magnesium sulfate and silica gel, and concentrated to provide **25** (100 mg, 73%) as a white solid whose TLC behavior and ^1H NMR spectrum was identical with an authentic sample.[5a]

Conversion of Nosylate 16 to Quinoxaline 27. Nosylate **16** (322 mg, 1 mmol) was dissolved in a mixture of benzene (80 mL) and triethylamine (1 mL) and stirred overnight at room temperature. (Attempts to isolate tricarbonyl **26** by flash chromatography led to extensive decomposition during chromatography and low (20-30%) yield of product.) To the reaction mixture were added *o*-phenylenediamine (200 mg, 1.85 mmol) and *p*-toluenesulfonic acid (50 mL, 0.3 mmol). A Dean-Stark apparatus was fitted to the reaction flask and the mixture was refluxed for 1 h. The reaction mixture was concentrated by rotary evaporation, and the residue was taken up in ethyl acetate (50 mL), washed with HCl (1 N, 50 mL) and then saturated sodium bicarbonate (50 mL), passed through a short pad of magnesium sulfate and silica gel, and concentrated to give **27** as a yellow oil. The crude product showed only traces of other components. Flash chromatography (hexane/ethyl acetate, 9:1) yielded **27** as a pale pink solid (160 mg, 74%) with mp 65-66 °C: IR (KBr) cm^{-1} 3040, 2970 (CH), 1720 (C=O), 1500 (C=N); ^1H NMR (200 MHz, $CDCl_3$) δ 1.50 (t, 3 H, OCH_2CH_3), 2.96 (s, 3 H, CH_3), 4.57 (q, 2 H, OCH_2CH_3), 7.75-8.3 (m, 4 H, Ar CH). Anal. Calcd for $C_{12}H_{12}N_2O_2$: C, 66.67; H, 5.56; N, 12.96. Found: C, 66.29; H, 5.55; N, 12.74.

Reduction of Nosylate 17 to Nosyl Alcohol 28. A stirred solution of 3-keto-2-nosyl ester **17** (360 mg, 1 mmol) in ethanol (10 mL) was cooled to 0 °C and sodium borohydride (40 mg, 1 mmol) was added in one portion. After stirring this mixture at 0 °C for 1 h, 1 N hydrochloric acid (5 mL) was added slowly. Most of the ethanol was removed from the reaction mixture by rotary evaporation, the aqueous residue was mixed with ethyl acetate (50 mL), and the layers were separated. The organic extract was washed with brine (50 mL), passed through a short pad of magnesium sulfate and silica gel, and evaporated to 3-hydroxy-2-nosyl ester **28** as a yellow oil. The crude product was purified by flash chromatography (hexane/ethyl acetate 4:1) to give pure **28** (260 mg, 72%) with mp 101-102 °C: IR (CH_2Cl_2 solution) cm^{-1} 3550 (OH), 3100, 2960 (CH), 1725 (C=O), 1530 (NO_2); ^1H NMR (200 MHz, $CDCl_3$) δ 0.97, 1.04 (d's, 6 H, J = 7 Hz, $CH(CH_3)_2$), 1.23 (t, 3 H, J = 6.6 Hz, OCH_2CH_3), 1.83 (m, 1 H, $CH(CH_3)_2$), 2.30 (br s, 1 H, OH), 3.70 (dd, 1 H, J = 2.8, 2.6 Hz, CHOH), 4.17 (q, 2 H, J = 6.6 Hz, OCH_2CH_3), 5.19 (d, 1 H, J = 2.8 Hz, CHONs), 8.19-8.39 (AB q, 4 H, Ar H). Anal. Calcd for $C_{14}H_{17}NO_8S$: C, 46.54; H, 5.26; N, 3.88. Found: C, 46.64; H, 5.52; N, 3.68.

On the basis of the relatively small coupling constant (J = 2.8 Hz) of the doublet at δ 5.19, the product was assigned as the syn isomer **28s**.[18] A very small doublet was observed at δ 5.09 with J = 4.8 Hz, which was assigned to the anti isomer **28a**. From the relative intensities of these two signals, the syn stereoselectivity is 97:3.

Acknowledgment. This work was supported by the National Science Foundation (87-09853). We also thank Prof. Gerald Koser for communicating his unpublished results and for helpful discussions.

Registry No. **3**, 6209-72-9; **5**, 105-45-3; **6**, 141-97-9; **7**, 7152-15-0; **8**, 22502-03-0; **9**, 1694-31-1; **10**, 94-02-0; **11**, 838-57-3; **12**, 609-14-3; **13**, 10472-24-9; **14**, 123-54-6; **15**, 124716-78-5; **16**, 124716-79-6; **17**, 124716-80-9; **18**, 124716-81-0; **19**, 124716-82-1; **20**, 124716-83-2; **21**, 124716-84-3; **22**, 124716-85-4; **23**, 124716-86-5; **24**, 124716-87-6; **25**, 98990-66-0; **26**, 1723-25-7; **27**, 3885-38-9; **28a**, 124716-77-4; **28s**, 124716-76-3; *o*-$NH_2C_6H_4NH_2$, 95-54-5.

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Intramolecular Diels-Alder Reactions of Sulfur-Substituted Dienes via 3-Sulfolenes

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Received July 27, 1989

Sulfur-substituted dienes containing an unsaturated alkyl chain were readily prepared from 3-sulfolenes. The intramolecular Diels-Alder (IMDA) reaction of these derivatives was studied for the first time. A sulfonyl group on the diene was found to facilitate the IMDA reaction. Hexahydroindenes were produced in good yield and with high stereoselectivity. Octahydronaphthalenes were also obtained, but the stereoselectivity was low and the IMDA reaction was more sensitive to steric hindrance.

