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Practical preparation of *N*-(1-alkynyl)sulfonamides and their synthetic utility in titanium alkoxide-mediated coupling reactions

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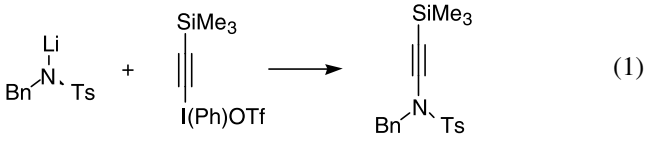
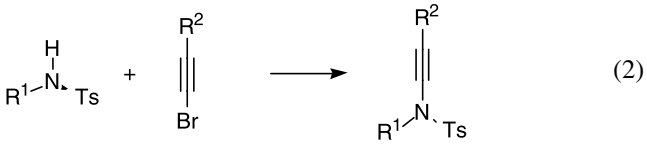
Abstract—Aliphatic and aromatic sulfonamides were alkynylated with 1-bromo-1-alkynes in the catalytic presence of CuI to give *N*-(1-alkynyl)sulfonamides in good to excellent yields. Racemization of optically active sulfonamides was not observed during this alkynylation. The acetylene–titanium complexes generated from the resultant *N*-(1-alkynyl)sulfonamides and Ti(O–*i*-Pr)$_4$/2 *i*-PrMgCl underwent regio-, olefinic stereo-, and diastereoselective addition to aldehydes to give virtually single allyl alcohols. Alternatively, inter- or intramolecular coupling reaction between *N*-(1-alkynyl)sulfonamides and another acetylene or olefin with the above titanium alkoxide reagent generated the corresponding titanacycles, hydrolysis of which furnished stereo-defined (sulfonylamino)dienes or cyclic compounds.

1. Introduction

Acetylenes are versatile starting materials for transition metal-mediated coupling reactions with other unsaturated compounds.[1] As far as the group 4 metal-mediated coupling reactions are concerned,[2–4] functionalized acetylenes such as alkoxycarbonyl-, chloro-, alkoxy-, sulfur-, or phosphorus-functionalized ones were utilized to effect unique transformations.[5] However, (protected) amino-substituted acetylenes had not yet been studied, until we reported the first example 2 years ago.[6,7] There are a wide variety of methods to prepare amino-substituted acetylenes,[8] among which the displacement of alkynyliodonium salts with amino-nucleophiles has been one of the most dependable methods (Eq. 1).[9] However, as the prior preparation of alkynyliodonium salts needs additional steps, a more straightforward synthesis of these acetylenes is called for. The recent success in the transition-metal catalyzed displacement at an sp^2 or sp-carbon center bearing a leaving group with a heteroatom nucleophile[10,11] led us to examine a new and facile preparation of *N*-(1-alkynyl)sulfonamides from sulfonamides and haloacetylenes (Eq. 2) and, eventually, their application to titanium-mediated coupling reactions.



(1)



(2)

2. Results and discussion

2.1. Preparation of *N*-(1-alkynyl)sulfonamides

Considering the broad applicability of palladium-catalyzed coupling reactions between aryl or vinyl halides and amino-nucleophiles,[10] we first attempted N-alkynylation of sulfonamide **1**[12] with 1-bromo-1-octyne (**2**) under palladium catalysis. A few selected conditions are summarized in Table 1, which did not show a fruitful result. During the course of our study along this line, copper-catalyzed alkynylation of amides by Hsung and co-workers[11b] and the copper-mediated alkynylation of sulfonamides by Danheiser's group[11c] appeared. In addition to these pioneering works, we report here our results on a copper-catalyzed coupling reaction between 1-halo-1-alkynes and sulfonamides to give various *N*-(1-alkynyl)-sulfonamides.[6b] Some typical conditions are summarized

Keywords: Alkynylation; Copper catalyst; Sulfonamides; Titanium alkoxide; Titanacycle; Ynamide; Enamide.
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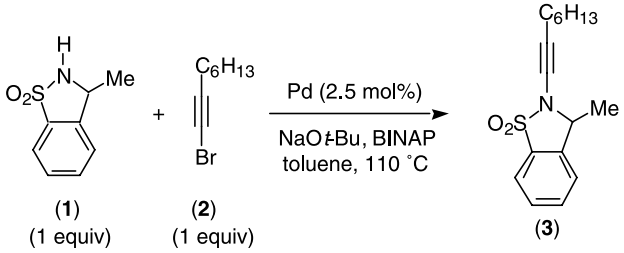
Table 1. Attempted Pd-catalyzed alkynylation of benzosultam **1**

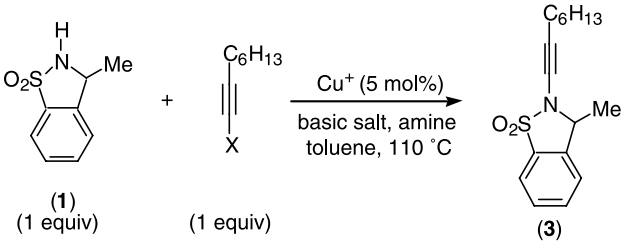


(**1**) (1 equiv) (**2**) (1 equiv) (**3**)

Entry	Pd	Yield (%)[a]
1	$Pd(PPh_3)_4$	<1
2	$PdCl_2(C_6H_5CN)_2$	<1
3	$Pd_2(dba)_3$	<1

[a] Yield determined by ^1H NMR spectroscopy with $CHCl{=}CCl_2$ as an internal standard.

Table 2. Optimum conditions for the alkynylation of benzosultam **1**



(**1**) (1 equiv) (1 equiv) (**3**)

Entry	X	Cu^+	Basic salt	Amine	Yield (%)[a]
1	Br	CuI	Cs_2CO_3	$(CH_2NHMe)_2$	68
2	Br	CuI	K_2CO_3	$(CH_2NHMe)_2$	94 (68)
3	Br	CuCN	K_3PO_4	$(CH_2NHMe)_2$	87
4	Br	CuSPh	K_3PO_4	$(CH_2NHMe)_2$	93
5	Br	CuI	K_3PO_4	$(CH_2NH_2)_2$	62
6	Br	CuI	K_3PO_4	$(CH_2NHMe)_2$	97 (79)
7	I	CuI	K_3PO_4	$(CH_2NHMe)_2$	77

[a] Yield determined by ^1H NMR spectroscopy with $CHCl{=}CCl_2$ as an internal standard. Isolated yield in parantheses.

in Table 2. The best yield was obtained in entry 6 with alkynyl bromide rather than iodide (cf. entry 7), with K_3PO_4 rather than K_2CO_3 or Cs_2CO_3 (entries 1 and 2), and with *N*,*N*′-dimethylethylenediamine rather than ethylenediamine (entry 5). Under the optimum conditions, a virtually quantitative yield of the desired product **3** was attained.

Table 3 shows the generality of this transformation. Open-chain sulfonamide **4** was alkynylated with 1-bromo-1-octyne (**2**) to give **12** in good yield (entry 1). This compound was previously prepared via a stepwise sequence, involving (i) coupling of (silylethynyl)iodonium salt with *N*-benzyl-*p*-toluenesulfonamide (**4**) (to give **13**, see Eq. 1), (ii) desilylation of **13** to the terminal acetylene, and (iii) its alkylation.[6a] Thus, the one-step synthesis from **4** to **12** proved to be advantageous over the conventional method shown in Eq. 1. The trimethylsilyl group of bromide **10** survived the reaction conditions to give *N*-(silylethynyl)-sulfonamide **13** in good yield, which is a precursor of the versatile terminal acetylene as mentioned above (entry 2). Another open-chain sulfonamide **5** afforded the coupling products **14** and **15**, although the yield was not satisfactory under the standard conditions and thus the excess use of the alkynylating agent is required (entry 3). It should be noted that the product **15** (and also **14**) were hardly obtained by the alkynyliodonium method (Scheme 1). Sterically more congested benzosultams **6**–**8** were successfully alkynylated to afford the desired products (entries 7–12). The enantiopurity of optically active sultam **7** was completely retained in the product (**19**, entry 9). In addition to aromatic sulfonamides **1** and **4**–**8**, an aliphatic cyclic sulfonamide **9**, a useful chiral auxiliary known as Oppolzer's camphorsultam,[13] underwent this coupling reaction to give **23** or **24**. In the latter case, the product yield was improved by the use of excess alkylating agent (entry 14).

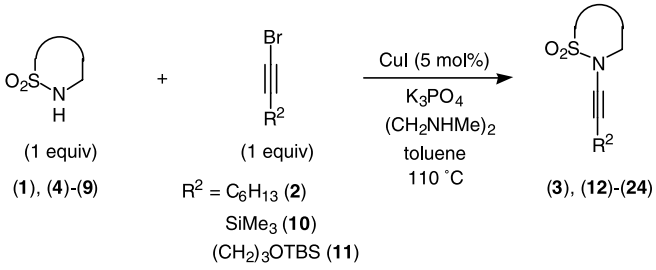
2.2. Coupling of *N*-(1-alkynyl)sulfonamides with aldehyde

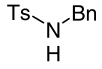
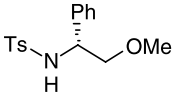
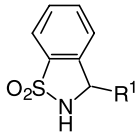
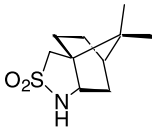
With *N*-(1-alkynyl)sulfonamides in hand, we began to investigate the generation and synthetic application of a new class of *N*-(1-alkynyl)sulfonamide–titanium alkoxide complexes. As the aminoacetylenes having a chiral element were conveniently prepared as shown in Table 3, the titanation of these acetylenes followed by the aldehyde addition should lead to an interesting approach for asymmetric synthesis (Table 4). Thus, *N*-(silylethynyl)-sultam **16** was first treated with a titanium(II) alkoxide reagent, Ti(O–*i*-Pr)$_4$/2 *i*-PrMgCl (**25**),[4] to generate the acetylene–titanium complex **26**, to which was added benzaldehyde as **27**. After hydrolysis, the adduct **29** was obtained in good yield, showing virtually complete regio- and olefinic stereoselectivities[6a,14,15] and with high 1,5-diastereoselectivity (ds=96:4) (entry 1). The excellent level of the remote asymmetric induction (=1,5-diastereoselectivity) is noteworthy.[16] Other sultams **18**, **20**, and **24** having the same acetylenic moiety gave the analogous adducts with benzaldehyde in the following yields and diastereoselectivities: 73%, 97:3; 62%, 79:21; and 46%, 84:16, which revealed that sultam **16** is the most effective one. The structure of **29** was established by spectroscopic means as well as appropriate derivatization. The deuteriolysis confirmed the presence of the remaining vinyl–titanium bond in the intermediate oxatitanacycle **28**, which may serve for further transformations.[17] Other types of aldehydes gave the adducts **30**–**34** in good to excellent diastereoselectivities (entries 2–6).

Chart 1 shows a proposed stereochemical course of the above reaction. The intermediate shown below, which fulfills (i) the least hindered conformation of the sultam moiety to the substituent (Me_3Si) of the titanated acetylene, (ii) the approach of the aldehyde from the less hindered side (opposite the Me group on the sultam), and (iii) the less hindered orientation of the side chain (R) of the aldehyde, may account for the observed stereochemistry of the products in entries 1–6.

On the other hand, when the same reaction between the sultams having an *N*-octynyl group and aldehydes is performed, benzosultam **19** with a *tert*-butyl side chain was found to be the substrate of choice and its titanation and subsequent addition to aldehydes afforded the coupling

Table 3. Alkynylation of various sulfonamides

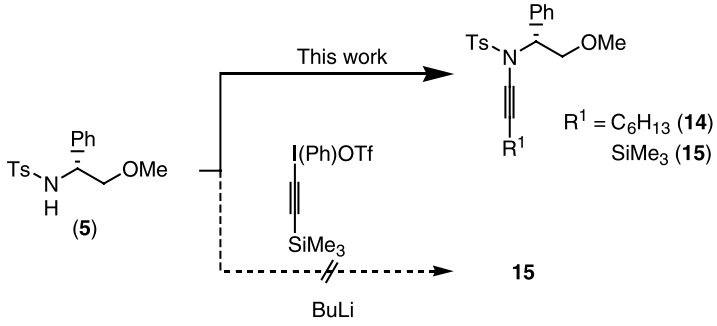


Entry	Starting sulfonamide		Bromoalkyne	Product		
				R^2		Yield (%)[a]
1		(**4**)	**2**	C_6H_{13}	(**12**)	93
2		(**4**)	**10**	$SiMe_3$	(**13**)	84
3		(**5**)	**2**	C_6H_{13}	(**14**)	28, 44,[b] 57,[c] 67[d]
4		(**5**)	**10**	$SiMe_3$	(**15**)	23
5		R^1=Me (**1**)	**2**	C_6H_{13}	(**3**)	79
6		Me (**1**)	**10**	$SiMe_3$	(**16**)	71
7		Bu (**6**)	**2**	C_6H_{13}	(**17**)	84
8		Bu (**6**)	**10**	$SiMe_3$	(**18**)	66
9		*t*-Bu (**7**)[e]	**2**	C_6H_{13}	(**19**)[e]	94
10		*t*-Bu (**7**)	**10**	$SiMe_3$	(**20**)	71
11		*t*-Bu (**7**)	**11**	-$(CH_2)_3$OTBS	(**21**)	81
12		Ph (**8**)	**11**	-$(CH_2)_3$OTBS	(**22**)	91
13		(**9**)	**2**	C_6H_{13}	(**23**)	95
14		(**9**)	**10**	$SiMe_3$	(**24**)	58, 95[f]

[a] Isolated yield.
[b] Compound **2** (2 equiv) was used.
[c] Compound **2** (3 equiv) was used.
[d] Compound **2** (4 equiv) was used.
[e] The enantiopurity of (*S*)-**7** (96% ee) was completely preserved in the product (*S*)-**19** (96% ee).
[f] Compound **10** (2 equiv) was used.

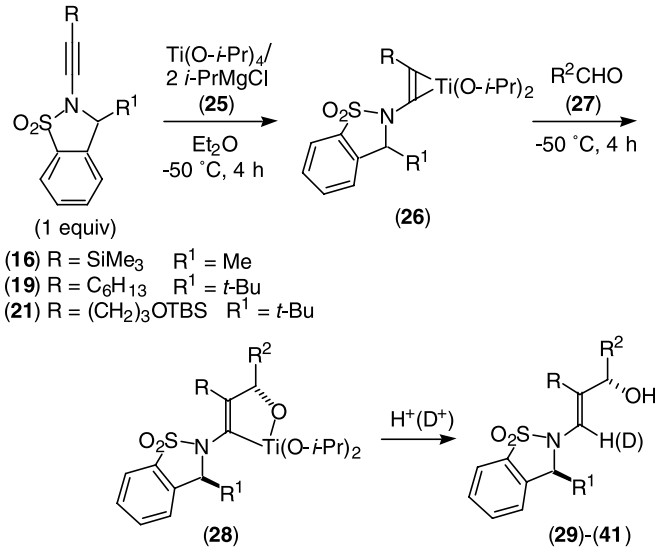
products **35**–**40**, again with exclusive regio- and olefinic stereoselectivities and good to excellent 1,5-diastereoselectivities (entries 7–12). Benzosultam **21** with a different acetylenic side chain also showed a similar result (entry 13). When the reaction was started with chiral alkynylsultam ((*S*)-**19**, 96% ee, prepared in entry 9 of Table 3), the optically active products **38** and **40** were obtained without loss of the enantiopurity (entries 10 and 12).

Chart 2 shows a proposed stereochemical course of the reaction discussed above. The intermediate shown below,



Scheme 1.

Table 4. Remote diastereoselective addition of *N*-alkynylsultams to aldehydes



Entry	Sultam	Aldehyde		Product		
		R^2	Equiv		Yield (%)[a]	1,5-Ds[b]
1	**16**	Ph	0.8	(**29**)	87 (97%D)[c]	96:4[d]
2	**16**	*p*-ClC$_6$H$_4$–	1	(**30**)	54	96:4
3	**16**	(*E*)-C$_5$H$_{11}$CH=CH–	0.8	(**31**)	73	94:6
4	**16**	(*E*)-MeCH=CH–	1	(**32**)	52	95:5
5	**16**	C$_8$H$_{17}$	0.8	(**33**)	94	88:12
6	**16**	*c*-C$_6$H$_{11}$	0.8	(**34**)	89	68:32
7	**19**	Ph	1	(**35**)	74	88:12
8	**19**	(*E*)-MeCH=CH–	1	(**36**)	59	81:19
9	**19**	C$_8$H$_{17}$	1	(**37**)	62	88:12
10[e]	**19**[f]	*i*-Pr	1	(**38**)[f]	88 (96%D)[c]	93:7
11	**19**	*c*-C$_6$H$_{11}$	0.8	(**39**)	79	93:7
12	**19**[f]	*t*-Bu	0.8	(**40**)[f]	93	98.2
13	**21**	*i*-Pr	1.5	(**41**)	84	>95:5[g]

[a] Isolated yields.
[b] Diasterioselectivity.
[c] Result of deuteriolysis.
[d] Isomerically pure sample of **29** could be obtained by recrystallization from hexane–CH_2Cl_2.
[e] In this case, a small amount of a regioisomer (less than 4%) was detected and was easily separated from **38** by silica gel chromatography. In other entries, we were unable to identify the regioisomeric product(s).
[f] The enantiopurity of (*S*)-**19** (96% ee) was retained in the product **38** (95% ee) or **40** (96% ee).
[g] We were unable to identify the characteristic peaks of minor diastereoisomer by ^{1}H NMR spectroscopy, and deduced that the diastereoselectivity of **41** was > 95:5.

which fulfills (i) the least hindered conformation of the sultam moiety to the substituent (C_6H_{13}) of the titanated acetylene, (ii) the approach of the aldehyde from the less hindered side (opposite the *t*-Bu group on the sultam), and (iii) the less hindered orientation of the side chain (R) of the aldehyde, may account for the observed stereochemistry of the products of entries 7–13.

Some derivatizations based on the coupling products obtained in Table 4 demonstrated their synthetic utility.

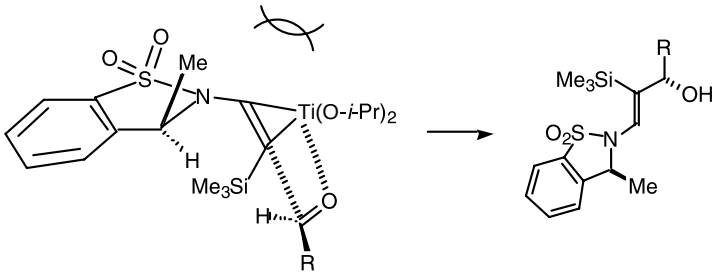


Chart 1.

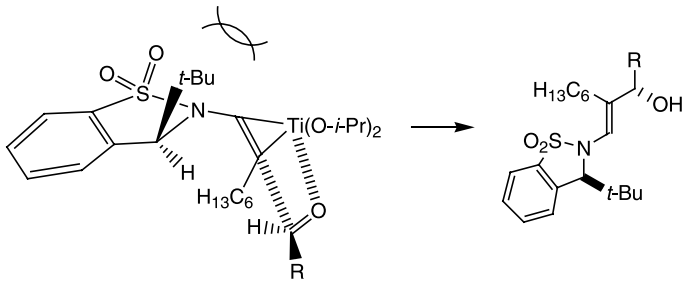
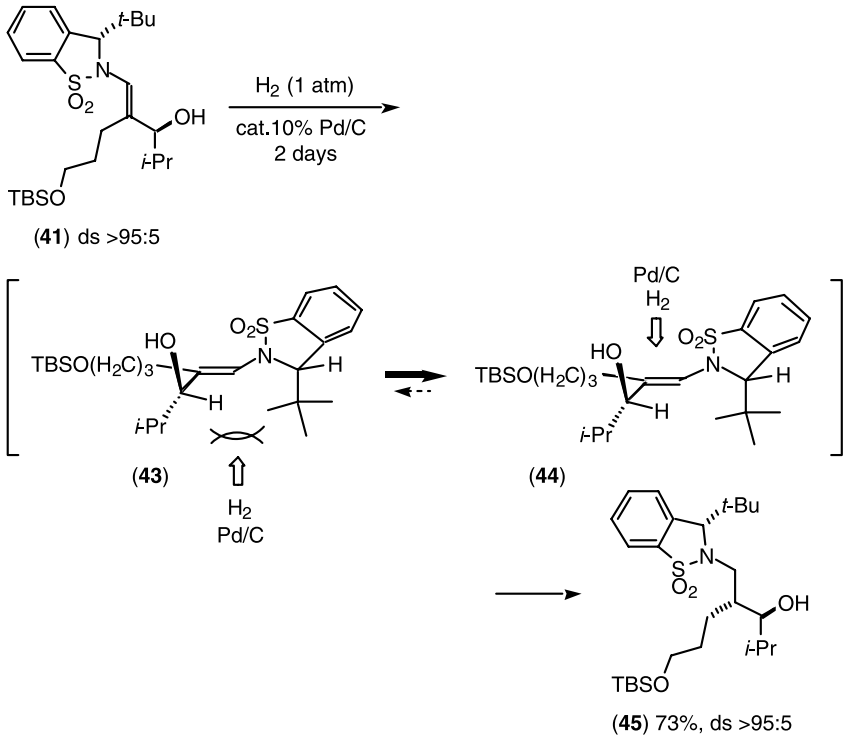
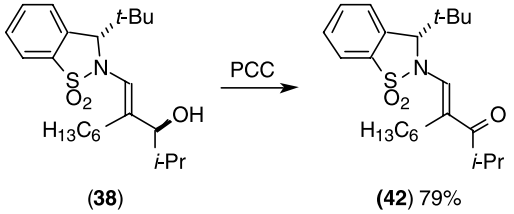


Chart 2.



