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Easy Synthesis of 7-Alkylbicyclo[3.3.1]non-6-en-3-ones by Silica Gel-Promoted Fragmentation of 3-Alkyl-2-oxaadamant-1-yl Mesylates

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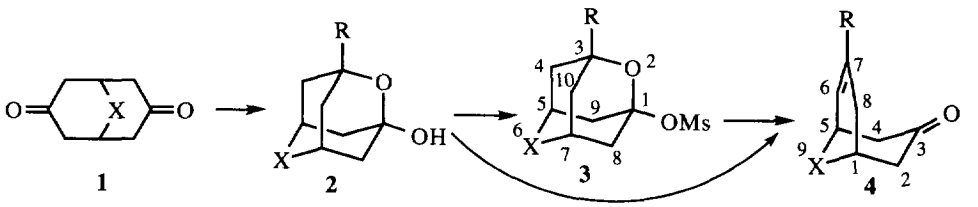
Abstract: A synthesis of 7-alkylbicyclo[3.3.1]non-6-en-3-ones **4b-f** and **4j,k** by reaction of the corresponding 3-alkyl-2-oxaadamant-1-yl mesylates **3** with silica gel in methylene chloride at room temperature, is described. The method failed to give enones **4a,g** and the related compounds **4l,m**, what can be rationalized on mechanistic grounds. Copyright © 1996 Elsevier Science Ltd

In connection with the synthesis of a series of compounds with antiacetylcholinesterase activity, which may be considered as tacrine-huperzine A hybrids, of interest for the treatment of Alzheimer's disease[1], ketones of general structure **4** were required.

Bicyclo[3.3.1]non-6-en-3-one, **4a**, and its 7-methyl derivative, **4b**, are known compounds which have been prepared by several procedures, through multi-step sequences starting normally from adamantane derivatives[2,3]. However, the lack of generality and the complexity of these methods made us look for an alternative procedure to prepare enones **4** from the readily available diketones **1**[4] (Scheme 1).



	X
1a	CH_2
1b	$(CH_3O)_2C$
1c	$(CH_3O)(CH_3)C$
1d	*o*-phenylene

	X	R
2-4a	CH_2	H
2-4b	CH_2	Me
2-4c	CH_2	Et
2-4d	CH_2	Pr
2-4e	CH_2	*n*-Bu
2-4f	CH_2	Ph
2-4g	CH_2	CN

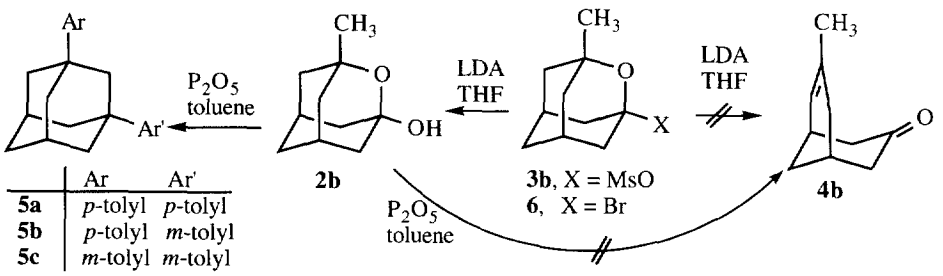
	X	R
2-4h	$(CH_3O)_2C$	Me
2-4i	C=O	Me
2-4j	(*syn*-CH_3O)$(CH_3)C$	Me
2-4k	(*anti*-CH_3O)$(CH_3)C$	Me
2-4l	*o*-phenylene	H
2-4m	*o*-phenylene	Me

Scheme 1. Synthesis of bicyclic enones **4** from diketones **1**[a].
[a] Numbering corresponds to the derivatives of diketones **1a-c**, except **2-4g**.

It is known that diketones **1a** and **1d** undergo transannular reactions on nucleophilic addition to give polycyclic hemiacetals of general structure **2**[5] where R represents the added nucleophile. Moreover, polycyclic hemiacetals such as 5-substituted 9-oxabicyclo[3.3.1]nonan-1-ols or 3,5,9-triphenyl-2-oxatricyclo[4.4.0.0^{3,8}]decan-1-ol have been dehydrated by reaction with *p*-TsOH in refluxing benzene[6] or sulfuric acid in acetic acid[7], respectively, to the corresponding enones, i.e. 5-substituted 4-cycloocten-1-ones or *exo*-4,6,*exo*-8-triphenylbicyclo[3.3.1]non-6-en-2-one.

According to these facts, enones **4** could be obtained by dehydration of the corresponding hemiacetals **2** (Scheme 1). Reaction of the known oxaadamantanol **2b**[5c] with *p*-TsOH or 4 Å molecular sieves in refluxing toluene left the starting material unchanged. The same result was obtained on attempted dehydration of oxaadamantanol **2c**, with conc. H_2SO_4 or HCl in refluxing methanol. On the other hand, reaction of **2b** with P_2O_5 in refluxing toluene gave a mixture of isomeric 1,3-ditolyladamantanes, **5a-c**, in which the *p,p*-isomer **5a**, was the major product (Scheme 2). Chalais et al.[8] obtained a similar mixture of 1,3-ditolyladamantanes, by reaction of adamantane with $FeCl_3$ in the presence of a K 10 clay when toluene was used as solvent.

As an alternative way to transform oxaadamantanol **2b** into enone **4b**, we attempted the base-induced heterolytic fragmentation[9] of its derived mesylate **3b**, obtained from **2b** by a standard procedure[10]. However, reaction of **3b** with lithium diisopropylamide (LDA) in THF did not lead to the expected enone **4b**, but to oxaadamantanol **2b** in 94% yield, a fact that can be explained by 1,2-elimination with sulfene formation via a $E1_{cb}$ mechanism[11] (Scheme 2). Also, the known 1-bromo-3-methyl-2-oxaadamantane[12], **6**, in which such a 1,2-elimination can not take place, failed to give **4b** on reaction with LDA (Scheme 2).



Scheme 2. Attempted synthesis of enone **4b** from hemiacetal **2b**, mesylate **3b** or bromo derivative **6**.

On attempted purification of mesylate **3b** by column chromatography on silica gel only enone **4b** and oxaadamantanol **2b** were isolated, what suggests that an acid-induced heterolytic fragmentation[9] had taken place. This result prompted us to study the use of silica gel to transform mesylates **3** into enones **4**. Reaction of **3b** with silica gel in CH_2Cl_2 at room temperature until all mesylate was transformed (TLC) afforded a mixture of enone **4b** and oxaadamantanol **2b** which were isolated in 71 and 11% yield, respectively, by column chromatography (Scheme 1).

To establish the scope of this reaction, the known oxaadamantanols **2a**[5a,b], **2b**[5c], **2f**[5c] and **2g**[5d] were prepared following the described procedures. Oxaadamantanols **2c**, **2d** and **2e** were prepared in moderate to high yields by reacting diketone **1a** with the corresponding organolithium or organomagnesium reagent in anhydrous THF, following a procedure similar to that described for **2b**. Similarly, reaction of diketone **1b** with methyllithium or methylmagnesium chloride in THF afforded **2h**. The same reaction carried out starting from

9-methoxy-9-methylbicyclo[3.3.1]nonane-3,7-dione, **1c**, afforded a mixture of oxaadamantanols **2j** and **2k**, from which pure samples of these products were isolated by column chromatography in 36 and 18% yield, respectively. Diketone **1c** is a new compound which was obtained by a procedure similar to that described for **1b**, i.e., reaction of 4-methoxy-4-methylcyclohexa-2,5-dienone[13] with dimethyl acetondicarboxylate under basic catalysis followed by hydrolysis and decarboxylation.

