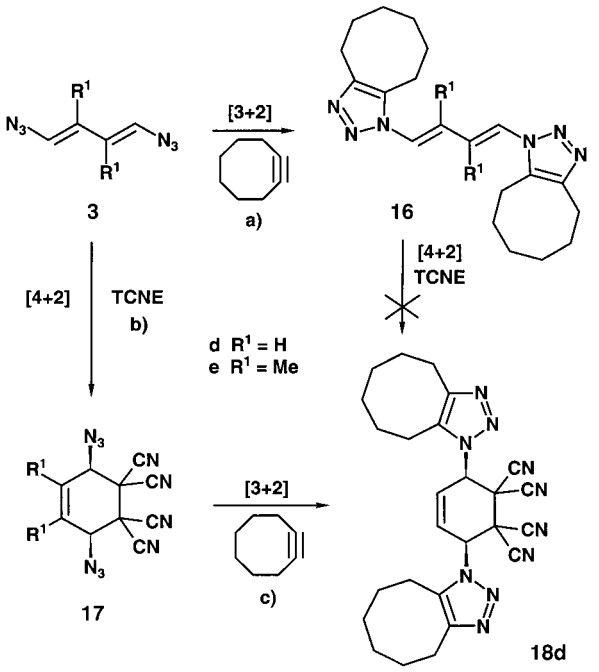


Scheme 3. Cycloaddition reactions of 1,4-diazidobuta-1,3-dienes **3d**,**e**. a) Chloroform, 20 °C, 30 – 60 min, 86 % **16d**, 99 % **16e**; b) acetone, tetracyanoethylene (TCNE) 20 °C, 2 – 20 h, 95 % **17d**, 91 % **17e**; c) chloroform, 20 °C, 3 h, 96 % **18d**.

[8] a) G. L'abbé, A. Hassner, *Angew. Chem.* **1971**, *83*, 103 – 109; *Angew. Chem. Int. Ed. Engl.* **1971**, *10*, 98 – 104; b) G. Smolinsky, C. A. Pryde in *The Chemistry of the Azido Group* (Ed.: S. Patai), Wiley, London, **1971**, pp. 555 – 585; c) A. Hassner in *Azides and Nitrenes: Reactivity and Utility* (Ed.: E. F. V. Scriven), Academic Press, Orlando, **1984**, pp. 35 – 94; d) K. Banert, *Methoden Org. Chem. (Houben-Weyl) 1952-*, Vol. E15, **1993** pp. 818 – 875, 1344 – 1347, 2348 – 2349, 3105 – 3107.

[9] H. Hoberg, C. Fröhlich, *Synthesis* **1981**, 830 – 831.

[10] D. Landini, A. Maia, F. Montanari, *J. Am. Chem. Soc.* **1978**, *100*, 2796 – 2801; D. Landini, A. Maia, F. Montanari, *Nouv. J. Chim.* **1979**, *3*, 575 – 577; D. Landini, A. Maia, F. Montanari, F. Rolla, *J. Org. Chem.* **1983**, *48*, 3774 – 3777; K. Banert, W. Kirmse, *J. Am. Chem. Soc.* **1982**, *104*, 3766 – 3767; K. Banert, *Chem. Ber.* **1985**, *118*, 1564 – 1574.

[11] Caution should be exercised during isolation of azides, particularly (*E*,*E*)-**3d** which is explosive.

[12] Isolated yield; the yield of unstable products, which could not be isolated, e.g. **4** and **9**, was determined by ^{1}H NMR spectroscopy (internal standard).

[13] W. Kirmse, N. G. Rondan, K. N. Houk, *J. Am. Chem. Soc.* **1984**, *106*, 7989 – 7991.

[14] H. A. Brune, W. Schwab, *Tetrahedron* **1969**, *25*, 4375 – 4378.

[15] R. Criegee, A. Moschel, *Chem. Ber.* **1959**, *92*, 2181 – 2184.

[16] G. Maier, M. Schneider, G. Kreiling, W. Mayer, *Chem. Ber.* **1981**, *114*, 3922 – 3934.

[17] R. S. Hansen, W. S. Trahanovsky, *J. Org. Chem.* **1974**, *39*, 570 – 571.

[18] W. Zieliński, *Heterocycles* **1985**, *23*, 1639 – 1644.

[19] Also under these conditions, **7f** and **10f** were photochemically stable as shown in control experiments.

[20] H. Hoberg, C. Fröhlich, *J. Organomet. Chem.* **1980**, *197*, 105 – 109.

