Tandem Photocyclization-Intramolecular Addition Reactions of Aryl Vinyl Sulfides. Observation of a Novel [2 + 2] Cycloaddition-Allylic Sulfide Rearrangement

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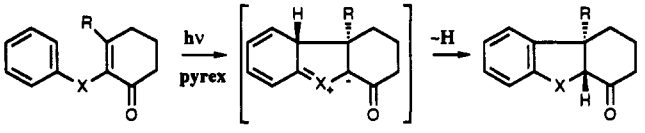
Photocyclization of aryl vinyl sulfides reportedly proceeds via thiocarbonyl ylide intermediates. The photochemical behavior of several aryl vinyl sulfides, which incorporate a pendant alkene side chain, was explored. In general, naphthyl and phenyl vinyl thioethers provided products which are consistent with photocyclization to a thiocarbonyl ylide intermediate followed by either intramolecular hydrogen shift or subsequent intramolecular ylide–alkene addition. Product distribution is influenced by solvent and temperature effects. Novel secondary photoprocesses were also observed during some reactions. Thus, irradiation of naphthyl vinyl sulfide **20** gave dihydrothiophene **22** which underwent subsequent intramolecular [2 + 2] cycloaddition to provide **24**. Upon prolonged irradiation **24** undergoes a novel allylic sulfide rearrangement to provide **25**.

Introduction

The photochemical six-electron heterocyclization reaction of aryl vinyl ethers **1a** and aryl vinyl thioethers **1b** reportedly proceeds via the corresponding carbonyl ylide and thiocarbonyl ylide intermediates **2**. In the absence of other effects these systems rearrange by a process involving hydrogen shifts to provide dihydrofuran and dihydrothiophene products **3**.[1,2] There is now substantial evidence, both chemical and spectroscopic, to support the intermediacy of the ylide systems **2**.[2-4] Surprisingly, this method has received only limited attention in recent years. Moreover, few experiments have been carried out involving reactions of the transient species. We recently reported on the sequential photocyclization and intramolecular ylide–alkene cycloadditions involving aryl vinyl ethers.[5-8] Herein we detail our efforts in the area of photoinitiated intramolecular ylide–alkene cycloaddition reactions of aryl vinyl sulfides. In addition we describe some novel secondary photoprocesses which were observed in the course of this work.

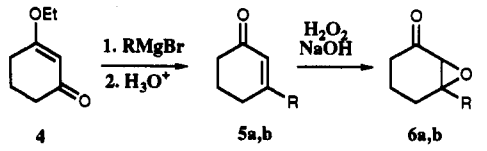


1a, X = O
b, X = S

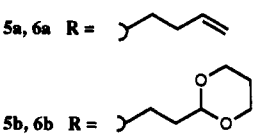
2 **3**

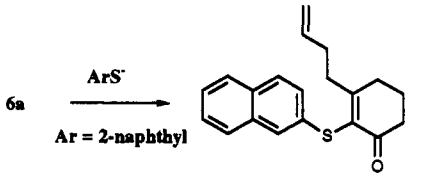
Results and Discussion

Preliminary investigations were carried out with the naphthyl vinyl sulfide **7**.[5,6] The preparation of **7** illustrates the general procedure employed for the synthesis of several different aryl vinyl sulfides and aryl vinyl ethers for use in this study.



4 **5a,b** **6a,b**





7

Irradiation of a solution of **7** in benzene (2×10^{-3} M) for 1 h at 25 °C provided the photocyclized product **8** in 81% isolated yield (no trapping observed).[5,9] Interestingly, low-temperature irradiation of a solution of **7** in toluene (3×10^{-3} M, -78 °C) provided **8** in quantitative yield after only 20 min. In contrast to these experiments, high-temperature photolysis of a solution of **7** in toluene (3×10^{-3} M, 110 °C) for 3.5 h resulted in formation of the addition product **9** which was obtained as a mixture of diastereoisomers (79% isolated yield). The structural assignment for each diastereoisomer **9a** and **9b** is based on IR, mass spectral, ^{1}H NMR, and ^{13}C NMR analyses. Confirmation of the structure **9a** was obtained by X-ray crystallographic analysis.[10] The formation of **9** is rather unusual. We had

(1) For reviews see: Schultz, A. G. *Acc. Chem. Res.* **1983**, *16*, 210. Schultz, A. G.; Motyka, L. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1983; Vol. 6, p 1.
(2) Herkstroeter, W. G.; Schultz, A. G. *J. Am. Chem. Soc.* **1984**, *106*, 5563.
(3) Wolff, T. J. *J. Am. Chem. Soc.* **1978**, *100*, 6158. Wolff, T. *J. Org. Chem.* **1981**, *46*, 978–983.
(4) Schultz, A. G.; Detar, M. B. *J. Am. Chem. Soc.* **1976**, *98*, 3574.
(5) Dittami, J. P.; Ramanathan, H.; Breining, S. *Tetrahedron Lett.* **1989**, *30*, 795.
(6) Dittami, J. P.; Nie, X.-Y. *Synth. Commun.* **1990**, *20* (4), 541.
(7) Dittami, J. P.; Nie, X.-Y.; Buntel, C.; Rigatti, S. *Tetrahedron Lett.* **1990**, 3821.
(8) Dittami, J. P.; Nie, X.-Y.; Nie, H.; Ramanathan, H.; Breining, S.; Bordner, J.; Decosta, D.; Kiplinger, J.; Reiche, P.; Ware, R. *J. Org. Chem.* **1991**, *56*, 5572.

(9) Photochemical experiments were conducted using a 450-W Canrad-Hanovia medium-pressure quartz mercury-vapor lamp. The lamp was placed in a water-cooled Pyrex immersion well. Reaction solutions were saturated with argon prior to irradiation. For high- and low-temperature runs a vacuum-jacketed quartz immersion well was employed with a Pyrex sleeve filter. The immersion well was placed in a large scale (~200 mL) reactor. Heating was carried out with a silicon oil bath, and cooling was achieved with a Neslab ULT-80DD low-temperature circulating bath.

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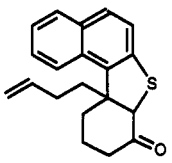
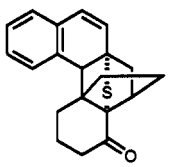
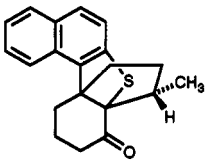
expected to observe formation of the [3 + 2] adduct **10**. However, none of this product was isolated from the reaction mixture. We note that ring closure in the naphthyl vinyl sulfide **7** occurs only toward the 1-position of the naphthalene system. This result is consistent with previous observations.[1]



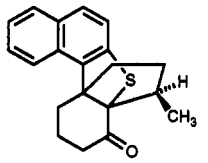
8



10



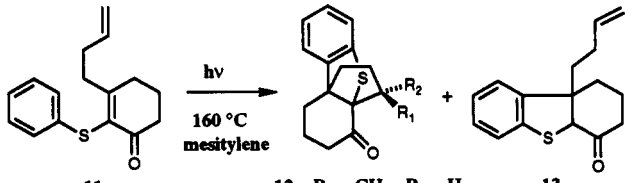
9a



9b

Control experiments demonstrate that both light and heat are required to effect the formation of **9**. Thus, on heating a solution of **7** in toluene at reflux temperature for 6 h in the dark, only starting material is recovered. Likewise, **8** was found to be stable in both refluxing toluene and under the reaction conditions (heat and light) used for formation of **9**. These data suggest that a transient species generated from **7** via a photochemical process undergoes a thermally induced addition reaction to give **9**.

Photolysis of the phenyl vinyl sulfide **11**, which is readily available from **6a**, yielded the intramolecular addition product **12** (41% isolated yield). However, the conversion **11** → **12** requires a higher reaction temperature (4×10^{-3} M, mesitylene, 160 °C) than the corresponding transformation **7** → **9**. In addition, a significant amount of photocyclized "untrapped" product **13** was observed in the reaction mixture (31% isolated yield). Control experiments carried out in the absence of light demonstrate that **11** is thermally stable at 160 °C. Furthermore, **13** remains unchanged under the conditions of the photolysis. Thus, both heat and light are required to effect the transformation of **11** to **12** and **13** is not an intermediate in the formation of **12**.



11 → **12a**, $R_1 = CH_3$, $R_2 = H$; **b**, $R_1 = H$, $R_2 = CH_3$ (41%) + **13** (31%)

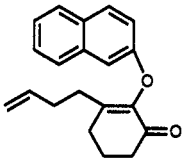
Earlier we reported that photolysis of aryl vinyl ethers such as **14** provides a means for the preparation of carbonyl ylide intermediates.[8] These intermediates exhibit reactivity which is considerably different from the aryl vinyl sulfide analogues. Thus, photolysis of a solution of **14** in toluene (3×10^{-3} M) for 1 h at room temperature afforded

(10) Single-crystal X-ray data for compound **9a** were obtained by P. G. Williard at Brown University. All other single crystal X-ray analyses were determined by Jon Bordner and Debra Decosta at Pfizer Central Research. A representative crystal was surveyed and a 1-Å data set (maximum $\sin\theta/\lambda = 0.5$) was collected on a Nicolet R3m/μm diffractometer.

