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EXO-TRICYCLO[3.2.1.$0^{2,4}$]OCT-6-ENE *EXO*-OXIDE

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Abstract—Epoxidation of *exo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**3**) affords the *exo*-oxide **2** which upon treatment with lithium in ammonia yields the known tricyclic alcohol **4** in almost quantitative yield. Lithium aluminium hydride reduction of oxide **2** gives a mixture of the same alcohol **4** and the rearranged, bicyclic alcohol **5**. Vapour phase chromatography of oxide **2** under most conditions effected acid catalysed isomerization of **2** to the bicyclic aldehyde **6** which was oxidized to the known carboxylic acid **7** as proof of structure. Above 120°, aldehyde **6** is converted quantitatively to the cyclohexadienyl acetaldehyde **8**. The kinetics of this transformation have been studied and suggest that the reaction proceeds by a thermal [1, 5] sigmatropic shift of hydrogen.

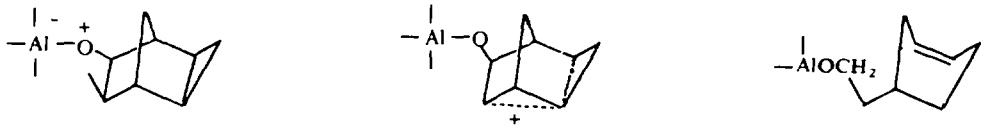
IN AN earlier communication[1] we described the preparation of *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene *exo*-oxide (**1**) and the rearrangements which accompany heterolytic cleavage of the oxirane ring of this oxide. These results have been reported in detail in the accompanying paper.[2] In an effort to gain some knowledge of the effect of the configuration of the cyclopropane ring on the course of these rearrangements work was initiated in these laboratories on a similar study of the isomeric *exo*-tricyclo-[3.2.1.$0^{2,4}$]oct-6-ene *exo*-oxide (**2**). Since our first communication Sargent, Harrison and Khoury[3] have described the results of their investigations of both these oxides. We report here the results of our study of the oxide **2**.

RESULTS AND DISCUSSION

Oxidation of *exo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene (**3**)[4] with peracetic acid afforded epoxide **2** in good yield. NMR spectroscopy and vpc analysis showed that within the limits of detection epoxidation occurred stereospecifically to give one oxide only. The NMR spectrum of **2** displayed a two proton signal at τ 6·83 which was assigned to the oxirane methine protons at C-2 and C-4. This signal occurred as a singlet, $W_{\frac{1}{2}h}$ = 2·5Hz, suggesting that the oxirane ring of **2** was in the *exo* configuration with no appreciable coupling between the oxirane methine protons at C-2, C-4 and the vicinal bridgehead protons at C-1, C-5.[5] This configurational assignment was confirmed by reduction of oxide **2** with Li in NH_3 which afforded the known *exo*-tricyclo-[3.2.1.$0^{2,4}$]octan-*exo*-6-ol (**4**).[6] This reduction has proved to be an effective means of establishing the structures of oxides **1** and **2** since cleavage of the oxirane proceeds without complication due to skeletal rearrangement.

