Table I

concntrn (ppm)	synthetic antheridic acid[a]	natural antheridic acid[a]
0.5	95.8 ± 1.4	95.7 ± 1.1
0.05	83.4 ± 3.7	87.8 ± 1.9
0.005	4.9 ± 1.1	5.6 ± 1.2
0.0005	0	0
0 (blank)	0	

[a] Each value is the average percent germination from four replicates.

(1 H, dd, $J_{3,2}$ = 11.16 Hz, $J_{3,2'}$ = 5.19 Hz, H3), 3.31 (1 H, dd, $J_{6,5}$ = 9.38 Hz, $J_{6,14}$ = 2.74 Hz, H6), 3.16 (1 H, dt, $J_{13,14}$ = 6.41 Hz, $J_{13,12}$ = ca. 3 Hz), 3.5-3.0 (1 H, s, br, CO_2H), 2.85 (1 H, d, $J_{5,6}$ = 9.38 Hz, H5), 2.4-2.0 (4 H, m), 1.74-1.26 (6 H, m), 1.19 (3 H, s, H18); ^{13}C NMR (75 MHz, acetone-d_6) 176.39, 173.65, 155.25, 146.01, 127.24, 110.21, 93.66, 74.25, 73.91, 61.17, 57.00, 55.37, 49.00, 42.73,[40] 28.45, 26.38, 21.83, 14.44; capillary GC-LRMS [tri-TMS derivative] 562 (M^+), 547, 534, 416, 400, 367, 129; HRMS 562.2606, $C_{28}H_{46}O_6Si_3$ (M^+) requires 562.2602.

Bioassay (induction of dark germination): Approximately 150 *Anemia phyllitidis* spores, sterilized by soaking in 0.5% NaOCl solution for 1 min, were innoculated on the surface of 0.2 mL of solidified growth medium ($MgSO_4$, 0.25 g; $Ca(NO_3)_2$, 1.0 g; KNO_3, 0.12 g; KH_2PO_4, 0.25 g; ferric citrate, 5 mg; agar, 9 g; and H_2O, 1 L) containing the sample to be tested. The samples were incubated in the dark in small round glass vessels (8 mm i.d., 7 mm depth) for 10 days at 25 °C, and the percentage of germinated spores in each vessel was determined under a microscope at 60-fold magnification.[38]

(40) One ^{13}C resonance is obscured by the acetone-d_6 solvent peaks.

2-(Phenylsulfonyl)-1,3-dienes as Versatile Synthons in Organic Transformations. Multicoupling Reagents and Diels-Alder Dienes with a Dual Electron Demand

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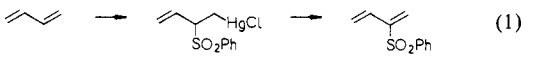
Abstract: 2-(Phenylsulfonyl)-1,3-dienes were stereo- and regioselectively functionalized via Michael addition of nucleophiles and subsequent addition of nucleophiles and/or electrophiles to the resulting allylic sulfones. The second nucleophile is introduced via a palladium-catalyzed or a cuprate-promoted nucleophilic substitution of the allylic sulfone. The strategy was applied to the synthesis of a Monarch butterfly pheromone. The sulfonyldienes were shown to undergo [4 + 2] cycloadditions with both electron-rich and electron-deficient dienophiles. Enamines and enol ethers gave highly regioselective reactions, whereas the regioselectivity in the reaction with methyl acrylate depends on the structure of the sulfonyldiene. The sulfonyl group in the cycloaddition products allows further useful transformations, which was demonstrated in a few cases.

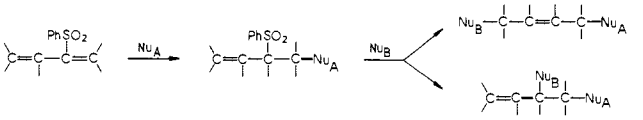
We recently reported a procedure for the synthesis of 2-(phenylsulfonyl)-1,3-dienes from conjugated dienes.[2] The method is based upon a sulfonylmercuration-elimination sequence and allows a one-pot synthesis of the sulfonyldiene (eq 1). The



(1)

reaction is highly regioselective for a number of dienes. The sulfonyldienes obtained are useful building blocks for further functionalization,[2] and furthermore, they are potentially interesting Diels-Alder dienes.[3,4] In view of these aspects and the general synthetic potential of unsaturated sulfones[5-9] we decided to explore the synthetic utility of the readily available 2-(phenylsulfonyl)-1,3-dienes. In this paper we report (i) that they can be regio- and stereoselectively functionalized via sequential nucleophilic addition of carbon and nitrogen nucleophiles and (ii) that they show a duality in their Diels-Alder cycloadditions and give [4 + 2] adducts with *both* electron-deficient and electron-rich olefins.

Scheme I



Results and Discussion

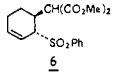
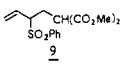
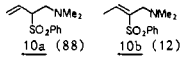
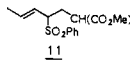
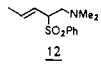
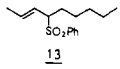
Stereo- and Regioselective Additions of Nucleophiles. The principle for the sequential nucleophilic additions to 2-(phenylsulfonyl)-1,3-dienes is shown in Scheme I. After a Michael-type addition of the first nucleophile, the second nucleophile can substitute the allylic sulfonyl group in a copper-[6] or palladium-catalyzed[7] reaction. A variety of different nucleophiles can be used in the first addition, and a few representative examples for the preparation of allylic sulfones are shown in Table I.

The Michael addition to sulfonyldiene **1** was found to be diastereoselective for all nucleophiles tried, leading preferentially to the trans isomer (entries 1-5, Table I). For the addition of dimethyl malonate and dimethylamine, the selectivity for the trans isomer was >95%, whereas for the cuprate addition (or copper-assisted alkyllithium addition), the trans:cis ratio was 90:10. In the latter case, however, treatment of the crude product with

(1) Address correspondence to this author at the University off Uppsala.
(2) Andell, O. A.; Bäckvall, J. E. *Tetrahedron Lett.* **1985**, *26*, 4555.
(3) Sauer, J.; Sustman, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779.
(4) (a) Boger, D. L.; Mullican, M. D. *J. Org. Chem.* **1984**, *49*, 4033. (b) Boger, D. L.; Panek, J. S. *J. Am. Chem. Soc.* **1985**, *107*, 5745. (c) Posner, G. H.; Harrison, W. *J. Chem. Soc., Chem. Commun.* **1985**, 1786.
(5) (a) Magnus, P. D. *Tetrahedron* **1977**, *33*, 2019. (b) Schank, K. In *Methoden Org. Chem. (Houben-Weyl)*, **1985** *Band E 11*, 1132.
(6) (a) Masaki, Y.; Sakuma, K.; Kaji, K. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1171. (b) Julia, M.; Righinie-Tapie, A.; Verpeaux, J. N. *Tetrahedron* **1983**, *39*, 3283. (c) Julia, M.; Verpeaux, J. N. *Ibid.* **1983**, *39*, 3289.
(7) (a) Trost, B. M.; Schmuff, N. R.; Miller, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 5981. (b) Trost, B. M.; Schmuff, N. R. *Ibid.* **1985**, *107*, 396. (c) Cuvigny, T.; Julia, M.; Rolando, C. *J. Organomet. Chem.* **1985**, *285*, 395.
(8) (a) Trost, B. M.; Ghadiri, M. R. *J. Am. Chem. Soc.* **1984**, *106*, 7260. (b) Trost, B. M.; Ghadiri, M. R. *Ibid.* **1986**, *108*, 1098.
(9) (a) Auvray, P.; Knochel, P.; Normant, J. F. *Tetrahedron Lett.* **1985**, *26*, 2329. (b) Knochel, P.; Normant, J. F. *Ibid.* **1985**, *26*, 425. (c) Kinney, W. A.; Crouse, G. D.; Paquette, L. A. *J. Org. Chem.* **1983**, *46*, 4986.

0002-7863/87/1509-6396$01.50/0

Table I. Addition of Nucleophiles to 2-(Phenylsulfonyl)-1,3-dienes

Entry	Sulfonyl diene	Nucleophile	Allylic sulfone	Yield (%)[a]
1	 1	$MeLi/Cu_2I_2$	 4	94[b]
2	1	$n\text{-}BuLi/Cu_2I_2$ $n\text{-}Bu_2CuLi$	 5	95[b] 71[c]
3	1	$NaHC(CO_2Me)_2$	 6	92[d]
4	1	$HNMe_2$	 7	91[d]
5	1	KCN	 8	74[d]
6	 2	$NaHC(CO_2Me)_2$	 9	83
7	2	$HNMe_2$	 10a (88) 10b (12)	96[e]
8	 3	$NaHC(CO_2Me)_2$	 11	94
9	3	$HNMe_2$	 12	96
10	3	$n\text{-}Bu_2CuLi$	 13	79

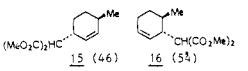
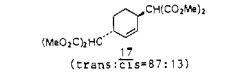
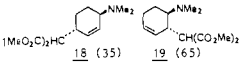
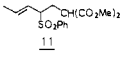
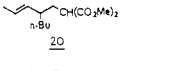
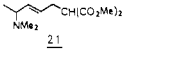
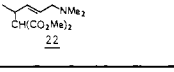
[a] Isolated yields. [b] Trans:cis = 92:8. [c] Trans:cis = 90:10. [d] >95% trans. [e] **10a** isomerized to **10b** on standing.

catalytic amounts of sodium methoxide in methanol led exclusively to the trans isomer. This shows that the high selectivity for the trans stereochemistry is thermodynamically controlled. The ^1H NMR spectra of these adducts are consistent with a configuration in which the two substituents are trans to one another.[10] Conclusive evidence for the trans configuration follows from the subsequent stereospecific transformations shown in Table II. Michael addition of cyanide to **1** under controlled conditions gave adduct **8** in 74% yield. During this reaction, small amounts of 1-cyano-1,3-cyclohexadiene were formed. The latter product could be obtained in high yield on prolonged reaction time.[11] Addition of a number of nucleophiles to sulfonyldienes **2** and **3** proceeded smoothly to give allylic sulfones **9–13**.

