

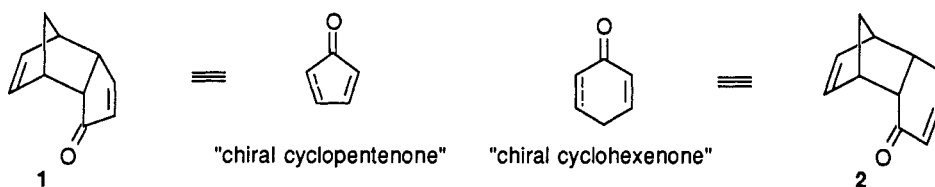
## Enantiocontrolled route to natural products using chiral equivalents of cyclopentenone and cyclohexenone

Kunio Ogasawara

Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980, Japan

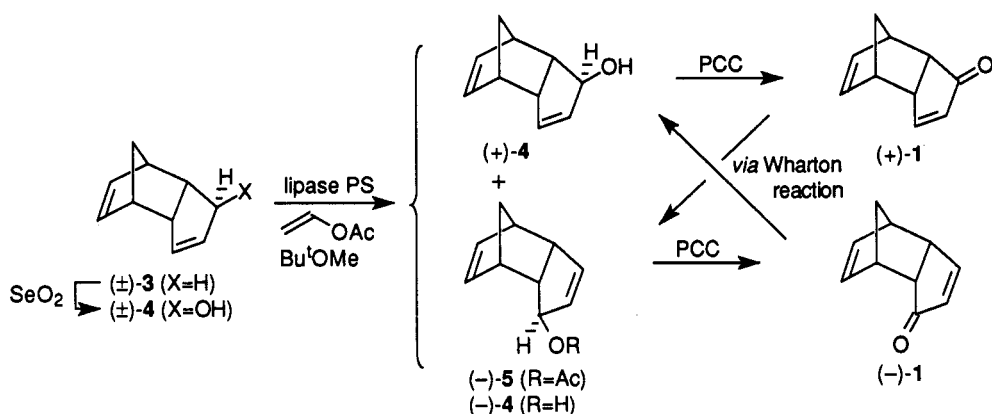
**Abstract:** Efficient preparation of two tricyclic dienones, (1) and (2), in both enantiomeric forms has been developed by employing lipase-mediated resolution. A variety of natural products have been synthesized in enantiocontrolled manners by utilizing the former as a chiral equivalent of 2-cyclopentenone (as well as cyclopentadienone) and the latter as a chiral equivalent of 2-cyclohexenone (as well as 2,5-cyclohexadienone).

Enantiocontrolled functionalization of cyclopentane and cyclohexane derivatives is one of the most important subjects in the synthesis of optically active materials. In this regard the enantiotopical preparation of two tricyclic dienones **1** and **2** was investigated with intent to use the former as a chiral equivalent of cyclopentenone (as well as cyclopentadienone) and the latter as a chiral equivalent of cyclohexenone (as well as 2,5-cyclohexadienone) in the chiral synthesis of natural products. Because of their biased framework and thermal susceptibility, they allowed highly stereoselective functionalization and generation of the olefin functionality which led to enantiocontrolled synthesis of a variety of natural products.