Scheme 2.

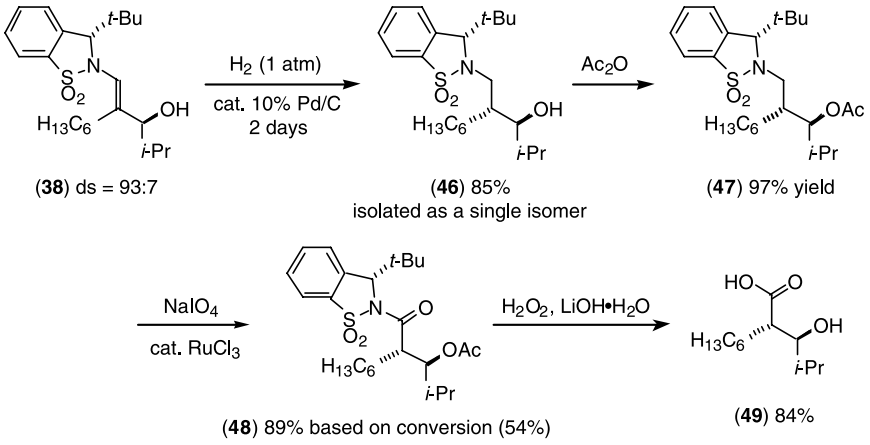
Oxidation of alcohol **38** afforded an α,β-unsaturated ketone **42** having a chiral amino group at its β-position (Eq. 3).[18] On the other hand, hydrogenation of **41** on Pd/C produced γ-aminoalcohol **45** in a highly stereoselective manner (Scheme 2). The stereochemical outcome of the hydrogenation could be interpreted in terms of the less hindered approach of hydrogen on Pd/C to the depicted conformation of **44**[19] rather than **43**. After protection of its hydroxy group, a similar hydrogenated product **46** prepared from **38** was oxidized at the methylene group adjacent to the benzosultam with $RuCl_3$–$NaIO_4$ to afford chiral amide **48**, which, in turn, was smoothly hydrolyzed to afford hydroxy ester **49** (Scheme 3).



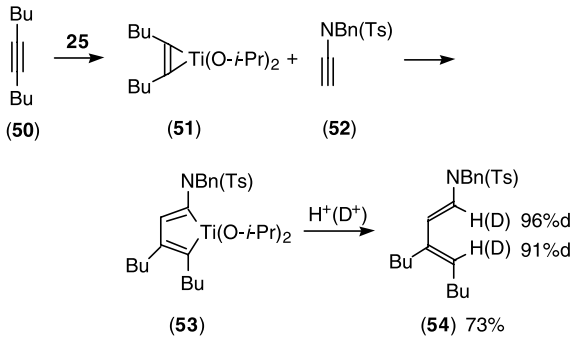
(3)

2.3. Coupling of *N*-(1-alkynyl)sulfonamides with another acetylene or olefin

One of the most characteristic features of acetylene–titanium alkoxide complexes is their capability of undergoing the coupling reaction with another acetylene. When this reaction is successfully applied to the *N*-(1-alkynyl)-sulfonamides, stereoselective construction of aminodienes, which are versatile compounds for the preparation of nitrogen-functionalized cyclic systems via a concerted process such as the Diels–Alder reaction, will be readily achieved.[20] Acetylene–titanium complex **51**, generated from 5-decyne (**50**) and **25**[4] by a known procedure,[21] was found to undergo a coupling reaction with the amino-substituted acetylene **52** (prepared by desilylation of **13** as described in Section 2.1) at −50 °C in a regio- and stereoselective manner to give single dienamide **54** after hydrolytic workup (Scheme 4).[22,23] Its structure was verified by ^{1}H NMR spectroscopy. In addition to the simple hydrolysis, deuteriolysis gave bis-deuterated dienamide **54**-d_2, confirming the presence of titanacyclopentadiene **53** as the intermediate.



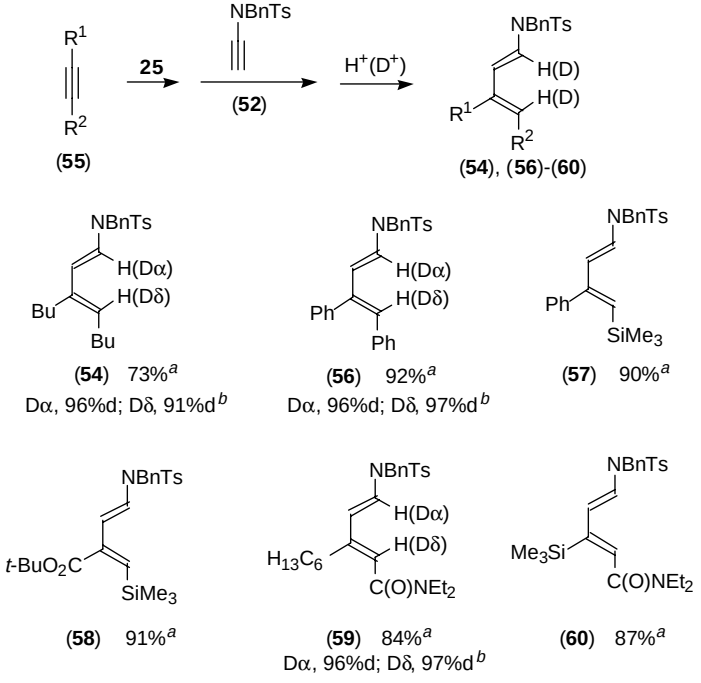
Scheme 3.



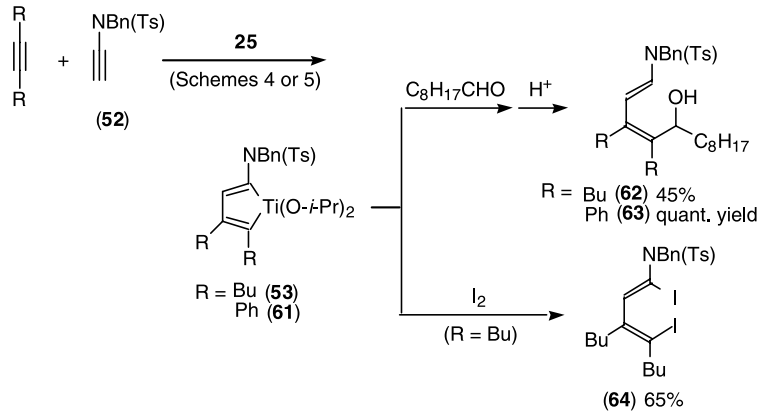
Scheme 4. Preparation of dienamide.

The generality of this reaction is shown in Scheme 5. As the first acetylene **55**, dialkylacetylene, diphenylacetylene, silylacetylene, and acetylenic esters and amides participated in the coupling reaction to give a variety of dienamides **54** and **56–60** in good to excellent yields. All reactions afforded the products as a single regio- as well as stereoisomer. In addition, further carbon-chain elongation and functionalization of the intermediate titanacycles **53** and **61** were exemplified by the regio- and stereoselective aldehyde addition to furnish **62** and **63** or by iodinolysis of **53** to give diiodide **64** (Scheme 6).[17]

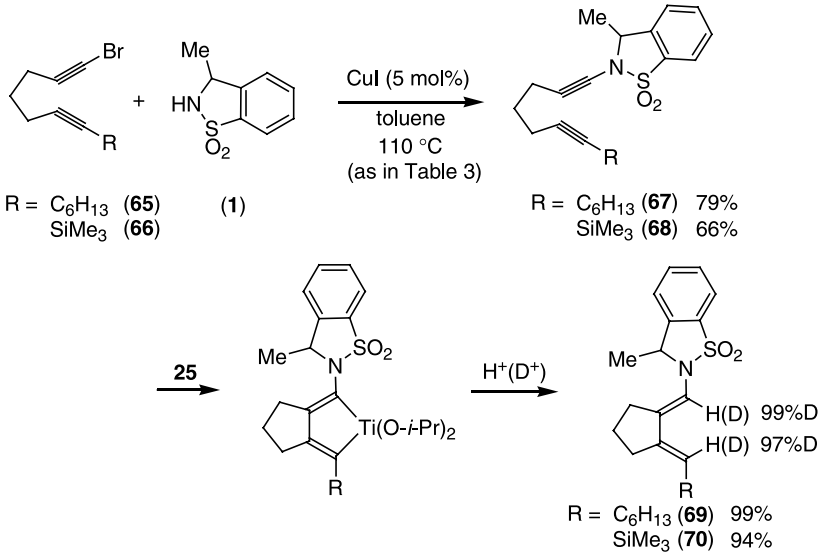
Intramolecular coupling of two acetylenic moieties is an attractive method to prepare cyclic compounds (Scheme 7). The starting diynes **67** and **68** were readily prepared by the standard protocol, copper-catalyzed *N*-alkynylation of sulfonamide **1** with bromodiynes **65** and **66** without any complication. The resultant dinynes **67** and **68** were then cyclized with the titanium reagent to give, upon hydrolysis or deuteriolysis, the desired



Scheme 5. Preparation of various dienamides according to Scheme 4. Isomeric products were not observed. The stereochemistry was unambiguously determined in several representative cases. [a]Isolated yields. [b]Results of deuteration.



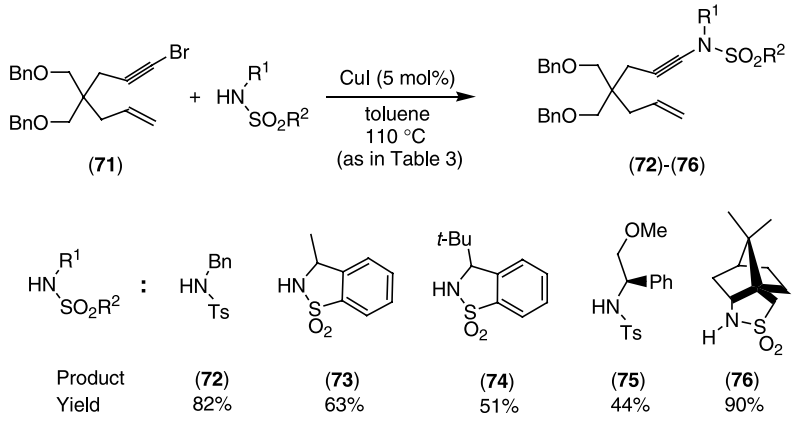
Scheme 6. Synthetic utility of the titanacycle.



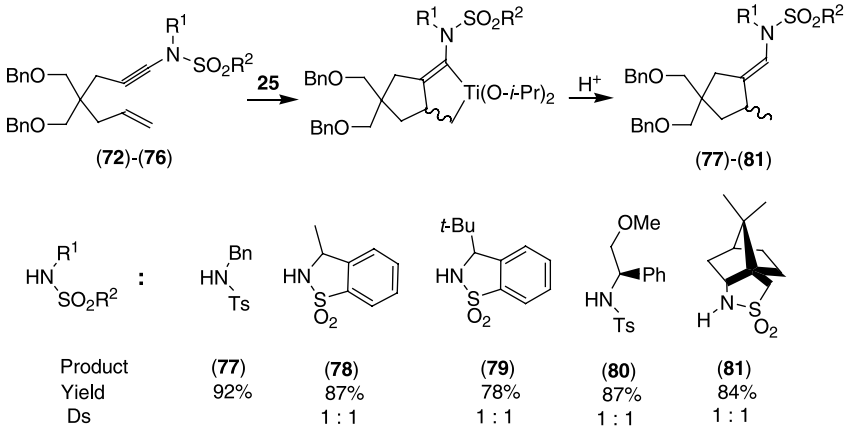
Scheme 7. Preparation of *N*-alkadiynylsulfonamides and its intramolecular cyclization with titanium reagent **25**.

amino-substituted, *exo*-cyclic dienes **69** and **70** in excellent yields.

In contrast to the above successful inter- and intramolecular coupling reactions between two acetylenes, the attempted intermolecular coupling of an *N*-(1-alkynyl)sulfonamides with an olefin failed. Accordingly, we moved to investigate an intramolecular version, that is, enyne cyclization,[24] and were glad to find that this type of reaction was, in fact, viable (Schemes 8 and 9). The copper-catalyzed alkynylation of sulfonamides with bromoenyne **71** proceeded as usual, unaffected by the neighboring olefinic moiety in the



Scheme 8. Preparation of *N*-alkadiynylsulfonamides having an olefin moiety.



Scheme 9. Intramolecular enyne cyclization of *N*-alkynylsulfonamides.

same molecule, to give the starting *N*-(1-alkynyl)sulfonamides **72–76** having an olefinic appendix (Scheme 8). Although the observed diastereoselectivities of the subsequent titanium alkoxide-mediated coupling reaction fell in an unsatisfactory range, the desired cyclic products **77–81** were obtained in good yields (Scheme 9).

3. Conclusion

A variety of *N*-(1-alkynyl)sulfonamides are now conveniently prepared from readily available starting materials and reagents. This improved synthesis enhanced the utility of these amino-substituted acetylenes to promising compounds that serve for the stereoselective construction of enamides and dienamide. Further application of the present transformation as well as the resultant amino-substituted compounds in organic synthesis will be reported in due course.

4. Experimental

4.1. General

^{1}H and ^{13}C NMR spectra were taken on a Varian Gemini-300 spectrometer at 300 and 75 MHz, respectively. $CDCl_3$ was used as the solvent, unless otherwise specified. Chemical shifts are reported in parts per million shift (δ value) from Me_4Si (δ 0 ppm for ^{1}H) or based on the middle peak of the solvent ($CDCl_3$) (δ 77.00 ppm for ^{13}C NMR) as an internal standard. When a sample was dissolved in C_6D_6 for ^{1}H NMR spectroscopy, the peak of the residual proton of the solvent is the internal standard (δ 7.20 ppm). Signal patterns are indicated as br, broad; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants (J) are given in Hertz. Infrared (IR) spectra were recorded on a JASCO A-100 spectrometer and are reported in wave numbers (cm^{-1}). Optical rotation was measured on JASCO DIP-370 digital polarimeter. All reactions were carried out under argon. Dry solvents were purchased from Kanto Chemicals Co. (Japan). Chemicals were purified or dried in a standard manner, if necessary.

4.1.1. Typical procedure for Table 3. *N*-(1-Octynyl)-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (19). To a heterogeneous mixture of 3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (**7**) (90.1 mg, 0.400 mmol), powdered K_3PO_4 (170 mg, 0.80 mmol), and CuI (3.8 mg, 0.020 mmol) in 1 mL of toluene was added 1-bromo-1-octyne (**2**) (75.6 mg, 0.400 mmol) in 3 mL of toluene followed by *N*,*N*′-dimethylethylenediamine (0.010 mL) under argon. After the mixture was stirred overnight in an oil bath maintained at 110 °C, it was cooled to room temperature and was filtered through a short pad of silica gel with the aid of ethyl acetate. The combined filtrates were concentrated in vacuo to give a crude oil, which was chromatographed on silica gel (hexane–ethyl acetate) to give the title compound (125.2 mg, 94%) as an oil. ^{1}H NMR δ 0.87 (t, J=6.9 Hz, 3H), 1.10 (s, 9H), 1.19–1.45 (m, 6H), 1.46–1.58 (m, 2H), 2.32 (t, J=7.2 Hz, 2H), 4.45 (s, 1H), 7.45 (d, J=7.5 Hz, 1H), 7.54 (t, J=7.5 Hz, 1H), 7.59 (t, J=7.5 Hz, 1H), 7.78 (d, J=7.5 Hz, 1H); ^{13}C NMR δ 13.87, 18.53, 22.39, 26.74, 28.53, 28.69, 31.17, 38.23, 71.13, 72.63, 75.26, 121.84, 125.77, 129.49, 132.54, 134.13, 135.59; IR (neat) 2958, 2931, 2858, 2256, 1472, 1328, 1276, 1178, 1139, 1041, 1015, 897, 758, 709 cm^{-1}. Anal. Calcd for $C_{19}H_{27}NO_2S$: C, 68.43; H, 8.16. Found: C, 68.54; H, 8.23.

4.1.2. *N*-(1-Octynyl)-3-methyl-1,2-benzisothiazoline 1,1-dioxide (3). ^{1}H NMR δ 0.87 (t, J=6.9 Hz, 3H), 1.21–1.47 (m, 6H), 1.48 –1.61 (m, 2H), 1.64 (d, J=6.6 Hz, 3H), 2.35 (t, J=6.9 Hz, 2H), 4.76 (q, J=6.6 Hz, 1H), 7.40 (d, J=7.5 Hz, 1H), 7.54 (t, J=7.5 Hz, 1H), 7.66 (t, J=7.5 Hz, 1H), 7.78 (d, J=7.5 Hz, 1H); ^{13}C NMR δ 13.82, 18.53, 19.01, 22.34, 28.32, 28.66, 31.11, 58.96, 66.96, 74.29, 121.56, 123.93, 129.53, 132.68, 133.59, 137.33; IR (neat) 2968, 2935, 2911, 2862, 2250, 1377, 1324, 1273, 1178, 1138, 1070, 903, 760, 717, 653 cm^{-1}. Anal. Calcd for $C_{16}H_{21}NO_2S$: C, 65.95; H, 7.26. Found: C, 66.11; H, 7.09.

4.1.3. *N*-Benzyl-*N*-(1-octynyl)-*p*-toluenesulfonamide (12). ^{1}H NMR δ 0.85 (t, J=6.9 Hz, 3H), 1.10–1.41 (m, 8H), 2.14 (t, J=6.9 Hz, 2H), 2.41 (s, 3H), 4.42 (s, 2H), 7.22–7.30 (m, 7H), 7.73 (d, J=8.4 Hz, 2H); ^{13}C NMR δ 13.84, 18.15, 21.38, 22.34, 28.07, 28.52, 31.12, 55.43, 70.77, 73.27, 127.66, 128.06, 128.36, 128.68, 129.54, 134.74, 134.85, 144.30; IR (Nujol) 3091, 3063, 3040, 2921, 2845, 2250, 1454, 1354, 1303, 1170, 1093, 1055, 812, 735, 698 cm^{-1}. Anal. Calcd for $C_{22}H_{27}NO_2S$: C, 71.51; H, 7.36. Found: C, 71.45; H, 7.02. Mp 47–48 °C.

4.1.4. *N*-Benzyl-*N*-[2-(trimethylsilyl)ethynyl]-*p*-toluenesulfonamide (13). ^{1}H NMR δ 0.08 (s, 9H), 2.44 (s, 3H), 4.48 (s, 2H), 7.24–7.34 (m, 7H), 7.73 (d, J=8.4 Hz, 2H); ^{13}C NMR δ −0.22, 21.48, 55.37, 73.84, 95.32, 127.85, 128.28, 128.40, 128.96, 129.56, 134.42, 134.65, 144.64; IR (Nujol) 3090, 3062, 3045, 3038, 2924, 2862, 2168, 1454, 1374, 1253, 1175, 1090, 1049, 946, 892, 842, 748 cm^{-1}. Anal. Calcd for $C_{19}H_{23}NO_2SSi$: C, 63.83; H, 6.48. Found: C, 63.92; H, 6.33. Mp 76–77 °C.

4.1.5. (*R*)-*N*-(*p*-Toluenesulfonyl)-*N*-(1-octynyl)-(2-methoxy-1-phenylethyl)amine (14). ^{1}H NMR δ 0.88 (t, J=6.9 Hz, 3H), 1.19–1.36 (m, 6H), 1.39–1.51 (m, 2H), 2.29 (t, J=6.9 Hz, 2H), 2.39 (s, 3H), 3.25 (s, 3H), 3.62 (d/d, J=5.1, 10.5 Hz, 1H), 3.84 (d/d, J=9.6, 10.5 Hz, 1H), 5.18 (d/d, J=5.1, 9.6 Hz, 1H), 7.14–7.21 (m, 2H), 7.22–7.33 (m, 5H), 7.61–7.69 (m, 2H); ^{13}C NMR δ 13.91, 18.52, 21.41, 22.46, 28.32, 28.77, 31.24, 58.61, 61.60, 70.64, 72.41, 73.08, 127.39, 127.96, 128.22, 128.43, 129.03, 135.66, 136.67, 143.83; IR (neat) 3095, 3065, 3033, 2960, 2935, 2862, 2250, 1457, 1363, 1261, 1168, 1133, 1092, 976, 764, 715 cm^{-1}. Anal. Calcd for $C_{24}H_{31}NO_3S$: C, 69.70; H, 7.56. Found: C, 69.51; H, 7.31; $[\alpha]_D^{24}$ 69.3 (c 1.39, $CHCl_3$).

