Preparation of N-substituted sulfoximines by benzotriazole methodology

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Abstract
Diverse *N*-substituted sulfoximines **5a–n** were prepared by nucleophilic replacement of the benzotriazole moiety in *N*-(benzotriazol-1-ylalkyl)sulfoximines **3a–e** using organozinc reagents or allylsilanes. *N*-(Benzotriazol-1-ylalkyl)sulfoximines **3**, in turn, were obtained by condensation of sulfoximines **1** with aldehydes **2** and benzotriazole.

Keywords: N-Substituted sulfoximines, condensation, nucleophilic substitution, organozinc reagents, allylsilanes

Introduction

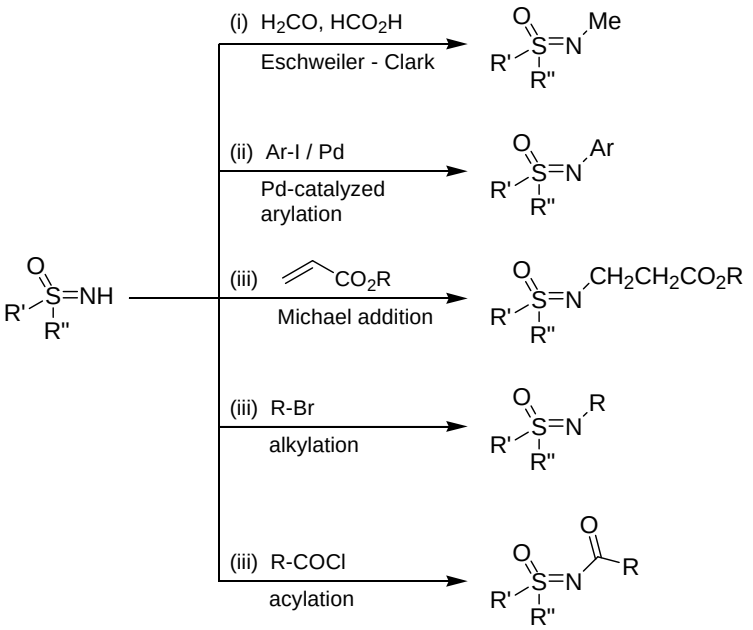
N-Functionalized sulfoximine derivatives are antimuscarinic, spasmolytic,[1] antiarrhythmic,[2] γ-glutamylcysteine synthetase inhibitors,[3] possess antitumor activity,[4] and are important synthetic intermediates.[5] Several methods have been developed for the preparation of *N*-substituted sulfoximines from *NH*-sulfoximines: (i) Eschweiler-Clark conditions for *N*-methylated sulfoximines;[6] (ii) palladium-catalyzed reactions for *N*-arylated sulfoximines;[7] and (iii) base-catalyzed Michael-type additions[8] or base-promoted alkylations[9a] or acylations[9b] (Scheme 1).

Nucleophilic substitution of the benzotriazole moiety in benzotriazolylmethyl amines is an efficient method to prepare *N*-alkylated amines,[10] amides,[11] thioamides,[12] or sulfonamides.[13] Herein, we report the preparation of *N*-(benzotriazol-1-ylalkyl)sulfoximines **3** as intermediates and subsequent nucleophilic replacement of the benzotriazolyl anion to introduce a simple route to *N*-substituted sulfoximines **5**.

Results and Discussion

Preparation of *N*-(benzotriazol-1-ylmethyl)sulfoximines 3a–e

A variety of benzotriazolyl intermediates, which provide convenient routes to diverse heterocycles,[14a] are readily available by condensations of benzotriazole and aldehydes with amides, thio



