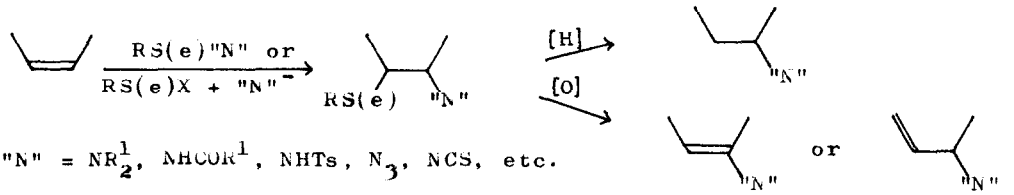
Tetrahedron Letters,Vol.25,No.34,pp 3759-3762,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

AMIDINOSULPHENYLATION OF ALKENES

Peter Brownbridge
University Chemical Laboratory, Lensfield Road, Cambridge, CB2 1EW.

Summary: Phenylsulphenamides react chemoselectively with an alkene and a nitrile in the presence of trifluoromethanesulphonic acid to give N-(β-phenylthioalkyl)amidines; in the absence of nitrile an amine is formed.

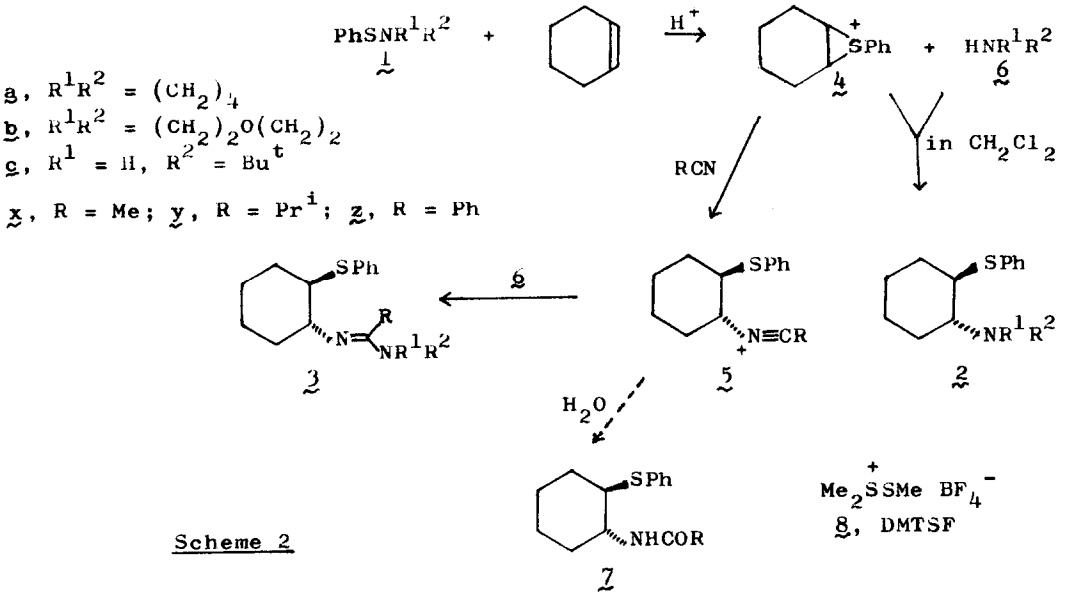
Regioselective 1,2-difunctionalization of alkenes with a nitrogen nucleophile and an alkylthio[1-3] or alkylseleno[1,4] group has attracted a good deal of interest recently, because it presents a simple answer to the lack of nitrogen electrophiles capable of attacking a weak nucleophile such as an alkene.[5] Reductive or oxidative elimination of the RS(e) group leads to overall addition to or substitution at the alkene by the nitrogen nucleophile ("N") respectively (Scheme 1).



Scheme 1

I now report a new reaction of this type, in which a phenylsulphenamide (1)[6] reacts with an alkene in dichloromethane to give moderate yields of an amine (2),[7] but in the presence of a nitrile undergoes a chemoselective three-molecule condensation to form an amidine (3) in high yield (Scheme 2). Results with cyclohexene are presented in Table 1, and with other alkenes in Table 2.

