# [4+2] Cyclohexane Ring Formation by a Tandem of a Free Radical Alkylation of a Non-Activated δ-Carbon Atom and Intramolecular Carbanion Cyclo-alkylation

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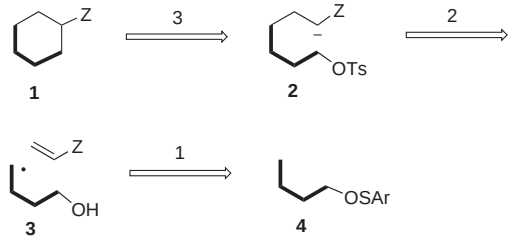
**Abstract:** A [4+2] cyclohexane ring formation was achieved by the combination of free radical and ionic reaction sequences. Free radical alkylation of the remote non-activated δ-carbon atom involves addition of δ-carbon radicals, generated by 1,5-hydrogen transfer in alkoxyl radical intermediates, to the radicophilic olefins, while the polar sequence involves the enolate anions as intermediates which undergo a cycloalkylation reaction. The cyclohexane rings were constructed using diverse acyclic compounds **15** and **18** as well as cyclic alkyl arenesulfenates (e.g., **5**, **24**, **27**) as the precursors of alkoxyl radicals (four-carbon atom fragment) and methyl vinyl ketone or other activated olefins as two-carbon atom fragments. Annulation of the cyclohexane ring was applied for the synthesis of a variety of cyclic systems including monocyclic (**17** and **20**), fused-rings (e.g. **23, 26, 29**) and spirocyclic systems (**7**).

**Key words:** annulations, radicals, 1,5-hydrogen transfer, radical reactions, cycloalkylations, δ-alkylations, alkyl arenesulfenates

Reactions and methods for carbocyclic ring construction are of great importance in organic synthesis. A variety of cyclization reactions were developed, which may involve cationic, radical and anionic intermediates, in addition to pericyclic and metal-catalyzed reactions.[1] In addition to the numerous classical reactions we recently discovered a new sequence of free radical and carbanionic reactions for the [4+2] annulation of cyclohexane ring **1**, involving a carbon-carbon bond formation on the remote non-activated carbon atom (Scheme 1, step 2).[2]

This cyclohexane ring annulation methodology is based on the recently discovered reaction of the δ-carbon radical **3**, generated by 1,5-hydrogen transfer in the alkoxyl radical intermediates (Scheme 1, step 1). It undergoes intermolecular addition to activated olefins and thus a functionalized alkyl chain was introduced at a remote non-activated carbon atom (Scheme 1, phase 2).[3,4] In these sequential free radical reactions the hydroxy compounds, possessing an electron-withdrawing group attached to the 6-position, are obtained. Compounds **2**, possessing a suitably disposed procarbanionic carbon atom and leaving group offer the possibility for cyclohexane ring **1** closure (Scheme 1, step 3).[5] This method for the construction of a cyclohexane rings requires [4+2] carbon fragments and could be complementary to the Robinson annulation.[6] The four-carbon atom fragment must be a precursor of the alkoxyl radical generated from the alkyl arenesulfenates **4**, while the two-carbon atom fragment is preferably an electron-deficient olefinic compound.




**Scheme 1**

The cyclohexane ring annulation methodology was verified using various structurally different four-carbon atom fragments as precursors of alkoxyl radicals.[3a] Cycloalkylation reactions were applied to the synthesis of a variety of cyclic compounds including monocyclic, fused-ring and spirocyclic systems (Scheme 2, Table 1). The alkyl arenesulfenates, used as precursors of the alkoxyl radicals, were part of acyclic, monocyclic and polycyclic systems and methyl vinyl ketone was used as an activated (radicophilic) olefin.

The method for [4+2] cyclohexane ring annulation was also successfully used for the construction of spirocyclic systems. Thus, in the reaction of 3-(cyclohexyl)-propyl-*p*-nitrobenzenesulfenate (**5**, Scheme 2) with tributyltin hydride (TBTH), in the presence of a 10 molar excess of methyl vinyl ketone, the hydroxy ketone **6** was obtained. Upon treatment of keto tosylate, derived from ketone **6**, with sodium hydride the cycloalkylation occurred and the 1-spiro[5,5]undec-2-ylethanone (**7**) was obtained in 36% overall yield (Scheme 2).

The alkoxyl radicals **11** were generated from the corresponding alkyl benzene- and *p*-nitrobenzenesulfenates (Scheme 3) by reaction with TBTH, and δ-alkylation was carried out in the presence of a 10 molar excess of methyl vinyl ketone as an activated olefin.[2–4,7] The reactions were performed under irradiation conditions in benzene solution. Translocation of the radical center from the oxygen in **11** to the non-activated carbon atom in δ-position occurs by 1,5-hydrogen transfer.[3a,8] δ-Carbon radical **12** undergoes intermolecular addition to methyl vinyl ketone[9] to give the corresponding δ-alkylated products **9** containing

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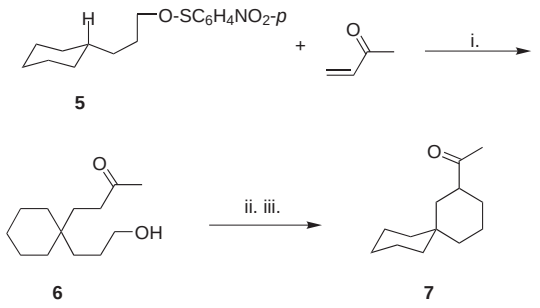



i. $Bu_3SnH$, h$\nu$, $C_6H_6$ (47%)
ii. TsCl, pyridine (80%)
iii. NaH, DME (72%)

**Scheme 2**

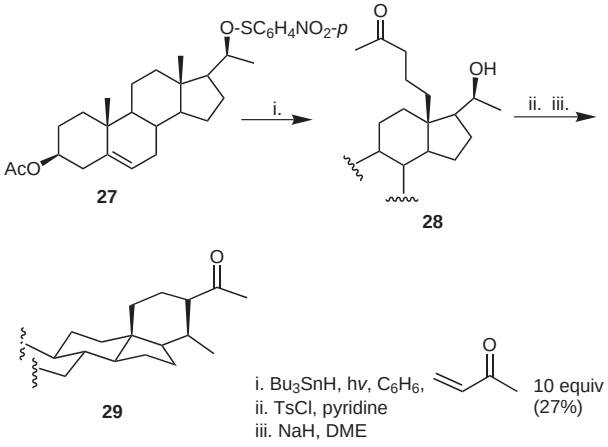
an electron-withdrawing group. Products **9** were isolated and fully characterized.

In the δ-alkylated products the relationship of functional groups is appropriate for the ionic 6-*exo*- and 8-*endo* cycloalkylation, depending of the reaction conditions and the reagents used.

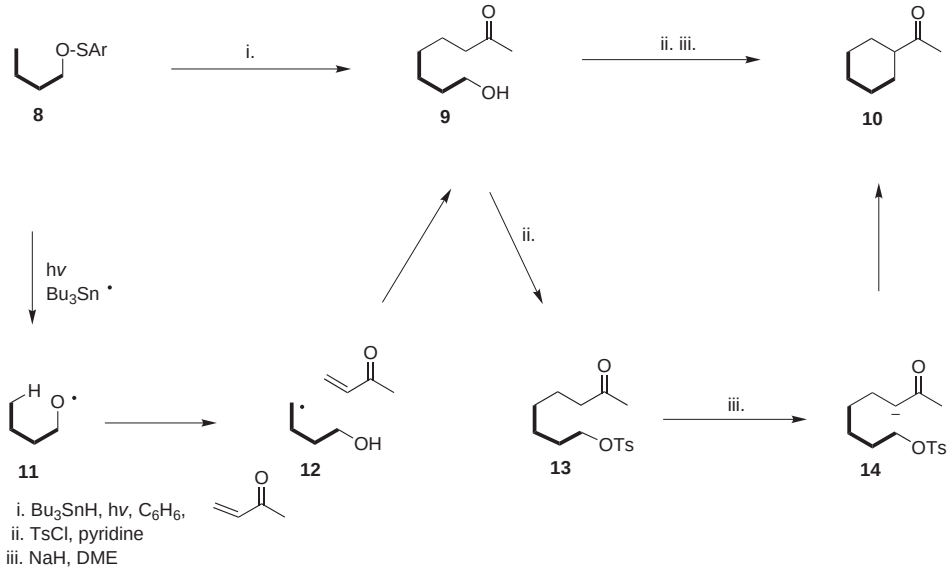
The hydroxyl group in **9** was converted into the corresponding toluenesulfonate or methanesulfonate esters **13** by reaction with the corresponding sulfonyl chloride in the presence of pyridine (Scheme 3).[10] In the next step, the keto sulfonate esters **13** were treated under equilibrium-controlled conditions with sodium hydride in DME thus furnishing the corresponding more stable enolate anions **14**.[5] In the presence of a suitably disposed sulfonate leaving group the enolate anions **14** undergo an intramolecular 6-*exo* alkylation to yield cyclohexane **10** with an exocyclic electron-withdrawing group. Under these reaction conditions the enolate anions **14** undergo exclusively C-alkylation. We suppose that under kinetic conditions deprotonation at the terminal position of the keto tosylate **13** could occur and 8-*endo* cycloalkylation products could also be obtained.[11]

