Cycloaddition Chemistry of 1,3- and 2,3-Bis(phenylsulfonyl) 1,3-Dienes with Enamines and Ynamines

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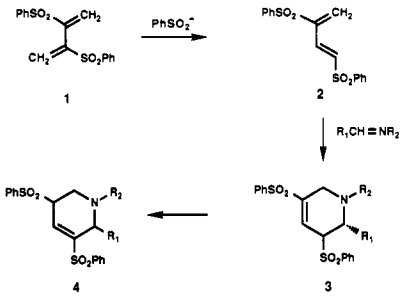
1,3- and 2,3-bis(phenylsulfonyl) dienes were found to react smoothly with a variety of enamines and enamine equivalents to give [4 + 2]-cycloadducts in excellent yields. The cycloaddition proceeds with high regioselectivity affording carbocycles as well as heterocycles. The reactivity of the 1,3-isomer was found to be much greater than the 2,3-isomer and is a consequence of both conformational and electronic factors. Formation of rearranged cycloadducts occurs when unactivated enamines are used with the 2,3-substituted diene. This reaction occurs by an initial rearrangement of the 2,3-diene to the 1,3-isomer followed by cycloaddition with the enamine. Cycloaddition of several 4-substituted 1,3-bis(phenylsulfonyl)butadienes with amidines and thioformamide gave dihydropyridines and thiopyrans, respectively. Indole reacts with both the 1,3- and 2,3-dienes to give the same product distribution of epimeric carbazoles. An entirely different reaction occurred when 1-indolylmagnesium iodide was used. The 2,3-diene reacts with 1-(diethylamino)-1-propyne at low temperatures to give a [2 + 2]-cycloadduct. Reaction of the isomeric 1,3-diene with the same ynamine gave [4 + 2]-cycloadducts as did several 4-substituted 1,3-bis(phenylsulfonyl)butadienes.

Hetero Diels–Alder cycloaddition processes have received increased attention owing to their obvious use in the area of heterocyclic synthesis.[1-7] The comprehensive review by Boger and Weinreb[8] contains numerous examples demonstrating the broad application of [4 + 2]-cycloadditions with heteroatom-containing dienes and dienophiles. Our interest in this area was initiated by a study of the reaction of 2,3-bis(phenylsulfonyl)-1,3-butadiene (1) and various C–N π-bonds.[9] In our first report, we described the cycloaddition reaction of 1 with various oximes as a method for piperidine formation.[9] In an



investigation which followed, we demonstrated that bissulfone 1 undergoes cycloaddition to a variety of simple imines under mild conditions to produce novel rearranged piperidines.[10] The formation of the rearranged cycloadduct 4 proceeds by a mechanism that involves addition of benzene sulfinate anion onto the terminal π-bond of the activated diene. The resulting carbanion undergoes proton transfer followed by aryl sulfinate ejection to give 1,3-bis(phenylsulfonyl)-1,3-butadiene (2) as a transient intermediate. This reactive diene undergoes a rapid [4 + 2]-cycloaddition to give 3 followed by a subsequent hydrogen 1,3-shift. The 1,3-substituted butadiene 2 is more highly activated toward [4 + 2]-cycloaddition than the 2,3-isomer as a consequence of its markedly lowered LUMO energy level (−1.39 vs −0.29 eV). In an attempt to ascertain whether the 2,3-isomer would undergo [4 + 2]-cycloaddition chemistry, we decided to explore its behavior with electron-rich π-systems. Herein we detail the results of such a study.

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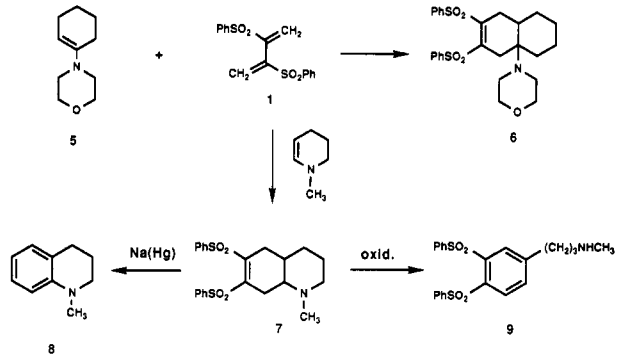
Results and Discussion

There are two major problems that must be addressed in the development of 2,3-bis(phenylsulfonyl)-1,3-butadiene as a reactant in the Diels–Alder reaction: (1) this diene exists exclusively in the transoid conformation and possesses a high barrier for rotation about the 2,3-π bond, and (2) the conditions necessary to induce the cycloaddition result in rearrangement of the 2,3-isomer into the more reactive 1,3-isomer.[10] One approach to overcome these difficulties involves the use of an electron-rich dienophile which would be expected to accelerate the inverse electron demand [4 + 2]-cycloaddition.[11]

We initially decided to test the feasibility of the [4 + 2]-cycloaddition of 1 by using 1-morpholino-2-cyclohexene (5) as the dienophile. A typical reaction was carried out



(1) Schmidt, R. R. *Acc. Chem. Res.* **1986**, *19*, 250.
(2) Danishefsky, S.; Webb, R. R. *J. Org. Chem.* **1984**, *49*, 1955.
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(10) Padwa, A.; Harrison, B.; Norman, B. H. *Tetrahedron Lett.* **1989**, *30*, 3259. Padwa, A.; Gareau, Y.; Harrison, B.; Norman, B. H. *J. Org. Chem.* **1991**, *56*, 2713.
(11) For related reactions of enamines with other phenylsulfonyl-substituted dienes, see: Bäckvall, J. E.; Rise, F. *Tetrahedron Lett.* **1989**, *30*, 5347. Bäckvall, J. E.; Juntunen, S. K. *J. Am. Chem. Soc.* **1987**, *109*, 6396. Bäckvall, J. E.; Juntunen, S. K. *J. Org. Chem.* **1988**, *53*, 2398. Masuyama, Y.; Yamazaki, H.; Toyoda, Y.; Kurusu, Y. *Synthesis* **1985**, 964. Lee, S. J.; Lee, J. C.; Peng, M. L.; Chou, T. S. *J. Chem. Soc., Chem. Commun.* **1989**, 1020.

