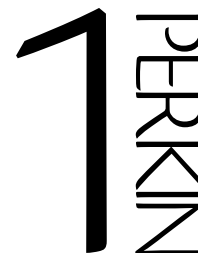


Dipolarophilic behaviour of (arylsulfonyl)allenes towards nitrilimines



Gianluigi Brogini^a and Giorgio Molteni^{*b}

^a Dipartimento di Scienze Chimiche, Fisiche e Matematiche, Università dell'Insubria, via Lucini 3, 22100 Como, Italy

^b Dipartimento di Chimica Organica e Industriale, Università di Milano, via Golgi 19, 20133 Milano, Italy

Received (in Cambridge, UK) 10th March 2000, Accepted 5th April 2000

Published on the Web 16th May 2000

The dipolarophilic behaviour of 1-[2-(acetylamino)phenylsulfonyl]propa-1,2-diene **1** towards a series of nitrilimines is here described. Mechanistic possibilities for the formation of pyrazolic products **4–7** are discussed.

Introduction

Owing to the presence of two cumulative unsaturations, allenes¹ are interesting dipolarophiles.² In fact, both C=C bonds are suitable positions for dipolar attack which can proceed with two opposite orientations. Hence, both site- and regioselectivity are involved in their cycloadditions.

The dipolarophilic behaviour of arylsulfonylallenes with nitrilium betaines has been extensively investigated in the field of nitrile oxide cycloadditions.³ Conversely, nitrile imines were only the object of occasional reports,^{3c,4} as recently stated.² Aiming to acquire a better understanding of this subject, we examined the reaction between 1-[2-(acetylamino)phenylsulfonyl]propa-1,2-diene **1**^{3b} and a series of properly substituted nitrilimines.

Results and discussion

Among the hydrazoneyl chlorides **2**, which we devised as precursors of the desired nitrilimines, substrates **2a,b,d,e** were synthesised as previously reported,⁵ while the new substrates **2c,f** were synthesised in an analogous manner as depicted in Scheme 1.

The *in situ* generation of nitrilimines was accomplished in the presence of **1** by treating the appropriate hydrazoneyl chloride with a two-fold molar excess of silver carbonate in dry 1,4-dioxane at room temperature. The choice of such an unconventional basic agent in the place of more common organic bases, like triethylamine or DABCO,⁶ comes from

the following considerations: (i) the allene \rightarrow acetylene isomerisation is suppressed under these conditions; (ii) room temperature and heterogeneous reaction medium allow a smooth generation of the nitrilimine, so minimising the degradative processes of the 1,3-dipole.

Cycloaddition reactions were carried out by using different proportions of the reactants, which are summarised in Table 1 along with reaction times, products, eluents and yields. When using a 2:1 molar ratio between a hydrazoneyl chloride **2** and the allene **1**, shorter reaction times and yield enhancement of cycloaddition products **4** and **5** were observed. Some quantity of the starting allene **1** was always recovered.