Thus starting from the primary acyclic alkyl benzenesulfenates **15** and **18** the 1,3-substituted cyclohexane derivatives **17** and **20**, respectively, were obtained (Table 1). The described methodology was also applied to the annulation of the fused cyclohexane ring of monocyclic and polycyclic arenesulfenates such as **21** and **24.** Starting from the 2-(cycloalkyl)-ethyl *p*-nitrobenzenesulfenates **21** and **24** the corresponding *trans*-decaline derivative **23** and adamantane derivative **26** were obtained.

Annulation of the cyclohexane ring into the steroid skeleton was realized by free radical alkylation of the C-18 angular methyl group of pregnane-20β-*O*-*p*-nitrobenzenesulfenate derivative **27** by radical addition to methyl vinyl ketone followed by intramolecular alkylation of the intermediary keto mesylate, prepared from the hydroxy ketone **28**. Thus, the ring E was constructed and 18,20-ethanopregnane derivative **29** was obtained in 26% overall yield (Scheme 4).

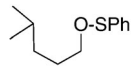
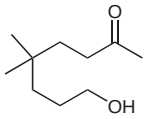
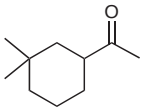
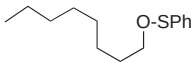
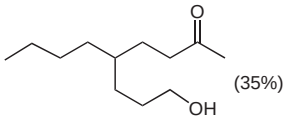
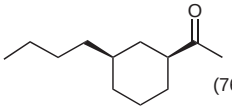
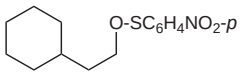
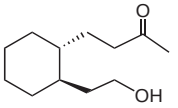
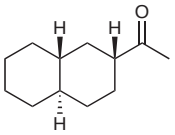
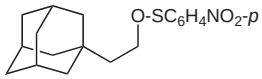
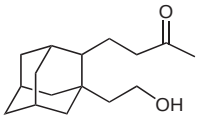
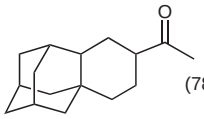



**Scheme 4**




**Scheme 3**

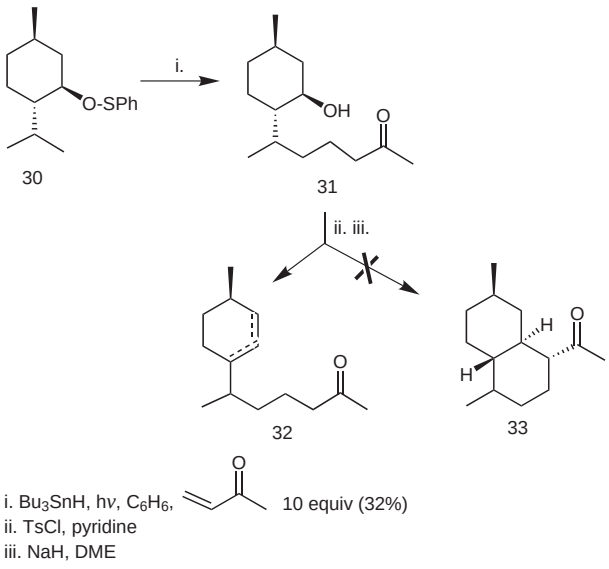
**Table 1** Annulation of the Cyclohexane Ring by a Sequence of Free Radical and Carbanionic Reactions Using Methyl Vinyl Ketone as the Activated Olefin

| Alkyl arenesulfenates[a] | δ-Alkylated products (yields in %)[b] | Annulated (cyclic) products (yields in %)[b,c] |
|---|---|---|
|  **15** |  (41%) **16** |  (74%) **17** |
|  **18** |  (35%) **19** |  (76%)[d] **20** |
|  **21** |  (36%)[e] **22** |  (76%) **23** |
|  **24** |  (42%) **25** |  (78%) **26** |

[a] The alkyl benzenesulfenates were purified by distillation under reduced pressure, while the alkyl *p*-nitrobenzenesulfenates were purified by dry flash chromatography.
[b] Yields of isolated products (yields by GC analysis were 10–20% higher).
[c] The hydroxyl group of the δ-alkylated products was converted into the corresponding tosylate or mesylate groups (80–90% yields) and then the cycloalkylation reaction was carried out under basic conditions (see experimental part).
[d] Only the *cis* isomer was obtained.
[e] The ratio of *cis* and *trans* isomers was 1:3.

Cycloalkylation reaction of open-chain or cyclic keto sulfonate esters, derived from primary alcohols and possessing appropriately oriented reactive centers, is a favorable reaction (Table 1). However, the modes of cycloalkylation reactions of cyclic keto sulfonate esters, are very sensitive to the stereoelectronic effects and side reactions can occur. When the stereochemical relationship of the reacting groups is not suitable for the intramolecular substitution reactions, the sulfonate esters derived from the secondary hydroxy group rather undergo an elimination as a side reaction, to give unsaturated products.[12]

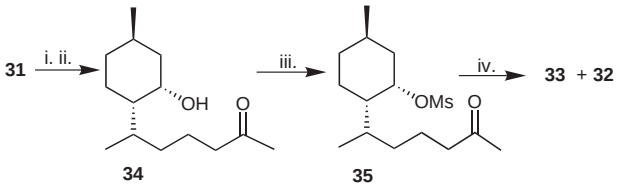
The importance of the appropriate stereochemistry at the reactive centers in the cycloalkylation reaction was observed in the annulation of (–)-menthyl benzenesulfenate **30** (Scheme 5). In the reaction with methyl vinyl ketone the methyl group in position 9 was alkylated and hydroxy ketone **31** was obtained (the ratio of 6*R* and 6*S* is 1:3.5) which was then converted into the corresponding keto-tosylate.[13] The enolate anion **31a** (Scheme 7) derived from the keto-tosylate, possessing an equatorial leaving group, did not undergo a substitution reaction, but rather an elimination reaction to give the unsaturated ketones **32**. No traces of the cycloalkylation product **33** was obtained (Scheme 5).[14]




**Scheme 5**

In order to carry out the cycloalkylation reaction, the equatorial hydroxyl group in the δ-alkylated product **31** was epimerized to give the axial alcohol **34** via its *p*-nitrobenzoate ester (Scheme 6).[15] The enolate anion **35a** derived from the corresponding keto-methanesulfonate **35**

with an axial leaving group, has the appropriate stereochemistry for an intramolecular substitution. Thus, cycloalkylation occurs to give the bicyclic product (tetrahydrokhusitone)[13] **33** (Schemes 6 and 7). However, in addition to the bicyclic product **33**, the unsaturated ketone **32** was also formed as a product of the elimination reaction (yields 53% and 34% respectively).[14,16] It is well known that the intramolelcular cycloalkylation reaction is less favorable when the leaving group (i.e. sulfonate ester group) is attached to a secondary carbon atom and its elimination becomes a serious side reaction.[17]




i. p-$O_2NC_6H_4COOH$, $Ph_3P$, DEAD, $C_6H_6$, (82%)
ii. KOH, THF, MeOH, $H_2O$, (97%)
iii. MsCl, pyridine, $CH_2Cl_2$, (100%)
iv. NaH, DME, (53%)

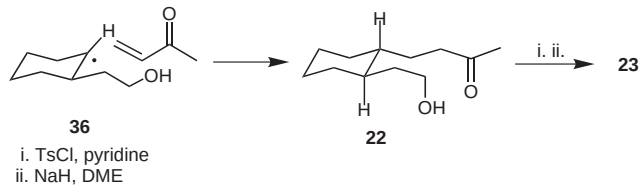
**Scheme 6**

When the described annulation method was applied to open-chain non-branched alkyl benzenesulfenates, e.g. *n*-octyl benzenesulfenate **18**, the *cis* isomer of 1,3-disubstituted cyclohexane derivative **20** was obtained (Table 1). Formation of the *cis* isomer is favorable because the 'axial' interaction of the substituents disfavor the transition state leading to the *trans* isomer.

