Rearrangements of Pinane Derivatives. Part VI.[1] Rearrangement *via* a [1,3] Shift of Carbon during Reaction of 2α*H*-10-Aminopinane (*cis*-Myrtanylamine) with Nitrous Acid[2]

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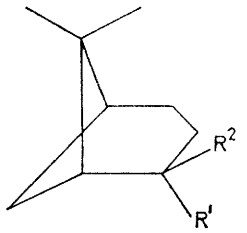
Reaction of 2α*H*-10-aminopinane (*cis*-mytranylamine) with nitrous acid gives a product mixture which includes six different rearranged carbon skeletons. In addition to rearrangements observed in the ester solvolysis, ring expansion to the bicyclo[4.1.1]octane system is observed, together with an unusual ring expansion *via* a [1,3] carbon shift to give the bicyclo[2.2.2]octane system.

SOLVOLYSES of 2α*H*- (I; $R^1 = H$, $R^2 = CH_2OTs$) and 2β*H*- (I; $R^1 = CH_2OTs$, $R^2 = H$) pinan-10-yl toluene-*p*-sulphonates in methanol containing sodium methoxide has been shown to proceed by simultaneous unimolecular and bimolecular reactions.[3] The unimolecular reaction involves a rate-determining hydride shift to give the pinan-2-yl cation; the reaction path subsequently follows the established route for this reaction,[4] giving a mixture of pinanyl, bornyl, fenchyl, and terpinyl derivatives.



(I)

In these reactions, the cyclobutane ring can either open or expand to cyclopentane, but there is no trace of expansion of the cyclohexane ring to cycloheptane. The first step of the reaction sequence involving the cyclobutane ring, hydride migration, is favoured over a carbon migration, in agreement with the lower energy needed for the former process relative to the latter.[5] Formation of a carbonium ion by reaction of an amine with nitrous acid is, however, known to favour ring expansion over formation of a carbonium ion by ester heterolysis,[5] consistent with evidence that this reaction involves a high energy carbonium ion.[6] Since reactions involving change in size of the cyclohexane ring of the pinane skeleton are extremely rare, we used the high energy ion in an attempt to carry out a ring expansion.[7]

EXPERIMENTAL

2α*H*-10-aminopinane (*cis*-myrtanylamine) was prepared from pin-2(10)-ene by reaction of the borane complex with hydroxylamine *O*-sulphonic acid.[8] The hydrochloride was prepared by passing dry hydrogen chloride into an ethereal solution of the amine.

5,5-*Dimethylbicyclo*[2.2.2]*oct*-2-*yl Acetate*.—Reduction of dimedone with lithium aluminium hydride [9] gave 5,5-dimethylcyclohex-2-enol, b.p. 76—78° at 10 mmHg (lit.,[9] 83—84° at 17 mmHg). Heating the product to 140° with potassium hydrogen sulphate [10] gave 5,5-dimethylcyclohex-1,3-adiene, b.p. 110—112° (lit.,[10] 111·6—111·8°), τ 9·05 (6H, m, 2 × Me), 7·95 (2H, m), and 4·2—4·7 (4H, m). Reaction of 5,5-dimethylcyclohexa-1,3-diene (17 g) with vinyl acetate (27 g) and a trace of hydroquinone for 4 days at 180°, following the published procedure for synthesis of bicyclo[2.2.2]oct-5-en-2-ol,[11] gave a mixture of 8,8-dimethylbicyclo[2.2.2]oct-5-en-2-yl acetate (56% by g.l.c.) and the 3-acetoxy-isomer (34%). These were separated by g.l.c. On oxidation,[12] both gave a single ketone, but reduction of the 2-ketone with sodium borohydride gave a mixture of the *exo*- and *endo*-alcohols, separable by g.l.c., while the 3-ketone gave only the *endo*-alcohol, on account of steric effects of the *gem*-dimethyl group. Although these three alcohols can be resolved by g.l.c., the acetates have not been resolved. Hydrogenation of 8,8-dimethylbicyclo[2.2.2]oct-5-en-2-yl acetate over 10% palladium–charcoal in ethyl acetate at atmospheric pressure gave 5,5-dimethylbicyclo-[2.2.2]oct-2-yl acetate.

