# Ring Opening of α-Pinene Epoxide

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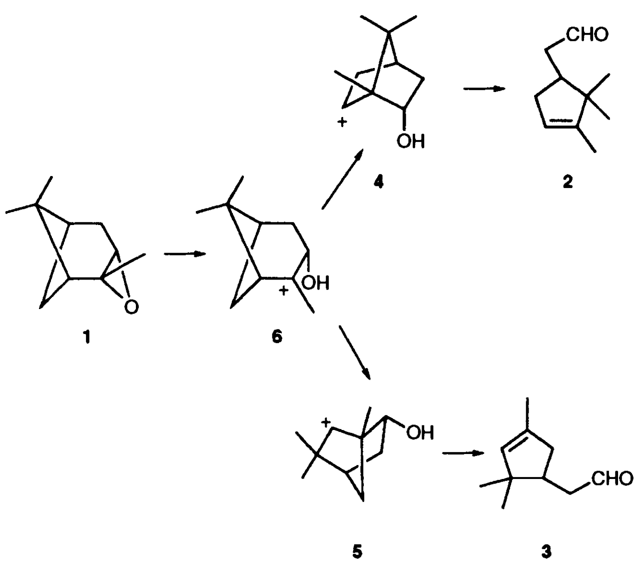
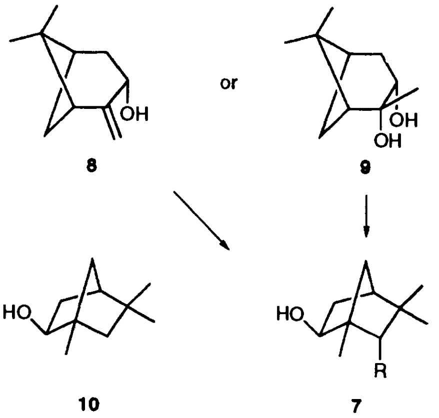
The acid-catalysed opening of the epoxide ring of α-pinene epoxide (2α,3α-epoxypinene) has been shown to proceed without participation of cyclobutane ring expansion in the rate-determining step. The reaction cannot proceed by initial C–O bond fission, as intermediates generated by either fission are on other reaction pathways. It is suggested that the reaction proceeds by fission of the C–C bond to give a heterocyclic intermediate, which can ring open, and finally expand the cyclobutane ring in the product-determining step. Reactions which could proceed by a similar mechanism are discussed. The corresponding reaction of β-pinene epoxide (2β,10-epoxypinene) in which the epoxide ring is not part of a strained bicyclic system, proceeds *via* this route to the extent of only 0.5%. The main reaction involves conventional C–O bond fission.

The boron trifluoride[1] catalysed ring opening of α-pinene epoxide (**1**) yields 2,2,3-trimethylcyclopent-3-enylacetaldehyde (**2**), 2,2,4-trimethylcyclopent-3-enylacetaldehyde (**3**), and pinocamphone as the main products. The use of zinc bromide as a catalyst gives similar products; hydrogen fluoride gives an unknown fluoro alcohol as the main product, plus the same mixture.[1] Ring opening with toluene-*p*-sulfonic acid and quinaldine[2] gives the same aldehydes (**2** is described as α-campholenic aldehyde) together with hydrocarbons, mainly monocyclic terpenoids. The authors point out that the ratio of **2** to **3** is approximately 3:17, the ratio reported by several previous authors whenever α-pinene oxide is treated with homogeneous catalysts. On solid acid catalysts, such as alumina or silica gel, the ratio is variable; the literature has been summarised by Tanabe, Ohnishi and Arata.[3] In alkaline conditions, α-pinene epoxide does not react.[4]

It has been suggested[1] that the reaction takes place by opening of the epoxide ring to give the ions **4** and **5**, which then collapse to give the aldehydes.



