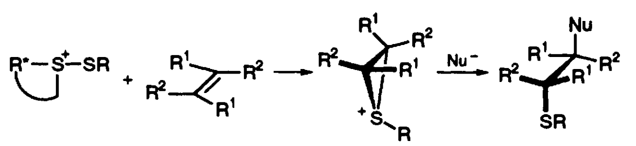
Enantiopure Thiosulfonium Salts in Asymmetric Synthesis. Face Selectivity in Electrophilic Additions to Unfunctionalised Olefins[†]

Vittorio Lucchini,[a] Giorgio Modena[b] and Lucia Pasquato*[b]

[a] *Dipartimento di Scienze Ambientali, Università di Venezia, Dorsoduro 2137, I-30123 Venezia, Italy*
[b] *Centro Meccanismi Reazioni Organiche del CNR, Dipartimento di Chimica Organica, via Marzolo 1, I-35131 Padova, Italy*

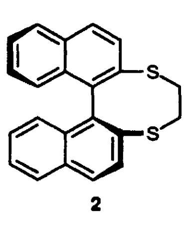
Enantiopure *S*-methylthiodinaphtho[2,1-*c*:1′,2′-*e*][1,2]dithiinium hexachloroantimonate **3** transfers enantioselectively the MeS$^+$ group to *trans*-hex-3-ene, leading to non-racemic thiiranium ion **4**, which, in turn, reacts with MeCN–H_2O allowing the synthesis of optically active double functionalised alkanes with enantiomeric excesses of up to 86%.

Thiiranium ions are interesting species from a mechanistic point of view[1] and versatile intermediates in organic synthesis.[2] They are the intermediates in the *anti*-stereoselective electrophilic additions of sulfenyl halides to carbon–carbon double bonds and we thought it would be interesting to apply this chemistry to the enantioselective double functionalisation of alkenes, which remains an important synthetic target despite the great progress achieved recently.[3] On the basis of previous studies by other authors[4] and by ourselves[1,2,5] in this field, we thought it would be feasible to synthesise enantiopure carriers able to transfer the RS$^+$ moiety to unfunctionalised alkenes. The rationale was that the association of an asymmetric auxiliary with the inherent chirality of the sulfonium ion could lead to a highly efficient transmission of the chiral information even to unfunctionalised double bonds. The chiral thiiranium ion generated would eventually react with nucleophiles to afford β-functionalised sulfides without loss of optical activity (see Scheme 1).



Scheme 1

We selected for our preliminary experiments the dinaphtho[2,1-*c*:1′,2′-*e*][1,2]dithiine **1** and the dinaphtho[2,1-*e*:1′,2′-*g*][1,4]dithiocine **2** as they both have C_2 symmetry, in order to minimise the number of possible steroisomers;[6] they contain a 1,1′-binaphthyl unit, and 2,2′-substituted 1,1′-binaphthalenes are widely used in asymmetric synthesis because of the excellent discriminating power reported for many reactions.[7–9] Both substrates are characterised by strong preference for addition at either sulfur atom from the equatorial direction. We concentrated on the disulfide **1**, which is a quite poor nucleophile and a good RS$^+$ transfer agent,[2] and which seems to give better results.



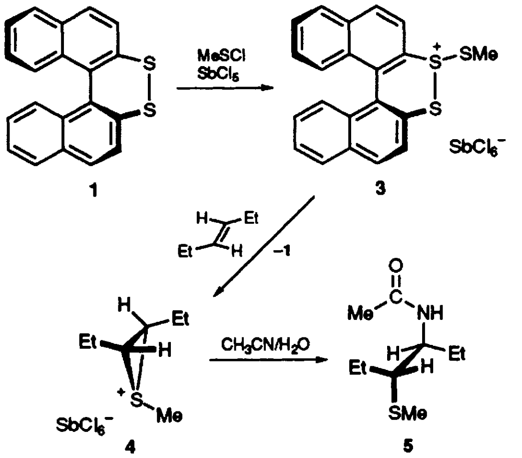
2

Compound **1** is readily prepared,[8,10] in enantiopure form, from commercially available 1,1′-binaphthalene-2,2′-diol with about 40% overall yield and good optical purity [enantiomeric excess (e.e.) >98%].

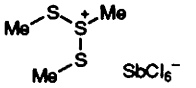
The *S*-methylthio sulfonium salt **3** was prepared by the reaction of the disulfide **1** with 1 equivalent each of methanesulfenyl chloride and $SbCl_5$ in dry methylene chloride at 0 °C under nitrogen. By addition of pentane and rapid filtration the thiosulfonium salt was isolated as a yellow powder in >90% yield.