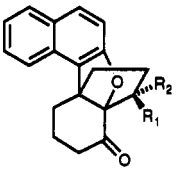
Table I. Variable-Temperature Photolyses of 20

	product ratio (NMR)		
reaction temp (°C)	**21**	**22**	**24**
−70	12.8	1	1.3
25	18	1	0.7
110	61	1	

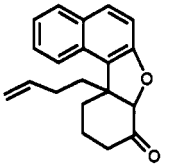
the intramolecular addition product **15** (38%) along with photocyclized product **16** (54%). Notably, the temperature required for the formation of the oxygen-containing system **15** (27 °C) is well below that which is needed for preparation of the corresponding sulfur analogue **9** (110 °C). We presume that formation of **15** occurs by a mechanism similar to formation of **9**. The difference in reaction temperature for each process may reflect the differences in reactivity (or stability) of the intermediate carbonyl ylide and thiocarbonyl ylide systems. High-temperature irradiation of **14** (10^{-3} M, toluene, 110 °C) provides significant amounts of the intramolecular [3 + 2] adduct **17** (~5:1, **17**:**15** by ^{1}H NMR analysis).[8] This result is in sharp contrast to the sulfur analogue **7** for which the formation of [3 + 2] adduct has never been observed.



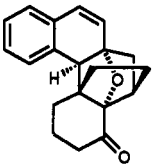
14



15a, $R_1 = CH_3$, $R_2 = H$; **b**, $R_1 = H$, $R_2 = CH_3$

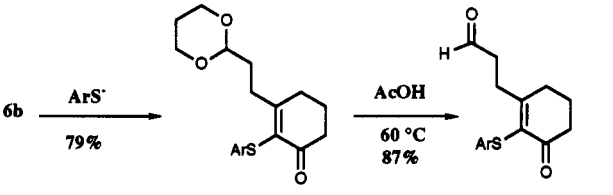


16

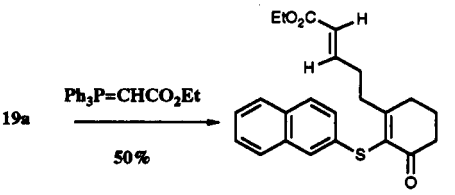


17

Aryl vinyl sulfides which incorporate an activating substituent in the side chain were also examined. The preparation of **20** illustrates the general method which was used in the synthesis of photoprecursors. The yields shown are typical for each step.[7]



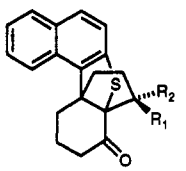
18a, Ar = 2-naphthyl; **b**, Ar = phenyl → **19a**, Ar = 2-naphthyl; **b**, Ar = phenyl



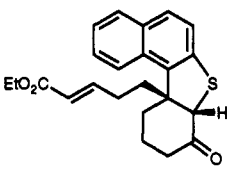
20

Incorporation of the butenoate function markedly influences the facility and outcome of the intramolecular addition reaction. Thus, Pyrex-filtered irradiation of a solution of **20** in toluene (10^{-3} M) at room temperature provided predominantly intramolecular addition product

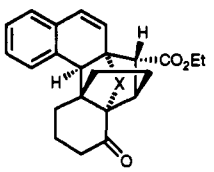
21 (84% isolated yield). Indeed, formation of 21 can even be observed at −70 °C (~60% isolated yield) (Table I). These results contrast those obtained for the low-temperature photolysis of 7 (−70 °C, toluene) where formation of photocyclized (untrapped) 8 was observed to the exclusion of any intramolecular addition product 9. In general, we have observed that substitution of the side chain with an ester group results in reduced reaction temperatures and increased yields of intramolecular addition products relative to the corresponding unsubstituted systems.



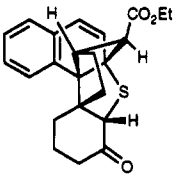
21a, $R_1 = CH_2CO_2Et$, $R_2 = H$
b, $R_1 = H$, $R_2 = CH_2CO_2Et$



22



23a, X = S
b, X = O



24

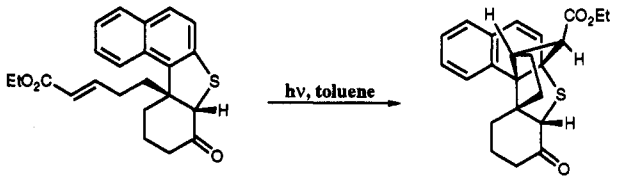
Two additional products were isolated from the room-temperature photolysis of 20. Formation of 22 is consistent with a six-electron cyclization to provide a thiocarbonyl ylide intermediate followed by an intramolecular hydrogen shift.[1] Compound 22 was assigned a cis-fused geometry on the basis of comparison with similar dihydrothiophene systems.[4] Notably, the photolyses of aryl vinyl sulfides in aprotic solvents usually provides dihydrothiophene products with a trans-fused geometry.[1] These systems are readily converted to the cis-fused isomers on treatment with base.

The third product isolated from the low-temperature photolysis of 20 was originally assigned the structure 23a on the basis of ^1H and ^{13}C NMR and by comparison with data from 23b for which an X-ray structure had been determined.[7,8] Recent results on the photolysis of related aryl vinyl ethers in methanol–toluene, however, led us to reconsider this assignment.[8] Subsequent single-crystal X-ray analysis[10] revealed that the product originally assigned structure 23a actually has the structure 24. It is noteworthy that the relative stereochemical relationships which were present in 22 are maintained in 24. Consistent with this observation 24 presumably results from a photoinitiated intramolecular [2 + 2] cycloaddition of the dihydrothiophene 22.[11,12] The following experiments support this pathway.

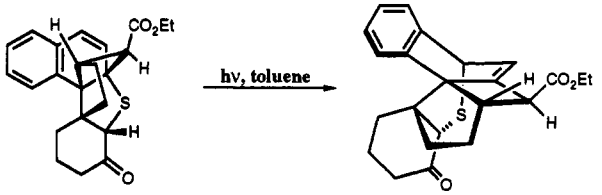
Table II. Variable-Temperature Photolyses of 26

reaction temp (°C)	% yield (isolated) 27	28
−70 °C	>42	<8
room temp	49	14
110 °C	53	10
160 °C	35	34

A solution of 20 in toluene–methanol was irradiated with a 350-nm light source to provide a mixture of 21 and 22. The use of a protic solvent and a lower energy light source provides enhanced yield of the dihydrofuran product 22 with product ratios as high as 2:1 22:21.[13] Isolation and irradiation of pure 22 in toluene with a Pyrex-Hanovia light source at room temperature results in clean conversion to adduct 24 (major product) accompanied by the product of allylic rearrangement 25.[14] Prolonged irradiation of 24 (room temperature, ~3 h) results in complete conversion to rearranged product 25. Confirmation of structure 25 was obtained by single-crystal X-ray analysis.[10]



22 24



24 25

The observation of [2 + 2] adducts and allylic rearrangement products as secondary photoproducts provides an added dimension to the synthetic utility of our photochemical reactions. We have shown that it is possible to direct the course of the photoreaction to favor intramolecular addition products 21, ring closed products 22, and [2 + 2] and [2 + 2]-allylic rearrangement products 24 and 25.

Consistent with our earlier studies, the intramolecular addition reaction is less favorable for systems which incorporate a phenyl group as the aromatic component. Thus, low-temperature photolysis of a solution of phenyl vinyl sulfide 26 (10^{-3} M, −70 °C) provides predominantly ring closed product 27 with less than 8% of the intramolecular addition product 28 (Table II). As shown, an increase in the reaction temperature for the photolysis results in an increase in the formation of intramolecular addition product. The temperature required for the conversion of 26 → 28 is significantly higher than that observed for the conversion 20 → 21 (naphthalene analogue). This difference may reflect the differences in resonance stabilization afforded the intermediate thiocarbonyl ylides derived from 20 and 26. In the case of 20 aromatic character is retained in the intermediate thiocarbonyl ylide

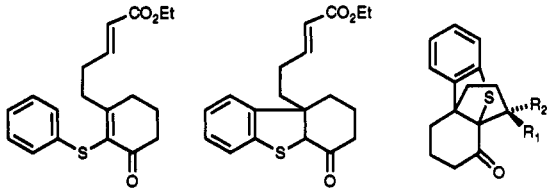
(11) For recent reviews of [2 + 2] cycloaddition reactions see: Oppolzer, W. *Acc. Chem. Res.* **1982**, *15*, 135. Baldwin, S. *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1981; Vol. 5, p 123.