In view of the trans-addition observed with cyclohexene,† a likely mechanism for this reaction involves generation of the episulphonium ion 4, followed by attack of the nitrile on this in a Ritter-type reaction,[8] and finally capture of the nitrilium ion 5 by the liberated amine 6.[9] Smit et al. have previously observed incorporation of nitriles (to give amides such as 7) in their examination of the reactions of isolated episulphonium ions,[10] but it does not occur during the azasulphenylation of alkenes using DMTSF (8),[2a,c] nor in the addition of alkanesulphenyl halides to alkenes.[11]



Scheme 2

Table 1: reaction of cyclohexene with sulphenamides 1

sulphenamide	solvent, products[a] MeCN	Pr^iCN	$PhCN^b/CH_2Cl_2$	CH_2Cl_2
1a	3ax, 91[c], 69[d]	3ay, 92[c]	3az:2a = 4:1[c], 73	2a, 44[c], 46[d]
1b	3bx, 73[c]	3by, 78[c]	3bz:2b = 3:1[c]	2b, 45[c]
	3bx, 74 + 7x, 12[ce]		3bz, 76[d]	
1c	3cx, 71[c]	3cy, 84[f]	-	2c, 50[f]

[a] Isolated yields based on sulphenamide (%), 2 - 5 mmol scale; [b] 5 equivalents; [c] 1 equiv. HOTf used; [d] 1 equiv. Me_3SiOTf + 1 drop HOTf used; [e] 20 mmol scale reaction; [f] 2 equivs. HOTf used.

Table 2: reaction of 1 with other alkenes

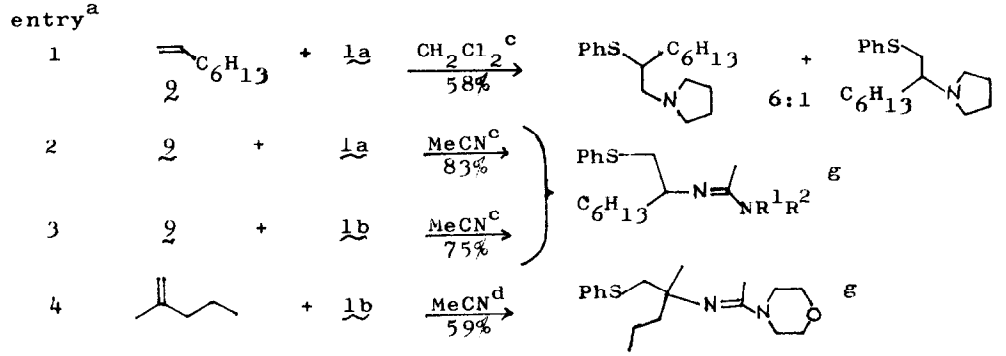
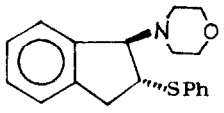


Table 2 continued

5 indene + 1b $\xrightarrow[69\%]{CH_2Cl_2}{}^{c}$  g

a, c, d see Table 1; g single regioisomer produced.

The best promotor for this reaction is trifluoromethanesulphonic acid (HOTf), but for particularly acid-sensitive systems (such as entry 4 of Table 2), trimethylsilyl trifluoromethanesulphonate (Me_3SiOTf) containing a catalytic quantity (1 drop) of HOTf, is superior. The reaction occurs rapidly (1 - 2 h) at -23°C, using the nitrile as solvent if it is volatile, otherwise with dichloromethane as co-solvent. Since benzonitrile is comparatively less nucleophilic than alkanecarbonitriles, it competes less successfully with the liberated amine 6 for the episulphonium ion 4, with the result that a little 2 is formed in addition to the amidine 3z, although this appears to be suppressed by using Me_3SiOTf. The benzamidine products 3z are also considerably more sensitive to hydrolysis during work-up than their alkyl counterparts.

From Table 2 it will be seen that amidinosulphenylation of unsymmetrical alkenes results in Markovnikoff regiochemistry exclusively (entries 2 - 4), whereas when the electronic bias of the episulphonium ion intermediate is not pronounced, aminosulphenylation is observed to be mainly anti-Markovnikoff (entry 1, but c.f. entry 5).[2] This suggests that, as might be expected, a nitrile is a nucleophile of particularly low steric demand.