The configuration of compounds **2j** and **2k** was established by X-ray diffraction analysis of the less polar stereoisomer **2j**. Figure 1 shows the ORTEP representation of this compound in which a double hydrogen bridge between pairs of molecules of **2j** can be clearly observed.

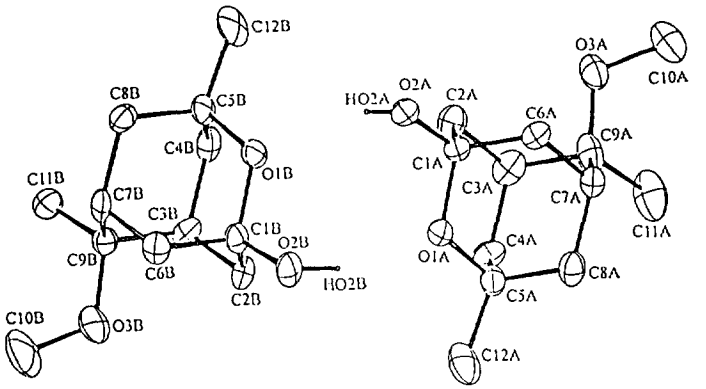


Figure 1. Perspective drawing (ORTEP) of **2j**. The numbering is that used for the X-ray analysis[a].
[a] Selected distances [Å] and angles [°] between the two molecules: HO2B-O1A 2.113, HO2A-O1B 2.003, O2A-HO2A-O1B 162.58, O1A-HO2B-O2B 155.86.

Mesylates **3a-h**, and **3j,k** were prepared in high yields by reaction of the corresponding oxaadamantanols with methanesulfonyl chloride following a standard procedure[10] (Scheme 1).

Treatment of mesylates **3c-f** under the same reaction conditions used for **3b** afforded the expected enones **4c-f** in 42, 47, 41 and 68 yield, respectively. In all cases except **3f**, oxaadamantanols (**2c-e**) were also obtained as by-products in different yields (14, 11 and 28% yield, respectively).

It is worth noting the different behaviour of the stereoisomeric mesylates **3j** and **3k** which gave mixtures of the corresponding enones (**4j** and **4k**, 45 and 22% yield, respectively) and oxaadamantanols (**2j** and **2k**, 26 and 60% yield, respectively) in a very different ratio.

Mesylate **3a** gave only oxaadamantanol **2a** when treated with silica gel under the standard conditions or with conc. H_2SO_4 in refluxing methanol. On the other hand, mesylate **3g** remained unchanged after refluxing with silica gel in dichloromethane or dioxane.

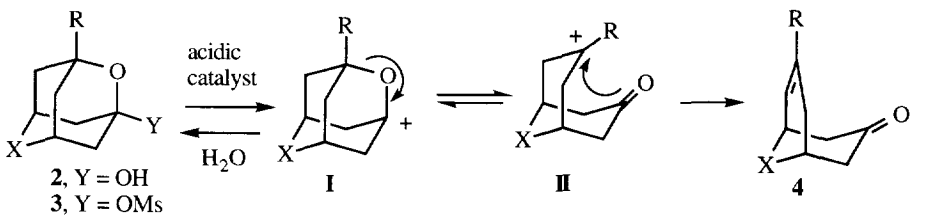
Unexpectedly, mesylate **3h** did not react with silica gel under the standard conditions. However, under more forcing conditions (dichloromethane under reflux) mesylate **3i** was obtained in 93% yield. This fact implies that acetal hydrolysis of **3h** takes place more rapidly than fragmentation to **4h**, and that the resulting mesylate **3i** is stable under these reaction conditions.

Reaction of **2h** with P_2O_5 in refluxing dichloromethane for 8 h gave a mixture of enone **4i** (20% yield) and the new oxaadamantanol **2i** in which the acetal function of **2h** has been hydrolyzed (37% yield). Mesylation

of **2i** gave **3i** which on reaction with conc. H_2SO_4 in dichloromethane at room temperature for 4 d afforded enone **4i** in 24% yield.

Enone **4f** was also obtained in an improved yield (94%) by reacting oxaadamantanol **2f** with sulfuric acid in refluxing methanol for 1 h. Recently, Quast et al.[14] described a synthesis of **4f** (84% yield) by reaction of **2f** with boron trifluoride-diethyl ether in the presence of acetic anhydride for 48 h, pointing out that the reaction failed when other dehydrating agents such as conc. H_2SO_4 in acetic acid, conc. H_2SO_4 in acetic anhydride or trifluoroacetic anhydride, or trimethylsilyl triflate in the presence of 2,6-di(*tert*-butyl)pyridine were used instead.

According to Grob and Schiess[9], these fragmentation reactions could take place through the intermediacy of carbocations such as those indicated in Scheme 3.



Scheme 3. Possible pathway for the acidic fragmentation of hemiacetals **2** or mesylates **3** to enones **4**.

Such a mechanism allows us to explain the competitive formation of enones **4** and oxaadamantanols **2** in most of these reactions as a function of the relative stability of the corresponding intermediate carbocations. The highly preferred formation of enone **4f** from either mesylate **3f** or oxaadamantanol **2f** can be explained on the basis of the greater relative stability of the benzylic carbocation **II** (R = C_6H_5, X = CH_2), a situation which seems to be reversed in the case of mesylate **3a**, where the corresponding carbocation **II** (R = H, X = CH_2) is secondary, oxaadamantanol **2a** being the only observed product in this case.

The absence of reaction of mesylate **3g** may be due to the decreased stability of the initially formed carbocation due to the electronwithdrawing effect of the cyano substituent. The lower reactivity of mesylate **3i** may also reflect a destabilization of the tricyclic carbocation **I** (R = CH_3, X = CO), due to the presence of the carbonyl function at position 9, thus more drastic acidic conditions being required for its fragmentation to **4i**.

To extend the scope of this procedure to related enones, mesylates **3l** and **3m** were prepared from the known[4c, 5e] benzo-fused 2-oxahomoadamantanols **2l** and **2m**, respectively. Reaction of these mesylates with silica gel under the standard conditions gave only the corresponding alcohols **2l** and **2m**. The failure of mesylate **3m** to give enone **4m** may be due to the greater relative stability of the initially formed carbocation, **I** (R = CH_3, X = *o*-phenylene), in this kind of polycyclic systems.

Enones **4a**, **4l** and **4m** have been obtained by different procedures, what will be described elsewhere.

All new compounds have been fully characterized through their spectroscopic and analytical data. Except for compounds **2d,e** and **3e,j,k**, COSY $^1H/^1H$ and $^1H/^{13}C$ experiments were carried out to assign the ^1H- and ^{13}C-NMR spectra. For the compounds where no such experiments were done, assignment was made by comparison with related compounds. Tables 1-6 collect the ^{13}C- and ^1H-NMR data of all of the new compounds, the known compounds **2b,f**, for which these data had not been previously published, and **4f**.

Other kind of experiments were required to completely assign the ^1H- and ^{13}C-NMR spectra of diketone **1c**. A NOESY experiment allowed us to distinguish between 2(4)-H*exo* and 6(8)-H*exo*, the last ones

being close to the 9-methyl substituent while a COSY $^{1}H/^{13}C$ using the HMBC sequence allowed us to differentiate the two carbonyl carbon atoms, through the coupling with their *vicinal* protons.

