New Mechanistic Evidence on the Reaction between Sulfonylallenes and Nitrile Oxides

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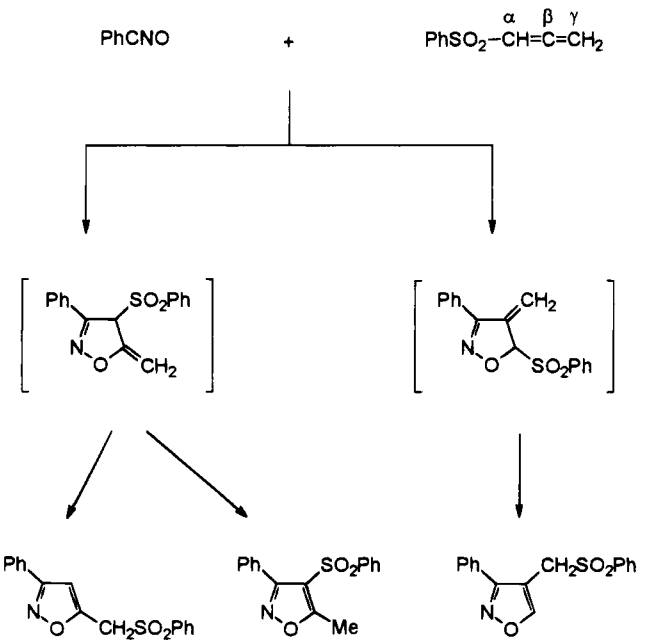
The use of allenes as dipolarophiles is receiving growing attention due to some advantages, the most important of which is that the resulting cycloadducts are versatile intermediates for synthetic purposes.[1-6] However, the dipolarophilic reactivity of the allene moiety is intrinsically modest in the absence of proper activating substituents. Among them, the sulfonyl group occupies a prominent position owing to the following features: (i) it enhances the reactivity of the cumulated double bonds,[7] (ii) it facilitates the further functionalization of the cycloadducts,[8] and (iii) it can be easily removed in the final stage of the synthetic sequence.[9] For these reasons, 1-(phenylsulfonyl)-1,2-propadiene has been advanced as the synthetic equivalent of the unreactive 1,2-propadiene.[10]

Examples of nitrile oxide cycloadditions to sulfonyl-substituted allenes have been reported independently by two research groups,[7,11] both of which found a disappointing degree of site selectivity and regioselectivity in contrast to the prediction of CNDO computations.[10] To accommodate this discrepancy, the American research group[7] has proposed a reaction pathway involving cycloaddition across the α,β double bond and subsequent 1,3-shift of the sulfonyl moiety, thus simulating a β,γ-cycloaddition (Scheme 1).

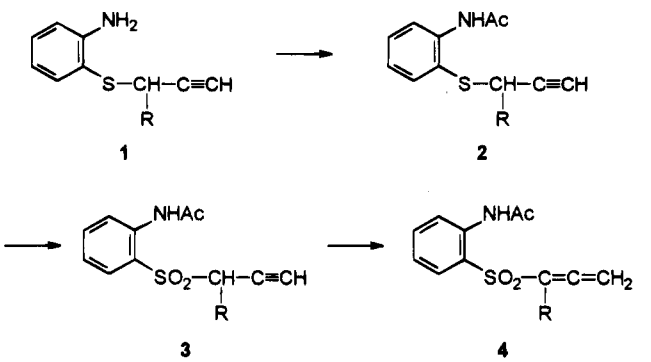
We now wish to report new results on the same subject, which confirm the previously observed trend but are not consistant with Padwa's mechanistic picture. To improve the interest of our work for synthesis, we have chosen the sulfonylallenes **4a,b**, which would have given compounds containing a masked amino group.

The desired allenes **4a,b** were synthesized through the sequence outlined in Scheme 2. Compounds **4a,b** were

Scheme 1



Scheme 2[a]



[a] **a**; R = H; **b**; R = Me.

reacted with 3,5-dichloro-2,4,6-trimethylbenzonitrile oxide (**5**) in boiling tetrachloromethane by using different proportions of the reactants (see Scheme 3). Reaction times, products, and yields are summarized in Table 1.

