Arylsulfenium Ion Promoted Cascade Cyclizations of Deactivated Aryldienes. An Investigation into Reagent-Based Acceleration of Cationic Annulation

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The efficiency of sulfenylative cyclization has been shown to be strongly influenced by both substrate substitution pattern and the structure of the external sulfenium ion source. Of the various reagents examined, 2-methoxyethyl 4-chlorobenzenesulfenate (**9b**) has been found a particularly effective initiator for the regioselective cyclization of a range of aryldienes at low temperature.

Introduction

Biomimetic polyene cyclizations have played a crucial role in the stereodefined synthesis of a wide variety of multiply fused polycyclic substances.[2] The vast majority of these transformations involve substrates possessing functionally differentiated sites of incipient cation formation which are often time consuming to synthesize.[3] Over the last few years, investigations in several laboratories have revealed procedures by which simple alkenes can be used directly as initiating moieties for cationic cyclizations via chemical activation by external reagents.[4] Our own efforts in this area have led to the discovery that $PhSOCH_3$, when used in combination with $BF_3{\cdot}CH_3NO_2$ or Me_3SiOTf, is capable of promoting the sulfenylative cyclization of simple 4-aryl-1-butenes[5a] as well as selected 9-aryl-2,6-nonadienes.[5b,c] In several instances involving the latter class of substrates, only modest yields of tricyclic products arising from the intended cyclization cascade were obtained when the prototypical reagent $PhSOCH_3$ was used as the sulfenium ion source. In this account, we document the development and application of an unusually effective arylsulfenium ion equivalent that is able to promote efficient cascade cyclizations of problematic substrates, as well as those which proved comparatively inert to the reaction conditions described previously.[5]

The issue of site selectivity of initial cation generation is of paramount importance to the successful implementation of cascade cyclizations involving substrates bearing simple alkene moieties. We have previously shown that certain aryldienes possessing (*E*)-internal alkenes (e.g., **1a**) are well behaved in this context and provide fully cyclized products in good yield upon exposure to $PhSOCH_3/BF_3{\cdot}CH_3NO_2$.[5b] By way of contrast, substrates which lack a "deactivating" cyano function can suffer competitive sulfenylative cyclization proceeding by initial attack at the internal alkene to provide product mixtures contaminated with bicyclic materials (Scheme 1). Unfortunately, even substrates that possess a suitably disposed cyano moiety undergo cyclization with reduced efficiency when the internal alkene is of the (*Z*)-geometry.[5b]

Cyclization Studies

As mentioned above, we had previously demonstrated the beneficial directing effect that a homoallylic cyano substituent can exert on the site selectivity of cation generation.[5b] For synthetic as well as mechanistic reasons it was of interest to examine the behavior of the corresponding *allylic* cyanide **4**[6] under our standard set of conditions for sulfenylative cyclization.[5b] In this connection, it is significant that exposure of **4** to $PhSOCH_3$ (1.05 equiv) and BF_3 (2.10 equiv) in CH_3NO_2 at −30 °C for 1 h, followed by the addition of aqueous $NaHCO_3$ provided the diastereomeric β-phenylthio alcohols **6a** (48% isolated) to the exclusion of the expected cyclization products **7a**,**b** (Scheme 2). Similarly, addition of EtOH to the reaction mixture at −30 °C prior to quenching with $NaHCO_{3(aq)}$ furnished the β-phenylthio ethers **6b** in 69% isolated yield. The regiochemistry of nucleophilic attack leading to **6a** and **6b** is consistant with that expected for a Markovnikov type addition. These results are indicative of a pronounced directive effect of the cyano substituent on sulfenylative regioselection, in addition to a marked suppression of cyclization via engagement of the inductively deactivated internal alkene. In consonance with this hypothesis, conversion of the putative episulfonium ion **5**[7] to the expected diastereomeric tricycles **7a**,**b** could only be achieved at elevated temperatures over a prolonged period (45−50 °C for 2 h). Under these rather drastic conditions, **7a**,**b** could be obtained as a 1:1 mixture of 10-cyano epimers in 73% isolated yield after chromatography.

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(1) Recipient of a Japan Society for the Promotion of Science Fellowship, 1997.

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(3) Several noteworthy accounts involving highly stereoselective polyene cyclizations have recently appeared. (a) Corey, E. J.; Wood, H. B., Jr. *J. Am. Chem. Soc.* **1996**, *118*, 11982 and references therein. (b) Johnson, W. S.; Fletcher, V. R.; Chenera, B.; Bartlett, W. R.; Tham, F. S.; Kullnig, R. K. *J. Am. Chem. Soc.* **1993**, *115*, 497. (c) Johnson, W. S.; Plummer, M. S.; Reddy, S. P.; Bartlett, W. R. *J. Am. Chem. Soc.* **1993**, *115*, 515.

