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OXAICEANE AND ABEO-OXAICEANE

David P.G. Hamon,* Garry F. Taylor and R.N. Young.

Department of Organic Chemistry, University of Adelaide,
Adelaide, South Australia, 5000.

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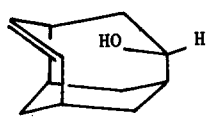
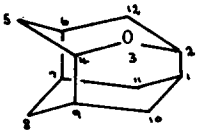
The recent publication[1] of a synthesis of 3-Oxawurtzitane[2] prompts us to report our observations of a parallel synthetic scheme in which the key step, the oxymercuration-reduction reaction of the olefinic alcohol 1,† leads not only to 3-oxa-tetracyclo[5,3,1,$1^{2,6}0^{4,9}$] dodecane 2 (oxaiceane) as reported by the Swiss workers, but also to a structural isomer 12-oxa-tetracyclo[5,3,1,$1^{2,5}0^{4,9}$] dodecane 3 (abeo-oxaiceane).[3] The structures of these isomers are differentiated by the novel use of a chiral nmr shift reagent as well as by ^{13}C nmr. In the light of the recent calculations of Schleyer et al.[4] concerning the carbon analogues, of which only one isomer is known,[5] these two oxa isomers should prove of theoretical interest. The key compound which allowed us to prepare them, and also the hydrocarbon Iceane 4,[5] is the keto-olefin 5, the structure of which was confirmed by independent chemical correlations. Since our route to compound 2 is different from that reported and involves a new fragmentation reaction, we take this opportunity to report it.

The olefinic acid 6[6] was brominated (N-bromosuccinimide in CCl_4) to give the bromoacid 7 (mp 156-8°). Treatment of the crude bromoacid with oxalylchloride and thence with diazomethane gave the diazoketone. This was decomposed with copper powder in refluxing cyclohexane[7] to give the bromocyclopropyl ketone 8[8,9] (mp 78-9°) (43% based on acid 6); ν_{max}^{nujol} 3000 (shoulder) and 1680 cm^{-1}; nmr (CCl_4) no vinylic hydrogens, δ 4.52 br, s (CHBr)[10] and 3.0-0.6 (methylene envelope).

† The oxymercuration was done in THF rather than in water.[1]



1



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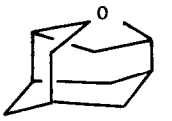

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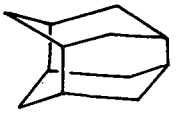

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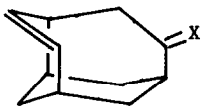
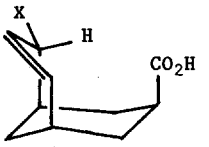
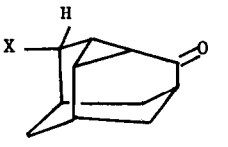


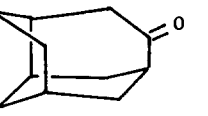
5 X=O
11 X=CH_2



6† X=H
7† X=Br



8† X=Br
10† X=H



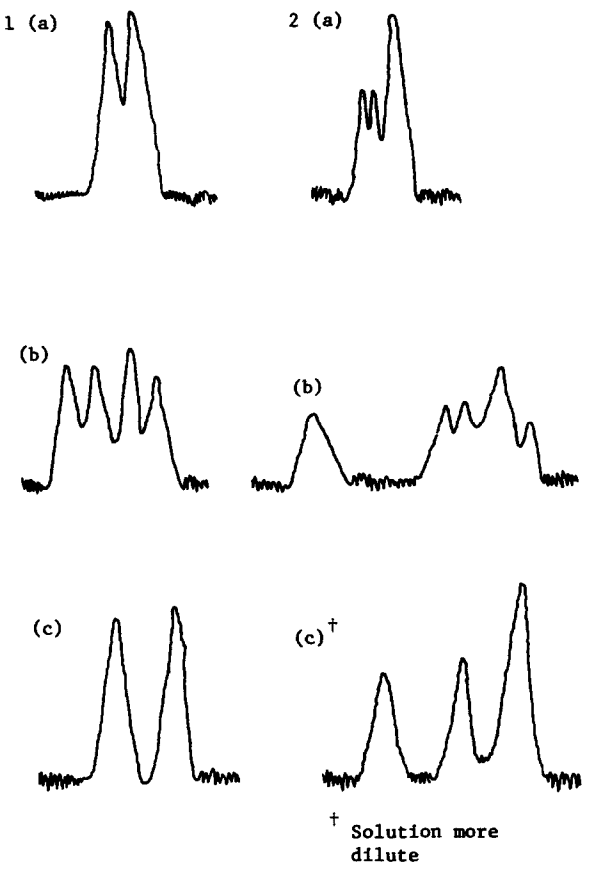
9

† Enantiomeric series of the (±) compounds shown for clarity.