4.1.6. (*R*)-*N*-(*p*-Toluenesulfonyl)-*N*-[2-(trimethylsilyl)-ethynyl]-(2-methoxy-1-phenylethyl)amine (15). ^{1}H NMR δ 0.16 (s, 9H), 2.40 (s, 3H), 3.23 (s, 3H), 3.62 (d/d, J=4.8, 10.5 Hz, 1H), 3.82 (d/d, J=9.6, 10.5 Hz, 1H), 5.13 (d/d, J=4.8, 9.6 Hz, 1H), 7.15–7.21 (m, 2H), 7.22–7.32 (m, 5H), 7.60–7.68 (m, 2H); ^{13}C NMR δ −0.08, 21.46, 58.65, 62.07, 72.33, 76.34, 93.05, 127.42, 128.11, 128.40, 128.47, 129.03, 135.34, 136.32, 144.17; IR (neat) 3058, 3017, 2957, 2919, 2895, 2158, 1597, 1457, 1364, 1249, 1168, 971, 844, 760, 698, 665 cm^{-1}. Anal. Calcd for $C_{21}H_{27}NO_3SSi$: C, 62.81; H, 6.78. Found: C, 63.12; H, 6.87; $[\alpha]_D^{24}$ 70.2 (c 1.06, $CHCl_3$).

4.1.7. *N*-[2-(Trimethylsilyl)ethynyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (16). ^{1}H NMR δ 0.21 (s, 9H), 1.67 (d, J=6.6 Hz, 2H), 4.86 (q, J=6.6 Hz, 1H), 7.41 (d, J=7.5 Hz, 1H), 7.56 (t, J=7.5 Hz, 1H), 7.68 (t, J=7.5 Hz, 1H), 7.79 (d, J=7.5 Hz, 1H); ^{13}C NMR δ −0.04, 19.16, 59.06, 77.40, 88.66, 121.66, 124.02, 129.70, 132.54, 133.82, 137.01; IR (neat) 2960, 2903, 2166, 1474, 1328, 1250, 1181, 1139, 1067, 1029, 844, 749, 694 cm^{-1}. Anal. Calcd for $C_{13}H_{17}NO_2SSi$: C, 55.88; H, 6.13. Found: C, 55.90; H, 6.36.

4.1.8. *N*-(1-Octynyl)-3-butyl-1,2-benzisothiazoline 1,1-dioxide (17). ^{1}H NMR δ 0.85 (t, J=7.2 Hz, 3H), 0.89 (t, J=6.9 Hz, 3H), 0.93–1.07 (m, 1H), 1.22–1.48 (m, 9H), 1.49–1.64 (m, 2H), 1.91–2.07 (m, 1H), 2.08–2.23 (m, 1H), 2.37 (t, J=6.9 Hz, 2H), 4.83 (t, J=4.5 Hz, 1H), 7.38 (d, J=7.5 Hz, 1H), 7.55 (t, J=7.5 Hz, 1H), 7.66 (t, J=7.5 Hz, 1H), 7.80 (d, J=7.5 Hz, 1H); ^{13}C NMR δ 13.62, 13.88, 18.61, 22.27, 22.41, 24.77, 28.37, 28.72, 31.20, 31.84, 63.07, 67.23, 74.15, 121.76, 123.96, 129.48, 133.41, 133.46, 135.94; IR (neat) 2968, 2935, 2895, 2845, 2250, 1466, 1327, 1279, 1189, 1140, 1050, 903, 764 cm^{-1}. Anal. Calcd for $C_{19}H_{27}NO_2S$: C, 68.43; H, 8.16. Found: C, 68.51; H, 8.17.

4.1.9. *N*-[2-(Trimethylsilyl)ethynyl]-3-butyl-1,2-benzisothiazoline 1,1-dioxide (18). ^{1}H NMR δ 0.21 (s, 9H), 0.86 (t, J=7.2 Hz, 3H), 0.96–1.13 (m, 1H), 1.21–1.44 (m, 3H), 1.92–2.07 (m, 1H), 2.08–2.24 (m, 1H), 4.91 (t, J=4.5 Hz, 1H), 7.39 (d, J=7.5 Hz, 1H), 7.56 (t, J=7.5 Hz, 1H), 7.68 (t, J=7.5 Hz, 1H), 7.80 (d, J=7.5 Hz, 1H); ^{13}C NMR δ −0.04, 13.58, 22.15, 24.84, 32.08, 63.22, 77.21, 89.09, 121.77, 124.02, 129.62, 133.18, 133.68, 135.65; IR (neat) 2959, 2935, 2854, 2169, 1451, 1321, 1250, 1179, 1138, 1048, 840, 757, 697 cm^{-1}. Anal. Calcd for $C_{16}H_{23}NO_2SSi$: C, 59.77; H, 7.21. Found: C, 59.57; H, 7.05.

4.1.10. (*S*)-3-(*tert*-Butyl)-1,2-benzisothiazoline 1,1-dioxide (96% ee) ((*S*)-7). This was prepared according to the following literature: Oppolzer, W.; Kingma, A. J.; Pillai, S. K. *Tetrahedron Lett*. **1991**, *32*, 4893–4896. $[\alpha]_D^{25}$ −51.7 (c 1.0, $CHCl_3$) for a sample of 96% ee. Lit. $[\alpha]_D^{18}$ −54.0 (c 1.0, $CHCl_3$) for an enantiopure (*S*)-sample [Ahn, K. H.; Ham, C.; Kim, S. -K.; Cho, C. -W. *J. Org. Chem*. **1997**, *62*, 7047–7048]; $[\alpha]_D^{20}$ −53.9 (c 1, $CHCl_3$) for a pure (*S*)-sample [Oppolzer, W.; Kingma, A. J.; Pillai, S. K. *Tetrahedron Lett*. **1991**, *32*, 4893–4896; however, the nomenclature of *R*/*S* in this reference is wrong].

4.1.11. (*S*)-*N*-(1-Octynyl)-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (96% ee) ((*S*)-19) prepared from (*S*)-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (96% ee) ((*S*)-7). For ^{1}H and ^{13}C NMR, IR, and elemental analyses, see the racemic sample listed above. $[\alpha]_D^{29}$ −21.1 (c 1.06, $CHCl_3$) for a sample of 96% ee. The enantiopurity was determined to be 96% ee by HPLC analysis [CHIRALCEL OD-H column (silica gel, 0.46ϕ×15.25 cm), *i*-PrOH/hexane (1:10 v/v) at a rate of 0.5 mL/min: retention time=13.8 min for (*R*) and 16.0 min for (*S*)]. Thus, no racemization was observed during this copper-catalyzed coupling reaction.

4.1.12. *N*-[2-(Trimethylsilyl)ethynyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (20). ^{1}H NMR δ 0.18 (s, 9H), 1.11 (s, 9H), 4.54 (s, 1H), 7.46 (d, J=7.5 Hz, 1H), 7.55 (t, J=7.5 Hz, 1H), 7.61 (t, J=7.5 Hz, 1H), 7.79 (d, J=7.5 Hz, 1H); ^{13}C NMR δ −0.10, 26.72, 38.50, 75.36, 75.66, 92.72, 121.91, 125.86, 129.64, 132.75, 134.00, 135.26; IR (Nujol) 2922, 2845, 2161, 1464, 1376, 1333, 1245, 1175, 1010, 846, 746, 671 cm^{-1}. Anal. Calcd for $C_{16}H_{23}NO_2SSi$: C, 59.77; H, 7.21. Found: C, 59.81; H, 7.26. Mp 73–74 °C.

4.1.13. *N*-[5-((*tert*-Butyl)dimethylsiloxy)-1-pentynyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (21). To a heterogeneous mixture of 3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (**7**) (1.13 g, 5.00 mmol), powdered K_3PO_4 (2.12 g, 10.0 mmol), and CuI (47.6 mg, 0.250 mmol) in 10 mL of toluene was added 1-bromo-[5-(*tert*-butyl)dimethylsiloxy]-1-pentyne (**11**) (1.39 g, 5.00 mmol) in 40 mL of toluene followed by *N*,*N*′-dimethylethylenediamine (0.125 mL) under argon. After the mixture was stirred overnight in an oil bath maintained at 110 °C, it was cooled to room temperature and was filtered through a short pad of silica gel with the aid of ethyl acetate. The combined filtrates were concentrated in vacuo to give a crude oil, which was chromatographed on silica gel (hexane–ethyl acetate) to give the title compound (1.70 g, 81%) as an oil. ^{1}H NMR δ 0.04 (s, 6H), 0.88 (s, 9H), 1.10 (s, 9H), 1.72 (quintet, J=6.6 Hz, 2H), 2.40 (t, J=6.6 Hz, 2H), 3.69 (t, J=6.6 Hz, 2H), 4.44 (s, 1H), 7.45 (d, J=7.8 Hz, 1H), 7.49–7.64 (m, 2H), 7.77 (d, J=7.8 Hz, 1H); ^{13}C NMR δ −5.25, 15.18, 18.33, 25.96, 26.89, 31.99, 38.34, 61.59, 71.27,

72.09, 75.23, 121.64, 125.58, 129.30, 132.35, 133.88, 135.30; IR (neat) 3074, 2955, 2903, 2845, 2256, 1472, 1331, 1252, 1179, 1140, 1104, 1010, 836, 777, 709 cm^{-1}. Anal. Calcd for $C_{22}H_{35}NO_3SSi$: C, 62.66; H, 8.37. Found: C, 62.53; H, 8.50.

4.1.14. *N*-[5-((*tert*-Butyl)dimethylsiloxy)-1-pentynyl]-3-phenyl-1,2-benzisothiazoline 1,1-dioxide (22). ^1H NMR δ 0.00 (s, 6H), 0.86 (s, 9H), 1.59 (quintet, $J=6.6$ Hz, 2H), 2.29 (t, $J=6.6$ Hz, 2H), 3.53 (t, $J=6.6$ Hz, 2H), 5.67 (s, 1H), 7.08–7.16 (m, 1H), 7.28–7.43 (m, 5H), 7.50–7.61 (m, 2H), 7.79–7.88 (m, 1H); ^{13}C NMR δ −5.61, 14.79, 18.06, 25.73, 31.57, 61.16, 67.17, 67.23, 74.18, 121.39, 125.32, 128.00 (2 peaks), 129.03, 129.31, 129.75, 132.39, 133.66, 136.27; IR (neat) 3074, 3025, 2928, 2895, 2862, 2250, 1466, 1325, 1270, 1189, 1115, 838, 772, 707 cm^{-1}.

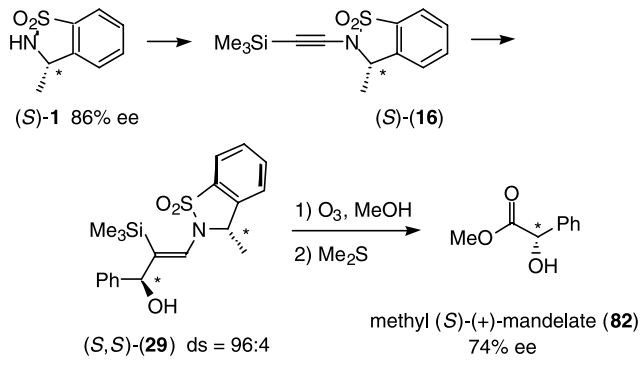
4.1.15. (1*S*,2*S*)-*N*-(1-Octynyl)-2,10-camphorsultam (23). ^1H NMR δ 0.84 (t, $J=6.9$ Hz, 3H), 0.89 (s, 3H), 1.06 (s, 3H), 1.17–1.58 (m, 10H), 1.70 (d/d, $J=8.1$, 13.2 Hz, 1H), 1.76–1.94 (m, 3H), 2.13 (d/d/d, $J=13.2$, 6.6, 3.9 Hz, 1H), 2.25 (t, $J=6.9$ Hz, 2H), 3.18 (s, 2H), 3.47 (d/d, $J=4.2$, 8.1 Hz, 1H); ^{13}C NMR δ 13.78, 18.37, 19.68, 19.93, 22.27, 26.80, 28.19, 28.65, 31.04, 31.34, 34.17, 44.16, 47.68, 49.27, 50.63, 67.00, 67.29, 72.27; IR (neat) 2960, 2935, 2250, 1457, 1335, 1224, 1166, 1144, 1116, 1068, 875, 833, 772, 669 cm^{-1}. Anal. Calcd for $C_{18}H_{29}NO_2S$: C, 66.83; H, 9.04. Found: C, 66.83; H, 8.70; $[\alpha]_D^{29}$ −99.9 (*c* 1.02, $CHCl_3$).

4.1.16. (1*S*,2*S*)-*N*-[2-(Trimethylsilyl)ethynyl]-2,10-camphorsultam (24). ^1H NMR δ 0.16 (s, 9H), 0.93 (s, 3H), 1.09 (s, 3H), 1.20–1.46 (m, 2H), 1.76 (d/d, $J=8.1$, 13.2 Hz, 1H), 1.83–1.99 (m, 3H), 2.20 (d/d/d, $J=13.2$, 6.6, 3.9 Hz, 1H), 3.23 (s, 2H), 3.59 (d/d, $J=4.2$, 8.1 Hz, 1H); ^{13}C NMR δ 0.08, 19.82, 20.02, 26.92, 31.49, 34.12, 44.28, 47.88, 49.79, 51.07, 66.87 (2 peaks), 75.53; IR (neat) 2952, 2927, 2895, 2166, 1344, 1246, 1156, 1075, 851, 822, 781, 748, 668 cm^{-1}. Anal. Calcd for $C_{15}H_{25}NO_2SSi$: C, 57.83; H, 8.09. Found: C, 57.75; H, 7.97; $[\alpha]_D^{29}$ −119.0 (*c* 1.01, $CHCl_3$).

4.1.17. Typical procedure for Table 4. (*RS*)-*N*-[(*RS*)-(*Z*)-3-Hydroxy-3-phenyl-2-(trimethylsilyl)-1-propenyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (29). To a stirred solution of *N*-[2-(trimethylsilyl)ethynyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (**16**) (34.4 mg, 0.123 mmol) and $Ti(O\text{–}i\text{-}Pr)_4$ (0.073 mL, 0.246 mmol) in 1.2 mL of Et_2O was added *i*-PrMgCl (1.46 M in Et_2O, 0.337 mL, 0.492 mmol) at −78 °C under argon to give a yellow homogeneous solution. The solution was warmed to −50 °C over 30 min, during which period its color turned black. After stirring at −50 °C for an additional 4 h, benzaldehyde (0.010 mL, 0.098 mmol) was added at −50 °C and the solution was stirred for another 4 h. Then, the reaction was terminated by the addition of H_2O (0.123 mL) and the reaction mixture was allowed to warm to room temperature, stirred for 30 min, and was filtered through Celite with the aid of ether. The combined filtrates were concentrated in vacuo to give a crude oil, careful analysis of which by ^1H NMR spectroscopy showed the presence of a 96:4 mixture of diastereoisomers. The crude product was chromatographed on silica gel (hexane–ethyl acetate) to give the title compound (33.3 mg, 87%) as a colorless solid and as a 96:4 mixture of diastereoisomers. ^1H NMR δ 0.02 (s, 9H), 1.61 (d, $J=6.6$ Hz, 3H), 1.91 (br s, 1H, OH), 4.60 (q, $J=6.6$ Hz, 1H), 5.48 (s, 1H), 6.71 (s, 1H), 7.22–7.58 (m, 7H), 7.66 (t, $J=7.5$ Hz, 1H), 7.80 (d, $J=7.5$ Hz, 1H). Irradiation of proton at δ 4.60 ppm (CHN) showed 12% NOE enhancement to the peak at δ 6.71 ppm (CH=C). Irradiation of proton at δ 5.48 ppm (C*H*OH) showed 4% NOE enhancement to the peak at δ 6.71 ppm (CH=C). Irradiation of proton at δ 6.71 ppm (CH=C) showed 12% NOE enhancement to the peak at δ 4.60 ppm (CHN) and 4% NOE enhancement to the peak at δ 5.48 ppm (C*H*OH). Thus, the regio- and stereochemistries have been confirmed. ^1H NMR (C_6D_6) δ 0.22 (s, 9H), 1.14 (d, $J=6.6$ Hz, 3H), 1.35 (br s, 1H, OH), 4.00 (q, $J=6.3$ Hz, 1H), 5.33 (s, 1H), 6.59 (d, $J=7.5$ Hz, 1H), 6.72 (t, $J=7.5$ Hz, 1H), 6.76 (s, 1H), 6.88 (t, $J=7.5$ Hz, 1H), 7.00–7.24 (m, 3H), 7.36 (d, $J=7.5$ Hz, 1H), 7.53 (d, $J=7.8$ Hz, 2H). A characteristic peak of the minor diastereoisomer: ^1H NMR (C_6D_6) δ 5.26 (s, 1H). ^{13}C NMR δ 0.23, 19.05, 60.20, 77.21, 121.48, 123.53, 127.94, 128.32, 128.69, 129.11, 130.63, 133.11, 134.40, 138.77, 141.60, 149.50; IR (Nujol) 3509, 2952, 2923, 2854, 1597, 1457, 1375, 1297, 1172, 974, 844, 757 cm^{-1} for a 96:4 mixture of diastereoisomers. Anal. Calcd for $C_{20}H_{25}NO_3SSi$: C, 61.98; H, 6.50. Found: C, 61.61; H, 6.48 for a 96:4 mixture of diastereoisomers. Mp 165–168 °C (recrystallized from CH_2Cl_2–hexane).

4.1.18. (*RS*)-*N*-[(*RS*)-(*Z*)-1-Deuterio-3-hydroxy-3-phenyl-2-(trimethylsilyl)-1-propenyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (29-*d*$_1$). ^1H NMR δ 0.02 (s, 9H), 1.61 (d, $J=6.6$ Hz, 3H), 1.91 (br s, 1H, OH), 4.60 (q, $J=6.6$ Hz, 1H), 5.48 (s, 1H), 7.22–7.58 (m, 7H), 7.66 (t, $J=7.5$ Hz, 1H), 7.80 (d, $J=7.5$ Hz, 1H). The peak at δ 6.71 ppm (CH=C) of (*RS*)-*N*-[(*RS*)-(*Z*)-3-hydroxy-3-phenyl-2-(trimethylsilyl)-1-propenyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (**29**) disappeared to show 97% deuterium incorporation.

4.1.19. Structural determination of adduct 29. (*S*)-*N*-[(*S*)-(*Z*)-3-Hydroxy-3-phenyl-2-(trimethylsilyl)-1-propenyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide ((*S*,*S*)-29). For determination of the relative stereochemistry of the (racemic) adduct **29**, optically active (*S*)-**16** prepared from known benzosultam (*S*)-**1** (86% ee, $[\alpha]_D^{25}$ −25.8 (*c* 1.00, $CHCl_3$). Lit. $[\alpha]_D^{20}$ −30 (*c* 1.21, $CHCl_3$) for a pure (*S*)-sample [Oppolzer, W.; Wills, M.; Starkemann, C.; Bernardinelli, G. *Tetrahedron Lett*. **1990**, *31*, 4117–4120]) was allowed to react with benzaldehyde to give (*S*,*S*)-**29** (ds=96:4). The olefinic bond of (*S*,*S*)-**29** was oxidatively cleaved by ozonolysis in methanol, affording directly (*S*)-methyl mandelate (**82**), the absolute stereochemistry and ee value of which were determined to be *S* and 74% ee, respectively, by ^1H NMR analyses of the derived MTPA esters in comparison with an authentic sample of methyl (*S*)-(+)-mandelate. The ee value of the methyl mandelate (74% ee) derived from the adduct (*S*,*S*)-**29** was in good agreement with the expected value (79% ee) based on the ee value of the starting **29** (86% ee) and the diastereoselectivity (ds=96:4). Thus, the relative stereochemistry of adduct **29** has been established.



4.1.20. Methyl (*S*)-(+)-mandelate (82) from (*S*,*S*)-29. Adduct (*S*,*S*)-**29** (153.2 mg, 0.305 mmol) dissolved in dry MeOH (2.35 mL) was cooled to −78 °C, and ozone was bubbled into this solution. After the blue color of ozone appeared, argon was bubbled for 10 min in place of ozone and then methyl sulfide (0.427 mL) was added. The reaction mixture was allowed to warm to room temperature and stirred for 3 h. The solution was concentrated to give a crude oil, which was chromatographed on silica gel (hexane–ethyl acetate) to give the title compound (14.4 mg, 29%) as an oil. ^{1}H NMR δ 3.46 (br s, 1H, OH), 3.76 (s, 3H), 5.18 (s, 1H), 7.29–7.47 (m, 5H).

$[\alpha]_D^{25}$ +111.3 (*c* 0.96, $CHCl_3$) for a sample of 74% ee. Lit. $[\alpha]_D^{20}$ +144 (*c* 1.00, MeOH) for a sample of 98% ee [Aldrich Handbook of Fine Chemicals and Laboratory Equipment; Sigma–Aldrich: 2003–2004, p 1255].