6,6-*Dimethylbicyclo*[3.2.1]*oct*-2-*yl Acetate*.—Treatment of 5,5-dimethylbicyclo[2.2.2]oct-2-yl acetate with lithium aluminium hydride gave the corresponding alcohol, a white solid, m.p. 96—97°; reaction with toluene-*p*-sulphonyl chloride in pyridine [13] gave the toluene-*p*-sulphonate as a pale yellow oil. Acetolysis of the toluene-*p*-sulphonate in anhydrous acetic acid containing sodium acetate at 48·5° for 48 h gave a mixture [14] of 5,5-dimethylbicyclo[2.2.2]oct-2-yl acetate and 6,6-dimethylbicyclo[3.2.1]oct-2-yl acetate in the ratio 8 : 5. These acetates could only be separated by preparative scale g.l.c.

4,4-*Dimethylbicyclo*[3.2.1]*oct*-2-*yl Acetate*.—Oxidation of

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camphene with lead tetra-acetate gave [15] 4,4-dimethylbicyclo[3.2.1]octan-2-one; reduction with sodium borohydride gave a mixture of 66% of the *endo*-alcohol and 34% of the *exo*-alcohol. Acetylation of the mixture with acetic anhydride and sodium acetate gave an oil which is a mixture of 4,4-dimethylbicyclo[3.2.1]oct-*endo*- and -*exo*-2-yl acetates. We were unable to resolve the acetate mixture by g.l.c., but their retention times differed from those of all acetates from our product mixture.

3-*Acetyl*-2,2-*dimethylcyclobutylacetyl Chloride*.—A commercial sample of 3-acetyl-2,2-dimethylcyclobutylacetic acid (1·12 g) was converted into the sodium salt by reaction with sodium hydride (0·145 g) in dry benzene. Addition of a solution of oxalyl chloride (0·8 ml) in dry benzene, followed by stirring at 70° for 2 h, filtration through Celite, and removal of the solvent gave the acid chloride as a yellow oil, $\nu_{max.}$ 1700 and 1795 cm^{-1} (*cf.* for the acid, $\nu_{max.}$ 1675, 1725, and 3220 cm^{-1}), τ 9·20 (Me), 8·72 (Me), and 8·05 (Me).

Methyl 3-(3-*Acetyl*-2,2-*dimethylcyclobutyl*)*propionate*.—Treatment of the above acid chloride (1·06 g) with an excess of diazomethane in ether at 0° for 1 h gave, after removal of solvent, the diazo-ketone as a yellow oil (1·07 g). The i.r. spectrum showed the peak at 1795 cm^{-1} to have disappeared, while that at 1700 cm^{-1} remained, and peaks at 1635 and 2100 cm^{-1} had appeared. To a solution of this diazoketone (1·07 g) in dry methanol (25 ml) at 60° was added over a period of 15 min a slurry of silver oxide (made by treatment of 1 ml of 10% aqueous silver nitrate with potassium hydroxide) in dry methanol. The mixture was refluxed for 1 h, cooled, decolourising charcoal added, and filtered through Celite. Removal of the solvent left a yellow oil (0·89 g), $\nu_{max.}$ 1700 and 1735 cm^{-1}, τ 9·20 (Me), 8·75 (Me), 8·05 (Me), and 6·41 (Me).

Methyl 3-(2,2-*Dimethyl*-3-*methoxycarbonylcyclobutyl*)*propionate*.—The method of Welenkiwar *et al.*[16] was used. A bromoform reaction on the above ester gave the diacid, whose i.r. spectrum showed a broad maximum at 1700 cm^{-1}, and n.m.r. spectrum showed methyl proton peaks at τ 9·05 and 8·82. Esterification with diazomethane gave the dimethyl ester, b.p. 92° at 0·25 mmHg, $\nu_{max.}$ 1720 cm^{-1}, τ 9·08 (Me), 8·80 (Me), and 6·38 (2 × Me).

