Regioselective and Stereoselective Transformations of Enantiopure *p*-Benzoquinone Equivalents

Ina Gerstenberger[a], Martin Hansen[a], Antony Mauvais[b], Rudolf Wartchow[c] and Ekkehard Winterfeldt*[a]

Institut für Organische Chemie der Universität Hannover[a],
Schneiderberg 1 B, D-30167 Hannover, Germany
Fax: (internat.) + 49(0)511/762-3011
E-mail: winterfeldt@mbox.oci.uni-hannover.de

Fondation Nationale Alfred Kastler de l'Académie des Sciences[b],
2, rue Brulée, F-67000 Strasbourg, France
Fax: (internat.) + 33(0)3/88222477

Institut für Anorganische Chemie der Universität Hannover[c],
Callinstraße 9, D-30167 Hannover, Germany
Fax: (internat.) + 49(0)511/762-3006

Received October 9, 1997

Keywords: Cycloaddition / High pressure chemistry / Quinones / Cyclohexanones / Retro Diels-Alder process

The selectivities of typical transformations of the *p*-benzoquinone Diels-Alder adduct **2** and its dihydro derivative **3** are shown to be highly dependent on the mechanistic path followed. To avoid ambiguities and to make sure of clearly defined regioselectivity, the monoketal **13** was examined and proven not only to be an excellent dienophile but, of course, also to lead to reliable regioselectivity in subsequent transformations. This led to the correction of an earlier provisional assignment of the alkylation products **11** and **12**.

Since Diels-Alder adduct **2** is formed smoothly and quantitatively from *p*-benzoquinone and the enantiopure cyclopentadiene **1**[1], we became interested in studying the regioselectivity of its transformations. Having observed a quite remarkable regioselectivity with anhydride[2] and imide[3] adducts, we expected **2** to show a similar behaviour and envisaged it as being an excellent source of enantiopure cyclohexenones (see below).

This was borne out by experiment. L-Selectride reduction of the dihydro compound **3**, as well as of the epoxide **4**, proved to be completely regioselective with the carbonyl group distant from the phenyl substituent again being attacked preferentially (Scheme 1).

Subsequent pyrolysis furnished the enantiopure hydroxycyclohexenones **7**[1] and **8**[4] cleanly and with *ee*'s $> 98\%$.

If the regioselectivities of oxidations were to parallel those of reductions, the enantiomer of **8** should be obtainable from diol **9**, which can be obtained in a highly diastereoselective manner by DIBAH reduction of adduct **2**. With this diol at hand, we were in a position to study the regioselectivities of the oxidation processes. The best results were obtained with the Bobbit reagent[5]. As is clear from the formula **10**, this space-demanding reagent indeed attacked at the same position as found previously in the L-Selectride reduction (Scheme 2). On subsequent pyrolysis, the enantiomer of **8** was formed as predicted[5].

