

YU ISSN 0351—8655
Original Scientific Paper**Asymmetric Synthesis of Sulfoxides from Alkenyl Sulphides, Disulphides and Related Compounds, with (1S)-(+)-Percamphoric Acid. Gem-Disulphides and Related Compounds, Part XXIII.¹**

*Ante Deljac, (the late) Ranajit Purkayastha,^{1a} Micheline Popović-Tkalčić, Mira Novak, Jadranka Blažević and Krešimir Balenović**

*Centre for the Chemistry of Organic Natural Compounds
of the Yugoslav Academy of Sciences and Arts,
Strossmayerov trg 14, YU 41001 Zagreb, Croatia, Yugoslavia*

Received April 8, 1988.

Accepted May 10, 1988.

Partial asymmetric oxidation of sulphides **1**, **2**, **5** and **6** with percamphoric acid is described. The results are summarized on Tables 1—3 and interpreted in terms of the earlier proposed transition state with diamond-lattice structure for the oxidation of sulphides and sulfoxides with percamphoric acid (Schemes 1 and 3). Subclasses of sulphides **1** and **2** gave sulfoxides with the same sign of optical rotation. Sulfoxides from subclasses **5** and **6** have opposite rotations. These facts, as well as the fact that sulfoxides **4a** and **4b** (Table 1) on the one side, and the sulfoxides **7a** and **7b** (Table 2) on the other, have opposite signs of rotation, are strongly in favour of the proposed transition state illustrated on Scheme 1.

Several asymmetric sulfoxide syntheses have been accomplished, although in low optical yields, by oxidizing the appropriate sulphides with such optically active peracids as percamphoric acid, perhydratropic acid, and α -substituted perglutaric acid.^{2,2a,3}

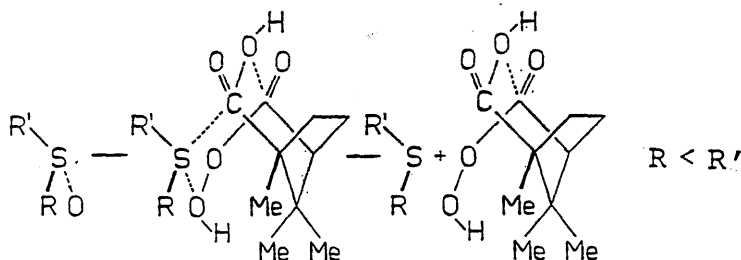
Regarding in retrospect the work on the asymmetric synthesis of sulfoxides in our Laboratory, we attempted to gain information about the absolute configuration of sulfoxides by means of active peracids.³ However, it soon became evident that other laboratories were simultaneously and independently working on the same problem.^{2, 2a}

We later found that during the reaction of butyl methyl sulfoxide⁴ with L-cysteine or (+)-2-mercaptopropionic acid, the (—)-(*R*)-sulfoxide accumulated, indicating that the (*S*)-enantiomer was reduced faster by the thiol⁵ (Scheme 2a).

It is true that our experiments with the optically active reagents we have used gave comparatively low optical yields, but the configuration assigned

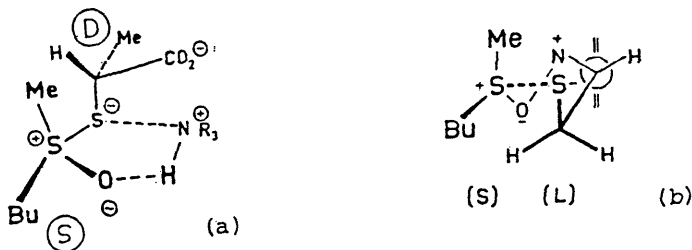
* To whom inquiries should be addressed.

to the few sulfoxides obtained were proven in later investigations to be correct. We also proposed a hypothetical transition state for these oxidations with diamond-lattice structure (Scheme 1).