In compound **2b**, the greater deshielding effect of the hydroxy group in comparison with that of the methyl group on the *exo*-methylene protons, allowed us to assign 8(9)-H*exo*[15]. Differentiation of the 8(9)-H*exo*/8(9)-H*endo* and 4(10)-H*exo*/4(10)-H*endo* pairs could be easily carried out since a W-coupling for 4(10)-H*exo*/9(8)-H*exo* was observed (see Table 4). In passing from compound **2b** to **2h**, deshielding effects around 0.2 ppm for the *exo*-methylene protons and shielding effects around 0.1 ppm for their *endo* pairs, were observed. To assign the 8(9)-H*exo*/8(9)-H*endo* and 4(10)-H*exo*/4(10)-H*endo* pairs of the stereoisomeric compounds **2j** and **2k**, the different effects of the methyl and methoxy groups at position 6 were taken into account[15].

Assignment of the ^{1}H- and ^{13}C-NMR spectra of mesylates **3a-k** was straightforward due to their symmetry and by comparison with the corresponding oxaadamantanols. In a similar way, the ^{1}H- and ^{13}C-NMR spectra of mesylates **3l,m** were assigned.

In the case of enones **4b-f** and **4i-k**, the observed *vicinal* and W-couplings (Table 6) were of capital importance to fully assign their ^{1}H- and ^{13}C-NMR spectra.

In conclusion, we have developed a short synthetic sequence to obtain 7-alkylbicyclo[3.3.1]non-6-en-3-ones **4** from the easily available diketones **1**, based on a silica gel-mediated fragmentation reaction of 3-alkyl-2-oxaadamant-1-yl mesylates under very mild reaction conditions. This reaction seems to work only with 2-oxaadamant-1-yl mesylates bearing an electronreleasing group at position 3. The reaction fails to give the related enones **4l** and **4m** from the corresponding mesylates **3l** and **3m**.

Experimental

Melting points (open capillary tubes) were determined on a Gallenkamp melting point apparatus, model MFB 595010M. IR spectra were recorded on a FT/IR Perkin Elmer model 1600. ^{1}H- and ^{13}C-NMR spectra were taken on Varian Gemini 200 or 300 or VXR 500 spectrometers. The chemical shifts are given in ppm (δ scale) relative to internal TMS and coupling constants are given in Hertz (Hz). COSY $^{1}H/^{1}H$ experiments were performed by using standard procedures while for COSY $^{1}H/^{13}C$ the HMQC and HMBC sequences with an indirect detection probe were used. Numbering of diketone **1c** assigns the lower values to the carbon atoms *syn* to the 9-methoxy group. The *endo*/*exo* notation of the protons at positions 2, 4, 6 and 8 in diketones **1a**, **1b** and **1c** has been retained for the corresponding protons of diketone **1d** and in all of the compounds **2**, **3** and **4** derived from diketones **1a-d**. The *syn*-notation of compounds **2j**, **3j** and **4j** means that the methoxy group is on the same side of the hydroxy, mesyloxy or ketone functions, respectively, while the *anti*-notation of **2k**, **3k** and **4k** means that the methoxy substituent is on different side of the above mentioned groups. Silica gel (SDS 60, 60-200 μm) was used without any pretreatment for the fragmentation reactions and column chromatography. For the TLC, silica gel 60 F254 (alugran R sil G / UV 254) was used. Mycroanalyses were carried out at the Mycroanalysis Service of the Centro de Investigación y Desarrollo, C.I.D., Barcelona, Spain. Diketones **1a**[4a], **1b**[4b] and **1d**[4c] and hemiacetals **2a**[5a,b], **2b**[5c], **2f**[5c], **2g**[5d], **2l**[4c] and **2m**[5e] were prepared using literature methods. NMR data are collected in Tables: ^{13}C-NMR, Tables 1, 2 and 3; ^{1}H-NMR, Tables 4, 5 and 6.

9-Methoxy-9-methylbicyclo[3.3.1]nonane-3,7-dione (1c). To a solution of sodium (40 mg, 1.73 at-g) in methanol (30 ml), a solution of 4-methoxy-4-methylcyclohexa-2,5-dienone[13] (2.40 g, 17.4 mmol) in methanol (60 ml) and a solution of dimethyl acetondicarboxylate (6.10 g, 35.0 mmol) in methanol (60 ml) were successively added dropwise and the reaction mixture was heated under reflux for 48 h. To the cold mixture, water (80 ml) and NaOH pellets (2.00 g, 35.0 mmol) were added and the reaction mixture was heated under

reflux overnight. The organic solvent was evaporated *in vacuo*, the resulting aqueous mixture was made acidic with 2 N HCl (30 ml), stirred for 1 h and extracted with CH_2Cl_2 (4 x 50 ml). The combined organic extracts were dried with anhydrous Na_2SO_4 and evaporated at reduced pressure to give a residue (3.00 g) which was sublimed at 110°C / 1 Torr affording pure diketone **1c** (2.73 g, 81% yield), mp 144°C (CH_2Cl_2). IR (KBr): ν 1714 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.60 (s, 3 H, 9-CH_3), 2.13 [broad d, J = 15.5 Hz, 2 H, 2(4)-H_{endo}], 2.36 [dm, J = 16.5 Hz, 2 H , 6(8)-H_{endo}], 2.60 [m, 2 H, 1(5)-H], 2.66 [dm, J = 16.5 Hz, 2 H, 6(8)-H_{exo}], 2.94 [ddd, J = 15.5 Hz, J' = 6.0 Hz, J" = 1.5 Hz, 2 H, 2(4)-H_{exo}], 3.36 (s, 3 H, 9-OCH_3). ^{13}C-NMR (50.3 MHz, $CDCl_3$): δ 19.3 (CH_3, 9-CH_3), 39.0 [CH, C1(5)], 43.7 [CH_2, C2(4)], 45.0 [CH_2, C6(8)], 49.0 (CH_3, 9-OCH_3), 73.4 (C, C9), 207.7 (C, C7), 208.9 (C, C3). Anal. Cald. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.33; H, 8.27.

General procedure for the preparation of alcohols 2 from diketones 1. To a solution of the organomagnesium or organolithium reagent (1.5 mmol) in diethyl ether, THF or hexane, cooled to 0°C (ice bath), a solution of diketone **1** (1 mmol) in anhydrous THF (5 ml) was added dropwise in a 30 minute period and the reaction mixture was stirred for 0.5-3 h at 0°C. 10% NH_4Cl aqueous solution was added until the resulting white precipitate was completely dissolved. The organic phase was separated and the aqueous one extracted with CH_2Cl_2 (3 x 5 ml). The combined organic extracts were dried with anhydrous Na_2SO_4 and concentrated *in vacuo* to give a residue that was purified by sublimation, crystallization or column chromatography affording the corresponding oxaadamantanol **2**, or the mixture of **2j** and **2k** in the case of diketone **1c**.

3-Ethyl-2-oxa-1-adamantanol (2c). From diketone **1a** (6.00 g, 39.4 mmol) and ethyllithium [prepared from lithium (1.50 g, 0.22 at-g) and 1-bromoethane (4.50 ml, 60.3 mmol) in anhydrous pentane], **2c** (76% yield) was obtained. Alternatively, from **1a** (1.00 g, 6.57 mmol) and 22% ethylmagnesium chloride in THF (2.2 ml, 6.5 mmol), **2c** (74% yield), mp 109-110.5°C (sublimed at 90°C / 0.5 Torr) was obtained. IR (KBr): ν 3318 cm^{-1}. Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.48; H, 9.96. Found: C, 72.46; H, 9.97.

