Tetrahedron Vol. 45, No. 22, pp. 7149 to 7160. 1989
Printed in Great Britain.

0040-4020/89 $3.00+.00

SELECTIVE BIS-HYDRIDE REDUCTION OF TOSYLMETHYL-SUBSTITUTED TRICYCLIC ENONES BY LITHIUM ALUMINIUM HYDRIDE SYNTHESIS OF α-METHYLENE CYCLOPENTENOIDS[1]

Adrie A. M. Houwen-Claassen, A. J. H. Klunder, and B. Zwanenburg*
Department of Organic Chemistry, University of Nijmegen,
Toernooiveld, 6525 ED NIJMEGEN, The Netherlands

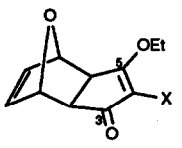
(*Received in UK* 26 *July* 1989)

Abstract: On treatment with LAH the 4-tosylmethyl substituted exo-*10-oxatricyclo[5.2.1.0^{2,6}]decadienones* **1** *and* **3** *undergo two consecutive, regioselective and stereospecific reductions. The first reduction constitutes an S_N2' displacement of the allylic tosyl group, the second a 1,2-reduction of the resulting* exo-*cyclic enone to form the α-methylene cyclenols* **7** *and* **8**, *respectively. These products are smoothly converted into α-methylene-cyclopentenols and α-methylene-cyclopentenones, using the Flash Vacuum Thermolysis techmique for the required cycloreversion.*

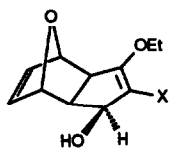
Introduction

Functionalized cyclopentenones are of general interest in natural product synthesis. In several papers we showed that a broad range of cyclopentenones can conveniently be obtained from appropriately substituted tricyclo[5.2.1.0^{2,6}]decadienones[2]. In connection with studies on the synthesis of cyclopentadienone epoxides[3,4], we needed to convert the tosylmethyl substituted 10-oxatricyclo[5.2.1.0^{2,6}]decadienone **1** into the tricyclic sulphone **3**. Such a transformation, which actually involves the conversion of a β-alkoxy enone into an α,β-unsaturated carbonyl compound, can in principle be achieved via complex metal hydride reduction of the ketone function followed by acid hydrolysis of the resulting γ-hydroxy enol ether[5-7]. The Lithium Aluminium Hydride (LAH) reduction of tricyclodecadienone **4** indeed follows this course. This was demonstrated by the isolation of the intermediate enol ether **5** and its subsequent hydrolysis to enone **6**[3,8]. We expected that the LAH reduction of the structurally related tricyclic sulphone **1** would proceed in the same way and thus would lead to the desired sulphone **3**, or to the intermediate enolether **2**, if neutral or alkaline hydrolysis conditions were applied.

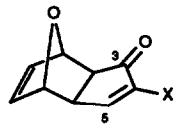
Most unexpectedly, however, the reduction of sulphone **1** with LAH provided neither **2** nor its hydrolyzed derivative **3**. Instead, an entirely different compound was obtained, *viz.* the exo-cyclic methylene derivative **7**. The intended conversion of **1** into sulphone **3** could eventually be achieved by applying Di-iso-Butyl Aluminium Hydride (DIBAL) as the reducing agent[3]. Treatment of sulphone **3** with LAH also resulted in the formation of an exo-cyclic methylene compound, *viz.* **8**. The surprising outcome of these LAH reductions led us to investigate this deviant reduction process in more detail. In this paper we will elucidate the crucial role of the allylic tosyl group in the whole process. Furthermore, we will demonstrate that the formation of the α-methylene alcohols **7** and **8** offers a unique entry to α-alkylidene-cyclopentenols and α-alkylidene-cyclopentenones.



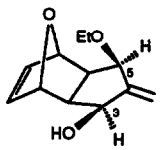
1 X=CH_2Tos
4 X=H



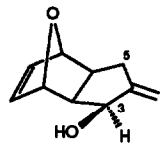
2 X=CH_2Tos
5 X=H



3 X=CH_2Tos
6 X=H



7



8

Results and Discussion

The LAH reductions of sulphones **1** *and* **3.**

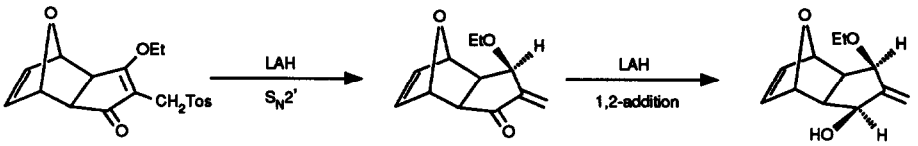
The LAH reduction of sulphone **1** was carried out in THF/ether (3:2), at room temperature. Neutral work-up with sat NH_4Cl afforded **7** as the only product in 70% yield. No trace of **3** or its precursor **2** was found in the crude reaction mixture.

The basic structure of **7** could be deduced from its spectral data. A strong OH absorption at 3365 cm^{-1} and the absence of a C=O band in the IR spectrum indicated complete reduction of the ketone function. The absence of the tosyl group was apparent from the ^{1}H-NMR spectrum. As its spectral data did not allow an unambiguous assignment of the configuration at C-3 and C-5, the product was subjected to an X-Ray analysis[9]. This structure determination confirmed the reduction of the carbonyl function and the reductive elimination of the tosyl group. In addition, it revealed that both these processes had taken place with complete stereospecifity, implying hydride attack from the least hindered *exo*-face of the substrate, *anti* to the 10-oxa bridge. This stereo control is in agreement with previous observations for the *exo*-10-oxa-tricyclodecadienone system[3,4]. The conceivable involvement[10] of the 10-oxa bridge in the complexation of LAH, favouring the formation of a product with the opposite stereochemistry at C-3 and C-5, was not observed.

