.7, 137.1, and 184.7. Anal. Calcd for $C_{18}H_{17}NO_4S_2$: C, 57.58; H, 4.56; N, 3.73. Found: C, 57.51; H, 4.58; N, 3.78.

10-(Ethylthio)-2-phenyl-5-(phenylsulfonyl)-5*H*-pyrrolo-[3,4-*b*]carbazole-1,3-dione (47) was obtained from 188 mg (0.5 mmol) of sulfoxide **45** and 173 mg (1 mmol) of *N*-phenylmaleimide as a colorless solid in 90% yield: mp 249−250 °C; IR (KBr) 1760, 1708, 1370, and 1350 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.25 (t, 3H J = 7.5 Hz), 3.21 (q, 2H, J = 7.5 Hz), 7.39−7.69 (m, 10H), 7.91 (d, 2H, J = 7.8 Hz), 8.46 (d, 1H, J = 8.4 Hz), 8.92 (s, 1H), and 9.27 (d, 1H, J = 8.1 Hz); ^{13}C-NMR ($CDCl_3$) δ 15.0, 31.3, 110.0, 114.6, 124.4, 125.4, 125.7, 126.5, 126.6, 127.2, 128.0, 129.0, 129.3, 129.5, 131.6, 131.7, 131.9, 132.8, 134.5, 137.4, 139.6, 141.1, 165.9, and 166.2. Anal. Cacld for $C_{28}H_{20}N_2O_4S_2$: C, 65.61; H, 3.93; N, 5.47. Found: C, 65.67; H, 3.96; N, 5.46.

10-(Ethylthio)-5-(phenylsulfonyl)-5*H*-furo[3,4-*b*]carbazole-1,3-dione (48) was obtained from 188 mg (0.5 mmol) of sulfoxide **45** and 98 mg (1 mmol) of maleic anhydride as a colorless solid in 89% yield: mp 209−210 °C; IR (KBr) 1839, 1805, 1771, and 1272 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.25 (t, 3H, J = 7.5 Hz), 3.22 (q, 2H, J = 7.5 Hz), 7.44−7.73 (m, 6H), 7.91 (d, 2H, J = 7.5 Hz), 8.46 (d, 1H, J = 8.4 Hz), 8.92 (s, 1H), and 9.17 (d, 1H, J = 8.1 Hz); ^{13}C-NMR ($CDCl_3$) δ 15.1, 31.2, 111.0, 114.6, 124.8, 124.9, 125.6, 126.5, 126.6, 129.6, 130.2, 130.4, 134.1, 134.2, 134.9, 137.2, 140.0, 141.9, 161.1, and 162.5. Anal. Calcd for $C_{22}H_{15}NO_5S_2$: C, 60.40; H, 3.46; N, 3.20. Found: C, 60.33; H, 3.52; N, 3.23.

1-(Ethylthio)-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole (46) was obtained from 188 mg (0.5 mmol) of sulfoxide **45** as a clear oil in 78% yield: IR (neat) 1448, 1368, 1134, and 956 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.22 (t, 3H, J = 7.5 Hz), 2.84 (q, 2H, J = 7.5 Hz), 7.22−7.51 (m, 5H), 7.75 (d, 1H, J = 7.5 Hz), 7.82 (m, 3H), and 7.96 (d, 1H, J = 8.4 Hz); ^{13}C-NMR ($CDCl_3$) δ 15.3, 30.4, 114.8, 121.8, 122.2, 124.4, 125.6, 126.7, 126.9, 127.7, 128.9, 133.6, 133.9, 134.4, 136.5, 144.0; MS m/e 357 (M^+), 328, 216, 188, 141, and 77; HRMS (EI) calcd for $C_{18}H_{15}NO_3S_2$ 357.0493, found 357.0492.