(4) (a) Harring, S. R.; Edstrom, E. D.; Livinghouse, T. *Adv. Heterocycl. Nat. Prod. Synth.* **1992**, *2*, 299−376. (b) McMurry, J. E.; Erion, M. D. *J. Am. Chem. Soc.* **1985**, *107*, 2712. (c) White, J. D.; Avery, M. A.; Carter, J. P. *J. Am. Chem. Soc.* **1982**, *104*, 3923. (d) Hoye, T. R.; Caruso, A. J.; Dellaria, J. F.; Kurth, M. *J. Am. Chem. Soc.* **1982**, *104*, 6704. (e) Nishizawa, M.; Yamada, H.; Hayashi, Y. *Tetrahedron Lett.* **1987**, *28*, 3255.

(5) (a) Edstrom, E. D.; Livinghouse, T. *J. Am. Chem. Soc.* **1986**, *108*, 1334. (b) Edstrom, E. D.; Livinghouse, T. *J. Org. Chem.* **1987**, *52*, 949. (c) Harring, S. R.; Livinghouse, T. *Tetrahedron Lett.* **1989**, *27*, 1499.

(6) Harring, S. R.; Livinghouse, T. *Tetrahedron* **1994**, *50*, 9229.

(7) (a) The true nature of the initiating species has not been definitively established. Although reference is made to an episulfonium ion, it is possible that an episulfurane[7b,c] may be serving as the electrophile. (b) Smit, W. A.; Zefirov, N. S.; Bodrikov, I. V.; Krimer, M. Z. *Acc Chem. Res.* **1979**, *12*, 282 and references therein. (c) Smit, W. S.; Zefirov, N. S.; Bodrikov, I. V. *Org. Sulfur Chem. Invited Lect. Int. Symp., 9th, 1980* **1981**, 159.

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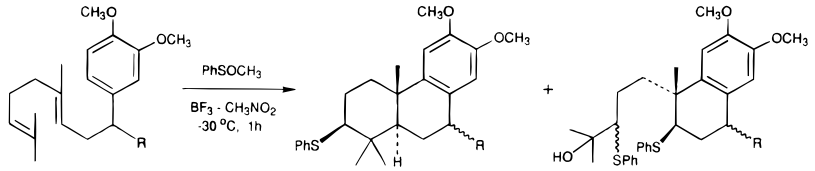
Scheme 1

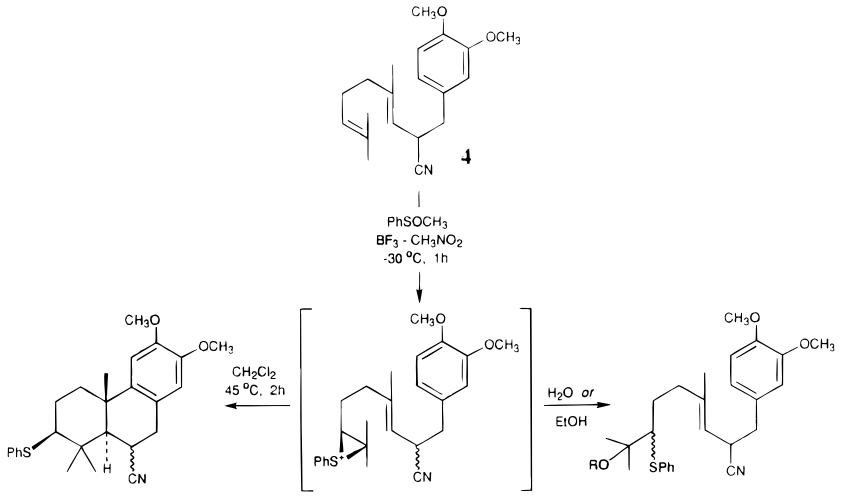


1a: R = CN
1b: R = H

2a (85%)
2b (51%)

3a (0%)
3b (8%)

Scheme 2



7a,b (73%)

6a: R = H (48%)
6b: R = Et (69%)

In principle, the restoration of cascade cyclization efficiency might be achieved by utilizing modified sulfenylating reagents that could generate episulfonium ions possessing enhanced electrophilicity so as to overcome the attenuated reactivity of the allylically substituted alkene. An obvious strategy to investigate this possibility would involve the synthesis and empirical evaluation of a series of $ArSOCH_3$ derivatives bearing electron-withdrawing substituents. To this end, the prospective sulfenylating reagents **8a**−**c** were prepared by the reaction of the corresponding sulfenyl chlorides with CH_3OH in the presence of Et_3N.[8] Unfortunately, **8a**−**c** admixed with BF_3 in CH_3NO_2 proved surprisingly ineffective for the cyclization of **4** at temperatures below 0 °C. We next turned our attention to sulfenylating reagents of the type $ArSOCH_2CH_2OCH_3$, **9a**−**e**, with the expectation that facile dissociative ionization of the bidentate 2-methoxyethoxy moiety could be achieved through the use of chelate-forming Lewis acids such as $TiCl_4$ or $SnCl_4$.