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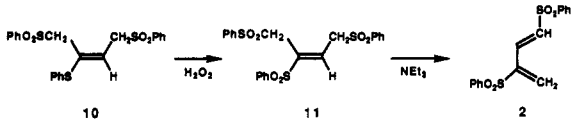
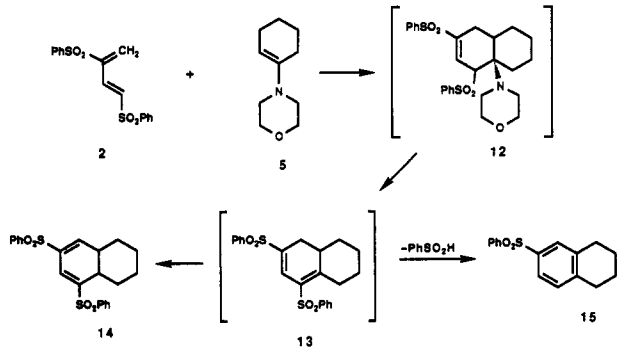
by simply stirring the two reagents in methylene chloride at 25 °C for 24 h. The structure of the resulting [4 + 2]-cycloadduct **6** (61%) was assigned on the basis of its characteristic spectral data.[12] A similar reaction occurred using *N*-methyl-1,2,3,4-tetrahydropyridine as the 2π-reactant. Exposure of the resulting cycloadduct **7** to sodium amalgam in methanol[13] afforded *N*-methyl-1,2,3,4-tetrahydroquinoline (**8**).[14] When cycloadduct **7** was heated in chloroform at 80 °C, the compound slowly disappeared ($t_{1/2} \sim 90$ min) and *N*-methyl-3-[3,4-bis(phenylsulfonyl)-phenyl]propylamine (**9**) was formed. The transformation of **7** into **9** most likely proceeds by an initial elimination followed by a subsequent oxidation to the thermodynamically stable aromatic ring.

The isomeric 1,3-bis(phenylsulfonyl)-1,3-butadiene (**2**) is highly activated toward cycloaddition as a consequence of its markedly lowered LUMO energy level compared with the 2,3-disubstituted isomer **1**.[10] Consequently, we decided to explore the behavior of **2** with the same set of enamines as was used with **1** so as to evaluate its synthetic potential. The sequence of reactions that was used to prepare diene **2** involved the oxidation of 1,4-bis(phenylsulfonyl)-2-(phenylthio)-2-butene (**10**)[15,16] to the corresponding trisulfone **11** with a 30% hydrogen peroxide solution. Elimination of benzene sulfinate to give diene **2** was accomplished by stirring **11** with triethylamine in benzene at 25 °C. Because of the problem of self-dimerization, we opted to generate **2** in situ in the presence of the appropriate dienophile.



10 11 2

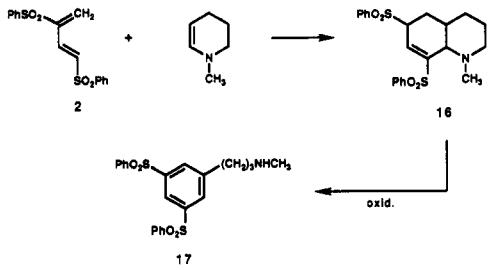
The in situ generation of **2** and subsequent reaction with 1-morpholino-1-cyclohexene (**5**) resulted in a 1:9 mixture of 5,7-bis(phenylsulfonyl)-1,2,3,4,4a,8a-hexahydronaphthalene (**14**) and 6-(phenylsulfonyl)-1,2,3,4-tetrahydronaphthalene (**15**). Heating a sample of **14** in benzene



2 5 12 14 13 15

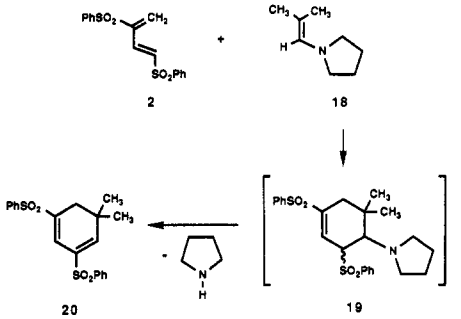
in the presence of base resulted in elimination of phenylsulfinic acid and the quantitative formation of **15**. The formation of **14** undoubtedly occurs by elimination of morpholine from the initially formed Diels–Alder adduct **12** followed by a 1,5-sigmatropic hydrogen shift from the resulting diene **13**.

Cycloaddition of **2** with *N*-methyl-1,2,3,4-tetrahydropyridine resulted in the isolation of the expected Diels–Alder adduct **16** in 84% yield. This compound is air sensitive and upon standing was converted into the 1,3,4-trisubstituted benzene amine **17** in 68% yield.



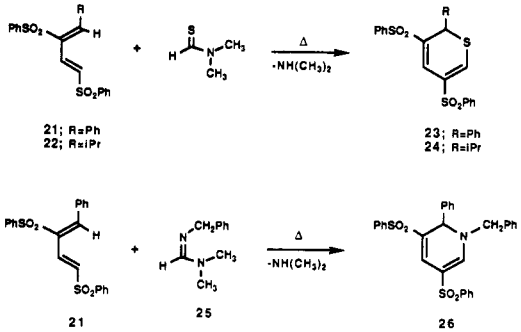
2 16 17

We also studied the [4 + 2]-cycloaddition chemistry of several 4-substituted 1,3-bis(phenylsulfonyl)-1,3-butadienes. These compounds were prepared by treatment of a benzene solution of 1,3-bis(phenylsulfonyl)-1-propene and an aldehyde in the presence of a catalytic amount of piperidine and acetic acid followed by azeotropic removal of water. This procedure was used to prepare dienes **21** and **22** starting from benzaldehyde and isobutyl aldehyde.[10] The reaction of **2** with 1-(2-methylpropenyl)pyrrolidine (**18**) in methylene chloride at 25 °C for 6 h afforded cycloadduct **19** which spontaneously lost pyrrolidine to give **20** in 74% yield.



2 18 20 19

Heating a sample of **21** or **22** with *N*,*N*-dimethylthioamide in benzene afforded products **23** and **24** in 84% and 64% yield, respectively. The initial Diels–Alder adducts readily lose dimethylamine to produce the substituted 2*H*-thiopyran ring system. A related reaction occurred



21 25 26

with **21** and *N*,*N*-dimethyl-*N*-benzyl methanimidamide (**25**) and produced adduct **26** in 83% yield. It should be noted that the incorporation of a substituent onto the 4-position of the diene significantly diminished the rate of cycloaddition relative to the unsubstituted case.

We have also studied the cycloaddition reaction of both the 2,3- and 1,3-bis(phenylsulfonyl)-substituted dienes with amidine **25** and indole since these reagents formally cor-

(12) It is conceivable that the 4 + 2-cycloaddition takes place in a stepwise fashion via a transient zwitterionic intermediate.

