

TOTAL SYNTHESIS OF COLEONS, U AND V

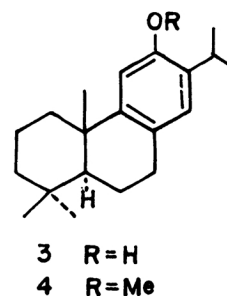
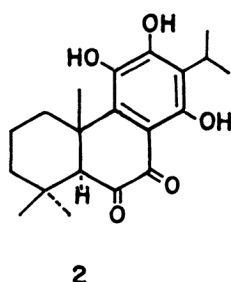
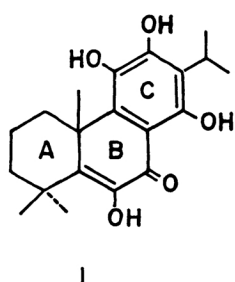
Takashi MATSUMOTO* and Shoji TAKEDA

Department of Chemistry, Faculty of Science, Hiroshima University

Higashisenda-machi, Hiroshima 730

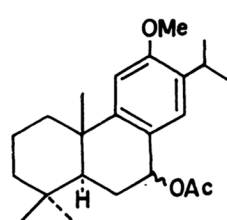
The highly-oxygenated tricyclic diterpenes, coleon U and coleon V, were successfully synthesized starting from (+)-ferruginol via an intermediate, (+)-12-benzoyloxyabieta-8,11,13-triene-6 β ,11-diol.

Coleon U and coleon V, highly-oxygenated tricyclic diterpenes possessing an abietane skeleton, were isolated from leaf-glands of Plectranthus myrianthus Briq. (Labiatae) by Eugster et al.¹⁾ It is known that the introduction of oxygen function in ring B of tricyclic diterpenes with a fully substituted aromatic C ring is very difficult.^{2,3)} This communication⁴⁾ will describe a successful conversion of (+)-ferruginol (3) into coleon U (1) and coleon V (2) via an intermediate, (+)-12-benzoyloxyabieta-8,11,13-triene-6 β ,11-diol (13). Since the total synthesis of (+)-3 has recently been achieved in our laboratory,⁵⁾ the present conversion can be regarded as the total syntheses of coleon U and coleon V.

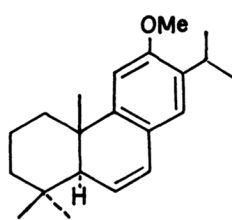


The intermediate, (+)-13, was easily synthesized from (+)-3 by a procedure⁶⁾ similar to that used for (±)-13. Ferruginyl methyl ether (4),⁷⁾ $[\alpha]_D + 63.1^\circ$, prepared from (+)-3,^{5,8)} was treated with lead tetraacetate to yield a mixture of 7 α - and 7 β -acetoxy compounds (5), which was refluxed with dilute hydrochloric acid in ethanol to give a tetraene derivative (6: 84% from 4), $[\alpha]_D - 88.5^\circ$. The