The Diels-Alder reaction is one of the most useful methods in organic synthesis.[1] The intramolecular version of this reaction (IMDA) has also been widely used in the construction of polycyclic ring systems with different levels of stereocontrol.[2] The problem of using the IMDA reaction is often the efficient and selective synthesis of the required diene and dienophile within the same molecule.

It is well established that 3-sulfolenes are useful precursors to 1,3-dienes[3] and have been often used in the IMDA reaction.[4] We have been interested in the synthesis and reactions of sulfur-substituted dienes via 3-sulfolenes.[5] Although there are many examples of sulfur-substituted dienes in the intermolecular Diels-Alder reaction,[6] they

(1) Carruthers, W. *Some Modern Methods of Organic Synthesis*, 3rd ed.; Cambridge University Press: Cambridge, 1986; Chapter 3, and references therein.

(2) (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. (b) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63. (c) Taber, D. F. *Intramolecular Diels-Alder Reactions and Alder Ene Reactions*; Springer Verlag: New York, 1984. (d) Ciganek, E. *Org. React.* **1984**, *32*, 1. (e) Craig, D. *Chem. Soc. Rev.* **1987**, *16*, 238.

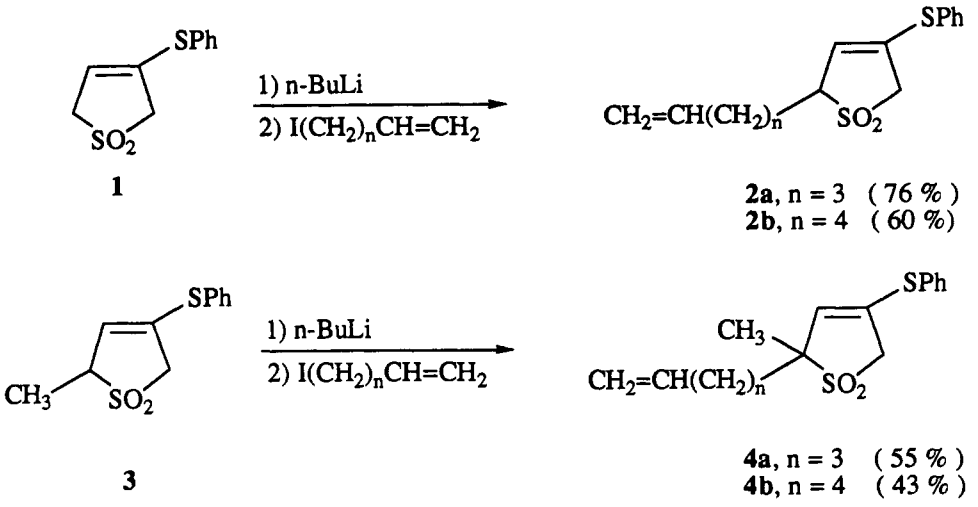
(3) Chou, T. S.; Hung, S. C. *J. Org. Chem.* **1988**, *53*, 3020, and references therein.

(4) (a) Nicolaou, K. C.; Barnette, W. E.; Ma, P. *J. Org. Chem.* **1980**, *45*, 1463. (b) Schmitthenner, H. F.; Weinreb, S. M. *J. Org. Chem.* **1980**, *45*, 3372. (c) Martin, S. F.; Tu, C.; Kimura, M.; Simonsen, S. H. *J. Org. Chem.* **1982**, *47*, 3634. (d) Nomoto, T.; Takayama, H. *Heterocycles* **1985**, *23*, 2913. (e) Chou, T. S.; Tso, H. H.; Chang, L. J. *J. Chem. Soc., Chem. Commun.* **1985**, 236. (f) Tso, H. H.; Chang, L. J.; Lin, C. L.; Chou, T. S. *J. Chin. Chem. Soc.* **1985**, *32*, 333. (g) Lee, S. J.; Chou, T. S. *J. Chem. Soc., Chem. Commun.* **1988**, 1188.

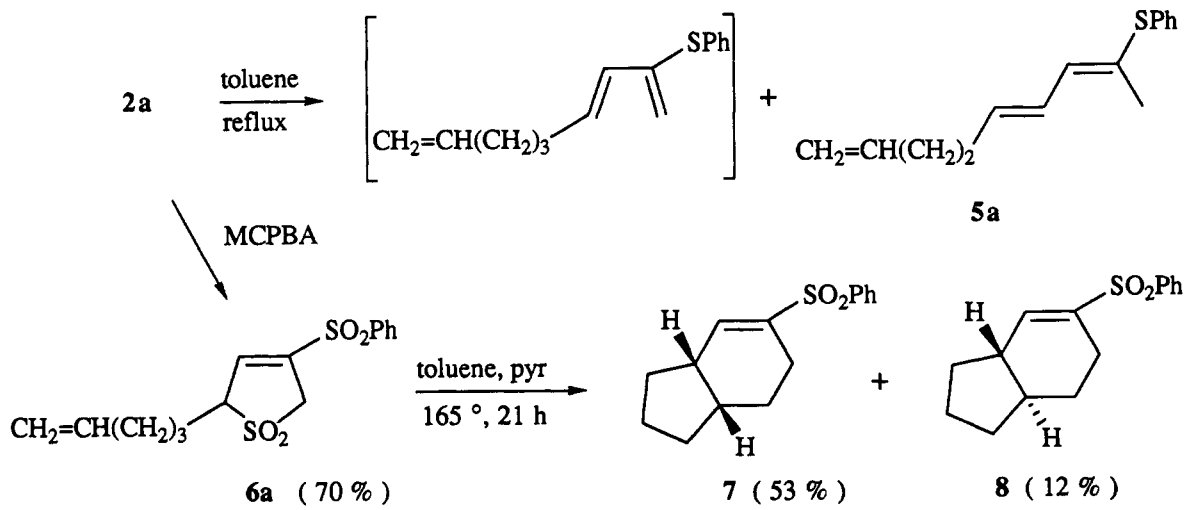
(5) (a) Chou, S. S. P.; Liou, S. Y.; Tsai, C. Y.; Wang, A. J. *J. Org. Chem.* **1987**, *52*, 4468. (b) Chou, T. S.; Lee, S. J.; Peng, M. L.; Sun, D. J.; Chou, S. S. P. *J. Org. Chem.* **1988**, *53*, 3027. (c) Chou, S. S. P.; Sun, D. J. *J. Chem. Soc., Chem. Commun.* **1988**, 1176. (d) Chou, S. S. P.; Liou, S. Y.; Tsai, C. Y. *J. Chin. Chem. Soc.* **1988**, *35*, 379. (e) Chou, S. S. P.; Tsai, C. Y. *J. Org. Chem.* **1988**, *53*, 5305. (f) Chou, S. S. P.; Sun, D. J. *J. Chin. Chem. Soc.* **1988**, *35*, 437. (g) Chou, S. S. P.; Tsai, C. Y.; Sun, C. M. *J. Chim. Chem. Soc.* **1989**, *36*, 149. (h) Chou, S. S. P.; Tsai, C. Y.; Sun, C. M. *J. Chin. Chem. Soc.* **1989**, *36*, 227.