[21] There are several reports on the thermal transformation of other 1-azido-1,2-diphenylethenes into azirines which occurred already at low temperatures: a) F. W. Fowler, A. Hassner, L. A. Levy, *J. Am. Chem. Soc.* **1967**, *89*, 2077 – 2082; b) K. Banert, M. Hagedorn, C. Liedtke, A. Melzer, C. Schöffler, *Eur. J. Org. Chem.* **2000**, 257 – 267.

[22] R. A. Carboni, R. V. Lindsey, *J. Am. Chem. Soc.* **1959**, *81*, 4342 – 4346.

Highly Enantioselective Isomerization of 4,7-Dihydro-1,3-dioxepins Catalyzed by Me-DuPHOS-Modified Dihalogenonickel Complexes and Determination of the Absolute Configuration of the Isomerization Products**

Herbert Frauenrath,* Dirk Brethauer, Stefan Reim, Martin Maurer, and Gerhard Raabe

Dihalogenonickel complexes bearing chiral ligands have proved to be efficient catalyst precursors for the asymmetric isomerization of cyclic allyl acetals. In the isomerization of 5-methylen-1,3-dioxanes to 5-methyl-4*H*-1,3-dioxins, for example, DIOP-modified (DIOP = 2,3-*O*-isopropylidene-2,3-dihydroxy-1,4-bis(diphenylphosphanyl)butane) dihalogenonickel complexes activated with lithium triethylborohydride gave selectivities of up to 92 % *ee*.[1] The enantioselectivities significantly decreased, when 4,7-dihydro-1,3-dioxepins (**1**) were used as substrates. However, we have shown previously that the selectivities depend on the relationship between the chelate-ring size of the catalyst and the ring size of the substrate.[1, 2] Thus, isomerization of **1a** by using a five-membered CHIRAPHOS-modified (CHIRAPHOS = 2,3-bis(diphenylphosphanyl)butane) dichloronickel complex (**2a**) at room temperature in THF afforded 2-*tert*-butyl-4,5-dihydro-1,3-dioxepin (**3a**) with 67 % *ee*. In contrast, the seven-membered DIOP-modified dichloronickel complex gave **3a** under the same reaction conditions with only 38 % *ee*.[3]

Searching for other diphosphanes that form five-membered-ring nickel chelates we found that 1,2-bis(phospholanyl)benzenes (Me-DuPHOS, Et-DuPHOS) are suitable ligands for the asymmetric nickel-catalyzed isomerization of **1**.[4, 5] In fact, by employing Me-DuPHOS as a ligand a breakthrough was achieved in terms of enantioselectivity (Table 1). Treatment of **1a** with [$NiCl_2$((−)-Me-DuPHOS)] (**2c**) at room temperature and activation with $LiBHEt_3$ in toluene provided (−)-**3a** already with 85 % *ee* (Table 1, entry 5), but incomplete conversion at this temperature indicated a decreased catalytic activity of the dichloronickel complex (**2c**). However, we found that replacing the chloro by bromo or iodo ligands drastically enhanced the activity of the nickel catalysts. Thus, isomerizations of **1** with CHIRAPHOS and DuPHOS bearing $NiBr_2$– or NiI_2 – phosphane complexes could be performed even at low temperatures yielding vinyl

[*] Prof. Dr. H. Frauenrath, D. Brethauer, Dr. S. Reim, Dr. M. Maurer
Universität Gh Kassel
Fachbereich 19 - Biologie/Chemie
Heinrich-Plett-Strasse 40, 34109 Kassel (Germany)
Fax: (+49) 561-8044649
E-mail: frauenra@hrz.uni-kassel.de
Piv.-Doz. Dr. G. Raabe[+]
Rheinisch-Westfälische Technische Hochschule Aachen
Institut für Organische Chemie
Prof.-Pirlet-Strasse 1, 52074 Aachen (Germany)

