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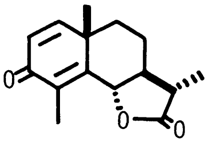
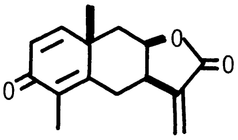
TRANSPOSITION OF LACTONE IN SESQUITERPENE LACTONE: CHEMICAL TRANSFORMATION OF α-SANTONIN INTO SESQUITERPENE α-METHYLENE-γ-LACTONE, YOMOGIN (1)

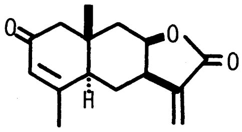
Koji YAMAKAWA,* Kiyoshi NISHITANI, and Akihiro YAMAMOTO
Faculty of Pharmaceutical Sciences, Science University of Tokyo
Ichigaya-funagawara-machi, Shinjuku-ku, Tokyo 162

The chemical transformation of α-santonin (I) into yomogin (II) was investigated. Introduction of an oxygen function at C-8 of trienone (V) was effected by tert-butyl chromate to give dione (VII). Partial reductive lactonization converted VII to XIII-XV. Phenylselenenylation of XIII gave XVI which was then syn-eliminated to give yomogin (II).

The eudesmane type sesquiterpenoid lactones possessing a 6,12-olide moiety as typically shown in α-santonin (I) are widely distributed in plants. While, sesquiterpenoid α-methylene-8,12-olides have also been well-known, for example, in yomogin (II),(2) pinnatifidine (II),(3) alantolactone (IV),(4) and encelin(5) etc. in the family of Compositae.


(I)


(II)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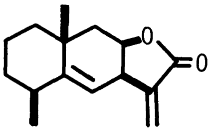
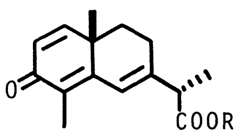
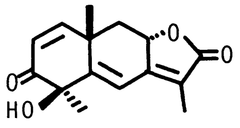

(IV)

In this communication, we will report the transposition of γ-lactone of santan-6,12-olide, α-santonin (I) into santan-8,12-olide, yomogin (II) and its related compounds. Introduction of an oxygen function at C-8 of 1,4,6-trienone (V)(6) was attempted by several oxidative methods for the purpose of transposition of 6,12-olide into 8,12-olide. Oxidation of the methyl trienone carboxylate (Vb) with chromium trioxide-pyridine complex gave unsatisfactory results. Allylic bromination of Vb at C-8 using N-bromosuccinimide gave complex products, and a desired C-8 bromide could not be isolated.



(Va): R=H

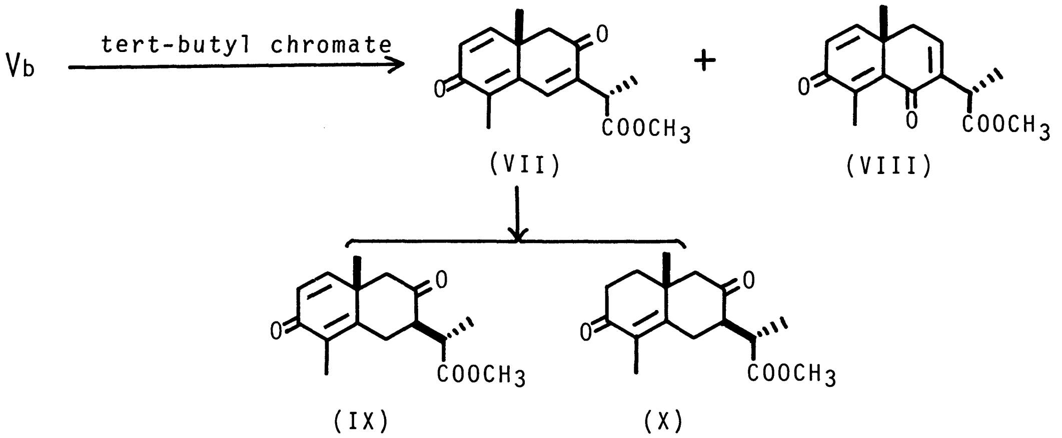
(Vb): R=CH_3



(VI)