This explanation is unsatisfactory for two reasons. Firstly, the formation of **4** and **5** from **6** is irreversible, so decomposition of **6** must be the product-determining step. Reactions of ions similar to **6**, except for the hydroxy group, favour shift of the *gem*-dimethyl group over shift of the methylene, and so would give rise to **2** as the main product.[5] Secondly, Schmidt[6] has shown that either isopinene glycol or pinocarveol (**8**) rearrange in acids to give only fenchanediol (**7**; R=OH). The subsequent demonstration[7] that isopinene glycol has the structure **9** suggests that both these reactions occur *via* the ion **6**, indicating that the latter does not lie on the route to formation of the aldehyde **3**. Schmidt did obtain **3** from **7**; R=Br but in only 38% yield, and accompanied by 52% of α-fenchol (**10**) on reduction with zinc dust or sodium in ethanol. A similar yield of **3** was obtained during solvolysis of the benzoate of **7**; R=Cl in alkaline ethanol. Formation of **3** was not observed under acid conditions, and may proceed by offering the only route for a bimolecular elimination from **7**; R=Cl.

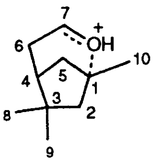


## Results and Discussion

The reaction of α-pinene epoxide with fluorosulfuric acid in sulfur dioxide at −70 °C gave a product whose $^{13}$C NMR spectrum was identified as that of **11**. Confirmation of the identification was obtained by direct generation of **11** from the parent aldehyde, **3**.

Assignment of the spectrum is straightforward. The main charge is spread over C-7 at 232, and C-1 at 147. C-6, at $\delta$ 56, is affected by the charge on C-7. C-2, at $\delta$ 39 and C-5, at $\delta$ 32 are not appreciably shifted by the charge on C-1; these assignments could be reversed, as could C-3 at $\delta$ 49 and C-4 at $\delta$ 43. The *gem*-dimethyl carbons are at $\delta$ 25 and 23, while the single methyl group is at $\delta$ 19.

It will readily be seen that **11** is formed from **3** by interaction of the carbonyl oxygen atom with the protonated double bond. It is the sole detectable product of the reaction. There is no



**11**

**Table 1** Rates of reaction of epoxides in aqueous 80% ethanol containing 0.000 498 mol dm$^{-3}$ toluene-*p*-sulfonic acid at 0 °C

| Substrate | $k_1/10^{-4}$ s$^{-1}$ |
|---|---|
| α-Pinene oxide | 4.1 |
| 1-Methyl-1,2-epoxy cyclohexene | 1.5 |
| Epoxycyclohexane | 0.005 |

evidence of formation of **2**, but a low yield would not be detected by our method.

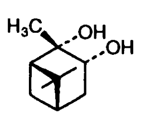
We then added β-pinene epoxide to fluorosulfuric acid in sulfur dioxide at −70 °C, but obtained only polymeric material.

Clearly the reaction in superacid parallels closely the reaction in normal acids, and offers no clue as to why **3** is formed in a reaction which presumably involves a methylene bridge shift, rather than forming **2**, which involves a *gem*-dimethyl bridge shift.

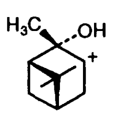
It has been pointed out[8] that the acid-catalysed opening of the epoxide ring rarely involves a carbocation unless the charge is stabilised by a group such as phenyl or vinyl. To check whether the rate-determining step of α-pinene epoxide ring opening involved interaction of the developing carbocation with the bond shift involved in expansion of the cyclobutane ring, we measured the rate of acid-catalysed hydrolysis of α-pinene epoxide, and compared it with the rates of reaction of some monocyclic epoxides.

If expansion of the cyclobutane ring were involved in the rate-determining step of the hydrolysis, the rate should be increased[5] by a factor of approximately $10^5$, resulting from the formation of a delocalised ion.[9] This clearly has not occurred, so it is unlikely that fission of the C-2 to oxygen bond is involved in the rate-determining step. This offers further evidence that the ion **6** is not involved in the overall reaction.

