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ORGANIC REACTIONS IN A SOLID MATRIX—IV†

OXIRANE REARRANGEMENT ON MODIFIED-ALUMINA‡

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Abstract—Rearrangement of methyldialkyl-substituted oxiranes to the corresponding allylic secondary alcohols with active Al_2O_3 is accompanied by carbonium ion rearrangements. The effect of modifying the Al_2O_3 with various bases or salts has been studied. With NaOH-modified Al_2O_3, the carbonium ion-rearrangements are significantly suppressed, and rearrangement to the allylic alcohols becomes the major pathway. Rearrangement of 2,10-epoxypinane (both isomers) on Al_2O_3–NaOH is reported.

Oxiranes, irrespective of their degree of substitution and carbon-skeletal features, are quite sensitive[1,2] to active Al_2O_3 at ambient temperatures and, in general, four different types of reactions have been observed,[1d] (i) transformation into an allylic alcohol; (ii) hydration to *trans*-glycol; (iii) isomerisation to carbonyl compounds; (iv) typical carbonium ion rearrangements.

With trisubstituted 1,2-epoxides, generally, reactions (ii) and (iii) are not very significant. The present work was undertaken to see if Al_2O_3 can be modified in such a way as to suppress reaction (iv) so that transformation to allylic alcohols {reaction (i)} becomes the dominant pathway with trialkyl-substituted 1,2-epoxides.

It is generally agreed that alumina has dipolar character[3] and there are both electron-donor[4] and electron-acceptor[5] sites on its surface. The nature of these sites has been investigated and several types of catalytic and adsorption sites have been identified.[6] Of the acidic sites, there are protonic acid sites and Lewis acid sites of different acidity;[5] at low temperatures (100°C), the surface hydroxyls of alumina are not acidic, hence protonic acid sites are unimportant[5c] under these conditions. Both acid and basic sites have been implicated[1d,1e] in the transformation of oxirane to allylic alcohols on Al_2O_3 surface. Making the reasonable assumption that acid sites involved in the carbonium ion rearrangements and oxirane-to-allylic alcohol transformations are different, the behaviour of oxirane compounds on different surface-modified aluminas was studied in an effort to suppress the carbonium ion rearrangements. Acidic sites on Al_2O_3 surface have been modified/neutralised by treatment with ammonia,[7] organic amines,[8] sodium hydroxide,[5a,9] or sodium chloride.[5a,9] Using the readily accessible (+)-2α,3α-epoxypinane[1c] (**1**) as the substrate, we have evaluated the effect of doping alumina surface with LiOH, NaOH, KOH, LiCl, NaCl and KCl. The results are summarised in Table 1. It is clear from these data that with Al_2O_3–NaOH, rearrangement to allylic alcohol (*trans*-pinocarveol, **3**) is the dominant pathway; Al_2O_3-alkali halides, on the other hand, suppress this reaction and aid isomerisation to the ketone (pinocamphone, **2**).

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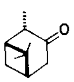

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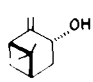

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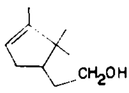

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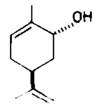

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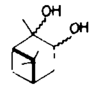

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In order to assess the generality of these findings, action of Al_2O_3–NaOH and Al_2O_3–NaCl on 1-methyl-1,2-epoxycycloheptane and (+)-3α,4α-epoxycarane (**9**) was next investigated.

1-Methyl-1,2-epoxycycloheptane[1c] on exposure to Al_2O_3-NaOH yielded 2-methylene-cycloheptanol (**7**, 87%) and 1-methyl-1-hydroxy-methylcyclohexane (**8**, 13%), while rearrangement on Al_2O_3–NaCl resulted in **7** (38%), **8** (41)% and α-methylcycloheptanone (21%). Under the same conditions Al_2O_3 (water-washed) led to the formation of **7** (72%), **8** (21%) and α-methylcycloheptanone (7%).[11] The total recovery in each case was ~60% and substrate modified alumina ratio was 1:25.