(12) For a recent report on the photochemical [2 + 2] cycloadditions of butenoxyacetonaphthones see: Wagner, P. J.; Sakamoto, M. *J. Am. Chem. Soc.* **1989**, *111*, 9255. For a report on the intramolecular [2 + 2] cycloadditions of naphthonitrile systems see: McCullough, J. J.; MacInnis, W. K.; Lock, C. J. L.; Faggiani, R. *J. Am. Chem. Soc.* **1982**, *104*, 4644. For a report on the inter- and intramolecular [2 + 2] photocycloadditions of enol ethers to naphthalene see: Gilbert, A.; Heath, P.; Kashoulis-Koupparis, A.; Ellis-Davies, G. C. R.; Firth, S. M. *J. Chem. Soc., Perkin Trans. 1*, **1988**, 31. For studies on the [2 + 2] photocycloaddition of acrylonitrile to naphthalene see: Bowman, R. M.; Chamberlain, T. R.; Huang, C. W.; McCullough, J. J. *J. Am. Chem. Soc.* **1974**, *96*, 692. Bowman, R. M.; Calvo, C.; McCullough, J. J.; Miller, R. C.; Singh, I. *Can. J. Chem.* **1973**, *51*, 1060. Bowman, R. M.; McCullough, J. J. *Chem. Commun.* **1970**, 948.

(13) The 350-nm irradiations were conducted in a Rayonet photochemical reactor equipped with a carousel and RPR-3500 Å lamps. Reaction solutions were saturated with argon prior to irradiation.

(14) Brownbridge, P.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2126. Kwart, H.; Johnson, N. A.; Eggerichs, T.; George, T. J. *J. Org. Chem.* **1977**, *42*, 172. Kwart, H.; Johnson, N. A. *J. Am. Chem. Soc.* **1977**, *99*, 3441. Kwart, H.; Stanulonis, J. *J. Am. Chem. Soc.* **1976**, *98*, 4009.

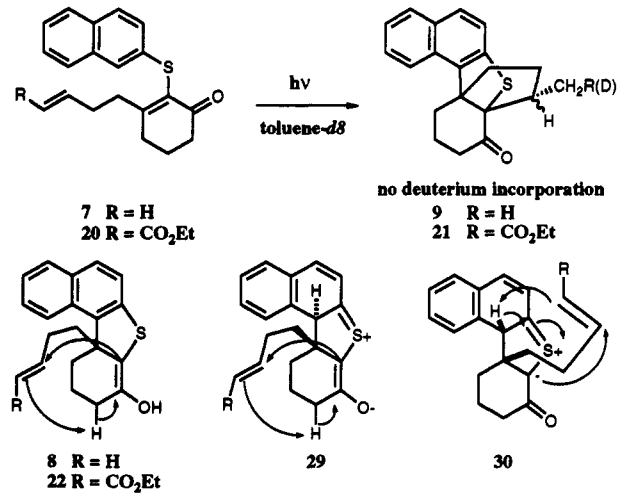
whereas aromaticity is lost in the intermediate derived from **26**.



26 **27** **28a**, $R_1 = CH_2CO_2Et$, $R_2 = H$; **b**, $R_1 = H$, $R_2 = CH_2CO_2Et$

Labeling experiments were conducted to determine a mechanism for the hydrogen abstraction which is required for the formation of **9** and **21**.[7,15] These experiments demonstrate that hydrogen abstraction does not involve the solvent. Thus, photolysis of a solution of **7** in toluene-d_8 (110 °C) provided **9** which did not show any detectable deuterium incorporation. Likewise, irradiation of a solution of **20** in toluene-d_8 (30 °C) provided **21** which was free of deuterium.

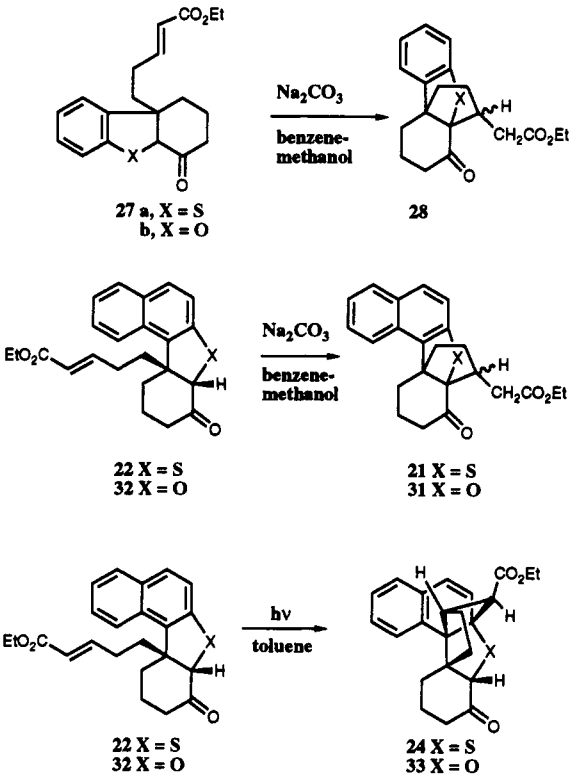
The effect of concentration on formation of **21** was also examined. Photolyses were conducted over a wide range of concentrations with no noticeable impact on product distribution. These data are consistent with a mechanism for formation of **9** and **21** which involves intramolecular hydrogen abstraction. One pathway to **9** and **21** could involve an ene reaction from the primary photoproducts **8** and **22**.[16] However, we can rule out this pathway for **8** on the basis of control experiments which demonstrate that it is stable to the reaction conditions. Also **22** is thermally stable at temperatures well above those used in the photolysis of **20** (110 °C). Other pathways include enelike rearrangements from either the trans-fused ylide **29** or the cis-fused ylide **30**. Most data on the mechanism of the heteroatom directed photoarylation reaction is consistent with the intermediacy of the trans-fused ylide.[1] However, recent studies support the presence of other transient species postulated to be the cis-fused systems.[2]



7 R = H; **20** R = CO_2Et — hν, toluene-*d8* — no deuterium incorporation — **9** R = H; **21** R = CO_2Et

8 R = H; **22** R = CO_2Et **29** **30**

In an effort to enhance the utility of the photocyclization intramolecular addition process we explored alternative conditions which provide greater control over product formation. Earlier we noted a yield improvement for formation of **22** in protic media. Similar improvements can be realized for **27** and **32**. These dihydrofuran and dihydrothiophene products can in turn be employed for the high yield preparation of intramolecular addition products such as **21** and [2 + 2] adducts such as **24**. Thus, reaction of **22**, **27**, or **32** with sodium carbonate–methanol/benzene at room temperature in the dark provides the corresponding Michael adducts **21**, **28**, and **31** in yields of ~60–90%. Conversely, photolysis of **22** or **32** in toluene at room temperature affords the corresponding [2 + 2] adducts **24** and **33** in 82% and ~76% yield, respectively.



27 a, X = S; b, X = O — Na_2CO_3, benzene-methanol — **28**

22 X = S; **32** X = O — Na_2CO_3, benzene-methanol — **21** X = S; **31** X = O

22 X = S; **32** X = O — hν, toluene — **24** X = S; **33** X = O

Summary

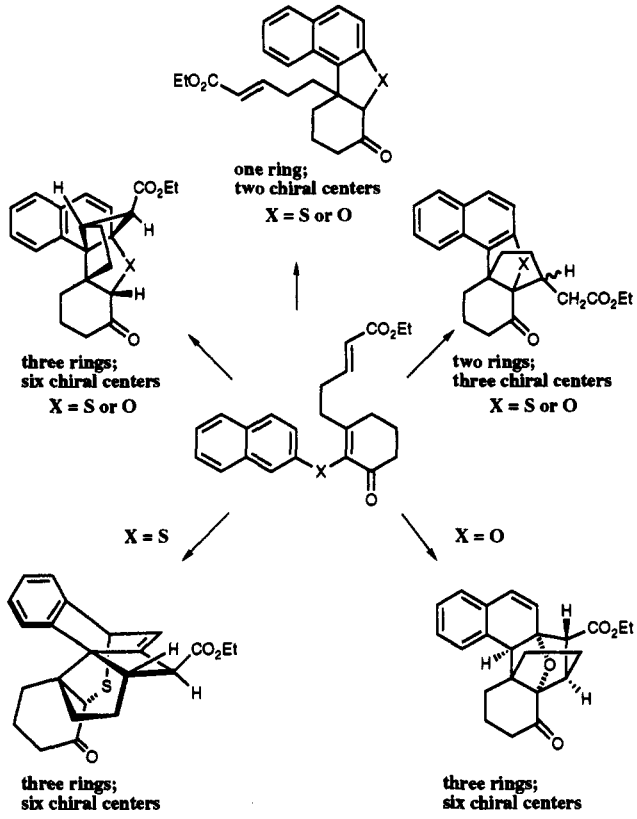
In summary, the tandem photocyclization–intramolecular addition reactions of aryl vinyl sulfides offers considerable flexibility in the formation of complex systems from relatively simple starting materials. We have demonstrated that it is possible to direct formation of one ring and two chiral centers, two rings and three chiral centers, or three rings and six chiral centers from a single starting material. In addition, sequential secondary photoprocesses which proceed in good yield and with excellent stereocontrol result in formation of three rings and six chiral centers. The products formed in each of these reactions are obtained as racemates. However, photoprecursors which incorporate a chiral auxiliary will be examined for the synthesis of optically pure materials. We are currently developing methods which we anticipate will provide even greater control over product formation, and we are exploring applications for these reactions in synthesis.

