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A NOVEL SKELETAL REARRANGEMENT OF BICYCLO(2.2.2)OCTENES THROUGH BICYCLO(3.2.1)OCTENE SYSTEM: SYNTHESIS OF (±)-HINESOL AND (±)-10-epi-HINESOL

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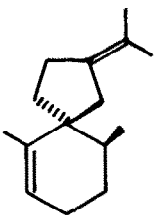
SUMMARY: Acid catalysed rearrangement of the endo-alcohol (9) leads to the ketones (11) and (12) having the bicyclo(3.2.1) and bicyclo(2.2.2) moieties. An efficient entry into spiro(4.5)decane and eremane system, as exemplified by the total synthesis of (±)-hinesol (2) and its 10-epimer (3) is reported.

The facile stereocontrolled skeletal rearrangement[1] of the bridgehead substituted bicyclo(2.2.2) system followed by oxidative cleavage of the resultant bicyclo(3.2.1)enone provides a simple and novel synthetic route to the spiro(4.5)decane system belonging to the β-vetivone (1) family[2]. In this communication we wish to report the application of this strategy to the synthesis of (±)-hinesol (2) and its 10-epimer (3)[3] starting from readily available aromatic compounds.



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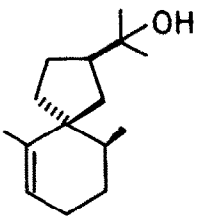

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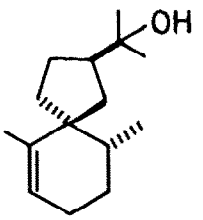

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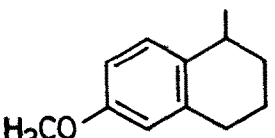

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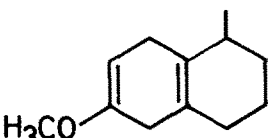

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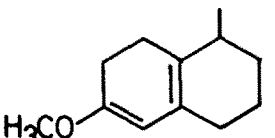

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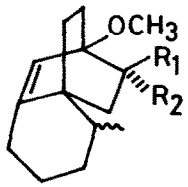
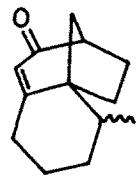


(7) $R_1, R_2 = Cl, CN$

(8) $R_1, R_2 = O$

(9) $R_1 = H$; $R_2 = OH$

(10) $R_1 = OH$; $R_2 = H$



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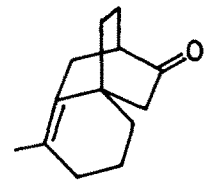

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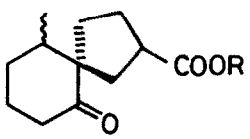
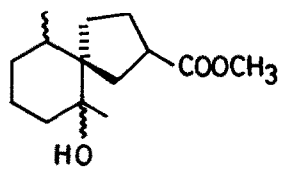


(13) R = H

(14) $R = CH_3$



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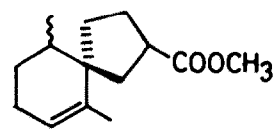

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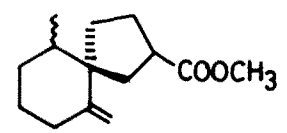

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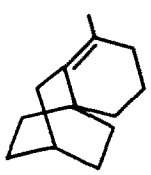

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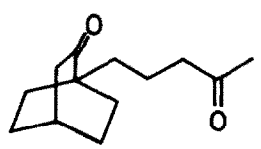

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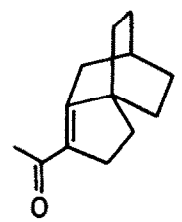

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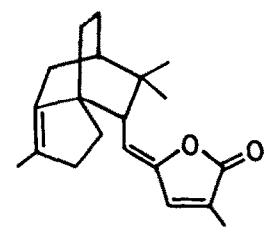

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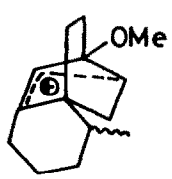

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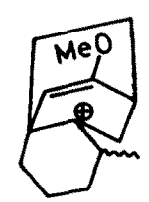

(24)