Treatment of compound 8 with liquid Na-K alloy in anhydrous ether (0.5 hr, 20°) followed by protonation (EtOH: petrol (40°-60°) 1:9) gave a mixture of ketonic and alcoholic products which on oxidation (chromic acid, acetone) afforded the olefinic ketone 5 (mp 258-260°) (90% based on 8); ν_{max}^{nujol} 1710 cm^{-1}; nmr CCl_4 δ 6.1 and 5.5 m (vinylic)[11] and 3.0-0.6 (methylene envelope). This novel metal reaction[12] has considerable general synthetic potential in that it provides a keto-olefin product rather than a diolefin or diketone available from alternative methods.[13] Further work, demonstrating the utility of this procedure, will be reported in the near future. Catalytic hydrogenation of compound 5 gave a dihydroketone 9, which was not homoadamantanone,[14] but which was identical in all respects to a compound obtained by reduction (Li, liq NH_3) of the cyclopropylketone 10.[15]

The alcoholic material obtained from the metal reaction was a mixture of two compounds (glc) both of which gave the ketone 5 on oxidation. Sodium borohydride reduction of ketone 5 gave only one of these alcohols (mp 269-270°) (> 95%); ν_{max}^{nujol} 3400, 3000 (shoulder) 1650 cm^{-1}; nmr ($CDCl_3$) δ 6.4-5.8 complex m (vinylic) 4.1 m (-CHO-) and 2.8-1.2 (methylene envelope and OH). By analogy[5] with the hydroboration of diolefin 11, it was expected that this alcohol would have the stereochemistry shown in structure 1. Indeed, oxymercuration[16] of the olefinic alcohol followed by reduction ($NaBH_4$) gave a mixture of two compounds (ca. 1:1) isomeric with the starting material (glc - ms). These could be separated into two crystalline compounds (prep. glc).[17]

That which eluted first was abeo-oxaiceane (3) (mp 256-7°) followed closely by oxaiceane (2) (mp 314-5°). The structures were assigned on the basis of the following data.



Both gave analytical data and molecular ions consistent with the formula $C_{11}H_{16}O$. The main feature of the pmr spectrum of each isomer was the absorption of the protons on carbon bearing oxygen. That for oxaiceane was a symmetrical broadened doublet at δ 4.22 (fig. 1a) whereas for the isomer this absorption was an unsymmetrical multiplet centred at δ 4.2 (fig. 2a). The remainder of the spectrum of oxaiceane revealed a more symmetrical structure than that of its isomer. The symmetry of oxaiceane and the asymmetry of abeo-oxaiceane were clearly revealed by the use of optically active shift reagent[18] in the nmr samples (fig. 1b and 2b). Figure 2c (the decoupled spectrum of fig. 2b) clearly reveals that there are four different protons present (although clearly two are almost co-incident in chemical shift) as would be expected[18] for diastereoisomeric interactions between enantiomers of compound 3 and the shift reagent. Figure 1c shows that in this sample there are two different protons in this region consistent with diastereotopism[19] induced[18] in the prochiral molecule 2 by the optically active shift reagent.

The $^{13}C\{^1H\}$ nmr spectra further confirmed the structural assignments. Oxaiceane showed absorptions (relative to TMS) at δ 69.7 (C_2, C_4) 31.2 (C_5, C_{12} co-incident with C_8, C_{11}) 29.9 (C_1, C_9) 27.8 two almost superimposed absorptions (C_6, C_7) and 24.3 (C_{10}) ppm. The off-resonance decoupled spectrum was consistent with the assignments. abeo-Oxaiceane showed in its $^{13}C\{^1H\}$

spectrum eleven absorptions (unassigned) at δ 76.7, 76.2, 38.4, 36.2, 35.5, 34.6, 34.4, 31.8, 29.7, 29.3 and 26.6 ppm.

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2. Although these authors give good reasons for their choice of a trivial name, we believe precedent has been claimed.
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8. We have been unable, as yet, to obtain satisfactory analytical data for this compound.
9. Conversion of 6 to 8 was effected without purification of intermediates.
10. The small coupling constant between this proton and its neighbors is consistent with the configuration depicted since models indicate that in this configuration, but not in the epimer, the dihedral angles between this proton and both of its two neighbors are about 90°.
11. Each multiplet was a doublet of doublets i.e. an AB pattern further split by the neighboring protons.
12. A similar reaction has been observed as a minor pathway in the zinc reduction of π-bromocamphor. K.M. Baker and B.R. Davis, Tetrahedron, 24, 1655 (1968).
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15. Compound 10 was prepared by an analogous route starting from acid 6 but omitting the bromination step. Compound 10 has been prepared independently, R.K. Murray private communication.
16. The procedure of Brown was used. H.C. Brown and Min-Hon Rei, J.Amer.Chem.Soc., 91, 5646 (1969).
17. 2 m x 8 mm 20% FFAP at 210°.
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