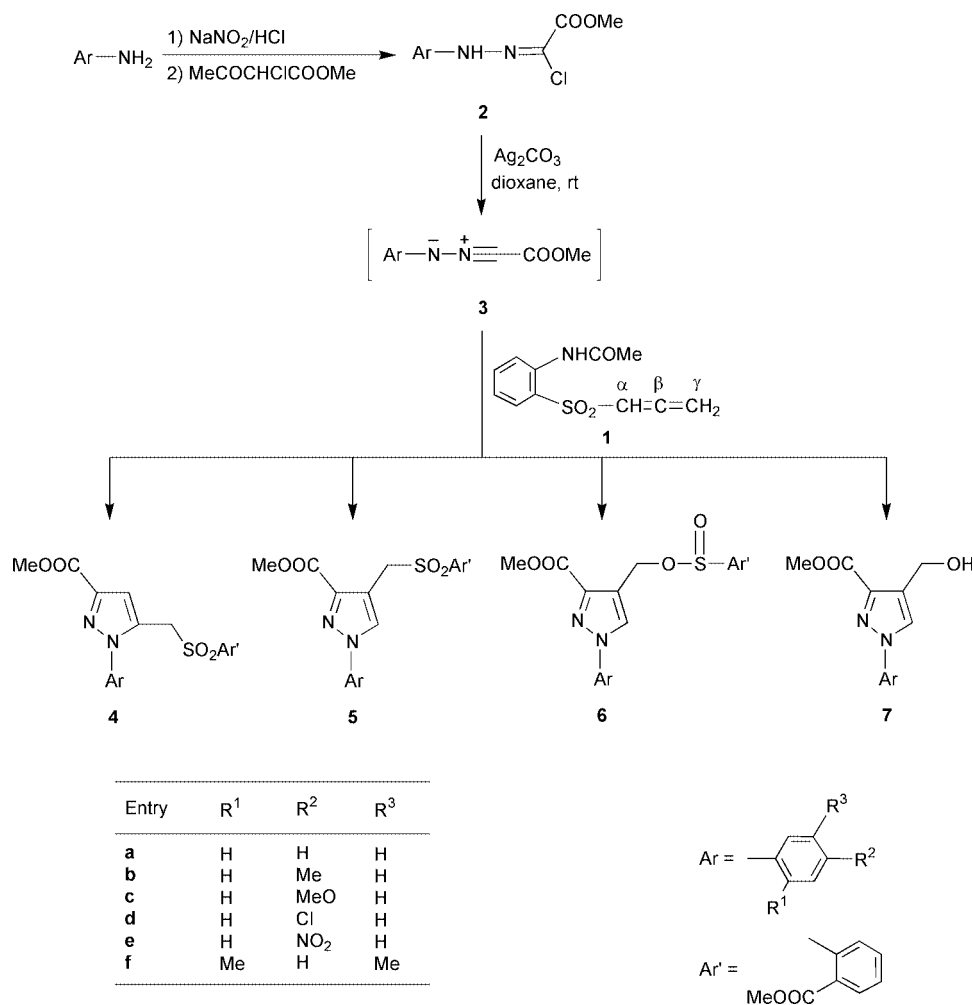
The regioisomeric formulae of **4** and **5** were distinguished on the basis of ¹H NMR chemical shifts of the pyrazolic hydrogens,⁷ while the 1-aryl-4-hydroxymethyl-3-(methoxycarbonyl)-pyrazole structure **7** was assigned based upon analytical and spectral data. The sulfinic ester **6f**, which was fully characterised, was shown to undergo a complete conversion to **7f** under mild hydrolytic conditions (aq. HCl–1,4-dioxane, rt). Such lability plausibly justifies the lack of isolation of analogous intermediates **6a–e** in the other cases.

The experimental findings can be accounted for by two independent mechanistic hypotheses. The first one, which is outlined in Scheme 2, implies competitive cycloadditions of nitrilimines **3** across the α,β and the β,γ positions, in analogy with the behaviour of **1** towards 2,4,6-trimethyl-3,5-dichloro benzonitrile oxide.^{3b} According to this picture, the primary cycloadducts **A** and **B** give pyrazoles **4** and **5**, respectively, *via* 1,3-prototropic shift facilitated by the basic medium. Such a