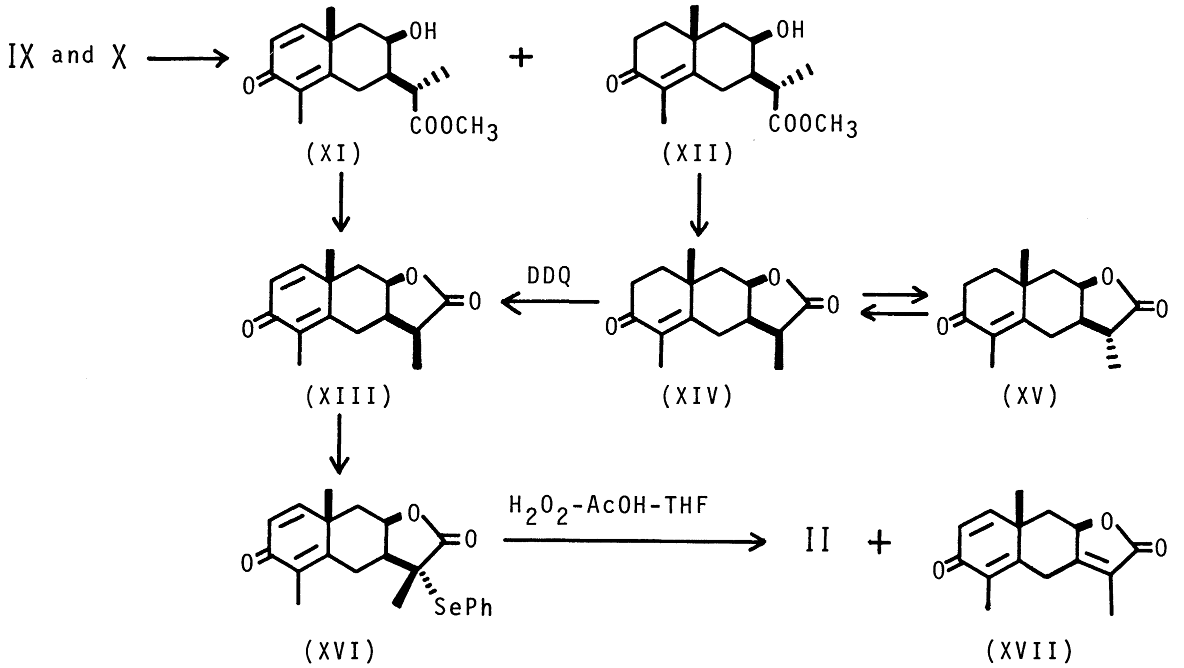
Oxidation of the trienone carboxylic acid (Va) with selenium dioxide gave complex products, whereas, oxidation of the methyl ester (Vb) with selenium dioxide in dioxane under reflux afforded unexpected 8,12-olide (VI), mp 199-200° in 11% yield [MS: m/e 260 M^+; IR ν_{OH} 3400, ν_{CO} 1740 and 1695; UV λ_{max}^{EtOH} 277 nm; PMR δ: 1.59 (t, *J*=12 Hz; 9α-H), 1.60 and 1.66 (s each, 4,10-Me), 1.90 (d, *J*=2 Hz; 11-Me), 2.39 (dd, *J*=12, 5 Hz; 9β-H), 5.16 (m; 8-H), 6.07 and 6.67 (d each, *J*=10 Hz; 2,1-H), 7.04 (s; 6-H)].

Oxidation of the methyl ester (Vb) with tert-butyl chromate[7)] in carbon tetrachloride containing acetic anhydride afforded a desired 8-oxo compound (VII), mp 125-126° [MS: m/e 274, M^+; IR ν_{max} 1735, 1670, 1645, 1620; UV λ_{max}^{EtOH} 252 and 310 nm (ε 6,900 and 16,400); PMR δ: 2.56 (AB-d, *J*=15 Hz; 9-H), 6.33 and 6.83 (d each, *J*=10 Hz; 2,1-H), 7.50 (s; 6-H)] in 28-39% yield, together with 3,6-dioxo-1,4,7-trienone (VIII), mp 97-98° [MS: m/e 274, M^+; IR ν_{max} 1725, 1660, 1645, 1630; UV λ_{max}^{EtOH} 253 and 280 nm (ε 10,500 and 8,300); PMR δ: 2.59 (d, *J*=4.5 Hz; 9-H), 6.32 and 6.84 (d each, *J*=10 Hz; 2,1-H), 6.78 (t, *J*=4.5 Hz; 8-H)] in 20-10% yield.