In order to rationalize the formation of **7** from **1** by reduction with LAH, initial attack at either of the two electrophilic centres in the substrate, C-3 or C-5, can be envisaged. Attack at C-3 would lead to the alcoholate of sulphone **2**. In the next step this alcoholate must then undergo a reductive S_N2' type substitution of the tosyl group in order to arrive at the final product **7**. This reaction sequence, however, could be excluded by subjecting sulphone **2**, obtained from the reduction of **1** with DIBAL[3], to the reaction conditions of the LAH reduction.

Sulphone **2** was not affected by this treatment and was recovered almost quantitatively[11]. Even an excess of LAH and a prolonged reaction time did not produce the slightest trace of **7**. This result convincingly proves that the first step in the LAH reduction of **1** does *not* involve C-3 attack leading to reduction of the ketone group. The primary process apparently is the reductive elimination of the tosyl group, initiated by hydride attack at C-5. This elimination leads to the unsaturated ketone **9**, which then *in situ* is reduced, in a 1,2-fashion, to form the exo-cyclic methylene compound **7** (Scheme 1).

Scheme 1.

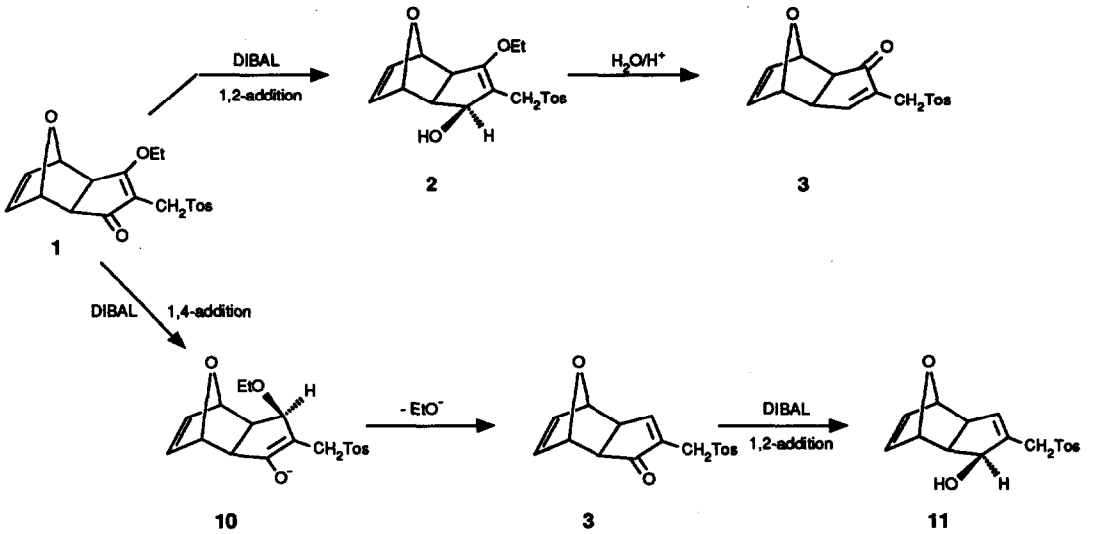


1 **9** **7**

The regioselectivity of the second step is certainly not trivial, since cyclic enones possessing an exo-cyclic double bond have been reported to be reactive Michael acceptors[12-14]. Evidence for the 1,2-selectivity of this step was obtained independently from the LAH reduction of enone **9**, which could be prepared by MnO_2 oxidation of the allylic alcohol **7** (*vide infra*). Under conditions identical to the LAH reduction of sulphone **1**, enone **9** was converted regioselectively and quantitatively into alcohol **7**.

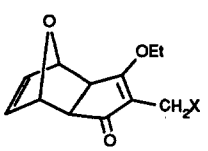
The mechanistic course of the first step is supposed to proceed via the S_N2' pathway. The occurrence of such an S_N2' process has been established for the nucleophilic displacement of the tosyl group in **1** by other nucleophiles such as alcoholates and thiolates[3]. Strong evidence against the alternative pathway, involving initial conjugate addition of the hydride to the enone moiety of sulphone **1** to form the intermediate enolate **10**, was provided by an observation during the investigation of the DIBAL reduction of this sulphone. In contrast to LAH, DIBAL reduces **1** preferentially in a 1,2-fashion to afford **2** as the major product. Subsequent acid hydrolysis of **2** led to enone **3** (Scheme 2). However, when an excess of DIBAL was applied in this reaction, in addition to **2** some bis-reduction product **11** was isolated. The formation of **11** can only be explained by assuming initial 1,4-hydride addition, leading to the formation of enolate **10**. This enolate eliminates *in situ* the C-5 ethoxy group to give enone **3**, which then, under the conditions of the reaction, is converted into alcohol **11** via a regioselective 1,2-reduction (Scheme 2). If such a conjugate addition in the LAH reduction of sulphone **1** would play a role of any importance, then formation of **11** would certainly have been observed. However, no trace of **11** was found in the crude reaction mixture of the LAH reduction. In the DIBAL reductions on the other hand, no α-methylene product **7** was observed. This allows the conclusion that in the LAH- and 1,4-DIBAL reduction, we are dealing with two different processes, both involving initial hydride attack at C-5. The different results with DIBAL, as compared with LAH, after the attack at C-5, can be explained by assuming that DIBAL coordinates more strongly with the carbonyl group[15], thus promoting the 1,4-addition. For LAH, which coordinates less efficiently, both the 1,2- and the 1,4-addition are overruled by the S_N2' displacement of the tosyl group. The absence of any **7** in the product mixtures of the DIBAL reactions not only excludes the S_N2' pathway for the DIBAL reduction, it also proves that elimination of the tosyl group from enolate **10** does not take place. The exclusive elimination of the C-5 ethoxy group from **10** can be explained by an enhanced leaving ability of

Scheme 2.

