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A NEW δ-LACTONE FROM THE FLOWERS OF *GREWIA ASIATICA*

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Key Word Index—*Grewia asiatica*; Tiliaceae; flowers; 3, 21, 24 trimethyl-5,7-dihydroxyhentriacontanoic acid δ-lactone.

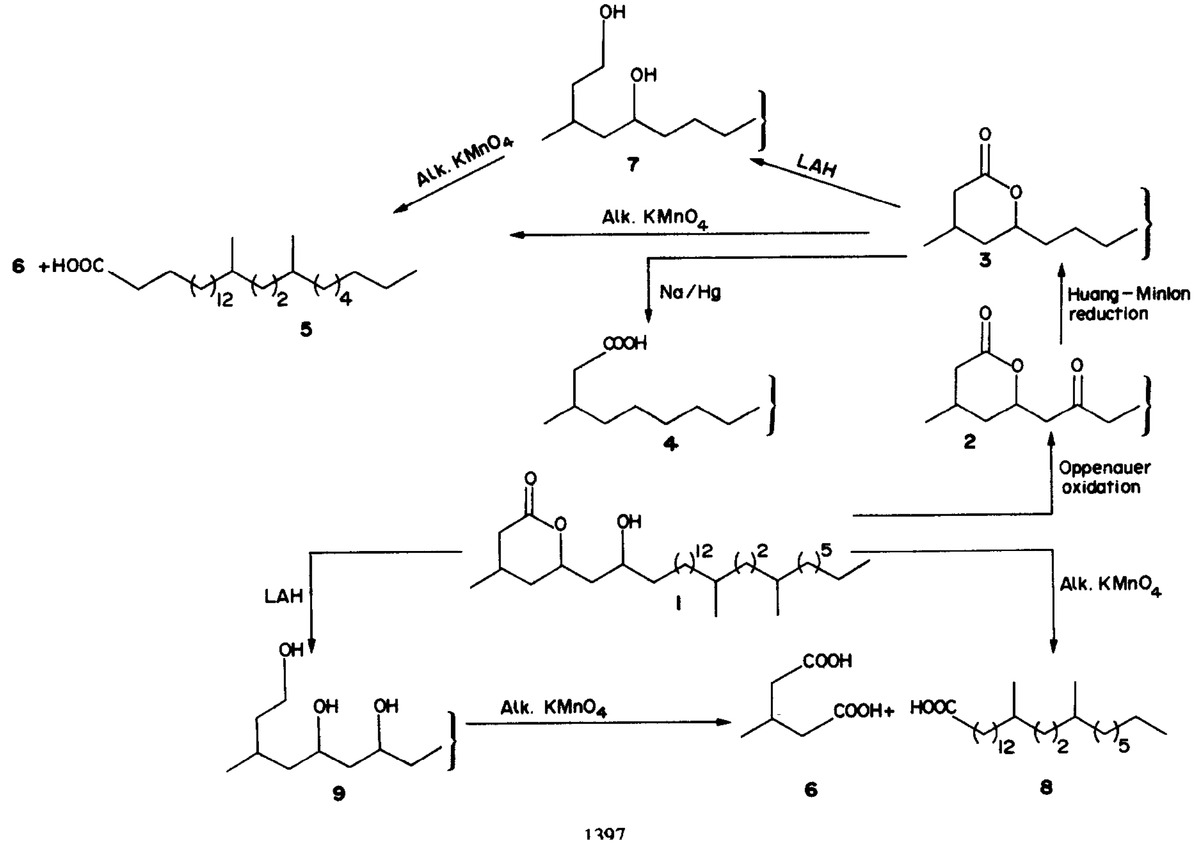
Abstract—The structure of 3, 21, 24 trimethyl-5,7-dihydroxyhentriacontanoic acid δ-lactone, a new δ-lactone, isolated from the flowers of *Grewia asiatica* has been deduced on the basis of physico-chemical studies.

INTRODUCTION

Grewia asiatica (Tiliaceae) is extensively cultivated in various parts of India, flowering from January to April. It is also distributed in Asia, Africa, Australia, especially in tropical regions. Medicinally, the unripe fruit of the plant is bitter, acrid, sour, removes Vata and causes Kapha and biliousness. The ripe fruit is pleasant to taste, digestible, tonic, aphrodisiac and allays thirst and burning sensation. It is also useful in diarrhoea and fevers [1–3]. Previously, palmitic, stearic, oleic, linoleic acids, sitosterol have been isolated from its seeds [4]. The present investigation with *G. asiatica* flowers reports the isolation and structure elucidation of a new lactone.