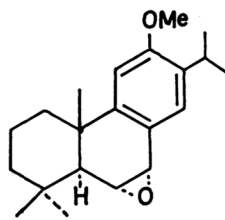
tetraene (6) was then oxidized with m-chloroperbenzoic acid in chloroform (3-8°C, 1.5 h) and the resulting crude epoxide (7) was further treated with p-toluenesulfonic acid in refluxing chloroform (1 h) to give 12-methoxyabieta-8,11,13-trien-6-one (8: 78% from 6), mp 93-94°C, $[\alpha]_D + 128^\circ$. Demethylation of 8 with boron tribromide in dichloromethane (r.t., 4 h) afforded a phenol derivative (9: 93%), mp 165.5-167°C, $[\alpha]_D + 129^\circ$, which on reduction with lithium aluminium hydride gave abieta-8,11,13-triene-6 β ,12-diol (10: 87%), mp 171.5-173.5°C, $[\alpha]_D + 45.7^\circ$, along with its 6 α -isomer (11: 12%), $[\alpha]_D + 8.7^\circ$. The stereochemistry of hydroxyl groups at C-6 in 10 and 11 was supported by half-height widths of C-6 protons in their NMR spectra.⁹⁾ Alternatively, the β -alcohol (10: 83%) was also obtained by a similar demethylation of 12-methoxyabieta-8,11,13-trien-6 β -ol (12), mp 59-69°C, $[\alpha]_D + 43.1^\circ$, NMR: 4.55 (1H, m, $W_{1/2}=10$ Hz, C₆-H), which was prepared from 8 (93%) by reduction with lithium aluminium hydride. Oxidation of C-11 in 10 with benzoyl peroxide in chloroform yielded the intermediate (13: 53%),¹⁰⁾ mp 226-228°C, $[\alpha]_D + 46.8^\circ$, together with 13-benzoyloxy-6 β -hydroxyabieta-8(14),9(11)-dien-12-one (14: 31%)¹¹⁾ which was converted into the phenol (10: 77%) by reduction with lithium aluminium hydride. To introduce an oxygen function at C-14, the diol (13) was oxidized with m-chloroperbenzoic acid in dichloromethane (r.t., 20 h) to afford 12-benzoyloxy-6 β -hydroxyabieta-8,12-diene-11,14-dione (15: 64%), mp 247.5-249.5°C, $[\alpha]_D + 18.0^\circ$, IR: 3610, 3350, 1740, 1660, 1647sh, 1605 cm⁻¹, NMR (CDCl₃): 1.02 (3H, s, C_{4 α} -CH₃), 1.23 and 1.25 (each 3H, d, and J=7 Hz, -CH(CH₃)₂), 1.28 (3H, s, C_{4 β} -CH₃), 1.68 (3H, s, C₁₀-CH₃), 3.21 (1H, m, -CH(CH₃)₂), 4.69 (1H, m, $W_{1/2}=9$ Hz, C₆-H), 7.45-8.3 (5H, m, -C₆H₅). Oxidation of 15 with Jones reagent (0-5°C, 5 min) afforded the corresponding 6-oxo compound (16) which, for protection of the C ring, was immediately reduced with a mixture of zinc powder and dilute hydrochloric acid in refluxing benzene (20 min) and the resulting crude phenol (17) was further acetylated with acetic anhydride in pyridine (85-90°C, 2 h) to give 11,14-diacetoxy-12-benzoyloxyabieta-8,11,13-trien-6-one (18: 94% from 15), mp 188.5-190.5°C dec., $[\alpha]_D + 134^\circ$, IR: 1765, 1740, 1720 cm⁻¹, NMR (CDCl₃): 1.03 (3H, s, C_{4 β} -CH₃), 1.25 (6H, bd, J=7 Hz, -CH(CH₃)₂), 1.31 (6H, s, C_{4 α} -CH₃ and C₁₀-CH₃), 1.92 and 2.36 (each 3H and s, 2-OCOCH₃), 2.69 (1H, bs, C₅-H), 3.33 (2H, bs, -COCH₂-), 7.4-8.3 (5H, m, -C₆H₅). Similarly, the α -alcohol (11) was also converted into 18 via 12-benzoyloxy-6 α -hydroxyabieta-8,12-diene-11,14-dione (19), mp 210-212°C, $[\alpha]_D + 67.9^\circ$. Oxidation of C-7 in 18 was carried out with Jones reagent (r.t., 4 h) and the crude product was



