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The 1,3-Dipolar Cycloaddition Reactions of *C*, *N*-Diphenyl Nitrone with Vinyl Sulfoximines

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Abstract: The reactions of vinyl sulfoximines (**1a-e**) with *C,N*-diphenylnitrone (**2**) are highly regioselective and give only 4-sulfonimidoyl-isoxazolidine cycloadducts. These reactions proceed with modest π-facial diastereoselectivity with respect to the dipolarophile. The stereochemical outcome of these reactions is consistent with attack on the favoured ground state conformation of the vinyl sulfoximine through an '*endo*' like transition state.

The 1,3-dipolar cycloaddition reaction of nitrones with alkenes is an important method for preparing isoxazolidines in a regioselective and stereoselective manner.[1] Isoxazolidines have been successfully transformed into alkaloids and other important natural products and bioactive molecules.[2] While the 1,3-dipolar cycloaddition of nitrones and vinyl sulfones[3] and sulfoxides[4] has been studied we were not aware of a similar study on vinyl sulfoximines.[5] This is surprising since the use of enantiomerically pure vinyl sulfoximines[6] as dipolarophiles would allow the opportunity for the asymmetric synthesis of chiral isoxazolidines. In this paper we report our studies on the reactions of racemic vinyl sulfoximines (**1a-e**) with *C, N*-diphenylnitrone (**2**).

Results and Discussion

Heating a chloroform solution of racemic vinyl sulfoximine (**1a**) or racemic vinyl sulfoximines (**1b**)-(**1e**) with *C, N*-diphenyl nitrone (**2**) (1.1-1.2 molar equivalents) at 60 °C or 75-80 °C, respectively, in a sealed tube for 16 h to 14-28 days respectively, gave a mixture of two racemic diastereoisomeric cycloadducts (**3**) and (**4**) (Scheme 1, although (**3**) and (**4**) are racemic only one enantiomer of (**3**) and (**4**) are shown for convenience). The results of this investigation are summarized in the Table 1. The diastereoselectivities of these reactions were measured by ^{1}H NMR (400 MHz) on the crude reaction products. The products appeared to be formed under irreversible (i.e. kinetically controlled) conditions since the diastereoisomeric product ratios did not vary significantly with time over the course of the reaction. In general, the two diastereoisomeric cycloadducts could not be separated by column chromatography and the yields reported in

Scheme 1

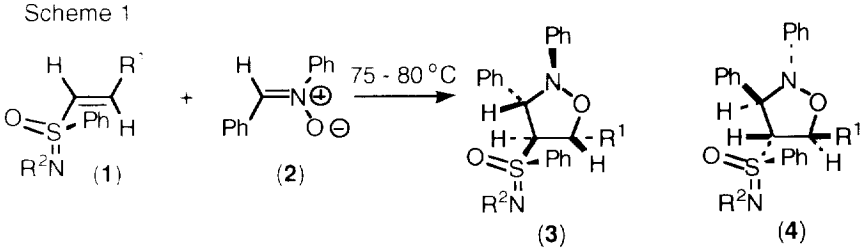


Table 1. Reactions of vinyl sulfoximines (**1a**)-(**1e**) with nitrone (**2**).

Entry	Vinyl sulfoximine (**1**) R^1	R^2	Time (days)	Yield[b] (%)	Diastereoselection (**3**) : (**4**)
1	(**a**) H	Tos	12h[a]	46	65 : 35
2	(**b**) Me	Tos	14	55	64 : 36
3	(**c**) Ph	Tos	28	67	67 : 33
4	(**d**) Ph	2,4,6-$(Pr^i)_3C_6H_2$	28	66	75 : 25
5	(**e**) Ph	Me	28	43	47 : 53

[a] Reaction temperature 60 °C. [b] Combined yield of (**3**) and (**4**) after column chromatography.

Table 1 refer to the yield of the mixture of (**3**) and (**4**) after purification of the crude product by column chromatography. In each case the diastereomerically pure cycloadducts could be obtained by separation by preparative HPLC on a porasil column. ^{1}H NMR analysis of the pure adducts (**3a**) and (**4a**) from the reaction of vinyl *N*-tosyl sulfoximine (**1a**) with (**2**), revealed that these adducts were two diastereoisomeric 4-sulfonimidoyl-isoxazolidines rather than the regio-isomeric 5-sulfonimidoyl-isoxazolidines (**5a**). This is in contrast to the reaction of phenyl vinyl sulfone[3] and *p*-tolyl vinyl sulfoxide[4] with nitrones. The reaction of the former alkene with *C*-phenyl-*N*-methylnitrone was not regioselective and gave a mixture of 4-phenylsulfonyl- and 5-phenylsulfonyl-isoxazolidines (68 : 32, respectively).[3] The reaction of the latter alkene with (**2**) however, was completely regioselective and gave in 54% and 3% isolated yields two diastereoisomeric 4-*p*-tolylsulfinylisoxazolidines.[4]

The reaction of *N*-tosyl (*E*)-propenyl sulfoximine (**1b**) and (**2**) proceeded with a similar diastereoselectivity as the reaction of (**1a**) and (**2**) and gave a 64 : 36 mixture of cycloadducts (**3b**) and (**4b**) respectively (Table 1, entry 2). The regiochemistry of these adducts was evident from analysis of their ^{1}H and COSY NMR spectra. The relative '*endo*' stereochemistry of (**3b**) and (**4b**), rather than the relative '*exo*' stereochemistry as shown in structure (**6**), was determined from NOESY NMR experiments. The results of these experiments are summarized in the Experimental section of this paper. The high regioselectivity and preference for '*endo*' diastereoselectivity in this reaction is similar to that found in the reaction of the analogous (*E*)-propenyl phenyl sulfone with *C*-phenyl-*N*-methylnitrone which gave 84% isolated yield of the

'*endo*'-4-phenylsulfonyl-isoxazolidine cycloadduct and 5% isolated yield of the '*exo*'-4-phenylsulfonyl-isoxazolidine cycloadduct.[3b]

The reaction of *N*-tosyl β-styryl sulfoximine (**1c**) with (**2**) proceeded with similar diastereoselectivity as the other *N*-tosyl vinyl sulfoximines, (**1a**) and (**1b**), and gave a 67 : 33 mixture of the cycloadducts (**3c**) and (**4c**) (Table 1 , entry 3). The relative stereochemistry of (**3c**) was unequivocally determined by a single crystal structural analysis, as shown in Fig. 1. The structural analysis showed (**3c**) had the '*endo*' relative stereochemistry and this knowledge was used to assign the relative stereochemistry of the major and minor cycloadducts (**3a, b**) and (**4a, b**), respectively.

