

Activation of hydrogen peroxide for asymmetric epoxidation by chiral arenesulfonimidoylimidazoles †

Ralph Kluge,* Heiko Hocke ‡ and Manfred Schulz

Martin-Luther-Universität Halle-Wittenberg, Institut für Organische Chemie, Geusaer Straße, D-06217 Merseburg, Germany

Abstract: Different types of olefins were oxidized by using the chiral (arenesulfonimidoyl)imidazoles **3a,b** and H₂O₂ in the presence of 2N NaOH or K₂HPO₄. The corresponding epoxides were isolated in moderate to good yields. *Cis*- and *trans*-olefins were converted stereospecifically (retention of the configuration). Enantiomeric excesses up to 42% were obtained. © 1997 Elsevier Science Ltd

The search for effective new reagents for asymmetric oxidations is an important field in modern organic chemistry. In stoichiometric asymmetric epoxidations, the application of hydrogen peroxide (in the presence of an effective chiral activator) is of special interest, because it is an inexpensive oxidant with a high content of active oxygen. Attempts to activate H₂O₂ by transformation to chiral carboxylic peracids resulted in ee values of 10% max in asymmetric epoxidations.¹ Recently, the activation of H₂O₂ by a chiral phosphoryl chloride was described, the corresponding epoxides were obtained with ees up to 22%.²

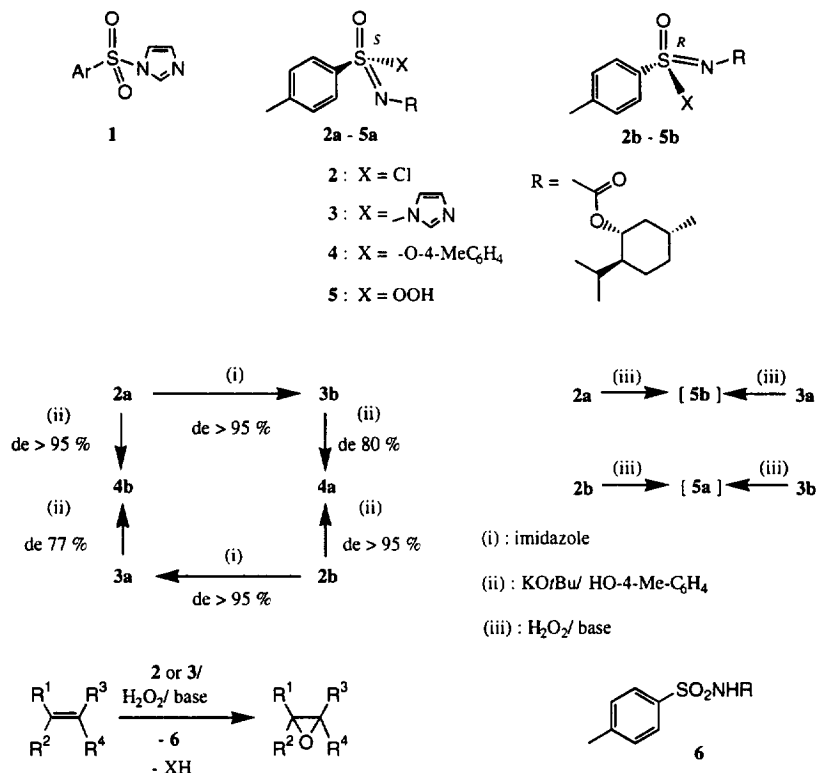
Our own results in the highly diastereoselective epoxidation by arenesulfonic peracids (generated *in situ* from 1/H₂O₂/base)³ prompted us to investigate whether the heteroanalogous (arenesulfonimidoyl)imidazoles **3** could be useful new chiral activators for H₂O₂. The enantiomerically pure diastereomeric 1-(arenesulfonimidoyl)imidazoles **3a** and **3b** were prepared⁴ in near-quantitative yields by the reaction of the corresponding known enantiomerically pure sulfonimidoyl chlorides **2a,b**⁵ with imidazole. Complete inversion of the configuration at the sulfur atom (de >> 95%) was observed,⁶ thus, **2a** gave **3b** and **2b** led to **3a**.

Different types of olefins (mono-, di- and trisubstituted olefins, allylic and homoallylic alcohols) were epoxidized with **3a** or **3b**/H₂O₂/base (2N NaOH or K₂HPO₄) in MeOH at 25°C or 65°C (the product resulting from **3a,b** the sulfonamide **6** was isolated; yield 85–95%). The results are summarized in Table 1. Generally, the oxidations proceeded under retention of the stereochemistry (*cis*-olefins gave *cis*-epoxides and *trans*-olefins led to *trans*-epoxides, de > 99%). Nonfunctionalized olefins (entries 1–9) gave moderate epoxide yields and ees up to 11%. Significantly higher yields were obtained, when allylic or homoallylic alcohols were employed (entries 10–16) and, in the case of *cis*-2-hexen-1-ol, increased enantioselectivity was observed (ee 37%, entry 10), indicating an association of the oxidant with the substrate (compare with the findings of Kluge et al.³). The more reactive sulfonimidoyl chlorides **2a,b** were also used, but led to lower epoxide yields (4-fold excess of the olefin was necessary to get acceptable conversions; entries 7, 9, 11, 13). However, comparable ees were obtained and the configuration of the epoxide was the same, when the analogous diastereoisomers **2a/3a** or **2b/3b** were introduced.