RESULTS AND DISCUSSION

The lactone (1), mp 70–71°, analysed for $C_{34}H_{66}O_3$. IR spectra and colour reactions for esters and lactones indicated that it was either an aliphatic (saturated) ester or lactone. Its PMR spectrum exhibited four Mes in the methylene and methine region (9.10τ), and it formed a monoacetate $C_{36}H_{68}O_4$ mp 68°. Disappearance of the



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OH absorption in the IR and the appearance of a three proton singlet at 7.86τ for acetyl and a 0.92 ppm shift for one methine proton indicated it to be a monohydroxy compound and the OH to be secondary. This was confirmed by forming a ketone (**2**), $C_{34}H_{64}O_3$ mp 56° by Oppenauer oxidation [5]. Reduction of **2** by the Huang–Minlon [6] modification of the Wolf–Kishner method yielded **3**, $C_{34}H_{66}O_2$, mp 76°, which on $LiAlH_4$ reduction gave a diol **7**, $C_{34}H_{70}O_2$, mp 86–8°. Oxidation of **3** as well as the diol **7** with alkaline $KMnO_4$ [10] produced the same two major acids. Acid **5**, $C_{28}H_{56}O_2$, mp 52.4° exhibited IR absorption at 1700 cm^{-1} and three Mes (9.05τ) in the PMR spectrum besides other peaks. It formed an amide and a Me ester whose MS fragmentation showed the presence of one Me on C-16 and C-19 and consequently the acid **5** was established as 16, 19-dimethylhexacosanoic acid. Acid **6**, mp 84°, a dibasic acid was identified as β-methyl glutaric acid [7] (mmp., TLC. diamide formation). **3** with Na–Hg in acid solution yielded a monobasic acid **4** $C_{34}H_{68}O_2$, mp 51–2° which with CH_2N_2 gave a mono Me ester M^+ at *m/e* 522. Its MS fragmentation [8] indicated the presence of three Me groups on C-3, C-21, C-24 establishing its structure as 3, 21, 24 trimethylhentriacontanoic acid. On this basis the structure for **3** and diol **7** were elucidated as 3, 21, 24-trimethylhentriacontanoic acid δ-lactone and 3, 21, 24-trimethylhentriacontane 1,5-diol respectively.

$LiAlH_4$ reduction of **1** gave a triol **9** mp 92–3°. Alkaline $KMnO_4$ oxidation of **1** as well as triol **9** gave the same two acids **6** and **8**, 14, 17-dimethyltetracosanoic acid [9] (amide mp 62°). Thus from the foregoing chemical and spectral studies it is evident that **1** is either 3, 21, 24-trimethyl-6-hydroxyhentriacontanoic acid δ-lactone or 3, 21, 24-trimethyl-7-hydroxyhentriacontanoic acid δ-lactone. Since the triol **9** is highly resistant to $NaIO_4$, it lacks vicinal OH groups and therefore the first possibility was ruled out. Hence the structures of triol **9** and **1** were established as 3, 21, 24-trimethylhentriacontane-1,5,7-triol and 3, 21, 24-trimethylhentriacontanoic acid δ-lactone.