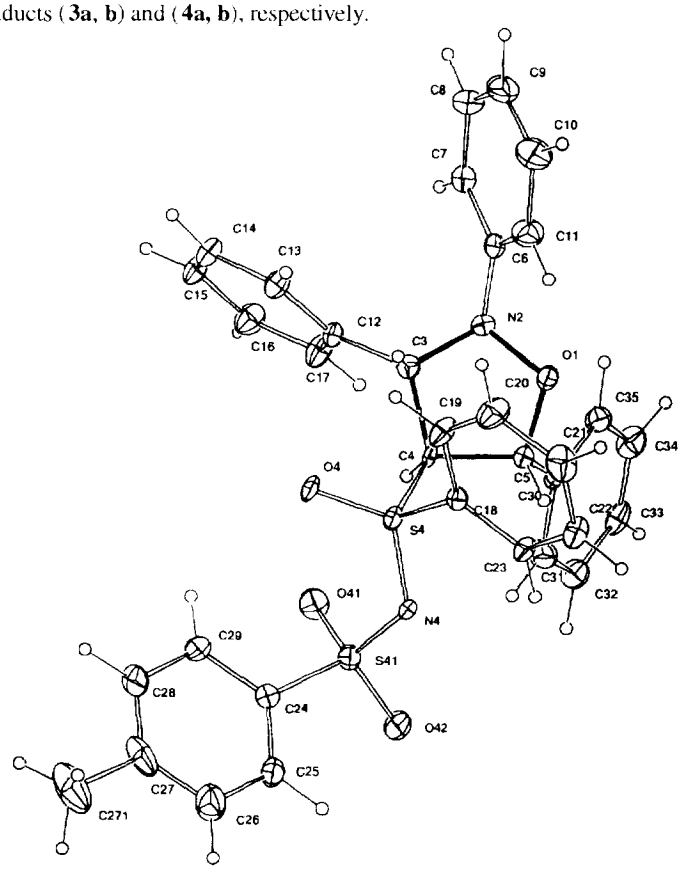
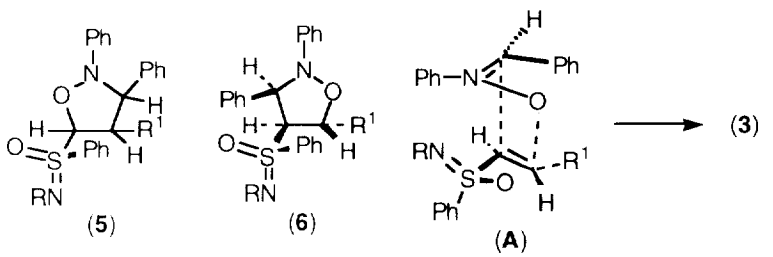


Figure 1. Molecular projection of (**3c**) normal to the central ring plane; 20% thermal ellipsoids are shown for the non-hydrogen atoms, hydrogen atoms having arbitrary radii of 0.1 Å.

The sterically demanding analogue of (**1c**), the *N*-2,4,6-triisopropylphenylsulfonyl β-styryl sulfoximine (**1d**) upon reaction with nitrone (**2**) gave a 75 : 25 mixture of the cycloadducts (**3d**) and (**4d**) respectively. The relative stereochemistry assigned to the cycloadducts (**3d**) and (**4d**) was based upon the close similarity of their ^{1}H NMR spectra to those of (**3c**) and (**4c**) respectively.

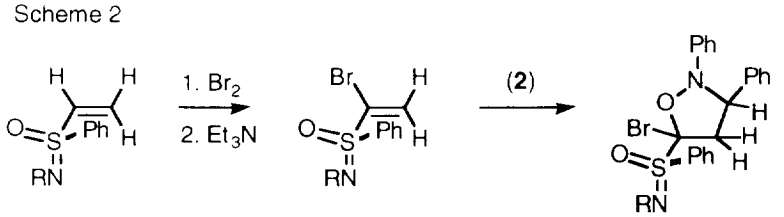
The reaction of the *N*-methyl β-styryl sulfoximine (**1e**) with nitrone (**2**) was poorly diastereoselective and gave a 53 : 47 mixture of the diastereoisomeric '*endo*' cycloadducts (**4e**) and (**3e**) respectively. Thus unlike vinyl sulfones,[3] the regioselectivity and diastereoselectivity of the reaction of the *N*-tosyl vinyl sulfoximines (**1a-c**) with nitrone (**2**) was independent upon the nature of the β-vinyl substituent (R^1). The

diastereoselectivities of the reactions, although only modest, increased as the steric demand of the *N*-substituent (R^2) of the sulfoximine was increased from methyl through to 2,4,6-triisopropylphenylsulfonyl. The stereochemical outcome of the reaction of (**1c**) and (**2**) can be accounted for by invoking the '*endo*' transition state (**A**) in which the least sterically demanding substituent on the sulfoximine, the oxygen substituent, is approximately syn-coplanar with the β-vinyl hydrogen. Addition of the nitrone then occurs from the less hindered β-face of the alkene, that is *anti* to the bulky *S*-phenyl substituent. We have recently found a similar s-*cis* conformation for (**1c**) in the solid state to that shown for (**1c**) in transition state structure (**A**).[7]