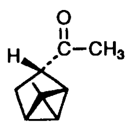
Reaction probably involves the protonated epoxide ring, so we must next consider the possibility of involvement of the C-3 to oxygen bond in the rate-determining step, although this appears unlikely, as no mechanism for stabilising the resultant carbocation can be found in this case. Evidence that this bond is not broken in the first step of the reaction comes from the work of Hirata,[4] who obtained the ion **12** by solvolysis of the mono toluene-*p*-sulfonate of the *cis*-pinanediol **13**, and showed that it underwent a pinacol shift to give the bicyclo[2.1.1]hexane **14** and the methylnopinone **15**.



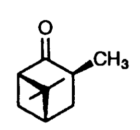
**13**



**12**



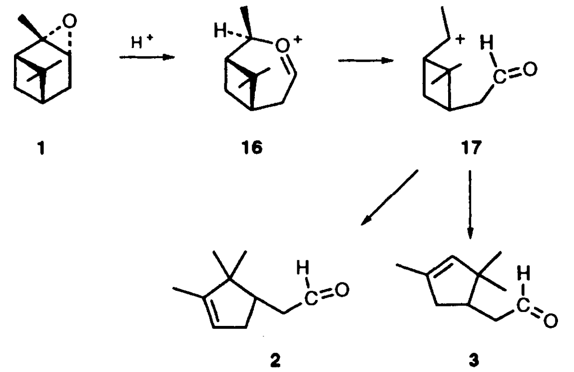
**14**



**15**

This leaves only fission of the C–C bond of the epoxide as the first step of the reaction. This is a most unexpected reaction, even though the products reveal that this bond is broken at some stage. However, the mechanism outlined in Scheme 1 shows that this is consistent with the results obtained.

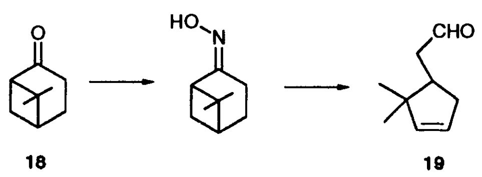
Protonation of the epoxide oxygen of **1** is followed by fission of the epoxide C–C bond, and hydride shift. The shift proceeds only to the tertiary carbon; it may be influenced by spread of charge from the oxygen to the carbon atoms on protonation. The heterocycle formed in this step is rapidly hydrolysed to **17**. The cyclobutane ring of **17** is flexible, unlike that of **1** so its direction of ring opening is now influenced by its conformation and the stability of the products, with the electronic effect of the *gem*-dimethyl bridge making a diminished contribution to the control of the reaction direction. Consistent with this, the ratio of **2** to **3**, constant in homogeneous reactions, varies substantially in heterogeneous reactions, when the surface on which the substrate is absorbed can control the reaction.[3]



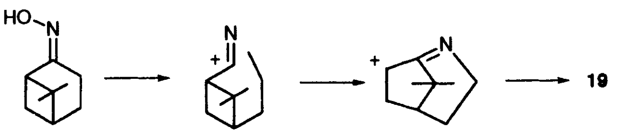
Scheme 1

We looked for similar examples of expansion of the six-membered pinene ring to a heterocyclic ring as a route to fission, and found two possible examples.

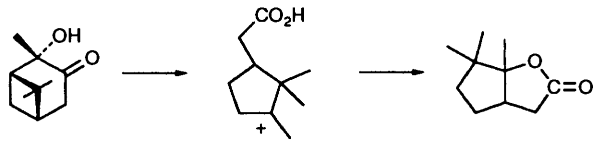
Firstly,[10] the oxime of nopinone (**18**) (6,6-dimethylbicyclo[3.1.1]hexan-2-one) on reduction with lithium aluminium hydride in ether, gave 2,2-dimethylcyclopent-3-enylacetaldehyde (**19**) in 78% yield.



The reaction has not been studied, but could proceed *via* a Beckman-type rearrangement.



Secondly,[11] 2α-hydroxypinan-3-one (**20**) rearranges in the presence of oxalic acid to yield the lactone **21** in 28% yield. The intermediate is believed to be **22**.