2-Oxa-3-propyl-1-adamantanol (2d). From diketone **1a** (15.0 g, 98.7 mmol) and 2 M propylmagnesium chloride in diethyl ether (74.0 ml, 148 mmol), **2d** (38% yield), mp 66-67°C (sublimed at 80°C / 0.5 Torr) was obtained. IR (KBr): ν 3317 cm^{-1}. Anal. Calcd. for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.51; H, 10.23.

Table 1. ^{13}C-NMR Chemical Shifts[a] of Oxaadamantanols **2**.

Carbon	**2b**	**2c**	**2d**	**2e**	**2f**[b]	**2h**	**2i**	**2j**	**2k**
C1	94.7	94.6	94.5	94.5	95.0	94.6	93.9	94.5	94.4
C3	74.6	77.0	76.7	76.8	77.6	74.2	74.3	73.9	74.1
C4	40.2	37.8	38.5	38.4	40.6	37.3	41.6	38.3	36.3
C5	29.2	29.3	29.5	29.4	29.7	33.7	44.8	36.9	36.9
C6	33.5	34.0	34.1	34.1	33.6	100.3	215.6	75.0	75.2
C8	40.7	41.2	41.4	41.3	41.0	37.4	42.5	36.4	38.6
3-CH_3	28.5	7.1	14.6	14.1		27.6	27.1	27.7	28.2
3-CH_2-Me		34.4	16.0	23.2					
3-$\underline{C}H_2$-Et			44.4	25.0					
3-$\underline{C}H_2$-Pr				41.8					
6-CH_3								19.3	19.7
6-OCH_3						47.0		47.8	48.2
						47.2			

[a] All these spectra were recorded at 50.3 MHz in $CDCl_3$. For equivalent carbon atoms, only the lowest numbered atom is indicated.

[b] The following signals were also observed: *Cipso* 146.7, *Cortho* 124.1, *Cmeta* 128.0 and *Cpara* 126.7.

Table 2. ^{13}C-NMR Chemical Shifts[a] of Mesylates **3**.

Carbon	**3a**	**3b**	**3c**[b]	**3d**	**3e**	**3f**[c]	**3g**[d,e]	**3h**	**3i**	**3j**	**3k**[b]
C1	107.0	108.0	108.0	108.0	108.0	108.2	72.4	107.0	104.5	107.4	107.0
C3	73.9	77.4	79.6	79.5	79.5	80.4	105.7	76.8	76.5	76.4	76.8
C4	34.0	40.0	37.5	38.0	38.0	40.0	38.8	36.9	41.8	37.5	35.8
C5	29.6	30.0	29.9	29.9	29.9	30.3	28.9	34.2	44.7	37.5	37.3
C6	34.0	33.2	33.7	33.6	33.6	33.2	32.5	99.4	212.7	74.4	74.3
C8	40.4	39.7	39.9	39.9	39.9	39.8	37.6	36.0	39.9	35.1	37.1
3-CH_3		28.3	7.0	14.5	13.9			27.3	26.5	27.3	27.7
3-CH_2-Me			33.9	15.9	23.0						
3-CH_2-Et				43.8	24.8						
3-CH_2-Pr					41.2						
6-CH_3										19.1	19.5
6-OCH_3								47.1		48.0	48.2
								47.3			
CH_3SO_3	41.8	42.0	42.0	42.0	42.0	41.9	42.1	42.0	42.0	41.9	42.0

[a] Unless otherwise stated, the spectra were taken at 50.3 MHz in $CDCl_3$. For equivalent carbon atoms, only the lowest numbered atom is indicated. [b] This spectrum was taken at 75.4 MHz. [c] The following signals were also observed: *Cipso* 145.5, *Cortho* 124.1, *Cmeta* 128.3, *Cpara* 127.3. [d] Systematic numbering for this compound has been used, what interchanges C1 / C3 and C4 / C8 with respect to the rest of compounds. [e] The following signal was also observed: CN 118.7.

Table 3. ^{13}C-NMR Chemical Shifts[a] of Enones **4**.

Carbon	**4b**	**4c**	**4d**	**4e**	**4f**[b]	**4i**	**4j**	**4k**
C1	30.1	30.2	30.0	30.1	30.0	44.1	37.4	36.9
C2	49.0	49.1	48.9	49.0	48.9	48.5	45.0	46.5
C3	212.2	212.3	212.0	212.1	211.5	212.5	212.2	211.1
C4	46.4	46.7	46.4	46.5	46.2	46.6	41.3	43.6
C5	31.0	30.9	30.9	31.0	31.3	45.0	39.7	38.7
C6	124.5	123.0	124.2	124.0	127.2	123.5	124.5	122.4
C7	132.7	138.3	136.3	136.7	135.2	134.1	131.4	132.7
C8	37.3	35.7	35.4	35.6	34.7	41.9	37.3	35.9
C9	30.1	30.5	30.3	30.4	29.9	206.2	73.8	73.7
7-CH_3	23.1	12.3	13.4	13.8		22.1	22.3	22.9
7-CH_2-Me		29.8	20.5	22.1				
7-CH_2-Et			39.0	29.7				
7-CH_2-Pr				36.7				
9-CH_3							19.0	19.9
9-OCH_3							48.3	49.4

[a] All these spectra were taken at 50.3 MHz in $CDCl_3$. [b] The following signals were also observed: *Cipso* 141.0, *Cortho* 125.1, *Cmeta* 128.1 and *Cpara* 127.1.

3-Butyl-2-oxa-1-adamantanol (2e). From diketone **1a** (10.0 g, 65.8 mmol) and 1.6 M butyllithium in hexane (70.0 ml, 112 mmol), **2c** (65% yield), mp 58-59°C (sublimed at 60°C / 0.5 Torr) was obtained. IR (KBr): ν 3334 cm^{-1}. Anal. Calcd. for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.45; H, 10.66.

6,6-Dimethoxy-3-methyl-2-oxa-1-adamantanol (2h). From diketone **1b** (4.82 g, 22.7 mmol) and 1.6 M methyllithium in diethyl ether (43.0 ml, 68.8 mmol), **2h** (67% yield) was obtained. Alternatively, from **1b** (1.21 g, 5.70 mmol) and 22% methylmagnesium chloride in THF (2.91 ml, 8.55 mmol), **2h** (53% yield), mp 132°C (diethyl ether) was obtained. IR (KBr): ν 3327 cm^{-1}. Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83. Found: C, 63.08; H, 8.90.

***Syn*-3,6-dimethyl-6-methoxy-2-oxa-1-adamantanol (2j) and *anti*-3,6-dimethyl-6-methoxy-2-oxa-1-adamantanol (2k).** From diketone **1c** (1.10 g, 5.61 mmol) and 22% methylmagnesium chloride in THF (3.00 ml, 8.82 mmol), a mixture of **2j** and **2k** in the approximate ratio **2j / 2k** = 4 / 3 (1.05 g, 88% yield) was obtained.

In order of elution, pure **2j** (36% yield) and **2k** (18% yield) were isolated from this mixture by column chromatography [silica gel (50 g SiO_2 / g material), mixtures hexane / ethyl acetate as eluent]. By using a 1.6 M solution of methyllithium in diethyl ether the yield of the mixture of **2j** and **2k** raised to 97%.
Spectroscopic and analytical data of **2j**: mp 124-126°C (diethyl ether). IR (KBr): ν 3361 cm^{-1}. Anal. Calcd. for $C_{12}H_{20}O_3$: C, 67.89; H, 9.50. Found: C, 67.73; H, 9.65.
Spectroscopic and analytical data of **2k**: mp 88-90°C (hexane / ethyl acetate 8:2). IR (KBr): ν 3318 cm^{-1}. Anal. Calcd. for $C_{12}H_{20}O_3 \cdot 1/4H_2O$: C, 66.48; H, 9.54. Found: C, 66.69; H, 9.34.