Regiospecific addition[4] of α-chloroacrylonitrile to the diene (6), obtained by the metal-ammonia reduction of 6-methoxy-1-methyltetralin (4) followed by base catalysed conjugation of the diene (5), furnished the adduct (7, 50%) as a mixture of endo and exo isomers (5:2). Hydrolysis of this mixture with aq KOH in DMSO afforded the ketone (8, 61%), ν_{max} 1720 cm^{-1}, δ 0.87 and 0.94(2d, 3H, -CH-$\underline{CH_3}$), 3.52(s, 3H, -O$\underline{CH_3}$) and 5.85(s, 1H, =$\underline{CH}$). Reduction of this ketone with $NaBH_4$ yielded a mixture (3:1) of endo and exo alcohols (9 and 10), which was separated by chromatography. Rearrangement of the endo-alcohol (9) with BF_3-Et_2O gave a (3:2) mixture of the enone (11) and the ketone (12). The tricyclic ketone (11), ν_{max} 1680 and 1600 cm^{-1}; λ_{max} (EtOH) 242nm(ε, 10,000); δ 0.92 and 1.0(2d, J=6.4Hz, 3H, -CH$\underline{CH_3}$). 2.75(m, 1H, bridgehead proton) and 5.7(m, 1H, =$\underline{CH}$); M^+ 190, was obtained as a mixture of diastereoisomers. This was oxidised with $RuCl_3.3H_2O$-$NaIO_4$ according to the procedure of Sharpless[5] to furnish the keto acid (13, 75%), characterised as its methyl ester[6] (14). ν_{max} 1735 and 1700 cm^{-1}; δ 0.9 and 0.93(2d, J=7Hz, 3H, -CH$\underline{CH_3}$), 2.72(br. quintet, 1H, C$\underline{H}$-$COOCH_3$), 3.65 and 3.67(2s, 3H, -O$\underline{CH_3}$), M^+ 224. Addition of methylmagnesium iodide to the keto acid (13), followed by esterification afforded the hydroxy ester (15) in 87% overall yield. Dehydration of the ester (15) gave a mixture (1:1) of the olefins (16 and 17) which was separated by chromatography over silica gel impregnated with 15% silver nitrate. The exo-olefin (17) was readily isomerised to (16, 90%) with PTS. Grignard reaction of the ester (16) with methylmagnesium iodide afforded a mixture of (±)-hinesol (2) and its 10-epimer (3) in 95% yield, the spectral data of which were identical with the reported values[3].

The ketone (12), ν_{max} 1720 cm^{-1}; ^{13}C NMR δ 215.9, 128.8, 125.9, 49.6, 43.5, 35.7, 33.7, 31.2, 30.5, 29.8, 22.9, 18.6 and 17.7; M^+ 190, was deoxygenated via the thioacetalization, followed by desulfurization with Raney-Ni in ethanol to yield the compound (18): ^{13}C NMR showed 11 lines due to the symmetry in the molecule (δ, 134.3, 123.9, 46.6, 35.8, 33.5 (2C), 31.7, 26.8 (2C) 20.0 and 18.4). The compound (18) was oxidised with $RuCl_3.3H_2O$-$NaIO_4$ to the dione (19), ν_{max} 1710 cm^{-1}; ^{13}C NMR showed 11 lines (δ, 217.1, 208.7, 44.7, 44.5, 44.1, 33.0, 29.5, 27.9, 27.5, 25.0 and 18.1); M^+ 208. Aldol condensation of (19) yielded the unsaturated ketone (20), ν_{max} 1670 and 1625 cm^{-1}; ^1H NMR, δ 2.2 (s, 3H, -CO $\underline{CH_3}$) and 2.62(m, 1H, bridgehead proton); M^+ 190, thus establishing the position of the double bond in the ketone (12). The compounds (12), (18) and (20) had the structural features of eremane skeleton[7,8] and with proper appendages, can be elaborated into isoeremolactone[8] (21) and is being examined.

Although reaction of the unsaturated ketone (11) with BF_3-Et_2O is unchanged, ketalisation of (11) with ethylene glycol and BF_3-Et_2O in benzene, followed by hydrolysis yielded the ketone (12) in 40% yield. The mechanism of this novel

cationic rearrangement of (9) into (11) and (12) seemed to involve the intermediacy of the carbocations (22), (23) and (24) thus (23) leading to (11) and (24) to (12) respectively.

Thus a novel rearrangement of a (2.2.2)bicyclic system into an isomeric(2.2.2)-bicyclic moiety through a (3.2.1)bicyclic intermediate is observed for the first time.

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References

1. G.S.R. Subba Rao and K. Pramod, Proc. Indian Acad. Sci., (Chem. Sci), 93, 573 (1984).
2. J.A. Marshall, D.D. Syradal and N.H. Anderson, Fortshr. Chem. Org. Naturstoffe, 31, 283 (1974).
3. (a) J.A. Marshall and S.F. Brady, J. Org. Chem., 35, 4068 (1970).
   (b) P.D. Magnus, D. Bhuddhasukh and D. Ayalon Chass, J. Org. Chem., 43, 1750 (1978).
4. A.J. Birch and K.P. Dastur, Tet. Lett., 4195 (1972).
5. P.H.J. Carlsen, T. Katsuki, V.S. Martin and K.P. Sharpless, J. Org. Chem., 46, 3936 (1981).
6. M. Deighton, C.R. Hughes and R. Ramage, J.C.S. Chem. Comm., 662 (1975).
7. R. Jeffries, J.R. Knox and E.I. Middleton, Aust. J. Chem., 15, 532 (1962).
8. A.J. Birch, G.S.R. Subba Rao and J.P. Turnbull, Tet. Lett., 4749 (1966).

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