# Rearrangements of Pinane Derivatives. Part VII.[1] Reactions of ' High Energy ' 6,6-Dimethylnorpinan-2-yl Cations

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The 6,6-dimethylnorpinan-2-yl cation has been generated (a) as a solvated ion, or (b) in close proximity to a water molecule, or (c) a counterion and the products of its decomposition have been determined in each case. The reactions have been compared with the deamination of 2α-amino-6.6-dimethylnorpinane : the results suggest that the latter reaction involves a high energy classical ion associated with a counterion.

A COMPARISON of the products of deamination and toluene-$p$-sulphonate solvolysis of the appropriate pinan-3-yl derivatives led to the conclusion that the deamination was best rationalised in terms of the intermediacy of unsolvated classical ions.[2] This is consistent with the general picture of deamination in bicyclic systems.[3] $exo$-Norbornylamine is believed to react $via$ competing pathways only one of which involves σ-bond participation.[4] Deamination of nor-pinan-2-yl derivatives involves rearrangement, but the symmetry of the system conceals the reaction stereochemistry.[5]

The 6,6-dimethylnorpinan-2-yl system is ideal for testing the effects of σ-bond participation on deamination, since it can form either a classical ion which can react $via$ two independent pathways or a delocalised ion which can react $via$ only one pathway.[6,7] Since

either a counterion[8] or the water molecule produced in the deamination reaction may influence the behaviour of the cation, we have formed the 6,6-dimethylnorpinan-2-yl cation under conditions which would favour[9] its production (a) as part of an ion pair, (b) in association with a water molecule, and (c) as a solvated ion. The products of decomposition of these systems are compared with the products of deamination.

EXPERIMENTAL

$Materials.$—The 6,6-dimethylnorpinan-2-ols were prepared[10] from 6,6-dimethylnorpinan-2-one,[11] and 6,6-di-methylnorpin-2-ene[12] was obtained from pin-2-en-10-al.[13]

[1] Part VI, P. I. Meikle and D. Whittaker, $J.C.S. Perkin II$, 1974, 318.

[2] D. G. Cooper and R. A. Jones, $J. Chem. Soc. (C)$, 1971, 3920.

[3] L. Friedman, in ' Carbonium Ions,' eds. G. A. Olah and P. von R. Schleyer, Wiley-Interscience, New York, 1970, p. 655.

[4] J. A. Berson and A. Remanick, $J. Amer. Chem. Soc.$, 1964, 86, 1749; E. J. Corey, J. Casanova, P. A. Vatakencherry, and R. Winter, $ibid.$, 1963, 85, 169.

[5] W. Kirmse and R. Siegfried, $J. Amer. Chem. Soc.$, 1968, 90, 6564.

[6] E. C. Friedrich and S. Winstein, $J. Amer. Chem. Soc.$, 1964, 86, 2721.

[7] J. R. Salmon and D. Whittaker, $J. Chem. Soc. (B)$, 1971, 1249.

[8] T. Cohen and E. Jankowski, $J. Amer. Chem. Soc.$, 1964, 86, 4217.

[9] H. Indyk and D. Whittaker, $J.C.S. Perkin II$, 1974, 313.

[10] S. Winstein and N. J. Holness, $J. Amer. Chem. Soc.$, 1955, 77, 3054.

[11] W. Hückel and E. Gelchsheimer, $Annalen$, 1959, 625, 12.

[12] H. E. Eschinazi and H. Pines, $J. Org. Chem.$, 1995, 24, 1369.

[13] W. D. Stallcup and J. E. Hawkins, $J. Amer. Chem. Soc.$, 1941, 63, 3339.

*2α-Amino-6,6-dimethylnorpinane.*— 6,6-Dimethylnorpinan-2-one was converted into its oxime (a yellow oil), then reduced by refluxing with lithium aluminium hydride in tetrahydrofuran for 20 h.[14] After conventional extraction procedures, the amine was purified by precipitation of its hydrochloride from ether. The *amine hydrochloride*, a white solid, decomposed slowly over a wide temperature range above 150° (Found: C, 61·3; H, 10·1; Cl, 20·7; N, 7·9. $C_9H_{18}ClN$ requires C, 61·5; H, 10·2; Cl, 20·2; N, 8·0%), $\nu_{max.}$ 1610 and 2000 cm⁻¹, τ 6·24br (C-2 proton) and 8·74 and 8·78 (sharp, methyl groups). The absence

