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The Synthesis of Friedelan-3-on-24-al

Tokiko HOSHINO, Takahiko TSUYUKI and Takeyoshi TAKAHASHI

Department of Chemistry, Faculty of Science, The University of Tokyo, Hongo, Tokyo

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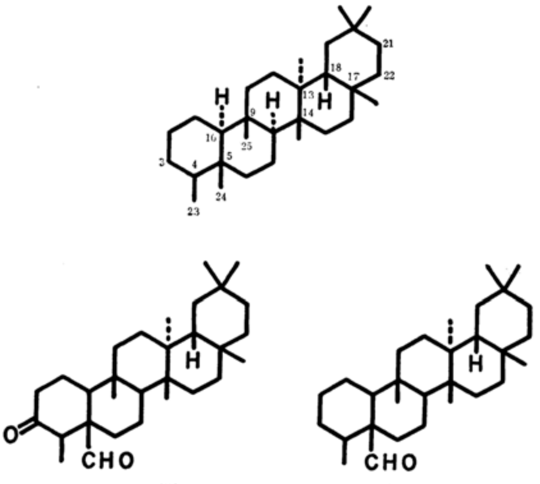
24-Oximinofriedelan-3β-ol (V) was converted *via* either lactone (VI) or hemiacetal (VIII) into diol (VII). Monoacetylation of the diol gave 24-acetoxyfriedelan-3β-ol (X), which was oxidized to keto acetate (XI). Hydrolysis of XI afforded the corresponding keto alcohol, followed by Jones' oxidation giving rise to friedelan-3-on-24-al (I), mp 248—249°C, $[\alpha]_{578}$ +66°. The physical constants of I are not identical with those of friedelan-3-on-y-al, isolated by Courtney *et al.* from *Siphonodon australe* Bent. This furnishes a further evidence that friedelan-3-on-y-al is not friedelan-3-on-24-al (I), but friedelan-3-on-25-al, confirming the recent Courtney's proposal.

In 1956 Courtney and others reported the isolation of over a dozen pentacyclic triterpenes of the friedelane type from *Siphonodon australe* Bent.,[1,2] and revealed that this series of compounds consists of carbonyl, hydroxy-carbonyl and polyhydroxy derivatives. Among them, the carbonyl compounds are classified into friedelan-3, x-dione, friedelan-3, y-dione and friedelan-3, x, y-trione. The exact positions of C-x and C-y in the friedelane skeleton have not yet determined; however, the studies[3,4] in mass spectrometry have indicated that C-x must be located either at C_{21} or at C_{22} and that C-y is not in fact a keto group, but is an angular aldehyde group, which is situated at either C-5 or, preferably, C-9. Thus friedelan-3, y-dione corresponds to either friedelan-3-on-24-al (I) or -25-al.

To decide the exact position of C-y, we first tried to synthesize friedelan-3-on-24-al (I), which was more accessible to synthesis than in the case of friedelan-3-on-25-al.

During our investigation, Courtney and Stern[5] have reported the chemical evidence to show that C-y aldehyde group cannot be at C-5 and it must be located at C-9. They have synthesized friedelan-24-al (II), whose physical properties were not identical with those of friedelan-y-al, therefore, they have inferred that friedelan-y-al must be friedelan-25-al.

The present paper deals with the synthesis of friedelan-3-on-24-al (I). Nitrosolation of friedelan-3β-ol (III) gave a crystalline nitrite (IV) which on irradiation underwent rearrangement to yield oxime (V).[6] The oxime was oxidized with Jones' reagent to γ-lactone (VI) in 23% yield,[7a,b] which was reduced with lithium aluminum hydride to diol (VII) in 68% yield. Treatment of the oxime (V) with acetic acid and apueous sodium nitrite gave hemiacetal (VIII);[8] however, the reaction products showed a weak ester band at 1740 cm^{-1} and two spots on thin layer chromatogram. The larger spot with lower R_f value was due to the hemiacetal and the upper one was attributed to the hemiacetal acetate. The reaction mixture, on treatment with sodium hydroxide in



(I) (II)

Fig. 1

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[1] J. L. Courtney and R. M. Gascoigne, *J. Chem, Soc.*, **1956**, 2115.