EXPERIMENTAL

Isolation of lactone (**1**). Air dried flowers of *Grewia asiatica* (10 kg) was extracted with C_6H_6 and $CHCl_3$ which on concn. yielded a semi-solid yellow mass (100 g). This was resolved into Et_2O soluble and Et_2O-insoluble fractions. The former was treated with animal charcoal and was chromatographed over neutral Al_2O_3. Elution with C_6H_6–$CHCl_3$ (1:1) yielded a colourless solid which was fractionally crystallized as colourless needles (14.2 g), mp 70–71°, homogeneous by TLC in different solvents, $[\alpha]_D^{30}$ −10.3($CHCl_3$). $IR\nu_{max}^{KBr}$: 3450(OH), 2900, 2820, 1475(>CH_2), 1750(δ-lactone), 1380(Me), 735 and 725 cm^{-1}. PMR($CDCl_3$, τ): 9.10(12H, 4 × Me), 8.72(42H, 21 × CH_2), 8.54(3H, 3 × ≡CH), 8.49(2H, $-C\underline{H}_2CHO$), 8.26(2H, $O{=}CHC\underline{H}_2$), 6.72(2H, $-CH_2COO$), 6.12(1H, −CHO), 5.32(1H) and 4.92(1H, =CHOCO–). (Found: C, 74.24; H, 12.60; C-Me 10.82 $C_{34}H_{66}O_3$ requires: C, 74.33; H, 12.64; C-Me 11.49%). Acetylation with C_5H_5N–Ac_2O afforded colourless flakes (1.5 g) mp 68°(MeOH), $[\alpha]_D^{25}$ −13.4($CHCl_3$) $IR\nu_{max}^{KBr}$: 2910, 2820, 1750(broad), 1480, 1870, 1080, 730 and 722 cm^{-1}. PMR ($CDCl_3$, τ): 9.10(12H, 4 × Me), 8.72(42H, 21 × CH_2), 8.54(3H, 3 × CH), 8.42(2H, $-C\underline{H}_2CHO$), 8.22(2H, $O{=}CHC\underline{H}_2$), 7.86(3H, MeCOO), 6.70(2H, $-CH_2COO$), 5.20(1H, =CHO) and 4.90(1H, =CHOCO). (Found: C, 76.56; H, 12.10; $C_{36}H_{68}O_4$ requires: C, 76.60; H, 12.05%). Oppenauer oxidation of lactone (**1**) (10 g) gave a waxy product which on chromatography over neutral Al_2O_3(C_6H_6–$CHCl_3$ 1:1) gave (**2**), mp 55–6°(MeOH–$CHCl_3$). $IR\nu_{max}^{KBr}$: 2910, 2840, 1750(δ-lactone), 1725(C=O, enhanced), 1460, 1385, 1140 and 720 cm^{-1}. (Found: C, 78.26; H, 12.15; C-Me 11.04 $C_{34}H_{64}O_3$ requires: C, 78.46; H, 12.30; 4 × C-Me 11.54%). Formed 2, 4 DNP derivative mp 125–6°(MeOH) and an oxime, mp 68–9°(EtOH) (Found: C, 78.46; H, 11.08; N, 4.48 $C_{40}H_{70}O_2N_2$ requires: C, 78.69; H, 11.47; N, 4.59%). Reduction of **2** (4.50 g) by Huang–Minlon modification of the Wolff–Kishner reduction method with hydrazine hydrate and KOH in ethylene glycol yielded a syrupy product which was purified on Al_2O_3($CHCl_3$) to afford colourless flakes **3** (3.33 g), mp 75–6°(MeOH–$CHCl_3$) $[\alpha]_D^{30}$ = −7.40($CHCl_3$). $IR\nu_{max}^{KBr}$: 2925, 2860, 1750, 1460, 1375, 1180, 730 and 725 cm^{-1}. PMR($CDCl_3$, τ): 9.15(12H), 8.76(46H), 8.48(3H), 8.30(2H), 6.62(2H) and 4.90(1H). (Found: C, 80.46; H, 13.08; C-Me 11.20 $C_{34}H_{66}O_2$ requires: C, 80.63; H, 13.04; C-Me 11.85%). **3** (2.2 g) on treatment with Na–Hg in acid soln, usual work up and purification on Si gel(MeOH–$CHCl_3$) yielded waxy flakes **4**, mp 51–2°(MeOH), $[\alpha]_D^{30}$ +14.2°($CHCl_3$). $IR\nu_{max}^{KBr}$: 3250–3200(broad, OH), 2920, 2850, 2725, 1710(COOH), 1460, 1380, 1260, 1130 and 720 cm^{-1}. (Found: C, 80.22; H, 13.40; C-Me 11.84 $C_{34}H_{68}O_2$ requires: C, 80.32; H, 13.38; C-Me, 11.80%). Formed an amide, mp 84–5°(aq. MeOH). (Found: C, 80.34; H, 13.45; N, 2.64 $C_{34}H_{69}ON$ requires C, 80.47; H, 13.61; N, 2.76%). Me ester, mp 28–30°(at 0°). MS(*m/e*): 522(M^+), 493, 491, 