(13) DeLucchi, O.; Pasquato, L. *Tetrahedron* **1988**, *44*, 4755. Paquette, L. A.; Lin, H.; Gunn, B. P.; Coghlan, M. J. *J. Am. Chem. Soc.* **1988**, *110*, 5818.

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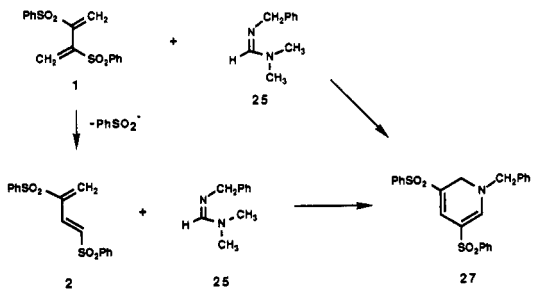
(17) Padwa, A.; Harrison, B.; Murphree, S. S.; Yeske, P. E. *J. Org. Chem.* **1989**, *54*, 4232.

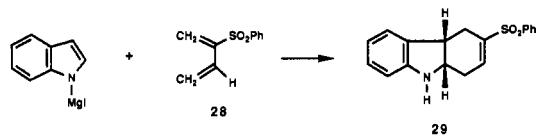
respond to enamine equivalents.[18] Reaction of the 2,3-



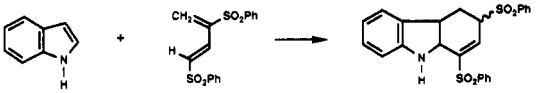
substituted diene 1 with amidine 25 required 12 h of heating at 80 °C. The only material that was isolated in 52% yield corresponded to the rearranged dihydropyridine 27. This same compound was generated (87%) from the reaction of the 1,3-substituted diene 2 with amidine 25. The formation of 27 from diene 1 and 25 implies that the simple [4 + 2]-cycloaddition path is sufficiently slow so that rearrangement of 1 → 2 first occurs under the experimental conditions. Presumably, some trace of phenylsulfinate anion was present in the reaction mixture and served as an initiator for the diene isomerization step.

The indole skeleton is a fundamental structural unit of numerous biologically active alkaloids.[19] As such, the chemistry of indole has been widely investigated[20] and the indole-based alkaloids have been the target of countless synthetic efforts.[21-23] Indole could prove to be an appropriate starting material for further alkaloid synthesis if suitable chemistry can be induced from this parent skeleton. Since the enamine functionality of indole dominates its reactivity,[24] we felt successful [4 + 2]-cycloaddition of the bis(phenylsulfonyl)-substituted dienes with the 2,3-double bond was possible.

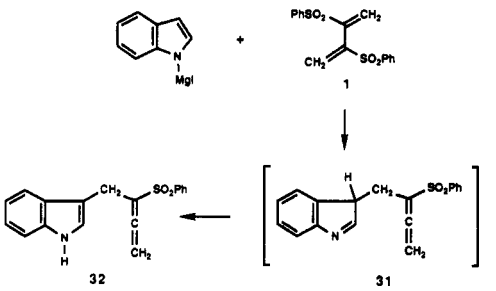
Bäckvall and co-workers have recently reported on the preparation and synthetic use of 2-(phenylsulfonyl)buta-1,2-diene (28).[11,25] Unlike the bis(phenylsulfonyl)-sub-



stituted dienes (1 and 2), the Bäckvall diene reacts with both electron-rich and electron-deficient olefins. Enol ethers and enamines were used as dienophiles in the inverse electron-demand Diels–Alder reaction.[26] Although the cycloaddition of 28 with indole failed, it was possible to induce reaction by using the magnesium salt of indole as a dienophile.[27] The enamine-like reactivity of indole is increased sufficiently in the presence of a weak base[18] or on formation of the magnesium salt[28] to allow for a [4 + 2]-cycloaddition. In contrast to the results obtained with the monoactivated phenylsulfonyl diene 28, the more highly activated bis(phenylsulfonyl) diene 2 cycloadds directly with indole to give a mixture of epimeric carbazoles (30a and 30b) in 61% yield. A similar result was obtained using the 2,3-substituted diene 1, and presumably a prior diene isomerization (i.e., 1 → 2) is involved here.

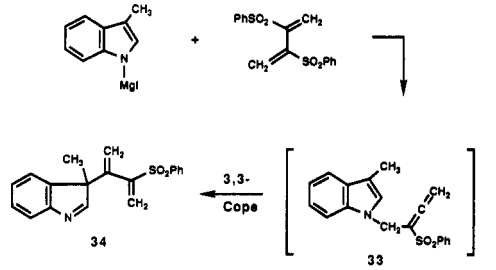


An entirely different reaction took place when 1-indolylmagnesium iodide was allowed to react with 2,3-bis(phenylsulfonyl) diene 1. The product formed (80%) corresponded to 3-(2-(phenylsulfonyl)-2,3-butadienyl)-indole (32). The formation of 32 appears to involve en-



amine addition to the terminal methylene carbon of diene 1, and the resulting carbanion rapidly ejects a phenylsulfinate anion to form the allene. This is then followed by a 1,3-sigmatropic hydrogen shift to regenerate the indole skeleton.

The reaction of 1 with 3-methyl-1-indolylmagnesium iodide was also examined and was found to give 3*H*-indole 34 in 67% yield. In this case, alkylation at the C_3-position of the indole skeleton is retarded as a consequence of the methyl substituent. Instead, attack of the magnesium salt occurs on the nitrogen atom producing allene 33 as a transient intermediate which rapidly undergoes a 3,3-sigmatropic Cope rearrangement to give 3*H*-indole 34.



