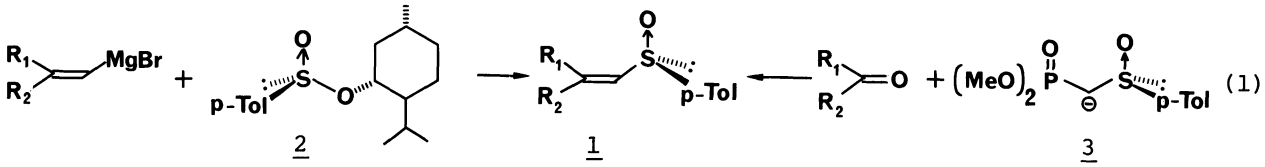
CHEMISTRY LETTERS, pp. 805-808, 1985. © 1985 The Chemical Society of Japan

A SIMPLE PREPARATIVE METHOD FOR OPTICALLY PURE 1-ALKENYL p-TOLYL SULFOXIDES VIA 1-ALKYNYL p-TOLYL SULFOXIDES

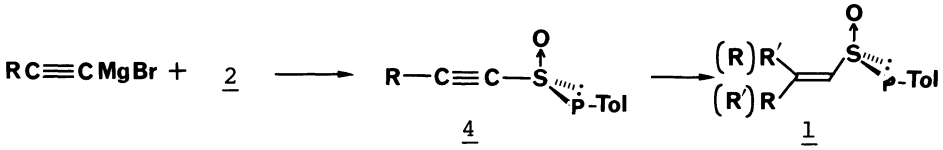
Hiroshi KOSUGI,* Masaki KITAOKA, Katsuya TAGAMI, and Hisashi UDA
Chemical Research Institute of Non-Aqueous Solutions,
Tohoku University, Katahira, Sendai 980

1-Alkynyl Grignard reagents react with (S_S)-(-)-menthyl p-toluenesulfinate in toluene to give optically active 1-alkynyl p-tolyl sulfoxides in high yields. The 1-alkynyl sulfoxides thus obtained undergo a stereoselective hydroalumination followed by hydrolysis to afford the corresponding (E)-1-alkenyl p-tolyl sulfoxides with high optical purity.

Optically active 1-alkenyl sulfoxides (1), chiral by virtue of asymmetry at sulfur, have been used successfully to direct carbon-carbon or carbon-heteroatom bond formation in asymmetric synthesis.[1-3] They are usually prepared by the reaction of (S_S)-(-)-menthyl p-toluenesulfinate (2) with vinylic Grignard reagents (Andersen's method),[4] or by the reaction of (R_S)-(+)-dimethylphosphorylmethyl p-tolyl sulfoxide (3) with carbonyl compounds[5] (Eq. 1). However, the former method depends on the availability of the starting 1-halovinyl compounds, and the latter usually leads to a mixture of the geometrical isomers. In connection with our study on the asymmetric synthesis of acyclic compounds using chiral sulfoxides,[6] we needed a variety of chiral α,β-unsaturated sulfoxides with high optical purity. This paper describes a new route to a variety of chiral 1-alkenyl sulfoxides (1) via 1-alkynyl sulfoxides (4) (Eq. 2).



(1)



(2)

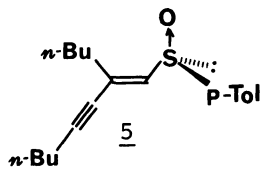
Despite recent success on the asymmetric oxidation of sulfides to chiral sulfoxides,[7] the Andersen's method, which involves the reaction of chiral sulfinate (2) with Grignard reagents, has been still valuable for the preparation of diaryl, aryl alkyl, and alkenyl aryl sulfoxides with high optical purity.[8] To our knowledge, however, the synthesis of chiral acetylenic sulfoxides has not been reported

Table 1. Preparation of 1-Alkynyl p-tolyl sulfoxides (4)

