# A NOVEL APPROACH TO CHIRAL CYCLOBUTANES--AN ENANTIOSELECTIVE TOTAL SYNTHESIS OF (+)-(S,Z)-5-(1-DECENYL)DIHYDRO-2(3H)-FURANONE AND (-)-(R,Z)-5-(1-DECENYL)DIHYDRO-2(3H)-FURANONE

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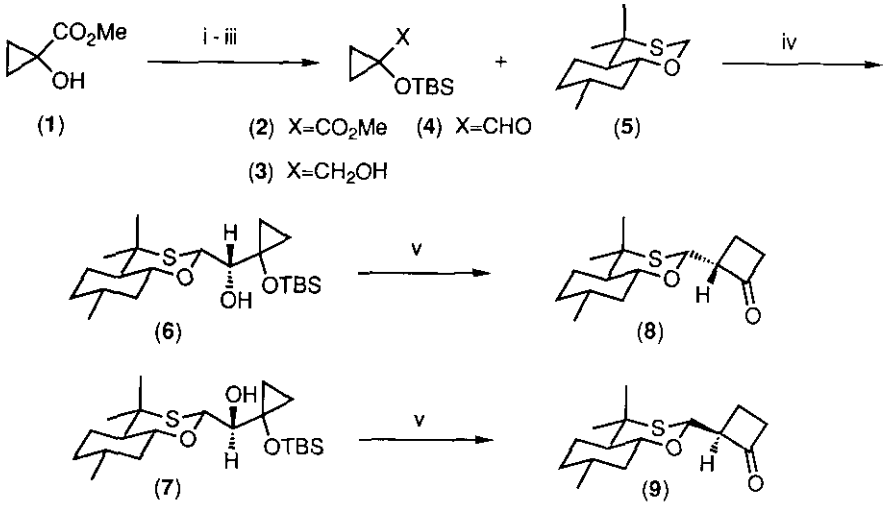
Abstract — An enantioselective synthesis of (+)-(S,Z)-5-(1-decenyl)-dihydro-2(3H)-furanone (**25**) and (-)-(R,Z)-5-(1-decenyl)dihydro-2(3H)-furanone (**26**) was achieved starting with either (**10**) or (**11**) prepared by reduction of the chiral cyclobutanone (**8**) which was derived stereospecifically from the cyclopropyl carbinol (**6**) by ring expansion reaction.

There have been intense interests in the chemistry[1] of cyclobutane and cyclobutanone derivatives mainly because of its occurrence as the basic structure of some natural products[2] and its flexibility for the synthesis of a wide variety of derivatives.[3] But there are few reports[1,4] on the synthesis of optically active cyclobutane or cyclobutanone derivatives. Herein, we wish to report a facile and enantioselective synthesis[5] of cyclobutanones which lead to a total synthesis of (+)-(S,Z)-5-(1-decenyl)dihydro-2(3H)-furanone (**25**) and (-)-(R,Z)-5-(1-decenyl)dihydro-2(3H)-furanone (**26**) (the pheromone of the Japanese beetle).

The synthesis of the key compounds (**8** and **9**) (*Scheme I*) for further transformation was initiated by protection [t-butyldimethylchlorosilane (TBSCl), imidazole, dimethylaminopyridine (DMAP)]of readily available methyl 1-hydroxycyclopropanecarboxylate (**1**)[6] to give (**2**) (89 %) which on reduction [diisobutylaluminium hydride (DIBAL)] yielded the alcohol (**3**) (78 %). Oxidation (Swern conditions) of (**3**) followed by a condensation of the resulted aldehyde (**4**) with the anion of the oxathiane[7] (**5**) to give the threo and erythro compounds (**6** and **7** ; 1:1) (73 % overall from (**3**) ) as a readily separable mixture. The stereospecific ring expansion of a cyclopropane was effected by a reaction of (**6**)

and (**7**) with mesyl chloride (MsCl) followed by acid treatment (10 % HCl) to give (**8**) and (**9**) in 88 % and 92 % yields respectively. Base [diazabicycloundecene (DBU)] treatment of (**9**) yielding the mixture of (**8**) and (**9**) (3:1) in favoring (**8**) (mp 105-106 °C) revealed that (**8**) was the thermodynamically favored product. Thus, the cyclobutanone (**8**) could be prepared selectively by subjecting the mixture of (**6**) and (**7**) directly to the ring expansion reaction followed by base treatment of the crude product.