It is well documented that the reaction of nitrones with 1,1-disubstituted alkenes gives 5,5-disubstituted isoxazolidines.[1b] Therefore in an attempt to reverse the regiochemistry of these dipolar cycloadditions we prepared the α-bromo vinyl sulfoximines (**7**) and (**8**) (Scheme 2). ^{1}H NMR analysis of the reaction of (**2**) and (**7**) in $CDCl_3$ solution after 24 h at room temperature revealed 66% conversion to the expected 5,5-disubstituted isoxazolidine cycloadduct (**9**) which was a 2.6:1 mixture of diastereoisomers. (Major diastereoisomer: ^{1}H NMR ($CDCl_3$) δ 5.84 (dd, J= 8.4, 3.9 Hz, 1H, H3), 4.09 (dd, J = 14.4, 3.9 Hz, 1H, H4), 3.65 (dd, J = 14.4, 8.4 Hz, 1H, H4'). Minor diastereoisomer: ^{1}H NMR ($CDCl_3$) δ 5.92 (dd, J = 7.8, 5.1 Hz, 1H, H3), 3.96 (dd, J = 14.4, 5.1 Hz, 1H, H4), 3.97 (dd, J= 14.4, 7.8 Hz, 1H, H4'). Similarly, the reaction between (**2**) and (**8**) showed 60% conversion to the cycloadduct (**10**) as a 1.8:1 mixture of diastereoisomers after 24 h at room temperature . (Major diastereoisomer: ^{1}H NMR ($CDCl_3$) δ 5.78 (dd, J = 8.8, 4 .4 Hz, 1H, H3), 4.09 (dd, J = 14.0, 4.4 Hz, 1H, H4), 3.65 (dd, J = 14.0, 8.8 Hz, 1H, H4'). Minor diastereoisomer: δ 6.03 (dd, J = 3.9, 7.2 Hz, 1H, H3), 3.90 (dd, J = 14.4, 3.9 Hz, 1H, H4), 3.59 (dd, J = 14.4, 7.2 Hz, 1H, H4')). However, after 48 h these cycloadducts were no longer evident and a mixture of unidentified products resulted. We assume that these compounds are thermally unstable due to the sensitive tertiary bromide group. These reactions were therefore not further studied.

Scheme 2

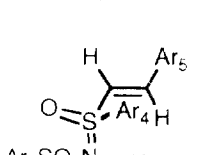


(**1a**); R = tosyl (**7**); R = tosyl (**9**); R = tosyl
(**1f**); R = 2,4,6-$(Pr^i)_3C_6H_2$- (**8**); R = 2,4,6-$(Pr^i)_3C_6H_2$- (**10**); R = 2,4,6-$(Pr^i)_3C_6H_2$-

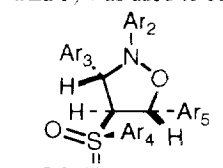
In summary, the reaction of vinyl sulfoximines (**1a-e**) with *C,N*-diphenylnitrone (**2**) are highly regioselective and only 4-sulfonimidoyl-isoxazolidine cycloadducts are obtained. These reactions proceed with modest π-facial diastereoselectivity with respect to the dipolarophile. The stereochemical outcome of these reactions is consistent with attack on the favoured ground state conformation of the vinyl sulfoximine through an '*endo*' like transition state.

Experimental

Vinyl sulfoximines (**2b**), (**2c**) and (**2e**) were prepared as previously reported.[7] All NMR spectra (^{1}H NMR and ^{13}C NMR) were recorded on a Varian unity 400 or 300 NMR spectrometer in $CDCl_3$ solution unless otherwise indicated. Aromatic protons have been assigned as belonging to the aromatic rings Ar_1-Ar_5 as shown in the structures below. 2-D NMR (COSY and NOESY) was used to confirm the ^{1}H assignments.



(**1**)



(**3**)

Melting points were measured on a capillary melting point apparatus and are uncorrected. HPLC separations were performed using a Waters Model 510 pump, a Waters 25 x 10 cm Radial-Pak HPLC porasil cartridge with detection at 254 nm.

X-ray Structure Determinations. A unique room temperature (~295K) diffractometer data set (molybdenum Mo *Kα* monochromatic radiation, λ = 0.71093 Å; $(2\theta/\theta)_{max}$ = 50°, 2θ/θscan mode) yielded 5335 independent reflections (gaussian absorption correction), 2043 with $I > 3\sigma(I)$ being considered 'observed' and used in the full matrix least squares refinement. Anisotropic thermal parameters were refined for C, N, O, S; (*x*, *y*, *z*, U_{iso})$_H$ were included constrained at estimated values after observation in difference maps. Conventional residuals *R*, R_w on |*F*| were 0.063, 0.059 (statistical weights derivative of $\sigma^2(I) = \sigma^2(I_{diff}) + 0.0004\ \sigma^4(I_{diff})$). Full tabulations of atom coordinates and thermal parameters, molecular geometries and structure factor amplitudes have been deposited with the Cambridge Crystallographic Data Centre. Crystal data for (3c): $C_{34}H_{30}N_2O_4S_2$, *M* = 594.8 Monoclinic, space group $P2_1/c$ (C_{2h}^5, No. 14), *a* = 10.398 (2), *b* = 111.885(6), *c* = 26.036(5) Å, β = 109.42(2)°, *V* = 3034(2) Å^3, D_c(*Z* = 4) = 1.30 g. cm^{-3}; *F*(000) = 1248, μ_{Mo} = 2.2 cm.$^{-1}$; specimen: 0.23 x 0.42 x 0.09 mm; $A^*_{min,max}$ = 1.02 [illegible]

***N*-Tosyl *S*-ethenyl *S*-phenyl sulfoximine (1a).** *N*-Tosyl *S*-methyl *S*-phenyl sulfoximine[8] (4.0 g, 13 mmol) was dissolved in freshly distilled dry THF (55 mL) under N_2 and then cooled to -78 °C. Butyllithium / hexanes (16 mmol) was added slowly at this temperature then the reaction was allowed to warm up to rt over 35 min. The reaction was recooled to -78 °C and Eschenmoser's salt (4.8g, 26 mmol) was added under N_2 and the reaction stirred at -78 °C for 1 h. The mixture was then allowed to come to room temperature then rotary evaporated to remove solvent. The residue was dissolved in methanol (40 mL) then iodomethane (12 mL, 190 mmol) was added and the mixture was left stirring overnight. The reaction was placed in a 40 °C water bath for 2 h to remove excess iodomethane before being rotary evaporated to remove solvent. The crude product was then shaken with a 5% aqueous solution of sodium bicarbonate (280 mL) and CH_2Cl_2 (200 mL) until all the oil and solid had dissolved. The CH_2Cl_2 layer was separated and the aqueous layer washed with a further 150 mL of CH_2Cl_2. The organic extracts were combined, washed with a 10% aqueous solution

of sodium thiosulfate (100 mL) then with a saturated aqueous solution of NaCl (200 mL), dried over $MgSO_4$ and rotary evaporated to dryness. The orange oil was chromatographed on silica gel using 50% ethyl acetate / hexane as eluent to give 1.1 g (26 %) of (**1a**) as a white solid, m.p 126-128 °C. ^{1}H NMR ($CDCl_3$) δ 7.97 (dd, J = 7.8, 0.9 Hz, 2H, Ar_4 'ortho'), 7.85 (dd, J = 8.1, 1.8 Hz, 2H, Ar_1 'ortho'), 7.68 (t, J = 7.8 Hz, 1H, Ar_4 'para'), 7.57 (t, J = 7.8 Hz, 2H, Ar_4 'meta'), 7.26 (d, J = 8.1 Hz, 2H, Ar_1 'meta'), 6.83 (dd, J = 16.2, 9.6 Hz, 1H, H1), 6.48 (dd, J = 16.2, 1.5 Hz, H2'), 6.19 (dd, J = 9.6, 1.5 Hz, H2), 2.40 (s, 3H $ArCH_3$). ^{13}C NMR ($CDCl_3$) δ 161.77 (C), 142.85 (C), 137.73, 134.23, 129.64, 129.24, 129.14 (CH_2), 128.04, 126.68, 102.37(C), 21.49 (CH_3). HRMS (EI) calcd for $C_{15}H_{15}NO_3S_2$ 321.04931 found 321.05039.