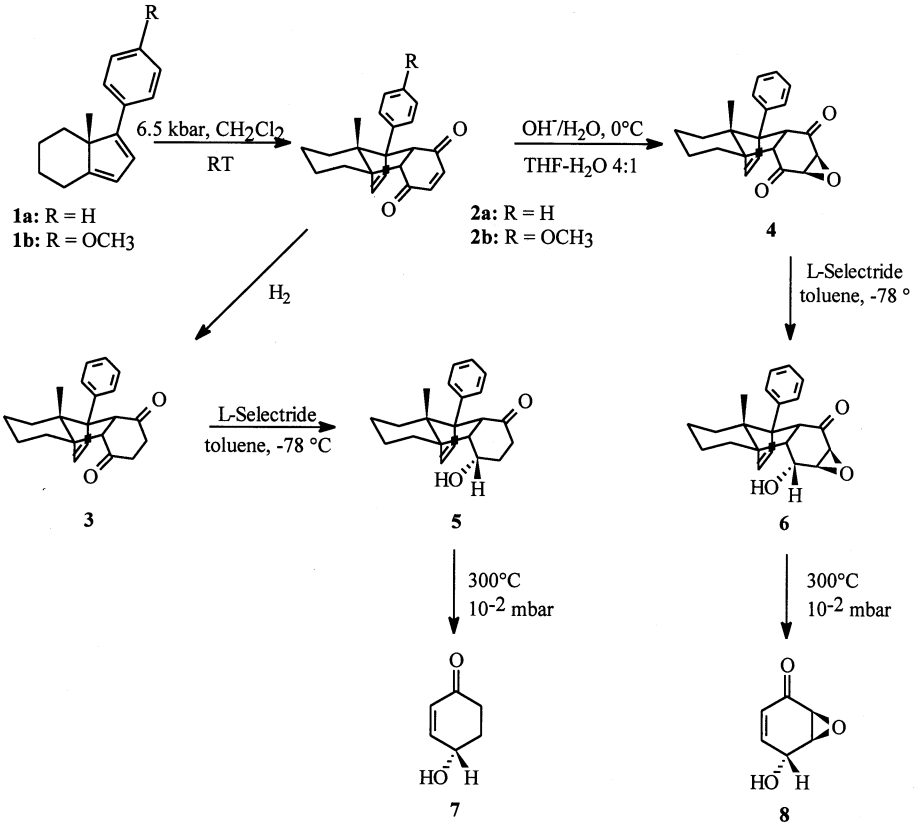
Compared to these two operations, only modest regioselectivity was observed in the enolate alkylation of the dihydro derivative **3**[5] (Table 1).

As shown in Table 1, a mixture of the monoalkylated compounds **11** and **12** was obtained in this case and, bearing in mind the aforementioned results on reduction and oxidation, we provisionally assigned structure **12** to the main reaction product. Since the differences in the NMR data were, however, quite small, we decided to resolve any ambiguities by obtaining definitive experimental data. The quinone mono ketal **13** emerged as the most obvious candidate for enabling regioselective transformations of the corresponding cycloadduct **14**, and hence we studied the Diels-Alder chemistry of this dienophile. As expected, the cycloaddition of diene **1b** and quinone monoketal **13** provided one single regioisomer (**14**) in quantitative yield. The structure of **14** was proven by an X-ray investigation (see Figure 1)[8]. Since adduct **14** was obtained quantitatively after 3 days at 6.5 kbar, the reaction rate is somewhat lower than that observed with *p*-benzoquinone itself (1 d, 6.5 kbar) (Scheme 3). However, adduct formation is considerably faster than with spiro ether **15** (2 weeks, 6.5 kbar), which illustrates the remarkable effect of a second electronegative atom adjacent to the dienophile double bond. In contrast, the carbocyclic spiro compound **17** did not give rise to any cycloadducts at all, once again demonstrating the higher spatial demand of a CH_2 group, which is fully in line with our earlier reports on kinetic resolution, as well as on the differentiation of enantiotopic groups.

Although cycloadduct **14** already looked quite promising as far as chemo-, regio-, and diastereoselectivity were concerned, the first set of hydride reductions additionally re-

  1434–193X/98/0404–0643 $ 17.50+.50/0

Scheme 1



Scheme 2

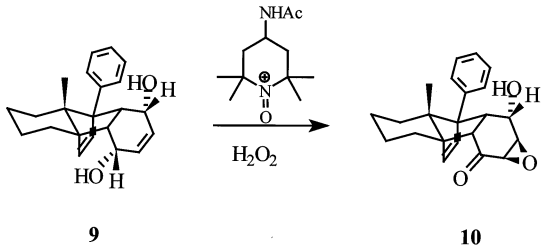
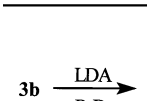