In the annulation of the cyclohexane ring starting from 2-cyclohexylethyl *p*-nitrobenzenesulfenate (**21**) and methyl vinyl ketone a mixture of *cis*- and *trans*-hydroxy ketones **22** was obtained in a ratio of 1:3. The excess of *trans* isomer is obtained because the addition of the intermediary cyclohexyl radical (of type **36**, Scheme 8) to methyl vinyl ketone preferentially takes place from the equatorial side to give the *trans*-diequatorial intermediary hydroxy ketone **22**,[18] which upon cycloalkylation reaction gives the *trans*-decaline derivative **23** (Scheme 8 and Table 1).

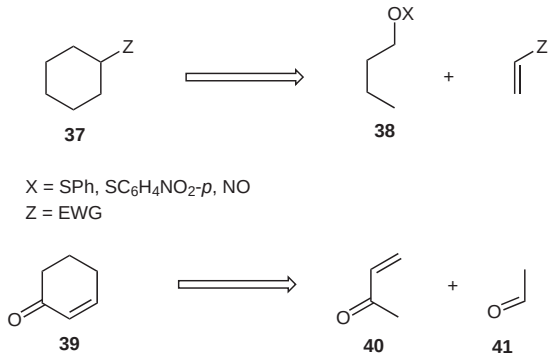
The described annulation methodology consists of a sequence of three reactions. It is more convenient to perform all of the reactions separately, and to isolate the intermediary hydroxy ketones as products of the free radical δ-alkylation as well as their tosyl or mesyl derivatives. The pure keto sulfonate esters must be used in the cycloalkylation reaction.

The sequence of a free radical δ-alkylation and enolate anion cycloalkylation offers a new method for the annulation of cyclohexane rings which require two fragments: an activated olefin (Michael acceptor) and a four-carbon atom chain of type **38** with a proalkoxy radical functional group, preferably alkyl arenesulfenates (**38**, X = SPh, $SC_6H_4NO_2$-*p*, Scheme 9). The cyclohexane derivative **37**, formed by applying this methodology, contains only an exocyclic electron-withdrawing group. The presented method herein could be complementary to the Robinson annulation of the cyclohexane ring **39** which requires two fragments: conjugated and saturated ketones **40** and **41** and two procarbanionic carbon atoms (Scheme 9).[6]



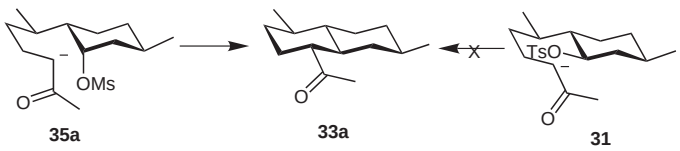

i. TsCl, pyridine
ii. NaH, DME

**Scheme 8**




**Scheme 9**

The solvents and commercial reagents used in all of the experiments were purified by distillation before use (benzene distilled over $CaH_2$ and $CH_2Cl_2$ over $P_2O_5$). Purifications and separations of the reaction products were carried out by distillation and preparative column chromatography using silica gel 100–200 mesh (60 Å) and by dry flash chromatography using silica gel (60 Å). The reactions were monitored by TLC using silica gel (TLC 60 Å, plates were visualized using ultraviolet light or by $H_2SO_4$) or by GC (Varian 3400, column OV-101 1% on Chromosorb W-AW). Optical rotations were measured using a Perkin-Elmer 141 MC polarimeter. IR spectra were recorded on a Perkin-Elmer 457 grating instrument. $^1H$ NMR spectra were recorded in $CDCl_3$ solution (unless otherwise stated) at 200 MHz, using a Varian Gemini 200 spectrometer. The chemical shifts (δ) are expressed in ppm using TMS as the internal standard. $^{13}C$ NMR spectra were measured on the same instrument at 50 MHz. Mass spectra were performed on a Finningan ITDS 700 instrument.




**Scheme 7**

### Synthesis of Alkyl Arenesulfenates

### Alkyl Benzenesulfenate; General Procedure[3b–3d,6,19]

To the solution of starting alcohol (0.02 mol) and $Et_3N$ (0.05 mol) in $CH_2Cl_2$ (150 mL), cooled to –78 °C under an Ar atmosphere, benzenesulfenyl chloride (0.025 mol) was added during 10 min at –78 °C and left to reach r.t. The mixture was diluted with $CH_2Cl_2$ (400 mL) and washed successively with 2 M HCl (50 mL), sat. aq $NaHCO_3$ (50 mL) and $H_2O$ (50 mL). The solution was dried over $Na_2SO_4$. The solvent was removed by evaporation and the residual oil distilled on a short path under reduced pressure. Solid alkyl benzenesulfenates were purified by dry flash chromatography. Alkyl benzenesulfenates were obtained in 71–87% yield.

### 4-Methylpentyl Benzenesulfenate (15)

Yield: 76%; yellow-green oil, bp 80–83 °C/0.02 mmHg.

IR (neat): 3063, 1583, 1477, 1455, 1440, 1387, 1097, 1024, 981, 959, 892, 737, 690 $cm^{-1}$.

$^1H$ NMR (200 MHz, $CDCl_3$): δ = 0.87 (d, *J* = 6.6 Hz, 6 H), 1.15–1.27 (m, 2 H), 1.52 (hept, *J* = 6.6 Hz, 1 H), 1.60–1.75 (m, 2 H), 3.78 (t, *J* = 6.4 Hz, 2 H), 7.15–7.38 (m, 5 H).

$^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 140.8, 128.8, 126.3, 123.6, 78.8, 34.7, 28.2, 27.7, 22.4.

Anal. Calcd. for $C_{12}H_{18}OS$: C, 68.57; H, 8.57; S, 15.23. Found: C, 68.90; H, 8.40; S, 15.02.

### Octyl Benzenesulfenate (18)[3b,c]

Yield: 71%; bp 103–105 °C/0.02 mmHg.

IR (neat): 3060, 1583, 1478, 1440, 1378, 1148, 1068, 1024, 968, 894, 737, 690 $cm^{-1}$.

$^1H$ NMR (200 MHz): δ = 0.88 (t, *J* = 6.2 Hz, 3 H), 1.20–1.40 (m, 10 H), 1.58–1.73 (m, 2 H), 3.80 (t, *J* = 6.6 Hz, 2 H), 7.13–7.40 (m, 5 H).

$^{13}C$ NMR (50 MHz): δ = 140.8. 128.9, 126.3, 123.6, 78.6, 31.7, 30.3, 29.1, 25.7, 22.6, 14.0.

### (1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl Benzenesulfenate [(–)-Menthyl benzenesulfenate, (30)][13]

Yield 87%; bp 108–110 °C/0.07 mmHg; $[\alpha]_D^{22}$ –256.7 (c = 1, $CHCl_3$) of 92% purity of compound (determined by $^1H$ NMR spectrum).

IR (neat): 3062, 1583, 1477, 1455, 1440, 1387, 1370, 1345, 1097, 1024, 1004, 981, 959, 914, 851, 778, 738, 690 $cm^{-1}$.