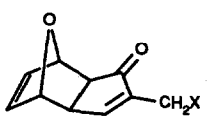


the ethoxy group due to complexation with the excess of DIBAL. On the other hand, strain factors favouring the formation of an endo-cyclic enone system instead of a cyclic enone with an exo-cyclic olefinic bond, also may be involved.

Both the mechanistic course and the regiospecifity of the first step in this LAH reduction are exceptional. In contrast to sulphone **1**, the analogous alkoxymethyl and thiomethyl substituted tricyclic enones **12a** and **12b** undergo exclusively 1,2-reduction of the carbonyl group when treated with LAH, to afford the corresponding α,β-unsaturated enones **13a** and **13b**, respectively. In these LAH reductions the formation of **7** was not



12a X=OiPr
12b X=SPh



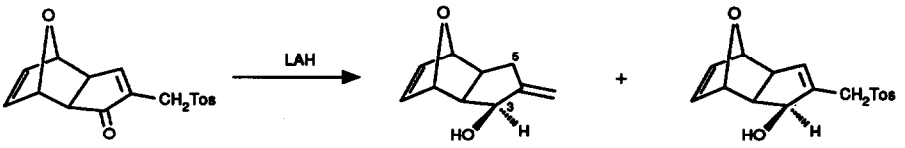
13a X=OiPr
13b X=SPh

observed[3]. Hence, the exceptional regiospecifity of the LAH reduction of sulphone **1** is attributable to the presence of the tosyl group. Most likely, this is connected with the strongly electronegative character of the sulphonyl group which causes a substantial electron deficiency at C-5 of sulphone **1**.

In order to investigate the influence of the C-5 ethoxy group on this reductive process, sulphone **3**, lacking this substituent, was treated with LAH under conditions as applied for sulphone **1**. This afforded the bis-hydride reduction product **8** and sulphone **11**[3], in a ratio of 4:1 (Scheme 3). Compound **11** was isolated by

chromatography. The amount of this by-product could be diminished by performing the reduction at a lower temperature (0°C). In that case, only a negligible amount of **11** was formed (≤ 5%).

Scheme 3.



3 **8** **11**

Apart from the signals for the substituents at C-5, the ^{1}H-NMR features of **8** resemble those of **7**. The assignment of the configuration at C-3 is based on the assumption that the stereochemical course of this bis-hydride reduction is the same as that of the LAH reduction of sulphone **1**.

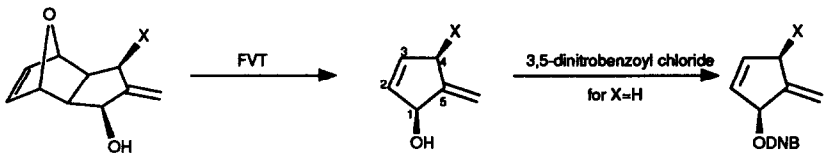
The decreased regioselectivity in the LAH reduction of sulphone **3**, as compared with the LAH reduction of sulphone **1**, can be explained as follows. Due to the absence of the electron releasing C-5 ethoxy group, the electron deficiency at C-3 in sulphone **3** will be more pronounced than at C-3 in sulphone **1**. This electronic effect, favouring 1,2-reduction, is apparently large enough to bring about some competition between hydride attack at C-3 and C-5 in **3**.

Synthesis of α-methylene cyclopentenoids.

The finding of an efficient and stereospecific route to the tricyclic α-methylene alcohols **7** and **8** offers an interesting possibility to synthesize the α-methylene cyclopentenols, **14** and **15**, and the α-methylene cyclopentenones, **17** and **18**.

For the preparation of **14** and **15** only a cycloreversion reaction had to be accomplished. This was carried out by subjecting **7** and **8**, respectively, to Flash Vacuum Thermolysis (FVT) (Scheme 4).

Scheme 4.



7 X=OEt
8 X=H

14 X=OEt
15 X=H

16 X=H

Sublimation of **7** at 0.1 mbar through a quartz pyrolysis tube (16 x 1.3cm), heated at 400°C, afforded **14** as the only product (yield 81%). Under these conditions the conversion of **8** into **15** was not entirely complete. Apparently, a longer contact time or a higher thermolysis temperature was needed in this case. Employment of a

longer pyrolysis tube (25 x 1.3 cm) without changing the other thermolysis parameters indeed provided alcohol **15** (yield 86%) without any substrate **8** remaining.

The spectral data of the α-methylene cyclopentenols **14** and **15** are characteristic for their structure. Both compounds display a strong broad OH absorption in the IR spectrum at ~ 3300 cm^{-1}. For **15** also a less intense OH band at 3595 cm^{-1}, indicative of a free OH group, is found.

The ^{1}H-NMR spectrum of **14** reveals a typical pattern for the ring protons, *viz.* a singlet for H_2 and H_3 at δ 6.12 ppm, a broad singlet for H_1 at δ 4.81 ppm and a broad singlet for H_4 at δ 4.71 ppm. The assignment of the last two signals is based on the different downward shifts caused by a hydroxy (*ca.* 1.7 ppm) and an alkoxy substituent (*ca.* 1.5 ppm)[16], respectively. For the α-methylene protons of **14** a set of two broad singlets is found at δ 5.52 and δ 5.47 ppm. The configuration at C-1 and C-4, which could not be deduced from ^{1}H-NMR data, is assumed to be the same as that at C-3 and C-5, respectively, in precursor **7**.