R-C≡C-MgBr	R-C≡C-S(O)-p-Tol	Yield/%[a]	$[\alpha]_D^{20}$/° ($CHCl_3$)	Absolute configuration
R=n-C_3H_7-	4a	83	+88.6 (c 1.009)	S
R=n-C_4H_9-	4b	80	+77.6 (c 1.195)	S
R=n-C_5H_{11}-	4c	86	+73.6 (c 0.469)	S
R=n-C_6H_{13}-	4d	82	+70.0 (c 1.087)	S
R=Me_3Si-	4e (R=H)[b]	80	+154 (c 0.182)	R

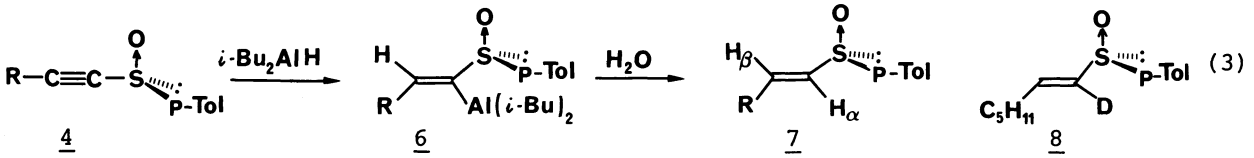
a) Yields are for the isolated pure products based on 2.
b) See Text.

so far. We first examined the reaction of (S_S)-(-)-menthyl p-toluenesulfinate (2) {$[\alpha]_D^{20}$ -202° (c 0.50, acetone)} with 1-hexynyllithium or 1-hexynylmagnesium bromide under a variety of conditions. The reaction of 2 with 1-hexynyllithium was unsuccessful, yielding the 2:1 adduct (5) as the major product. Exposure of the Grignard reagent to 2 in Et_2O, THF, or benzene, which are commonly used for the Andersen's method,[8] was also unsatisfactory, affording the desired 1-hexynyl p-tolyl sulfoxide (4b) in only 20% yield along with the recovery (60%) of 2. On the other hand, when the reaction of the Grignard reagent with 2 was conducted in toluene as the solvent, it was found that the reaction proceeded cleanly even at low temperature, and a great superior yield of 4b was achieved. The results from the reaction of 2 with other Grignard reagents are summarized in Table 1. In the case of trimethylsilylethynylmagnesium bromide, the initial product (4, R=Me_3Si-) was hydrolyzed during chromatographic purification on silica gel, giving (R)-(+)-ethynyl p-tolyl sulfoxide (4e) in 80% yield. The absolute configurations of these new chiral sulfoxides were assigned on the basis of the reasonable assumption that this type of the reaction would proceed with inversion of the chirality at the sulfur atom analogous to many other Andersen-type procedures. This was finally confirmed by the conversion of the acetylenic sulfoxides (4) to the corresponding vinylic sulfoxides as described below.



5

The acetylenic sulfoxides thus obtained were then subjected to hydroalumination. Thus, treatment of 4 with diisobutylaluminum hydride (DIBAH) in toluene or THF followed by hydrolysis of the resulting adducts (6) with water afforded the 1-(E)-alkenyl sulfoxide (7) in high yields (Eq. 3 and Table 2). The stereochemistry of the double bond in these products was easily determined by their ^1H NMR spectra; the olefinic proton signals appear around at δ 6.1 (d, J=15.5 Hz, H_α) and 6.4 (dt, J=15.5 and 6 Hz, H_β).[9] In contrast to usual hydroalumination of simple unactivated acetylenes,[10] the hydroalumination of these acetylenic sulfoxides proceeded smoothly even at low temperature (-78— -100 °C) in a trans addition manner, and the orientation of addition (formation of 6) was proved by the hydrolysis of the adduct (6c) with D_2O to give 1-(E)-1-D-heptenyl p-tolyl sulfoxide (8) [δ 6.43 (br t, J=6.0 Hz, H_β)] (Eq. 3). The vinylic sulfoxides (7) thus obtained were shown to be optically pure by HPLC analysis on a chiral stationary phase.[11] Consequently, the



4 6 7 8 (3)

Table 2.

