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The Synthesis of 24-Norfriedel-4-en-3-one

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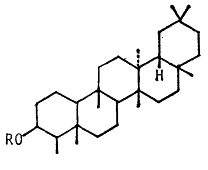
Synopsis. The lead tetraacetate oxidation of 24-hydroxyfriedel-3-ene, prepared from friedelin, afforded a 3-acetoxy-24-norfriedel-4-ene, which was then convered into the title compound.

Pristimerin and celastrol have been shown to have the carbon skeleton of 24-norfriedelane.[1] In connection with the structural investigation of these compounds, we studied the removal of the 24-methyl group from friedelin.

The functionalization of the 24-methyl group in friedelin was studied by Fukuda *et al*;[2] they prepared 3β-hydroxyfriedelan-24-oic acid lactone from 3β-friedelanol (I R=H) by lead tetraacetate–iodine oxidation, followed by chromic oxidation, or by the photolysis of a nitrile (I R=NO), followed by the oxidation of the resulting oxime. Although photoirradiation on 3β-friedelanol (I R=H) in the presence of iodine and mercuric oxide had been reported to form 3β,24-oxidofriedelane (II R=CH_3),[3] Wenkert and Mylari pointed out that the same reaction in the presence of lead tetraacetate instead of mercuric oxide affords 25-iodo-3β,24-oxidofriedelane (II R=CH_2I) besides 3β,24-oxide (II R=CH_3).[4] The formation of the iodo ether seems to be due to an excess of the oxidizing reagent in the photolysis. The photolysis of 3β-friedelanyl hypobromite (I R=Br), which had been prepared from friedelanol, bromine, and mercuric oxide in a dark place, is found to afford 3β,24-oxidofriedelane (II R=CH_3) in a modest yield.

Upon treatment with boron trifluoride-etherate and acetic anhydride, the ether linkage of 3β,24-oxide (II R=CH_3) was cleaved to afford a homoallyl acetate (III R=Ac),[3] which was then further converted into the corresponding alcohol (III R=H) by alkaline hydrolysis. Attempts to remove the hydroxymethyl group of (III R=H) *via* an epoxy derivative (IV) were unsuccessful. However, it was found that the reaction of (III R-H) with lead tetraacetate caused the elimination of the methylol group, affording a norcompound with the composition of $C_{31}H_{50}O_2$. This product showed an acetoxyl absorption band in the IR spectrum at 1730 cm^{-1} and gave a postive test with tetranitromethane. The NMR spectrum indicated a singlet at δ 2.05 due to the methyl group bonded to an olefin group and a multiplet at δ 5.06 assignable to either a carbinyl proton of allyl acetate or a vinyl proton. The product, therefore, appeared to be an unsaturated noracetate, most probably either 3-acetoxy-24-norfriedel-4-ene (V R=Ac) or 5-acetoxy-24-norfriedel-3-ene (VI). The base hydrolysis of the acetate afforded a corresponding allyl alcohol, the NMR spectrum of which showed a new signal at δ 3.86 instead of the signal at δ 5.06 in the original acetate. This change indicates that the signal at δ 5.06 is due to a carbinyl proton of allyl acetate, and



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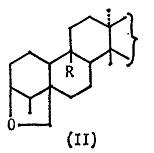

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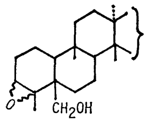
(III)



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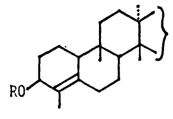

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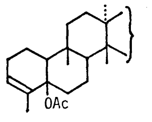

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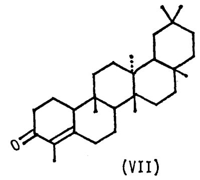

(VII)

so the structure (V) is assigned to the lead tetraacetate oxidation product. The allyl alcohol (V R=H) was finally converted by oxidation with manganese dioxide into the α,β-unsaturated ketone (VII), which has the desired 24-norfriedelane carbon skeleton.