The distinction between the regioisomeric formulae **7** and **8** was easily made on the basis of the chemical shifts of the isoxazolinic protons, while the structures **6** and **11** were assigned upon examination of the literature data dealing with ^{1}H NMR of 5-methylisoxazoles.[12] Moreover, both **6** and **11** were obtained independently by cycloaddition of **5** to α-sulfonyl ketone **13** and 2-butyn-1-ol, respectively.

The diadduct structural assignments **9** and **10** rely upon analytical and spectral data, including ^{1}H and ^{13}C NMR. The depicted stereochemistry, although not proven with full certainty, is plausible in light of that found for similar spirobi(4,5-dihydroisoxazoles) by ^{13}C–H coupling constant correlation[13] and X-ray analysis.[5a] The unusual structure **10** was chemically confirmed by base-promoted fragmentation to give a mixture of **14** and **15**.

The above results support two mechanistic conclusions. First, the β,γ-cycloadducts **7** cannot be ascribed to the

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Scheme 3

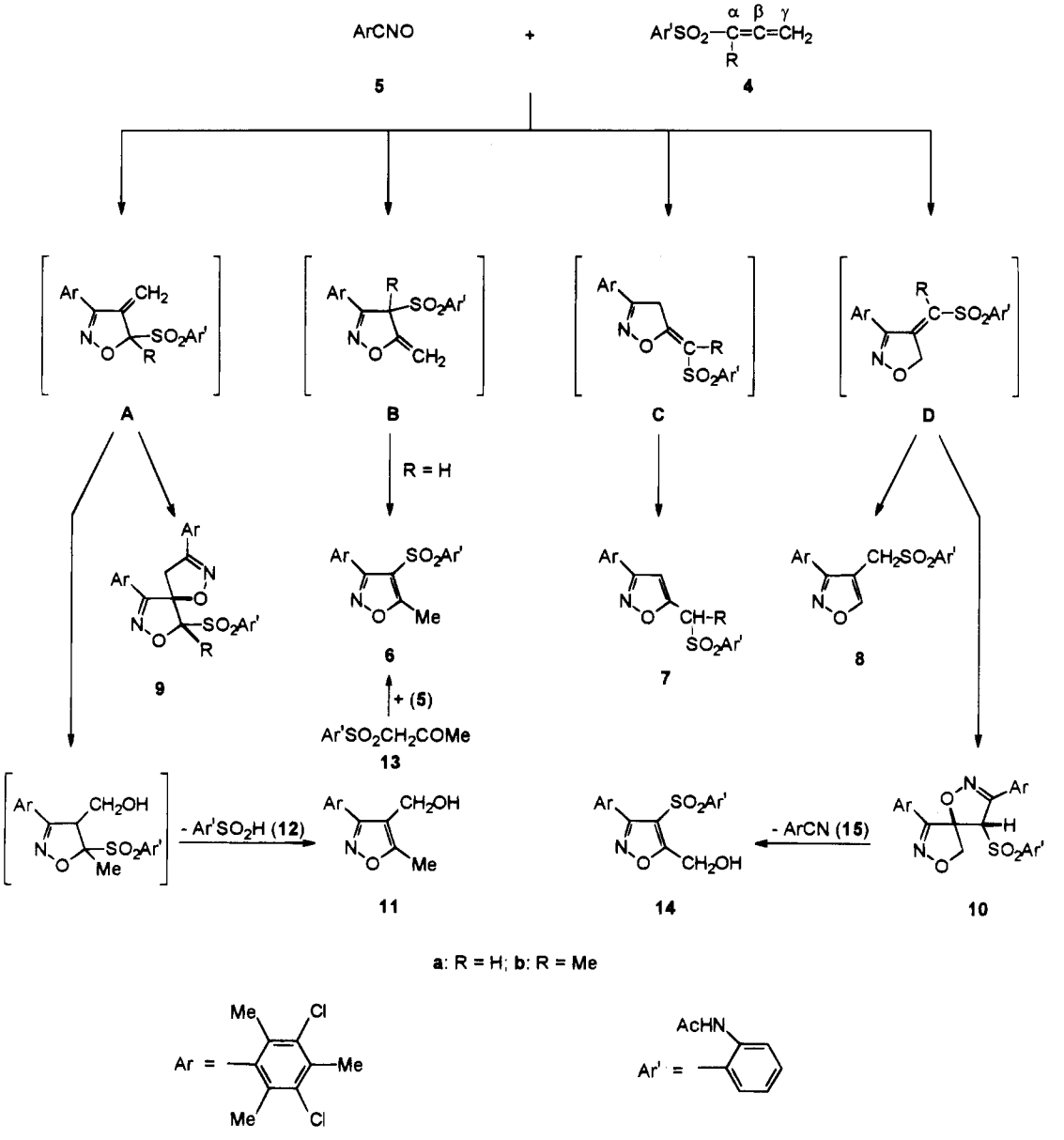

Table 1. Reaction of Nitrile Oxide 5 with Allenes 4[a]