$^1H$ NMR (200 MHz): δ = 0.62 (d, *J* = 7.0 Hz, 3 H), 0.87 (d, *J* = 7.2 Hz, 3 H), 0.88 (d, *J* = 7.2 Hz, 3 H), 0.72–1.00 (m, 3 H), 1.20–1.38 (m, 2 H),1.54–1.66 (m, 2 H), 2.18–2.38 (m, 2 H), 3.37 (td, $J_1$ = 10.7 Hz, $J_2$ = 4.4 Hz, 1 H), 7.10–7.40 (m, 5 H).

$^{13}C$ NMR (50 MHz): δ = 141.3, 128.5, 126.6, 125.4, 87.0, 48.6, 40.9, 34.1, 31.5, 25.1, 22.9, 22.0, 20.9, 15.6.

Elemental analysis was not performed because the compound decomposes with explosion in the Pregl apparatus (determined by $^1H$ NMR spectrum).

### Alkyl *p*-Nitrobenzenesulfenates

### *p*-Nitrobenzenesulfenyl Chloride[20]

To a solution of chlorine in $CCl_4$ (14%, 80 mL) cooled to –20 °C, *p*-nitrothiophenol (14.0 g, 0.09 mol) was added during 20 min (vigorous reaction). The reaction mixture was stirred for additional 30 min at –20 °C and 3 h at r.t. The solvent was evaporated and the red residual oil solidified. The product was dissolved in anhyd $Et_2O$ (50 mL), concentrated, and 17.0 g of brown crystalline *p*-nitrobenzenesulfenyl chloride was obtained in 99% yield.

IR (KBr): 2000–1600, 1597, 1576, 1509, 1475, 1398, 1362, 1341, 1317, 1107, 855, 841, 739 $cm^{-1}$.

### Alkyl *p*-Nitrobenzenesulfenates; General Procedure[21]

To a solution of starting alcohol (10.5 mmol) and $Et_3N$ (2.66 g, 26.4 mmol) in $CH_2Cl_2$ (55 mL), cooled to –40 °C under an Ar atmosphere, the solution of *p*-nitrobenzenesulfenyl chloride (2.2 g, 11.6 mmol) in $CH_2Cl_2$ (10 mL) was added drop-wise during 10 min. The reaction mixture was stirred at –40 °C for 20 min and then allowed to reach r.t. with stirring for 1.5 h. The mixture was diluted with $CH_2Cl_2$ (200 mL) and washed successively with HCl (30 mL, 2 M), sat. aq $NaHCO_3$ (30 mL) and $H_2O$ (50 mL). The solution was dried over $Na_2SO_4$. The solvent was removed by evaporation and the residual oil purified by dry flash chromatography on a silica gel column (toluene). Alkyl *p*-nitrobenzenesulfenates were obtained in 74–86% yield.

### 2-Cyclohexylethyl *p*-Nitrobenzenesulfenate (21)[3b,c]

Yield: 82%; red oil.

IR (neat): 1594, 1581, 1515, 1475, 1448, 1424, 1337, 1178, 1111, 1088, 1030, 963, 890, 852, 840, 802, 741 $cm^{-1}$.

$^1H$ NMR (200 MHz, $CDCl_3$): δ = 0.85–1.55 (m, 7 H), 1.64 (q, *J* = 6.8 Hz, 2 H), 1.59–1.75 (m, 4 H), 3.95 (t, *J* = 6.8 Hz, 2 H), 7.73 (AA′BB′ system, $\delta_A$ = 7.25, $\delta_B$ = 8.21, $J_{AB}$ = 9.0 Hz, $J_{AB'}$ = 2.0 Hz, 4 H).

$^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 151.7, 144.9, 124.0, 119.6, 77.6, 37.5, 34.05, 30.0, 26.2, 25.9.

### 3-Cyclohexylpropyl *p*-Nitrobenzenesulfenate (5)

Yield: 80%; red oil.

IR (neat): 1594, 1581, 1515, 1475, 1449, 1366, 1337, 1178, 1111, 1088, 1037, 994, 974, 949, 920, 911, 852, 841, 742 $cm^{-1}$.

$^1H$ NMR (200 MHz, $CDCl_3$): δ = 0.78–1.09 (m, 2 H), 1.10–1.40 (m, 6 H), 1.60–1.85 (m, 7 H), 3.89 (t, *J* = 6.8 Hz, 2 H), 7,73 (AA′BB′ system, $\delta_A$ = 7.25, $\delta_B$ = 8.21, $J_{AB}$ = 9.0 Hz, $J_{AB'}$ = 2.0 Hz, 4 H).

$^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 151.8, 145.0, 124.2, 119.7, 79.9, 37.2, 33.1, 27.6, 26.5, 26.2.

### 2-(1-Adamantyl)ethyl *p*-Nitrobenzenesulfenate (24)

Yield: 74%; yellow crystals.

IR (KBr): 1593, 1577, 1509, 1474, 1448, 1333, 1317, 1253, 1188, 1176, 1109, 1088, 951, 937, 853, 837 $cm^{-1}$.

$^1H$ NMR (200 MHz, $CDCl_3$): δ = 1.47–1.68 (m, 12 H), 1.56 (t, *J* = 7.4 Hz, 2 H), 1.90–2.00 (m, 3 H), 3.98 (t, *J* = 7.4 Hz, 2 H), 7.73 (AA′BB′ system, $\delta_A$ = 7.25, $\delta_B$ = 8.21, $J_{AB}$ = 9.0 Hz, $J_{AB'}$ = 2.0 Hz, 4 H).

$^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 151.8, 146.0, 124.2, 119.7, 76.1, 44.1, 42.5, 38.9, 36.8, 28.4.

Anal. Calcd for $C_{18}H_{23}NO_3S$: C, 64.86; H, 6.90; N, 4.20; S, 9.60. Found: C, 64.55; H, 7.05; N, 4.08; S, 9.78.

### Methyl (3β,20*S*)-20-{[(4-nitrophenyl)thio]oxo}pregn-5-ene-3-carboxylate (27)

Yield: 86%; yellow crystals.

IR (KBr): 1732, 1637, 1593, 1583, 1517, 1747, 1446, 1366, 1350, 1250, 1148, 1112, 1089, 1071, 1039, 866, 853, 837, 738 $cm^{-1}$.

$^1H$ NMR (200 MHz, $CDCl_3$): δ = 0.78 (s, 3 H), 1.04 (s, 3 H), 1.20 (d, *J* = 6.2 Hz, 3 H), 0.96–1.34 (m, 7 H), 1.39–1.71 (m, 8 H), 1.85–1.97 (m, 2 H), 2.04 (s, 3 H), 2.07–2.15 (m, 1 H), 2.31–2.35 (m, 2 H), 3.92 (m, 1 H), 4.61 (m, 1 H), 5.38 (d, *J* = 4.2 Hz, 1 H), 7.75 (AA′BB′ system, $\delta_A$ = 7.32, $\delta_B$ = 8.18, $J_{AB}$ = 9.0 Hz, $J_{AB'}$ = 2.0 Hz, 4 H).

$^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 170.5, 153.4, 144.9, 139.9, 123.9, 122.3, 120.4, 88.0, 73.8, 56.4, 55.9, 49.9, 42.3, 39.3, 38.0, 36.9, 36.5, 31.8, 31.7, 27.7, 25.6, 24.3, 21.4, 20.8, 19.3, 19.0, 12.5.

Anal. Calcd for $C_{29}H_{39}NO_5S$: C, 67.83; H, 7.60; N, 2.72; S, 6.23. Found: C, 67.55; H, 7.38; N, 2.80; S, 6.11.

**Free Radical Alkylation of the Non-Activated δ-Carbon Atom; General Procedure[2]**

A solution of alkyl benzenesulfenates (or *p*-nitrobenzenesulfenates) (2.24 mmol), 10 molar equiv of methyl vinyl ketone (1.57 g, 22.4 mmol) and $Bu_3SnH$ (0.727 g, 2.5 mmol) in benzene (220 mL) was irradiated at r.t. by visible light (xenon lamp 250W λ > 300 nm or by UV lamp) for 1 h in an Ar atmosphere. After the reaction was completed, benzene was evaporated and the residual oil was dissolved in $Et_2O$ (50 mL) and washed with aq solution of NaF (0.5 g in 10 mL). The ethereal solution was separated and the aqueous solution extracted with $Et_2O$ (2 × 20 mL). The ethereal solutions were dried ($Na_2SO_4$). The ether was evaporated and the reaction products were separated by chromatography on a silica gel column (benzene–EtOAc, 7:3).