Its ^1H NMR spectrum in liquid SO_2 shows only one set of six aromatic signals;[‡] *i.e.* the two naphthyl moieties give the same resonances. This may be explained by a rapid migration of the methylthio residue from one sulfur atom to the other one of **1** very likely *via* an intermolecular process.[§] The equilibrium remains fast even at −90 °C. No significant chemical shift variation is observed in the temperature range studied (−20 to −90 °C). This suggests that the migration is between two identical species. Thus, in analogy with the oxidation to the monosulfoxide of dinaphtho[2,1-*e*:1′,2′-*g*][1,4]dithiocine **2**[8] we assume that the electrophile adds to either sulfur atom of **1** specifically along the equatorial direction.

In the complete reactions sequence (Scheme 2) a solution of the thiosulfonium salt in dry methylene chloride at the given temperature was allowed to react with the olefin (*trans*-hex-3-ene) and, after an appropriate time, which depends on the



Scheme 2 The stereochemistry shown in the drawings is arbitrary



6

Table 1 Enantioselective transfer of MeS$^+$ to *trans*-hex-3-ene from the enantiopure hexachloroantimonate salt **3**

Olefin equivalents	*T*/°C	Time before MeCN addition (*t*/min)	**5**, e.e. (%)[a]
1.1	−20	10	40[b]
1.1	−20	10	49[b]
1.1	−60	60	56[c]
1.0	−78	120	86[c]

[a] Determined for the isolated product *via* ^1H NMR utilising (+)-(*S*)- or (−)-(*R*)-1-(9-anthryl)-2,2,2-trifluoroethanol. [b] The chemical yields for product **5** and recovered **1** are about 80%. [c] A byproduct containing the MeS–S–binaphtho–S–residue is formed in about 30% yield.

temperature, acetonitrile was added as nucleophile.[4i,12] The reaction mixture was then treated with a saturated solution of $NaHCO_3$, and after the usual work-up, the disulfide **1** and the product **5**[¶] were separated by chromatography on silica gel. The reaction was also monitored by ^{1}H NMR spectroscopy in CD_2Cl_2; at 25 °C, **3** reacts instantaneously with the olefin giving the thiiranium ion **4**, which is stable under the reaction conditions. Thiiranium ion **4** has been independently prepared and isolated in the racemic form, using methylbis(methylthio)sulfonium hexachloroantimonate **6**.[13]

The results obtained with the preformed enantiopure salt **3** taken as a representative example are collected in Table 1.

It should be pointed out that thiiranium ions may react with other nucleophilic species present in solution. Thus adventitious nucleophiles with thiophilic properties may strongly depress the enantioselection because of reversible attack at the sulfonium sulfur. As a consequence the e.e. value measured for the final adduct **5** may be lower than that for the thiiranium ion **4**. In principle, the problem may be solved by rapid precipitation and isolation of thiiranium ion **4** followed by determination of the e.e. However, there is, so far, no method available to measure the optical purity of thiiranium salts.

The data in Table 1 suggest the following: (*i*) the thiosulfonium salt **3** is effective for the face-selective transfer of the electrophile MeS$^+$ to *trans*-hex-3-ene; (*ii*) as frequently observed in asymmetric synthesis, lower temperatures lead to better e.e. values.

Although the first two entries of Table 1 reveal that some difficulties, due to the high reactivity of thiiranium salts, are still present, the present results strongly encourage us to develop this new enantioselective double functionalisation of simple olefins as a useful synthetic route.

Received, 31st March 1994; Com. 4/01967I

Footnotes

[†] Part of this work was presented at the ESOC 8, Barcelona, Spain 29th August–4th September, 1993.

[‡] Mp 105 °C (decomp.); ^{1}H NMR (200 MHz, SO_2, $SiMe_4$) δ 3.17 (3H, s, CH_3), 7.31 (2H, m), 7.50 (2H, m), 7.82 (2H, m), 7.99 (2H, m); 8.35 (2H, m). Elemental analyses were satisfactory. The optical rotation could not be measured because a solution of **3** absorbs at all the wavelengths of Na and Hg lamps.

[§] A similar process was observed for methylbis(methylthio)sulfonium hexachloroantimonate. It was proved that the rearrangement is catalysed by dimethyl disulfide, *i.e.* the reaction is intermolecular.[11]

[¶] Oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.92 (3H, t, *J* 7.02 Hz), 1.07 (3H, t, *J* 7.02 Hz), 1.31 (2H, m), 1.62 (2H, m), 2.02 (3H, s), 2.10 (3H, s), 2.52 (1H, m), 4.08 (1H, m), 5.83 (br d, *J* 8.54 Hz). For the 4-$MeOC_6H_4S$ substituted analogue see ref. 12(*c*).