[2] J. L. Courtney, R. M. Gascoigne and A. Z. Szumer, *ibid.*, **1856**, 2119.

[3] J. L. Courtney and J. S. Shannon, *Tetrahedron Letters*, **1963**, 13.

[4] J. S. Shannon, C. G. Macdonald and J. L. Courtney, *ibid.*, **1963**, 173.

[5] J. L. Courtney and W. Stern, *ibid.*, **1965**, 1607.

[6] *Cf.* D. H. R. Barton, J. M. Beaton, L. E. Geller and M. M. Pechet, *J. Am. Chem. Soc.*, **82**, 2640 (1960); **83**, 4076 (1961), and related papers.

[7] a) T. Fukuda, T. Tsuyuki, Y. Tanahashi and T. Takahashi, This Bulletin, **38**, 1808 (1965). b) *Ibid.*, **40**, 370 (1967).

[8] *Cf.* M. Akhtar and D. H. R. Barton, *J. Am. Chem. Soc.*, **86**, 1528 (1964).

methanol,[9] gave one spot with the lower R_f value on thin layer chromatogram. The hemiacetal (VIII) thus was obtained in 81% yield based on the oxime, and converted into the same diol (VII) by the action of lithium aluminum hydride in about 88% yield.

We reported that the γ-lactone (VI) was also obtained by an alternative route.[7a,b] A solution of friedelan-3β-ol in cyclohexane was heated with lead tetraacetate in the presence of iodine under irradiation with a 250 W lamp. The residue obtained, was oxidized with chromium trioxide-sulfuric acid to afford, after separation by preparative thin layer chromatography, the same γ-lactone (VI) in a lower yield.

Dehydration of the oxime (V) with boiling acetic anhydride afforded the nitrile acetate (IX).

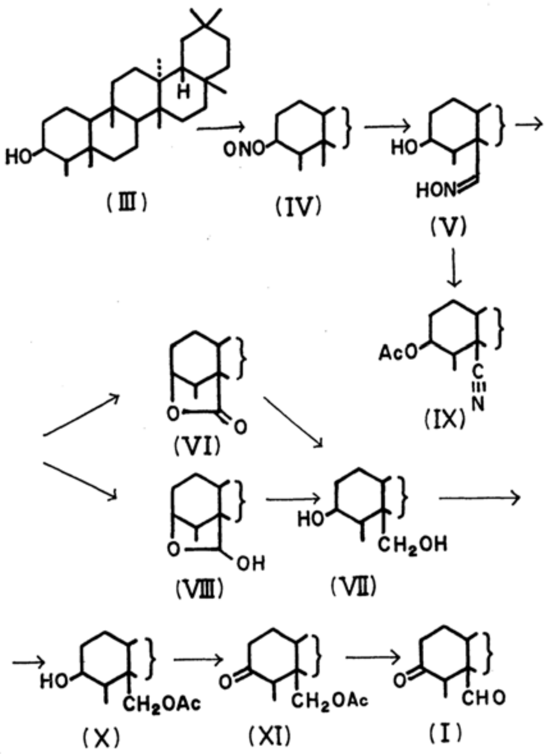

Fig. 2

The diol (VII), on acetylation with acetic anhydride and pyridine, gave a mixture of diacetate and the two monoacetate alcohols, which were separated by column chromatography. 24-Acetoxyfriedelan-3β-ol (X) was characterized by oxidation to the corresponding 3-keto compound (XI). The NMR spectrum of the 3-keto acetate (XI) exhibits peaks at $\delta=1.92$ (3H, singlet) and $\delta_A=4.09$, $\delta_B=4.31$ ppm (2H, AB quartet, $J_{AB}=-13.5$ cps), indicating that the acetoxy group is attached to C-24, not to C-3. Hydrolysis of the keto acetate (XI) with methanolic potassium hydroxide gave the corresponding hydroxy ketone, which upon further oxidation with Jones' reagent gave rise to friedelan-3-on-24-al (I), mp 248—249°C, $[\alpha]_{578}$ +66° (c 0.97).