Acyloin Condensation.—To a suspension of sodium (2·3 g) in refluxing toluene (100 ml) was added, over a period of 2 h, a solution of the above diester (5·0 g) and chlorotrimethylsilane (20 ml) in toluene (50 ml). The mixture was then refluxed and stirred for 20 h. On cooling, filtration, and removal of solvent, a yellow oil (5·1 g) was left. This was refluxed in ethanol under nitrogen for 6 h, the solvent removed, and the product chromatographed on alumina. Excess of silane and diester were eluted with light petroleum, and the acyloin with diethyl ether; it had $\nu_{max.}$ 3450 and 1715 cm^{-1}. Treatment of the acyloin with toluene-*p*-sulphonyl chloride in pyridine gave the toluene-*p*-sulphonate, $\nu_{max.}$ 1725, 1190, and 1180 cm^{-1}. Reduction of this ester with lithium aluminium hydride gave a pale yellow oil, which g.l.c. showed to be the expected mixture of four alcohols, the *exo*- and *endo*-isomers of 7,7-dimethylbicyclo-[4.1.1]octan-2-ol and -3-ol. The penultimate peak of the g.l.c. trace had the same retention time as one of the deamination products after lithium aluminium hydride reduction. On acetylation with acetic anhydride and sodium acetate, it gave a product with identical i.r. spectrum and retention time to one of the deamination products of 2α*H*-10-aminopinane. The last peak of the trace was identical in retention time to the main unidentified deamination product both as alcohol and acetate. Our condensation gave it in very poor yield (*ca.* 1% of the product) so that we were unable to record its i.r. spetrum.

6,6-*Dimethylnorpin*-3-*en*-7-*one*.— 6,6-Dimethylnorpin-3-en-2-one [17] (283 mg) in cyclohexane (28 ml) was irradiated [18] for 3 h at 350 nm. Chromatography on silica gel, with 3% ether in pentane gave the 7-one (142 mg), $\nu_{max.}$ 1780 cm^{-1}. Hydrogenation at room temperature over 10% palladium–charcoal gave the saturated ketone, $\nu_{max.}$ 1770 cm^{-1}, as an oil.

Attempts to add diazomethane to either the saturated or unsaturated ketone, with or without catalysts, to give the bicyclo[3.2.1]octan-2-one system, were all unsuccessful; the strained ring appears to be resistant to addition reactions.

Reaction of 2αH-10-*Aminopinane with Nitrous Acid*.—Reaction of 2α*H*-10-aminopinane (as its hydrochloride) with nitrous acid in acetic acid followed the method of Jones,[19] except that sodium acetate was not used. Extraction of products and g.l.c. analysis followed previous techniques,[20] and products were identified by comparison of i.r. spectra with those of known samples.[4]

The main unknown product (17%) had $\nu_{max.}$ 609, 909, 969, 1013, 1024, 1043, 1110, 1131, 1147, 1241, 1365, 1449, 1469, and 1731 cm^{-1}, τ 8·89 (Me) and 9·00 (Me). Its retention time on g.l.c. analysis was identical to that of a very minor component of the bicyclo[4.1.1]octanol synthesis, but we were unable to obtain an i.r. spectrum of the latter, and so must regard the product as unidentified.

The last product (3%) had a retention time identical with that of 5,5-dimethylbicyclo[2.2.2]octan-2-ol.