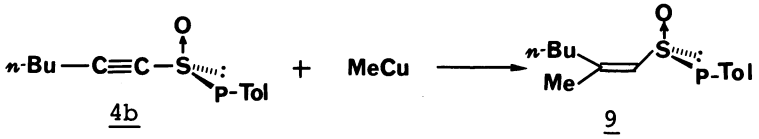
Compound	Product	Yield/%[a]	$[\alpha]_D^{20}$/° (acetone)
4a	7a	84	+178 (*c* 1.003)
4b	7b	87	+158 (*c* 1.027)
4c	7c	74	+148 (*c* 0.517)
4d	7d	81	+138 (*c* 0.503) (ref. +104°)[b]

a) Yields are for the isolated pure products.
b) See Ref. 9.

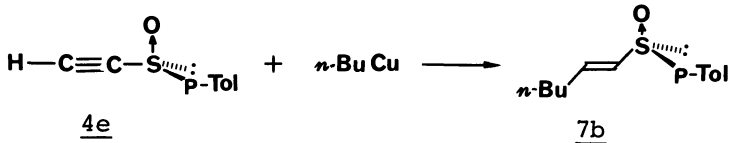
optical purity of the acetylenic sulfoxides prepared by the present method was estimated to be 100%.

An additional advantage of the present method has also been shown by the fact that the acetylenic sulfoxides (4) undergo stereoselectively a facile 1,4-conjugate addition with organocopper reagents to give the β-mono or β,β-disubstituted vinylic sulfoxides.[12] For example, the reaction of 4b with MeCu in THF proceeded well to furnish a single product, (Z)-2-methyl-1-hexenyl p-tolyl sulfoxide (9)[13] {$[\alpha]_D^{20}$ +260° (*c* 0.50, acetone)} in 77% yield (Eq. 4). Similarly, 4e reacted with n-BuCu in THF, affording 7b {$[\alpha]_D^{20}$ +154° (*c* 1.02, acetone)} in 80% yield (Eq. 5).

Thus, the present method offers an easy access to a variety of optically pure 1-alkenyl p-tolyl sulfoxides as well as 1-alkynyl p-tolyl sulfoxides because of the ready availability of acetylenic Grignard reagents. We are currently investigating the utility of these α,β-unsaturated sulfoxides as a chiral synthon for asymmetric syntheses.



4b 9 (4)



4e 7b (5)

A representative procedure is described for 1-(E)-hexenyl p-tolyl sulfoxide (7b). 1-Hexyne (2.26 g, 28.8 mmol) was added to an ethereal solution of EtMgBr (11 mL of 2.17 M solution) and the mixture was refluxed for 1 h under nitrogen. To the cooled solution[14] was added a solution of 2 (5.88 g, 20 mmol) in toluene (70 mL) at -20 °C. After stirring for 1 h, the reaction was quenched by the addition of saturated aqueous ammonium chloride. Extractive work-up followed by chromato-

graphic purification on silica gel (hexane-EtOAc=20:1) afforded 3.52 g (80% yield) of 4b. To a solution of 4b (1.41 g, 6.4 mmol) in 20 mL of THF was added dropwise a solution of DIBAH (5 mL of 1.53 M solution, 7.65 mmol) at -90 – -95 °C. The reaction was usually complete within 10 min. Addition of saturated aqueous ammonium chloride and extractive work-up followed by purification (silica gel chromatography; 3:1 hexane-EtOAc as eluent) gave 1.23 g (87% yield) of 7b.

References

1) For a recent review of the Michael addition reaction, see: G. H. Posner, "Addition of Organometallic Reagents to Chiral Vinylic Sulfoxides," in "Asymmetric Synthesis," ed by J. D. Morrison, Academic Press, N.Y. (1983), Vol. 2, Part A, Chap. 8, p. 225.

