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LABELLING STUDIES OF THE FORMATION OF CYCLOPENTADIENES FROM THE REACTION OF 1,1-DIBROMO-2-VINYLCYCLOPROPANES WITH METHYL LITHIUM

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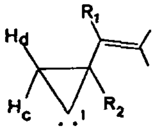
Labelling studies of the conversion of (5, $R_1 = R_2 =$ Me) to (9) on reaction with methyl lithium are consistent with an intermediate (4, $R_1 = R_2 =$ Me) or a carbenoid with no plane of symmetry through the ring, in which selective migration of H_a (H_b and H_d in (1, $R_1 = R_2 =$ Me)) occurs.

The reaction of 1,1-dibromo-2-vinylcyclopropanes with methyl lithium provides a versatile route to cyclopentadienes (3), in some cases accompanied by allenes.[1] The process has been explained in terms of the formation of a vinylcyclopropylidene (1) (or a related carbenoid) which rearranges to a cyclopentenylidene (2); a 1,2-shift of hydrogen then produces (3). Labelling studies have shown that the fate of C-1 of the cyclopropane is consistent with this type of rearrangement [2] and various calculations on the (1) to (2) transformation have been reported.[3] The formation of a simple cyclopentenylidene, eg., (2, $R_1 = R_2 =$ Me) from (1, $R_1 = R_2 =$ Me) is unusual in that a species with no planes of symmetry, in which all the labelled hydrogens are inequivalent, is formally converted into one with two planes of symmetry in which all four hydrogens are equivalent, (2, $R_1 = R_2 =$ Me). This in turn rearranges to (3, $R_1 = R_2 =$ Me) in which they are in three different environments.



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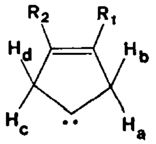

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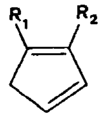

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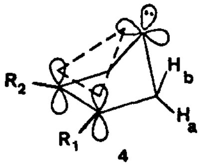

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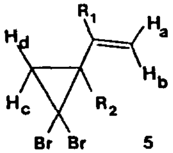

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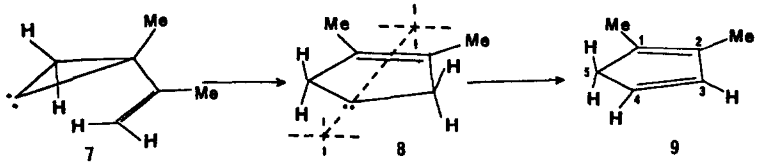
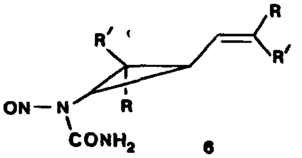
Although the free carbenes (1) and (2) are formally involved, there are a number of reports of very high regiocontrol in the rearrangement. A careful study of the effect of alkyl substituents has recently been published.[4] The dibromides (5, $R_1 =$ Me, $R_2 =$ H) and (5, $R_1 =$H, $R_2 =$ Me) both lead to the same 53:47 mixture of 1- and 2-methyl-cyclopentadienes, suggesting that a commmon intermediate (2, $R_1 =$H, $R_2 =$ Me) is indeed involved, and that hydrogen migration takes place with about equal facility in each direction unaffected by the substituent. However, the corresponding phenyl-substituted systems (5,

R_1= Ph, R_2= H) and (5, R_1= H, R_2= Ph) both lead only to migration of the hydrogen furthest from the phenyl-group in the resulting carbene (2, R_1= H, R_2= Ph), an indication of the extreme sensitivity of carbene rearrangements to substituents. Moreover an elegant study of the formation of 4-methoxycyclopentenes from the cleavage of (6) by sodium methoxide in methanol,[5] indicates that a planar cyclopentenylidene is not involved; thus the two labelled species (6, R=H, R'=D) and (6, R=D, R'=H) lead to different diastereoisomers of 3,5-dideuterio-4-methoxycyclopentene, consistent with trapping of a 'foiled' carbene (4) by methanol. In order to examine the nature of the 'cyclopentenylidene' intermediate in the dibromocyclopropanemethyl lithium reaction, we have examined the symmetrically substituted reaction in Scheme 1 using labelled compounds.