RESULTS AND DISCUSSION

In experiments on the formation and decomposition of the pinan-2-yl cation, product mixtures were obtained consistent with formation of a solvated ion by addition of acid to olefin in aqueous dioxan, and of an ion pair by addition of acid to olefin in anhydrous acetic acid. Reaction of the alcohol with acid in anhydrous acetic acid gave the ion in close association with a water molecule. Products of reactions of 6,6-dimethylnorpin-2-ene and the 6,6-dimethylnorpinan-2-ols under these

TABLE 1

Products of acid-catalysed rearrangement of 6,6-dimethylnorpin-2-ene and the 6,6-dimethylnorpinan-2-ols in dioxan–water (4 : 1 v/v)

| Substrate | Temp. (°C) | Perchloric acid (M) | Time (h) | Olefin 1 | Olefin 2 | Olefin 3 | (VI) | (VII) | (VIII) | (IX) | (X) | (XI) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6,6-Dimethylnorpin-2-ene | 105 | 0·37 | 23 | 6 | 12 | 6 | 5 | 5 | | 45 | 8 | |
| | | | 48 | 2 | 11 | 10 | 6 | 5 | | 45 | 8 | |
| 6,6-Dimethylnorpinan-2α-ol | 70 | 0·025 | 3·5 | | | | 52 | 4 | 35 | 9 | | |
| | | | 16·5 | | | | 56 | 4 | 27 | 10 | | |
| 6-6-Dimethylnorpinan-2β-ol | 70 | 0·025 | 24 | | | | 4 | 25 | 12 | | 22 | 37 |
| | | | 162 | | | | 2 | 23 | 10 | | 25 | 28 |

TABLE 2

Products of acid-catalysed rearrangement of 6,6-dimethylnorpin-2-ene and the 6,6-dimethylnorpinan-2-ols in anhydrous acetic acid

| Substrate | Catalyst (0·1M) | Temp. (°C) | Time (h) | Olefin 1 | Olefin 2 | Olefin 3 | Acetate of (VI) | Acetate of (VII) | Acetate of (VIII) | Acetate of (IX) | Acetate of (X) | Acetate of (XI) | (VI) | (IX) | (X) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6,6-Dimethyl-norpin-2-ene | HClO₄ | 40 | 3 | | | 1 | 4 | 8 | 8 | 70 | 6 | 2 | | | |
| | p-MeC₆H₄·SO₃H | 90 | 3 | 2 | | 4 | 5 | 8 | 11 | 66 | 4 | 2 | | | |
| 6,6-Dimethyl-norpinan-2α-ol | H₂SO₄ | 25 | 0·25 | | | 1 | 13 | 2 | 27 | 21 | | | 25 | 3 | |
| | HClO₄ | 25 | 0·025 | | | 1 | 9 | 2 | 19 | 23 | | | 39 | 2 | |
| 6,6-Dimethyl-norpinan-2β-ol | H₂SO₄ | 25 | 0·5 | 2 | 8 | | | 3 | 29 | 21 | 7 | 3 | 3 | | 7 |
| | HClO₄ | 25 | 0·08 | 13 | 8 | 2 | | 2 | 18 | 22 | 8 | 3 | 1 | | 13 |

of methyl proton peaks attributable to the β-isomer is taken as evidence of the stereochemical purity of the product.[15]

*Deamination.*—The method of Jones was used.[2]

*Deoxidation.*—The method described by Jones was used.[16]

*Identification of Products.*—Reaction mixtures were analysed by g.l.c. as outlined in earlier papers.[17] The alcohols in the reaction mixtures were separated by preparative scale g.l.c., and the i.r. and n.m.r. spectra of each were obtained. 3,3-Dimethylnorbornan-2-*endo*-ol was identified by comparison with a sample prepared by reduction of 3,3-dimethylnorbornan-2-one with lithium aluminium hydride. We thank Dr. E. C. Friedrich (University of California, Davies, California) for supplying spectroscopic data for the other alcohols, on which our identifications are based. Three olefinic products (olefins 1—3 in Tables 1 and 2) were not identified.

*Kinetics.*—Rate constants for the disappearance of substrate were obtained as outlined earlier.[17] Although there is some evidence of reversible olefin protonation,[9,17] the observed values are probably close to the rates of olefin protonation. Rates quoted are accurate to ±5%.

[14] D. R. Smith, M. Maienthal, and J. Tipton, *J. Org. Chem.*, 1952, **17**, 294.

[15] R. J. Abraham, M. A. Cooper, J. R. Salmon, and D. Whittaker, *Org. Magnetic Resonance*, 1972, **4**, 489.

conditions are given in Tables 1 and 2. The rate constants for reactions of all three substrates in aqueous dioxan are given in Table 3.