RESULTS AND DISCUSSION

Reaction of 2α*H*-10-aminopinane hydrochloride with nitrous acid in acetic acid gave a mixture of products, the analysis of which is given in the Table. The products clearly show the complex nature of the reaction; they

Products of reaction of 2α*H*-10-aminopinane with sodium nitrite in acetic acid containing sodium acetate at 25°

	Product (%)
Unknown	(13)
p-Mentha-1,8-diene	(2)
1,3,3-Trimethylnorborn-2-yl acetate	(1)
Pinan-2α-ol	(2)
1,3,3-Trimethylnorbornan-2α-ol	(2)
Bornyl acetate + pinan-2β-ol	(3)
p-Menth-1-en-4-ol	(2)
p-Menth-1-en-8-ol	(5)*
p-Menth-1-en-8-yl acetate	(5)
5,5-Dimethylbicyclo[2.2.2]oct-2-yl acetate	(9)*
6,6-Dimethylbicyclo[3.2.1]oct-2-yl acetate	(11)*
7,7-dimethylbicyclo[4.1.1]oct-2-yl acetate	(11)*
Unknown	(17)
Unknown	(3)

Analysis by g.l.c. on a 14 ft packed capillary column 15% C20M on Chromosorb W at 170°. Components <1% are neglected.

* Identities checked by examination of the i.r. spectra of samples separated by preparative g.l.c.

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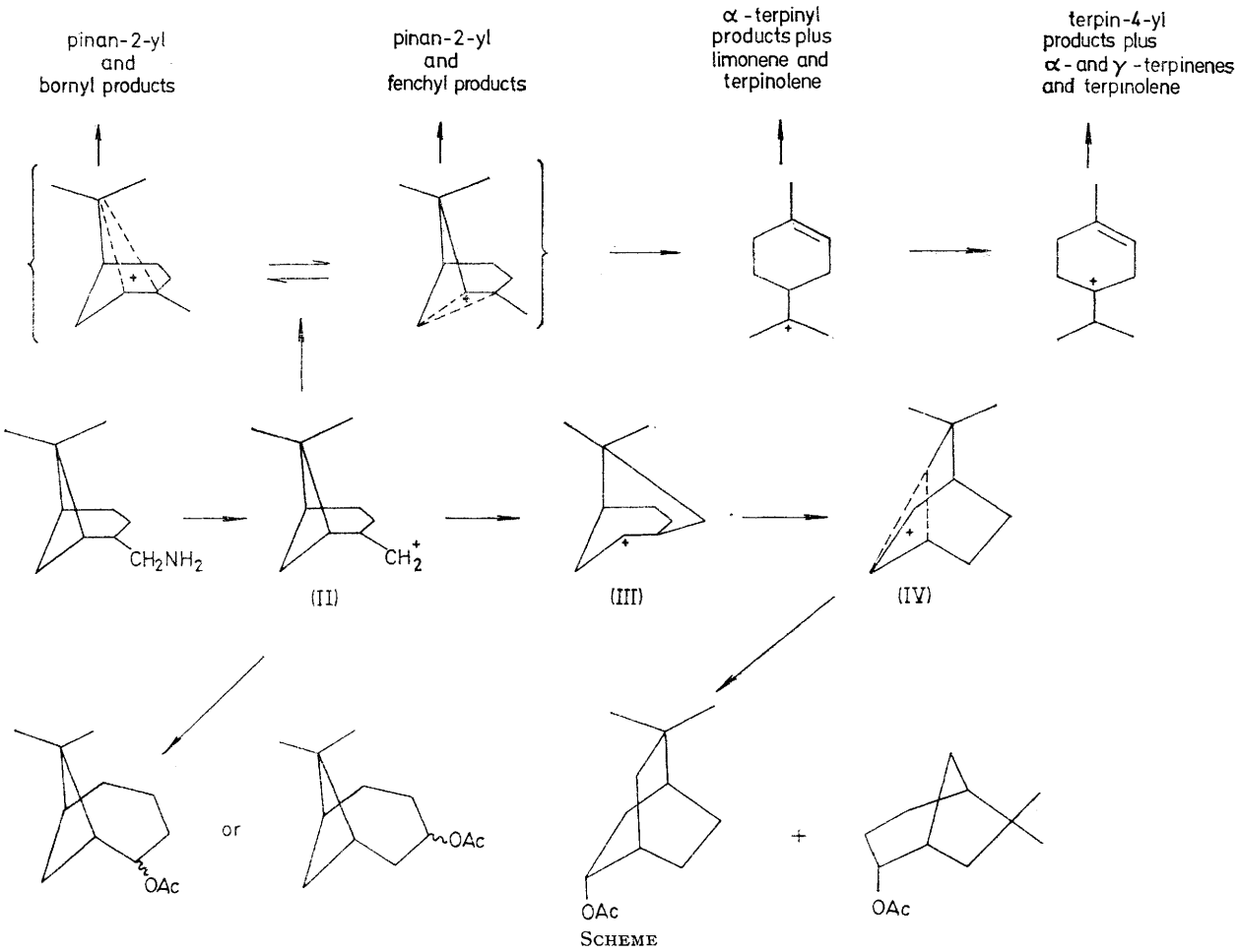
contain compounds with six different rearranged carbon skeletons. The pinanyl, bornyl, fenchyl, and terpinyl products have been detected in products of rearrangement of the pinenes in acid,[20] and in products of pinanyl ester solvolysis [4] and so require no further comment here. The three ring-expanded products, however, having the bicyclo[2.2.2]octane, the bicyclo[3.2.1]octane, and the bicyclo[4.1.1]octane skeletons have not previously been detected in reactions of the pinanes.