0022-3263/90/1955-1270$02.50/0

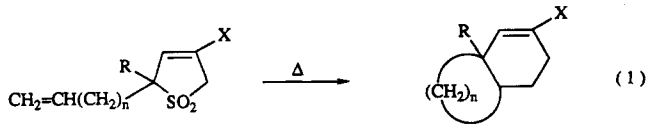
Scheme I



Scheme II



have not been used in the IMDA reaction.[7] In this paper we report the first examples of such a reaction via 3-sulfolenes (eq 1). The oxidation state of the sulfur group as well as the chain length and the substituent on the diene affect the reactivity and stereoselectivity of this reaction.



R = H, Me X = PhS, $PhSO_2$ n = 3, 4

Results and Discussion

Treatment of 3-(phenylthio)-3-sulfolene (1)[8] with *n*-BuLi (1 equiv) at −105 °C followed by the addition of 5-iodo-1-pentene or 6-iodo-1-hexene[9] gave the alkylation products **2a** and **2b**, respectively. Similar reaction with 2-methyl-4-(phenylthio)-3-sulfolene (3)[5a] gave the methylated products **4a** and **4b** (Scheme I).

Thermolysis of compound **2a** in refluxing toluene for 20 min gave only the isomerized triene **5a** as the result of a 1,5-hydrogen shift from the expected triene.[5a] Heating of **2a** at 165 °C for 21 h in the presence of pyridine (5 equiv) to remove the SO_2 generated did not give any of the Diels–Alder product either. The sulfide **2a** was then oxidized with MCPBA (2.2 equiv) to give the corresponding sulfone **6a** in the hope that the electron-withdrawing sulfonyl group would increase the reactivity of the IMDA reaction. Indeed, the thermolysis of **6a** in toluene at 165 °C for 21 h gave smoothly the Diels–Alder products **7** and **8** (cis/trans = 82:18, Scheme II). The stereochemistry of **7** and **8** was determined by the double-resonance technique and NOE study of the ^1H NMR spectra. Decoupling of the vinylic proton of **7** at δ 7.01 (t, J = 1.9 Hz) simplified the adjacent methine hydrogen (δ 2.55–2.65 (m)) as a quartet. Irradiation of this methine hydrogen resulted in a positive NOE effect for the vinylic proton, indicating the ring junction is cis. On the other hand, the vinylic proton

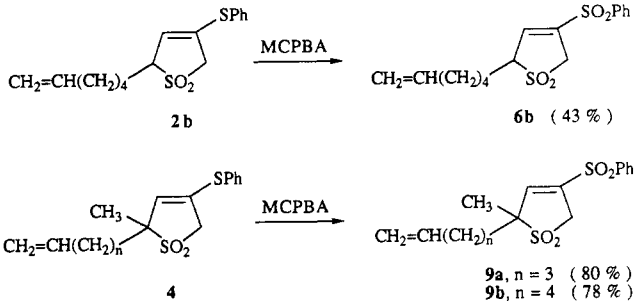
(6) (a) Petrzilka, M.; Grayson, J. I. *Synthesis* **1981**, 753. (b) Cohen, C.; Kosarych, Z. *J. Org. Chem.* **1982**, *47*, 4005. (c) Kozikowski, A. P.; Huie, E. M. *J. Am. Chem. Soc.* **1982**, *104*, 2923. (d) Overman, L. E.; Petty, C. B.; Ban, T.; Huang, G. T. *J. Am. Chem. Soc.* **1983**, *105*, 6335. (e) Bridges, A. J.; Fischer, J. W. *Tetrahedron Lett.* **1983**, *24*, 447. (f) Proteau, P. J.; Hopkins, P. B. *J. Org. Chem.* **1985**, *50*, 141. (g) Liotta, C. L.; Verbicky, Jr., J. W. *Tetrahedron Lett.* **1985**, *26*, 1395. (h) Backvall, J. E.; Juntunen, S. K. *J. Am. Chem. Soc.* **1987**, *109*, 6396. (i) Boucher, J. L.; Stella, L. *J. Chem. Soc., Chem. Commun.* **1989**, 187.

(7) The closest system we could find was that reported by Craig et al. (Craig, D.; Fischer, D. A.; Kemal, O.; Plessner, T. *Tetrahedron Lett.* **1988**, *29*, 6369), where a sulfonyl-substituted dienophile was reacted with a diene intramolecularly.

(8) (a) Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, *43*, 1208. (b) Gundermann, K. D.; Holtman, P. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 678.