R	molar equiv of 5	time (h)	products and yields (%)[b] 6	7	8	9	10	11	α,β:β,γ ratio[e]
H	1[c]	32	14	22	26	10			33:67
	2	24	11	29	25	8	1		26:74
	4	18	9	37	10	8	14		22:78
Me	1[c]	48		39		6		5[d]	22:78
	2	24		49		13			21:79
	4	12		56		19			35:75

[a] In boiling tetrachloromethane. [b] Isolated yield of pure compounds. [c] Some allene was recovered (10–12%). [d] The corresponding quantity of arenesulfinic acid **12** was also obtained. [e] In light of the mechanistic conclusions given in the text.

primary formation of (**B**) and subsequent 1,3-shift of the sulfonyl group because such a process would have given 3-aryl-4-methyl-5-((arylsulfonyl)methyl)isoxazole in place of the observed 3-aryl-5-(1-(arylsulfonyl)ethyl)isoxazole **7b**. Second, the formation of diadduct **10** is facilitated by an excess of nitrile oxide at the expense of monoadduct **8**, thus suggesting that **10** and **8** arise from a common precursor *via* two concurrent reactions of different kinetic order; the first-formed β,γ-cycloadduct (**D**) is the reasonable candidate for this role.

In conclusion, the present work demonstrates that (i) both of the cumulated double bonds of sulfonylallenes are reactive toward nitrile oxides and (ii) the regiochemical course for each site of cycloaddition follows from an interplay of steric and electronic factors. Since such evidence does not agree with the prediction based on the frontier orbital properties of 1-(methylsulfonyl)-1,2-propadiene,[10] it must be inferred that the FMO model is inadequate for the reaction under study, similarly to what has previously been found for nitrile oxide cycloadditions to sulfonylethylenes.[14,15] Searching for a rationalization of the observed results, one may tentatively consider two suggestions: (1) the subtle electronic effect of the sulfonyl group (which has been shown to include inductive, conjugative, and hyperconjugative components)[16–18] could markedly affect both α,β and β,γ double bonds of the allene; (2) due to the nonplanar geometry of the system under study, secondary orbital

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interactions could be operative to enhancing the reactivity of the β,γ double bond. In this context, the dipolarophilic behavior of 1,1-difluoroallene is mentioned as a significant case of β,γ-activation.[6]

Experimental Section

Melting points are not corrected. Analytical and spectroscopic instruments were as described in detail in a recent paper.[5c]

Compounds **1a**[19] and **5**[20] were prepared according to the literature methods.

3-((2-Aminophenyl)thio)butyne (1b). A mixture of sodium 2-aminothiophenoxide (2.35 g, 15.7 mmol) and 3-bromobut-1-yne[21] (2.0 g, 15.0 mmol) in EtOH (40 mL) was stirred under nitrogen for 4 h. The solvent was evaporated under reduced pressure, and the residue was poured in water (40 mL) and extracted with $CHCl_3$. The organic layer was washed with a 4% aqueous solution of NaOH, dried over Na_2SO_4, and evaporated to give 1.90 g (72%) of **1b**. Bp: 125–130 °C (0.2 mmHg). ^{1}H NMR ($CDCl_3$) δ: 1.48 (3H, d, J = 7.0 Hz), 2.33 (1H, d, J = 2.4 Hz), 3.80 (1H, dq, J = 7.0, 2.4 Hz), 4.40 (2H, br s), 6.60–6.80 (2H, m), 7.10–7.20 (1H, m), 7.40–7.50 (1H, m). IR (Nujol) 3350–3490 cm^{-1}. Anal. Calcd for $C_{10}H_{11}NS$: C, 67.76; H, 7.90; N, 24.83; S, 18.09. Found: C, 67.70; H, 7.81; N, 24.72; S, 17.90.