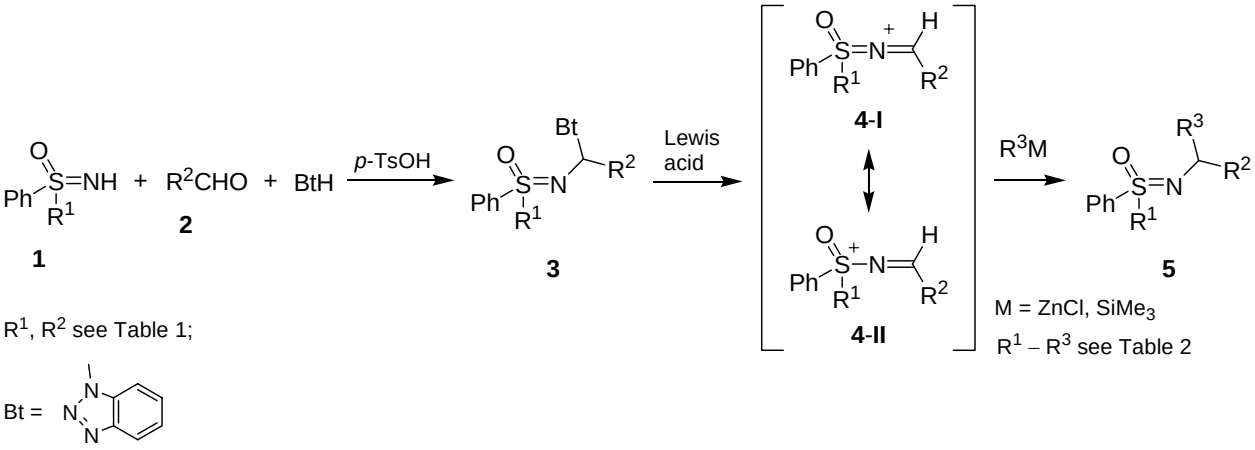
Scheme 1

amides, sulfonamides or acylhydrazines.[14b] We have now similarly prepared *N*-functionalized sulfoximines *via* *N*-(benzotriazol-1-ylmethyl)sulfoximines **3a–e** (Scheme 2, Table 1). Thus, condensation of (±)-*S*-methyl-*S*-phenylsulfoximine (**1a**) with formaldehyde and benzotriazole in the presence of catalytic amounts of *p*-toluenesulfonic acid in refluxing toluene gave *N*-(benzotriazol-1-ylmethyl)-*S*-methyl-*S*-phenylsulfoximine (**3a**) in 73% yield. Similarly, reaction of **1a** with benzotriazole and ethyl glyoxylate gave the desired ethyl 2-(1*H*-1,2,3-benzotriazol-1-yl)-2-[[methyl(oxo)phenyl-λ^6-sulfanylidene]amino]acetate (**3b**) in 82% yield. Condensation of diphenyl sulfoximine with formaldehyde or ethyl glyoxylate and benzotriazole gave the corresponding benzotriazole adducts **3c** and **3d** in 78% and 71% yield, respectively. Use of (1*R*)-(–)-menthyl glyoxylate in this condensation reaction provided the adduct **3e** in 62% yield as a mixture of diastereomers in 1:1 ratio, as determined by the ^{1}H-NMR spectrum of the crude product. Condensation of (*S*)-(–)-*S*-methyl-*S*-phenylsulfoximine (*S*)-**1a** with formaldehyde and benzotriazole afforded the enantiopure benzotriazole intermediate (*S*)-**3a** in 69% yield. Structures of intermediates **3a–e** are supported by their ^{1}H and ^{13}C NMR spectra and by elemental analysis or high-resolution MS data.

Nucleophilic substitution of 3a–c with organozinc reagents

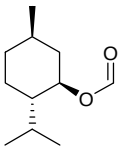
Lewis acid ($ZnCl_2$) facilitates the loss of the benzotriazolyl anion in *N*-(benzotriazol-1-ylalkyl)-sulfoximines **3** to form *N*-methylene-(λ^6-sulfanylidene)iminium ions **4-I** ↔ 1-(methyleneamino)-λ^4-sulfonium ions **4-II**, which can undergo nucleophilic addition by organozinc reagents. Nucleophilic substitution of the benzotriazolyl group in **3a–c** by allyl or aryl groups was achieved by treatment of **3a–c** with allyl- or arylzinc reagents prepared *in situ* by reaction of zinc chloride with the corresponding Grignard reagents. The desired *N*-functionalized sulfoximines

5a–h were obtained in 41–65% yields (Scheme 2, Table 2). Reaction of **3b** with benzylzinc chloride gave **5e** as a mixture of diastereoisomers in a 2:3 ratio. Attempts to improve the diastereoselectivity by lowering the reaction temperature or increasing the reaction time remained unsuccessful.



Scheme 2

Table 1. Preparation of *N*-(benzotriazol-1-ylalkyl)sulfoximines **3a**–**e**

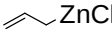
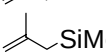
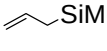
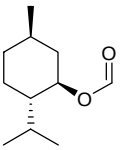
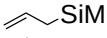
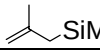
Sulfoximine	Aldehyde	R^1	R^2	Product	Yield [%]
1a	**2a**	Me	H	**3a**	73
1a	**2b**	Me	CO_2Et	**3b**	82
1b	**2a**	Ph	H	**3c**	78
1b	**2b**	Ph	CO_2Et	**3d**	71
1b	**2c**	Ph		**3e**	62
(*S*)-**1a**	**2a**	Me	H	(*S*)-**3a**	69