Despite its simplicity, the ^{1}H-NMR pattern of **15** did not immediately allow a definite assignment of the signals. The olefinic ring protons H_2 and H_3, which in contrast to **14** are clearly distinguishable from each other due to the absence of the C-4 ethoxy group, appear at δ 6.04 and δ 5.89 ppm, respectively. As compared with the H_4 proton of **14**, the protons H_{4A} and H_{4B} of **15** have shifted upfield (*ca.* 1.7 ppm) and are found at δ 3.03 ppm. For H_1 and both α-methylene protons a set of three singlets is observed at δ 5.39, δ 5.17 and δ 5.01 ppm. In order to assign these latter resonances, cyclopentenol **15** was converted into its dinitrobenzoate **16**. Comparison of the ^{1}H-NMR spectrum of **16** with that of **15** revealed a downfield shift for all the ring protons, except for one of the H_4 protons. For this particular proton an upfield shift of 0.36 ppm was observed. This upfield shift is most likely due to a shielding effect of the dinitrobenzoate group. This proton must thus be the proton, that is in *cis*-position with respect to the benzoate group (H_{4A}). The resonances for H_1 and the α-methylene protons were found at δ 6.30 and δ 5.16/5.04 ppm, respectively. On the basis of this information the singlet at δ 5.39 ppm in the ^{1}H-NMR spectrum of **15** was assigned to H_1 and the remaining singlets at δ 5.17 and δ 5.01 ppm to the α-methylene protons.

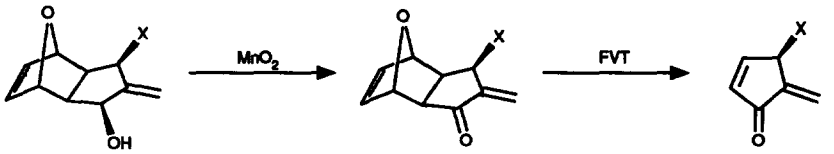
Cyclopentenol **14** decomposes slowly, even when stored in the freezer. In its IR spectrum a strong absorption band at ~ 1730 cm^{-1} and a weaker one at 1650 cm^{-1} gradually appeared, while in the ^{1}H-NMR spectrum an extra set of doublets at δ 7.53 and δ 6.48 ppm was observed along with three new singlets at δ 6.21, δ 5.70 and δ 5.04 ppm, respectively. Both the IR data and the low field ^{1}H-NMR signals pointed to an α,β-unsaturated carbonyl system. GCMS(EI)-analysis of the new structure revealed a mass loss of only two m/e units as compared with the molecular mass of **14**. On the basis of these data we tentatively assigned structure **17** to this compound, which was confirmed in a later stage by an independent synthesis (*vide infra*).

This apparent oxidation of **14** to **17** is typical for **14**. Cyclopentenol **15** was found to be much more stable on storage in the freezer. This suggests that the C-4 ethoxy group plays a role in the formation of **17** from **14**.

The synthesis of the α-methylene cyclopentenones, **17** and **18**, from the tricyclic precursors **7** and **8**, respectively, required, apart from a cycloreversiom step, the oxidation of the allylic alcohol group at C-3. The precursor for **17** *viz.* **9**, was readily prepared from **7** by an MnO_2 oxidation (Scheme 5, *cf.* discussion of Scheme 1). Similarly, **19** was obtained from **8** in good yield.

Both enones appeared to be sensitive compounds. Attempts to obtain an analytically pure sample of **19**, using various chromatographic techniques, failed due to decomposition of the product. Flash chromatography of enone **9** over SiO_2 also led to considerable decomposition. Most unexpectedly, in this case, besides enone **9**, a small amount of the cycloreversion product **17** was isolated[17]. Since the purity of both **9** and **19**, as obtained

Scheme 5.



7 X=OEt **9** X=OEt **17** X=OEt
8 X=H **19** X=H **18** X=H

directly from the oxidation, was sufficient for the subsequent thermolyses, no further attempts were made to prepare analytically pure samples. The spectral data obtained for **9** and **19** were in full accord with their structures.

The cycloreversions of enones **9** and **19** to give **17** and **18**, respectively, were carried out under FVT conditions. When **9** was subjected to the same thermolysis conditions (400°C, 0.1 mbar), that had been applied for its precursor **7** in the synthesis of **14**, it was quantitatively converted into a mixture of the desired cyclopentenone **17** and an unknown by-product in a ratio of *ca.* 3:1 (capillary GC and ^{1}H-NMR data). Comparison of the ^{1}H-NMR data of the mixture with those obtained for **14** and **18** (*vide infra*), confirmed the presence of structure **17** as the major product. The structure of the by-product has not been elucidated yet. In order to prevent the formation of a similar by-product in the thermolysis of **19**, or at least to diminish its relative amount, the cycloreversion of enone **19** was attempted at a lower temperature, *viz.* 310°C instead of 400°C. This experiment afforded cyclopentenone **18** as the only product.

Both α-methylene cyclopentenones **17** and **18** are characterized by their spectral properties. Most typical are the ^{1}H-NMR resonances of the endo-cyclic H_β protons at low field, *viz.* δ 7.59 and δ 7.61 ppm, respectively, and those of the exo-cyclic H_β protons at much higher field, *viz.* δ 5.69/6.23 ppm and δ 5.44/6.12 ppm, respectively. The ^{1}H-NMR data of **18** are in agreement with those reported by Siwapinyoyos and Thebtaranonth[18] for this compound. Both cyclopentenones appeared to be stable on storage in the freezer. No indications of a spontaneous polymerization[18] were found.

Concluding remarks

The bis-hydride reduction of the sulphones **1** and **3** by LAH involves the initial S_N2' displacement of the tosyl group and subsequent 1,2-reduction of the carbonyl function. Both these processes proceed in a stereocontrolled manner from the *exo*-side of the substrate molecule, *anti* with respect to the oxa-bridge. This special behaviour of the sulphones **1** and **3** during LAH reductions finds its origin in the electron attracting character and the leaving ability of the allylic tosyl group.