References

1 V. Lucchini, G. Modena and L. Pasquato, *J. Am. Chem. Soc.*, 1988, **110**, 6900; *J. Am. Chem. Soc.*, 1991, **113**, 6600.

2 G. Capozzi, G. Modena and L. Pasquato, *The Chemistry of Sulfenic Acids and Their Derivatives*, ed. S. Patai, Wiley, New York, 1990, ch. 10; G. Capozzi and G. Modena, *Studies in Organic Chemistry 19. Organic Sulfur Chemistry. Theoretical and Experimental Advances*, ed. F. Bernardi, I. G. Csizmadia and A. Mangini, Elsevier, New York, 1985, ch. 10; U. Zoller, *Small Ring Heterocycles*, vol. 42, ed. A. Hassner, Wiley, Chichester, 1983, p. 450.

3 Recent examples are: K. C. Kolb, P. G. Andersson, Y. L. Bennani, G. A. Crispino, K.-S. Jeong, H.-L. Kwong and K. B. Sharpless, *J. Am. Chem. Soc.*, 1993, **115**, 12226 and references cited therein; Z. Li, K. R. Conser and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1993, **115**, 5326; D. A. Evans, M. M. Faul, M. T. Bilodeau, B. A. Anderson and D. M. Barnes, *J. Am. Chem. Soc.*, 1993, **115**, 5328; T. Schwenkreis and A. Berkessel, *Tetrahedron Lett.*, 1993, **34**, 4785.

4 Chiral olefins: (*a*) F. Effenberger, T. Beisswenger and H. Isak, *Tetrahedron Lett.*, 1985, **26**, 4335; (*b*) F. Effenberger and H. Isak, *Chem. Ber.*, 1989, **122**, 545; (*c*) G. Grewal, N. Kaila and R. W. Franck, *J. Org. Chem.*, 1992, **57**, 2084; (*d*) N. Kaila, M. Blumenstein, H. Bielawska and R. W. Franck, *J. Org. Chem.*, 1992, **57**, 4576; (*e*) R. W. Franck; N. Kaila, M. Blumenstein, A. Geer, X. L. Huang and J. J. Dannenderg, *J. Org. Chem.*, 1993, **58**, 5335. Selenium chemistry, with enantiopure RSeBr reagents: (*f*) S. Tomoda and M. Iwaoka, *Chem. Lett.*, 1988, 1895; (*g*) S. Tomoda, K. Fujita and M. Iwaoka, *J. Chem. Soc., Chem. Commun.*, 1990, 129; (*h*) R. Déziel, S. Goulet, L. Grenier, J. Bordeleau and J. Bernier, *J. Org. Chem.*, 1993, **58**, 3619; (*i*) from enantiopure epoxides: A. Toshimitsu, C. Hirosawa and S. Tanimoto, *Tetrahedron Lett.*, 1991, **32**, 4317.

5 V. Lucchini, G. Modena and L. Pasquato, *J. Am. Chem. Soc.*, 1993, **115**, 4527.

6 J. K. Whitesell, *Chem. Rev.*, 1989, **89**, 1581.

7 C. Rosini, L. Franzini, A. Raffaelli and P. Salvadori, *Synthesis*, 1992, 503.

8 F. Di Furia, G. Licini, G. Modena and G. Valle, *Bull. Soc. Chim. Fr.*, 1990, **127**, 734.

9 O. De Lucchi, *Phosphorus, Sulfur, and Silicon*, 1993, **74**, 195.

10 D. Fabbri, G. Delogu and O. De Lucchi, *J. Org. Chem.*, 1993, **58**, 1748; J.-M. Brunel and G. Buono, *J. Org. Chem.*, 1993, **58**, 7313; M. Kawashima and A. Hirayama, *Chem. Lett.*, 1990, 2299.

11 G. Capozzi, V. Lucchini, G. Modena and F. Rivetti, *J. Chem. Soc., Perkin Trans. 2*, 1975, 900.

12 (*a*) B. M. Trost and T. Shibata, *J. Am. Chem. Soc.*, 1982, **104**, 3225; (*b*) A. Berwick, D. E. Coe, J. M. Mellor and W. M. Owton, *J. Chem. Soc., Perkin Trans. 1*, 1985, 1033; (*c*) M. Tiecco, M. Tingoli, L. Testaferri and R. Baeducci, *J. Org. Chem.*, 1992, **57**, 4025.

13 G. Capozzi, O. De Lucchi, V. Lucchini and G. Modena, *Tetrahedron Lett.*, 1975, 2603.