Nucleophilic substitution of 3a–e with allylsilanes

Lewis acid promoted reactions of allylsilanes with benzotriazole intermediates result in nucleophilic substitution.[15] Reaction of **3b** with allyltrimethylsilane in the presence of BF_3•Et_2O gave *N*-substituted sulfoximine **5i** in 64% yield (Table 2). Similarly, (benzotriazol-1-yl-methyl)diphenylsulfoximine **3c** reacted with allyltrimethylsilane or (2-methylpropenyl)-trimethylsilane to give **5j** and **5k** in 74% and 92% yields, respectively. Bulky intermediates **3d,e**, which showed no reactivity towards organozinc reagents, reacted readily with

allyltrimethylsilane to afford *N*-substituted sulfoximines **5l** and **5m** in 71% and 60% yields, respectively. However, the sulfur chiral center did not exert any diastereoselectivity, and sulfoximine **5i** was obtained as a 1:1 mixture of diastereoisomers as determined by ^{1}H and ^{13}C NMR spectra. Use of (*R*)-(–)-menthyl group as an additional chiral moiety in **3e** also resulted in the formation of a 1:1 mixture of diastereomers **5m** in 60% yield upon reaction with allyl(trimethyl)silane. Similarly, reactions of (*S*)-**3a** with allyl(trimethyl)silane or 2-methyl-3-(trimethyl)silyl-1-propene gave sulfoximines (*S*)-**5a** or (*S*)-**5n** in 77 and 67% yields, respectively.

Table 2. Preparation of *N*-substituted sulfoximines **5a–n**

Staring material	Nucleophile	R^1	R^2	R^3	Product	Yield [%]
3a		Me	H		**5a**	45
3a	PhZnCl	Me	H	Ph	**5b**	45
3a	4-ClC_6H_4ZnCl	Me	H	4-ClC_6H_4	**5c**	62
3a	$PhCH_2ZnCl$	Me	H	$PhCH_2$	**5d**	65
3b	$PhCH_2ZnCl$	Me	CO_2Et	$PhCH_2$	**5e**	41
3c	4-ClC_6H_4ZnCl	Ph	H	4-ClC_6H_4	**5f**	62
3c	$PhCH_2ZnCl$	Ph	H	Ph	**5g**	49
3c	(2-mesityl)ZnCl	Ph	H	2-mesityl	**5h**	53
3b		Me	CO_2Et		**5i**	64
3c		Ph	H		**5j**	74
3c		Ph	H		**5k**	92
3d		Ph	CO_2Et		**5l**	71
3e		Ph			**5m**	60
(*S*)-**3a**		Me	H		(*S*)-**5a**	77
(*S*)-**3a**		Me	H		(*S*)-**5n**	67

Conclusions

In summary, we have introduced a general and convenient method for the preparation of *N*-substituted sulfoximines *via* readily available *N*-(benzotriazol-1-ylmethyl)sulfoximines.

Experimental Section

General Procedures. ^{1}H NMR spectra were determined at 300 MHz and ^{13}C NMR at 75 MHz in $CDCl_3$ (with TMS for ^{1}H and $CDCl_3$ for ^{13}C as the internal reference). HRMS was measured on an AEI-30 mass spectrometer. Tetrahydrofuran (THF) was distilled from Na/benzophenone, dichloromethane was distilled from CaH_2 under N_2. Sulfoximines **1a**, **1b** and (*S*)-**1a** were prepared according to literature procedures.[16]

General procedure for the preparation of *N*-(benzotriazol-1-ylalkyl)sulfoximines 3a–e
A mixture of aldehyde **2** (10 mmol), benzotriazole (1.19 g, 10 mmol), sulfoximine **1** (10 mmol) and catalytic *p*-TsOH (30 mg) in toluene was refluxed overnight under N_2 in a Dean-Stark apparatus. After removal of water, toluene was evaporated under reduced pressure, and the residue was purified by column chromatography with hexanes/ethyl acetate (from 1:1 to 1:3) to give the desired product **3**.

1-[[[Methyl(oxo)phenyl-λ^6-sulfanylidene]amino]methyl]-1*H*-1,2,3-benzotriazole (3a). Colorless plates (from hexanes/chloroform); mp 88–89 °C; yield 73%. ^{1}H NMR: δ 7.93 (d, *J* = 8.4 Hz, 1H), 7.72–7.68 (m, 3H), 7.53–7.29 (m, 5H), 5.95 (d, *J* = 13.2 Hz, 1H), 5.84 (d, *J* = 13.2 Hz, 1H), 3.09 (s, 3H); ^{13}C NMR: δ 146.0, 139.0, 133.3, 132.5, 129.3, 127.7, 127.1, 123.7, 119.6, 110.3, 57.0, 45.4. Anal. Calcd for $C_{14}H_{14}N_4OS$: C, 58.72; H, 4.93; N, 19.57. Found: C, 58.86; H, 4.79; N, 19.95.