While the [4 + 2]-cycloaddition reactions of vinyl sulfones with enamines have been well investigated, much less attention has been paid to the carbon–carbon bond-forming reaction of vinyl sulfones with ynamines. Thiete, 1,1-dioxide (35) had previously been reported to undergo [2 + 2]-cycloadditions with ynamines.[29] More recently, Eisch and co-workers found that such [2 + 2]-cycloadditions are not restricted to strained vinyl sulfones, such as 35, but are general for vinylic, acetylenic, and 1,3-dienylic sulfones.[30] We have investigated the reaction of

(18) Bergman, J.; Bäckvall, J. E.; Lindstrom, J. O. *Tetrahedron* **1973**, *29*, 971.
(19) Sundberg, R. J. *The Chemistry of Indoles*; Academic Press: New York, 1970.
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(26) Bäckvall, J. E.; Rise, F. *Tetrahedron Lett.* **1989**, *30*, 5347.
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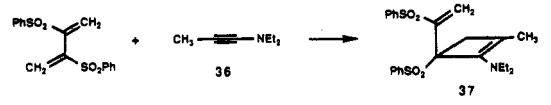
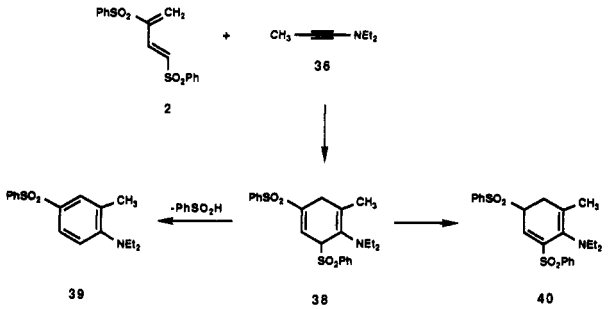
(29) Paquette, L. A.; Houser, R. W.; Rosen, M. *J. Org. Chem.* **1970**, *35*, 905.
(30) Eisch, J. J.; Galle, J. E.; Hallenbeck, L. E. *J. Org. Chem.* **1982**, *47*, 1608. Eisch, J. J.; Hallenbeck, L. E.; Lucarelli, M. A. *J. Org. Chem.* **1991**, *56*, 4095.

diene 1 with a typical ynamine with the aim of evaluating its potential in organic synthesis. It was found that the reaction of 1 with (*N*,*N*-diethylamino)propyne (36) in CH_2Cl_2 proceeded smoothly and gave the [2 + 2]-cycloaddition product 37 in 81% yield.



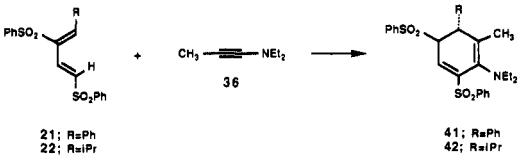
We also studied the cycloaddition behavior of the isomer 1,3-bis(phenylsulfonyl)butadiene 2 with ynamine 36. When a mixture of 2 and 36 was heated in benzene at 80 °C, *N*,*N*-diethyl-4-(phenylsulfonyl)-*o*-toluidine (39) was obtained in 85% yield. The formation of 39 may proceed



by an initial [4 + 2]-cycloaddition, and the resulting adduct 38 undergoes loss of phenylsulfinic acid. When the reaction was carried out in CH_2Cl_2 at 25 °C, compounds 39 (21%) and 40 (67%) were formed. Under the milder conditions used, the initially produced Diels–Alder adduct 38 undergoes a competitive 1,3-hydrogen shift to give 40 in addition to losing phenylsulfinic acid.[31] Molecular mechanics calculations using the Steliou Model program indicate that the lowest energy conformer of the 1,3-isomer corresponds to the cisoid conformation necessary for the Diels–Alder reaction.[32] The 2,3-substituted diene 1 exists exclusively in the transoid form and consequently cannot undergo a concerted [4 + 2]-cycloaddition with ynamine 36.

In an extension of this work we studied the reaction of the 4-substituted 1,3-bis(phenylsulfonyl)-1,3-butadienes 21 and 22 with ynamine 36. Treatment of a methylene chloride solution of diene 21 or 22 with ynamine 36 afforded cycloadducts 41 and 42 in good yield. Once again, the initially formed Diels–Alder adduct rapidly undergoes a 1,3-sigmatropic hydrogen shift to produce the observed products.

In summary, 1,3- and 2,3-bis(phenylsulfonyl)-1,2-butadienes have been observed to be reactive substrates with



a variety of enamines and ynamines. The resulting cycloadducts contain several reactive sites for subsequent chemistry and should find useful application in organic synthesis.

Experimental Section

Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70 eV. Unless otherwise noted, all reactions were performed in oven-dried glassware under an atmosphere of extra dry nitrogen. Solutions were evaporated under reduced pressure with a rotary evaporator, and the residue was chromatographed on a silica gel column using an ethyl acetate–hexane mixture as the eluent unless specified otherwise.

Reaction of 2,3-Bis(phenylsulfonyl)-1,3-butadiene (1) with 1-Morpholino-1-cyclohexene (5). A solution containing 229 mg (0.7 mmol) of 1 and 0.12 mL of 1-morpholino-1-cyclohexene in 10 mL of CH_2Cl_2 was stirred at 25 °C for 24 h. Removal of the solvent was followed by purification of the crude orange oil by silica gel chromatography using a 2:3 mixture of ethyl acetate–hexane as the eluent. The major fraction contained 210 mg (61%) of a white solid whose structure was assigned as 2,3-bis(phenylsulfonyl)-4a-(1-morpholino)-1,4,4a,5,6,7,8,8a-octahydronaphthalene (6): mp 163–164 °C; IR (KBr) 1470, 1265, 1085, 730, 720, and 690 cm^{-1}; *m/e* (M + H) 502; NMR ($CDCl_3$, 300 MHz) δ 1.10–1.80 (m, 9 H), 1.88–2.02 (m, 1 H), 2.15–2.25 (m, 2 H), 2.32–2.60 (m, 3 H), 2.68 (s, 1 H), 2.75–2.92 (m, 1 H), 3.30–3.50 (m, 4 H), 7.45–7.75 (m, 6 H), and 7.96 (d, 4 H, *J* = 7.9 Hz). Anal. Calcd for $C_{26}H_{31}NO_5S_2$: C, 62.25; H, 6.23; N, 2.79. Found: C, 62.39; H, 6.24; N, 2.80.

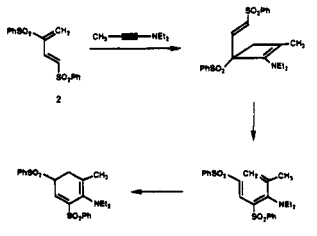
Reaction of 2,3-Bis(phenylsulfonyl)-1,3-butadiene (1) with *N*-Methyl-1,2,3,4-tetrahydropyridine. To a 100-mg (0.3 mmol) sample of 1 in 10 mL of CH_2Cl_2 was added 30 mg (0.3 mmol) of *N*-methyl-1,2,3,4-tetrahydropyridine in 2 mL of CH_2Cl_2 under a nitrogen atmosphere. After the mixture was stirred for 8 h, the solvent was removed under reduced pressure and the residue was purified by flash silica gel chromatography to give 105 mg (81%) of a white solid whose structure was assigned as 1,2,3,4,4a,5,8,8a-octahydro-1-methyl-6,7-bis(phenylsulfonyl)quinoline (7): mp 141–142 °C; IR (KBr) 1445, 1330, 1160, 1085, and 690 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.33 (m, 3 H), 1.66 (m, 1 H), 1.96 (s, 3 H), 2.12 (m, 1 H), 2.42–2.62 (m, 5 H), 2.85 (dt, 2 H, *J* = 15.6 and 4.5 Hz), 7.45–7.58 (m, 6 H), and 7.97 (t, 4 H, *J* = 8.4 Hz). Anal. Calcd for $C_{22}H_{25}NO_4S_2$: C, 61.24; H, 5.84; N, 3.25. Found: C, 61.08; H, 5.67; N, 3.10.

