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Asymmetric epoxidation of olefins by chiral dioxiranes generated in situ from ketones of D-(−)-quinic acid

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Abstract

The in situ generated dioxiranes (Caroate as peroxide source) of the optically active ketones **4a** and **4b**, which may be conveniently prepared from D-(−)-quinic acid, serve as effective oxidants for the asymmetric epoxidation (ee values up to ca. 90% with **4a**) of prochiral olefins. © 1999 Elsevier Science Ltd. All rights reserved.

1. Introduction

Dioxiranes are reactive yet selective oxygen-transfer reagents,[1] which are readily generated from Caroate (also known as Oxone) and ketones. Since the ketone is regenerated after the oxygen transfer, in principle, only a catalytic amount is required for the in situ method.[2] Therefore, with optically active ketones, asymmetric oxidations may be conducted.

Since the pioneering work by Curci[3] as early as 1984,[3a] considerable progress has been made recently in the catalytic asymmetric epoxidation of olefins with in situ generated optically active dioxiranes.[4–9] For example, Shi et al. have reported[5a] the fructose-derived ketone **1** for highly asymmetric epoxidation of *trans* disubstituted and trisubstituted prochiral olefins. While this ketone performed adequately under catalytic conditions even at pH ca. 10.5, its persistence is limited due to oxidative destruction.[5a] The same group also reported the ketones **2** and **3** derived from D-(−)-quinic acid, which also yield good enantioselectivities for some *cis* and terminal olefins;[5b] however, the major drawback is their lengthy synthesis. Moreover, all these pseudo C_2-symmetric ketones have the sterically controlling groups at both α positions, which makes it difficult[5c] to modify their structures for more effective asymmetric oxidations, especially for the asymmetric epoxidation of electron-poor olefins[5b] and asymmetric C–H insertion.[10] In our search for new optically active ketones as more effective oxygen-transfer catalysts and to elucidate the structural requirements for efficient asymmetric oxidations,[6] we chose the ketones **4** as

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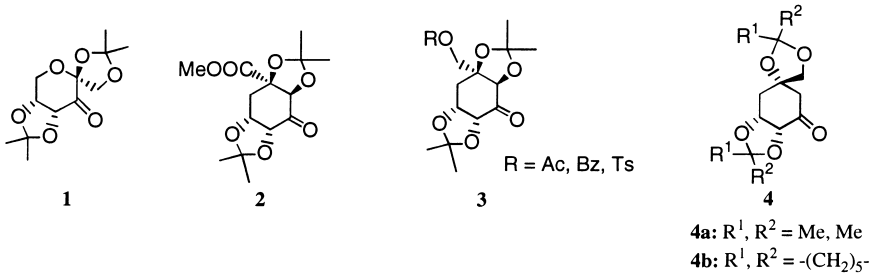
target structures, in which the free α position would allow further modification. Herein we report our results on the asymmetric epoxidation of prochiral olefins with the optically active ketones **4**.

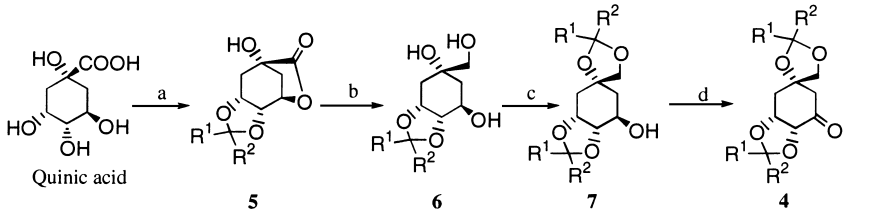


1 **2** **3** **4**

4a: R^1, R^2 = Me, Me
4b: R^1, R^2 = -$(CH_2)_5$-

2. Results and discussion

Ketones **4** were conveniently prepared in good yields from D-(−)-quinic acid, a cheap precursor from the chiral pool. As shown in Scheme 1, quinic acid was converted to **6a** and **6b** in high yields by following the literature procedures.[5b,11] Selective acetalation yielded the known **7a**[12] and the new **7b**, which were oxidized by the Swern method or pyridinium chlorochromate (PCC) to give the new ketones **4a** and **4b** in good yields.



