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TRANSFORMATION OF SPERGULAGENIC ACID, A DICARBOXYLIC TRITERPENOID, TO EUPTELEOGENIN, A UNIQUE NORTRITERPENOID

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Interested in the photochemical reactions which are potentially applied in the biogenetic-type chemical derivations of natural products, we have studied so far the photooxidation of Δ^{12}-oleanene triterpenoids, such as oleanolic acid$^{1)}$ and erythrodiol$^{2)}$. In the former, the 11α,12α-epoxy-13,28-lactone system(as in Ia) has been induced in one step from Δ^{12}-17-carboxylic acid(as in IIa), while in the latter, the 11α,12α-epoxy-13,28-oxide moiety has been introduced from Δ^{12}-17-carbinol along with the skeletal rearrangement furnishing the 11α,12α-epoxy-taraxerene derivative.

As a continuation of the investigation, the transformation of spergulagenic acid(IIa)$^{3)}$, a dicarboxylic Δ^{12}-oleanene sapogenin of Mollugo spergula L.(Molluginaceae) to eupteleogenin(Ia)$^{4)}$, a unique nortriterpenoid sapogenin(obtainable from Euptelea polyandra Sieb. et Zucc., Trochodendraceae) possessing the 11α,12α-epoxy-13,28-lactone moiety, by way of the photooxidation followed by the lead tetraacetate decarboxylation has been accomplished, with which the present communication deals.

Irradiation(500W high pressure Hg arc lamp, with Pyrex filter) of spergulagenic acid(IIa) in ethanol(adjusted to pH ca. 2 by c.HCl) for 80 hr. at room temperature with occasional agitation by shaking yielded a mixture. Subsequent TLC separation of the mixture furnished a compound tentatively designated MS-1(IIIa), $C_{30}H_{44}O_6$, mp. 320-323°; $[\alpha]_D$ +116° (c=1.0, pyridine); IR(KBr, cm^{-1}): 3440(hydroxyl), 1769(γ-lactone), 1708(carboxyl), 872(epoxy) in 12.5 % yield with a recovery of IIa(37.4 %).

Acetylation of MS-1 with acetic anhydride and pyridine afforded MS-1-Ac(IIIb), $C_{30}H_{43}O_5(OCOCH_3)$, mp. 301-303°; $[\alpha]_D$ +86° (c=0.5, $CHCl_3$); IR(KBr, cm^{-1}): no hydroxyl, 1768(γ-lactone), 1734, 1247(acetate), 1702(sh.)(carboxyl), 873(epoxy), whereas diazomethane methylation of MS-1 yielded MS-1-Me(IIIc), $C_{29}H_{43}O_4(COOCH_3)$, mp. 324-326°, $[\alpha]_D$ +46° (c=1.0, $CHCl_3$); IR(KBr, cm^{-1}): 3502(hydroxyl), 1768(γ-lactone), 1710(ester), 874(epoxy); NMR(100 Mc, $CDCl_3$, τ): 9.21, 9.02, 8.97, 8.90, 8.78, 8.75(3H each, all singlets, $-\overset{|}{\underset{|}{C}}-C\underline{H}_3 \times 6$), 7.01(2H, s., $W_{\frac{h}{2}}$=2.5 cps., $C_{(11)}-\underline{H}$, $C_{(12)}-\underline{H}$), 6.78(1H, t.-like, $C_{(3)}-\underline{H}$), 6.32(3H, s., $COOC\underline{H}_3$).

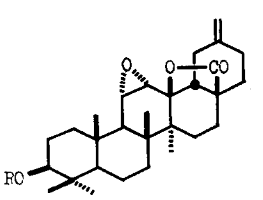
Based on the above physical data, the formulation of IIIa, b, c having the epoxy-lactone moiety has been substantiated analogously as for eupteleogenin(Ia)[4], and our previous work on the photooxidation product of oleanolic acid[1]. Thus, two significant absorption bands at 1768-1769 and 872-874 cm^{-1} in the IR spectra of MS-1, MS-1-Ac, and MS-1-Me are respectively ascribed to γ-lactone and epoxy ring. In addition, a characteristic singlet at 7.01τ(2H, $w_{\frac{h}{2}}$=2.5 cps.) of MS-1-Me is assignable to protons attached to $C_{(11)}$ and $C_{(12)}$ constituting an epoxy ring.