Scheme 1

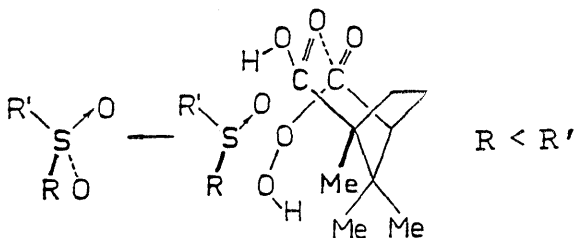
Our hypothetical transition states for the reductions with thiols are presented in Scheme 2a, b.



Scheme 2a, b

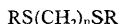
It is evident today that no simple rationalization of the optical induction in terms of the eclipsic effect of small, medium and large groups in the respective transition states is possible, because electronic and other effects are important in the formation of transition states. Therefore, at best one might derive particular heuristic rules for predicting absolute configurations for different substrate series. These hypothetical transition states, proposed more than twenty years ago³, were severely criticized at that time as superfluous, since the geometry of the relevant transition states of oxidation remains unknown.⁶ Today the real transition state for the oxidation of sulfoxides still does not exist, and the criticized transition states remain useful in certain cases: for instance, the interesting fact that opposite stereospecificity is found in asymmetric oxidations of sulfoxides and of sulphides with the same peroxy-acid; *i.e.*, the enantiomeric sulfoxides which are preferentially formed,

from the sulphides are found to be those which are oxidized more slowly to sulphones.^{7, 8} Both asymmetric inductions can be interpreted with the same model of transition states proposed earlier.² Our model of the transition state with diamond-lattice structure³ for the oxidation of asymmetric sulphoxides with (1S)-(+)-percamphoric acid has enabled us to interpret both asymmetric inductions^{9, 14} (Scheme 3).



Scheme 3

Therefore, in the present modest experimental contribution we have given new examples of the asymmetric oxidations of several classes of new asymmetric sulphides (**1**, a: R, *t*-butyl, R', allyl; b: R, *n*-amyl, R', allyl) and disulphides (**2**, a: R, *t*-butyl, *n* = 1; b: R, *t*-butyl, *n* = 2)

**1****2**

The resulting sulfoxides were the following: *t*-butylallyl sulfoxide (**3a**); *n*-amylallyl sulfoxide (**3b**); *t*-butylsulphinyl-*t*-butylthio methane (**4a**); 1-*t*-butylsulphinyl-2-*t*-butylthio ethane (**4b**). The results are summarized on Table 1.

TABLE 1

Sulfoxides obtained by oxidation with (1S)-(+)-percamphoric acid in Et₂O solution at -5°

Compound	B.p./mm; m.p.	$[\alpha]_D^{25}$	Solvent
3a	b.p. 55—60°/0.1	+1,62°	MeOH
3b	b.p. 65—70°/0.1	0,0°	"
4a	m.p. 73—74°	+3,5°	"
4b	b.p. 85—89°/0.07	+1,56°	dioxane

We also oxidized the following mercaptals (**5**) and *trans*-1-methylthio-1-alkenes (**6**) with (1S)-(+)-percamphoric acid: 1,1-bismethylthio-3-phthalimido propane (**5a**); 1,1-bismethylthio-4-phthalimido butane (**5b**); *trans*-1-methylthio-1-heptene (**6a**); *trans*-1-methylthio-4-phthalimido-1-butene.

Table 2 summarizes the properties of the resulting sulfoxides: 1-methylsulphanyl-1-methylthio-3-phthalimidopropane (**7a**); 1-methylsulphanyl-1-methylthio-4-phthalimidobutane (**7b**); *trans*-1-methylsulphanyl-1-heptene (**8a**); *trans*-1-methylsulphanyl-4-phthalimido-1-butene (**8b**).