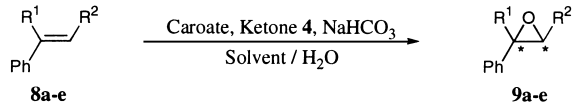
Quinic acid **5** **6** **7** **4**

4a: R^1, R^2 = Me, Me
4b: R^1, R^2 = -$(CH_2)_5$-

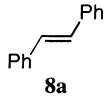
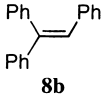
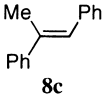
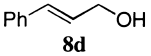
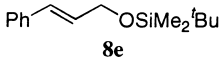
Scheme 1. Synthesis of ketones **4a** and **4b**. Reaction conditions: (a) **5a**: 2,2-dimethoxypropane, TsOH (cat.), benzene, reflux, 88%; **5b**: cyclohexanone, H_2SO_4 (cat.), reflux, 85%. (b) $NaBH_4$, EtOH, ca. 20°C, 100%. (c) **7a**: 2,2-dimethoxypropane, *p*-TsOH (cat.), ca. 20°C, Ar, 75%; **7b**: cyclohexanone, *p*-TsOH (cat.), toluene, reflux, 44%. (d) **4a**: $(COCl)_2$/DMSO then Et_3N, −70°C, 70%; **4b**: pyridinium chlorochromate (PCC), CH_2Cl_2, ca. 20°C, 34%

The results of the asymmetric epoxidation of the prochiral olefins **8** by the in situ generated optically active dioxiranes of the ketones **4** are collected in Table 1. At room temperature (20°C) in acetonitrile with $NaHCO_3$ as the buffer (pH ca. 8), the asymmetric epoxidation of *trans*-stilbene **8a** mediated by ketone **4a** afforded the epoxide **9a** in good enantioselectivity (ee value of 62%) (entry 1); however, the conversion was only 26% even when a stoichiometric amount of ketone **4a** was used. A decrease of the temperature to 0°C led to an increase of the ee value to 78% in a slightly lower (20%) conversion (entry 2). At an even lower temperature (−10°C), the conversion was significantly reduced to 6%, with no improvement in the ee value (entry 3). These results imply that the ketone **4a** does not persist under the reaction conditions, most probably due to Baeyer–Villiger oxidative decomposition.[13] When 3.0 equiv. of ketone **4a** were used, the conversion was increased only to 35%; however, the ee value of the epoxide **9a** was further enhanced to 85% (entry 4). In dimethoxyethane (DME) as solvent at room temperature, the conversion was better than in acetonitrile (42% vs 26%), but with a much lower (37%) ee value (entries 5 and 1). At a lower temperature (−10°C), the conversion dropped dramatically (6%), with no improvement in the ee value (entry 6). In dimethoxymethane (DMM) a high enantioselectivity (77% ee) was obtained

Table 1
Asymmetric epoxidation of prochiral olefins mediated by ketones **4a** and **4b**



8a-e **9a-e**

entry	substrate[a]	ketone (equiv.)	solvent	t (h)	T (°C)	convn (%)[b]	ee (%)[c]	confign[d]
1		**4a** (1.0)	CH_3CN	5	20	26	62	*R*,*R* (+)
2		**4a** (1.0)	CH_3CN	5	0	20	78	*R*,*R* (+)
3		**4a** (1.0)	CH_3CN	6	-10	5	75	*R*,*R* (+)
4		**4a** (3.0)	CH_3CN	6.5	0	35	85	*R*,*R* (+)
5		**4a** (1.0)	DME[e]	5	20	42	37	*R*,*R* (+)
6		**4a** (1.0)	DME[e]	6	-10	<5	38	*R*,*R* (+)
7	**8a**	**4a** (1.0)	DMM[f]	5	0	<5	77	*R*,*R* (+)
8		**4b** (1.0)	CH_3CN	24	20	12	32	*R*,*R* (+)
9		**4b** (1.0)	dioxane	3	20	31	25	*R*,*R* (+)
10		**4b** (1.0)	CH_3CN/ DMM[g]	24	20	<5	45	*R*,*R* (+)
11		**4a** (3.0)	CH_3CN	2.5	0	36	85	*R* (-)
12		**4a** (3.0)	CH_3CN	6	-10	22	84	*R* (-)
13	**8b**	**4b** (1.0)	dioxane	3	20	32	25	*R* (-)
14	 **8c**	**4a** (3.0)	CH_3CN	5	0	47	70	*R*,*R* (+)
15	 **8d**	**4a** (1.0)	CH_3CN	6.5	0	26	18	*R*,*R* (+)
16		**4a** (1.0)	CH_3CN	5	20	23	57[h]	*R*,*R* (+)
17	**8e**	**4a** (3.0)	CH_3CN	6.5	0	29	87[h]	*R*,*R* (+)