On the basis of this reaction path, we suggest that the [1,3] carbon shift by which (III) is produced from 2α*H*-10-aminopinane probably results in formation of a classical ion since it can subsequently delocalise to (IV). It must also follow that the delocalisation of (III) is restricted, since it would be expected to give two possible delocalised ions, (IV) and (V). Subsequent reaction of (V) with acetic acid should give rise to *exo*-4,4-dimethylbicyclo[3.2.1]oct-2-yl acetate (VI) which we have

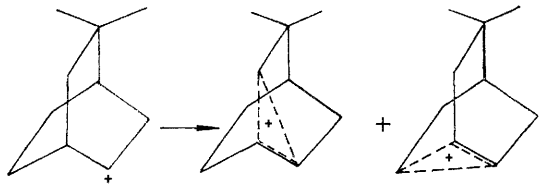


SCHEME

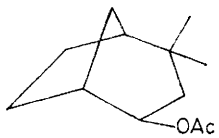
Suggested reactions by which these products may have been found are outlined in the Scheme. We suggest that 5,5-dimethylbicyclo[2.2.2]oct-2-yl acetate and 6,6-dimethylbicyclo[3.2.1]oct-2-yl acetate both arise from ion (IV). This ion must itself arise from 2α*H*-10-aminopinane *via* a [1,3] carbon shift; two successive [1,2] shifts in this system could not give rise to (III). After formation, we suggest that (III) forms (IV), from which the observed products are obtained. In support of this, acetolysis of *endo*-5,5-dimethylbicyclo[2.2.2]oct-2-yl toluene-*p*-sulphonate gives rise to these products, though the ratio of bicyclo[2.2.2]- to bicyclo[3.2.1]-octane derivative observed in toluene-*p*-sulphonate acetolysis (8 : 5) differs from the ratio (9 : 11) observed from the amine.

synthesised and shown to be absent from the products. The restriction forcing delocalisation to proceed in one direction only is, we suggest, a solvating molecule or ion very close to the ion centre; electron shift to the delocalised ion could displace this molecule or ion. Deaminations are known to produce a water molecule close to the carbonium ion centre generated in the reaction; and we showed in the preceding paper [1] that a water molecule close to a carbonium ion centre can remain in place during a bond shift. We suggest that the water molecule formed in deamination moves to the ion centre as ion (III) is generated, and then controls its subsequent reactions. This would be expected to generate a small amount of *endo*-5,5-dimethylbicyclo[2.2.2]octan-2-ol; the final peak listed in the Table has the same retention

time as this alcohol, though we have been unable to obtain a sufficient sample to prove its identity. Ring