Experimental Section

General Methods. The general experimental procedures including equipment, analytical methods, and solvent and chemical purification have been reported elsewhere.[8] Unless otherwise

(15) Analyses of products from the deuterium labeling studies were carried out with a Hewlett-Packard GC–MS system consisting of a Hewlett-Packard 5990A gas chromatograph, a 25-m × 0.31-mm capillary column (Perkin-Elmer p.n. 009-23-27) comprised of bonded methyl 5% phenyl silicone (25-μm film thickness), and a Hewlett-Packard 5970B mass selective detector with 70-eV electron energy. All products were compared with products obtained in control experiments (methanol-*d* vs methanol-*h* or toluene-d_8 vs toluene-h_8). Deuterium NMR was measured on a Bruker ACE-200 spectrometer at 30.72-MHz in CH_2Cl_2 as solvent with $CDCl_3$ (δ 7.24) internal standard.

(16) For reviews see: Oppolzer, W.; Snieckus, V. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 476. Taber, D. F. *Intramolecular Diels–Alder and Alder Ene Reactions*; Springer-Verlag: Berlin, 1984.



noted, removal of solvent was carried out on a rotary evaporator at reduced pressure.

3-(3-Butenyl)-2-cyclohexenone (5a). To a mixture of magnesium turnings (0.55 g, 23 mmol) in dry THF (5 mL) under argon was added 4-bromo-1-butene (2.6 g, 19 mmol) and THF (15 mL). The mixture rapidly achieved reflux temperature. When the exothermic reaction had subsided a solution of 3-ethoxy-2-cyclohexenone (2.8 g, 20 mmol) in THF (15 mL) was added. The mixture was stirred at room temperature for 1.5 h and then cooled to 0 °C. Saturated aqueous ammonium choride solution (10 mL) was added, and the solvent was removed. The crude product was partitioned between CH_2Cl_2 and a saturated aqueous solution of oxalic acid. The aqueous phase was further washed with CH_2Cl_2, and the combined organic phases were washed with water and brine and dried (Na_2SO_4). Removal of solvent followed by distillation provided **5a** as an oil (1.75 g, 58%): bp 80–90 °C (4 mmHg); IR (film) 2940, 1670, 1625 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.95–2.2 (m, 2 H), 2.25–2.45 (m, 8 H), 4.9–5.1 (m, 2 H), 5.7–5.9 (m with overlapping singlet at 5.88, 2 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 22.4, 29.5, 30.7, 36.9, 37.1, 115.3, 125.6, 136.7, 165.3, 199.5; GC/MS (EI, 70 eV) m/e 150 (M^+), 135, 121.

6-(3-Butenyl)-7-oxabicyclo[4.1.0]heptan-2-one (6a). Enone **5a** (1.75 g, 11 mmol) was dissolved in methanol (11 mL), and hydrogen peroxide (30%, 3.2 mL) was added. The solution was cooled to 15 °C, and a solution of NaOH (6 N, 1 mL) was added slowly. The resulting mixture was stirred at room temperature for 1 h after which the solvent was removed. Product was extracted with ether–hexane (1:1), and the organic phase was washed with water and brine and was dried ($MgSO_4$). Removal of the solvent followed by distillation gave **6a** (1.72 g, 86%): bp 100 °C (5 mmHg); IR (film) 2920, 1700, 1630 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.6–2.3 (m, 9 H), 2.4–2.6 (m, 1 H), 3.1 (s, 1 H), 4.97–5.1 (m, 2 H), 5.7–5.9 (m, 1 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 17.2, 26.3, 28.8, 35.1, 35.8, 61.0, 64.9, 115.4, 137.1, 206.6; GC/MS (EI, 70 eV) m/e 166 (M^+), 137, 125, 112. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.65; H, 8.58.

3-(3-Butenyl)-2-(2-naphthalenylthio)-2-cyclohexen-1-one (7). To a 0 °C suspension of KH (35% in oil, 133 mg, 1 mmol) in dry THF (25 mL) was added 2-naphthalenethiol (480 mg, 3 mmol). After 5 min, a solution of **6a** (500 mg, 3 mmol) in THF (10 mL) was added. The mixture was stirred at room temperature for 24 h. THF was removed, and the residue was partitioned between CH_2Cl_2 and water. The organic extracts were washed with water and brine and were dried (Na_2SO_4). Removal of the solvent gave an oil which was purified by silica gel column chromatography (hexane–ethyl acetate (10:1)) to afford **7** (564 mg, 61%) as an oil which crystallized on standing: mp 72–73 °C; IR (film) 3060, 2920, 1675, 1640, 1625, 1580, 1500 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.95–2.05 (m, 2 H), 2.10–2.20 (m, 2 H), 2.50–2.60 (m, 4 H), 2.75–2.85 (m, 2 H), 4.95–5.05 (m, 2 H), 5.68–5.86 (m, 1 H), 7.2–7.7 (m, 7 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.8 (CH_2), 31.9 (CH_2), 32.4 (CH_2), 37.0 (CH_2), 38.3 (CH_2), 115.7 (CH_2), 125.1 (CH), 125.2 (CH), 125.7 (CH), 126.3 (CH), 126.8 (CH), 127.5 (CH), 128.2 (CH), 129.7 (C), 131.4 (C), 133.6 (C), 134.3 (C), 136.8 (CH), 172.1 (C), 194.3 (C=O); UV (MeOH) λ_{max} (ϵ) 217 (32 000), 250 (33 000) nm. Anal. Calcd for $C_{20}H_{20}OS$: C, 77.88; H, 6.54. Found: C, 78.08; H, 6.71.

3-(3-Butenyl)-2-(phenylthio)-2-cyclohexen-1-one (11). A solution of epoxide **6a** (1.64 g, 10 mmol) in THF (25 mL) was treated with thiophenol (1.1 g, 10 mmol) and KH (35% in oil, 75 mg, 0.65 mmol) in dry THF (75 mL) according to the procedure described for preparation of **7**. Chromatography of the resulting oil on silica gel (hexane–ethyl acetate (5:1)) provided **11** (1.28 g, 50%): IR (film) 3080, 2930, 1680, 1640, 1590, 1480 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.97–2.10 (m, 2 H), 2.20–2.31 (m, 2 H), 2.51–2.64 (m, 4 H), 2.74–2.82 (m, 2 H), 4.96–5.07 (m, 2 H), 5.68–5.90 (m, 1 H), 7.0–7.3 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.7, 31.9, 32.3, 36.9, 38.3, 115.6, 125.2, 127.0 (2 C), 128.6 (2 C), 129.6, 136.7, 172.0 (2 C), 194.3; GC/MS (EI, 70 eV) m/e 258 (M^+), 229, 147; UV (MeOH) λ_{max} (ϵ) 205 (11 000), 245 (16 000) nm. Anal. Calcd for $C_{16}H_{18}OS$: C, 74.38; H, 7.02. Found: C, 74.29; H, 7.20.

3-[2-(1,3-Dioxan-2-yl)ethyl]-2-(2-naphthalenylthio)-2-cyclohexen-1-one (18a). Epoxide **6b**[8] (2.39 g, 10.6 mmol) in THF (10 mL) was allowed to react with 2-naphthalenethiol (1.73 g, 10.8 mmol) in THF (20 mL) and 4 drops of potassium hydride (40% in mineral oil) according to the procedure described for preparation of **7**. The solvent was removed, and the residue was poured into water (50 mL) and extracted with CH_2Cl_2. The product obtained as a solid was purified by column chromatography on silica gel which had been deactivated with triethylamine (hexane–ethyl acetate (3:1)) to give **18a** (3.07 g, 79%): mp 111.5–112.5 °C; IR (film) 2930, 2860, 1680, 1620, 1575 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.23–1.30 (d, 1 H, J = 13.4 Hz), 1.65–1.95 (m, 2 H), 2.0–2.15 (m, 3 H), 2.50–2.65 (m, 4 H), 2.75–2.84 (m, 2 H), 3.59–3.72 (dt, 2 H, J = 12.2 and 2.2 Hz), 3.99–4.07 (m, 2 H), 4.46–4.51 (t, 1 H, J = 4.8 Hz), 7.2–7.7 (m, 7 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.8, 25.4, 32.1, 32.9, 38.2, 66.6 (2 C), 101.0, 124.9, 125.0, 125.5, 126.1, 126.7, 127.4, 128.1, 129.2, 131.3, 133.5, 134.2, 172.6, 194.2; GC/MS (EI, 70 eV) m/e 368 (M^+), 265, 160. Anal. Calcd for $C_{22}H_{24}O_3S$: C, 71.71; H, 6.56. Found: C, 71.59; H, 6.62.

