Tetrahedron: Asymmetry Vol. 3, No. 6, pp. 701-704, 1992
Printed in Great Britain

0957-4166/92 $5.00+.00
Pergamon Press Ltd

HOMOCHIRAL 1-METHOXY-3-SULFINYL-1,3-BUTADIENES DERIVED FROM 10-MERCAPTOISOBORNEOL

Maria C. Aversa,[a*] Paola Bonaccorsi,[a] Placido Giannetto,[a] Sedigheh M.A. Jafari,[b] and D. Neville Jones[b*]

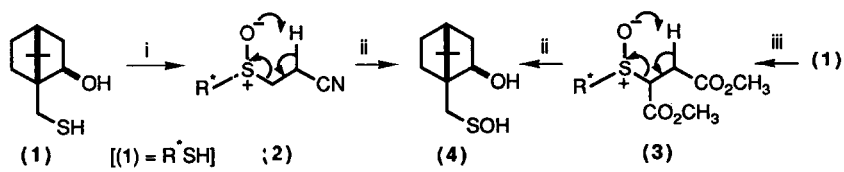
[a]Dipartimento di Chimica organica e biologica, Università, 98166 Messina, Italy
[b]Department of Chemistry, The University, Sheffield S3 7HF, U.K.

(*Received* 30 *April* 1992)

Summary. Simple syntheses of homochiral (Z)- and (E)-1-methoxy-3-alkylsulfinyl-1,3-butadienes were provided by the cycloaddition of (1S)-d-isobornyl-10-sulfenic acid to (Z)- and (E)-1-methoxybut-1-en-3-yne. Asymmetric induction pertained for such cycloadditions, which also provided homochiral dienes from 1-ethynylcyclohex-1-ene.

Sulfoxides homochiral at sulfur play an important role in asymmetric transformations.[1] Among these, asymmetric Diels-Alder reactions with optically active α,β-unsaturated sulfoxides as dienophiles are well exemplified,[2,3] but there are no reports of Diels-Alder reactions of homochiral sulfinyl dienes, examples of which compounds were unknown until recent reports of the synthesis of optically active 1-sulfinyl dienes[4] and 2-sulfinyl dienes.[5] We now report a simple procedure for the synthesis of homochiral 1-substituted-3-sulfinyl dienes derived from 10-mercaptoisoborneol (1), which was chosen because of its ready availability, and because the presence of the hydroxy group was expected to facilitate the separation and conformational rigidity of derived sulfoxides homochiral at sulfur.[3]

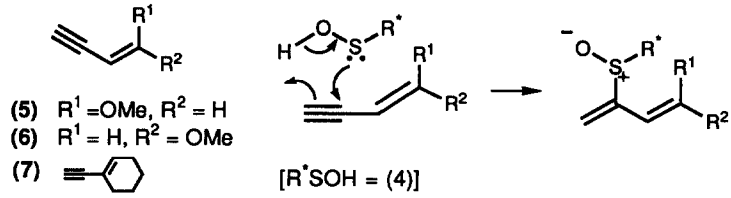
The syntheses were based on the regioselective addition of sulfenic acids to enynes,[6] (Scheme 2) and proceeded in three simple steps commencing with the base-catalysed addition of 10-mercaptoisoborneol (1) to either acrylonitrile or dimethyl maleate, followed by oxidation of the adducts with 3-chloroperbenzoic acid to give the corresponding sulfoxides (2) and (3) respectively as mixtures of diastereoisomers at sulfur (Scheme 1).



Scheme 1. Reagents: i, (a) CH_2=CHCN, THF, Triton B, -78 → 0 °C; (b), mCPBA, CH_2Cl_2, 0 °C; ii, heat; iii, (a) dimethyl maleate, Et_3N, toluene, 1.5h; (b) mCPBA, CH_2Cl_2, 0 °C

Although these mixtures could be separated into their components by chromatography, they were used without separation for the next step, which involved thermolysis to give the sulfenic acid (4) in which sulfur is achiral. Of these sulfenic acid precursors, the cyano-sulfoxides (2) were the more convenient because they are stable up to 110 °C, whereas the sulfoxides (3) decomposed slowly at room temperature (and quite rapidly at

80 °C) and so required fresh preparation for each subsequent reaction. However, the more ready thermal decomposition of the sulfoxides (3) to the sulfenic acid (4) was an advantage when the products of sulfenic acid-alkyne additions were themselves thermally labile. Like most other sulfenic acids,[7] the hydroxy-sulfenic acid (4) was too unstable to be isolated, so it was generated *in situ* by thermolysis of the the precursors (2) and (3) in the presence of appropriate enynes (5), (6), and (7) (Scheme 2).