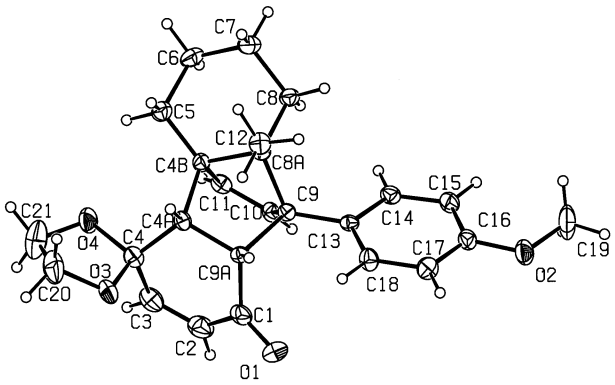
Table 1. Regioselectivity of alkylation



	11	12	
R = CH_2–Ph	86%	20%	**a**
R = CH_2–C≡CH	71%	29%	**b**
R = CH_2–CH=CH_2	88%	12%	**c**
R = CH_3	80%	20%	**d**

vealed a quite remarkable directing effect of the ketal moiety. Whereas the *p*-benzoquinone adduct **2** was smoothly

Figure 1. Structure of compound **14**

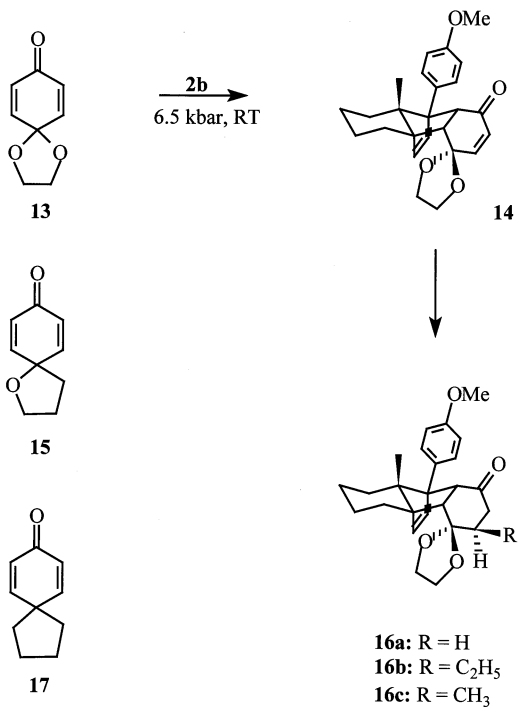


reduced to the corresponding unsaturated diol **9**, under the same conditions ketal **14** underwent reduction of the double bond to yield mixtures of the saturated ketone **18** and the corresponding α-carbinol **20a**. Exclusive formation of **20a** could only be achieved using an excess of the reducing agent.

Similar treatment with a simple Grignard reagent, such as that derived from bromoethane, afforded exclusively the conjugate addition product **16b**, which corresponds to alkylation products of type **11** (see below).

As expected, cuprate additions in the presence of trimethylsilyl chloride also gave rise to 1,4-adducts (e.g. **16c**) and although exclusive conjugate addition is quite normal in

Scheme 3



this case, the outcome of the hydride reduction and the Grignard attack may well be due to a chelating effect of the ketal group. In any event, **16c** should, in principle, have served quite well for the structural assignment of the alkylation products **11** and **12**. It turned out, however, that ketal hydrolysis to give the corresponding diketones was accompanied by epimerization at the α-carbonyl carbon atom, leading to an inseparable mixture of epimers.

To simplify matters and to ensure the exclusive formation of a single β-alkylation product, we investigated the alkylation of dihydro compound **18**, which is readily obtained from adduct **14** under the Luche conditions employing zinc and nickel dichloride under sonification (Scheme 4).