$ArSOCH_3$	$ArSOCH_2CH_2OCH_3$
8a: Ar = *p*-ClC_6H_4	**9a:** Ar = C_6H_5
8b: Ar = C_6F_5	**9b:** Ar = *p*-ClC_6H_4
8c: Ar = *o*-$NO_2C_6H_4$	**9c:** Ar = *p*-$CF_3C_6H_4$
	9d: Ar = *m*-$CF_3C_6H_4$
	9e: Ar = *o*-$CF_3C_6H_4$

The reagents of interest, **9a**−**e**, were readily prepared by the Et_3N-mediated condensation of 2-methoxyethanol with the requisite sulfenyl chlorides.[8] In light of the documented inductive electron-withdrawing properties of a *p*-chloro substituent and the nominal cost of 4-chlorothiophenol, sulfenate ester **9b** was selected for initial evaluation in the cascade cyclization of the lethargic aryldiene **4**. Several Lewis acids, solvents, and temperature schemes were examined to determine the most effective set of conditions for promoting the transformation shown in Table 1. In all instances examined, 1.05 equiv of **9b** and an appropriate quantity of the Lewis acid of interest were employed. The results of this study are compiled in Table 1.

The following observations deserve comment. Despite our initial expectation that chelating Lewis acids [e.g., $SnCl_4$, $TiCl_4$, and $Me_2Si(OTf)_2$] would effectively promote sulfenylative cyclization, BF_3 proved the superior activator of **9b**. In addition, 3.15 equiv of BF_3 was determined optimum, presumably as a consequence of a second oxygen moiety in **9b**.[9]

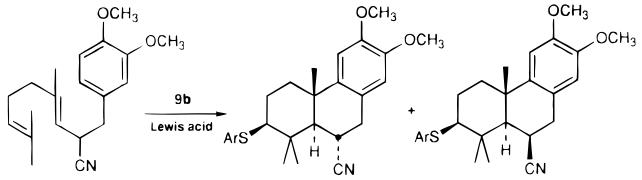
That **4** could be induced to undergo clean cyclization at −20 °C (entry 2) was most gratifying. Support for fully cyclized structures was garnered by the absence of vinyl protons and the presence of two aromatic singlets in the ^{1}H-NMR. The relative stereochemistry of the individual diastereomers was readily deduced from the coupling constants of their methine and benzylic protons. In addition, an X-ray structure of **12b** confirmed the stereochemical assignments of this diastereomer (Figure 1).

After determination of the optimum Lewis acid, solvent, and temperature (in conjunction with sulfenate ester **9b**) for providing the highest yield of cyclized adducts **12a**,**b**, an examination of two additional facets of these reagents was undertaken. Specifically, alternative leaving groups and aryl substituents were investigated to determine if higher yields of octahydrophenan-

(8) (a) Harring, S. R.; Livinghouse, T. *Synth. Commun.* **1997**, submitted for publication. (b) For the preparation of $PhSOCH_3$, see: Chang, L. L.; Denney, D. B.; Denney, D. Z.; Kazior, R. J. *J. Am. Chem. Soc.* **1977**, *99*, 2293.

(9) The use of BF_3 in quantities exceeding 3.15 equiv resulted in no observable increase in yield.

Table 1. Cyclizations of Aryldiene 4 with Sulfenylating Reagent 9b (1.05 equiv). The Effect of Lewis Acids and Reaction Conditions on the Yield of Octahydrophenanthrene Derivatives 12a and 12b



4 **12a** **12b**

(Ar = *p*-Cl)

entry	Lewis acid (equiv)	solvent	temp, °C	time[a]	yield of **12** (**a**:**b**), %
1	$BF_3{\cdot}CH_3NO_2$ (2.10)	CH_3NO_2	−20	5 min	35−40[c]
2	$BF_3{\cdot}CH_3NO_2$ (3.15)	CH_3NO_2	−20	5 min	81[b]
3	$SnCl_4$ (1.05)	CH_3NO_2	−20 → 25	6 h	0[c]
4	$SnCl_4$ (2.10)	CH_2Cl_2:CH_3NO_2 (2:1)	−20	6 h	36[b] (1.0:1.0)
5	$TiCl_4$ (1.05)	CH_3NO_2	−20 → 25	6 h	0[c]
6	$TiCl_4$ (2.10)	CH_3NO_2	−20 → 25	6 h	0[c]
7	TMSOTf (1.05)	CH_3NO_2	−20 → 25	6 h	0[c]
8	TMSOTf (2.10)	CH_3NO_2	−20 → 25	6 h	0[c]
9	$Me_2Si(OTf)_2$ (1.05)	CH_2Cl_2	−78 → 25	4 h	25−30[c]
10	$Me_2Si(OTf)_2$ (1.05)	CH_2Cl_2:CH_3NO_2 (2:1)	−78 → 25	4 h	25−30[c]

[a] Time the reaction was allowed to proceed at the final temperature before quenching. [b] Yield after chromatography; the ratios were determined from the weight of the separated diastereomers. [c] Uncorrected GLC yield; the ratios of diastereomers were not determined.

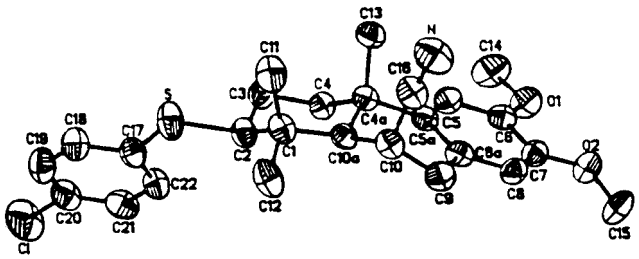


Figure 1.