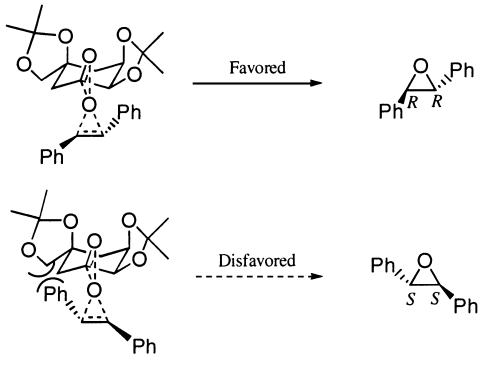
[a] Carried out at pH 8.0 with olefin (0.1 mmol), ketone **4** (0.1-0.3 mmol), Caroate (0.5 mmol) and $NaHCO_3$ (1.55 mmol) in the appropriate solvent (1.5 mL) and 4×10^{-4} M aqu. EDTA solution (1.0 mL). [b]Determined by ^{1}H-NMR analysis, error limit *ca*. 5% of the stated values, yields ≥95% based on conversion in all cases. [c]Determined by chiral HPLC analysis (Chiralcel OD-H or OB-H, UV detection at 220 nm, 9:1 hexane/isopropanol, flow rate 0.5-0.6 mL/min), error limits *ca*. 2% of the stated values. [d]Configuration of the major enantiomer of **9** determined by comparing the sense of the optical rotation with literature values (Ref 5). [e]Dimethoxyethane (DME). [f]Dimethoxymethane (DMM). [g]2:1 (v/v) CH_3CN/DMM. [h]Determined for the desilylated epoxy alcohol **9d** (Ref 5a).

in very low conversion (entry 7), while no consumption of **8a** could be achieved in methylene chloride as solvent (data not shown). Although it is known that the efficiency of some ketones may be improved at elevated pH,[5,6] substrate **8a** resisted conversion at pH 10.5[5] (data not shown). Presumably, the oxidative decomposition of ketone **4a** was much more effective than dioxirane formation at these more basic conditions.[14] Ketone **4b**, which possesses cyclohexylidene instead of isopropylidene groups, gave a lower ee value (32%) in poor conversion (12%) for the epoxidation of the test substrate **8a** in acetonitrile (entry 8), as compared to **4a** (entry 1). In dioxane, better conversions were obtained, but at the expense of the enantioselectivity (entries 9 and 8). In a mixture of acetonitrile:DMM (2:1 v/v), the best ee value of 45%

was achieved, but in a very low (<5%) conversion (entry 10). Again, at pH 10.5 no conversion of **8a** was observed (data not shown). Thus, ketone **4b** is in all respects inferior to **4a** for asymmetric epoxidation.

The representative prochiral olefins **8b**–**e** were epoxidized under the optimal conditions (3.0 equiv. of **4a** at 0°C in acetonitrile with $NaHCO_3$ as buffer), to extend the scope of this asymmetric epoxidation. A high ee value of 85% was obtained for triphenylethylene (**8b**) at a conversion of 36% (entry 11), while lower temperature (−10°C) did not improve the ee values (entry 12). With ketone **4b** (entry 13), a much lower (25%) ee value was found. The epoxidation of *E*-α-methylstilbene **8c** also gave a good ee value of 70% at a conversion of 47% (entry 14). The worst (18%) ee value was observed for the epoxidation of cinnamyl alcohol **8d** with 1.0 equiv. of ketone **4a** (entry 15). Substrate **8d** is known to give lower ee values at pH 8, which has been explained in terms of its susceptibility towards direct oxidation of the alcohol functionality by Caroate under neutral conditions.[5d] Indeed, a high ee value (57%) was achieved with the derivative **8e**, in which the hydroxy group was protected by silylation (entry 16). When 3.0 equiv. of ketone **4a** were used, the ee value could be improved to as high as 87% (entry 17).