(+)-3α,4α-Epoxycarane[1c] (**9**) and Al_2O_3-NaOH (substrate alumina ratio, 1:50) gave a product (72%) consisting of **10** (63%), **11** (26%) and 12 (11%). The product (yield 62%) from Al_2O_3–NaCl (1:25, substrate alumina ratio) exposure was very complex (at least 12 components, GLC), in which the following were identified (decreasing RT): **10** (30%), **11** (4%), **12** (19%), **13** (6%), p-cymene (6%) and 3,7,7-trimethyltropilidene (**14**: 28%). (cf. rearrangement of this oxirane over silica gel[10]).

The identification of all compounds described above has been discussed earlier[1c,10] and in the present investigation the various products were identified by mixed GLC with authentic samples.

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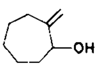
Table 1. Rearrangement of $2\alpha,3\alpha$-epoxypinane on surface-modified alumina[a]

Solid matrix	Total recovery (%)	Product composition (%)[b]							
		—increasing RRT—							
		U[c]	U	**2**	**3**	U	**4**	**5**	**6**
Al_2O_3/I	52	—	—	13	57	—	27	—	3
Al_2O_3-LiOH-I	62	—	—	12	75	—	13	—	—
Al_2O_3-NaOH/II	75	—	—	4	93	—	3	—	—
Al_2O_3-KOH/II	60	—	—	6	90	—	4	—	—
Al_2O_3-LiCl/I	30	1	4	84	4	2	5	—	—
Al_2O_3-NaCl/II	53	—	1	31	30	2	30	6	—
Al_2O_3-KCl/II	43	—	1	36	42	1	19	1	—

[a] Substrate alumina ratio, 1:25.

[b] GLC: 300 cm × 0.6 cm column, 20% carbowax (20M) on 60–80 mesh Chromosorb W; temp. programmed, 125–190°, 4°C/min.; 70 mlH_2/min.

[c] Unidentified.



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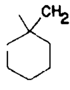

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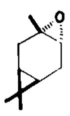

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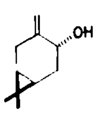

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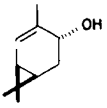

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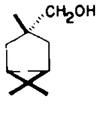

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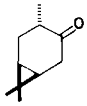

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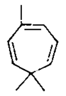

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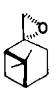
From the present investigation it is clear that Al_2O_3–NaOH is superior to Al_2O_3 for the isomerisation of trisubstituted oxiranes to allylic alcohols.

In view of the above demonstrated superiority of Al_2O_3–NaOH as a solid matrix for oxirane-allylic alcohol rearrangement it was thought of interest to examine its effect on 2,10-epoxypinane (**15**), as a representative of 2,2-disubstituted oxiranes which have propensity for isomerisation to aldehydes.[12] Isomerisation of 2-10-epoxypinane (**16**) has also been included in this study to discern any steric factors, similar to those observed for the pair 3α-4α-epoxycarane and 3β, 4β-epoxycarane, in an earlier investigation.[1c,1d]

2α,10-Epoxypinane (**15**) has been reported[13] to furnish *trans*-myrtanal (**17**) and myrtenol (**21**) in a ratio of 3:1 on exposure to Al_2O_3 (at reflux temp.). When **15** was treated with Al_2O_3–NaOH in hexane at 25° (24 h), the product consisted of four components (GLC), which were separated by preparative GLC and identified from spectral characteristics (IR, PMR) as *trans*-myrtanal[14] (**17**; 6%), myrtenal[15,16] (**22**; 18%), myrtenol[15,17] (**21**, 28%) and *trans*-myrtanol[18,19] (**18**: 48%). Epoxide **16** likewise on treatment with Al_2O_3-NaOH, gave the same four products in essentially the same proportions (see below).

The formation of **17** and **21** from 2,10-epoxypinane is readily understandable. *trans*-Myrtanol (**18**), in part (see below), arises from **17** by a Cannizzaro reaction on Al_2O_3 surface, for which there is ample previous analogy;[1c,20] this is further supported by the isolation of myrtanic acid[21] (**19**) as the methyl ester (**20**) from the spent alumina. The formation of myrtenal (**22**) during this reaction suggests a hydride transfer reaction (of a type similar to the Meerwein-Ponndorf-Oppenauer equilibrium) between **17** and **21** leading to myrtenal (**22**) and *trans*-myrtanol (**18**). This aspect is under further exploration.