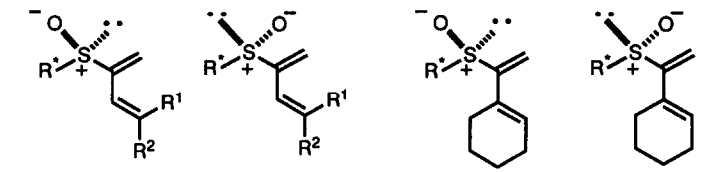


Scheme 2.

Thermolysis of the cyano-sulfoxides (2) in boiling xylene (150 °C) containing (Z)-1-methoxybut-1-en-3-yne (5) gave a mixture of (R_S,Z)-3[(1S)-isobornyl-10-sulfinyl]-1-methoxy-1,3-butadiene (8) (35%) and its (S_S,Z)-isomer (9) (5%). Yields were improved when the sulfoxides (3) were thermolysed in boiling benzene (80 °C) containing the same enyne (Table).[8]

Table

Sulfinyldienes from addition of sulfenic acid (4) to enynes (5) - (7)

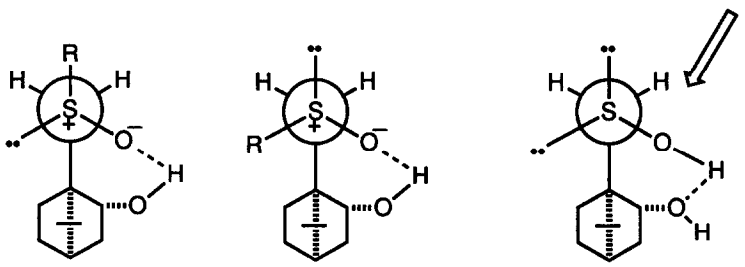


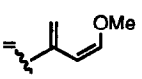
Enyne	Method†	Time	Products (% yield)	
(5)	a	1h	(8) (35%)	(9) (5%)
(5)	b	3h	(8) (63%)	(9) (14%)
(6)	a	1h	(10) (30%)	
(6)	b	1h	(10) (60%)	(11) (10%)
(7)	c	3.5h	(12) (66%)	(13) (20%)

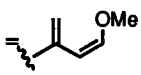
† a, Sulfoxides (2) (≈ 1 mmol) and enyne (0.25 ml ,≈ 3 mmol) in boiling xylene (2 ml) (≈ 150 °C): b, sulfoxides (3) (≈ 1 mmol) and enyne (1 ml ,≈ 12 mmol) in boiling benzene (10 ml) (≈ 80 °C): c, sulfoxides (2) in neat (7) at 110 °C.

The isomers (8) and (9) were readily separated by chromatography on silica, and the chromatographically more mobile major isomer (8) was allocated the (R_S) configuration at sulfur on the basis of the following considerations. Sulfoxides form strong intramolecular hydrogen bonds with suitably orientated proximal hydroxy groups,[9] a phenomenon which is associated with enhanced chromatographic mobility by virtue of the consequent reduction in the effective polarity of the sulfoxide group. Models reveal that the (R_S) isomer (8) can readily adopt an unhindered (and therefore highly populated) conformation (A) which involves intramolecular

hydrogen bonding, whereas for the (S_S) isomer (9) intramolecular hydrogen bonding requires the adoption of a less favourable (and less highly populated) conformation (B) which is sterically compressed by virtue of non-bonded interactions between the bicyclic skeleton and the diene moiety. Support for this interpretation is provided by the behaviour of the sulfoxides (2) in which the epimers at sulfur were formed in the ratio 7:1 (85% yield) by peroxyacid oxidation of the corresponding sulfide (Scheme 1). The major isomer is the more mobile chromatographically, and therefore may be allocated the (S_S) configuration (C) by the preceding arguments,[10] which is in complete accord with the configuration assigned on the basis of the well-established[11] directing effect of a proximal hydroxy group on the stereoselectivity of peroxyacid oxidation at sulfur in the preferred conformation of the corresponding sulfide.[12]



(A) R = 

(B) R = 

(D)

(C) R = CH_2CH_2CN

Thermolysis of the sulfoxides (2) and (3) in the presence of (E)-1-methoxybut-1-en-3-yne (6) and 1-ethynylcyclohexene (7) furnished the homochiral sulfinyl dienes (10) and (11), and (12) and (13) respectively (Table), for which allocations of configuration at sulfur were made as before on the basis of the relative chromatographic mobilities of the epimers.

The predominance of the (R_S)-3-sulfinyldienes in each case (Table) provides the first examples of asymmetric induction in sulfenic acid-alkyne additions. Such additions are pericyclic processes which proceed *via* a five membered transition state (Scheme 2),[6] and the observed stereoselectivities are rationalized in terms of additions of the alkyne to the unhindered "face" of the sulfenic acid (4) which is constrained in a conformation such as that depicted in (D) by intramolecular hydrogen bonding with the proximal hydroxy group. This hypothesis is supported by observations that intramolecular hydrogen bonding in other hydroxy sulfenic acids is strong,[7] and contributes so significantly to their stability that in some cases they may be isolated.