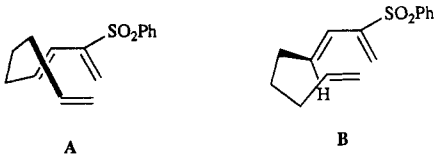
(9) These compounds were prepared from the corresponding alcohols (Aldrich Chemical Co.) by first treatment with mesyl chloride/Et_3N to give the mesylates which were reacted with sodium iodide in acetone. Both the mesylates and iodides were vacuum distilled.

Scheme III



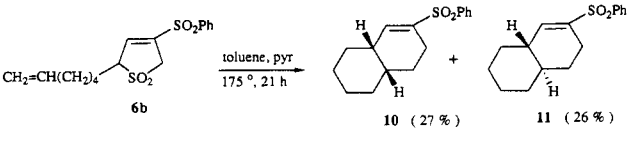
of 8 appeared as a singlet at δ 7.19. Irradiation of its adjacent methine hydrogen at δ 2.10–2.25 (m) did not give a positive NOE effect for the vinylic proton, indicating the ring junction is trans. The molecular models show clearly that the vinylic proton and the adjacent methine hydrogen of the trans isomer **8** are farther away from each other than those of the cis isomer **7**, so that only the latter would give rise to a positive NOE effect. The larger coupling constant for the vinylic proton of the cis isomer **7** than that of the trans isomer **8** also attests to the ring configuration.[10]

The above results indicate that the oxidation state of the sulfur group on the diene has a strong effect on the rate of 1,5-hydrogen shift as well as the success of the IMDA reaction. In comparison with the unsubstituted case where Houk et al.[11] reported that 1,3,8-nonatriene upon heating at 162 °C for 90 h gave only a 45% yield of the cyclization product (cis/trans = 76:24), it can be seen that the phenylsulfonyl group activates the diene toward the dienophile in the IMDA reaction. This enhanced reactivity of sulfonylated diene could be due to the more favorable LUMO (diene)–HOMO (dienophile) interaction which was found by Alston et al.[12] to be significant in determining the regioselectivity of some thio-substituted 1,3-butadienes in the intermolecular Diels–Alder reaction. The preference for the cis transition state A is probably due to the disfavored interaction of the connecting chain with the vinylic hydrogen at C4 in the trans transition state B.[13]

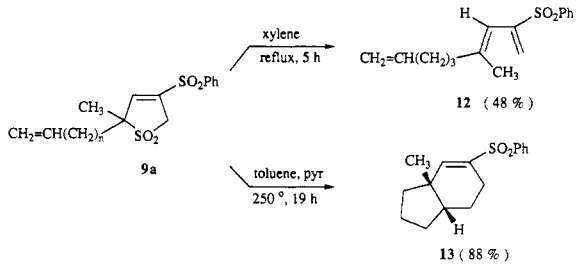


Since the phenylsulfonyl group is more effective than the phenylthio group in activating the diene for the IMDA reaction (vide supra), sulfides **2b**, **4a**, and **4b** were all oxidized by MCPBA (2.2 equiv) to the corresponding sulfones **6b**, **9a**, and **9b** (Scheme III).

Thermolysis of **6b** in toluene at 175 °C for 21 h gave the cis and trans cyclization products **10** and **11** in 27% and 26% yield, respectively. The stereochemistry of **10** and **11** was also determined by the double-resonance technique and NOE study of the ^{1}H NMR spectra. Decoupling of the vinylic proton of **10** at δ 6.88 (t, J = 1.3 Hz) simplified the adjacent methine hydrogen (δ 2.35–2.45 (m)) to appear as a doublet of doublets. Irradiation of this methine hydrogen resulted in a positive NOE effect for the vinylic proton, indicating the ring junction is cis. On the other hand, the vinylic proton of **11** appeared as a singlet at δ 6.83. Irradiation of its adjacent methine hydrogen at δ 2.05–2.15 (m) did not give a positive NOE effect for the vinylic proton, indicating the ring junction is trans. The larger coupling constant for the vinylic proton of the cis isomer **10** than that of the trans isomer **11** is also consistent with the assigned ring configuration.[10] Formation of the octahydronaphthalene system for **6b** required a higher temperature than that for the hexahydroindene system from **6a**, and a much closer ratio of cis/trans isomers was obtained. In the IMDA reaction of unsubstituted 1,3,9-decatriene system, the cis product was only slightly more favored than the trans product.[11]

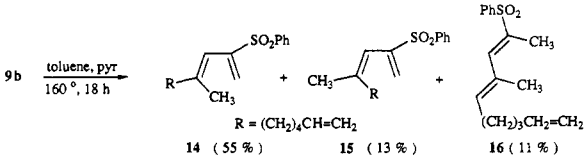


Thermolysis of **9a** in xylene at reflux for 5 h gave the diene **12** together with some cyclization product **13**. The



diene **12** was found by NOE study of its ^{1}H NMR spectrum to be exclusively the *E* isomer. When **9a** was heated in toluene in a sealed tube at 250 °C for 19 h, the cyclization product **13** was obtained in 88% yield. The stereochemistry of **13** was determined by using the COSY/NOESY technique of its 2D ^{1}H NMR spectrum. The two allylic protons appeared at δ 2.02 (triplet of doublets, J = 5.66, 1.67 Hz). The adjacent methylene protons and the methine hydrogen were then identified as appearing at δ 1.67 and 1.76, respectively. The NOESY spectrum showed a positive NOE effect for the angular methyl group and the methine hydrogen, indicating the ring junction is cis. The exclusive formation of the cis product **13** is also consistent with the argument for the IMDA reaction of **6a** (vide supra). The extra methyl group in the diene **12** should cause a very severe interaction with the exo alkyl chain in the trans transition state.