Friedelan-3-on-y-al has been registered[1] to have mp 305—309°C and $[\alpha]_D$ −62° (c 2.3) and it now appears that friedelan-3-on-y-al is friedelan-3-on-25-al.

Experimental*

Friedelan-3β-ol (III). Friedelin (1 g) was dissolved in hot methanol (*ca.* 2 *l*) and treated with excess of sodium borohydride. After allowing to stand overnight, the precipitate was filtered and dried, which weighed about 1 g. This material showed one spot on TLC, which was identical with authentic friedelan-3β-ol.

3β-Friedelanyl Nitrite (IV). Excess nitrosyl chloride was passed through a solution of friedelan-3β-ol (III, 4 g) in pyridine (1 *l*) at room temperature and was treated as described in the preceding paper.[7b] The white precipitate was dissolved in a small quantity of methylene dichloride and dried over sodium sulfate. After filtration, a large amount of methanol was added to the filtrate. The precipitate was collected on a filter paper. This procedure is available for a large quantity of nitrite, mp 261—263°C, ν_{max}^{Nujol} 1645 and 1610 cm^{-1} (nitrite), identical with authentic 3β-friedelanyl nitrite.

24-Oximinofriedelan-3β-ol (V) and 3β-Hydroxyfriedelan-24-oic Lactone (VI). V and VI were synthesized by the procedure described in the preceding paper.[7b]

Friedelan-3β-ol-24-al Hemiacetal (VIII). The oxime (V, 100 mg) in glacial acetic acid (17 m*l*) and water (3.4 m*l*) was treated at 70°C with sodium nitrite (100 mg). After 2 min, the reaction mixture was poured into ice and water, and extracted with methylene dichloride. After washing with water and then with aqueous sodium hydrogen carbonate, the organic layer was dried over sodium sulfate and the solvent was removed under reduced pressure. The crude hemiacetal (VIII), which contained hemiacetal acetate, was dissolved in 4 m*l* of 1% methanolic sodium hydroxide solution and was allowed to stand for 20 min. The precipitate was collected on a filter paper and washed with water and dried, which weighed 75.7 mg (81%), mp 240—242°C.

Friedelan-3β, 24-diol (VII). *A) From γ-Lactone (VI).* To a solution of the γ-lactone (VI, 135 mg) in tetrahydrofuran (20 m*l*) was added 100 mg of lithium aluminum hydride. The suspension was heated at reflux for 3 hr. Ethyl acetate and water were added and the reaction product was extracted with ether. The ether solution was washed with water and then

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[9] *Cf.* R. H. Hesse and M. M. Pechet, *J. Org. Chem.*, **30**, 1723 (1965).

* Melting points were determined on a hot block and are reported uncorrected. All column chromatographies were carried with silica gel, Davison 200 mesh. As a routine check on the purity of various products, thin layer chromatography (TLC) on silica gel G was employed. The NMR spectra were determined in deuteriochloroform with TMS as an internal standard. Optical rotation was measured in chloroform.

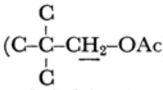
with aqueous sodium hydrogen carbonate solution. After drying over sodium sulfate, the solvent was removed. Recrystallization from dioxane gave 93 mg (68%) of the diol (VII), mp >291°C (with sublimation).

B) From Hemiacetal (VIII). To a solution of the hemiacetal (VIII, 711 mg) in 75 m*l* of tetrahydrofuran was added 840 mg of lithium aluminum hydride. The suspension was refluxed for 3 hr. After the usual work-up, the product was extracted with chloroform, and recrystallized from dioxane, giving rise to 627 mg (87.5 %) of the diol (VII), mp >291°C (with sublimation), ν_{max}^{Nujol} 3226, 1038 and 948 cm^{-1}.