Ethyl 2-(1*H*-1,2,3-benzotriazol-1-yl)-2-[[methyl(oxo)phenyl-λ^6-sulfanylidene]amino]acetate (3b). A 1:1 mixture of diastereomers as determined by ^{1}H NMR spectrum of the crude product. After recrystallization, one isomer was separated and characterized. Colorless plates (from hexanes/chloroform); mp 114–115 °C; yield 82%. ^{1}H NMR: δ 8.07–7.99 (m, 1H), 7.74–7.62 (m, 3H), 7.51 (t, *J* = 7.4 Hz, 1H), 7.38 (t, *J* = 8.1 Hz, 1H), 6.63 (s, 1H), 4.25–4.10 (m, 2H), 3.07 (s, 3H), 1.15 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR: δ 167.5, 146.5, 137.6, 133.9, 132.1, 129.7, 128.6, 127.2, 123.9, 119.7, 112.5, 70.3, 62.3, 45.1, 13.8. Anal. Calcd for $C_{17}H_{18}N_4O_3S$: C, 56.97; H, 5.06; N, 15.63. Found: C, 57.31; H, 4.95; N, 15.92.

1-[[[Oxo(diphenyl)-λ^6-sulfanylidene]amino]methyl]-1*H*-1,2,3-benzotriazole (3c). White prisms (from hexanes/chloroform); mp 123–124 °C; yield 78%. ^{1}H NMR: δ 7.96 (d, *J* = 8.4 Hz, 1H), 7.86 (d, *J* = 7.4 Hz, 4H), 7.79 (d, *J* = 8.4 Hz, 1H), 7.50–7.28 (m, 8H), 6.04 (s, 2H). ^{13}C NMR: δ 146.1, 140.0, 132.9, 132.6, 129.2, 128.0, 127.1, 123.7, 119.6, 110.6, 57.3. Anal. Calcd for $C_{19}H_{16}N_4OS$: C, 65.50; H, 4.63; N, 16.08. Found: C, 65.80; H, 4.48; N, 16.17.

Ethyl 2-(1*H*-1,2,3-benzotriazol-1-yl)-2-[[oxo(diphenyl)-λ^6-sulfanylidene]amino]acetate (3d). White prisms (from hexanes/ethyl acetate); mp 86–87 °C; yield 71%. ^{1}H NMR: δ 8.05–7.96 (m, 4H), 7.67–7.64 (m, 2H), 7.62–7.25 (m, 8H), 6.77 (s, 1H), 4.22 (q, *J* = 7.0 Hz, 2H), 1.20 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR: δ 167.7, 146.4, 139.0, 133.3, 133.0, 132.1, 129.4, 129.1, 128.4, 128.0, 127.2, 123.9, 119.6, 112.6, 70.0, 62.4, 13.9. Anal. Calcd for $C_{22}H_{20}N_4O_3S$: C, 62.84; H, 4.79; N, 13.32. Found: C, 62.96; H, 4.77; N, 13.27.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 2-(1*H*-1,2,3-benzotriazol-1-yl)-2-[[diphenyl(oxo)-λ^6-sulfanylidene]amino]acetate (3e). Isolated as a 1:1 mixture of diastereomers; colorless oil; yield 62%. ^{1}H NMR: δ 8.03–7.94 (m, 4H), 7.75–7.68 (m, 2H), 7.60–7.25 (m, 8H), 6.77 (s, 0.5×1 H), 6.76 (s, 0.5×1 H, isomer), 4.76 (dt, *J* = 10.9, 4.4 Hz, 0.5×1H), 4.67 (dt, *J* = 10.9, 4.4 Hz, 0.5×1 H), 2.07–1.81 (m, 2H), 1.65–0.73 (m, 13H), 0.58 (d, *J* = 6.9 Hz, 0.5×3 H), 0.42 (d, *J* = 6.9 Hz, 0.5×3H, isomer); ^{13}C NMR: δ 167.3 (167.2), 146.3 (146.3), 139.2 (139.1), 138.9, 133.2, 133.0 (132.9), 132.1 (132.0), 129.3, 129.0 (128.9), 128.5 (128.4), 128.0 (127.9), 127.1 (127.0), 123.8 (123.7), 119.5, 112.7 (112.5), 70.2 (70.1), 46.8 (46.6), 40.2 (40.1), 33.9, 31.2 (31.2), 25.9 (25.4), 23.1 (22.8), 21.8, (21.8), 20.6 (20.4), 16.1 (15.6). HRMS calcd for $C_{30}H_{35}N_4O_3S$: 531.2429, found: 531.2425.