Support for the structure of 7 was obtained by its reduction to *N*-methyl-1,2,3,4-tetrahydroquinoline (8).[14] To a 400-mg (0.93 mmol) sample of 7 in 30 mL of methanol was added 2.5 g (17.6 mmol) of dibasic sodium phosphate and 2.8 g (7.3 mmol) of sodium amalgam (6%). The reaction mixture was allowed to stir at 25 °C overnight and filtered, and the solvent was removed under reduced pressure. The crude solid was purified by flash silica gel chromatography to give 78 mg (57%) of *N*-methyl-1,2,3,4-tetrahydroquinoline (8) whose spectral properties were identical in all detail with an authentic sample: NMR ($CDCl_3$, 300 MHz) δ 1.98 (m, 2 H), 2.77 (t, 2 H, *J* = 6.5 Hz), 2.88 (s, 3 H), 3.22 (t, 2 H, *J* = 5.7 Hz), 6.61 (m, 2 H), 6.95 (d, 1 H, *J* = 7.2 Hz), and 7.08 (t, 1 H, *J* = 7.5 Hz).

Heating a 50-mg (0.12 mmol) sample of 7 in 2 mL of $CHCl_3$ at 80 °C for 3 h afforded *N*-methyl-3-[3,4-bis(phenylsulfonyl)-phenyl]propylamine (9) in 92% yield: mp 189–190 °C; IR (KBr) 1480, 1300, 1225, 1150, 730, and 700 cm^{-1}; NMR (CD_3OD, 300 MHz) δ 1.93 (q, 2 H, *J* = 7.8 Hz), 2.64 (s, 3 H), 2.74 (t, 2 H, *J* = 7.8 Hz), 2.95 (t, 2 H, *J* = 7.8 Hz), and 7.35–7.94 (m, 13 H). Anal. Calcd for $C_{22}H_{23}NO_4S_2$: C, 61.52; H, 5.40; N, 3.26. Found: C, 61.45; H, 5.26, N; 3.18.

Reaction of 1,3-Bis(phenylsulfonyl)-1,3-butadiene (2) with 1-Morpholino-1-cyclohexene (5). To a solution containing 110 mg (0.23 mmol) of trisulfone 11 and 0.4 mL of the enamine in

(31) It is also conceivable that the formation of 40 proceeds via an initial [2 + 2]-cycloaddition followed by consecutive electrocyclic ring opening 6π-electrocyclization reactions.



(32) MM2 calculations were performed on a VAX 8550 using Model 2.98 with the "statistical coordinate" option in TTY (i.e., CONF) to write the appropriate batch files for minimization with the use of BAKMDL to find the global minimum. We thank Professor Kosta Steliou for making this program available to us.

8 mL of benzene was added 1 equiv of triethylamine in 1 mL of benzene. This solution was heated at reflux under nitrogen for 20 h. The reaction mixture was filtered through a pad of silica gel, and this was followed by removal of the solvent under reduced pressure to leave behind a light yellow oil. Purification of the oil by silica gel chromatography afforded two fractions. The main fraction contained 56 mg (89%) of 6-(phenylsulfonyl)-1,2,3,4-tetrahydronaphthalene (**15**): mp 92–93 °C; IR (KBr) 1600, 1585, 1320, 1205, 1195, and 690 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.70–1.85 (m, 4 H), 2.70–2.85 (m, 4 H), 7.15 (d, 1 H, J = 7.8 Hz), 7.43–7.58 (m, 3 H), 7.58–7.70 (m, 2 H), and 7.92 (d, 2 H, J = 7.2 Hz). Anal. Calcd for $C_{16}H_{16}O_2S$: C, 70.56; H, 5.92. Found: C, 70.64; H, 5.95.

The second fraction contained 10 mg (9%) of a white solid whose structure was assigned as 5,7-bis(phenylsulfonyl)-1,2,3,4,4a,5-hexahydronaphthalene (**14**): mp 212–213 °C; IR (KBr) 1580, 1445, 1385, 1300, 1220, 1135, 1085, 815, and 690 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.07–1.25 (m, 1 H), 1.25–1.45 (m, 2 H), 1.62–2.35 (m, 6 H), 4.03–4.18 (m, 1 H), 7.07 (bs, 1 H), 7.25 (bs, 1 H), 7.45–7.55 (m, 2 H), 7.55–7.67 (m, 3 H), 7.67–7.80 (m, 3 H), and 7.89 (d, 2 H, J = 7.4 Hz). Anal. Calcd for $C_{22}H_{22}O_4S_2$: C, 63.74; H, 5.35. Found: C, 63.63; H, 5.41. Heating a sample of **14** in benzene in the presence of triethylamine afforded tetrahydronaphthalene **15** in quantitative yield.

Reaction of 1,3-Bis(phenylsulfonyl)-1,3-butadiene (2) with *N*-Methyl-1,2,3,4-tetrahydropyridine. To 246 mg (0.51 mmol) of trisulfone **11** in 10 mL of methylene chloride was added 126 mg (1.27 mmol) of *N*-methyl-1,2,3,4-tetrahydropyridine[33] in 3 mL of CH_2Cl_2 which contained 2 equiv of triethylamine. After being stirred for 8 h under a nitrogen atmosphere, the mixture was filtered through a pad of silica gel and washed with ethyl acetate. The solvent was removed under reduced pressure, and the crude oil obtained was purified by flash silica gel chromatography to give 175 mg (84%) of a white solid whose structure was assigned as 1,2,3,4,4a,5,6,8a-octahydro-1-methyl-6,8-bis(phenylsulfonyl)-quinoline (**16**): mp 112–113 °C; IR (neat) 1590, 1450, 1320, 1150, 730, and 695 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.40–2.05 (m, 8 H), 2.07 (s, 3 H), 2.50 (m, 1 H), 2.75 (m, 2 H), 6.80 (m, 1 H), 7.44–7.66 (m, 6 H), and 7.83 (t, 4 H, J = 8.4 Hz); m/e (M + H) 432. Anal. Calcd for $C_{22}H_{25}NO_4S_2$: C, 61.24; H, 5.84; N, 3.25. Found: C, 61.07; H, 5.69; N, 3.04.

