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EXCEPTIONAL DESULPHONYLATION OF β-EPOXY SULPHONYL CONTAINING 10-OXATRICYCLODECENONES

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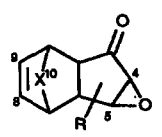
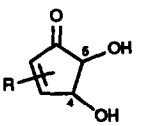
Abstract: Treatment of 4,5-epoxy-4-tosylmethyl-10-oxatricyclo[5.2.1.$0^{2,6}$]-8-en-3-ones with sodium methanolate in methanol and subsequent acid hydrolysis leads in high yield to 4-formyl-10-oxatricyclo-[5.2.1.$0^{2,6}$]-8-en-3-ones. The reaction sequence involves successively, a base induced epoxide ring opening of a β-epoxy sulphone, three consecutive S_N2' type reactions and a hydrolysis of a dimethyl acetal.

Tricyclodecadienone epoxides **1** (X=O,CH_2) are suitable precursors for a stereoselective synthesis of both *trans*- and *cis*-4,5-dihydroxy-2-cyclopentenones **2**. This has has been demonstrated previously during the syntheses of pentenomycin[1], terrein[2] and *epi*-pentenomycin[3]. The conversion of **1** into **2** requires two essential



1



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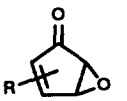

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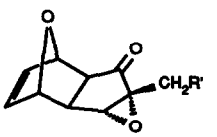


4 R' = OEt
5 R' = $SO_2C_6H_4CH_3$

transformations, *viz.* a thermal [4 + 2] cycloreversion and an epoxide ring opening. In a recent paper[4] we showed that the thermal reaction of 10-oxatricyclodecadienone epoxides **1** (X=O) to give cyclopentadienone epoxides **3** is conveniently accomplished using the technique of Flash Vacuum Thermolysis. The hydrolysis of the epoxide function in **3** can subsequently readily be achieved under mild acidic conditions and leads usually to *trans*-4,5-dihydroxy-2-cyclopentenones **2**[5].

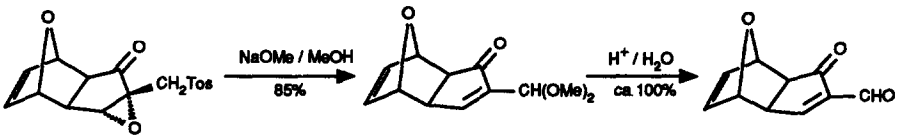
The ease with which the epoxide ring in **3** is converted into a diol considerably contrasts with the reluctance of the tricyclodecadienone epoxides **1** (X=CH_2; R=4-CH_2OMe; R=4-Me) to undergo epoxide opening[1,6]. These tricyclic epoxides completely fail to react under conditions that normally result in a smooth reaction of the epoxide ring of α,β-epoxy ketones. Their inertness to undergo epoxide ring opening is ascribed to the typical structural feature that the reactive rear side of the epoxide ring is shielded against nucleophilic attack, by either the C_8-C_9 ethylene bridge in the *endo* form or the C_{10} methylene bridge in the *exo* form.

As various 10-oxatricyclodecadienone epoxides **1** (X=O) became recently conveniently accessible[4,7], we decided to investigate whether these compounds would show a similar reluctance to epoxide ring opening as the related 10-carbon analogues **1** (X=CH_2). The substrates selected for this study were the 4-ethoxymethyl- and 4-tosylmethyl-substituted epoxides, **4** and **5**[4], respectively. In this communication we report that β-epoxy

sulphone **5** in contrast to its ethoxymethyl substituted congener **4** rapidly reacts under basic methanolysis conditions. It will be shown that compound **5** undergoes an exceptional desulphonylation reaction.

Treatment of **4** with 2.2 eq of sodium methanolate in boiling methanol for 24 hrs did not give any product indicative of an epoxide ring opening. The substrate was recovered in *ca.* 80% yield. The loss of material was most probably due to decomposition initiated by β-elimination of the 10-oxa bridge. When epoxy sulphone **5**[8] was treated in the same way as **4** an entirely different result was obtained. Complete conversion of the substrate was observed within 1.5 hrs. After work-up a single product was isolated, which by means of its IR and ^{1}H-NMR spectrum was identified as the dimethylketal **6** (*ca.* 85% yield) (Scheme 1). The characteristic