† Dedicated to Prof. Dr Dr hc Waldemar Adam on the occasion of his 60th birthday.

* Corresponding author.

‡ Dissertation in progress, Martin-Luther-Universität Halle-Wittenberg. Email: hocke@mailserv.rz.fh-merseburg.de



A plausible interpretation of the results may be given by the intermediate formation of the hitherto unknown⁸ arenesulfonimidic peracids **5a,b** (a new type of chiral peracids with an asymmetric centre directly bound to the peroxy group) as the active oxygen transfer reagents. In agreement with the known S_N^2 -like reactions of **2a,b** with different N-, O- and C-nucleophiles,⁵ we assume that **2a/3a** should react to give the (*R*)-peracid **5b** and the (*S*)-peracid **5a** is formed from **2b/3b**. This is also in agreement with the reaction of **2a** and **3a** to the known ester **4b**⁵ (**2b** and **3b** yielded **4a**) under inversion of the configuration at the sulfur atom.

The results represent the first examples for a chiral induction by sulfur peroxy intermediates (chiral at the sulfur atom) in stoichiometric epoxidations.







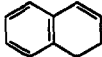
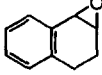









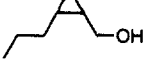

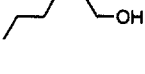


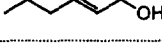
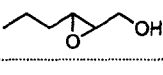
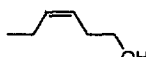
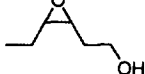
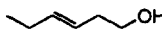
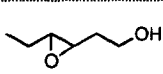
Acknowledgements

The financial support both by the Deutsche Forschungsgemeinschaft (DFG-Schwerpunktprogramm: "Sauerstofftransfer/ Peroxidchemie") and the Fonds der Chemischen Industrie is gratefully acknowledged.

References

- (a) Montanari, F.; Moretti, I.; Torre, G. *Chem. Commun.* **1969**, 135. (b) Pirkle, W. H.; Rinaldi, P. *L. J. Org. Chem.* **1977**, *42*, 2080–2082.
- Berkessel, A.; Frauenkron, M. *Tetrahedron: Asymmetry* **1996**, *7*, 671–672.
- Kluge, R.; Schulz, M.; Liebsch, S. *Tetrahedron* **1996**, *52*, 2957–2976.
- (+)-(*S*)-1-*N*-[Carbo-(1*R*)-menthoxy]-*p*-toluenesulfonimidoyl]imidazole **3a**: the (–)-(*R*)-sulfonimidoyl chloride **2b**⁵ (371 mg, 1 mmol) was stirred with 204 mg (3 mmol) imidazole in 5 ml dry THF at 0°C for 24 h. After filtration, evaporation of the solvent *in vacuo* and column chromatography (silica gel; *n*-hexane/EtOAc 3/1), 392 mg (97%) **3a** were obtained as colourless oil. Elemental analysis: calc. (found) C: 62.50 (62.35), H: 7.24 (7.36), N: 10.41 (10.37), S: 7.94

Table 1. Asymmetric epoxidation of olefinic substrates with **2a,b** or **3a,b**/H₂O₂/base

Entry ^{a)}	Educt	Product ^{b)}	Conditions ^{c)}	Conv. [%] ^{d)}	Yield [%] ^{e)}	ee [%] ^{f)} (Config.) ^{g)}
1			3b , A), 25 °C, 24h	73	32	7 (<i>S</i>)
2			3b , A), 65 °C, 4h	61	74	9 (<i>S,S</i>)
3			3a , A), 65 °C, 4h	60	72	5 (<i>R,R</i>)
4			3b , A), 65 °C, 4h	79	36	6 (<i>1S,2R</i>)
5			3b , B), 25 °C, 24h	-	68 ^{h)}	11 (<i>R,R</i>)
6			3b , A), 65 °C, 4h	63	81	11 (<i>R,R</i>)
7			2b , B), -5 °C, 0.5h	-	60 ^{h)}	8 (<i>R,R</i>)
8			3a , A), 65 °C, 4h	68	72	2 (<i>S,S</i>)
9			2a , B), -5 °C, 0.5h	-	45 ^{h)}	2 (<i>S,S</i>)
10			3b , B), 25 °C, 24h	84	95	37 (<i>2R,3S</i>)
11			2b , B), -5 °C, 1h	-	56 ^{h)}	41 (<i>2R,3S</i>)
12			3a , B), 25 °C, 24h	100	90	29 (<i>2S,3R</i>)
13			2a , B), -5 °C, 1h	-	69 ^{h)}	42 (<i>2S,3R</i>)
14			3b , B), 25 °C, 24h	86	93	8 (<i>2S,3S</i>)
15			3b , B), 25 °C, 24h	100	76	0
16			3b , B), 25 °C, 24h	91	80	7 (<i>3R,4R</i>)