(*S*)-1-[[[Methyl(oxo)phenyl-λ^6-sulanylidene]amino]methyl]-1*H*-1,2,3-benzotriazole (*S*)-(3a). $[\alpha]_D^{25}$ = +32.6 (*c* 1.32, $CHCl_3$); other data same as **3a.**

General procedure for the nucleophilic substitution of 3a–c with organozinc reagents

A solution of zinc chloride (1.0 M, 1.2 mL, 1.2 mmol) in THF was added to a flask containing a solution of the Grignard reagent (1.0 M, 1.2 mL, 1.2 mmol) in THF (10 mL) under nitrogen at 0 °C. The reaction mixture was stirred at 25 °C for 45 min and then cooled to 0 °C again, and *N*-(benzotriazol-1-ylalkyl)sulfoximine **3** (1 mmol) in THF (10 mL) was added dropwise. The reaction mixture was stirred overnight at 25 °C, quenched with dil. aqueous NH_4Cl and extracted with diethyl ether. The organic layer was washed with $NaHCO_3$, brine, dried over Na_2SO_4 and then removed. The residue was purified by column chromatography on silica gel using hexanes/ethyl acetate (1:2) as eluent to afford the desired *N*- substituted sulfoximines **5a–h**.

(3-Butenylimino)(methyl)oxo(phenyl)-λ^6-sulfane (5a). Colorless oil; yield 45%. ^{1}H NMR: δ 7.93–7.90 (m, 2H), 7.65–7.54 (m, 3H), 5.90–5.76 (m, 1H), 5.08–4.97 (m, 2H), 3.14–3.00 (m, 4H), 2.90–2.81 (m, 1H), 2.32 (q, *J* = 7.1 Hz, 2H). ^{13}C NMR: δ 139.5, 136.6, 132.8, 129.4, 128.6, 115.7, 45.1, 43.5, 37.1. Anal. Calcd for $C_{11}H_{15}NOS$: C, 63.12; H, 7.22; N, 6.69. Found: C, 62.64; H, 7.51; N, 6.89.

(Benzylimino)(methyl)oxo(phenyl)-λ^6-sulfane (5b).[17] Colorless oil; yield 45%. ^{1}H NMR: δ 7.95–7.92 (m, 2H), 7.64–7.53 (m, 3H), 7.37–7.16 (m, 5H), 4.21 (d, *J* = 14.3 Hz, 1H), 3.97 (d, *J* = 14.3 Hz, 1H), 3.14 (s, 3H). ^{13}C NMR: δ 141.2, 139.4, 132.9, 129.4, 128.6, 128.2, 127.6, 126.5, 47.3, 45.3. Anal. Calcd for $C_{14}H_{15}NOS$: C, 68.54; H, 6.16; N, 5.71. Found: C, 68.07; H, 6.32; N, 5.92.

[(4-Chlorobenzyl)imino](methyl)oxo(phenyl)-λ^6-sulfane (5c).[9b] White prisms (from hexanes /ethyl acetate); mp 61–62 °C; yield 62%. ^{1}H NMR: δ 7.93–7.90 (m, 2H), 7.66–7.52 (m, 3H), 7.31–7.23 (m, 4H), 4.15 (d, *J* = 14.6 Hz, 1H), 3.93 (d, *J* = 14.6 Hz, 1H), 3.15 (s, 3H). ^{13}C NMR: δ 139.7, 139.3, 133.0, 132.2, 129.5, 128.9, 128.6, 128.3, 46.7, 45.3. Anal. Calcd for $C_{14}H_{14}ClNOS$: C, 60.10; H, 5.04; N, 5.01. Found: C, 60.06; H, 5.12; N, 4.97.

Methyl(oxo)(phenethylimino)(phenyl)-λ^6-sulfane (5d). Colorless oil; yield 65%. ^{1}H NMR: δ 7.79–7.76 (m, 2H), 7.61–7.48 (m, 3H), 7.27–7.16 (m, 5H), 3.28–3.19 (m, 1H), 3.06–2.96 (m,

4H), 2.90–2.85 (m, 2H). ^{13}C NMR: δ 140.4, 139.4, 132.8, 129.3, 128.9, 128.6, 128.2, 125.9, 45.8, 45.1, 39.4. HRMS calcd for $C_{15}H_{18}NOS$: 260.1109, found: 260.1107.