The allylic sulfones obtained in Table I underwent smooth nucleophilic substitution of the allylic sulfonyl group when palladium catalysis or cuprates were used. Some representative examples are given in Table II. Cuprate or copper-catalyzed Grignard reactions of allylic sulfones are known to proceed with a preference for γ-substitution.[6] This occurred in the reaction with allylic sulfone **4** (entry 1, Table II). Interestingly, cuprate addition to **11**, which contains a malonic ester substituent, did not give the γ-substitution but selectively afforded the α-substitution product (entry 5). This result is probably due to formation of an anion of the malonate, which directs copper and hence the cuprate addition to the α-position. Reaction of **4** with lithium dimethylcuprate gave *cis*-1,4-dimethyl-2-cyclohexene as expected from an anti substitution of the phenylsulfonyl group in the trans isomer **4** (entry 1).[12] The stereochemistry of the product was unambiguously established by ^1H NMR.[13]

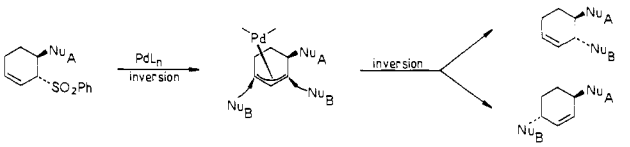
Palladium-catalyzed substitution of the sulfonyl group by dimethyl malonate was stereoselective (retention) as shown by reaction of **4**, **6**, and **7** (entries 2, 3, and 4, Table II). These reactions proceed via a π-allyl intermediate,[7a,14] and the regioselectivity of the reaction depends on the substituent Nu_A (Scheme II). It is known that an electronegative substituent in the 4-position of a π-allyl complex may direct the attack to the 1-position.[15–17] In accordance, **6** afforded only the 1,4-isomer **17** (entry 3, Table II), while **4** and **7** gave a mixture of 1,2- and

Table II. Palladium-Catalyzed or Cuprate Nucleophilic Substitution of Allylic Sulfones Obtained from Sulfonyldienes

Entry	Allylic sulfone	Nucleophile/catalyst	Product[a]	Yield (%)[b]
1	 4	Me_2CuLi	 14 (> 95 % cis)	54
2	4	$NaHC(CO_2Me)_2$ $Pd(PPh_3)_4$, PPh_3	 15 (46) 16 (54)	64
3	 6	$NaHC(CO_2Me)_2$ $Pd(OAc)_2$, diphos	 17 (trans:cis=87:13)	86
4	 7	$NaHC(CO_2Me)_2$ $Pd(PPh_3)_4$, diphos	 18 (35) 19 (65)	64
5	 11	$n\text{-}Bu_2CuLi$	 20	57
6	11	$HNMe_2$, $Pd(PPh_3)_4$ PPh_4, diphos	 21	47
7	 12	$NaHC(CO_2Me)_2$ $Pd(dba)_2$, diphos	 22	64

[a] The stereochemistry of the products was determined by ^1H NMR spectroscopy. [b] Isolated yields.

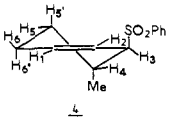
Scheme II



not give the γ-substitution but selectively afforded the α-substitution product (entry 5). This result is probably due to formation of an anion of the malonate, which directs copper and hence the cuprate addition to the α-position. Reaction of **4** with lithium dimethylcuprate gave *cis*-1,4-dimethyl-2-cyclohexene as expected from an anti substitution of the phenylsulfonyl group in the trans isomer **4** (entry 1).[12] The stereochemistry of the product was unambiguously established by ^1H NMR.[13]

Palladium-catalyzed substitution of the sulfonyl group by dimethyl malonate was stereoselective (retention) as shown by reaction of **4**, **6**, and **7** (entries 2, 3, and 4, Table II). These reactions proceed via a π-allyl intermediate,[7a,14] and the regioselectivity of the reaction depends on the substituent Nu_A (Scheme II). It is known that an electronegative substituent in the 4-position of a π-allyl complex may direct the attack to the 1-position.[15–17] In accordance, **6** afforded only the 1,4-isomer **17** (entry 3, Table II), while **4** and **7** gave a mixture of 1,2- and

(10) For example, the ^1H NMR spectrum of **4** indicates the conformation depicted. The fact that J_{34}, J_{45}, and J_{45} are small (4–5.5 Hz) requires that the methyl group occupy an axial position. Furthermore, it has recently been shown that allylic sulfones are more stable with the phenylsulfonyl group in the axial position.[7b] Thus, we conclude that **4** is the trans isomer, since the cis isomer is expected to have an equatorial methyl and an axial sulfonyl group.



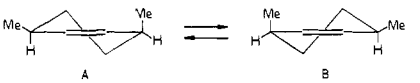
4

$J_{1,2}$ = 10.0 Hz; $J_{1,6} \sim J_{1,6'}$ = 4 Hz; $J_{2,3}$ = 4 Hz
$J_{3,4}$ = 4.2 Hz; $J_{1,3} \sim J_{3,6} \sim J_{3,6'}$ = 2 Hz
$J_{4,5'} \sim$ 5.5 Hz; $J_{4,5}$ = 4.0 Hz

(11) A similar addition–elimination sequence has been reported in the reaction of vinylsulfones with KCN: Taber, D. F.; Saleh, S. A. *J. Org. Chem.* **1981**, *46*, 4817.

(12) The anti stereochemistry in cuprate substitutions of allylic sulfones is consistent with the stereochemistry observed with other allylic leaving groups in cuprate reactions: (a) Goering, H. L.; Singleton, V. D., Jr. *J. Am. Chem. Soc.* **1976**, *98*, 7854. (b) Claesson, A.; Olsson, L. I. *J. Chem. Soc., Chem. Commun.* **1978**, 621. (c) Yamamoto, Y.; Yamamoto, S.; Yatagai, H.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 2318. (d) Tanigama, Y.; Ohta, H.; Sonoda, A.; Murashi, S. I. *Ibid.* **1978**, *100*, 4610.

(13) The ^1H NMR spectrum indicates two rapidly interconverting conformations, since the allylic methine protons at δ = 2.15 upon decoupling of the methyl groups become a broad triplet with $J \sim$ 5.5 and 5.5 Hz.



A B

(14) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 385.

(15) (a) Bäckvall, J. E. *Acc. Chem. Res.* **1983**, *16*, 335. (b) Bäckvall, J. E. *Pure Appl. Chem.* **1983**, *55*, 1669. (c) Bäckvall, J. E.; Byström, S. E.; Nordberg, R. E. *J. Org. Chem.* **1984**, *49*, 4619. (d) Bäckvall, J. E.; Nyström, J. E.; Nordberg, R. E. *J. Am. Chem. Soc.* **1985**, *107*, 3676.

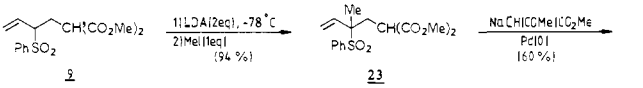
(16) (a) Genêt, J. P.; Balabane, H.; Charbonnier, F. *Tetrahedron Lett.* **1982**, *23*, 5027. (b) Genêt, J. P.; Balabane, H.; Bäckvall, J. E.; Nyström, J. E. *Tetrahedron Lett.* **1983**, *24*, 2745.

(17) (a) Tsuji, J.; Kataoka, H.; Kobayashi, Y. *Tetrahedron Lett.* **1981**, *22*, 2575. (b) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 5969.

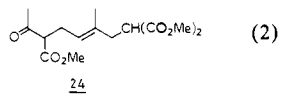
1,4-isomers. A high selectivity for 1,4-isomer was obtained in the palladium-catalyzed nucleophilic substitution of acyclic allylic sulfones **11** and **12** (entries 6 and 7).

Since the 2-(phenylsulfonyl)-1,3-dienes are obtained from 1,3-dienes, the method developed here allows the formal addition of nucleophiles to the 1- and 4-positions of a conjugated diene. It thus complements our previously developed method via 1,4-chloroacetoxylation and subsequent nucleophilic substitution.[15] Interestingly, the present method allows a regiochemical choice also for terminal 1,3-dienes. The functionalization of 1,3-pentadiene by $CH(COOMe)_2$ and NMe_2 can be made either 1,4 (**21**) or 4,1 (**22**) via **3** and **11** or via **3** and **12**, respectively (entries 8 and 9, Table I; entries 6 and 7, Table II).

The allylic sulfones obtained from the Michael-type addition to the sulfonyldienes (Table I) can be functionalized in a number of ways.[5-9] Besides the nucleophilic substitutions shown in Table II they allow introduction of an electrophile at the α-position of the sulfone. A demonstration of the versatility of the approach is given in eq 2. Alkylation of the dianion of **9** by methyl iodide



9 23



24 (2)

followed by palladium-catalyzed substitution of **23** by sodium methyl acetoacetate afforded **24**, which is the key intermediate in a recent synthesis of a Monarch butterfly pheromone.[18]

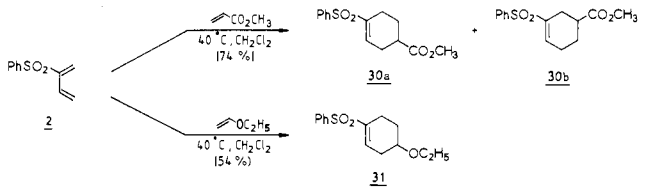
Diels–Alder Dienes with a Dual Electron Demand. It was found that some of the 2-(phenylsulfonyl)-1,3-dienes undergo Diels–Alder dimerization on standing. In particular **2** and **3** readily underwent a dimerization and therefore these dienes were usually not isolated before use but handled in a solution of ether or methylene chloride. Because of this property we decided to study their cycloaddition with other olefins. The alkenylsulfone moiety formed in the Diels–Alder adduct from reaction of 2-(phenylsulfonyl)-1,3-dienes with olefins masks numerous latent functional groups.

Reaction of **3** with methyl acrylate in toluene in the presence of aluminum trichloride[19] afforded the cycloaddition product **25** in 95% yield. Mainly one stereo- and regioisomer (~93%)[20] was

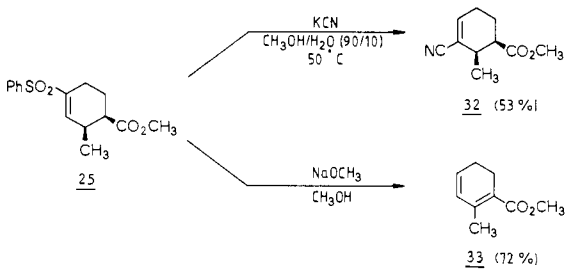
3 25 R = OCH_3 (95 %)
26 R = CH_3 (68 %)

formed according to ^1H NMR and HPLC. From the ^1H NMR spectrum it follows that the regioisomer with the methyl and carbomethoxy groups vicinal to one another is formed. This regiochemistry is in line with that observed from reaction of 2-cyano-1,3-butadiene with methyl acrylate[21] and in accord with

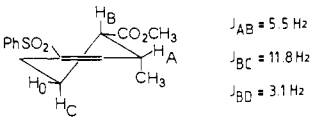
Scheme III



Scheme IV

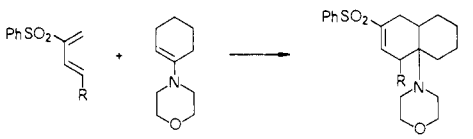


predictions by frontier orbital theory and theoretical calculations.[3,22,23] The cis stereochemistry of **2** is easily assigned from the ^1H NMR spectrum. The vicinal coupling constants J_{AB} and J_{BC} of 5.5 and 11.8 Hz, respectively, are only compatible with



a conformation in which the methyl group is axial and the carbomethoxy group is equatorial and hence cis to one another. Analogously, **3** reacted with methyl vinyl ketone in the absence of catalyst to give **26** as the major isomer. In this case, however, the regioselectivity was much lower and a ratio of about 2.3:1 between **26** and the other regioisomer was formed.[24] The cis stereochemistry of **25** and **26** is consistent with secondary orbital interactions and an endo transition state.[3]

Since diene **1** is electron deficient, it occurred to us that it may undergo inverse electron demand cycloadditions[3,4,25] with electron-rich olefins. Indeed reaction of **3** with enamine **27** proceeded with complete and predictable regiospecificity to give **28**. The stereochemistry of **28** has not yet been determined. Reaction of 2-(phenylsulfonyl)-1,3-butadiene (**2**) with **27** also proceeded smoothly to give **29** as the single product.