**8-Hydroxy-5,5-dimethyloctan-2-one (16)**

The compound was obtained as a colorless oil in 41% yield according to the described general procedure.

IR (neat): 3443,1715, 1585, 1472, 1417, 1387, 1366, 1299, 1261, 1223, 1164, 1060, 1022, 897, 851, 801, 750, 692 $cm^{-1}$.

$^1H$ NMR (200 MHz, $CDCl_3$): δ = 0.86 (s, 6 H), 1.18−1.27 (m, 2 H), 1.44−1.56 (m, 4 H), 1.85 (br s, 1 H), 2.16 (s, 3 H), 2.35−2.43 (m, 2 H), 3.61 (t, *J* = 6.4 Hz, 2 H).

$^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 209.8, 63.5, 38.8, 37.4, 35.0, 31.9, 29.8, 27.3, 26.73.

Anal. Calcd for $C_{10}H_{20}O_2$: C, 69.76; H, 11.62. Found: C, 69.95; H, 11.51.

**5-(3-Hydroxypropyl)nonan-2-one (19)**

Yield: 35%; colorless oil.

IR (neat): 3418, 1713, 1456, 1413, 1359, 1308, 1266, 1226, 1166, 1059 $cm^{-1}$.

$^1H$ NMR (200 MHz, $CDCl_3$): δ = 0.89 (t, *J* = 6.8 Hz, 3 H), 1.24–1.33 (m, 9 H), 1.48–1.64 (m, 4 H), 1.82 (br s, 1 H), 2.15 (s, 3 H), 2.38–2.45 (m, 2 H), 3.63 (t, *J* = 6.6 Hz, 2 H).

$^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 209.7 C, (62.9, 40.9) $CH_2$, 36.5 $CH_3$, 32.8 $CH_2$, 29.7 CH, (29.5, 29.1, 28.5, 27. 22.8) $CH_2$, 13.9 $CH_3$.

***cis*- and *trans*-4-[2-(2-Hydroxyethyl)cyclohexyl]butan-2-one (22)**

The compound was obtained from the 2-cyclohexylethyl *p*-nitrobenzenesulfenate **21** and the mixture of *cis*- and *trans*-hydroxy ketones **22,** with the ratio of 1:3, was isolated as a colorless viscous oil in 35% yield.

IR (neat): 3417, 1714, 1654, 1596, 1577, 1559, 1447, 1412, 1360, 1272, 1165, 1048 $cm^{-1}$.

$^1H$ NMR (200 MHz, $CDCl_3$): δ = 0.85–1.97 (m, 15 H), 2.15 (s, 3 H), 2.30–2.58 (m, 2 H), 3.57–3.78 (m, 2 H).

$^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 209.8, 61.4, 60.8, 41.8, 40.8, 40.6, 38.6, 38.1, 36.3, 35.1, 31.7, 31.3, 29.9, 28.4, 28.2, 27.04, 25.9, 25.9, 23.5, 23.2.

**4-[1-(3-Hydroxypropyl)cyclohexyl]butan-2-one (6)**

Yield: 47%; viscous, colorless oil.

IR (neat): 3405, 1713, 1596, 1519, 1459, 1416, 1358, 1339, 1164, 1057, 1018, 964, 918, 852, 822 $cm^{-1}$.

$^1H$ NMR (200 MHz, $CDCl_3$): δ = 0.9 (t, *J* = 7.2 Hz, 2 H), 1.21–1.62 (m, 14 H), 1.93 (br s, 1 H), 2.16 (s, 3 H), 2.29–2.38 (m, 2 H), 3.61 (t, *J* = 6.4 Hz, 2 H).

$^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 210.0, 63.5, 37.7, 35.6, 33.9, 32.5, 30.4, 29.9, 27.7, 26.9, 26.3, 26.1, 21.4.

Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.58; H, 11.32. Found: C, 73.40, H, 11.48.

**4-[1-(2-Hydroxyethyl)-2-adamantyl]butan-2-one (25)**

Yield: 42%; viscous, colorless oil.

IR (neat): 3412, 1713, 1596, 1572, 1518, 1460, 1410, 1356, 1230, 1163, 1058, 916 $cm^{-1}$.

$^1H$ NMR (200 MHz, $CDCl_3$): δ = 1.22–1.94 (m, 19 H), 2.14 (s, 3 H), 2.26–2.54 (m, 2 H), 3.70 (t, *J* = 6.6 Hz, 2 H).

Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.80; H, 10.40. Found: C, 76.62; H, 10.35.

**Acetic Acid 17-(1-Hydroxy-ethyl)-10-methyl-13-(4-oxo-pentyl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl Ester [4-(3β-Acetoxy-20β-hydroxy-5-pregnen-18-yl)-butan-2-one] (28)**

Yield: 27% (from **27**); white, crystals.

IR (KBr): 3456, 1732, 1718, 1646, 1596, 1519, 1458, 1374, 1339, 1247, 1156, 1133, 1082, 1032 $cm^{-1}$.

$^1H$ NMR (200 MHz, $CDCl_3$): δ = 1.02 (s, 3 H), 0.85–1.97 (m, 22 H), 1.15 (d, *J* = 5.8 Hz, 3 H), 2.04 (s, 3 H), 2.14 (s, 3 H), 2.20–2.51 (m, 5 H), 3.64–3.84 (m, 1 H), 4.51–4.68 (m, 1 H), 5.36–5.39 (m, 1 H).

$^{13}C$ NMR (50 MHz, $CDCl_3$): δ = 209.2, 170.6, 139.7, 122.4, 73.9, 70.2, 59.4, 57.5, 49.8, 44.9, 44.3, 38.0, 36.9, 36.6, 35.8, 31.6, 29.8.

Anal. Calcd for $C_{27}H_{42}O_4$: C, 75.34; H, 9.76. Found: C, 75.48; H, 9.90.

**(6*R*) and (6*S*)-[(1*S*,2*R*,4*R*)-2-Hydroxy-4-methylcyclohexyl]heptan-2-one (31)[13]**

(6*R*) and (6*S*)-[(1*S*,2*R*,4*R*)-2-Hydroxy-4-methylcyclohexyl]-heptan-2-one was obtained [from (–)-menthyl benzenensulfenate **30**] in 32% yield (0.2 g) as a yellow-green oil containing a mixture of two diastereoisomers (6*R* and 6*S*) in a ratio of 1:3.5.

IR (neat): 3420, 1713, 1456, 1411, 1363, 1262, 1226, 1170, 1103, 1080, 1044, 991, 969, 922 $cm^{-1}$.

$^1H$ NMR (200 MHz): δ = 0.80 (d, *J* = 7.0 Hz, 3 H), 0.91 (d, *J* = 6.4 Hz, 3 H), 0.92 (d, J = 7.0 Hz, 3 H), 0.86–1.71 (m, 9 H), 1.22 (q, *J* = 7.8 Hz, 2 H), 1.90–2.06 (m, 2 H), 2.14 (s, 3 H), 2.43 (t, *J* = 7.4 Hz, 2 H), 3.43 (td, $J_{aa}$ = 10.0 Hz, $J_{ae}$ = 4.0 Hz, 1 H).

$^{13}C$ NMR (50 MHz): δ = 209.5, 70.7, 70.5, 50.3, 48.1, 44.8, 43.8, 43.6, 34.52, 34.3, 31.4, 31.0, 30.2, 29.7, 24.3, 22.8, 22.1, 22.0, 21.8, 17.5, 13.6.

MS (CI, isobutane): *m*/*z* (%) = 209 [$M^+$ + 1] (100), 191 [($M^+$ + 1) – $H_2O$] (25).

**Tosylation (or Mesylation) of Hydroxy Ketones; General Procedure**

To a stirred solution of hydroxy ketones (δ-alkylated products) (2.0 mmol) and pyridine (0.47 g, 6.0 mmol) in $CH_2Cl_2$ (2 mL), *p*-toluenesulfonyl chloride (0.76 g, 4.0 mmol) was added at r.t. The reaction was completed after 12 h of stirring at r.t. After standard work up procedure the crude product was purified by dry flash chromatography (petrolether–acetone, 95:5) to give the pure tosylate.[10]

**5,5-Dimethyl-8-*p*-toluenesulfonyloxyoctan-2-one (from Hydroxy Ketone 16)**

Following the general procedure this compound is prepared as a pale yellow oil (87% yield).