3-[2-(1,3-Dioxan-2-yl)ethyl]-2-(phenylthio)-2-cyclohexen-1-one (18b). A solution of epoxide **6b**[8] (1.70 g, 7.5 mmol) in ethanol (2 mL) and potassium hydroxide solution (15% in EtOH, 0.11 mL) was stirred at ice-bath temperature under a nitrogen atmosphere while a solution of thiophenol (0.91 g, 8.3 mmol) in dry THF (2.5 mL) was added over 20 min. Stirring was continued at 0 °C for 8 h after which water was added. The reaction mixture was extracted with ether and benzene (1:1), the organic layer was washed with brine and dried ($MgSO_4$). Solvent was removed, and the crude product was purified by column chromatography on silica gel which had been deactivated with triethylamine (hexane–ethyl acetate (3:1)) to provide **18b** (1.87 g, 78%). The product could be purified further by recrystallization from ether and hexane to give **18b**: mp 101–102 °C; IR (film) 2940, 2830, 1668, 1570 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.22–1.32 (d, 1 H, J = 13.5 Hz), 1.66–1.84 (m, 2 H), 1.99–2.08 (m, 2 H), 2.49–2.64 (m, 5 H), 2.77 (m, 2 H), 3.64–3.75 (t, 2 H, J = 11 Hz), 4.02–4.10 (m, 2 H), 4.50 (t, 1 H, J = 5 Hz), 7.09–7.19 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 22.0, 25.6, 32.2, 32.3, 33.1, 38.5, 66.8 (2 C), 101.3, 125.3, 127.1 (2 C), 128.7 (2 C), 129.6, 136.8, 172.4, 194.4; GC/MS (EI, 70 eV) m/e 318 (M^+), 242, 218. Anal. Calcd for $C_{18}H_{22}O_3S$: C, 67.89; H, 6.97. Found: C, 67.84; H, 7.01.

2-(2-Naphthalenylthio)-3-oxo-1-cyclohexene-1-propanal (19a). A solution containing **18a** (2.5 g, 6.8 mmol) in acetic acid (80%, 100 mL) was heated at 65 °C for 16 h after which product was extracted with CH_2Cl_2. The organic phase was washed with saturated sodium bicarbonate, water, and brine and dried ($MgSO_4$). Removal of the solvent followed by chromatography on silica gel which had been deactivated with triethylamine

(hexane–ethyl acetate (2:1)) gave an oil (1.90 g, 90%) which was crystallized from ethyl acetate and hexane to provide **19a**: mp 78.0–78.5 °C; IR (film) 3040, 2940–2920, 2720, 1715, 1670 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.06–2.16 (m, 2 H), 2.56–2.72 (m, 4 H), 2.95–3.03 (m, 2 H), 7.21–7.74 (m, 7 H), 9.74 (t, 1 H, J = 2.1 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.9, 30.1, 32.5, 38.2, 41.6, 125.3, 125.4, 125.6, 126.5, 126.9, 127.6, 128.5, 130.4, 131.5, 133.6, 133.7, 170.7, 194.2, 199.9; GC/MS (EI, 70 eV) m/e 310 (M^+), 160, 153, 141, 128. Anal. Calcd for $C_{19}H_{18}O_2S$: C, 73.52; H, 5.84. Found: C, 73.34; H, 5.98.

2-(Phenylthio)-3-oxo-1-cyclohexene-1-propanal (19b). Aldehyde **19b** was prepared from **18b** (1.91 g, 60 mmol) according to the same procedure used for preparation of **19a**. The product was purified by chromatography on silica gel which had been deactivated with triethylamine (hexane–ethyl acetate (3:1)) to give **19b** (1.24 g, 79%): IR (film) 3040, 2940, 2800, 2705, 1710, 1665 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 2.05 (m, 2 H), 2.45–2.70 (m, 6 H), 2.9 (m, 2 H), 7.0–7.3 (m, 5 H), 9.7 (s, 1 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 21.9, 30.1, 32.5, 38.3, 41.7, 125.7, 127.3 (2 C), 128.9 (2 C), 130.6, 136.3, 170.3, 194.1, 200.0; GC/MS (EI, 70 eV) m/e 260 (M^+), 231, 218, 185; HRMS calcd for $C_{15}H_{16}O_2S$ 260.0871, found 260.0868.

(*E*)-5-[2-(2-Naphthalenylthio)-3-oxo-1-cyclohexen-1-yl]-2-pentenoic Acid, Ethyl Ester (20). Sodium hydride (0.076 g, 3.2 mmol) and DMSO (5.1 mL) were warmed to 55 °C and stirred for 60 min resulting in a pale green solution. To this solution was slowly added a solution of (carbethoxymethyl)triphenylphosphonium bromide (1.155 g, 2.7 mmol) in DMSO (4.1 mL). During this period the color of the solution changed to dark red and then to yellow brown. After 50 min, the mixture was transferred via cannula to a solution of aldehyde **19a** (0.56 g, 1.8 mmol) in DMSO (5.0 mL) at room temperature. The reaction mixture was stirred for 15 min and poured into water (50 mL), and the aqueous phase was extracted with ethyl acetate. The combined organic extracts were washed with water and brine and dried ($MgSO_4$). Removal of the solvent gave crude product which was purified by column chromatography on silica gel which had been deactivated with triethylamine (hexane–ethyl acetate (3:1)) to give **20** (0.53 g, 77%) as an oil: IR (film) 3115, 2920, 1710, 1665, 1640, 1610 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.25 (t, 3 H, J = 7.1 Hz), 2.07 (m, 2 H), 2.40 (q, 2 H, J = 7.0 Hz), 2.54–2.66 (m, 4 H), 2.81–2.90 (m, 2 H), 4.09–4.20 (q, 2 H, J = 7.0 Hz), 5.76–5.84 (dt, 1 H, J = 15.6 and 1.4 Hz), 6.89–6.99 (dt, 1 H, J = 15.6 and 7.0 Hz), 7.22–7.71 (m, 7 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.1, 21.8, 30.4, 32.4, 36.2, 38.3, 60.3, 122.4, 125.3, 125.4, 125.7, 126.4, 126.9, 127.6, 128.4, 130.4, 131.5, 133.6, 133.9, 146.4, 166.1, 170.6, 194.3; GC/MS (EI, 70 eV) m/e 380 (M^+), 335, 265; UV (MeOH) λ_{max} (ϵ) (48 000), 250 (41 000) nm. Anal. Calcd for $C_{23}H_{24}O_3S$: C, 72.60; H, 6.36. Found: C, 72.55; H, 6.33.

5-[3-Oxo-2-(phenylthio)-1-cyclohexen-1-yl]-2-pentenoic Acid, Ethyl Ester (26). Using the same procedure described for preparation of **20**, aldehyde **19b** (0.65 g, 2.5 mmol) was converted to **26** (0.61 g, 75%). The product was purified by chromatography on silica gel which had been deactivated with triethylamine (hexane–ethyl acetate (3:1)): IR (film) 3040, 2930, 1710, 1670 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.29 (t, 3 H, J = 7.1 Hz), 1.99–2.12 (m, 2 H), 2.33–2.44 (m, 2 H), 2.52–2.64 (m, 4 H), 2.83 (m, 2 H), 4.18 (q, 2 H, J = 7.1 Hz), 5.77–5.87 (dt, 1 H, J = 15.6 and 1.5 Hz), 6.85–7.06 (dt, 1 H, J = 15.6 and 7.0 Hz), 7.07–7.26 (m, 5 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.2, 21.9, 30.4, 32.4, 36.2, 38.4, 60.3, 122.5, 125.6, 127.3 (2 C), 128.9 (2 C), 130.5, 136.5, 146.5, 166.2, 170.3, 194.2; GC/MS (EI, 70 eV) m/e 330 (M^+), 301, 257, 218, 175; UV (MeOH) λ_{max} (ϵ) 207 (20 000), 248 (29 000) nm. Anal. Calcd for $C_{19}H_{22}O_3S$: C, 69.06; H, 6.71. Found: C, 68.76; H, 6.57.

Variable-Temperature Pyrex-Filtered Irradiations of 7. 11a-(3-Butenyl)-9,10,11,11a-tetrahydrobenzo[*b*]naphtho-[1,2-*d*]thiophen-8(7a*H*)-one (8). A solution of **7** (150 mg, 0.49 mmol) in dry toluene (150 mL) was degassed with argon and cooled to −78 °C. The solution was irradiated with a Pyrex-filtered light source[9] for 15 min during which time all of the starting material was consumed. Solvent was removed to provide **8** in quantitative yield. Product was purified by crystallization from petroleum ether and ether: mp 92–94 °C; IR (Nujol) 3050, 2940, 1700, 1640, 1620, 1585 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.8–2.6 (m, 9 H), 2.75–2.92 (m, 1 H), 4.27 (s, 1 H), 4.9 (m, 2 H), 5.8 (m, 1 H), 7.25 (d, 1 H, J = 8.5 Hz), 7.33–7.50 (m, 2 H), 7.68 (d, 1 H, J = 8.6 Hz), 7.81 (d, 1 H, J = 7.9 Hz), 7.99 (d, 1 H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 19.6 (CH_2), 28.6 (CH_2), 34.1 (CH_2), 36.1 (CH_2), 39.9 (CH_2), 60.9 (C), 61.0 (CH), 114.9 (CH_2), 120.8 (CH), 121.3 (CH), 124.3 (CH), 126.9 (CH), 129.6 (CH), 129.7 (CH), 130.4 (C), 132.5 (C), 137.7 (CH), 138.5 (C), 208.3 (C=O); GC/MS (EI, 70 eV) m/e 308 (M^+), 253, 237; UV (MeOH) λ_{max} (ϵ) 219 (32 000), 256 (47 000) nm. Anal. Calcd for $C_{20}H_{20}OS$: C, 77.88; H, 6.54. Found: C, 77.80; H, 6.43.

