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FORMATION OF COLEON A SKELETON FROM (-)-ABIETIC ACID

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By the treatment of Δ^6-6-hydroxy-5βH-dehydroabietic acid (18-6)-lactone with potassium hydrogensulfate or conc. sulfuric acid, the B ring aromatization and the C_1-C_{10} bond cleavage occurred to give 1,10-secoabietane derivatives possessing coleon A skeleton.

Coleon A (I), which has been isolated[1] by Eugster et al. as a pigment of Coleus igniarius Schweinf. (Labiatae), is a rare diterpene possessing a highly oxygenated 1,10-secoabietane skeleton.[2] In their biogenetic view, coleon A is derived from ferruginol (II), by hydroxylation or/and dehydration at the positions marked with arrows, aromatization of ring B, and cleavage of C_1-C_{10} bond (Fig. 1). During the course of our study on the reactivity of (-)-abietic acid (1) derivatives, we now found that, when Δ^6-6-hydroxy-5βH-dehydroabietic acid (18-6)-lactone (3) was treated with potassium hydrogensulfate or conc. sulfuric acid, both the B ring aromatization and the C_1-C_{10} bond cleavage occurred. This communication[3] describes a novel synthesis of coleon A skeleton.

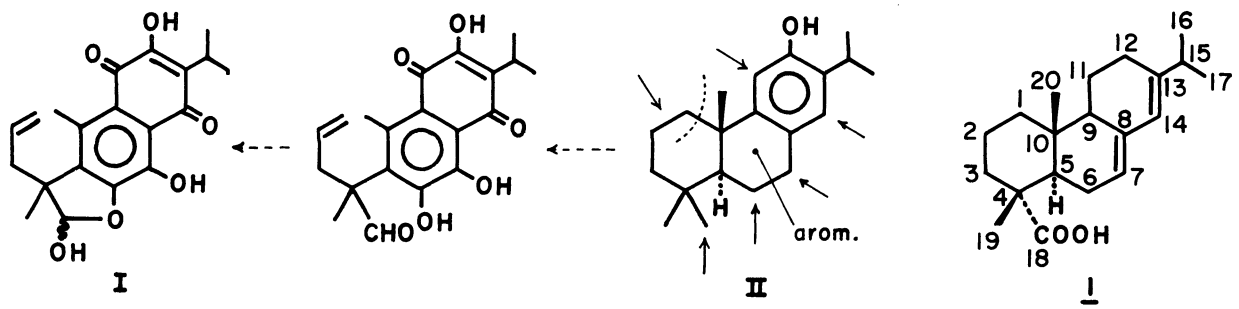
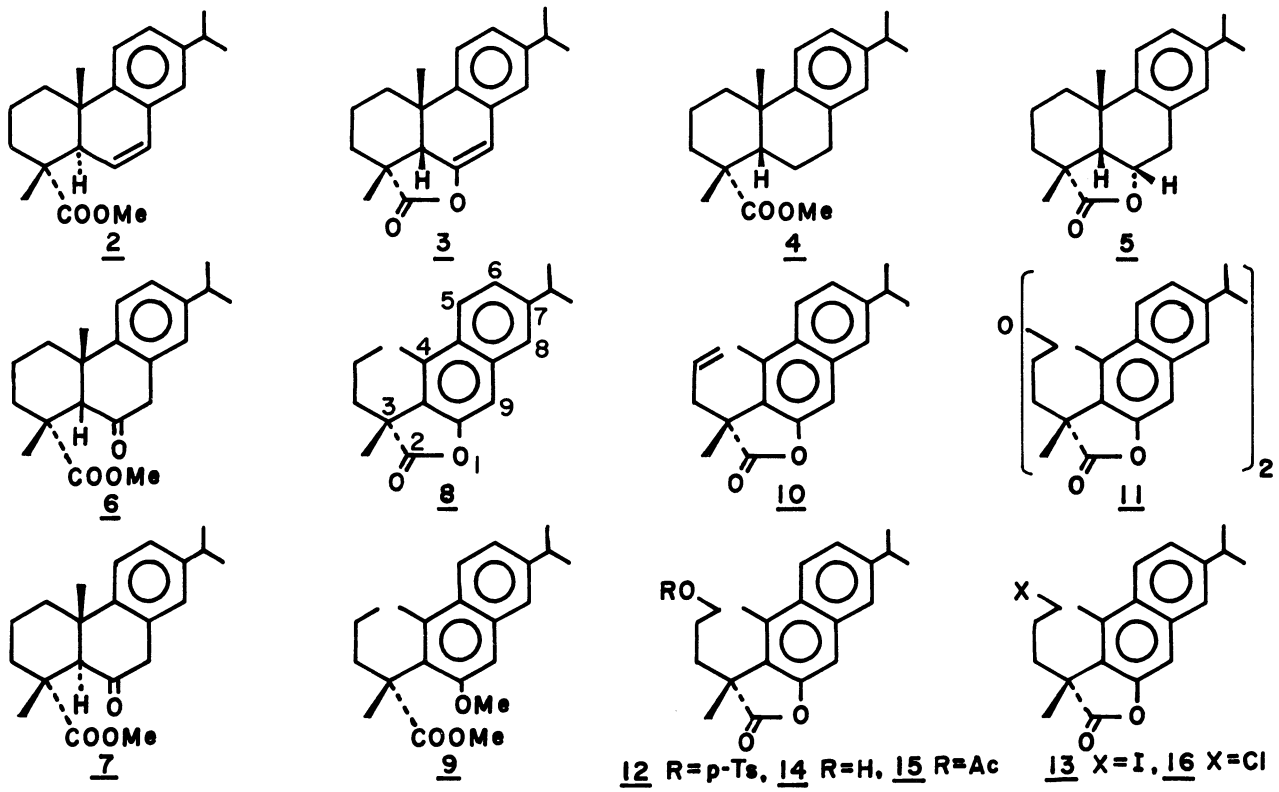