General procedure for the preparation of mesylates 3 from alcohols 2. A solution of the alcohol **2** (1 mmol) and anhydrous triethylamine (1.5 mmol) in anhydrous CH_2Cl_2 (5 ml) was cooled at -10°C. Methanesulfonyl chloride (1.5 mmol) was added dropwise over a period of 10 min and the reaction mixture was stirred for 30 min at -10°C. The solution was poured onto a mixture of 2 N HCl (5 ml) and crushed ice. The organic layer was separated and the aqueous one was extracted with CH_2Cl_2 (3 x 5 ml). The combined organic extracts were washed with saturated $NaHCO_3$ aqueous solution (5 ml) and brine (5 ml), dried with anhydrous Na_2SO_4 and evaporated at reduced pressure to afford the corresponding mesylate **3**.

2-Oxa-1-adamantyl methanesulfonate (3a). From **2a** (1.50 g, 9.73 mmol) and methanesulfonyl chloride (1.0 ml, 12.9 mmol), **3a** (1.65 g, 73% yield), mp 127-129°C (ethyl acetate) was obtained. IR (KBr): ν 1320, 1163 cm^{-1}. Anal. Calcd. for $C_{10}H_{16}O_4S \cdot 1/4H_2O$: C, 50.72; H, 7.03; S, 13.54. Found: C, 50.89; H, 6.89; S, 13.39.

3-Methyl-2-oxa-1-adamantyl methanesulfonate (3b). From **2b** (29.8 g, 177 mmol) and methanesulfonyl chloride (22.0 ml, 284 mmol), mesylate **3b** (43.4 g, quantitative yield) was obtained, mp 79-81°C (dichloromethane). IR (KBr): ν 1345, 1175 cm^{-1}. Anal. Calcd. for $C_{11}H_{18}O_4S \cdot 1/4H_2O$: C, 52.67; H, 7.44; S, 12.78. Found: C, 52.38; H, 7.22; S, 12.71.

Table 4. ^{1}H-NMR Chemical Shifts[a] and Coupling Constants of Oxaadamantanols **2**.

	2b[b]	**2c**	**2d**	**2e**	**2f**[c,d,e]	**2h**	**2i**	**2j**	**2k**
δ (ppm)									
4-H*exo*	1.47	1.45	1.45	1.45	1.6-2.0	1.68	1.92	1.63	1.88
4-H*endo*	1.62	1.57	1.59	1.54	1.6-2.0	1.50	1.96	1.56	1.37
5-H	2.30	2.32	2.30	2.30	2.44	2.32	2.69	2.10	2.08
6-H*syn*	1.65	1.66	1.65	1.65	1.6-2.0				
6-H*anti*	1.65	1.66	1.65	1.65	1.6-2.0				
8-H*exo*	1.75	1.76	1.76	1.75	1.6-2.0	1.98	1.96	2.17	1.85
8-H*endo*	1.68	1.67	1.67	1.67	1.6-2.0	1.55	2.19	1.44	1.66
3-C<u>H</u>3	1.15	0.86	0.88	0.87		1.16	1.29	1.15	1.15
3-C<u>H</u>2-Me		1.44	1.35	1.28					
3-C<u>H</u>2-Et			1.35	1.28					
3-C<u>H</u>2-Pr				1.40					
6-C<u>H</u>3								1.24	1.28
6-OC<u>H</u>3						3.15		3.18	3.17
						3.16			
OH	---	2.73	2.76	2.86	3.15	3.64	2.22	---	---
J (Hz)									
4-H*exo*/4-H*endo*	12.0	12.5	12.5	12.5		12.5	14.0	12.5	12.5
8-H*exo*/8-H*endo*	12.0	12.5	12.5	13.0		11.5	13.0	12.0	13.5

[a] Unless otherwise stated, these spectra were taken at 500 MHz in $CDCl_3$. For equivalent protons, only the lowest numbered is indicated. [b] The following coupling constants were also observed: 4-H*exo*/5-H and 7-H/8-H*exo* 3.5 and 4-H*exo*/9-H*exo* 2.0. [c] This spectrum was taken at 200 MHz. [d] The following signals were also observed: H*ortho* 7.46, H*meta* 7.15-7.40 and H*para* 7.15-7.40. [e] The following coupling constants were also observed: H*ortho*/H*meta* 7.5.

Table 5. ^{1}H-NMR Chemical Shifts[a] and Coupling Constants of Mesylates **3**.

	3a[b,c]	**3b**	**3c**	**3d**	**3e**	**3f**[d,e]	**3g**[f]	**3h**	**3i**	**3j**[g]	**3k**[b]
δ (ppm)											
4-H*exo*	1.60	1.50	1.46	1.47	1.46	1.94	2.36	1.74	1.97	1.62	1.92
4-H*endo*	2.01	1.69	1.70	1.70	1.69	2.01	1.97	1.60	2.07	1.70	1.48
5-H	2.39	2.36	2.38	2.37	2.36	2.53	2.49	2.40	2.78	2.17	2.18
6-H*syn*	1.80	1.67	1.70	1.70	1.69	1.82	1.80				
6-H*anti*	1.80	1.67	1.70	1.70	1.69	1.82	1.80				
8-H*exo*	2.33	2.18	2.20	2.20	2.18	2.36	2.27	2.16	2.33	2.33	2.03
8-H*endo*	2.01	1.92	1.93	1.93	1.91	2.04	1.94	2.08	2.53	1.93	2.20
3-C<u>H</u>3		1.19	0.89	0.90	0.87			1.23	1.38	1.21	1.23
3-C<u>H</u>2-Me			1.50	1.36	1.28						
3-C<u>H</u>2-Et				1.44	1.28						
3-C<u>H</u>2-Pr					1.46						
6-C<u>H</u>3										1.24	1.34
6-OC<u>H</u>3								3.16		3.12	3.16
								3.18			
CH3SO3	3.16	3.11	3.13	3.12	3.11	3.15	3.17	3.14	3.22	3.19	3.20
J (Hz)											
4-H*exo*/4-H*endo*	12.6	12.5	12.5	12.7		12.5	13.0	12.5	13.5		12.9
8-H*exo*/8-H*endo*	12.6	11.5	12.0	10.0	10.5	13.0	13.0	13.5	13.0		

[a] Except otherwise stated, the spectra were taken at 500 MHz in $CDCl_3$. For equivalent protons, only the lowest numbered is indicated. [b] This spectrum was taken at 300 MHz. [c] The following signal was also observed: 3-H 4.46. [d] The following signals were also observed: H*ortho* 7.44, H*meta* 7.35 and H*para* 7.26. [e] The following coupling constants were also observed: H*ortho*/H*meta* and H*meta*/H*para* 7.5 and H*ortho*/H*para* 1.5. [f] Systematic numbering for this compound has been used, what interchanges 4-H and 8-H with respect to the rest of compounds. [g] This spectrum was taken at 200 MHz.

3-Ethyl-2-oxa-1-adamantyl methanesulfonate (3c). From **2c** (5.47 g, 30.0 mmol) and methanesulfonyl chloride (3.60 ml, 46.4 mmol), **3c** (7.0 g, 89% yield), mp 44-46°C (CH_2Cl_2) was obtained. IR (KBr): ν 1356, 1178 cm^{-1}. Anal. Calcd. for $C_{12}H_{20}O_4S$: C, 55.36; H, 7.75; S, 12.29. Found: C, 55.43; H, 7.74; S, 12.26.