The reduction products, *i.e.* the alcohols **7** and **8**, are excellent precursors for the stereospecific synthesis of functionalized α-methylene cyclopentenols and α-methylene cyclopentenones, using the FVT technique for the required cycloreversions. Such cyclopentenoids, in particular the α-methylene cyclopentenones, are potentially valuable synthons in natural product synthesis[18,19].

Experimental

General remarks

Melting points were measured with a Reichert Thermopan microscope and are uncorrected. IR spectra were taken on a Perkin Elmer 298 infrared spectrophotometer. ^{1}H-NMR spectra were recorded on a Varian EM-390 or a Bruker WH-90 spectrometer using TMS as internal standard. For mass spectra a Varian SM-1B or a double focussing VG 7070E mass spectrometer was used. Column chromatography under light pressure ("flash chromatography"[20]) was carried out at a pressure of *ca* 1.5 bar, a column length of *ca* 15 cm and a column diameter of 1-4 cm, using Merck Kieselgel 60 H or Merck Aluminium Oxid 150 neutral (Typ T).

Endo-*5-ethoxy-4-methylene*-exo-*10-oxatricyclo[5.2.1.0^{2,6}]deca-8-ene*-endo-*3-ol* (**7**).

Sulphone **1**[3] (450 mg; 1.25 mmol) was added to 57 mg of LAH (1.50 mmol), suspended in a mixture of dry ether (12 ml) and dry THF (18 ml), under nitrogen, at room temperature. After 40 min of stirring, acetone (1 ml) was added to decompose the excess of LAH. The mixture was stirred for another 5 min and was then diluted with saturated NH_4Cl (5 ml). Stirring was continued for 15 min. Then more water was added to obtain a better separation between the organic and the aqueous layer. The aqueous phase was extracted with dichloromethane (3x60 ml). The combined organic layers were washed with water(3x), dried ($MgSO_4$), filtered and concentrated. The crude product (247 mg, purity *ca*, 90%) was crystallized in hexane-ethyl acetate (5:1) to give 108 mg of pure **7**, mp 132-134°C. Flash chromatography (SiO_2/hexane-ethyl acetate (3:1)) of the mother liquor afforded an additional amount of pure **7** (83 mg) (70% total yield). IR(KBr) ν: 3365(s), 3020(w), 2975(m), 2885(m), 1430(br w), 1372(w), 1350(w), 1308(m), 1230/1225(m), 1160(w), 1145(w), 1123(m), 1100/1088(s), 1073(m), 1008(m), 948(m), 918(m), 905/898(s), 830(m), 698(s) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.21(3H,t,J=7Hz;OCH_2CH_3), 2.11-2.31 (2H,m;H_6,H_2), 2.42(1H,br d,J=8Hz;OH), 3.57(2H,q,J=7Hz;OCH_2CH_3), 4.10(1H,m;H_5), 4.40(1H,m;H_3), 4.92 (d,J=1.8Hz)/4.97(d,J=1.8Hz)($C=CH_2$)[21]//4.99(br s;H_7)/5.07(br s;H_1)(4H in all), 6.28(2H,m;H_8,H_9). MS(CI) m/e(%): 209(43;M+1$^+$), 191(16;-H_2O), 163(14;-C_2H_5OH), 162(13;M$^+$-C_2H_5OH), 147(14), 146(24), 145(100), 141(10; -furan), 139(12), 137(14), 123(42;-H_2O,-furan), 117(19), 113(62), 95(23;-furan,-C_2H_5OH), 85(20), 68(15;furan$^+$). (Found: C 69.55, H 7.86. Calc. for $C_{12}H_{16}O_3$: C 69.21, H 7.74%.)

Attempted reduction of sulphone **2** *with LAH.*

Sulphone **2**[3] (206 mg; 0.57 mmol) was stirred with LAH (24 mg; 0.63 mmol) in a mixture of dry ether (4 ml) and dry THF (6 ml), under nitrogen, at room temperature, for 2.5 hr. About half the amount of the reaction mixture was then treated with acetone (0.5 ml; 5 min of stirring) to decompose the excess of LAH. Subsequent hydrolysis was carried out with 10% NaOH. The aqueous layer was extracted with dichloromethane (3x3 ml). The combined organic extracts were washed with water (1x), dried ($MgSO_4$) and concentrated, affording 147 mg of sulphone **2**. No trace of **7** was found in this product (^{1}H-NMR). The remaining part of the reaction mixture was stirred overnight with an extra amount of LAH (8 mg). Subsequent work-up in the same way as above, afforded 40 mg of sulphone **2**. Although its purity was less than that of the first batch, again no trace of **7** could be detected (^{1}H-NMR).

4-Methylene-exo-*10-oxatricyclo[5.2.1.0^{2,6}]deca-8-ene*-endo-*3-ol* (**8**).