3-((2-(Acetylamino)phenyl)thio)propyne (2a). A solution of **1a** (2.12 g, 13.0 mmol) and Ac_2O (1.40 g, 13.7 mmol) in AcOH (10 mL) was refluxed for 20 min. The mixture was poured in water (60 mL), and the precipitate was filtered to give 1.80 g (68%) of **2a**. Mp: 73 °C (from EtOH). ^{1}H NMR ($CDCl_3$) δ: 2.27 (3H, s), 2.32 (1H, t, J = 2.5 Hz), 3.42 (2H, d, J = 2.5 Hz), 7.02–7.10 (1H, m), 7.32–7.48 (1H, m), 7.53–7.58 (1H, m), 8.38–8.42 (1H, m), 8.54 (1H, br s). IR (Nujol) 3200, 2100, 1630 cm^{-1}. Anal. Calcd for $C_{11}H_{11}NOS$: C, 64.36; H, 5.40; N, 6.82; S, 15.62. Found: C, 64.20; H, 5.46; N, 6.71; S, 15.50.

3-((2-Acetylamino)phenyl)thio)butyne (2b). A solution of **1b** (2.00 g, 11.3 mmol) and Ac_2O (1.28 g, 12.5 mmol) in AcOH (6 mL) was refluxed for 20 min. The mixture was poured in water (80 mL), and the precipitate was filtered to give 1.43 g (58%) of **2b**. Mp: 81 °C (from hexane–benzene). ^{1}H NMR ($CDCl_3$) δ: 1.48 (3H, d, J = 7.0 Hz), 2.20 (3H, s), 2.35 (1H, d, J = 2.4 Hz), 3.69 (1H, dq, J = 7.0, 2.4 Hz), 6.95–7.10 (1H, m), 7.27–7.35 (1H, m), 7.50–7.60 (1H, m), 8.32–8.45 (1H, m), 8.63 (1H, br s). IR (Nujol) 3180, 2110, 1640 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NOS$: C, 65.72; H, 5.98; N, 6.39; S, 14.62. Found: C, 65.60; H, 6.11; N, 6.46; S, 14.71.

3[(2-(Acetylamino)phenyl)sulfonyl]propyne (3a). A mixture of **2a** (5.03 g, 24.5 mmol), 30% aqueous H_2O_2 (51.0 g, 0.45 mol), and AcOH (200 mL) was warmed to 45 °C for 5 h. The mixture was poured in water/ice (500 mL), and $NaHSO_3$ was added until the excess of oxidant was completely removed. The precipitate was filtered to give 3.50 g (60%) of **3a**. Mp: 137 °C (from EtOH). ^{1}H NMR ($CDCl_3$) δ: 2.20 (3H, s), 2.35 (1H, t, J = 2.8 Hz), 3.99 (2H, d, J = 2.8 Hz), 7.15–7.28 (1H, m), 7.58–7.70 (1H, m), 7.85–7.93 (1H, m), 8.45–8.55 (1H, m), 9.62 (1H, br s). IR (Nujol) 3310, 2120, 1660 cm^{-1}. Anal. Calcd for $C_{11}H_{11}NO_3S$: C, 55.68; H, 4.67; N, 5.90; S, 13.51. Found: C, 55.79; H, 4.61; N, 5.94; S, 13.39.

3-[(2-(Acetylamino)phenyl)sulfonyl]butyne (3b). A mixture of **2b** (3.00 g, 13.7 mmol), 30% aqueous H_2O_2 (34.0 g, 0.30 mol), and AcOH (110 mL) was warmed to 45 °C for 5.5 h. The mixture was poured in water/ice (400 mL), and $NaHSO_3$ was added until the excess of oxidant was completely removed. The solvent was evaporated under reduced pressure, and the residue was taken up with water (80 mL) and extracted with CH_2Cl_2. The organic layer was washed with water, dried over Na_2SO_4, and evaporated to give 2.70 g (79%) of **3b**. Mp: 149 °C (from diisopropyl ether). ^{1}H NMR ($CDCl_3$) δ: 1.57 (3H, d, J = 7.0 Hz), 2.18 (3H, s), 2.40 (1H, d, J = 2.8 Hz), 3.95 (1H, dq, J = 7.0, 2.8 Hz), 7.10–7.25 (1H, m), 7.55–7.68 (1H, m), 7.75–7.90 (1H, m), 8.45–8.55 (1H, m), 9.75 (1H, br s). IR (Nujol) 3300, 2110, 1660 cm^{-1}. Anal. Calcd for $C_{12}H_{13}NO_3S$: C, 57.35; H, 5.21; N, 5.57; S, 12.76. Found: C, 57.23; H, 5.10; N, 5.42; S, 12.85.