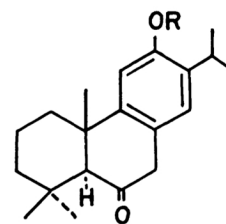
5



6

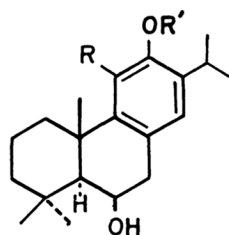


7

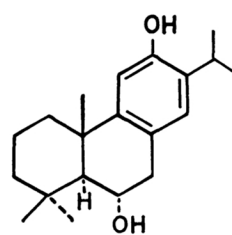


8 R=Me

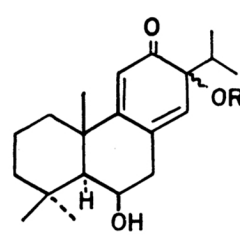
9 R=H



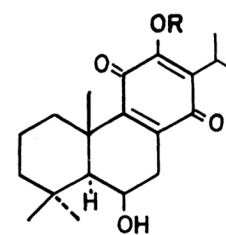
10 R=R'=H
12 R=H, R'=Me
13 R=OH, R'=COPh



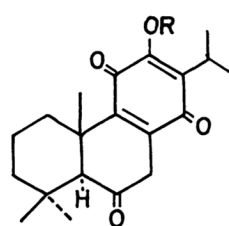
11



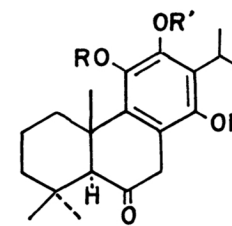
14 R=COPh



15 R=COPh

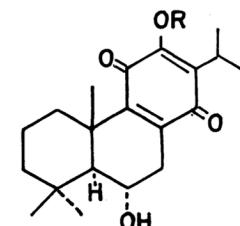


16 R=COPh

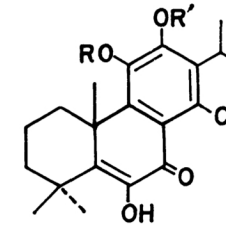


17 R=H, R'=COPh

18 R=Ac, R'=COPh



19 R=COPh



20 R=Ac, R'=COPh

21 R=H, R'=Me

purified by repeated column chromatography on silica gel to afford 11-acetoxy-12-benzoyloxy-6,14-dihydroxyabieta-5,8,11,13-tetraen-7-one (20: 44%), mp 171-172.5°C, $[\alpha]_D + 24.1^\circ$, IR: 3420, 1775, 1745, 1645, 1605 cm^{-1} , NMR: 1.87 (3H, s, $-\text{OCOCH}_3$), 6.90 (1H, s, $\text{C}_6\text{-OH}$), 13.05 (1H, s, $\text{C}_{14}\text{-OH}$). The compound (20) was finally hydrolyzed with aqueous sodium hydrogencarbonate in methanol (40-45°C, 1 h) under an atmosphere of nitrogen to give coleon U (1) and coleon V (2) in a ratio of ca. 1:1. 1; mp 172-175.5°C dec., IR: 3675, 3600, 3485sh, 3400, 3225sh, 1620, 1600 cm^{-1} , NMR (CDCl_3): 1.37 (6H, bd, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 1.44 (9H, s, $-\text{C}(\text{CH}_3)_2$ and $\text{C}_{10}\text{-CH}_3$), 6.98 (1H, s, $\text{C}_6\text{-OH}$). 2; mp 159-164°C dec., IR: 3300, 1720, 1610 cm^{-1} , NMR (CDCl_3): 1.03 (3H, s) and 1.42 (6H, s) ($-\text{C}(\text{CH}_3)_2$ and $\text{C}_{10}\text{-CH}_3$), 1.35 (6H, d, $J=7$ Hz, $-\text{CH}(\text{CH}_3)_2$), 2.96 (1H, s, $\text{C}_5\text{-H}$), 13.22 (1H, s, $\text{C}_{14}\text{-OH}$). Interconversion of the synthetic 1 and 2 was also carried out as follows. Treatment of 1 with aqueous

potassium hydroxide in ethanol (r.t., 90 min) under an atmosphere of nitrogen yielded 1 and 2 in a ratio of ca. 1:1. On the other hand, treatment of 2 with dilute hydrochloric acid in ethanol (r.t., 72 h) afforded 1 which was further characterized as coleon U 12-methyl ether (21), mp 174-176°C dec., $[\alpha]_D - 11.3^\circ$.