IR (neat): 1714, 1599, 1495, 1471, 1358, 1292, 1176, 1098, 1020, 968, 913, 816, 733, 665 $cm^{-1}$.

$^1$H NMR ($CDCl_3$, 200 MHz): δ = 0.81 (s, 6 H), 1.12–1.21 (m, 2 H), 1.38–1.47 (m, 2 H),1.54–1.65 (m, 2 H), 2.15 (s, 3 H), 2.30–2.38 (m, 2 H), 2.45 (s, 3 H), 4.00 (t, *J* = 6.4 Hz, 2 H), 7.57 (AA′BB′ system, $\delta_A$ = 7.36, $\delta_B$ = 7.79, $J_{AB}$ = 8.4 Hz, $J_{AB'}$ = 1.6 Hz, 4 H).

$^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 209.3, 144.7, 133.0, 129.8, 127.8, 71.2, 38.6, 37.1, 34.8, 31.8, 29.9, 26.5, 23.6, 21.5.

MS (CI, isobutane): *m*/*z* (%) = 327 [$M^+$ + 1] (100), 156 [($M^+$ + 1) – *p*-$MePhSO_3H$] (68).

**5-(3-*p*-Toluenesufonyloxypropyl)nonan-2-one (from Hydroxy Ketone 19)**
Yield: 90%.

IR (neat): 2000–1600, 1715, 1599, 1456, 1413, 1360, 1307, 1292, 1211, 1189, 1177, 1098, 958, 920, 816, 665 $cm^{-1}$.

$^1$H NMR ($CDCl_3$, 200 MHz): δ = 0.87 (t, *J* = 6.8 Hz, 3 H), 1.18–1.27 (m, 9 H), 1.40–l.75 (m, 4 H), 2.13 (s, 3 H), 2.33–2.41 (m, 2 H), 2.45 (s, 3 H), 4.01 (t, *J* = 6.6 Hz, 2 H), 7.57 (AA′BB′ system, $\delta_A$ = 7.35, $\delta_B$ = 7.79, $J_{AB}$ = 8.4 Hz, $J_{AB'}$ = 0.6 Hz, 4 H).

$^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 209.1, 144.6, 133.1, 129.8, 127.8, 70.8, 40.7, 36.2, 32.6, 29.8, 28.9, 28.5, 26.9, 25.9, 22.9, 21.5, 13.9.

Anal. Calcd for $C_{19}H_{30}O_4S$: C, 64.40; H, 8.47; S, 9.03. Found: C, 64.18; H, 8.60; S, 8.85.

***cis*- and *trans*-4-[2-(2-*p*-Tolenesulfonyloxyethyl)cyclohexyl]butan-2-one (from Hydroxy Ketone 22)**
Obtained as viscous colorless oil in 92% yield (mixture of *cis*- and *trans*-isomers in a ratio of 1:3).

IR (neat): 1714, 1599, 1450, 1360, 1177, 1098, 1023, 960, 911, 818, 752 $cm^{-1}$.

$^1$H NMR (200 MHz, $CDCl_3$): δ = 0.90–1.42 (m, 9 H), 1.57–1.80 (m, 4 H), 1.85–2.05 (m, 1 H), 2.13 (s, 3 H), 2.25–2.50 (m, 2 H), 2.45 (s, 3 H), 4.02–4.15 (m, 2 H), 7.57 (AA′BB′ system, $\delta_A$ = 7.35, $\delta_B$ = 7.79, $J_{AB}$ = 8.0 Hz, $J_{AB'}$ = 1.8 Hz, 4 H).

$^{13}$C NMR (50 MHz, $CDCl_3$): δ = 209.2, 144,7, 133.1, 129.8, 127.9, 69.2, 68.8, 41.5, 40.6, 40.4, 38.0, 37.6, 34.8, 32.2, 31.1, 29.9, 28.39, 28.0, 27.8, 26.7, 25.6, 23.1, 21.6.

Anal. Calcd for $C_{19}H_{28}O_4S$: C, 64.77; H, 7.97; S, 9.09. Found: C, 64.56; H, 8.10; S, 9.22.

**4-[1-(3-*p*-Toluenesulfonyloxypropyl)cyclohexyl]-butan-2-one (from Hydroxy Ketone 6)**
Yield: 80%; pale yellow oil.

IR (neat): 2000–1600, 1715, 1599, 1496, 1460, 1359, 1308, 1292, 1211, 1189, 1177, 1120, 1098, 1041, 1020, 990, 945, 922, 817, 793, 736, 665 $cm^{-1}$.

$^1$H NMR ($CDCl_3$, 200 MHz,): δ = 1.16–1.25 (m, 6 H), 1.34–1.52 (m, 10 H), 2.14 (s, 3 H), 2.13–2.32 (m, 2 H), 2.45 (s, 3 H), 4.01 (t, *J* = 6.2 Hz, 2 H), 7.57 (AA′BB′ system, $\delta_A$ = 7.35, $\delta_B$ = 7.79, $J_{AB}$ = 8.4 Hz, $J_{AB'}$ = 0.6 Hz, 4 H).

$^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 209.4, 144.7, 133.1, 129.8, 127.8, 71.4, 37.49, 35.4, 33.9, 32.2, 30.1, 29.9, 26.2, 22.6, 21.5, 21.3.

**4-{2-[1-(2-*p*-Toluenesulfonylethyl)]-adamantyl}-butan-2-one (from Hydroxy Ketone 25)**
Yield: 79%; viscous, colorless oil.

IR (neat): 1715, 1598, 1495, 1452, 1412, 1361, 1308, 1293, 1189, 1176, 1098, 1020, 958, 841, 816 $cm^{-1}$.

$^1$H NMR (200 MHz, $CDCl_3$): δ = 1.17–1.90 (m, 18 H), 2.13 (s, 3 H), 2.26–2.42 (m, 2 H), 2.45 (s, 3 H), 4.00–4.20 (m, 2 H), 7.57 (AA′BB′ system, $\delta_A$ = 7.35, $\delta_B$ = 7.80, $J_{AB}$ = 8.0 Hz, $J_{AB'}$ = 1.8 Hz, 4 H).

$^{13}$C NMR (50 MHz, $CDCl_3$): δ = 209.2, 144.6, 133.2, 129.8, 127.9, 67.1, 45.6, 42.88, 41.7, 38.7, 38.5, 37.8, 37.4, 14.4, 30.6, 29.9, 29.6, 28.3, 28.0, 21.6, 20.9.

Anal. Calcd for $C_{23}H_{32}O_4S$: C, 68.31; H, 7.92; S, 7.92. Found: C, 68.18; H, 7.95; S, 8.09.

**Acetic Acid 17-(1-Methanesulfonyloxy-ethyl)-10-methyl-13-(4-oxo-pentyl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl Ester [4-(3β-Acetoxy-20β-methanesulfonyl-5-pregnen-18-yl)butan-2-one] (from Hydroxy Ketone 28)**
Yield: 99%; viscous, pale yellow oil.

IR (KBr): 1732, 1715, 1456, 1343, 1246, 1196, 1173, 1033, 971, 944, 908, 855 $cm^{-1}$.

$^1$H NMR (200 MHz, $CDCl_3$): δ = 0.86–1.99 (m, 21 H), 1.02 (s, 3 H), 1.47 (d, *J* = 6.0 Hz, 3 H), 2.04 (s, 3 H), 2.15 (s, 3 H), 2.20–2.50 (m, 5 H), 3.06 (s, 3 H), 4.52–4.68 (m, 1 H), 4.80–4.92 (m, 1 H), 5.36–5.39 (m, 1 H).

$^{13}$C NMR (50 MHz, $CDCl_3$): δ = 209.0, 170.6, 139.8, 122.2, 82.6, 73.8, 57.4, 56.3, 49.8, 44.7, 44.3, 40.0, 38.0, 36.9, 36.5, 35.2, 31.6, 29.8, 27.6, 25.4, 23.3, 21.4, 21.2, 21.0, 19.3, 18.6.

