New Carbon–Carbon Bond Formation by the Pummerer-type Reaction of Vinylic Sulphoxides with Allylmagnesium Bromide

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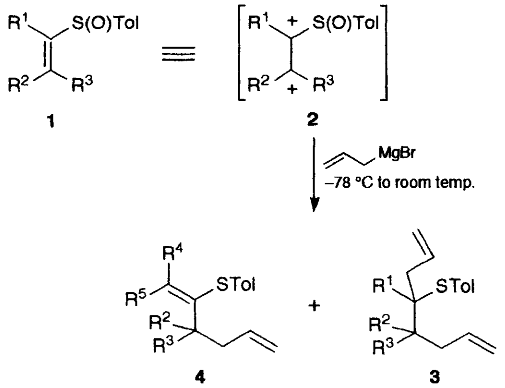
Vinylic sulphoxides underwent Pummerer-type reactions with allylmagnesium bromide to give diallylated sulphides together with monoallylated vinylic sulphides.

1,4-Conjugate addition to vinylic sulphoxides is an attractive method for carbon–carbon bond formation because of the potential applicability to asymmetric synthesis using sulphinyl chirality.[1] Carbon nucleophiles, however, are generally less reactive to vinylic sulphoxides, except for the malonate anion.[1i] In order to overcome this problem, two representative solutions have been employed. One of them, developed by Posner and coworkers,[1j] is based on the activation of the alkene unit by substitution with another electron-withdrawing group such as a ketone or an ester. The other approach is the Pummerer-type reaction,[2] which is initiated by the attack of an electrophile on the nucleophilic oxygen atom of the sulphinyl group to give a highly reactive intermediate. As a result, the electrophilicity of the position β to the sulphinyl group is enhanced and the nucleophilic attack becomes easier. Another aspect of the Pummerer-type reaction is the formation of an α,β-disubstituted sulphide along with cleavage of the S–O bond, *i.e.* vinylic sulphoxides act as a 1,2-dication equivalent, as shown in Scheme 1.

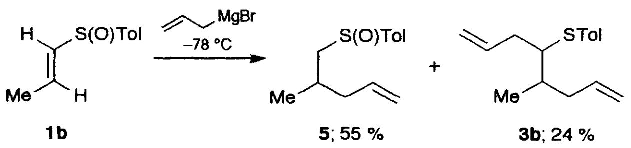
In this communication, we report the first successful Pummerer-type reaction of vinylic sulphoxides with allylmagnesium bromide providing synthetically versatile α- and β-allylated sulphides.

(*E*)-1-(*p*-Tolylsulphinyl)propene **1b** reacted with a large excess of allylmagnesium bromide in diethyl ether at −78 °C to give 4-methyl-5-(*p*-tolylsulphinyl)pent-1-ene **5** and 5-methyl-4-(*p*-tolylthio)octa-1,7-diene **3b** in 55 and 24% yields, both as diastereoisomeric mixtures (Scheme 2).

The minor unexpected product **3b** is especially attractive, since the vinylic sulphoxide reacted as a 1,2-dication equivalent and two versatile allyl groups were introduced at once. We examined the conditions suitable for diallylation.



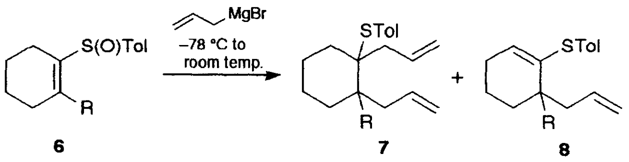
Scheme 1 Tol = p-MeC$_6$H$_4$



Scheme 2

After a few fruitless examinations, we found that diallylation occurred exclusively when the temperature was raised from −78 °C to room temperature. We applied these conditions to other acyclic vinylic sulphoxides to examine the limitation of this reaction. For several acyclic vinylic sulphoxides, the Pummerer-type reaction proceeded in fair yields. An α-substituted vinylic sulphoxide provided a diallylated compound along with a vinylic sulphide. The results are summarized in Table 1.

The general procedure for diallylation is followed. A solution of allylmagnesium bromide (6 equiv.) in dry diethyl ether was added to a solution of the vinylic sulphoxide in dry diethyl ether with stirring at −78 °C under N$_2$. The resulting mixture was stirred at −78 °C for 30 min, allowed to reach room temperature, and stirred for an additional 6–12 h. Work-up and purification by column chromatography gave the products.



Scheme 3

Table 1 The Pummerer-type reaction of the acyclic vinylic sulphoxides **1** with allylmagnesium bromide

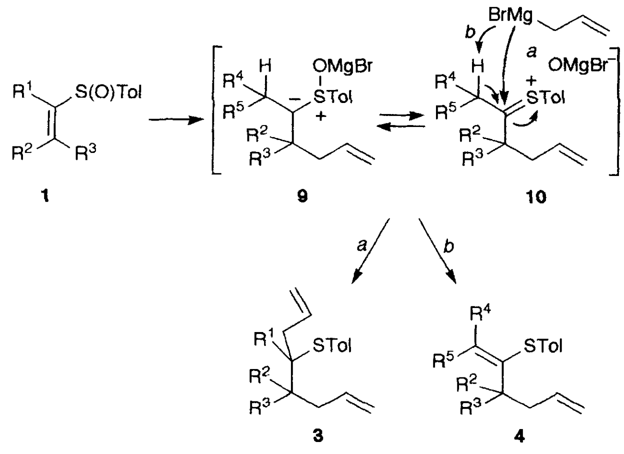
	Compound 1			Yield (%)[a]	
	R^1	R^2	R^3	**3**	**4** (R^4 = R^5 = H)
a	H	H	H	44	—
b	H	Me	H	85[b]	—
c	H	H	Me	87[c]	—
d	H	Ph	H	78[b]	—
e	H	H	Ph	78[c]	—
f	Me	Ph	H	43[c]	18