TABLE 3

Rate constants for the acid-catalysed rearrangement of 6,6-dimethylnorpin-2-ene and the 6,6-dimethylnorpinan-2-ols in dioxan–water (4 : 1 v/v) catalysed by perchloric acid

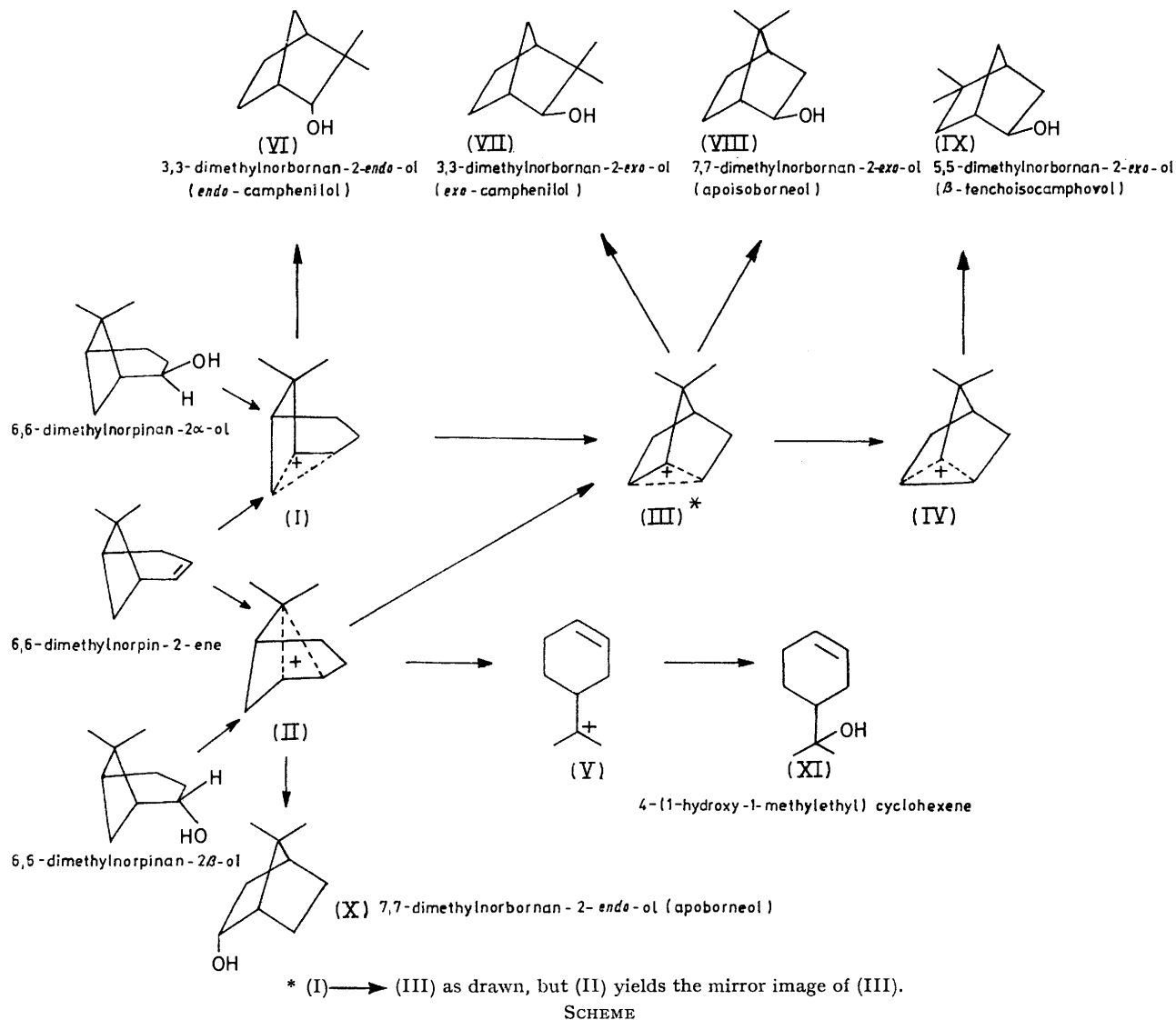| Substrate | [HClO₄]/M | Temp. (°C) | $k_1 \times 10^6$/ mol l⁻¹ s⁻¹ |
|---|---|---|---|
| 6,6-Dimethylnorpin-2-ene | 0·366 | 90·0 | 1·45 |
| | | 97·5 | 3·88 |
| | | 105·0 | 9·75 |
| 6,6-Dimethylnorpinan-2α-ol | 0·025 | 70·0 | 2·56 |
| | | 90·0 | 24·7 |
| 6,6-Dimethylnorpinan-2β-ol | 0·025 | 70·0 | 0·17 |
| | | 90·0 | 2·44 |