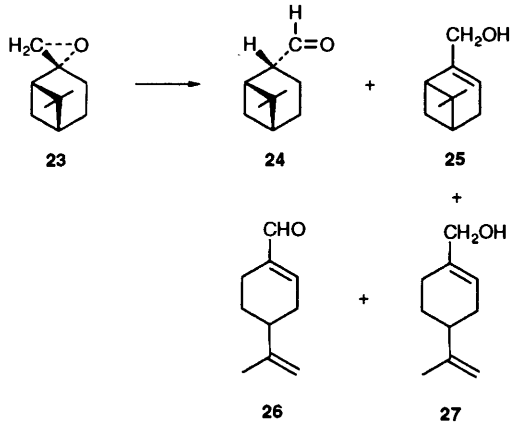


**20** **22** **21**

The authors suggest ring opening occurs by fission of a carbocation with a β-keto substituent; however, C–C bond fission was not detected[12] in the solvolysis of 7-keto norbornyl toluene-*p*-sulfonates.

A possible route from **20** to **22** is formation of a seven-membered oxygen-heterocyclic ring, then ring opening and rearrangement.

We next studied the acid-catalysed ring opening of β-pinene epoxide (**23**). In this case, the epoxide ring is outside the bicyclo[3.1.1] system, so should not be strained. While C–C bond fission should yield nopinone (**18**) the main reaction would be expected to be C-2 to oxygen bond fission, yielding C-10 alcohols and aldehydes. This was in fact the case; reaction of β-pinene epoxide in aqueous 80% alcohol containing 0.1 mol dm$^{-3}$ toluene-*p*-sulfonic acid yielded a complex mixture of products from which we were able to isolate *trans*-myrtanal (**24**) 17%, myrtenol (**25**) 10%, perillaldehyde (**26**) 9% and perillyl alcohol (**27**) 8%. In addition, we found 0.5% nopinone (**18**).



Thus, reaction of an unstrained epoxide proceeds mainly along the expected pathway of fission of a C–O bond to yield the more stable carbocation, but a small amount of C–C bond fission is still detectable.

Epoxide reaction by C–C bond fission is unexpected, but not unprecedented. Thermal C–C bond fission in phenyl-substituted epoxides has been reported on flash heating to 370 °C for 15 s.[13] The α-cyano-*cis*- and -*trans*-stilbene oxides can undergo C–C fission thermally or photolytically to yield 1,3-dipoles,[14] and photolytic C–C bond fission in alkyl-substituted epoxides is well documented.[15] Similar thermal and photolytic fission has also been reported in the aziridines.[16] Fission of the C–C bond in an acid-catalysed reaction has not been previously reported. There is no doubt, however, that C–C bond fission does take place during the reaction, and it seems more likely that this will occur when the bond is under maximum strain, rather than when some strain has been released by C–O fission in the epoxide ring. Strain does facilitate all modes of ring opening.

We conclude that the epoxide ring of α-pinene epoxide is probably opened by C–C bond fission. It does not involve cyclobutane ring expansion, which takes place later along the reaction pathway to determine the product composition. This opening of the epoxide ring is exceptional, and is observed only in substrates where the ring is strained.

## Experimental

$^1$H NMR spectra were recorded on a Perkin-Elmer R34 (220 MHz) spectrometer, using $CDCl_3$ as the solvent and tetramethylsilane as an internal standard. $^{13}$C NMR spectra were recorded on a Varian XL 100 (25.2 MHz) spectrometer with $CDCl_3$ as the solvent and tetramethylsilane as an internal standard; for superacid solutions, liquid sulfur dioxide was used as the solvent, with an external deuterium lock of [$^2H_6$]acetone or [$^2H_4$]methanol and an external standard of $Me_4Si$ enclosed within a 5 mm tube.

IR spectra were recorded on a Perkin-Elmer 1320 spectrometer using either liquid films or Nujol mulls.

Reaction mixtures were analysed on a Dani 3800 gas liquid chromatograph with a flame ionisation detector using nitrogen as the carrier gas. The instrument used a 25 m capillary column with 0.3 mm, internal diameter, coated with OV351. A similar instrument was connected to a VG 7070E mass spectrometer for GLC–MS analyses.