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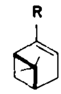
17: R = CHO
18: R = CH_2OH
19: R = COOH
20: R = COOMe



21: R = CH_2OH
22: R = CHO

The fact that 2,10-epoxypinane (**16**) also furnished *trans*-myrtanal (and *trans*-myrtanol) and not the *cis*-isomer, requires epimerisation of the expected *cis*-aldehyde to the more stable *trans*-isomer[22] on Al_2O_3 surface, a reaction which is not unexpected.[23]

The above results suggest that even with Al_2O_3–NaOH the dominant reaction of 2,2-disubstituted oxiranes would be isomerisation to the corresponding aldehyde.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Light petroleum refers to the fraction b.p. 40–60°. All solvent extracts were finally washed with brine, before drying (Na_2SO_4). All yields are on a w/w basis. Optical rotations were determined in $CHCl_3$ at 25°, on a Perkin-Elmer polarimeter, model 141. IR spectra were recorded as smears on a Perkin-Elmer Infracord, model 137-E. PMR spectra were taken with 10–20% soln in CCl_4 with TMS as internal standard, on a Varian A-60 spectrometer. GLC were carried out on "Aerograph", model A-350-B using a 300 cm × 0.5 cm column (20% diethyleneglycol polysuccinate on 60–80 mesh Chromosorb-W) for analytical chromatography and, a 300 cm × 0.8 cm column (30% diethyleneglycol polysuccinate on 30–60 mesh Chromosorb-W) for preparative runs, unless stated to the contrary; H_2 was used as the carrier gas.

Alumina and modified alumina

(i) *Water-washed alumina.* Commercial alumina (−100, +250 mesh) was repeatedly washed with boiling water till washings were neutral (phenolphthalein). The product was filtered, washed with distilled water and then with alcohol. It was dried in air and activated at 450°/6 h.

(ii) *Alumina doped with alkali hydroxides.* The above Al_2O_3 (50 g) was covered with alkali hydroxide aq (100 ml containing 1.5 g of the hydroxide). After 48 h at ~25°, the excess soln was drained off, Al_2O_3 dried at 120° in air for 16 h and then calcined at 450° for 1 h under N_2.

(iii) *Alumina doped with alkali metal chlorides.* This treatment was carried out exactly as above, except that a soln of 5.0 g of salt in 100 ml of H_2O was used. Al_2O_3 and modified alumina, obtained as above, were graded according to Brockmann[24] and the activity found is indicated in Table 1.

Standard procedure for reaction with alumina

The epoxide is added to a thick slurry of 25 (or 50) times its wt. of Al_2O_3 or modified alumina suspended in hexane (30 ml for every 25 g of Al_2O_3), in a suitable stoppered flask, flushed with N_2, and shaken mechanically for 6 h and then kept aside for 18 h, at room temp. (22–28°). The alumina is filtered off and washed with Et_2O–MeOH (5%, 800 ml for 1 g of epoxide; added in several portions). The combined filtrates and washings are freed of solvent by careful fractionation to furnish the product. A part of the product was distilled for temp. programmed GLC.

Products from 2α,10-epoxypinane (**15**)

2α,10-Epoxypinane was prepared by the action of perbenzoic acid (20.3 g of per acid in 360 ml of ether soln) on β-pinene (20.0 g) in ether (30 ml) at 0° to 5° (20 h), in the usual manner. The product (18.3 g) had: b.p. 96–98°/20 mm, n_d^{20} 1.4751, $[\alpha]_D + 10.92$ (*c*, 10%). (Lit.[25]: n_D^{16} 1.4770, $[\alpha]_{578} + 7.8°$). IR: 1058, 1040, 1010, 990, 962, 938, 908, 898, 860, 828, 812 cm^{-1}. PMR: Me (3H singlets at 0.91 and 1.25 ppm), $C\underline{H}_2OC$ (2H, AB-q, 2.50 ppm, J = 6 Hz).