In anhydrous acetic acid, the alcohols reacted too fast for accurate rate measurements. Reaction of the olefin with sulphuric acid in anhydrous acetic acid did

[16] Ee Chong-Sen, R. A. Jones, and T. C. Webb, *J.C.S. Perkin II*, 1974, 38; J. T. Keating and P. S. Skell in 'Carbonium Ions,' vol. II, eds. G. A. Olah and P. von R. Schleyer, Wiley-Interscience, New York, 1970, p. 573.

[17] C. M. Williams and D. Whittaker, *J. Chem. Soc. (B)*, 1971, 668.

not show first-order behaviour, so this reaction was not used in product studies; however first-order kinetics were shown by the reactions with perchloric acid and toluene-$p$-sulphonic acid in anhydrous acetic acid. Rates of reaction of the alcohols are in satisfactory agreement with those reported earlier,[6] being greater

The basic pattern of the rearrangements is consistent with the modified version[7] of Winstein's original theory,[6] and is outlined in the Scheme. 4-(1-Hydroxy-1-methylethyl)cyclohexene was not observed as a product of olefin hydration, since it is unstable under the reaction conditions.[9]



(VI)
3,3- dimethylnorbornan-2-endo-ol
( endo - camphenilol )

(VII)
3,3-dimethylnorbornan-2-exo-ol
( exo - camphenilol )

(VIII)
7,7-dimethylnorbornan-2-exo-ol
( apoisoborneol )

(IX)
5,5-dimethylnorbornan- 2-exo-ol
(β-fenchoisocamphovol )

6,6-dimethylnorpinan -2α-ol

(I)

6,6-dimethylnorpin- 2- ene

(II)

6,6-dimethylnorpinan - 2β-ol

(X) 7,7-dimethylnorbornan - 2- endo-ol ( apoborneol )

(III)*

(IV)

(V)

(XI)

4-(1-hydroxy -1- methylethyl) cyclohexene

* (I)——► (III) as drawn, but (II) yields the mirror image of (III).

SCHEME

than for butan-2-ol [18] by factors of *ca.* $10^3$ for the β-alcohol and $10^4$ for the α-isomer.

From these data, activation enthalpies and entropies were calculated:

|  | $\Delta H^{\ddagger}$/ kcal mol$^{-1}$ | $\Delta S^{\ddagger}$/ cal mol$^{-1}$ K$^{-1}$ |
|---|---|---|
| Hydration of 6,6-dimethylnorpin-2-ene | 34 | 10 |
| Rearrangement of 6,6-dimethyl-norpinan-2α-ol | 27 | 7 |
| Rearrangement of 6,6-dimethyl-norpinan-2β-ol | 32 | 16 |

For comparison, the activation enthalpy for the acid-catalysed racemisation of butan-2-ol [18] is 34 kcal mol$^{-1}$.

Effects of external stabilisation would be expected to be greater than for the tertiary pinan-2-yl cation; indeed the water molecule produced in heterolysis of the α-alcohol in acetic acid can capture up to 39% of the ion. The effect is less in the reaction of the β-alcohol, since the *gem*-dimethyl group has less shielding effect. The counterion has less effect than in the tertiary system, possibly because the ion formed, like the pinan-2-yl ion, has its charge delocalised, but a much greater amount of positive charge is on C-1 rather than C-2 in comparison with the tertiary ion. Hence

[18] C. A. Bunton, K. Khaleeluddin, and D. Whittaker, *J.C.S. Perkin II*, 1972, 1154.

the positive charge is moved rapidly away from the counterion, diminishing its effect. Since the same argument could be applied to the effect of the associated water molecule, it must be assumed that the latter is more mobile than a counterion, possibly because it is smaller and closer to the ion centre.