4.1.21. The MTPA ester of methyl (*S*)-(+)-mandelate (82). A characteristic peak of the (*R*)-MTPA ester prepared from (*S*)-MTPACl and **82**: ^{1}H NMR δ 6.12 (s, 1H, CHOMTPA). A characteristic peak of the (*S*)-MTPA ester prepared from (*R*)-MTPACl and **82**: ^{1}H NMR δ 6.10 (s, 1H, CHOMTPA).

4.1.22. (*RS*)-*N*-[(*RS*)-(*Z*)-3-(*p*-Chlorophenyl)-3-hydroxy-2-(trimethylsilyl)-1-propenyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (30). ^{1}H NMR δ 0.03 (s, 9H), 1.59 (d, *J*=6.6 Hz, 3H), 2.18 (br s, 1H, OH), 4.58 (q, *J*=6.6 Hz, 1H), 5.44 (s, 1H), 6.65 (s, 1H), 7.30–7.46 (m, 5H) 7.55 (t, *J*=7.5 Hz, 1H), 7.66 (t, *J*=7.5 Hz, 1H), 7.79 (d, *J*=7.5 Hz, 1H). Characteristic peaks of the minor diastereoisomer: ^{1}H NMR δ 4.51 (q, *J*=6.6 Hz, 1H), 6.41 (s, 1H). ^{13}C NMR δ 0.01, 18.88, 60.21, 75.78, 121.63, 123.73, 128.96, 129.34, 129.46, 131.57, 133.37, 134.17, 134.48, 138.95, 140.47, 149.54; IR (Nujol) 3482, 2952, 2919, 2862, 2723, 1458, 1376, 1290, 1175, 1134, 1083, 854 cm^{-1} for a 96:4 mixture of diastereoisomers. Anal. Calcd for $C_{20}H_{24}ClNO_3SSi$: C, 56.92; H, 5.73. Found: C, 57.17; H, 5.70 for a 96:4 mixture of diastereoisomers.

4.1.23. (*RS*)-*N*-[(*RS*)-(1*Z*,4*E*)-3-Hydroxy-2-(trimethylsilyl)-1,4-decadien-1-yl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (31). ^{1}H NMR δ 0.22 (s, 9H), 0.88 (t, *J*=7.2 Hz, 3H), 1.10–1.48 (m, 6H), 1.54 (d, *J*=6.6 Hz, 3H), 1.69 (br s, 1H, OH), 2.06 (q, *J*=6.9 Hz, 2H), 4.52 (q, *J*=6.6 Hz, 1H), 4.87 (d, *J*=7.2 Hz, 1H), 5.53 (d/d, *J*=7.2, 15.3 Hz, 1H), 5.79 (d/t, *J*=15.3, 6.9 Hz, 1H), 6.50 (s, 1H), 7.40 (d, *J*=7.5 Hz, 1H), 7.53 (t, *J*=7.5 Hz, 1H), 7.63 (t, *J*=7.5 Hz, 1H), 7.78 (d, *J*=7.5 Hz, 1H). A characteristic peak of the minor diastereoisomer: ^{1}H NMR δ 6.45 (s, 1H). ^{13}H NMR δ 0.31, 13.90, 18.51, 22.38, 28.57, 31.37, 32.13, 59.87, 74.94, 121.59, 123.67, 129.24, 130.28, 132.00, 133.19, 134.69, 134.94, 139.02, 151.39; IR (neat) 3486, 2968, 2926, 2895, 2856, 1606, 1456, 1377, 1313, 1245, 1174, 973, 843, 759 cm^{-1} for a 94:6 mixture of diastereoisomers. Anal. Calcd for $C_{21}H_{33}NO_3SSi$: C, 61.87; H, 8.16. Found: C, 62.05; H, 7.93 for a 94:6 mixture of diastereoisomers.

4.1.24. (*RS*)-*N*-[(*RS*)-(1*Z*,4*E*)-3-Hydroxy-2-(trimethylsilyl)-1,4-hexadien-1-yl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (32). ^{1}H NMR δ 0.21 (s, 9H), 1.54 (d, *J*=6.6 Hz, 3H), 1.67 (br s, 1H, OH), 1.73 (d/d, *J*=1.5, 6.6 Hz, 3H), 4.52 (q, *J*=6.6 Hz, 1H), 4.86 (d, *J*=7.2 Hz, 1H), 5.55 (d/d/q, *J*=7.2, 15.3, 1.5 Hz, 1H), 5.80 (d/q, *J*=15.3, 6.6 Hz, 1H), 6.49 (s, 1H), 7.40 (d, *J*=7.5 Hz, 1H), 7.53 (t, *J*=7.5 Hz, 1H), 7.63 (t, *J*=7.5 Hz, 1H), 7.78 (d, *J*=7.5 Hz, 1H). A characteristic peak of the minor diastereoisomer: ^{1}H NMR δ 6.44 (s, 1H). ^{13}C NMR δ 0.26, 17.60, 18.50, 59.83, 74.78, 121.56, 123.66, 129.22, 129.46, 130.22, 133.20, 133.31, 134.64, 139.00, 151.36; IR (Nujol) 3509, 2951, 2923, 2854, 2723, 1600, 1457, 1376, 1300, 1165, 1096, 1067, 973, 843, 761 cm^{-1} for a 95:5 mixture of diastereoisomers. Anal. Calcd for $C_{17}H_{25}NO_3SSi$: C, 58.08; H, 7.17. Found: C, 58.06; H, 6.93 for a 95:5 mixture of diastereoisomers.

4.1.25. (*RS*)-*N*-[(*RS*)-(*Z*)-3-Hydroxy-2-(trimethylsilyl)-1-undecenyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (33). ^{1}H NMR δ 0.24 (s, 9H), 0.88 (distorted t, *J*=6.9 Hz, 3H), 1.18–1.43 (br m, 12H), 1.53 (d, *J*=6.6 Hz, 3H), 1.58–1.90 (m, 3H), 4.44 (q, *J*=3.6 Hz, 1H), 4.52 (q, *J*=6.6 Hz, 1H), 6.44 (s, 1H), 7.40 (d, *J*=7.5 Hz, 1H), 7.53 (t, *J*=7.5 Hz 1H), 7.63 (t, *J*=7.5 Hz, 1H), 7.78 (d, *J*=7.5 Hz, 1H). Characteristic peaks of the minor diastereoisomer: ^{1}H NMR δ 4.36 (q, *J*=3.6 Hz, 1H), 4.79 (q, *J*=6.6 Hz, 1H), 6.43 (s, 1H). ^{13}C NMR δ 0.32, 13.97, 18.47, 22.55, 25.51, 29.16, 29.38, 29.47, 31.76, 37.95, 59.87, 74.24, 121.57, 123.68, 129.24, 130.14, 133.18, 134.62, 139.00, 153.29; IR (neat) 3503, 3072, 2960, 2923, 2854, 1608, 1456, 1376, 1308, 1247, 1173, 1134, 1067, 1027, 842, 759, 689 cm^{-1} for an 88:12 mixture of diastereoisomers. Anal. Calcd for $C_{22}H_{37}NO_3SSi$: C, 62.37; H, 8.80. Found: C, 62.44; H, 9.10 for an 88:12 mixture of diastereoisomers.

4.1.26. (*RS*)-*N*-[(*RS*)-(*Z*)-3-Cyclohexyl-3-hydroxy-2-(trimethylsilyl)-1-propenyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (34). ^{1}H NMR δ 0.23 (s, 9H), 0.78–1.38 (m, 9H), 1.46–2.03 (m, 6H), 4.21 (d, *J*=4.8 Hz, 1H), 4.51 (q, *J*=6.6 Hz, 1H), 6.33 (s, 1H), 7.39 (d, *J*=7.5 Hz, 1H), 7.51 (t, *J*=7.5 Hz, 1H), 7.62 (t, *J*=7.5 Hz, 1H), 7.76 (d, *J*=7.5 Hz, 1H). Characteristic peaks of the minor diastereoisomer: ^{1}H NMR δ 7.38 (d, *J*=7.5 Hz, 1H), 7.50 (t, *J*=7.5 Hz, 1H), 7.61 (t, *J*=7.5 Hz, 1H). ^{13}C NMR δ 0.30, 18.57, 25.92, 26.02, 26.27, 26.43, 30.60, 42.38, 59.92, 78.87, 121.49, 123.64, 129.20, 131.00, 133.18, 134.52, 138.95, 151.29; IR (neat) 3515 (OH), 2922, 2854, 2659, 1603, 1313, 1246, 1130, 1027, 853, 755, 721 cm^{-1} for a 68:32 mixture of diastereoisomers. Anal. Calcd for $C_{20}H_{31}NO_3SSi$: C, 61.03; H, 7.94. Found: C, 60.97; H, 7.66 for a 68:32 mixture of diastereoisomers.

4.1.27. (*RS*)-*N*-[(*RS*)-(*E*)-2-Hexyl-3-hydroxy-3-phenyl-1-propenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (35). ^{1}H NMR δ 0.84 (t, J=7.2 Hz, 3H), 1.09 (s, 9H), 1.15–1.31 (m, 6H), 1.37–1.49 (m, 2H), 2.01–2.14 (m, 2H, including OH), 2.55–2.63 (m, 1H), 4.24 (s, 1H), 5.28 (s, 1H), 5.87 (s, 1H), 7.27–7.39 (m, 4H), 7.45–7.60 (m, 4H), 7.79 (d, J=7.5 Hz, 1H). Characteristic peaks of the minor diastereoisomer: ^{1}H NMR δ 4.17 (s, 1H), 5.34 (s, 1H), 5.80 (s, 1H). ^{13}C NMR δ 13.90, 22.42, 27.16, 27.23, 28.83, 29.54, 31.43, 38.13, 75.61, 76.20, 121.76, 125.50, 125.75, 127.46, 128.11, 128.70, 129.21, 132.08, 137.08, 138.15, 141.24, 141.84; IR (neat) 3464, 3064, 3028, 2956, 2927, 2871, 1654, 1602, 1454, 1312, 1179, 1049, 911, 760, 731, 701 cm^{-1} for an 88:12 mixture of diastereoisomers. Anal. Calcd for $C_{26}H_{35}NO_3S$: C, 70.71; H, 7.99. Found: C, 70.94; H, 8.37 for an 88:12 mixture of diastereoisomers.

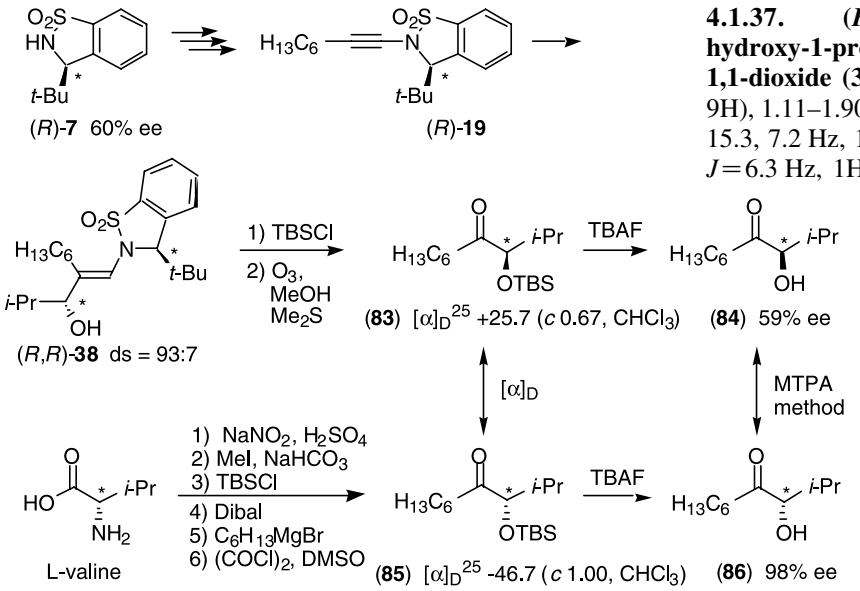
4.1.28. (*RS*)-*N*-[(*RS*)-(1*E*,4*E*)-2-Hexyl-3-hydroxy-1,4-hexadien-1-yl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (36). ^{1}H NMR δ 0.88 (t, J=7.2 Hz, 3H), 1.06 (s, 9H), 1.22–1.42 (m, 6H), 1.48–1.60 (m, 2H), 1.71 (d/d, J=1.5, 6.3 Hz, 3H), 1.75 (br s, 1H, OH), 2.30 (d/t, J=14.7, 8.1 Hz, 1H), 2.62 (d/t, J=14.7, 8.1 Hz, 1H), 4.18 (s, 1H), 4.64 (d, J=7.2 Hz, 1H), 5.54 (d/d/q, J=7.2, 15.3, 1.5 Hz, 1H), 5.70 (s, 1H), 5.81 (d/q, J=15.3, 6.3 Hz, 1H), 7.42–7.60 (m, 3H), 7.77 (d, J=7.5 Hz, 1H). Characteristic peaks of the minor diastereoisomer: ^{1}H NMR δ 4.17 (s, 1H), 4.67 (d, J=7.2 Hz, 1H), 5.44 (d/d/q, J=6.9, 15.3, 1.5 Hz, 1H), 5.72 (s, 1H). ^{13}C NMR δ 13.94, 17.62, 22.49, 27.14, 27.42, 28.87, 29.65, 31.53, 38.10, 73.65, 76.08, 121.74, 124.54, 125.70, 128.90, 129.15, 132.01, 132.16, 136.17, 137.07, 142.13; IR (neat) 3482 (OH), 2968, 2927, 2870, 1662, 1471, 1367, 1314, 1179, 1135, 966, 911, 756, 740 cm^{-1} for an 81:19 mixture of diastereoisomers. Anal. Calcd for $C_{23}H_{35}NO_3S$: C, 68.11; H, 8.70. Found: C, 68.38; H, 8.87 for an 81:19 mixture of diastereoisomers.

4.1.29. (*RS*)-*N*-[(*RS*)-(*E*)-2-Hexyl-3-hydroxy-1-undecenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (37). ^{1}H NMR δ 0.82–0.95 (m, 6H), 1.06 (s, 9H), 1.18–1.45 (m, 18H), 1.55 (m, 4H), 1.78 (br s, 1H, OH), 2.37 (d/t, J=10.2, 6.3 Hz, 1H), 2.54 (d/t, J=10.2, 6.3 Hz, 1H), 4.16 (s, 1H), 4.19 (t, J=6.6 Hz, 1H), 5.63 (s, 1H), 7.45–7.61 (m, 3H), 7.78 (d, J=7.5 Hz, 1H). A characteristic peak of the minor diastereoisomer: ^{1}H NMR δ 5.65 (s, 1H). ^{13}C NMR δ 13.97, 22.55, 25.28, 26.49, 27.15, 27.97, 28.60, 29.16, 29.46, 29.51, 29.59, 29.86, 31.57, 31.78, 35.51, 38.14, 73.81, 76.07, 121.79, 125.08, 125.70, 129.20, 132.04, 136.16, 137.00, 143.51; IR (Nujol) 3498, 2960, 2935, 2862, 1646, 1468, 1367, 1313, 1179, 1135, 1050, 910, 757, 731, 707 cm^{-1} for an 88:12 mixture of diastereoisomers. Anal. Calcd for $C_{28}H_{47}NO_3S$: C, 70.39; H, 9.92. Found: C, 70.41; H, 9.75 for an 88:12 mixture of diastereoisomers.

4.1.30. (*RS*)-*N*-[(*RS*)-(*E*)-2-Hexyl-3-hydroxy-4-methyl-1-pentenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (38). ^{1}H NMR δ 0.88 (t, J=7.2 Hz, 3H), 0.92 (d, J=6.3 Hz, 3H), 0.95 (d, J=6.3 Hz, 3H), 1.06 (s, 9H), 1.22–1.42 (m, 6H), 1.50–1.70 (m, 2H), 1.78 (br s, 1H, OH), 1.94 (octet, J=6.6 Hz, 1H), 2.29 (d/t, J=14.4, 8.1 Hz, 1H), 2.61 (d/t, J=14.4, 8.1 Hz, 1H), 3.92 (d, J=6.6 Hz, 1H), 4.17 (s, 1H), 5.61 (s, 1H), 7.42–7.60 (m, 3H), 7.76 (d, J=7.5 Hz, 1H). Irradiation of proton at δ 5.61 ppm (C=CH) showed 7% NOE enhancement to the peak at δ 3.92 ppm (C*H*OH) and 15% NOE enhancement to the peak at δ 4.17 ppm (NCH). Irradiation of proton at δ 3.92 ppm (C*H*OH) showed 9% NOE enhancement to the peak at δ 5.61 ppm (CH=C). Thus, the regio- and stereochemistries have been confirmed. ^{1}H NMR (C_6D_6) δ 0.88–0.93 (m, 12H), 1.16 (d, J=6.6 Hz, 6H), 1.26–1.58 (m, 7H, including OH), 1.70–1.85 (m, 2H), 1.95 (octet, J=6.6 Hz, 1H), 2.54 (d/t, J=14.4, 8.1 Hz, 1H), 2.92 (d/t, J=14.4, 8.1 Hz, 1H), 3.72 (s, 1H), 3.89 (d, J=6 Hz, 1H), 5.56 (s, 1H), 6.72–6.78 (m, 1H), 6.84–6.92 (m, 2H), 7.42 (d, J=7.8 Hz, 1H). Characteristic peaks of the minor diastereoisomer: ^{1}H NMR (C_6D_6) δ 3.67 (s, 1H), 3.96 (d, J=6 Hz, 1H), 5.62 (s, 1H). ^{13}C NMR δ 13.94, 16.60, 19.45, 22.53, 27.15, 27.81, 28.97, 29.84, 31.39, 31.56, 38.06, 76.11, 78.59, 121.74, 125.53, 125.70, 129.15, 132.02, 136.15, 137.05, 142.43; IR (Nujol) 3502, 2968, 2923, 2854, 1457, 1377, 1304, 1169, 1135, 1042, 1024, 830, 707 cm^{-1} for a 93:7 mixture of diastereoisomers. Anal. Calcd for $C_{23}H_{37}NO_3S$: C, 67.77; H, 9.15. Found: C, 67.53; H, 9.30 for a 93:7 mixture of diastereoisomers.

4.1.31. (*RS*)-*N*-[(*RS*)-(*E*)-1-Deuterio-2-hexyl-3-hydroxy-4-methyl-1-pentenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (38-d_1). ^{1}H NMR δ 0.88 (t, J=7.2 Hz, 3H), 0.92 (d, J=6.3 Hz, 3H), 0.95 (d, J=6.3 Hz, 3H), 1.06 (s, 9H), 1.22–1.42 (m, 6H), 1.50–1.70 (m, 2H), 1.78 (br s, 1H, OH), 1.94 (octet, J=6.6 Hz, 1H), 2.29 (d/t, J=14.4, 8.1 Hz, 1H), 2.61 (d/t, J=14.4, 8.1 Hz, 1H), 3.92 (d, J=6.6 Hz, 1H), 4.17 (s, 1H), 7.42–7.60 (m, 3H), 7.76 (d, J=7.5 Hz, 1H). The peak at δ 5.61 ppm (CH=C) of (*RS*)-*N*-[(*SR*)-(*E*)-2-hexyl-3-hydroxy-4-methyl-1-pentenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (**38**) disappeared to show 96% deuterium incorporation.

4.1.32. Structural determination of adduct 38. (*R*)-*N*-[(*R*)-(*E*)-2-Hexyl-3-hydroxy-4-methyl-1-pentenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide ((*R*,*R*)-38). For determination of the relative stereochemistry of the (racemic) adduct **38**, optically active (*R*)-**19** prepared from known benzosultam (*R*)-**7** (60% ee, $[\alpha]_D^{25}$ +32.1 (*c* 1.00, $CHCl_3$); Lit. see (*S*)-**7**) was allowed to react with benzaldehyde to give (*R*,*R*)-**38** (ds=93:7). After protection as a TBS ether, the olefinic bond of (*R*,*R*)-**38** was oxidatively cleaved by ozonolysis in methanol to afford siloxy ketone (**83**), which was desilylated to give hydroxy ketone **84**. The absolute configuration and ee value of this ketone **84** were determined to be *R* and 59% ee, respectively, by ^{1}H NMR analyses of the derived MTPA esters in comparison with an authentic antipode **86** prepared from L-valine. The ee value of hydroxy ketone **84** (59% ee) prepared from (*R*,*R*)-**38** was in good agreement with the expected value (52% ee) based on the ee value of (*R*)-**7** (60% ee) and the diastereoselectivity of (*R*,*R*)-**38** (ds=93:7). The comparison between the samples of **83** and **85** at the stage of α-siloxyketones was also consistent with the above assignment.



4.1.33. (*R*)-3-[(*tert*-Butyl)dimethylsiloxy]-2-methyl-4-decanone (83) derived from (*R*,*R*)-38. ^{1}H NMR δ 0.00 (s, 3H), 0.03 (s, 3H), 0.81–0.91 (m, 9H), 0.93 (s, 9H), 1.18–1.35 (m, 6H), 1.44–1.64 (m, 2H), 1.92 (octet, J=6.9 Hz, 1H), 2.43 (d/t, J=18.0, 7.5 Hz, 1H), 2.54 (d/t, J=18.0, 7.5 Hz, 1H), 3.71 (d, J=5.4 Hz, 1H); ^{13}C NMR δ −5.21, −4.94, 13.91, 17.37, 18.03, 18.83, 22.40, 22.92, 25.68, 28.92, 31.59, 32.51, 37.75, 83.70, 214.04; $[\alpha]_D^{25}$ +25.7 (c 0.67, $CHCl_3$) for a sample of 59% ee.