Ethyl 2-[[methyl(oxo)phenyl-λ^6-sulfanylidene]amino]-3-phenylpropanoate (5e). Isolated as a mixture of diastereomers in 2:3 ratio; colorless oil; yield 41%. ^{1}H NMR: δ 7.91–7.89 (m, 1H), 7.60–7.50 (m, 2H), 7.32–7.17 (m, 7H), 4.20–3.60 (m, 3H), 3.20–2.90 (m, 5H), 1.23 (t, *J*= 7.2 Hz, 0.4×3H, diastereomer 1), 1.02 (t, *J* = 7.1 Hz, 0.6×3H, diastereomer 2). ^{13}C NMR: δ 173.6 (172.8), 138.3 (137.8), 133.0 (132.7), 129.9, 129.6, 129.2, 129.1, 128.5, 128.4, 128.1, 126.1, 60.8 (60.4), 59.4 (58.3), 45.2 (45.1), 42.3 (41.4), 14.0 (13.9). Anal. Calcd for $C_{18}H_{21}NO_3S$: C, 65.23; H, 6.39; N, 4.23. Found: C, 65.41; H, 6.52; N, 4.49.

[(4-Chlorobenzyl)imino](oxo)diphenyl-λ^6-sulfane (5f). Colorless oil; yield 62%. ^{1}H NMR: δ 8.01–7.98 (m, 4H), 7.53–7.45 (m, 6H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 4.24 (s, 2H). ^{13}C NMR: δ 140.5, 140.1, 132.5, 132.1, 129.2, 128.8, 128.5, 128.3, 46.5. Anal. Calcd for $C_{19}H_{16}ClNOS$: C, 66.76; H, 4.72. Found: C, 66.39; H, 4.96.

(Benzylimino)(oxo)diphenyl-λ^6-sulfane (5g).[18] Colorless oil; yield 49%. ^{1}H NMR: δ 8.03–8.00 (m, 4H), 7.53–7.44 (m, 8H), 7.32 (t, *J* = 7.1 Hz, 2H), 7.25–7.19 (m, 1H), 4.28 (s, 2H). ^{13}C NMR: δ 141.5, 140.7, 132.4, 129.1, 128.6, 128.2, 127.4, 126.4, 47.1. Anal. Calcd for $C_{19}H_{17}NOS$: C, 74.23; H, 5.57; N, 4.56. Found: C, 74.13; H, 5.59; N, 4.62.

[(Mesitylmethyl)imino](oxo)diphenyl-λ^6-sulfane (5h). White microcrystals (from ethyl acetate/hexanes); mp 97 °C; yield 53%. ^{1}H NMR: δ 7.96–7.93 (m, 4H), 7.48–7.42 (m, 6H), 6.78 (s, 2H), 4.20 (s, 2H), 2.35 (s, 6H), 2.23 (s, 3H). ^{13}C NMR: δ 141.3, 136.9, 136.1, 134.5, 132.1, 128.9, 128.8, 128.3, 40.7, 20.8, 19.6. Anal. Calcd for $C_{22}H_{23}NOS$: C, 75.61; H, 6.63; N, 4.01. Found: C, 75.29; H, 6.75; N, 4.01.

General procedure for the nucleophilic substitution of 3a–e with allyl(trimethyl)silanes

To a mixture of *N*-(benzotriazol-1-ylalkyl)sulfoximine **3** (1 mmol) and allyl(trimethyl)silane (1 mmol) in CH_2Cl_2 (20 mL) was added BF_3•Et_2O (2 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 2 h and then at room temperature for 18 h. The reaction was quenched by aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2. The combined solvent extract was dried over anhydrous Na_2SO_4 and removed *in vacuo*. The residue was purified by column chromatography with hexanes/ethyl acetate (2:1) as eluent to give the desired *N*-substituted sulfoximine **5**.

Ethyl 2-[[methyl(oxo)phenyl-λ^6-sulfanylidene]amino]-4-pentenoate (5i). Isolated as a 1:1 mixture of diastereomers; colorless oil; yield 64%. ^{1}H NMR: δ 7.96–7.92 (m, 2H), 7.67–7.52 (m, 3H), 5.93–5.70 (m, 1H), 5.13–5.02 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 0.5×2H, diastereomer 1), 4.12–3.91 (m, 0.5×2H, diastereomer 2), 3.76 (t, *J* = 6.5 Hz, 0.5×1H, diastereomer 1), 3.69 (t, *J* = 6.7 Hz, 0.5×1H, diastereomer 2), 3.15 (s, 3H), 2.64–2.40 (m, 2H), 1.27 (t, *J* = 7.1 Hz, 0.5×3H, diastereomer 1), 1.15 (t, *J* = 7.1 Hz, 0.5×3H, diastereomer 2). ^{13}C NMR: δ 173.2, 172.7 (other diastereomer), 139.7, 139.4 (other diastereomer), 134.1, 134.0 (other diastereomer), 132.9, 129.2, 128.5, 128.3 (other diastereomer), 117.4, 117.3 (other diastereomer), 60.5, 60.3 (other diastereomer), 56.9, 56.4 (other diastereomer), 45.4, 45.0 (other diastereomer), 40.4, 39.5 (other

diastereomer), 14.04, 13.98 (other diastereomer). Anal. Calcd for $C_{14}H_{19}NO_3S$: C, 59.76; H, 6.81; N, 4.98. Found: C, 60.17; H, 7.18; N, 4.92.