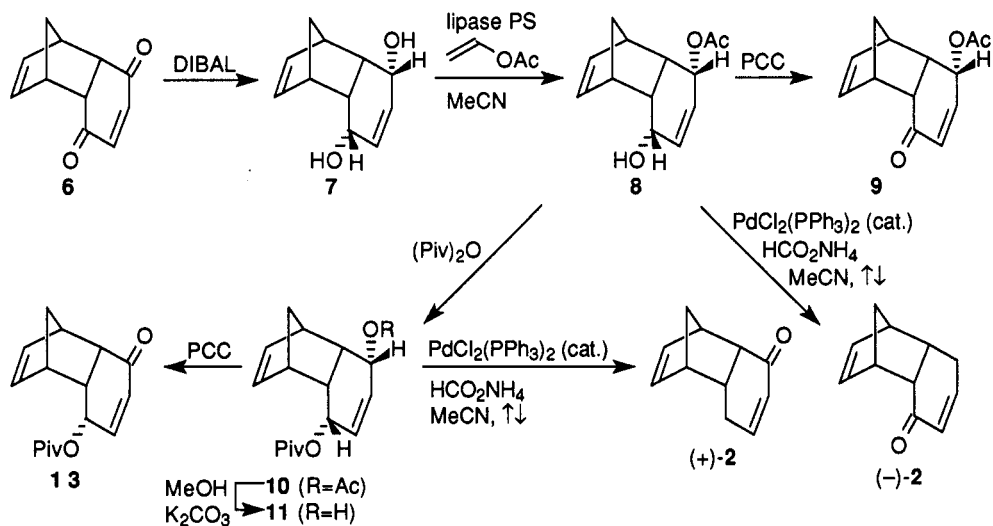


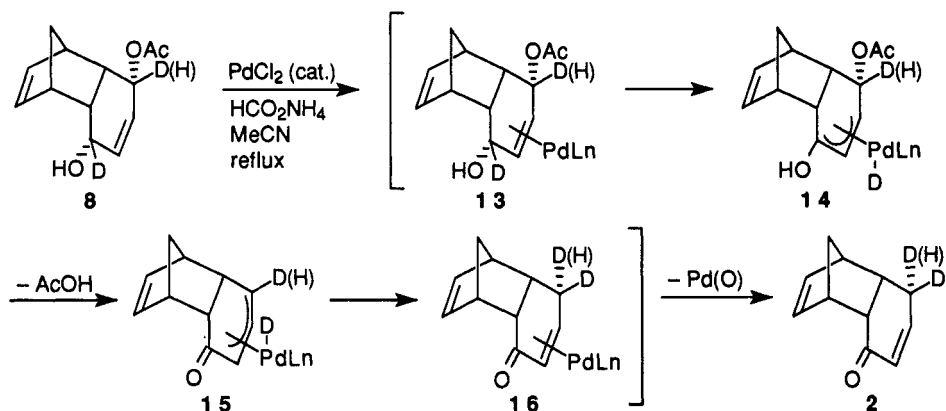
### SYNTHESIS OF OPTICALLY PURE SUBSTRATES

(a) **Synthesis of Optically Pure "Cyclopentenone" (1)** — Treatment of the readily accessible *exo*-alcohol (4) with vinyl acetate in the presence of lipase PS (*pseudomonas*, sp.) or lipase MY (*candida cylindraceae*) in organic solvent yielded the optically active acetate (5) and the optically active alcohol (4) both in ca. 80% ee. Fortunately, the alcohol (4) crystallized and the optically pure 4 could be obtained after recrystallization. "Cyclopentenone" (1) was obtained from 4 in a satisfactory yield on oxidation. Moreover, the configuration of 1 could be inverted by a 1,3-ketone transposition *via* the Wharton reaction.



