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PURE ENANTIOMERS FROM SIMPLE, SYMMETRIC DIENOPHILES

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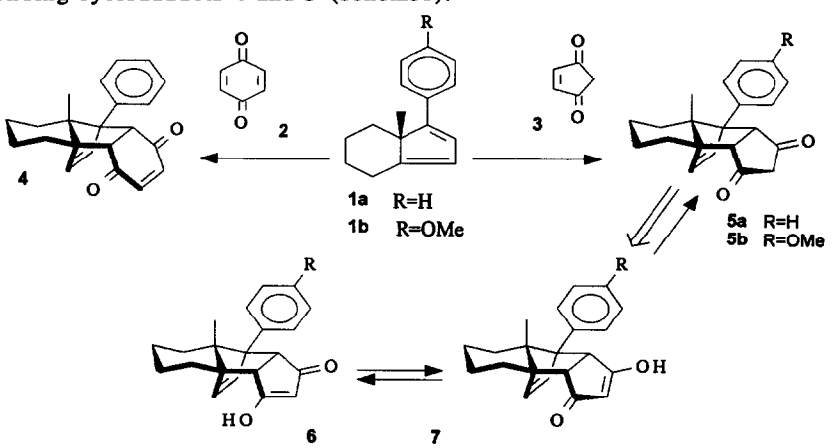
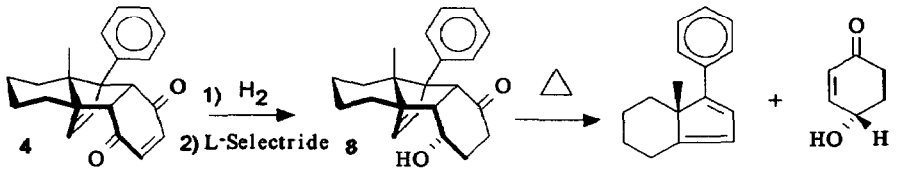
***Abstract** : Starting from p-benzoquinone or 2-cyclopentene-1,4-dione as dienophiles and the enantiomerically pure dienes **1a** and **1b**, high pressure cycloadditions led to chiral adducts.These were transformed in a regioselective manner to generate well defined stereogenic centres. A remarkably efficient electron density directed regioselectivity was discovered with **18c** and **18d**.*

While the use of chiral catalysts and auxiliary modified dienophiles has found wide application in enantioselective synthesis[1] much less has been published on enantiomerically pure dienes and their employment as chiral templates[2]. Since we have easy access to both enantiomers of the cyclopentadienes **1a** and **1b**, we investigated their high-pressure cycloadditions to the achiral symmetric dienophiles quinone **2** and 2-cyclopentene-1,4-dione[3] **3** as well as the regioselectivity of various transformations of the corresponding cycloadducts **4** and **5** (scheme1).



Scheme 1

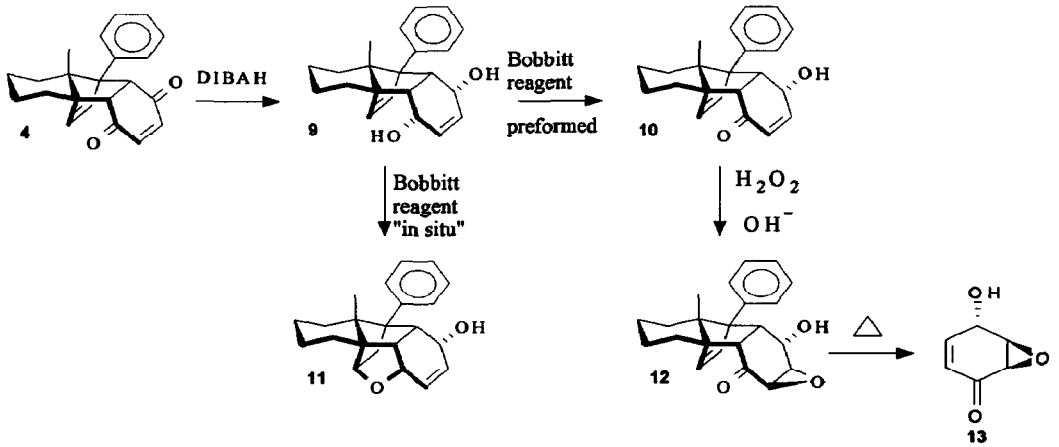
While with adduct **4**[4]these subsequent reactions just pose regioselectivity problems, matters become more complicated in the case of the 1,3-dicarbonyl adduct **5**, since here fast enolisation establishes the enol-equilibrium **6** ⇔ **7** and it then probably will be a matter of kinetic versus thermodynamic control to achieve regioselective carbonyl transformations. The regioselectivity in these reactions is however of great interest with respect to obtaining enantiomerically pure cyclopentenones[5,6]. Once this regioselective change from sp^2 to well defined, template directed sp^3 centres is achieved, one can easily prepare pure enantiomers by chemoselective reactions and subsequent retro-Diels-Alder-processes.



Scheme 2

Since the first examples demonstrating these sequences were recently published from our laboratory[7] (see scheme 2) starting from the benzoquinone-adduct **4**, the first examples reported in this paper have been chosen from this area, too. Having noticed that, probably owing to the shielding by the phenyl group, selectride® reduction takes place exclusively at the carbonyl group distant from this substituent (see **8**), we became interested in the regioselectivity of the corresponding oxidation process, (scheme 3). As diol **9** can easily be prepared from **4** in a DIBAH-reduction in 92% yield, we activated Bobbitts'4-acetylamino-"tempo"-reagent[8] by p-toluenesulfonic acid prior to the addition of diol **9** and were pleased to notice the formation of just one hydroxy-ketone (**10**) which could easily be shown to be derived from attack at the hydroxy-group away from the phenyl-residue (NMR-data-see experimental part). The subsequent epoxidation of this ketol **10** occurred with high diastereoselectivity and was followed by a high yield pyrolysis to regenerate the diene and epoxide **13**. This epoxide represents the enantiomer of the one we recently generated from the corresponding reduction product[4], which is the regioisomer of **10**.

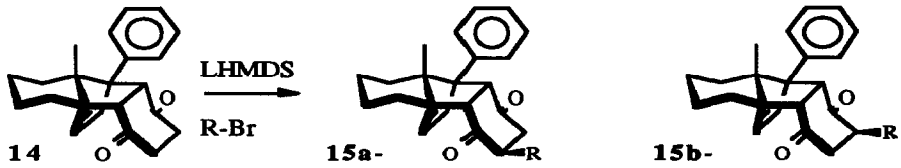
The reaction conditions of the selective tempo-oxidation turned out to be crucial, however, as the generation of the reagent in the presence of diol **9** exclusively provided the cyclic ether **11** in quantitative yield, probably via radical-addition to the strained double bond.



Scheme 3

As this result shows that oxidations can take place with excellent regioselectivity, we decided next to investigate a deprotonation-alkylation sequence and chose the bulky base lithium-hexamethyldisilazide hopefully again to benefit from the sterical demand of the

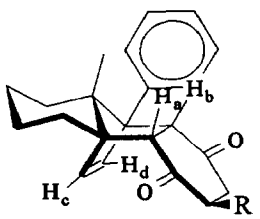
phenyl-ring. Although the deprotonation as well as the alkylation were conducted at -78°C the regioselectivity was in this case not as good as in the reduction-oxidation experiments.



15	R = Benzyl	86	:	14
16	R = Propargyl	84	:	16
17	R = Allyl	82	:	18
18	R = Methyl	72	:	28

Scheme 4

15, **16** and **17** were generated with satisfactory and comparable regioselectivity, which dropped significantly however with methylbromide as the electrophile (see **18**). While owing to the concave-convex bending of the molecule, β-attack is guaranteed, to yield in both cases the configuration indicated, the regioselectivity was first of all concluded from the general preferences noticed with these molecules but gained additional support from NMR-data which showed a consistent low-field shift for proton H_a, going along with a comparable high-field shift for proton H_c (see table 1).



15a - 18a

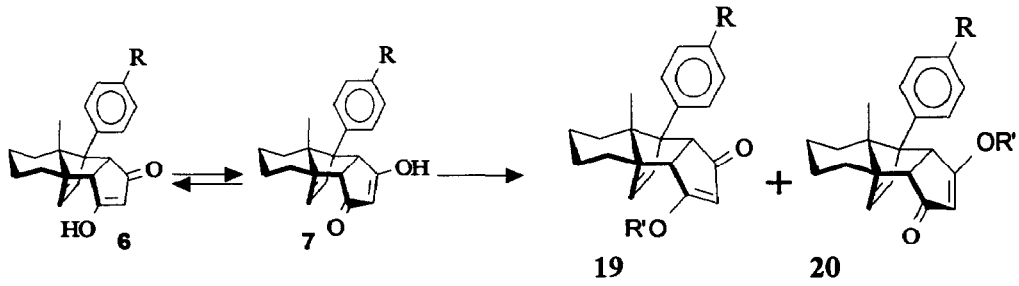
Compound		Ha	Hb	Hc	Hd
14	R=H	3.17	4.06	6.05	6.30
15a	R=Benzyl	3.11	4.08	6.11	6.25
16a	R=Allyl	3.12	4.05	6.13	6.23
17a	R=Propargyl	3.13	4.13	6.18	6.24
18a	R=Methyl	3.09	4.07	6.13	6.20

Table 1

As with these compounds regioselectivity is translated into enantioselectivity on further transformations and retro-Diels-Alder splitting, additional support for this assignment will be obtained from these sequences. To continue with the desymmetrisation experiments we next turned to 1,3-diketone **5**, which easily can be shown to massively populate the enol-equilibrium **6** ⇔ **7** (IR-data, NMR-data, solubility).