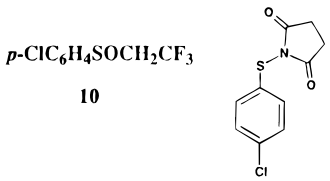
Table 2. Cyclizations of Aryldiene 4 with Sulfenylating Reagents 8a, 9b, 10, and 11 (1.05 equiv) and $BF_3{\cdot}CH_3NO_2$ (3.15 equiv). The Effect of the Leaving Group on the Yield of Octahydrophenanthrene Derivatives 12a and 12b

entry	sulfenylating reagent	leaving group	yield of **12**[a] (**a**:**b**), %
1	**8a**	OCH_3	0[b]
2	**9b**	$OCH_2CH_2OCH_3$	81 (1.3:1.0)[b]
3	**10**	OCH_2CF_3	38 (1.0:1.3)[b]
4	**11**	$N[C(O)CH_2]_2$	43 (1.0:1.0)[b]

[a] Yield after chromatography; ratios were determined from the weight of the separated diastereomers. [b] In all instances, sulfenylative cyclizations were conducted at −20 °C for 5 min prior to quenching with $NaHCO_{3(aq)}$ (procedure A).

threnes could be realized by further adjusting the structural and electronic characteristics of the sulfenylating reagent.

Since the outcome of annulations employing **8a** and **9b** as the episulfonium ion source was known, the ability of **10** and **11** to effect the transformation **4** → **12a**,**b** was



11

examined first. The results of this study are illustrated in Table 2, and show that the methoxyethoxy moiety is far superior to either the trifluoroethoxy or succinimido leaving groups in promoting the desired cascade reaction. Furthermore, these examples constitute the first cases in which the extent of cationic cyclizations was shown to be dramatically influenced by the leaving group of the episulfonium ion precursor.

The trend observed in Table 2 *may* reflect differences in the true nature of the initiating species (i.e. episulfonium ion vs episulfurane), which in turn can be attributed to the degree of dissociation of the S−O bond upon interaction with the substrate. At one extreme, complexation of BF_3 to the 2-methoxyethoxy portion of ester **9b** could possibly generate a 2:1 BF_3 adduct, or alternatively, a boronium ion chelate, thereby facilitating rupture of the S−O bond upon introduction of the substrate to generate a highly reactive episulfonium ion **13** (Scheme 3). On the other hand, treatment of the simple methyl ester with BF_3 might weaken but not induce complete cleavage of the S−O bond upon exposure to the aryldiene. Consequently, an episulfurane (e.g., **14**) with diminished reactivity may be produced with this sulfenylating system (Scheme 3).[7b,c] The extent of dissociation of the S−L bonds of reagents **10** and **11** would appear to be intermediate (and approximately to the same degree) in accord with the increased ability of these leaving groups to accommodate a negative charge relative to OCH_3. Several chelates between BF_3 and bidentate nitrogen donors are known;[10] however, TMEDA reacts with 2 equiv of BF_3 to form a simple, nonchelated 1:2 complex in which a BF_3 molecule is coordinated to each nitrogen atom.[11] Very little information currently exists regarding the chemistry of BF_3 and bidentate oxygen ligands. Studies of such systems are certainly warranted and should provide additional insight into the results of Table 2.[12]

(10) Axtell, D. D.; Cambell, A. C.; Keller, P. C.; Rund, J. V. *J. Coord. Chem.* **1976**, *5*, 129.

(11) Sigaram, B.; Pai, G. G. *Heterocycles* **1982**, *18* (Spec. Iss.), 387.

(12) The complex formed between BF_3 and **9b** is not stable after 30 min at −20 °C, as evidenced by the failure to observe (by GC and TLC) or isolate cyclized products from reactions in which the Lewis acid and sulfenate ester were allowed to age for 30 min at −20 °C before introducing the substrate.

Scheme 3

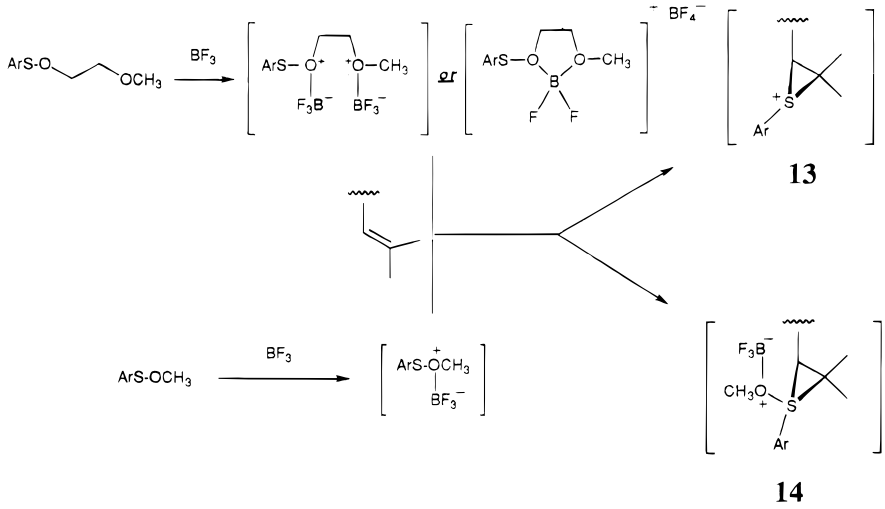
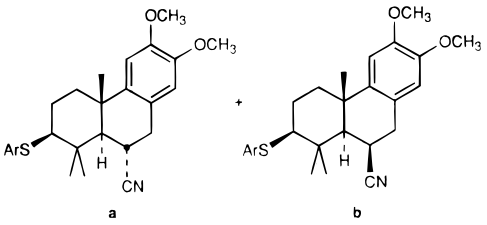