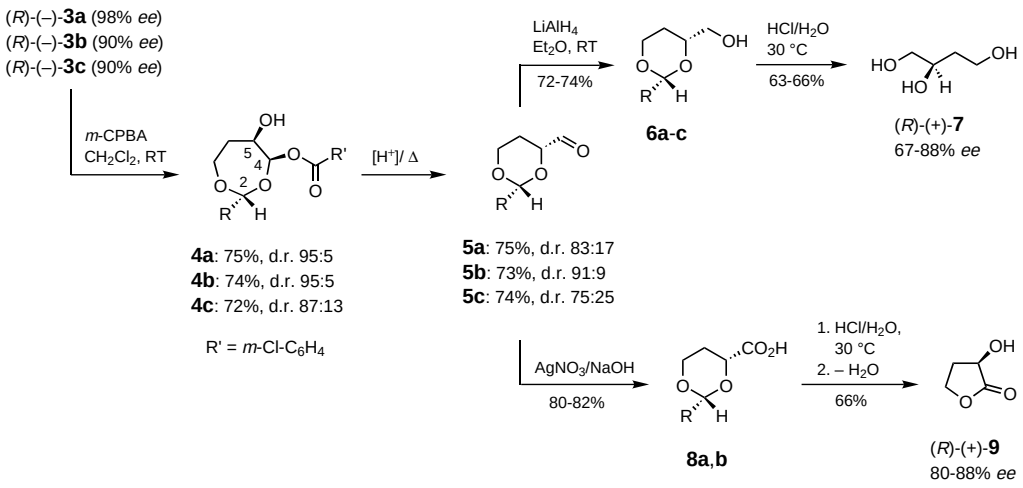
[+] X-ray crystallographic analysis

[**] This work was supported by the Fonds der Chemische Industrie. We would like to thank Prof. Dr. H. Brunner, Universität Regensburg, for help in questions concerning analytical data. Me-DuPHOS = 1,2-bis(2,5-dimethylphospholanyl)benzene.

  1433-7851/01/4001-0177 $ 17.50+.50/0

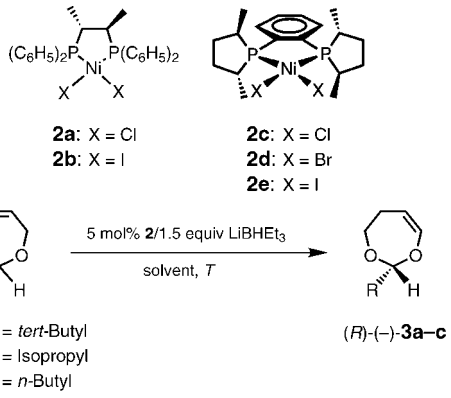
acetals (**3a**–**c**) in good to high enantioselectivities. Best results were achieved with [NiI_2((−)-Me-DuPHOS)] (**2e**) as a precatalyst and with activation by $LiBHEt_3$ in toluene at −55 °C. Under these conditions, the enantiomers(−)-**3b** and **3c** were obtained at acceptable rates with 90 % *ee*, and (−)-**3a** with an excellent selectivity of 98 % *ee* (Table 1, entries 11, 13, 15).

The absolute configuration of the isomerization products was established by the conversion of **3** into either 1,2,4-butanetriol (**7**) or 2-hydroxy-γ-butyrolactone (**9**). Both transformations proceed by a new oxidation ring-contraction sequence of **3** to give the carbaldehydes **5** (Scheme 1) according to our procedure for the synthesis of 4-methyl-1,3-dioxolan-4-carbaldehydes.[7] Thus, treatment of (−)-**3a**–**c** with *m*-chloroperbenzoic acid and heating the resulting crude mixture in vacuo in the presence of an acid led directly to distillation of a diastereomeric mixture of carbaldehydes **5a**–**c**. Subsequent reduction with lithium aluminum hydride and acetal cleavage or oxidation, acetal cleavage, and lactonization by azeotropic removal of water furnished (*R*)-(+)-**7** and (*R*)-(+)-**9**, respectively. Comparison of the specific rotation of the product with that of authentic (*R*)-(+)-**7** and (*R*)-(+)-**9** determined the 2*R*,4*R* configuration for the major diastereomers of **5a**–**c** and the 2*S*,4*R* configuration for the minor diastereomers. The absolute configuration of (−)-**3a**–**c** followed from the relative configuration of acylals **4a**–**c** obtained as the primary products of the *m*-chloroperbenzoic acid oxidation and isolated, by careful neutralization of the crude oxidation product, as a mixture of two diastereomers in a 95:5 to 83:17 ratio. As evidenced by NMR spectroscopic data, both diastereomers differ in the configuration at C4. In the case of *rac*-**4b**, the major diastereomer could be isolated in a diastereomerically pure crystalline form from pentane solution.



Scheme 1. Oxidation and rearrangement of *R*-(−)-**3** and the conversion of the carboxaldehydes **5** into (*R*)-(+)-1,2,4-butanetriol (**7**) and (*R*)-(+)-2-hydroxy-γ-butyrolactone (**9**), respectively.