2) For the Diels-Alder reaction, see: C. Maignan and R. A. Raphael, Tetrehedron, 39, 3249 (1983); T. Koizumi, I. Hatamada, and E. Yoshii, Tetrahedron Lett., 25, 87 (1984); C. Maignan, A. Guessous, and F. Rouessac, ibid., 25, 1727 (1984).

3) For examples of other types of asymmetric reactions using chiral vinylic sulfoxides, see: R. W. Hoffmann and N. Maak, Tetrahedron Lett., 1976, 2237 ; T. Koizumi, H. Hirai, and E. Yoshii, J. Org. Chem., 47, 4005 (1982); J. P. Marino and A. D. Perez, J. Am. Chem. Soc., 106, 7643 (1984); G. Solladié and G, Moine, ibid., 106, 6097 (1984).

4) D. J. Abbott, S. Colonna, and C. L. M. Stirling, J. Chem. Soc., Chem. Commun., 1971, 471 and Ref. 9.

5) M. Mikołajczyk, S. Grzejszczak, and A. Zatorski, J. Org. Chem., 40, 1979 (1975); M. Mikołajczyk, W. Midura, S. Grzejszczak, A. Zatorski, and A. Chefrezynska, ibid., 43, 473 (1978).

6) H. Kosugi, H. Konta, and H. Uda, J. Chem. Soc., Chem. Commun., 1985, 211.

7) Oxidation using microorganisms: H. Ohta, Y. Okamoto, and G. Tsuchihashi, Chem. Lett., 1984, 205 , and references cited therein. Oxidation by chiral chemical reagents: P. Pitchen, E. Dũnach, M. N. Desmukh, and H. B. Kagan, J. Am. Chem. Soc., 106, 8188 (1984), and references cited therein.

8) K. K. Andersen, Tetrahedron Lett., 1962, 93; K. Mislow, M. M. Green, P. Laur, J. K. Melillo, T. Simmons, and A. L. Ternary, Jr., J. Am. Chem. Soc., 87, 1958 (1965). For a recent review, see: G. Solladié, Synthesis, 1981, 185.

9) G. H. Posner and P. W. Tang, J. Org. Chem., 43, 4131 (1978).

10) T. Mole and E. A. Jeffery, "Organoaluminium Compounds," Elservier, Amsterdam (1972), p. 263.

11) Chiralcel OB (cellulose tribenzoate coated silica gel, Daicel Chemical Industries Ltd.). The racemates of 7 were completely resolved on this column, whereas the acetylenic sulfoxides were not resolved. For example, this column showed resolving power for 7b; separation factor α=1.6, resolution factor R_s= 1.1 [HPLC conditions: column, 25 x 0.46 cm (i.d.); hexane - 2-propanol (85:15); flow rate 0.88 mL/min; a 254 nm UV detector].

12) W. E. Truce and M. J. Lusch, J. Org. Chem., 43, 2252 (1978).

13) ^{1}H NMR (100 MHz, $CDCl_3$) of 9: δ 0.97 (t, J=7.0 Hz, 3H), 1.2-1.7 (4H), 1.86 (d, J=1.2 Hz, 3H), 2.38 (s, 3H), 2.58 (br t, J=7 Hz, 2H), 6.00 (br s, 1H), 7.32 (d, J=8.0 Hz, 2H), and 7.48 (d, J=8.0 Hz, 2H). The stereoisomer of 9 could not be detected from the analysis of the ^{13}C NMR and ^{1}H NMR spectra. The Z stereochemistry of 9 is based on the result of the analogous system reported in Ref. 12.

14) In the case of trimethylsilylethynyl Grignard reagent, it is necessary to suspend the Grignard reagent in toluene after evaporation of the ether.

(Received March 14, 1985)