Catalytic reduction of 3,8-dioxotriene (VII) with tris(triphenylphosphine)chlororhodium catalyst in benzene gave 3,8-dioxo-1,4-diene (IX) and 3,8-dioxo-4-ene (X). Reduction of IX and X with sodium borohydride in methanol at 0° gave stereoselectively ketol (XI), oil, and (XII), mp 162-165°, respectively. [(XII): MS: m/e 280, M^+, 248 $[M-MeOH]^+$; IR ν_{max} 3450, 1730, 1655, 1615; UV λ_{max}^{EtOH} 249 nm; PMR δ: 4.16 (m, W $\frac{1}{2}$=8 Hz; 8-H)].

XI was heated at 170° for 15 min or hydrolyzed with an alkaline and then acidified to form an 8,12-olide (XIII), mp 180-180.5° [MS: m/e 246, M^+; IR ν_{max} 1755, 1655, 1625, 1605; UV λ_{max}^{EtOH} 238 and 262 (shoulder) nm; PMR δ: 1.27 (d, *J*=7 Hz; 11-Me), 1.29 (s; 10-Me), 4.50 (m, W ½=10 Hz; 8-H), 6.20 and 6.78 (d each, *J*=10 Hz; 2,1-H)]. Treatment of XII under the same conditions described above gave another 8,12-olide (XIV), mp 111-112° [MS: m/e 248, M^+; IR ν_{max} 1765, 1660, 1620; UV λ_{max}^{EtOH} 246 nm; PMR δ: 1.21 (d, *J*=7 Hz; 11-Me), 1.23 (s; 10-Me), 1.73 (s; 4-Me), 4.45 (q, W ½=10 Hz; 8-H)] quantitatively. A mixture of IX and X was reduced with tris-tert-butoxy lithium aluminum hydride, and the resulting mixture (XI and XII) was treated with NaOH and then acidified to give XIII, XIV, and XV. [(XV): mp 189°, MS: m/e 248, M^+; IR ν_{max} 1770, 1660, 1625; UV λ_{max}^{EtOH} 247 nm; PMR δ: 1.25 (s; 10-Me), 1.30 (d, *J*=7 Hz; 11-Me), 4.50 (m, W ½=12 Hz; 8-H)]. Treatment of XIV and XV with potassium carbonate in xylene under reflux afforded an equlibrium mixture of XIV and XV, respectively. Dehydrogenation of XIV with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in dioxane afforded XIII.



Phenylselenenylation of XIII by Grieco's procedure[8)] gave a phenylselenide (XVI), mp 215-218°, in 42 % yield [PMR δ: 1.60 (s; 11-Me), 7.20-7.70 (m, Ph)]. Oxidative syn-elimination of XVI produced a selenoxide as an intermediate which immediately converted to a 1.2:1 mixture of exocyclic isomer (II) and endocyclic isomer (XVII). Exocyclic isomer (II), mp 210-211°; 37% yield, was crystallized out from ethyl acetate solution of the above mixture [(II): IR ν_{max} 1770, 1665, 1633, and 1615; PMR δ: 1.32 (s; 10-Me), 1.93 (s; 4-Me), 4.48 (m, $W_{1/2}$=12 Hz; 8-H), 5.72 and 6.26 (d, each, *J*=2 Hz; $=\!\!<^{H}_{H}$), and 6.22 and 6.77 (d, each, *J*=10 Hz; 2,1-H)]. The IR and PMR spectra of II were identical with those of yomogin (II) which was isolated from *Artemisia princeps* Pamp. by Geissman.²⁾

References and Notes

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