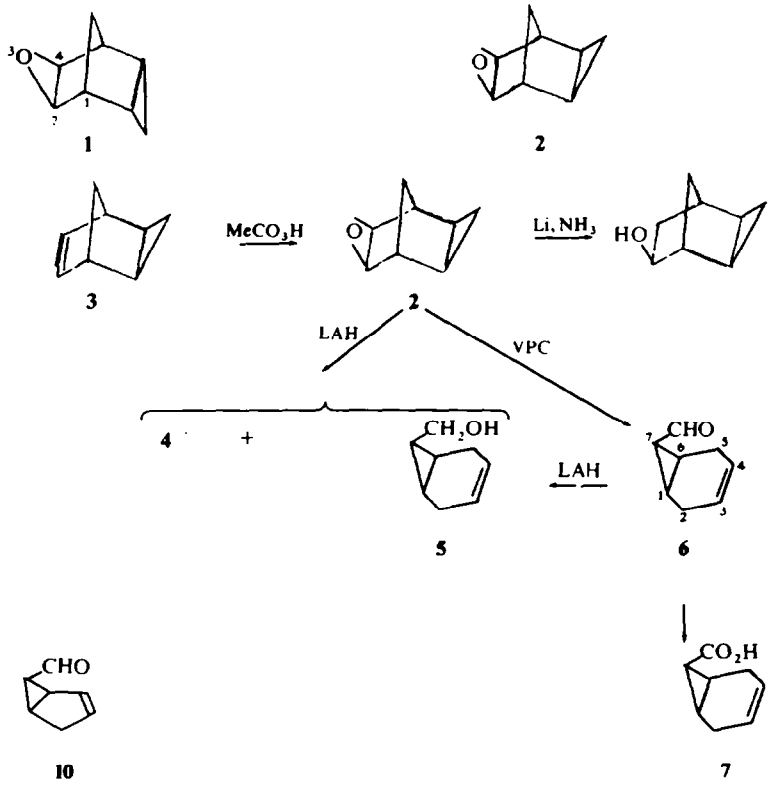
LAH reduction of **2** gave a mixture of the unrearranged alcohol **4** and the rearranged, bicyclic alcohol **5** in roughly equal proportions. The components of this mixture were separated by vpc and identified by comparison with authentic sample of **4**[6] and **5**.[2] By analogy with the known reaction of LAH with norbornadiene *exo*-oxide[7] and in line with the proposals of Sargent *et al.*[3] the formation of the

bicyclic alcohol **5** may be rationalized most simply in terms of the mechanism shown in Scheme I. However, the formation of the unrearranged alcohol **4** is difficult to explain, particularly when one recalls that under similar conditions both norbornadiene *exo*-oxide and *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene *exo*-oxide (**1**) afford rearranged alcohols exclusively. One might argue, for example, that oxide **2** is more



SCHEME I

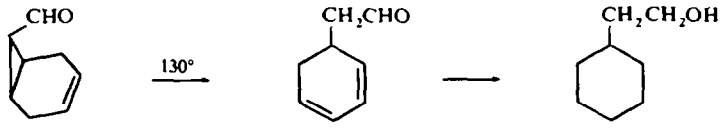
susceptible to intermolecular hydride attack at C-2, C-4 from the *endo* direction than the isomeric oxide **1** which should be extremely hindered towards *endo* attack at C-2, C-4. In this event one might expect norbornadiene *exo*-oxide, which is less hindered to *endo* attack than **2**, to yield some unrearranged alcohol on reduction with LAH. This is contrary to the experimental results. We believe that the explanation of these anomalies lies in some unique structural feature of the initial carbonium ion derived by Al catalysed cleavage of **2** and that this feature of the ion allows intramolecular capture of hydride from within the complexed ion. However, further experimentation is required before any definite conclusion can be drawn.



Epoxide **2** was found to be stable at 200°C and to vpc at 100°C on freshly prepared stainless steel columns with TCEP stationary phase. However, vpc of **2** on most other stationary phases resulted in catalysed isomerization to a single product (**6**) of longer retention. With column temperatures above 120° this product, **6**, underwent thermal isomerization (discussed further on) to the cyclohexadienyl acetaldehyde **8** with a retention time similar to that of oxide **2**.

In our hands, vpc under these conditions proved to be the most efficient method for effecting smooth, acid catalysed isomerization of oxide **2** to the bicyclic aldehyde **6**. Aldehyde **6** gave NMR and IR spectra consistent with the assigned structure. One feature of the NMR spectrum of **6** deserves further comment. The NMR signal at τ 0·8 due to the aldehyde proton occurs as a complex multiplet and this contrasts with the NMR signal of the aldehyde proton in the homologous aldehyde **10** which occurs as a doublet, J = 3 Hz.[8] The NMR spectrum of the aldehyde **6** shows the three cyclopropane protons as a narrow multiplet between τ 8·23 to 8·39 and it is obvious that these three protons constitute a strongly coupled system. Consequently, the aldehydic proton of **6** is not only directly coupled to the vicinal proton at C-7 but virtually coupled to the bridgehead protons at C-1 and C-6 giving rise to the observed complex multiplet for the NMR signal of the aldehydic proton in **6**. In contrast, the bridgehead protons at C-1 and C-5 of the homologous aldehyde **10** are not equivalent and presumably their chemical shift difference is large relative to their coupling constant. If in addition these two protons are not strongly coupled to the third cyclopropane at C-6 then the aldehydic proton will experience only direct vicinal coupling giving a doublet for the pmr signal of the aldehydic proton.