Reduction of sulphone **3**[3] (187 mg; 0.6 mmol) with LAH (30 mg; 0.8 mmol) in a mixture of dry ether (6

ml) and dry THF (9 ml), as described above for sulphone **1** (see **7**), afforded 117 mg of a crude product mixture, containing alcohol **8** and sulphone **11**[3] in a ratio of 4:1 (combined yield *ca.* 100%). Separation of the products was accomplished by flash chromatography over SiO_2, using hexane-ethyl acetate (3:1) as the eluent. An analytically pure sample of **8**, mp 104-106°C, was obtained by subsequent crystallization in hexane-ethyl acetate (3:1). With the above eluent, sulphone **11** severely dragged behind and could not be collected. However, by applying a more polar eluent, this sulphone indeed could be isolated. By performing the reduction at 0°C instead of room temperature, the relative amount of **11** was substantially reduced. IR(KBr) ν: 3405(s), 3000(m), 2965(m), 2885(m), 1428(m), 1310(m), 1110/1105(s), 1005/998(m), 945(m), 905(s), 880(s), 862(s), 830(s), 678(s) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.80-2.68(5H,m; *endo*-H_5,H_6,H_2,OH,*exo*-H_5), 4.48(1H,br m;H_3), 4.65(1H,s;H_7), 4.85(d,J~1Hz)/4.93(d,J~1Hz)(2H;C=CH_2)[21], 5.12(1H,s;H_1), 6.36(2H,narrow m;H_8,H_9). (Found: C 72.55, H 7.46. Calc. for $C_{10}H_{12}O_2$: C 73.15, H 7.37%.)

Endo-*5-ethoxy-4-methylene*-exo-*10-oxatricyclo[5.2.1.0^{2,6}]deca-8-ene-3-one* (**9**).

A mixture of **7** (108 mg; 0.52 mmol), activated MnO_2 (1851 mg; 21.2 mmol) and dry ether (15 ml) was stirred for 3 hrs at room temperature. Subsequent filtration and evaporation afforded 51 mg of **9** as an almost pure (^{1}H-NMR), pale tinted oil (50% yield). Attempts to purify the product by flash chromatography (SiO_2/hexane-ethyl acetate (3:1)) afforded two fractions, the first of which was **17** (9 mg) (^{1}H-NMR and capillary GC data identical to those of **17**, *vide infra*), while the second consisted of pure **9** (18 mg; colourless oil). IR(CCl_4) ν: 2980(w), 2872(w), 1725(s;C=O), 1645(w;C=C), 1145(w), 1120/1110(s), 1015(w), 955/945(w), 918(w), 898(w), 870(w), 855(w), 683(m) cm^{-1}. ^{1}H-NMR(CCl_4) δ: 1.33(3H,t,J=7Hz;OCH_2CH_3), 2.39(2H,m; H_6,H_2), 3.44-3.83(2H,m,ABX_3 system,J_{AX}=J_{BX}=7Hz;OCH_2CH_3), 4.53(1H,m;H_5), 4.97(1H,br s;H_7), 5.13(1H,br s;H_1), 5.37(1H,dd,J~1.5Hz,J_{gem}=3Hz)/5.91(1H,dd,J~1.5Hz,J_{gem}=3Hz)(C=CH_2)[21], 6.35(d,$J_{8,9}$=5.4Hz)/6.44(dd, J=1.5Hz,$J_{8,9}$=5.4Hz)(2H;H_8,H_9).

Conversion of **9** *into* **7** *via LAH reduction*.

Enone **9** (29 mg; 0.14 mmol) was treated with LAH (5 mg; 0.13 mmol) in a mixture of dry ether (2 ml) and dry THF (4 ml), under nitrogen, at room temperature. After 5 min all starting material had reacted (TLC). Acetone (0.5 ml) was added to quench the reaction. Work-up was carried out as described above for **7**. This afforded 28 mg (*ca.* 100%) of crude **7**, as a thick white oil. The IR spectrum of this product showed no carbonyl absorption. Crystallization from hexane-ethyl acetate (5:1) gave analytically pure **7**.

4-Methylene-exo-10-oxatricyclo[5.2.1.0^{2,6}]deca-8-ene-3-one (**19**).

A mixture of **8** (90 mg; 0.55 mmol), activated MnO_2 (7.6 mg; 8 mmol) and dry ether (12 ml) was stirred for 2.5 hr at room temperature. The mixture was then filtered and evaporated to give 88 mg (98% yield) of **19** as a colourless oil, which solidified in the freezer. Attempts to obtain an analytically pure sample by means of preparative TLC (SiO_2/ethyl acetate) or flash chromatography (Al_2O_3/hexane-ethyl acetate (3:1)) failed, due to decomposition of the product during these purifications. IR(CCl_4) ν: 3000(w), 2965(w), 2935(w), 1722(s;C=O), 1638(m;exocyclic C=C), 1270(s), 1148(s), 1112(m), 1020(m), 940(s), 920/910/902(m), 875(s), 690(m) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 2.24-2.57(~2H,m;H_6,H_2 and upfield part of ABXY pattern of *endo*-H_5), 2.67(~1H,narrow q,$J_{5,5'}$~3Hz;downfield part of ABXY pattern of *endo*-H_5), 2.77-3.21(1H,m;*exo*-H_5), 4.83(1H,br s;H_7), 5.10(1H,br s;H_1), 5.25(1H,narrow t, $J_{5',5}$~3Hz)/5.94(1H,narrow t,$J_{5',5}$~3Hz)(C=CH_2)[21], 6.41(2H,narrow m;H_8,H_9). MS(CI) m/e(%): 163(3;M+1$^+$), 162(7;M$^+$), 145(12), 135(10;-CO), 123(17), 117(24), 95(100;-furan), 68(furan$^+$).

Flash vacuum thermolysis: general procedure.

The substrate is sublimed or distilled in vacuo, at moderate temperature (T_1) through a quartz pyrolysis tube (25 or 16 x 1.3 cm; oven heated (T_2)). The pyrolysate is collected immediately after the tube in a cold trap at -78°C. After the reaction the cold trap is disconnected from the equipment[22] and allowed to warm up under nitrogen. The product is then obtained by rinsing the cold trap with a suitable solvent, followed by removal of the solvent in vacuo.

Cis-*4-ethoxy-5-methylene-2-cyclopentenol* (**14**).