***N*-Tosyl *S*-(1-bromo-1-ethenyl) *S*-phenylsulfoximine (7).** To a solution of (1a) (0.521 g, 1.6 mmol) in CCl_4 / CH_2Cl_2 (1:1, 12 mL) was added Br_2 (3.2 mmol) in CCl_4 solution (5 mL) and the reaction stirred over night under N_2 in a flask that was covered in aluminium foil to exclude light. After 24 h an aqueous 10% solution of sodium thiosulfate was added until the bromine colour disappeared and then CH_2Cl_2 (20 mL) was added. The organic layer was separated, dried ($MgSO_4$) then rotary evaporated to remove solvent. The residue was redissolved in CH_2Cl_2 (15 mL) and treated with triethylamine (0.181g, 1.78 mmol) for 40 min. The solution was washed with 5% aqueous HCl and then water. The solution was then dried ($MgSO_4$) and evaporated to dryness. Purification by column chromatography using 40% EtOAc / hexane as eluent gave pure (**7**) (0.223 g , 32%) as an oil. ^{1}H NMR δ 8.01 (dd, J = 6.0, 1.2 Hz, 2H, Ar_4 'ortho'), 7.89 (dd, J = 6.6, 1.8 Hz, 2H, Ar_1 'ortho'), 7.71 (t, 1H, Ar_4 'para'), 7.58 (t, 2H, Ar_4 'meta'), 7.30 (d, J = 3.6 Hz, 1H, H1), 6.47 (d, J = 3.9 Hz, 1H, H1'), 2.340 (s, 3H, $ArCH_3$). ^{13}C NMR δ 143.10 (C), 140.42 (C), 134.81, 134.44, 131.43 (CH_2), 129.39, 129.26, 129.11, 128.69 (C), 126.75, 21.49 (CH_3). Mass spectrum (ES+) *m/z* 402/400 (84%/100%, $[M]^+$), 294 (25) 283 (65). HRMS (EI) calcd for $C_{15}H_{14}Br^{79}NO_3S_2$ 398.95991, found 398.95910.

***N*-2,4,6-(Triisopropylbenzenesulfonyl) *S*-methyl *S*-phenylsulfoximine.** To a solution of *S*-methyl *S*-phenyl sulfoximine[8] (7.6 g, 49 mmol) of in dry CH_2Cl_2 (20 mL) was added dry pyridine (6 mL) and a crystal of dimethylaminopyridine. The mixture was cooled to 0 °C then 2,4,6-triisopropylbenzenesulfonyl chloride (14.85 g, 49 mmol) was added in small lots under a flow of N_2. After addition the mixture was warmed to rt and was stirred under N_2 for 16 h. The reaction was filtered, the solids washed with dry pyridine (10 mL) and the filtrate was diluted with water (50 mL) and extracted three times with CH_2Cl_2. The combined extracts were washed with 10% aqueous HCl (2 x 25 mL) then dried over $MgSO_4$, filtered and rotary evaporated to dryness. The residue was recrystallized from ethanol to give 11 g (53%) of the title compound as white crystals mp 138-139 °C. ^{1}H NMR δ 7.99 (dd, J = 8.4, 15 Hz, 2H, ArH), 7.69 (tt, 1H, ArH), 7.58 (tt, 2H, ArH), 7.11 (s, 2H, Ar_1 'meta'), 4.38 (hept, 2H, Me_2CH), 3.11 (s, 3H, CH_3), 2.88 (hept, 1H, Me_2CH), 1.255 1.251 1.233 1.230 1.207 (3 x d, overlapping, $6CH_3$). ^{13}C NMR δ 151.95, 149.05, 138.99, 137.26, 134.18, 129.59, 127.42, 123.37, 46.95, 34.12, 29.25, 24.65 ($2CH_3$), 24.60 ($2CH_3$), 23.63 (CH_3), 23.61 (CH_3). Mass spectrum (ES+) *m/z* 422/400 (100%, $[M+H]^+$).

***N*-(2,4,6-Triisopropylbenzenesulfonyl) *S*-ethenyl *S*-phenylsulfoximine (1f)** The title compound was prepared from *N*-2,4,6-(triisopropylbenzenesulfonyl)*S*-methyl *S*-phenylsulfoximine (4.44 g, 11.0 mmol) using the procedure described above for the synthesis of (**1a**). Recrystallisation from ethanol gave 1.94g (42%) of white crystals, m.p. 155-156 °C. ^{1}H NMR δ 7.96 (dd, J = 8.1, 1.5 Hz, 2H, Ar_4 'ortho'), 7.66 (t, J = 7.5 Hz, 1H, Ar_4 'para'), 7.59 (t, J = 8.1 Hz, 2H, Ar_4 'meta'), 7.12 (s, 2H, Ar_1 'meta'), 6.82 (dd, J = 16.5, 9.6 Hz, 1H, H1), 6.48 (dd, J = 1.2, 16.2 Hz, 1H, H2'), 6.16 (dd, J = 9.6, 1.2 Hz, 1H, H2), 4.38 (quin, 2H, Me_2CH), 2.88 (quin, 1H, Me_2CH), 1.25 (d, J = 1.8 Hz, 6H , $2CH_3$), 1.23 (d, J = 1.2 Hz, 12H, $4CH_3$). ^{13}C NMR δ 151.99, 149.11,

138.09, 134.10, 129.55, 128.76, 127.98, 127.41, 123.35, 34.11 (CH), 29.24 (CH), 24.66 ($\underline{C}H_3$), 24.58 ($\underline{C}H_3$), 23.63 ($\underline{C}H_3$). HRMS (EI) calcd for $C_{23}H_{31}NO_3S_2$ 433.1745 found 433.17359.

