Halogenovinyl Sulfones. 6.[1] Synthesis of Condensed Heterocycles by Diastereoselective Intramolecular Diels−Alder Reactions of Sulfonyl-Substituted Trienes

Hideki Takeuchi,[†] Tetsuya Fujimoto,[†] Kenji Hoshino,[†] Jiro Motoyoshiya,[‡] Akikazu Kakehi,[§] and Iwao Yamamoto*[,†]

Department of Functional Polymer Science, Faculty of Textile Science and Technology, Shinshu University, Ueda, Nagano 386-8567, Japan, Department of Materials Creation Chemistry, Faculty of Textile Science and Technology, Shinshu University, Ueda, Nagano 386-8567, Japan, and Department of Chemistry and Material Engineering, Faculty of Engineering, Shinshu University, Wakasato, Nagano 380-8553, Japan

Received February 3, 1998

Sulfonyl trienes having a chiral center on the allyl carbon of the diene moiety were prepared from L-amino acid as chiral building blocks. Intramolecular Diels−Alder reaction of the sulfonyl trienes having *E*-geometry on the diene moiety proceeded on the si-face and exo-selectively to give *cis*-isoindoles as a sole product in good yields. But using the sulfonyl trienes having *Z*-geometry on the diene part, the ratio of the diastereomers of the products decreased to about 80:20. The observed stereoselectivity can be explained by calculations with semiempirical and ab initio methods.

Many reports about Diels−Alder reactions of dienes with sulfonyl-substituted dienophiles can be found in the literature, because vinyl sulfones have higher reactivity than the other electron-withdrawing groups such as nitro, cyano, esters, and ketones and the sulfonyl substituents of the products are easily removed under mild conditions.[2] That complex molecules can be constructed in a single step under mild conditions stereo- and regioselectively via intramolecular Diels−Alder reactions of vinyl sulfones might be expected; however, examples of the reactions are rare.[3] Recently, we reported the synthesis of racemic mixtures of dibenzopyran derivatives via a diastereoselective intramolecular Diels−Alder reaction of vinyl sulfones.[1] We were interested in this procedure because it might be applied to the diastereoselective synthesis of heterocyclic compounds having more than one chiral center.

Generally, facial selectivity of cycloaddition can be influenced by a chiral building block in which one face of the diene or dienophile is blocked preferentially. Incorporation of a single stereogenic center in an allylic position of either a dienophile or a diene, particularly, when a heteroatom is present, is known to exert a direction influence.[4] In this paper, we wish to report highly diastereoselective intramolecular Diels−Alder reactions of vinyl sulfones with dienes having a chiral building block at the allylic position.

Results

Synthesis of Sulfonyl Trienes and Their Intramolecular Diels−Alder Reactions. Reaction of *N*-benzylphenylalaninol (**1c**)[5] with 1,3-dichloro-2-(phenylsulfonyl)propane[6] in the presence of triethylamine at room temperature gave alcohol **2c** in 76% yield. A Swern oxidation of the alcohol **2c** using oxalyl chloride, dimethyl sulfoxide, and triethylamine afforded aldehyde **3c** quantitatively. A Wittig reaction of **3c** with phosphonium salt **6** in the presence of potassium *tert*-butoxide in THF at room temperature gave desired sulfonyl triene **4c** in 36% yield.

The ^{1}H NMR spectrum of **4c** showed the signals of olefinic protons at 5.84 and 5.40 ppm with a coupling constant of 15.6 Hz which correspond to *E* geometry. No signals assigned to a *Z*-diene were observed.

The intramolecular Diels−Alder reaction of **4c** was performed in boiling benzene to give isoindole derivative **5c** in 83% yield as a single diastereomer ($[\alpha]^{26}_D$ = +69.74°). The structure of **5c** was determined by spectral data and confirmed by X-ray analysis that indicated the absolute configuration of bridge head methine carbon was *S* and that of the other bridge head carbon was *R* (Figure 1). Intramolecular Diels−Alder reactions under the same conditions using **4a**,**b** instead of **4c** gave **5a**,**b** in 79% and 69% yields, respectively. The ^{13}C NMR spectra of these products **5a**,**b** were similar to that of **5c**, which suggested that these compounds had the same configuration (Table 1).

On the basis of the above results, these reactions proceeded *exo*- and π-face (*si*-face)-selectively[7] to give isoindoles having the same configuration, and the stereoselectivity did not depend on the bulk of the substituent at the allylic position.

[†] Department of Functional Polymer Science.
[‡] Department of Materials Creation Chemistry.
[§] Department of Chemistry and Material Engineering.

(1) Yamamoto, I.; Kohara, T.; Fujimoto, T.; Ohta, K. *Phosphorus, Sulfur, Silicon* **1996**, *116*, 203.
(2) (a) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhorven, T. R.; *Tetrahedron Lett*. **1976**, 3477. (b) Julia, M.; Mark, J. *Tetrahedron Lett*. **1973**, 4833.
(3) (a) Craig, D.; Fiacher, S. A.; Kemal, O.; Plessner, T. *Tetrahedron Lett*. **1988**, *29*, 6369. (b) Kametani, T.; Aizawa, M.; Nemoto, H. *Tetrahedron* **1981**, *37*, 2547. (c) Jung, M. E.; Truc, V. C. *Tetrahedron Lett*. **1988**, *29*, 6059.
(4) (a) Tripathy, R.; Franck, R.; Onan, L. D. *J. Am. Chem. Soc.* **1988**, *110*, 3257. (b) Fisher, M. J.; Hehre, W. J.; Kahn, S. D.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 4625. (c) Datta, S. C.; Frank, R. R. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2023. (d) Bloch, R.; Chaptal-Gradoz, N. *J. Org. Chem*. **1994**, *59*, 4162.
(5) Davidsen, S. K.; Chu-Moyer, M. Y. *J. Org. Chem*. **1989**, *54*, 5558.
(6) Anzeveno, P. B.; Mattews, D. P.; Barney, C. L.; Barbuch, R. J. *J. Org. Chem*. **1989**, *49*, 3134.
(7) Franck, R. W.; Argade, S.; Subramaniam, C. S.; Frechet, D. M. *Tetrahedron Lett*. **1985**, *27*, 3187.

S0022-3263(98)00181-9 CCC: $15.00
Published on Web 09/22/1998

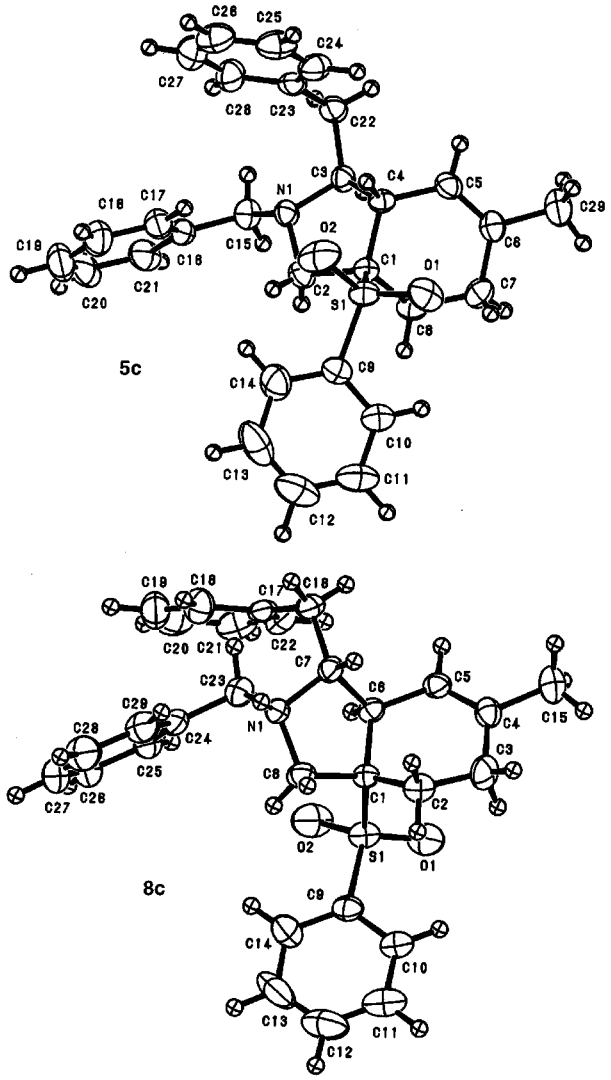


Figure 1. X-ray crystal structures of **5c** and **8c**.