Flash vacuum thermolysis (16 cm tube/0.1 mbar/80°C(T_1)/400°C(T_2)) of **7** (106 mg; 0.50 mmol) provided **14** (57 mg; 81% yield) as a colourless oil (GLC: one peak, 99%). IR(film) ν: 3380(br s;OH), 2970(m), 2870(m), 1390(m), 1350(m), 1060(s), 1010(s), 990(s), 900(m) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.18(3H,t,J=7Hz; OCH_2CH_3), 1.97(1H,br m;OH), 3.53(2H,q,J=7Hz;OCH_2CH_3), 4.71(1H,br s;H_4), 4.81(1H,br s;H_1), 5.47(1H,br s)/5.52 (1H,br s)($C=CH_2$)[21], 6.12(2H,s;H_2,H_3). MS(EI) m/e(%): 140(2;M^+), 139(10;M-1), 123(17;-OH), 112(23;-CO), 111(49;-C_2H_5), 95(100;-OC_2H_5), 83(36), 77(11;C_6H_6), 67(48), 55(60), 41(48), 39(59). HRMS(EI) m/e: 140.0839 (calc. for $C_8H_{12}O_2$(M): 140.0837).

5-Methylene-2-cyclopentenol (**15**).

Flash vacuum thermolysis (25 cm tube/0.06 mbar/80°C(T_1)/420°C(T_2)) of **8** (46 mg; 0.28 mmol) provided **15** (23 mg; 86% yield) as a colourless oil. IR(CCl_4) ν: 3595(m;free OH), 3500-3200(br m), 3060(m), 2985(w), 2900(m), 2825(w), 1432(w), 1380(m), 1110(m), 1040(m), 1000(s), 960(m), 910(s), 837(m), 715(m), 688(w) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.72(1H,s;OH), 3.03(2H,narrow m;H_{4A},H_{4B}), 5.01(1H,br s)/5.17(1H,br s)($C=CH_2$)[21], 5.39(1H,br s;H_1), 5.89(1H,d,$J_{3,2}$=6.7Hz;H_3), 6.04(1H,d,$J_{2,3}$=6.7Hz;H_2).

5-Methylene-2-cyclopentenyl 3,5-dinitrobenzoate (**16**).

Benzoylation of **15** (21 mg; 0.21 mmol) with 50 mg of 3,5-dinitrobenzoyl chloride (0.22 mmol) and a catalytic amount of DMAP (9 mg; 0.08 mmol) in a mixture of dichloromethane (5 ml) and triethylamine (5 drops) at 0°C during 1 hr, afforded, after the usual work-up, repeated flash chromatography (SiO_2/hexane-ethyl acetate (3:1); SiO_2/hexane-ethyl acetate (9:1)) followed by crystallization (hexane), 11 mg of pure, white **16**, mp 103-106°C. IR(KBr) ν: 3080(w;vinyl H), 1720(s;C=O), 1623(m;C=C), 1540(s;NO_2), 1342(s;NO_2), 1268(s), 1160(s), 730(m), 720(s) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 2.57(d,$J_{4A,3}$~2Hz)/2.76(d,$J_{4A,3}$~2Hz)//3.04(br d,$J_{4B,3}$=6.7Hz)/ 3.24(br d,$J_{4B,3}$=6.7Hz)(2H,ABX system,J_{AB}=18Hz;H_{4A},H_{4B}), 5.04(1H,br s)/5.16(1H,br s)($C=CH_2$)[21], 6.16(m, $J_{3,2}$~$J_{3,4B}$=6-7Hz,$J_{3,4A}$~2Hz;H_3)/6.30(br s;H_1)(2H), 6.59(1H,d,$J_{2,3}$=6.2Hz;H_2), 9.16(3H,m;ArH). NB H_{4A} is the proton at C-4 that is in *cis*-position towards the dinitrobenzoate group. (Found: C 53.67, H 3.44, N 9.50. Calc. for $C_{13}H_{10}N_2O_6$: C 53.80, H 3.47, N 9.65%.)

4-Ethoxy-5-methylene-2-cyclopentenone (**17**).

Flash vacuum thermolysis (16 cm tube/0.03 mbar/80°C(T_1)/400°C(T_2)) of **14** (17 mg; 0.08 mmol) afforded a mixture (11 mg) containing **17** as major component (73%). Since the amount of product material was rather small, no attempts to separate cyclopentenone **17** from the by-product were made. Its spectral data could easily be deduced from the spectra of the crude pyrolysate. IR(CCl_4) ν: 1728(s;C=O) and 1652(w;exocyclic C=C) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.22(3H,t,J=7Hz;OCH_2CH_3), 3.57(2H,q,J=7Hz;OCH_2CH_3), 5.04(1H,br s;H_4),

5.69(1H,br s)/6.23(1H,br s)($C=CH_2$)[21], 6.50(1H,d,$J_{2,3}$=6Hz;H_2), 7.59(1H,d(d),$J_{3,2}$=6Hz;H_3). GCMS(EI) m/e(%): 138(48;M^+), 110(81;-CO), 109(52;-C_2H_5), 94(27), 93(72;-OC_2H_5), 82(81), 81(53), 65(100), 55(99), 39(99), 27(84).

5-Methylene-2-cyclopentenone (**18**).

Flash vacuum thermolysis (16 cm tube/0.03 mbar/60°C(T_1)/310°C(T_2)) of **19** (12-20 mg; 0.07-0.12 mmol) provided **18** as the only product (colourless oil; capillary GC: one peak (99%)). IR(CCl_4) ν: 1708(s;C=O), 1650(m;exocyclic C=C), 1582(w), 1428/1415/1402/1388(w), 1342(w), 1250(m), 1195(m), 1135(m), 1080(w), 950(m), 937(s), 838(m), 698(m) cm^{-1}. ^{1}H-NMR($CDCl_3$)[18] δ: 3.24(2H,narrow m; H_{4A},H_{4B}), 5.44(1H,br s)/6.12(1H,br s)($C=CH_2$)[21], 6.42(1H,br d,$J_{2,3}$=6Hz;H_2), 7.61(1H,m;H_3). MS(CI) m/e(%): 95(100;M+1$^+$), 79(18), 68(29), 57(21). HRMS(CI) m/e: 95.0500 (calc. for C_6H_7O(M+1): 95.0497).