(3-Butenylimino)(oxo)diphenyl-λ^6-sulfane (5j). Colorless oil; yield 74%. ^{1}H NMR: δ 8.00–7.96 (m, 4H), 7.53–7.43 (m, 6H), 5.97–5.84 (m, 1H), 5.13–4.99 (m, 2H), 3.12 (t, *J* = 7.3 Hz, 2H), 2.46–2.39 (m, 2H). ^{13}C NMR: δ 140.7, 136.8, 132.2, 129.0, 128.5, 115.7, 43.5, 37.3. Anal. Calcd for $C_{16}H_{17}NOS$: C, 70.81; H, 6.31; N, 5.16. Found: C, 71.16; H, 6.47; N, 5.36.

[(3-Methyl-3-butenyl)imino](oxo)diphenyl-λ^6-sulfane (5k). Colorless oil; yield 92%. ^{1}H NMR: δ 7.99–7.96 (m, 4H), 7.50–7.43 (m, 6H), 4.75–4.74 (m, 2H), 3.17 (t, *J* = 7.6 Hz, 2H), 2.39 (t, *J* = 7.6 Hz, 2H), 1.71 (s, 3H). ^{13}C NMR: δ 144.2, 140.8, 132.2, 129.0, 128.5, 110.9, 42.5, 41.2, 22.7. Anal. Calcd for $C_{17}H_{19}NOS$: C, 71.54; H, 6.71; N, 4.91. Found: C, 71.37; H, 6.78; N, 4.80.

Ethyl 2-[[oxo(diphenyl)-λ^6-sulfanylidene]amino]-4-pentenoate (5l). Colorless oil; yield 71%. ^{1}H NMR: δ 8.04–7.96 (m, 4H), 7.54–7.42 (m, 6H), 5.98–5.84 (m, 1H), 5.17–5.06 (m, 2H), 4.19–4.06 (m, 2H), 3.83 (t, *J* = 6.7 Hz, 1H), 2.67–2.60 (m, 2H), 1.23 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR: δ 173.0, 140.3, 134.3, 132.4, 132.4, 128.9, 128.9, 128.6, 128.3, 117.3, 60.5, 56.9, 40.1, 14.1. Anal. Calcd for $C_{19}H_{21}NO_3S$: C, 66.45; H, 6.16; N, 4.08. Found: C, 66.56; H, 6.28; N, 4.28.

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl 2-[[oxo(diphenyl)-λ^6-sulfanylidene]amino]-4-pentenoate (5m). Isolated as a 1:1 mixture of diasteromers; colorless oil; yield 60%. ^{1}H NMR: δ 8.08–8.04 (m, 2H), 7.96–7.92 (m, 2H), 7.54–7.42 (m, 6H), 6.01–5.83 (m, 1H), 5.15–5.06 (m, 2H), 4.78–4.67 (m, 1H), 3.80 (t, *J* = 6.7 Hz, 1H), 2.71–2.54 (m, 2H), 2.06–1.78 (m, 2H), 1.69–1.64 (m, 2H), 1.55–1.35 (m, 2H), 1.10–0.84 (m, 9H), 0.78–0.72 (m, 3H). ^{13}C NMR: δ 172.7 (172.6), 140.6, 140.4 (140.3), 134.5 (134.4), 132.5 (132.4), 129.1 (129.0), 129.0, 128.9 (128.8), 128.5 (128.4), 117.4 (117.3), 74.4, 57.5 (57.3), 46.9 (46.8), 40.7 (40.5), 40.4 (40.3), 34.1, 31.3, 25.8 (25.7), 23.2 (22.9), 22.0, 20.8 (20.7), 16.1 (15.8). Anal. Calcd for $C_{27}H_{35}NO_3S$: C, 71.49; H, 7.78; N, 3.09. Found: C, 71.33; H, 7.99; N, 3.24.

(*S*)-(3-Butenylimino)(methyl)oxo(phenyl)-λ^6-sulfane [(*S*)-5a]. $[\alpha]_D^{25}$ = +136.9 (*c* 2.08, $CHCl_3$). Other data same as **6a**.

