A New Rearrangement: Conversion of a Diepoxycyclohexane into a Dihydropyrancarbaldehyde

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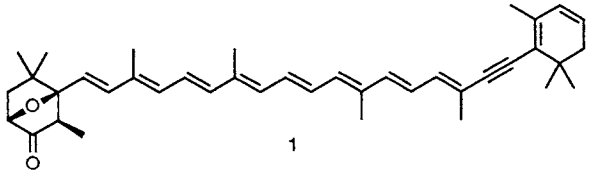
Treatment of 2,7,7-trimethyl-3,8-dioxatricyclo[3.2.1.$0^{2,4}$]octane **5** and derivatives with BF_3 gave the corresponding 4,4,5-trimethyl-3,4-dihydro-2*H*-pyran-2-carbaldehyde **7** and traces only of 3,5,5-trimethyl-7-oxabicyclo[2.2.1]-heptan-2-one **8**.

The carotenoid, eutreptiellanone **1** was reported[1] having a novel 7-oxabicyclo[2.2.1]heptan-2-one end-group. In an approach to the synthesis of this end-group the diepoxycyclohexane **5a** was prepared and treated with BF_3–Et_2O. Only trace amounts of the expected ketone **8a** were formed. The major product isolated was the dihydropyrancarbaldehyde **7a**. Further examples of this new rearrangement are reported and a mechanism of the reaction suggested. The minor product **8a** was converted to its isomer **9a** corresponding to the carotenoid end-group.

The diepoxycyclohexane **5a** was prepared by the method of Kato *et al.*[2] from the *trans*-diol **2a** *via* the epoxide **3a** and the tosylate **4a** (Scheme 1). Base treatment of the tosylate **4a** gave mainly the diepoxycyclohexane **5a** (79.2%) but also traces of the isomeric epoxyketone **6a** (1.65%).[3] The latter is presumably formed by loss of the tosyloxy group and hydride migration to the resulting carbocation site followed by ketone formation and then ring closure by the alkoxide to give the epoxide **6a**.

When the diepoxycyclohexane **5a** was treated with BF_3–Et_2O the expected[4] ketone **8a** was only formed in trace amounts. The major product formed was the dihydropyrancarbaldehyde **7a**. At room temperature the reaction was complete in 90 s giving isolated yields of 88% of **7a** and 8.7% of **8a**. At −77 °C 95% of **7a** was isolated while at 80 °C there



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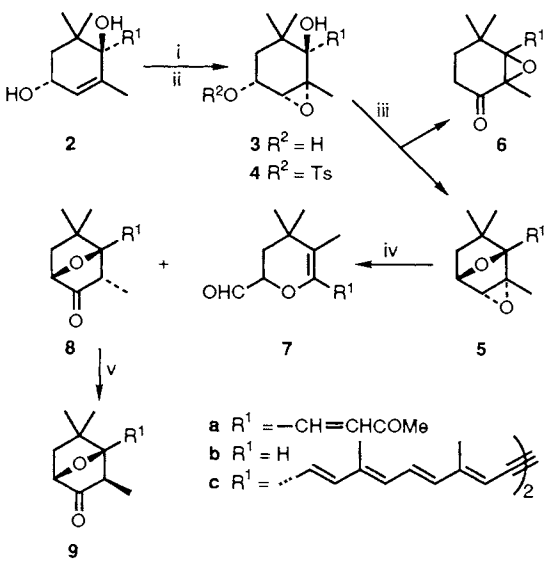
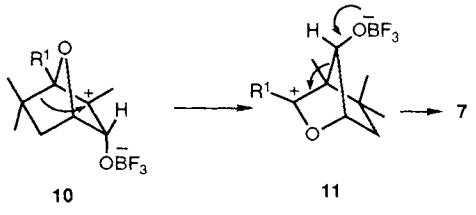


Scheme 1 *Reagents and conditions*: i, *m*-$ClC_6H_4CO_3H$, room temp.; ii, TsCl, py, 0 °C; iii, NaH, THF, 25 °C; iv, BF_3·Et_2O, PhH; v, MeONa, MeOH, room temp., 5 h; Ts = *p*-$MeC_6H_4SO_2$, THF = tetrahydrofuran



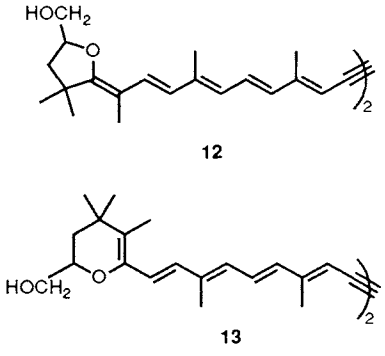
Scheme 2

was a reduced yield due to decomposition. The rearrangement was also detected after leaving a chloroform solution for 4 h presumably due to traces of HCl present. The aldehyde **7a**† was not very stable and was fully characterised after reduction to the corresponding diol and conversion to its diacetate. Its structure was only identified by comparison with the related product **7b**† prepared in the model studies described below.