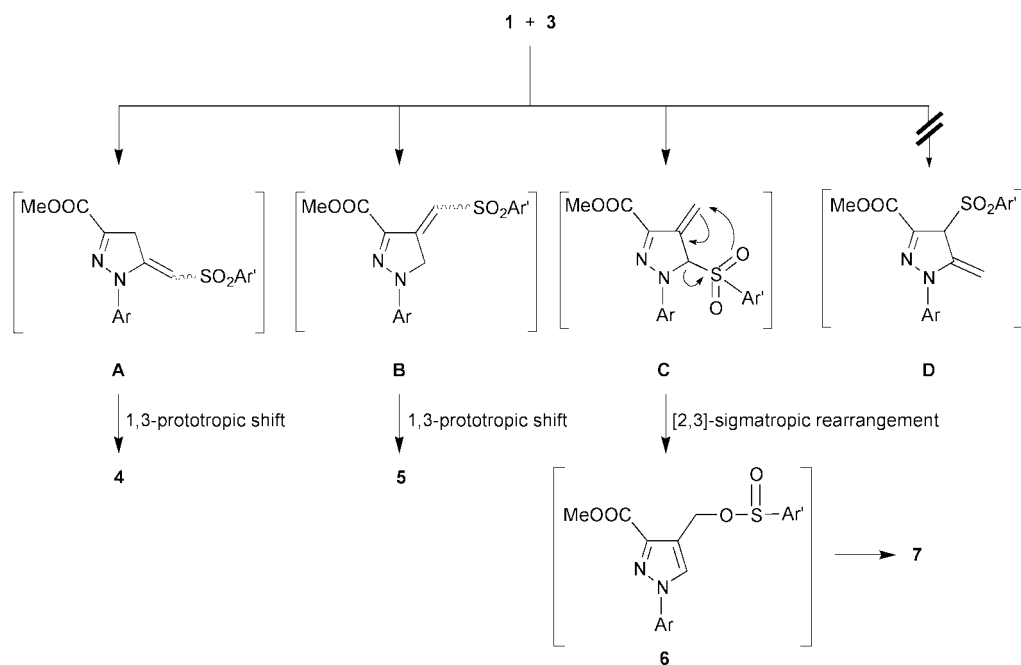
Table 1 Reaction of hydrazoneyl chlorides **2** with the allene **1**^a

Entry	Molar equiv. of 2	t/h	Products and Yields (%)					$\alpha,\beta:\beta,\gamma$ ratio ^a	Eluent ^b
			1	4	5	6	7		
a	1	67	44	18	8		20	43:57	Et ₂ O
	2	28	30	22	23		8	15:85	Et ₂ O
b	1	120	54	16	7		12	34:66	Et ₂ O–LP (9:1)
	2	48	32	26	20			0:100	CH ₂ Cl ₂ –Et ₂ O (4:1)
c	1	140	47	18	11		18	38:62	Et ₂ O–LP (9:1)
	2	48	27	26	12		15	28:72	Et ₂ O
d	1	96	70	8	1		3	25:75	Et ₂ O–LP (9:1)
e	1	170	80						
f	1	160	40	12	14	17		40:60	Et ₂ O–LP (9:1)

^a At rt (20 °C). ^b In light of the mechanistic pathway outlined in Scheme 2. ^c LP = light petroleum (distillation range 40–60 °C).



Scheme 1



Scheme 2

mechanism, however, does not provide a convincing rationalisation of the very variable α,β,γ ratio (Table 1), since the latter was roughly constant in the case of nitrile oxide cyclo-additions.^{3b}

The second mechanistic pathway requires the α,β position as the exclusive site for dipolar attack (see Scheme 3), and reflects

the expectations based upon early CNDO computations on (methylsulfonyl)allene.⁸ By performing PM3 calculations⁹ on the allene **1**,¹⁰ we found that the LUMO atomic coefficients of the α and β carbons are only slightly different (+0.33 on the α carbon and -0.43 on the β carbon, see Fig. 1), so allowing the formation of both regioisomers **C** and **D**. Within this pathway,