Table 3. Cyclizations of Aryldiene 4 with Sulfenylating Reagents 9a−e (1.05 equiv) and BF_3·CH_3NO_2 (3.15 equiv). The Effect of the Aromatic Substituent on the Yield of Octahydrophenanthrene Derivatives of General Structures a and b



entry	sulfenylating reagent	Ar	products	yield[a] (a:b), %
1	**9b**	*p*-Cl	**12a**; **12b**	81 (1.3:1.0)
2	**9a**	*p*-H	**7a**; **7b**	14 (1.0:1.0)
3	**9c**	*p*-CF_3	**15a**; **15b**	48 (1.5:1.0)
4	**9d**	*m*-CF_3	**16a**; **16b**	58 (1.4:1.0)
5	**9e**	*o*-CF_3	**17a**; **17b**	59 (1.5:1.0)

[a] Yield after chromatography; the ratios were determined by the weight of the separated diastereomers.

The final aspect regarding these preliminary experiments concerned the influence of substituents on the aromatic ring of the sulfenylating reagent in determining the efficiency of cascade cyclization. To this end, aryldiene **4** was subjected to treatment with 1.05 equiv of reagents **9a**−**e** and 3.15 equiv of BF_3·CH_3NO_2 in CH_3NO_2 for 5 min at −20 °C. The results of these cyclizations are presented in Table 3. Evidence supporting the formation of octahydrophenanthrenes in this study was obtained by standard spectroscopic techniques. The ^{1}H- and ^{13}C-NMRs for all of the compounds in entries 2−5 were very similar to those already discussed for **12a** and **12b**. In general, the yields of cyclized adducts correlate reasonably well with the inductive destabilizing effects of the substituents toward the inherent positive charge developed prior to the onset of cyclization. Given the increase in yield observed in entry 4 as compared to entry 3, a steric effect from the *o*-CF_3 group may account for the lower than anticipated yield of **17a**,**b** (entry 5) than might have been expected based solely on electronic considerations.

The data compiled in Tables 1−3 indicate that the combination of **9b** and BF_3 is a very reactive sulfenylation system which is capable of efficiently promoting the cyclization of **4** at −20 °C, a transformation that failed with the more conventional reagent $PhSOCH_3$. Given the modest yields of functionalized octahydrophenanthrenes obtained in many of our early efforts to cyclize aryldienes with $PhSOCH_3$,[5b] it was decided to reinvestigate the cyclization of problematic substrates utilizing the more reactive sulfenylating combination cited above. Accordingly, exposure of precyclization substrates **18**,[6] **20**,[6] and **22**[6] to **9b** (1.05 equiv) and BF_3·CH_3NO_2 (3.15 equiv) in CH_3NO_2 for 5 min at −20 °C resulted in smooth conversion to the desired cyclized compounds **19a**,**b**, **21a**,**b** and **23**, as illustrated in Table 4. It was pleasing to discover that substantially higher yields of tricyclic materials were realized in each case via the agency of **9b** versus those obtained through the use of $PhSOCH_3$. Moreover, the formation of polar byproducts (analogous to **6a**) were minimized by the use of this reagent relative to $PhSOCH_3$. Aside from subtle differences in the aromatic region, the ^{1}H- and ^{13}C-NMR spectra of the resultant tricycles were nearly identical to those of the corresponding PhS-derivatized products reported previously.[5b]

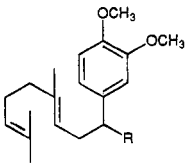
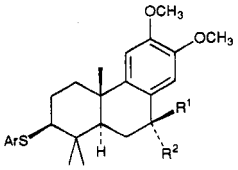
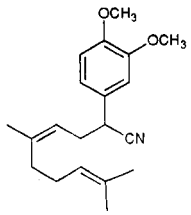
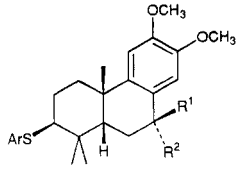
In conclusion, this study has shown that 2-methoxyethyl 4-chlorobenzenesulfenate (**9b**) in combination with BF_3·CH_3NO_2 is a remarkably effective reagent for promoting efficient sulfenylative cascade cyclizations of representative aryldienes. The utilization of this method for the synthesis of alternative carbocyclic structures will be described in due course.

