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A SYNTHESIS OF (±)-CRYPTOJAPONOL AND (±)-TAXODIONE

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Abstract. A new method for the synthesis of highly substituted catechols involving the decarboxylation of an α,β-epoxyenone was developed and employed in a synthesis of two diterpenes, cryptojaponol and taxodione.

Previous methods for introducing the catechol subunit in abietane diterpenes have involved either carrying a protected catechol through an annelation sequence[2] or oxidizing a phenol at the C-11 position.[3,4] We have now developed an alternate approach which involves the concomitant decarboxylation of a vinylogous β-ketoacid and the rearrangement of an epoxide to generate a catechol. We wish to report a formal total synthesis of cryptojaponol[5] (1) and taxodione[6] (2) which utilizes this approach.

We have already reported an efficient synthesis of the enone 3 from 2-carboethoxycyclohexanone in seven steps.[7] The hindered nature of the bridged ring system in 3 precluded the direct base-catalyzed hydrogen peroxide[8] or tert-butylhydroperoxide[9] oxidation of 3 to an epoxyketone 8. We resorted instead to the three-step sequence shown in Scheme 1. Reduction of 3 with sodium borohydride furnished a 2.5 to 1 ratio of the 12α-alcohol 4 [52% yield; mp 190-192°; nmr ($CDCl_3$) δ 5.47 (d, $J_{11,12\beta}$ = 1.8 Hz, C-11 vinyl H)] and 12β-alcohol 5 [21% yield; mp 195-197°; nmr ($CDCl_3$) δ 5.72 (d, $J_{11,12\alpha}$ = 5.9 Hz, C-11 vinyl H)] which displayed nmr coupling constants in good agreement with values calculated for dihedral angles measured from models. In accord with Henbest's findings,[10] epoxidation of 4 provided the 9α,11α-epoxy-12α-alcohol 6 [72% yield; mp 214-215.5°; ir (KBr) 2.88, 5.82 μ; nmr ($CDCl_3$) δ 3.26 (s, C-11 H) and 3.72 (d, J = 9 Hz, C-12β H)]. Unequivocal support for structure 6 was obtained by a single crystal x-ray diffraction study[11] (Figure 1). Epoxidation of the 12β-epimer 5 led to a mixture of the enone 3 and the 9α,11α-epoxy-12β-alcohol 7 [51% yield] presumably because the hindered nature of the β-face of 5 overrode the directing effect of the 12β-hydroxyl group. Support for this stereochemical outcome was found in the chromium trioxide oxidation of either 6 or 7 to the epoxyketone 8 [73% from 6;

89% from 7; mp 210-211.5°; ir (KBr) 5.72, 5.82 μ; nmr ($CDCl_3$) δ 3.20 (s, C-11 H)] in 53% overall yield from 3.

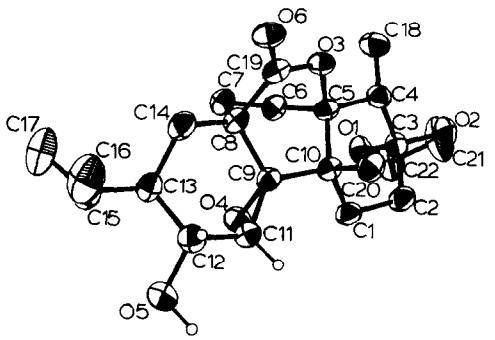
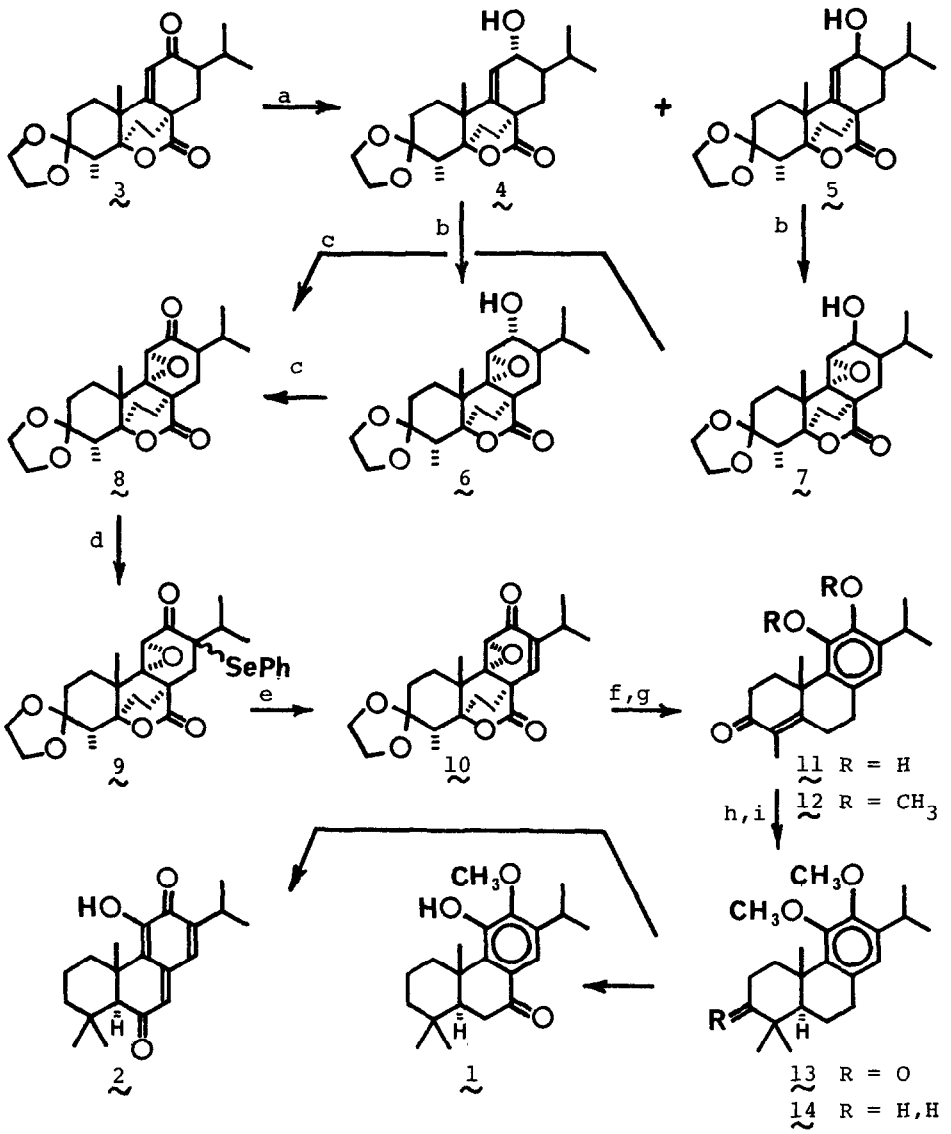