10,11-Dihydro-14-methyl-7a,11a-propanobenzo[*b*]-naphtho[1,2-*d*]thiophen-8(9*H*)-one (9). A solution of **7** (220 mg, 0.71 mmol) in dry toluene (150 mL) was degassed with argon for 30 min and brought to reflux temperature after which it was irradiated for 4 h. Solvent was removed and the residue was purified by chromatography on silica gel (hexane–ethyl acetate (10:1)) to provide **9** as a mixture of diastereoisomers (172 mg, 78%). The individual isomers were separable by HPLC chromatography on silica gel (hexane–ethyl acetate (16:1)).

10,11-Dihydro-14-methyl-(7aβ,11aβ,14α)-7a,11a-propanobenzo[*b*]naphtho[1,2-*d*]thiophen-8(9*H*)-one (9a): IR (Nujol) 3020, 2940, 2860, 1700, 1620, 1590 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.25 (d, 3 H, J = 6.7 Hz), 1.42–1.58 (m, 4 H), 1.59–1.87 (m, 4 H), 2.04–2.18 (m, 1 H), 2.31–2.46 (m, 1 H), 2.71–2.87 (m, 3 H), 2.99–3.12 (m, 1 H), 7.28 (d, 1 H, J = 8.6 Hz), 7.41 (t, 1 H, J = 8 Hz), 7.51 (t, 1 H, J = 8.4 Hz), 7.73 (d, 1 H, J = 8.5 Hz), 7.86 (d, 1 H, J = 8 Hz), 8.01 (d, 1 H, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 16.3 (CH_3), 19.7 (CH_2), 32.3 (CH_2), 36.0 (CH_2), 36.5 (CH_2), 40.7 (CH_2), 41.0 (CH), 68.9 (C), 76.8 (C), 119.9 (CH), 122.4 (CH), 124.0 (CH), 126.4 (CH), 129.4 (CH), 129.5 (C), 129.6 (CH), 132.7 (C), 137.4 (C), 138.2 (C), 208.9 (C=O); GC/MS (EI, 70 eV) m/e 308 (M^+), 252, 237, 223; UV (CH_3CN) λ_{max} (ϵ) 194 (41 000), 219 (32 000), 256 (51 000) nm. Anal. Calcd for $C_{20}H_{20}OS$: C, 77.88; H, 6.54. Found: C, 78.06; H, 6.41.

10,11-Dihydro-14-methyl-(7aβ,11aβ,14β)-7a,11a-propanobenzo[*b*]naphtho[1,2-*d*]thiophen-8(9*H*)-one (9b): IR (Nujol) 2920, 1700, 1620, 1590 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.3 (d, 3 H, J = 7 Hz), 1.46–1.63 (m, 1 H), 1.80–2.04 (m, 3 H), 2.14–2.25 (m, 1 H), 2.27–2.53 (m, 3 H), 2.56–2.86 (m, 3 H), 7.27 (d, 1 H, J = 8.6 Hz), 7.42 (t, 1 H, J = 7.4 Hz), 7.52 (t, 1 H, J = 7.6 Hz), 7.72 (d, 1 H, J = 8.6 Hz), 7.87 (d, 1 H, J = 7.9 Hz), 7.96 (d, 1 H, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 15.2, 18.8, 32.5, 34.8, 38.7, 39.4, 48.1, 65.9, 76.3, 120.5, 123.0, 124.0, 126.3, 129.1, 129.5, 129.6, 132.7, 135.6, 139.2, 209.5; GC/MS (EI, 70 eV) m/e 308 (M^+). Anal. Calcd for $C_{20}H_{20}OS$: C, 77.88; H, 6.54. Found: C, 77.71; H, 6.49.

Irradiation of 11. A solution of **11** (200 mg, 0.77 mmol) in dry mesitylene (200 mL) was degassed with argon. The reaction mixture was brought to reflux temperature and then irradiated with a Pyrex-filtered light source[9] for 3 h. Evaporation of the solvent and chromatography of the resulting oil on silica gel (hexane–ethyl acetate (10:1)) provided **12** (82 mg, 41%) and **13** (62 mg, 31%).

2,3-Dihydro-12-methyl-4a,9b-propanodibenzothiophen-4-(1*H*)-one (12). Obtained as a mixture of diastereoisomers which were not separated: IR (film) 3020, 2960, 2860, 1700 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.10 and 1.15 (d, total 3 H, J = 7 Hz), 1.41–3.1 (m, 10 H), 7.9–7.71 (m, 4 H); GC/MS (EI, 70 eV) m/e 258 (M^+), 230, 225; UV (MeOH) λ_{max} (ϵ) 216 (12 000) nm. Anal. Calcd for $C_{16}H_{18}OS$: C, 74.38; H, 7.02. Found: C, 74.57; H, 6.63.

9b-(3-Butenyl)-2,3,4a,9b-tetrahydro-4(1*H*)-dibenzothiophenone (13): IR (film) 3060, 2920, 2860, 1710, 1640 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.6–2.6 (m, 10 H), 4.25 (s, 1 H), 4.65–4.9 (m, 2 H), 5.55–5.65 (m, 1 H), 6.95–7.45 (m, 4 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 22.6 (CH_2), 27.0 (CH_2), 27.4 (CH_2), 30.4 (CH_2), 40.3 (CH_2), 56.6 (C), 72.1 (CH), 114.8 (CH_2), 123.6 (CH), 124.2 (CH), 124.3 (CH), 127.9 (CH), 137.7 (C), 139.5 (C), 144.9 (C), 204.6 (C=O); GC/MS (EI, 70 eV) m/e 258 (M^+), 203; UV (MeOH) λ_{max} (ϵ) 215 (14 000) nm. Anal. Calcd for $C_{16}H_{18}OS$: C, 74.38; H, 7.02. Found: C, 74.11; H, 7.22.

Variable-Temperature Pyrex-Filtered Irradiations of 20.[9] Irradiation of 20 at −78 °C. Compound **20** (98 mg, 0.25 mmol) was dissolved in dry toluene (196 mL). The reaction mixture was degassed with argon for 30 min and then irradiated for 30 min at −78 °C. Removal of the solvent provided **24**, **22**, and **21** in a ratio of 1.3:1:12.8, respectively (NMR analysis). Isolation of products was carried out as described below.

Irradiation of 20 at Room Temperature. Compound **20** (98

mg, 0.25 mmol) was dissolved in dry toluene (197 mL). The reaction mixture was degassed with argon for 30 min and then irradiated for 30 min at room temperature. Removal of the solvent gave **24**, **22**, and **21** in a ratio of 0.7:1:18, respectively (NMR analysis). Isolation of products was carried out as described below.

Irradiation of 20 at 110 °C. Compound **20** (100 mg, 0.26 mmol) was dissolved in dry toluene (200 mL). The reaction mixture was degassed with argon for 30 min and then irradiated for 30 min at 110 °C. Removal of the solvent gave **22** and **21** in a ratio of 1:61, respectively (NMR analysis). Isolation of products was carried out as described below.

Purified products **24**, **22**, and **21** obtained in each of the foregoing reactions were isolated by silica gel chromatography (carbon tetrachloride–ethyl acetate (20:1)).

8,9,10,11-Tetrahydro-8-oxo-7a,11a-propanobenzo[*b*]naphtho[1,2-*d*]thiophene-14-acetic acid, ethyl ester (21): IR (film) 3030, 2930, 2850, 1715, 1690 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.23 (t, 3 H, J = 7.1 Hz), 1.34–2.18 (m, 7 H), 2.37–2.47 (m, 2 H), 2.70–3.20 (m, 4 H), 4.13 (q, 2 H, J = 7.1 Hz), 7.20 (d, 1 H, J = 8.6 Hz), 7.37 (t, 1 H, J = 6.9 Hz), 7.47 (t, 1 H, J = 6.9 Hz), 7.7 (d, 1 H, J = 8.6 Hz), 7.82 (d, 1 H, J = 7.8 Hz), 7.95 (d, 1 H, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.1 (CH_3), 19.4 (CH_2), 29.8 (CH_2), 35.9 (CH_2), 36.3 (CH_2, 2 C), 40.3 (CH_2), 42.8 (CH), 60.1 (CH_2), 68.5 (C), 75.1 (C), 119.7 (CH), 122.2 (CH), 124.2 (CH), 126.5 (CH) 129.3 (C), 129.5 (CH, 2 C), 132.7 (C), 137.0 (C), 137.4 (C), 172.7 (C=O), 208.1 (C=O); GC/MS (70 eV) m/e 380 (M^+); UV (CH_3CN) λ_{max} (ϵ) 219 (27000), 256 (36000) nm; HRMS calcd for $C_{23}H_{24}O_3S$ 380.1446, found 380.1440.