The preferential formation of the (*R*,*R*) enantiomers [(*R*) in the case of **8b**] in the epoxidation mediated by the ketones **4** may be explained by the transition structures shown in Scheme 2. The pseudo axial oxygen atom of the dioxirane is effectively shielded by the two exocyclic dioxolane rings, so that the substrate (illustrated for substrate **8a**) approaches the dioxirane only from the bottom side. Of the two possible π facial orientations for the substrate **8a**, in the disfavored *spiro* transition state[1,4,5] there is a steric interaction between the phenyl group and the exocyclic dioxolane ring at the β position of the dioxirane. This repulsion is absent in the favored one and, therefore, the (*R*,*R*) enantiomer of the epoxide **9a** is formed in preference. The high ee values (up to ca. 90%) obtained with ketone **4a** disclose that the stereocontrol by bulky substituents at the β position is quite efficient. This paves the way for designing still more effective oxidants of this structural type, particularly more persistent derivatives of ketone **4a**, to improve the catalytic activity.



Scheme 2. Favored and disfavored transition structures for the oxygen transfer

3. Experimental

3.1. General methods

^{1}H- and ^{13}C-NMR spectra were measured on a Brucker AC 200 (^{1}H: 200 MHz, ^{13}C: 50 MHz) spectrometer with TMS as internal standard. IR spectra were recorded on a Perkin–Elmer 1600 FT-IR spectrophotometer. Melting points were taken on a Büchi B-545 apparatus, and are not corrected. Optical rotation values were measured on a Perkin–Elmer 241 MC polarimeter at 20°C. MS spectra were

taken on a Finnigan MAT90 spectrometer in the Institute of Organic Chemistry, University of Würzburg. HPLC was conducted on a Kontron (Eching/München) analytic HPLC instrument with Kontron HPLC pumps (Model 322) and a Rheodyne 7725 injector (maximum sample volume: 20 μL). Enantiomers were detected by a tunable absorption detector (Kontron, Model UVIKON 720 LC micro) at 220 or 254 nm. The optical rotations were on-line detected by a CHRALYZER® (IBZ Meßtechnik, Hannover) polarimetric detector. Enantiomers were separated on a Chiralcel OD-H or a Chiralcel OB-H column (0.46 cmϕ×25 cm) from the Daicel Chemical Industries, Co. Ltd. (Exton, PA, USA). Elemental analyses were carried out by the Microanalytical Division of the Institute of Inorganic Chemistry, University of Würzburg. TLC analyses were conducted on precoated silica gel foils Polygram SIL G/UV_{254} (40×80 mm) from Macherey and Nagel (Düren, Germany). Spots were identified on UV-light exposure and/or by iodine vapor. Silica gel (63–200 μm, Woelm) was used for column chromatography. Compounds **5a**, **5b**, **6a** and **6b** were synthesized according to literature procedures from D-(−)-quinic acid.[5b,11]

3.2. (5R,7R,8R,9R)-7,8,9-Trihydroxy-8,9-O-isopropylidene-2,2-dimethyl-1,3-dioxaspiro-[4.5]-decane ***7a***[12]

To a solution of **6a** (3.30 g, 15.1 mmol) in 2,2-dimethoxypropane (10 mL) under an argon atmosphere was added *p*-toluenesulfonic acid (165 mg). The mixture was stirred at room temperature (ca. 20°C) for 3 h. Then Et_3N (3 mL) was added and the mixture was further stirred for 30 min. The solvent was removed (20°C/10 mbar) and the residue was purified by column chromatography (1:1 EtOAc:*n*-hexane) to give a colorless oil (2.92 g, 75%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.34 (s, 3H), 1.37 (s, 6H), 1.58 (s, 3H), 1.38–1.59 (m, 1H), 1.95–2.11 (m, 4H), 2.18 (br s, 1H, OH), 3.70–4.08 (m, 2H), 4.31 (m, 1H), 5.29 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.7 (q), 27.1 (q), 27.3 (q), 28.1 (q), 36.3 (t), 38.9 (t), 68.6 (d), 73.1 (d), 74.3 (t), 79.1 (s), 79.5 (d), 109.0 (s), 109.5 (s).