Similarly, we performed an intramolecular Diels–Alder reaction using D–*N*-benzylphenylalaninol as a starting material (Scheme 1) resulting in formation of the desired **8c** in 88% yield. The spectral data showed the same results as that of **5c** except for specific rotation. The compound **8c** showed a specific rotation of −69.51°. Furthermore, the X-ray analysis showed the absolute configuration of **8c** was that of an enantiomer of **5c** (Figure 1). This result suggests that the reaction would proceed by the attack on *re*-face of diene, selectively.

Relationship between Stereoselectivity and Geometry and/or Substituents of Dienes. With the hypothesis that the *exo*-orientation of cycloadditions in the above reactions might be the result of steric repulsion between the phenylsulfonyl group and methyl group on the 4-position of the diene, we tried to examine the intramolecular Diels–Alder reaction of sulfonyl trienes having a methyl group on the terminal position of diene moiety. A Wittig reaction of aldehyde **3c** with phosphonium salt **9** in the presence of *n*-butyllithium and lithium bromide,[8] however, gave geometrical isomers, which could not be separated. An alternative method to obtain a isomerically pure diene is shown in Scheme 2. Protection of the amino group followed by an oxidation of the hydroxy group gave aldehyde **11c** which reacted with phosphonium salt **9** to give diene **12c**. A deprotection of **12c** by trimethylsilyl iodide[9] and methanol gave a geometrical mixture of amino diene **13c** in 45% yield, which was separated to two components. One of them was a mixture of (3*E*,5*E*)- and (3*Z*,5*E*)-diene, and the other was pure (3*Z*,5*E*)-diene.

A reaction of (3*Z*,5*E*)-diene **13c** with 1,3-dichloro-2-(phenylsulfonyl)propane in the presence of triethylamine gave a desired sulfonyl triene (3*Z*,5*E*)-**14** in 79% yield. An intramolecular Diels–Alder reaction of (3*Z*,5*E*)-**14** in boiling toluene for 72 h gave two isoindoles in 98% yield in the ratio of 80 to 20, which were separated by column chromatography to give white crystals (major) and a pale yellow syrup (minor).

The structure and stereochemistry of the major product was determined by spectral data and confirmed by X-ray crystal analysis (Figure 2). A NOESY spectrum of the compound, *cis*-*β*-**15**, indicated that the each pair of H2 and H15, H1 and H5, and H2 and H11 was in a cis relation as shown in Figure 3.

On the other hand, the NOESY spectrum of a minor product, *cis*-α-**15**, showed a typical NOE between H1 and H2 and H2 and H15 which was compatible to the configuration assigned to *cis*-α-**15**. On the basis of these results, the product *cis*-*β*-**15** would come from endo-cycloaddition of vinyl sulfone to the si-face attack on the diene, and *cis*-α-**15** would come from endo-re-face attack on the diene moiety.

To clarify these stereoselectivities, we further examined the reactions of sulfonyl trienes having no substituents on dienyl group. The geometric mixture of amino diene **18**, obtained from a Wittig reaction of aldehyde **11c** and phosphonium salt **19**, was separated by column chromatography, and each diene, *E*-**18** and *Z*-**18**, was transformed to sulfonyl triene *E*-**21** and *Z*-**21**, as shown in Scheme 3.

An intramolecular Diels–Alder reaction of *E*-**21** in boiling toluene for 17 h gave *cis*-*β*-isoindoles, *cis*-*β*-**22** in 83% yield as a single diastereomer, and a reaction of *Z*-**21** under the same conditions gave a mixture of *β*-isoindoles, *cis*-*β*-**22**, and α-isoindoles, *cis*-α-**22**, in 96% yield in the ratio of 84 to 16 (Scheme 3). The structure of *cis*-*β*-**22** was determined by spectral data and confirmed by X-ray analysis (Figure 2), and that of *cis*-α-**22** was determined by comparing its NMR spectrum with that of *cis*-α-**15**.

Discussion

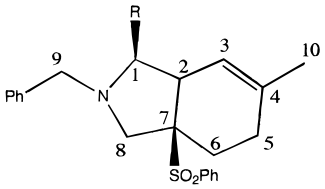
Intramolecular Diels–Alder reactions of sulfonyl triene having an *E*-configuration on the diene part proceeded in a manner of si-face selective exo-cycloaddition, and the reaction having a *Z*-configuration on the diene part proceeded in a manner of si-face selective endo-cycloaddition.

Asymmetric Diels–Alder reactions using chiral dienes have been a subject of interest. The effect of an allylic center on dienes which influences diastereoselectivity stimulated the interest, and many theoretical discussions

(8) (a) Vedejs, E.; Meier, G. P.; Snoble, K. A. J. *J. Am. Chem. Soc.* **1981**, *103*, 2823. (b) Hooper, D. L.; Gragan, S. *J. Org. Chem.* **1994**, *59*, 1226.

(9) (a) Olah, G. A.; Narang, S. C. *Tetrahedron* **1982**, *38*, 2225. (b) Rawal, V. H.; Michoud, C.; Monestel, R. F. *J. Am. Chem. Soc.* **1993**, *115*, 3030. (c) Jung, M. E.; Lyster, M. A. *J. Chem. Soc., Chem. Commun.* **1978**, 315. (d) Lott, R. S.; Chauhan, V. S.; Stammer, C. H. *J. Chem. Soc., Chem. Commun.* **1979**, 495.

Table 1. Proton NMR and Carbon-13 NMR Chemical Shifts and *J* Values (Hz) for 5 in $CDCl_3$



5a : R = Me
5b : R = i-Pr
5c : R = Bn

^{13}C Data

	carbon									
	1	2	3	4	5	6	7	8	9	10
5a	66.54	46.90	118.93	136.05	26.86	28.01	67.82	62.09	56.76	23.87
5b	75.07	40.86	121.75	135.77	26.64	28.70	68.36	61.62	58.22	24.04
5c	72.49	44.05	120.20	135.00	26.76	27.87	68.50	61.35	57.58	23.62

^{1}H Data

	proton		
	vinyl proton 3	methylene proton 8 or 9	methylene proton 9 or 8
5a	5.50−5.48 (multiplet)	3.81 (J_{gem} = 13.40) 2.82 (J_{gem} = 13.20)	3.42 (J_{gem} = 12.30) 2.04 (J_{gem} = 11.70)
5b	5.62−5.42 (multiplet)	3.91 (J_{gem} = 13.07) 2.80 (J_{gem} = 12.97)	3.42 (J_{gem} = 11.98) 2.11 (J_{gem} = 12.19)
5c	5.08−4.90 (multiplet)	4.00 (J_{gem} = 13.08) 2.91 (J_{gem} = 13.07)	3.34 (J_{gem} = 11.54) 2.11 (J_{gem} = 11.64)

have been reported in the past decade.[10−13] Tripathy et al.[14] and Scott et al.[15] reported that the selectivity of Diels−Alder reactions of chiral dienes depended on the conformational stability of the chiral center.

The IMDA reactions of **4a**−**c** gave compounds **5a**−**c** as a sole product (Scheme 1). These products came from the results of exo attack of the vinyl sulfone moiety. Furthermore, in the IMDA of (3*E*)-**21** we observed exo-addition, which would suggest that the methyl substituent on the diene moiety did not affect the topography (endo or exo) of the reactions. To clarify these stereoselectivities, we performed calculations of each transition state with the CAChe MOPAC PM3 method. The activation energy of the exo-addition of the vinylsulfonyl group on the si-face of diene in *E*-triene (**E-exo-si** to **TS-1**) was 26.23 kcal/mol (Figure 4). On the contrary, the activation energies of the endo-additions (**E-endo-si** to **TS-3** and **E-endo-re** to **TS-4**), which should give trans-fused isoindoles, were 34.52 and 33.04 kcal/mol, respectively. These values are much larger than that of **E-exo-si** to **TS-1** and suggest that the reactions could not proceed via endo-additions. In the case of exo-addition of the vinylsulfonyl group on the re-face of diene, the activation energy was 25.40 kcal/mol, which was 0.83 kcal/mol smaller than **E-exo-si** to **TS-1**. As this did not agree with the experimental results, we calculated again these transition state energies with the ab initio (3-21G*) method based on the structures located by PM3. The energies of **TS-1** and **TS-2** were estimated as −1213.181 320 and −1213.173 066 au, respectively, from whose values the difference in energies between **TS-1** and **TS-2** was calculated to be 0.008 245 au (5.18 kcal/mol) large enough to control the π-facial selectivity. The reversal found in PM3 and ab initio method would be due to the different appreciation of the repulsion of dipole moments between the sulfonyl and amino groups, which take the places more closely in **TS-2** than in **TS-1**. In addition, the heat of formation of the **E-exo-si** conformer was 22.9 kcal/mol and that of **E-exo-re** was 24.37 kcal/mol. The more stabilized **E-exo-si** conformer also supports the predominant cyclization to give *cis*-β-isoindoles.