The usual deprotonation (LDA)/alkylation sequence afforded in each case one single alkylation product (**19a**−**19d**), indicating excellent regioselectivity and exclusive β-attack of the alkyl bromide. To avoid epimerization during ketal hydrolysis, as well as to generate the corresponding enantiopure hydroxy ketones as potential chiral building blocks, the hydride reduction of ketone **19b** was investigated. Since hydride attack can only occur from the convex β-side, the β-alkyl residue, stereoselectively introduced in the alkylation process, hinders this transformation. Sodium tetrahydridoborate, L-Selectride or DIBAH either leave the molecule unchanged or induce decomposition under more forcing conditions. Finally, using an excess of lithium aluminium hydride at −49°C, a 99% yield of the pure α-hydroxy ketal **20** was obtained. The ketal could then be hydrolyzed without any epimerization. The hydroxy ketone **21** prepared in this way could easily be reoxidized to diketone **11c**, which proved to be identical in every respect to the major product of the alkylation reaction summarized in Table 1.

This proves very clearly that our earlier assignment has to be reversed and that, in contrast to L-Selectride reduction (nucleophilic attack), enolate formation with diketone **3** takes place preferentially at the carbonyl group adjacent to the phenyl residue. We have no straightforward explanation for this outcome and one may again speculate that complexation of the electron-rich aromatic π-system at an early stage of the interaction directs the proton-accepting species towards this particular carbonyl group. On the other hand, pyrolysis of **21** furnished an almost quantitative yield (97%) of the enantiomerically pure (*ee* > 98%) hydroxy ketone **22a**. Transformation of this material into the corresponding silyl ether **22b** led to the enantiomer of a chiral intermediate involved in the synthesis of "manzamine A", which was prepared from shikimic acid by Overman's group[6]. The constitutional identity of the two compounds was proved with the aid of a sample kindly provided by Professor Overman. Since the antipode of diene **1** is, of course, also at hand in our laboratory, the enantiomer of **22b** can be prepared as well.

In the light of the above results, it is clear that regioselective introduction of alkyl residues into adduct **14** can be achieved in a predictable manner, either by employing the aforementioned alkylation protocol or by means of a cuprate addition in the presence of a trialkylchlorosilane.

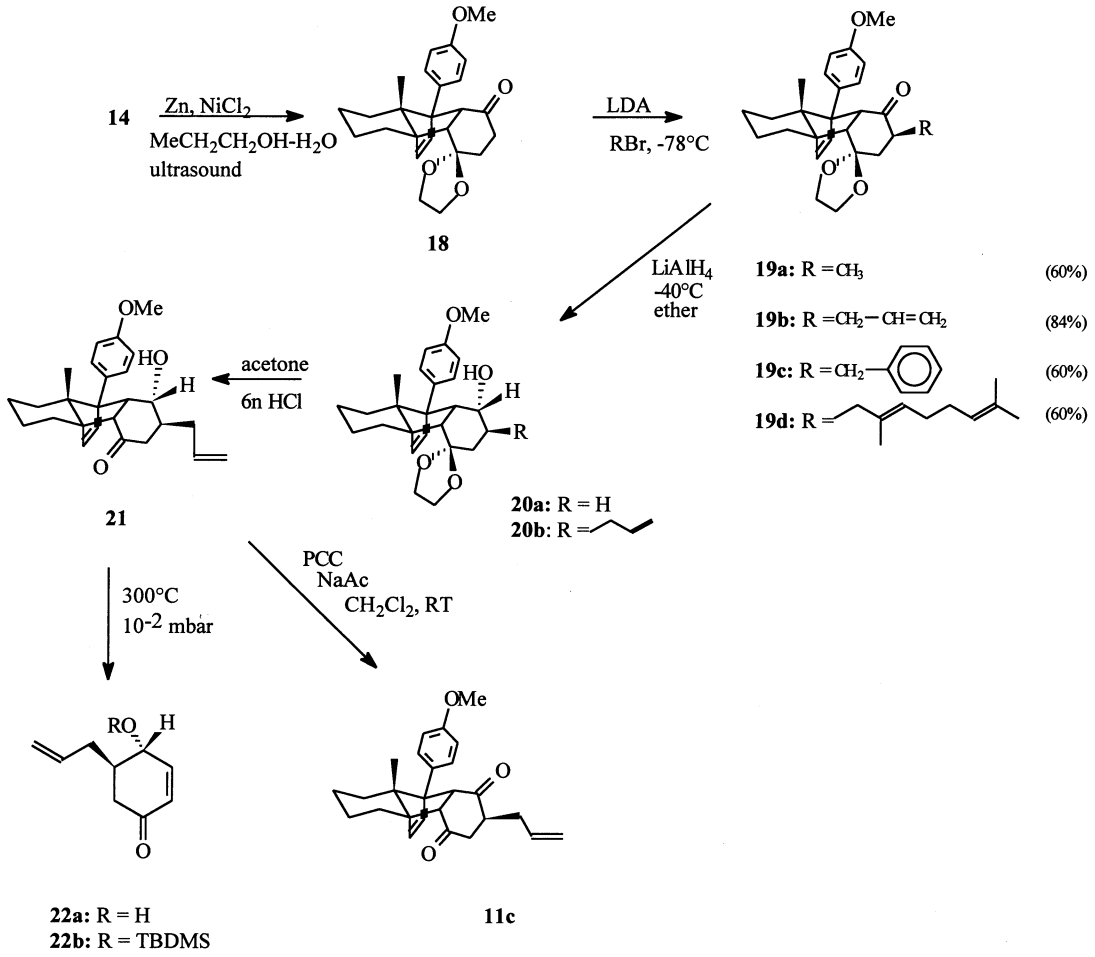
Finally, two standard double-bond transformations, epoxidation and cyclopropanation, were addressed, since these could also lead to useful enantiopure building blocks. Epoxidation under nucleophilic conditions leading to **23a** proceeded in high yield. Subsequent thermolysis of this compound provided the enantiomerically pure epoxide **25**, which is well-equipped for various highly selective transformations (Scheme 5).