423, 367, 199, 185, 171, 153, 143, 129, 127, 115, 101, 99, 74 and 56. **3** (0.8 g) was oxidized with 50 ml 10% $KMnO_4$ and 20 ml 12% KOH for *ca* 2 hr at 50° and the two products **5** and **6** were isolated in usual way [10]. **5** (H_2O insol) was purified over Si gel, mp 52.4°(MeOH), $[\alpha]_D^{20}$ +15.4°($CHCl_3$). $IR\nu_{max}^{KBr}$: 3170(OH), 2920, 2850, 2710, 1700(COOH), 1460, 1375, 1245, 1140 and 725 cm^{-1}. PMR($CDCl_3$, τ): 9.05(9H), 8.76(4OH), 8.42(2H), 8.22(2H, $C\underline{H}_2CH_2COOH$), 7.52(2H, $-C\underline{H}_2COOH$) and 0.86(1H, $COO\underline{H}$). (Found: C, 80.09, H, 12.56; C-Me 10.20 $C_{28}H_{56}O_2$ requires: C, 80.18; H, 12.61, 3 × C-Me 10.61%). Formed an amide mp 98–99°(aq. MeOH) (Found: C, 79.35; H, 13.38; N, 3.22 $C_{28}H_{57}ON$ requires C, 79.43; H, 13.47; N, 3.30%). Me ester, mp 35–6°. MS(*m/e*): 438(M^+), 409, 407, 381, 365, 339, 283, 227, 213, 143, 129, 127, 115, 99, 87 and 74. **6** (H_2O sol), mp 84°(C_6H_6) was recovered by Et_2O extraction of the aq. reaction mixture and purification on Si gel. (Found: C, 49.16; H, 6.76 $C_6H_{10}O_4$ requires: C, 49.31; H, 6.85%), amide mp 169–70°. It was identified as β-methyl glutaric acid (mmp and TLC with an authentic sample). $LiAlH_4$ reduction of **3** (0.5 g) gave a product which on purification over Al_2O_3 gave diol **7**, mp 86–8°(MeOH), $[\alpha]_D^{25}$ −10.2°($CHCl_3$). $IR\nu_{max}^{KBr}$: 3550 cm^{-1}(OH) (Found: C, 80.11; H, 13.64; C-Me, 11.54 $C_{34}H_{70}O_2$ requires: C, 80.00; H, 13.72; 4 × C-Me 11.76%). Formed diacetate(Ac_2O–NaOAc), mp 76–7°(MeOH–$CHCl_3$). (Found: C, 76.66; H, 12.45; acetyl, 13.06 $C_{38}H_{74}O_4$ requires: C, 76.76; H, 12.45; 2 × acetyl, 14.48%). Alkaline $KMnO_4$ oxidation of the diol **7** (100 mg) and usual work up gave **5** and **6** in major yields (mmp, TLC). Lactone **1** (0.85 g) was oxidized by alkaline $KMnO_4$ and the oxidation products **6** (H_2O sol) and **8** (H_2O insol) were isolated and purified as above. **8**, a syrupy mass $[\alpha]_D^{30}$ +44.6°($CHCl_3$). $IR\nu_{max}^{KBr}$: 1705 cm^{-1}(COOH). (Found: C, 78.64; H, 13.35; C-Me 10.90 $C_{26}H_{52}O_2$ requires: C, 78.78; H, 13.32; 3 × C-Me, 11.30%). Formed an amide mp 63–4°(aq. EtOH) (Found: 78.98; H, 13.42; N, 3.54 $C_{26}H_{53}ON$ requires: C, 78.98; H, 13.42; N, 3.54%), Me ester, mp. 30°(MeOH–$CHCl_3$). Ms(*m/e*): 410(M^+), 379, 353, 339, 311, 255, 183, 127, 99 and 88. **6**, mp 84°(C_6H_6). $LiAlH_4$ reduction of lactone **1** (0.85 g) gave a product which was purified by chromatography on Si gel to yield a triol **9**, needles mp 93°(EtOH–$CHCl_3$), $[\alpha]_D^{30}$ −12.2°($CHCl_3$). $IR\nu_{max}^{KBr}$: 3520 cm^{-1}(OH) (Found: C, 77.42; H, 13.22; C-Me, 10.74 $C_{34}H_{70}O_3$ requires: C, 77.57; H, 13,31; 4 × C-Me, 11.40%), Formed triacetate mp 80–1°(EtOH) (Found: C, 73.54; H, 11.45, acetyl 18.69 $C_{40}H_{76}O_6$ requires: C, 73.62; H, 11.66; 3 × acetyl 19.73%). The triol **9** (150 mg) was oxidized by alkaline $KMnO_4$ and the oxidation products were similarly isolated as H_2O insoluble and soluble portions, purified, crystallized and identified as **8** and **6** respectively (mmp, TLC).

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