Fig. 1

Methyl Δ^6-dehydroabietate[4] (2) was oxidized with perbenzoic acid in chloroform to give a mixture of C_6-oxygenated products[5] which was immediately treated with p-toluenesulfonic acid monohydrate in refluxing toluene to yield the Δ^6-lactone (3: 70% yield), mp 106.5-107°C, $[\alpha]_D$ - 116°, IR: 1800, 1692 cm^{-1}; NMR: 1.46, 1.52 (each 3H, s), 2.65, 5.96 (each 1H, d, J=2.5 Hz). The stereochemistry of C_5-position in 3 was established as follows; 3 was transformed by catalytic hydrogenation on platinum oxide in acetic acid followed by esterification with diazomethane to the known[6] methyl 5βH-dehydroabietate (4: 49% yield), together with an (18-6α)-lactone of 6α-hydroxy-5βH-dehydroabietic acid[7] (5: 30% yield), mp 109-109.5°C, $[\alpha]_D$ - 45°, IR: 1758 cm^{-1}, NMR: 1.18, 1.29 (each 3H, s), 2.21 (1H,

d, J=8.5 Hz), 3.06 (2H, d, J=4 Hz), 4.88 (1H, dt, J=8.5, 4, and 4 Hz). Methanolysis of 3 with conc. hydrochloric acid gave methyl 6-oxo-5βH-dehydroabietate (6: 81% yield), mp 126-127°C, $[\alpha]_D$ + 36°, IR: 1723, 1700 cm^{-1}; NMR: 1.09, 1.18 (each 3H, s), 2.04 (1H, s), 2.90 (3H, s), 3.44 (2H, bs). On the other hand, methyl 6-oxodehydroabietate[8] (7) was never epimerized to 6 under the same condition.

The Δ^6-lactone (3) was fused with potassium hydrogensulfate (15 mole equivalent, 220°C, 12 h) to give three naphthalene derivatives which were separated by a careful column chromatography on silica gel. The first compound (5% yield), mp 130-130.5°C, $[\alpha]_D$ + 81°, showed the presence of a naphthalene chromophore in UV spectrum, λ_{max}(ethanol): 235.5 nm (log ε=4.80), 281.5 (3.76), 293sh (3.63), 312 (3.07), 320sh (2.90), 327 (3.08), and γ-enol lactone function in IR spectrum, ν_{max}: 1798 cm^{-1}. In addition to those information, the observation of its NMR spectrum (Table 1) clarified its structure to be (3R)-2,3-dihydro-7-isopropyl-3,4-dimethyl-3-propylnaphtho[2,3-b]furan-2-one (8).[9] This structure was further confirmed by the transformation with dimethyl sulfate and potassium hydroxide in aqueous acetone to a methyl ester (9: 50% yield), $[\alpha]_D$ - 31°, IR: 1725 cm^{-1}, NMR: 2.63, 3.53, 3.78 (each 3H, s), 6.86 (1H, s, 27% NOE enhancement by saturation of the signal 3.78), 7.83 (1H, d, J=9 Hz, 22% NOE enhancement by saturation of the signal 2.63). Thus 8 has apparently coleon A (I) skeleton, a 1,10-secoabietane structure. The second (5% yield), mp 118-119°C, $[\alpha]_D$ + 130°, possesses an allyl group as a partial structure (IR: 987, 910 cm^{-1}; NMR: Table 1). On catalytic hydrogenation (5% palladium-carbon in methanol), it gave 8, so it must be a dehydro derivative (10). The last compound, which was a main product (32% yield, $[\alpha]_D$