Further confirmation of structure **6** was obtained by oxidation of the aldehyde to the known carboxylic acid **7**[9] and by reduction of the aldehyde to the known alcohol **5**.[2]



6 **8** **9**

The details of the mechanism of the acid catalysed isomerization of **2** to **6** coupled with the mechanistic implications of the differences in reactivity of and products derived from the two oxides **1** and **2** have been discussed by Sergent *et al.*[3] and this need not be pursued furthermore.

Scheme 2

When heated in the range 120° to 160° aldehyde **6**, either neat or in CCl_4 solution, was converted quantitatively to the isomeric cyclohexadienylacetaldehyde **8**. Above 160°C small amounts of an unidentified component were formed as evidence by the appearance of a NMR signal at *ca* τ 2.

The IR spectrum of **8** showed an absorption at 1726 cm^{-1} characteristic of the carbonyl stretching frequency of a nonconjugated aldehyde function[10] and the NMR spectrum displayed a one proton triplet (J = 2 Hz) at τ 0·30 due to the aldehyde proton as well as a four proton multiplet at τ 4·19 due to the olefinic protons. The UV

spectrum (λ_{max}^{EtOH} 266 nm. ε 2.300) was consistent with that of a 1.3-cyclohexadiene derivative.[11] Furthermore. catalytic reduction of **8** and subsequent reduction with LAH afforded 2-cyclohexylethanol **9**. identical with an authentic sample of **9**.

The rate of isomerization of **6** to **8** could be followed conveniently by integration of the NMR signals of the aldehyde protons of reactant (**6**) and product (**8**). Sample kinetic data are shown in Fig. I. The isomerization of **6** to **8** occurred by a well behaved first order process. Table 1 contains the rate constants and the kinetic parameters for the isomerization.

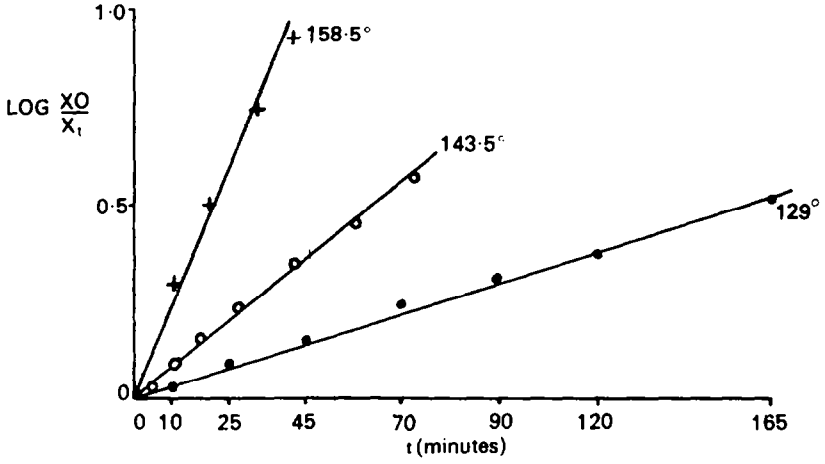
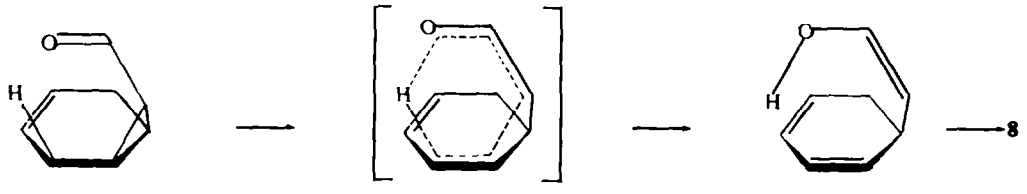


FIG. I First-order rate plots for the thermal isomerization of **6**.