Acknowledgement. The authors gratefully acknowledge financial support from the MURST of Italy.

References and Notes

1 G. Solladié, *Synthesis*, 1981, 185; M. Mikolajczyk and J. Drabowicz, in Topics in Stereochemistry, N.L. Allinger, E.L. Eliel, and S.H. Wilen, eds., Wiley, New York, 1982, vol.13, p.333; G.H. Posner, in The Chemistry of Sulphones and Sulphoxides, S. Patai, Z. Rappoport and C. Stirling, eds., Wiley, Chichester, 1988, p.823.

2 C. Maignan and R.A. Raphael, *Tetrahedron*, 1983, **39**, 3245; Y. Arai, S. Kuwayama, Y. Takeuchi, and T. Koizumi, *Synth. Commun.*, 1986, **16**, 233; I. Alonso, J.C. Carretero, and J.L. Garcia-Ruano, *Tetrahedron Lett.*, 1989, **30**, 3853; M.C. Carreño, J.L. Garcia-Ruano, and A. Urbano, *Tetrahedron Lett.*, 1989, **30**, 4003; B. Ronan and H.B. Kagan, *Tetrahedron Asymmetry*, 1991, **2**, 75.

3 O. De Lucchi, V. Lucchini, C. Marchioro, G. Valle, and G. Modena, *J. Org. Chem.*, 1986, **51**, 1457; Y. Arai, K. Hayashi, M. Matsui, T. Koizumi, M. Shiro, and K. Kuriyama, *J. Chem. Soc., Perkin Trans. 1*, 1991, 1709.

4 G. Solladié, P. Ruiz, F. Colobert, M. C. Carreño, and J.L. Garcia-Ruano, *Synthesis*, 1991, 1011; G. Solladié, F. Colobert, P. Ruiz, C. Hamdouchi, M. C. Carreño, and J.L. Garcia-Ruano, *Tetrahedron Lett.*, 1991, **3**, 3695; S. Goldmann, R.W. Hoffmann, N. Maak, and K.J. Geueke, *Chem. Ber.*, 1980, **113**, 831.

