

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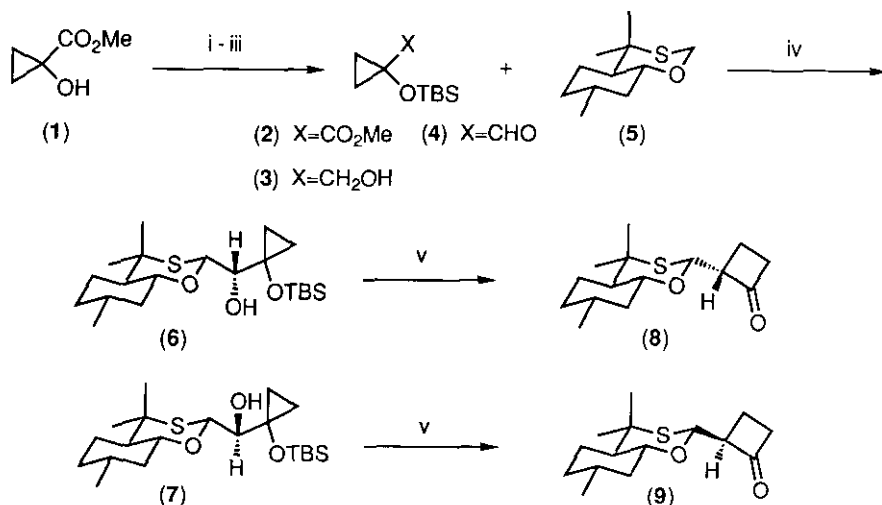
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Abstract — An enantioselective synthesis of (+)-(S,Z)-5-(1-decenyl)-dihydro-2(3H)-furanone (**25**) and (-)-(R,Z)-5-(1-decenyl)dihydro-2(3H)-furanone (**26**) was achieved starting with either (**10**) or (**11**) prepared by reduction of the chiral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

There have been intense interests in the chemistry¹ of cyclobutane and cyclobutanone derivatives mainly because of its occurrence as the basic structure of some natural products² 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 synthesis⁵ 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 [diisobutylaluminum 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 oxathiane⁷ (**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.

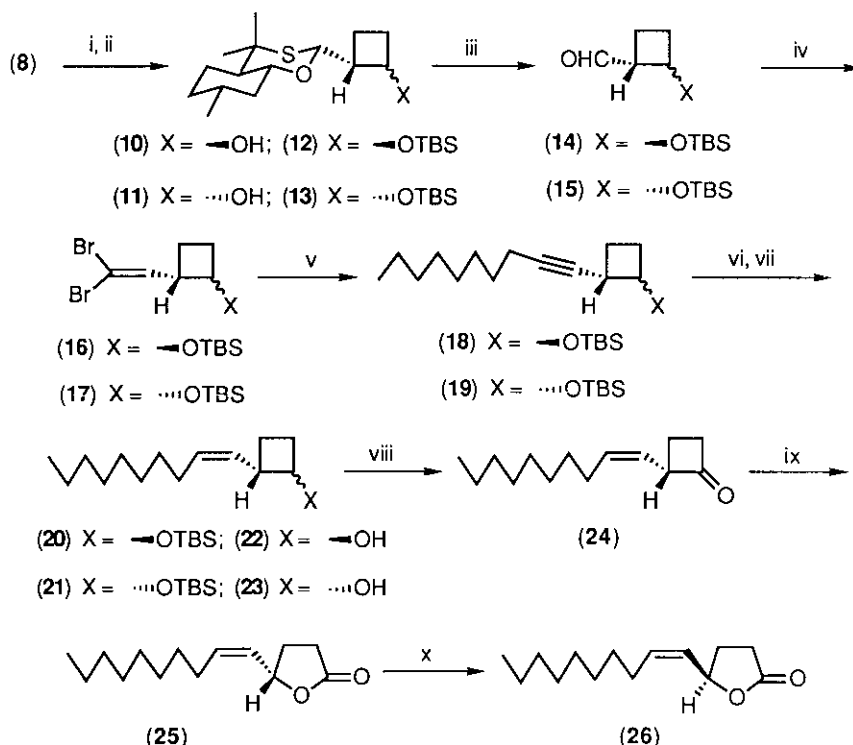


Scheme 1

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; Et₃N, 20 °C, 10 min; iv, 5, n-BuLi, THF, -78 °C, 15 min; then 4; v, MsCl, Et₃N, CH₂Cl₂, 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 (NaBH₄) 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), AgNO₃] to give the aldehyde (14). Conversion (CBr₄, Ph₃P)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 (H₂, Lindlar catalyst) of (18) followed by deprotection (n-Bu₄NF) 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 chirality⁹ was effectively achieved by successive treatment [KOH; then Ph₃P, 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, CDCl₃), ir (NaCl) and optical rotation ([α]_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, NaBH₄, MeOH, 0 °C, 30 min; ii, TBSCl, imidazole, DMAP, DMF; iii, NCS, AgNO₃, MeCN, 0 °C, 7 min; iv, CBr₄, Ph₃P, Et₃N, -78 °C, 1 h; v, *n*-BuLi, *n*-C₈H₁₇Br, Hexamethylphosphoramide, THF, -78 °C, 1 h; vi, H₂, Lindlar catalyst, AcOEt, 20 °C, 30 min; vii, *n*-Bu₄NF, THF, 20 °C, 2 h; viii, DMSO, (COCl)₂, THF, -78 °C, 30 min; Et₃N, 0 °C, 10 min; ix, *t*-BuOOH, 10 % NaOH, THF, 0 °C, 30 min; x, KOH, MeOH, 60 °C, 3 h; Ph₃P, 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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