When **5** was treated with diazomethane in anhydrous ether the product turned out to be a 66:34 ratio of the enolethers **19a** and **20a** and as this ratio proved to be independant on the reaction temperature (-78°C, -20°C and 20°C), we conclude that this reagent just traps the equilibrium **6** ⇔ **7**. For the formation of **19b** and **20b** adduct **5** was dissolved in anhydrous dichloromethane and mixed with a solution of 1.5 equivalents of p-toluenesulfonoyl chloride and dimethylaminopyridine (DMAP) at-78°C. In this case we obtained a 30:70 ratio favouring **20b** and as this ratio does not markedly change if

deprotonation is achieved with methilithium at-78°C (**19b:20b** = 26:74), we assume that π-stacking between the reagent and the phenyl ring in **5** may be responsible for this unusual result.

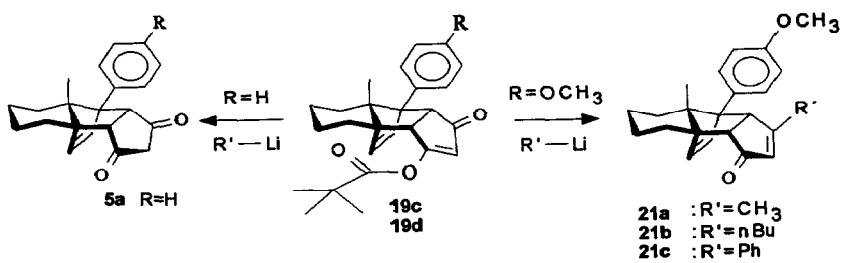


a) R=H; R'=CH_3	66	:	34
b) R=H; R'=Tosyl	30	:	70
c) R=H; R'=Pivaloyl	95	:	5
d) R=OCH_3; R'=Pivaloyl	95	:	5

Scheme 5

As a consequence of this we next decided on a bulky, non aromatic reagent and chose pivaloyl chloride which with **5a** as well as with **5b** yielded a 95:5 ratio of the two regioisomers. Similar to other bulky reagents, again the carbonyl group distant to the phenyl ring is attacked with high regioselectivity. Having this way an easy access to the enolesters **19c** and **19d** we next investigated their transformation into cyclopentenones. With this aim both compounds were treated with organolithium reagents and the products were formed with a high regioselectivity, which indicates an unexpected directing effect of the aromatic rings in these compounds.

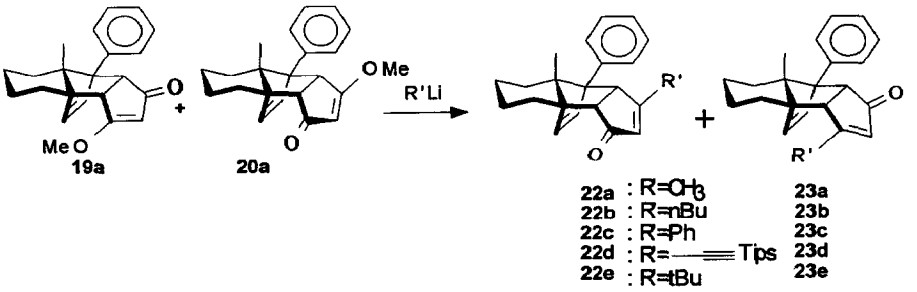
While **19c** was exclusively attacked at the pivalate moiety to regenerate **5a**, the corresponding p-methoxy derivative **19d** underwent attack at the five-membered ring to provide the cyclopentenones **21a**, **21b** and **21c**. The only exception turned out to be the lithium derivative of trialkylsilylacetylenes which again attacked at the pivalate group. Since the only difference between **19c** and **19d** is the substituent on the phenyl ring, we are dealing here with electron density directed regioselectivity.



Scheme 6

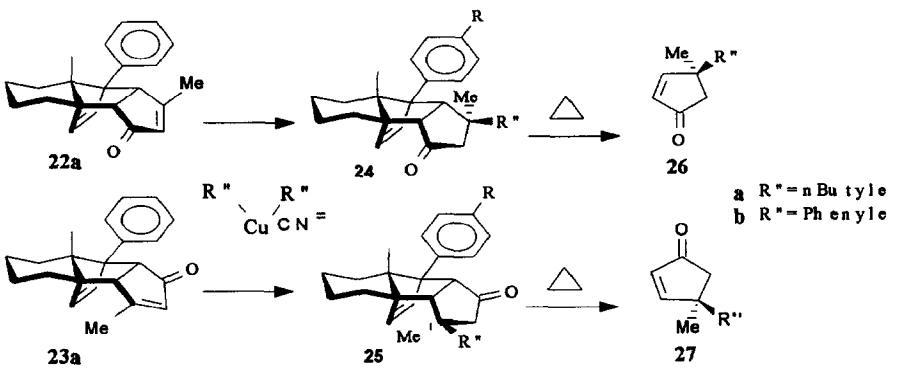
A possible explanation could be a favourable electronic interaction between the metal atom and the more electron rich aromatic ring in **19d** (R=OCH_3) which directs the

Organolithium compounds into the carbonyl group neighbouring this aromatic ring. The exceptional behaviour of the acetylide may well be due to the acidity of the sp-centre, leading to the less aggregated and probably predissociated species.



Scheme 7

The cyclopentenones of type **22** do also represent the major isomers from the treatment of the inseparable methylether mixture **19a/20a** with organolithium compounds (scheme 7). In this case the same 66:34 ratio which is observed on diazomethane treatment is obtained after hydrolysis and, as at this stage the two regioisomers **22** and **23** may be separated by chromatography, they also represent useful precursors for enantiomerically pure cyclopentenones. To demonstate this we conducted cuprate additions to both regioisomers.



Scheme 8

These transformations generate cyclopentenones of type **24** (R=H) from **22a** and the corresponding regioisomers **25** (R=H) from **23a**. On pyrolysis one obtains the enantiomerically pure cyclopentenones **26a** and **26b** and their antipodes **27a** and **27b**. These observations provide two options for the easy preparation of these enantiomers.

On one hand one may treat adduct **19d** with a well defined sequence of metallorganic compound and cuprate, which, depending on the selection of the first or second nucleophile, will either generate the ketones of type **24** (R=OMe) or their epimers. On the other hand the cyclopentenones generated from the methylethers **19a** and **20a** afford ketones **24** and **25** upon cuprate additions. In each case both enantiomers of disubstituted cyclopentenones (see **26** and **27**) will be obtained on pyrolysis. In this way the symmetric

2-cyclopenten-1,4-dione may be converted into enantiomerically pure cyclopentenones with a quaternary carbon atom in a few simple steps.

EXPERIMENTAL

Melting points were measured on a Büchi hotstage and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker WP-200. MS assays (MS m/z) were obtained using a Finnigan MAT 312 spectrometer with an ionization potential of 70 eV. IR spectra were recorded in $CHCl_3$ or in KBr with a Perkin-Elmer 580. UV spectra were measured on a Beckmann 3600 spectrometer. Elemental analysis were obtained using a Heraeus CHN rapid analyzer. For flash chromatography Baker silica gel 30-60 μm was used, TLC analysis were carried out on DC aluminium foils, covered with silica gel $^{60}F_{254}$ (E. Merck) ; the spots were detected by UV (254 nm) an in addition to that by a dipping bath of Cerium(IV)-sulphate/phosphomolybdic acid reagent. Optical rotations were measured on a Perkin-Elmer 241. Organic solvents were purified by standard procedures. Anhydrous THF was distilled from potassium/benzophenone and ,air- and moisture-sensitive reactions were carried out in flame-dried reaction vessels under nitrogen using dry syringes.

Diketone **14**: A 10 mL flask was charged with **4** (300 mg, 0.94 mmol) and Zn powder (246 mg, 3.76 mmol) in glacial AcOH (3 mL) and was sonicated at 18°C for 5 min. The reaction mixture was then filtered and diluted with water (10 mL) and extracted 3 times with Et_2O (10 mL). The combined organic phases were washed with sat. $NaHCO_3$ (10 mL), brine (10 mL) and dried over $MgSO_4$. Evaporation to dryness gave **14** (287 mg, 95%), which could be crystallized as colorless needles from AcOEt/petroleum ether.