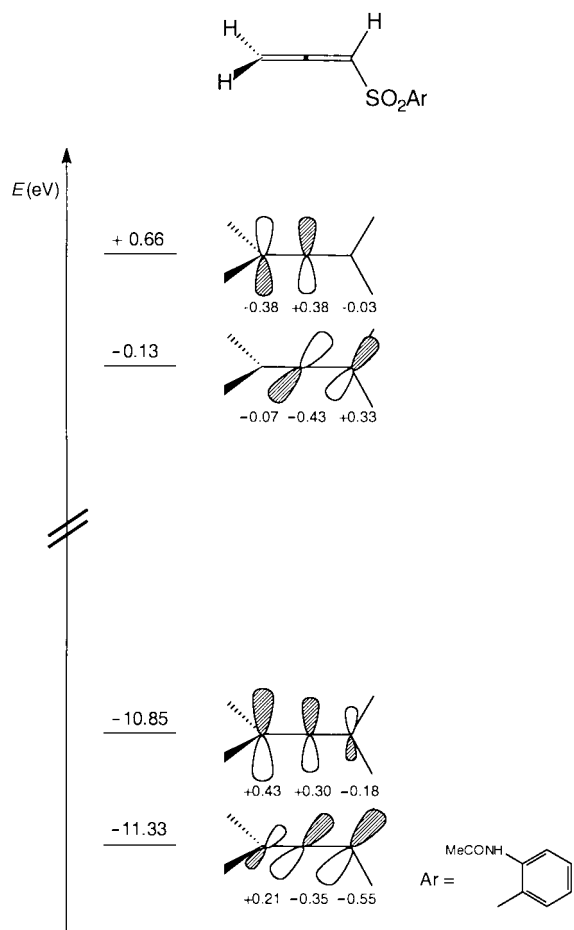
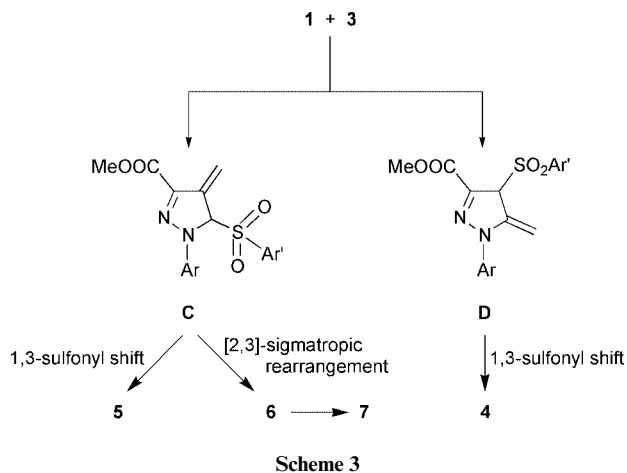


Fig. 1 Frontier molecular orbitals of the allene **1** calculated by the PM3 method.



the final pyrazoles **4** and **5** would originate from **C** and **D** via 1,3-allylic shift of the sulfonyl group.^{3c,11} Such a mechanism suggests that the ratio of **5** to **7** should be very sensitive to pH and solvent, but it also predicts that the ratio of **4** to **5** + **7** should be constant, and this is not the case.

Irrespective of the above mechanistic hypothesis, the formation of the sulfinic esters **6** can be rationalised by invoking a [2,3]sigmatropic rearrangement of cycloadduct **C** via a sulfur-to-oxygen bond migration.¹²

As a final remark, it can be stated that the mechanistic pictures outlined in Schemes 2 and 3 are only partly in accord with experimental results. However, we note that the course of cycloaddition is strongly dependent on the electronic nature of the 1,3-dipole. While electron-rich nitrilimines gave good results, the cycloaddition pathway appeared impervious with