Scheme 1

To establish the formation of an intermediate with the vertical plane of symmetry in Scheme 1, compound (10) was prepared in which the marked carbons were labelled with ^{13}C.[6] Reaction of (10) with methyl lithium in ether at -78°C for 5min, quenching with water at that temperature, and removal of the solvent at -40° and 1mmHg and flash distillation of the residue at 20° and 1mmHg led to labelled (9).[**] The ^{13}C spectrum showed signals at δ_c 136.4 (C-3), 45.2 (C-5), 13.2 (CH_3-C-1) and 12.5 (CH_3-C-2) which were all six times as large (within 10%) when compared to the signal at δ 129 (C-4) as those in the unlabelled compound. The proton spectrum showed only one olefinic hydrogen (that at δ 6.29) with large ^{13}C-side bands (ca.6% total, J 161Hz). Moreover the signal for the methylene group of (9) also showed large side bands (6% total, J 125Hz). These results are consistent with a reaction proceeding through an intermediate (8) having a vertical plane of symmetry as shown in Scheme 1.[8]



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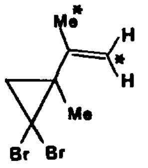

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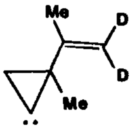
* = ^{13}C



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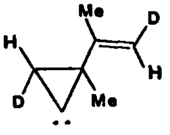

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Since the above results indicate an intermediate involving the vertical plane of symmetry, if a second plane of symmetry is also present both (11) and (12) should lead to the same ratio of hydrogen to deuterium migration in forming a cyclopentadiene from (13) or (14), determined by the primary isotope effect for the 1,2-shift (ignoring secondary effects due to differences between CH_2, CHD, and CD_2 groups). If, however, only intermediates lacking this plane are involved then either deuterium or hydrogen migration may be preferred in (14), depending on the nature of the intermediate. Treatment of the dibromide (15)[9] with methyl lithium in ether at -78°C followed by work up as before led to a mixture of (16, R= H, R'= D) and (16, R= D, R'= H); the ratios of the total alkene to methylene signals in the ^1H and ^2H n.m.r. spectra were 2.2 and 0.43 respectively, indicating an average isotope effect of 2.25 for migration of hydrogen relative to deuterium; isotope effects of this order have been reported for insertion of carbenes (carbenoids) into C-H bonds.[11] Reaction of the E,E-dideuterio-compound (17)[10] with methyl lithium in ether as above led to a 6:1 mixture of (18, R_1= H, R_2= D) and (18, R_2= D, R_1= H); the ^2H n.m.r. showed one major signal at δ 6.06 corresponding to H_3 in (9); a minor peak was observed at δ 6.14 corresponding to H_4. Hydrogen rather than deuterium migration is therefore preferred. There can be no second plane of symmetry in the intermediate; moreover the preferred migration of hydrogen, ie. of H_b and H_d in (1, R_1= R_2= Me) is consistent with movement of H_a in a foiled carbene (4)[3] as expected from the alignment of the C-H_a bond with the 'vacant' carbene orbital.

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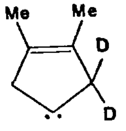

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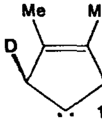

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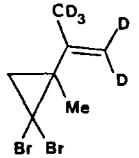

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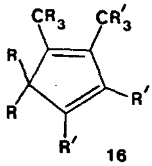

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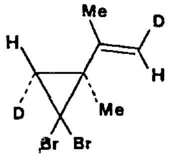