Dimethyl 4-(ethylthio)-1-hydroxy-9-(phenylsulfonyl)-carbazole-2,3-dicarboxylate (50). A solution containing 60 mg (0.17 mmol) of furoindole **46** and 57 mg (0.48 mmol) of dimethyl acetylenedicarboxylate in 10 mL of dry benzene was heated at reflux under argon for 2 h. The benzene solution was passed through a plug of silica gel and was concentrated under reduced pressure. The crude material was purified by silica gel chromatography to give 67 mg (67%) of **50** as a pale yellow solid: mp 161−162 °C; IR (KBr) 1733, 1668, 1437, 1362, and 1330 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.14 (t, 3H, J = 7.5 Hz), 2.78 (q, 2H, J = 7.5 Hz), 3.93 (s, 3H), 3.95 (s, 3H), 7.43−7.63 (m, 5H), 7.92 (dd, 2H, J = 8.4 and 1.2 Hz), 8.42 (d, 1H, J = 8.4 Hz), 9.03 (d, 1H, J = 8.4 Hz), and 11.97 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 14.2, 31.1, 52.4, 53.2, 108.0, 116.5, 117.0, 124.3, 124.4, 126.0, 127.0, 128.2, 128.7, 129.3, 133.4, 135.2, 139.6, 139.7, 142.4, 152.0, 168.0, and 169.4. Anal. Calcd for $C_{24}H_{21}NO_7S_2$: C, 57.70; H, 4.24; N, 2.80. Found: C, 57.55; H 4.30; N, 2.84.

2-((Ethylthio)methyl)-1-(phenylsulfonyl)-1*H*-indole-3-carbaldehyde (53). A sample of aldehyde **51**[41] (8.97 g, 30 mmol) was allowed to react with excess *tert*-butylamine in the same manner as described above for aldehyde **42** to give 10.2 g (96%) of the corresponding *tert*-butylimine as a colorless solid, mp 117−118 °C (lit.[41] mp 113−114 °C). The imine was used without further purification in the next step.

A mixture containing 3.54 g (10 mmol) of the above imine, 1.96 g (11 mmol) of *N*-bromosuccinimide, 100 mg of benzoyl peroxide, and 120 mL of carbon tetrachloride was heated at reflux under argon for 1.5 h. After cooling to rt, the mixture was filtered and the solvent was removed under reduced pressure. Crystallization of the residue gave 3.84 g (89%) of *N*-*tert*-butyl-2-bromomethyl-1-(phenylsulfonyl)-1*H*-indole-3-methanimine (**52**) as a colorless solid: mp 134−135 °C; IR (KBr) 2970, 1643, 1450, 1364, and 1164 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.34 (s, 9H), 5.37 (s, 2H), 7.32−7.58 (m, 5H), 7.96 (m, 2H), 8.13 (m, 1H), 8.34 (m, 1H), and 8.62 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 22.0, 29.6, 58.4, 114.4, 120.5, 122.5, 124.5, 126.2, 127.0, 127.5, 129.2, 134.1, 136.6, 136.9, 138.5, and 147.2. Anal. Calcd for $C_{20}H_{21}BrN_2O_2S$: C, 55.43; H, 4.88; N, 6.46. Found: C, 55.35; H, 4.85; N, 6.43.

Bromomethyl imine **52** was converted into aldehyde **53** following the procedure previously described for **43**, affording 1.40 g (78%) of **53**: mp 91−92 °C; IR (KBr) 1654, 1546, 1379, and 1191 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.24 (t, 3H, J = 7.5 Hz), 2.61 (q, 2H, J = 7.5 Hz), 4.59 (s, 2H), 7.32−7.59 (m, 6H), 8.03 (m, 2H), 8.25 (m, 1H), and 10.31 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 14.2, 25.3, 26.5, 114.3, 119.4, 121.3, 125.1, 125.8, 125.9, 127.1, 129.3, 134.4, 135.7, 138.2, 147.5, and 185.1; MS m/e 359 (M^+), 218, 204, 190, 158, 156, 128, 117, 102, and 77. Anal. Calcd for $C_{18}H_{17}NO_3S_2$: C, 60.15; H, 4.77; N, 3.90. Found: C, 59.89; H, 4.83; N, 3.76.

