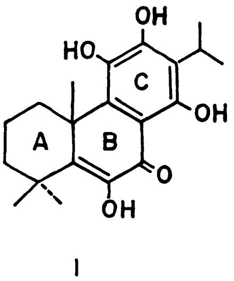
CHEMISTRY LETTERS, pp. 409-412, 1979. Published by the Chemical Society of Japan

TOTAL SYNTHESIS OF COLEONS, U AND V

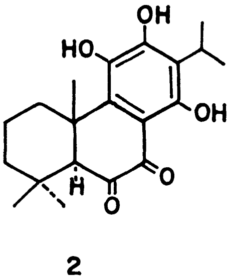
Takashi MATSUMOTO* and Shoji TAKEDA
Department of Chemistry, Faculty of Science, Hiroshima University
Higashisenda-machi, Hiroshima 730

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-6β,11-diol.

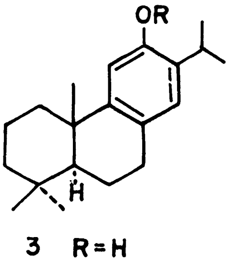
Coleon U and coleon V, highly-oxygenated tricyclic diterpenes possessing an abietane skeleton, were isolated from leaf-glands of *Plectranthus myrianthus* Briq. (Labiatae) by Eugster et al.[1] It is known that the introduction of oxygen function in ring B of tricyclic diterpenes with a fully substituted aromatic C ring is very difficult.[2,3] This communication[4] 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-6β,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.



1

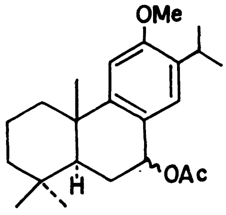


2

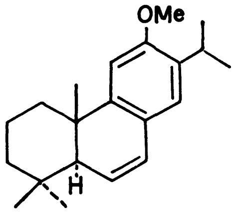


3 R=H
4 R=Me

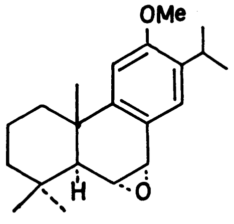
The intermediate, (+)-13, was easily synthesized from (+)-3 by a procedure[6] similar to that used for (±)-13. Ferruginyl methyl ether (4),[7] $[\alpha]_D$ + 63.1°, prepared from (+)-3,[5,8] was treated with lead tetraacetate to yield a mixture of 7α- and 7β-acetoxy compounds (5), which was refluxed with dilute hydrochloric acid in ethanol to give a tetraene derivative (6: 84% from 4), $[\alpha]_D$ - 88.5°. 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°. 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°, which on reduction with lithium aluminium hydride gave abieta-8,11,13-triene-6β,12-diol (10: 87%), mp 171.5-173.5°C, $[\alpha]_D$ + 45.7°, along with its 6α-isomer (11: 12%), $[\alpha]_D$ + 8.7°. 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-6β-ol (12), mp 59-69°C, $[\alpha]_D$ + 43.1°, NMR: 4.55 (1H, m, $W_{1/2}$=10 Hz, C_6-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°, together with 13-benzoyloxy-6β-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-6β-hydroxyabieta-8,12-diene-11,14-dione (15: 64%), mp 247.5-249.5°C, $[\alpha]_D$ + 18.0°, IR: 3610, 3350, 1740, 1660, 1647sh, 1605 cm^{-1}, NMR ($CDCl_3$): 1.02 (3H, s, $C_{4\alpha}$-CH_3), 1.23 and 1.25 (each 3H, d, and J=7 Hz, -CH($\underline{C}\underline{H}_3$)$_2$), 1.28 (3H, s, $C_{4\beta}$-CH_3), 1.68 (3H, s, C_{10}-CH_3), 3.21 (1H, m, -$\underline{C}\underline{H}$($CH_3$)$_2$), 4.69 (1H, m, $W_{1/2}$=9 Hz, C_6-H), 7.45-8.3 (5H, m, -C_6H_5). 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°, IR: 1765, 1740, 1720 cm^{-1}, NMR ($CDCl_3$): 1.03 (3H, s, $C_{4\beta}$-CH_3), 1.25 (6H, bd, J=7 Hz, -CH($\underline{C}\underline{H}_3$)$_2$), 1.31 (6H, s, $C_{4\alpha}$-CH_3 and C_{10}-CH_3), 1.92 and 2.36 (each 3H and s, 2-$OCOCH_3$), 2.69 (1H, bs, C_5-H), 3.33 (2H, bs, -$COCH_2$-), 7.4-8.3 (5H, m, -C_6H_5). Similarly, the α-alcohol (11) was also converted into 18 via 12-benzoyloxy-6α-hydroxyabieta-8,12-diene-11,14-dione (19), mp 210-212°C, $[\alpha]_D$ + 67.9°. Oxidation of C-7 in 18 was carried out with Jones reagent (r.t., 4 h) and the crude product was