Table 2 Elemental analyses of compounds **4**, **5**, **6f** and **7**

Compound (Formula)	Found (%) (Required)				
	C	H	Cl	N	S
4a (C ₂₀ H ₁₉ N ₃ O ₅ S)	58.03 (58.10)	4.61 (4.64)		10.11 (10.17)	7.69 (7.74)
4b (C ₂₁ H ₂₁ N ₃ O ₅ S)	59.09 (59.00)	4.91 (4.96)		9.78 (9.84)	7.56 (7.49)
4c (C ₂₁ H ₂₁ N ₃ O ₆ S)	56.80 (56.87)	4.77 (4.78)		9.44 (9.48)	7.16 (7.22)
4d (C ₂₀ H ₁₈ ClN ₃ O ₅ S)	53.74 (53.68)	4.04 (4.06)	7.77 (7.82)	9.43 (9.40)	7.21 (7.15)
4f (C ₂₂ H ₂₃ N ₃ O ₅ S)	59.88 (59.85)	5.22 (5.25)		9.50 (9.52)	7.32 (7.25)
5a (C ₂₀ H ₁₉ N ₃ O ₅ S)	58.15 (58.10)	4.66 (4.64)		10.15 (10.17)	7.78 (7.74)
5b (C ₂₁ H ₂₁ N ₃ O ₅ S)	59.01 (59.00)	4.96 (4.96)		9.88 (9.84)	7.56 (7.49)
5c (C ₂₁ H ₂₁ N ₃ O ₆ S)	56.92 (56.87)	4.81 (4.78)		9.51 (9.48)	7.14 (7.22)
5d (C ₂₀ H ₁₈ ClN ₃ O ₅ S)	53.73 (53.68)	4.07 (4.06)	7.93 (7.82)	9.41 (9.40)	7.21 (7.15)
5f (C ₂₂ H ₂₃ N ₃ O ₅ S)	59.88 (59.85)	5.23 (5.25)		9.49 (9.52)	7.20 (7.25)
6f (C ₂₂ H ₂₃ N ₃ O ₅ S)	59.85 (59.85)	5.21 (5.25)		9.50 (9.52)	7.32 (7.25)
7a (C ₁₂ H ₁₂ N ₂ O ₃)	63.02 (62.05)	5.23 (5.21)		12.11 (12.07)	
7b (C ₁₃ H ₁₄ N ₂ O ₃)	63.43 (63.39)	5.69 (5.73)		11.41 (11.38)	
7c (C ₁₃ H ₁₅ N ₂ O ₄)	59.33 (59.29)	5.75 (5.75)		10.71 (10.64)	
7d (C ₁₂ H ₁₁ ClN ₂ O ₃)	54.10 (54.13)	4.15 (4.17)	13.08 (13.14)	10.57 (10.53)	
7f (C ₁₄ H ₁₆ N ₂ O ₃)	64.62 (64.59)	6.22 (6.20)		10.84 (10.77)	

electron-poor nitrilimines: recovery of considerable amounts of unchanged allene **1** and very poor product yields were the rule here. These disappointing results are, however, explained in the light of the HOMO-dipole-controlled nature of these cycloadditions onto an electron-deficient dipolarophile.¹³

Experimental

Mps were determined with a Büchi apparatus and are uncorrected. IR spectra were recorded with a Perkin-Elmer 1725X spectrophotometer. Mass spectra were determined with a VG-70EQ apparatus. ¹H NMR spectra were taken with a Bruker AC 300 instrument for samples in CDCl₃ solution; chemical shifts are given as ppm from tetramethylsilane, *J*-values are given in Hz. All new compounds **4**–**7** gave satisfactory elemental analyses, which are given in Table 2.

General procedure for the preparation of hydrazoneyl chlorides **2c,f**

A solution of the properly substituted aniline (15 mmol) in a mixture of water (25 cm³) and methanol (15 cm³) was treated with hydrochloric acid (10 mol dm⁻³, 4.5 cm³) and then cooled to 0 °C. Sodium nitrite (15 mmol) as a solution in water (5 cm³) was added dropwise to the cooled and stirred reaction mixture. After 30 min, the cold mixture was adjusted to pH 5 with sodium acetate and then a solution of methyl 2-chloroacetate (15 mmol) in methanol (15 cm³) was added with cooling and stirring of the mixture, which was stirred overnight at room temperature and then extracted with diethyl ether. The organic layer was washed with aq. sodium hydrogen carbonate, dried over sodium sulfate and evaporated. Recrystallisation from diisopropyl ether gave the pure hydrazoneyl chloride in 67% (**2c**) or 91% (**2f**) yield.