1-[(2-(Acetylamino)phenyl)sulfonyl]-1,2-propadiene (4a). A solution of **3a** (2.50 g, 10.5 mmol) in benzene (200 mL) was treated with Et_3N (1.06 g, 10.5 mmol) and refluxed for 20 min. The evaporation of the solvent gave 2.27 g (91%) of **4a**. Mp: 90 °C (from hexane–benzene). ^{1}H NMR ($CDCl_3$) δ: 2.22 (3H, s), 5.47 (2H, d, J = 6.0 Hz), 6.20 (1H, t, J = 6.0 Hz), 7.10–7.14 (1H, m), 7.50–7.80 (1H, m), 7.80–8.10 (2H, m), 9.40 (1H, br s). ^{13}C NMR ($CDCl_3$) δ: 25.0 (q), 84.5 (t), 100.2 (d), 120.8–136.8, 168.5 (s), 209.5 (s). IR (Nujol) 3370, 1950, 1690 cm^{-1}. MS *m/e*: 237 (M). Anal. Calcd for $C_{11}H_{11}NO_3S$: C, 55.68; H, 4.67; N, 5.90; S, 13.51. Found: C, 55.49; H, 4.60; N, 5.74; S, 13.40.

3-[(2-(Acetylamino)phenyl)sulfonyl]-1,2-butadiene (4b). A solution of **3b** (2.01 g, 8.0 mmol) in benzene (160 mL) was treated with Et_3N (8.08 g, 80.0 mmol) and stirred at room temperature for 20 min. The evaporation of the solvent gave 1.81 g (90%) of **4b**. Mp: 66 °C (from diisopropyl ether). ^{1}H NMR ($CDCl_3$) δ: 1.88 (3H, t, J = 3.3 Hz), 2.18 (3H, s), 5.33 (2H, q, J = 3.3 Hz), 7.16–7.24 (1H, m), 7.55–7.62 (1H, m), 7.82–7.87 (1H, m), 8.40–8.45 (1H, m), 9.40 (1H, br s). ^{13}C NMR ($CDCl_3$) δ: 13.0 (q), 25.2 (q), 83.4 (t), 120.5–136.8, 168.0 (s), 207.8 (s). IR (Nujol) 3340, 1940, 1710 cm^{-1}. MS *m/e*: 251 (M). Anal. Calcd for $C_{12}H_{13}NO_3S$: C, 57.35; H, 5.21; N, 5.57; S, 12.76. Found: C, 57.20; H, 5.10; N, 5.65; S, 12.88.