***N*-(2,4,6-Triisopropylbenzenesulfonyl) *S*-(1-bromo-1-ethenyl) *S*-phenylsulfoximine (8).** To a stirred solution of (**1f**) (0.518 g 1.01 mmol) in CH_2Cl_2 (5 mL) was added Br_2 (0.21 g, 1.3 mmol) in dry CCl_4 (3 mL) and the reaction stirred under N_2 for 16 h. TLC showed the reaction was 50% complete so another equivalent of bromine was added and the reaction was left stirring for a further 24h. The reaction mixture was worked up as described above for the preparation of (**7**). The residue was then treated with triethylamine (0.149g, 1.47 mmol) for 2.5 h and then worked up as described above for the synthesis of (**7**) to give an oil. (0.585 g). ^1H NMR analysis showed a showed a 2:1 mixture of (**8**) and (**1f**). Purification by column chromatography using 25% EtOAc / hexane as eluent gave 0.162 g (26%) of (**8**) as an oil. ^1H NMR δ 8.01 (dd, J = 8.8, 1.2 Hz, 2H, Ar_4 'ortho'), 7.70 (t, J = 7.6 Hz, 1H, Ar_4 'para'), 7.57 (t, J = 8.4 Hz, 2H, Ar_4 'meta'), 7.31 (d, J = 3.6 Hz, 1H, H2), 7.13 (s, 2H, Ar_1 'meta'), 6.47 (d, J = 3.2 Hz, 1H, H2'), 4.43 (hept, J = 6.8 Hz, 2H, $Me_2C\underline{H}$), 2.88 (hept, J = 6.8 Hz, 1H, $Me_2C\underline{H}$), 1.27 (d, J = 6.4 Hz, 6H, $2C\underline{H}_3$), 1.24 (d, J = 6.4 Hz, 6H, $2C\underline{H}_3$), 1.22 (d, J = 6.4 Hz, 6H, $2C\underline{H}_3$); ^{13}C NMR δ 152.13 (C), 149.15 (C), 137.13 (C), 135.08 (C), 134.65 (CH), 130.92 (CH_2), 129.31 (CH), 128.96 (CH), 123.36 (CH), 34.06 ($Me_2\underline{C}H$), 29.23 ($2Me_2\underline{C}H$), 24.67 ($\underline{C}H_3$), 24.55 ($2\underline{C}H_3$), 23.54 ($2\underline{C}H_3$). HRMS (+LSIMS) calcd for $C_{23}H_{30}{}^{81}BrNO_3S_2$+H 514.090786 found 514.08506.

***N*-2,4,6-(Triisopropylbenzenesulfonyl) *S*-2-phenylethenyl *S*-phenylsulfoximine (1d).** To a stirred solution of *N*-2,4,6-(triisopropylbenzenesulfonyl) *S*-methyl *S*-phenyl sulfoximine (2.1 g, 4.95 mmol) in dry THF (20 mL) under N_2 at -78 °C was added butyllithium in hexanes (5.88 mmol). The reaction mixture was then allowed to come to rt and was stirred for 10 min. The mixture was then recooled to -78 °C and benzaldehyde (0.74g, 7.5 mmol) was added, the reaction was warmed slowly to 0 °C and stirred for 45 min. Dry triethylamine (0.73 mL, 5.5 mmol) was added followed by the dropwise addition of methanesulfonyl chloride (0.629 g, 5.49 mmol). The reaction was stirred for 20 min then triethylamine (0.73 mL) was added and the reaction allowed to come to rt and stirred another 20 min. A 10% aqueous solution of NH_4Cl (10 mL) was added and the mixture was extracted with CH_2Cl_2. The extracts were dried ($MgSO_4$) and rotary evaporated to dryness to give a solid material. Recrystallization from ethyl acetate gave fine white crystals. (0.447g, 17%), mp 202-206 °C. ^1H NMR δ 8.01 (d, J = 7.6 Hz, 2H, Ar$\underline{H}$), 7.67 (d, J = 15.2 Hz, 1H, $C\underline{H}$), 7.63 (d, J = 7.6 Hz, 1H, Ar$\underline{H}$), 7.55 (dd, J = 8 Hz, 2H Ar$\underline{H}$), 7.45-7.38 (m, 5H, Ar$\underline{H}$), 7.11 (m, 2H, Ar_1 'meta'), 6.88 (d, J = 15.2 Hz, 1H, $C\underline{H}$), 4.41 (m, 2H, $Me_2C\underline{H}$), 2.87 (m, 1H, $Me_2C\underline{H}$), 1.23 (ddd, 18H, $6C\underline{H}_3$). Anal. Calcd for $C_{29}H_{35}NO_3S_2$: C, 68.34; H, 6.92; N, 2.75. Found C, 68.28; H, 7.03; N, 2.68.

Reaction of Vinyl Sulfoximines (1a) with Nitrone (2)-A General Procedure: The vinyl sulfoximine (**1a**) (0.203 g, 0.632 mmol) nitrone (**2**) (0.142 g, 0.758 mmol) and chloroform (3 mL) were placed in a sealed tube, with a stirring bar, under N_2. The tube was covered with foil to exclude light and the solution was heated at 60 °C overnight. The crude ^1H NMR indicated the ratio of diastereoisomers was 65:35. The reaction mixture was purified by column chromatography on silica gel using 40% ethyl acetate in hexane as eluent. Fractions were obtained that contained a mixture of the two diastereoisomers (**3a**) and (**4a**) (0.152g, 46%). A small sample of this mixture was separated by HPLC using 15% ethyl acetate / hexane as the mobile phase. The first compound to elute was (**3a**), the second, (**4a**).