Although L-Selectride reduction of **23a** furnished the α-hydroxy compound **23b** in high yield (96%) and with excellent diastereoselectivity, all our efforts to prepare the corresponding α-hydroxy- or α-acetoxycyclohexenone ketals from **23a** or **23c** by means of thermal retro reactions met with failure.

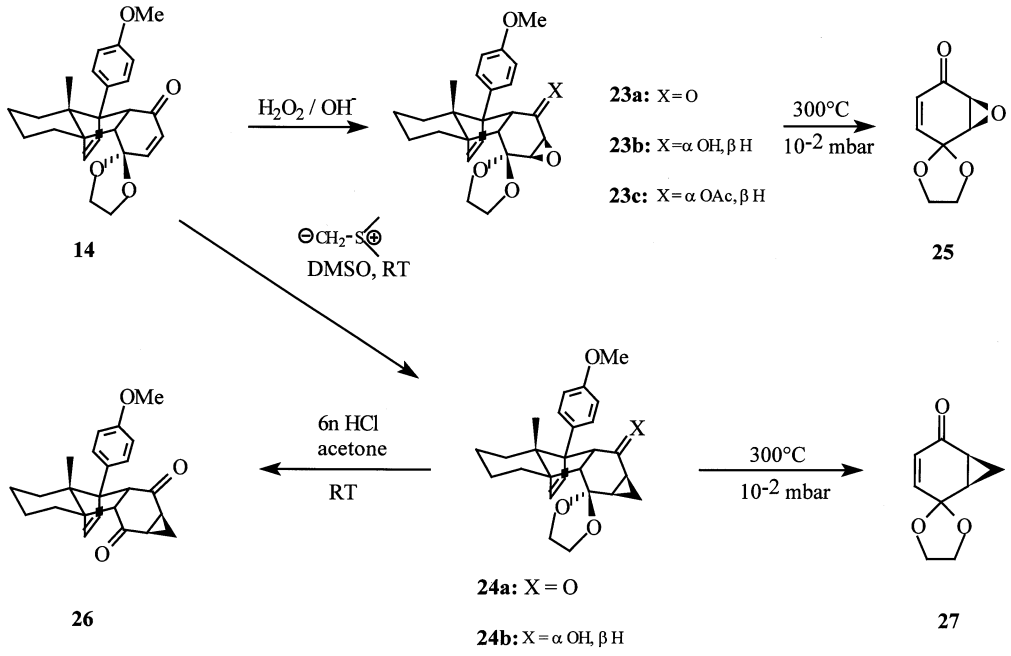
In contrast to the simple *p*-benzoquinone adduct **2**, which had resisted all our efforts to introduce a cyclopropane ring under various conditions, cyclopropanation of ketal **14** proved to be a very efficient process. Under Corey-Chaykovsky conditions[7], the product of exclusive β-attack (**24**) was obtained in 90% yield and proved to be a stable and easy to handle compound. The retro process occurred readily at 300°C and generated 90% of the enantiopure bicycloheptane **27**. Since attempted cyclopropanation of the *p*-benzoquinone adduct **2** had failed, we were particularly pleased to find that ketal hydrolysis of **24a** proceeded very efficiently (90%) to provide this particular diketone **26**, which could not be generated directly.

