CHEMISTRY LETTERS, pp. 921-922, 1988.

Synthesis of (R)-(+)-4-Butyl-2,6-cycloheptadienone, a Constituent of Marine Algae

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The title compound was synthesized from (R)-(-)-5-trimethylsilyl-2-cyclohexenone in 19% overall yield.

(+)-4-Butyl-2,6-cycloheptadienone (**1**) was isolated as a minor constituent of the essential oil of Hawaiian Dictyopteris. The unique dihydrotropone derivative is a metabolite of the structurally related dictyopterene C' and the structure was confirmed by the derivatization from natural dictyopterene C'.[1)]

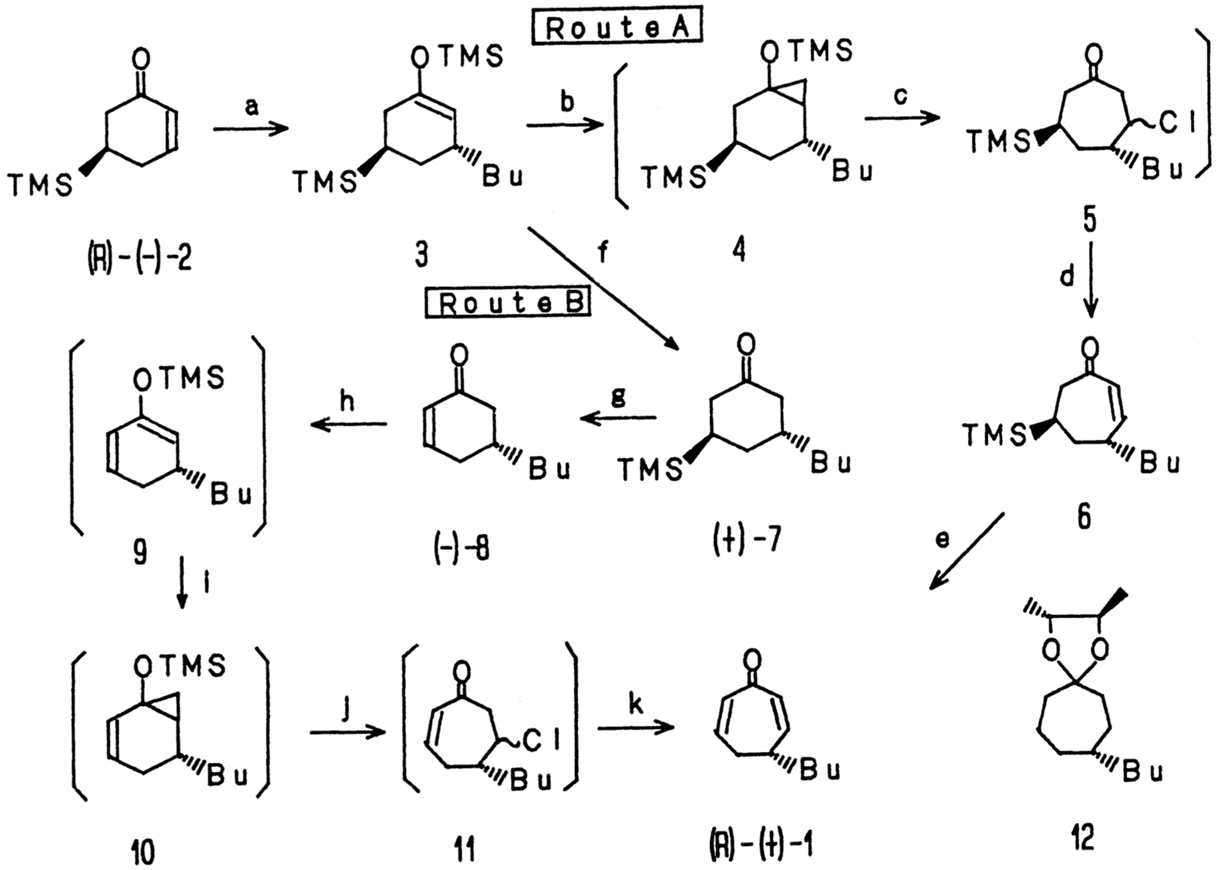
In this paper we will describe a short step synthesis of the above compound by utilizing (R)-(-)-5-trimethylsilyl-2-cyclohexenone (**2**).[2)]