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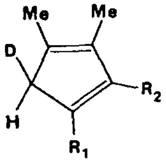
1. L.Skattebol, Chem. and Ind., 1962, 2146; Tetrahedron, 1967, 23, 1107. For a review see P.Weyerstahl, 'Cyclopropanes', in The Chemistry of Functional Groups, Suppl.D, Eds. S.Patai and Z.Rappoport.
2. K.H.Holm and L.Skattebol, Tetrahedron Letters, 1977, 2347.
3. W.W.Schoeller and U.H.Brinker, J.Amer.Chem.Soc., 1978, 100, 6012.
4. K.H.Holm and L.Skattebol, Acta.Chem.Scand., 1984, 38B, 783.
5. W.Kirmse, P.Van Chiem and P.G.Henning, J.Amer.Chem.Soc., 1983, 105, 1695.
6. Reaction of methyl methacrylate with two equivalents of methyl magnesium iodide (prepared from methyl iodide enriched with 12% ^{13}C) in ether gave labelled 2,3-dimethylbut-3-en-2-ol (60%) which was converted to (19) by reaction with bromoform-aq.sodium hydroxide-cetrimide under phase transfer conditions. Treatment with phosphorus oxychloride in pyridine led to (10); the ^1H n.m.r. showed ^{13}C side bands on both vinylic hydrogen signals (J 155Hz) and on the methyl signal at δ1.94 (J 127Hz). The ^{13}C n.m.r. showed a major enhancement in the signals at 113.8 and 20.2 compared to those in unlabelled (10) (δ_C 145.9s, 113.8t, 36.6s, 36.2s, 34.1t, 23.8q, 20.2q).
7. Unlabelled (9) showed δ_H 6.2 (1H, d, J 5.2Hz), 6.06 (1H, d, J 5.2Hz), 2.76

(2H, br.s), 1.91 (3H, s), 1.83 (3H, s).



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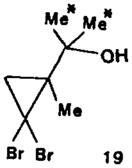

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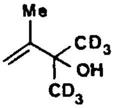

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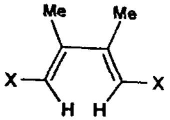

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8. The effect of labelling on the proton spectrum also shows that the olefinic signal at 6.29 must be that due to the hydrogen on C-4.
9. Prepared by treatment of isopropenyl magnesium bromide with $^2H_6$-acetone to give (20), reaction with bromoform- aq.NaOH-cetrimide and then dehydration of the resulting dibromcyclopropane with $POCl_3$-pyridine. Compound (15) showed δ_H 1.92 (1H, d, J 7Hz), 1.56 (1H, d, J 7Hz), 1.48 (3H, s); δ^2_H 4.95 (1H, br.s), 4.81 (1H, s), 1.91 (3H, s).
10. Reaction of 2,3-dimethylbuta-1,3-diene with 2mol.equiv. of bromine in dichloromethane at -78° followed by dehydrohalogenation with potassium hydroxide at 0.01mmHg and 100° (E.Z.Said and A.E.Tipping, J.Chem.Soc. Perkin I, 1972, 1399, and private communication) gave a mixture of 1,4-dibromo-2,3-dimethylbuta-1,3-dienes. Fractional crystallisation from methanol at low temperature led to the major isomer, (21, X=Br), m.p. 19-21°, which showed δ_H 6.39 (2H, br.s), 1.97 (6H, br.s); ν_{max} 1574m, 757s, 727s cm^{-1}. Reaction with zinc-copper couple in D_2O- diglyme (L.M.Stephenson, R.V.Gemmer and S.P.Current, J.Org. Chem., 1977, 42, 212) led to (21, X=D) which showed δ_H 5.04 (2H, s), 1.92(6H, s), together with a small peak at 4.97 (0.25 of the size of that at 5.04). The E-stereochemistry, and therefore that of (21, X=Br), was deduced from the fact that the lower field alkene signal of 2,3-dimethylbuta-1,3-diene was absent in the deuterated species (see eg., R.Harris, Org.Magn.Resn., 1977, 9, 483). The ^2H n.m.r. showed signals at 4.97 and 5.04 in ratio 12:1, indicating 92:8 E- to Z-deuteration. Reaction of (21, X= D) with bromoform- aq.NaOH-cetrimide at 20° led to (17). The ^2H-n.m.r. of this showed two major signals at chemical shifts corresponding to those of H_a and H_c in (5, R_1= R_2= Me) and two minor signals corresponding to H_b and H_d again in ratio 12:1.
11. M.J.Goldstein and S.J.Baum, J.Amer.Chem.Soc., 1963, 85, 1885; M.J.Goldstein and W.R.Dolbier, ibid., 1965, 87, 2293. See also W.Kirmse, H-D.von Scholz and H.Arold, Annalen, 1968, 711, 22.
12. The results available do not allow an exact figure for the preference to be determined but, assuming equal isotope effects for migration of H_a and H_b in (4), an estimate of 4 may be made.

** Model n.m.r. studies showed that (9) was stable under these conditions.

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