Reaction of 5 with Allene 4a in a 1:1 Molar Ratio. A solution of **4a** (5.40 g, 23.0 mmol) and **5** (5.20 g, 23.0 mmol) in CCl_4 (470 mL) was refluxed for 32 h. The solvent was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with toluene–AcOEt (4/1) as eluent. The first fraction gave 1.60 g (10%) of 5-[(2-acetylamino)-phenyl)sulfonyl]-3,3′-bis(3,5-dichloro-2,4,6-trimethylphenyl)-4,5′-spirobis(4,5-dihydroisoxazole) (**9a**). Mp: 270 °C (from hexane–benzene). ^{1}H NMR ($CDCl_3$) δ: 1.89 (6H, s), 2.21 (3H, s), 2.40 (3H, s), 2.47 (3H, s), 2.51 (3H, s), 2.62 (3H, s), 3.23, 4.57 (2H, AB type, J = 19.0 Hz), 5.60 (1H, s), 7.10–7.40 (1H, m), 7.60–7.90 (1H, m), 7.90–8.10 (1H, m), 8.60–8.80 (1H, m), 9.50 (1H, br s). ^{13}C NMR ($CDCl_3$) δ: 17.2 (q), 19.1 (q), 19.6 (q), 25.1 (q), 40.9 (t), 97.3 (d), 99.8 (s), 122.7–139.8, 157.6 (s), 157.8 (s), 168.4 (s). IR (Nujol) 3400, 1700 cm^{-1}. MS *m/e*: 695 (M). Anal. Calcd for $C_{31}H_{29}Cl_4N_3O_5S$: C, 53.38; H, 4.19; Cl, 20.33; N, 6.02; S, 4.59. Found: C, 53.21; H, 4.07; Cl, 20.22, N, 5.90; S, 4.41. The second fraction contained 1.50 g (14%) of **6a** (*vide infra*). The third fraction contained 2.36 g (22%) of 5-[[(2-(acetylamino)phenyl)-sulfonyl]methyl]-3-(3,5-dichloro-2,4,6-trimethylphenyl)isoxazole (**7a**). Mp: 206 °C (from hexane–benzene). ^{1}H NMR ($CDCl_3$) δ: 2.09 (6H, s), 2.29 (3H, s), 2.58 (3H, s), 4.67 (2H, s), 6.11 (1H, s), 7.00–7.30 (1H, m), 7.50–7.80 (2H, m), 8.50–8.70 (1H, m), 9.50 (1H, br s). IR (Nujol) 3360, 1700 cm^{-1}. MS *m/e*: 466 (M). Anal. Calcd for $C_{21}H_{20}Cl_2N_2O_4S$: C, 53.97; H, 4.31; Cl, 15.17; N, 5.99; s, 6.86. Found: C, 54.11; H, 4.40; Cl, 15.23; N, 6.10; S, 6.94. The fourth fraction was chromatographed on a silica gel column with Et_2O–light petroleum ether (1/1) as eluent, obtaining 2.79 g (26%) of 4-[[(2-(acetylamino)phenyl)-sulfonyl]methyl]-3-(3,5-dichloro-2,4,6-trimethylphenyl)isoxazole (**8a**). Mp: 177 °C (from hexane–benzene). ^{1}H NMR ($CDCl_3$) δ: 2.02 (6H, s), 2.04 (3H, s), 3.93 (2H, s), 7.10–7.30 (1H, m), 7.50–7.80 (2H, m), 8.40–8.50 (1H, m), 8.57 (1H, s), 9.20 (1H, br s). IR (Nujol) 3230, 1650 cm^{-1}. MS (*m/e*: 466 (M). Anal. Calcd for $C_{21}H_{20}Cl_2N_2O_4S$: C, 53.94; H, 4.31; Cl, 15.17; N, 5.99; S, 6.86. Found: C, 53.78; H, 4.36; Cl, 15.22; N, 6.11; S, 7.00.

1-[2-((Acetylamino)phenyl)sulfonyl]-2-propanone (13). A solution of **4a** (1.00 g, 4.2 mmol) in EtOH (42 mL) was refluxed for 18 h. The solvent was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with AcOEt–light petroleum ether (3/1) as eluent, obtaining 110 mg (10%) of **13**. Mp: 96 °C (from hexane–benzene). ^{1}H NMR ($CDCl_3$) δ: 2.22 (3H, s), 2.32 (3H, s), 4.13 (2H, s), 7.21–7.26 (1H, m), 7.60–7.66 (1H, m), 7.82–7.86 (1H, m), 8.44–8.49 (1H, m), 9.39 (1H, br s). IR (Nujol) 1740 cm^{-1}. MS *m/e*: 257 (M). Anal. Calcd for $C_{11}H_{13}NO_4S$: C, 51.75; H, 5.13; N, 5.49; S, 12.56. Found: C, 51.89; H, 5.20; N, 5.44; S, 12.73.