2-((Ethylsulfinyl)methyl)-1-(phenylsulfonyl)-1*H*-indole-3-carbaldehyde (54). A 718 mg (2 mmol) sample of sulfide **53** was oxidized in a manner similar to that outlined for sulfide **44** using sodium periodate/dioxane to give **54** in 92% yield, mp 119−120 °C; IR (KBr) 1670, 1444, 1385, and 1186 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.41 (t, 3H, J = 7.5 Hz), 2.88 (m, 2H), 4.80 (d, 1H, J = 13.8 Hz), 4.96 (d, 1H, J = 13.8 Hz), 7.35−7.64 (m, 5H), 7.85 (m, 2H), 8.07 (m, 1H), 8.32 (m, 1H), and 10.19 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 6.8, 46.1, 48.3, 114.1, 121.7, 123.5, 125.3, 126.0, 126.3, 126.4, 129.5, 134.7, 135.8, 137.5, 138.2, and 185.7. Anal. Calcd for $C_{18}H_{17}NO_4S_2$: C, 57.58; H, 4.56; N, 3.74. Found: C, 57.68; H, 4.57; N, 3.68.

4-(Ethylthio)-2-phenyl-5-(phenylsulfonyl)-5*H*-pyrrolo-[3,4-*b*]carbazole-1,3-dione (56) was prepared from 188 mg (0.5 mmol) of sulfoxide **54** and 173 mg (1 mmol) of *N*-phenylmaleimide as a colorless solid in 51% yield: mp 251−252 °C; IR (KBr) 1767, 1708, 1363, and 1174 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.00 (t, 3H, J = 7.5 Hz), 2.99 (q, 2H, J = 7.5 Hz), 7.25−7.56 (m, 12H), 7.85 (d, 1H, J = 7.8 Hz), 8.16 (d, 1H, J = 8.4 Hz), and 8.26 (s, 1H); ^{13}C-NMR ($CDCl_3$) δ 14.2, 31.7, 113.6, 118.8, 121.0, 125.8, 126.2, 126.6, 126.9, 128.0, 128.4, 128.8, 129.0, 129.3, 130.7, 131.0, 131.6, 133.5, 134.7, 137.0, 142.7, 146.3, 165.6, and 166.2. Anal. Calcd for $C_{28}H_{20}N_2O_4S_2$: C, 65.61; H, 3.93; N, 5.47. Found: C, 65.34; H, 3.97; N, 5.42.

4-(Ethylthio)-5-(phenylsulfonyl)-5*H*-furo[3,4-*b*]carbazole-1,3-dione (57) was prepared from 188 mg (0.5 mmol) of sulfoxide **54** and 98 mg (1 mmol) of maleic anhydride as a colorless solid in 53% yield: mp 224−225 °C; IR (KBr) 1838, 1775, 1607, 1444, 1363, 1263, and 1173 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.98 (t, 3H, J = 7.5 Hz), 2.96 (q, 2H, J = 7.5 Hz), 7.28−7.63 (m, 7H), 8.16 (d, 1H, J = 7.5 Hz), 8.16 (d, J = 8.4 Hz), and 8.27 (s, 1H). Anal. Calcd for $C_{22}H_{15}NO_5S_2$: C, 60.44; H, 3.46; N, 3.20. Found: C, 60.24; H, 3.49; N, 3.16.

3-(Ethylthio)-4-(phenylsulfonyl)-4*H*-furo[3,4-*b*]indole (55) was prepared from 188 mg (0.5 mmol) of sulfoxide **54** as a colorless oil in 36% yield: IR (neat) 1449, 1373, 1260, and 1091 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 1.31 (t, 3H, J = 7.5 Hz), 2.99 (q, 2H, J = 7.5 Hz), 7.24−7.54 (m, 6H), 7.68 (s, 1H), 7.87 (d, 2H, J = 8.1 Hz), and 8.16 (d, 1H, J = 8.5 Hz); ^{13}C-NMR ($CDCl_3$) δ 15.3, 30.3, 116.3, 121.4, 122.0, 124.0, 124.6, 127.4, 127.5, 127.6, 128.9, 132.9, 133.7, 134.2, 137.1, and 145.7; HRMS (EI) calcd for $C_{18}H_{15}NO_3S_2$ 357.0493, found 357.0504.

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Supporting Information Available: ^{1}H-NMR and ^{13}C-NMR spectra for new compounds lacking analyses (15 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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