Compound **2c** (2.11 g, 67%), mp 102 °C (from diisopropyl ether) (Found: C, 49.66; H, 4.62; Cl, 14.56; N, 11.65. C₁₀H₁₁-

Table 3 Physical and spectral data of compounds **4**, **5**, **6f** and **7a–d**

Compd.	Mp/°C	ν_{\max} /cm ⁻¹	δ_{H}	m/z (M ⁺)
4a	152 ^a	3370, 1730, 1705	2.00 (3H, s), 3.90 (3H, s), 4.45 (2H, s), 6.95 (1H, s), 7.00–8.60 (9H, m), 9.25 (1H, br s)	413
4b	165 ^b	3345, 1715, 1700	2.05 (3H, s), 2.40 (3H, s), 3.95 (3H, s), 4.45 (2H, s), 6.95 (1H, s), 7.00–8.60 (8H, m), 9.25 (1H, br s)	427
4c	125 ^a	3350, 1730, 1700	2.05 (3H, s), 3.85 (3H, s), 3.90 (3H, s), 4.40 (2H, s), 6.90 (1H, s), 7.00–8.60 (8H, m), 9.25 (1H, br s)	443
4d	168 ^a	3340, 1745, 1680	2.10 (3H, s), 3.95 (3H, s), 4.45 (2H, s), 6.90 (1H, s), 7.10–8.60 (8H, m), 9.20 (1H, br s)	447
4f	160 ^c	3370, 1730, 1710	1.85 (3H, s), 2.05 (3H, s), 2.25 (3H, s), 3.92 (3H, s), 4.30 (2H, d, J_{AB} 10.5), 6.92 (1H, s), 7.01–8.60 (7H, m), 9.30 (1H, br s)	441
5a	201 ^b	3360, 1720, 1700	2.20 (3H, s), 3.80 (3H, s), 4.80 (2H, s), 7.00–7.80 (8H, m), 7.95 (1H, s), 8.40–8.65 (1H, m), 9.45 (1H, br s)	413
5b	187 ^a	3380, 1715, 1700	2.20 (3H, s), 2.40 (3H, s), 3.85 (3H, s), 4.80 (2H, s), 7.00–7.80 (7H, m), 7.90 (1H, s), 8.50–8.60 (1H, m), 9.48 (1H, br s)	427
5c	170 ^c	3355, 1720, 1700	2.18 (3H, s), 3.80 (3H, s), 3.85 (3H, s), 4.75 (2H, s), 6.80–7.80 (7H, m), 7.85 (1H, s), 8.45–8.65 (1H, m), 9.50 (1H, br s)	443
5d	208 ^b	3370, 1720, 1700	2.20 (3H, s), 3.90 (3H, s), 4.80 (2H, s), 7.00–7.85 (7H, m), 7.90 (1H, s), 8.55–8.60 (1H, m), 9.50 (1H, br s)	447
5f	168 ^a	3360, 1715, 1700	2.15 (3H, s), 2.28 (3H, s), 2.35 (3H, s), 3.85 (3H, s), 4.80 (2H, s), 6.95–7.80 (6H, m), 7.82 (1H, s), 8.45–8.60 (1H, m), 9.55 (1H, br s)	441
6f	104 ^b	3350, 1720, 1710, 1120	2.08 (3H, s), 2.20 (3H, s), 2.34 (3H, s), 3.94 (3H, s), 5.20 (2H, d, J_{AB} 12.0), 6.90–7.80 (6H, m), 7.88 (1H, s), 8.15–8.35 (1H, m), 9.60 (1H, br s)	441
7a	91 ^a	3370, 1715	3.85 (1H, br s), 3.95 (3H, s), 4.75 (2H, s), 6.90–7.80 (5H, m), 7.85 (1H, s)	232
7b	84 ^b	3365, 1715	2.30 (3H, s), 3.45 (1H, br s), 3.95 (3H, s), 4.70 (2H, s), 6.80–7.60 (4H, m)	246
7c	133 ^a	3355, 1720	3.40 (1H, br s), 3.82 (3H, s), 3.98 (3H, s), 4.72 (2H, s), 6.90–7.70 (4H, m)	263
7d	95 ^b	3485, 1705	3.99 (3H, s), 4.10 (1H, br s), 4.75 (2H, s), 7.40–7.70 (4H, m), 7.88 (1H, s)	266
7f	89 ^a	3370, 1715	2.11 (3H, s), 2.22 (3H, s), 3.50 (1H, br s), 3.90 (3H, s), 4.72 (2H, s), 6.95–7.60 (3H, m), 7.82 (1H, s)	260