14 : **Mp**=153-154°C; **TLC** R_f (MTBE/PE 1:1)=0.21 ; **MS** m/z 320 (M^+, 5), 236 (32), 221 (22), 210 (100), 167 (26), 109 (19) ; **IR** (KBr) 2955s, 1703s, 1446s, 1303s, 1141s, 752s, 704s, cm^{-1} ; ^{1}H **NMR** ($CDCl_3$) 0.51 (bd, J=13 Hz, 1H), 0.76 (d, J=1Hz), 2.27-2.49 (m, $w_{1/2}$=39 Hz, 3H), 2.63 (bd, J=9 Hz, 1H), 3.17 (d, J=9.5 Hz, 1H), 4.06 (d, J=9.5 Hz, 1H), 6.05 (d, J=6 Hz, 1H), 6.30 (d, J=6 Hz, 1H), 7.20-7.40 (m, $w_{1/2}$=4 Hz, 5H) ; ^{13}C **NMR** ($CDCl_3$) 15.4, 21.1, 23.4, 26.1, 27.7, 38.5, 54.2, 56.1, 61.7, 63.0, 69.1, 116.1, 126.5, 127.3, 127.8, 127.9, 137.5, 138.8, 139.1. **Microanalysis** calcd. for $C_{22}H_{24}O_2$ (320.44) ; C, 82.5 ; H, 7.55. Found : C, 82.3 ; H, 7.55 ; **HRMS** calcd. ; 320.1787, found ; 320.1776.[α] = -33.6 ($CHCl_3$, 0.995).

Diol **9**: DIBAH (630 mL, 0.63 mmol) was added dropwise at -78°C and under inert atmospher to a solution of **4** (100 mg, 0.31 mmol) in dry toluene (4 mL). After 5 to 10 min, the reaction mixture was poured into 20 mL of cold 1N NaOH. After extraction with Et_2O or CH_2Cl_2, drying over $MgSO_4$ and evaporation to dryness, we obtained **9**, which was crystallized from PE/CH_2Cl_2, to give 93 mg of pure **9** (92%).

9 : **Mp**=176-178°C ; **TLC** R_f (Et_2O)=0.47 ; **MS** m/z 322 (M^+, 4), 210 (100), 195 (32), 167 (37), 116 (23), 91 (35) ; **IR** (KBr) 3397w, 2921s, 2856s, 1445s, 999s, 763s, 701s cm^{-1} ; ^{1}H **NMR** (CD_2Cl_2) 0.46.(bd, J=13 Hz, 1H), 0.80 (d, J=1 Hz, 3H), 2.36 (dd, J_1=10 Hz, J_2=5 Hz, 1H), 3.23 (dd, J_1=10 Hz, J_2=5 Hz, 1H), 4.31 (bdd, J_1=6 Hz, J_2=6 Hz, 2H), 6.12 (bs, 2H), 6.38 (dd, J_1=3 Hz, J_2=1 Hz, 1H), 6.41 (dd, J_1=3 Hz, J_2=1 Hz, 1H), 7.18-7.42 (m, $w_{1/2}$=2 Hz, 5H) ; ^{13}C **NMR** ($CDCl_3$) 15.5, 21.6, 23.4, 25.7, 27.8,

47.6, 50.0, 59.1, 63.1, 63.4, 65.4, 66.0, 126.3, 127.5, 128.1, 133.5, 136.2, 137.0, 137.5, 139.0. **Microanalysis** calcd. for $C_{22}H_{26}O_2$ (322.45); C, 82.0; H, 8.15. Found: C, 81.5 ; H, 8.15 ; **HRMS** calcd.; 322.1933, found ; 322.1933.[α] = -25.1 ($CHCl_3$, 1).

Hydroxy-ketone **10**: A solution of 4-(acetylamino)-TEMPO, was prepared by stirring a suspension of pTsOH monohydrate (227 mg, 1.19 mmol) with the corresponding nitroxide (254 mg, 1.19 mmol), in CH_2Cl_2 (5 mL) for 20 min at 0°C. An orange color developed from the oxoammonium salt. This solution was added dropwise to **9** (183 mg, 0.568 mmol) in cold CH_2Cl_2 (5 mL) over 30 min. The orange solution was then stirred at 0°C for 1h and then at room temperature until the color had essentially disapeared and a dense white precipitate formed. The reaction mixture was then cooled in ice, and the precipitate was removed by filtration and washed with cold CH_2Cl_2 (2 mL). The filtrate was washed with saturated $NaHCO_3$ (15 mL) and dried over $MgSO_4$. After removal of the solvent, the product **10** was purified by flash chromatography with Et_2O.

10 : Mp=137°C ; **TLC** R_f (Et_2O)=0.36 ; **MS** m/z 320 (M^+, 45), 319 (42), 210 (75), 163 (100), 91 (77) ; **IR** ($CHCl_3$) 3584w, 2928m, 2860s, 1660s, 1496s, 1444s cm^{-1} ; ^{1}**H NMR** ($CDCl_3$) 0.46 (bd, J=13 Hz, 1H), 0.83 (bs, 3H), 2.13 (bd, J=13 Hz, 1H), 2.93 (d, J=9 Hz, 1H), 4.00 (bt, J=9 Hz, 1H), 4.88 (td, J_1=10 Hz, J_2=3 Hz, 1H), 5.72 (d, J=6 Hz, 1H), 5.83 (dd, J_1=10 Hz, J_2=3 Hz, 1H), 6.26 (d, J=6 Hz, 1H), 6.55 (dd, J_1=10 Hz, J_2=3 Hz, 1H), 7.22-7.42 (m, $w_{1/2}$=5 Hz, 5H); **HRMS** calcd for $C_{22}H_{24}O_2$; 320.1779, found ; 320.1776.[α] = -119.7 ($CHCl_3$, 0.685).

Ether **11**: pTsOH monohydrate (186 mg, 0.98 mmol) was suspended in CH_2Cl_2 (3 mL) containing compound **9** (150 mg, 0.47 mmol) and cooled to 0°C. A solution of the nitroxide (210 mg, 0.98 mmol) in CH_2Cl_2 (2 mL) was added dropwise over 30 min. The solution was then stirred at room temperature until it was almost completely decolorized. During the last minutes of the reaction a precipitate formed. The reaction mixture was then cooled in ice, and the precipitate was removed by filtration and washed with cold CH_2Cl_2 (1 mL). The filtrate was washed with saturated H_2O (10 mL) an dried over $MgSO_4$. After removal of the solvent, the resulting oil was chromatographed through silica (PE/MTBE) to yield pure **11** (149 mg, quant.).: **11** : **TLC** R_f (Et_2O/PE 1:1)=0.52 ; **MS** m/z 322 (M^+, 2), 303 (100), 275 (16), 211 (50), 171 (65), 144 (88), 127 (58), 91 (66) ; **IR** ($CHCl_3$) 3520w, 3056m, 2976m, 2936m, 2864s, 1444s, 1084s cm^{-1} ; ^{1}**H NMR** ($CDCl_3$) 0.80 (s, 3H), 2.05 (tdd, J_1=5 Hz, J_2=1 Hz, J_3=1 Hz, 1H), 2.42 (bt, J=5 Hz, 1H), 2.61-2.76 (m, $w_{1/2}$=24 Hz, 2H), 4.04-4.11 (m, $w_{1/2}$=9 Hz, 1H), 5.12 (s, 1H), 5.22 (td, J_1=5 Hz, J_2=1 Hz, 1H), 6.03 (ddd, J_1=8 Hz, J_2=7 Hz, J_3=2 Hz, 1H), 6.17 (ddd, J_1=8 Hz, J_2=7 Hz, J_3=2 Hz, 1H), 7.15-7.36 (m, $w_{1/2}$=6 Hz, 5H). **HRMS** calcd. for $C_{22}H_{26}O_2$; 322.1926, found ; 322.1933.[α] = -62.1 ($CHCl_3$, 0.470).

Epoxide **12**: A solution of NaOH (32 mg, 0.78 mmol) and 35% H_2O_2 (68 μL, 0.78 mmol) in H_2O (1 mL) was added in one portion to a solution of **10** (50 mg, 0.16 mmol) in THF (2 mL) cooled to 0°C, with the help of an addition funnel. The mixture was allowed to warm up to r. t. and stirred for 30 min. The resulting mixture was extracted 3 times with Et_2O (10 mL) and the combined organic layers were washed 2 times with 5% aqueous

$FeSO_4$ (10 mL), dried over $MgSO_4$ and evaporated to dryness. Chromatography through neutral alumina eluted with PE/Et_2O lead to **12** (47 mg, 89%): **12** : **Mp**=170-171°C (Decomp.) ; **TLC** R_f (Et_2O)=0.56 ; **MS** m/z 336 (M^+, 16), 241 (36), 221 (36), 210 (100), 167 (53), 91 (39) ; **IR** (KBr) 3443w, 2923m, 2859s, 1713s, 1446s, 765s, 702s : **^{1}H NMR** ($CDCl_3$) 0.49 (bdd, J_1=13 Hz, J_2=3 Hz, 1H), 0.81 (d, J=1 Hz, 3H), 2.34 (bd, J=11 Hz, 1H), 3.11 (d, J=11 Hz, 1H), 3.30 (d, J=4 Hz, 1H), 3.57 (dd, J_1=4 Hz, J_2=3 Hz, 1H), 3.77 (dd, J_1=11 Hz, J_2=6 Hz, 1H), 4.68 (bs, 1H), 6.23 (bt, J=6 Hz, 2H), 7.23-7.42 (m, $w_{1/2}$=8 Hz, 5H) ; **HRMS** calcd for $C_{22}H_{24}O_3$. ; 336.1727, found; 336.1725.[α] = -53.6 ($CHCl_3$, 0.470).

