Stereoselective Oxylactonization. Preparation of 2-Deoxy-DL-ribono-1,4-lactone Derivatives from 3-Silyloxy-4-alkenamides

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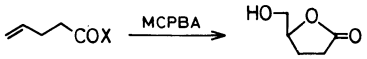
The oxylactonization of 3-silyloxy-4-alkenamides proceeds stereoselectively by treatment with *m*-chloroperbenzoic acid to give the corresponding 2-deoxy-DL-ribono-1,4-lactone derivatives.

Halolactonization reaction of acyclic alkenoic acids or their derivatives has been used to functionalize double bonds in a stereoselective manner,[1] and widely applied to the synthesis of natural products.[2] It was expected that the development of oxylactonization in which alkenoic acid derivatives are converted to the corresponding hydroxy lactones in a one-pot manner would provide an effective method for the preparation of polyhydroxy compounds. Hence, the oxylactonization of 4-alkenoic acid derivatives was undertaken using *m*-chloroperbenzoic acid (MCPBA) as an oxidant.

When 4-pentenoic acid (**1a**) and the corresponding 3-phenylpropyl ester **1b** were treated with MCPBA at room temperature, the generation of the epoxides was observed. The successive lactonization to 5-hydroxy-4-pentanolide (**2**), however, proceeded very slowly.[3] On the other hand, the reaction of *N,N*-dimethyl-4-pentenamide (**1c**) with MCPBA was found to afford 5-hydroxy-4-pentanolide (**2**), however, even at room temperature.[4]



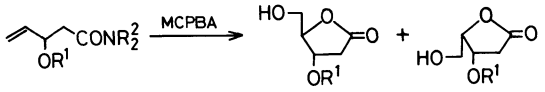
1a X=OH
b X=O(CH$_2$)$_3$Ph
c X=NMe$_2$

2

As an alkenamide is susceptible to the oxylactonization with MCPBA, we next investigated the stereochemical course of the oxylactonization of 3-hydroxy-4-pentenamide **3a**. The treatment of *N,N*-diisopropyl-3-hydroxy-4-pentenamide (**3a**) with a 4-molar amount of MCPBA in benzene at room temperature generated 3,4-*trans*(*erythro*)-3,5-dihydroxy-4-pentanolide (**4a**) predominantly along with the 3,4-*cis*(*threo*)-isomer **5a** (**4a**:**5a**=2.6:1).

Particularly interesting was that the oxylactonization of **3a** with MCPBA shows the opposite stereoselectivity to the halolactonization of 3-hydroxy-(or silyloxy)-4-alkenoic acids, which are generally converted to the 3,4-cis-substituted butanolides.[1c] Therefore, the stereoselectivity of this oxylactonization was examined in detail by introducing various protecting groups to the 3-hydroxyl group of the amide **3a**. When acyl groups such as acetyl, benzoyl, pivaloyl, and ethoxycarbonyl groups were employed for the protection of the 3-hydroxyl group, the yields of oxylactones **4** and **5** were very low because of the elimination of acyloxyl groups occurred under the reaction conditions. The reaction of the benzyl (Bn) ether **3b** and the methoxymethyl (MOM) ether **3c** with MCPBA proceeded smoothly, however, the stereoselectivity toward the *trans*(*erythro*)-lactone **4** was not improved (**4**:**5**=*ca.* 2:1).

The high selectivity was observed when the *t*-butyldimethylsilyl (TBS) ether **3d** was employed. The reaction of **3d** with MCPBA in benzene afforded the trans-substituted isomer **4d** in favorable selectivity. The structure of **4d** was confirmed by the transformation to 2-deoxy-DL-ribono-1,4-lactone[5] by removal of the TBS group with aqueous acetic acid in tetrahydrofuran at 80 °C.

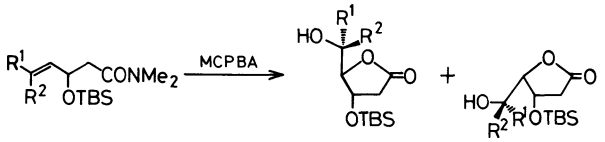


3 4 5

Table 1. Oxylactonization of the 3-hydroxy-4-pentenamide derivatives **3**

	R^1	R^2	Yield/%	(**4** : **5**)
3a	H	*i*-Pr	88	(2.6 : 1)
3b	Bn	Me	70	(2.1 : 1)
3c	MOM	Me	54	(1.9 : 1)
3d	TBS	*i*-Pr	90	(4.3 : 1)

Furthermore, (*E*) and (*Z*)-isomers of 3-silyloxy-4-hexenamide (**6a** and **6b**) were prepared and submitted to the reaction with MCPBA. In the oxylactonization of the (*Z*)-amide **6a**, the both stereoisomers **7a** and **8a** were formed in comparable amounts. On the other hand, it was noted that the 3,4-*trans*-substituted lactone **7b** was generated in good selectivity (**7b**:**8b**=3.9:1) from the (*E*)-hexenamide **6b**.