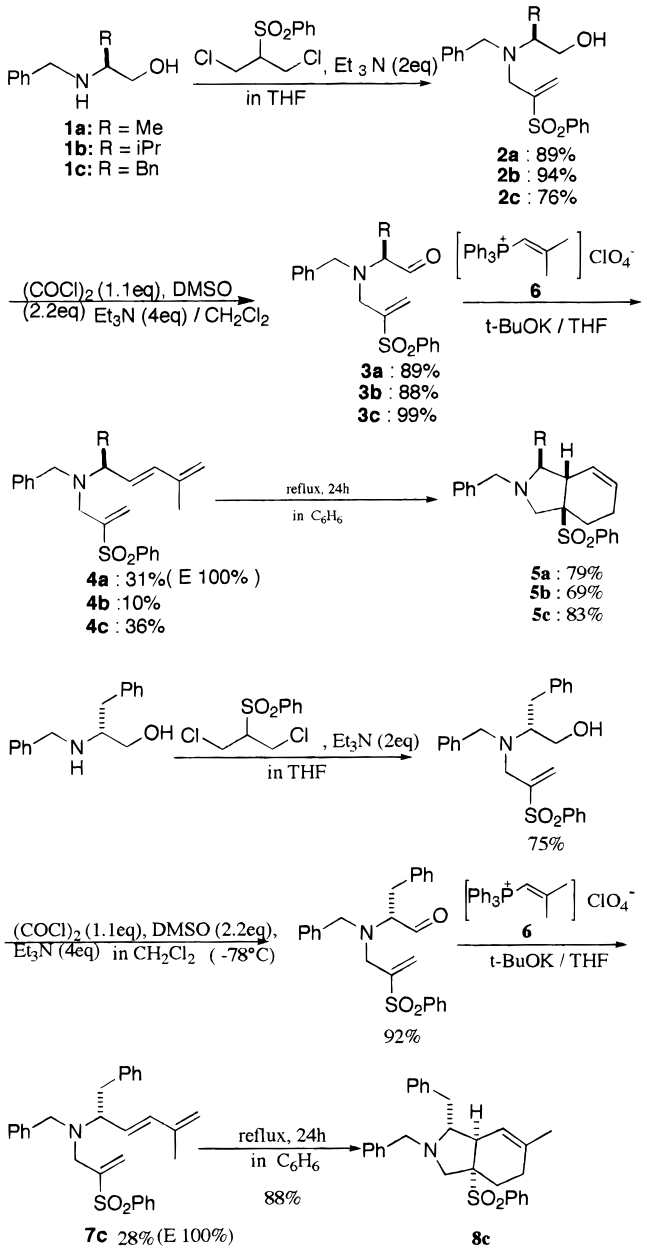
On the other hand, in the case of the IMDA of *Z*-triene, the ratio of si-face to re-face selectivity was about 80 to 20. In the IMDA of (3*Z*)-**14** and (3*Z*)-**21**, the reactions proceeded through the endo-transition states, selectively. These results suggest that the terminal methyl substituent does not affect the stereoselectivity of the reactions. Every product was a cis-fused condensed heterocycle which has the same skeleton. In this case, the preferable transition states in the cycloaddition would be **TS-5** and **TS-6**. The activation energy of **TS-5** from **Z-endo-si** was 29.64 kcal/mol, and that of **TS-6** was 30.85 kcal/mol (Figure 5). The difference between these energies (1.21 kcal/mol) would predict that the si-face attack would be predominant. The exo transition state for the *Z*-triene is geometrically impossible for the dienophile to approach both termini of the diene simultaneously, which was indicated by inspection of molecular models. Furthermore, the cyclization reactions of *E*-trienes (ΔE_a = 26.23 kcal/mol) proceeded in boiling benzene. In the case of *Z*-triene (ΔE_a = 29.64 kcal/mol), the reactions did not proceed in the same conditions but required higher temperature (boiling toluene). The difference in activation energies, 3.41 kcal/mol, should affect the reaction conditions.

Experimental Section

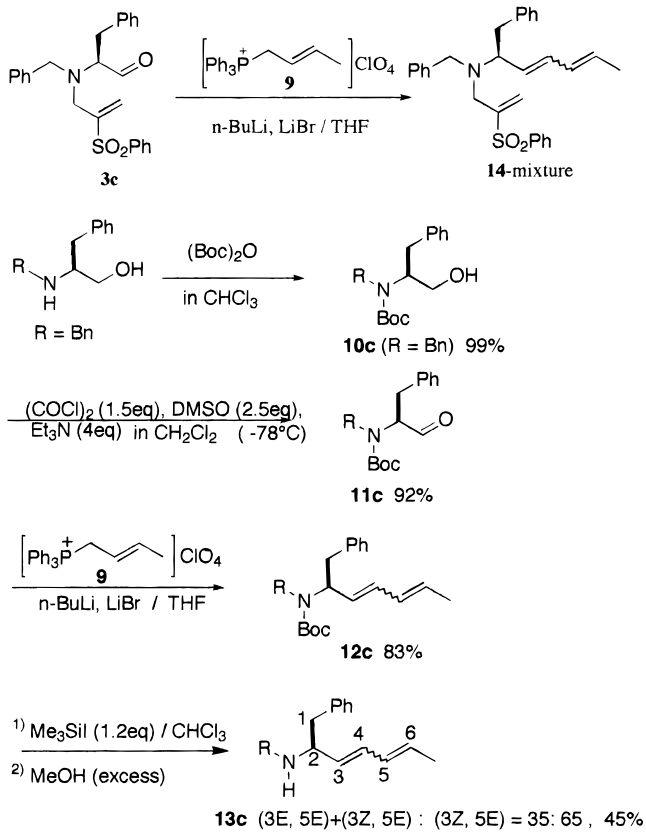
***N*-Benzyl-*N*-[(2*S*)-5-methyl-3,5-hexadien-2-yl]-*N*-[2-(phenylsulfonyl)-2-propen-1-yl]amine (4a).** To potassium *tert*-butoxide (0.59 g, 4.75 mmol) was added dropwise a solution of (2-methyl-1-propenyl)triphenylphosphonium perchlorate (2.18 g, 5.23 mmol) in THF (50 mL) at room temperature, and the

(10) Houk, K. N.; Bock, C. W. *J. Org. Chem.* **1992**, *57*, 4862.
(11) Raimondi, L.; Brown, F. K.; Gonzalez, J.; Houk, K. N. *J. Am. Chem. Soc.* **1992**, *114*, 4796.
(12) Houk, K. N.; Moses, S. R.; Wu, Y. D.; Rondan, D. G.; Jager, V.; Schohe, R.; Fronczek, F. R. *J. Am. Chem. Soc.* **1984**, *106*, 3880.
(13) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63 and references cited therein.
(14) Tripathy, R.; Franck, R. W.; Onan, K. D. *J. Am. Chem. Soc.* **1988**, *110*, 3257.
(15) Scott, D. K.; Warrem, J. H. *Tetrahedron Lett.* **1985**, *26*, 3647.

Scheme 1



Scheme 2



mixture was stirred for 30 min. Then a solution of **3a** (1.63 g, 4.75 mmol) in THF (20 mL) was added dropwise to the solution and stirred for 3 h. To the solution was added an aqueous ammonium chloride, and then THF was evaporated in vacuo. The residue was extracted CH_2Cl_2, and the organic extract was washed with saturated NaCl solution and dried over anhydrous Na_2SO_4. The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel (1:40EtOAc/$CHCl_3$) to give **4a** as yellow syrup in 31% (0.56 g) yield: IR (neat) 3000, 1450, 1300, 1140, 1080, 750, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83−6.97 (m, 10H, Ph × 2), 6.48 (s, 1H, H10), 6.26 (s, 1H, H10), 5.94 (d, 1H, H4, J_{H3H2} = 15.8 Hz), 5.49 (dd, 1H, H3, J_{H2H3} = 7.1 Hz, J_{H3H4} = 15.9 Hz), 4.93 (s, 1H, H6 or H6′), 4.86 (s, 1H, H6 or H6′), 3.46 (s, 1H, H7), 3.42 (s, 1H, H7), 3.36−2.97 (m, 3H, H2, H8), 1.79 (s, 3H, Me), 1.07 (d, 3H, Me, J = 6.4 Hz); ^{13}C NMR (22.63 MHz, $CDCl_3$) δ 149.5, 141.5, 139.5, 139.4, 134.5, 133.5, 130.2, 129.3, 128.6, 128.4, 128.3, 127.1, 125.4, 116.3, 55.9, 54.3, 48.6, 18.8, 16.1; $[\alpha]^{25}_D$ −32.857° (c = 1.05, $CHCl_3$). HRMS: calcd for $C_{23}H_{27}NSO_2$, M 381.1761; found M^+, m/z 381.1793.