Benzyl products **15a and 15b**: To a solution of LiHMDS in 2 mL dry THF (prepared from HMDS, 100 µL, 0.47 mmol and BuLi 1.6 M in hexanes, 375 µL, 0.47 mmol at -78°C) was added dropwise compound **6** (50 mg, 0.16 mmol) in THF (1 mL), with the help of a canula. After 10 min, benzyl bromide (110 µL, 0.94 mmol) was added and allowed to react for 15 min. The reaction mixture was then poured into sat. NH_4Cl (10 mL) and extracted with Et_2O (3 times 10 mL). The organic phase was dried over $MgSO_4$ and evaporated to dryness. Chromatography over silica gel eluted with PE/Et_2O lead to a mixture of **12a** and **12b** (52 mg, 81%).**15a** : **TLC** R_f (MTBE/PE 1:1)=0.60 ; **IR** ($CHCl_3$) 2928w, 2860s, 1700s, 1496s, 1384s, 1120w, 908s, 620s cm^{-1} ; **^{1}H NMR** ($CDCl_3$) 0.49 (bd, J=13 Hz, 1H), 0.77 (d, J=1 Hz, 3H), 2.62 (bd, J=8 Hz, 1H), 3.12 (d, J=9 Hz, 1H), 4.08 (d, J=9 Hz, 1H), 6.12 (d, J=6 Hz, 1H), 6.25 (d, J=6 Hz, 1H), 7.03-7.13 (m, $w_{1/2}$=2 Hz, 5H). **HRMS** calcd. for $C_{29}H_{30}O_2$; 410.2250, found ; 410.2246.

Propargyl products **16a and 16b**: These (43 mg, 76%) were obtained in a similar procedure as for **15a** and **15b** upon treatment with propargyl bromide.**16a** : **TLC** R_f (MTBE/PE 1:1)=0.46 ; **MS** m/z 358 (M^+, 3), 210 (100), 195 (32), 167 (50), 165 (28), 149 (34), 91 (35) ; **IR** ($CHCl_3$) 3308s, 2928m, 2122m, 1700s, 1444s, 908s, 636s, 616s cm^{-1} ; **^{1}H NMR** ($CDCl_3$) 0.49 (bd, J=13 Hz, 1H), 0.78 (d, J=1 Hz, 3H), 1.99 (t, J=3 Hz, 1H), 2.63 (s, 1H), 3.13 (d, J=9 Hz, 1H), 4.13 (d, J=9 Hz, 1H), 6.18 (d, J=6 Hz, 1H), 6.24 (d, J=6 Hz, 1H), 7.21-7.24 (m, $w_{1/2}$=6 Hz, 5H). **Microanalysis** calcd. for $C_{25}H_{26}O_2$ (358.48) ; C, 83.8 ; H, 7.30. Found ; C, 83.8 ; H, 7.35. **HRMS** calcd.; 358.1933, found ; 358.1933.

Allyl products **17a and 17b**: These (44 mg, 79%) were obtained in a similar procedure as for **15a** and **15b** upon treatment with allyl bromide.**17a** : **TLC** R_f (MTBE)=0.58 ; **MS** m/z 360 (M^+, 2), 210 (100), 195 (34), 181 (28), 167 (54), 115 (15) ; **IR** ($CHCl_3$) 2928m, 2860s, 1700s, 1600w, 1496s, 1444s cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.49 (bd, J=13 Hz, 1H), 0.77 (d, J=1 Hz, 3H), 3.12 (d, J=9 Hz, 1H), 4.05 (d, J=9 Hz, 1H), 5.01 (dd, J_1=7 Hz, J_2=2 Hz, 1H), 5.06 (dd, J_1=12 Hz, J_2=2 Hz, 1H), 5.53-5.79 (m, $w_{1/2}$=36 Hz, 1H), 6.13 (d, J=6 Hz, 1H), 6.24 (d, J=6 Hz, 1H), 7.21-7.41 (m, $w_{1/2}$=2 Hz, 5H). **Microanalysis** calcd. for $C_{25}H_{28}O_2$ (360.50) ; C, 83.30 ; H, 7.80. Found ; C, 83.20 ; H, 7.80. **HRMS** calcd. ; 360.2086, found ; 360.2089.

Cyclopentadienone adduct **5a**: A solution of the diene **1a** (2.10 g, 10 mmol) and the cyclopentene-1,4-dione (0.96 g, 10 mmol) in anhydrous CH_2Cl_2 (6 mL) were introduced

in a Teflon® tube and pressurized at 7Kbar at 25°C during 24h. The product was filtered and washed with 5mL Et_2O. The reaction gave 3 g of the vinylogous acid **5a** (98%). **5a**: **Mp** ; 191°C (Decomp.) ; Solubility: 40mg in 4ml DMSO ; **MS** m/z 306 (M^+ 15), 305 (65), 236 (77), 221 (59), 210 (100), 167 (50), 152 (16) ; **IR** (KBr) 2859s, 1572s, 1291s, 783s, 758w, 699w cm^{-1} ; **^{1}H-NMR** (DMSO D_6) 0.48 (bd, J=13Hz, 1H), 0.78 (bs, 3H), 4.87 (s, 1H), 5.89 (bs, 2H), 7.18-7.47 (m, 5H), 11.75 (bs, 1H) ; **^{13}C NMR** δ 14.5, 20.3, 21.1, 22.9, 26.1, 29.8, 39.3, 40.6, 58.5, 66.3, 107.7, 126.2, 127.8, 133.8, 136.4, 139.2; **HRMS** calcd for $C_{21}H_{22}O_2$; 306.1619, found ; 306.1620.[α] = -166.1 (DMSO, 0.620).

Cyclopentadienone adduct **5b**: A solution of the diene **1b** (2.40 g, 10 mmol) and the cyclopentene-1,4-dione (0.96 g, 10 mmol) in anhydrous CH_2Cl_2 (6 mL) were introduced in a Teflon® tube and pressurized at 7Kbar at 25°C during 24h. The product was filtered and washed with 5mL Et_2O. The reaction gave 3.3 g of the vinylogous acid **5b** (98%). The same yield was obtained when the reaction was performed at room temperature, although the reaction was longer. This Diels-Alder reaction was then achieved using high pressure.

5b : **Mp** ; 232-233°C (Decomp.) ; solubility: 40mg in 4ml DMSO ; **MS** m/z 336 (M^+ 2), 266 (17), 241 (100), 225 (25), 197 (28), 165 (14), 153 (11) ; **IR** (KBr) 2928s, 1575s, 1516s, 1251s, 782w, cm^{-1} ; **^{1}H-NMR** (DMSO D_6) 0.48 (bd, J=13 Hz, 1H), 0.77 (bs, 3H), 2.85 (bd, J=6 Hz, 1H), 3.76 (s, 3H), 3.90 (bd, J=6 Hz), 4.87 (bs, 1H), 5.89 (bs, 2H), 6.90 (bd, J=8 Hz, 2H), 7.30 (bd, J=8 Hz, 2H), 11.75 (bs, 1H) ; **HRMS** calcd for $C_{22}H_{24}O_3$; 336.1725, found ; 336.1728.[α] = -188.2 (DMSO, 0.500).

Enol ethers **19a and 20a**: In a two necked round flask equipped with a magnetic spin bar were introduced the Diels-Alder adduct **5a** (306 mg, 1 mmol) and 10 mL of freshly distilled anhydrous Et_2O. The suspension kept under nitrogen was cooled to -78°C and a diazomethane/Et_2O solution (10 mL) was added via a double needle. The reaction mixture was then warmed up to r.t. and stirred until the colour disappeared. The solvent was evaporated to dryness and cristallization from PE/ether gave a 66:34 inseparable mixture of the regioisomeres **19a** and **20a** . The same procedure was used in order to conduct this reaction at -20°C and at 20°C. In those two cases the same ratio and the same yields were obtained: The mixture of **19a** and **20a** were obtained with 95% yield: **19a** and **20a**: **Mp**=135-137°C ; **TLC R_f** (Et_2O)=0.38 ; **MS** m/z 320 (M^+, 33), 273 (21), 223 (22), 210 (100), 167 (25), 91 (31), 69 (47) ; **IR** (KBr) 2857w, 1685s, 1595s, 1578s, 1363s, 781s, 759s cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.65 (bd, J=13 Hz, 1H), 0.85 (bs, 3H), 2.28 (d, J=13 Hz, 1H), 3.13 (d, J=6 Hz, 1H), 3.72 (s, 3H), 3.81 (d, J=6 Hz, 1H), 5.10 (s, 1H), 5.82 (d, J=6 Hz, 1H), 6.02 (d, J=6 Hz, 1H), 4.01 (d, J=9 Hz, 1H), 5.05 (bd, J=5 Hz, 1H), 6.19 (bs, 2H), 7.20-7.45 (m, 5H) ; **HRMS** calcd for $C_{22}H_{24}O_2$; 320.1776, found ; 320.1774.