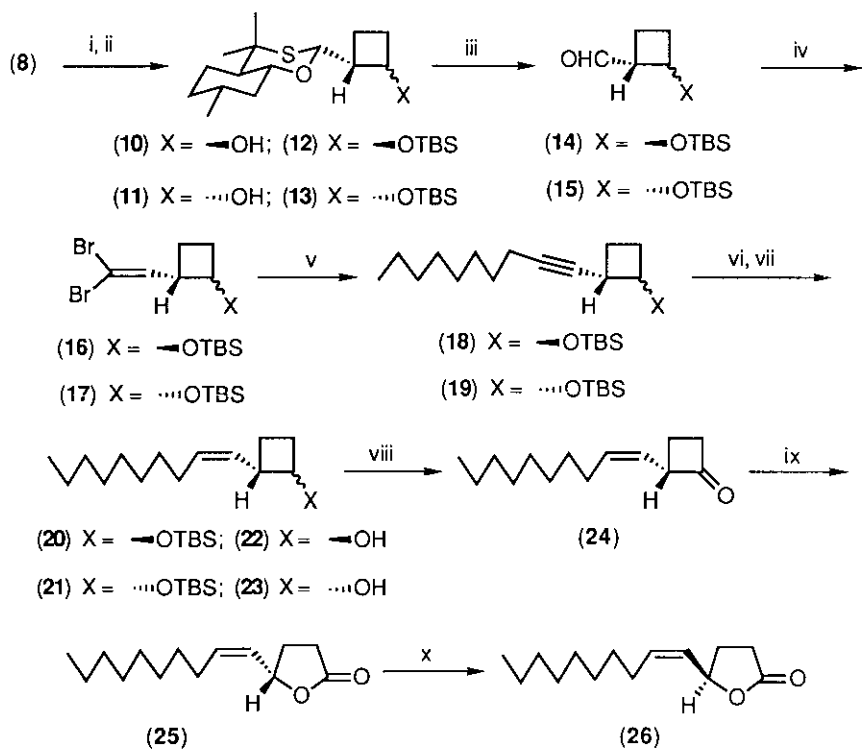



**Scheme 1**

*Reagents and conditions:* **i**, TBSCl, imidazole, DMAP, DMF, 25°C, 24 h; ii, DIBAL, THF, -40 °C, 1 h; iii, DMSO, $(COCl)_2$, THF, -78 °C, 30 min; $Et_3N$, 20 °C, 10 min; iv, **5**, *n*-BuLi, THF, -78 °C,15 min; then **4**; v, MsCl, $Et_3N$, $CH_2Cl_2$, 0 °C, 1 h; 10 % HCl, 6 h

Then, the compound (**8**), keeping the chirality on cyclobutanone in tact, was effectively converted into (+)-(S,Z)-5-(1-decenyl)dihydro-2(3H)-furanone and (-)-(R,Z)-5-(1-decenyl)dihydro-2(3H)-furanone as follows (Scheme II). Reduction ($NaBH_4$) of (**8**) gave the readily separable mixture of (**10**) and (**11**) (7:3) in 100 % yield. Protection (TBSCl) of (**10**) afforded (**12**) (99 %), which was then subjected to the oxidative solvolysis [N-chlorosuccinimide (NCS), $AgNO_3$] to give the aldehyde (**14**). Conversion ($CBr_4$, $Ph_3P$)[8] of the aldehyde (**14**) into (**16**) was then carried out by Wittig reaction (64 % from (**12**)). Base (n-BuLi) treatment of (**16**) and alkylation of *in situ* generated lithium acetylide gave (**18**) (85 %). Semihydrogenation ($H_2$, Lindlar catalyst) of (**18**) followed by deprotection (n-$Bu_4NF$) of (**20**) afforded the alcohol (**22**) (69 % overall from (**18**)), which on Swern oxidation yielded (**24**). Baeyer-

Villiger oxidation (t-BuOOH, 10 % NaOH) of (**24**) furnished (+)-(S,Z)-5-(1-decenyl)dihydro-2(3H)-furanone (**25**) (30 % overall from (**22**)). By following the same chemical treatments described above (**25**) was also prepared starting with (**11**) through (**13**), (**15**), (**17**), (**19**), (**21**), (**23**) and (**24**). Inversion of chirality[9] was effectively achieved by successive treatment [KOH ; then $Ph_3P$, diethyl azodicarboxylate (DEAD)] of (**25**) to yield (-)-(R,Z)-5-(1-decenyl)dihydro-2(3H)-furanone (**26**) (76 %), which was identical with an authentic sample in all aspects including $^1H$ nmr (500 MHz, $CDCl_3$), ir (NaCl) and optical rotation ($[\alpha]_D$ -70.82°), (lit.[10] -70.4°, lit.[11,12] -70.0°, lit.[13] -69.93°, lit.[14] -69.7°).