4.1.34. (*R*)-3-Hydroxy-2-methyl-4-decanone (84). ^{1}H NMR δ 0.69 (d, J=6.9 Hz, 3H), 0.86 (distorted t, J=6.9 Hz, 3H), 1.10 (d, J=6.9 Hz, 3H), 1.20–1.38 (m, 6H), 1.50–1.68 (m, 2H), 2.15 (heptet/d, J=6.9, 2.7 Hz, 1H), 2.43 (t, J=6.9 Hz, 2H), 3.40 (d, J=5.1 Hz, 1H, OH), 4.05 (d/d, J=2.7, 5.1 Hz, 1H); ^{13}C NMR δ 13.84, 14.57, 19.91, 22.32, 23.44, 28.79, 31.08, 31.40, 38.04, 80.62, 212.56.

4.1.35. The MTPA ester of (*R*)-3-hydroxy-2-methyl-4-decanone (84). A characteristic peak of the (*R*)-MTPA ester prepared from (*S*)-MTPACl and **84**: ^{1}H NMR δ 3.61 (s, 3H, OCH_3). A characteristic peak of the (*S*)-MTPA ester prepared from (*R*)-MTPACl and **84**: ^{1}H NMR δ 3.57 (s, 3H, OCH_3).

4.1.36. (*S*)-*N*-[(*S*)-(*E*)-2-Hexyl-3-hydroxy-4-methyl-1-pentenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide ((*S*,*S*)-38) (95% ee). This was prepared from (*S*)-**19** (96% ee). For ^{1}H and ^{13}C NMR, IR, and elemental analyses, see the racemic sample **38** listed above. $[\alpha]_D^{25}$ −11.7 (c 0.81, $CHCl_3$) for a 93:7 mixture of diastereoisomers, in which the major diastereoisomer is 95% ee. The ee value of the major diastereoisomer was determined by ^{1}H NMR chiral shift study and integration of the separated peaks: (+)-Eu(hfc)$_3$, 0 mol%: δ 5.61 (s, 1H, C=CH) ppm; 2.5 mol%: major enantioisomer 5.66, minor enantioisomer 5.67; 5 mol%: major enantioisomer 5.73, minor enantioisomer 5.75; 7.5 mol%: major enantioisomer 5.80, minor enantioisomer 5.84; 10 mol%: major enantioisomer 5.86, minor enantioisomer 5.93.

4.1.37. (*RS*)-*N*-[(*RS*)-(*E*)-3-Cyclohexyl-2-hexyl-3-hydroxy-1-propenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (39). ^{1}H NMR δ 0.79–0.93 (m, 5H), 1.05 (s, 9H), 1.11–1.90 (m, 17H), 2.00 (br s, 1H, OH), 2.30 (d/t, J=15.3, 7.2 Hz, 1H), 2.60 (d/t, J=15.3, 7.2 Hz, 1H), 3.92 (d, J=6.3 Hz, 1H), 4.17 (s, 1H), 5.59 (s, 1H), 7.43–7.61 (m, 3H), 7.77 (d, J=7.5 Hz, 1H); ^{1}H NMR (C_6D_6) δ 0.86–0.98 (m, 12H), 1.04–1.94 (m, 19H), 2.37 (br s, 1H, OH), 2.60 (d/t, J=15.3, 7.2 Hz, 1H), 2.91 (d/t, J=15.3, 7.2 Hz, 1H), 3.74 (s, 1H), 3.93 (d, J=6 Hz, 1H), 5.58 (s, 1H), 6.68–6.80 (m, 1H), 6.80–6.90 (m, 2H), 7.42 (d, J=7.8 Hz, 1H). Characteristic peaks of the minor diastereoisomer: ^{1}H NMR (C_6D_6) δ 3.70 (s, 1H), 3.98 (d, J=6 Hz, 1H), 5.61 (s, 1H). ^{13}C NMR δ 13.96, 22.54, 25.92, 26.22, 26.39, 26.48, 27.16, 27.90, 29.04, 29.76, 29.87, 31.57, 38.08, 41.31, 76.12, 78.02, 121.78, 125.63, 125.70, 129.17, 132.03, 136.14, 137.04, 142.22; IR (Nujol) 3498, 2952, 2927, 2845, 1458, 1377, 1299, 1170, 1045, 1020, 757, 733 cm^{-1} for a 93:7 mixture of diastereoisomers. Anal. Calcd for $C_{26}H_{41}NO_3S$: C, 69.76; H, 9.23. Found: C, 70.04; H, 9.20 for a 93:7 mixture of diastereoisomers.

4.1.38. (*RS*)-*N*-[(*RS*)-(*E*)-4,4-Dimethyl-2-hexyl-3-hydroxy-1-pentenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (40). ^{1}H NMR δ 0.88 (t, J=7.2 Hz, 3H), 0.97 (s, 9H), 1.07 (s, 9H), 1.20–1.42 (m, 6H), 1.48–1.72 (m, 3H, including OH), 2.04–2.20 (m, 1H), 2.78–3.05 (m, 1H), 3.98 (s, 1H), 4.21 (s, 1H), 5.65 (s, 1H), 7.44–7.60 (m, 3H), 7.76 (d, J=7.5 Hz, 1H). Characteristic peaks of the minor diastereoisomer: ^{1}H NMR δ 3.94 (s, 1H), 4.14 (s, 1H). ^{13}C NMR δ 14.17, 22.68, 26.10, 27.32, 27.58, 29.80, 31.60, 31.75, 36.33, 38.22, 76.26, 79.34, 121.57, 125.57, 126.66, 128.98, 131.83, 135.92, 136.70, 140.72; IR (Nujol) 3506, 2960, 2919, 2854, 1464, 1377, 1169, 1136, 1096, 1015, 855, 755, 723, 707 cm^{-1} for a 98:2 mixture of diastereoisomers. Anal. Calcd for $C_{24}H_{39}NO_3S$: C, 68.37; H, 9.32. Found: C, 68.29; H, 9.62 for a 98:2 mixture of diastereoisomers.

4.1.39. (*S*)-*N*-[(*S*)-(*E*)-4,4-Dimethyl-2-hexyl-3-hydroxy-1-pentenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide ((*S*,*S*)-40) (96% ee). This was prepared from (*S*)-**19** (96% ee). For ^{1}H and ^{13}C NMR, IR, and elemental analyses, see the racemic sample **40** listed above. $[\alpha]_D^{28}$ −9.4 (c 0.96, $CHCl_3$) for a 98:2 mixture of diastereoisomers, in which the major diastereoisomer is 96% ee. The ee value of the major diastereoisomer was determined by ^{1}H NMR chiral shift study and integration of the separated peaks: (+)-Eu(hfc)$_3$,

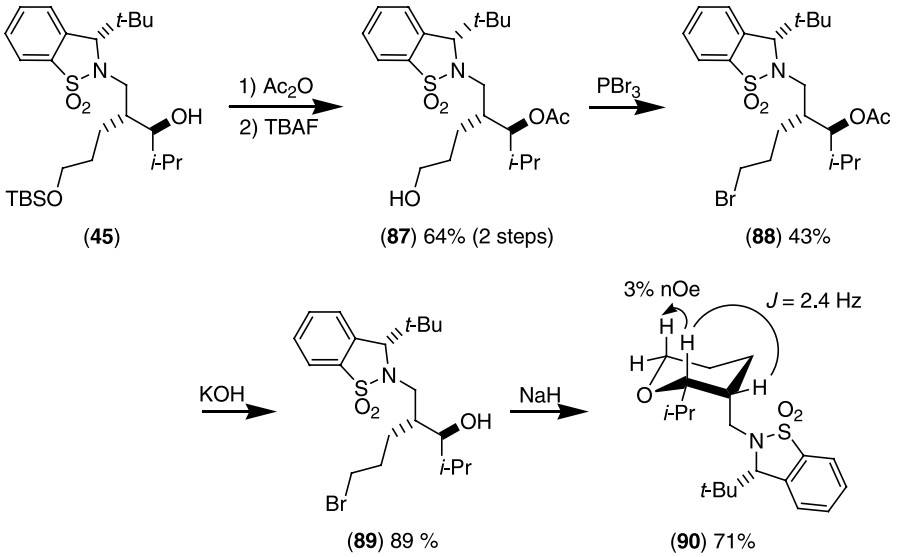
0 mol%: δ 5.65 (s, 1H, C=CH) ppm; 7.5 mol%: major enantioisomer 5.73, minor enantioisomer 5.76; 10 mol%: major enantioisomer 5.76, minor enantioisomer 5.80; 12.5 mol%: major enantioisomer 5.79, minor enantioisomer 5.83; 15 mol%: major enantioisomer 5.81, minor enantioisomer 5.86; 17.5 mol%: major enantioisomer 5.84, minor enantioisomer 5.89.

4.1.40. (*RS*)-*N*-[(*RS*)-(*E*)-2-(3-(*tert*-Butyl)dimethylsiloxypropyl)-3-hydroxy-4-methyl-1-pentenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (41). To a stirred solution of *N*-[5-((*tert*-butyl)dimethylsiloxy)-1-pentynyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (**21**) (713 mg, 1.69 mmol) and Ti(O–*i*-Pr)$_4$ (0.998 mL, 3.38 mmol) in 17 mL of Et_2O was added *i*-PrMgCl (1.50 M in Et_2O, 4.51 mL, 6.76 mmol) at −78 °C under argon to give a yellow homogeneous solution. The solution was warmed to −50 °C over 30 min, during which period its color turned black. After stirring at −50 °C for an additional 4 h, isobutyraldehyde (0.230 mL, 2.54 mmol) was added at −50 °C and the solution was stirred for another 4 h. Then, the reaction was terminated by the addition of H_2O (1.7 mL) and the reaction mixture was allowed to warm to room temperature, stirred for 30 min, and was filtered through Celite with the aid of ether. The combined filtrates were concentrated in vacuo to give a crude oil, ^{1}H NMR analysis of which did not show the peaks corresponding to the minor diastereoisomer within the limits of detection. Thus the diastereoselectivity was judged to be >95:5. The crude product was chromatographed on silica gel (hexane–ethyl acetate) to give the title compound (700 mg, 84%) as a colorless solid. ^{1}H NMR δ 0.07 (s, 6H), 0.90 (s, 9H), 0.97 (d, J=6.9 Hz, 6H), 1.06 (s, 9H), 1.66–2.05 (m, 4H), 2.30–2.45 (m, 1H), 2.58–2.73 (m, 1H), 3.68 (d/t, J=10.2, 6.0 Hz, 1H), 3.74 (d/t, J=10.2, 6.0 Hz, 1H), 3.90 (d, J=6.3 Hz, 1H), 4.17 (s, 1H), 5.63 (s, 1H), 7.42–7.68 (m, 3H), 7.77 (d, J=7.5 Hz, 1H); ^{13}C NMR δ −5.13, 17.09, 18.47, 19.62, 25.45, 26.09, 27.35, 31.26, 31.61, 38.21, 63.63, 76.15, 78.91, 121.64, 125.53, 125.72, 129.01, 131.89, 135.85, 136.84, 142.05; IR (Nujol) 3492 (OH), 3278, 3066, 2925, 2854, 1457, 1377, 1298, 1168, 1134, 1107, 836, 759 cm^{-1} for a >95:5 mixture of diastereoisomers. Anal. Calcd for $C_{26}H_{45}NO_4SSi$: C, 62.99; H, 9.15. Found: C, 62.61; H, 8.82 for a >95:5 mixture of diastereoisomers. Mp 114–116 °C.

4.1.41. *N*-[(*E*)-2-Hexyl-4-methyl-3-oxo-1-pentenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (42). ^{1}H NMR δ 0.88 (t, J=6.9 Hz, 3H), 1.07 (s, 9H), 1.09 (d, J=6.9 Hz, 3H), 1.11 (d, J=6.9 Hz, 3H), 1.20–1.76 (m, 8H), 2.58–2.80 (m, 2H), 3.09 (septet, J=6.9 Hz, 1H), 4.31 (s, 1H), 6.50 (s, 1H), 7.46–7.66 (m, 3H), 7.80 (d, J=7.2 Hz, 1H); ^{13}C NMR δ 13.95, 18.80, 19.31, 22.53, 27.07, 27.68, 27.93, 29.55, 31.49, 35.65, 38.26, 76.73, 121.86, 125.66, 129.54, 132.46, 135.82, 136.07, 136.51, 136.82, 205.34; IR (neat) 2960, 2927, 2870, 1668 (C=O), 1627, 1468, 1325, 1266, 1198, 1181, 1136, 1050, 872, 755, 700 cm^{-1}.

4.1.42. (*RS*)-*N*-[(2*SR*,3*RS*)-2-(3-(*tert*-Butyl)dimethylsiloxypropyl)-3-hydroxy-4-methyl-1-pentyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (45). A solution of (*RS*)-*N*-[(*RS*)-(*E*)-2-(3-(*tert*-butyl)dimethylsiloxypropyl)-3-hydroxy-4-methyl-1-pentenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (**41**) (399 mg, 0.805 mmol) and 10% Pd/C (12 mg) in 8 mL of EtOH was stirred at room temperature under 1 atm of hydrogen gas for 2 days. Then, the reaction mixture was filtered through Celite with the aid of ethyl acetate. The combined filtrates were concentrated in vacuo to give a crude oil, ^{1}H NMR analysis of which did not show the peaks corresponding to the minor diastereoisomer within the limits of detection. Thus the diastereoselectivity was judged to be > 95:5. The crude product was chromatographed on silica gel (hexane–ethyl acetate) to give the title compound (293 mg, 73%) as a colorless solid. ^{1}H NMR δ 0.05 (s, 6H), 0.89 (s, 9H), 0.95 (d, J=6.0 Hz, 3H), 0.97 (d, J=6.0 Hz, 3H), 1.06 (s, 9H), 1.44–1.94 (m, 5H), 1.98–2.12 (m, 1H), 2.31–2.46 (m, 1H), 3.18 (t, J=12.0 Hz, 1H), 3.33 (d/d, J=3.0, 8.4 Hz, 1H), 3.52–3.74 (m, 3H), 4.07 (s, 1H), 7.39–7.57 (m, 3H), 7.70–7.76 (m, 1H); ^{13}C NMR δ −5.48, −5.44, 18.28, 18.93, 19.49, 24.59, 25.92, 27.12, 29.63, 30.55, 38.02, 39.54, 52.00, 63.65, 75.32, 76.66, 121.41, 125.87, 129.19, 131.78, 136.63, 137.62; IR (Nujol) 3511 (OH), 2952, 2923, 2862, 1458, 1377, 1295, 1173, 1108, 963, 835, 763 cm^{-1}. Anal. Calcd for $C_{26}H_{47}NO_4SSi$: C, 62.73; H, 9.52. Found: C, 62.68; H, 9.51. Mp 117–119 °C.

The stereochemistry of the title compound was unambiguously determined by the following derivatization (**45**→**87**→**88**→**89**→**90**).



4.1.43. (*RS*)-*N*-[((2*SR*,3*RS*)-3-Oxa-2-isopropyl-1-cyclohexyl)methyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (90). ^{1}H NMR δ 0.95 (d, J=6.6 Hz, 6H), 1.07 (s, 9H), 1.20–1.36 (m, 4H), 1.56–1.72 (m, 1H), 2.55–2.67 (m, 1H), 2.94 (d/d, J=2.4, 10.2 Hz, 1H), 3.36–3.57 (m, 3H), 4.07 (s, 1H), 4.09 (d/d, J=6.6, 17.4 Hz, 1H), 7.38–7.45 (m, 1H), 7.46–7.60 (m, 2H), 7.72–7.79 (m, 1H). Decoupling experiment was carried out as follows: Irradiation of the peak at δ 1.56–1.72 ppm (C*H*(CH$_3$)$_2$) changed the doublet–doublet peak at δ 2.94 ppm (*i*-PrC*H*O–) to a doublet peak (d, J=2.4 Hz). Irradiation of proton at δ 3.36–3.57 ppm (CH$_2$O–) showed 3% NOE enhancement to the peak at δ 2.94 ppm (*i*-PrC*H*O–). These coupling constants and NOE experiment established the depicted structure of **90** and, hence, that of **45**. ^{13}C NMR δ 17.89, 21.20, 24.35, 27.23, 29.61, 29.73, 33.25, 49.13, 69.95, 75.24, 77.20, 86.82, 121.48, 125.60, 125.75, 129.25, 131.80, 137.82; IR (neat) 2960, 2923, 2845, 1457, 1308, 1172, 1066, 757 cm^{-1}.

4.1.44. (*RS*)-*N*-[(2*SR*,3*RS*)-2-Hexyl-3-hydroxy-4-methylpentyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (46). A solution of (*RS*)-*N*-[(*RS*)-(*E*)-2-hexyl-3-hydroxy-4-methyl-1-pentenyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (**38**) (100 mg, 0.244 mmol, a 93:7 mixture of diastereoisomer) and 10% Pd/C (5 mg) in 2 mL of EtOH was stirred at room temperature under 1 atm of hydrogen gas for 2 days. Then, the reaction mixture was filtered through Celite with the aid of ethyl acetate. The combined filtrates were concentrated in vacuo to give a crude oil, ^{1}H NMR analysis of which showed the presence of a 93:7 mixture of diastereoisomers. The crude product was chromatographed on silica gel (hexane–ethyl acetate) to give the isomerically pure title compound (84.8 mg, 85%) as an oil. ^{1}H NMR δ 0.87 (t, J=6.9 Hz, 3H), 0.95 (d, J=6.6 Hz, 3H), 0.96 (d, J=6.6 Hz, 3H), 1.06 (s, 9H), 1.18–1.52 (m, 9H), 1.60–1.85 (m, 2H), 1.87–2.05 (m, 1H), 2.30–2.45 (symmetric m, 1H), 3.18 (t, J=12.6 Hz, 1H), 3.31 (d/d, J=2.7, 8.4 Hz, 1H), 3.57 (d/d, J=3.6, 12.6 Hz, 1H), 4.07 (s, 1H), 7.38–7.58 (m, 3H), 7.69–7.78 (m, 1H); ^{13}C NMR δ 13.97, 19.00, 19.30, 22.47, 26.59, 27.09, 28.27, 29.32, 30.67, 31.72, 37.99, 39.32, 51.87, 75.14, 76.95, 121.35, 125.84, 129.15, 131.73, 136.64, 137.61; IR (neat) 3535 (OH), 3278, 3066, 2956, 2927, 2870, 1471, 1367, 1301, 1171, 1107, 1001, 928, 759, 707 cm^{-1}. Anal. Calcd for C$_{23}$H$_{39}$NO$_3$S: C, 67.44; H, 9.60. Found: C, 67.12; H, 9.81.

4.1.43. (*RS*)-*N*-[(2*SR*,3*RS*)-3-Acetoxy-2-hexyl-4-methylpentyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (47). A solution of (*RS*)-*N*-[(2*SR*,3*RS*)-2-hexyl-3-hydroxy-4-methylpentyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (**46**) (398 mg, 0.800 mmol), NEt$_3$ (0.450 mL, 3.20 mmol), Ac$_2$O (0.150 mL, 1.60 mmol), and DMAP (5 mg, 0.04 mmol) in CH$_2$Cl$_2$ (8 mL) was stirred at room temperature overnight. The organic layer was washed with water, dried, and concentrated to give an oil, which was chromatographed on silica gel to afford the title compound (419 mg, 97%). This sample was directly used in the next step.

4.1.46. (*RS*)-*N*-[(2*RS*,3*RS*)-3-Acetoxy-2-hexyl-4-methylpentanoyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (48). To a stirred solution of (*RS*)-*N*-[(2*SR*,3*RS*)-3-acetoxy-2-hexyl-4-methylpentyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (**47**) (67.5 mg, 0.149 mmol) in 0.3 mL of CCl$_4$, 0.3 mL of CH$_3$CN, and 0.45 mL of H$_2$O were added NaIO$_4$ (95.9 mg, 0.448 mmol) and RuCl$_3$ (3.1 mg, 0.015 mmol) at room temperature. After being stirred overnight, the reaction mixture was filtered through Celite with the aid of ethyl acetate. The combined filtrates were concentrated in vacuo to give a crude oil, which was chromatographed on silica gel (hexane–ethyl acetate) to give the title compound (33.6 mg, 89% based on conversion (54%)) as an oil. ^{1}H NMR δ 0.74–1.04 (m, 18H), 1.16–2.10 (m, 14H), 3.88 (d/d/d, J=4.2, 6.9, 9.0 Hz, 1H), 5.31 (d/d, J=3.0, 9.0 Hz, 1H), 5.67 (s, 1H), 7.45–7.85 (m, 4H); ^{13}C NMR δ 13.90, 15.65, 19,97, 20.76, 22.42, 25.86, 27.15, 28.72, 29.31, 30.51, 31.44, 38.22, 48.85, 66.12, 75.93, 121.91, 126.07, 129.53, 132.96, 135.35, 135.73, 170.63, 173.38; IR (neat) 2976, 2928, 2870, 1733 (OC=O), 1711 (NC=O), 1456, 1322, 1123, 1025, 830 cm^{-1}. Anal. Calcd for C$_{25}$H$_{39}$NO$_5$S: C, 64.48; H, 8.44. Found: C, 64.17; H, 8.78.