Table 1. Asymmetric isomerization of 4,7-dihydro-1,3-dioxepins (**1a**–**c**) using (*R*,*R*)-(+)-CHIRAPHOS- and (*R*,*R*)-(−)-Me-DuPHOS-modified nickel complexes.



Entry	Product	Pre-catalyst	Solvent	T [°C]	Conversion [%][a]/ Time(h)[b]	*ee* [%][c]	$[\alpha]_D^{20}$ (neat)
1	**3a**	**2a**	THF	20	100(71)/48	67	−23.6
2	**3a**	**2a**	THF	−40	0/48		
3	**3a**	**2b**	THF	20	100/48	73	
4	**3a**	**2b**	THF	−40	100(83)/72	82	−28.4
5	**3a**	**2c**	toluene	20	80/96	85	
6	**3a**	**2c**	toluene	−55	0/48		
7	**3a**	**2d**	toluene	20	100/18	80	
8	**3a**	**2d**	toluene	−55	16/72	92	
9	**3a**	**2e**	toluene	20	100/2.5	80	
10	**3a**	**2e**	toluene	−20	100/48	92	
11	**3a**	**2e**	toluene	−55	100(74)/72	98	−34.9
12	**3b**	**2e**	toluene	20	100/2.5	70	
13	**3b**	**2e**	toluene	−55	100(75)/72	90	−27.2
14	**3c**	**2e**	toluene	20	100/2.5	78	
15	**3c**	**2e**	toluene	−55	100(75)/72	90	−22.1

[a] Determined by gas chromatography (GC). Values in parentheses: yields of isolated product. [b] No further conversion on prolonged reaction times. [c] Determined by GC. Capillary column: Rt-βDEXcst (30 m, internal diameter 0.32 mm);[6] carrier gas H_2.

Crystal structure analysis of *rac*-**4b** unambiguously confirmed the 2*RS*,4*RS*,5*RS* configuration for both conformers in the asymmetric unit (Figure 1) indicating a preferred *trans*

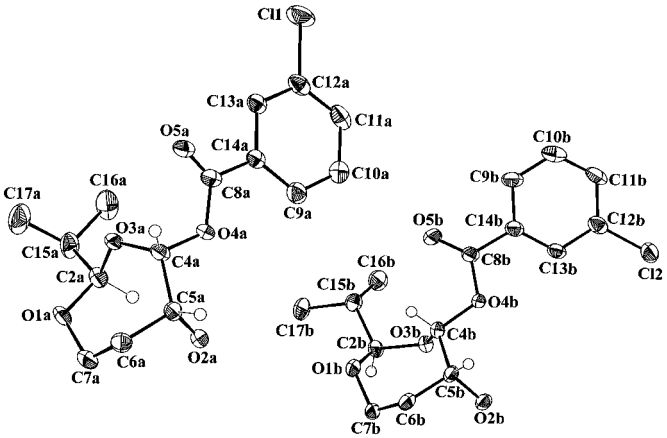


Figure 1. The symmetrically independent molecules of the asymmetric unit of *rac*-**4b**.

  1433-7851/01/4001-0178 $ 17.50+.50/0 *Angew. Chem. Int. Ed.* **2001**, *40*, No. 1

attack of *m*-chloroperbenzoic acid in the reaction with **3**.[8] The results reveal, that (−)-**3b** and, on the basis of similar coupling constants in the ^{1}H NMR spectra and similar nuclear Overhauser enhancement (NOE) effects , most probably (−)-**3a**, **c** have the *R* configuration.

In conclusion, 4,5-dihydro-1,3-dioxepins (**3**) are readily available with high enantiomeric excess by asymmetric isomerization of **1** employing [NiI_2(Me-DuPHOS)] as a precatalyst. The conversions of **3** into 2-hydroxy-γ-butyrolactone (**9**) and 1,2,4-butanetriol (**7**) demonstrate new applications for compounds **3** as chiral synthons in asymmetric synthesis. Derivates of carbaldehydes **5** and alcohols **6**, prepared by different methods, have already been used for the synthesis of optical active α-amino acetals, α-amino acids, and 1,2- and 1,3-diols.[9]

Experimental Section

(*R*)-(−)-**3a**: Catalyst precursor **2e** (0.20 g, 0.32 mmol) was dissolved in toluene at room temperature and activated by $LiBHEt_3$ (0.5 mL, 0.5 mmol, 1M in THF). After cooling to −55 °C, a solution of **1a** (1.0 g, 6.40 mmol) in toluene (5 mL) was added, and the mixture was left at this temperature for 48 h. The conversion is monitored by GC. After complete conversion the mixture was allowed to warm to room temperature and quenched with a saturated NH_4Cl solution (10 mL). The organic layer was separated, and after removal of the solvent the residue was distilled in vacuo; b.p. 55–60 °C/18 Torr; yield 0.74 g (4.7 mmol, 74%).