Figure 1.

Conversion of the epoxyketone 8 to the epoxyenone 10 required for a catechol synthesis was not without obvious pitfalls. Although the enolate derived from 8 could suffer a well-precedented Favorskii rearrangement,[12] this potential difficulty was circumvented by adding a 1:1 THF-HMPA solution of 8 and phenylselenyl chloride (4 equiv) to an LDA (3 equiv)/THF solution at -78° to obtain the phenylselenide 9 as a mixture of diastereomers [59% yield; mp 219-225°; ir ($CHCl_3$) 5.75, 5.95 μ; nmr ($CDCl_3$) δ 3.41 (s, C-11 H)]. We anticipated that oxidative elimination of the phenylseleno group would proceed without incident, but we noted that variable amounts of hydrogen peroxide[13] were often required to consume all the starting material 9 and that the reaction proceeded after variable induction periods. We avoided these problems by irradiating (300W Sunlamp) 9 in the presence of 3.5 equiv of hydrogen peroxide[14] in dichloromethane to afford the epoxyenone 10 [ir ($CHCl_3$) 5.73, 5.93 μ; uv (EtOH) λ_{max} 240 nm; nmr ($CDCl_3$) δ 3.39 (s, C-11 H) and 6.17 (s, C-14 H)].

Acid hydrolysis (25% $HClO_4$, H_2O-THF, 60°, 2.5 hr) of 10 proceeded with concomitant deketalization, β-elimination, decarboxylation of the vinylogous β-ketoacid and rearrangement of the epoxide to give the air-sensitive catechol 11. Methylation (K_2CO_3, $(CH_3)_2SO_4$, acetone) provided the stable derivative 12 [ir ($CHCl_3$) 6.04, 6.20 μ; nmr ($CDCl_3$) δ 3.73, 3.89 (two s, OCH_3) and 6.66 (s, aromatic H)] in 32% overall yield from 9. To complete a formal total synthesis of (±)-cryptojaponol (1) and (±)-taxodione (2), we employed a standard sequence of reactions to convert the enone 12 to 11-methoxyferruginyl methyl ether 14 which Wenkert[5a] has converted to cryptojaponol (1) and which Mori and Matsui[4b] have converted to taxodione (2).[15]

Scheme 1



a, $NaBH_4$, ethanol; b, MCPBA, CH_2Cl_2; c, $CrO_3 \cdot Py$, CH_2Cl_2; d, LDA, PhSeCl, THF-HMPA, -78°; e, H_2O_2, hν; f, $HClO_4$, H_2O-THF, 60°; g, $(CH_3)_2SO_4$, K_2CO_3; h, Li, NH_3-THF, CH_3I (see procedure in reference 7); i, $HSCH_2CH_2SH$ followed by Raney Ni.

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13. Other oxidizing agents including ozone, sodium periodate and tert-butyl hydroperoxide proved less satisfactory than hydrogen peroxide.

14. Irradiation of the phenylselenide 9 in the absence of hydrogen peroxide does not lead to the epoxyenone 10.

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