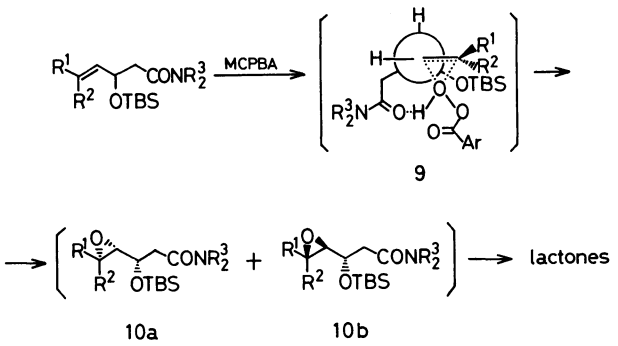


6 7 8

Table 2. Oxylactonization of the 3-silyloxy-4-hexenamides **6**

	R^1	R^2	Yield/%	(**7** : **8**)
6a	H	Me	63	(1.1 : 1)
6b	Me	H	79	(3.9 : 1)

From these results, the following speculation might be suggested for the *trans* stereoselection in the present oxylactonization. The lactonization is considered to proceed *via* unstable epoxy amides **10**, which are successively converted to hydroxy lactones by the intramolecular attack of the amide oxygen. The stereoselectivity is consequently directed in the epoxidation step. The epoxidation maybe proceeds through "the inside alkoxy transition state **9**"[6] in which MCPBA forms a hydrogen bond with the amide group[7] to result in the predominant formation of the *threo*-epoxide **10a**. The remarkable decrease of the selectivity in the case of the (*Z*)-amide **6a** is well explained by the steric interaction between the (*Z*)-methyl group and the TBS group in the preferred transition state **9**.



In conclusion, the oxylactonization of 3-silyloxy-4-alkenamides was found to proceed by the simple treatment with MCPBA to yield 2-deoxy-DL-ribono-1,4-lactone derivatives in good stereoselectivity. In contrast to *cis*-selective halolactonization, the present oxylactonization provides a useful method for the preparation of polyoxygenated 3,4-*trans*-substituted butyrolactones.

Experimental

All the melting and boiling points are uncorrected. The IR spectra were determined on a Hitachi Model 260-30 spectrometer. The ^{1}H NMR spectra were recorded with Hitachi R-24B and Varian EM-390 spectrometers in $CDCl_3$ with tetramethylsilane as an internal standard. Benzene was distilled and dried over sodium wire. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl. *N,N*-Dimethylformamide (DMF) was distilled from CaH_2 and stored over Molecular Sieve. Purification of products was performed by column chromatography on silica gel (Wakogel C-200 or Merck, Art. 9385 Kieselgel 60, 230—400 mesh).

Preparation of N,N-*Diisopropyl-3-hydroxyl-4-pentenamide (**3a**).* To a solution of lithium diisopropylamide (55 mmol) in THF (100 mL) was added a solution of *N,N*-diisopropylacetamide (7.16 g, 50 mmol) in THF (10 mL) at −78 °C, and the mixture was stirred for 1 h at −78 °C.[8] A THF (5 mL) solution of acrylaldehyde (3.36 g, 60 mmol) was added and then stirred for 15 min at −78 °C. To the mixture was added sat. aqueous NH_4Cl and the organic layer was extracted with dichloromethane. The separated organic layer was dried over Na_2SO_4 and was condensed under reduced pressure. Purification by column chromatography (hexane:ethyl acetate=3:1, v/v) and distillation gave the amide **3a** (8.21 g, 82%): Bp 101—102 °C/0.8 mmHg (1 mmHg=133.322 Pa). IR (neat) 3420, 1625 cm^{-1}. ^{1}H NMR δ=1.22 (6H, d, J=6.8 Hz), 1.38 (6H, d, J=6.8 Hz), 2.33 (1H, dd, J=8.3, 16.0 Hz), 2.55 (1H, dd, J=3.3, 12.0 Hz), 3.22—4.17 (2H, m), 4.32—4.70 (2H, m), 5.00—5.42 (2H, m), 5.88 (1H, ddd, J=5.4, 10.0, 17.0 Hz).