First, the synthetic route A was examined by using racemic **2** (Scheme 1). The route involves the Simmons-Smith type cyclopropanation of enol silyl ether **3**, which was obtained in 93% yield by 1,4-addition of butylmagnesium bromide to **2** in the presence of chlorotrimethylsilane,[2,3)] and subsequent oxidative ring opening as a ring expansion method. Among cyclopropanation conditions of **3** examined, the use of CH_2I_2-Et_2Zn[4)] in benzene at 0 °C-rt gave the best result. Oxidative ring opening of **4** with $FeCl_3$[5)] and dehydrochlorination afforded cycloheptenone derivative **6** in 77% overall yield from **3**.

Disappointingly, oxidative removal of TMS group from **6** under various reported conditions[6)] resulted in a failure. After further trials, the conversion was accomplished by three-step operation to give the desired dienone **1**, but the yield was low (28%). Therefore, alternative route was examined by using (±)-**2**. The second route (route B) involves the removal of TMS group in an early stage. Hydrolysis of crude enol silyl ether **3** with KF and subsequent removal of TMS group under oxidative conditions ($CuCl_2$ in DMF)[7)] gave enone **8** in 85% overall yield from **2**. After the conversion of **8** to the enol silyl ether **9** (84%), cyclopropanation followed by oxidative ring cleavage and dehydrochlorination gave expected dienone (±)-**1** in 44% overall yield from **9**.

Thus, the synthesis of (R)-(+)-**1** was carried out by the second route. The 1,4-addition of butylmagnesium bromide to (R)-(-)-**2** proceeded in a stereospecific manner to give ketone (+)-**7** [$[\alpha]_D^{22}$+78.3°(c 2.17, $CHCl_3$)] in 99% yield.[2,7)] Removal of TMS group gave cyclohexenone (-)-**8** [85%, $[\alpha]_D^{22}$-51.2°(c 1.40, $CHCl_3$)] which was converted to enol silyl ether **9**. Cyclopropanation of **9** followed by oxidative ring opening with $FeCl_3$, and dehydrochlorination furnished (R)-(+)-**1**[8)] [22% from (-)-**8**, $[\alpha]_D^{15}$+35.8°(c 3.34, MeOH).[9)] To confirm the optical purity of synthesized (R)-(+)-**1**, it was hydrogenated and converted to acetal derivative of

2(R), 3(R)-butane diol **12** (98% yield). Comparison of the ^{13}C-NMR spectrum of **12** with that of the corresponding acetal derivative obtained from $(\pm)$-**1** indicated optical homogeneity of **12**.



a)BuMgBr, cat. CuBr, TMSCl, HMPT; b)CH_2I_2, Et_2Zn; c)$FeCl_3$, DMF; d)AcONa; e)LDA/NCS/TBAF; f)KF, MeOH; g)$CuCl_2$, DMF; h)LDA/TMSCl; i)CH_2I_2, Et_2Zn; j)$FeCl_3$, DMF; k)AcONa.

This work was financially supported by Grant-in Aid from the Ministry of Education.

References

1) R. E. Moore and G. Yost, Chem. Commun., 1973, 937. 2) M. Asaoka, K. Shima, and H. Takei, Tetrahedron Lett., 28, 5669 (1987). 3) Y. Horiguchi, S. Matsuzawa, E. Nakamura, and I. Kuwajima, Tetrahedron Lett., 27, 4025 (1986). 4) J. Furukawa, N. Kawabata, and J. Nishimura, Tetrahedron, 24, 53 (1968). 5) Y. Itoh, S. Fujii, and T. Saegusa, J. Org. Chem., 41, 2073 (1976). 6) I. Fleming and J. Goldhill, J. Chem. Soc., Perkin Trans. 1, 1980, 1943; J. Ager, I. Fleming, and S. K. Patel, ibid., 1980, 2520; I. Fleming and D. A. Perry, Tetrahedron, 37, 4027 (1981) and references cited therein. 7) M. Asaoka, K. Shima, and H. Takei, J. Chem. Soc., Chem. Commun., in the press. 8) The structure was confirmed by ^{1}H-NMR, ^{13}C-NMR, and IR spectra and elemental analysis. 9) Lit.$^{1)}$ $[\alpha]_D$+96°(isooctane-MeOH).

(Received February 26, 1988)