**Epimerization of (1*S*,2*R*,4*R*)-Hydroxy Ketone 31 into (1*S*,2*S*,4*R*)-Hydroxy Ketone 34[15] [(1*S*,2*S*,4*R*)-4-Methyl-2-*p*-nitrophenylcarbonyloxycyclohexyl]heptan-2-one (from Hydroxy Ketone 31)[13]**
To a solution of (6*R*) and (6*S*)-[(1*S*,2*R*,4*R*)-2-hydroxy-4-methylcyclohexyl]heptan-2-one (**31**, 0.163 g, 0.72 mmol), $PPh_3$ (1.13 g, 4.31 mmol) and *p*-nitrobenzoic acid (0.72 g, 4.31 mmol) in benzene (14 mL) was slowly added with stirring diethyl azodicarboxylate (0.75 g, 0.67 ml, 4.31 mmol) at r.t. and in an Ar atmopsphere. Esterification was completed during 6 h; silica gel (3 g) was added to the mixture and from the resulting suspension benzene was evaporated. The residual powder was transferred onto a silica gel column and eluted with petrolether, petrolether–acetone (95:5), successively. The title compound was obtained in 82% yield (0.22 g) as an oily mixture of two diastereoisomers (6*R* and 6*S*) in a ratio of 1:3.5.

IR (neat): 1718, 1609, 1530, 1457, 1411, 1352, 1320, 1273, 1166, 1116, 1104, 1015, 921, 875, 839, 785, 722 $cm^{-1}$.

$^1$H NMR (200 MHz): δ = 0.88 (d, *J* = 6.4 Hz, 3 H), 0.91 (d, *J* = 4.8 Hz, 3 H), 0.98–1.89 (m, 12 H), 2.03–2.10 (m, 1 H), 2.07 and 2.12 (s, 3 H), 2.35 (t, *J* = 7.2 Hz, 2 H), 5.48 (br s, 1 H), 8.26 (AB q, $\delta_{AB}$ = 0.11, $J_{AB}$ = 8.6 Hz, 4 H).

$^{13}$C NMR (50 MHz): δ = 208.9, 164.0, 150.4, 136.3, 130.6, 123.5, 73.3, 72.99, 44.6, 43.8, 39.1, 34.7, 34.2, 34.0, 33.4, 29.8, 26.8, 24.8, 22.0, 20.5, 16.9.

**(6*R*) and (6*S*)-[(1*S*,2*S*,4*R*)-2-Hydroxy-4-methyl-cyclohexyl]heptan-2-one (34)[13]**
(6*R*)- and (6*S*)-[(1*S*,2*S*,4*R*)-4-Methyl-2-*p*-nitrophenylcarbonyloxycyclohexyl]heptan-2-one (0.21 g, 0.57 mmol) was dissolved in MeOH (1.1 mL) and THF (0.25 mL) and then an aq solution of KOH (0.13 g, 2.3 mmol in 0.2 mL) was added. The mixture was stirred at r.t. for 30 h. $Et_2O$ (150 mL) was added to the reaction mixture and then washed with 2 M HCl (2 mL), sat. aq NaCl (5 mL) and the resulting solution was dried over $Na_2SO_4$. The solvent was evaporated and the residual oil was purified by dry flash chromatography on silica gel column (petrolether–acetone, 95:5). Isomerized hydroxy ketone **34** was obtained in 97% yield (0.125 g) as a colorless oil containing two diastereoisomers (6*R* and 6*S*) in the ratio of 1:3.5.

IR (neat): 3492, 1713, 1531, 1456, 1410, 1363, 1258, 1167, 1129, 1031, 962, 936, 722 $cm^{-1}$.

$^1$H NMR (200 MHz): δ = 0.87 (d, *J* = 6.6 Hz, 3 H), 0.90 (d, *J* = 7.0 Hz, 3 H), 0.95–1.88 (m, 14 H), 2.14 (s, 3 H), 2.42 (t, *J* = 7.0 Hz, 2 H), 4.08 (br s, 1 H).

$^{13}$C NMR (50 MHz): δ = 209.7, 67.8, 45.7, 45.7, 44.0, 43.9, 42.6, 35.0, 33.8, 33.7, 33.5, 33.2, 29.8, 29.6, 25.9, 24.1, 23.8, 22.3, 20.8, 20.7, 17.2, 16.8.

**(6*R*) and (6*S*)-[(1*S*,2*S*,4*R*)-2-Methanesulfonyl-4-methylcyclohexyl]heptan-2-one 35 (from Hydroxy Ketone 34)[13]**

To the solution of hydroxy ketone **34** (45 mg, 0.20 mmol) and pyridine (114 mg, 1.4 mmol) in $CH_2Cl_2$ (2 mL), cooled to 0 °C, methanesulfonyl chloride (91.3 mg, 0.79 mmol) was added drop-wise during 3 min. The mixture was stirred for 15 h at r.t. to complete the reaction. The solvent was evaporated and the residue was dissolved in $Et_2O$ (150 mL), the solution was washed successively with $H_2O$ (10 mL), 1.5 M HCl (2 mL), a sat. aq solution of $NaHCO_3$ (5 mL) and $H_2O$ (10 mL) and dried over $Na_2SO_4$. The solvent was removed by evaporation to give the pure title compound as a viscous oil in quantitative yield (61 mg). The mesylate was obtained as a mixture of diastereoisomers (6*R* and 6*S*) in a ratio of 1:5.

IR (neat): 1714, 1457, 1413, 1348, 1223, 1173, 1085, 1007, 974, 952, 911, 896, 840, 796 cm$^{-1}$.

$^1$H NMR (200 MHz): δ = 0.90 (d, *J* = 6.6 Hz, 6 H), 0.94–1.82 (m, 13 H), 2.14 (s, 3 H), 2.44 (t, *J* = 7.0 Hz, 2 H), 3.02 (s, 3 H), 5.11 (br s, 1 H).

$^{13}$C NMR (50 MHz): δ = 209.3, 81.2, 45.3, 45.0, 43.8, 43.7, 40.0, 39.1, 39.0, 34.3, 33.4, 33.2, 32.9, 29.8, 26.0, 24.0, 23.7, 21.8, 20.5, 20.3, 16.7, 16.5.

Anal. Calcd for $C_{15}H_{28}O_4S$: C, 59.21; H, 9.21; S, 10.52. Found: C, 59.50; H, 9.45; S, 10.28.

**Cycloalkylation of Ketosulfonate Esters; General Procedure[22]**

To a solution of tosylate (or mesylate) from the above experiments (0.2 mmol) in DME (2.0 mL), NaH (9.6 mg, 0.4 mmol, as a 80% suspension) was added under an Ar atmosphere and the mixture was heated to 80 °C during 8 h. After the reaction was complete EtOH (2 mL) was carefully added followed by $H_2O$ (5 mL). The mixture was extracted with $Et_2O$ (3 × 25 mL), the ethereal solution washed with brine and dried ($Na_2SO_4$). The solvent was evaporated and the oily residue was purified by dry flash chromatography on a silica gel column (petrolether–acetone, 95:5) to give the cyclic ketone.

**1-(3,3-Dimethylcyclohexyl)ethanone (17)**

Ketone **17** was obtained as colorless oil according to the described procedure (yield 74%).

IR (neat): 1748, 1462, 1378, 1268, 1164, 779 cm$^{-1}$.

$^1$H NMR ($CDCl_3$, 200 MHz): δ = 0.92 (s, 3 H), 0.94 (s, 3 H), 1.02–l.71 (m, 7 H), 1.80–1.94 (m, 1 H), 2.14 (s, 3 H), 2.50 (tt, $J_{aa}$ = 12.4 Hz, $J_{ae}$ = 3.6 Hz, 1 H).

$^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 212.6 (C), 47.7 (CH), 41.0, 38.5 ($CH_2$), 33.1 ($CH_3$), 30.5 (C), 28.2 ($CH_2$), 27.9, 24.4 ($CH_3$), 21.5 ($CH_2$).

MS (CI, isobutane): *m*/*z* (%) = 155 [M + 1] (100).