5-(8,9,10,11-Tetrahydro-8-oxobenzo[*b*]naphtho[1,2-*d*]thien-11a(7a*H*)-yl)-2-pentenoic acid, ethyl ester (22): IR (film) 3060, 2950, 2880, 1710, 1650 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.25 (t, 3 H, J = 7.1 Hz), 1.85–3.00 (m, 10 H), 4.15 (q, 2 H, J = 7.1 Hz), 4.20 (s, 1 H), 5.70 (d, 1 H, J = 15.6 Hz), 6.84 (dt, 1 H, J = 15.7 and 6.4 Hz), 7.29 (d, 1 H, J = 8.5 Hz), 7.40 (dt, 1 H, J = 6.6 and 1.5 Hz), 7.50 (dt, 1 H, J = 6.8 and 1.5 Hz), 7.73 (d, 1 H, J = 8.5 Hz), 7.85 (d, 1 H, J = 7.8 Hz), 7.96 (d, 1 H, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.2 (CH_3), 19.5 (CH_2), 27.1 (CH_2), 34.2 (CH_2), 36.1 (CH_2), 39.1 (CH_2), 60.2 (C), 60.7 (CH_2), 61.0 (CH), 120.8 (CH), 120.9 (CH), 121.6 (CH), 124.5 (CH), 127.1 (CH), 129.8 (CH), 130.0 (CH), 130.3 (C), 132.6 (C), 134.6 (C), 138.7 (C), 147.6 (CH), 166.3 (C=O), 208.6 (C=O); GC/MS (EI, 70 eV) m/e 380 (M^+); UV (MeOH) λ_{max} (ϵ) 256 (14000), 218 (12000) nm. Anal. Calcd for $C_{23}H_{24}O_3S$: C, 72.60; H, 6.36. Found: C, 72.27; H, 6.15.

Compound 24: mp 156–157 °C; IR (film) 2870, 1730, 1705 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.25 (t, 3 H, J = 7.2 Hz), 1.75–2.70 (m, 10 H), 3.05 (m, 1 H), 3.23 (d, 1 H, J = 6.0 Hz), 4.07 (s, 1 H), 4.15 (dq, 2 H, J = 7.2 and 2.2 Hz), 5.78 (d, 1 H, J = 9.9 Hz), 6.38 (d, 1 H, J = 9.8 Hz), 6.95–7.23 (m, 4 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.4 (CH_3), 24.2 (CH_2), 29.7 (CH_2), 31.3 (CH_2), 38.4 (CH_2), 40.1 (CH_2), 46.5 (CH), 59.7 (CH), 60.2 (C), 60.8 (CH_2), 62.6 (CH), 66.4 (C), 71.8 (C), 122.7 (CH), 126.3 (CH), 126.8 (CH), 127.8 (CH), 127.9 (CH), 128.5 (CH), 131.0 (C), 136.6 (C), 171.1 (C=O), 207.7 (C=O); GC/MS (EI, 70 eV) m/e 380 (M^+); UV (MeOH) λ_{max} (ϵ) 225 (46000), 231 (39000) nm. Anal. Calcd for $C_{23}H_{24}O_3S$: C, 72.60; H, 6.36. Found: C, 72.67; H, 6.26.

Room-Temperature Irradiation of 22 with a 350-nm Light Source. A solution of **22** (4 mg, 0.01 mmol) in toluene (4 mL) was degassed with argon and irradiated with a 350-nm light source[13] for a total of 190 min during which time the progress of the reaction was monitored by ^1H NMR analysis. At 60-min irradiation time the reaction mixture consisted of starting material **22** and **24** in a ratio of 0.9:1. After 90 min the appearance of **25** was noted in the reaction mixture (**22**:**24**:**25** (0.5:1:0.4)). After 190-min irradiation time all of the starting material had been consumed and the product mixture consisted of **24** and **25** in a ratio of 1:8 by ^1H NMR analysis. Compound **25**: mp 124–126 °C; IR (KBr) 2960, 2930, 1720, 1705, 1090 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.21 (t, 3 H, J = 7.1 Hz), 1.63–2.16 (m, 8 H), 2.40–2.53 (m, 2 H), 3.44 (t, 1 H, J = 5.3 Hz), 3.73 (m, 2 H), 4.08 (q, 2 H, J = 7.1 Hz), 4.45 (d, 1 H, J = 6.7 Hz), 6.20 (dd, 1 H, J = 6.6 and 2.6 Hz), 7.11 (br s, 4 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.1 (CH_3), 22.5 (CH_2), 26.4 (CH_2), 30.3 (CH_2), 35.0 (CH_2), 39.0 (CH_2), 43.9 (C), 44.7 (CH), 45.7 (CH), 47.0 (CH), 60.9 (C), 61.0 (CH_2), 62.6 (CH), 117.8 (CH), 123.5 (CH), 125.2 (CH), 125.3 (CH), 126.2 (CH), 141.7 (C), 143.6 (C), 146.9 (C), 170.6 (C=O), 206.8 (C=O); GC/MS (EI, 70 eV) m/e 380 (M^+), 254, 253, 235; UV (MeOH) λ_{max} (ϵ) 203 (3000) nm; HRMS calcd for $C_{23}H_{24}O_3S$ 380.1446, found 380.1424.

Pyrex-Filtered Irradiation of 22 at −72 °C. A solution of **22** (14 mg, 0.04 mmol) in toluene (7 mL) was degassed with argon for 30 min, cooled to −72 °C, and irradiated with a Pyrex-filtered Hanovia light source[9] for 130 min during which time the progress of the reaction was monitored by ^1H NMR analysis. At 110 min the reaction mixture consisted of a 7:1 mixture of **25**:**24**. After 130 min the ratio of products **25**:**24** increased to 15:1. The product was subjected to chromatography on silica gel (carbon tetrachloride–ethyl acetate (20:1)) to provide **25** (11.5 mg, 82%).

Variable-Temperature Pyrex-Filtered Irradiations of 26.[9] Irradiation of 26 at −75 °C. Compound **26** (101 mg, 0.32 mmol) was dissolved in dry toluene (140 mL). The reaction mixture was degassed with argon for 30 min and was then irradiated for 3 h at −75 °C. The solvent was removed to give the dihydrothiophene **27** and product **28**. The products were isolated by chromatography on silica gel which had been deactivated with triethylamine (hexane–ethyl acetate (5:1)) to give pure **27** (42 mg, 42%) and **28** (8 mg, 8%).

Irradiation of 26 at Room Temperature. Compound **26** (140 mg, 0.44 mmol) was dissolved in dry toluene (180 mL). The reaction mixture was degassed with argon for 30 min and was then irradiated for 2.0 h at room temperature. The solvent was removed to give dihydrothiophene **27** and product **28**. The crude product was purified by chromatography on silica gel which had been deactivated with triethylamine (hexane–ethyl acetate (5:1)) to provide **27** (68 mg, 49%) and **28** (19 mg, 14%).

Irradiation of 26 at 110 °C. Compound **26** (100 mg, 0.32 mmol) was dissolved in dry toluene (130 mL). The reaction mixture was degassed with argon for 30 min and was irradiated for 4 h at 110 °C. The solvent was removed to give dihydrothiophene **27** and product **28**. The crude product was purified by silica gel chromatography which had been deactivated with triethylamine (hexane–ethyl acetate (5:1)) to give **27** (53 mg, 53%) and **28** (10 mg, 10%).

Irradiation of 26 at 160 °C. Compound **26** (100.0 mg, 0.318 mmol) was dissolved in dry mesitylene (90 mL). The reaction mixture was degassed with argon for 30 min and was then irradiated for 2.8 h at 160 °C. The solvent was removed to give dihydrothiophene **27** and product **28**. The crude product was purified by silica gel chromatography which had been deactivated with triethylamine (hexane–ethyl acetate (5:1)) to give **27** (35 mg, 35%) and **28** (34 mg, 34%).

5-(1,3,4,9a-Tetrahydro-1-oxo-4a(2*H*)-dibenzothienyl)-2-pentenoic acid, ethyl ester (27): IR (film) 3070, 2950, 2880, 1720, 1660 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.25 (t, 3 H, J = 7.1 Hz), 1.80–2.40 (m, 9 H), 2.65–2.80 (m, 1 H), 3.98 (d, 1 H, J = 1.1 Hz), 4.2 (q, 2 H, J = 7.2 Hz), 5.77 (d, 1 H, J = 15.8 Hz) 6.83–6.91 (dt, 1 H, J = 15.6 and 6.2 Hz), 6.95–7.20 (m, 4 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.2 (CH_3), 20.0 (CH_2), 27.0 (CH_2), 33.7 (CH_2), 37.1 (CH_2), 38.5 (CH_2), 57.5 (C), 60.2 (CH_2), 62.0 (CH), 121.7 (CH), 122.5 (CH), 123.5 (CH), 125.0 (CH), 128.3 (CH), 140.5 (C), 142.6 (C), 147.8 (CH), 166.4 (C=O), 208.0 (C=O); GC/MS (EI, 70 eV) m/e 330 (M^+), 302, 285, 256; UV (MeOH) λ_{max} (ϵ) 212 (25000), 246 (7000) nm. Anal. Calcd for $C_{19}H_{22}O_3S$: C, 69.06; H, 6.71. Found: C, 69.01; H, 6.64.