5 E. Bonfrand, P. Gosselin, and C. Maignan, *Tetrahedron Lett.*, 1992, **33**, 2347.

6 R. Bell, P.D. Cottam, J. Davies, and D.N. Jones, *J. Chem. Soc., Perkin Trans. 1*, 1981, 2106.

7 D.R. Hogg, in The Chemistry of Sulphenic Acids and their Derivatives, S. Patai, ed., Wiley, Chichester, 1990, Ch.9.

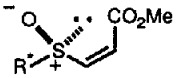
8 All new compounds were characterized by IR, ^{1}H NMR, and MS or elemental analysis. Selected data: (specific rotations in $CHCl_3$; ^{1}H NMR at 250 or 300 MHz in $CDCl_3$): **(2)**[(S$_S$)-isomer) oil, $[\alpha]_D$ -46 (c 0.012); [Rf = 0.33, ethyl acetate-light petroleum (1:4)]; δ 0.85 (3H, s, 9-Me), 1.11 (3H, s, 8-Me), 2.42 (1H, AB, J = 13Hz, H$_B$-10), 2.90-3.15 (4H, m, C*H*$_2$C*H*$_2$CN), 3.37 (1H, AB, H$_A$-10), 4.05 (1H, dd, J 8 and 4 Hz, 2-H); **(2)**[(R$_S$)-isomer) oil, $[\alpha]_D$ -53 (c 0.1) (Rf=0.16) δ 0.9 (3H, s, 9-Me), 1.10 (3 H, s, 8-Me), 2.60 (1H, AB, J = 13Hz, H$_B$-10), 2.90-3.10 (4H, m, C*H*$_2$C*H*$_2$CN), 3.15 (1H, AB, J = 13 Hz, H$_A$-10), 4.03 (1 H, dd, 2-H); **(3)**,oil, two isomers, (Rf = 0.22 and 0.08, ether/light petroleum, 1:1), H^1 NMR (220 MHz, in $CDCl_3$,for major isomer) δ 0.88 (3H, s, 9-Me), 1.05 (3H, s, 8-Me), 2.28 (1H, AB, J = 12 Hz, H$_B$-10), 2.75 (1H, AB, H$_A$-10), 3.05 (2H, m, C*H*$_2$CO$_2$), 3.30 (1H, dd, C*H*CO$_2$), 3.70 (3H, s, OMe), 3.78 (3H, s, OMe), 4.0 (1H, m, 2-H). These compounds were used immediately for the next step since they were not stable; **(8)** m.p. 95-97 °C, $[\alpha]_D$ + 78 (c, 0.07), δ 6.17 (1H, d, J 7Hz, =C*H*(OMe); 5.92 (1H, s, *H*HC=), 5.89 (1H, s, H*H*C=), 5.07 (1H, d, J 7Hz, -C*H*=CHOMe), 4.14 (1H, dd, J = 8 and 4 Hz, H-2), 3.75 (3H, s, OMe), 2.99 (1H, AB, H$_A$-10), 2.66 (1H, AB, J = 13Hz, H$_B$-10), 1.07 (3H, s, 8-Me), 0.81 (3H, s, 9-Me); **(9)**, oil, $[\alpha]_D$ -34 (c, 0.004), δ 6.17 (1H, d, J 7Hz, =C*H*(OMe); 6.01 (1H, s, *H*HC=), 5.99 (1H, s, H*H*C=), 5.03 (1H, d, J 7Hz, -C*H*=CHOMe), 4.12 (1H, dd, J = 8 and 4 Hz, H-2), 3.77 (3H, s, OMe), 3.32 (1H, AB, J 14 Hz, H$_A$-10), 2.51 (1H, AB,, H$_B$-10), 1.10 (3H, s, 8-Me), 0.81 (3H, s, 9-Me); **(10)**, oil, $[\alpha]_D$ +39 (c, 0.002), δ 6.86 (1H, d, J 13Hz, =C*H*(OMe); 5.71 (1H, s, *H*HC=), 5.59 (1H, s, H*H*C=), 5.53 (1H, d, J 13Hz, -C*H*=CHOMe), 4.13 (1H, dd, J = 8 and 4 Hz, H-2), 3.67 (3H, s, OMe), 3.13 (1H, AB, J 13.5 Hz, H$_A$-10), 2.60 (1H, AB, H$_B$-10), 1.08 (3H, s, 8-Me), 0.82 (3H, s, 9-Me); **(11)**, oil, with ca. 10% impurity, δ 6.90 (1H, d, J 12Hz, =C*H*(OMe); 5.71 (1H, s, *H*HC=), 5.56 (1H, s, H*H*C=), 5.50 (1H, d, J 12Hz, -C*H*=CHOMe), 4.09 (1H, m, H-2), 3.70 (3H, s, OMe), 3.15 (1H, AB, J 12 Hz, H$_A$-10), 2.48 (1H, AB, H$_B$-10), 1.08 (3H, s, 8-Me), 0.82 (3H, s, 9-Me); **(12)** m.p. 110 °C, $[\alpha]_D$ +44.3 (c 0.09) [Rf=0.5 ethyl acetate-light petroleum (1:4)]; δ 5.92 (1H, s, *H*HC=), 5.88 (1H, m, vinyl), 5.72 (1H, s, H*H*C=), 4.15 (1 H, dd, J 8 and 4 Hz, H-2), 2.95 (1H, AB, J 14 Hz, H$_A$-10), 2.72 (1 H, AB, H$_B$-10), 1.07 (3 H, s, 8-Me),0.8 (3 H, s, 9-Me); **(13)** m.p. 165 °C, $[\alpha]_D$ -41 (c 0.08), (Rf=0.28), δ 6.0 (1H, m, vinyl), 5.95 (1H, s, *H*HC=), 5.75 (1H, s, H*H*C=), 4.12 (1 H, dd, J 8 and 3 Hz, H-2), 3.40 (1H, AB, J 14 Hz, H$_A$-10), 2.55 (1 H, AB, H$_B$-10), 1.12 (3 H, s, 8-Me),0.8 (3 H, s, 9-Me).

9 N. Furukawa and H Fujihara, in The Chemistry of Sulfones and Sulfoxides, S. Patai, Z. Rappoport and C. Stirling, eds., Wiley, Chichester, 1988, p.541.

10 Note that the configuration at sulfur in (A) is identical to that in (C), although they have different designations according to the CIP system.

11 R.S. Glass, W.N. Setzer, U.D.G. Prabhu, and G.S. Wilson, *Tetrahedron Lett.*,1982, **23**, 2335.

12 Similar considerations of hydroxy-directed oxidation at sulfur were employed by De Lucchi et. al. to assign configuration at sulfur in the related vinyl sulfoxide (14), a conclusion which was anchored by X-ray analysis of a Diels-Alder adduct of (14) with cyclopentadiene.[3] It is clear that the major sulfoxide formed by peroxyacid oxidation of a hydroxy sulphide should always be chromatographically less polar than its epimer at sulfur, since similar intramolecular hydrogen bonding effects influence both stereoselectivity of oxidation and chromatographic characteristics.



(14) R = (1)