3.3. (5R,8R,9R)-8,9-Dihydroxy-8,9-O-isopropylidene-2,2-dimethyl-1,3-dioxaspiro-[4.5]-decan-7-one ***4a***

To a solution of oxalyl chloride (1.2 mL) in dry CH_2Cl_2 (4.0 mL) was added DMSO (2.0 mL) slowly at −78°C while stirring vigorously. Then a solution of **7a** (1.20 g, 4.65 mmol) in dry CH_2Cl_2 (5.8 mL) was added dropwise over 30 min. The mixture was further stirred for 1 h and then Et_3N (4.5 mL) was added slowly. After 10 min the mixture was poured into an ice–water mixture (20 mL) with vigorous stirring. The solution was saturated with NaCl and extracted with EtOAc (3×50 mL). The organic phases were washed with brine (50 mL) and dried over $MgSO_4$. The solvent was evaporated (20°C/10 mbar) and the residue was purified by silica gel (buffered with 1% Et_3N) chromatography with EtOAc:*n*-hexane (1:1.5 to 1.5:1) as eluent to give a white powder (0.83 g, 70%), m.p. 104.3°C (sublimes). $[\alpha]_D^{20}$=−54.8 (c=0.5 in $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.36 (s, 3H), 1.38 (s, 3H), 1.40 (s, 3H), 1.47 (s, 3H), 2.16 (d d, J_1=15.2 Hz, J_2=5.0 Hz, 1H), 2.37 (d t, J_1=15.1 Hz, J_2=2.6 Hz, 1H), 2.56 (d, J=13.8 Hz, 1H), 2.73 (d d, J_1=13.8 Hz, J_2=2.2 Hz, 1H), 3.82 (s, 2H), 4.33 (d, J=6.2 Hz, 1H), 4.64 (d d d, J_1=6.2 Hz, J_2=5.0 Hz, J_3=3.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 25.5 (q), 26.3 (q), 26.8 (q), 26.9 (q), 35.5 (t), 48.6 (t), 73.4 (t), 74.9 (d), 78.3 (d), 81.4 (s), 109.8 (s), 110.3 (s), 204.3 (s). IR ($CHCl_3$): ν=3686, 3622, 3030, 2894, 2401, 1737, 1602, 1522, 1478, 1424, 1229, 1207, 1045, 928, 801 cm^{-1}. MS: 43 (100%), 59 (27%), 72 (22%), 85 (29%), 95 (41%), 141 (26%), 155 (12%), 183 (9%), 213 (10%), 241 (63%), 256 (M^+, 2%). HRMS calcd for $C_{13}H_{20}O_5$: 256.1311; found: 256.1308.

3.4. (5R,7R,8R,9R)-7,8,9-Trihydroxy-8,9-O-cyclohexylidene-2-cyclohexylidene-1,3-dioxaspiro-[4.5]-decane **7b**

To a solution of **6b** (2.75 g, 10.63 mmol) and cyclohexanone (2.07 g, 21.25 mmol) in toluene (50 mL) was added *p*-toluenesulfonic acid (54.90 mg). The mixture was heated at reflux for 30 min and then the toluene was slowly distilled off until ca. 25 mL solution remained. K_2CO_3 (1.0 g) was added to the cooled solution and the mixture was stirred for 1 h, the solid was filtered off and washed with $CHCl_3$ (2×5 mL). The filtrate was concentrated in vacuo (20°C/10 mbar) to yield a yellow solid which was recrystallized from EtOAc to afford white plates (1.82 g, 44%), m.p. 124.9–125.4°C. $[\alpha]_D^{20}$=−14.5 (c=1.3 in $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.37–1.69 (m, 20H), 1.81–2.10 (m, 4H), 2.43 (br s, 1H), 3.75 (s, 2H), 3.85 (m, 1H), 4.16 (m, 1H), 4.22 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 23.7 (t), 23.9 (t), 24.0 (t), 24.1 (t), 25.1 (t), 25.2 (t), 35.2 (t), 36.7 (t), 36.8 (t), 37.0 (t), 38.1 (t), 39.6 (t), 69.4 (d), 72.9 (d), 73.8 (t), 78.8 (s), 79.7 (d), 109.6 (s), 110.0 (s). IR ($CHCl_3$): ν=3690, 3605, 3600–3200 (br), 3022, 2940, 2862, 1727, 1603, 1448, 1365, 1277, 1240, 1164, 1105, 1044, 934 cm^{-1}. Anal. calcd for $C_{19}H_{30}O_5$ (338. 4): C, 67.43; H, 8.93; found: C, 67.05; H, 8.76.