4.1.47. (2*RS*,3*RS*)-2-Hexyl-3-hydroxy-4-methylpentanoic acid (49). To a stirred solution of (*RS*)-*N*-[(2*RS*,3*RS*)-3-acetoxy-2-hexyl-4-methylpentanoyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (**48**) (36.0 mg, 0.077 mmol) in 1.2 mL of THF and 1.2 mL of H$_2$O were added H$_2$O$_2$ (35%, 0.027 mL, 0.309 mmol) and LiOH·H$_2$O (6.4 mg, 0.155 mmol) at 0 °C. After the reaction mixture was stirred overnight at room temperature, most of the THF was evaporated. The aqueous solution was extracted with CH$_2$Cl$_2$ and the organic layer was discarded. Then the aqueous solution was acidified with 1 N HCl until pH~1 and extracted a few times with CH$_2$Cl$_2$. The combined CH$_2$Cl$_2$ solution was dried over Na$_2$SO$_4$ and concentrated to give a crude oil, which was chromatographed on silica gel (hexane–ethyl acetate) to give the title compound (14.0 mg, 84%) as an oil. ^{1}H NMR δ 0.87 (t, J=6.6 Hz, 3H), 0.95 (d, J=6.6 Hz, 3H), 0.96 (d, J=6.6 Hz, 3H), 1.18–1.42 (m, 9H), 1.53–1.82 (m, 3H), 2.60 (d/t, J=9.0, 5.4 Hz, 1H), 3.38 (d/d, J=5.4, 6.3 Hz, 1H), 3.56 (br s, 1H); ^{13}C NMR δ 17.44, 19.42, 22.46, 27.15, 29.04, 29.61, 29.82, 31.51, 31.90, 47.90, 77.30, 179.03; IR (neat) 3409 (OH), 2960, 2925, 2854, 1700, 1559, 1457 cm^{-1}. Anal. Calcd for C$_{12}$H$_{24}$O$_3$: C, 66.63; H, 11.18. Found: C, 66.99; H, 10.71.

4.1.48. Typical procedure for Schemes 4 and 5. *N*-Benzyl-*N*-[(1*E*,3*E*)-3-butyl-1,3-octadienyl]-*p*-toluenesulfonamide (54). To a stirred solution of 5-decyne (**50**) (0.021 mL, 0.117 mmol) and Ti(O–*i*-Pr)$_4$ (0.043 mL, 0.146 mmol) in 2 mL of Et$_2$O was added *i*-PrMgCl (1.44 M in Et$_2$O, 0.203 mL, 0.292 mmol) at −78 °C under argon to give a yellow homogeneous solution. The solution was warmed to −50 °C over 30 min, during which period its color turned black. After stirring at −50 °C for 2 h, pulverized *N*-benzyl-*N*-ethynyl-*p*-toluenesulfonamide (**52**) (27 mg, 0.094 mmol) was added in one portion to the reaction mixture at −50 °C. After being stirred for 4 h at the same temperature, the reaction was terminated by the addition of H$_2$O (0.2 mL) and the heterogeneous mixture was filtered through Celite with the aid of ether. The organic phase was concentrated in vacuo to give a crude oil. Careful analysis of the crude product by ^{1}H NMR spectroscopy did not show the presence of any isomeric products. The crude

product was chromatographed on silica gel (hexane–ethyl acetate) to afford the title compound (29 mg, 73%) as a colorless oil. ^{1}H NMR δ 0.86 (t, J=6.9 Hz, 3H), 0.92 (t, J=6.9 Hz, 3H), 1.23–1.33 (m, 8H), 2.00 (q, J=7.2 Hz, 2H), 2.13 (t, J=7.2 Hz, 2H), 2,42 (s, 3H), 4.53 (s, 2H), 5.10 (t, J=7.2 Hz, 1H), 5.31 (d, J=14.4 Hz, 1H), 6.80 (d, J=14.4 Hz, 1H), 7.23–7.33 (m, 7H), 7.68 (d, J=8.1 Hz, 2H). Irradiation of proton at δ 5.10 ppm (C=C*H*(Bu)) showed 12% NOE enhancement to the peak at δ 5.31 ppm (C*H*=CHN). Thus, the stereochemistry has been confirmed. ^{13}C NMR δ 13.82, 13.97, 21.42, 22.33, 22.78, 26.62, 27.67, 31.02, 31.84, 49.44, 117.42, 123.74, 127.01 (2 peaks), 127.42, 128.64, 129.86, 130.50, 135.92, 136.07, 136.12, 143.84; IR (neat) 3088, 3065, 3030, 2957, 2928, 2871, 2859, 1638, 1620, 1598, 1496, 1465, 1456, 1401, 1358, 1322, 1307, 1289, 1265, 1210, 1185, 1165, 1119, 1093, 1044, 1025, 1018, 1003, 938, 887, 812, 778, 735, 704, 696, 663 cm^{-1}. Anal. Calcd for $C_{26}H_{35}NO_2S$: C, 73.37; H, 8.29. Found: C, 73.57; H, 7.92.

4.1.49. *N*-Benzyl-*N*-[(1*E*,3*E*)-3-butyl-1,4-dideuterio-1,3-octadienyl]-*p*-toluenesulfonamide (54-d_2). ^{1}H NMR δ 0.86 (t, J=6.9 Hz, 3H), 0.92 (t, J=6.9 Hz, 3H), 1.23–1.33 (m, 8H), 2.00 (t, J=7.2 Hz, 2H), 2.13 (t, J=7.2 Hz, 2H), 2.42 (s, 3H), 4.53 (s, 2H), 5.31 (s, 1H), 7.23–7.33 (m, 7H), 7.68 (d, J=8.1 Hz, 2H). The peak at δ 5.10 ppm (C=C*H*(Bu)) of **54** disappeared to show 91% deuterium incorporation. The peak at δ 6.80 ppm (CH=C*H*(N)) of **54** disappeared to show 96% deuterium incorporation.

4.1.50. *N*-Benzyl-*N*-[(1*E*,3*Z*)-3,4-diphenyl-1,3-butadienyl]-*p*-toluenesulfonamide (56). ^{1}H NMR δ 2.44 (s, 3H), 4.61 (s, 2H), 5.77 (d, J=14.1 Hz, 1H), 6.25 (s, 1H), 6.51 (d, J=14.1 Hz, 1H), 6.74–6.77 (m, 2H), 7.01–7.03 (m, 3H), 7.08–7.12 (m, 2H), 7.29–7.42 (m, 10H), 7.54 (d, J=8.1 Hz, 2H); ^{13}C NMR δ 21.44, 49.65, 118.33, 126.36, 126.95, 127.00, 127.61, 127.76, 127.92, 128.22, 128.78, 128.98, 129.03, 129.45, 129.78, 129.87, 135.66, 135.83, 136.99, 138.02, 139.82, 144.05; IR (Nujol) 3089, 3065, 3032, 2953, 2924, 2854, 1629, 1594, 1456, 1377, 1364, 1341, 1312, 1286, 1273, 1239, 1211, 1200, 1184, 1163, 1117, 1089, 1078, 1042, 1028, 1017, 1000, 972, 951, 932, 911, 897, 867, 852, 835, 809, 799, 775, 759, 751, 733, 694, 674, 654 cm^{-1}. Anal. Calcd for $C_{30}H_{27}NO_2S$: C, 77.39; H, 5.84. Found: C, 77.19; H, 5.63. Mp 127–129 °C.

4.1.51. *N*-Benzyl-*N*-[(1*E*,3*Z*)-3,4-diphenyl-1,4-dideuterio-1,3-butadienyl]-*p*-toluenesulfonamide (56-d_2). ^{1}H NMR δ 2.44 (s, 3H), 4.61 (s, 2H), 5.77 (s, 1H), 6.74–6.77 (m, 2H), 7.01–7.03 (m, 3H), 7.08–7.12 (m, 2H), 7.29–7.42 (m, 10H), 7.54 (d, J=8.1 Hz, 2H). The peak at δ 6.25 ppm (C=C*H*(Ph)) of **56** disappeared to show 97% deuterium incorporation. The peak at δ 6.51 ppm (CH=C*H*(N)) of **56** disappeared to show 96% deuterium incorporation.

4.1.52. *N*-Benzyl-*N*-[(1*E*,3*Z*)-3-phenyl-4-(trimethylsilyl)-1,3-butadienyl]-*p*-toluenesulfonamide (57). ^{1}H NMR δ −0.28 (s, 9H), 2.43 (s, 3H), 4.55 (s, 2H), 5.45 (s, 1H), 5.65 (d, J=14.4 Hz, 1H), 6.45 (d, J=14.4 Hz, 1H), 7.04–7.07 (m, 2H), 7.26–7.36 (m, 10H), 7.50 (d, J=8.4 Hz, 2H). Irradiation of proton at δ −0.28 ppm ($SiMe_3$) showed 5% NOE enhancement to the peak at δ 5.45 ppm (C=C*H*($SiMe_3$)). Irradiation of proton at δ 5.45 ppm (C=C*H*($SiMe_3$)) showed 10% NOE enhancement to the peak at δ 5.65 ppm (C*H*=CH(N)). Thus, the regio- and stereochemistries have been confirmed. ^{13}C NMR δ −0.33, 21.44, 49.55, 119.11, 126.92, 126.98, 127.56, 128.00, 128.76, 129.27, 129.87, 130.39, 130.63, 135.66, 135.92, 140.32, 144.06, 154.42; IR (neat) 3078, 3064, 3029, 2953, 2926, 2898, 2857, 1623, 1598, 1559, 1491, 1456, 1442, 1400, 1363, 1316, 1260, 1247, 1215, 1185, 1167, 1107, 1090, 1039, 1028, 945, 864, 837, 775, 739, 703, 664 cm^{-1}. Anal. Calcd for $C_{27}H_{31}NO_2SSi$: C, 70.24; H, 6.77; N, 3.03. Found: C, 70.10; H, 6.73; N, 2.82.

4.1.53. *tert*-Butyl (3*E*)-4-[benzyl(*p*-toluenesulfonyl)-amino]-2-[(*Z*)-(trimethylsilyl)methylene]-3-butenoate (58). ^{1}H NMR δ 0.09 (s, 9H), 1.53 (s, 9H), 2.42 (s, 3H), 4.54 (s, 2H), 5.40 (d, J=14.7 Hz, 1H), 5.72 (s, 1H), 7.24–7.32 (m, 7H), 7.35 (d, J=14.7 Hz, 1H), 7.67 (d, J=8.4 Hz, 2H). Irradiation of proton at δ 0.09 ppm ($SiMe_3$) showed 8% NOE enhancement to the peak at δ 5.72 ppm (C=C*H*($SiMe_3$)). Irradiation of proton at δ 5.72 ppm (C=C*H*($SiMe_3$)) showed 5% NOE enhancement to the peak at δ 0.09 ppm ($SiMe_3$) and 14% NOE enhancement to the peak at δ 5.40 ppm (C*H*=CH(N)). Thus, the regio- and stereochemistries have been confirmed. ^{13}C NMR δ −0.54, 21.43, 28.07, 49.29, 81.93, 111.82, 126.87, 127.02, 127.59, 128.75, 129.06, 130.03, 135.27, 136.05, 136.46, 144.22, 145.56, 167.21; IR (Nujol) 3087, 3063, 3032, 2952, 2924, 2854, 1715 (C=O), 1653, 1624, 1596, 1569, 1559, 1539, 1507, 1495, 1457, 1375, 1319, 1259, 1228, 1169, 1090, 1026, 971, 939, 894, 860, 845, 803, 755, 729, 694, 661 cm^{-1}. Anal. Calcd for $C_{26}H_{35}NO_4SSi$: C, 64.29; H, 7.26; N, 2.88. Found: C, 64.16; H, 7.29; N, 2.71. Mp 101–103 °C.

4.1.54. (2*E*,4*E*)-*N*,*N*-Diethyl-5-[benzyl(*p*-toluenesulfonyl)-amino]-3-hexyl-2,4-pentadienamide (59). ^{1}H NMR δ 0.89 (t, J=6.9 Hz, 3H), 1.06 (t, J=7.2 Hz, 3H), 1.09 (t, J=7.2 Hz, 3H), 1.25–1.33 (m, 6H), 1.40 (m, 2H), 2.42 (s, 3H), 3.23 (q, J=7.2 Hz, 2H), 3.36 (q, J=7.2 Hz, 2H), 4.60 (s, 2H), 5.27 (d, J=14.4 Hz, 1H), 5.60 (s, 1H), 7.17 (d, J=14.4 Hz, 1H), 7.23–7.31 (m, 7H), 7.66 (d, J=8.4 Hz, 2H). Irradiation of proton at δ 5.60 ppm (C=CH(C=O)) showed 13% NOE enhancement to the peak at δ 5.27 ppm (C*H*=CH(N)). Thus, the regio- and stereochemistries have been confirmed. ^{13}C NMR δ 12.90, 13.98, 14.08, 21.43, 22.51, 28.39, 29.29, 29.43, 31.65, 39.26, 42.26, 49.31, 114.14, 119.11, 126.84, 127.00, 127.58, 128.70, 128.88, 130.00, 135.29, 135.92, 144.27, 147.69, 167.24; IR (neat) 3089, 3065, 3032, 2958, 2930, 2871, 2858, 1634 (C=O), 1618, 1598, 1496, 1456, 1428, 1362, 1321, 1281, 1272, 1220, 1185, 1165, 1140, 1119, 1090, 1046, 1028, 1017, 1002, 944, 911, 863, 813, 785, 734, 704, 696, 663 cm^{-1}. Anal. Calcd for $C_{29}H_{40}N_2O_3S$: C, 70.12; H, 8.12. Found: C, 70.11; H, 7.78.

4.1.55. (2*E*,4*E*)-*N*,*N*-Diethyl-5-[benzyl(*p*-toluenesulfonyl)-amino]-2,5-dideuterio-3-hexyl-2,4-pentadienamide (59-d_2). ^{1}H NMR δ 0.89 (t, J=6.9 Hz, 3H), 1.06 (t, J=7.2 Hz, 3H), 1.09 (t, J=7.2 Hz, 3H), 1.25–1.33 (m, 6H), 1.40 (m, 2H), 2.42 (s, 3H), 3.23 (q, J=7.2 Hz, 2H), 3.36 (q, J=7.2 Hz, 2H), 4.60 (s, 2H), 5.27 (s, 1H), 7.23–7.31 (m, 7H), 7.66 (d, J=8.4 Hz, 2H). The peak at δ 5.60 ppm (C=CH(C=O)) of **59** disappeared to show 97% deuterium

incorporation. The peak at δ 7.17 ppm (CH=C*H*(N)) of **59** disappeared to show 96% deuterium incorporation.

4.1.56. *N*-Benzyl-*N*-[(1*E*,3*Z*)-4-(*N*,*N*-diethylcarbamoyl)-3-(trimethylsilyl)]-*p*-toluenesulfonamide (60). ^{1}H NMR δ 0.01 (s, 9H), 1.12 (t, *J*=7.2 Hz, 3H), 1.16 (t, *J*=7.2 Hz, 3H), 2.43 (s, 3H), 3.33 (q, *J*=7.2 Hz, 2H), 3.36 (q, *J*=7.2 Hz, 2H), 4.54 (s, 2H), 5.42 (d/d, *J*=1.2, 13.8 Hz, 1H), 6.47 (d, *J*=1.2 Hz, 1H), 6.98 (d, *J*=13.8 Hz, 1H), 7.24–7.33 (m, 7H), 7.68 (d, *J*=8.4 Hz, 2H). Irradiation of proton at δ 0.01 ppm ($SiMe_3$) showed 7% NOE enhancement to the peak at δ 5.42 ppm (C*H*=CH(N)) and 6% NOE enhancement to the peak at δ 6.98 ppm (CH=C*H*(N)). Irradiation of proton at δ 6.47 ppm (C=CH(C=O)) showed 1% NOE enhancement to the peak at δ 3.33 ppm (NCH_2CH_3), 4% NOE enhancement to the peak at δ 5.42 ppm (C*H*=CHN), and 13% NOE enhancement to the peak at δ 6.98 ppm (CH=C*H*(N)). Thus, the regio- and stereochemistries have been confirmed. ^{13}C NMR δ −0.48, 12.90, 14.18, 21.44, 39.84, 42.48, 49.69, 116.59, 126.47, 126.93, 127.03, 127.59, 128.71, 129.25, 129.97, 135.35, 135.93, 144.18, 151.11, 167.41; IR (neat) 3087, 3065, 3031, 2973, 2933, 2899, 2873, 1633, 1622, 1616, 1563, 1558, 1496, 1475, 1456, 1446, 1429, 1379, 1361, 1314, 1290, 1261, 1221, 1185, 1165, 1103, 1090, 1040, 1028, 1017, 1002, 944, 841, 812, 780, 734, 705, 696, 660 cm^{-1}. Anal. Calcd for $C_{26}H_{36}N_2O_3SSi$: C, 64.42; H, 7.49; N, 5.78. Found: C, 64.18; H, 7.68; N, 5.49.

4.1.57. Typical procedure for Scheme 6. *N*-Benzyl-*N*-[(1*E*,3*Z*)-5-hydroxy-3,4-dibutyl-1,3-tridecadienyl]-*p*-toluenesulfonamide (62). To a stirred solution of 5-decyne (**50**) (0.016 mL, 0.088 mmol) and Ti(O–*i*-Pr)$_4$ (0.032 mL, 0.110 mmol) in 1 mL of Et_2O was added *i*-PrMgCl (1.47 M in Et_2O, 0.149 mL, 0.219 mmol) at −78 °C under argon to give a yellow homogeneous solution. The solution was warmed to −50 °C over 30 min, during which period its color turned black. After stirring at −50 °C for 2 h, pulverized *N*-benzyl-*N*-ethynyl-*p*-toluenesulfonamide (**52**) (20 mg, 0.070 mmol) was added in one portion to the reaction mixture at −50 °C and the solution was stirred for another 4 h. Then, nonanal (0.023 mL, 0.131 mmol) was added and the reaction mixture was subsequently allowed to warm to room temperature. After being stirred for 5 h at the same temperature, the reaction was terminated by the addition of H_2O (0.2 mL) and the heterogeneous mixture was filtered through Celite with the aid of ether. The organic phase was concentrated in vacuo to give a crude oil. Careful analysis of the crude product by ^{1}H NMR spectroscopy did not show the presence of any isomeric products. The crude product was chromatographed on silica gel (hexane–ethyl acetate) to afford the title compound (18 mg, 45%) as a colorless oil. ^{1}H NMR δ 0.88 (t, *J*=6.9 Hz, 3H), 0.89 (t, *J*=6.9 Hz, 3H), 0.92 (t, *J*=6.9 Hz, 3H), 1.11–1.34 (m, 20H), 1.59 (br s, 2H), 1.96 (m, 3H), 2.12 (t, *J*=8.7 Hz, 2H), 2.43 (s, 3H), 4.16 (t, *J*=7.8 Hz, 1H), 4.45 (d, *J*=15.6 Hz, 1H), 4.64 (d, *J*=15.6 Hz, 1H), 5.64 (d, *J*=14.4 Hz, 1H), 6.86 (d, *J*=14.4 Hz, 1H), 7.23–7.36 (m, 7H), 7.70 (d, *J*=8.1 Hz, 2H). Irradiation of proton at δ 5.64 ppm (C*H*=CH(N)) showed 20% NOE enhancement to the peak at δ 4.16 ppm (C*H*OH). Thus, the stereochemistry has been confirmed. ^{13}C NMR δ 13.74, 13.91, 13.97, 21.42, 22.56, 22.98, 23.37, 25.92, 28.13, 29.03, 29.18, 29.45, 29.54, 31.43, 31.80, 33.04, 35.87, 49.61, 71.95, 111.28, 125.53, 126.92, 127.04, 127.57, 128.73, 129.81, 129.94, 132.11, 135.77, 138.68, 143.97; IR (neat) 3303 (OH), 3089, 3065, 3032, 2956, 2927, 2871, 2857, 1598, 1496, 1456, 1402, 1339, 1306, 1290, 1239, 1163, 1120, 1092, 1060, 926, 814, 738, 698, 663 cm^{-1}. Anal. Calcd for $C_{35}H_{53}NO_3S$: C, 74.03; H, 9.41. Found: C, 74.21; H, 9.16.