*Preparation of Materials.*—Samples of α-pinene epoxide (2α,3α-epoxypinane), β-pinene epoxide (a mixture of 2α,10-epoxypinane and 2β,10-epoxypinane) and cyclohexane epoxide were obtained from Aldrich and were distilled under reduced pressure before use. A sample of 2β,10-epoxypinane was prepared from nopinone[17] by the method of Coxon.[5] Samples for identification of the products of β-pinene decomposition were obtained from Aldrich, except for myrtenol, which was prepared by reduction of commercial myrtenal with sodium borohydride.

2,2,4-*Trimethylcyclopenten*-3-*enylacetaldehyde.*[1]—Distilled $BF_3$–diethyl ether (15 cm$^3$) was added dropwise to an ice-cold stirred solution of α-pinene oxide (15 g) in 50 cm$^3$ ether. This was then poured onto a solution of 100 g of hydrated sodium acetate in 250 cm$^3$ of water, and extracted with ether. The aldehyde (51% yield) had *m*/*z* 152; δ 1.2 (3 H, s, Me) 1.14 (3 H, s, Me), 1.6 (3 H, br s, Me), 1.7 (1 H, m, CH), 1.7 (2 H, d, $CH_2$), 2.3 (2 H, br s, $CH_2$CHO), 5.2 (1 H, s, CH) and 9.8 (1 H, s, CHO); $\nu_{max}$/cm$^{-1}$ 2900, 1700, 1440, 1360 and 1040.

1-*Methyl*-1,2-*epoxycyclohexane.*—1-Methylcyclohexene (10 g) was added to a solution of *m*-chloroperbenzoic acid (18 g) in 250 cm$^3$ of chloroform and stirred at 0 °C for 24 h. 0.1 mol dm$^{-3}$ NaOH was then added until the solution was just basic. The chloroform layer was washed with water, dried, and concentrated to give the epoxide, b.p. 118–120 °C (lit.,[18] 137–138 °C), *m*/*z* 112; δ 1.3 (3 H, s, Me), 1.4–1.9 (8 H, m, ring $CH_2$) and 2.95 (1 H, br s, O–C–H).

*Kinetics.*—Rate measurements were made on the reactions in aqueous 80% ethanol (made up by volume) in an ice–water bath at 0 °C. Samples were quenched by being poured into water and the reaction mixture was extracted with pentane and analysed by GLC. Mesitylene was used as an internal standard.

*Product Studies.*—Products of the acid-catalysed decomposition of β-pinene epoxide were studied by extraction of the products of the completed reaction and analysis by GLC–MS. In all cases, identification was supported by checking retention times against those of known samples of the product. Identification of nopinone among the products of β-pinene epoxide hydrolysis was repeated on three separate samples. In each case, the substrate was checked by GLC for the presence of nopinone before the reaction was carried out.

*Generation and Study of Carbocations.*—Sulfur dioxide (1 cm$^3$) was condensed in a 10 cm$^3$ round-bottomed flask and $FSO_3H$ (2 cm$^3$) added. The solution was cooled to −78 °C, and the substrate (250–500 mg) in $SO_2$ (1 cm$^3$) at −78 °C was added dropwise with stirring. The mixture was placed in a 12 mm bore NMR tube cooled to −78 °C. An external lock of [$^2H_6$]acetone or [$^2H_4$]methanol in a sealed 5 mm tube held in place by two guides was added and the 12 mm tube stoppered and placed in the Varian X-L 100 spectrometer. The tube was cooled in a stream of nitrogen passing through a cooling coil immersed in liquid nitrogen. The temperature of the probe was controlled using a heating coil in the nitrogen stream. The tube was spun at 14 rps. A sweep width of 10 000 Hz was used in conjunction with an acquisition time of 0.4 s.

*Reaction of α-pinene epoxide.*—The $^{13}C$ NMR spectrum of **11** had peaks at $\delta$ 232 (C-7), 147 (C-1), 56 (C-6), 49 (C-3), 43 (C-4), 39 (C-2), 32 (C-5), 25 (C-9), 23 (C-8) and 19 (C-10). It was identical with the spectrum of 2,2,4-trimethylcyclopent-3-enylacetaldehyde in $FSO_3H$.

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