Enol tosylates **19b and 20b**: A suspension of the Diels-Alder adduct **5a** (306 mg, 1 mmol) in anhydrous CH_2Cl_2 (10 mL) was cooled to -78°C, and a solution of dimethyaminopyridine (150 mg, 1.23 mmol) and anhydrous CH_2Cl_2 (2 mL) was added dropwise under nitrogen atmosphere. The reaction mixture was stirred 10 to 15 min and a

solution of p-toluenesulfonylchloride (285 mg, 1.5 mmol) and CH_2Cl_2 (3mL) was introduced dropwise. This mixture was stirred 2 hours at -78°C and was allowed to warm slowly up to rt. A saturated aqueous solution of $NaHCO_3$ (10 mL) was added and the resulting mixture extracted with CH_2Cl_2 (3x50 mL) . The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ (10 mL), dried ($MgSO_4$) and evaporated. The crude product was filtered through silica gel with Et_2O as eluent to afford 310 mg (67%) of a 70:30 regioisomers mixture. The same results were obtained on deprotonation with methyllithium: **19b** and **20b** : **Mp**=132-133°C ; **TLC** R_f (PE/AcOEt : 9/2)=0.32 ; **MS** m/z 460 (M^+, 2), 304 (15), 236 (13), 210 (100), 167 (20), 91 (31), 69 (33) ; **IR** ($CHCl_3$) 2928w, 1696s, 1600s, 1140s, 1088s, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) 0.65 (bd, J=13 Hz, 1H), 0.78 (bs, 3H), 2.48 (s, 3H), 3:19 (d, J=6 Hz, 1H), 3.73 (d, J=6 Hz, 1H), 5.43 (d, J=6 Hz, 1H), 5.72 (s, 1H), 5.92 (d, J=6 Hz, 1H), 7.15-7.35 (m, 5H), 7.41 (d, J=8 Hz, 2H), 7.85 (d, J=8 Hz, 2H) ; **^{13}C NMR** 14.7, 21.0, 21.7, 22.2, 26.4, 29.9, 52.7, 55.6, 66.8, 67.3, 67.7, 116.7, 127.6, 128.0, 128.5, 130.2, 135.8, 137.1, 137.4, 146.6, 204.2 ; **HRMS** calcd for $C_{28}H_{28}O_4S$; 460.1708, found ; 460.1705.

Enol pivalates **19c and 20c**: To a suspension of the Diels-Alder adduct **5a** (306 mg, 1 mmol) in absoluted CH_2Cl_2 (10 mL), at -78°C, was added dropwise, under nitrogen atmosphere, a solution of dimethylaminopyridine (150 mg, 1.23 mmol) and anhydrous CH_2Cl_2 (2 mL). After 10 to 15 min a solution of pivaloyl chloride (180 mg, 1.5 mmol, 0,184 mL) and CH_2Cl_2 (1 mL) was added dropwise. This resulting mixture was stirred 2 hours at -78°C and was taken to rt. The reaction was quenched with a saturated aqueous solution of $NaHCO_3$ (10 mL), extracted with CH_2Cl_2 (3x50 mL). The organic layer was washed with a saturated $NaHCO_3$ aqueous solution, dried ($MgSO_4$) and evaporated. The crude product underwent a column filtration through silica gel with Et_2O as eluent to afford 370 mg (95%) of a 95:5 regioisomer mixture.

19c : **Mp**=127-128°C ; **TLC** R_f (Et_2O)=0.71 ; **MS** m/z 390 (M^+, 5), 288 (2), 210 (100), 167 (15), 69 (17) ; **IR** ($CHCl_3$) 1768s, 1688s, 1592s, 1152s, 1080s, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.60 (bd, J=13 Hz, 1H), 0.83 (bs, 3H), 1.21 (s, 9H), 2.26 (bd, J=13 Hz, 1H), 2.87 (d, J=6 Hz, 1H), 4.30 (d, J=6 Hz, 1H), 5.90 (d, J=6 Hz, 1H), 6.00 (d, J=6 Hz, 1H), 6.03 (s, 1H), 7.22-7.42 (m, 5H) ; **^{13}C NMR** δ 14.8, 21.3, 23.2, 26.3, 27.1, 29.4, 39.1, 49.5, 54.3, 60.7, 66.6, 67.5, 118.7, 126.7, 127.6, 128.0, 133.4, 137.4, 137.5, 173.8, 179.3, 207.2 ; **HRMS** calcd for $C_{26}H_{30}O_3$; 390.2194, found; 390.2207.

Enol esters **19d and 20d**: This enol ester was prepared by the same method as the former with **5b**. Yield : 95%: **19d** : **Mp**=182-183°C ; **TLC** R_f (Et_2O)=0.69 ; **MS** m/z 420 (M^+, 4), 335 (4), 240 (100), 225 (9), 197 (7), 121 (5), 91 (5) ; **IR** (KBr) 2933s, 1772s, 1698s, 1593s, 1517s, 1255m, 1182s, 1084s, cm^{-1} ; **^{1}H NMR** (CD_2Cl_2) 0.55 (bd, J=13 Hz, 1H), 0.88 (bs, 12H), 2.18 (bd, J=13 Hz, 1H), 2.80 (d, J=6 Hz, 1H), 3.79 (s, 3H), 4.23 (d, J=6 Hz, 1H), 5.88 (d, J=6 Hz, 1H), 5.91 (d, J=1 Hz, 1H), 5.95 (d, J=6 Hz, 1H), 6.89 (d, J=9 Hz, 2H), 7.32 (d, J=9 Hz, 2H) ; **^{13}C NMR** 14.8, 21.7, 23.7, 26.3, 26.7, 29.9, 39.5, 50.0, 54.7, 55.6, 60.8, 66.4, 67.6, 113.7, 118.7, 129.0, 130.0, 159.0, 174.3, 179.5, 206.8 ; **HRMS** calcd for $C_{27}H_{32}O_4$; 420.2300, found ; 420.2296.

Methyl enones **21a**: To a solution of **19d** and **20d** (183 mg, 0.52 mmol) in 5 mL anhydrous THF, MeLi (1.09 mmol, 0.73 mL of a 1.5M solution) was added dropwise, at -78°C, under nitrogen. This mixture was stirred 1h (TLC control) and three drops of trifluoroacetic acid were added. The solution was warmed up to r.t. and stirred an additional hour. A aqueous solution of $NaHCO_3$ was added and the mixture was extracted with CH_2Cl_2 (3x15 mL). The organic layer was washed with aqueous $NaHCO_3$, dried and evaporated. The crude product was purified by chromatography to afford the pure regioisomer **21a**. (Yield 156 mg, 90%): **21a** : **TLC** R_f (Et_2O/PE : 1/1)= 0.24 ; **MS** m/z 334 (M^+, 9), 279 (31), 241 (21), 240 (75), 167 (51), 149 (100), 113 (25) ; **IR** ($CHCl_3$) 2926s, 1726m, 1691s, 1612s, 1515s, 1253s, 1180m, 1069w, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) 0.56 (bd, J=13 Hz, 1H), 0.88 (bs, 3H), 1.67 (s, 3H), 2.87 (bd, J=13 Hz, 1H), 3.02 (d, J=6 Hz, 1H), 3.81 (s, 3H), 4.04 (d, J=6 Hz, 1H), 5.67 (s, 1H), 5.83 (d, J=6 Hz, 1H), 5.91 (d, J=6 Hz, 1H), 6.90 (d, J=9 Hz, 2H), 7.32 (d, J=9 Hz, 2H) ; **HRMS** calcd for $C_{23}H_{26}O_2$; 376.1933, found, 376.1934.[α] = -476.5 (CH_2Cl_2, 0.200).