+ 45°), showed the molecular weight 606 (mass spectrum: M^+=606). In the NMR spectrum (Table 1), a triplet signal (3.07) suggested the structure to be a dimer (11) possessing an ether linkage at both the ω-positions of propyl groups in two monomers (8). This ether dimer (11) was converted to a tosylate (12: 45% yield, $[\alpha]_D$ + 69°, IR: 1795, 1637, 1360, 1172 cm^{-1}; NMR: Table 1) by heating with p-toluenesulfonic acid monohydrate in sym-tetrachloroethane. Subsequently 12 was converted to an iodide (13: 89% yield, $[\alpha]_D$ + 19°, NMR: Table 1) by refluxing with sodium iodide in acetone. Treatment of 13 with potassium t-butoxide in dimethyl sulfoxide gave 10 (6% yield) and a hydroxyl derivative (14: 25% yield), $[\alpha]_D$ + 50°, IR: 3620, 3450br, 1795, 1637 cm^{-1}; NMR: Table 1.

Our next effort was directed toward the more effective condition. When the Δ^6-lactone (3) was treated with conc. sulfuric acid in refluxing toluene (2 h), the tosylate (12: 17% yield) was obtained. The yield of this reaction was further improved by treatment of 3 with conc. sulfuric acid in refluxing acetic acid (3 h), and in this case, an acetate (15: 47% yield, $[\alpha]_D$ + 11°, IR: 1797, 1730, 1640 cm^{-1}; NMR: Table 1) was obtained. Hydrolysis of 15 with conc. hydrochloric acid in aqueous methanol gave 14 which was converted to the tosylate (12: 49% yield) by treatment with p-toluenesulfonyl chloride in pyridine or to a chloride (16: 83% yield, mp 63-65.5°C, $[\alpha]_D$ + 10°, NMR: Table 1) with triphenylphosphine in carbon tetrachloride. The latter (16) was also subjected to the elimination reaction to yield the allyl compound (10: 6% yield).

Table 1. NMR spectra of 2,3-dihydronaphtho[2,3-b]furan-2-one derivatives[3,a)]

Compd.	C_3-Me	C_4-Me	C_5-H	C_6-H	C_7-^{i}Pr	C_8-H	C_9-H	C_3-substituent	
8	1.59s	2.61s	7.82d[b)] (8.5)	7.26dd (8.5;2)	1.32d,6H(7) 3.02qui,1H(7)	7.50d (2)	7.20s	0.70-1.25m,5H ca.2.05m,2H	
10	1.64s	2.67s	7.86d[c)] (9)	7.29dd (9;2)	1.35d,6H(6.5) 3.04qui,1H(6.5)	7.52d (2)	7.22s	2.79d,2H(6.5) 4.75-5.60m,3H[d)]	
11	1.58s	2.59s	7.83d (9)	7.26dd (9;2)	1.31d,6H(7) 3.00m*,1H	7.47d (2)	7.13s	ca.2.1m,2H ca.1.1m,2H	3.07t* 2H(6)
12[e)]	1.54s	2.57s	7.84d (8.5)	7.28dd (8.5;2)	1.31d*,6H(7) 3.01qui,1H(7)	7.50d (2)	7.14s	ca.2.05m,2H ca.1.2m*,2H	3.77t 2H(6)
13	1.64s	2.69s	7.82d (8)	7.27dd (8;2)	1.33d*,6H(7) 3.03m*,1H	7.49d (2)	7.18s	ca.2.2m,2H ca.1.4m*,2H	3.03t* 2H(6)
14[f)]	1.59s	2.61s	7.84d (9)	7.27dd (9;2)	1.32d,6H(7) 3.02qui,1H(7)	7.51d (2)	7.21s	ca.2.1m,2H ca.1.1m,2H	3.33t 2H(6)
15[g)]	1.62s	2.62s	7.81d (8)	7.26dd (8;2)	1.33d*,6H(7) 3.01qui,1H(7)	7.49d (2)	7.20s	ca.2.1m,2H ca.1.2m*,2H	3.83t 2H(6)
16	1.63s	2.64s	7.82d (9)	7.26dd (9;2)	1.33d*,6H(7) 3.02qui,1H(7)	7.48d (2)	7.20s	ca.2.25m,2H ca.1.4m*,2H	3.35t 2H(6)