The foregoing results have been compared with those for the deamination of 2α-amino-6,6-dimethyl-pinane (Table 4). The products show a close parallel

increase the rate of separation of an ion pair, but not affect a direct intramolecular displacement of the leaving group. We therefore repeated the deamination in 4 : 1 v/v acetic acid–water, and in water. The results are given in Table 4. Changing the solvent to aqueous acetic acid produced no significant changes in the product composition, but changing to water resulted in the formation of 6% of the tertiary alcohol (XI). This product has not been observed, and would not be

TABLE 4

Products of (A) deamination of 2α-amino-6,6-dimethylpinan and (B) deoxidation of 6,6-dimethylnorpinan-2α-ol

| | | | | Composition of products (mole %) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Reaction | Solvent | Temp. (°C) | Time (h) | 6,6-Dimethyl-norpinan-2α-yl acetate | Acetate of (VI) | Acetate of (VII) | Acetate of (VIII) | Acetate of (IX) | 6,6-Dimethyl-norpinan-2α-ol | (VI) | (VII) | (VIII) | (IX) | (XI) |
| (A) | AcOH | 30 | 2 | 7 | 18 | 6 | 31 | 8 | 1 | 7 | | 2 | 1 | |
| | AcOH–H₂O (4 : 1 v/v) | 30 | 2 | 4 | 14 | 4 | 24 | 6 | 1 | 13 | | 10 | 4 | |
| | H₂O | 30 | 2 | | | | | | | 39 | 7 | 34 | 13 | 6 |
| (B) | H₂O | 100 | 3 | | | | | | | 8 | | 6 | 1 | 68 |

to those from the acid-catalysed reaction of the 2α-alcohol, in that reaction proceeds entirely through the ion (I). Reaction via the ion (II) would give the tertiary alcohol (XI) and 7,7-dimethylnorbornan-2-endo-ol (X) or their acetates; both are absent from the reaction mixture. The parallel between reactions of alcohol and amine is, however, only superficial. The amine yields less 5,5-dimethylnorbornan-2-exo-yl acetate [acetate of (IX)] formed from the ion (IV), and more of the acetates of 7,7-dimethylnorbornan-2-exo-ol (VIII) and 3,3-dimethylnorbornan-2-exo-ol (VII), formed from the ion (III). Since the ion (IV) is formed from (III) by a 2,6-hydride shift, which has been shown to be of less importance in conditions favouring a short lifetime of (III),[19] we conclude that the ion produced in deamination has a shorter lifetime than the ion from alcohol heterolysis, as would be expected. The water molecule has less effect on the ion than that produced in alcohol heterolysis, consistent with the expected higher energy of the ion from the amine, which also accounts for its greater reactivity.

The stereospecificity of formation of the ion (I) from 2α-amino-6,6-dimethylnorpinane indicates that the reaction cannot involve an unsolvated classical ion. Either the ion (I) must be formed directly from the amine, the necessary electron shift occurring during loss of nitrogen, or the amine must yield a classical ion with a counterion holding a position close to the leaving group.[20] Displacement of this ion by an electron shift would then give the ion (I). This latter explanation is consistent with the results of Berson,[4] which require some reaction of a classical ion, and would also be consistent with our stereospecific reaction.

To distinguish between these routes one could raise the dielectric constant of the medium, which would

expected, from the ion (I). It could, however, arise from a classical 6,6-dimethylnorpinan-2-yl cation, either directly or via (II). The change in solvent from acetic acid to water is, however, substantial, and also involves a change of counterion, so the result should be considered as no more than an indication that the reaction in acetic acid involves initial formation of a classical ion as part of an ion pair, the counterion being displaced by an electron shift faster than the classical ion can react by any other route.

An unexpected feature of the reaction in water was the failure to form endo-7,7-dimethylnorbornan-2-ol, indicating that the classical ion underwent ring opening directly, rather than via the ion (II). To examine the reactions of high energy ions under conditions which would not favour association with a counterion, we carried out the deoxidation of 6,6-dimethylnorpinan-2α-ol. The results of this experiment are also in Table 4. The dominant product was the ring-opened product (XI). This arose without any corresponding amount of the expected product of decomposition of the ion (II), 3,3-dimethylnorbornan-2-exo-ol (VII), suggesting that it was formed via a classical ion. We suggest that this is probably the source of ring-opened product in aqueous deamination.

Our results are consistent with the theory of Collins[10] that reaction of amine with nitrous acid gives rise to a high energy classical ion with an associated counterion. Displacement of the counterion by an electron shift is rapid, so that reaction of an undelocalised ion can be detected only under extreme conditions. Under normal conditions the reaction proceeds entirely through the delocalised ion.

[19] A. Colter, E. C. Friedrich, N. J. Holness, and S. Winstein, J. Amer. Chem. Soc., 1965, 87, 378.
[20] C. J. Collins, Accounts Chem. Res., 1971, 4, 315.

It is probable that separation of an ion pair, particularly in a good ionising solvent, would be fast compared with intermolecular attack on the cation. Consequently, in a system in which delocalisation was unlikely, products consistent with reaction of an unsolvated or a solvated ion would be expected, as has been observed.[2]