(*S*)-Methyl[(3-methyl-3-butenyl)imino]oxo(phenyl)-λ^6-sulfane [(*S*)-5n]. Colorless oil; yield 67%. $[\alpha]_D^{25}$ = +130.6 (*c* 1.75, $CHCl_3$); ^{1}H NMR: δ 7.94–7.90 (m, 2H), 7.62–7.54 (m, 3H), 4.72 (s, 1H), 4.68 (s, 1H), 3.15–3.05 (m, 4H), 2.95–2.86 (m, 1H), 2.29 (t, *J* = 7.7 Hz, 2H), 1.69 (s, 3H). ^{13}C NMR: δ 144.0, 139.6, 132.8, 129.4, 128.6, 110.8, 45.2, 42.5, 40.9, 22.7. Anal. Calcd for $C_{12}H_{17}NOS$: C, 64.53; H, 7.67; N, 6.27. Found: C, 64.16; H, 7.97; N, 6.23.

References

1. Alker, D.; Kemp, J. E. G.; Cross, P. E. PCT Int. Appl. 9110648, 1991; *Chem. Abstr.* **1991**, *115*, 207864.
2. Hellberg, M. R.; Shanklin, J. R., Jr. U.S. Pat. 5140026, 1992; *Chem. Abstr*. **1993**, *118*, 147299.

3. Griffith, O. W.; Anderson, M. E.; Meister, A. *J. Biol. Chem.* **1979**, *254*, 1205.
4. Harvison, P. J.; Kalman, T. I. *J. Med. Chem.* **1992**, *35*, 1227.
5. (a) Johnson, C. R. *Acc. Chem. Res*. **1973**, *6*, 341. (b) Reggelin, M.; Zur, C. *Synthesis* **2000**, 1. (c) Craig, D.; Geach, N. J.; Sardharwala, F. E.; White, A. J. P.; Williams, D. J. *Arkivoc* **2002**, (*vi*), 104.
6. Johnson, C. R.; Schroeck, C. W.; Shanklin, J. R. *J. Am. Chem. Soc*. **1973**, *95*, 7424.
7. (a) Bolm, C.; Hildebrand, J. P. *Tetrahedron Lett*. **1998**, *39*, 5731. (b) Bolm, C.; Simic, O. *J. Am. Chem. Soc*. **2001**, *123*, 3830. (c) Bolm, C.; Martin, M.; Gibson, L. *Synlett* **2002**, 832.
8. Johnson, C. R.; Rigau, J. J.; Haake, M.; McCants Jr. D.; Keiser, J. E.; Gertsema, A. *Tetrahedron Lett*. **1968**, 3719.
9. (a) Johnson, C. R.; Lavergne, O. M. *J. Org. Chem*. **1993**, *58*, 1922. (b) Bolm, C.; Hackenberger, C. P. R.; Simic, O.; Verrucci, M.; Muller, D.; Bienewald, F. *Synthesis* **2002**, 879.
10. (a) Katritzky, A. R.; Yannakopoulou, K.; Lue, P.; Rasala, D.; Urogdi, L. *J. Chem. Soc., Perkin Trans. 1* **1989**, 225. (b) Katritzky, A. R.; Fan, W.-Q. *J. Fluorine Chem*. **1991**, *51*, 33.
11. (a) Katritzky, A. R.; Drewniak, M.; Lue, P. *J. Org. Chem*. **1988**, *53*, 5854. (b) Katritzky, A. R.; Urogdi, L. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1853.
12. Katritzky, A. R.; Denisko, O.; Lang, H. *Tetrahedron* **1995**, *51*, 8703.
13. Katritzky, A. R.; Oniciu, D. C.; Ghiviriga, I. *Synth. Commun*. **1997**, *27*, 907.
14. (a) Katritzky, A. R. *J. Heterocycl. Chem.* **1999**, *36*, 1501. (b) Katritzky, A. R.; Lan, X.; Yang, J. Z.; Denisko, O. V. *Chem. Rev*. **1998**, *98*, 409.
15. Katritzky, A. R.; Qiu, G.; He, H.-Y.; Yang, B. *J. Org. Chem.* **2000**, *65*, 3683.
16. Misani, F.; Fair, T. W.; Reiner, L. *J. Am. Chem. Soc.* **1951**, *73*, 459.
17. Johnson, C. R.; Lavergne, O. M. *J. Org. Chem.* **1993**, *58*, 1922.
18. Hoffmann, H.; Gescher, A. *J. Electroanal. Chem.* **1976**, *74*, 329.