***N*-Benzyl-*N*-[(2*S*)-2,6-dimethyl-4,6-hexadien-3-yl]-*N*-[2-(phenylsulfo-nyl)-2-propen-1-yl]amine (4b).** This compound was obtained in 10% yield as a yellow syrup, after being chromatographed on silica gel (2:5EtOAc/*n*-hexane): IR (neat) 2990, 1450, 1310, 1140, 1080, 980, 750, 680 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.90−7.35 (m, 5H, SO_2Ph), 7.12(S, 5H, Ph), 6.42 (s, 1H, H11), 6.30 (s, 1H, H11), 5.73 (d, 1H, H5, J_{H3H2} = 14.0 Hz), 5.25 (d, d, 1H, H4, J_{H2H1} = 9.0 Hz, J_{H2H3} = 14.4 Hz), 4.90 (s, 1H, H7 or H7′), 4.81 (s, 1H, H7 or H7′), 3.97−2.87 (m, 4H, H8, H9), 2.43(t, 1H, H3, J_{H1H2} = 9.0 Hz, J_{H1H6} = 9.0 Hz), 2.07−1.50 (m, 4H, H2, CH_3), 1.00 (d, 3H, CH_3, J = 7.0 Hz), 0.70 (d, 3H, CH_3, J = 7.0 Hz); ^{13}C NMR (22.63 MHz, $CDCl_3$/TMS) δ 149.28, 141.31, 139.19, 137.58, 133.42, 129.20, 128.63, 128.52, 128.35, 128.13, 127.03, 126.16, 124.67, 116.20, 68.67, 54.28, 48.19, 29.90, 20.759, 18.74; $[\alpha]^{25}_D$= +3.95° (c = 0.50, $CHCl_3$); HRMS m/z calcd for $C_{25}H_{31}NSO_2$, M, 409.2073. Found, M+, 409.2051.

***N*-Benzyl-*N*-[(2*S*)-1-phenyl-5-methyl-3,5-hexadien-3-yl]-*N*-[2-(phenylsulfonyl)-2-propen-1-yl]amine (4c).** This compound was obtained in 36% yield as yellow crystals, after being chromatographed on silica gel (1:3EtOAc/*n*-hexane): mp 110.5−112.5 °C; IR (neat) Å@2900, 2800, 1580, 1440, 1290, 1120, 1060, 960, 870, 730, 680 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.97−6.80 (m, 15H, Ph × 3), 6.28 (s, 1H, H7 or H7′), 5.84 (d, 1H, H4, J_{H3H2} = 15.6 Hz), 5.73 (s, 1H, H10), 5.40 (d, d, 1H, H3, J_{H3H4} = 15.6 Hz, J_{H2H3} = 7.9 Hz), 4.94 (s, 1H, H6 or H6′), 4.85 (s, 1H, H6 or H6′), 3.79−2.58 (m, 6H, CH_2 × 3), 1.88 (m, 4H, H2, CH_3); ^{13}C NMR (22.63 MHz, $CDCl_3$/TMS) δ 149.04, 141.37, 139.27, 138.95, 136.41, 133.33, 129.52, 129.17, 128.48, 128.31, 128.20, 127.09, 126.77, 126.18, 125.10, 116.41, 63.10, 54.37, 48.43, 39.05, 18.61; $[\alpha]^{26}_D$ = +8.34° (c = 0.99, $CHCl_3$). Anal. Calcd for $C_{29}H_{31}NSO_2$: C, 76.1; H, 6.83; N, 3.06. Found: C, 75.7; H, 6.880; N, 3.24.

***N*-Benzyl-*N*-[(2*R*)-1-phenyl-5-methyl-3,5-hexadien-3-yl]-*N*-[2-(phenylsulfonyl)-2-propen-1-yl]amine (7c).** This compound was obtained in 28% yield as yellow crystals, after being chromatographed on silica gel (1:3EtOAc/*n*-hexane); mp 110.3−112.5 °C; $[\alpha]^{29}_D$ = −9.86° (c = 1.11, $CHCl_3$).

Isoindole 5a. A solution of sulfonyl triene **4a** (0.47 g, 0.23 mmol) in benzene (30 mL) was refluxed for 24 h, and the mixture was concentrated in vacuo. The residue was chromatographed on silica gel (1:3EtOAc/$CHCl_3$) to give **5a** (0.37

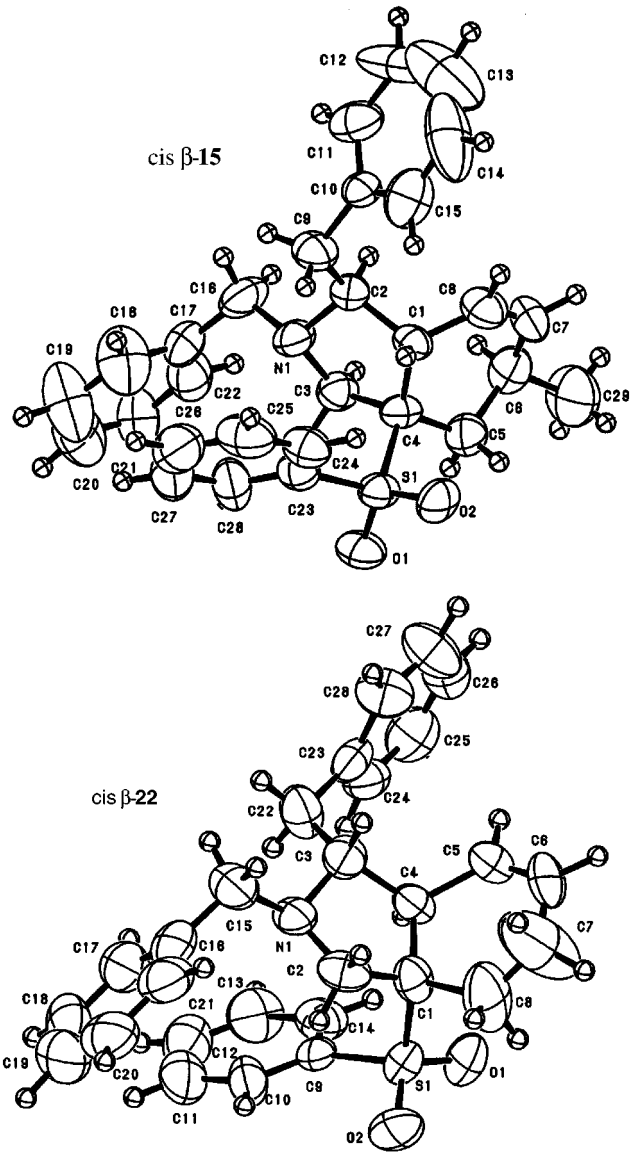


Figure 2. X-ray crystal structures of *cis*-*β*-**15** and *cis*-*β*-**22**.