2-Oxa-3-propyl-1-adamantyl methanesulfonate (3d). From **2d** (0.80 g, 4.08 mmol) and methanesulfonyl chloride (0.48 ml, 6.18 mmol), **3d** (1.02 g, 91% yield) was obtained as an oil. IR (NaCl): ν 1357, 1178 cm^{-1}. Anal. Calcd. for $C_{13}H_{22}O_4S$: C, 56.91; H, 8.08; S, 11.68. Found: C, 57.02; H, 8.13; S, 11.41.

3-Butyl-2-oxa-1-adamantyl methanesulfonate (3e). From **2e** (8.83 g, 42.0 mmol) and methanesulfonyl chloride (5.0 ml, 64.4 mmol), mesylate **3e** (10.6 g, 88% yield) was obtained as an unstable oil. IR (NaCl): ν 1356, 1177 cm^{-1}.

2-Oxa-3-phenyl-1-adamantyl methanesulfonate (3f). From **2f** (250 mg, 1.09 mmol) and methanesulfonyl chloride (0.25 ml, 3.22 mmol), **3f** (300 mg, 89% yield), mp 69-71°C (diethyl ether) was obtained. IR (KBr): ν 1350, 1175 cm^{-1}. Anal. Calcd. for $C_{16}H_{20}O_4S$: C, 62.31; H, 6.54; S, 10.40. Found: C, 62.00; H, 6.56; S, 10.17.

3-Methanesulfonyloxy-2-oxaadamantane-1-carbonitrile (3g). From **2g** (0.50 g, 2.80 mmol) and methanesulfonyl chloride (0.24 ml, 3.10 mmol), mesylate **3g** (0.68 g, 94% yield), mp 119-120.5°C (acetonitrile) was obtained. IR (KBr): ν 2246, 1356, 1186 cm^{-1}. Anal. Calcd. for $C_{11}H_{15}NO_4S$: C, 51.35; H, 5.88; N, 5.44; S, 12.46. Found: C, 51.39; H, 5.89; N, 5.43; S, 12.40.

Table 6. ^{1}H-NMR Chemical Shifts[a] and Coupling Constants of Enones **4**.

	4b	**4c**	**4d**	**4e**	**4f**[b,c]	**4i**	**4j**[d]	**4k**
δ (ppm)								
1-H	2.55	2.56	2.55	2.55	2.77	2.78	2.27	2.34
2-H*exo*	2.48	2.47	2.47	2.47	2.58	2.85	2.71	2.54
2-H*endo*	2.24	2.23	2.23	2.23	2.37	2.54	1.93	2.25
4-H*exo*	2.40	2.41	2.40	2.41	2.54	2.85	2.74	2.54
4-H*endo*	2.28	2.29	2.28	2.28	2.44	2.61	2.01	2.30
5-H	2.63	2.65	2.64	2.64	2.91	2.94	2.45	2.54
6-H	5.40	5.40	5.40	5.40	6.10	5.41	5.31	5.30
8-H*exo*	2.33	2.33	2.30	2.30	2.81	2.85	2.27	2.54
8-H*endo*	1.78	1.80	1.79	1.80	2.36	2.39	1.89	1.71
9-H*syn*	1.97	1.98	1.97	1.97	2.09			
9-H*anti*	1.90	1.92	1.91	1.91	2.09			
7-C$\underline{H}_3$	1.57	0.92	0.80	0.84		1.68	1.53	1.63
7-C$\underline{H}_2$-Me		1.86	1.33	1.24				
7-C$\underline{H}_2$-Et			1.83	1.24				
7-C$\underline{H}_2$-Pr				1.85				
9-C$\underline{H}_3$							1.25	1.53
9-OC$\underline{H}_3$							3.27	3.26
J (Hz)								
1-H/2-H*exo*	6.5	6.5	6.5	6.5	6.5		6.0	
1-H/2-H*endo*	2.0	2.0	2.0	2.0	2.0		2.0	2.0
1-H/8-H*exo*	6.0	6.0	6.0	6.0	6.0			
2-H*exo*/2-H*endo*	15.5	15.5	15.5	15.5	15.5	14.5	16.0	17.0
2-H*exo*/8-H*exo*		1.0		1.0			2.0	
2-H*endo*/4-H*endo*	2.0	2.0	2.0	2.0	2.0	3.0	2.0	2.0
2-H*endo*/9-H*anti*	2.0	2.0	2.0	2.0	2.0			
4-H*exo*/4-H*endo*	14.5	14.5	14.5	14.5	14.5	15.0	15.0	15.5
4-H*exo*/5-H	4.5	4.0	4.5	4.0	4.0		4.5	
4-H*endo*/5-H	2.0	2.0	2.0	2.0	2.0	3.0	2.0	2.0
4-H*endo*/9-H*anti*	2.0	2.0	2.0	2.0	2.0			
5-H/6-H	6.0	6.0	6.0	6.0	6.0	5.5	6.0	
8-H*exo*/8-H*endo*	18.0	18.0	17.5	18.0	16.5	17.0	18.0	17.5
9-H*syn*/9-H*anti*	12.5	12.5	12.5	12.5				

[a] All these spectra were taken at 500 MHz in $CDCl_3$. [b] The following signals were also observed: H*ortho* 7.31, H*meta* 7.30 and H*para* 7.22. [c] The following coupling constants were also observed: H*ortho*/H*meta* 6.5, H*ortho*/H*para* 1.5 and H*meta*/H*para* 7.0. [d] The following coupling constant was also observed: 1-H/8-H*endo* 3.5.

6,6-Dimethoxy-3-methyl-2-oxa-1-adamantyl methanesulfonate (3h). From **2h** (440 mg, 1.92 mmol) and methanesulfonyl chloride (0.22 ml, 2.80 mmol), **3h** (580 mg, 98% yield) was obtained as an oil. IR (NaCl): ν 1359, 1173 cm^{-1}. Anal. Calcd. for $C_{13}H_{22}O_6S$: C, 50.96; H, 7.24; S, 10.46. Found: C, 50.94; H, 7.38; S, 10.30.

3-Methyl-2-oxa-6-oxo-1-adamantyl methanesulfonate (3i). a) **From alcohol 2i.** From **2i** (see further on) (1.19 g, 6.53 mmol) and methanesulfonyl chloride (0.76 ml, 9.80 mmol), mesylate **3i** (1.64 g, 96% yield), mp 106-107°C (ethyl ether) was obtained. IR (KBr): ν 1732, 1358, 1183 cm^{-1}. Anal. Calcd. for $C_{11}H_{16}O_5S$: C, 50.75; H, 6.20; S, 12.32. Found: C, 50.80; H, 6.22; S, 12.31.

b) **From mesylate 3h.** A suspension of **3h** (770 mg, 2.52 mmol) and silica gel (2.10 g) in CH_2Cl_2 (50 ml) was heated under reflux for 2 h. The mixture was filtered, and the solid residue was washed with CH_2Cl_2 (2 x 50 ml). The combined organic phases were evaporated at reduced pressure to give mesylate **3i** (610 mg, 93% yield).

***Syn*-6-methoxy-3,6-dimethyl-2-oxa-1-adamantyl methanesulfonate (3j).** From **2j** (530 mg, 2.50 mmol) and methanesulfonyl chloride (0.38 ml, 4.89 mmol), mesylate **3j** (630 mg, 87% yield) was obtained as an unstable oil. IR (NaCl): ν 1368, 1173 cm^{-1}.