By the same procedure, the corresponding *N,N*-dimethyl amide (**3**, R^1=H, R^2=Me) was prepared in 82% yield: Bp 84—88 °C/0.35 mmHg. IR (neat) 3400, 1615 cm^{-1}. ^{1}H NMR δ=2.37 (1H, dd, J=7.8, 16.2 Hz), 2.59 (1H, dd, J=4.0, 16.2 Hz), 2.98 (3H, s), 3.03 (3H, s), 4.25—4.70 (2H, m), 5.02—5.43 (2H, m), 5.90 (1H, ddd, J=5.5, 10.0, 16.5 Hz).

Preparation of N,N-*Diisopropyl-3-t-butyldimethylsilyloxy-4-pentenamide (**3d**).* A mixture of **3a** (1.99 g, 10 mmol), triethylamine (1.52 g, 15 mmol), *t*-butyldimethylsilyl chloride (1.81 g, 12 mmol) and a catalytic amount of 4-dimethylaminopyridine in DMF (30 mL) was stirred for 3 h at room temperature.[9] Then pH 7 phosphate buffer (100 mL) was added, and the mixture was extracted with ether. The ether extract was washed with water and sat. aqueous NaCl and dried over Na_2SO_4. The ether solution was concentrated and the residue was purified by column chromatography on silica gel (hexane:ethyl acetate=10:1, v/v) and distillation to give the silylated amide **3d** (3.02 g, 96%): Bp 122 °C/0.4 mmHg. IR (neat) 1640 cm^{-1}. ^{1}H NMR δ=0.07 (6H, s), 0.88 (9H, s), 1.19 (6H, d, J=6.5 Hz), 1.34 (6H, d, J=6.5 Hz), 2.32 (1H, dd, J=6.0, 14.5 Hz), 2.62 (1H, dd, J=6.8, 14.5 Hz), 3.37—4.20 (2H, m), 4.73 (1H, br, q, J=6.5 Hz), 4.91—5.34 (2H, m), 5.90 (1H, ddd, J=5.5, 10.0, 16.5 Hz). Found: C, 64.59; H, 11.52; N, 4.52%. Calcd for $C_{17}H_{35}NO_2Si$: C, 65.12; H, 11.25; N, 4.47%.

*Preparation of (Z)-*N,N-*Dimethyl-3-t-butyldimethylsilyloxy-4-hexenamide (**6a**).* The reaction of lithiated *N,N*-dimethylacetamide with 2-butynal according to the procedure described above yielded *N,N*-dimethyl-3-hydroxy-4-hexynamide in 85% yield: Bp 125—126 °C/0.7 mmHg. The acetylenic amide was hydrogenated over 5% Pd/$BaSO_4$-quinoline catalyst[10] in methanol under usual pressure, and the hydroxyl group was silylated to give **6a** in 86% overall yield: Bp 120 °C (bath temp)/0.1 mmHg. IR (neat) 1650 cm^{-1}. ^{1}H NMR δ=0.02 (6H, s), 0.81 (9H, s), 1.60 (3H, d, J=5.5 Hz), 2.15 (1H, dd, J=4.8, 14.0 Hz), 2.63 (1H, dd, J=8.0, 14.0 Hz), 2.86 (3H, s), 2.98 (3H, s), 4.76—5.04 (1H, m), 5.10—5.55 (1H, m). Found: C, 61.77; H, 11.07; N, 5.20%. Calcd for $C_{14}H_{29}NO_2Si$: C, 61.93; H, 10.77; N, 5.16%.

*Preparation of (E)-*N,N-*Dimethyl-3-t-butyldimethylsilyloxy-4-hexenamide (**6b**).* As mentioned above, (*E*)-*N,N*-dimethyl-3-hydroxy-4-hexenamide was prepared by the reaction of lithiated *N,N*-dimethylacetamide with crotonaldehyde in 86% yield: Bp 99—100 °C/0.5 mmHg. The hydroxy amide was then silylated to give **6b** in 82% yield:

Bp 125—130 °C (bath temp)/0.3 mmHg. IR (neat) 1650 cm^{-1}. ^1H NMR δ=0.02 (6H, s), 0.87 (9H, s), 1.64 (3H, d, J=5.0 Hz), 2.22 (1H, dd, J=5.0, 13.5 Hz), 2.63 (1H, dd, J=8.0, 13.5 Hz), 2.88 (3H, s), 2.98 (3H, s), 4.33—4.73 (1H, m), 5.13—5.82 (2H, m). Found: C, 61.61; H, 11.00; N, 5.01%. Calcd for $C_{14}H_{29}NO_2Si$: C, 61.93; H, 10.77; N, 5.16%.