Thermolysis of **9b** in toluene in the presence of pyridine (5 equiv) at 160 °C for 18 h did not give any of the cyclization product. Instead, a mixture of dienes **14**, **15**, and **16** was obtained. Heating **9b** at 250 °C for 24 h gave only



14 (30%) and **15** (30%). Compound **16** was a product of a 1,5-hydrogen shift from **15**, which itself was obtained from the double-bonded isomerization of diene **14**. Apparently, the extra methyl group in **14** slowed down the IMDA reaction to the extent that isomerization of the diene as well as the hydrogen shift predominate. Inspection of the molecular model of **9b** indicated that in the

(10) Inspection of the molecular models shows that in the preferred conformation of the trans isomer the vinylic proton is almost perpendicular to the adjacent methine hydrogen and the allylic hydrogens, whereas in the preferred conformation of the cis isomer the vinylic proton is coupled with the adjacent methine hydrogen and one of the allylic hydrogens through a W-shaped interaction.

(11) Lin, Y. T.; Houk, K. N. *Tetrahedron Lett.* **1985**, *26*, 2269.

(12) Alston, P. V.; Gordon, M. D.; Ottenbrite, R. M.; Cohen, T. *J. Org. Chem.* **1983**, *48*, 5051.

(13) Brown, F. K.; Houk, K. N. *Tetrahedron Lett.* **1985**, *26*, 2297.

trans transition state the interaction of the methyl group with the connecting chain would be very severe, whereas in the cis transition state the repulsion between the C3 hydrogen and the C5 methylene group would also be quite serious. Thus, the IMDA reaction of **9b** was not observed.

In summary, the sulfur-substituted dienes containing an unsaturated alkyl chain can be readily prepared from 3-sulfolenes. The reactivity and stereoselectivity of the intramolecular Diels–Alder reaction of these dienes depend on the oxidation state of the sulfur group as well as the chain length and the substituent on the diene. Hexahydroindenes can be obtained in good yield and with high stereoselectivity, especially when there is an angular methyl group present. Octahydronaphthalenes can also be obtained, but the stereoselectivity is low and the reaction is more sensitive to steric hindrance. The products obtained from these reactions contain the functional group of vinylic sulfone, which should be useful for further synthetic transformations.[14]

Experimental Section

Infrared spectra were recorded with an Analect RFX-65 FTIR spectrometer. ^{1}H NMR spectra were taken in deuteriochloroform with a Varian-360L spectrometer or a Bruker AM-400 or AM-300 FT NMR spectrometer, with tetramethylsilane as the internal standard. Mass spectra were recorded with a JEOL JMS-D-100 or a Finnigan MAT TSQ-46C spectrometer. High-resolution mass spectra (HRMS) were taken with a JEOL JMS-D-300 mass spectrometer. Elemental analyses were taken with a Perkin-Elmer 240C analyzer. High-performance liquid chromatography (HPLC) was carried out with a Shimadzu LC-6A chromatograph using LiChrosorb (Merck) as the column. Melting points were taken with a Mel-Temp apparatus and were uncorrected. The sealed tube used for thermolysis was made by Ace Glass (catalog no. 8648-23). The silica gel used for flash column chromatography was made by Merck (60H). All reagents were of reagent grade and were purified prior to use.

2-(4-Pentenyl)-4-(phenylthio)-3-sulfolene (2a). To a solution of 3-(phenylthio)-3-sulfolene[8] (1, 0.83 g, 3.68 mmol) in THF (35 mL) and HMPA (2.6 mL, 4 equiv) at −105 °C was added dropwise a solution of *n*-BuLi in hexane (1.45 M, 2.5 mL, 3.63 mmol). This solution was slowly warmed to −90 °C, and 5-iodo-1-pentene[9] (1.57 g, 8.0 mmol) was then added in one portion. The reaction mixture was poured into saturated ammonium chloride solution at −50 °C, extracted with CH_2Cl_2, dried ($MgSO_4$), and evaporated. The crude product was purified by flash column chromatography using hexane/ethyl acetate (4:1) as eluent to give **2a** (0.82 g, 76%): IR (neat) 3073, 3062, 2977, 2929, 1440, 1311, 1216, 1128, 914, 750, 692 cm^{-1}; ^{1}H NMR (60 MHz) δ 1.4–2.4 (6 H, m), 3.6–4.0 (3 H, m), 4.8–5.2 (2 H, m), 5.5–6.1 (2 H, m), 7.5 (5 H, br s); mass spectrum (rel intensity), m/z 294 (M$^+$, 1), 230 (100), 189 (42), 121 (50); exact mass calcd for $C_{15}H_{18}O_2S_2$ m/z 294.0748, found 294.0735.

2-(5-Hexenyl)-4-(phenylthio)-3-sulfolene (2b). The procedure was similar to that for **2a** except that the reaction was quenched at −35 °C, and hexane/ethyl acetate (6:1) was the eluent; IR (neat) 3073, 2975, 2929, 2859, 1639, 1581, 1447, 1440, 1313, 1218, 1128, 748, 701, 692 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.3–1.7 (5 H, m), 1.85–2.1 (3 H, m), 3.65–3.85 (3 H, m), 4.85–5.05 (2 H, m), 5.65–5.85 (2 H, m), 7.35–7.5 (5 H, m); mass spectrum (rel intensity), m/z 308 (M$^+$, 20), 135 (100); exact mass calcd for $C_{16}H_{20}O_2S_2$ m/z 308.0905, found 308.0910.

2-Methyl-2-(4-pentenyl)-4-(phenylthio)-3-sulfolene (4a). The procedure was similar to that used for **2b** except that **3**[5a] and 6-iodo-1-hexene[9] were used as the starting material, and the reaction was quenched at −78 °C; IR (neat), 2937, 1440, 1309, 1120, 916, 744, 692 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.36 (3 H, s), 1.4–1.6 (2 H, m), 1.7–1.9 (2 H, m), 2.02 (2 H, q, J = 5.3 Hz), 3.62 (2 H, d, J = 0.84 Hz), 4.95–5.05 (2 H, m), 5.7–5.85 (2 H, m), 7.3–7.4 (5 H, m); mass spectrum (rel intensity), m/z 308 (M$^+$, 15), 244 (90), 202 (85), 135 (100); exact mass calcd for $C_{16}H_{20}O_2S_2$ m/z 308.0904, found 308.0901.