***Anti*-6-methoxy-3,6-dimethyl-2-oxa-1-adamantyl methanesulfonate (3k).** From **2k** (560 mg, 2.64 mmol) and methanesulfonyl chloride (0.41 ml, 5.30 mmol), **3k** (680 mg, 89% yield) was obtained as an oil. IR (NaCl): ν 1369, 1173 cm^{-1}. Anal. Calcd. for $C_{13}H_{22}O_5S$: C, 53.77; H, 7.64; S, 11.04. Found: C, 53.65; H, 7.56; S, 10.83.

7,11-Epoxi-6,7,8,9-tetrahydro-5,9-propano-5*H*-benzocyclohepten-7-yl methanesulfonate (3l). From **2l** (500 mg, 2.31 mmol) and methanesulfonyl chloride (0.30 ml, 3.90 mmol), mesylate **3l** (630 mg, 93% yield), mp 136-137°C (ethyl acetate) was obtained. IR (KBr): ν 1346, 1175 cm^{-1}. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 1.64 [dd, J = 13.5 Hz, J' = 1.0 Hz, 2 H, 10(12)-H*exo*], 2.06 [d, J = 13.0 Hz, 2 H, 6(8)-H*exo*], 2.29 [dt, J = 13.5 Hz, J' = 5.5 Hz, 2 H, 10(12)-H*endo*], 2.61 [m, 2 H, 6(8)-H*endo*], 3.17 (s, 3 H, CH_3SO_3), 3.22 [t, J = 5.5 Hz, 2 H, 5(9)-H], 4.68 [t, J = 5.5 Hz, 1 H, 11-H], 7.20 (m, 4 H, ar-H). ^{13}C-NMR (50.3 MHz, $CDCl_3$): δ 31.7 [CH_2, C10(12)], 38.5 [CH_2, C6(8)], 39.0 [CH, C5(9)], 41.9 (CH_3, CH_3SO_3), 74.8 (CH, C11), 107.7 (C, C7), 126.8 (CH) and 128.3 (CH) [C1(4) and C2(3)], 144.4 [C, C4a(9a)]. Anal. Calcd. for $C_{15}H_{18}O_4S$: C, 61.20; H, 6.17; S, 10.89. Found: C, 61.08; H, 6.15; S, 10.79.

7,11-Epoxi-6,7,8,9-tetrahydro-11-methyl-5,9-propano-5*H*-benzocyclohepten-7-yl methanesulfonate (3m). From **2m** (460 mg, 2.00 mmol) and methanesulfonyl chloride (0.20 ml, 2.60 mmol), mesylate **3m** (425 mg, 69% yield), mp 143-145°C (ethyl acetate) was obtained. IR (KBr): ν 1345, 1175 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.33 (s, 3 H, CH_3), 1.65 [d, J = 14.0 Hz, 2 H, 10(12)-H*exo*], 1.85-2.10 [complex signal, 4H, 6(8)-H*exo* and 10(12)-H*endo*], 2.55 [m, 2 H, 6(8)-H*endo*], 3.21 (s, 3 H, CH_3SO_3), 3.25 [m, 2 H, 5(9)-H], 7.14 (m, 4 H, ar-H). ^{13}C-NMR (50.3 MHz, $CDCl_3$): δ 30.7 (CH_3, 11-CH_3), 37.9 (CH_2) and 38.0 (CH_2) [C6(8) and C10(12)], 39.3 [CH, C5(9)], 42.3 (CH_3, CH_3SO_3), 78.7 (C, C11), 109.4 (C, C7), 127.1 (CH) and 128.5 (CH) [C1(4) and C2(3)], 144.4 [C, C4a(9a)]. Anal. Calcd. for $C_{16}H_{20}O_4S$: C, 62.31; H, 6.54; S, 10.40. Found: C, 62.34; H, 6.52; S, 10.38.

Attempted synthesis of 4b from oxaadamantanol 2b: Isomeric mixture of 1,3-bis(methylphenyl)adamantane (5). A suspension of oxaadamantanol **2b** (1.00 g, 6.06 mmol) and P_2O_5 (8.60 g, 60.5 mmol) in toluene (50 ml) was heated under reflux for 2 h. The mixture was concentrated at reduced pressure and the residue was taken in CH_2Cl_2 (30 ml) and water (30 ml) and made alkaline with solid Na_2CO_3. The organic layer was separated and the aqueous one was extracted with CH_2Cl_2 (3 x 50 ml). The combined organic extracts were dried with anhydrous Na_2SO_4 and evaporated at reduced pressure to afford an isomeric mixture of *p,p-*, *p,m-* and *m,m-* 1,3-ditolyladamantane **5** (0.81 g, 42% yield).

Attempted synthesis of 4b from mesylate 3b and LDA. A solution of **3b** (1.10 g, 4.47 mmmol) in anhydrous THF (60 ml) at 0°C (ice-bath) was treated with 2 M LDA in heptane/THF/ethylbenzene (6.70 ml, 13.4 mmol) for 5 h to afford, after a standard work-up **2b** (700 mg, 94% yield).

Procedure for the preparation of enones 4 from mesylates 3. A suspension of mesylate **3** and silica gel in CH_2Cl_2 was stirred at room temperature until all mesylate had disappeared. The mixture was concentrated at reduced pressure and the resulting residue was chromatographed through silica gel using mixtures hexane / ethyl acetate as eluent to give, in order of elution, the ketone **4** and the corresponding oxaadamantanol **2**.

Attempted synthesis of bicyclo[3.3.1]non-6-en-3-one (4a). a) **From mesylate 3a.** A mixture of **3a** (500 mg, 2.10 mmol) and silica gel (5 g), after stirring for 3 d, gave oxaadamantanol **2a** (330 mg, quantitative yield).

b) **From mesylate 3a and sulfuric acid**. A solution of **3a** (200 mg, 0.86 mmol) and 5 N H_2SO_4 (20 ml) in methanol (10 ml) was heated under reflux for 1 h. The cold mixture was extracted with ethyl acetate (3 x 25 ml) and the combined organic extracts were dried with anhydrous Na_2SO_4 and evaporated at reduced pressure to give oxaadamantanol **2a** (130 mg, 97% yield).

7-Methylbicyclo[3.3.1]non-6-en-3-one (4b). From mesylate **3b** (33.2 g, 135 mmol) and silica gel (33 g), after stirring for 3 h, enone **4b** (14.30 g, 71% yield) as an oil and **2b** (2.40 g, 11% yield) were obtained. IR (NaCl): ν 1709 cm^{-1}.

7-Ethylbicyclo[3.3.1]non-6-en-3-one (4c). From mesylate **3c** (7.31 g, 28.1 mmol) and silica gel (7.5 g), after stirring for 3 h, **4c** (1.94 g, 42% yield) as an oil and **2c** (0.72 g, 14% yield) were obtained. IR (NaCl): ν 1709 cm^{-1}. Anal. Calcd. for $C_{11}H_{16}O{\cdot}0.1H_2O$: C, 79.56; H, 9.84. Found: C, 79.83; H, 9.92.

7-Propylbicyclo[3.3.1]non-6-en-3-one (4d). From mesylate **3d** (0.88 g, 3.21 mmol) and silica gel (1 g), after stirring for 3 h, enone **4d** (0.27 g, 47% yield) as an oil and **2d** (70 mg, 11% yield) were obtained. IR (NaCl): ν 1718 cm^{-1}. Anal. Calcd. for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.90; H, 10.23.