TABLE 2

Sulfoxides obtained from 1-methylthio derivatives 5 and 6 by oxidation with (1S)-(+)-percamphoric acid in Et₂O at 0°C

Compound	m.p.	$[\alpha]_D^{25}$	Solvent
7a *	135—137°	—0.8°	CHCl ₃
7b	101—114°	—5.4°	MeOH
8a	b.p. 62—67°/0.02	—0.6°	MeOH
8b	151—153°	—1.4°	CHCl ₃

* See ref. 9a

Our experiments on the partial asymmetric oxidations of sulphides **1**, **2**, **5**, and **6** with (1S)-(+)-percamphoric acid are summarized on Table 3 in which the sign of optical rotation is correlated with the structure of substituents R and R' as proposed in the hypothetical transition state with diamond-lattice structure illustrated in Scheme 1. It is evident that some subclasses of our sulphides (**1** and **2**) gave the same sign of optical rotation. Other subclasses of sulphides (**5** and **6**) gave opposite signs of rotation. In terms of the large, medium, and small sizes of substituents R and R' as proposed for our transition state, the fact that sulfoxides **4a** and **4b** on the one side and sulfoxides **7a** and **7b** on the other side have opposite signs of optical rotation, is strongly in favour of our proposition for the transition state illustrated on Scheme 1.

TABLE 3

Sulfoxides of the structures 3, 4, 7, 8 (RSOR', R < R') obtained by oxidation from the corresponding sulphides with (1S) — (+) — percamphoric acid: sign of optical rotation correlated with the nature of substituents R and R'.

Compound	R	<	R'	sign of $[\alpha]_D$
3a	allyl	<i>t</i> -butyl		+
3b	allyl	<i>n</i> -amyl		0
4a	<i>t</i> -BuSCH ₂ —	<i>t</i> -butyl		+
4b	<i>t</i> -BuS(CH ₂) ₁ —	<i>t</i> -butyl		+
7a	CH ₃	CH(SCH ₃) (CH ₂) ₂ R''		—
7b	CH ₃	CH(SCH ₃) (CH ₂) ₃ R''		—
8a	CH ₃	<i>trans</i> -CH=CH(CH ₂) ₄ CH ₃		—
8b	CH ₃	<i>trans</i> -CH=CH(CH ₂) ₅ R''		—

R'' = phthalimido

EXPERIMENTAL

M. ps. are uncorrected. Tlc was performed on Silica Gel HF₂₅₄ (E. Merck) and spots developed with 1% KMnO₄ solution. Organic sulphides and sulfoxides were detectable with this reagent as intense yellow spots on a pink background. Light petroleum refers to the fraction with the b.p. 40–60°C. IR spectra were taken on a Perkin-Elmer Infracord 137. Optical rotations were measured on a Bendix NPL Automatic Polarimeter 143D. Sulphides **1** and **2** were prepared in liquid ammonia according to the procedure described earlier for the preparation of S-alkyl-cysteines from cystine¹⁰, from di-*t*-butyl disulphide resp. di-*n*-amyl disulphide and the appropriate alkyl halogenide. 1,1-bismethylthio-3-phthalimido propane (**5a**), 1,1-bis methylthio-4-phthalimido butane (**5b**), *trans*-1-methylthio-1-heptene (**6a**) and *trans*-1-methylthio-4-phthalimido-1-butene (**6b**) were prepared following the procedure described earlier.¹¹

Oxidations of 1, 2 5 and 6 with (1S)-(+)-monopercamphoric acid. 1S-(+)-monopercamphoric acid was prepared by oxidation of (+)-camphoric anhydride with sodium peroxide, acidification, and extraction with CHCl₃.¹² Oxidations in Et₂O were performed as described earlier.¹¹ Oxidations in CHCl₃ solution: The titrated CHCl₃ solution of peroxy-acid was added dropwise to a stirred CHCl₃ solution of appropriate sulphide with the temperature maintained at -5°C until the oxidant had disappeared (iodimetric test). At the end of the reaction (after 6–7 hrs.), the CHCl₃ solution was repeatedly extracted with saturated aqueous NaHCO₃, washed with water and dried (MgSO₄). Removal of the solvent and crystallization from CH₂Cl₂-light petroleum gave the corresponding sulfoxides.