[a] The stereochemistry of the diastereoisomers was not determined. [b] The ratio of diastereoisomers measured by ^{1}H NMR spectroscopy (500 MHz) was 3 : 2. [c] The ratio of diastereoisomers measured by ^{1}H NMR spectroscopy (500 MHz) was 1 : 1.

Table 2 The Pummerer-type reaction of the cyclic vinylic sulphoxides **6** with allylmagnesium bromide

	Compound **6** R	Yield (%)[a] (**7** + **8**)	Ratio **7** : **8**[b]	(diastereoisomer ratio of **7**)
a	H	80	81 : 19	(6 : 5)
b	Me	78	54 : 46	(2 : 1)
c	CH$_2$CH$_2$CH=CH$_2$	88	39 : 61	(2 : 1)
d	CHMe(OMe)	83	33 : 67	(—)

[a] The stereochemistry of the products was not determined. The two compounds could be separated by silica gel chromatography. [b] Determined by 500 MHz ^{1}H NMR spectroscopy.



Scheme 4

The Pummerer-type reaction also proceeded in good yields with cyclic vinylic sulphoxides to give diallylated compounds and vinylic sulphides (Scheme 3). As the β-substituent (R) became bulkier, the proportion of vinylic sulphide increased. The results are shown in Table 2.

We suggest the following mechanism. The initially formed ylide **9** gives the sulphonium cation **10** by cleavage of the S–O bond. Attack of the Grignard reagent on the α-position affords the diallylated compound (pathway *a*). Alternatively, increase of the steric hindrance of the β-substituent prevents the second approach of the Grignard reagent. As a result, the Grignard reagent acts as a base and the product from pathway *b* predominates (Scheme 4). The determination of the stereochemistry of the process and its application to natural product synthesis are in progress.

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References

1 Other examples of asymmetric induction using sulphinyl chirality: *Diels–Alder reaction*: (*a*) T. Koizumi, *J. Synth. Org. Chem., Jpn.*, 1986, **44**, 576; *1,3-Dipolar reaction*: (*b*) T. Koizumi, H. Hirai and E. Yoshii, *J. Org. Chem.*, 1982, **47**, 4004; (*c*) T. Takahashi, T. Hagi, K. Kitano, Y. Takeuchi and T. Koizumi, *Chem. Lett.*, 1989, 593; (*d*) T. Takahashi, K. Kitano, T. Hagi, H. Nihonmastu and T. Koizumi, *Chem. Lett.*, 1989, 597; *Conjugate addition*: (*e*) with amines: D. J. Abbott, S. Colonna and C. J. M. Stirling, *Chem. Commun.*, 1971, 471; (*f*) with amides: S. G. Pyne and S. L. Chapman, *J. Chem. Soc., Chem. Commun.*, 1986, 1688; (*g*) with alkoxides: C. Iwata, M. Fujita, K. Hattori, S. Uchida and T. Imanishi, *Tetrahedron Lett.*, 1985, **26**, 2221; (*h*) C. Iwata, M. Fujita, Y. Moritani, K. Hattori and T. Imanishi, *Tetrahedron Lett.*, 1987, **28**, 3135; (*i*) with malonate anions: G. Tsuchihashi, S. Mitamura, S. Inoue and K. Ogura, *Tetrahedron Lett.*, 1973, 323; (*j*) G. H. Posner in *Asymmetric Synthesis*, ed. J. D. Morrison, Academic Press, New York, 1983, vol. 2, p. 225.

2 For other Pummerer-type reactions, see: J. P. Mariro and A. D. Perez, *J. Am. Chem. Soc.*, 1984, **106**, 7643; G. H. Posner, E. Asirvatham and S. F. Ali, *J. Chem. Soc., Chem. Commun.*, 1985, 542; J. P. Marino and R. F. Pradilla, *Tetrahedron Lett.*, 1985, **26**, 5381; H. Kosugi, K. Tagami, A. Takahashi, H. Kanna and H. Uda, *J. Chem. Soc., Perkin Trans. 1*, 1989, 935; Y. Kita, O. Tamura, F. Itoh, H. Yasuda, T. Miki and Y. Tamura, *Chem. Pharm. Bull.*, 1987, **35**, 562; D. Craig and K. Daniels, *Tetrahedron Lett.*, 1990, **31** 6441 and references cited therein.

3 For reactions of sulphoxides with Grignard reagents, see: P. Manya, A. Sekera and P. Rumpf, *Tetrahedron*, 1970, **26**, 467; M. Hori, T. Kataoka and H. Shimizu, *Chem. Lett.*, 1974, 1073; A. Ohno, M. Uohama, K. Nakamura and S. Oka, *J. Org. Chem.*, 1979, **44**, 2244; M. Hojo, R. Masuda, T. Saeki, K. Fujimori and S. Tsutsumi, *Synthesis*, 1977, 789.