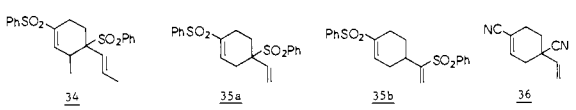


1 R = CH_3 27 28 R = CH_3 (50 %)
2 R = H 29 R = H (70 %)

The 2-(phenylsulfonyl)-1,3-dienes thus show an interesting duality in their [4 + 2] cycloadditions with olefins by reacting with both electron-deficient and electron-rich olefins. This duality in reactivity is further demonstrated in Scheme III with the reactions of **2** with methyl acrylate and ethyl vinyl ether, which

(18) Nyström, J. E.; Bäckvall, J. E. *J. Org. Chem.* **1983**, *48*, 3947.

(19) (a) The reaction was slow in the absence of $AlCl_3$, and in this case Diels–Alder dimerization of **1** competes. The structure of the Diels–Alder dimer of **3** is **34**. From **2** the corresponding dimer was **35a**. In the latter case also two other isomeric dimerization products **35b** and **35c** were formed, the ratio **35a**:**35b**:**35c** being 57:19:24. An analogous Diels–Alder dimerization has been observed for 2-cyano-1,3-butadiene, which afforded **36**.[19b] (b) Marvel, C. S.; Brace, N. O. *J. Am. Chem. Soc.* **1949**, *71*, 37.



34 35a 35b 36

(20) The trans isomer of **25** and another regioisomer were present in relative amounts of 4 and 3%, respectively, according to ^1H NMR. A mixture of these two minor isomers was isolated by preparative HPLC.

(21) Inukari, T.; Kojima, T. *J. Org. Chem.* **1971**, *36*, 924.

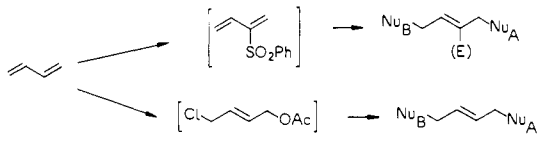
(22) (a) Fleming, I *Frontier Orbitals and Organic Chemical Reactions*; Wiley: 1976. (b) Houk, K. N. *J. Am. Chem. Soc.* **1973**, *95*, 4092.

(23) Eisenstein, O.; Lefour, J. M.; Nguyên Trong Ahn; Hudson, R. F. *Tetrahedron* **1977**, *33*, 523.

(24) (a) In accordance, it has recently been observed by Julia[24b] that reaction of 5-(phenylsulfonyl)-3,5-dodecadiene with methyl vinyl ketone gives a mixture of regioisomers. (b) Cuvigny, T.; Hervée du Penhoat, C.; Julia, M. *Tetrahedron* **1986**, *42*, 5329.

(25) For recent use of other sulfonyldienes in reactions with electron-rich olefins, see: (a) Masuyama, Y.; Sata, H.; Kurusu, Y. *Tetrahedron Lett.* **1985**, *26*, 67. (b) Masuyama, Y.; Yamazaki, H.; Toyoda, Y.; Kurusu, Y. *Synthesis* **1985**, 964. (c) Posner, G. H.; Wettlaufer, D. G. *Tetrahedron Lett.* **1986**, *27*, 667.

Scheme V



afforded **30** and **31**, respectively. Methyl acrylate afforded a mixture of regioisomers **30a** and **30b** in a ratio of 2:1,[26] whereas ethyl vinyl ether gave a single regioisomer. The regioisomer **31** is the one expected, where the nucleophilic carbon of the dienophile attaches to carbon-1 of the 2-(phenylsulfonyl)-1,3-diene. Also, from a frontier orbital analysis **31** is the regioisomer predicted.[3,22] The low regioselectivity in the reaction of **2** with methyl acrylate is in accordance with the poor regioselectivity usually found when $2\pi + 4\pi$ components of similar electrophilic nature react.[4a,21,24b,27,28] In this case **30a** is the regioisomer predicted from a frontier orbital analysis.[22]

There are few examples reported in the literature where a conjugated diene undergoes [4 + 2] cycloadditions with both electron-deficient and electron-rich olefins.[29] The dual reactivity of the 2-(phenylsulfonyl)-1,3-dienes in [4 + 2] cycloadditions with olefins increases the role they can play in organic synthesis.

By transforming a conjugated diene into a 2-(phenylsulfonyl)-1,3-diene,[2] one may obtain a richer Diels–Alder chemistry. The cycloaddition products obtained from the latter with olefins contain a lot of masked functionality in the vinyl sulfone group.[5] Thus, further functionalization can be made by Michael addition and cycloadditions.[5,30,31] Examples of transformations where the sulfonyl group is eliminated are shown in Scheme IV. Reaction of **25** with KCN gave an intermediate Michael adduct, which eliminates phenylsulfinic acid on prolonged reaction to give **32**.[32] Treatment of **25** with sodium methoxide in methanol gave **33** most likely via an intermediate allylic sulfone and subsequent 1,4-elimination of phenylsulfinic acid.

2-(Phenylsulfonyl)-1,3-dienes and 2-cyano-1,3-dienes show the same regiochemistry[21,33] in Diels–Alder reaction as expected, since the phenylsulfonyl and cyano groups are electron-withdrawing groups with comparable strength. By transforming the 1-(phenylsulfonyl)alkene moiety in the cycloalkene (cf. **25** → **32**), one obtains a complementary regiochemistry to that achieved by cycloaddition of 2-cyano-1,3-dienes to the same dienophile.

A method for the preparation of the isomeric 1-(phenylsulfonyl)-1,3-dienes from the corresponding diene has recently been described.[34] Also these sulfonyldienes are useful in cycloaddition reaction and it should be possible to use them in sequential nucleophilic functionalizations.

Related cycloadditions of (phenylsulfinyl)-[35] and (phenylthio)-1,3-dienes[36] with olefins have been reported. These dienes can be considered as synthetic equivalents to (phenylsulfonyl)-1,3-dienes in Diels–Alder reactions since the sulfur in the cycloadducts of the former can be oxidized.

2-(Arylsulfonyl)-1,3-dienes have previously been prepared from condensation of an allyl sulfone with an aldehyde and subsequent acetylation and elimination.[24b,37] They can also be obtained from the corresponding 2-(arylsulfonyl)sulfolene by thermal SO_2 extrusion.[28b]

Conclusions

2-(Phenylsulfonyl)-1,3-dienes are useful synthons for organic transformations. They can be functionalized by nucleophiles in the 1- and 4-positions and, as an option, with electrophiles in the 2-position. In this way they constitute multicoupling reagents and can be compared with 1-acetoxy-4-chloro-2-alkenes (Scheme V), which have been utilized as analogous multicoupling reagents.[15,38] In both cases the multicoupling synthon is obtained from the corresponding conjugated diene.

The 2-(phenylsulfonyl)-1,3-dienes undergo [4 + 2] cycloadditions with both electron-rich and electron-deficient olefins. This is of both theoretical and preparative interest. The cycloaddition products are vinyl sulfones and allow a variety of further functionalizations.

Experimental Section

High-pressure liquid chromatography (HPLC) was performed on a Waters M-45 instrument with a μ-Porasil column (silica, 10-μm packing, 0.4 × 30 cm) and a differential refractometer as detector. 1-Morpholino-1-cyclo-hexene,[39] tetrakis(triphenylphosphino)palladium-(0),[15d] and bis(dibenzylideneacetone)palladium(0)[40] were prepared according to the literature procedures.

2-(Phenylsulfonyl)-1,3-cyclohexadiene (1). To a suspension of 3-(phenylsulfonyl)-4-(chloromercuri)cyclohexene[2] (22.16 g, 48 mmol) in ether (200 mL) was added aqueous 2 M NaOH (75 mL, 150 mmol) under vigorous stirring. After 30 min of stirring the reaction mixture at room temperature, the layers were separated. The water phase was extracted with ether (3 × 50 mL). The combined ethereal phases were then filtered through a short (20 × 20 mm) silica gel column and dried with anhydrous $MgSO_4$. Removal of the solvent at reduced pressure gave an oil, which spontaneously started to crystallize; further drying at reduced pressure in a desiccator afforded 10.10 g (96%) of pure **1**: mp 61–63 °C; IR (KBr) 3060, 2950, 2880, 2830, 1585, 1450, 1305, 1150, 1090, 710, 690, 630 cm^{-1}; ^1H NMR δ 7.91–7.48 (m, 5 H, ArH), 6.95 (m, J = 4.6, 4.6, 1.4, 0.9 Hz, 1 H, H-1) 6.09 (ddd, J = 9.9, 3.4, 1.8 Hz, 1 H, H-3), 5.96 (m, J = 9.9, 4.1, 4.1, 0.9 Hz, 1 H, H-4), 2.49–2.36 (m, 2 H, H-6), 2.24–2.11 (m, 2 H, H-5); ^{13}C NMR δ 139.53, 138.27, 133.94, 132.39, 129.15, 128.41, 127.04, 118.01, 22.30, 20.79. Anal. Calcd for $C_{12}H_{12}O_2S$: C, 65.43; H, 5.49. Found: C, 65.27; H, 5.48.

2-(Phenylsulfonyl)-1,3-butadiene (2). To a suspension of 3-(phenylsulfonyl)-4-(chloromercuri)but-1-ene[2] in ether (10 mL/mmol) was added aqueous 2 M NaOH (3–4 equiv) at ambient temperature under vigorous stirring. A black precipitate was soon formed. The reaction mixture was stirred for 20–30 min and the layers were separated. The aqueous phase was extracted with ether. The combined ethereal phases were filtered through silica gel and diluted to ~50 mM solution and dried ($MgSO_4$ or $CaCl_2$). The product was usually used in reactions within a few hours, but it can be stored in solution in a freezer (−20 °C) for several days (<5% dimerization). If the sulfonyldiene was needed in Diels–Alder reactions, dichloromethane was used as the solvent with the same procedure as that described above. The yields are between 75 and 90%: ^1H NMR δ 7.90–7.47 (m, 5 H, ArH), 6.36 (br s, 1 H, H-1), 6.34 (ddd, J = 17.5, 11.0, 0.8 Hz, 1 H, H-3), 5.99 (br s, 1 H, H-1), 5.67 (d, J = 17.5 Hz, 1 H, H-4), 5.32 (d, J = 11.0 Hz, 1 H, H-4).

2-(Phenylsulfonyl)-1,3-pentadiene (3). The same procedure as that described for preparation of **2** was used. Since the sulfonyldiene **2** is more reactive toward Diels–Alder dimerization it was kept at lower concentration (10–50 mM). Yields were 90–100%: ^1H NMR δ 7.92–7.48 (m, 5 H, ArH), 6.22 (s, 1 H, H-1), 6.15 (dq, J = 15.7, 6.0 Hz, 1 H,

(26) In the presence of $AlCl_3$ a 1:1 mixture between **30a** and **30b** was obtained.

(27) Reed, J. E.; Schilling, C. L., Jr.; Tarvin, R. F.; Rettig, T. A.; Stille, J. K. *J. Org. Chem.* **1969**, *34*, 2188.

(28) (a) In contrast to the results obtained here, it was reported[28b] that 2-(*p*-tolylsulfonyl)-1,3-butadiene, generated in situ from 3-(*p*-tolylsulfonyl)-sulfolane, reacted with methyl acrylate to give only one isomer (the one corresponding to **30a**). (b) Inomata, K.; Kinoshita, H.; Takemoto, H. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 3341.