Acknowledgements. We want to thank M. G. Kooy and M. J. F. M. Crul for their assistence in some of the experiments.

References and notes

1. Part of this work was published as a short communication: Klunder, A. J. H.; Crul, M. J. F. M.; Houwen-Claassen, A. A. M.; Kooy, M. G.; Zwanenburg, B. *Tetrahedron Lett.* **1987**, *28*, 3147.
2. (a) Klunder, A. J. H.; Bos, W.; Verlaak J. M. J.; Zwanenburg, B. *Tetrahedron Lett.* **1981**, *22*, 4553; (b) Klunder, A. J. H.; Bos, W.; Zwanenburg, B. *ibid.* **1981**, *22*, 4557; (c) Verlaak, J. M. J.; Klunder, A. J. H.; Zwanenburg, B. *ibid.* **1982**, *23*, 5463; (d) Klunder, A. J. H.; Huizinga, W. B.; Sessink, P. J. M.; Zwanenburg, B. *ibid.* **1987**, *28*, 357; (e) Klunder, A. J. H.; Houwen-Claassen, A. A. M.; Kooy, M. G.; Zwanenburg, B. *ibid.* **1987**, *28*, 1329; (f) Lange, J. H. M.; Klunder, A. J. H.; Zwanenburg, B. *ibid.* **1989**, *30*, 127.
3. Houwen-Claassen, A. A. M.; Klunder, A. J. H.; Kooy, M. G.; Steffann, J.; Zwanenburg, B., submitted for publication in *Tetrahedron*.
4. Houwen-Claassen, A. A. M.; Klunder, A. J. H.; Zwanenburg, B., submitted for publication in *Tetrahedron*.
5. Gannon, W. F.; House, H. O. In *Organic Syntheses*; Wiley: New York, 1973; Coll. Vol. V, p 294.
6. Funk, R. L.; Vollhardt, K. P. *Synthesis* **1980**, 118.
7. Gill, M.; Herlt, A. J.; Richards, R. W. *Tetrahedron* **1982**, *38*, 3527.
8. Oda, M.; Kanao, Y.; Kasai, M.; Kitahara, Y. *Bull. Chem. Soc. Jpn.* **1977**, *45*, 2497.
9. Smits, J. M. M.; Beurskens, P. T.; Klunder, A. J. H.; Crul, M. J. F. M. *J. Cryst. Spectrosc. Res.* **1986**, *16*, 665.
10. For an example of the participation of an oxygen containing functionality in the reduction of a carbonyl group, see: Klunder, A. J. H.; de Valk, W. C. G. M.; Verlaak, J. M. J.; Schellekens, J. W. M.; Noordik, J. H.; Parthasarathi, V.; Zwanenburg, B. *Tetrahedron*, **1985**, *41*, 963.
11. Previously, we mentioned also the inertness of sulphone **2** on treatment with sodium methanolate in refluxing methanol[3].
12. Siwapinyoyos, T.; Thebtaranonth, Y. *Tetrahedron Lett.* **1984**, *25*, 353.

13. Smith III, A. B.; Wexler, B. A.; Slade, J. S. *Tetrahedron Lett.* **1980**, *21*, 3237.
14. Verlaak, J. M. J. *Ph.D. Thesis*, University of Nijmegen, Febr. 1983; Chpt. 3.3.
15. House, H. O. *Modern Synthetic Reactions*, 2nd ed.; W. A. Benjamin: Menlo Park, California, 1972; p 67.
16. Hesse, M.; Meier, H.; Zeeh, B. *Spektroskopische Methoden in der organischen Chemie*, 3. Auflage; Georg Thieme: Stuttgart-New York, 1987; p 114.
17. A similar result has recently been reported by Marchand and Vidyasagar, who demonstrated that the tricyclic enones, *exo*-2-carbomethoxy-*exo*-3-methyl- and *exo*-2-carbomethoxy-*exo*-3,7-dimethyl-tricyclo[5.2.1.$0^{2,6}$]deca-8-en-5-one undergo a rapid, Lewis acid promoted cycloreversion at room- or even lower temperatures (Marchand, A. P.; Vidyasagar, V. *J. Org. Chem.* **1988**, *53*, 4412). Their explanation for this acid catalyzed fragmentation may also be applicable to the SiO_2 mediated cycloreversion of **13**.
18. Siwapinyoyos, T.; Thebtaranonth, Y. *J. Org. Chem.* **1982**, *47*, 598.
19. (a) Sasai, H.; Shibasaki, M. *Tetrahedron Lett.* **1987**, *28*, 333; (b) Shibasaki, M.; Ogawa, Y. *ibid.* **1985**, *26*, 3841; (c) Nagaoka, H.; Miyakoshi, T; Yamada, Y. *ibid.* **1984**, *25*, 3621; (d) Smith III, A. B.; Branca, S. J.; Pilla, N. N.; Guaciaro, M. A. *J. Org. Chem.* **1982**, *47*, 1855; (e) Nakanishi, K. *Natural Product Chemistry;* Nakanishi, K. Ed.; 1983; Vol. 3.
20. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
21. Increment calculations (ref 16, p. 115) lead to the conclusion that the highest field signal of this pair should be assigned to the *exo*-cyclic H_β proton, that is in *cis*-position to the carbonyl group.
22. ref 14, p.154.