Experimental Section

General. ^{1}H-NMR chemical shifts are reported in ppm relative to the residual proton in chloroform-*d* assigned at 7.24 ppm. ^{13}C-NMR chemical shifts are reported in ppm relative to the center line in chloroform-*d* assigned at 76.90 ppm. DEPT experiments were performed on all compounds to identify the number of protons attached to each carbon. Either an Alltech Econocap SE-54 bonded phase 15 m length, 0.54 mm i.d., and 1.2 μm film size column or a J & W Scientific DB-5 bonded phase 15 m megabore, 0.53 mm i.d. column were utilized for obtaining GLCs.

Molar solutions of BF_3·CH_3NO_2 were routinely prepared by passing BF_3 gas (3−4 g) via a syringe needle (6 cm, 20 gauge) into a preweighed 50-mL volumetric flask fitted with a rubber septum and 35−40 mL of CH_3NO_2 at 0 °C, reweighing, and then diluting to the mark with additional CH_3NO_2. These solutions were stored in the dark at −20 °C for up to three weeks. Solutions of *n*-BuLi (2−3 M) were routinely prepared by diluting commercially available (Aldrich Chemical Co.) *n*-BuLi (10.0 M in hexane) with freshly distilled heptane (Na), and were titrated against (±)-2-butanol (2.0 M in toluene) using 1,10-phenanthroline as the indicator prior to use.

Table 4. Polyene Cyclizations of Aryldienes 18, 20, and 22 Mediated by 9b (1.05 equiv) and $BF_3{\cdot}CH_3NO_2$ (3.15 equiv)

Entry	Aryl-Diene	Products[a]	Yield[b,c]
1			92% (85%)
	18 (R = CN)	19a: R^1 = CN; R^2 = H (50%) 19b: R^1 = H; R^2 = CN (50%)	
2	22 (R = H)	23: $R^1 = R^2$ = H	77% (57%)
3			80% (54%)
	20	21a: R^1 = CN; R^2 = H (50%) 21b: R^1 = H; R^2 = CN (50%)	

[a] Ar = *p*-Cl. [b] Yield after chromatography, the ratios were determined by the weight of the separated diastereomers. [c] Yields in parentheses refer to cyclizations mediated by $PhSOCH_3$ (1.05 equiv) and $BF_3{\cdot}CH_3NO_2$ (2.10 equiv).[5b]

LDA·THF complex was prepared by dropwise addition of *n*-BuLi (5.0 mL, 50 mmol, 10.0 M in hexanes) to a 0 °C solution of *N,N*-diisopropylamine (7.0 mL, 50 mmol) and THF (4 mL, 50 mmol) in methylcyclohexane (34 mL). This complex was titrated by the method of Vedejs[13] prior to use.

General Procedures for Sulfenylative Cyclizations. Procedure A. A flame-dried, 25 × 150 mm test tube equipped with a magnetic stirring bar, rubber septum, and N_2 inlet was flushed with N_2, charged with the sulfenylating reagent (0.335 mmol) and dry CH_3NO_2 (4.8 mL), and cooled to −20 °C. $BF_3{\cdot}CH_3NO_2$ (1.24 mL, 1.24 mmol, 1.0 M) was added in one portion via syringe, and the resulting solution was stirred for 5 min at −20 °C. A solution of the nitrile (0.319 mmol) in dry CH_3NO_2 (1.0 mL) was then added in one portion via syringe, and the resulting mixture was stirred for 5 min at −20 °C. The reaction mixture was quenched (at −20 °C) with saturated $NaHCO_3$ (5 mL) and was then allowed to warm to room temperature. The layers were separated, and the organic phase was washed with H_2O (2 × 5 mL). The combined aqueous layers were back extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic phase was dried over anhydrous $MgSO_4$. The solvents were evaporated in vacuo to furnish the crude product which was purified by MPLC (5−10% ethyl acetate in hexane was used for elution).

Procedure B. The same as for procedure A except 2.10 equiv of $BF_3{\cdot}CH_3NO_2$ (instead of 3.15 equiv) was used, and the reactions were stirred at −30 °C for 1 h before quenching.

Procedure C. The same for procedure B except the reaction was quenched with absolute ethanol (at −30 °C), and the resulting mixture was stirred 30 min at room temperature before adding $NaHCO_3$ and workup in the usual manner.

Procedure D. The same for procedure B except the reaction was stirred 5 min at −30 °C and then 2 h at 45−50 °C, cooled to room temperature, quenched with $NaHCO_3$, and worked-up as described.