2-Methyl-2-(5-hexenyl)-4-(phenylthio)-3-sulfolene (4b). The procedure was similar to that for **4a** except that the eluent was hexane/ethyl acetate (4:1), IR (neat) 2975, 2935, 1477, 1440, 1309, 1122, 912, 748, 692 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.40 (3 H, s), 1.35–1.55 (4 H, m), 1.7–1.85 (2 H, m), 2.0–2.15 (2 H, m), 3.66 (2 H, d, J = 1.73 Hz), 4.9–5.05 (2 H, m), 5.65–5.85 (2 H, m), 7.3–7.4 (5 H, m); mass spectrum (rel intensity), m/z 322 (M$^+$, 75), 258 (46), 243 (86), 181 (54), 149 (100); exact mass calcd for $C_{17}H_{22}O_2S_2$ m/z 322.1061, found 322.1069.

2-(4-Pentenyl)-4-(phenylsulfonyl)-3-sulfolene (6a). To a solution of **2a** (104 mg, 0.35 mmol) in CH_2Cl_2 (5 mL) in an ice bath was added dropwise a solution of MCPBA (158 mg, 0.78 mmol) in CH_2Cl_2 (3 mL). The mixture was stirred for 1 h, washed with 5% $NaHCO_3$, dried ($MgSO_4$), and evaporated. The crude product was purified by flash column chromatography using hexane/ethyl acetate (2:1) as eluent to give **6a** (81 mg, 70%): mp 87–89 °C; IR (KBr) 3066, 2979, 2931, 1448, 1322, 1155, 734, 597, 565 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.5–1.8 (3 H, m), 1.95–2.05 (1 H, m), 2.12 (2 H, q, J = 6.9 Hz), 3.82 (2 H, t, J = 1.6 Hz), 3.9–4.0 (1 H, m), 4.95–5.05 (2 H, m), 5.65–5.85 (1 H, m), 6.98 (1 H, q, J = 2.1 Hz), 7.59 (2 H, t, J = 7.6 Hz), 7.70 (1 H, t, J = 7.4 Hz), 7.85 (2 H, d, J = 7.4 Hz); mass spectrum (rel intensity), m/z 262 (M$^+$ − 64, 8), 120 (100). Anal. Calcd for $C_{15}H_{18}O_4S_2$: C, 55.19; H, 5.56. Found: C, 55.14; H, 5.53.

2-(5-Hexenyl)-4-(phenylsulfonyl)-3-sulfolene (6b). The procedure was similar to that for **6a**; mp 51–53 °C; IR (KBr) 3066, 2977, 2931, 1859, 1448, 1322, 1155, 1132, 734, 597, 565 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.45–1.6 (4 H, m), 1.6–1.75 (1 H, m), 1.9–2.1 (3 H, m), 3.76 (2 H, t, J = 1.5 Hz), 3.89 (1 H, Δ, J = 7.2, 2.0 Hz), 4.85–5.05 (2 H, m), 5.65–5.8 (1 H, m), 6.93 (1 H, q, J = 2.1 Hz), 7.5–7.6 (2 H, m), 7.6–7.7 (1 H, m), 7.8–7.9 (2 H, m); mass spectrum (rel intensity), m/z 276 (M$^+$ − 64, 2), 135 (17), 119 (76), 93 (100). Anal. Calcd for $C_{16}H_{20}O_4S_2$: C, 56.45; H, 5.92. Found: C, 56.66; H, 5.94.

***cis*-6-(Phenylsulfonyl)-2,3,4,5,3a,7a-hexahydroindene (7) and *trans*-6-(Phenylsulfonyl)-2,3,4,5,3a,7a-hexahydroindene (8).** A solution of **6a** (80 mg, 0.30 mmol) in toluene (3 mL) and pyridine (0.1 mL) was heated in a sealed tube at 165 °C for 21 h. The solvent was removed by a rotary evaporator, and the crude product was purified by flash column chromatography using hexane/ethyl acetate (10:1) as eluent to give **7** (40 mg, 53%) and **8** (10 mg, 12%). **7**: IR (neat) 2940, 2867, 1446, 1303, 1290, 1151, 1091, 719, 690, 644, 574 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.2–1.4 (3 H, m), 1.45–1.65 (3 H, m), 1.65–1.8 (1 H, m), 1.9–2.05 (3 H, m), 2.1–2.2 (1 H, m), 2.55–2.65 (1 H, m), 7.01 (1 H, t, J = 1.9 Hz), 7.45–7.55 (2 H, m), 7.55–7.6 (1 H, m), 7.8–7.9 (2 H, m); mass spectrum (rel intensity), m/z 262 (M$^+$, 100), 137 (22), 121 (83), 120 (63); exact mass calcd for $C_{15}H_{18}O_2S$ m/z 262.1028, found 262.1020. **8**: IR (neat) 2940, 2867, 1446, 1303, 1151, 721, 690, 638, 561 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.0–1.2 (1 H, m), 1.2–1.4 (3 H, m), 1.6–1.8 (3 H, m), 1.8–2.0 (3 H, m), 2.1–2.25 (1 H, m), 2.25–2.4 (1 H, m), 7.20 (1 H, s), 7.45–7.5 (2 H, m), 7.5–7.55 (1 H, m), 7.75–7.85 (2 H, m); mass spectrum (rel intensity), m/z 262 (M$^+$, 100), 137 (29), 121 (75), 120 (71); exact mass calcd for $C_{15}H_{18}O_2S$ m/z 262.1028, found 262.1031.