3.5. (5R,8R,9R)-8,9-Dihydroxy-8,9-O-cyclohexylidene-2-cyclohexylidene-1,3-dioxaspiro-[4.5]-decan-7-one **4b**

To a solution of **7b** (1.02 g, 3.00 mmol) in dry CH_2Cl_2 (15 mL) under argon was added pyridinium chlorochromate (PCC, 1.75 g, 8.11 mmol) in portions over 15 min. The mixture was stirred at ca. 20°C for 22 h and then diluted with ether (50 mL), passed through a Celite pad and washed with ether (3×10 mL). The combined organic layers were dried over $MgSO_4$, and after removal of the solvent (20°C/10 mbar), the crude product was recrystallized from *n*-hexane to give ketone **4b** (0.34 g, 34%) as white powder, m.p. 131.2–132.0°C. $[\alpha]_D^{20}$=−37.3 (c=1.2 in $CHCl_3$). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 1.24–1.65 (m, 20H), 2.13 (d d, J_1=4.8 Hz, J_2=15.1 Hz, 1H), 2.38 (d, J=15.1 Hz, 1H), 2.53 (d, J=13.6 Hz, 1H), 2.68 (d d, J_1=1.9 Hz, J_2=13.6 Hz, 1H), 3.82 (s, 2H), 4.31 (d, J=6.1 Hz, 1H), 4.61 (m, 1H); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 23.6 (t), 23.8 (2×t), 23.9 (t), 24.9 (t), 25.0 (t), 35.4 (t), 36.2 (t), 36.6 (t), 36.8 (t), 36.9 (t), 49.5 (t), 73.5 (t), 75.0 (d), 78.5 (d), 81.3 (s), 111.1 (s), 111.6 (s), 204.6 (s). IR ($CHCl_3$): ν=3038, 3022, 3011, 2941, 2865, 1736, 1678, 1462, 1448, 1431, 1366, 1333, 1279, 1242, 1164, 1140, 1099, 1040, 976 cm^{-1}. Anal. calcd for $C_{19}H_{28}O_5$ (336.4): C, 67.83; H, 8.39; found: C, 67.44; H, 8.73.

3.6. General procedure for asymmetric epoxidation

To a solution of the olefin **8** (0.1 mmol) and Bu_4NHSO_4 (1.5 mg, 4.0 μmol) in acetonitrile (1.5 mL) was added 4×10^{-4} M Na_2EDTA (1.0 mL) at 0°C while stirring. Ketone **4a** (76.9 mg, 0.3 mmol) and a mixture of Caroate (307 mg, 0.5 mmol) and $NaHCO_3$ (130 mg, 1.55 mmol) were added simultaneously in portions over a period of 2.5 h. The reaction mixture was further stirred for the time indicated in Table 1, diluted with water (20 mL), and extracted with hexane (3×20 mL). The combined extracts were washed with water (10 mL), dried over $MgSO_4$, concentrated (20°C/10 mbar), and purified by silica gel chromatography (buffered with 1% Et_3N solution in hexane), with hexane:ethyl acetate (1:0 to 10:1) as the eluent, to afford the epoxide **9**.