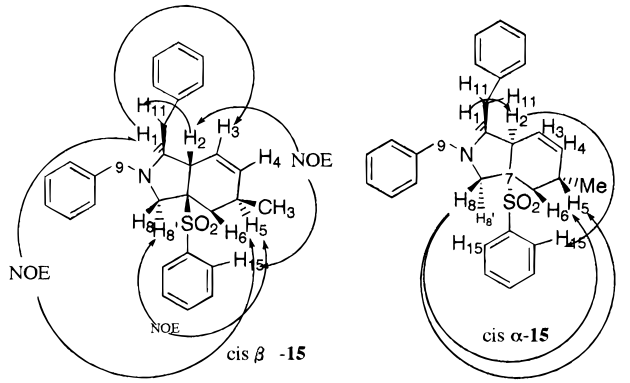
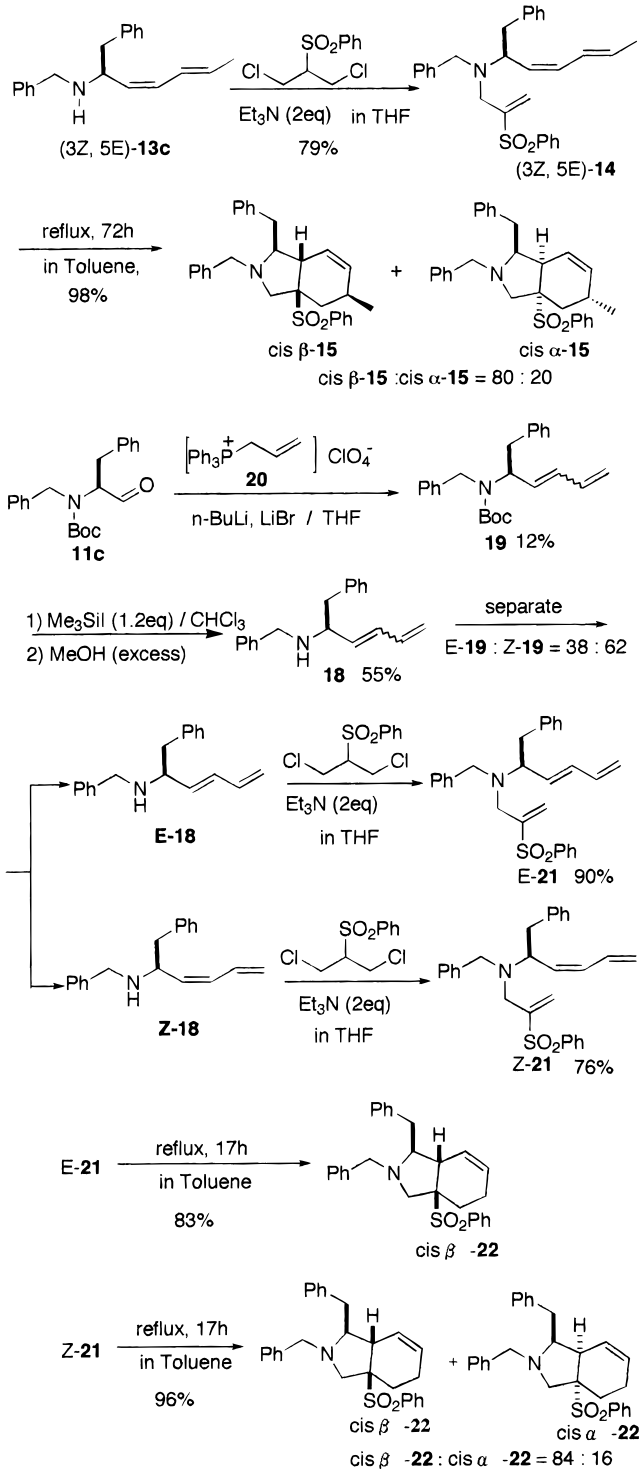


Figure 3. H−H NOE correlation of *cis*-*β*-**15** and *cis*-α-**15**.

g, 79%) as a yellow syrup along with starting **4a** (0.07 g, 15% recovery): IR (neat) 2925, 1450, 1380, 1300, 1140, 1080, 750, 680 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76−6.97 (m, 10H, Ph × 2), 5.50−5.48 (m, 1H, H3), 3.81 (d, 1H, H8 or H9, J_{gem} = 13.4 Hz), 3.42 (d, 1H, H8 or H9, J_{gem} = 12.3 Hz), 2.82 (m, 1H, H8 or H9, J_{gem} = 13.2 Hz), 2.75(br, 1H, H1), 2.44−2.37 (m, 1H, H5 or H6), 2.29−2.27 (m, 1H, H5 or H6), 2.06 (d, 1H, H2, J_{H2H1} = 14.9 Hz), 2.04 (d, 1H, H8 or H9, J_{gem} = 11.7 Hz), 1.90−1.85 (m, 1H, H5 or H6), 1.75 (s, 3H, H10, 1.71−1.64 (m, 1H, H5 or H6), 1.07 (d, 3H, H11, J = 5.9 Hz); ^{13}C NMR (22.63 MHz, $CDCl_3$) δ138.24(Cipso), 137.20 (Cipso), 136.05(C4), 133.19, 130.38, 128.88, 128.67, 128.62, 128.40, 128.25, 128.10, 126.95, 118.93 (C3), 67.86 (C7), 66.54 (C1), 62.09 (C8 or C9), 56.76 (C8 or C9), 46.90 (C2), 28.01 (C5 or C6), 26.86 (C5 or C6), 23.87 (C10), 17.20 (C11); $[\alpha]^{24}_D$ = +66.18° (c = 1.00, $CHCl_3$); MS (m/z) 381 (M^+). HRMS (m/z): calcd for $C_{23}H_{26}NSO_2$, M − 1, 380.1682; found, M^+ − 1, 380.1641.

Isoindole 5b: 69% yield, yellow syrup; IR (neat) 2990, 1450, 1300, 1140, 1070, 730, 690 cm^{-1}; ^1H NMR (90 MHz, $CDCl_3$) δ 7.98−7.01 (m, 10H, Ph × 2), 6.62−5.42 (m, 1H, H3), 3.91 (d, 1H, H8 or H9, J_{gem} = 13.07 Hz), 3.42 (d, 1H, H8 or H9, J_{gem} = 11.98 Hz), 3.12−2.78 (m, 1H, H2), 2.80 (d, 1H, H8 or H9, J_{gem}

Scheme 3



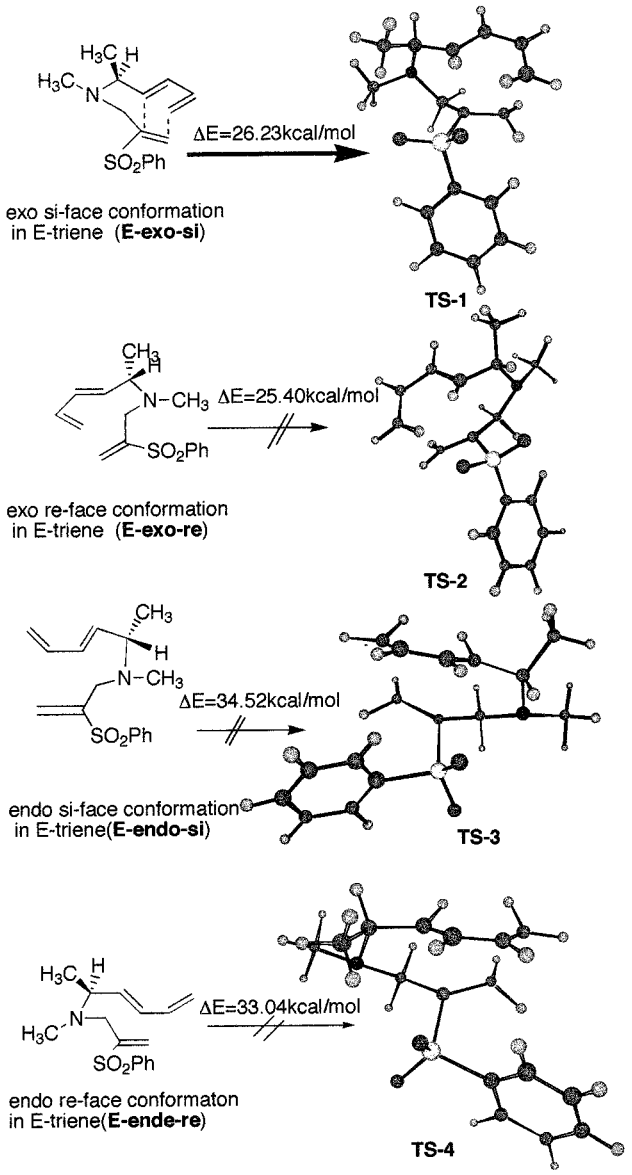


Figure 4. Transition states of *E*-sulfonyl trienes calculated by MOPAC PM3.

= 12.97 Hz), 2.43−1.06 (m, 10H, H1, H2, H5, H6, H11, H8), 0.95 (d, 3H, H12, J = 6.92 Hz), 0.79 (d, 3H, H12, J = 6.81 Hz); ^{13}C NMR (90 MHz, $CDCl_3$) δ139.04 (Cipso), 137.61 (Cipso), 135.77 (C4), 133.33, 130.53, 128.79, 128.40, 127.21, 121.75 (C3), 75.07 (C1), 68.36 (C7), 61.62 (C8 or C9), 58.22 (C8 or C9), 40.86 (C2), 28.70 (C5 or C6), 28.29 (C11), 26.64 (C5 or C6), 24.04 (C10) 19.84 (C12), 17.24 (C12); $[\alpha]^{24}_D$ = +80.98° (c = 0.97, $CHCl_3$); MS (m/z) 409 (M^+). HRMS (m/z): calcd for $C_{25}H_{31}NSO_2$, M, 409.2074; found, M^+, 409.2102.