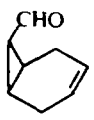
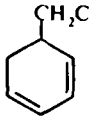
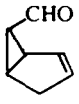
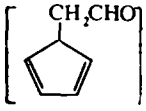
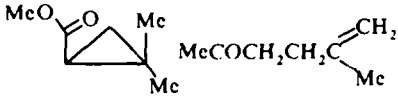
Included in Table 1 are the reported kinetic and thermodynamic data for several other pertinent thermal isomerizations. This type of thermal isomerization was first reported by Roberts [12a] and subsequently classified by Winstein[13] as a homodienyl 1.5-hydrogen shift in which the terminal double bond is replaced by a carbonyl group.



SCHEME 2

Other examples of this type of reaction have been reported since.[14, 15] The mechanism of these thermal reactions involves a suprafacial [1.5] sigmatropic shift of hydrogen from carbon to oxygen to give the enol tautomer of the final product. The rates and activation parameters for the isomerization **6** to **8** are comparable to those for the other isomerization listed in Table 1 and consequently this reaction proceeds via a similar mechanism which is represented in Scheme 2.

TABLE 1 KINETIC AND THERMODYNAMIC DATA FOR SOME [1, 5] SHIFTS OF HYDROGEN IN A HOMODIENYL SYSTEM IN WHICH THE DOUBLE BOND IS REPLACED BY A CARBONYL GROUP. (a) REF. 14. THE PRODUCT LISTED IN THE TABLE IS NOT IN FACT THE ISOLATED PRODUCT SINCE UNDER THE REACTION CONDITIONS IT UNDERGOES FURTHER, CONSECUTIVE DIENYL [1, 5] SHIFTS OF HYDROGEN. (b) REF. 12.

Reactant	Product	Temperature °C	Rate Constant $k \times 10^5$. sec^{-1}	$\Delta H^{\ddagger}_{25}$. Kcal $Mole^{-1}$	$\Delta S^{\ddagger}_{25}$ E.U.
		129·0 ± 0·5 143·5 ± 0·5 158·5 ± 1·0	1·27 ± 0·04 3·0 ± 0·1 9·9 ± 0·8	22·7 ± 1·4	−20·5 ± 4·1
(a) 				24·7 ± 0·6	−15·7 ± 1·5
(b) 		152 163	0·400 0·980	30	−10

EXPERIMENTAL

General introductory comments are the same as for the accompanying paper.[2] The following columns were used for vpc:- A. 10 ft × 0·125 in. O.D. stainless steel column of 5% TCEP on non-acid-washed Chromosorb W. 80–100. B. 10 ft × 0·125 in. O.D. copper column of 5% Ucon 50 HB 2000 on non-acid-washed Chromosorb W. 80–100. C. 10 ft × 0·25 in. O.D. aluminium column of 8% TCEP on non-acid-washed Chromosorb W. 60–80.

Epoxidation of exo-*tricyclo*[3.2.1.$0^{2,4}$]*oct-6-ene* (3). Commercial peracetic acid (32% W/V. 5 ml. 0·021 mol) containing dissolved anhyd NaOAc (0·32 g. 3·9 mmol) was added dropwise during 30 min to a stirred soln of the tricyclic olefin (3)[4] (2·0 g. 0·019 mol) in CH_2Cl_2 (120 ml) at 0°. The soln was allowed to warm to room temp and after 5 hr was washed with satd aq Na_2CO_3 (5 × 20 ml). water (2 × 20 ml) and dried ($MgSO_4$). Evaporation of the solvent under vac (20 mm) gave a colourless oil (2·0 g. 87%) which was distilled under vac to give an analytical sample of *exo*-3-oxa-*exo*-tetracyclo[3.3.1.$0^{2,4}$.$O^{6,8}$]nonane (2). (Found: C 78·87. H 8·33; Calc for $C_8H_{10}O$: C 78·65. H 8·25%). NMR: τ 6·83. s. $W_{\frac{1}{2}h}$ 2·5 Hz (2·03. oxirane methine); 7·54. br s. $W_{\frac{1}{2}h}$ 5·5 Hz (2·23. bridge head); 9·08. m (3·92. bridge and cyclopropane methine); 9·58. m (1·82. cyclopropane methylene); IR: 3071. 3029. 1036 and 864 cm^{-1}. NMR spectroscopy indicated that the crude oil contained > 95% of 2. VPC analysis (col A. 100°) of the crude oil showed > 95% one component. The component corresponding to this peak was collected and displayed an IR spectrum identical to that of epoxide 2.