Scheme 1



5 **6** **7**

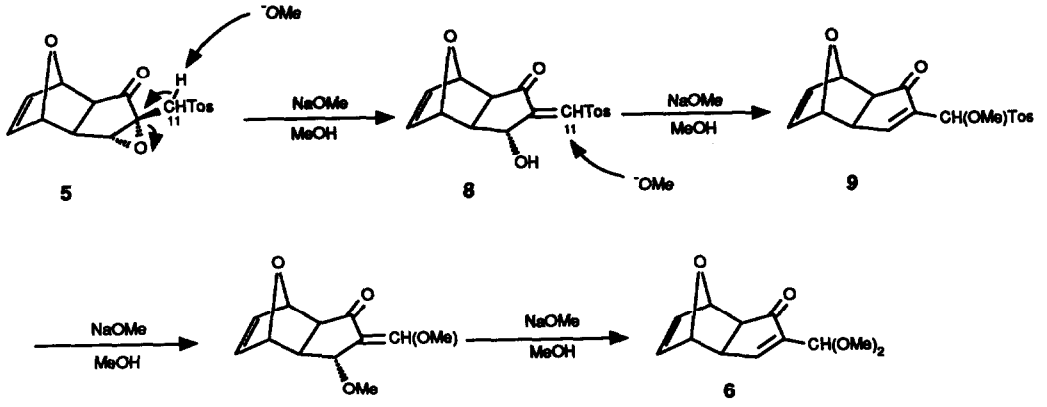
absorption in the IR spectrum at 1710 cm^{-1} and a typical low field resonance for the β-enone proton at δ 7.61 ppm in the ^{1}H-NMR spectrum clearly established the presence of the enone moiety. The ^{1}H-NMR spectrum revealed further the absence of the tosyl group, the presence of a dimethoxy unit and the retention of the tricyclic skeleton (see Table). Independent prove that the dimethoxy moiety was an acetal was obtained from the acid catalysed hydrolysis of **6** in a 2:1 mixture of dichloromethane and 3% HClaq. This hydrolysis produced the expected aldehyde **7** as a crystalline solid in almost quantitative yield.

The reluctance of epoxide **4** to undergo epoxide ring opening under the above conditions must be attributed to a shielding effect of the 10-oxa bridge, similar to that exerted by the C_8-C_9 ethylene or C_{10} methylene bridge in the *endo*- or *exo*-tricyclodecadienone epoxides **1** (X=CH_2). It is highly unlikely that this shielding effect of the 10-oxa bridge in sulphone **5** would be less pronounced. Direct bimolecular epoxide ring opening as the initial step in the formation of **6** from **5** can therefore be excluded.

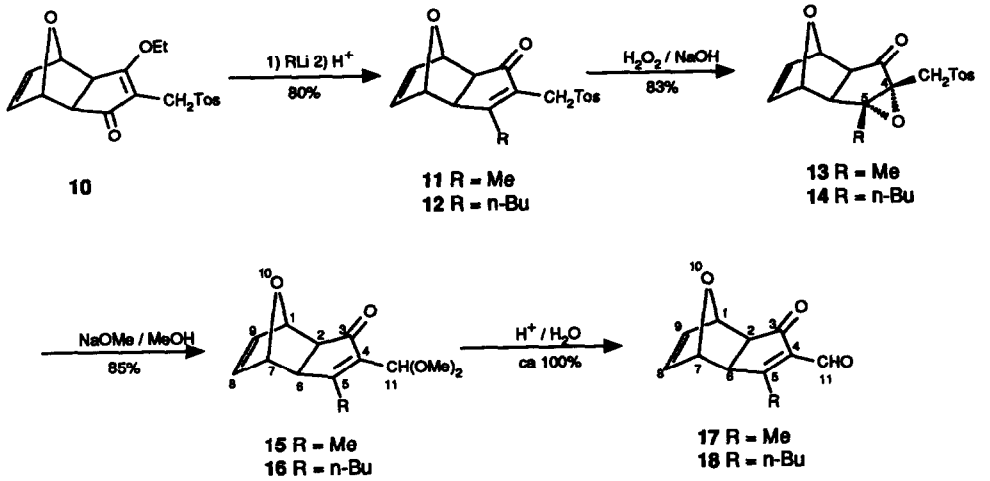
An essential difference between the substrates **4** and **5** is that the latter has an active methylene group, adjacent to the sulphone function, which permits a reaction of compound **5** commencing with proton abstraction. In view of this the conversion of **5** into **6** can satisfactorily be rationalized as follows. Initial deprotonation at C_{11}, followed by intramolecular opening[9] of the epoxide ring, generates alcohol **8** (Scheme 2). Subsequent attack[10] of a methoxide anion at C_{11} in **8** leads to sulphone **9**, most probably by a reaction involving an S_N2' type substitution[11]. Sulphone **9** is then converted into dimethyl acetal **6** by two consecutive S_N2' displacement reactions, as indicated in Scheme 2.