(29) It has been reported that the electron-deficient dienes 3-(carboxymethoxy)-2-pyrones, which are known to react with electron-rich olefins, also react with electron-deficient acetylenes.[4a]

(30) (a) Hutchinson, D. K.; Hardinger, S. A.; Fuchs, P. L. *Tetrahedron Lett.* **1986**, *27*, 1425. (b) Posner, G. H.; Brunelle, D. J. *J. Org. Chem.* **1973**, *38*, 2747. (c) Agawa, T.; Yoshida, Y.; Komatsu, M.; Oshiro, Y. *J. Chem. Soc., Perkin Trans. 1* **1981**, 751. (d) Ponton, J.; Helquist, P.; Conrad, P. C.; Fuchs, P. L. *J. Org. Chem.* **1981**, *46*, 118.

(31) Carr, R. V. C.; Paquette, L. A. *J. Am. Chem. Soc.* **1980**, *102*, 853. Kinney, W. A.; Crouse, G. D.; Paquette, L. A. *J. Org. Chem.* **1983**, *48*, 4986.

(32) A modified procedure to that reported by Taber and Saleh[11] was used.

(33) Interestingly 2-cyano-1,3-butadiene gives an analogous dimerization as the 2-(phenylsulfonyl)-1,3-dienes with the same regiochemistry.[19]

(34) Åkermark, B.; Nyström, J. E.; Rein, T.; Bäckvall, J. E.; Helquist, P.; Aslanian, R. *Tetrahedron Lett.* **1984**, *50*, 5719.

(35) Evans, D. A.; Bryan, C. A.; Sims, C. L. *J. Am. Chem. Soc.* **1972**, *94*, 2891.

(36) (a) Trost, B. M.; Vladuchick, W. C.; Bridges, A. J. *J. Am. Chem. Soc.* **1980**, *102*, 3554. (b) Cohen, T.; Kosarych, Z. *J. Org. Chem.* **1982**, *47*, 4005.

(37) Cuvigny, T.; Hervée du Penhoat, C.; Julia, M. *Tetrahedron Lett.* **1983**, *24*, 4315.

(38) Bäckvall, J. E. In *Organic Synthesis: An Interdisciplinary Challenge*; Streith, J., Prinzbach, H., Schill, G., Eds.; Blackwell Scientific: Oxford, UK, 1985; p 69.

(39) Hünig, S.; Lücke, E.; Brenninger, W. *Org. Synth., Collect. Vol. V*, **1972**, 808.

(40) Rettig, M. F.; Maitlis, P. M. *Inorg. Chem.* **1977**, *17*, 135.

MeCH=CH), 6.03 (dq, J = 15.7, 0.9 Hz, 1 H, MeCH=CH), 5.86 (s, 1 H, H-1), 1.74 (br d, J = 6.0 Hz, 3 H, CH_3).

Dimer 34: mp 144–148 °C; ^{1}H NMR δ 7.85–7.45 (m, 10 H, ArH), 6.81 (m, 1 H, vinylic H), 5.54 (dq, J = 15.9, 1.4 Hz, 1 H, MeCH=CH), 5.32 (dq, J = 15.9, 6.3 Hz, 1 H, MeCH=CH), 3.31 (m, 1 H, HC-Me), 2.18 (unresolved m, 2 H, allylic H), 1.92 (br t, 2 H, homoallylic H), 1.63 (dd, J = 6.3, 1.4 Hz, 3 H, HC=CHCH$_3$), 1.42 (d, J = 7.35 Hz, 3 H, HCCH$_3$); ^{13}C NMR δ 141.50, 138.69, 137.41, 134.77, 133.78, 133.25, 130.56, 129.04, 128.34, 127.81, 121.90, 67.90, 33.74, 25.43, 20.46, 18.47, 16.77.

4-Methyl-3-(phenylsulfonyl)cyclohexene (4). To a mixture of 2-(phenylsulfonyl)-1,3-cyclohexadiene (2.0 g, 9.1 mmol) and CuI (1.9 g, 10 mmol) was added THF (50 mL) via a syringe under nitrogen. After the mixture was stirred for 5 min under nitrogen, it was cooled to −65 °C. Then methyllithium (20 mL of a 1.5 M solution in ether, 30 mmol) was added via syringe during 7 min. After 30 min of stirring at −65 to −25 °C, the reaction flask was removed from the cooling bath. After an additional stirring for 15 min (the solution was dark red and homogeneous), a 23% aqueous solution of NH_4Cl (10 mL) and ether (10 mL) was added, followed by separation of the layers. The water phase was extracted with ether (2 × 25 mL), and the combined organic phases were dried with anhydrous $MgSO_4$. Finally, filtration through a silica gel column (70 × 25 mm) and concentration at reduced pressure afforded 2.0 g (94%) of **4** as an oil (trans/cis = 92/8): IR (neat) 3075, 3040, 2965, 2940, 2880, 1450, 1310, 1150, 1090, 765, 725, 695, 680 cm^{-1}; ^{1}H NMR δ 7.93–7.47 (m, 5 H, ArH), 6.10 (m, J = 10.0, 3.75, 3.75, 1.9 Hz, 1 H, H-1), 5.62 (m, J = 10.0, 4.0, 2.0, 2.0 Hz, 1 H, H-2), 3.42 (m, J = 4.0, 4.0, 2.0, 2.0, 2.0 Hz, 1 H, $HCSO_2Ph$), 2.32 (dddq, J = 6.9, 5.5, 4.2, 4.0 Hz, 1 H, HCMe), 2.0–1.88 (m, 2 H, allylic H), 1.83–1.68 (m, 1 H, one of the homoallylic H), 1.40–1.22 (m, 1 H, the other homoallylic H), 1.09 (d, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR δ 137.58, 135.12, 133.43, 128.81, 117.57, 67.38, 26.72, 25.96, 21.51, 19.81.

Anal. Calcd for $C_{13}H_{16}O_2S$: C, 66.07; H, 6.82. Found: C, 65.93; H, 6.66.

4-*n*-Butyl-3-(phenylsulfonyl)cyclohexene (5). The same procedure as for the preparation of **4** was applied. The amounts used were as follows: Sulfonyldiene **4** (230 mg, 1.04 mmol), CuI (218 mg, 1.14 mmol), THF (10 mL), and *n*-butyllithium (1.6 mL, 1.5 M in hexane, 2.4 mmol). The reaction was stirred at −70 °C for 30 min and then allowed to warm to room temperature during 1 h. After workup, 275 mg (95%) of essentially pure **5** was isolated as an oil (trans/cis = 92/8): IR (neat) 3070, 3040, 2940, 2870, 1450, 1310, 1150, 1090, 725, 695, 680 cm^{-1}; ^{1}H NMR δ 7.93–7.50 (m, 5 H, ArH), 6.12 (m, 1 H, H-1), 5.61 (m, 1 H, H-2), 3.46 (m, 1 H, $HCSO_2Ph$), 2.24 (m, 1 H, H-4), 2.01–1.73 (m, 3 H, allylic and one homoallylic H), 1.47–1.12 (m, 7 H), 0.84 (t, J = 6.5 Hz, 3 H, CH_3); ^{13}C NMR δ 137.99, 135.59, 133.43, 128.86, 117.10, 65.33, 32.33, 30.93, 28.88, 22.33, 20.93, 13.85.

Anal. Calcd for $C_{16}H_{22}O_2S$: C, 69.03; H, 7.96. Found: C, 69.06; H, 7.92.

Dimethyl (*trans*-2-(Phenylsulfonyl)cyclohex-3-en-1-yl)malonate (6). To a solution of 2-(phenylsulfonyl)-1,3-cyclohexadiene (1.20 g, 5.4 mmol) in THF (15 mL) was added a solution of sodium dimethyl malonate, prepared from dimethyl malonate (820 mg, 6.2 mmol) and NaH (80%, in paraffin oil, 30 mg, 1.0 mmol) in THF (5 mL). The resulting solution was stirred under a nitrogen atmosphere at room temperature for 2 h 45 min and then concentrated in vacuo. To the residue was added ether (25 mL) and a 10% aqueous solution of NH_4Cl (5 mL), followed by separation of the layers. The organic phase was washed with 10% NH_4Cl solution (3 mL), dried ($MgSO_4$), and concentrated. The excess of dimethyl malonate was removed by Kugelrohr distillation (100 °C, 1 Torr), giving 1.76 g (92%) of **6** as a colorless oil, which crystallized on standing: mp 93–96 °C; IR (KBr) 3050, 2955, 2910, 2895, 1730, 1440, 1305, 1280, 1240, 1150, 1085, 1020, 890, 750, 720, 685 cm^{-1}; ^{1}H NMR δ 7.93–7.51 (m, 5 H, ArH), 6.17 (m, J = 10.0, 3.75, 3.75, 1.9 Hz, 1 H, H-4), 5.68 (m, J = 10.0, 4.0, 2.0, 2.0 Hz, 1 H, H-3), 3.87 (unresolved m, 1 H, $HCSO_2Ph$), 3.80 (d, J = 8.4 Hz, 1 H, $HC(CO_2Me)_2$), 3.73 (s, 3 H, CO_2CH_3), 3.65 (s, 3 H, CO_2CH_3), 2.86 (m, 1 H, $HCCH(CO_2Me)_2$), 2.23–1.92 (m, 3 H, allylic and equatorial homoallylic H), 1.54–1.37 (m, 1 H, axial homoallylic H); ^{13}C NMR δ 167.49, 167.20, 136.98, 134.73, 132.97, 128.47, 128.26, 116.73, 62.86, 52.87, 52.25, 52.16, 32.06, 21.79, 21.39.

Anal. Calcd for $C_{17}H_{20}O_6S$: C, 57.94; H, 5.72. Found: C, 57.78; H, 5.77.

***trans*-4-(Dimethylamino)-3-(phenylsulfonyl)cyclohexene (7).** A solution of 2-(phenylsulfonyl)-1,3-cyclohexadiene (4.0 g, 18 mmol) and dimethylamine (2.43 g, 54 mmol) in ether (100 mL) was allowed to react at room temperature for 1.5 h. The white crystals formed were collected by filtration. The mother liquor was then evaporated at reduced pressure, without any heating, to leave ~20 mL of ether. The crystals formed were collected. This procedure was repeated once again. Drying in a desiccator gave 4.22 g (91%) of pure **7**: mp 90–91 °C; IR (KBr) 3060, 3030, 2970, 2935, 2830, 2790, 2775, 1450, 1300, 1285, 1140, 1080, 1045, 840, 760, 725, 695, 665 cm^{-1}; ^{1}H NMR δ 7.93–7.47 (m, 5 H, ArH), 6.15 (m, J = 10.0, 4.0, 4.0, 2.0 Hz, 1 H, H-1), 5.86 (m, J = 10.0, 3.5, 2.0, 2.0 Hz, 1 H, H-2), 3.87 (m, J = 6.1, four ~2.6 Hz, 1 H, $HCSO_2Ph$), 3.01 (ddd, J = 8.5, 6.1, 3.7 Hz, 1 H, $HCNMe_2$), 2.15–1.98 (m, 2 H, allylic H, partly hidden under the NMe_2 signal), 2.03 (s, 3 H, NMe_2), 1.88–1.73 (m, 1 H, homoallylic H), 1.70–1.48 (m, 1 H, homoallylic H); ^{13}C NMR δ 139.63, 134.95, 132.96, 128.51, 128.34, 117.87, 63.63, 58.66, 40.58, 23.27, 19.93.

Anal. Calcd for $C_{14}H_{19}O_2NS$: C, 63.37; H, 7.22. Found: C, 63.34; H, 7.16.