4.1.58. *N*-Benzyl-*N*-[(1*E*,3*E*)-5-hydroxy-3,4-diphenyl-1,3-tridecadienyl]-*p*-toluenesulfonamide (63). ^{1}H NMR δ 0.90 (t, *J*=6.9 Hz, 3H), 1.12–1.39 (m, 14H), 1.58 (br s, 1H, OH), 2.45 (s, 3H), 4.47 (d, *J*=15.6 Hz, 1H), 4.47 (br s, 1H), 4.74 (d, *J*=15.5 Hz, 1H), 6.06 (d, *J*=14.4 Hz, 1H), 6.46 (d, *J*=14.4 Hz, 1H), 6.85 (d/t, *J*=1.8, 7.8 Hz, 4H), 6.99–7.12 (m, 6H), 7.29–7.38 (m, 7H), 7.50 (d, *J*=8.4 Hz, 2H). Irradiation of proton at δ 6.06 ppm (C*H*=CH(N)) showed 26% NOE enhancement to the peak at δ 4.47 ppm (C*H*OH). Thus, the stereochemistry has been confirmed. ^{13}C NMR δ 14.00, 21.46, 22.56, 25.83, 29.17, 29.44 (2 peaks), 31.78, 36.37, 49.84, 71.26, 111.80, 126.26, 126.54, 126.92, 127.01, 127.38, 127.54, 127.75, 128.89, 129.91, 130.41, 130.60, 131.65, 135.65, 135.71, 136.98, 138.58, 139.50, 139.94, 144.10; IR (neat) 3553 (OH), 3077, 3056, 3028, 2926, 2855, 1625, 1598, 1490, 1456, 1441, 1399, 1362, 1318, 1289, 1268, 1212, 1186, 1167, 1119, 1091, 1073, 1038, 1029, 1018, 1009, 946, 911, 833, 813, 768, 736, 701, 666 cm^{-1}. Anal. Calcd for $C_{39}H_{45}NO_3S$: C, 77.06; H, 7.46. Found: C, 76.91; H, 7.54.

4.1.59. Typical procedure for Scheme 6. *N*-Benzyl-*N*-[(1*Z*,3*Z*)-3-butyl-1,4-diiodo-1,3-octadienyl]-*p*-toluenesulfonamide (64). To a stirred solution of 5-decyne (**50**) (0.022 mL, 0.120 mmol) and Ti(O–*i*-Pr)$_4$ (0.044 mL, 0.150 mmol) in 1 mL of Et_2O was added *i*-PrMgCl (1.46 M in Et_2O, 0.213 mL, 0.311 mmol) at −78 °C under argon to give a yellow homogeneous solution. The solution was warmed to −50 °C over 30 min, during which period its color turned black. After stirring at −50 °C for 2 h, pulverized *N*-benzyl-*N*-ethynyl-*p*-toluenesulfonamide (**52**) (27 mg, 0.096 mmol) was added in one portion and the mixture was stirred for 4 h at the same temperature. Then, iodine (91 mg, 0.359 mmol) in 1.0 mL of Et_2O was added. After 30 min, to the cold reaction mixture was added an aqueous solution of $Na_2S_2O_3$ (0.2 mL). The resulting heterogeneous solution was filtered through Celite with the aid of ether. The organic phase was concentrated in vacuo to give a crude oil, which was chromatographed on silica gel (hexane–ethyl acetate) to afford the title compound (42 mg, 65%) as a colorless oil. Its stereochemistry was assigned based on that of the protonated and deuterated products. ^{1}H NMR δ 0.86 (t, *J*=6.9 Hz, 3H), 0.88 (t, *J*=6.9 Hz, 3H), 1.13–1.50 (m, 8H), 2.15 (t, *J*=7.5 Hz, 2H), 2.44 (t, *J*=7.5 Hz, 2H), 2.46 (s, 3H), 4.44 (s, 2H), 6.47 (s, 1H), 7.23–7.41 (m, 7H), 7.79 (d, *J*=8.1 Hz, 2H); ^{13}C NMR δ 13.68, 13.81, 21.53, 22.52, 30.00, 31.45, 33.13, 39.99, 54.11, 102.69, 107.28, 128.08, 128.71 (2 peaks), 129.59, 129.70, 134.84, 134.94, 142.58, 144.45, 149.24; IR (neat) 3087, 3064, 3031, 2956, 2927, 2870, 2858, 1598, 1495, 1456, 1359, 1305, 1291, 1259, 1216, 1185, 1168, 1140, 1091, 1041, 946, 838, 813, 774, 742, 697, 662 cm^{-1}. Anal. Calcd for $C_{26}H_{33}I_2NO_2S$: C, 46.10; H, 4.91. Found: C, 46.38; H, 5.24.

4.1.60. Typical procedure for Scheme 7. *N*-(1,6-Tridecadiyn-1-yl)-3-methyl-1,2-benzisothiazoline 1,1-dioxide (67). To a heterogeneous mixture of 3-methyl-1,2-benzisothiazoline 1,1-dioxide (**1**) (293 mg, 1.60 mmol), powdered K_3PO_4 (679 mg, 3.20 mmol), and CuI (15.2 mg, 0.080 mmol) in 4 mL of toluene was added 1-bromo-1,6-tridecadiyne (**65**) (408 mg, 1.60 mmol) in 12 mL of toluene, followed by *N*,*N*′-dimethylethylenediamine (0.040 mL) under argon. The mixture was stirred overnight in an oil bath maintained at 110 °C. The reaction mixture was cooled to room temperature and was filtered through a short pad of silica gel with the aid of ethyl acetate. The combined filtrates were concentrated in vacuo to give a crude oil, which was chromatographed on silica gel (hexane–ethyl acetate) to give the title compound (455 mg, 79%) as an oil. ^{1}H NMR δ 0.89 (t, J=6.9 Hz, 3H), 1.26–1.54 (m, 8H), 1.67 (d, J=6.6 Hz, 3H), 1.76 (quintet, J=6.9 Hz, 2H), 2.15 (t/t, J=6.9, 2.4 Hz, 2H), 2.30 (t/t, J=6.9 Hz, 2.4 Hz, 2H), 2.51 (t, J=6.9 Hz, 2H), 4.79 (q, J=6.6 Hz, 1H), 7.40 (d, J=7.5 Hz, 1H), 7.57 (t, J=7.5 Hz, 1H), 7.68 (t, J=7.5 Hz, 1H), 7.83 (d, J=7.5 Hz, 1H); ^{13}C NMR δ 13.39, 17.84, 17.93, 18.65, 19.15, 22.46, 28.38, 28.47, 28.98, 31.28, 59.05, 67.45, 73.61, 78.94, 81.11, 121.81, 123.91, 129.62, 132.86, 133.62, 137.41; IR (neat) 3074, 3025, 2863, 2241, 1453, 1328, 1178, 1091, 928, 736, 699 cm^{-1}. Anal. Calcd for $C_{21}H_{27}NO_2S$: C, 70.55; H, 7.61. Found: C, 70.42; H, 7.48.

4.1.61. *N*-[7-(Trimethylsilyl)-1,6-tridecadiyn-1-yl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (68). ^{1}H NMR δ 0.15 (s, 9H), 1.67 (d, J=6.6 Hz, 3H), 1.79 (quintet, J=7.2 Hz, 2H), 2.37 (t, J=7.2 Hz, 2H), 2.51 (t, J=7.2 Hz, 2H), 4.79 (q, J=6.6 Hz, 1H), 7.40 (d, J=7.5 Hz, 1H), 7.57 (t, J=7.5 Hz, 1H), 7.68 (t, J=7.5 Hz, 1H), 7.82 (d, J=7.5 Hz, 1H); ^{13}C NMR δ −0.02, 17.81, 18.95, 19.15, 27.82, 59.03, 67.64, 73.33, 85.20, 106.28, 121.78, 123.93, 129.62, 132.79, 133.65, 137.36; IR (Nujol) 2923, 2854, 2731, 2266, 2184, 1457, 1376, 1303, 1180, 1033, 848, 763, 715 cm^{-1}. Anal. Calcd for $C_{18}H_{23}NO_2SSi$: C, 62.57; H, 6.71. Found: C, 62.40; H, 6.49. Mp 88–90 °C.

4.1.62. Typical procedure for Scheme 7. *N*-[(*E*)-((*E*)-2-Heptylidene-1-cyclopentylidene)methyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (69). To a stirred solution of *N*-(1,6-tridecadiyn-1-yl)-3-methyl-1,2-benzisothiazoline 1,1-dioxide (**67**) (38 mg, 0.106 mmol) and Ti(O–*i*-Pr)$_4$ (0.063 mL, 0.212 mmol) in 1.1 mL of Et_2O was added *i*-PrMgCl (1.50 M in Et_2O, 0.283 mL, 0.424 mmol) at −78 °C under argon to give a yellow homogeneous solution. The solution was warmed to −50 °C over 30 min, during which period its color turned red. After stirring at −50 °C for 3 h, the reaction was terminated by the addition of H_2O (0.11 mL) and the heterogeneous mixture was filtered through Celite with the aid of ether. The organic phase was concentrated in vacuo to give a crude oil. Careful analysis of the crude product by ^{1}H NMR spectroscopy did not show the presence of any isomeric products. The crude product was chromatographed on silica gel (hexane–ethyl acetate) to afford the title compound (37 mg, 99%) as a colorless oil. ^{1}H NMR δ 0.88 (t, J=6.9 Hz, 3H), 1.20–1.46 (m, 8H), 1.52 (d, J=6.6 Hz, 3H), 1.57–1.86 (m, 2H), 2.04–2.13 (m, 2H), 2.34–2.44 (m, 2H), 2.56–2.69 (m, 2H), 4.59 (q, J=6.6 Hz, 1H), 5.93–6.00 (m, 1H), 6.07 (t, J=1.8 Hz, 1H), 7.40 (d, J=7.5 Hz, 1H), 7.53 (t, J=7.5 Hz, 1H), 7.63 (t, J=7.5 Hz, 1H), 7.80 (d, J=7.5 Hz, 1H); ^{13}C NMR δ 14.09, 19.23, 22.61, 23.71, 29.12, 29.24, 29.79, 29.86, 31.58, 31.75, 58.73, 108.83, 121.44, 122.43, 123.60, 129.07, 132.91, 134.48, 138.75, 138.87, 148.30; IR (neat) 2976, 2927, 2862, 2837, 1660, 1455, 1308, 1262, 1172, 1132, 761 cm^{-1}. Anal. Calcd for $C_{21}H_{29}NO_2S$: C, 70.15; H, 8.13. Found: C, 69.91; H, 8.10.

4.1.63. *N*-[(*E*)-[(*E*)-2-(Trimethylsilyl)methylidene-1-cyclopentylidene]methyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (70). ^{1}H NMR δ 0.14 (s, 9H), 1.53 (d, J=6.6 Hz, 3H), 1.60–1.75 (m, 1H), 1.75–1.96 (m, 1H), 2.45–2.53 (m, 2H), 2.63–2.68 (m, 2H), 4.69 (q, J=6.6 Hz, 1H), 6.02 (t, J=2.1 Hz, 1H), 6.27 (t, J=2.1 Hz, 1H), 7.41 (d, J=7.5 Hz, 1H), 7.54 (t, J=7.5 Hz, 1H), 7.64 (t, J=7.5 Hz, 1H), 7.81 (d, J=7.5 Hz, 1H). NOESY experiments showed the correlation between the peaks at δ 4.69 ppm (NCH) and at δ 6.02 ppm (vinylic H), and that between the peaks at δ 6.02 ppm (vinylic H) and at δ 6.27 ppm (vinylic H). Thus, the stereochemistry of the olefinic bond has been confirmed. ^{13}C NMR δ −0.57, 19.57, 24.04, 30.78, 33.44, 58.72, 112.44, 118.33, 121.55, 123.73, 129.26, 133.12, 134.42, 138.88, 145.69, 155.48; IR (Nujol) 2952, 2924, 2854, 1653, 1457, 1376, 1303, 1172, 1134, 879, 836, 757 cm^{-1}. Anal. Calcd for $C_{18}H_{25}NO_2SSi$: C, 62.21; H, 7.25. Found: C, 61.96; H, 7.11.

4.1.64. Typical procedure for Scheme 8. *N*-[4,4-Bis(benzyloxymethyl)-6-hepten-1-yn-1-yl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (73). To a heterogeneous mixture of 3-methyl-1,2-benzisothiazoline 1,1-dioxide (**1**) (293 mg, 1.60 mmol), powdered K_3PO_4 (679 mg, 3.20 mmol), and CuI (15.2 mg, 0.080 mmol) in 4 mL of toluene was added 4,4-bis(benzyloxymethyl)-1-bromo-6-hepten-1-yne (**71**) (617 mg, 1.60 mmol) in 12 mL of toluene, followed by *N*,*N*′-dimethylethylenediamine (0.040 mL) under argon. The mixture was stirred overnight in an oil bath maintained at 110 °C. The reaction mixture was cooled to room temperature and was filtered through a short pad of silica gel with the aid of ethyl acetate. The combined filtrates were concentrated in vacuo to give a crude oil, which was chromatographed on silica gel (hexane–ethyl acetate) to give the title compound (515 mg, 63%) as an oil. ^{1}H NMR δ 1.60 (d, J=6.6 Hz, 3H), 2.28 (d, J=7.2 Hz, 2H), 2.49 (s, 2H), 3.44 (s, 4H), 4.52 (s, 4H), 4.72 (q, J=6.6 Hz, 1H), 5.06 (d, J=9.9 Hz, 1H), 5.12 (d, J=17.1 Hz, 1H), 5.76–5.89 (m, 1H), 7.25–7.33 (m, 10H), 7.39 (d, J=7.8 Hz, 1H), 7.57 (t, J=7.8 Hz, 1H), 7.68 (t, J=7.8 Hz, 1H), 7.83 (d, J=7.8 Hz, 1H); ^{13}C NMR δ 19.20, 22.49, 36.43, 42.45, 59.00, 71.32, 72.05 (2 peaks), 73.34 (2 peaks), 77.21, 118.24, 121.79, 123.91, 123.91, 127.41, 127.54, 128.33, 129.62, 132.96, 133.60, 133.97, 137.41, 138.97; IR (neat) 3058, 3025, 2968, 2919, 2258, 1453, 1325, 1270, 1179, 1107, 1025, 911, 797, 736, 715 cm^{-1}. Anal. Calcd for $C_{31}H_{33}NO_4S$: C, 72.20; H, 6.45. Found: C, 72.01; H, 6.57.

4.1.65. *N*-Benzyl-*N*-[4,4-bis(benzyloxymethyl)-6-hepten-1-yn-1-yl]-*p*-toluenesulfonamide (72). ^{1}H NMR δ 1.99 (d, J=7.5 Hz, 2H), 2.24 (s, 2H), 2.41 (s, 3H), 3.20 (s, 4H), 4.38 (s, 4H), 4.43 (s, 2H), 4.86–4.90 (m, 2H), 5.55–5.72 (m, 1H), 7.22–7.30 (m, 17H), 7.72 (d, J=8.4 Hz, 2H); ^{13}C NMR δ 21.46, 21.98, 35.96, 42.29, 55.26, 67.64, 71.64 (2 peaks),

73.02 (2 peaks), 74.73, 117.83, 127.14, 127.21, 127.52, 128.00, 128.12, 128.36, 128.46, 129.52, 133.73, 134.65, 134.71, 138.71, 144.21; IR (neat) 3041, 2919, 2860, 2250, 1496, 1453, 1364, 1169, 1092, 1034, 928, 854, 813, 756, 698 cm^{-1}. Anal. Calcd for $C_{37}H_{39}NO_4S$: C, 74.84; H, 6.62. Found: C, 74.83; H, 6.51.

4.1.66. *N*-[4,4-Bis(benzyloxymethyl)-6-hepten-1-yn-1-yl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide (74). ^1H NMR δ 1.10 (s, 9H), 2.28 (d, $J=7.5$ Hz, 2H), 2.47 (s, 2H), 3.44 (s, 4H), 4.39 (s, 1H), 4.53 (s, 4H), 5.07 (d, $J=9.9$ Hz, 1H), 5.13 (d, $J=17.4$ Hz, 1H), 5.75–5.89 (m, 1H), 7.25–7.34 (m, 10H), 7.47 (d, $J=7.5$ Hz, 1H), 7.54–7.65 (m, 2H), 7.82 (d, $J=6.6$ Hz, 1H); ^{13}C NMR δ 22.36, 26.77 (*t*-Bu), 36.30, 38.16, 42.50, 69.45, 71.98 (2 peaks), 72.92, 73.22 (2 peaks), 75.19, 118.11, 121.89, 125.79, 127.34, 127.45 (2 peaks), 128.27, 129.53, 132.54, 134.03, 135.57, 138.95; IR (neat) 3082, 3025, 2960, 2919, 2862, 2250, 1466, 1328, 1254, 1181, 1115, 1091, 936, 736, 707 cm^{-1}. Anal. Calcd for $C_{34}H_{39}NO_4S$: C, 73.22; H, 7.05. Found: C, 73.09; H, 6.87.

4.1.67. (*R*)-*N*-(*p*-Toluenesulfonyl)-*N*-[4,4-bis(benzyloxymethyl)-6-hepten-1-yn-1-yl]-*N*-(2-methoxy-1-phenylethyl)amine (75). ^1H NMR δ 1.99 (d, $J=7.8$ Hz, 2H), 2.35 (s, 3H), 2.38 (s, 2H), 3.22 (s, 3H), 3.33 (s, 4H), 3.60 (d/d, $J=4.8$, 9.9 Hz, 1H), 3.80 (t, $J=9.9$ Hz, 1H), 4.44 (s, 4H), 5.01 (m, 2H), 5.21 (d/d, $J=4.8$, 9.9 Hz, 1H), 5.73 (m, 1H), 7.11 (d, $J=8.4$ Hz, 2H), 7.22–7.34 (m, 15H), 7.64 (d, $J=8.4$ Hz, 2H); ^{13}C NMR δ 21.44, 22.34, 36.20, 42.54, 58.65, 61.58, 70.04, 72.02 (2 peaks), 72.30, 72.39, 73.24 (2 peaks), 118.05, 127.36, 127.39, 127.44, 128.00, 128.27, 128.35, 128.54, 129.16, 134.00, 135.76, 136.72, 138.91, 143.91; IR (neat) 3066, 3025, 2927, 2861, 2258, 1597, 1491, 1453, 1363, 1181, 1092, 1034, 958, 928, 813, 748, 701 cm^{-1}. Anal. Calcd for $C_{39}H_{43}NO_5S$: C, 73.44; H, 6.80. Found: C, 73.18; H, 6.57; $[\alpha]_D^{28}$ +51.2 (*c* 3.36, $CHCl_3$).

4.1.68. (1*S*,2*S*)-*N*-[4,4-Bis(benzyloxymethyl)-6-hepten-1-yn-yl]-2,10-camphorsultam (76). ^1H NMR δ 0.99 (s, 3H), 1.09 (s, 3H), 1.28–1.31 (m, 1H), 1.38–1.44 (m, 1H), 1.64 (d/d, $J=5.1$, 8.1 Hz, 1H), 1.85–1.92 (m, 3H), 2.05–2.15 (m, 1H), 2.24 (d, $J=7.5$ Hz, 2H), 2.40 (s, 2H), 3.21 (s, 2H), 3.41 (s, 4H), 3.46 (t, $J=7.8$ Hz, 1H), 4.51 (s, 4H), 5.05 (d, $J=10.4$ Hz, 1H), 5.10 (d, $J=17.4$ Hz, 1H), 5.72–5.86 (m, 1H), 7.24–7.36 (m, 10H); ^{13}C NMR δ 19.79, 20.04, 22.24, 26.87, 31.44, 34.28, 36.30, 42.31, 44.27, 47.78, 49.44, 50.80, 67.04, 69.28, 69.37, 71.99 (2 peaks), 73.25 (2 peaks), 118.11, 127.35, 127.43, 128.28, 133.96, 138.94; IR (neat) 3066, 2959, 2895, 2854, 2250, 1638, 1453, 1338, 1320, 1270, 1140, 1095, 919, 737, 699 cm^{-1}. Anal. Calcd for $C_{33}H_{41}NO_4S$: C, 72.36; H, 7.54. Found: C, 72.51; H, 7.59; $[\alpha]_D^{28}$ +8.3 (*c* 0.936, $CHCl_3$).