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Reaction of 5 with Ketone 13. A solution of **5** (2.00 g, 8.7 mmol) and **13** (2.22 g, 8.7 mmol) in EtOH (350 mL) was treated with 0.2 M ethanolic NaOH (3.5 mL) and refluxed for 30 min. The solvent was partly removed under reduced pressure, and the residue was taken up with Et_2O, washed with water, and dried over sodium sulfate. After evaporation of the solvent, the residue was chromatographed on a silica gel column with benzene–AcOEt (4/1) as eluent to give 2.47 g (61%) of 4-[(2-(acetylamino)phenyl)sulfonyl]-3-(3,5-dichloro-2,4,6-trimethylphenyl)-5-methylisoxazole (**6a**). Mp: 273 °C (from hexane–benzene). ^1H NMR ($CDCl_3$) δ: 1.74 (6H, s), 2.00 (3H, s), 2.60 (3H, s), 3.05 (3H, s), 6.80–7.10 (1H, m), 7.20–7.70 (2H, m), 8.40–8.60 (1H, m), 9.30 (1H, br s). IR (Nujol) 3360, 1705 cm^{-1}. MS *m/e*: 466 (M). Anal. Calcd for $C_{21}H_{20}Cl_2N_2O_4S$: C, 53.97; H, 4.31; Cl, 15.17; N, 5.99; S, 6.86. Found: C, 53.79; H, 4.40; Cl, 15.23; N, 6.09; S, 7.00.

Reaction of 5 with Allene 4a in a 2:1 Molar Ratio. A solution of **4a** (3.00 g, 12.7 mmol) and **5** (5.82 g, 25.4 mmol) in CCl_4 (130 mL) was refluxed for 24 h. The solvent was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with Et_2O as eluent. First fractions contained 706 mg (8%) of **9a**. Subsequent fractions contained 650 mg (11%) of **6a**, 1.72 g (29%) of **7a**, and 1.48 g (25%) of **8a**. Further elution allowed for isolation of 88 mg (1%) of 4-[(2-(acetylamino)phenyl)sulfonyl]-3,3′-bis(3,5-dichloro-2,4,6-trimethylphenyl)-5,4′-spirobis(4,5-dihydroisoxazole) (**10**). Mp: 265 °C dec (from hexane–diisopropyl ether). ^1H NMR ($CDCl_3$) δ: 0.93 (3H, s), 2.19 (3H, S), 2.34 (3H, s), 2.44 (9H, s), 2.54 (3H, s), 4.94 (1H, s), 5.00, 5.65 (2H, AB type, J = 12.0 Hz), 6.70–7.00 (1H, m), 7.20–7.40 (2H, m), 8.20–8.40 (1H, m), 9.10 (1H, br s). ^{13}C NMR ($CDCl_3$) δ: 12.5–29.2, 25.2 (q), 73.3 (d), 73.4 (t), 99.8 (s), 119.5–137.7, 149.0 (s), 154.3 (s), 167.8 (s). IR (Nujol) 3450, 1720 cm^{-1}. MS *m/e*: 695 (M). Anal. Calcd for $C_{31}H_{29}Cl_4N_3O_5S$: C, 53.38; H, 4.19; Cl, 20.33; N, 6.02; S, 4.59. Found: C, 53.22; H, 4.24; Cl, 20.37; N, 6.11; S, 4.70.

Reaction of 5 with Allene 4a in a 4:1 Molar Ratio. A solution of **4a** (2.50 g, 10.5 mmol) and **5** (9.71 g, 42.0 mmol) in CCl_4 (105 mL) was refluxed for 18 h. The solvent was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with Et_2O as eluent. The following products was isolated in order of elution: **9a** (580 mg, 8%), **10** (1.02 g, 14%), **6a** (290 mg, 9%), **7a** (1.81 g, 37%), **8a** (490 mg, 10%).

Reaction of 10 with Triethylamine. A solution of **10** (200 mg, 0.29 mmol) and Et_3N (2.93 g, 29.0 mmol) in benzene (40 mL) was refluxed for 1 h. The solvent was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with CH_2Cl_2–AcOEt (3/1) to give 28 mg (45%) of nitrile **15**[22] followed by 63 mg (45%) of 4-[(2-(acetylamino)-phenyl)sulfonyl]-3-(3,5-dichloro-2,4,6-trimethylphenyl)-5-methylisoxazole (**14**). Mp: 244 °C (from diisopropyl ether). ^1H NMR ($CDCl_3$) δ: 1.69 (6H, s), 1.99 (3H, s), 2.55 (3H, s), 3.29 (1H, t, J = 7.5 Hz), 5.18 (2H, d, J = 7.5 Hz), 6.96–7.02 (1H, m), 7.35–7.43 (1H, m), 7.54–7.59 (1H, m), 8.50–8.56 (1H, m), 9.20 (1H, br s). IR (Nujol) 3330, 1690 cm^{-1}. MS *m/e*: 482 (M). Anal. Calcd for $C_{21}H_{20}Cl_2N_2O_5S$: C, 52.18; H, 4.17; Cl, 14.67; N, 5.80; S, 6.63. Found: C, 52.00; H, 4.12; Cl, 14.74; N, 5.88; S, 6.66.