5a: A solution of purified *m*-chloroperbenzoic acid (3.40 g, 20 mmol)[10] in dichloromethane (50 mL) was added dropwise at room temperature to a stirred solution of **3a** (2.34 g, 15 mmol) in dichloromethane (10 mL). After stirring for 30 min and removal of the solvent in vacuo the diastereomeric aldehydes **5a** were distilled off by heating the colorless residue to 130 °C ; b.p. 75–80 °C/18 Torr; yield 1.50 g (8.70 mmol, 58%). ^{1}H NMR (500 MHz, $CDCl_3$, 22 °C, TMS); major diastereomer: $\delta = 0.95$ (s, 9H, *t*Bu), 1.65 (ddddd, 1H (eq), $J = 13.3, 3.0, 2.7, 1.5, 0.8$ Hz, OCH_2CH_2), 1.77 (dddd, 1H (ax), $J = 13.3, 12.2, 11.8, 5.1$ Hz, OCH_2CH_2), 3.75 (ddd, 1H (ax), $J = 12.2, 11.4, 2.7$ Hz, OCH_2CH_2), 4.08 (ddd, 1H (ax), $J = 11.6, 3.0, 0.8$ Hz, $OCHCH_2$), 4.19 (ddd, 1H (eq), $J = 11.5, 4.9, 1.5$ Hz, OCH_2CH_2), 4.20 (s, 1H, OCHO), 9.66 (dd, 1H, $J = 0.8, 0.8$ Hz, CHO); ^{13}C NMR (125 MHz, $CDCl_3$, 22 °C, TMS); major diastereomer: $\delta = 24.6$ ($C(CH_3)_3$), 26.0 ($C(CH_3)_3$), 35.0 (OCH_2CH_2), 66.0 (OCH_2CH_2), 80.0 ($OCHCH_2$), 107.2 (OCHO), 201.5 (CHO). MS (PCI): *m/z* (%) = 173 (100), 157 (13), 127 (20).

8a: A solution of $AgNO_3$ (2.55 g, 15 mmol) in water (70 mL) was added to a stirred solution of NaOH (1.20 g, 30 mmol) in water (70 mL). A solution of aldehyde **5a** (0.86 g, 5 mmol) in diethyl ether (15 mL) was added dropwise to the resulting suspension. After stirring for 12 h at room temperature, the mixture was filtered and the solid washed with hot water. The aqueous phase was acidified with 2M HCl, and the precipitated acid extracted with diethyl ether. After drying the combined ethereal extracts ($MgSO_4$) the solvent was removed, and the residue recrystallized from petroleum ether; yield 0.80 g (4.30 mmol, 85%); m.p. 95 °C. ^{1}H NMR (500 MHz, $CDCl_3$, 22 °C, TMS); major diastereomer: $\delta = 0.95$ (s, 9H, *t*Bu), 1.91 (m, 2H, OCH_2CH_2), 3.77 (ddd, 1H (ax), $J = 11.6, 11.5, 3.6$ Hz, OCH_2CH_2), 4.21 (ddd, 1H (eq), $J = 11.5, 4.5, 1.7$ Hz, OCH_2CH_2), 4.22 (s, 1H, OCHO), 4.30 (dd, 1H (ax), $J = 10.6, 4.3$ Hz, $OCHCH_2$), 8.21 (s, 1H, COOH); ^{13}C NMR (125 MHz, $CDCl_3$, 22 °C, TMS); major diastereomer: $\delta = 25.3$ ($C(CH_3)_3$), 28.7 ($C(CH_3)_3$), 35.7 (OCH_2CH_2), 67.1 (OCH_2CH_2), 85.0 ($OCHCH_2$), 108.0 (OCHO), 173.4 (COOH).