Experimental

3β-Friedelanol (I R=H). Sodium borohydride (4 g) was added portion by portion to a solution of friedeline (3 g) in diglyme (800 ml), and then the mixture was allowed to stand for 15 hr. After the addition of water (1000 ml), the separated precipitate was collected, washed with water, and dried. The material was recrystallized from chloroform to give 2.2 g of 3β-friedelanol (mp 270—273°C), which was identical with the sample prepared by the authentic method.[1]

3β,24-Oxidofriedelane (II R=CH_3). To a solution of 3β-friedelanol (500 mg) in carbon tetrachloride (1000 ml) containing yellow mercury oxide (900 mg), was added drop by drop a solution of bromine (0.08 ml) in carbon tetrachloride (3 ml) at 0 °C over 1-hr period in a place protected from light. After it had been stirred for 3 hr at 0°C, the mixture was filtered and the filtrate was irradiated with a tungsten lamp (300 W; 15 cm from the liquid level) at 0 °C under a nitrogen atmosphere for 1 hr, after which period the orange color of the solution had faded. The solution was washed with an aqueous sodium chloride solution, dried, and evaporated to give a white solid. The crude product was dissolved in benzene. The solution was purified through a column of alumina (15 g). Elution with benzene yielded 240 mg of pure oxide, which was then recrystallized from chloroform; mp 210—212 °C, ν (KBr) 2980—2850, 1450, 1380 cm^{-1}, $\delta(CDCl_3)$ 3.40(1H,d,J=8 Hz), 3.86(1H,m), 4.24(1H), 4.24(1H,d,J=8 Hz).

24-Hydroxyfriedel-3-ene (III R=H) was prepared from the oxide (II R=CH_3) by the method developed by Courtney and Stern.[3]

3-Acetoxy-24-norfriedel-4-ene (V R=Ac). To a stirred solution of the hydroxyfriedelene (III R=H) (150 mg) in 30 ml of benzene containing 0.07 ml of pyridine, was added 300 mg of lead tetraacetate. The mixture was stirred for 30 min. After subsequent treatment with water, the mixture was extracted with ether. The ether extract was washed successively with aqueous cupric sulfate and an aqueous sodium chloride solution, and dried. The ether was then removed, and the residue was fractionated by the column chromatography of alumina to give white crystals of the allyl acetate (159 mg); mp 172—175 °C, ν(KBr) 1730, 1240 cm^{-1}, $\delta(CDCl_3)$ 2.05(3H,s), 1.68(3H,s), 5.06(1H,m). Found: $(M-HOAc)^+$, 394.36102. Calcd for $C_{29}H_{46}$: 394.35990.

3-Hydroxy-24-norfriedel-4-ene (V R=H). The allyl acetate (V R=Ac, 140 mg) dissolved in ethanol (100 ml) was hydrolysed by means of a reaction with potassium hydroxide (4 g) under an atmosphere of nitrogen to give the allyl alcohol (V R=H, 125 mg); mp 209 °C, ν(KBr) 3430 cm^{-1}, $\delta(CDCl_3)$ 1.78(3H,s), 3.86(1H,bs). Found: $(M-H_2O)^+$, 394.36001. Calcd for $C_{29}H_{46}$: 394.35990.

24-Norfriedel-4-en-3-one (VII). A mixture of the allyl alcohol (V R=H, 45 mg), active manganese dioxide (450 mg), and methylene chloride (5 ml) was stirred for 4 hr. The inorganic substance was removed by filtration, and the filtrate was evaporated *in vacuo* to give a crude α,β-unsaturated ketone (45 mg). A pure compound was obtained by recrystallization from chloroform–methanol; mp 201 °C, ν(KBr) 1675, 1610 cm^{-1}, $\delta(CDCl_3)$ 1,78(3H,s). λ_{max} 252 nm (ε 14900). Found: 410.3566. Calcd for $C_{29}H_{46}O$: 410.3548.

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