***trans*-4-Cyano-3-(phenylsulfonyl)cyclohexene (8).** To a solution of 2-(phenylsulfonyl)-1,3-cyclohexadiene (220 mg, 1 mmol) and acetic acid (60 μL, 63 mg, 1.05 mmol) in ethanol (4 mL) was added a solution of potassium cyanide (133 mg, 2.05 mmol) in water (0.4 mL). The mixture was stirred at 20 °C and an additional amount of acetic acid (30 μL) was added in three portions over 30 min. The mixture was stirred at 20 °C for an additional 1.5 h, and then ether (25 mL) and saturated NaCl solution (15 mL) were added. The mixture was shaken and the organic layer was collected. The aqueous phase was extracted with ether (20 mL). The combined organic phases were washed with aqueous 2 M NaOH (2 × 5 mL), water (5 mL), and saturated aqueous NaCl solution (5 mL) and finally dried ($MgSO_4$). The solvent was removed and the crude product was purified by flash chromatography on silica gel (EtOAc/hexane = 10/90) to give 182 mg (74%) of **8** as a colorless oil: ^{1}H NMR δ 7.95–7.55 (m, 5 H, ArH), 6.25 (m, J = 10.2, 4.0, 3.0, 1.8 Hz, 1 H, H-1), 5.61 (m, J = 10.2, 4.2, 2.0, 2.0 Hz, 1 H, H-2), 3.90 (m, J = 4.2, 4.0, 1.8, sum of the remaining 4 Hz, 1 H, $HCSO_2Ph$), 3.51 (unresolved m, 1 H, HCCN), 2.45–2.15 (m, 3 H, allylic and equatorial homoallylic H), 2.00–1.85 (m, 1 H, axial homoallylic H); ^{13}C NMR δ 136.98, 135.62, 134.57, 129.55, 119.16, 115.77, 61.85, 24.80, 21.99, 21.70.

Dimethyl (2-(Phenylsulfonyl)but-3-en-1-yl)malonate (9). To a 52 mM ethereal solution of **2** (60 mL, 3.12 mmol) was added a solution of sodium dimethyl malonate, prepared from dimethyl malonate (793 mg, 6 mmol), NaH (80%, in paraffin oil, 36 mg, 1.2 mmol), and THF (20 mL). After the solution was stirred at room temperature under a nitrogen atmosphere for 2.5 h, a 10% aqueous solution of NH_4Cl (10 mL) and ether (10 mL) was added, and the phases were separated. The aqueous phase was extracted with ether (2 × 10 mL), and the combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. The excess dimethyl malonate was removed by distillation in a Kugelrohr apparatus (100 °C, 1 Torr), affording 850 mg (83%) of **9** as crystals: mp 63–70 °C; IR (KBr) 2960, 1745, 1440, 1350, 1310, 1290, 1240, 1220, 1145, 1085, 1000, 940, 755, 730, 690 cm^{-1}; ^{1}H NMR δ 7.98–7.48 (m, 5 H, ArH), 5.62 (ddd, J = 17.0, 10.1, 9.4 Hz, 1 H, H_2C=CH), 5.34 (dd, J = 10.1, 0.9 Hz, 1 H, H-4), 5.09 (br d, J = 17.0 Hz, 1 H, H-4), 3.72 and 3.71 (two s, 3 H each, CO_2CH_3), ~3.70 (m, partly hidden under the CO_2Me signal, 1 H, $HCSO_2Ph$), 3.50 (dd, J = 9.3, 5.6 Hz, 1 H, $HC(CO_2Me)_2$), 2.66 (ddd, J = 14.0, 9.3, 4.3 Hz, 1 H, one of the methylene H), 2.24 (ddd, J = 14.0, 10.7, 5.6 Hz, 1 H, one of the methylene H); ^{13}C NMR δ 168.81, 168.53, 137.14, 133.89, 129.23, 128.96, 124.64, 67.36, 52.72, 48.63, 26.67.

Anal. Calcd for $C_{15}H_{18}O_6S$: C, 55.20; H, 5.56. Found: C, 55.00; H, 5.59.

Mixture of 1-(Dimethylamino)-2-(phenylsulfonyl)but-3-ene (10a) and 1-(Dimethylamino)-2-(phenylsulfonyl)but-2-ene (10b). To a 50 mM ethereal solution of **2** (20 mL, 1 mmol) was added dimethylamine (250 mg, 5.5 mmol). After 1 h of stirring at room temperature the ether and the excess dimethylamine were removed at reduced pressure on a rotary evaporator. Further drying in a desiccator afforded 232 mg (96%) of **10a** and **10b** in a ratio of 88:12 as an oil. Upon standing, **10a** isomerizes to **10b**.

10a: ^{1}H NMR δ 7.93–7.40 (m, 5 H, ArH), 5.71 (ddd, J = 17.0, 10.0, 9.3 Hz, 1 H, H_2C=CH), 5.33 (br d, J = 10.0 Hz, 1 H, H-4), 5.10 (br d, J = 17.0 Hz, 1 H, H-4), 3.75 (ddd, J = 10.0, 9.3, 4.5 Hz, 1 H, $HCSO_2Ph$), 2.87 (dd, J = 12.2, 4.5 Hz, 1 H, $HCNMe_2$), 2.79 (dd, J = 12.2, 9.3 Hz, 1 H, $HCNMe_2$), 2.20 (s, 6 H, $N(CH_3)_2$).

10b: IR (neat) 2940, 2820, 2770, 1450, 1305, 1150, 1090, 740, 690 cm^{-1}; ^{1}H NMR δ 7.93–7.41 (m, 5 H, ArH), 7.16 (q, J = 7.0 Hz, 1 H, HC=C), 3.17 (s, 2 H, H_2CNMe_2), 1.96 (s, 6 H, $N(CH_3)_2$), 1.95 (d, J = 7.0 Hz, 3 H, C=CHCH$_3$); ^{13}C NMR δ 141.34, 140.99, 140.27, 132.69, 128.50, 128.28, 54.02, 44.39, 14.51.

Anal. Calcd for $C_{12}H_{17}O_2NS$: C, 60.22; H, 7.16. Found: C, 60.17; H, 7.24.

Dimethyl ((*E*)-2-(Phenylsulfonyl)pent-3-en-1-yl)malonate (11). A 50 mM ethereal solution of 2-(phenylsulfonyl)-1,3-pentadiene was prepared according to the procedure given above, starting with 1 g (2.25 mmol) of the corresponding sulfonylmercury compound. To that ethereal solution (45 mL) was added a solution of sodium dimethyl malonate,

prepared from dimethyl malonate (595 mg, 4.5 mmol) and NaH (80% in paraffin oil, 27 mg, 0.9 mmol) in THF (8 mL). The mixture was stirred for 40 min at room temperature and then worked up in the same way as for compound **9**, giving 723 mg (94%) of **11**: IR (neat) 3085, 3020, 2960, 2860, 1745, 1445, 1310, 1150, 1090, 1040, 975, 770, 740, 695 cm^{-1}; ^1H NMR δ 7.90–7.47 (m, 5 H, ArH), 5.50 (dq, J = 15.0, 6.4 Hz, 1 H, HC=C*H*Me), 5.23 (ddq, J = 15.0, 9.5, 1.4 Hz, 1 H, *H*C=CHMe), 3.72 and 3.71 (two s, each 3 H, CO_2CH_3), 3.64 (ddd, J = 10.5, 9.5, 4.5 Hz, 1 H, $HCSO_2Ph$), 3.48 (dd, J = 9.5, 5.5 Hz, 1 H, HC-$(CO_2Me)_2$), 2.61 (ddd, J = 13.7, 9.5, 4.5 Hz, 1 H, methylene H), 2.20 (ddd, J = 13.7, 10.5, 5.5 Hz, 1 H, methylene H), 1.65 (dd, J = 6.4, 1.4 Hz, 3 H, C=$CHCH_3$); ^{13}C NMR δ 168.65, 168.30, 136.88, 136.53, 133.54, 128.81, 128.69, 121.26, 66.44, 52.46, 48.42, 26.54, 17.94.

Anal. Calcd for $C_{16}H_{20}L_6S$: C, 56.46; H, 5.92. Found: C, 56.61; H, 5.76.

(*E*)-1-(Dimethylamino)-2-(phenylsulfonyl)pent-3-ene (12). To a suspension of 5-(chloromercuri)-4-(phenylsulfonyl)pent-2-ene[2] (4.45 g, 10 mmol) in ether (100 mL) was added, under vigorous stirring, aqueous 2 M NaOH (15 mL, 30 mmol). After 5 min the layers were separated, and the aqueous phase was extracted with ether (2 × 20 mL). The combined ethereal phases were diluted to 200 mL and dried ($MgSO_4$). Then dimethylamine (1.35 g, 30 mmol) was added. After 2.5 h of stirring at room temperature the ether was removed at reduced pressure on a rotary evaporator. Further drying in a desiccator afforded 2.44 g (96%) of **12** as white crystals: mp 58–61 °C; IR (KBr) 2940, 2825, 2770, 1450, 1310, 1290, 1140, 1085, 970, 770, 740, 690 cm^{-1}; ^1H NMR δ 7.86–7.48 (m, 5 H, ArH), 5.46 (dq, J = 15.2, 6.1 Hz, 1 H, HC=C*H*Me), 5.32 (ddq, J = 15.2, 8.5, 0.9 Hz, 1 H, *H*C=CHMe), 3.68 (ddd, J = 9.8, 8.5, 4.2 Hz, 1 H, $HCSO_2Ph$), 2.86 (dd, J = 12.4, 4.2 Hz, 1 H, $HCNMe_2$), 2.74 (dd, J = 12.4, 9.8 Hz, 1 H, $HCNMe_2$), 2.19 (s, 6 H, $N(CH_3)_2$), 1.65 (dd, J = 6.1, 0.9 Hz, 3 H, HC=$CHCH_3$); ^{13}C NMR δ 137.99, 135.48, 133.49, 129.15, 128.69, 122.66, 67.64, 56.97, 45.51, 18.26.

(*E*)-4-(Phenylsulfonyl)non-2-ene (13). To a suspension of CuI (1.14 g, 6 mmol) in ether (25 mL) was added a 1.6 M butyllithium solution in hexane (7.5 mL, 12 mmol) at −60 °C under a nitrogen atmosphere during 15 min. The mixture was allowed to reach −10 °C during 1 h and cooled again to −60 °C. To that was then added a 60 mM ethereal solution (concentrated just before use) of **3** (100 mL, 6 mmol) from a dropping funnel during 1 h at a temperature interval off −60 to −10 °C. After the usual workup, the crude product was purified by flash chromatography on silica gel (EtOAc/hexane = 10/90), giving 1.24 g (79%) of **13** as a colorless oil: ^1H NMR δ 7.85–7.45 (m, 5 H, ArH), 5.41 (dq, J = 15.0, 6.2 Hz, 1 H, HC=C*H*Me), 5.21 (ddq, J = 15.0, 9.0, 1.3 Hz, 1 H, *H*C=CHMe), 3.42 (ddd, J = 11.0, 9.0, 3.0 Hz, 1 H, $HCSO_2Ph$), 2.05 (m, 1 H, *H*C$CHSO_2Ph$), 1.64 (dd, J = 6.2, 1.3 Hz, 3 H, HC=$CHCH_3$), 1.60 (m, partly hidden under the Me signal, 1 H, *H*C$CHSO_2Ph$), 1.25 (m, 6 H, methylene H), 0.86 (t, J = 6.4 Hz, 3 H, CH_3).