***cis*-1-(3-Butylcyclohexyl)ethanone (20)**

Following the described procedure compound **20** was obtained in 76% yield as a colorless oil.

IR (neat) : 1712, 1448, 1353, 1259, 1296, 1175, 968 cm$^{-1}$.

$^1$H NMR ($CDCl_3$, 200 MHz): δ = 0.78–1.01 (m, 3 H), 1.17–1.39 (m, 10 H), 1.68–1.96 (m, 5 H), 2.14 (s, 3 H), 2.34 (tt, $J_{aa}$ = 12.0 Hz, $J_{ae}$ = 3.2 Hz, 1 H).

$^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 212.4 (C),51.7 (CH), 37.1 ($CH_3$), 37.0, 34.9, 32.5, 28.9, 28.5 ($CH_2$), 27.9, (CH), 25.6, 22.9 ($CH_2$), 14.1 ($CH_3$).

Anal. Calcd for $C_{12}H_{22}O$: C, 79.12; H, 12.08. Found: C, 78.88; H, 12.25.

**1-[(1*R*,4a*S*,7*R*,8a)-4,7-Dimethyldecahydronaphthalen-1-yl]ethanone [Tetrahydrokhusitone (33)][13]**

Mesylate **35** (30 mg, 0.098 mmol) was dissolved in dimethoxy ethane (1.5 mL) and then NaH (9.4 mg, 0.39 mmol) was added at r.t. under an Ar atmosphere. The mixture was stirred and heated to 80 °C during 20 h. After the reaction was complete EtOH (2 mL) was added to react with the excess of NaH. $H_2O$ (2 mL) was added to the mixture and then extracted with $Et_2O$ (3 × 25 mL). The combined ethereal solutions were washed with sat. aq NaCl (10 mL) and dried over $Na_2SO_4$. The solvent was evaporated and the oily residue purified by preparative TLC chromatography (petrolether–acetone, 97.5:2.5). Tetrahydrokhusitone (**33**) was obtained (10.9 mg) in 53% yield as a viscous oil.

IR (neat): 1701, 1595, 1453, 1355, 1178, 935 cm$^{-1}$.

$^1$H NMR (200 MHz): δ = 0.50–0.67 (m, 1 H), 0.82 (d, *J* = 6.4 Hz, 3 H), 0.88 (d, *J* = 6.0 Hz, 3 H), 0.90–1.81 (m, 12 H), 1.96 (dt, $J_1$ = 9.0 Hz, $J_2$ = 3.2 Hz, 1 H), 2.12 (s, 3 H), 2.19 (td, $J_{aa}$ = 12.8 Hz, $J_{ae}$ = 4.0 Hz, 1 H).

$^{13}$C NMR (50 MHz): δ = 212.7 (C), 58.1 (CH), 47.7 (CH), 43.3 (CH), 40.2 ($CH_2$), 36.8 (CH), 35.13 ($CH_2$), 34.9 ($CH_2$), 32.2 (CH), 30.1 ($CH_2$), 29.7 ($CH_2$), 29.5 ($CH_3$), 22.53 ($CH_3$), 19.7 ($CH_3$).

In addition to tetrahydrokhusitone (**33**) as a cyclization product (6*R*)- and (6*S*)-[(4*R*)-4-methylcyclohexen-1-yl]heptan-2-one (**32**) was isolated (7 mg, 34% yield) as a colorless oil. This olefinic compound is the product of an elimination reaction and has the same $^1$H NMR spectrum as a product obtained in the reaction of the tosylate derived from **31** with NaH.[13]

***cis*- and *trans*-(Decahydronaphthalen-2-yl)ethanone (23)**

Obtained by cycloalkylation of the tosylate derived from **22**, in 81% yield as viscous colorless oil.

IR (neat): 1731, 1470, 1441, 1372, 1245, 1103, 1029, 956, 864, 803 cm$^{-1}$.

$^1$H NMR (200 MHz, $CDCl_3$): δ = 0.82–1.94 (m, 16 H), 2.13 (s, 3 H), 2.39 (tt, $J_{aa}$ = 11.8 Hz, $J_{ae}$ = 3.4 Hz, 1 H).

$^{13}$C NMR (50 MHz, $CDCl_3$): δ = 212.6, 51.7, 42.6, 42.4, 35.5, 33.8, 33.6, 33.0, 28.3, 27.9, 26.5.

Anal. Calcd for $C_{12}H_{20}O$: C, 80.00; H, 11.11. Found: C, 79.77; H, 11.28.

**1-Spiro[5.5]undec-2-ylethanone (7)**

Following the described procedure bicyclic ketone **7** was obtained in 77% yield as a colorless oil.

IR (neat): 1709, 1451, 1372, 1354, 1270, 1236, 1189, 1164, 964, 903, 843 cm$^{-1}$.

$^1$H NMR ($CDCl_3$, 200 MHz): δ = 0.89–1.90 (m, 18 H), 2.13 (s, 3 H), 2.50 (tt, $J_{aa}$ = 12.2 Hz, $J_{ae}$ = 3.4 Hz, 1 H).

$^{13}$C NMR ($CDCl_3$, 50 MHz): δ = 212.8 (C), 46.7 (CH), 41.8 ($CH_3$), 38.7, 35.8 ($CH_2$), 32.6 (C), 32.1, 28.7 ($CH_2$), 27.9, 26.8, 21.5, 20.7 ($CH_2$).

MS (CI, isobutane): *m*/*z* (%) = 195 [M + 1] (100).

**1-Acetyl-cyclohexyl[3,4:2,1]adamantane (26)**

Yield: 78%; viscous, colorless oil.

IR (neat): 1709, 1456, 1352, 1313, 1274, 1238, 1200, 1158, 1106, 962, 906, 746 cm$^{-1}$.

$^1$H NMR (200 MHz, $CDCl_3$): δ = 0.82–2.12 (m, 20 H), 2.15 (s, 3 H), 2.38 (tt, $J_{aa}$ = 11.8 Hz, $J_{ae}$ = 3.8 Hz, 1 H).

$^{13}$C NMR (50 MHz, $CDCl_3$): δ = 212.5, 52.3, 46.9, 46.7, 39.6, 39.2, 38.2, 35.2, 33.6, 31.1, 29.7, 29.3, 29.2, 28.6, 28.1, 23.3.

Anal. Calcd for $C_{16}H_{24}O$: C, 82.75, H, 10.34. Found: C, 82.70, H, 10.25.

**1-(10-Hydroxy-4,12a-dimethyl-eicosahydro-indeno[1,7a-*a*]phenanthren-3-yl)-ethanone [1-(18,20-Ethano-3β-hydroxy-5-pregnen-22-yl)ethanone] (29)**
Yield: 95%; white crystals.

IR (KBr): 3431, 1694, 1638, 1441, 1362, 1298, 1243, 1106, 1066, 1009, 956 $cm^{-1}$.

$^1$H NMR (200 MHz, $CDCl_3$): δ = 0.79 (d, $J$ = 6.8 Hz, 3 H), 0.88–1.14 (m, 5 H), 1.00 (s, 3 H), 1.24–1.67 (m, 15 H), 2.14 (s, 3 H), 1.80–2.40 (m, 7 H), 3.44–3.62 (m, 1 H), 5.33–5.36 (m, 1 H).

$^{13}$C NMR (50 MHZ, $CDCl_3$): δ = 213.5 (C), 140.9 (C), 121.6 (CH), 71.7 (CH), 56.9 (CH), 53.4 (CH), 52.1 (CH), 50.5 (CH), 42.2 ($CH_2$), 41.9 (C), 37.2 ($CH_2$), 36.6 (C), 33.0 ($CH_2$), 31.9 ($CH_2$), 31.6 ($CH_2$), 31.3 (CH), 31.2 (CH), 29.3 ($CH_3$), 25.1 ($CH_2$), 23.5 ($CH_2$), 21.9 ($CH_2$), 21.7 ($CH_2$), 20.4 ($CH_2$), 19.5 ($CH_3$), 17.9 ($CH_3$).

Anal. Calcd for $C_{27}H_{40}O_3$: C, 78.64; H, 9.70. Found: C, 78.34, H, 9.84.

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