A sample of **16** was found to readily air oxidize to *N*-methyl-3-[3,5-bis(phenylsulfonyl)phenyl]propylamine (**17**) in 68% yield: IR (KBr) 1620, 1480, 1300, 1230, 1150, and 700 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.99 (q, 2 H, J = 7.8 Hz), 2.42 (s, 3 H), 2.63 (t, 2 H, J = 7.8 Hz), 2.71 (t, 2 H, J = 7.8 Hz), and 7.28–7.94 (m, 13 H). Anal. Calcd for $C_{22}H_{23}NO_4S_2$: C, 61.52; H, 5.40; N, 3.26. Found: C, 61.36; H, 5.28; N, 3.15.

Reaction of 1,3-Bis(phenylsulfonyl)-1,3-butadiene (2) with 1-(2-Methylpropenyl)pyrrolidine (18). To a solution containing 103 mg (0.22 mmol) of trisulfone **11** and 0.03 mL of 1-(2-methylpropenyl)pyrrolidine (**18**)[3] in 7 mL of CH_2Cl_2 was added 1 equiv of triethylamine in 1 mL of CH_2Cl_2. The solution was stirred at 25 °C under nitrogen for 6 h. The reaction mixture was filtered through a pad of silica gel followed by removal of the solvent to leave behind a light yellow oil. Purification of this material by silica gel chromatography gave 62 mg (74%) of 1,3-bis(phenylsulfonyl)-5,5-dimethyl-1,3-cyclohexadiene (**20**) as a white solid: mp 163–164 °C; IR (KBr) 1620, 1575, 1445, 1310, 1080, 785, 720, and 685 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 0.93 (s, 6 H), 2.17 (brs, 2 H), 6.90 (d, 1 H, J = 10 Hz), 7.16 (d, 1 H, J = 1.0 Hz), 7.45–7.70 (m, 6 H), and 7.75–7.90 (m, 4 H). Anal. Calcd for $C_{20}H_{20}O_4S_2$: C, 61.83; H, 5.19. Found: C, 61.67; H, 5.22.

Reaction of 1,3-Bis(phenylsulfonyl)-4-phenyl-1,3-butadiene (21) with *N,N*-Dimethylthioformamide. A mixture containing 138 mg (0.34 mmol) of diene **21**[10] and 0.03 mL (0.39 mmol) of *N,N*-dimethylthioformamide in 15 mL of benzene was heated at 95 °C in a sealed tube for 96 h. The solvent was removed under reduced pressure and the residue was crystallized from methylene chloride–ether to give 128 mg (84%) of 3,5-bis(phenylsulfonyl)-2-phenyl-2*H*-thiopyran (**23**) as a yellow solid: mp 179–180 °C; IR (KBr) 1780, 1595, 1450, 1310, 1085, 800, and 690 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 5.05 (s, 1 H), 6.62 (d, 2 H, J = 7.6 Hz), 6.89 (t, 2 H, J = 7.6 Hz), 7.06 (t, 1 H, J = 7.3 Hz), 7.28 (t, 2 H, J = 7.8 Hz), 7.41 (t, 1 H, J = 7.3 Hz), 7.53–7.73 (m, 5 H), 7.77 (s, 2 H), and 7.87 (d, 2 H, J = 7.5 Hz); calcd for $C_{23}H_{18}O_4$ 454.0367, found 454.0355. Anal. Calcd for $C_{23}H_{18}O_4$: C, 77.07; H, 5.07. Found: C, 77.14; H, 4.93.

Reaction of 1,3-Bis(phenylsulfonyl)-4-isopropyl-1,3-butadiene (22) with *N,N*-Dimethylthioformamide. A mixture containing 100 mg (0.27 mmol) of diene **22**[10] and 0.03 mL (0.39 mmol) of *N,N*-dimethylthioformamide in 10 mL of benzene was heated at 100 °C in a sealed tube for 40 h. The solvent was removed under reduced pressure, and the residue was crystallized from methylene chloride–ether to give 71 mg (64%) of 3,5-bis(phenylsulfonyl)-2-isopropyl-2*H*-thiopyran (**24**) as a yellow solid: mp 134–135 °C; IR (KBr) 1610, 1580, 1445, 1305, 1080, 790, and 685 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 0.46 (d, 3 H, J = 6.7 Hz), 0.79 (d, 3 H, J = 6.9 Hz), 1.78–1.96 (m, 1 H), 3.68 (dd, 1 H, J = 4.1 and 1.3 Hz), 7.45–7.65 (m, 7 H), and 7.75–7.90 (m, 5 H). Anal. Calcd for $C_{20}H_{20}O_4S_3$: C, 57.12; H, 4.79. Found: C, 57.05; H, 4.84.

Reaction of 1,3-Bis(phenylsulfonyl)-4-phenyl-1,3-butadiene (21) with *N,N*-Dimethyl-*N*-benzylmethanimidamide (25). A mixture containing 200 mg (0.49 mmol) of diene **21** and 78 mg (0.49 mmol) of *N,N*-dimethyl-*N'*-benzylmethanimidamide (**25**) in 10 mL of benzene was heated at reflux for 7 d under a nitrogen atmosphere. The solvent was removed under reduced pressure, and the residue was crystallized from a methylene chloride–hexane mixture to give 212 mg (83%) of *N*-benzyl-2-phenyl-3,5-bis(phenylsulfonyl)-1,2-dihydropyridine (**26**) as a yellow solid: mp 200–201 °C; IR (KBr) 1620, 1450, 1305, 1185, 985, 960, and 695 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 4.28 (AB_q, 2 H, J = 15.0 Hz), 5.25 (s, 1 H), and 6.99–7.88 (m, 22 H). Anal. Calcd for $C_{30}H_{25}NO_4S_2$: C, 68.28; H, 4.79; N, 2.65. Found: C, 68.11; H, 4.86; N, 2.57.

Preparation of *N*-Benzyl-3,5-bis(phenylsulfonyl)-1,2-dihydropyridine (27). A mixture containing 167 mg (0.5 mmol) of diene **1** and 0.064 mL of amidine **25** in 10 mL of benzene was heated at 80 °C for 12 h. After removal of the solvent under reduced pressure, the crude oil was subjected to silica gel flash chromatography to give 91 mg (52%) of *N*-benzyl-3,5-bis(phenylsulfonyl)-1,2-dihydropyridine (**27**) as a yellow solid: mp 190–191 °C; IR (KBr) 1630, 1555, 1445, 1300, 1140, 1085, and 695 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 3.99 (s, 2 H), 4.28 (s, 2 H), and 7.06–7.85 (m, 17 H); m/e (M + H) 452. Anal. Calcd for $C_{24}H_{21}NO_4S_2$: C 63.83; H, 4.70; N, 3.10. Found: C, 63.58; N, 4.63; N, 3.07.