Oxylactonization of ***3d***. A benzene (2 mL) solution of the amide **3d** (152 mg, 0.48 mmol) was added to a suspension of MCPBA (70% pure, 478 mg, 1.94 mmol) in benzene (2 mL), and the mixture was stirred at 20—30 °C overnight. A mixture of sat. aqueous Na_2SO_3 and 10% aqueous K_2CO_3 was added and the mixture was extracted with ether. The ether extract was washed successively with 10% aqueous K_2CO_3 and sat. aqueous NaCl. After being dried over Na_2SO_4, the ether solution was condensed *in vacuo*. The residue was purified by column chromatography (hexane:ethyl acetate=3:1—1:1, v/v) to give the less polar **4d** (87.6 mg, 73%) and the more polar **5d** (20.7 mg, 17%).

*3-O-t-Butyldimethylsilyl-2-deoxy-*DL-erythro-*pentono-1,4-lactone (**4d**)*: Mp 54—55 °C (hexane). IR (CH_2Cl_2) 3620, 1785 cm^{-1}. ^1H NMR δ=0.09 (6H, s), 0.78 (9H, s), 2.28 (1H, dd, J=4.0, 16.5 Hz), 2.57 (1H, br s), 2.78 (1H, dd, J=6.5, 16.5 Hz), 3.53—3.82 (2H, m), 4.07—4.56 (2H, m). Found: C, 53.46; H, 9.23%. Calcd for $C_{11}H_{22}O_4Si$: C, 53.62; H, 9.00%. Hydrolysis of **4d** (49 mg, 0.20 mmol) in THF (0.5 mL), H_2O (0.5 mL), and acetic acid (1.5 mL) at 80 °C gave 2-deoxy-DL-ribono-1,4-lactone.[5]

*3-O-t-Butyldimethylsilyl-2-deoxy-*DL-threo-*pentono-1,4-lactone (**5d**)*: Mp 99—100 °C (cyclohexane). IR (CH_2Cl_2) 3620, 1785 cm^{-1}. ^1H NMR δ=0.09 (6H, s), 0.89 (9H, s), 2.37 (1H, br s), 2.40 (1H, dd, J=3.0, 17.5 Hz), 2.74 (1H, dd, J=5.7, 17.5 Hz), 3.58—4.07 (2H, m), 4.34—4.70 (2H, m). Found: C, 53.37; H, 8.93%. Calcd for $C_{11}H_{22}O_4Si$: C, 53.62; H, 9.00%.

*The Oxylactonization of **6a** and **6b** was Carried out by the Same Procedure.* *3-O-t-Butydimethylsilyl-2,6-dideoxy-*DL-lyxo-*hexono-1,4-lactone (**7a**)*: Bp 180—185 °C (bath temp)/2.5 mmHg. IR (CH_2Cl_2) 3480, 1775 cm^{-1}. ^1H NMR δ=0.09 (6H, s), 0.77 (9H, s), 1.19 (3H, d, J=6.0 Hz), 2.22 (1H, dd, J=4.0, 17.5 Hz), 2.37 (1H, br s), 2.78 (1H, dd, J=7.0, 17.5 Hz), 3.43—4.13 (2H, m), 4.22—4.60 (1H, m). Found: C, 55.26; H, 9.56%. Calcd for $C_{12}H_{24}O_4Si$: C, 55.34; H, 9.29%.

*3-O-t-Butyldimethylsilyl-2,6-dideoxy-*DL-xylo-*hexono-1,4-lactone (**8a**).* Mp 82—83.5 °C (cyclohexane). IR (CH_2Cl_2) 3580, 1785 cm^{-1}. ^1H NMR δ=0.12 (6H, s), 0.89 (9H, s), 1.25 (3H, d, J=6.2 Hz), 2.47 (1H, dd, J=3.3, 17.5 Hz), 2.65 (1H, br s), 2.77 (1H, dd, J=6.2, 17.5 Hz), 3.97—4.32 (2H, m), 4.42—4.69 (1H, m). Found: C, 55.24; H, 9.53%. Calcd for $C_{12}H_{24}O_4Si$: C, 55.34; H, 9.29%.