7-Butylbicyclo[3.3.1]non-6-en-3-one (4e). From mesylate **3e** (13.6 g, 47.2 mmol) and silica gel (14 g), after stirring for 3 h, **4e** (3.70 g, 41% yield) as an oil and **2e** (2.80 g, 28% yield) were obtained. IR (NaCl): ν 1718 cm^{-1}. Anal. Calcd. for $C_{13}H_{20}O{\cdot}0.1H_2O$: C, 80.44; H, 10.50. Found: C, 80.42; H, 10.47.

7-Phenylbicyclo[3.3.1]non-6-en-3-one (4f). a) **From oxaadamantanol 2f**. A solution of **2f** (9.00 g, 39.1 mmol) and concentrated H_2SO_4 (25 ml) in methanol (250 ml) was heated under reflux for 1 h and concentrated *in vacuo*. The resulting residue was extracted with ethyl acetate (3 x 100 ml) and the combined organic extracts were washed with water, dried with anhydrous Na_2SO_4 and evaporated at reduced pressure to give a yellow solid (8.70 g) which was sublimed at 170°C / 0.5 Torr affording pure ketone **4f** (7.80 g, 94% yield) as a white solid, mp 94-96°C. IR (KBr): ν 1700 cm^{-1}.
b) **From mesylate 3f.** A mixture of **3f** (300 mg, 0.97 mmol) and silica gel (8 g), after stirring for 3 h, enone **4f** (140 mg, 68% yield) was obtained, alcohol **2f** being not detected.

7-Methylbicyclo[3.3.1]non-6-ene-3,9-dione (4i). a) **From mesylate 3i**. To a solution of **3i** (400 mg, 1.53 mmol) in CH_2Cl_2 (10 ml), concentrated H_2SO_4 (0.2 ml, 2.0 mmol) was added and the reaction mixture was stirred at room temperature for 4 d. The solution was washed with water (2 x 15 ml), dried with anhydrous Na_2SO_4 and concentrated at reduced pressure to give a brown oil which was distilled at 125°C / 1 Torr affording diketone **4i** (60 mg, 24% yield), mp 66-67°C (sublimed at 60°C / 0.5 Torr). IR (NaCl): ν 1739, 1710 cm^{-1}. Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.22; H, 7.33.
b) **From oxaadamantanol 2h**. To a solution of **2h** (4.79 g, 21.0 mmol) in CH_2Cl_2 (200 ml), P_2O_5 (40.0 g, 282 mmol) was added and the reaction mixture was heated under reflux for 8 h. The cold mixture was filtered at reduced pressure and the filtrate was evaporated *in vacuo* to give a black solid (4.14 g). The solid material was taken in water and extracted with CH_2Cl_2 (4 x 40 ml). The combined organic extracts were evaporated *in vacuo* to give a black oil (330 mg). The mixture of both residues was chromatographed through silica gel using mixtures hexane / ethyl acetate to give in order of elution, diketone **4i** (690 mg, 20% yield) and oxaadamantanol **2i** (1.41 g, 37% yield). Spectroscopic and analytical data of **2i**: mp 136-139°C (diethyl ether). IR (KBr): ν 3334, 1727 cm^{-1}. Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.90; H, 7.75. Found: C, 65.87; H, 7.79.

***Syn*-9-methoxy-7,9-dimethylbicyclo[3.3.1]non-6-en-3-one (4j).** From mesylate **3j** (630 mg, 2.17 mmol) and silica gel (6 g), after stirring for 8 h, enone **4j** (190 mg, 45% yield) as a white solid, mp 37-38°C (sublimed at 100°C / 1.5 Torr) and oxaadamantanol **2j** (120 mg, 26% yield) were obtained. IR (KBr): ν 1711 cm^{-1}. Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.35. Found: C, 74.18; H, 9.44.

***Anti*-9-methoxy-7,9-dimethylbicyclo[3.3.1]non-6-en-3-one (4k).** From mesylate **3k** (680 mg, 2.34 mmol) and silica gel (6 g) after stirring for 36 h, enone **4k** (100 mg, 22% yield) as an oil and oxaadamantanol **2k** (300 mg, 60% yield) were obtained. IR (NaCl): ν 1713 cm^{-1}. Anal. Calcd. for $C_{12}H_{18}O_2$: C, 74.19; H, 9.35. Found: C, 74.25; H, 9.48.

Attempted synthesis of 5,6,8,9-tetrahydro-5,9-[1]propenobenzocyclohepten-7-one (4l). From mesylate **3l** (385 mg, 1.31 mmol) and silica gel (10 g), after stirring for 2 h, oxahomoadamantanol **2l** (290 mg, quantitative yield) was obtained.

Attempted synthesis of 5,6,8,9-tetrahydro-11-methyl-5,9-[1]propenobenzocyclohepten-7-one (4m). From mesylate **3m** (100 mg, 0.32 mmol) and silica gel (1 g), after stirring for 3 d, oxahomoadamantanol **2m** (72 mg, 97% yield) was obtained.

Table 7. Experimental data of the X-ray crystal structure determination of **2j**.

Molecular formula	$C_{12}H_{20}O_3$	Size of crystal [mm]	0.1 x 0.1 x 0.2
Molecular mass	212.28	Measured reflections	3458
Crystal system	orthorhombic	Independent reflections	3458
Space grup	$P2_12_12_1$	Observed reflections	1973
Cell parameters	[a]	μ(Mo-*K*α) [mm^{-1}][b]	0.086
a [Å]	20.622(4)	*R*	0.0606
b [Å]	14.706(3)	*R*w	0.1342
c [Å]	15.211(3)	Absolute structure parameter	1(2)
V [$Å^3$]	4613(2)	Diff. Four. $\Delta\rho_{max}$[c]	0.246
Z	16	$\Delta\rho_{min}$[d]	-0.237
F(000)	1856	Refined parameters	349
d(calcd) [Mg m^{-3}]	1.223	Max. shift / e.s.d.	0.04

[a] Determined by automatic centering of 25 reflections ($8 \le \theta \le 12°$). [b] μ(Mo-*K*α), Linear absorption coefficient. Radiation Mo-*K*α (λ = 0.71069Å). [c] Maximum and [d] minimum peaks in final difference synthesis.

X-ray Crystal-Structure Determinations of 2j. A prismatic crystal was selected and mounted on a Philips PW-1100 four-circle diffractometer. Unit cell parameters were determined by automatic centering of 25 reflections and refined by the least-squares method. Intensities were collected with graphite-monochromatized Mo-*K*α radiation, using w/2θ scan technique. Reflections were measured in the range $2.16 \le \theta \le 29.99$ and were assumed as observed by applying the condition $I \ge 2\,\sigma(I)$. Three reflections were measured every two hours as orientation and intensity control; significant intensity decay was not observed. Lorentz polarization but no absorption corrections were made. The structure was solved by Patterson synthesis, using the SHELXS computer program[16] and refined by the full-matrix least-squares method with the SHELX-93 computer program[17]. The function minimized was $\Sigma\, w\, [|F_o|^2 - |F_c|^2]^2$, where $w = [\sigma^2(I) + (0.0797\,P)^2 + 1.3654\,P]^{-1}$, being $P = (|F_o|^2 + 2\,|F_c|^2) / 3$. f, f' and f'' were taken from International Tables of X-ray Crystallography[18]. The extinction coefficient was 0.012514. 14 H atoms were located from a difference synthesis and refined with an overall isotropic temperature factor and 23 H atoms were computed and refined with an overall isotropic temperature factor by using a riding model.

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