(*E*)-2-[(3,4-Dimethoxyphenyl)methyl]-4,8-dimethyl-8-hydroxy-7-(phenylthio)non-3-enenitrile (6a). Treatment of nitrile **4** (84 mg, 0.27 mmol) with $PhSOCH_3$ (39 mg, 0.28 mmol) and $BF_3{\cdot}CH_3NO_2$ (0.57 mL, 0.56 mmol, 0.988 M) in CH_3NO_2 (4.0 mL) according to procedure B afforded 57 mg (48%) of **6a** as an undetermined mixture of diastereomers following MPLC [(1:9) ethyl acetate:hexane for elution]. For **6a** as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 7.45−7.14 (cm, SAr*H*), 6.73 (m, Ar*H*), 4.88 (t, J = 9.4 Hz, =C*H*), 3.82 (s, OCH_3), 3.81 (s, OCH_3), 3.46 (m, C*H*CN), 2.98−2.55 (cm, C*H*SAr, CH_2Ar), 2.43−2.08 (cm, CH_2, CH′-*H*), 1.90 (m, CH-*H*′), 1.50 (s, CH_3), 1.35 (s, O*H*), 1.28 (s, CH_3), 1.20 (s, CH_3) ppm; ^{13}C-NMR ($CDCl_3$) δ 148.7 (*C*), 148.1 (*C*), 140.4, 140.3 (*C*), 137.2 (*C*), 130.6 (*C*H), 130.3 (*C*H), 129.0 (*C*), 128.9, 128.8 (*C*H), 126.5, 126.3 (*C*H), 121.1 (*C*H), 120.5 (*C*), 119.2, 119.0 (*C*H), 112.5 (*C*H), 111.1 (*C*H), 72.80, 72.75 (*C*), 63.8, 63.2 (*C*H), 55.7 (2 OCH_3), 38.7, 38.6 (CH_2), 37.3 (CH_2), 32.0, 31.8 (*C*H), 30.2, 30.1 (CH_2), 26.7 (CH_3), 26.2, 26.1 (CH_3), 16.1, 16.2 (CH_3) ppm; IR (thin film) 3504 (br, OH), 3075−2832 (CH envelope), 2216 (CN), 1630, 1516, 1264, 1240, 1158, 1028 cm^{-1}; HRMS calcd for $C_{26}H_{33}NO_3S$: 439.2181. Found: 439.2173.

(*E*)-2-[(3,4-Dimethoxyphenyl)methyl]-4,8-dimethyl-8-ethoxy-7-(phenylthio)non-3-enenitrile (6b). Treatment of nitrile **4** (71 mg, 0.23 mmol) with $PhSOCH_3$ (33 mg, 0.28 mmol) and $BF_3{\cdot}CH_3NO_2$ (0.48 mL, 0.48 mmol, 0.988 M) in CH_3NO_2 (3.4 mL) according to procedure C afforded 73 mg (69%) of **6b** as an undetermined mixture of diastereomers, following MPLC [(1:19) ethyl acetate:hexane for elution]. For **6b** as a colorless oil: ^{1}H-NMR ($CDCl_3$) δ 7.35−7.09 (cm, SAr*H*), 6.69 (m, Ar*H*), 4.99 (d, J = 8.8 Hz, =C*H*), 4.91 (d, J = 8.8 Hz, =C*H*), 3.78 (s, OCH_3), 3.77 (s, OCH_3), 3.43 (q, J = 7.8 Hz, C*H*CN), 3.27 (m, OCH_2CH$_3$), 2.95 (m, CH_2Ar), 2.80 (m, CH_2Ar), 2.66 (m, C*H*SAr), 2.32 (m, CH′-*H*), 2.19−2.03 (m, CH_2), 1.48 (s, CH_3), 1.35 (m, CH-*H*′), 1.18 (s, CH_3), 1.14 (s, CH_3), 1.03 (t, J = 6.9 Hz, OCH$_2$CH_3) ppm; ^{13}C-NMR ($CDCl_3$) δ 148.7 (*C*), 148.0 (*C*), 141.1, 140.9 (*C*), 138.1, 138.0 (*C*), 130.5 (*C*H), 130.1 (*C*H), 129.1 (*C*), 128.8, 128.7 (*C*H), 126.1, 125.9 (*C*H), 121.1 (*C*H), 120.7 (*C*), 118.9 (*C*H), 118.4 (*C*H), 112.1 (*C*H), 111.1 (*C*H), 78.1 (*C*), 58.4, 57.3 (*C*H), 56.6 (CH_2), 55.7 (2 OCH_3), 38.83, 38.76 (CH_2), 37.3, 37.2 (CH_2), 32.1, 32.0 (*C*H), 28.6, 28.3 (CH_2), 24.1 (CH_3), 21.9 (CH_3), 16.4, 16.1 (CH_3), 15.8 (CH_3) ppm; IR (thin film) 3054−2825 (CH envelope), 2234 (CN), 1592, 1515, 1460, 1439, 1265, 1237, 1025 cm^{-1}; HRMS calcd for $C_{28}H_{37}NO_3S$: 467.2494. Found: 467.2487.

2-[(4′-Chlorophenyl)thio]-10-cyano-6,7-dimethoxy-1,2α,3,4,4aα,9,10β,10aβ-octahydro-1,1,4a-trimethylphenanthrene (12a) and 2-[(4′-Chlorophenyl)thio]-10-cyano-6,7-dimethoxy-1,2α,3,4,4aα,9,10α,10aβ-octahydro-1,1,4a-trimethylphenanthrene (12b). Cyclization of nitrile **4** (0.348 g, 1.11 mmol) with **9b** (0.255 g, 1.17 mmol) and $BF_3{\cdot}CH_3NO_2$ (4.26 mL, 3.50 mmol, 0.823 M) in CH_3NO_2 (17.0 mL), according to procedure A, afforded 0.408 g (81%) of **12a** and **12b** as a 1.3:1.0 mixture of diastereomers.