Epoxide **15** (5.0 g) on treatment with Al_2O_3-NaOH (125 g), afforded 2.5 g of a product, b.p. 98–120°/18 mm. The product was separated by preparative GLC (temp. 150°; gas flow 90 ml/min) and the components had RRT of 1, 1.25, 1.77 and 2.16.

Component of RRT 1.0 (trans-*myrtanal*, **17**). The product was converted into its semicarbozone, m.p. 177–179° (dil. EtOH) (Lit[13] m.p. 179.5–180°), from which pure **17** was regenerated (aq. oxalic acid-heptane[26]): b.p. 125° (bath)/40 mm, n_D^{20} 1.4855. IR: HCO 2700, 1720 cm^{-1}; (lit.[13]). PMR: Me (3H singlets at 0.91 and 1.27 ppm), $C\underline{H}O$ (1H, bs, 9.73 ppm).

Component with RRT 1.25 (*myrtenal*, **22**). IR: CHO 2700, 1675 cm: C = C 1615 cm^{-1}; 1175, 1128, 970, 915, 890, 800, 782, 700 cm^{-1}; (Lit.[15]). PMR: Me (3H singlets at 0.75 and 1.35 ppm), $C = C\underline{H}$ (1H, m, 6.58 ppm), $C\underline{H}O$ (1H, s, 9.47 ppm); (lit.[16]).

An authentic sample[27] of **22** was prepared by SeO_2 oxidation of α-pinene, for direct comparison.

Component with RRT 1.77 (*myrtenol*, **21**). B.p. 130° (bath)/20 mm, n_D^{20} 1.4920, $[\alpha]_D^{25} - 48.65°$ (*c*, 3.1%). (Lit.[28] n_D^{20} 1.4938; $[\alpha]_D$-47.1, 1.2% in EtOH). IR: 3300, 1120, 1080, 1060, 1012, 988, 960, 888, 802 cm^{-1};[15] PMR: Me (3H, singlets at 0.85 and 1.32 ppm), $C\underline{H}_2OH$ (2H, q, 3.87 ppm, J = 1.5 Hz), $C = C\underline{H}$ (1H, m, 5.37 ppm).[17]

Component with RRT 2.16 (trans-*myrtanol*, **18**). B.p. 108°/10 mm, n_D^{20} 1.4882, $[\alpha]_D$-25.46 (*c*, 4%). (Lit.[18] n_D^{25} 1.4863; $[\alpha]_D$-28°, 14.7% in p-cymene). IR: 3300, 1058, 1018 cm^{-1};[18] PMR: Me (3H singlets at 0.87 and 1.22 ppm), $C\underline{H}_2OH$ (2H, d, 3.27 ppm, J = 7 Hz).[19]

Myrtanic acid (**19**). The spent alumina from the above experiment was extracted with aq. ethanolic Na_2CO_3 (10%) and the extract worked up in the usual manner[1c] to give an acid, which was esterified (CH_2N_2) and distilled to give the methyl ester **20** (0.524 g): b.p. 150° (bath)/48 mm, n_D^{20} 1.4700. (lit.[21] n_D^{25} 1.4680). PMR: Me (3H, singlets at 0.89 and 1.25 ppm), COOMe (3H, s, 3.58 ppm).

Products from 2β,10-epoxypinane (**16**)

2β,10-Epoxypinane from nopinone by a known procedure:[29] b.p. 115–116°/40 mm, n_D^{20} 1.4762, $[\alpha]_D + 28.63$ (*c*, 1.5%). IR: 975, 935, 910, 863, 835, 810, 768, 715 cm^{-1}. PMR: Me (3H singlets at 1.05 and 1.25 ppm), $C\underline{H}_2OC$ (2H, "d", 2.36 ppm).

Epoxide **16** (5.0 g) on treatment with Al_2O_3-NaOH (125 g) in the usual manner afforded 3.08 g of product, b.p. 98–120°/18 mm. Analytical GLC showed the same four components as obtained from 2,10-epoxypinane: **17** (4%), **22** (14%), **21** (34%) and **18** (48%).

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