***cis*-3,6-Dimethylcyclohexene (14).** To a stirred suspension of CuI (10 g, 52.5 mmol) in ether (70 mL) was added methyllithium (65 mL, 1.6 M in ether, 104 mmol) via a syringe at −40 °C under a nitrogen atmosphere during 20 min. The homogeneous solution was allowed to warm to 0 °C during 1 h. The solution was then cooled to −40 °C, and **4** (2.0 g, 8.46 mmol) dissolved in ether (10 mL) was added (during 10 min). The reaction mixture was allowed to warm to 0 °C during 1.5 h, followed by addition of a saturated solution of NH_4Cl (10 mL), and filtered through silica gel. The ether was distilled off at ambient pressure, and the residue was applied to a silica gel column, using pentane as the eluent. The pentane was distilled off, affording 0.50 g (54%) of pure **14** as a colorless oil (>95% cis):[41] ^1H NMR δ 5.52 (s, 2 H, HC=CH), 2.15 (m, J = 7.1, 5.5, 5.5 Hz, 2 H, HCMe), 1.85–1.15 (m, 4 H, H_2CCH_2), 0.97 (d, J = 7.1 Hz, 6 H, CH_3).

Mixture of Dimethyl (*trans*-4-Methylcyclohex-2-en-1-yl)malonate (15) and Dimethyl (*trans*-6-Methylcyclohex-2-en-1-yl)malonate (16). To a mixture of **4** (350 mg, 1.48 mmol), $Pd(PPh_3)_4$ (90 mg, 0.078 mmol), and PPh_3 (75 mg, 0.286 mmol) was added a solution of sodium dimethyl malonate, prepared from dimethyl malonate (900 mg, 6.8 mmol), NaH (80% in paraffin oil, 203 mg, 6.76 mmol), and THF (12 mL). After the reaction mixture was refluxed under a nitrogen atmosphere for 22 h, a saturated aqueous solution of Na_2CO_3 (10 mL) and ether (10 mL) was added followed by separation of the layers. The aqueous phase was extracted with ether (2 × 10 mL), and the combined organic phases were filtered through silica gel, dried ($MgSO_4$), and concentrated in vacuo. Purification by flash chromatography on silica gel (EtOAc/pentane = 10/90) afforded 227 mg (64%) as a 46:54 mixture of **15** and **16**. Since the starting material consists of ~10% of the cis isomer, ~10% of the *cis*-**15** could be detected in the ^1H NMR spectrum. The 1,2- and 1,4-isomers could not be separated by HPLC (EtOAc/hexane = 20/80, silica gel). The spectroscopic data (NMR) given for the isomers were obtained from the spectrum of this mixture. Decoupling experiments were used in the assignment.

15: ^1H NMR δ 5.67 (ddd, J = 10.0, 3.0, 2.0 Hz, 1 H, H-2), 5.51 (ddd, J = 10.0, 3.0, 2.0 Hz, 1 H, H-3), 3.74 (s, 6 H, $C(CO_2CH_3)_2$), 3.31 (d, J = 9.5 Hz, 1 H, $HC(CO_2Me)_2$), 2.87 (m, 1 H, *H*C$CH(CO_2Me)_2$), 2.18 (m, 1 H, HCMe), 1.55–1.20 (m, 4 H, H_2CCH_2), 0.98 (d, J = 7.0 Hz, 3 H, CH_3).

16: ^1H NMR δ 5.77 (m, J = 10.0, 3.5, 3.5, 2.0 Hz, 1 H, H-2), 5.56 (m, J = 10.0, 5.0, 3.0, 1.8 Hz, 1 H, H-3), 3.75 and 3.72 (two s, each 3 H, $C(CO_2CH_3)$), 3.54 (d, J = 7.0 Hz, 1 H, $HC(CO_2Me)_2$), 2.57 (m, 1 H, *H*C$CH(CO_2Me)_2$), 2.01 (m, 2 H, H-4), 1.80–1.58 (m, 3 H, HCMe and H-5).

cis-**15**: ^1H NMR δ (distinguishable signals in mixture with **15** and **16**) 3.25 (d, J = 9.0 Hz, 1 H, $HC(CO_2Me)_2$), 0.96 (d, J = 7.5 Hz, 1 H, CH_3).

Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found (for the isomeric mixture): C, 63.44; H, 7.90.

***trans*-1,4-Bis(dicarbomethoxymethyl)cyclohex-2-ene (17).** To a mixture of **6** (715 mg, 2.0 mmol), $Pd(OAc)_2$ (22 mg, 0.1 mmol), and diphos (96 mg, 0.24 mmol) in THF (3 mL) was added a solution of sodium dimethyl malonate, prepared from dimethyl malonate (818 mg, 6.2 mmol) and NaH (80%, in paraffin oil, 180 mg, 6.0 mmol) in THF (8 mL). The reaction mixture was refluxed for 3.5 h under a nitrogen atmosphere. After the mixture cooled to room temperature, ether (10 mL) and saturated aqueous $NaHCO_3$ (5 mL) were added. The layers were separated and the aqueous phase was extracted with ether (3 × 5 mL). The combined organic phases were dried (Na_2SO_4) and concentrated in vacuo, followed by silica gel filtration (column: 1 × 3 cm) using EtOAc/hexane (50/50) as the eluent. The excess of dimethyl malonate was removed by Kugelrohr distillation (100 °C, 1 Torr). The crude product was purified by flash chromatography on silica gel (EtOAc/hexane = 20/80), giving 586 mg (86%) of *trans*-**17** and *cis*-**17** in a ratio of 87:13 as a colorless oil. For analytical purposes *trans*-**17** and *cis*-**17** were separated by preparative HPLC.

trans-**17**: ^1H NMR δ 5.63 (br s, 2 H, HC=CH), 3.74 and 3.73 (two s, each 6 H, $HC(CO_2CH_3)_2$), 3.27 (d, J = 8.7 Hz, 2 H, *H*C$(CO_2Me)_2$), 2.90 (m, 2 H, *H*C$CH(CO_2Me)_2$), 1.85 (m, J_{tol} = 11 Hz, 2 H, equatorial H), 1.40 (m, J_{tot} = 20 Hz, 2 H axial H); ^{13}C NMR δ 168.35, 129.45, 56.20, 52.17, 35.43, 25.90.

cis-**17**: ^1H NMR δ 5.69 (d, 2 H, HC=CH), 3.74 (s, 12 H, HC-$(CO_2CH_3)_2$), 3.32 (d, J = 9.5 Hz, 2 H, *H*C$(CO_2Me)_2$), 2.90 (m, 2 H, *H*C$HC(CO_2Me)_2$), 1.88–1.34 (m, 4 H, H_2CCH_2).

Anal. Calcd for $C_{16}H_{22}O_8$: C, 56.13; H, 6.48. Found (for the mixture of *trans*-**17** and *cis*-**17**): C, 56.02; H, 6.51.

Mixture of Dimethyl (*trans*-4-(Dimethylamino)cyclohex-2-en-1-yl)-malonate (18) and Dimethyl (*trans*-6-(Dimethylamino)cyclohex-2-en-1-yl)malonate (19). To a mixture of **7** (256 mg, 1 mmol), $Pd(PPh_3)_4$ (73 mg, 0.063 mmol), and diphos (21 mg, 0.052 mmol) in THF (2 mL) was added a solution of sodium dimethyl malonate, prepared from dimethyl malonate (285 mg, 2.2 mmol), NaH (80% in paraffin oil, 36 mg, 1.2 mmol), and THF (7 mL). After the reaction mixture was heated at reflux temperature for 13.5 h under a nitrogen atmosphere, it was concentrated on a rotary evaporator. Then ether (10 mL) and 1 M HCl (5 mL) were added and the layers were separated. The organic phase was extracted with 1 M HCl (4 × 3 mL). The aqueous phase was cooled in an ice bath and made alkaline with solid K_2CO_3. The aqueous phase was extracted with ether (4 × 5 mL). To the aqueous phase was added 2 M NaOH (3 mL) followed by extraction with ether (2 × 10 mL). The combined organic phases were then dried ($MgSO_4$) and concentrated. The excess of dimethyl malonate was removed by bulb-to-bulb distillation, affording 163 mg (64%) as a 35:65 mixture of **18** and **19**. The isomers were separated by flash chromatography on silica gel. Elution with ether/dichloromethane afforded **18** (95 mg, 37%). Subsequent elution with THF gave **19** (50 mg, 20%) as an oil.

18: ^1H NMR δ 5.77 (br d, J = 10 Hz, 1 H, HC=C (H-2)), 5.68 (br d, J = 10 Hz, 1 H, C=CH (H-3)), 3.75 and 3.74 (two s, each 3 H, $C(CO_2CH_3)_2$), 3.25 (d, J = 8.8 Hz, 1 H, $HC(CO_2Me)_2$), 3.23 (m, 1 H, $HCNMe_2$), 2.91 (m, 1 H, *H*C$CH(CO_2Me)_2$), 2.30 (s, 6 H, $N(CH_3)_2$), 1.88 (m, 2 H, homoallylic equatorial H), 1.66–1.25 (m, 2 H, homoallylic axial H).

19: ^1H NMR δ 5.70 (m, J = 10.0, the rest of J = 9 Hz, HC=C (H-2)), 5.50 (m, J = 10.0, the rest of J = 5.6 Hz, C=CH (H-3)), 3.71 and 3.69 (two s, each 3 H, $C(CO_2CH_3)_2$), 3.61 (d, J = 7.1 Hz, 1 H, $HC(CO_2Me)_2$), 2.99 (m, 1 H, *H*C$CH(CO_2Me)_2$), 2.52 (ddd, J = 12.0, 10.2, 2.7 Hz, 1 H, $HCNMe_2$), 2.19 (s, 6 H, $N(CH_3)_2$), 2.24–1.99 (m, 2 H, allylic H (H-4)), 1.91–1.78 (m, 1 H, homoallylic equatorial H (H-5)), 1.5–1.3 (m, 1 H, homoallylic axial H (H-5)); ^{13}C NMR δ 169.52, 169.35, 128.63, 127.05, 62.11, 54.45, 52.11, 40.29, 39.88, 25.49, 19.29.

(41) Hückel, W.; Feltkamp, H. *Chem. Ber.* **1959**, *92*, 2851.