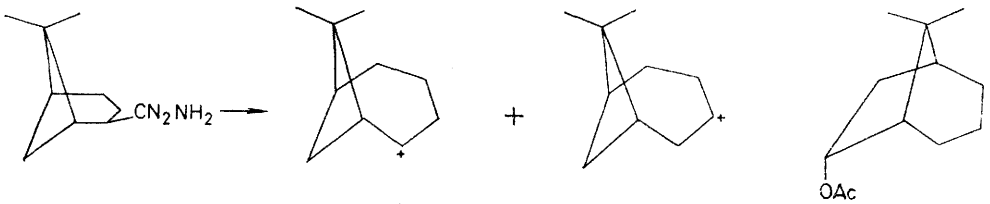
(III) (IV) (V)



(VI)

expansion to yield the 7,7-dimethylbicyclo[4.1.1]octyl system can proceed *via* either ion (VII) or (VIII).

Reaction *via* (VII) would be expected to yield some (IX) *via* a delocalised ion, but difficulties in synthesising



(VII) (VIII) (IX)

these systems make the precise course of reaction *via* this pathway uncertain.

The reaction sequence *via* ion (III) is characteristic of a ' classical ' deamination in that it involves an intermediate which undergoes reaction *via* a pathway not observed when the ion is generated by ester heterolysis. Our evidence offers no distinction between reaction *via* a ' hot ' carbonium ion similar to (II), or *via* a diazonium ion in which the nitrogen is displaced by a bond shift, or any type of ion pair in which a bond shift displaced the solvating ion or molecule. The reactive intermediate, having rearranged to ion (III) then behaves in a manner similar to that of a carbonium ion produced by solvolysis.

The products show that a [1,3] carbon shift has taken place. Such reactions are uncommon. A [1,3] carbon shift was first suggested by Laughlin,[21] and further examples postulated by Whitmore and Mosher.[22] The first example of a [1,3] carbon shift which could not be explained as two [1,2] shifts was the dehydration of 3-ethyl-4,4-dimethylpentan-2-ol to 3-ethyl-2,4-dimethylpent-2-ene.[23] Since then, [1,3] carbon shifts have been observed from vinylcyclopropane and Cope rearrangements [24] but the only other simple [1,3] shift observed was in the reaction with nitrous acid of 2-cyclopropylethylamine.[25] In this case a [1,2] carbon shift was available and was followed to a greater extent than the [1,3] shift.

In the reaction of 2α*H*-10-aminopinane with nitrous acid, several factors favour a [1,3] carbon shift. First, the probable conformation [26] of 2α*H*-10-aminopinane would have the carbon atom carrying the amino-group displaced upwards from the plane of the ring towards the *gem*-dimethyl bridge. Models of the system show that relatively little movement of the bonding electrons is needed to bring about a [1,3] carbon shift. Secondly, this pathway causes a reduction in strain of the ring system, by expanding a cyclobutane ring to cyclohexane. The alternative, ring expansion of a cyclohexane ring to cycloheptane, leaving the cyclobutane ring intact, would cause little, if any, relief of strain. Expansion of the cyclobutane ring by the pathway followed in ester solvolysis reactions, a [1,2] hydride shift followed by a [1,2] carbon shift or ring opening, is probably less favoured since the first step, the [1,2] hydride shift, offers no relief of ring strain. Thirdly, expansion of the cyclohexane ring of pinane is difficult. Prior to our work, the only reported case was the addition of dibromocarbene to pin-2-ene.[27] We have been unable to expand the cyclohexane ring by a pinacol reaction on the monotoluene-*p*-sulphonate of the diol from pin-2(10)-ene,[28] which would favour observation of a [1,2] carbon shift. We conclude that it is a particular feature of the system being studied rather than an observation of general significance in pinane chemistry.

Direct comparison with the pinan-10-yl toluene-*p*-sulphonates is restricted by the solvolysis of the latter involving a [1,2] hydride shift in the rate-determining step. It is unlikely that any carbon or hydride shift is involved in removal of nitrogen from the amine.

Our results show the expected behaviour of a high energy carbonium ion. It initially undergoes a reaction which gives the maximum possible relief of strain in the system and then undergoes further reactions in a manner similar to species generated by heterolytic ester fission. This type of behaviour is exactly as predicted for a ' hot ' carbonium ion.

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