Tetrahedron: Asymmetry Vol. 4, No. 11, pp. 2277-2278, 1993
Printed in Great Britain

0957-4166/93 $6.00+.00
Pergamon Press Ltd

Highly Enantioselective Synthesis of (+) and (−)Endo-Tricyclo [5.2.1.$0^{2,6}$]Deca-4,8-dien-3-one and (−)-4-t-Butyldimethylsilyloxy-Cyclopentenone by Enzyme-Catalyzed Acetylation[1]

Zhi-Yu Liu[*a], **Ling He**[b] and **Hu Zheng**[b]

[a]Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China
[b]College of Pharmacy, West China University of Medical Sciences, Chengdu, Sichuan 610041, China

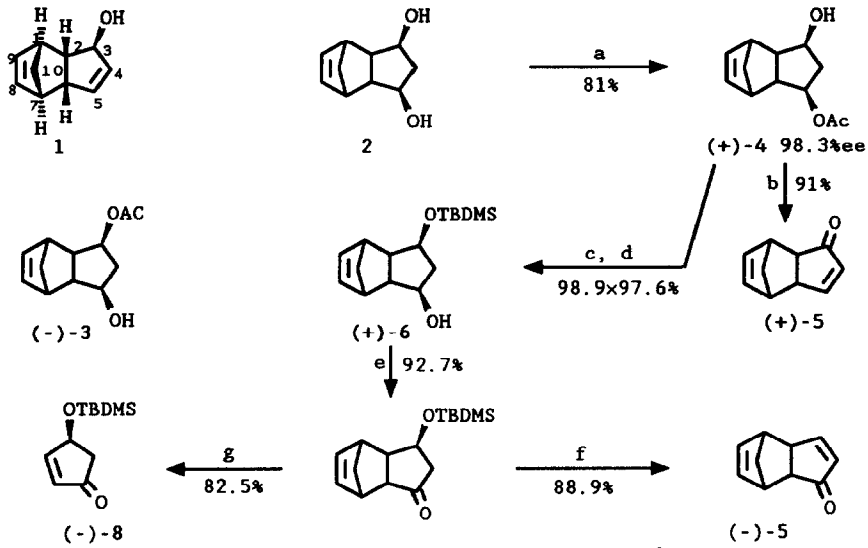
(*Received in Japan* 15 *July* 1993)

Abstract: Asymmetric syntheses of enantiomerically pure (+)- and (−)-**5** and (−)-**8** are described with enzyme-catalyzed acetylation of the meso-diol **2** as the key step.

The optically active title compounds are useful chiral synthons for the synthesis of optically active natural products[2]. (−)-**5** has been prepared by resolution of (±)-**1** via 3-acetoxy-5-etiocholenate and oxidation of (−)-**1**[3]. Sharpless kinetic resolution of (±)-**1** provided (+)-**1** and its absolute configuration has been assigned as 1S,2S,3R,6R,7R[4]. (+)- and (−)-**5** also have been prepared by enzyme-catalyzed kinetic resolution[5-7] and by the chiron approach[8,9]. Recently we succeeded in the asymmetric synthesis of both (+)- and (−)-**5** using an enzyme-catalyzed hydrolysis of the diacetate of meso-**2** to give (−)-**3** as the key step in 84% yield with 62%ee: optically pure (+) and (−)-**5** were obtained by recrystallization[10]. Herein we wish to report a novel asymmetric synthesis of the title compounds via an enzyme-catlyzed esterification in highly enantioselective manner as a key step.