2-Methyl-2-(4-pentenyl)-4-(phenylsulfonyl)-3-sulfolene (9a). The procedure was similar to that for **6a** except that the reaction mixture was stirred for 1.5 h and was eluted with hexane/ethyl acetate (3:1), mp 122–123 °C; IR (KBr) 3015, 2981, 2933, 1446, 1303, 1149, 736, 568 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.44 (3 H, s), 1.45–1.55 (2 H, m), 1.75–1.95 (2 H, m), 2.03 (2 H, q, J = 11 Hz), 3.73 (2 H, d, J = 1.35 Hz), 4.95–5.05 (2 H, m), 5.65–5.8 (1 H, m), 6.90 (1 H, t, J = 1.7 Hz), 7.55–7.65 (2 H, m), 7.65–7.75 (1 H, m), 7.8–7.9 (2 H, m); mass spectrum (rel intensity), m/z 276 (M$^+$ − 64, 36), 135 (100), 93 (62). Anal. Calcd for $C_{16}H_{20}O_4S_2$: C, 56.45; H, 5.92. Found: C, 56.40; H, 5.91.

2-Methyl-2-(5-hexenyl)-4-(phenylsulfonyl)-3-sulfolene (9b). The procedure was the same as that for **9a**; mp 102–104 °C; IR (KBr) 3073, 2983, 2933, 1448, 1309, 1151, 916, 757, 738, 688, 568 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.43 (3 H, *s*), 1.35–1.5 (4 H, m), 1.75–1.95 (2 H, m), 2.0–2.15 (2 H, m), 3.73 (2 H, t, J = 1.8 Hz), 4.9–5.05 (2 H, m), 5.65–5.8 (1 H, m), 6.65 (1 H, t, J = 1.7 Hz) 7.55–7.65 (2 H, m), 7.65–7.75 (1 H, m), 7.8–7.9 (2 H, m); mass

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spectrum (rel intensity), m/z 290 ($M^+ - 64$, 1), 149 (68), 133 (43), 107 (94), 93 (100). Anal. Calcd for $C_{17}H_{22}O_4S_2$: C, 57.60; H, 6.26. Found; C, 57.63; H, 6.26.

***cis*-7-(Phenylsulfonyl)-1,2,3,4,5,6,4a,8a-octahydronaphthalene (10) and *trans*-7-(Phenylsulfonyl)-1,2,3,4,5,6,4a,8a-octahydronaphthalene (11).** A solution of **6b** (87 mg, 2.56 mmol) in toluene (2 mL) and pyridine (0.1 mL) was heated in a sealed tube at 175 °C for 21 h. The workup procedure was the same as that for the preparation of **7** and **8** to give **10** (19 mg, 27%) and **11** (18 mg, 26%). **10**: IR (neat) 2927, 2856, 1446, 1301, 1151, 1089, 690, 584, 563 cm^{-1}; ^1H NMR (400 MHz) δ 1.15–1.75 (1 H, m), 2.0–2.2 (2 H, m), 2.35–2.45 (1 H, m), 6.88 (1 H, t, J = 1.3 Hz), 7.46 (2 H, t, J = 7.6 Hz), 7.53 (1 H, t, J = 7.4 Hz), 7.79 (2 H, d, J = 7.5 Hz); mass spectrum (rel intensity), m/z 276 (M^+, 41), 274 (45), 167 (31), 151 (72), 135 (100); exact mass calcd for $C_{16}H_{20}O_2S$ m/z 276.1184, found 276.1180. **11**: IR (neat) 2925, 2854, 1315, 1301, 1151, 1089, 584, 563 cm^{-1}; ^1H NMR (400 MHz) δ 0.9–1.4 (6 H, m), 1.55–1.85 (6 H, m), 2.05–2.25 (2 H, m), 6.83 (1 H, s), 7.46 (2 H, t, J = 7.6 Hz), 7.54 (1 H, t, J = 7.3 Hz), 7.79 (2 H, d, J = 7.3 Hz); mass spectrum (rel intensity), m/z 276 (M^+, 24), 274 (61), 167 (20), 151 (26), 135 (100); exact mass calcd for $C_{16}H_{20}O_2S$ m/z 276.1184, found 276.1178.

(*E*)-4-Methyl-2-(phenylsulfonyl)-1,3,8-nonatriene (12). A solution of **9a** (70 mg, 0.21 mmol) in *p*-xylene (10 mL) was heated at reflux for 5 h. The solvent was removed by a rotary evaporator, and the crude product was purified by flash column chromatography using hexane/ethyl acetate (6:1) as eluent to give **12** (23 mg, 48%) and **13** (6 mg, 11%). **12**: IR (neat) 2933, 1446, 1313, 1305, 1157, 1133, 1081, 746, 688 cm^{-1}; ^1H NMR (400 MHz) δ 1.44 (3 H, s), 1.3–1.4 (2 H, m), 1.92 (2 H, q, J = 7.3 Hz), 2.03 (2 H, t, J = 7.4 Hz), 4.85–4.95 (2 H, m), 5.6–5.75 (1 H, m), 5.69 (1 H, d, J = 1.3 Hz), 5.78 (1 H, s), 6.51 (1 H, s), 7.4–7.5 (2 H, m), 7.5–7.55 (1 H, m), 7.7–7.8 (2 H, m); the NOE experiment showed that irradiation at δ 1.44, 2.03, and 6.51 resulted in enhancements at δ 5.68, 5.78, and 5.68, respectively; mass spectrum (rel intensity), m/z 276 (M^+, 18), 135 (100), 93 (68); exact mass calcd for $C_{16}H_{20}O_2S$ m/z 276.1184, found 276.1191.

