

THE TOTAL SYNTHESIS OF *dl*-RIMUENE

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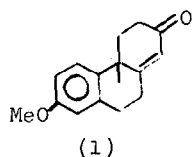
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For a number of years the chemistry of the diterpene rimuene (11) has commanded the attention of several laboratories to an extent that is out of proportion to the hydrocarbon's importance in the natural order of things. This has been partly due to the biogenetic implications of the originally suggested pimaradiene-type structures^{1,2}, as well as the void left when these structural postulates were proved incorrect by recent synthetic work.³ Very recent results, disclosed independently from two groups, have brought forth yet another structure,^{4,5} (11), for rimuene, that removes it from its key role as an intermediate in diterpene biogenesis, and establishes the hydrocarbon as merely another manifestation of the possible rearrangement pathways open to the polyene cyclisation process. While the evidence presented by these groups leaves little doubt as to the validity of their conclusions, it seemed worthwhile to add the final touch to this story by providing a total synthesis of the diterpenoid hydrocarbon. We record here such a synthesis of *dl*-rimuene (11) that verifies the structural

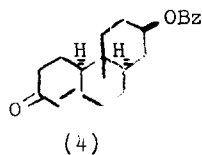
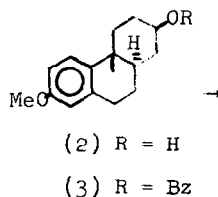
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deductions made by the English and New Zealand groups.

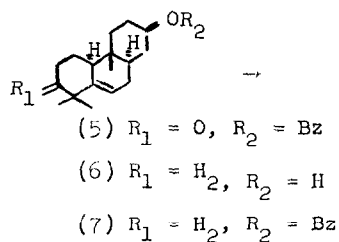
The starting material for our work was the familiar tricyclic ketone (1)⁶ which was obtained in 85% yield from 6-methoxy-1-methyl-2-tetralone by homoannulation with methyl vinyl ketone. However, rather than use this tricyclic derivative in the more customary sense, the aromatic ring was envisaged as the A ring of rimuene (11). The trans fusion between the B and C rings was established by lithium-ammonia reduction⁷ of the unsaturated ketone (1) which gave the dihydro derivative (m.p. 100-102°, C, 78.60; H, 8.26%) in 74% yield. Further reduction with lithium aluminum hydride gave the oily alcohol (2) which was characterized as the benzoate (3) (86% overall yield, m.p. 120-121°, C, 78.68; H, 7.42%).

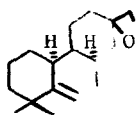


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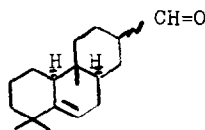


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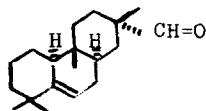




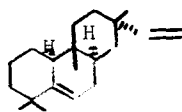
(8)



(9)



(10)



(11)

Introduction of the C-13 substituents was then postponed until elaboration of the A ring was completed. To this end, the alcohol (2) was reduced with lithium-ammonia-tert. butanol,⁸ the resulting dihydroanisolediol (86% yield, m.p. 134-136°, C, 77.38; H, 9.71%) hydrolysed with aqueous hydrochloric acid in ethanol and then esterified with benzoyl chloride-pyridine. The unsaturated keto benzoate (4) (m.p. 177-180°, C, 78.13; H, 7.84%) was thus obtained in 82% overall yield. Methylation of (4) with methyl iodide-potassium tert. butoxide in tert.butanol-benzene afforded the 4,4 dimethyl derivative (5)⁹ (82% yield, m.p. 179-181°, C, 78.58; H, 8.38%). A signal at 5.7 p.p.m. in the n.m.r. spectrum of this product was ascribed to the C-6 olefinic proton and corroborated that the 4,5 double bond in the parent compound had shifted to the 5,6 position rather than the 5,10 location by this treatment. The modification of ring A was then completed by Huang Minlon

reduction¹⁰ of the 3-ketone with concomitant hydrolysis of the 13-benzoate to give the olefinic alcohol (6) (m.p. 116-118°, C, 82.07; H, 11.33%) in 94% yield. An alternative procedure which employed desulfurisation of the 3-dithioketal of (5) (m.p. 181-183°, C, 70.22; H, 7.72%), gave the benzoate (7) (m.p. 119-123°, C, 81.74; H, 9.17) in 82% overall yield.

Oxidation of the alcohol (6) with "Jones reagent" gave the 13-ketone (96% yield, m.p. 108-111°, C, 82.73; H, 10.51%), which was smoothly converted to the oxide (8) (m.p. 71-72°, C, 82.89; H, 10.70%) in 72% yield by treatment with dimethyl sulfoxonium methylide.¹¹ The oxide (8) was rearranged to the corresponding aldehyde (9) (90% yield, m.p. 58-61°, C, 82.76; H, 10.88%) by brief treatment with boron trifluoride-etherate in benzene.¹² The final elaboration of the C-13 substituents was effected by methylation with methyl iodide in the presence of potassium tert. butoxide, which gave a mixture of the desired aldehyde (10) (37%, m.p. 46-48°, C, 83.24; H, 10.94%), a small amount (7%) of the C-13 epimer of (10), and dimeric material (30%). The infra red spectrum of the aldehyde (10) was identical with that of the aldehyde obtained from the degradation of rimuene, and on treatment of the *dl*-compound with methylene triphenyl phosphorane,¹³ there resulted a 75% yield of *dl*-rimuene (11) (m.p. 85-88°, C, 88.19; H, 11.62%). Again, spectral (IR and NMR) comparison with the natural substance proved the identity of the synthetic and naturally occurring material, and thus, the total synthesis of the elusive rimuene was complete.

ACKNOWLEDGEMENTS

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