Reaction of 5 with Allene 4b in a 1:1 Molar Ratio. A solution of **4b** (5.00 g, 19.9 mmol) and **5** (4.64 g, 20.0 mmol) in CCl_4 (200 mL) was refluxed for 48 h. The solvent was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with Et_2O as eluent. First fractions gave 3.73 g (39%) of 5-[1-[(2-(acetylamino)phenyl)-sulfonyl]ethyl]-3-(3,5-dichloro-2,4,6-trimethylphenyl)isoxazole (**7b**). Mp: 153 °C (from hexane–benzene). ^1H NMR ($CDCl_3$) δ: 1.85 (3H, d, J = 7.2 Hz), 2.06 (6H, s), 2.24 (3H, s), 2.53 (3H, s), 4.63 (1H, q, J = 7.2 Hz), 6.07 (1H, s), 7.13–7.34 (1H, m), 7.60–7.69 (2H, m), 8.54–8.59 (1H, m), 9.56 (1H, br s). IR (Nujol) 3375, 1710 cm^{-1}. MS *m/e*: 480 (M). Anal. Calcd for $C_{22}H_{22}Cl_2N_2O_4S$: C, 54.89; H, 4.68; Cl, 14.73; N, 5.82; S, 6.66. Found: C, 54.76; H, 4.51; Cl, 14.90; N, 5.99; S, 6.74. Subsequent fractions contained 850 mg (6%) of 5-[(2-(acetylamino)phenyl)-sulfonyl]-5-methyl-3,3′-bis(3,5-dichloro-2,4,6-trimethylphenyl)-4,5′-spirobis(4,5-dihydroisoxazole) (**9b**). Mp: 270 °C (from $CHCl_3$–Me_2CO). ^1H NMR ($CDCl_3$) δ: 1.83 (9H, s), 2.16 (3H, s), 2.44 (3H, s), 2.49 (3H, s), 2.51 (3H, s), 2.60 (3H, s), 3.28, 4.49 (2H, AB type, J = 19.5 Hz), 7.25–7.31 (1H, m), 7.70–7.75 (1H, m), 7.91–7.95 (1H, m), 8.63–8.68 (1H, m), 9.36 (1H, br s). ^{13}C NMR ($CDCl_3$) δ: 11.8–26.3, 41.7 (t), 100.4 (s), 102.9 (s), 120.6–138.5, 157.8 (s), 158.5 (s), 168.5 (s). IR (Nujol) 3405, 1726 cm^{-1}. MS *m/e*: 709 (M). Anal. Calcd for $C_{32}H_{31}C_4N_3O_5S$: C, 54.02; H, 4.39; Cl, 19.93; N, 5.91; S, 4.51. Found: C, 54.16; H, 4.47; Cl, 20.08; N, 6.02; S, 4.59. Further elution gave 300 mg (5%) of **11b** (*vide infra*) and 200 mg (5%) of **12**.[23]

Reaction of 5 with 2-Butyn-1-ol. A solution of **5** (500 mg, 2.2 mmol) and 2-butyn-1-ol (145 mg, 2.2 mmol) in CCl_4 (20 mL) was refluxed for 24 h. The solvent was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column with Et_2O as eluent, obtaining 236 mg (36%) of 4-(hydroxymethyl)-3-(3,5-dichloro-2,4,6-trimethylphenyl)-5-methylisoxazole (**11**). Mp: 146 °C (from hexane–benzene). ^1H NMR ($CDCl_3$) δ: 1.56 (1H, br s), 2.14 (6H, s), 2.55 (3H, s), 2.58 (3H, s), 4.27 (2H, s). IR (Nujol) 3430 cm^{-1}. MS *m/e*: 299 (M). Anal. Calcd for $C_{14}H_{15}Cl_2NO_2$: C, 56.02; H, 5.04; Cl, 23.62; N, 4.66. Found: C, 56.16; H, 5.11; Cl, 23.71; N, 4.79.

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