Isoindole 5c: 83% yield; mp 167.5−169.4 °C; IR (KBr) 3025, 2900, 2800, 1440, 1370, 1290, 1140, 1070, 730, 690 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.71−6.79 (m, 15H, Ph × 3), 5.00 (m, 1H, H3), 4.00 (d, 1H, H8 or H9, J_{gem} = 13.08 Hz), 3.34 (d, 1H, H8 or H9, J_{gem} = 11.54 Hz), 3.05−1.70 (m, 8H, H1, H2, H5, H6, H11), 2.91 (d, 1H, H8 or H9, J_{gem} = 13.07 Hz), 2.11 (d, 1H, H8 or H9, J_{gem} = 11.64 Hz), 1.64 (s, 3H, H10); ^{13}C NMR (22.63 MHz, $CDCl_3$) δ138.51(Cipso), 138.32 (Cipso), 137.67 (Cipso), 135.00 (C4), 132.99, 130.47, 129.78, 128.65, 128.44, 128.26, 127.09, 126.36, 120.20 (C3), 72.49 (C1), 68.50 (C7), 61.35 (C9), 57.58 (C8), 44.05 (C2), 37.64 (C11), 27.87 (C5 or C6), 26.76 (C5 or C6), 23.62(C10); $[\alpha]^{26}_D$ = +69.74° (c = 0.90, $CHCl_3$); MS (m/z) 366 (M − 91). Anal. Calcd for $C_{29}H_{31}NSO_2$: C, 76.11; H, 6.83; N, 3.06. Found: C, 76.40; H, 6.82; N, 3.24.

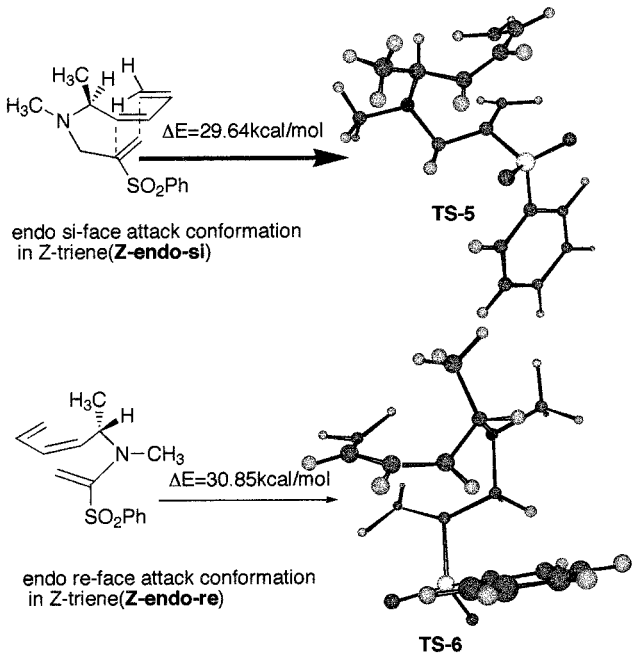


Figure 5. Transiton states of *Z*-sulfonyl trienes calculated by MOPAC PM3.

Isoindole 8c: 88% yield; mp 167.6−169.5 °C; $[\alpha]^{28}_D$ = −69.51° (c = 1.03, $CHCl_3$).

(2*S*)-2-(*N*-Benzyl-*N*-(*tert*-butoxycarbonyl)amino)-1-phenyl-3,5-heptadiene (12c). To a solution of 2-butenyltriphenylphosphonium perchlorate (**9**) (4.46 g, 10.7 mmol) and lithium bromide (3.72 g, 47.2 mmol) in THF (80 mL) was added a 1.6 M solution of *n*-butyllithium in *n*-hexane (7.36 mL, 11.8 mmol, 1.1 equiv), and the solution was stirred at 0 °C for 30 min. Then a solution of *N*-benzyl-*N*-Boc-phenylalaninal (**11c**) (3.6 g, 10.7 mmol) in THF (40 mL) was added to the mixture. After the mixture was stirred for 24 h, a saturated ammonium chloride solution (30 mL) was added and the solvent THF was evaporated in vacuo. The residue was extracted with dichloromethane, and the organic layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel (1:10EtOAc/$CHCl_3$) to give **12c** (1:1 geometrical mixture) in 83% (3.34 g) yield as a yellow syrup: IR (neat) 3000, 1690, 1500, 1450, 1360, 1320, 1250, 1160, 1110, 980, 740, 700 cm^{-1}; ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.40−6.90 (m, 10H, Ph × 2), 6.35−5.34 (m, 4H, olefin proton), 5.18−4.65 (m, 1H, CH), 4.65−3.93 (m, 2H, CH_2), 3.18−2.53 (m, 2H, CH_2), 1.70 (d, 3H, CH_3, J = 7.1 Hz), 1.38 (s, 9H, Boc); ^{13}C NMR (22.63 MHz, $CDCl_3$) δ 155.42 (C=O), 139.58 (Cipso), 139.45 (Cipso), 138.71 (Cipso), 138.51 (Cipso), 132.14, 131.60, 131.54, 131.05, 129.46, 129.30, 128.81, 128.24, 128.16, 128.00, 127.51, 127.33, 126.83, 126.70, 126.66, 126.40, 126.18, 79.74 (C−O), 60.41 (CH), 55.45 (CH), 49.41 (CH_2), 48.63 (CH_2), 40.65 (CH_2), 39.55 (CH_2), 28.41 (CH_3), 18.25 (CH_3), 18.01 (CH_3); MS (m/z) 377 (M^+).

(2S)-2-(*N*-Benzylamino)-1-phenyl-3,5-heptadiene (13c). To a solution of *N*-Boc-amino diene **12c** (2.50 g, 6.9 mmol) in chloroform (30 mL) was added dropwise by syringe iodotrimethylsilane (1.18 mL, 8.3 mmol, 1.2 equiv), and the mixture was heated at 50 °C. After 30 min, 5 mL of methanol was added, and the solvent was evaporated in vacuo. Then 40 mL of ether and 40 mL of 30% aqueous acetic acid was added and stirred for a few minutes. The solution was neutralized by aqueous sodium bicarbonate and extracted with ether. The ether layer was washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated in vacuo, and the residue was chromatographed on silica gel (1:3EtOAc/*n*-hexane) to give a 1:1 mixture of (3*E*,5*E*)- and (3*E*,5*Z*)-amino diene **13c** (0.26 g) and pure (3*Z*,5*E*)-amino diene **13c** (0.61 g).

Mixture of (3*E*,5*E*)-13c and (3*Z*, 5*E*)-13c: IR (neat) 3025, 2925, 2850, 1600, 1500, 1450, 1100, 1030, 980, 740, 700 cm^{-1};

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.31−7.11 (m, 10H, Ph), 6.44−6.37 (m, 2H, H4, H5), 6.11−5.99 (m, 1H, H6), 5.68−5.41 (m, 1H, H3), 3.83−3.77 (m, 1H, methylene proton H8), 3.61−3.56 (m, 1H, methylene proton H8), 3.40−3.28 (m, 1H, H2), 2.86−2.70 (m, 2H, methylene proton H7), 1.75−1.71 (m, 3H, CH_3), 1.26 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 140.54 (Cipso), 138.64 (Cipso), 135.66, 133.44, 131.91, 131.21, 129.44, 129.02, 128.82, 128.41, 128.33, 127.98, 126.82, 126.77, 126.75, 126.36, 126.34, 126.16, 61.07 (C2), 60.91 (C2), 51.29 (C8), 51.24 (C8), 42.83 (C1), 42.76 (C1), 18.11 (C7), 13.42 (C7); MS *m*/*z* 278 (M + 1), 210, 186, 171, 129, 91. HRMS (*m*/*z*): calcd for $C_{20}H_{24}N$, M + 1, 278.1909; found, M^+ + 1, 278.1898.

(3*Z*,5*E*)-13c: IR (neat) 3025, 2925, 2850, 1600, 1500, 1450, 1100, 1030, 980, 940, 820, 740, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29−7.13 (m, 10H, Ph), 6.45−6.04 (m, 2H, H4, H5), 5.71−5.62 (m, 1H, H6), 5.18 (t, 1H, H3, J_{H3H4} = 9.36 Hz), 3.83−3.75 (m, 1H, H2), 3.80 (d, 1H, methylene proton H8, J_{gem} = 13.55 Hz), 3.59 (d, 1H, methylene proton H8, J_{gem} = 13.58 Hz), 2.80−2.71 (m, 2H, methylene proton H1), 1.75−1.71 (m, 3H, CH_3), 1.53 (s, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 140.51 (Cipso), 138.59 (Cipso), 131.43 (C3), 130.69, 130.64, 129.45, 128.36, 128.26, 128.10, 128.04, 126.94, 126.74, 126.32, 55.39 (C2), 51.26 (C8), 42.50 (C1), 18.23 (CH_3); $[\alpha]^{27}_D$ = +12.56° (*c* = 1.06, $CHCl_3$); MS *m*/*z* 278 (M + 1). HRMS (*m*/*z*): calcd for $C_{20}H_{24}N$, M + 1, 278.1909; found, M^+ + 1, 278.1866.