The same cycloadduct was prepared in 87% yield from the reaction of trisulfone **11** with 2 equiv of triethylamine and amidine **25** in 10 mL of benzene at 80 °C for 12 h.

Reaction of Indole with 2,3-Bis(phenylsulfonyl)-1,3-butadiene (1). To a 106-mg (0.9 mmol) sample of indole and 0.073 mL (0.9 mmol) of dry pyridine in 10 mL of benzene was added 150 mg (0.45 mmol) of diene **1**. The mixture was heated at reflux under nitrogen for 24 h. After being cooled, the solution was quenched with water and the organic phase was separated. The aqueous phase was extracted with benzene, and the combined organic extracts were dried over magnesium sulfate. Removal of the solvent followed by silica gel chromatography gave 134 mg (68%) of a 2:1 mixture of 1,3-bis(phenylsulfonyl)-3,4,4a,9a-tetrahydrocarbazole (**30a** and **30b**). The two isomers were separated by crystallization from methylene chloride–hexane. The major adduct **30a** was a white solid: mp 175–176 °C; IR (KBr) 1605, 1480, 1300, 1140, 1080, 755, and 685 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 2.07 (m, 1 H), 2.36 (m, 1 H), 3.61 (m, 1 H), 3.92 (m, 1 H), 4.14 (d, 1 H, J = 8.1 Hz), 5.02 (m, 1 H), 6.61 (d, 1 H, J = 7.5 Hz), 6.73 (t, 1 H, J = 7.5 Hz), 6.98 (m, 2 H), and 7.55–7.85 (m, 11 H); m/e (M + H) 452. Anal. Calcd for $C_{24}H_{21}NO_4S_2$: C, 63.83; H, 4.70; N, 3.10. Found: C, 63.70; H, 4.71; N, 3.05.

The minor adduct **30b** was a white solid: mp 171–172 °C; IR (KBr) 1615, 1490, 1320, 1155, 765, and 695 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.47 (m, 1 H), 2.14 (m, 1 H), 3.08 (m, 1 H), 3.92 (m, 1 H), 4.21 (m, 1 H), 4.53 (d, 1 H, J = 3.3 Hz), 6.55 (d, 1 H, J = 7.8 Hz), 6.71 (t, 1 H, J = 7.8 Hz), 7.05 (q, 2 H, J = 3.3 Hz), 7.29 (s, 1 H), and 7.52–7.88 (m, 10 H). Anal. Calcd for $C_{24}H_{21}NO_4S_2$: C, 63.83; H, 4.70; N, 3.10. Found: C, 63.73; H, 4.74; N, 3.06.

The same mixture of cycloadducts was prepared in 79% yield from the reaction of trisulfone **11** with 2 equiv of triethylamine and indole in 10 mL of benzene at 80 °C for 12 h.

(33) Beeken, P.; Fowler, F. W. *J. Org. Chem.* **1980**, *45*, 1336.

Reaction of 1-Indolylmagnesium Iodide with 2,3-Bis(phenylsulfonyl)-1,3-butadiene (1). To a 28-mg sample of magnesium turnings in 3 mL of ether was added 0.062 mL of methyl iodide. After being stirred for 30 min, the solution was transferred dropwise to a solution containing 116 mg (1.0 mmol) of indole in 6 mL of a 1:1 benzene–ether mixture. The solution was stirred for 30 min under nitrogen, and then 150 mg (0.45 mmol) of diene 1 in 8 mL of benzene was added dropwise via a syringe. After being stirred for 2 h, the mixture was quenched with ammonium chloride and the organic phase was separated. The aqueous phase was extracted with benzene, and the organic solution was dried over magnesium sulfate. Removal of the solvent under reduced pressure followed by silica gel chromatography gave 98 mg (80%) of 3-(2-(phenylsulfonyl)-2,3-butadienyl)indole (**32**): IR (neat) 1970, 1940, 1450, 1310, 1150, 750, and 690 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 3.78 (t, 2 H, J = 3.0 Hz), 5.19 (t, 2 H, J = 3.0 Hz), 6.92–7.85 (m, 10 H), and 8.14 (bs, 1 H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 23.5, 89.9, 109.6, 110.6, 112.1, 117.9, 118.8, 121.4, 122.6, 126.2, 127.3, 128.3, 132.7, 135.5, 139.7, and 208.1. Anal. Calcd for $C_{18}H_{15}NO_2S$: C, 69.88; H, 4.89; N, 4.53. Found: C, 69.69; H, 5.04; N, 4.47.

Reaction of 3-Methyl-1-indolylmagnesium Iodide with 2,3-Bis(phenylsulfonyl)-1,3-butadiene (1). To 23 mg of magnesium turnings in 3 mL of ether was added 0.058 mL of methyl iodide. After being stirred for 30 min, the solution was transferred dropwise to a solution containing 123 mg (1.24 mmol) of 3-methylindole in 6 mL of a 1:1 mixture of benzene–ether. The mixture was stirred for 30 min under nitrogen, and then 160 mg (0.48 mmol) of diene 1 in 8 mL of benzene was added dropwise. The solution was quenched after 2 h with aqueous ammonium chloride, and the organic phase was separated. The aqueous phase was extracted with benzene, and the combined organic solution was dried over magnesium sulfate. Removal of the solvent under reduced pressure followed by silica gel chromatography gave 102 mg (67%) of 3-methyl-3-(1-methylene-2-(phenylsulfonyl)-2-propenyl)-3*H*-indole (**34**): IR (neat) 1605, 1450, 1310, 1160, 950, 780, and 695 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 1.36 (s, 3 H), 4.79 (s, 1 H), 5.38 (s, 1 H), 5.60 (s, 1 H), 5.94 (s, 1 H), and 7.14–7.81 (m, 10 H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 18.6, 61.4, 120.8, 120.9, 121.5, 124.3, 126.2, 127.9, 128.5, 128.7, 133.3, 137.1, 137.6, 141.4, 147.3, 154.5, and 175.7. Anal. Calcd for $C_{19}H_{17}NO_2S$: C, 70.57; H, 5.30; N, 4.33. Found: C, 70.41; H, 5.18; N, 4.07.