Treatment of several of the β-phenylthioalkylamidines with Raney Nickel provided the desulphurized amidines in yields of 87-93%;[12] however, thermolysis of the corresponding sulphoxides has not given any characterizable products so far.

Acknowledgements: I thank Dr D. J. Cavalla and Dr A. J. Kirby for useful discussions, and am grateful to Jesus College, Cambridge, for a Research Fellowship.

References and Notes

1. D. H. R. Barton, M. R. Britten-Kelly, D. Ferreira J. Chem. Soc., Perkin Trans. I 1978, 1090 and 1682; A. Bewick, D. E. Coe, J. M. Mellor, D. J. Walton J. Chem. Soc., Chem. Commun. 1980, 51.

2. a) B. M. Trost, T. Shibata J. Am. Chem. Soc. 1982, 104, 3225; b) M. C. Caserio, J. K. Kim ibid. 3231; c) see also B. M. Trost, T. Shibata, S. J. Martin ibid. 3228.

3. T. Ohsawa, M. Ihara, K. Fukumoto, T. Kametani J. Org. Chem. 1983, 48, 3644; M. Ihara, Y. Haga, M. Yonekura, T. Ohsawa, K. Fukumoto, T. Kametani J. Am. Chem. Soc. 1983, 105, 7345.

4. For recent results see T. Hayama, S. Tomoda, Y. Takeuchi, Y. Nomura Tetrahedron Lett. 1982, 23, 4733; R. R. Webb, S. Danishefsky Tetrahedron Lett. 1983, 24, 1357; A. Toshimitsu, S. Uemura, M. Okano, N. Watanabe J. Org. Chem. 1983, 48, 5246.

5. For other solutions to this problem (e.g. azamercuration) see M. B. Gasc, A. Lattes, J. J. Perie Tetrahedron 1983, 39, 703; J. Barluenga, C. Jiménez, C. Nájera, M. Yus J. Chem. Soc., Perkin Trans. I 1983, 591, 1984, 721; A. P. Kozikowski, J. Scripko Tetrahedron Lett. 1983, 24, 2051 and references therein.

6. The phenylsulphenamides were prepared from N-phenylthiocaprolactam according to G. Sosnovsky, J. A. Krogh Synthesis 1979, 228, but using the amine as solvent.

7. For a previous similar reaction of N-methanethiodimethylamine see ref. 2b; for an entirely different approach to β-RS-alkylamines see J. Barluenga, C. Jiménez, C. Nájera, M. Yus Synthesis 1981, 201.

8. L. I. Krimen, D. J. Cota Org. React. 1969, 17, 246-7.

9. To ensure completion of this step, the reaction mixture was treated with an additional equivalent of the amine 6 before aqueous workup.

10. W. A. Smit, M. Z. Krimer, E. A. Vorob'eva Tetrahedron Lett. 1975, 2451; Izv. Akad. Nauk SSSR, Ser. Khim. 1975, 125, 1976, 1318.

11. W. A. Smit, N. S. Zefirov, I. V. Bodrikov, M. Z. Krimer Acc. Chem. Res. 1979, 12, 282; and in "IUPAC 9th International Symposium on Organic Sulfur Chemistry", R. K. Freidlina and A. E. Skorova, Eds., Pergamon, Oxford, 1981, pp. 159-173.

12. For recent syntheses of substituted amidines see V. G. Granik Russ. Chem. Rev. 1983, 52, 377; E. Haug, W. Kantlehner, P. Speh, H.-J. Bräuner Synthesis 1983, 35.

† The trans-diaxial coupling of the SCHCHN system in the cyclohexane ring is clearly shown in the proton nmr spectrum, e.g. in 3bz [δ 3.23 (1H, dt, J_d 4, J_t 10 Hz, SCH) and δ 2.80 (1H, dt, J_d 4, J_t 10 Hz, NCH)] and in 2c [δ 3.00 (1H, dt, J_d 4, J_t 9.5 Hz, SCH) and δ 2.62 (1H, dt, J_d 4.5, J_t 9.5 Hz, NCH)].

(Received in UK 18 May 1984)