Butyl enone **21b**: The same procedure was followed for the reaction with butyllithium and **21b** was obtained in 91%yield: **21b** : **TLC** R_f (Et_2O/PE : 1/1)= 0.42 ; **MS** m/z 376 (M^+, 1), 301 (4), 240 (100), 174 (24), 139 (35), 115 (72) ; **IR** ($CHCl_3$) 2928s, 1691s, 1680s, 1604s, 1512s, 1252s, 1036m, 828w, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) 0.50 (bd, J=13 Hz, 1H), 0.77 (t, 3H), 0.90 (d, j=1Hz, 3H), 2.24 (bd, J=13 Hz, 1H), 2.77 (d, J=6 Hz, 1H), 3.82 (s, 3H), 4.08 (d, J=6 Hz, 1H), 5.69 (s, 1H), 5.82 (d, J=6 Hz, 1H), 5.90 (d, J=6 Hz, 1H), 6.89 (d, J=8 Hz, 2H), 7.32 (d, J=8 Hz, 2H) ; **HRMS** calcd for $C_{23}H_{26}O_2$; 376.2402, found, 376.2401.[α] = -68.4 (CH_2Cl_2, 0.500).

Phenyl enone **21c**: The same procedure was followed for the reaction with the phenyllithium, **21c** was obtained in 85%yield: **21c** : **TLC** R_f (Et_2O/PE : 1/1)=0.43 ; **MS** m/z 396 (M^+, 3), 319 (31), 240 (100), 167 (57), 113 (24), 97 (19) ; **IR** ($CHCl_3$) 2928s, 1678s, 1590w, 1569m, 1253m, 1181m, 1039m, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) 0.37 (bd, J=13 Hz, 1H), 1.11 (bs, 3H), 3.02 (bd, J=6 Hz, 1H), 3.77 (s, 3H), 4.59 (d, J=6 Hz, 1H), 5.84 (d, J=6 Hz, 1H), 5.94 (d, J=6 Hz, 1H), 6.14 (s, 1H), 6.84 (d, J=9 Hz, 2H), 7.32 (m, 7H) ; **HRMS** calcd for $C_{28}H_{28}O_2$: 396.2089 ; found, 396.2098.[α] = -5.2 (CH_2Cl_2, 1.25).

Methyl enones **22a and 23a**: This mixture was obtained by a similar procedure as for **21a**. The starting material was the mixture **19a** and **20a** and the hydrolysis was carried out with 1 equivalent pTsOH monohydrate: **22a** was obtained in 63% yield (58 mg): **22a** : **MP**=105-106°C, **TLC** R_f (Et_2O/PE : 1/1)=0.28 ; **MS** m/z 304 (M^+, 3), 211 (100), 196 (23), 181 (17), 167 (28), 116 (19), 91 (21) ; **IR** ($CHCl_3$) 2928s, 1684s, 1612s, 1444m, 1192m, 984m, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.52 (bd, J=13 Hz, 1H), 0.90 (bs, 3H), 1.67 (s, 3H), 2.25 (d, J=13 Hz, 1H), 2.80 (bd, J=5 Hz, 1H), 4.11 (d, J=5 Hz, 1H), 5.68 (t, J=2 Hz, 1H), 5.87 (d, J=6 Hz, 1H), 5.93 (d, J=6 Hz, 1H), 7.25-7.47 (m, 5H) ; **^{13}C NMR** δ 14.7, 19.1, 21.3, 23.3, 26.3, 26.4, 53.1, 56.6, 60.7, 66.5, 67.3, 126.8, 127.4, 128.1, 132.8, 133.7, 137.1, 137.9, 177.8, 209.5 ; **HRMS** calcd for $C_{22}H_{24}O$: 304.1827; found, 304.1828. [α] = -23.3 (CH_2Cl_2, 1.200): **23a** was obtained in 32% yield: **23a** : **TLC** R_f (Et_2O/PE : 1/1)=0.27 ; **^{1}H NMR** ($CDCl_3$) δ 0.67 (bd, J=13 Hz, 1H), 0.85 (bs,

3H), 1.20 (s, 3H), 2.05 (d, J=13 Hz, 1H), 3.17 (bd, J=5 Hz, 1H), 3.70 (d, J=5 Hz, 1H), 5.70 (t, J=2 Hz, 1H), 5.78 (d, J=6 Hz, 1H), 5.98 (d, J=6 Hz, 1H), 7.25-7.47 (m, 5H); [α] = -61.6 (CH_2Cl_2, 1.03).

Butyl enones **22b and 23b**: This mixture was obtained following a similar procedure as before. The starting material was a mixture of **19a** and **20a** and the hydrolysis was carried out with 1 equivalent pTsOH monohydrate: **22b** was obtained in 64% yield: **22b** : **TLC** R_f (PE/EE : 9/1)=0.20 ; **MS** m/z 346 (M^+, 3), 267 (6), 210 (100), 197 (22), 181 (13), 167 (20), 115 (9), 91 (33) ; **IR** ($CHCl_3$) 2927s, 1694s, 1608s, 1445m, 758m, cm^{-1}; **^{1}H NMR** ($CDCl_3$) 0.45 (bd, J=13 Hz, 1H), 0.75 (t, 3H), 0.87 (bs, 3H), 2.79 (bd, J=5 Hz, 1H), 4.11 (d, J=5 Hz, 1H), 5.68 (d, J=2 Hz, 1H), 5.85 (d, J=6 Hz, 1H), 5.91 (d, J=6 Hz, 1H), 7.20-7.40 (m, 5H) ; **^{13}C NMR** 13.8, 14.7, 21.3, 22.1, 23.5, 26.2, 29.1, 29.3, 32.3, 52.4, 56.3, 58.9, 66.7, 67.5, 126.5, 127.3, 127.8, 132.8, 132.8, 134.6, 135.7, 137.8, 182.3, 209.6 ; **HRMS** calcd for $C_{25}H_{30}O$: 346.2296 ; found, 346.2285.[α] = -145 (CH_2Cl_2, 1.350).

23b was obtained with 33% yield: **23b** : **TLC** R_f (PE/EE : 9/1)=0.10 ; **^{1}H NMR** ($CDCl_3$) 0.67 (bd, J=13 Hz, 1H), 0.91 (bs, 3H), 0.95 (t, 3H), 3.21 (bd, J=5 Hz, 1H), 3.69 (d, J=5 Hz, 1H), 5.71 (d, J=2 Hz, 1H), 5.75 (d, J=6 Hz, 1H), 5.98 (d, J=6 Hz, 1H), 7.20-7.40 (m, 5H) ; **^{13}C NMR** 13.6, 14.9, 21.1, 22.4, 23.3, 27.2, 28.9, 29.9, 32.8, 53.1, 54.7, 60.8, 66.7, 67.2, 126.7, 127.8, 128.0, 132.0, 132.8, 136.8, 137.9, 181.0, 208.5; **HRMS** calcd for $C_{25}H_{30}O$: 346.2296 ; found, 346.2289.[α] = -14 (CH_2Cl_2, 0.250).

Phenyl enones **22c and 23c**: The reaction was carried out under the same conditions as before to afford pure **22c** in 57% yield: **22c** : **MP**=65-68°C : **TLC** R_f (Et_2O/PE : 2/3)=0.40 ; **MS** m/z 366 (M^+, 1), 210 (100), 195 (20), 167 (24), 165 (13), 128 (13), 91 (16), 69 (13) ; **IR** ($CHCl_3$) 2928s, 1680s, 1600s, 1444s, 1272m, 1192m, 908m, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.43 (bd, J=13 Hz, 1H), 1.12 (bs, 3H), 2.28 (d, J=13 Hz, 1H), 3.02 (bd, J=5 Hz, 1H), 4.64 (d, J=5 Hz, 1H), 5.86 (d, J=6 Hz, 1H), 5.93 (d, J=6 Hz, 1H), 6.14 (d, J=1 Hz, 1H), 7.00-7.40 (m, 10H) **^{13}C NMR** δ 15.4, 21.2, 23.2, 25.9, 29.3, 52.7, 57.4, 61.3, 66.0, 126.4, 127.3, 127.5, 127.6, 127.8, 129.9, 132.2, 132.5, 134.3, 136.3, 137.5, 176.7, 208.8 ; **HRMS** calcd. for $C_{27}H_{26}O$ 366.1983 ; found, 366.1992.[α] = -115.2 (CH_2Cl_2, 0.600).

23c was obtained as pure regioisomer in 29%: **23c** : **TLC** R_f (Et_2O/PE : 1/1)=0.46 : **^{1}H NMR** ($CDCl_3$) δ 0.68 (bd, J=13 Hz, 1H), 0.95 (bs, 3H), 3.90 (bd, J=5 Hz, 1H), 3.97 (d, J=5 Hz, 1H), 5.63 (d, J=6 Hz, 1H), 6.03 (d, J=6 Hz, 1H), 6.22 (d, J=1 Hz, 1H), 7.00-7.60 (m, 10H) **^{13}C NMR** δ 15.1, 21.2, 23.6, 27.5, 30.1, 52.0, 54.2, 59.5, 67.2, 67.8, 126.7, 127.1, 127.8, 127.9, 128.5, 130.6, 131.6, 134.7, 135.0, 136.1, 137.7, 173.9, 208.1 ; **HRMS** calcd. for $C_{27}H_{26}O$ 366.1983 ; found, 366.1989.[α] = -61.2 (CH_2Cl_2, 0.500).