The rearrangement of **5** to **7** can be explained as initially giving the expected carbocation **10** which on 1,2-hydride migration of the shown hydrogen atom gives the ketone **8**. However, the main reaction is rearrangement to the carbocation **11** (Scheme 2) followed by ring cleavage to give the dihydropyrancarbaldehyde **7**. Analogous rearrangements of carbocyclic systems similar to **11** have been observed.[5]

To identify the location of the methyl group attached to the double bond of **7** model studies with **5b** were undertaken. It

† *Spectroscopic data* for **7a**: ^1H NMR (250 MHz, $CDCl_3$): δ 1.13 (s, 4-Me), 1.18 (s, 4-Me), 1.85 (s, 5-Me), 4.28 (ddd, *J* 1,4, 11 Hz, 2-H), 9.83 (d, *J* 1 Hz, CHO), [side chain 2.30 (s, Me), 6.58 (d, *J* 16 Hz, 3-H), 7.38 (d, *J* 16 Hz, 4-H)]; ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 12.3 (q, 5-Me), 27.6 (q, 4-Me), 27.9 (q, 4-Me), 33.2 (s, C4), 38.4 (t, C3), 76.3 (d, C2), 126.5 (s, C5), 142.0 (s, C6), 201.4 (d, CHO), [side chain 28.6 (q, Me), 125.9, 133.5 (both d, CH=CH), 198.6 (s, CO)]. For **7b** ^1H NMR (80 MHz, $CDCl_3$): δ 1.05 (s, 4-Me), 1.17 (s, 4-Me), 1.53 (d, *J* 2 Hz, 5-Me) 4.30 (m, 2-H), 6.15 (br, 6-H), 9.75 (d, *J* 1.5 Hz, CHO); corresponding acetate of reduced **7b** ^1H NMR: δ 1.04 (s, 4-Me), 1.09 (s, 4-Me), 1.51 (d, *J* 1.5 Hz, 5-Me), 1.55 (m, 3-H), 2.11 (s, Ac), 4.04 (m, 2H), 4.07 (dd, *J* 6.5, 11 Hz, CH_2OAc), 4.19 (dd, *J* 3, 11 Hz, CH_2OAc), 6.08 (br, 6-H); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ 12.9 (q, 5-Me), 20.9 (q, Ac), 27.6 (q, 4-Me), 28.1 (q, 4-Me), 31.0 (s, C4), 40.2 (t, C3), 66.8 (t, CH_2OAc), 70.2 (d, C2), 115.9 (s, C5), 136.9 (d, C6), 170.9 (s, Ac).



was prepared in the same way (Scheme 1) as before and again traces of the ketone **6b** were isolated. Treatment of the diepoxycyclohexane **5b** with BF_3–Et_2O gave, after 20 s at −18 °C, **7b** and traces of **8b**. The NMR spectrum of **7b** showed the methyl was located at C-5 of the pyran ring (C-6 δ 6.15 for **7b** and after reduction at δ 6.11 and 136.7, C-5 at δ 116.0). A model compound with the two oxygen atoms *cis* to each other proved to be resistant to BF_3 catalysed rearrangement.

A similar rearrangement of a bisdiepoxy-derivative has been reported in the literature. When the synthetic carotenoid **5c** was treated with diisobutylaluminium hydride (DIBAH) it was claimed[6] to give the diol **12**. From our results it is clear that Eugster's product should be corrected to **13**. The NMR spectra quoted for the ring system are almost identical to our data with the expected slight variation due to the different side-chains. Thus, the DIBAH is acting as a Lewis acid giving a similar rearrangement followed by reduction of the aldehyde group formed. Another example of a DIBAH induced rearrangement of a diepoxy-derivative is reported by Finch *et al.*[7]

Base treatment of the minor rearrangement product **8a** resulted in isomerisation to the diketone **9a**. The NMR spectrum‡ was essentially the same as that assigned[1] to the relevant end-group of the natural carotenoid **1**. It is clear that the signal quoted for C-7′ (δ 92.7) should be assigned to C-6 with only C-3 at δ 80.5 (carotenoid numbering). It is probable that the signal for C-7′ was not detected owing to its long relaxation time.

We thank the Palm Oil Research Institute of Malaysia for a studentship (C. K. O.).

Received, 11th November 1991; Com. 1/057211

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‡ *Spectroscopic data* for **9a** ^1H NMR (250 MHz, $CDCl_3$): δ 0.92 (s, 5-*exo*-Me), 0.93 (d, *J* 7 Hz, 3-Me), 1.12 (s, 5-*endo*-Me), 1.57 (d, *J* 13.5 Hz, 6-*endo*-H), 1.92 (dd, *J* 7, 13.5 Hz, 6-*exo*-H), 2.51 (q, *J* 7 Hz, 3-H), 4.39 (d, *J* 7 Hz, 1-H), [side chain 2.26 (s, Me), 6.37 (d, *J* 16 Hz, α-H), 6.62 (d, *J* 16 Hz, β-H)]; ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 24.2 (3-Me), 28.6, 28.9 (2 × 5-Me), 42.6 (C5), 42.7 (C3), 44.7 (C6), 80.6 (C1), 92.1 (C4), 213.3 (C2), [side chain 12.8 (Me), 131.0, 139.0 (CH=CH), 197.4 (CO)].