1,2,3,4-Tetrahydro-4-oxo-4a,9b-propanodibenzothiophene-12-acetic acid, ethyl ester (28): IR (film) 3080, 2960, 2880, 1735, 1705 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.20 (t, 3 H, J = 7.1 Hz), 1.30–2.90 (m, 13 H), 4.05 (q, 2 H, J = 7.1 Hz), 6.90–7.05 (m, 4 H); ^{13}C NMR ($CDCl_3$, 50.3 MHz) δ 14.2 (CH_3), 19.7 (CH_2), 29.8 (CH_2), 36.2 (CH_2), 36.6 (CH_2), 37.5 (CH_2), 42.4 (CH_2), 43.2 (CH), 60.3 (CH_2), 66.4 (C), 76.1 (C), 121.0 (CH), 123.6 (CH), 125.2 (CH), 128.1 (CH), 140.2 (C), 146.4 (C), 172.7 (C=O), 209.0 (C=O); GC/MS (EI, 70 eV) m/e 330 (M^+), 285, 256, 214. UV (MeOH) λ_{max} (ϵ) 211 (18000), 251 (8000) nm. Anal. Calcd for $C_{19}H_{22}O_3S$: C, 69.06; H, 6.71. Found: C, 68.82; H, 6.52.

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Supplementary Material Available: Proton NMR spectra for **19b** and **25**; carbon NMR spectra for **19b** and **21**; full details on X-ray crystallographic analyses for compounds **9a**, **24**, and **25** including tables of coordinates, anisotropic temperature factors, distances, and angles (27 pages). This material is contained in many 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.

Diastereoselection in the Lewis Acid Catalyzed Cycloaddition Reaction of α-Alkoxy Imines[1]

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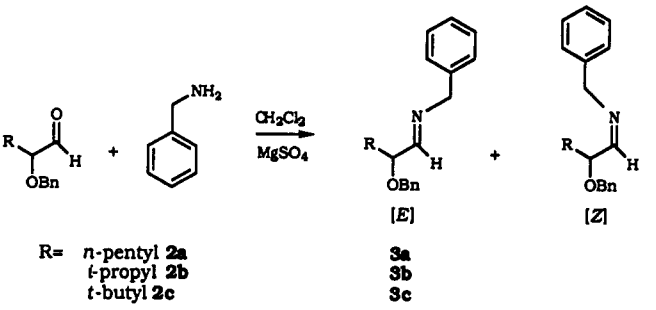
The Lewis acid catalyzed cycloaddition reactions of α-benzyloxy imines ($RCH(OCH_2C_6H_5)CH{=}NCH_2C_6H_5$) were investigated using 1,3-dimethoxy-1-[(trimethylsilyl)oxy]-1,3-butadiene. The observed diastereoselectivity was dependent on both the Lewis acid and substrate structure. Strong Lewis acids such as diethylaluminum chloride (DEAC) exhibited moderate to good success in promoting the cycloaddition reaction. When DEAC was used as the Lewis acid, the diastereoselectivity was also dependent on the stoichiometry of the Lewis acid to the substrate. In general, the diastereoselectivity increased with increasing steric bulk of the R group.

Introduction

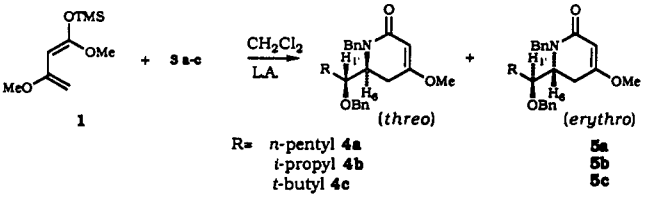
The use of heteroatom dienophiles in the Diels–Alder reaction has received much attention in recent years.[2] We have been interested in the cycloaddition reactions of α-heterosubstituted dienophiles such as α-alkoxy aldehydes,[3] α-amino aldehydes,[4] and α-alkoxy ketones.[5] The use of imines as dienophiles has also been of interest, and results using an α,β-dialkoxy imine have been reported.[6]

Cycloaddition reactions of imine and iminium species are of use in the construction of complex natural products and thus this reaction has received considerable attention.[2] Grieco has described cycloaddition reactions of iminium ion species generated under Mannich-type conditions.[7] Danishefsky has reported the Lewis acid catalyzed cycloaddition of simple alkyl imines in the synthesis of the natural product ipaldibine.[8] Ojima has observed reactions of imines with silyl ketene acetals catalyzed by titanium tetrachloride ($TiCl_4$).[9] Ojima provided evidence suggesting that the reaction proceeds by an addition–cyclization pathway rather than a cycloaddition pathway. Kunz has reported the Lewis acid mediated cycloaddition reaction of imines derived from pivaloylated sugars.[10] Kunz rationalized a "chelation-controlled" mechanism based upon the observed diastereoselectivities. The role of the group on the imine nitrogen has been the focus of recent work involving imine cycloadditions.[11] The endo/exo approach of the dienophile was influenced by the group on the imine nitrogen. The selectivity of these reactions was also dependent on whether kinetic or thermodynamic control was employed.

Scheme I



Scheme II



In our own laboratories, we have investigated the cycloaddition reactions of simple aldimines with an activated diene 1,3-dimethoxy-1-[(trimethylsilyl)oxy]-1,3-butadiene (Brassard's diene,[12] **1**).[13] The reaction proceeds efficiently when a strong Lewis acid such as diethylaluminum chloride (DEAC) or $TiCl_4$ is used. Boron trifluoride and magnesium dibromide ($MgBr_2$) were also efficient catalysts. Preliminary results also indicated that the choice of Lewis acid was important in the stereochemical outcome of cycloadditions involving α,β-dialkoxy imines.

Stereochemical results of cycloadditions using a variety of α-alkoxy imines and diene **1** are reported within. The nature of the Lewis acid in promoting the cycloaddition

(1) Taken in part from the Ph.D. Dissertation of R.W.K., University of California, Riverside, 1990.
(2) For reviews, see: Weinreb, S. M. *Chem. Rev.* **1989**, *89*, 1234. Weinreb, S. M.; Boger, D. L. *Hetero Diels-Alder Methodology in Organic Synthesis*; Academic Press: New York, 1987. Weinreb, S. M.; Staib, R. R. *Tetrahedron* **1982**, *38*, 3087.
(3) (a) Midland, M. M.; Koops, R. W. *J. Org. Chem.* **1990**, *55*, 5058. (b) Midland, M. M.; Graham, R. S. *J. Am. Chem. Soc.* **1984**, *106*, 4294. See also: (c) Danishefsky, S.; Pearson, W. H.; Harvey, D. F.; Maring, C. J.; Springer, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 1256 and references therein. (d) Sims, J. J.; Castellino, S. *Tetrahedron Lett.* **1984**, *25*, 2307.
(4) (a) Midland, M. M.; Afonso, M. M. *J. Am. Chem. Soc.* **1989**, *111*, 4368. (b) Jurczak, J.; Golebioswki, A. *Chem. Rev.* **1989**, *89*, 149. Jurczak, J. *J. Org. Chem.* **1989**, *54*, 2496.
(5) Midland, M. M.; Koops, R. W.; Carter, D. S., manuscript in preparation.
(6) Midland, M. M.; McLoughlin, J. I. *Tetrahedron Lett.* **1988**, *29*, 4653.
(7) Grieco, P. A.; Larsen, S. D. *J. Org. Chem.* **1986**, *51*, 3553. Grieco, P. A.; Larsen, S. D. *J. Am. Chem. Soc.* **1985**, *107*, 1768.
(8) Danishefsky, S.; Vogel, C. *J. Org. Chem.* **1986**, *51*, 3915.
(9) Ojima, I.; Brandstadter, S. M. *Tetrahedron Lett.* **1987**, *28*, 1067.
(10) Kunz, H.; Pfrengle, W. *J. Org. Chem.* **1989**, *54*, 4261. Kunz, H.; Pfrengle, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 1067.
(11) Wartski, L.; Seyden-Penne, J.; Veyrat-Martin, C.; Le Coz, L.; Bois, C.; Philoche-Levisalles, M. *J. Org. Chem.* **1990**, *55*, 4870.
(12) Brassard, P.; Savard, J. *Tetrahedron Lett.* **1979**, *20*, 4911.
(13) McLoughlin, J. I. Ph.D. Thesis Dissertation, University of California, Riverside, 1986.

0022-3263/92/1957-1158$03.00/0