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STEREOSELECTIVE TOTAL SYNTHESES OF (±)- AND OPTICALLY ACTIVE DEHYDROIRIDODIOLS

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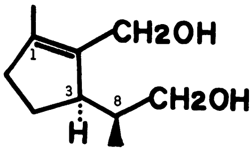
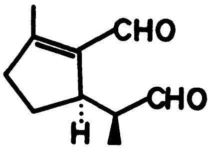
(±)-Dehydroiridodiol and its epimer (±)-isodehydroiridodiol were synthesized stereoselectively using the homoconjugate addition of cyanide anion to methyl 6-methyl-2-oxobicyclo[3.1.0]hexane-1-carboxylates. Both enantiomers of dehydroiridodiol were prepared after the resolution of *l*-menthyl 6-methyl-2-oxobicyclo[3.1.0]hexane-1-carboxylate, whose absolute configurations became clear as the result.

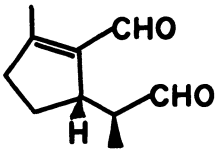
(-)-Dehydroiridodiol (1), isolated from *Actinidia polygama* Miq. as an attractant for members of the Chrysopidae, is a useful material for the synthesis of the other related cyclopentane monoterpenes.1) Syntheses of 1,1) a further oxidized product (2) (dehydroiridodial),2) and its C-3 epimer (3)(chrysomelidial)3) had been achieved from *l*- or *d*-limonene by the well-established method including a troublesome separation step, and recently stereoselective syntheses of (±)-24) and (±)-35) have been reported by two groups. Now we describe here selective syntheses of (±)-1 and its epimer (±)-(4)(isodehydroiridodiol)1b) using the homoconjugate addition6) of cyanide anion7) and preparations of (-)- and (+)-1 after the resolution of *l*-menthyl ester derivatives.



(1)



(2)



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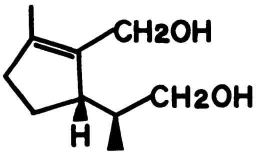
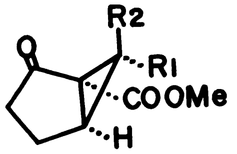


(4)

Methyl 6-methyl-2-oxobicyclo[3.1.0]hexane-1-carboxylate (±)-(5)8) was treated with sodium cyanide in DMSO at 70°C for two hours under nitrogen atmosphere to give the desired nitrile (±)-(6)9) in 72% yield. Although the epimerization at the α position of the cyano group occurred a little under that condition, the undesired isomer could be removed easily by the silica gel column chromatography. (±)-6 was then transformed into the α,β-unsaturated ester (±)-(7)10) in 66% yield by the treatmemt with sodium hydride and diethyl phosphorochloridate at 0°C, followed by the exposure of the resultant enol phosphate with lithium dimethylcuprate at 0°C.11) Reduction of (±)-7 with excess diisobutyl aluminum hydride in toluene at room temperature, followed by the hydrolysis, afforded the hemiacetal (±)-(8),12) which was reduced with lithium aluminum hydride to (±)-1 in 37% yield from (±)-7. Along the same reaction sequence, (±)-9 was converted to (±)-4 *via* (±)-10, (±)-11, and (±)-12 in about the same yield as (±)-1.13) The spectral data of synthetic (±)-1 and (±)-4 were identical with those in the literature.[1b)]

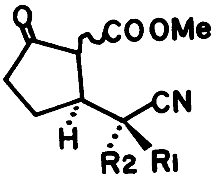
As (±)-dehydroiridodiol was synthesized shortly in a moderate yield, we decided to prepare the optical active materials. A diastereomeric mixture of *l*-menthyl esters (13) was obtained from *l*-menthyl acetoacetate[14)] in three steps, and resolved cleanly by the careful silicagel column chromatography(Et_2O-hexane) and recrystallization (hexane).[15)] The absolute configurations of these materials became clear after their derivation to (-)- and (+)-1. The less polar diastereomer was loaded on our established process[13)] to provide (-)-1, whose optical rotation($[\alpha]_D$=-27.9°($CHCl_3$, C=0.895), lit.[1b)] -20.7°) had the same sign as the natural product(-16.7°[1b)]). The same transformation of the more polar material produced (+)-1($[\alpha]_D$=+25.8°($CHCl_3$, C=1.20));thus the structure (13a) was given to the less polar one and (13b) to the more polar one.

Further synthetic studies of the other optical active natural products from 13a and/or 13b are now in progress.



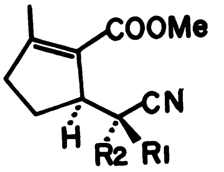
(5) $R_1=CH_3,R_2=H$

(9) $R_1=H,R_2=CH_3$



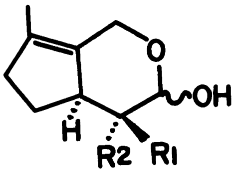
(6) $R_1=CH_3,R_2=H$

(10) $R_1=H,R_2=CH_3$



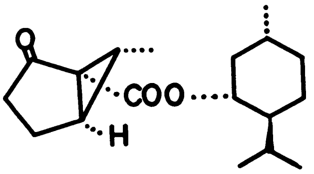
(7) $R_1=CH_3,R_2=H$

(11) $R_1=H,R_2=CH_3$

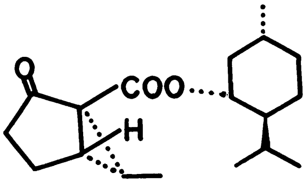


(8) $R_1=CH_3,R_2=H$

(12) $R_1=H,R_2=CH_3$



(13a)



(13b)

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9) (±)-6 was an unseparable mixture of keto-enol tautomers and/or cis-trans isomers. m/z 195(M^+); IR(CCl_4) 2250, 1760, 1730, 1665, 1620 cm^{-1}; NMR(CCl_4) δ 1.29, 1.35 (total 3H, each d, J=7,6), 3.76, 3.78(total 3H, each s).
10) (±)-7: m/z 193(M^+); IR($CHCl_3$) 2245, 1680, 1640 cm^{-1}; NMR(CCl_4) δ 1.31(3H, d, J=7) 2.15(3H, brs), 3.74(3H, s).
11) F.W.Sum and L.Weiler, Can. J. Chem., 57, 1431(1979).
12) (±)-8: m/z 168(M^+); IR(CCl_4) 3620, 3380, 1450 cm^{-1}; the NMR spectrum was complex for the isomerism at the C-9 position, but did not show the signal of the aldehyde proton.
13) All synthetic intermediates gave satisfactory analytical and spectral properties.
14) D.F.Taber, S.A.Saleh, and R.W.Korsmeyer, J. Org. Chem., 45, 4699(1980).
15) 13a: mp 64.5-65.5°C; $[\alpha]_D$=-70.2°($CHCl_3$,C=3.02). 13b: mp 97.5-98.5°C; $[\alpha]_D$=-39.7° ($CHCl_3$,C=5.59).

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