^a From diisopropyl ether. ^b From hexane–benzene. ^c From diisopropyl ether–propan-2-ol.

ClN₂O₃ requires C, 49.58; H, 4.58; Cl, 14.45; N, 11.57%; ν_{\max} (Nujol)/cm⁻¹ 3260, 1700; δ_{H} 3.80 (3H, s), 3.90 (3H, s), 6.90–7.20 (4H, m), 8.30 (1H, br s); m/z (EI) 242 (M⁺).

Compound **2f** (3.28 g, 91%), mp 112 °C (from diisopropyl ether) (Found: C, 55.09; H, 5.49; Cl, 14.65; N, 11.60. C₁₁H₁₃ClN₂O₂ requires C, 54.89; H, 5.44; Cl, 14.73; N, 11.64%); ν_{\max} (Nujol)/cm⁻¹ 3250, 1710; δ_{H} 2.25 (3H, s), 2.35 (3H, s), 3.95 (3H, s), 6.70–7.40 (3H, m), 8.25 (1H, br s); m/z (EI) 240 (M⁺).

General procedure for the reaction between the allene **1** and hydrazonoyl chlorides **2** in a 1 : 1 molar ratio

A solution of the allene **1** (1.19 g, 5 mmol) and a hydrazonoyl chloride **2** (5 mmol) in dry 1,4-dioxane (25 cm³) was treated with silver carbonate (2.76 g, 10 mmol). The mixture was stirred at room temperature in the dark for the time indicated in Table 1. The undissolved material was filtered off, the solvent was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column. Products, eluents and yields are collected in Table 1. Physical and spectral data of compounds **4**, **5**, **6f** and **7a–d,f** are collected in Table 3.

General procedure for the reaction between allene **1** and hydrazonoyl chlorides **2a–c** in a 1 : 2 molar ratio

A solution of the allene **1** (1.19 g, 5 mmol) and hydrazonoyl chlorides **2a–c** (10 mmol) in dry 1,4-dioxane (25 cm³) was treated with silver carbonate (2.76 g, 10 mmol). The mixture was stirred at room temperature in the dark for the time indicated in Table 1. The undissolved material was filtered off, the solvent was evaporated under reduced pressure, and the residue was chromatographed on a silica gel column. Products, eluents and yields are collected in Table 1. Physical and spectral data of compounds **4**, **5** and **7** are collected in Table 3.

Treatment of the allene **1** with silver carbonate in 1,4-dioxane

A solution of the allene **1** (1.19 g, 5 mmol) in dry 1,4-dioxane (25 cm³) was treated with silver carbonate (2.76 g, 10 mmol). The mixture was stirred at room temperature in the dark and

periodically monitored by ¹H NMR. After 200 h the undissolved material was filtered off, the filtrate was dried over sodium sulfate, and the solvent was evaporated under reduced pressure. The unchanged allene was quantitatively recovered.

Acidic hydrolysis of **6f**

A solution of **6f** (0.2 g, 0.5 mmol) in 1,4-dioxane (5 cm³) was treated under stirring with hydrochloric acid (10 mol dm⁻³; 0.1 cm³) for 6 h at room temperature. The mixture was dried over sodium sulfate and the solvent was removed under reduced pressure. The residue was chromatographed on a silica gel column with diethyl ether as eluent. First fractions gave 1-(2,5-dimethylphenyl)-4-hydroxymethyl-3-(methoxycarbonyl)pyrazole **7f** (83 mg, 64%). Further elution gave 2-(acetyl-amino)benzenesulfinic acid¹⁴ (35 mg, 35%).