A remarkable resistance of the keto group in **24a** towards hydride reduction needs to be mentioned in relation to further chemical transformations of this cyclopropane derivative. As in the case of the β-alkylation products **19a**−**19d**, reagents such as tetrahydridoborate, L-Selectride and DIBAH left the keto group untouched and again it

Scheme 4



Scheme 5



needed treatment with lithium aluminium hydride to obtain an 85% yield of the α-hydroxy compound **24b**. Clearly, since α-attack is, owing to the concave-convex conformation, impossible, any β-substituent adjacent to the carbonyl group hinders nucleophilic attack.

In summary, it is concluded that the system of *p*-benzoquinone monoketal in combination with the chiral diene **1** not only leads to the formation of cycloadducts with excellent regioselectivities, but that these cycloadducts additionally undergo highly selective chemical transformations. In the particular case of cyclopropanation, this reagent is certainly superior to the corresponding quinone adduct.

Thanks are due to the *Volkswagen Foundation* for support of this work, the *DFG (Deutsche Forschungsgemeinschaft)* for providing the high-pressure apparatus, and the *Alexander von Humboldt Foundation* for a postdoctoral fellowship for A. M.

Experimental Section

Melting points: Gallenkamp MPD 350, uncorrected values. − IR: Perkin-Elmer 581. − ^{1}H and ^{13}C NMR: Bruker AM 400; internal standard tetramethylsilane. − MS: Finnigan MAT 312; 70 eV. − Elemental analyses: Heraeus CHN rapid analyser. − Optical rotations: Perkin-Elmer 241 polarimeter, 10-cm cell, 589 nm (Na-D line), in solution.

2b: 2.0 g (8.52 mmol) of diene **1** and 900 mg (8.52 mmol) of *p*-benzoquinone were dissolved in 3 ml of dichloromethane. The resulting solution was sealed in a Teflon tube, which was pressurized at 6.5 bar for 48 h. After evaporation of the solvent and purification of the residue by flash chromatography (diethyl ether/petroleum ether, 2:1), 2.67 g (92%) of yellow crystals was obtained. − M.p. 127°C. − $[\alpha]_D = -355.2$ ($c = 0.88$, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu} = 2936$ cm^{-1}, 1752, 1668, 1516, 1288, 1252, 1108. − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.55 (br. d, $J = 12$ Hz, 1 H), 0.82 (s, 3 H), 2.24 (br. d, $J = 12$ Hz, 1 H), 3.14 (d, $J = 8$ Hz, 1 H), 4.01 (d, $J = 8$ Hz, 1 H), 5.96 (d, $J = 6$ Hz, 1 H), 6.10 (d, $J = 6$ Hz, 1 H), 6.48 (d, $J = 10$ Hz, 1 H), 6.56 (d, $J = 10$ Hz, 1 H), 6.87−6.96 (m, 2 H), 7.28−7.39 (m, 2 H). − MS (80°C); *m/z* (%): 348 (9) [M$^+$], 240 (100), 225 (26), 197 (20), 165 (12), 108 (19), 82 (10). − $C_{23}H_{24}O_3$ (348.44): calcd. 348.1725; found 348.1711 (MS).