4.1.69. Typical procedure for Scheme 9. *N*-[[(*E*)-4,4-Bis(benzyloxymethyl)-2-methyl-1-cyclopentylidene]-methyl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide as a 1:1 mixture of diastereoisomers (78). To a stirred solution of *N*-[4,4-bis(benzyloxymethyl)-6-hepten-1-yn-1-yl]-3-methyl-1,2-benzisothiazoline 1,1-dioxide (**73**) (47 mg, 0.097 mmol) and Ti(O–*i*-Pr)$_4$ (0.057 mL, 0.193 mmol) in 1.0 mL of Et_2O was added *i*-PrMgCl (1.50 M in Et_2O, 0.257 mL, 0.386 mmol) at −78 °C under argon to give a yellow homogeneous solution. The solution was warmed to −50 °C over 30 min, during which period its color turned red. After stirring at −50 °C for 3 h, the reaction was terminated by the addition of H_2O (0.10 mL) and the heterogeneous mixture was filtered through Celite with the aid of ether. The organic phase was concentrated in vacuo to give a crude oil, ^1H NMR analysis of which showed the diastereoselectivity to be 1:1. The crude product was chromatographed on silica gel (hexane–ethyl acetate) to afford the title compound (53 mg, 87%) as a colorless oil. ^1H NMR δ 1.15–1.21 (m, 4H), 1.43 (d, $J=6.6$ Hz, 1.5H) 1.45 (d, $J=6.6$ Hz, 1.5H), 2.04 (d/d, $J=10.2$, 13.8 Hz, 1H), 2.58 (br s, 2H), 2.77 (m, 1H), 3.35–3.43 (m, 4H), 4.46–4.51 (m, 5H), 5.55 (q, $J=2.4$ Hz, 0.5H), 5.64 (q, $J=2.4$ Hz, 0.5H), 7.26–7.33 (m, 10H), 7.37 (d, $J=7.5$ Hz, 1H), 7.52 (t, $J=7.5$ Hz, 1H), 7.62 (t, $J=7.5$ Hz, 1H), 7.80 (d, $J=7.5$ Hz, 1H). Irradiation of proton at δ 5.55–5.64 ppm (vinylic H) showed 3% NOE enhancement to the peak at δ 2.77 ppm (C=CC*H*Me). Irradiation of proton at δ 2.77 ppm (C=CC*H*Me) showed 3% NOE enhancement to the peak at δ 5.55–5.64 ppm (vinylic H). Thus, the stereochemistry has been confirmed. ^{13}C NMR δ 17.74, 18.55, 18.64, 19.87, 36.21, 36.74, 39.95, 40.36, 45.71, 46.25, 58.17, 58.33, 72.84, 73.22, 73.38, 74.65, 74.82, 77.21, 111.52, 111.99, 121.51, 123.63, 123.67, 127.41, 127.49, 127.52, 127.55, 128.28, 128.32, 128.35, 129.10, 132.89, 132.95, 134.72, 138.90, 139.16, 157.28, 157.84. (Peaks of diastereoisomers may be overlapping.) IR (neat) 3025, 2960, 2927, 2856, 1496, 1453, 1363, 1304, 1279, 1172, 1148, 1099, 1034, 910, 735, 699 cm^{-1} for a 1:1 mixture of diastereoisomers. Anal. Calcd for $C_{31}H_{35}NO_4S$: C, 71.92; H, 6.81. Found: C, 71.64; H, 6.56 for a 1:1 mixture of diastereoisomers.

4.1.70. *N*-Benzyl-*N*-[[(*E*)-4,4-bis(benzyloxymethyl)-2-methyl-1-cyclopentylidene]methyl]-*p*-toluenesulfonamide (77). ^1H NMR δ 0.96 (d, $J=6.0$ Hz, 3H), 1.22–1.36 (m, 1H), 1.82–1.92 (m, 1H), 2.18 (s, 2H), 2.44 (s, 3H), 2.40–2.54 (m, 1H), 2.99–3.14 (m, 4H), 4.18 (d, $J=3.9$ Hz, 2H), 4.32–4.50 (m, 4H), 4.97–5.05 (m, 1H), 7.16–7.40 (m, 17H), 7.70 (d, $J=8.1$ Hz, 2H); ^{13}C NMR δ 19.19, 21.51, 35.50, 37.00, 39.67, 45.73, 54.44, 72.48, 73.03 (2 peaks), 74.46, 117.36, 127.25, 127.50, 128.18, 129.05, 129.50, 135.20, 136.09, 138.89, 143.27, 155.85. Peaks of aromatic carbons may be overlapping. IR (neat) 3029, 2968, 2927, 2855, 1598, 1496, 1453, 1355, 1165, 1099, 815, 739, 697 cm^{-1}. Anal. Calcd for $C_{37}H_{41}NO_4S$: C, 74.59; H, 6.94. Found: C, 74.75; H, 6.93.

4.1.71. *N*-[[(*E*)-4,4-Bis(benzyloxymethyl)-2-methyl-1-cyclopentylidene]methyl]-3-(*tert*-butyl)-1,2-benzisothiazoline 1,1-dioxide as a 1:1 mixture of diastereoisomers (79). ^1H NMR δ 1.04 (s, 9H), 1.08 (d, $J=6.6$ Hz, 1.5H) 1.15 (d, $J=6.6$ Hz, 1.5H), 1,25–1,29 (m, 1H), 1.97–2.08 (m, 1H), 2.51–2.63 (m, 1H), 2.65–2.85 (m, 2H), 3.29–3.59 (m, 4H), 4.12 (s, 0.5H), 4.17 (s, 0.5H), 4.42–4.62 (m, 4H), 5.31 (d, $J=1.8$ Hz, 0.5H), 5.44 (d, $J=1.8$ Hz, 0.5H), 7.24–7.36 (m, 10H), 7.43–7.58 (m, 3H), 7.76–7.82 (m, 1H). ^{13}C NMR δ 17.10, 21.95, 27.13, 29.66, 35.82, 35.86, 37.00, 37.11, 38.06, 38.24, 39.69, 40.53, 45.98, 47.33, 72.19, 73.08, 73.19, 73.75, 7452, 74.79, 75.13, 75.38, 119.13, 120.45, 121.62, 121.65, 125.51, 127.20, 127.26, 127.41, 127.45, 128.15, 128.21, 128.94, 128.97, 131.75, 131.79, 136.19, 136.88, 136.97, 138.83, 147.25, 148.35. (Peaks of

diastereoisomers may be overlapping.) IR (neat) 3025, 2956, 2919, 2862, 1453, 1313, 1262, 1178, 1099, 919, 736, 699 cm^{-1} for a 1:1 mixture of diastereoisomers. Anal. Calcd for $C_{34}H_{41}NO_4S$: C, 72.95; H, 7.38. Found: C, 72.86; H, 7.59 for a 1:1 mixture of diastereoisomers.

4.1.72. (*R*)-*N*-(*p*-Toluenesulfonyl)-*N*-[[(*E*)-4,4-bis(benzyloxymethyl)-2-methyl-1-cyclopentylidene]methyl]-(2-methoxy-1-phenylethyl)amine as a 1:1 mixture of diastereoisomers (80). ^{1}H NMR δ 0.96–1.06 (m, 3H), 1.22–1.37 (m, 1H), 1.70–2.03 (m, 1H), 2.22 (d, J=15.6 Hz, 1H), 2.28 (d/d, J=15.6 Hz, 1H), 2.37 (s, 3H), 2.50–2.67 (m, 1H), 3.00–3.27 (m, 7H), 3.57–3.74 (m, 2H), 4.36–4.51 (m, 4H), 5.04 (q, J=2.1 Hz, 0.5H), 5.11 (q, J=2.1 Hz, 0.5H), 5.26–5.34 (m, 1H), 7.08–7.38 (m, 17H), 7.65 (d, J=8.1 Hz, 2H); ^{13}C NMR δ 19.02, 19.42, 19.49, 21.40, 35.89, 36.02, 36.58, 36.76, 39.63, 40.18, 45.73, 45.77, 58.48, 60.78, 60.86, 71.05, 71.26, 72.58, 73.02, 73.07, 73.14, 74.61, 74.74, 113.32, 113.69, 127.22, 127.27, 127.31, 127.75, 127.92, 128.10, 128.14, 128.19, 128.60, 126.63, 128.99, 129.02, 136.15, 136.47, 137.33, 137.39, 138.79, 138.85, 138.90, 142.73, 142.78, 159.51, 159.98. (Peaks of diastereoisomers may be overlapping.) IR (neat) 3031, 2952, 2927, 2858, 1598, 1496, 1453, 1345, 1197, 1159, 1096, 1028, 1001, 813, 777, 738, 698, 661 cm^{-1} for a 1:1 mixture of diastereoisomers. Anal. Calcd for $C_{39}H_{45}NO_5S$: C, 73.21; H, 7.09. Found: C, 73.02; H, 6.86 for a 1:1 mixture of diastereoisomers.

4.1.73. (1*S*,2*S*)-*N*-[[(*E*)-4,4-Bis(benzyloxymethyl)-2-methyl-1-cyclopentylidene]methyl]-2,10-camphorsultam as a 1:1 mixture of diastereoisomers (81). ^{1}H NMR δ 0.92 (s, 3H), 1.07–1.19 (m, 8H), 1.42–1.60 (m, 2H), 1.78–2.05 (m, 5H), 2.54 (s, 2H), 2.58–2.72 (m, 1H), 3.15 (d, J= 1.8 Hz, 2H), 3.16–3.25 (m, 1H), 3.28–3.41 (m, 4H), 4.49 (s, 2H), 4.50 (s, 2H), 5.11 (q, J=2.1 Hz, 0.5H), 5.19 (q, J= 2.1 Hz, 0.5H), 7.22–7.38 (m, 10H); ^{13}C NMR δ 17.70, 20.05, 20.15, 20.50, 27.06, 32.10, 35.04, 35.17, 36.03, 36.22, 36.37, 36.61, 39.77, 40.61, 44.49, 45.59, 46.19, 47,61, 49.48, 49.85, 49.87, 67.73, 67.78, 72.77, 73.09, 73.12, 73.17, 73.34, 74.46, 74.83, 112.53, 113.34, 127.27, 127.41, 128.17, 138.76, 138.84, 155.41, 155.73. (Peaks of diastereoisomers may be overlapping.) IR (neat) 3033, 2955, 2870, 1453, 1319, 1254, 1197, 1135, 1115, 1034, 816, 737, 698 cm^{-1} for a 1:1 mixture of diastereoisomers. Anal. Calcd for $C_{33}H_{43}NO_4S$: C, 72.10; H, 7.88. Found: C, 72.23; H, 7.98 for a 1:1 mixture of diastereoisomers.

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References and notes

1. Trost, B. M., Fleming, I., Eds.; Comprehensive Organic Synthesis; Pergamon Press: Oxford, 1991; Vols. 1–7. For applications of (1-alkynyl)amine derivatives in these reactions, see: Witulski, B.; Stengel, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 2426–2430. Rainier, J. D.; Imbriglio, J. E. *J. Org. Chem.* **2000**, *65*, 7272–7276. Witulski, B.; Gößmann, M. *Synlett* **2000**, 1793–1797. Witulski, B.; Alayrac, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 3281–3284. Saito, N.; Sato, Y.; Mori, M. *Org. Lett.* **2002**, *4*, 803–805. Huang, J.; Xiong, H.; Hsung, R. P.; Rameshkumar, C.; Mulder, J. A.; Grebe, T. P. *Org. Lett.* **2002**, *4*, 2417–2420. Shen, L.; Hsung, R. P. *Tetrahedron Lett.* **2003**, *44*, 9353–9358. Marion, F.; Coulomb, J.; Courillon, C.; Fensterbank, L.; Malacria, M. *Org. Lett.* **2004**, *6*, 1509–1511. Riddell, N.; Villeneuve, K.; Tam, W. *Org. Lett.* **2005**, *7*, 3681–3684.
2. *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: Weinheim, 2002.
3. Negishi, E.; Takahashi, T. *Acc. Chem. Res.* **1994**, *27*, 124–130. Negishi, E. In Trost, B. M., Fleming, I., Eds.; Comprehensive Organic Synthesis; Pergamon Press: Oxford, 1991; Vol. 5, pp 1163–1184. Buchwald, S. L.; Nielsen, R. B. *Chem. Rev.* **1988**, *88*, 1047–1058.
4. (a) Sato, F.; Urabe, H. In *Titanium and Zirconium in Organic Synthesis*; Marek, I., Ed.; Wiley-VCH: Weinheim, 2002; pp 319–354. (b) Sato, F.; Okamoto, S. *Adv. Synth. Catal.* **2001**, *343*, 759–784. (c) Sato, F.; Urabe, H.; Okamoto, S. *Chem. Rev.* **2000**, *100*, 2835–2886. (d) Eisch, J. J. *J. Organomet. Chem.* **2001**, *617–618*, 148–157. (e) Kulinkovich, O. G.; de Meijere, A. *Chem. Rev.* **2000**, *100*, 2789–2834.
5. Acetylenic esters and amides: Urabe, H.; Suzuki, K.; Sato, F. *J. Am. Chem. Soc.* **1997**, *119*, 10014–10027. Urabe, H.; Nakajima, R.; Sato, F. *Org. Lett.* **2000**, *2*, 3481–3484. Chloroacetylene: Averbuj, C.; Kaftanov, J.; Marek, I. *Synlett* **1999**, 1939–1941. Alkoxyacetylene: Nugent, W. A.; Thorn, D. L.; Harlow, R. L. *J. Am. Chem. Soc.* **1987**, *109*, 2788–2796. Sulfur-functionalized acetylenes: Van Wagenen, B. C.; Livinghouse, T. *Tetrahedron Lett.* **1989**, *30*, 3495–3498. Pagenkopf, B. L.; Lund, E. C.; Livinghouse, T. *Tetrahedron* **1995**, *51*, 4421–4438. Kemp, M. I.; Whitby, R. J.; Coote, S. J. *Synthesis* **1998**, 557–568. Suzuki, D.; Urabe, H.; Sato, F. *J. Am. Chem. Soc.* **2001**, *123*, 7925–7926. Suzuki, D.; Nobe, Y.; Watai, Y.; Tanaka, R.; Takayama, Y.; Sato, F.; Urabe, H. *J. Am. Chem. Soc.* **2005**, *127*, 7474–7479. Phosphorus-functionalized acetylene: Quntar, A. A. A.; Baum, O.; Shibli, A.; Dembitsky, V. M.; Srebnik, M. *Angew. Chem., Int. Ed.* **2003**, *42*, 4777–4779.
6. Portions of this work were already communicated. (a) Tanaka, R.; Hirano, S.; Urabe, H.; Sato, F. *Org. Lett.* **2003**, *5*, 67–70. (b) Hirano, S.; Tanaka, R.; Urabe, H.; Sato, F. *Org. Lett.* **2004**, *6*, 727–729.
7. Tanaka, R.; Yuza, A.; Watai, Y.; Suzuki, D.; Takayama, Y.; Sato, F.; Urabe, H. *J. Am. Chem. Soc.* **2005**, *127*, 7774–7780.
8. For a review on (1-alkynyl)amine derivatives, see: Katritzky, A. R.; Jiang, R.; Singh, S. K. *Heterocycles* **2004**, *63*, 1455–1475. Zificsak, C A.; Mulder, J. A.; Hsung, R. P.; Rameshkumar, C.; Wei, L.-L. *Tetrahedron* **2001**, *57*, 7575–7606. Himbert, G In Kropf, H., Schaumann, E., Eds. 4th ed.; Houben-Weyl Methods of Organic Chemistry; Thieme: Stuttgart, 1993; Vol. E15/3, pp 3267–3443.Collard-Motte, J; Janousek, Z. *Top. Curr. Chem.* **1986**, *130*, 89–131.
9. Witulski, B; Stengel, T. *Angew. Chem., Int. Ed.* **1998**, *37*, 489–492. Murch, P.; Williamson, B. L.; Stang, P. J. *Synthesis* **1994**, 1255–1256. Witulski, B.; Gößmann, M. *Chem. Commun.* **1999**, 1879–1880. Witulski, B.; Lumtscher, J.; Bergsträßer, U. *Synlett* **2003**, 708–710.

10. Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805–818. Hartwig, J. F. *Acc. Chem. Res.* **1998**, *31*, 852–860. Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046–2067. Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125–146. Prim, D.; Campagne, J.-M.; Joseph, D.; Andrioletti, B. *Tetrahedron* **2002**, *58*, 2041–2075.
11. (a) Klapars, A.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 7421–7428. During the course of our study that was communicated as Ref. 6b, the following report appeared: (b) Frederick, M. O.; Mulder, J. A.; Tracey, M. R.; Hsung, R. P.; Huang, J.; Kurtz, K. C. M.; Shen, L.; Douglas, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 2368–2369. However, this paper described that the sulfonamides and sultams are sluggish substrates toward the alkynylation. Furthermore, after the completion of the preparation of our communication (Ref. 6b), alkynylation of a couple of sulfonamides in the presence of a stoichiometric amount of a copper salt was reported: (c) Dunetz, J. R.; Danheiser, R. L. *Org. Lett.* **2003**, *5*, 4011–4014.
12. For review, see: Liu, Z.; Takeuchi, Y. *Heterocycles* **2002**, *56*, 693–709. Optically active benzosultams are readily prepared according to this literature.
13. For review, see: Oppolzer, W. *Pure Appl. Chem.* **1990**, *62*, 1241–1250. Kim, B. H.; Curran, D. P. *Tetrahedron* **1993**, *49*, 293–318.
14. Stereoselective preparation of tri-substituted enamides of the type **29**–**42**, which have two different β-alkyl (and -silyl) substituents, appears quite difficult. To the contrary, tri-substituted enamides having the same two β-substituents have been reported. Meuzelaar, G. J.; van Vliet, M. C. A.; Neeleman, E.; Maat, L.; Sheldon, R. A. *Liebigs Ann. Recl.* **1997**, 1159–1163. Murai, T.; Kasai, Y.; Ishihara, H.; Kato, S. *J. Org. Chem.* **1992**, *57*, 5542–5545. Shono, T.; Matsumura, Y.; Tsubata, K.; Sugihara, Y.; Yamane, S.; Kanazawa, T.; Aoki, T. *J. Am. Chem. Soc.* **1982**, *104*, 6697–6703. Stille, J. K.; Becker, Y. *J. Org. Chem.* **1980**, *45*, 2139–2145.
15. In addition, hydrolysis of the acetylene–titanium complexes **26** afforded (*Z*)-disubstituted enamides. For details, see Ref. 6a. For recent reports on the preparation of (*E*)- or (*Z*)-disubstituted enamides, see: Trost, B. M.; Surivet, J.-P. *Angew. Chem., Int. Ed.* **2001**, *40*, 1468–1471. Fürstner, A.; Brehm, C.; Cancho-Grande, Y. *Org. Lett.* **2001**, *3*, 3955–3957. Krompiec, S.; Pigulla, M.; Szczepankiewicz, W.; Bieg, T.; Kuznik, N.; Leszczynska-Sejda, K.; Kubicki, M.; Borowiak, T. *Tetrahedron Lett.* **2001**, *42*, 7095–7098. Miniere, S.; Cintrat, J.-C. *Synthesis* **2001**, 705–707. Snider, B. B.; Song, F. *Org. Lett.* **2000**, *2*, 407–408. Witulski, B.; Buschmann, N.; Bergsträßer, U. *Tetrahedron* **2000**, *56*, 8473–8480. Alonso, D. A.; Alonso, E.; Nájera, C.; Yus, M. *Synlett* **1997**, 491–492. Kondo, T.; Tanaka, A.; Kotachi, S.; Watanabe, Y. *J. Chem. Soc., Chem. Commun.* **1995**, 413–414. Ogawa, T.; Kiji, T.; Hayami, K.; Suzuki, H. *Chem. Lett.* **1991**, 1443–1446. Hudrlik, P. F.; Hudrlik, A. M.; Rona, R. J.; Misra, R. N.; Withers, G. P. *J. Am. Chem. Soc.* **1977**, *99*, 1993–1996.
16. Mitchell, H. J.; Nelson, A.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1899–1914. Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307–1370.
17. For synthetic application of organotitanium compounds, see: Reetz, M. T. *Organotitanium Reagents in Organic Synthesis*; Springer: Berlin, 1986. Ferreri, C.; Palumbo, G.; Caputo, R. In Trost, B. M., Fleming, I., Eds.; Comprehensive Organic Synthesis; Pergamon Press: Oxford, 1991; Vol. 1, pp 139–172. Reetz, M. T. In *Organometallics in Synthesis*; Schlosser, M., Ed.; Wiley: Chichester, 1994; pp 195–282.
18. Chiral enones are a promising substrate for asymmetric conjugate addition. Alexakis, A. In *Organocopper Reagents A Practical Approach*; Taylor, R. J. K., Ed.; Oxford University Press: Oxford, 1994; pp 159–173.
19. The most likely conformation in $CDCl_3$ was suggested by NOE study of ^1H NMR. See Ref. 6b.
20. Fringuelli, F.; Taticchi, A. *Dienes in the Diels–Alder Reaction*; Wiley: New York, 1990.
21. Harada, K.; Urabe, H.; Sato, F. *Tetrahedron Lett.* **1995**, *36*, 3203–3206.
22. For other reported preparations of 1-amino-1,3-butadiene derivatives, see: Overman, L. E.; Clizbe, L. A. *J. Am. Chem. Soc.* **1976**, *98*, 2352–2354 see also 8295. Overman, L. E.; Taylor, G. F.; Petty, C. B.; Jessup, P. J. *J. Org. Chem.* **1978**, *43*, 2164–2167. Yli-Kauhaluoma, J. T.; Ashley, J. A.; Lo, C.-H.; Tucker, L.; Wolfe, M. M.; Janda, K. D. *J. Am. Chem. Soc.* **1995**, *117*, 7041–7047. Kozmin, S. A.; Rawal, V. H. *J. Am. Chem. Soc.* **1997**, *119*, 7165–7166. Huang, Y.; Iwama, T.; Rawal, V. H. *Org. Lett.* **2002**, *4*, 1163–1166 and references cited therein.
23. For our previous effort to make non-functionalized or electron-deficient dienes, see: Hamada, Y.; Suzuki, D.; Urabe, H.; Sato, F. *J. Am. Chem. Soc.* **1999**, *121*, 7342–7344.
24. For a recent reviews on enyne cyclization, see: Aubert, C.; Buisine, O.; Malacria, M. *Chem. Rev.* **2002**, *102*, 813–834.