*3-O-t-Butyldimethylsilyl-2,6-dideoxy-*DL-ribo-*hexono-1,4-lactone (**7b**)*: Bp 150—160 °C (bath temp)/2 mmHg. IR (CH_2Cl_2) 3610, 1780 cm^{-1}. ^1H NMR δ=0.10 (6H, s), 0.76 (9H, s), 1.10 (3H, d, J=6.0 Hz), 2.18 (1H, dd, J=3.0, 17.5 Hz), 2.77 (1H, dd, J=6.5, 17.5 Hz), 2.80 (1H, br s), 3.57—4.13 (2H, m), 4.30—4.58 (1H, m). Found: C, 55.04; H, 9.51%. Calcd for $C_{12}H_{24}O_4Si$: C, 55.34; H, 9.29%.

*3-O-t-Butyldimethylsilyl-2,6-dideoxy-*DL-arabino-*hexono-1,4-lactone (**8b**)*: Mp 88.5—90.5 °C (cyclohexane). IR (CH_2Cl_2) 3610, 1780 cm^{-1}. ^1H NMR δ=0.13 (6H, s), 0.93 (9H, s), 1.35 (3H, d, J=6.0 Hz), 2.23 (1H, br d, J=4.5 Hz), 2.45 (1H, dd, J=3.0, 17.5 Hz), 2.75 (1H, dd, J=5.7, 17.5 Hz), 3.93—4.19 (2H, m), 4.57—4.80 (1H, m). Found: C, 55.04; H, 9.23%. Calcd for $C_{12}H_{24}O_4Si$: C, 55.34; H, 9.29%.

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References

1) a) P. A. Bartlett, "Olefin Cyclization Processes That Form Carbon-Heteroatom Bonds," in "Asymmetric Synthesis," ed by J. D. Morrison, Academic press, Inc., Orland (1984), Vol. 3, Chap. 6, pp. 417—425; b) P. A. Bartlett and J. Myerson, *J. Am. Chem. Soc.*, **100**, 3950 (1978); c) A. R. Chamberlin, M. Dezube, P. Dussault, and M. C. McMills, *ibid.*, **105**, 5819 (1983); d) Y. Tamaru, M. Mizutani, Y. Furukawa, S. Kawamura, Z. Yoshida, K. Yanagi, and M. Minobe, *ibid.*, **106**, 1079 (1984).

2) P. A. Bartlett, D. J. Tanzella, and J. F. Barstow, *Tetrahedron Lett.*, **23**, 619 (1982); N. J. Barnes, A. H. Davidson, L. R. Hughes, G. Procter, and V. Rajcoomar, *ibid.*, **22**, 1751 (1981); D. R. Williams, B. A. Barner, K. Nishitani, and J. G. Phillips, *J. Am. Chem. Soc.*, **104**, 4708 (1982).

3) By the treatment of **1a** with $HCOOH-H_2O_2$ at the elevated temperature, the lactone **2** was obtained in good yield: M. T. Dangyan and S. V. Arakelyan, *Nauch. Trudy Erevan. Gosudarst. Univ., Ser., Khim. Nauk*, **44**, 35 (1959); *Chem. Abstr.*, **53**, 21648i (1959).

4) During our investigation, it was reported that similar oxylactonization of an alkenamide proceeds by the acid catalyzed epoxidation ($CH_3COOH-H_2O_2$): M. Majewski and V. Snieckus, *J. Org. Chem.*, **49**, 2682 (1984).

5) The ^1H NMR and IR spectra are identical with those of the authentic sample: M. Murakami and T. Mukaiyama, *Chem. Lett.*, **1982**, 241.

6) K. N. Houk, S. R. Moses, Y.-D. Wu, N. G. Rondan, V. Jäger, R. Schohe, and F. R. Fronczek, *J. Am. Chem. Soc.*, **106**, 3880 (1984).

7) In the epoxidation of an olefinic amide, the interaction of the carbamoyl group with an peroxy acid by hydrogen bonding is probable from the following result. When ethyl 3-*t*-butyldimethylsilyloxy-4-pentenate was treated with MCPBA, almost equal amounts of both *threo* and *erythro* epoxides were obtained (*threo*:*erythro*=1.3:1). Furthermore, the formation of intermolecular hydrogen bonding between peroxy acids and amides has been reported: J. Škerjanc, A. Regent, and B. Plesničar, *J. Chem. Soc., Chem. Commun.*, **1980**, 1007.

8) D. Seebach and H. F. Leitz, *Angew. Chem., Int. Ed. Engl.*, **10**, 501 (1971).

9) S. K. Chaudhary and O. Hernandez, *Tetrahedron Lett.*, **1979**, 99.

10) D. J. Cram and N. L. Allinger, *J. Am. Chem. Soc.*, **78**, 2518 (1956).