(*R*)-(+)-**9**: A diastereomeric mixture of **8a** (1.88 g, 10 mmol) was stirred with 18% HCl (30 mL) at 30 °C for 12 h. After addition of $CHCl_3$ (100 mL) and the azeotropic removal of water the organic layer was dried ($MgSO_4$). The solvent was removed, and the residue distilled in high vacuum; b.p. 103–105 °C/0.1 Torr; yield 0.67 g (6.60 mmol, 66%); $[\alpha]_D^{20} = +17.8$ ($c = 1$ in H_2O) (ref. [11]: $[\alpha]_D^{20} = +20.29$ ($c = 4$ in H_2O)).

Received: July 11, 2000 [Z15436]

[1] H. Frauenrath, S. Reim, A. Wiesner, *Tetrahedron: Asymmetry* **1998**, *9*, 1103–1106.

[2] A. Wille, S. Tomm, H. Frauenrath, *Synthesis* **1998**, 305–308.

[3] For the isomerization of **1** with new Ru complexes, see: H. Brunner, M. Prommesberger, *Tetrahedron: Asymmetry* **1998**, *9*, 3231–3239.

[4] (−)-Me-DuPHOS = (−)-1,2-Bis[(2*R*,5*R*)-2,5-dimethylphospholanyl]-benzene; M. J. Burk, *J. Am. Chem. Soc.* **1991**, *113*, 8518–8519.

[5] J. Albrecht, U. Nagel, *Angew. Chem.* **1996**, *108*, 444–446; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 407–409, and references therein.

[6] Supplier: RESTEK GmbH, Sulzbacherstrasse 15, 65812 Bad Soden, Germany.

[7] C. Wattenbach, M. Maurer, H. Frauenrath, *Synlett* **1999**, 303–306.

[8] Crystal structure analysis of *rac*-**4b**: $C_{15}H_{19}O_5Cl$, $M_r = 314.77$; crystals were obtained from pentane (293 K); triclinic space group $P\bar{1}$ (no.2), $a = 11.716(3)$, $b = 11.721(4)$, $c = 12.388(3)$ Å, $\alpha = 73.21(2)$, $\beta = 73.90(3)$, $\gamma = 85.15(3)°$, $V = 1564.7$ Å^3, $Z = 2 \times 2$, $\rho_{calcd} = 1.336$ g cm^{-3}, 150 K. A total of 8974 reflections were collected on an Enraf-Nonius CAD4 four-circle diffractometer CAD4, graphite-monochromated $Cu_{K\alpha}$ radiation ($\lambda = 1.54179$ Å), $\mu = 11.7$ cm^{-1}, no absorption correction. The structure was solved by direct methods (GENSIN[12], GENTAN[13] as implemented in the XTAL3.4 program package[14]). Hydrogen atoms were fixed in idealized positions without refinement. Final full-matrix least-squares refinement of 379 parameters (involved 4855 observed reflections $I > 4\sigma(I)$), $R(R_w) = 0.091$ (0.094), $w = (\sigma^2(F) + 0.0004F^2)^{-1}$, residual electron density −0.90/+0.86 e Å^{-3}. The asymmetric unit contains two symmetrically independent molecules of *rac*-**4b** with different conformations (Figure 1). Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-134153. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[9] a) M. Thiam, F. Chastrette, *Tetrahedron Lett.* **1990**, *31*, 1429–1432; b) M. Thiam, A. Slassi, F. Chastrette, R. Amouroux, *Synth. Commun.* **1992**, *22*, 83–95.

[10] For purification of technical *m*-chloroperbenzoic acid, see: a) N. N. Schwartz, J. H. Blumbergs, *J. Org. Chem.* **1964**, *29*, 1976–1979; L. F. Fieser, M. Fieser, *Reagents for Organic Synthesis*, *Vol. 1*, Wiley, New York, **1967**, pp. 135–136.

[11] J. W. E. Glattfeld, F. V. Sanders, *J. Am. Chem. Soc.* **1921**, *43*, 2675–2682.

[12] V. Subramanian, S. Hall, GENSIN, *Xtal3.4 User's Manual* (Eds.: S. R. Hall, G. S. D. King, J. M. Stewart), Lamb, Perth, **1995**, pp. 141–148.

[13] S. Hall, GENTAN, *Xtal3.4 User's Manual* (Eds.: S. R. Hall, G. S. D. King, J. M. Stewart), Lamb, Perth, **1995**, pp. 148–159.

[14] *Xtal3.4 User's Manual* (Eds.: S. R. Hall, G. S. D. King, J. M. Stewart), Lamb, Perth, **1995**.

  1433-7851/01/4001-0179 $ 17.50+.50/0