a) Numerals in parentheses represent coupling constants in Hz.
b) 18% NOE enhancement by saturation of a signal 2.61 was observed.
c) 18% NOE enhancement by saturation of a signal 2.67 was observed.
d) The first-order analysis of this multiplet signal showed three vinyl protons at 4.87(dd,J=9.5 and 2.5 Hz), 5.00(dd,J=17 and 2.5 Hz), and 5.30(dd of t,J=17, 9.5, 6.5, and 6.5 Hz).
e) 2.33(3H,s), 7.14(2H,d,J=8 Hz), and 7.58(2H,d,J=8 Hz) for p-tosyloxy group.
f) 1.82(1H,bs,exchangeable with deuterium oxide) for hydroxyl group.
g) 1.91(3H,s) for acetoxy group.
* Signal partially overlapped.

Thus, coleon A skeleton was effectively obtained from (-)-abietic acid (1). The synthesis of coleon A (I) is proceeding now.

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References and Notes

1) C. H. Eugster, H. -P. Küng, H. Kühnis, and P. Karrer, Helv. Chim. Acta, 46, 530 (1963)

2) D. Karanatsios and C. H. Eugster, Helv. Chim. Acta, 48, 471 (1965)

3) All of communicated compounds were supported by elemental analysis. IR spectra and optical rotations were measured in chloroform. NMR spectra were taken with a Hitachi Model R-22 NMR spectrometer (90 MHz) in carbon tetrachloride. The chemical shifts are presented in terms of δ value; s: singlet, bs: broad singlet, d: doublet, dd: double doublet, td: triple doublet, t: triplet, dt: double triplet, qui: quintet, m: multiplet.

4) G. Dupont, R. Dulou, G. Ourisson, and C. Thibault, Bull. Soc. Chim. Fr., 1955, 708

5) G. Defaye-Duchateau, Bull. Soc. Chim. Fr., 1964, 1469; by a careful column chromatography of the mixture, we obtained methyl 6-oxo-[8] (7: 25-30% yield), 7ξ-benzoyloxy-6α-hydroxy- (7-epimer mixture: 30-35% yield), 6α,7α-dihydroxy- (8-10% yield), 6α,7β-dihydroxy-dehydroabietate (5-8% yield) and Δ^5-6-hydroxy-7-oxodehydroabietic acid (18-6)-lactone (2-3% yield).

6) E. Wenkert, A. Afonso, P. Beak, R. W. J. Carney, P. W. Jeffs, and J. D. McChesney, J. Org. Chem., 30, 713 (1965); E. Wenkert and B. L. Mylari, ibid., 30, 4387 (1965). Our sample (4) showed $[\alpha]_D$ - 79°.

7) Another (18-6β)-lactone of 6β-hydroxy epimer was obtained (0.5% yield), mp 133-134°C, $[\alpha]_D$ - 90°, IR: 1760 cm^{-1}, NMR: 1.41 (6H, s), 1.77 (1H, d, J=11 Hz), 2.88 (1H, dd, J=15 and 11 Hz), 3.18 (1H, dd, J=15 and 5 Hz), 4.38 (1H, td, J= 11, 11, and 5 Hz).

8) The compound (7) was obtained as described in reference 5 (7: $[\alpha]_D$ + 156°, IR: 1720, 1705 cm^{-1}; NMR: 1.18, 1.44 (each 3H, s), 3.15 (1H, s), 3.52 (2H, s), 3.58 (3H, s)). cf. R. C. Cambie and R. A. Franich, Aust. J. Chem., 24, 571 (1971)

9) The configuration regarding C_3-position in coleon A (I) has not been decided. All of the 2,3-dihydronaphtho[2,3-b]furan-2-one derivatives in this communication should retain the chirality R as shown in 3.

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