Treatment of epoxide 2 *with Li in liquid* NH_3. A soln of 2 (100 mg. 0·82 mmol) in anhyd ether (1 ml) was added to a soln of Li shot (65 mg. 9·4 mmol) in anhyd NH_3 (20 ml. at −33°) and the mixture stirred for 2 hr. EtOH was added to the reaction mixture until the blue colour had disappeared. The NH_3 was allowed to evaporate and the residue was diluted with water (10 ml) and then extracted with ether (3 × 20 ml). The ethereal soln was washed with 10% aq NH_4Cl (3 × 10 ml). water (2 × 10 ml) and dried ($MgSO_4$). Evaporation of the ether under vac gave *exo*-tricyclo[3.2.1.$0^{2,4}$]octan-*exo*-6-ol (4) as a colourless oil (93 mg. 91%) which was shown to > 98% one component by VPC (col B. 110°). The product gave VPC retention time. NMR and IR spectra which were identical with those of a sample of 4 prepared after the manner of Wiberg and Wenzinger.[6]

Treatment of epoxide 2 *with LAH in ether*. Epoxide 2 (170 mg. 1·39 mmol) in anhyd ether (30 ml) was refluxed for 24 hr with LAH (200 mg. 5·7 mmol). The reaction mixture was washed with satd aq Na_2SO_4

(10 ml), water (3 × 5 ml) and dried ($MgSO_4$). Evaporation of the ether gave a colourless oil (140 mg) which was shown by VPC (col A, 120°) to consist of three components in the proportion 10:42:48, in order of increasing retention time. These were separated by preparative VPC (col C, 140°) to give in order of increasing retention time, the following three components. Component (i), as collected gave a colourless liquid which was identified as epoxide **2** by spectral comparisons. Component (ii), as collected gave a colourless liquid which displayed IR and NMR spectra identical to those of a sample of *exo*-tricyclo[3.2.1.$0^{2,4}$]octan-*exo*-6-ol (**4**) prepared according to the published procedure.[6] Component (iii) was collected as a solid which after sublimation (4 mm, 81°) gave *endo*-7-hydroxmethylbicyclo[4.1.0]hept-3-ene (**5**), identical with (IR and NMR) a sample of this alcohol described in the accompanying publication.[2]

Rearrangement of epoxide **2** *under VPC conditions.* Injection of epoxide **2** (100 mg) onto a TCEP preparative VPC column (col C, 120°) yielded two peaks in the proportions 33:67 in order of increasing retention time. The component corresponding to the shorter retention time peak was collected and identified by spectral comparisons as epoxide **2**. Collection of the component having the longer retention time gave bicyclo[4.1.0]hept-3-en-*endo*-7-carboxaldehyde (**6**) as a colourless liquid. An analytical sample was prepared by vac distillation. (Found: C 78·45, H 7·96; Calc for $C_8H_{10}O$: C 78·65, H 8·25%). NMR: τ 0·77 m (1·07, aldehyde), 4·26, m (2·00, olefinic); 7·48, br s (3·87, allylic) and 8·29, m (3·06, cyclopropane); IR: 3029, 1701, 1126, 912 and 662 cm^{-1}.

Reduction of bicyclo[4.1.0]*hept-3-en-*endo*-7-carboxaldehyde* (**6**) *with LAH.* A soln of **6** (50 mg, 0·41 mmol) in anhyd ether (20 ml) was refluxed with LAH (100 mg, 2·8 mmol) for 2 hr. The reaction mixture was treated with satd aq Na_2SO_4 (10 ml) and the ether soln washed with water (3 × 5 ml) and dried ($MgSO_4$). The ether was evaporated to give a semicrystalline solid (45 mg) which was shown by VPC (col A, 120°) to consist of three components in the proportions 2:17:81. Preparative VPC (col C, 140°) gave the major component as a crystalline solid which displayed IR and PMR spectra identical to those of alcohol **5**.[2] The other components were not investigated further but presumably one of these may arise from rearrangement of **6** to **8** and subsequent reduction.