***cis*-7a-Methyl-6-(phenylsulfonyl)-2,3,4,5,4a,7a-hexahydroindene (13).** A solution of **9a** (14 mg, 0.041 mmol) in toluene (2 mL) and pyridine (0.1 mL) was heated in a sealed tube at 250 °C for 19 h. The crude product was purified by HPLC using hexane/ethyl acetate (10:1) as eluent to give **13** (10 mg, 88%): mp 66–67 °C; IR (KBr) 2950, 1446, 1303, 1149, 690, 570 cm^{-1}; ^1H NMR (300 MHz) δ 1.06 (3 H, s), 1.23–1.35 (1 H, m), 1.40–1.50 (1 H, m), 1.50–1.66 (5 H, m), 1.66–1.80 (2 H, m), 2.02 (2 H, td, J = 5.66, 1.67 Hz), 6.68 (1 H, s), 7.45–7.65 (3 H, m), 7.8–7.85 (2 H, m); mass spectrum (rel intensity), m/z 276 (M^+, 9), 135 (46), 108 (100); exact mass calcd for $C_{16}H_{20}O_2S$ m/z 276.1184, found 276.1187.

(*E*)-4-Methyl-2-(phenylsulfonyl)-1,3,9-decatriene (14), (*Z*)-4-Methyl-2-(phenylsulfonyl)-1,3,9-decatriene (15), and (2*E*,4*E*)-4-Methyl-2-(phenylsulfonyl)-2,4,9-decatriene (16). A solution of **9b** (67 mg, 0.19 mmol) in toluene (2 mL) and pyridine (0.1 mL) was heated in a sealed tube at 160 °C for 18 h. The crude product was purified by HPLC using hexane/ethyl acetate (10:1) as eluent to give **14** (30 mg, 55%), **15** (7 mg, 13%), and **16** (6 mg, 11%). **14**: IR (neat) 2933, 1446, 1315, 1305, 1160, 1133, 1081, 748, 688 cm^{-1}; ^1H NMR (300 MHz) δ 1.15–1.4 (4 H, m), 1.40 (3 H, d, J = 1.2 Hz), 1.95–2.05 (4 H, m), 4.9–5.0 (2 H, m), 5.65 (1 H, d, J = 1.6 Hz), 5.65–5.8 (2 H, m), 6.48 (1 H, s), 7.4–7.5 (2 H, m), 7.5–7.6 (1 H, m), 7.75–7.85 (2 H, m); the NOE experiment showed that irradiation at δ 2.0 and 5.65 resulted in enhancements for δ 6.8 and 6.47, respectively; mass spectrum (rel intensity), 290 (M^+, 13), 149 (100); exact mass calcd for $C_{17}H_{22}O_2S$ m/z 290.1341, found 290.1336. **15**: ^1H NMR (300 MHz) δ 1.0–1.15 (4 H, m), 1.71 (3 H, d, J = 0.8 Hz), 1.75–1.95 (4 H, m), 4.85–5.0 (2 H, m), 5.62 (1 H, d, J = 1.7 Hz), 5.6–5.8 (1 H, m), 5.76 (1 H, s), 6.44 (1 H, s), 7.75–7.85 (2 H, m); the NOE experiment showed that irradiation at δ 1.7, 5.6, and 6.4 resulted in enhancements at δ 5.76, 6.4, and 5.6, respectively. **16**: ^1H NMR (300 MHz) δ 1.4–1.55 (2 H, m), 1.77 (3 H, s), 1.94 (3 H, s), 2.0–2.2 (4 H, m), 4.9–5.05 (2 H, m), 5.65–5.85 (2 H, m), 7.19 (1 H, s), 7.45–7.65 (3 H, m), 7.8–7.9 (2 H, m).

Acknowledgment. Financial support of this work by the National Science Council of the Republic of China is gratefully acknowledged.

Registry No. 1, 64741-13-5; **2a**, 124243-68-1; **2b**, 124243-69-2; 3, 104664-79-1; **4a**, 124243-70-5; **4b**, 124243-71-6; **6a**, 124266-43-9; **6b**, 124243-72-7; **7**, 124243-73-8; **8**, 124243-74-9; **9a**, 124266-44-0; **9b**, 124266-45-1; **10**, 124243-75-0; **11**, 124243-76-1; **12**, 124243-77-2; **13**, 124243-78-3; **14**, 124243-79-4; **15**, 124243-80-7; **16**, 124243-81-8; $CH_2{=}CH(CH_2)_3I$, 7766-48-5; $CH_2{=}CH(CH_2)_4I$, 18922-04-8.

Application of NMR Techniques to the Structural Elucidation of Isomeric Phenolic Biphenyls

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Received August 4, 1989

3-Hydroxy-4-methoxybiphenyl has been synthesized and its structure confirmed by using NMR techniques. Complete ^{13}C NMR assignments of the biphenyl system were made by using a long-range HETCOR spectrum. The position of the hydroxy versus methoxy substituent was then established by using the long-range HETCOR spectrum, ^{13}C spin-lattice relaxation measurements, deuterium-induced ^{13}C chemical shift effects, and NOE difference spectroscopy.

Phenolic biphenyl compounds are natural products commonly observed as metabolites of biphenyl.[1] In many such substances, some of the phenolic hydroxyl groups are substituted, and O-methylation is often observed. In establishing the structures of partially O-methylated phenolic biphenyl compounds, ^{13}C NMR spectroscopy is a valuable and much used tool. However, signal assignment between hydroxylated and O-methylated carbons based on shift value calculations is often ambiguous since the substituent effects of OH and OCH_3 groups are comparable.[2] It was therefore necessary to develop NMR techniques to differentiate these carbons so that complete NMR assignments and therefore structure assignments could be made. The techniques used included 2D long-range heteronuclear correlated spectroscopy (HETCOR), spin-lattice relaxation

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