Triisopropylsilyacetylenyl enones **22d and 23d**: To a solution of triisopropylsilylacetylene (282 mg, 1.55 mmol) in THF (5 ml), at -78°C, was added dropwise n-butyllithium (1.5 mmol, 1 ml of 1.5M solution in hexanes) under nitrogen. After 10-15 min at this temperature the solution was introduced, via a double needle, into a mixture composed of **19a** and **20a** (100 mg, 0.31 mmol) and 3 mL THF. After 3 hours

at -78°C, pTsOH monohydrate (190 mg, 1 mmol) was added and the resulting mixture stirred one additional hour at r.t.. The products were extracted with Et_2O (3x20 mL) and the resulting organic layer was washed with aqueous $NaHCO_3$, dried ($MgSO_4$) and evaporated. The crude mixture was purified by chromatography on silica gel with PE as eluent to give the pure regioisomer **25a** (61 mg, 42%).

22d : **TLC** R_f (Et_2O/PE : 1/1)=0.71 ; **MS** m/z 470 (M^+, 4), 210 (100), 195 (11), 167 (14), 157 (10), 125 (11), 97 (10); **IR** ($CHCl_3$) 2940s, 1684s, 1572s, 1252s, 848s, cm^{-1}; ^{1}**H NMR** ($CDCl_3$) 0.51 (bd, J=13 Hz, 1H), 0.85 (s, 18H), 1.11 (bs, 3H), 2.24 (d, J=13 Hz, 1H), 2.82 (bd, J=5 Hz, 1H), 4.30 (dd, J_1=5 Hz, J_2=1 Hz, 1H), 5.90 (d, J=6 Hz, 1H), 5.98 (d, J=6 Hz, 1H), 6.07 (d, J=1 Hz, 1H), 7.20-7.45 (m, 5H) ; **HRMS** calcd. for $C_{32}H_{42}OSi$, 470.3004 ; found, 470.3008.[α] = -117.2 (CH_2Cl_2, 0.500).

23d was obtained in 19% yield: **23d** : **TLC** R_f (Et_2O/PE : 1/1)=0.63 : ^{1}**H NMR** ($CDCl_3$) δ 0.75 (bd, J=13 Hz, 1H), 0.85 (m, 21H), 2.39 (d, J=13 Hz, 1H), 2.35 (dd, J_1=5 Hz, J_2=1 Hz, 1H), 3.70 (bd, J=5 Hz, 1H), 5.87 (d, J=6 Hz, 1H), 5.96 (d, J=6 Hz, 1H), 6.05 (d, J=1 Hz, 1H), 7.20-7.45 (m, 5H) ; **HRMS** calcd. for $C_{32}H_{42}OSi$, 470.3004 ; found, 470.3010.[α] = -78.4 (CH_2Cl_2, 0.500).

t-Butyl enones **22e and 23e**: The same procedure as above was followed in order to obtain **22e** pure in 60% yield: **22e** : **MP**=66-67°C : **TLC** R_f (Et_2O/PE : 1/1)=0.47 ; **MS** m/z 346 (M^+, 3), 210 (100), 195 (12), 167 (13), 165 (6), 128 (3), 91 (7), 67 (4) ; **IR** ($CHCl_3$) 2942m, 1693s, 1590w, 756m, cm^{-1} ; ^{1}**H NMR** ($CDCl_3$) δ 0.31 (bd, J=13 Hz, 1H), 0.88 (s, 9H), 0.99 (bs, 3H), 2.28 (d, J=13 Hz, 1H), 2.87 (bd, J=5 Hz, 1H), 4.21 (d, J=5 Hz, 1H), 5.20 (d, J=1 Hz, 1H), 5.88 (d, J=6 Hz, 1H), 5.97 (d, J=6 Hz, 1H), 7.20-7.60 (m, 5H) ; ^{13}**C NMR** δ 15.0, 21.2, 23.1, 25.9, 29.2, 29.3, 35.1, 51.2, 57.4, 59.7, 66.9, 67.9, 126.6, 127.5, 128.0, 132.0, 132.7, 136.1, 138.2, 189.7, 209.8; **HRMS** calcd. for $C_{25}H_{30}O$, 346.2296 ; found, 346.2281.[α] = -77.2 (CH_2Cl_2, 0.370).

22e was obtained in 31% yield: **22e** : **TLC** R_f (Et_2O/PE : 1/1)=0.46 ; ^{1}**H NMR** ($CDCl_3$) δ 0.65 (bd, J=13 Hz, 1H), 0.90 (s, 3H), 1.20 (s, 9H), 2.25 (d, J=13 Hz, 1H), 3.41 (bd, J=5 Hz, 1H), 3.71 (d, J=5 Hz, 1H), 5.75 (d, J=6 Hz, 1H), 5.89 (d, J=1 Hz, 1H), 5.01 (d, J=6 Hz, 1H), 7.20-7.40 (m, 5H) ; ^{13}**C NMR** δ 14.1, 21.3, 22.7, 25.9, 29.2, 29.7, 35.1, 51.2, 57.4, 59.7, 66.9, 67.9, 126.7, 127.5, 128.4, 132.0, 132.7, 136.1, 138.2, 188.6, 208.1; **HRMS** calcd. for $C_{25}H_{30}O$, 346.2296 ; found, 346.2291.[α] = -187.9 (CH_2Cl_2, 0.580).

Cuprate addition. General procedure: To a suspension of copper(I) cyanide (110mg, 1.23mmol) in diethyl ether (10ml) at -30°C was dropped a solution of nucleophile (2:45mmol) in THF. The solution obtained was stirred 15min at -30°C and cooled to -78°C. To this solution was slowly added the enone (0.24mmol) dissolved in 3ml diethyl ether. After 5min at -78°C BF_3Et_2O (0.2mmol, 25µl) was added dropwise. The resulting solution was stirred for 90min at -78°C and quenched at this temperature by addition of a saturated aqueous NH_4Cl solution. The aqueous phase was extracted with diethyl ether (4x20ml), the combined organic phase was washed with brine and dried with $MgSO_4$.

Ketone **24a** (R=H): According to the general procedure described before, enone **22a** (0.24mmol, 75mg) reacted with n-butylcuprate to provide 80mg (90%) of the desired

product after flash chromatography (100%PE): **24a** : **TLC** R_f (Et_2O/PE : 1/1)=0.59 ; **MS** m/z 362 (M^+, 1), 236 (51), 221 (43), 210 (100), 167 (24) ; **IR** ($CHCl_3$) 2926s, 1720s, 1460w, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.41 (bd, J=13 Hz, 1H), 0.72 (s, 3H), 0.81 (d, J=1Hz, 3H), 0.91 (t, 3H), 1.95 (d, J=18 Hz, 1H), 2.15 (d, J=18Hz, 1H), 2.84 (d, J=8 Hz, 1H), 3.52 (d, J=8 Hz, 1H), 5.95 (d, J=6 Hz, 1H), 6.38 (d, J=6 Hz, 1H), 7.22-7.40 (m, 5H) **^{13}C NMR** δ 14.1, 15.0, 21.1, 23.3, 23.5, 24.2, 26.3, 26.4, 27.7, 29.7, 39.5, 47.5, 53.4, 54.5, 61.2, 62.4, 66.9, 67.9, 126.3, 127.4, 127.9, 136.3, 138.8, 139.4, 221.4; **HRMS** calcd. for $C_{26}H_{34}O$, 362.2609 ; found, 362.2609.[α] = -133.6 (CH_2Cl_2, 0.500).

Ketone **25a** (R=H): According to the general procedure described before, enone **23a** (0.24mmol, 75mg) reacted with nButylcuprate to provide 80mg (90%) of the desired product after flash chromatography (100%PE): **25a** : **TLC** R_f (Et_2O/PE : 1/1)=0.59 ; **MS** m/z 362 (M^+, 1), 251 (6), 223 (48), 210 (100), 167 (27), 111 (47) ; **IR** ($CHCl_3$) 2927s, 1730s, 1466s, 1379s, 758m, 698m, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.58 (bd, J=13 Hz, 1H), 0.79 (d, J=1Hz, 3H), 0.90 (t, 3H), 1.11 (s, 3H), 1.97 (d, J=18 Hz, 1H), 2.13 (d, J=18Hz, 1H), 2.52 (d, J=8 Hz, 1H), 3.79 (d, J=8 Hz, 1H), 6.01 (d, J=6 Hz, 1H), 6.29 (d, J=6 Hz, 1H), 7.22-7.42 (m, 5H) ; **HRMS** calcd. for $C_{26}H_{34}O$, 362.2609 ; found, 362.2609.[α] = -3.3 (CH_2Cl_2, 0.850).