TABLE 4

Sulfoxides obtained by oxidation with (1S)-(+)-percamphoric acid

Compound	B.p./mm or m.p.°	Formula	Found (%)		Required (%)	
			C	H	C	H
3a	55–60/0.1	C ₇ H ₁₆ OS	57.30	9.91	57.49	9.65
3b	65–70/0.1	C ₈ H ₁₈ OS	60.10	9.98	59.95	10.06
4a	73–74°	C ₉ H ₂₀ OS ₂	52.45	9.67	51.87	9.68
4b	85–89/0.07	C ₁₀ H ₂₂ OS ₂	55.46	10.48	54.00	9.97
7b	101–114°	C ₁₄ H ₁₇ O ₃ NS ₂	54.01	5.81	53.99	5.50
8a	62–67/0.02	C ₈ H ₁₆ OS	59.49	10.22	59.95	10.06
8b	151–153	C ₁₃ H ₁₉ O ₃ NS	59.44	5.12	59.30	4.98

Each of these compounds has a strong bifurcated absorption band in the IR spectrum characteristic for sulfoxides, ν_{max} (KBr) at 1040–1050 cm⁻¹.

Acknowledgements — We thank the Republic Research Fund of Croatia for financial support of this research.

REFERENCES AND NOTES

- Part XXII: Tetrahedron Lett. **21**, 3089 (1980). Part XXI: Tetrahedron, **36**, 1895 (1980).
- 1a. Part of the Doctor's Thesis, University of Zagreb, 1961, on leave of absence from the Department of Applied Chemistry, University of Calcutta, India.
2. A. Mayr, F. Montanari, and M. Tramontini, Gazz. chim. ital. **90**, 739 (1960).
- 2a. A. Maccioni, F. Montanari, M. Secci, and M. Tramontini, Tetrahedron Lett. 607 (1961).