To extend the scope of this interesting transformation, epoxy sulphones **13** and **14** were prepared and treated with NaOMe in MeOH in the same way as epoxy sulphone **5**. Both compounds **13** and **14** were readily obtained from sulphone **10**[7] via alkylation with MeLi or n-BuLi, followed by alkaline epoxidation of the resulting enones **11** and **12**, respectively (Scheme 3). The subsequent transformation into the corresponding dimethyl acetals **15** and **16** took place smoothly. Complete conversion was reached in less than 1 hr. Both ketals **15** and **16** are stable crystalline compounds. They were unequivocally characterized by their ^{1}H-NMR spectra

Scheme 2



Scheme 3



(see Table). Treatment with HClaq in dichloromethane led, as in the case of **6**, to a rapid and quantitative formation of aldehydes **17** and **18**, respectively (see Table for ^{1}H-NMR data).

The aldehydes **7**, **17** and **18** are thermolabile compounds. They slowly decompose on standing at room temperature. These aldehydes are interesting structures, which are expected to be highly reactive Michael acceptors and dienophiles. They deserve further synthetic elaboration, particularly when is taken into account that these tricyclic compounds in combination with Flash Vacuum Thermolysis can be considered as synthetic equivalents of α-formyl cyclopentadienones.

Table. ^{1}H-NMR spectra[a] of 4-dimethoxymethyl- and 4-formyl-10-oxatricyclodecadienones

no.	H_2	H_6	$(OMe)_2$	H_1/H_7	H_{11}	H_8/H_9	C_5-R
6	2.49(d)	2.98(m)	3.28(s)	4.74(s)	5.11(s)	6.42(dd)	R=H
			3.34(s)	5.02(s)		6.56(dd)	7.61(d)
15	2.42(d)	2.75(d)	3.30(s)	4.82(s)	5.13(s)	6.49(m)	R=Me
			3.40(s)	5.00(s)			2.32(s)
16	2.43(d)	2.90(d)	3.27(s)	4.80(d)	5.07(s)	6.41(dd)	R=n-Bu
			3.36(s)	4.98(s)		6.53(dd)	0.95(t); 1.47(m)
							2.43(d); 3.09(m)
7	2.58(d)	3.10(m)		4.87(s)	9.84(s)	6.43(dd)	R=H
				5.09(s)		6.58(dd)	8.23(d)
17	2.52(d)	2.90(d)		4.89(s)	9.90(s)	6.48(m)	R=Me
				5.23(s)			2.52(s)
18	2.48(d)	3.00(d)		4.88(s)	9.93(s)	6.47(m)	R=n-Bu
				5.07(s)			0.93(t); 1.50(m)
							2.48(m); 3.29(m)

a The spectra were measured in $CDCl_3$/TMS. Chemical shifts are recorded in ppm.

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8. This compound was prepared by alkaline epoxidation of 4-*p*-tolylsulphonylmethyl-*exo*-10-oxatricyclo[5.2.1.$0^{2,6}$]deca-4,8-dien-3-one[7].
9. Similar base-promoted epoxide opening reactions of β-epoxysulphones have been reported by (a) Bordwell, F. G.; Sokol, P. J.; Spainhour, J. D. *J. Am. Chem. Soc.* **1960**, *82*, 2881; (b) Conrad, P. C.; Fuchs, P. L. *Ibid.* **1978**, *100*, 346; (c) Donaldson, R. E.; Saddler, J. C.; Byrn, S.; McKenzie, A. T.; Fuchs, P. l. *J. Org. Chem.* **1983**, *48*, 2167.
10. Although the tosyl group discourages nucleophilic attack at an adjacent carbon, such an attack cannot be excluded here, since the carbon involved is an sp^2 centre and therefore less susceptible to steric and electronic shielding.
11. For evidence see ref 7.

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