For **12a** as a white solid: mp 157−159 °C [recrystallized from (1:9) toluene:heptane]; ^{1}H-NMR ($CDCl_3$) δ 7.34 (d, 2 H, J = 8.5 Hz, SAr*H*), 7.25 (d, 2 H, J = 8.5 Hz, SAr*H*), 6.67 (s, 1 H, Ar*H*), 6.65 (s, 1 H, Ar*H*), 3.85 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 3.33 (dd, 1 H, J = 8.2, 15.7 Hz, ArCH_a), 3.13 (td, 1 H, J = 3.5, 8.2 Hz, C*H*CN), 3.01 (dd, 1 H, J = 3.5, 15.7 Hz, ArCH_e), 2.85 (dd, 1 H, J = 8.7, 16.7 Hz, C*H*SAr), 2.19 (dt, 1 H, J = 3.1, 12.9 Hz, C(4)-H_e), 2.03 (m, 2 H, C(3)H_2), 1.74 (d, 1 H, J = 8.2 Hz, C*H* ring junction), 1.63 (m, 1 H, C(4)-H_a), 1.58 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 1.16 (s, 3 H, CH_3) ppm; ^{13}C-NMR ($CDCl_3$) δ 147.8 (*C*), 147.2 (*C*), 140.2 (*C*), 134.5 (*C*), 133.1 (2 *C*H), 132.8 (*C*), 129.0 (2 *C*H), 124.7 (*C*), 123.8 (*C*), 111.5 (*C*H), 106.7 (*C*H), 61.4 (*C*H), 55.9 (OCH_3), 55.8 (OCH_3), 55.1 (*C*H), 39.9 (*C*), 38.7 (CH_2), 38.0 (*C*), 33.0 (CH_2), 30.2 (CH_3), 27.1 (CH_2), 25.6 (*C*H), 21.9 (CH_3), 17.5 (CH_3) ppm; IR (KBr) 3096−2832 (CH envelope), 2234 (CN), 1512, 1474, 1272, 1212, 1156, 1093, 820, 680 cm^{-1}; HRMS calcd for $C_{26}H_{30}ClNO_2S$: 455.1652. Found: 455.1633. Anal. Calcd for $C_{26}H_{30}ClNO_2S$: C, 68.46; H, 6.63. Found: C, 68.49; H, 6.69.

For **12b** as a white solid: mp 182−184 °C [recrystallized from (1:9) toluene:heptane]; ^{1}H-NMR ($CDCl_3$) δ 7.33 (d, 2 H, J = 8.5 Hz, SAr*H*), 7.23 (d, 2 H, J = 8.5 Hz, SAr*H*), 6.70 (s, 1 H, Ar*H*), 6.49 (s, 1 H, Ar*H*), 3.83 (s, 6 H, 2 OCH_3), 3.47 (br s with fine structure, 1 H, C*H*CN), 3.14 (d, 2 H, J = 4.2 Hz, ArCH_2), 2.76 (dd, 1 H, J = 4.6, 12.1 Hz, C*H*SAr), 2.20 (dt, 1 H, J = 3.3, 13.1 Hz, C(4)-H_e), 2.03 (m, 2 H, C(3)H_2), 1.67 (s, 3 H, CH_3), 1.59 (d, 1 H, J = 2.4 Hz, C*H* ring junction), 1.37 (s, 6 H, 2 CH_3), 1.24 (m, 1 H, C(4)-H_a) ppm; ^{13}C-NMR ($CDCl_3$) δ

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148.1 (*C*), 147.4 (*C*), 138.9 (*C*), 134.6 (*C*), 133.0 (2 *C*H), 132.8 (*C*), 129.0 (2 *C*H), 123.1 (*C*), 121.6 (*C*), 110.9 (*C*H), 108.3 (*C*H), 61.4 (*C*H), 55.8 (OCH_3), 55.7 (OCH_3), 53.2 (*C*H), 41.9 (CH_2), 39.5 (*C*), 37.8 (*C*), 35.4 (CH_2), 30.1 (CH_3), 27.8 (CH_2), 24.5 (CH_3), 22.5 (*C*H), 18.1 (CH_3) ppm; IR (KBr) 3096−2825 (CH envelope), 2230 (CN), 1512, 1476, 1260, 1094, 816 cm^{-1}; HRMS calcd for $C_{26}H_{30}ClNO_2S$: 455.1652. Found: 455.1662. Anal. Calcd for $C_{26}H_{30}ClNO_2S$: C, 68.46; H, 6.63. Found: C, 68.06; H, 6.64.

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Supporting Information Available: ^1H and ^{13}C NMR, IR and high resolution mass spectral data for compounds **7a,b**, **15a**,**b**, **16a**,**b**, **17a**,**b**, **19a**,**b**, **21a**,**b** and **23**; ^{13}C NMR spectra for compounds **6a**,**b**, **15a**,**b**, **16a**,**b**, **17a**,**b**, **19b**, **21a**,**b** and **23** (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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