***N*-Benzyl-N-(1-phenyl-3*Z*,5*E*-heptadien-2-yl)-*N*-[2-(phenylsulfonyl)-2-propen-1-yl]amine (14) ((3*Z*,5*E*)-14).** This compound was obtained from the reaction between amino diene (3*Z*,5*E*)-**13c** (0.58 g, 2.1 mmol), triethylamine (0.42 g, 4.2 mmol, 2 equiv), and 1,3-dichloro-2-(phenylsulfonyl)propane (0.53 g, 2.1 mmol) in the presence of hydroquinone (0.02 g, 0.21 mmol) in 79% (0.76 g) yield as a yellow syrup, after being chromatographed on silica gel (1:3EtOAc/*n*-hexane): IR (neat) 3050, 3030, 2930, 2850, 1740, 1500, 1450, 1370, 1300, 1240, 1180, 1140, 1080, 960, 740, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.84−7.80 (m, 2H, Ph), 7.62−7.58 (m, 1H, Ph), 7.52−7.48 (m, 2H, Ph), 7.25−7.12 (m, 6H, Ph), 6.97−6.88 (m, 4H, H11, Ph), 6.34 (s, 1H, H11), 6.09(t, 1H, H4, J_{H4H5} = 10.64 Hz), 5.90 (s, 1H, H11), 5.71 (d, d, 1H, H5, J_{H4H5} = 10.69 Hz, J_{H5H6} = 14.91 Hz), 5.61(q, d, H6, J_{H6Me} = 6.35 Hz, J_{H6H5} = 14.91 Hz), 5.18(t, H3, J_{H3H4} = 10.53 Hz), 3.69(1H, d, d, H2, J_{H1H2} = 7.58 Hz, J_{H2H3} = 17.60 Hz), 3.54 (d, 1H, H9, J_{H8gem} = 16.92 Hz), 3.46 (d, 1H, H8, J_{H7gem} = 14.15 Hz), 3.24 (d, 1H, H8, J_{H7gem} = 14.13 Hz), 3.13 (d, 1H, H9, J_{H8gem} = 16.90 Hz), 2.76 (d, d, H1, J_{H1gem} = 13.76 Hz, J_{H1H2} = 6.85 Hz), 1.63 (d, 3H, Me, J_{MeH6} = 6.19 Hz); ^{13}C NMR ($CDCl_3$) δ 148.70 (Cipso), 139.15 (Cipso), 139.00 (Cipso), 138.68 (C10), 133.43, 132.72, 131.22 (C4), 129.54 (C6), 129.20, 128.48, 128.08, 128.04, 128.00, 126.96, 126.96, 126.86, 126.09, 125.32, 125.19 (C11), 57.33 (C2), 54.73 (C8), 47.52 (C9), 39.33 (C1), 18.11 (C6); $[\alpha]^{27}_D$ = +67.66° (*c* = 1.05, $CHCl_3$); MS *m*/*z* 458(M + 1). HRMS (*m*/*z*): calcd for $C_{29}H_{32}NSO_2$, M + 1, 458.2154; found, M^+ + 1, 458.2105.

Isoindole Derivative 15. A solution of (3*Z*,5*E*)-**14** (0.85 g, 1.86 mmol) in toluene (20 mL) was refluxed for 72 h. Then the solvent was evaporated and the residue was chromatographed on silica gel to give a epimeric mixture of *cis*-*β*-**15** and *cis*-α-**15** (0.83 g, 98%, α-**15**/*β*-**15** = 80/20), which was purified by chromatography again.

Isoindole derivative *cis*-*β*-15: mp 150.1−152.6 °C; IR (neat) 3050, 2975, 2950, 2800, 1680, 1500, 1450, 1300, 1220, 1140, 1080, 1030, 760, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.74−7.73 (m, 2H, Ph), 7.65−7.61 (m, 1H, Ph), 7.48−7.45 (m, 2H, Ph), 7.34−7.22 (m, 6H, Ph), 7.20−7.13 (m, 4H, H11, Ph), 5.40 (d, 1H, H4, J_{H4H3} = 9.82 Hz), 4.88−4.83 (m, 1H, H3), 3.90 (d, 1H, H9, J_{gem} = 12.77 Hz), 3.36 (d, 1H, H8, J_{gem} = 11.90 Hz), 2.96(t, 1H, H2, *J* = 5.97 Hz), 2.91−2.86 (m, 1H, H8), 2.87 (d, 1H, H9, J_{gem} = 12.68 Hz), 2.34 (d, 1H, H8, J_{gem} = 11.91 Hz), 2.29−2.21 (m, 2H, H1, H11), 2.09−1.97 (m, 1H, H5), 1.78−1.71 (m, 2H, H6), 1.01 (d, 3H, H10, J_{MeH5} = 6.93 Hz); ^{13}C NMR ($CDCl_3$) δ 138.35 (Cipso), 138.14 (Cipso), 137.07 (Cipso), 133.31, 132.76 (C4), 130.80,129.45, 129.13, 128.59, 128.57, 128.24, 127.29, 126.47, 74.85(C1), 71.09 (C7), 58.95 (C8), 58.11 (C9), 43.31 (C2), 39.40 (C11), 33.94 (C6), 25.98 (C5), 21.15 (C10); MS *m*/*z* 458(M + 1). HRMS (*m*/*z*): calcd for $C_{29}H_{32}NSO_2$, M + 1, 458.2154; found, M^+ + 1, 458.2144. Anal. Calcd for $C_{29}H_{31}NSO_2$: C, 76.11; H, 6.83; N, 3.06. Found: C, 75.94; H, 6.83; N, 3.06; $[\alpha]^{27}_D$ = +93.06° (*c* = 1.03, $CHCl_3$).

Isoindole Derivative *cis*-α-15. Yellow syrup: IR (neat) 3040, 2960, 2940, 2870, 1450, 1300, 1220, 1150, 1080, 750, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.80−7.75 (m, 2H, Ph, 7.63−7.60 (m, 1H, Ph), 7.51−7.45 (m, 2H, Ph), 7.33−7.20 (m, 10H, Ph), 5.76 (d, 1H, H4, J_{H4H3} = 10.03 Hz), 5.62−5.58 (m, 1H, H3), 4.09 (d, 1H, H9, J_{gem} = 13.26 Hz), 3.38−3.35 (m, 1H, H1), 3.19 (d, 1H, H9, J_{gem} = 13.17 Hz), 3.13−3.02 (m, 2H, H2, H11), 3.12 (d, 1H, H8, J_{gem} = 11.45 Hz), 2.84 (d, 1H, H8, J_{gem} = 11.73 Hz), 2.60−2.53 (m, 1H, H11), 2.27−2.23 (m, 1H, H5), 1.78−1.72 (m, 1H, H6), 1.48(t, 1H, H6, J_{gem} = 11.78 Hz), 0.95 (d, 3H, H10, J_{MeH5} = 7.08 Hz); ^{13}C NMR ($CDCl_3$) δ 138.35 (Cipso), 138.14 (Cipso), 137.07 (Cipso), 136.61 (C4), 133.66, 130.49, 128.96, 128.74, 128.57, 128.43, 128.37, 128.23, 127.01, 126.25, 124.78 (C3), 69.69 (C7), 67.90 (C1), 59.33 (C8), 57.34 (C9), 41.06 (C2), 35.87 (C11), 29.72 (C6), 25.87 (C5), 21.25 (C10); MS *m*/*z* 458 (M + 1). HRMS (*m*/*z*): calcd for $C_{29}H_{32}NSO_2$, M + 1, 458.2154; found, M^+ + 1, 458.2119.

2-(*N*-Benzylamino)-1-phenyl-3,5-hexadiene (18). Amino diene *E*-18: IR (neat) 3300, 3075, 3050, 3000, 2900, 2825, 1800, 1590, 1480, 1440, 1330, 1100, 1060, 1020, 990, 940, 890, 730, 680 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.41−6.90 (m, 10H, Ph × 2), 6.57−5.98 (m, 2H, H4, H5), 5.60 (d, d, 1H, H3, J_{H3H4} = 14.35 Hz, J_{H3H2} = 7.80 Hz), 5.30−5.00 (m, 2H, H6, H6′), 3.69 (d, d, 2H, methylene proton H7, J_{gem} = 13.51 Hz), 3.39−3.23 (m, 2H, methylene proton H1), 1.62 (br, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 140.46 (Cipso), 138.43 (Cipso), 136.67, 132.19, 129.39, 128.37, 128.29, 127.92, 126.72, 126.33, 116.43 (C6), 60.74 (C2), 51.27 (C7), 42.60 (C1); $[\alpha]^{26}_D$ = −1.57° (*c* = 1.07, $CHCl_3$).