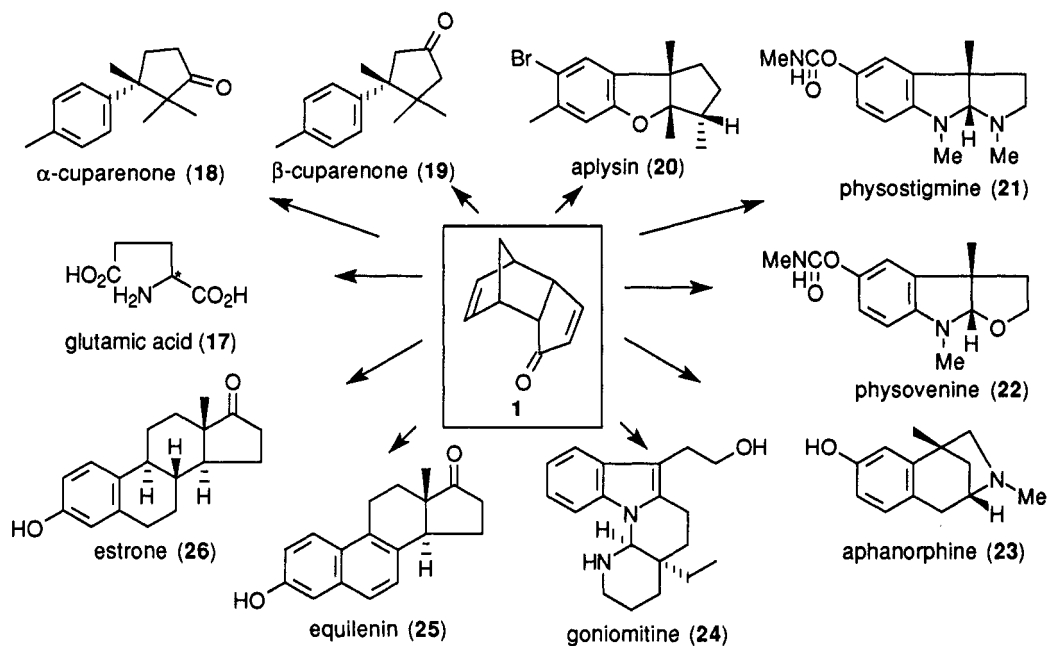
(b) **Synthesis of Optically Pure "Cyclohexenone" (2)** — Treatment of the readily accessible *meso*-diol (**7**) with vinyl acetate in the presence of lipase PS in acetonitrile furnished the optically pure (>99% ee) mono-acetate (**8**) in 79% yield. Oxidation of **8** gave the "4-substituted cyclohexenone" (**9**), while on sequential pivaloylation deacetylation, and oxidation, **8** afforded **12** which may be taken as enantiomer of **9**. The "cyclohexenone" (**2**) was obtained excellently in a rather surprising way when **8** was refluxed with ammonium formate in the presence of palladium dichloride (1.5 mol%) in acetonitrile. Similarly, the enantiomer was obtained excellently from the pivalate (**11**) under the same conditions. Deuterium labeling experiment revealed that this interesting reaction involved unprecedented suprafacial 1,4-hydrogen shift pathway.

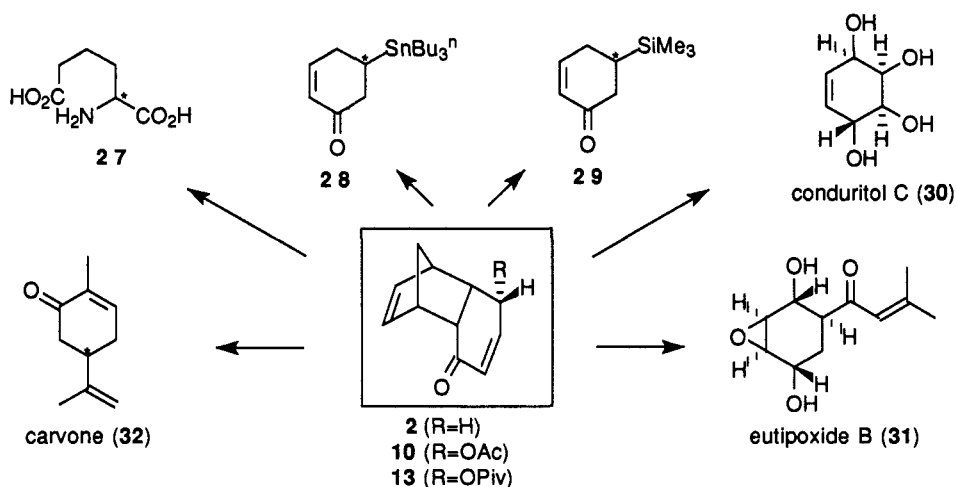




### SYNTHESIS OF NATURAL PRODUCTS

"Cyclopentenone" (1) and "cyclohexenone" (2) allowed highly stereospecific nucleophilic  $\beta$  and electrophilic  $\alpha$  functionalizations of the enone system from the *exo*-face and also allowed  $\alpha'$  functionalization under appropriate conditions. Moreover, Fischer indolization and Diels-Alder reactions also proceeded exclusively from the *exo*-face. Retro-Diels-Alder cleavage occurred generally at 200~250 °C in diphenyl ether to generate the double bond by removal of cyclopentadiene.





Natural products belonging to alkaloids, terpenes, and alkaloids, were prepared by standard  $\alpha$ - and  $\beta$ -functionalization procedures, by  $\alpha$ -arylation under the Fischer indolization conditions and by Diels-Alder functionalization, prior to retro-Diels-Alder reaction.

#### ACKNOWLEDGMENTS

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