Treatment of 4-hydroxymethyl-3-methoxycarbonyl-1-phenylpyrazole **7a** with silver carbonate in 1,4-dioxane

A solution of **7a** (210 mg, 0.91 mmol) in dry 1,4-dioxane (5.0 cm³) was treated with silver carbonate (500 mg, 1.82 mmol). The mixture was stirred at room temperature in the dark and periodically monitored by ¹H NMR. After 240 h the undissolved material was filtered off, the filtrate was dried over sodium sulfate, and the solvent was evaporated under reduced pressure. Unchanged **7a** was quantitatively recovered.

Acknowledgements

We thank MURST and CNR for financial support. We are grateful to Prof. Luisa Garanti and to Prof. Gaetano Zecchi for helpful suggestions.

References

- (a) W. Runge, in *The Chemistry of Allenes*, ed. S. R. Landor, Academic Press, New York, 1982; (b) W. Runge, in *The Chemistry of Ketenes, Allenes and Related Compounds*, ed. S. Patai, Wiley, New York, 1980; (c) H. F. Schuster and G. M. Coppola, *Allenenes in Organic Synthesis*, Wiley, New York, 1984.

- 2 G. Brogini and G. Zecchi, *Gazz. Chim. Ital.*, 1996, **126**, 479.
- 3 (a) L. Bruché, M. L. Gelmi and G. Zecchi, *J. Org. Chem.*, 1985, **50**, 3206; (b) G. Brogini, G. Molteni and G. Zecchi, *J. Org. Chem.*, 1994, **59**, 8271; (c) A. Padwa, S. P. Craig, U. Chiacchio and D. N. Kline, *J. Org. Chem.*, 1988, **53**, 2232.
- 4 L. Bruché and G. Zecchi, *J. Heterocycl. Chem.*, 1983, **20**, 1705.
- 5 Compound **2a**: R. Fusco and R. Romani, *Gazz. Chim. Ital.*, 1946, **76**, 419. Compounds **2b,d**: M. M. El-Abadelah, A. Q. Hussein, M. R. Kamal and K. H. Al-Adhami, *Heterocycles*, 1988, **27**, 917. Compound **2e**: M. T. Cocco, A. Maccioni and A. Plumitallo, *Farmaco, Ed. Sci.*, 1985, **40**, 272.
- 6 (a) P. K. Claus, in *Methoden der Organischen Chemie (Houben-Weil)*, ed. D. Klamann and H. Hagemann, Georg Thieme Verlag, Stuttgart, 1990, Band E14b, Teil 1, pp. 33–73; (b) A. S. Shawali and C. Párkányi, *J. Heterocycl. Chem.*, 1980, **17**, 833.
- 7 T. J. Batterham, *NMR Spectra of Simple Heterocycles*, Wiley, New York, 1973.
- 8 K. Hayakawa, N. Nishiyama and K. Kanematsu, *J. Org. Chem.*, 1985, **50**, 512.
- 9 J. J. P. Stewart, *J. Comput. Chem.*, 1989, **10**, 209, 221.
- 10 As implemented in the HyperChem Professional 5.1 version, Hypercube, Inc., 1998.
- 11 F. G. Bordwell and G. A. Pagani, *J. Am. Chem. Soc.*, 1975, **97**, 118.
- 12 S. Braverman, in *Chemistry of Sulphones and Sulphoxides*, ed. S. Patai, John Wiley and Sons, New York, 1998, p. 670.
- 13 (a) P. Caramella and P. Grünanger, in *1,3-Dipolar Cycloaddition Chemistry*, ed. A. Padwa, Wiley-Interscience, New York, vol. 1, p. 291; (b) P. Caramella and K. N. Houk, *J. Am. Chem. Soc.*, 1976, **98**, 6397.
- 14 G. Pappalardo, *Gazz. Chim. Ital.*, 1963, **93**, 630.