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SYNTHESIS OF ENANTIOMERICALLY PURE BI- AND TRICYCLIC LACTONES WITH QUATERNARY CHIRAL CENTERS.

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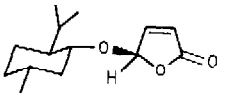
Abstract: Enantiomerically pure lactones, with a quaternary chiral center, were prepared by alkylation of enantiomerically pure bi- and tricyclic menthyloxyfuranones 2a and 3.

Currently there is a growing interest in the use of enantiomerically pure lactones as chiral building blocks in the synthesis of natural products[1]. Several routes to homochiral lactones have been developed e.g. by resolution, using a chiral alcohol as resolving agent[2], or by enzymatic resolution of bicyclic γ-butyrolactones using Horse Liver Esterase[3]. Also the ability of enzymes to discriminate between enantiotopic groups of meso-compounds has been exploited in the asymmetric synthesis of optically pure lactones[4].
We have shown that 5-(1-menthyloxy)-2(5H)-furanone 1 is an excellent chiral synthon for the preparation of enantiomerically pure aminodiols and epoxyalcohols.[5] Furthermore this compound serves as chiral maleic anhydride analogue in asymmetric Diels-Alder reactions with virtually complete π-face and endo selectivity with a variety of dienes.[6]
Recent reports on the formation of quaternairy centers in optically active lactones obtained by an enzymatic route [4b] or from D-ribonolactone [7] prompted us to report new asymmetric syntheses of enantiomerically pure bi- and tricyclic lactones with quaternary centers.



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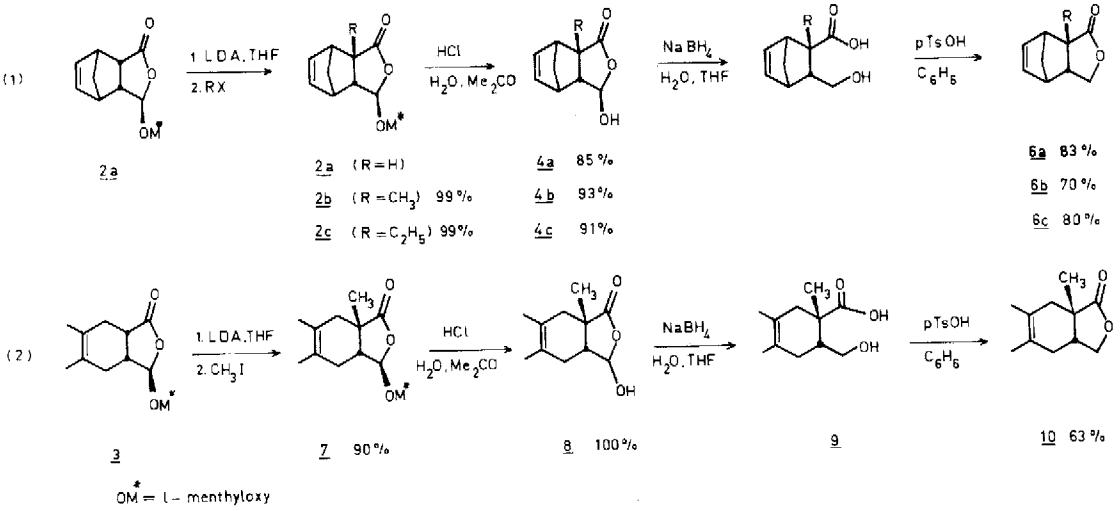
The starting lactones 2a and 3 were prepared by a diastereoselective Diels-Alder reaction between enantiomerically pure 5-(1-menthyloxy)-2(5H)-furanone 1 and cyclopentadiene and 2,3-dimethylbutadiene respectively[6]. Hydrolysis of the tricyclic compound 2a with HCl in water/acetone gave the dementhylated compound 4a in high yield (eq.1). The spectroscopic and physical properties were in complete agreement with those reported in the literature[2]. Reduction of the obtained hydroxyfuranone with $NaBH_4$ in THF/water gave the corresponding carboxylic acid which upon treatment with p-TsOH in benzene gave the desired tricyclic lactone in 83% yield. By starting from other bi- and tricyclic furanones, as prepared by Diels-Alder reactions between 5-(1-methyloxy)-2(5H)-furanone and a suitable diene[6], several bi- and tricyclic lactones should be accessible.
It was found that compounds 2a and 3 could be deprotonated and subsequently alkylated by various alkylating reagents to form new quaternary chiral centers. By using one equivalent of LDA and excess of alkylating reagent a mixture was found of starting material and alkylated product. By using two equivalents of LDA a complete conversion to the alkylated products 2b, 2c and 7 was found. Based on ^1H-and ^{13}C-NMR it was established that in all