Meso diol **2**, prepared by epoxidation of (±)-**1** and $LiAlH_4$ reduction of the resulted epoxide in 84% overall yield[10], was treated with vinyl acetate in the presence of Candida cyclindracea lipase(CCL purchased from Sigma Chemical Co.) to give (+)-**4** in 81% yield with 98.3%ee:as determined by GC on chiral phases. PDC (Pyridinium dichromate) oxidation of (+)-**4** with spontaneous β-elimination produced (+)-**5**.Analytical sample:mp.77-8°C (n-hexane), $[\alpha]_D^{20}$=+164.8($CHCl_3$, c=1.39), >99%ee(lit.[7]mp.59-60°C, $[\alpha]_D^{25}$= +158.8 (MeOH,c=1.01). Conversion of (+)-**4** to (−)-**5** has been accomplished by protecting the hydroxy of (+)-**4** as a silyl ether, base hydrolysis, PDC oxidation and base induced β-elimination. Analytical sample: mp.77-8°C(n-hexane), $[\alpha]_D^{20}$=−165.7 ($CHCl_3$, c=2.26), >99% ee. Lit: mp. 76.8-8°C[3], 59-60°C[7], $[\alpha]_D^{25}$=−162($CHCl_3$,c=3.15[3],$[\alpha]_D^{25}$=−152(MeOH, c=0.45)[7]. Thermolysis of (−)-**7** at 420°C/300 torr gave (−)-**8**, oil $[\alpha]_D^{20}$=−49.5 ($CHCl_3$, c=1.18).

Thus a highly enantioselective synthesis of both (+)- and (-)-**5** and (-)-**8** has been achieved.



Reagent and conditions: a, vinyl acetate, CCL, 28°C, 21 h. $[\alpha]_D^{20}$=1.6 ($CHCl_3$, c=2.17). b, PDC, CH_2Cl_2, rt, overnight. c, t-$BuMe_2SiCl$,imidazole, CH_2Cl_2, rt, 3h, d, 10% Na_2CO_3, MeOH, rt, 32h, $[\alpha]_D^{20}$=+11.9($CHCl_3$,c=1.01), >98%ee, e, PDC, CH_2Cl_2, m.s.4A, rt, 10h, mp 42-3°C, $[\alpha]_D^{20}$=-105.7($CHCl_3$, c=1.41), >98%ee, f, 10% Na_2CO_3, MeOH, rt, 10.5h, g, 420°/torr, 1 mim. $[\alpha]_D^{20}$=-49.5($CHCl_3$, c=1.18), >98%ee.

Acknowledgement. This project was supported by National Natural Sciences Fundation of China, we are grateful to Dr. Guong-Zhang Guo for the determination of ee by chiral GC.

REFERENCES:

1. Part VII on Natural Products Synthesis by Retro Diels-Alder Reaction. For part VI, see Z.-Y.Liu, X.-J.Chu, to be published.
2. a, Liu,Z.-Y., Chu,X.-J. Tetrahedron Lett., 1993, **34**, 349; b, Liu, Z.Y., He,L., Zheng,H., SYNLETT, 1993, 191; c, Klunder, A.J.H., Zwanenberg, B., Liu, Z.Y., Tetrahedron Lett., 1991, **26**, 3131; d, Verlack,J.M.J., Klunder,A.J.H., Zwanenberg,B., ibid, 1982, **23**, 5463, e, Takano,S., Moriya,M., Ogasawara,K., Tetrahdron Lett., 1992, **33**, 1909 and cited references therein.
3. Woodward,R.B., Katz,T.J., Tetrahedron, 1959, **5**, 70.
4. Ito, T., Okamoto, Y., Matsumoto,T., Bull. Chem. Soc. Jpn., 1985, **58**, 3631.
5. Klunder, A.J.H., Huijina, W.B., Hulshof, A.J.M., Zwanenberg, B., Tetrahedron Lett., 1986, **22**, 2543.
6. Takano,S., Inomata,K., Ogsawara,K., J. Chem. Soc., Chem. Commun., 1989, 271.
7. Takano,S., Inomata,K., Takahashi,M., Ogsawara,K., SYNLETT, 1991,636.
8. Takano,S., Inomata,K., Ogsawara,K., Chem. Lett., 1989, 359.
9. Dols,P.P.M.A., Laoroix,L., Klunder,A.J.H., Zwanenberg,B.,Tetrahedron Lett., 1991, **30**, 3739.
10. Zhang,L., Yang,J.-Y., Liu, Z.Y., Chinese Chem. Lett., 1992, **3**, 787 (Eng.).