Friedelan-3β, 24-diol 24-Acetate (X). To a solution of the diol (VII, 358 mg) in 60 m*l* of benzene and 60 m*l* of pyridine was added 7.2 m*l* of acetic anhydride. The solution was stored at room temperature for 20 hr. Then the acetic anhydride was decomposed with methanol and water. The product was extracted with benzene and washed with 1 N hydrochloric acid, with saturated sodium hydrogen carbonate solution and then with water. The benzene layer was dried over sodium sulfate, and the solvent was removed under reduced pressure. The product (259 mg) was dissolved in petroleum ether. The undissolved diol (VII, 64.4 mg) was filtered off and the filtrate was passed through a column of silica gel (20 g). Elution (300 m*l*) with benzene-ether (10 : 1) yielded 83.8 mg (27.4%) of pure mono-acetate (X), which was recrystallized from petroleum ether. Mp 222—223°C, ν_{max}^{Nujol} 3509, 1718, 1235 and 1036 cm^{-1}.

Found: C, 78.96; H, 11.18%. Calcd for $C_{32}H_{54}O_3$: C, 78.86; H, 11.39%.

24-Acetoxyfriedelan-3-one (XI). To a solution of 600 mg of chromium trioxide in 6 m*l* of pyridine was added the monoacetate (X, 60 mg) in 6 m*l* of pyridine. The mixture was stored overnight at room temperature. After addition of methanol and water, the product was extracted with ether, followed by the usual work-up. The residue was dissolved in benzene and was passed through a column of silica gel (5 g). Elution (250 m*l*) with benzene-ether (10 : 1) afforded 37.2 mg (62.5%) of pure keto acetate (XI), mp >270°C (with sublimation), ν_{max}^{Nujol} 1740, 1712, 1227 and 1042 cm^{-1}. NMR $\delta=1.92$ (O–CO–C$\underline{H}_3$); AB quartet $\delta_A=4.09$, $\delta_B=4.31$ ppm, $J_{AB}=-13.5$ cps



$(\mathrm{C{-}\overset{C}{\underset{C}{C}}{-}C\underline{H}_2{-}OAc})$.

Found: C, 79.28; H, 10.81%. Calcd for $C_{32}H_{52}O_3$: C, 79.37; H, 10.89%.

Friedelan-3-on-24-al (I). The keto acetate (XI, 47 mg) in ethanol (4 m*l*) and 0.3 m*l* of 0.5 N ethanolic potassium hydroxide solution was heated at reflux for 45 min. The reaction mixture was extracted with chloroform and dried over sodium sulfate. Chloroform was distilled off and the crude keto alcohol (37 mg) was dissolved in 160 m*l* of acetone. To the ice-cooled solution, 0.6 m*l* of Jones' reagent was dropped and stirred for 1 hr. A large amount of water was added and the product was extracted with ether. The extract was washed with saturated sodium hydrogen carbonate solution and with saturated sodium chloride solution. After drying over sodium sulfate, evaporation of ether gave 41.9 mg of crude keto aldehyde (I), which was purified by passing through a column of silica gel (2 g). Elution (125 m*l*) with benzene afforded 18 mg (48.8%) of friedelan-3-on-24-al (I), mp 248—249°C, ν_{max}^{Nujol} 1724 and 1709 cm^{-1}, NMR $\delta=9.73$ ppm (–C$\underline{H}$O). $[\alpha]_{365}$ +330°, $[\alpha]_{405}$ +204°, $[\alpha]_{436}$ +158°, $[\alpha]_{546}$ +78°, $[\alpha]_{578}$ +66° (*c* 0.97).

Found: C, 81.76; H, 10.98%. Calcd for $C_{30}H_{48}O_2$: C, 81.75; H, 10.84%.