Next, the attention was focussed to the transformation of geminary methyl and carboxylic functions at $C_{(20)}$ to the endo-methylene moiety.

At first for this purpose, we tried the photochemical decarboxylation[5] of IIIc using a low pressure Hg arc lamp, however the result was unsatisfactory although the decarboxylation has been observed in case of leucotylic acid derivative(VI)[6]. Finally, the lead tetraacetate oxidation after the procedure by Bennet and Cambie[7] has accomplished the desired decarboxylation. A reaction product, obtained by lead tetraacetate treatment of MS-1-Ac(IIIb) in pyridine under nitrogen at 20° for 2 hr. followed by heating at 50° for further 1 hr., showed two spots on TLC(SiO_2). Although the compound having higher Rf value coincided with eupteleogenin acetate(Ib) on ordinary TLC(SiO_2), it exhibited two spots on TLC using $AgNO_3$ impregnated SiO_2 and one of the spots showed the identical Rf value with Ib. Therefore the reaction product was separated by SiO_2 and SiO_2-$AgNO_3$ TLC successively furnishing three products: MS-1-Ac-A(28 %), mp. 322-323°; IR(KBr, cm^{-1}): 1769(γ-lactone), 1728, 1247(acetate), 1648, 892(endo-methylene), 873(epoxy), MS-1-Ac-B(36 %), mp. 319-321°; IR(KBr, cm^{-1}): 1770(γ-lactone), 1723, 1238(acetate), 876(epoxy), and MS-1-Ac-C(12 %), mp. 281-284°; IR($CHCl_3$, cm^{-1}): 1770(γ-lactone), 1723, 1248(acetate), 872(epoxy). The detailed examination on TLC behavior of these three products disclosed that MS-1-Ac-A and -B possess identical Rf value on SiO_2-TLC, while the former appears with lower Rf value(identical with eupteleogenin acetate(Ib)) than the latter on SiO_2-$AgNO_3$ TLC plate. The third one, MS-1-Ac-C is readily distinguished from the others on ordinary SiO_2-TLC(with lower Rf value). The final identification of MS-1-Ac-A with authentic eupteleogenin acetate(Ib) was established by mixed mp., TLC and IR(KBr), thus completing the transformation of spergulagenic acid(IIa) to eupteleogenin acetate(Ib) in two steps.

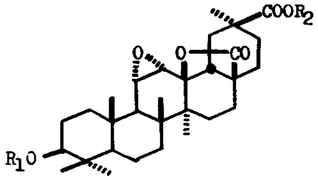
Based on the physical properties, the structures of the other products, MS-1-Ac-B and MS-1-Ac-C have been assumed respectively as Va+Vb(a mixture) and IV analogously as in case of the lead tetraacetate oxidation products of glycyrrhetic acid[8] and diterpenoid carboxylic acids[7].

Furthermore, the direct conversion of MS-1(IIIa) to eupteleogenin(Ia) itself has been also attempted, however the yield was rather unsatisfactory.



Ia : R=H eupteleogenin

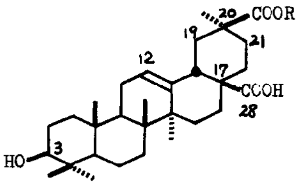
Ib : R=Ac



IIIa : $R_1=R_2=H$ MS-1

IIIb : $R_1=Ac$, $R_2=H$ MS-1-Ac

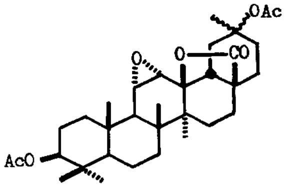
IIIc : $R_1=H$, $R_2=CH_3$ MS-1-Me



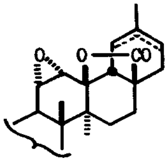
IIa : R=H

spergulagenic acid

IIb : $R=CH_3$

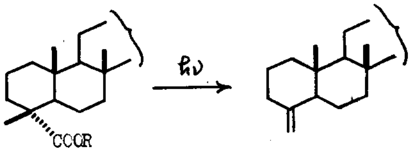


IV



Va : Δ^{19}

Vb : Δ^{20}



VI : R=H or CH_3

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9) Contrary to their report(cf. literatures cited in ref. 3), we isolated spergulagenic acid monomethyl ester(IIb) as the major sapogenin from the root of Mollugo spergula L.