**Scheme 2**

*Reagents and conditions:* i, $NaBH_4$, MeOH, 0 °C, 30 min; ii, TBSCl, imidazole, DMAP, DMF; iii, NCS, $AgNO_3$, MeCN, 0 °C, 7 min; iv, $CBr_4$, $Ph_3P$, $Et_3N$, -78 °C, 1 h; v, n-BuLi, n-$C_8H_{17}Br$, Hexamethylphosphoramide, THF, -78 °C, 1 h; vi, $H_2$, Lindlar catalyst, AcOEt, 20 °C, 30 min; vii, n-$Bu_4NF$, THF, 20 °C, 2h; viii, DMSO, $(COCl)_2$, THF,-78 °C, 30 min; $Et_3N$, 0 °C, 10 min; ix, t-BuOOH, 10 % NaOH, THF, 0 °C, 30 min; x, KOH, MeOH, 60 °C, 3 h; $Ph_3P$, DEAD, THF, 20 °C, 13 h

We believe that a facile synthesis of chiral cyclobutanones described above could provide a useful methodology for the synthesis of a variety of optically active cyclobutanones and the compounds readily derived from these compounds.

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**REFERENCES AND NOTES**

1. D. Bellus and B. Ernst, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 797.

2. (a) T. K. Devon and A. I. Scott, "Handbook of Naturally Occurring Compounds," Vol. II, Terpenes, Academic Press, New York, 1972 ; (b) A. F. Thomas and Y. Bessiere, "The Synthesis of Monoterpenes, 1980-1986" in "The Total Synthesis of Natural Products," ed. J. ApSimon, John Wiley and Sons, New York, 1988, Vol. 7, p. 275.

3. (a) J. M. Conia and M. J. Robson, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 473 ; (b) S. M. Ali, T. V. Lee, and S. M. Roberts, *Synthesis*, 1977, 155 ; (c) W. T. Brady, *Tetrahedron*, 1981, **37**, 2949 ; (d) C. S. Hwang and W. Reusch, *Heterocycles*, 1987, **25**, 589 ; (e) T. Cohen and L. Brockunier, *Tetrahedron*, 1989, **45**, 2917. Some representatives related to the reactions of 2-vinylcyclobutanones are cited therein.

4. (a) M. Nogradi, "Stereoselective Synthesis", VCH Verlagsgesellschaft, Weinheim, 1987, p. 275 ; (b) J. Salaun, B. Karkour, and J. Ollivier, *Tetrahedron*, 1989, **45**, 3151 ; (c) Y. Hayashi and K. Narasaka, *Chem. Lett.*, 1989, 793 ; (d) K. Hiroi, H. Nakamura, and T. Anzai, *J. Am. Chem. Soc.*, 1987, **109**, 1249.

5. All new substances exhibited spectroscopic data [IR, NMR (500MHz), and MS] in accord with the assigned structure and provided acceptable combustion or high resolution mass spectral data.

6. M. H. O'Leary, W. J. DeGooyer, T. M. Dougherty, and V. Anderson, *Biochem. Biophys. Res. Commun.*, 1981, **100**, 1320.

7. J. E. Lynch and E. L. Eliel, *J. Am. Chem. Soc.*, 1984, **106**, 2943.

8. E. J. Corey and P. L. Fuchs, *Tetrahedron Lett.*, 1972, 3769.

9. S. Takano, M. Yonaga, and K. Ogasawara, *Synthesis*, 1981, 265.

10. S. Senda and K. Mori, *Agric. Biol. Chem.*, 1983, **47**, 2595.

11. R. E. Doolittle, J. H. Tumlinson, A. T. Proveaux, and R. R. Heath, *J. Chem. Ecol.*, 1980, **6**, 473.

12. W. H. Pirkle and P. E. Adams, *J. Org. Chem.*, 1979, **44**, 2169.

13. M. M. Midland and N. H. Nguyen, *J. Org. Chem.*, 1981, **46**, 4107.

14. R. Baker and V. B. Rao, *J. Chem. Soc., Perkin Trans I*, 1982, 69.

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