3. K. Balenović, N. Bregant, and D. Francetić, *Tetrahedron Lett.* 20 (1960); K. Balenović, I. Bregovec, D. Francetić, I. Monković, and V. Tomašić, *Chem. & Ind.* **1961**, 469.
4. The absolute configuration of methyl *n*-butyl sulphoxide was determined by the synthesis from optically active *l*-butanesulphinic acid. K. Mislow, M. M. Green, P. Laur, and D. R. Chisholm, *J. Amer. Chem. Soc.* **87**, 665 (1965); K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr., *ibid.* **87**, 1958 (1965).
5. K. Balenović and N. Bregant, *Chem. & Ind.* **1964**, 1577; N. Bregant, K. Balenović, and V. Polak, *Bull. Sci. Cons. Acad. Sci. Arts RSF Yougoslavie, Sect. A* **17**, 289 (1972).
6. Cf. Mislow et al., reference 4 and experimentally extensively founded counter-arguments of F. Montanari et al., *Tetrahedron Lett.* **1965**, 3367 and U. Folli, D. Iarossi, and F. Montanari, *J. Chem. Soc. (C)* **1968**, 1317.
7. M. Kobayashi and A. Yabe, *Bull. Chem. Soc. Japan* **40**, 224 (1967).
8. U. Folli, D. Iarossi, and F. Montanari, *J. Chem. Soc. (C)* **1968**, 1372.
9. V. Polak, M. A. Thesis, University of Zagreb, 1967.
- 9a. O. Nota, M. A. Thesis, University of Zagreb, 1977. In our Laboratory O. Nota obtained **7a** by oxidation of **6a** in the presence of *Aspergillus niger* NRRL 337 Culture showing $[\alpha]_D^{25} + 24.9^\circ$ (CHCl₃), 1.13. Compound **7a** was oxidized with (1S)-(+)-percamphoric acid in CHCl₃ solution at -20°C . At temperatures above -20°C optically inactive products were obtained.
10. K. Balenović, I. Jambrešić, B. Gašpert, and D. Cerar, *Rec. trav. chim. Pays-Bas* **75**, 125 (1956); K. Balenović, D. Fleš, and I. Jambrešić, *Croat. Chem. Acta* **28**, 303 (1956).
11. A. Deljac, Z. Stefanac, and K. Balenović, *Tetrahedron, Suppl.* **8**, Part I, 33 (1966).
12. N. A. Milas and A. McAlevy, *J. Amer. Chem. Soc.* **55**, 349 (1933).
13. B. J. Aurret, D. R. Boyd, H. B. Henbest, C. G. Watson, K. Balenović, V. Polak, V. Johanides, and S. Divjak, *Phytochemistry* **13**, 65 (1974).
14. Note added during proof-reading (Dec 5, 1990): Vladimir Prelog and coworkers¹⁵ pointed out that as early as 1941, before the introduction of conformational analysis Speakman used diamond-lattice sectors in a discussion of the probable conformers of perhydrodiphenic acids and the influence of conformation on their dissociation constants, and expressly referred to this possibility.¹⁶ In our laboratory we have used the diamond lattice to interpret the transannular reaction course in cyclodecane derivatives¹⁷ and to characterize the stereoselectivity of oxido-reductases.¹⁸⁻²¹ A well-known chemist close to us (A. E.) has described the diamond lattice as the 'poor man's computer'.²²
15. V. Prelog, M. Kovačević and M. Egli, *Angew. Chem. Int. Ed. Engl.* **28**, 1147 (1989).
16. J. C. Speakman, *J. Chem. Soc.*, **1941**, 490
17. J. D. Dunitz, V. Prelog, *Angew. Chem.* **72**, 896, (1960).
18. V. Prelog, *J. Pure Appl. Chem.* **9**, 119, (1964).
19. H. Dutler, J. L. Van der Baan, E. Hochuli, Z. Kis, K. E. Taylor, V. Prelog, *Eur. J. Biochem.* **75**, 423, (1977).
20. J. M. H. Graves, A. Clarks, H. J. Ringold, *Biochemistry* **4**, 2655, (1965).
21. J. B. Jones, J. Jakovac, *Can. J. Chem.* **60**, 19, (1982).

SAZETAK

Asimetrijska sinteza sulfoksida oksidacijom alkenil sulfida, disulfida i srodnih spojeva sa (1S)-(+)-perkamfornom kiselinom. Gem-disulfidi i srodni spojevi, XXIII dio

Ante Deljac, Ranajit Purkayastha, Micheline Popović-Tkalčić,
Mira Novak, Jadranka Blažević i Krešimir Balenović

Opisana je parcijalna asimetrijska oksidacija sulfida **1**, **2**, **5** i **6** s perkamfornom kiselinom. Rezultati su prikazani u tablicama 1–3, a protumačeni su ranije pretpo-

stavljenom međufazom u ovoj oksidaciji (sheme 1 i 3). Iz sulfida podvrsti **1** i **2** nastaju sulfoksidi s istim predznakom optičke rotacije, dok sulfoksidi nastali iz podvrsti **5** i **6** pokazuju suprotan predznak. Ta činjenica, kao i podatak da sulfoksidi **4a** i **4b** (Tablica 1) imaju suprotan predznak rotacije od sulfoksida **7a** i **7b** (Tablica 2), podupire našu pretpostavku o strukturi međufaze ove oksidacije analogne kristalnoj mrežici diamanta kako je prikazano na shemama 1 i 3.

LABORATORIJ ZA KEMIJU ORGANSKIH
PRIRODNIH SPOJEVA JUGOSLAVENSKE
AKADEMIJE ZNANOSTI I UMJETNOSTI,
STROSSMAYEROV TRG 14,
YU-41000 ZAGREB

Prispjelo 8. travnja 1988.

Prihvaćeno 10. svibnja 1988.