Ketone **24b** (R=H): According to the general procedure described above, enone **22a** (0.24mmol, 75mg) reacted with phenylcuprate to provide 80mg (85%) of the desired product after flash chromatography (100%PE): **24b** : **TLC** R_f (PE)=0.38 ; **MS** m/z 382 (M^+, 1), 236 (69), 221 (47), 210 (100), 167 (23), 118 (21) ; **IR** ($CHCl_3$) 2928s, 1724s, 1446m, 763s, 699s, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.39 (bd, J=13 Hz, 1H), 0.69 (d, J=1Hz, 3H), 1.20 (s, 3H), 2.18 (bd, J=13 Hz, 1H), 2.45 (d, J=19Hz, 1H), 2.60 (d, J=19Hz, 1H), 2.88 (d, J=8 Hz, 1H), 3.81 (d, J=8 Hz, 1H), 6.07 (d, J=6 Hz, 1H), 6.50 (d, J=6 Hz, 1H), 7.18-7.45 (m, 10H) ; **HRMS** calcd. for $C_{28}H_{30}O$, 382.2296 ; found, 382.2296.[α] = -140.9 (CH_2Cl_2, 0.610).

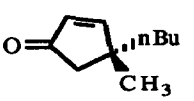
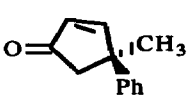
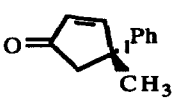
Ketone **25b** (R=H): The regioisomer of **24b** was obtained in 87% yield (82mg) from **23a**: **25b** : **TLC** R_f (PE)=0.27; **MS** m/z 382 (M^+, 1), 236 (31), 221 (24), 210 (100), 167 (32); **IR** ($CHCl_3$) 2927s, 1727s, 1445m, 760s, 701s, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.59 (bd, J=13 Hz, 1H), 0.69 (d, J=1Hz, 3H), 1.58 (s, 3H), 2.38 (bd, J=13 Hz, 1H), 2.45 (d, J=19Hz, 1H), 2.67 (d, J=19Hz, 1H), 2.89 (d, J=8 Hz, 1H), 3.73 (d, J=8 Hz, 1H), 6.12 (d, J=6 Hz, 1H), 6.41 (d, J=6 Hz, 1H), 7.18-7.40 (m, 10H) ; **HRMS** calcd. for $C_{28}H_{30}O$, 382.2296 ; found, 382.2295.[α] = -37.5 (CH_2Cl_2, 1).

Ketone **24a** (R=OMe): The ketone **24a** was obtained from the enone **21a** after n-butylcuprate addition. The yield was 84%: **24a** : **TLC** R_f (PE/Et_2O: 1/1)=0.60 ; **MS** m/z 392 (M^+, 0.5), 266 (22), 251 (18), 240 (100), 197 (10), 149 (17) ; **IR** ($CHCl_3$) 2956s, 2928s, 1720s, 1512s, 1248s, 1180s, 1036m, 832m, 576w, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.41 (bd, J=13 Hz, 1H), 0.73 (s, 3H), 0.78 (s, 3H), 0.91 (t, 3H), 1.95 (d, J=18Hz, 1H), 2.13 (d, J=18Hz, 1H), 2.81 (d, J=7.5 Hz, 1H), 3.48 (d, J=7.5 Hz, 1H), 3.81 (s, 3H), 5.92 (d, J=6 Hz, 1H), 6.33 (d, J=6 Hz, 1H), 6.89 (d, J=9Hz, 2H), 7.26 (d, J=9Hz, 2H) ; **^{13}C NMR** ($CDCl_3$) δ 14.0, 14.9, 21.1, 23.3, 23.5, 24.1, 26.3, 26.3,

27.7, 47.1, 53.5, 54.5, 55.1, 61.2, 62.2, 65.7, 67.2, 113.3, 123.3, 131.5, 136.4, 138.6, 158.1, 221.3 : **HRMS** calcd. for $C_{27}H_{36}O_2$, 392.2715 ; found, 392.2714.[α] = -20 (CH_2Cl_2, 0.950).

Epimer of ketone **24a** (R=OMe): This product was obtained from the enone **21b** after methylcuprate addition. The yield was 91%: **Epimer of 24a** : **TLC** R_f (PE/Et_2O: 1/1)=0.60 ; **MS** m/z 392 (M^+, 1), 266 (19), 251 (15), 240 (100), 197 (12), 167 (26), 149 (15) ; **IR** ($CHCl_3$) 2928s, 1720s, 1512s, 1288m, 1248s, 1180m, 1036m, 828w, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.39 (bd, J=13 Hz, 1H), 0.68 (t, 3H), 0.79 (d, J=1Hz, 3H), 1.04 (s, 3H), 1.81 (d, J=18Hz, 1H), 2.11 (d, J=13Hz, 1H), 2.19 (d, J=18Hz, 1H), 2.86 (d, J=8 Hz, 1H), 3.41 (d, J=8 Hz, 1H), 3.81 (s, 3H), 5.90 (d, J=6 Hz, 1H), 6.32 (d, J=6 Hz, 1H), 6.88 (d, J=8Hz, 2H), 7.25 (d, J=8Hz, 2H) ; **HRMS** calcd. for $C_{27}H_{36}O_2$, 392.2715; found, 392.2715.[α] = -78.2 (CH_2Cl_2, 2.540).

General procedure for the pyrolysis: A 3cm quartz tube containing the starting material was placed in a pyrolysis apparatus. The later was submitted to a 1.10^{-2}atm vacuum and the quartz tube was heated to 150-180°C while in the same time the pyrolysis tube (10cm long) was heated to 400°C. Both temperatures were maintained until the starting material had disappeared. The product and the diene were trapped at-190°C (liquid nitrogen).

	Starting material	Product	Yield	$[\alpha]_D^{24}$ in toluene
R=H	**24a**		93%	-30.6
R=OMe	**24a**		95%	-30.6
R=H	**25a**		94%	+30.6
R=OMe	**epimer of 24a**		90%	+30.6
R=H	**24b**		96%	-72.5
	25b		97%	+72.5

26a (4S)-4-butyl-4-methyl-2- cyclopenten-1-one

27a (4R)-4-butyl-4-methyl-2- cyclopenten-1-one

TLC R_f (PE/Et_2O)=0.62 ;**bp**: 145°C/20mmHg; **MS** m/z 152 (M^+, 17), 137 (9), 124 (7), 110 (30), 96 (74), 95 (100), 82 (32) ; **IR** (Cap film) 2959s, 2930s, 1718s, 1459w, 803w, cm^{-1} ; **^{1}H NMR** ($CDCl_3$) δ 0.83 (t, 3H), 1.17 (s, 3H), 1.18-1.50 (m, 6H), 2.06 (d, J=18 Hz, 1H), 2.25 (d, J=18 Hz, 1H), 5.98 (d, J=6 Hz, 1H), 7.39 (d, J=6 Hz, 1H) ; **^{13}C NMR** ($CDCl_3$) δ 13.9, 23.1, 26.2, 27.1, 40.2, 44.9, 47.8, 131.6, 173.7, 210.1 : **HRMS** calcd. for $C_{10}H_{16}O$, 152.1201 ; found, 152.1201

26b (4S)-4-methyl-4-phenyl-2- cyclopenten-1-one

27b (4R)-4-methyl-4-phenyl-2- cyclopenten-1-one
TLC R_f (PE)=0.25 ;**bp**: 79°C/0.05 mmHg; **MS** m/z 172 (M^+, 76), 157 (100), 129 (68), 128 (56), 77 (27) ; **IR** ($CHCl_3$) 2968m, 2928m, 1712s, 1588m, 1496m, 1076m, 908s, cm^{-1} ; ^1H **NMR** ($CDCl_3$) δ 1.63 (s, 3H), 2.55 (d, J=18 Hz, 1H), 2.68 (d, J=18 Hz, 1H), 6.21 (d, J=6 Hz, 1H), 7.20-7.40 (m, 5H), 7.70 (d, J=6 Hz, 1H) ; **HRMS** calcd. for $C_{12}H_{12}O$, 172.0888 ; found, 172.0888

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REFERENCES

1. Winterfeldt E, *Chem. Rev.*, **1993**, *93*, 827, and references cited therein.
2. Matcheva K., Beckmann M., Schomburg D., Winterfeldt E., *Synthesis*, **1989**, 814.
3. Rasmusson G. H., House O. H., Zaweski F. E., DePuy C. H., *Org. Synthesis.*, collective volume 5, **1973**, 324.
4. Mauvais A., Winterfeldt E., *Tetrahedron*, **1993**, *49*, 5817.
5. Meyers. A. I. and Westrum. L. J, *Tetrahedron Lett.*, **1993**, *48*, 7701.
6. Dols P. P. M. A., Verstappen. M. M. H., Klunder A. J. H., Zwanenburg B., *Tetrahedron* , **1993**, *48*, 11353., Dols P. P. M. A., Klunder A. J. H., Zwanenburg B., *Tetrahedron* , **1993**, *48*, 11373.
7. Brünjes R., Tilstam U., Winterfeldt E., *Chem Ber.*, **1991**, *124*, 1677.
8. Ma Z., Bobbitt J. M., *J. Org. Chem.*, **1991**, *56*, 6110.

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