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References

1. (a) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res*. **1989**, *22*, 205–211. (b) Murray, R. W. *Chem. Rev*. **1989**, *89*, 1187–1201. (c) Curci, R. In *Advances in Oxygenated Process*; Baumstark, A. L., Ed.; JAI: Greenwich CT, 1990; Vol. 2, Chapter 1, pp. 1–59. (d) Adam, W.; Hadjiarapoglou, L. P.; Curci, R.; Mello, R. In *Organic Peroxides*; Ando, W., Ed.; Wiley: New York, 1992; Chapter 4, pp. 195–219. (e) Curci, R.; Dinoi, A.; Rubino, M. F. *Pure Appl. Chem*. **1995**, *67*, 811–822. (f) Adam, W.; Smerz, A. K. *Bull. Soc. Chim. Belg*. **1996**, *105*, 581–599. (g) Adam, W.; Smerz, A. K.; Zhao, C.-G. *J. Prakt. Chem*. **1997**, *339*, 298–300.
2. (a) Curci, R.; Fiorentino, M.; Triosi, L.; Edwards, J. O.; Pater, R. H. *J. Org. Chem*. **1980**, *45*, 4758–4760. (b) Adam, W.; Hadjiarapoglou, L. P.; Smerz, A. *Chem. Ber*. **1991**, *124*, 227–232. (c) Yang, D.; Wong, M.-K.; Yip, Y.-C. *J. Org. Chem*. **1995**, *60*, 3887–3889. (d) Frohn, M.; Wang, Z.-X.; Shi, Y. *J. Org. Chem*. **1998**, *63*, 6425–6426.
3. (a) Curci, R.; Fiorentino, M.; Serio, M. R. *J. Chem. Soc., Chem. Commun*. **1984**, 155–156. (b) Curci, R.; D'Accolti, L.; Fiorentino, M.; Rosa, A. *Tetrahedron Lett*. **1995**, *36*, 5831–5834.
4. (a) Yang, D.; Wong, M.-K.; Yip, Y.-C.; Wang, X.-C.; Tang, M.-W.; Zheng, J.-H.; Cheung, K.-K. *J. Am. Chem. Soc*. **1998**, *120*, 5943–5952. (b) Yang, D.; Yip, Y.-C.; Chen, J.; Cheung, K.-K. *J. Am. Chem. Soc*. **1998**, *120*, 7659–7660.
5. (a) Wang, Z.-X.; Tu, Y.; Frohn, M.; Zhang, J.-R.; Shi, Y. *J. Am. Chem. Soc*. **1997**, *119*, 11224–11235. (b) Wang, Z.-X.; Shi, Y. *J. Org. Chem*. **1997**, *62*, 8622–8623. (c) Tu, Y.; Wang, Z.-X.; Frohn, M.; He, M.; Yu, H.; Tang, Y.; Shi, Y. *J. Org. Chem*. **1998**, *63*, 8475–8485. (d) Frohn, M.; Dalkiewicz, M.; Tu, Y.; Wang, Z.-X.; Shi, Y. *J. Org. Chem*. **1998**, *63*, 2948–2953.
6. Adam, W.; Zhao, C.-G. *Tetrahedron: Asymmetry* **1997**, *8*, 3995–3998.
7. Song, C. E.; Kim, Y. H.; Lee, K. C.; Lee, S.-g.; Jin, B. W. *Tetrahedron: Asymmetry* **1997**, *8*, 2921–2926.
8. Denmark, S. E.; Wu, Z.; Crudden, C. M.; Matsuhashi, H. *J. Org. Chem*. **1997**, *62*, 8288–8289.
9. Armstrong, A.; Hayter, B. R. *Chem. Commun*. **1998**, 621–622.
10. (a) Adam, W.; Saha-Möller, C. R.; Zhao, C.-G. *Tetrahedron: Asymmetry* **1998**, *9*, 4117–4123. (b) Adam, W.; Saha-Möller, C. R.; Zhao, C.-G. *J. Org. Chem*. submitted for publication.
11. (a) Elliott, J. D.; Kelson, A. B.; Purcell, N.; Stoodley, R. J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 2441–2449. (b) Flores-Parra, A.; Gutierrez-Avella, D. M.; Contreras, R.; Khuong-Huu, F. *Mag. Res. Chem*. **1989**, *27*, 544–555.
12. (a) White, J. D.; Cammack, J. H.; Sakuma, K.; Rewcastle, G. W.; Widener, R. K. *J. Org. Chem*. **1995**, *60*, 3600–3611. (b) Matsuo, K.; Matsumoto, T.; Nishiwaki, K. *Heterocycles* **1998**, *48*, 1213–1220.
13. Our efforts to identify the decomposed product from ketone **4a** were not successful.
14. Edwards, J. O.; Pater, R. H.; Curci, R.; Di Furia, F. *Photochem. Photobiol*. **1979**, *30*, 63–70. For a review see: Renz, M.; Meunier, B. *Eur. J. Org. Chem*. **1999**, 737–750.