Reaction of 1-(Diethylamino)-1-propyne (36) with 2,3-Bis(phenylsulfonyl)-1,3-butadiene (1). A solution containing 267 mg (0.8 mmol) of diene 1 in 10 mL of CH_2Cl_2 was cooled to −5 °C in an acetone/ice bath. To this solution was added dropwise 0.1 mL of ynamine **36**[34] in 2 mL of methylene chloride. After being stirred for 1 h, the solvent was removed under reduced pressure and the crude oil was subjected to flash silica gel chromatography to give 288 mg (81%) of 2-(diethylamino)-3-(1-phenylsulfonyl)-ethenyl)-1-methyl-3-(phenylsulfonyl)-1-cyclobutene (**37**) as a clear oil: IR (neat) 1675, 1450, 1310, 1150, 1085, 750, 730, and 695 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 0.99 (t, 6 H, J = 7.2 Hz), 1.29 (s, 3 H), 2.45 (AB_q, 2 H, J = 13.7 Hz), 2.94 (m, 2 H), 3.15 (m, 2 H), 6.84 (s, 1 H), 7.01 (s, 1 H), and 7.38–7.84 (m, 10 H). Anal. Calcd for $C_{23}H_{27}NO_4S_2$: C, 62.02; H, 6.11; N, 3.15. Found: C, 61.87; H, 6.06; N, 2.97.

(34) Brandsma, L. *Preparative Acetylenic Chemistry*; 2nd ed.; Elsevier: New York, 1988; p 235.

Reaction of 1-(Diethylamino)-1-propyne (36) with 1,3-Bis(phenylsulfonyl)-1,3-butadiene (2). To a solution containing 142 mg (0.35 mmol) of trisulfone 11 in 10 mL of benzene was added 0.1 mL (0.93 mmol) of ynamine **36** in 3 mL of benzene, and the mixture was heated at 80 °C for 3 h. The solvent was removed under reduced pressure, and the crude oil obtained was purified by flash silica gel chromatography to give 104 mg (85%) of *N,N*-diethyl-4-(phenylsulfonyl)-*o*-toluidine (**39**) on the basis of its spectral properties: mp 87–88 °C; IR (neat) 1585, 1445, 1325, 1145, 745, 720, and 690 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 0.98 (t, 6 H, J = 7.2 Hz), 2.27 (s, 3 H), 3.03 (q, 2 H, J = 7.2 Hz), and 6.99–7.91 (m, 8 H). Anal. Calcd for $C_{17}H_{21}NO_2S$: C, 67.30; H, 6.98; N, 4.62. Found: C, 67.26; H, 6.85; N, 4.49.

Carrying out the reaction in methylene chloride at 25 °C afforded a mixture of two compounds which could be separated by flash silica gel chromatography. The minor fraction (21%) was identified as **39** while the major component (67%) was assigned as 2-(diethylamino)-1-methyl-3,5-bis(phenylsulfonyl)-1,3-cyclohexadiene (**40**) on the basis of its spectral properties: IR (neat) 1445, 1315, 1145, 1085, 915 and 730 cm^{-1}.; NMR ($CDCl_3$, 300 MHz) δ 0.99 (t, 6 H, J = 7.2 Hz), 1.69 (s, 3 H), 2.05 (d, 1 H, J = 20 Hz), 2.40 (dd, 1 H, J = 20 and 2.2 Hz), 2.83 (m, 2 H), 3.07 (m, 2 H), 4.80 (s, 1 H), 6.74 (m, 1 H), and 7.25–7.83 (m, 10 H); m/e (M + H) 446. Anal. Calcd for $C_{23}H_{27}NO_4S_2$: C, 62.01; H, 6.11; N, 3.15. Found: C, 61.99; H, 6.15; N, 3.08.

Reaction of 1,3-Bis(phenylsulfonyl)-4-phenyl-1,3-butadiene (21) with 1-(Diethylamino)-1-propyne. To a solution containing 350 mg (0.85 mmol) of diene **21** in 10 mL of methylene chloride was added 0.11 mL of ynamine **36** in 2 mL of methylene chloride at 25 °C under a nitrogen atmosphere. After being stirred for 8 h, the solvent was removed under reduced pressure and the crude yellow solid was purified by flash silica gel chromatography to give 344 mg (89%) of a yellow solid whose structure was assigned as 2-(diethylamino)-1-methyl-6-phenyl-3,5-bis(phenylsulfonyl)-1,3-cyclohexadiene (**41**): mp 147–148 °C; IR (KBr) 1570, 1440, 1080, 840, 790, and 750 cm^{-1}; NMR ($CDCl_3$) δ 1.19 (t, 6 H, J = 7.1 Hz), 2.17 (s, 3 H), 3.40 (m, 4 H), 6.10 (s, 1 H), 6.63 (d, 1 H, J = 15.0 Hz), and 7.06–7.89 (m, 16 H). Anal. Calcd for $C_{29}H_{31}NO_4S_2$: C, 66.76; H, 6.00; N, 2.68. Found: C, 66.69; H, 5.93; N, 2.63.

Reaction of 1,3-Bis(phenylsulfonyl)-4-isopropyl-1,3-butadiene (22) with 1-(Diethylamino)-1-propyne. To a solution containing 200 mg (0.53 mmol) of diene **22** in 10 mL of methylene chloride was added 0.074 mL (0.7 mmol) of 1-(diethylamino)-1-propyne in 2 mL of methylene chloride under a nitrogen atmosphere at 25 °C. After the mixture was stirred for 8 h, the solvent was removed under reduced pressure to give a yellow oil. Purification of this material by silica gel chromatography gave 218 mg (85%) of 2-(diethylamino)-1-methyl-3,5-bis(phenylsulfonyl)-6-isopropyl-1,3-cyclohexadiene (**42**) as a bright yellow solid: mp 137–138 °C; IR (KBr) 1580, 1515, 1450, 1140, 730, and 700 cm^{-1}; NMR ($CDCl_3$, 300 MHz) δ 0.79 (bs, 6 H), 1.10 (t, 6 H, J = 7.2 Hz), 1.78 (s, 3 H), 2.47 (m, 1 H), 3.34 (m, 4 H), 5.27 (d, 1 H, J = 9.3 Hz), 6.32 (d, 1 H, J = 15.0 Hz), and 7.20–7.73 (m, 11 H). Anal. Calcd for $C_{26}H_{33}NO_4S_2$: C, 64.03; H, 6.83; N, 2.87. Found: C, 64.10; H, 6.86; N, 2.84.

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