cases one diastereoisomer was formed[7-9]. These alkylated products were hydrolysed and reduced in high yields, in the same manner as already described for the starting material 2a. (eqs. 1 and 2)[10].
Cyclization using p-toluenesulphonic acid under azeotropic conditions gave optically pure lactones 6a-6c and 10. The stereochemical assignment (eqs. 1 and 2) is based on the X-ray analysis of 3[1f] and the complete agreement of the spectral data of 4b with those reported [9]. Furthermore extensive 2D NMR studies established that in all lactones a cis-relationship is present between the C_3-alkyl group and C_4-hydrogen (see refs. 7, 8 for related systems).
It can be concluded that the asymmetric Diels-Alder and alkylation procedures described allow facile formation of various enantiomerically pure lactones containing quaternary centers. Furthermore 4a-4c and 8 can act as precursors to 5-alkyllactones as has been described for related racemic cases[8].



References
1. (a) Kano, S., Shibuya, S., Ebata, T. Heterocycles **1980**, 14, 661, (b) Hanessian, S., Sahoo, S.P., Botta, M. Tetrahedron Lett. **1987**, 28, 1143; (c) Hanessian, S., Sahoo, S.P., Botta, M. Tetrahedron Lett. **1987**, 28, 1147, (d) Ortuño, R.M., Mercé, R., Font, J. Tetrahedron Lett. **1986**, 27, 2519; (e) Vigneron, J.P., Méric, R. Tetrahedron **1984**, 40, 3521; (f) Feringa, B.L., de Lange, B., de Jong, J.C. J. Org. Chem. **1989**, 54, 2471.
2. Martel, J.J., Demoute, J.P., Tèche, A.P., Tessier. J.R. Pestic. Sci. **1980**, 11, 188.
3. Guibé-Jampel, E., Rousseau, G., Blanco, L. Tetrahedron Lett. **1989**, 30, 67.
4. (a) Lok, K.P., Jakovac, I.J., Jones, J.B. J. Am. Chem. Soc. **1985**, 107, 2521; (b) Shimada, M., Kobayashi, S., Ohno, M. Tetrahedron Lett. **1988**, 29, 6961; (c) Kaga, H., Kobayashi, S. Ohno, M. Tetrahedron Lett. **1989**, 30, 113; (d) Bloch R., Gilbert, L. J. Org. Chem. **1987**, 52, 4603.
5. (a) Feringa, B.L., de Lange, B. Tetrahedron Lett. **1988**, 29, 1303; (b) de Lange, B., Feringa, B.L. Tetrahedron, **1988**, 44, 7213.
6. Feringa, B.L., de Jong, J.C. J. Org. Chem. **1988**, 53, 1125.
7. Corbera, J., Font, J., Monsalvatje, M., Ortuño, R.M., Sánchez-Ferrando, F. J. Org. Chem. **1988**, 53, 4393.
8. Canonne, P., Akssira, M., Lemay, G. Tetrahedron Lett. **1983**, 24, 1929.
9. Canonne, P., Plamondon, J., Akssira, M. Tetrahedron, **1988**, 44, 2903.
10. All compounds were fully characterized by ^1H NMR, ^{13}C NMR, high resolution mass spectroscopy and elemental analysis.

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