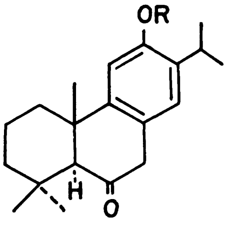
5



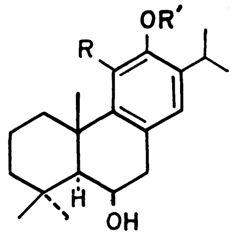
6



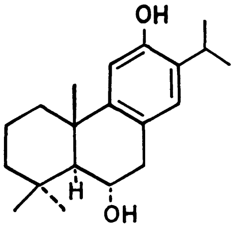
7



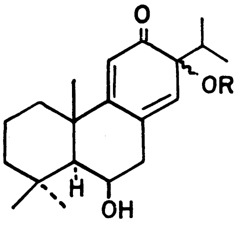
8 R=Me
9 R=H



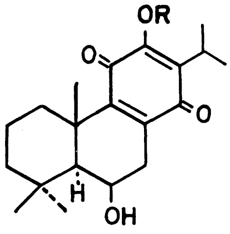
10 R=R'=H
12 R=H, R'=Me
13 R=OH, R'=COPh



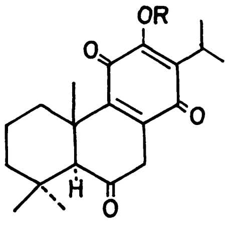
11



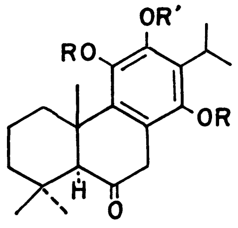
14 R=COPh



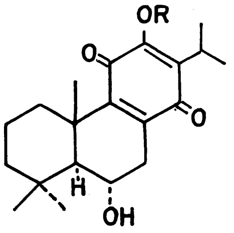
15 R=COPh



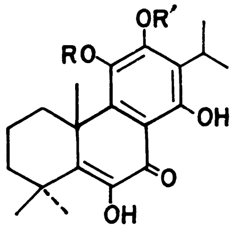
16 R=COPh



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°, IR: 3420, 1775, 1745, 1645, 1605 cm^{-1}, NMR: 1.87 (3H, s, $-OCOCH_3$), 6.90 (1H, s, C_6-OH), 13.05 (1H, s, C_{14}-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, $-CH(C\underline{H}_3)_2$), 1.44 (9H, s, $-\overset{|}{C}(CH_3)_2$ and $C_{10}-CH_3$), 6.98 (1H, s, C_6-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) ($-\overset{|}{C}(CH_3)_2$ and $C_{10}-CH_3$), 1.35 (6H, d, J=7 Hz, $-CH(C\underline{H}_3)_2$), 2.96 (1H, s, C_5-H), 13.22 (1H, s, C_{14}-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°.

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, $C_{4\alpha}$-CH_3), 1.22 (6H, d, J=7 Hz, -CH($C\underline{H}_3$)$_2$), 1.28 (3H, s, $C_{4\beta}$-CH_3), 1.53 (3H, s, C_{10}-CH_3), 4.67 (1H, $W_{1/2}$=10 Hz, C_6-H), 5.00 (1H, bs, -OH), 6.67 and 6.82 (each 1H and s, C_{11}-H and C_{14}-H). The NMR spectrum of 11 in CCl_4: 1.08 (6H, s, $-\overset{|}{C}(CH_3)_2$), 1.11 (3H, s, C_{10}-CH_3), 1.19 (6H, d, J=7 Hz, -CH($C\underline{H}_3$)$_2$), 4.20 (1H, $W_{1/2}$=16 Hz, C_6-H), 5.25 (1H, bs, -OH), 6.41 and 6.77 (each 1H and s, C_{11}-H and C_{14}-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, -CH($C\underline{H}_3$)$_2$), 0.98 (3H, s, $C_{4\alpha}$-CH_3), 1.23 (3H, s, $C_{4\beta}$-CH_3), 1.50 (3H, s, C_{10}-CH_3), 4.43 (1H, $W_{1/2}$=10 Hz, C_6-H), 5.79 and 5.98 (each 1H and s, C_{11}-H and C_{14}-H), 7.3-8.2 (5H, m, $-C_6H_5$). The above spectral data excluded the structure of 14 to be a para-substituted dienone.$^{8)}$

(Received February 17, 1979)