(a) For experimental details see Ref. 6. (b) All epoxides were characterized by ¹H NMR spectroscopy and by GC-MS. (c) A: K₂HPO₄; B: 2 N NaOH. (d) Conversion of the olefin, determined from the quantity of recovered starting material. (e) Isolated pure epoxides with respect to conversion. (f) The ee values of the epoxides were determined by ¹H NMR spectroscopy with Eu(hfc)₃ as a shift reagent (entries 1–9; solvent CDCl₃). The epoxy alcohols were converted to the acetates⁷ prior to the shift experiments [Eu(hfc)₃; solvent: C₆D₆; entries 10–16]. (g) The configuration was determined by optical rotation measurements.⁹ (h) Yield refers to introduced **2** and **3**, because a 4-fold excess of the olefin was used.

(7.90); MS (EI): m/z 403 [M+]; ¹H NMR (300 MHz, CDCl₃): δ (ppm) 0.6–2.1 (m, 18H), 2.42 (s, 3H), 4.55 (td, 1H, J₁ 10.65 Hz, J₂ 4.4 Hz), 7.07 (s, 1H), 7.24 (s, 1H), 7.34 (d, 2H, J 8.3 Hz), 7.92 (d, 2H, J 8.3 Hz), 7.99 (s, 1H); [α]₂₅²⁵ +53.8 (c 1.33, CHCl₃); de ≫ 95% (chiral HPLC: Chiralcel OJ, n-hexane/ iPrOH 9/1, 1 ml/min). The diastereomer **3b** was prepared in the same way from 371 mg (1 mmol) **2a**. **3b**: colourless oil, yield 390 mg (97%; de ≫ 95%, chiral HPLC—see above); elemental analysis: calc. (found) C: 62.50 (62.57), H: 7.24 (7.24), N: 10.41 (10.53), S: 7.94 (7.61); MS (EI): m/z 403 [M+]; ¹H NMR (300 MHz, CDCl₃): δ (ppm) 0.6–2.1 (m, 18H), 2.44 (s, 3H), 4.56 (td, 1H, J₁ 10.65 Hz, J₂ 4.4 Hz), 7.07 (s, 1H), 7.22 (s, 1H), 7.34 (d, 2H, J 8.3 Hz), 7.92 (d, 2H, J 8.3 Hz), 7.99 (s, 1H); [α]₂₅²⁵ -135.5 (c 1.33, CHCl₃).

5. Jones, M. R.; Cram, D. J. *J. Am. Chem. Soc.* **1974**, *96*, 2183–2190.

6. *Epoxidation Procedure.* Method A: the olefin (1 mmol), 1 mmol **3a** or **3b** and 5 mmol H₂O₂ (33%) were dissolved in 10 ml MeOH and 3 mmol K₂HPO₄ were added and the mixture was stirred at 25°C (24 h) or at 65°C (4 h), until **3** was completely consumed (TLC). After concentration of the mixture *in vacuo* to ca. 1/3, addition of 2 ml brine and 8 ml H₂O and extraction with CH₂Cl₂ (5×10 ml), the organic phase was dried over MgSO₄. After evaporation of the solvent *in vacuo*, the residue was purified by flash chromatography (silica gel; epoxides: *n*-hexane/EtOAc 50/1, epoxy alcohols: *n*-hexane/EtOAc 4/1). Method B: The reactions were carried out in an analogous manner as described for the oxidation with 1/H₂O₂/2N NaOH,³ by slowly adding 1 mmol 2N NaOH over a period of 3–4 h (microsyringe; pH ca. 8–10, unitest) to a solution of 1 mmol olefin, 1 mmol **3a** or **3b** and 5 mmol H₂O₂ (33%) in 5 ml MeOH at 25°C and additional stirring at 25°C (24 h). The work up procedure was the same as above. The oxidations with **2a,b** were performed analogously. But instead, 2 mmol olefin, 5 mmol H₂O₂ (33%), 0.5 mmol **2** and 0.5 mmol 2N NaOH were reacted in 10 ml THF/MeOH 1/1 (v/v) at –5°C (**2a,b** were consumed completely after the addition of NaOH over a period of 0.5–1 h).
7. Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765–5780.
8. Treatment of arenesulfonimidoyl chlorides with KO₂ led to an oxidant (probably a peroxy radical intermediate) which epoxidizes olefins nonstereospecifically: (a) Kim, Y. H.; Yoon, D. C. *Synth. Commun.* **1989**, *19*, 1569. (b) Kim, Y. H.; Lim, S. C.; Hoshino, M.; Obtsuka, Y.; Ohishi, T. *Chem. Lett.* **1989**, 167.
9. For example, *cis*-2,3-epoxyhexan-1-ol [ee 37% (2*R*,3*S*); entry 10 of Table 1]: [α]_{D₂₀} +1.43 (c 4.75, CHCl₃). Optically pure material: [α]_{D²⁷} +5.69 (c 1.41, CHCl₃); Mori, K.; Nakazono, Y. *Tetrahedron* **1986**, *42*, 6459–6466.

(Received in UK 5 June 1997; accepted 7 July 1997)