((*E*)-4-(2,2-Dicarbomethoxyethyl)oct-2-ene (20). To a suspension of CuI (580 mg, 3.05 mmol) in ether (10 mL) was added *n*-butyllithium (3.9 mL of a 1.54 M solution in hexane, 6 mmol) under a nitrogen atmosphere at −70 °C. The reaction mixture was allowed to warm to 0 °C over 30 min and then **11** (340 mg, 1 mmol), dissolved in ether (4 mL) and THF (1 mL), was added. After the mixture was stirred for 30 min at 0 °C, the reaction was quenched by adding a 20% aqueous solution of NH_4Cl. The layers were separated and the aqueous phase was extracted with ether (2 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo. Purification by flash chromatography on silica gel (CH_2Cl_2/pentane = 40/60) afforded 145 mg (57%) of **20** as a colorless oil: IR (neat) 2960, 2930, 2865, 1750, 1440, 1275, 1160, 975, cm^{-1}; ^1H NMR δ 5.37 (dq, J = 15.3, 6.3 Hz, 1 H, HC=C*H*Me), 5.05 (ddq, J = 15.3, 8.8, 1.5 Hz, 1 H, *H*C=CHMe), 3.74 and 3.71 (two s, each 3 H, $C(CO_2CH_3)_2$), 3.42 (dd, J = 9.3, 5.0 Hz, 1 H, *H*$C(CO_2Me)_2$), 2.03 (ddd, J = 12.5, 9.3, 3.2 Hz, 1 H, *H*CCH$(CO_2Me)_2$), 1.85 (m, 1 H, allylic methine H), 1.70 (ddd, partly hidden under the vinylic CH_3 signal, J = 12.5, 10.0, 5.0 Hz, 1 H, *H*CCH$(CO_2Me)_2$), 1.65 (dd, J = 6.3, 1.5 Hz, 3 H, HC=CHCH_3), 1.24 (m, 6 H, remaining methylene H), 0.86 (t, J = 6.5 Hz, 3 H, CH_3); ^{13}C NMR δ 170.23, 169.99, 134.01, 126.58, 52.34, 49.94, 41.34, 35.32, 34.21, 29.23, 22.62, 17.82, 13.96.

Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44. Found: C, 65.48; H, 9.57.

Dimethyl ((*E*)-4-(Dimethylamino)pent-2-en-1-yl)malonate (21). To a mixture of **11** (90 mg, 0.26 mmol), $Pd(PPh_3)_4$ (31 mg, 0.026 mmol), PPh_3 (14 mg, 0.056 mmol), and diphos (10 mg, 0.026 mmol) was added a solution of dimethylamine (450 mg, 10 mmol) in THF (5 mL). The reaction mixture was refluxed for 10 h under a nitrogen atmosphere. The reaction was then cooled to room temperature, ether (3 mL) and 2 M HCl (5 mL) were added, and the layers were separated. The organic phase was extracted with 1 M HCl (3 × 2 mL). The water phase was washed with ether (10 mL). The aqueous phase was made alkaline with solid K_2CO_3 and extracted with ether (4 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated in vacuo to give 30 mg (47%) of **21** as an oil: ^1H NMR δ 5.50 (m, 2 H, HC=CH), 3.73 (s, 6 H, $C(CO_2CH_3)_2$), 3.45 (t, J = 7.4 Hz, 1 H, $HC(CO_2Me)_2$), 2.83 (m, 1 H, $HCNMe_2$), 2.63 (m, 2 H, $H_2CCH(CO_2Me)_2$), 2.20 (s, 6 H, $N(CH_3)_2$), 1.11 (d, J = 6.6 Hz, 3 H, CH_3).

Dimethyl ((*E*)-1-(Dimethylamino)pent-2-en-4-yl)malonate (22). **12** (507 mg, 2.0 mmol), $Pd(dba)_2$ (86 mg, 0.15 mmol), diphos (60 mg, 0.15 mmol), dimethyl malonate (528 mg, 4.0 mmol), THF (5 mL), and a 0.4 M solution of sodium dimethyl malonate were mixed together and refluxed for 5 h under a nitrogen atmosphere. Workup as for **21** afforded 315 mg (64%) of **22** as an oil: IR (neat) 2960, 2820, 2780, 1750, 1460, 1440, 1240, 1155, 1020, 980 cm^{-1}; ^1H NMR δ 5.55 (m, 2 H, HC=CH), 3.73 and 3.69 (two s, each 3 H, $C(CO_2CH_3)_2$), 3.31 (d, J = 8.8 Hz, 1 H, $HC(CO_2Me)_2$), 2.96 (m, 1 H, HCMe), 2.85 (m, 2 H, H_2CNMe_2), 2.18 (s, 6 H, $N(CH_3)_2$), 1.09 (d, J = 6.8 Hz, 3 H, CH_3); ^{13}C NMR δ 168.65, 168.53, 134.66, 128.45, 61.53, 57.67, 52.34, 52.22, 44.97, 37.01, 18.35.

Dimethyl (2-Methyl-2-(phenylsulfonyl)but-3-en-1-yl)malonate (23). Diisopropylamine (506 mg, 5 mmol) in THF (1 mL) was added to a solution of *n*-butyllithium (3.2 mL of a 1.5 M solution in hexane, 4.8 mmol) in THF (2 mL) under nitrogen at −10 °C. After the solution was stirred for 30 min at −10 °C, it was cooled to −55 °C, and **9** (655 mg, 2.9 mmol) in THF (3 mL) was added. After 20 min methyl iodide (426 mg, 3 mmol) in THF (2 mL) was added during 1 min via a syringe. The reaction temperature was now allowed to increase slowly. After 2 h an additional portion of methyl iodide (50 mg, 0.35 mmol) in THF (1 mL) was added and the reaction was monitored by HPLC. After the solution was stirred for an additional 30 min between −10 and 0 °C, it was warmed to room temperature. Then a 10% aqueous solution of NH_4Cl (2 mL) and ether (5 mL) was added. The combined organic phases were separated and the aqueous phase was extracted with ether (2 × 5 mL). After drying ($MgSO_4$) and concentration the crude product was filtered through silica gel, affording 639 mg (94%) of **23** as white crystals: mp 74–77 °C; IR (KBr) 3060, 3000, 2960, 1740, 1440, 1355, 1290, 1230, 1140, 1075, 950, 725, 695 cm^{-1}; ^1H NMR δ 7.86–7.48 (m, 5 H, ArH), 5.88 (dd, J = 17.4, 10.7 Hz, 1 H, H_2C=C*H*), 5.38 (d, J = 10.7 Hz, 1 H, terminal C=CH), 5.11 (d, J = 17.4 Hz, 1 H, terminal C=CH), 3.74 and 3.70 (two s, each 3 H, $C(CO_2CH_3)_2$), 3.44 (t(dd), J = 6.5, 6.4 Hz, 1 H, *H*$C(CO_2Me)_2$), 2.69 (dd, J = 14.2, 6.4 Hz, 1 H, *H*CCH$(CO_2Me)_2$), 2.61 (dd, J = 14.2, 6.5 Hz, 1 H, *H*CCH$(CO_2Me)_2$), 1.35 (s, 3 H, CH_3); ^{13}C NMR δ 169.32, 169.16, 134.91, 134.19, 133.93, 130.84, 128.57, 121.38, 67.39, 52.88, 52.75, 47.55, 32.09, 16.09.

Anal. Calcd for $C_{16}H_{20}O_6S$: C, 56.46; H, 5.92. Found (for the crude product): C, 56.32; H, 5.81.

Methyl (*E*)-2,7-Dicarbomethoxy-4-methyl-8-oxo-4-nonenoate (24). To a mixture of **23** (165 mg, 0.48 mmol), $Pd(PPh_3)_4$ (31 mg, 0.026 mmol), and PPh_3 (10 mg, 0.026 mmol) was added a solution of sodium methyl acetoacetate, prepared from methyl acetoacetate (246 mg, 2.1 mmol), NaH (80% in paraffin oil, 30 mg, 1 mmol), and THF (5 mL). The reaction mixture was refluxed for 1 h under a nitrogen atmosphere and then cooled to room temperature, and 1 M HCl (1 mL), saturated $NaHCO_3$ (5 mL), and ether (10 mL) were added. The layers were separated and the aqueous phase was extracted with ether (3 × 5 mL), dried ($MgSO_4$), and concentrated at reduced pressure. The crude product was then purified by flash chromatography on silica gel (EtOAc/hexane = 15/85), affording 91 mg (60%) of **24**[18] (E/Z = 88/12).

***cis*-4-Carbomethoxy-3-methyl-1-(phenylsulfonyl)cyclohexene (25).** $AlCl_3$ (3.33 g, 25 mmol), toluene (30 mL), and methyl acrylate (2.15 g, 25 mmol) were mixed together and stirred under nitrogen until a homogeneous solution was formed. A 23 mM solution (217 mL) of 2-(phenylsulfonyl)-1,3-pentadiene (5 mmol) in CH_2Cl_2 was then concentrated to a volume of 60 mL on a rotary evaporator and added to the first solution during 10 min. After 4 h of stirring at room temperature, water (100 mL) was added and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (50 mL). The combined organic phases were filtered through silica gel, washed with water (2 × 50 mL), and dried ($MgSO_4$). Concentration at reduced pressure gave 1.4 g (95%) of **25** as an oil (~93%, plus ~7% other isomers[20]). A pure sample, for analytical purposes, was obtained by preparative HPLC: IR (neat) 3070, 3030, 2960, 2880, 1800, 1735, 1650, 1450, 1380, 1300, 1235, 1150, 1090, 1025, 760, 725, 695 cm^{-1}; ^1H NMR δ 7.90–7.45 (m, 5 H, ArH), 7.01 (ddd, J = 4.9, 2.1, 1.2 Hz, 1 H, HC=C), 3.67 (s, 3 H, CO_2CH_3), 2.90 (m, 1 H, HCMe), 2.61 (ddd, J = 11.7, 5.4, 3.0 Hz, 1 H, $HCCO_2Me$), 2.42–2.27 (m, 1 H, allylic H), 2.21–1.88 (m, 2 H, allylic and homoallylic H), 1.84–1.60 (m, 1 H, homoallylic H), 1.00 (d, J = 7.2 Hz, 3 H, CH_3); ^{13}C NMR δ 173.56, 141.38, 139.10, 138.93, 133.31, 129.16, 127.99, 51.64, 42.22, 31.57, 22.56, 19.35, 15.37.

***cis*-4-Acetyl-3-methyl-1-(phenylsulfonyl)cyclohexene (26).** To a 15.8 mM solution (CH_2Cl_2) of **3** (120 mL, 1.9 mmol) was added methyl vinyl ketone (5 mL), and the solution was concentrated on a rotary evaporator until ~50 mL was left. The reaction mixture was stirred at room temperature for 72 h and then concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (eluents: EtOAc/hexane = 10/90 and 20/80), yielding 380 mg (68%) as a mixture of four isomers in a ratio of 65:29:3:3, the main being the cycloadduct **26**, which could be separated by preparative HPLC (EtOAc/hexane = 30/70) from the three others.

26: ^1H NMR δ 7.88–7.48 (m, 5 H, ArH), 7.04 (ddd, J = 5.0, 2.2, 1.2 Hz, 1 H, HC=C), 2.96 (br sext, J_{tot} = 31.6 Hz, 1 H, HCMe), 2.64 (ddd, J = 11.5, 5.0, 3.0 Hz, 1 H, $HCCO_2Me$), 2.33 (m, J = 17.5, 5.7, 2.5, 1.2, 1 H, equatorial allylic H), 2.08 (m, 1 H, axial allylic H), 1.87 (m, 1 H, equatorial homoallylic H), 1.66 (m, 1 H, axial homoallylic H), 0.94 (d, J = 7.2 Hz, 3 H, CH_3).

Anal. Calcd for $C_{15}H_{18}O_3S$: C, 64.72; H, 6.52. Found (for the mixture of isomers): C, 64.59; H, 6.44.