Acknowledgment. The authors are grateful to Arakawa Chemical Co. Ltd. for a generous gift of rosin.

REFERENCES AND NOTES

- 1) T. Miyase, P. Rüedi, and C. H. Eugster, *Helv. Chim. Acta*, **60**, 2770 (1977).
- 2) T. Matsumoto, Y. Tachibana, M. Hayashi, and K. Fukui, *J. Sci. Hiroshima Univ. Ser. A*, **39**, 111 (1975).
- 3) R. H. Burnell and M. Ringust, *Can. J. Chem.*, **56**, 514 (1978).
- 4) The IR spectra and optical rotations were measured in chloroform. The NMR spectra were taken in carbon tetrachloride, unless otherwise stated. The chemical shifts are presented in terms of δ values; s: singlet, bs: broad singlet, d: doublet, bd: broad doublet, m: multiplet.
- 5) T. Matsumoto and S. Usui, *Bull. Chem. Soc. Jpn.*, **52**, 212 (1979).
- 6) T. Matsumoto, S. Usui, and T. Morimoto, *Bull. Chem. Soc. Jpn.*, **50**, 1575 (1977).
- 7) C. W. Brandt and L. G. Neubauer, *J. Chem. Soc.*, **1939**, 1031.
- 8) T. Matsumoto, Y. Ohsuga, S. Harada, and K. Fukui, *Bull. Chem. Soc. Jpn.*, **50**, 266 (1977).
- 9) The NMR spectrum of 10 in CDCl_3 : 1.03 (3H, s, $\text{C}_{4\alpha}\text{-CH}_3$), 1.22 (6H, d, $J=7$ Hz, $\text{-CH}(\text{CH}_3)_2$), 1.28 (3H, s, $\text{C}_{4\beta}\text{-CH}_3$), 1.53 (3H, s, $\text{C}_{10}\text{-CH}_3$), 4.67 (1H, $W_{1/2}=10$ Hz, $\text{C}_6\text{-H}$), 5.00 (1H, bs, -OH), 6.67 and 6.82 (each 1H and s, $\text{C}_{11}\text{-H}$ and $\text{C}_{14}\text{-H}$). The NMR spectrum of 11 in CCl_4 : 1.08 (6H, s, $\text{-C}(\text{CH}_3)_2$), 1.11 (3H, s, $\text{C}_{10}\text{-CH}_3$), 1.19 (6H, d, $J=7$ Hz, $\text{-CH}(\text{CH}_3)_2$), 4.20 (1H, $W_{1/2}=16$ Hz, $\text{C}_6\text{-H}$), 5.25 (1H, bs, -OH), 6.41 and 6.77 (each 1H and s, $\text{C}_{11}\text{-H}$ and $\text{C}_{14}\text{-H}$).
- 10) The IR and NMR spectra were identical with those of the racemate.⁶⁾
- 11) Although the compound (14) seemed to be a mixture of epimers regarding C-13, we did not further purification. The spectra of 14; IR: 3625, 3475, 1713, 1660, 1640sh cm^{-1} ; NMR: 0.92 and 1.09 (each 3H, d, and $J=7$ Hz, $\text{-CH}(\text{CH}_3)_2$), 0.98 (3H, s, $\text{C}_{4\alpha}\text{-CH}_3$), 1.23 (3H, s, $\text{C}_{4\beta}\text{-CH}_3$), 1.50 (3H, s, $\text{C}_{10}\text{-CH}_3$), 4.43 (1H, $W_{1/2}=10$ Hz, $\text{C}_6\text{-H}$), 5.79 and 5.98 (each 1H and s, $\text{C}_{11}\text{-H}$ and $\text{C}_{14}\text{-H}$), 7.3-8.2 (5H, m, $\text{-C}_6\text{H}_5$). The above spectral data excluded the structure of 14 to be a para-substituted dienone.⁸⁾

(Received February 17, 1979)