(3*SR*, 4*SR*, S*SR*) 2,3-Diphenyl-4(*N*-*p*-tolylsulfonyl *S*-phenylsulfonimidoyl)isoxazolidine (3a): Oil; ^1H NMR (C_6D_6) δ 8.18 (d, J = 7.8 Hz, 2H, Ar$\underline{H}$), 7.67 (m, 4H, Ar$\underline{H}$), 7.15 (m, 3H, Ar$\underline{H}$),6.88-6.61 (m, 10H, Ar $\underline{H}$), 5.14 (d, J = 3.9 Hz, 1H, $\underline{H}3$), 4.63 (quin, J = 3.9, 7.8, 11.4 Hz, 1H, $\underline{H}4$), 4.27 (dd, J = 10.6, 4.5 Hz, 1H, $\underline{H}5$), 3.87 (dd, J = 10.5, 7.5 Hz, $\underline{H}5'$), 1.87 (s, 3H, $C\underline{H}_3$). ^{13}C NMR δ 151.4, 148.6, 142.9, 140.5, 139.07,

134.85, 129.56, 129.41, 129.29, 129.12, 128.67, 128.44, 126.95, 126.63, 122.82, 115.39, 79.26, 69.70, 66.62, 29.69 (CH_3). Mass spectrum (ES+) *m/z* 519 (81% $[M+H]^+$), 501 (59), 443 (20), 279 (78), 275 (20), 165 (100). HRMS (+LSIM) calcd for $C_{28}H_{26}N_2O_4S_2$+H, 519.141184 found 519.14010. NOESY cross-peaks were observed between Ar_2'ortho' and H3 and H5.

(3*RS*, 4*RS*, S*SR*) 2,3-Diphenyl-4(*N*-*p*-tolylsulfonyl-*S*-phenylsulfonimidoyl)isoxazolidine (4a) Oil; ^{1}H NMR (C_6D_6) δ 8.17 (d, J = 8.1 Hz, 2H, ArH) , 7.67 (d, J = 7.2 Hz, 2H, ArH), 7.16 (m, 3H, ArH), 6.96 (m, 5H, ArH), 6.76 (m, 7H, ArH), 4.77 (d, J = 4.2 Hz, 1H, H3), 4.60 (dd, J = 10.2, 3.6 Hz, 1H, H5), 4.17 (m, 1H, H4), 3.94 (dd, J = 10.2, 7.2 Hz, H5'), 1.89 (s, 3H, CH_3). ^{13}C NMR δ 148.41, 142.91, 140.46, 138.06, 135.77, 134.67, 129.67, 129.25, 129.07, 128.93, 128.68, 128.44, 126.98, 126.60, 123.49, 116.46, 78.28, 70.44, 66.15, 29.70. Mass spectrum (ES+) *m/z* 519 (100%, $[M+H]^+$), 541 (17, $[M+Na]^+$), 501 (82).

(3*SR*, 4*SR*, 5*SR*, S*SR*) 5-Methyl-2,3-diphenyl-4(*N*-p-tolylsulfonyl *S*-phenylsulfonimidoyl)isoxazolidine (3b) and (3*RS*, 4*RS*, 5*RS*, S*SR*) 5-Methyl-2,3-diphenyl-4(*N*-*p*-tolylsulfonyl *S*-phenylsulfonimidoyl) isoxazolidine (4b). The title compounds were obtained from the reaction of the vinyl sulfoximine (**1b**) (97.5 mg, 0.29 mmol) and the nitrone (65.8 g, 0.33 mmol) in $CDCl_3$ (1 mL) at 75-80 °C for 14 days using the general procedure described above. ^{1}H NMR of the crude reaction mixture showed an diastereomeric ratio of 1.75:1. The reaction was chromatographed on silica gel using ethyl acetate / hexane (1 : 2) as eluent to give an almost pure sample of (**3b**) (12 mg) and a mixed fraction (73 mg) of (**3b**) and (**4b**) (total yield 55 %). A small sample of the mixture was separated by HPLC using 15% EtOAc / hexane as the mobile phase, the first compound from the column was (**3b**) and the second (**4b**).

(3b): Oil; ^{1}H NMR δ 7.88 (d, J = 7.6 Hz, 2H, Ar_4 ortho'), 7.77 (d, J = 8.0 Hz, 2H, Ar_1 'ortho'), 7.59 (t, 1H, Ar_4 'para'), 7.53 (d, J = 7.6 Hz, 2H, Ar_3 'ortho'), 7.45 (m, J = 8.0 Hz, 2H, Ar_4 'meta'), 7.36 (m, 2H, Ar_3, 'meta'), 7.31 (d, 1H, J = 7.2 Hz, Ar_3 'para'), 7.24 (d, 2H, J = 8.4 Hz, Ar_1 'meta'), 7.11 (dd, 2H, J = 7.6, 8.4 Hz, Ar_2 'meta'), 6.89 (t, 1H, Ar_2 'para'), 6.69 (d, 2H, Ar_2 'ortho'), 5.25 (d, J = 3.6 Hz, 1H, H3), 4.54 (quin, J = 6.4 Hz, 1H, H5), 4.23 (dd, J = 3.6, 6.4 Hz, 1H, H4), 2.41 (s, 3H, MeAr), 1.29 (d, J = 6.0 Hz, 3H, CH_3). ^{13}C NMR δ 149.00, 142.86, 140.62, 139.86, 134.92, 134.86, 129.64, 129.25, 129.16, 129.01, 128.91, 128.05, 126.68, 126.53, 122.09, 114.21, 84.21, 75.23, 70.20, 21.54, 18.55. Mass spectrum (EI+) *m/z* 533 (22%, $[M+H]^+$), 555 (68, $[M+Na]^+$), 570 (10, $[M+K]^+$), 489 (38), 288.5 (100)). NOESY cross-peaks were observed between, C5Me and H4; Ar_3 ortho and H4; Ar_2'ortho and H5 and H5.

(4b): Oil; ^{1}H NMR δ 7.88(d, J = 8.1Hz, 2H, Ar_4 ortho'), 7.69 (d, J = 8.4 Hz, 2H, Ar_1 'ortho'), 7.63 (m, 1H, Ar_4 para'), 7.48 (t, 2H, Ar_4 'meta'), 7.26-7.10 (m, 9H, Ar_1 'meta', Ar_2 'meta', Ar_3 'ortho +meta + para'), 6.92 (t, J = 6.9 Hz, 1H, Ar_2 'para'), 6.77 (d, J = 8.7 Hz, 2H, Ar_2 'ortho'), 4.92 (d, J = 4.8 Hz, 1H, H3), 4.82 (m, J = 6.3 Hz, 1H, H5), 4.01 (dd, J = 6.3, 4.8 Hz, 1H, H4), 2.40 (s, 3H, MeAr), 1.49 (d, J = 4.5 Hz 3H, CH_3). ^{13}C NMR δ 148.98, 142.81, 140.43, 139.27, 136.06, 134.75, 129.73, 129.20, 129.03, 128.92, 128.86, 128.05, 126.57, 126.53, 122.48, 120.46, 114.87, 83.71 (C4), 75.19 (C5), 70.81 (C3), 21.53, 19.24. HRMS (CI) calcd for 533.15683, found 533.15607. NOESY cross-peaks were observed between, H3 and H5;' and H3 and H5.