Cycloadduct 28. To a 60 mM solution (in CH_2Cl_2) of **3** (25 mL, 1.5 mmol) was added 1-morpholino-1-cyclohexene (5.0 g, 30 mmol), and the reaction mixture was stirred at room temperature for 60 h. Removal of the solvent in vacuo and purification by flash chromatography on silica gel (eluents: EtOAc/hexane = 10/90 and 20/80) afforded 282 mg (50%) of **28** as a colorless oil: IR (neat) 2950, 2860, 1450, 1310, 1275, 1155, 1120, 1090, 1000, 760, 725, 695, 645 cm^{-1}; ^1H NMR δ 7.87–7.48 (m, 5 H, ArH), 6.93 (m, 1 H, HC=C), 3.52 (m, 4 H, H_2COCH_2), 2.75–2.50 (m, 5 H, H_2CNCH_2, HCMe), 2.27–2.01 (m, 3 H, allylic H, methine H), 1.80–1.17 (m, 8 H, methylene H), 1.12 (d, J = 7.2 Hz, 3 H, CH_3); ^{13}C NMR δ 143.02, 139.34, 136.12, 133.19, 129.04, 127.87, 68.25, 58.19, 46.43, 35.73, 32.45, 29.99, 28.06, 27.65, 22.51, 21.74, 15.25.

Anal. Calcd for $C_{21}H_{29}O_3NS$: C, 67.17; H, 7.78. Found: C, 66.99; H, 7.69.

Cycloadduct 29. To a 50.8 mM solution (in CH_2Cl_2) of **2** (20 mL, 1 mmol) was added 1-morpholino-1-cyclohexene (1.67 g, 10 mmol), and the reaction mixture was stirred at room temperature for 2 h. Workup as for **28** afforded 253 mg (70%) of **29** as a colorless oil: IR (neat) 2930, 2860, 2820, 1450, 1310, 1295, 1270, 1155, 1120, 1090, 760, 725, 690, 645 cm^{-1}; ^1H NMR δ 7.88–7.48 (m, 5 H, ArH), 6.93 (br s, 1 H, HC=C), 3.51 (br s, 4 H, H_2COCH_2), 2.48 (br s, 4 H, H_2CNCH_2), 2.40–1.88 (m, 5 H, allylic and methine H), 1.76–1.10 (m, 8 H, methylene H); ^{13}C NMR δ 139.57, 137.81, 135.83, 133.02, 128.98, 127.69, 67.85, 56.20, 44.91, 34.38, 27.95, 27.36, 27.01, 26.78, 23.79, 23.44, 22.04.

Anal. Calcd for $C_{20}H_{27}O_3NS$: C, 66.45; H, 7.53. Found: C, 66.26; H, 7.65.

Mixture of 4-Carbomethoxy-1-(phenylsulfonyl)cyclohexene (30a) and 5-Carbomethoxy-1-(phenylsulfonyl)cyclohexene (30b). A 12.2 mM solution 90 mL of **2** (1.1 mmol) in CH_2Cl_2 was concentrated on a rotary evaporator until ~10 mL was left, and methyl acrylate (20 mL) was added. The reaction mixture was heated at reflux temperature for 45

h and, after cooling, concentrated in vacuo. Purification by flash chromatography on silica gel (EtOAc/hexane = 20/80) gave 227 mg (74%) as a 2:1 mixture of **30a** and **30b** as determined by ^{1}H NMR from the CO_2CH_3 signal: IR (KBr) 2950, 1730, 1440, 1305, 1150, 1090, 725, 690 cm^{-1}; ^{1}H NMR δ 7.89-7.48 (m, 5 H, ArH), 7.06 (m, 1 H, vinylic H), 3.66 (s, 3 H, OCH_3), 2.54 (m, 3 H), 2.28 (m, 2 H), 2.08 (m, 1 H), 1.70 (m, 1 H). The isomer **30b** is distinguishable in a mixture by ^{1}H NMR δ 3.62 (s, OCH_3).

Anal. Calcd for $C_{14}H_{16}O_4S$: C, 59.98; H, 5.75. Found: C, 60.03; H, 5.82.

1-(Phenylsulfonyl)-4-ethoxycyclohexene (31). A 12 mM solution (100 mL) of 2-(phenylsulfonyl)-1,3-butadiene (1.2 mmol) in CH_2Cl_2 was concentrated on a rotary evaporator to a volume of ca. 10 mL, and ethyl vinyl ether (30 mL) was added. The reaction mixture was heated at reflux temperature for 45 h, and then concentrated at reduced pressure. Purification by flash chromatography on silica gel (eluents: EtOAc/hexane = 10/90 and 20/80) afforded 173 mg (54%) of **31** as a colorless oil: IR (neat) 2985, 2930, 2878, 1450, 1310, 1290, 1155, 1090, 725, 690, 630 cm^{-1}; ^{1}H NMR δ 7.90-7.47 (m, 5 H, ArH), 6.94 (m, 1 H, HC=C), ~3.55 (m, 1 H, HCOEt), 3.48 (two q, J = 6.9 Hz, 2 H, OCH_2Me), 2.67-2.49 (m, 1 H), 2.40-2.15 (m, 3 H), 1.95-1.80 (m, 1 H), 1.78-1.62 (m, 1 H), 1.15 (t, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR δ 139.45, 139.28, 136.00, 133.19, 129.10, 127.93, 71.65, 63.52, 31.81, 26.83, 21.10, 15.48.

Anal. Calcd for $C_{14}H_{18}O_3S$: C, 63.13; H, 6.81. Found: C, 62.90; H, 6.70.

***cis*-1-Cyano-5-carbomethoxy-6-methylcyclohexene (32).** **25** (310 mg, 1.06 mmol) in MeOH (4 mL), acetic acid (58 μL, 1.0 mmol), and KCN in H_2O (0.4 mL) were mixed together and heated at 50 °C for 31 h. Ether (10 mL) and brine (5 mL) were added and the layers were separated. The aqueous phase was extracted with ether (10 mL). The combined organic phases were washed with aqueous 2 M NaOH (2 × 3 mL), H_2O (3 mL), and finally with brine (3 mL). After drying ($MgSO_4$) and removal of the solvent, the crude product was purified by flash chromatography on silica gel (EtOAc/hexane = 25/75), affording 97 mg (53%) of **32** as an oil: IR (neat) 2960, 2225, 1740, 1440, 1235, 1210, 1170 cm^{-1}; ^{1}H NMR δ 6.59 (m, unresolved, 1 H, HC=CCN), 3.72 (s, 3 H, CO_2CH_3), 2.82 (m, 1 H, HCMe), 2.69 (ddd, J = 12.2, 5.3, 3.2 Hz, 1 H, $HCCO_2Me$), 2.35-2.17 (m, 2 H, allylic H), 2.02-1.88 (m, 1 H, homoallylic H), 1.84-1.68 (m, 1 H, homoallylic H), 1.09 (d, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR δ 173.27, 144.07, 118.74, 117.28, 51.76, 42.45, 32.45, 25.55, 17.82, 15.48.

Anal. Calcd for $C_{10}H_{13}O_2N$: C, 67.02; H, 7.31. Found: C, 67.02; H, 7.44.

1-Carbomethoxy-2-methyl-1,3-cyclohexadiene (33). To a solution of **25** (330 mg, 1.12 mmol) in MeOH (5 mL) was added a solution of NaOMe in MeOH (prepared from 85 mg of Na (3.7 mmol) and 2.5 mL of MeOH). After the solution was refluxed for 6 h, $NaHCO_3$ (300 mg, 3.6 mmol) was added, and the resulting mixture was allowed to stir at room temperature overnight, followed by silica gel filtration (elution with ether). The solvent was removed by distillation at ambient pressure. The product was bulb-to-bulb distilled, yielding 123 mg (72%) of pure **33**[42] as a colorless oil: ^{1}H NMR δ 6.10 (m, J = 9.0, 4.5, 4.5 Hz, 1 H, H-4), 5.90 (m, J = 9.0, 1.5, 1.5 Hz, 1 H, H-3), 3.75 (s, 3 H, CO_2CH_3), 2.49-2.37 (m, 2 H), 2.22-2.07 (m, 2 H), 2.14 (s, 3 H, CH_3).

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Registry No. 1, 102860-22-0; **2**, 109802-71-3; **3**, 109802-72-4; *trans*-**4**, 109802-73-5; *cis*-**4**, 109802-96-2; *trans*-**5**, 109802-74-6; *cis*-**5**, 109802-97-3; **6**, 109802-75-7; **7**, 109802-76-8; **8**, 109802-77-9; **9**, 109802-78-0; **10a**, 109802-79-1; **10b**, 109802-98-4; **11**, 102860-24-2; **12**, 109802-80-4; **13**, 97663-39-3; **14**, 59356-67-1; *trans*-**15**, 109802-81-5; *cis*-**15**, 109802-99-5; **16**, 109802-82-6; *trans*-**17**, 109802-83-7; *cis*-**17**, 109803-00-1; **18**, 82736-46-7; **19**, 109802-84-8; **20**, 109802-85-9; **21**, 109802-86-0; **22**, 109802-87-1; **23**, 109802-88-2; (*E*)-**24**, 87040-04-8; (*Z*)-**24**, 109803-01-2; **25**, 109862-70-6; **26**, 109802-89-3; **27**, 670-80-4; **28**, 109802-90-6; **29**, 109802-91-7; **30a**, 109802-92-8; **30b**, 109803-02-3; **31**, 109802-93-9; **32**, 109802-94-0; **33**, 72359-60-5; **34**, 109802-95-1; MeLi, 917-54-4; BuLi, 109-72-8; $NaHC(CO_2Me)_2$, 18424-76-5; Me_2NH, 124-40-3; $Pd(PPh_3)_4$, 14221-01-3; $Pd(OAc)_2$, 3375-31-3; $Pd(dba)_2$, 32005-36-0; $H_2C(CO_2Me)_2$, 108-59-8; $NaHC(CO_2Me)COMe$, 34284-28-1; $H_2C{=}CHCO_2Me$, 96-33-3; $MeCOCH{=}CH_2$, 78-94-4; $EtOCH{=}CH_2$, 109-92-2; 3-(phenylsulfonyl)-4-(chloromercuri)cyclohexene, 102815-53-2; 3-(phenylsulfonyl)-4-(chloromercuri)but-1-ene, 102815-47-4; 3-(phenylsulfonyl)-4-(chloromercuri)-1-pentene, 109803-03-4; 5-(chloromercuri)-4-(phenylsulfonyl)pent-2-ene, 102815-50-9.

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A Novel Synthesis of Ikarugamycin: The Carbocyclic Portion

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Abstract: The tetracyclic glycol **2**, a potential intermediate for the synthesis of ikarugamycin (**1**), was synthesized. Key transformations involved were the following: the preparation with resolution of the enantiomeric esters **3**; their separate elaboration and ultimate recombination to form the trienes **17**; photocyclization of **17** with ground-state conformational bias to form diene **18**; and dissolving metal reduction of **20** with internal proton delivery to form predominantly monoene **22**.

In 1972 two Japanese groups described the isolation[1] and detailed, degradative structure elucidation[2] for the novel antimicrobial and amoebicide ikarugamycin (**1**). The interest of several synthetic groups, including this one, was attracted by the unusual carbocyclic portion of this unique natural product[3] and the obvious facility with which the three, linearly fused carbocyclic rings might be constructed by an intramolecular Diels-Alder reaction.[4] An alternate route could be devised that would take advantage of certain symmetry elements present in the carbocyclic moiety. In particular, we have depicted in Scheme I a retrosynthetic analysis which first disconnects the tetramic acid moiety at the two obvious junctions of the carbon-carbon π systems and then proceeds (with inversion of one stereochemical center) to the tetracyclic intermediate **2**.

Progression on to the natural product would involve the following: (1) cleavage of the glycol moiety with differentiation of the two resulting aldehyde functions; (2) inversion at the only

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