Oxidation of bicyclo[4.1.0]*hept-3-en-*endo*-7-carboxaldehyde* (**6**). The procedure was similar to that used by Meinwald *et al*[8] for the oxidation of bicyclo[3.1.0]hex-2-en-*endo*-6-carboxaldehyde (**10**). A mixture of **6** (200 mg, 1·64 mmol), $AgNO_3$ (1·1 g, 609 mol), H_2O (10 ml) and EtOH (5 ml) was stirred vigorously and aq NaOH (0·4 g in 10 ml) was added during 15 min. The reaction mixture was stirred at room temp for a further 8 hr and then filtered. The filtrate was washed with ether (2 × 10 ml), acidified with aq HCl (5M) and ether (4 × 10 ml) extracted. The extract was dried ($MgSO_4$) and evaporated to give a pale yellow solid (185 mg) which after crystallization (twice) from petroleum ether yielded bicyclo[3.1.0]hept-3-en-*endo*-7-carboxylic acid (**7**) (107 mg, 46%) as white needles, mp 129·5–131° (lit 130–131·5°[9a], 132°[9b], 130–131°[3]). The IR and NMR spectra of **7** were in agreement with those reported.[9b]

Thermal rearrangement of bicyclo[4.1.0]*hept-3-en-*endo*-7-carboxaldehyde* (**6**). *Kinetic measurements.* A soln (ca 2·1M) of aldehyde **6** in CCl_4 was sealed into an NMR tube and then immersed in a constant temp bath. The progress of the reaction was followed by removing the tube from the bath at appropriate intervals of time, chilling the tube and integrating the NMR signals due to the aldehyde protons at τ 0·77 and 0·30 of the reactant **6** and product **8** respectively. Each signal was integrated five times in the direction of increasing field strength and five times in the opposite direction and the average value was used in subsequent calculations. Within experimental error the reaction was quantitative.

This procedure was performed at three temperatures and the results are summarized in Fig. 1 and Table 1.

Product analysis. Aldehyde **6** (neat) was selaed into an ampoule and kept at 160° for 2 hr. The product was distilled under vac to give 2-(1-cyclohexa-2,4-dienyl)acetaldehyde (**8**) as a clear liquid. (Found: C 78·85, H 8·35; Calc for $C_8H_{10}O$: C 78·65, H 8·25%). NMR: τ 0·30, t, J = 2 Hz (0·93, aldehyde); 4·19, m (3·88, olefinic); 5·1 to 8·3, m (5·19); IR: 3031, 1726 and 672 cm^{-1}; UV: λ_{max}^{EtOH} 266 mμ (ε 2,300).

Reduction of 2-(1-*cyclohexa*-2,4-*dienyl*)*acetaldehyde* (**8**). A soln of aldehyde (**8**) (300 mg) in EtOAc (50 ml) was shaken with Pd/C (30 mg, 10%) in an atmosphere of H_2 (1 atmos pressure) for 20 hr. The mixture was filtered and the filtrate evaporated to give a colourless oil (280 mg) which was dissolved in anhyd ether (50 ml) and refluxed for 2 hr with LAH (300 mg). The reaction mixture was treated with satd aq Na_2SO_4 (30 ml) and the ethereal layer washed with H_2O (3 × 10 ml) and dried ($MgSO_4$). Evaporation of solvent gave a colourless liquid (195 mg) shown by VPC (col B, 120°) to be > 98% one component. The product was purified by preparative VPC to give 2-cyclohexylethanol (**9**) as a colourless liquid which displayed IR and NMR spectra identical to those of a sample of (**9**) prepared by reduction of 2-phenylethanol with Li/NH_3 and subsequent catalytic hydrogenation of the intermediate product.

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