(3*SR*, 4*SR*, 5*SR*, S*SR*) 2,3,5-Triphenyl-4(*N*-*p*-tolylsulfonyl S-phenylsulfonimidoyl)isoxazolidine (3c) and (3*RS*, 4*RS*, 5*RS*, S*SR*) 2,3,5-Triphenyl-4(*N*-*p*-tolylsulfonyl S-phenylsulfonimidoyl)isoxazolidine (4c). The title compounds were obtained from the reaction of the vinyl sulfoximine (**1c**) (0.083 g, 21.1 mmol) and the nitrone (0.42 g, 0.21 mmol) in $CHCl_3$ (1.5 mL) at 75-80 °C for 28 days using the general procedure described above. ^{1}H NMR of the crude reaction mixture showed an diastereomeric ratio of 2 : 1. The reaction was chromatographed on silica gel using ethyl acetate / hexane (1 : 2) as eluent to give 0.085 g (67%) of a mixture

of (**3c**) and (**4c**). A sample was separated by HPLC using 10% EtOAc / hexane as the mobile phase to give pure samples of (**3c**) and (**4c**) as white solids. A crystal structure was obtained on (**3c**), Fig. 1.

(3c): ^{1}H NMR δ 7.78 (d, J = 7.2 Hz, 2H, ArH), 7.75 (d, J = 8.1 Hz, 2H, ArH), 7.54 (t, J = 7.8 Hz 1H, ArH), 7.52 (dd, J = 8.4 Hz, 2H, ArH), 7.39 (d, J = 8.1 Hz, 2H, ArH), 7.34 (d, J = 7.8 Hz, 2H, ArH), 7.32 (t, 1H, ArH), 7.28 (d, J = 7.8 Hz, 2H, Ar H), 7.20 (d, J = 8.4 Hz, 2H, Ar H), 7.19 (t, J = 7.2 Hz, 1H, Ar H), 7.17 (d, J = 9.3 Hz, 2H, ArH), 7.14 (t, J = 6.6 Hz, 1H, ArH), 6.99 (t, 1H, ArH), 6.93 (dd, J = 6.9, 1.5 Hz, 2H, ArH), 6.86 (dd, J = 7.5, 1.2 Hz, 2H, ArH), 5.49 (d, J = 3.9 Hz, 1H, H3), 5.35 (d, J = 6.3 Hz, 1H, H5), 4.50 (dd, J = 4.2, 6.3 Hz, 1H, H4), 2.41 (s, 3H, CH_3). ^{13}C NMR δ 148.79, 142.82, 139.42, 135.64, 135.59, 134.62, 129.57, 129.22, 128.99, 128.77, 128.59, 128.12, 126.92, 126.76, 126.60, 122.64, 114.85, 84.79, 79.93, 70.21, 21.53. HRMS (CI), calcd for $C_{34}H_{30}N_2O_4S_2$ 595.17248, found 595.17388. NOESY cross-peaks were observed between Ar_2'ortho' and H3 and H5.

(4c): ^{1}H NMR δ 7.86 (d, J = 8.1 Hz, 2H, ArH), 7.73 (d, J = 8.4 Hz, 2H, ArH), 7.59 (t, J = 7.8 Hz, 1H, ArH), 7.44 (d, J = 8.1 Hz, 2H, ArH), 7.41 (m, 2H, ArH), 7.32 (m, 3H, ArH), 7.23 (d, J = 7.8 Hz, 2H, ArH), 7.18 (d, J = 8.7 Hz, 2H, ArH), 7.16 (t, 1H, ArH), 7.14 (d, J = 7.8 Hz, 2H, ArH), 7.00 (t, 1H, ArH), 6.92-6.86 (dd, 4H, ArH), 5.80 (d, J = 4.8 Hz, 1H, H3), 4.88 (d, J = 5.7 Hz, 1H, H5), 4.40 (t, J = 5.1 Hz, 1H, H4), 2.41 (s, 3H, CH_3). ^{13}C NMR (in part) δ 140.56, 138.32, 137.32, 134.66, 129.66, 129.23, 129.10, 128.90, 128.86, 128.69, 128.54, 128.32, 128.16, 126.98, 126.62, 123.32, 116.12, 84.69, 79.32, 70.99, 21.53. Mass spectrum (ES+) m/z 595.6 (22%, $[M+H]^+$), 338.9 (100).

(3*SR*, 4*SR*, 5*SR*, S*SR*) 2,3,5-Triphenyl-4(*N*-(2,4,6-triisopropylbenzenesulfonyl S-phenylsulfonimidoyl) isoxazolidine (3d) and (3*RS*, 4*RS*, 5*RS*, S*SR*) 2,3,5-Triphenyl-4(*N*-2,4,6-triisopropylbenzenesulfonyl S-phenylsulfonimidoyl) isoxazolidine (4d). The title compounds were obtained from the reaction of the vinyl sulfoximine (**1d**) (0.10 g, 0.20 mmol) and the nitrone (0.04 g, 0.20 mmol) in $CHCl_3$ (1.5 mL) at 75-80 °C for 28 days using the general procedure described above. ^{1}H NMR of the crude reaction mixture showed an diastereomeric ratio of 3 : 1. The reaction was chromatographed on silica gel using ethyl acetate / hexane (1 : 2) as eluent to give 0.096 g (66%) of a mixture of (**3d**) and (**4d**). A sample was separated by HPLC using 10% EtOAc / hexane as the mobile phase to give pure samples of (**3d**) and (**4d**) as white crystals.