Amino diene *Z*-18: IR (neat) 3300, 3075, 3050, 3000, 2900, 2825, 1800, 1720, 1590, 1480, 1440, 1350, 1320, 1280, 1190, 1060, 1020, 980, 960, 900, 740, 680 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.41−6.95 (m, 10H, Ph × 2), 6.63−5.99 (m, 2H, H3, H4), 5.45−4.97 (m, 3H, H5, H6, H6′), 3.93−3.81 (m, 1H, H2), 3.69 (d, d, 2H, methylene proton H7, J_{gem} = 13.62 Hz), 2.76 (d, d, 2H, methylene proton H1, J_{gem} = 6.7 Hz), 1.70(br, 1H, NH); ^{13}C NMR ($CDCl_3$) δ 140.23 (Cipso), 138.23 (Cipso), 134.42, 131.99, 131.12, 129.35, 128.31, 128.22, 128.07, 127.98, 127.25, 126.83, 126.75, 126.29, 118.21 (C5), 55.47 (C1), 51.18 (C7), 42.94 (C6); $[\alpha]^{26}_D$ = +3.13° (*c* = 0.82, $CHCl_3$).

***N*-Benzyl-*N*-[(2*S*)-1-phenyl-3*E*,5-hexadien-2-yl]-*N*-[2-(phenylsulfonyl)-2-propen-1-yl]amine (E-21).** This compound was obtained from the reaction between amino diene *E*-**18** (0.21 g, 0.8 mmol), triethylamine (0.16 g, 1.6 mmol, 2 equiv), and 1,3-dichloro-2-(phenylsulfonyl)propane (0.20 g, 0.8 mmol) in the presence of hydroquinone (0.02 g, 0.21 mmol) in 90% (0.32 g) yield as a yellow syrup, after being chromatographed on silica gel (1:3EtOAc/*n*-hexane): IR (neat) 3060, 3050, 3000, 2900, 2820, 1590, 1480, 1440, 1360, 1300, 1200, 1160, 1120, 1100, 1070, 1010, 990, 950, 740, 680 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.90−6.85 (m, 15H, Ph × 3), 6.49−6.00 (m, 1H, olefin proton), 6.28 (s, 1H, H10 or H10′), 5.70 (s, 1H, H10 or H10′), 5.86−5.47 (m, 2H, olefin proton), 5.20−4.98 (m, 2H, H6, H6′), 3.73−2.60 (m, 7H, H2, methylene proton H1, H7 and H8); ^{13}C NMR ($CDCl_3$) δ 148.31, 139.08, 138.99, 138.64, 136.28, 134.29, 133.40, 130.82, 129.43, 129.17, 128.39, 128.22, 128.05, 127.81, 127.01, 126.14 (C9), 125.21 (C10), 117.30 (C6), 62.47 (C2), 53.78 (C7), 47.89 (C8), 38.66 (C1); $[\alpha]^{26}_D$ = +1.23° (*c* = 0.60, $CHCl_3$).

***N*-Benzyl-*N*-[(2S)-1-phenyl-3*Z*,5-hexadien-2-yl]-*N*-[2-(phenylsulfonyl)-2-propen-1-yl]amine (Z-21).** This compound was obtained from the reaction between amino diene *Z*-**18** (0.21 g, 0.8 mmol), triethylamine (0.16 g, 1.6 mmol, 2equiv), and 1,3-dichloro-2-(phenylsulfonyl)propane (0.20 g, 0.8 mmol) in the presence of hydroquinone (0.02 g, 0.21 mmol) in 76% (0.27 g) yield as a yellow syrup, after being chromatographed on silica gel (1:3EtOAc/*n*-hexane): IR (neat) 3090, 3060, 2925, 2825, 1600, 1580, 1500, 1450, 1370, 1300, 1220, 1170, 1140, 1120, 1080, 1020, 1000, 970, 900, 740, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.87−6.80 (m, 15H, Ph × 3), 6.34 (s, 1H, H10 or H10′), 6.27−6.48 (m, 2H, olefin protons), 5.88 (s, 1H, H10 or H10′), 5.49−4.89 (m, 3H, olefin protons), 3.87−2.40 (m, 7H, H2, methylene protons); ^{13}C NMR ($CDCl_3$) δ

148.74, 139.23, 138.73, 138.56, 133.40, 133.05, 131.67, 129.46, 129.17, 128.83, 128.44, 128.35, 128.26, 128.13, 128.03, 127.01, 126.12, 125.19 (C10), 118.88 (C6), 57.69 (C2), 54.67 (C7), 47.85 (C8), 39.33 (C1); $[\alpha]^{26}_D = +17.18°$ ($c = 0.67$, $CHCl_3$).

Isoindole derivative *cis*-*β*-22 (from *E*-21): 83% yield as white crystals; mp 141.0−141.8 °C; IR (neat) 3030, 3020, 2980, 2820, 2800, 1740, 1610, 1590, 1500, 1450, 1300, 1220, 1040, 1080, 1030, 1000, 760, 700, 660 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 7.72−6.84 (m, 15H, Ph × 3), 5.92−5.60 (m, 1H, H4), 5.23 (d, d, 1H, H3, $J_{H3H2} = 4.28$ Hz, $J_{H3H4} = 10.60$ Hz), 4.01 (d, 1H, H8 or H9, $J_{gem} = 13.07$ Hz), 3.32 (d, 1H, H8 or H9, $J_{gem} = 11.76$ Hz), 3.05−1.45 (m, 8H, H1, H2, H5, H6, H10), 2.90 (d, 1H, H8 or H9, $J_{gem} = 12.96$ Hz), 2.12 (d, 1H, H8 or H9, $J_{gem} = 11.75$ Hz); ^{13}C NMR ($CDCl_3$) δ 138.14 (Cipso), 137.80 (Cipso), 136.97 (Cipso), 133.01, 130.28, 129.61, 128.59, 128.48, 128.35, 128.16, 127.16, 127.01, 126.31, 126.18, 71.94-(C1), 68.65 (C7), 61.00 (C8), 57.29 (C10), 43.04 (C2), 37.27 (C9), 26.89 (C6), 21.45 (C5). Anal. Calcd for $C_{28}H_{29}NSO_2$: C, 75.81; H, 6.59; N, 3.16. Found: C, 76.00; H, 6.60; N, 3.16. $[\alpha]^{26}_D = +1.47°$ ($c = 0.46$, $CHCl_3$).

Isoindole Derivatives *cis*-*β*-22, and cis-α-22 from *Z*-21. Isoindole derivative *cis*-*β*-22: 81% yield as white crystals; mp 138.4−140.3 °C.

Isoindole derivative *cis*-α-22: 15% yield as a yellow syrup; IR (neat) 3070, 3050, 2950, 2850, 1730, 1610, 1590, 1500, 1400, 1370, 1300, 1220, 1150, 1090, 1080, 1030, 1000, 750, 700 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 7.97−7.00 (m, 15H, Ph × 3), 6.10−5.81 (m, 1H, H4), 5.62 (d, d, 1H, H3, $J_{H3H2} = 3.95$ Hz, $J_{H3H4} = 10.34$ Hz), 4.05 (d, 1H, H8 or H9, $J_{gem} = 13.40$ Hz), 3.20 (d, 1H, H8 or H9, $J_{gem} = 12.96$ Hz), 3.56−2.44 (m, 6H, H1, H2, H8, H9, H10), 2.13−1.63 (m, 4H, H5, H6); ^{13}C NMR ($CDCl_3$) δ 139.12 (Cipso), 136.65 (Cipso), 133.59, 130.17, 129.37, 128.91, 128.76, 128.50, 128.35, 128.31, 126.94, 126.16, 124.97, 68.87 (C7), 67.85 (C1), 59.61 (C8), 57.45 (C10), 40.65 (C2), 36.23 (C9), 28.11 (C6), 20.82 (C5); MS (FAB) *m*/*z* 444 ($M^+ + 1$). FAB HRMS (*m*/*z*): calcd for $C_{28}H_{30}NSO_2$, M + 1, 444.2013; found, $M^+ + 1$, 444.1997.

Acknowledgment. We thank Mr. Takeya Ando, Osaka University, for useful suggestions for MOPAC PM3 calculations and Kissei Pharmaceutical Co., Ltd., for NMR measurements and valuable discussions.

Supporting Information Available: ^1H and ^{13}C NMR spectra of each new compound, vibrational spectra, x-ray crystallographic data for **7c**, **9c**, *cis*-*β*-**16**, and *cis*-*β*-**23**, and synthetic procedures of **2a**−**c**, **3a**−**c**, and (2*R*)-2-{*N*-benzyl-*N*-[2-(phenylsulfonyl)-2-propenyl]}amino-3-phenyl-1-propanal (73 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS: see any current masthead page for ordering information.

JO980181B