(3d): ^{1}H NMR δ 7.72 (dd, J = 8.0, 0.8 Hz, 2H, Ar_4 'ortho'), 7.56 (dd, J = 8.0, 1.6 Hz, 2H, Ar_3 'ortho'), 7.49 (t, J = 7.6 Hz, 1H, Ar_4 'para'), 7.34-7.28 (m, 5H, ArH), 7.21-7.14 (m, 5H, ArH), 7.05 (s, 2H, Ar_1 'meta'), 6.97 (dd, J = 8.8, 1.6 Hz, 2H, Ar_5 'ortho'), 6.96 (t, J = 7.2 Hz, 1H, Ar_2 'para'), 6.86 (dd, J = 8.8, 0.8 Hz, 2H, Ar_2 'ortho'), 5.54 (d, J = 4.0 Hz, 1H, H3), 5.38 (d, J = 6.0 Hz, 1H, H5), 4.51 (dd, J = 6, 4.0 Hz, 1H, H4), 4.17(quin, 2H, Me_2CH), 2.86 (quin, 1H, Me_2CH), 1.23 (d, J = 6.8 Hz, 6H, CH_3), 1.11 (d, J = 6.4 Hz, 6H, CH_3), 1.08 (d, J = 5.8 Hz, 6H, CH_3). ^{13}C NMR δ 152.06, 149.25, 148.78, 139.45, 137.06, 135.99, 135.34, 134.47, 129.36, 129.14, 128.97, 128.95, 128.65, 128.60, 128.07, 127.03, 126.68, 123.31, 122.61, 115.00, 85.29, 80.03, 70.21 34.10, 29.23, 24.68, 23.68, 23.63. Mass spectrum (ES+) m/z 729.4 (100%, $[M+Na]^+$), 707.3 (40, $[M+H]^+$), 601.3 (30). Anal. Calcd for $C_{42}H_{46}N_2O_4S_2$: C, 71.14; H, 6.56; N, 3.96. Found C, 71.48; H, 6.67; N, 3.91.

(4d): ^{1}H NMR δ 7.82 (dd, J = 8.4, 1.2 Hz, 2H, Ar_4 'ortho'), 7.59-7.57 (d+t, 3H, Ar_4 'para', Ar_3 'ortho'), 7.42 (d, J = 8.4 Hz, 2H, Ar_4 'meta'), 7.38 (d, J = 7.2 Hz, 2H, Ar_1 'ortho'), 7.36 (t, J = 6.8 Hz, 1H, Ar_3 para'), 7.17-7.12 (t, 2H, Ar_5 'meta'), t, 1H, Ar_5 'para'), 7.07 (d, J = 8.0 Hz, 2H, Ar_2 'meta'), 7.05 (s, 2H, Ar_1 ortho'), 6.97 (t, J = 7.6 Hz, 1H, Ar_2 'para'), 6.84 (dd, J = 8.8, 1.2 Hz, 2H, Ar_5 'ortho'), 6.75 (dd, J = 8.4, 1.2 Hz, 2H, Ar_2 'ortho'), 5.99 (d, 1H, H3), 4.74 (d, 1H, J = 5.4 Hz, H5), 4.45 (dd, 1H, J = 5.4, 4.5 Hz, H4), 4.16 (quin, 2H, Me_2CH), 2.85 (quin, 1H, Me_2CH) 1.22 (d, J = 6.9 Hz, 6H, 2 Me), 1.13 (d, J = 6.6 Hz, 6H, 2 Me), 1.03 (d, J = 6.9 Hz, 6H, 2Me). ^{13}C NMR (in part) δ 148.43, 138.32, 138.02, 135.97, 134.54, 129.55, 128.80, 128.76,

128.70, 128.30, 128.14, 84.85 (C4), 78.35 (C3), 71.12 (C5). Mass spectrum (ES+) m/z 729.2 (54%, $[M+Na]^+$) 707.2 (28, $[M+H]^+$), 601.1 (20), 287.9 (100).

(3*SR*, 4*SR*, 5*SR*, S*SR*) 2,3,5-Triphenyl-4(*N*-methyl S-phenylsulfonimidoyl)isoxazolidine (3e) and (3*RS*, 4*RS*, 5*RS*, S*SR*) 2,3,5-Triphenyl-4(*N*-methyl S-phenylsulfonimidoyl)isoxazolidine (4e). The title compounds were obtained from the reaction of the vinyl sulfoximine (**1e**) (0.209 g, 0.81 mmol) and the nitrone (0.160 g, 0.81 mmol) in $CHCl_3$ (1.5 mL) at 75-80 °C for 28 days using the general procedure described above. ^1H NMR of the crude reaction mixture showed an diastereomeric ratio of 1 : 1. The reaction was chromatographed on silica gel using 30 % ethyl acetate / hexane as eluent to give 0.160 g (43%) of a mixture of (**3e**) and (**4e**). A sample was separated by HPLC using 7.5 % EtOAc / hexane as the mobile phase to give pure samples of (**3e**) and (**4e**) as white solids.

(3e): ^1H NMR δ 7.74 (d, 2H, J = 7.5, 1.5 Hz, ArH), 7.52-7.49 (m, 3H, ArH), 7.42 (d, J = 7.8 Hz, 2H, ArH), 7.38-7.13 (m, 9H, ArH), 7.03-6.93 (m, 4H, ArH), 5.92 (d, J = 5.4 Hz, 1H, H3), 5.06 (d, J = 5.1 Hz, 1H, H5), 4.29 (t, J = 5.4 Hz, 1H, H4), 2.64 (s, 3H, CH_3). ^{13}C NMR δ 149.41, 139.79, 138.67, 137.02, 133.11, 129.99, 129.36, 128.75, 128.66, 128.47, 128.09, 127.65, 127.01, 126.80, 122.60, 115.85, 83.74, 79.85, 71.55, 29.71 (NMe), 29.29 (NMe). Mass spectrum (ES+) *m/z* 455 (100%, $[M+H]^+$), 317 (18), 258 (84).

(4e): ^1H NMR δ 7.71-7.63 (m, 4H, ArH), 7.44-7.22 (m, 8H, ArH), 7.13 (m, 3H, ArH), 7.01-6.94 (m, 5H, ArH), 5.70 (d, J = 3.9 Hz, 1H, H3), 5.36 (d, J = 7.2 Hz, 1H, H5), 4.38 (dd, J = 6.8, 4.0 Hz, 1H, H4), 2.63 (s, 3H, NMe). ^{13}C NMR δ 149.66, 141.04, 136.49, 136.26, 133.06, 129.94, 129.22, 128.94, 128.78, 128.39, 127.61, 127.03, 126.98, 122.06, 114.62, 83.65, 81.16, 70.65, 29.69 (NMe) 29.33 (NMe). Mass spectrum (ES+) *m/z* 455.7 (100%, $[M+H]^+$), 258.6 (84). HRMS (EI) calcd for $C_{28}H_{26}N_2O_2S$+H 455.179284 found 455.17934.

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