3b: An emulsion of 300 mg (0.86 mmol) of adduct **2** in 3 ml of acetic acid was treated with 225 mg (3.44 mmol, 5 equiv.) of zinc dust under ultrasound conditions for 5 min. The zinc was then filtered off, and the solution was diluted with water. After extraction with diethyl ether, the combined organic phases were washed with 10% aq. KOH and brine. The extract was dried with $MgSO_4$, filtered, and the solvent was evaporated under reduced pressure to yield 259.2 mg (86%) of a colourless solid. − M.p. 138°C. − $[\alpha]_D = 158.9$ ($c = 0.9$, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu} = 3000$ cm^{-1}, 2936, 1752, 1704, 1516, 1252, 1180, 1036. − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.51 (d, $J = 12$ Hz, 1 H), 0.75 (s, 3 H), 3.14 (d, $J = 9$ Hz, 1 H), 3.81 (s, 3 H), 3.99 (d, $J = 9$ Hz, 1 H), 6.04 (d, $J = 6$ Hz, 1 H), 6.26 (d, $J = 6$ Hz, 1 H), 6.89−6.91 (m, 2 H), 7.19−7.27 (m, 2 H). − MS (120°C); *m/z* (%): 350 (2) [M$^+$], 240 (100), 225 (16), 197 (13), 165 (8), 121 (9), 91 (8). − $C_{23}H_{26}O_3$ (350.46): calcd. 350.1882; found 350.1881 (MS).

11a−d *and* **12a−d**. − *General Procedure:* A solution of 0.304 ml (0.426 mmol) of *n*-butyllithium (1.6 M in toluene) and 0.06 ml (0.43 mmol) of diisopropylamine in 1.5 ml of THF was stirred for 30 min at 0°C. Then, a cold solution (−78°C) of 50 mg (0.14 mmol) of the dihydro adduct **3** in 3 ml of THF was added dropwise at −78°C. After stirring for 15 min, 2 equiv. of the alkylating reagent was added. On completion of the reaction (TLC control), the mixture was poured into an aqueous solution of ammonium chloride, the phases were separated, and the aqueous phase was extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. The remaining oil was purified by flash chromatography (diethyl ether/petroleum ether, 1:1) to yield 50−71% of the mixed products **11/12a−d**. The spectroscopic data were taken from the spectra of the mixtures.

11a: IR ($CHCl_3$): $\tilde{\nu} = 2940$ cm^{-1}, 2864, 1700, 1516, 1252, 1180, 1036, 908. − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.74 (s, 3 H), 3.08 (d, $J = 9$ Hz, 1 H), 3.82 (s, 3 H), 4.02 (d, $J = 9$ Hz, 1 H), 6.10 (d, $J = 6$ Hz, 1 H), 6.21 (d, $J = 6$ Hz, 1 H), 6.84−6.94 (m, 2 H), 7.03−7.14 (m, 2 H), 7.18−7.33 (m, 5 H). − MS (230°C); *m/z* (%): 439 (1.92) [M$^+$], 240 (100), 225 (39), 197 (34), 91 (75). − $C_{30}H_{32}O_3$ (440.58): calcd. 440.2351; found 440.2339 (MS).

11b: IR ($CHCl_3$): $\tilde{\nu} = 2928$ cm^{-1}, 2860, 1700, 1612, 1516, 1252, 1180. − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.76 (s, 3 H), 3.09 (d, $J = 9$ Hz, 1 H), 3.82 (s, 3 H), 3.98 (d, $J = 9$ Hz, 1 H), 4.97−5.05 (m, 1 H), 5.08 (s, 1 H), 5.54−5.76 (m, 1 H), 6.12 (d, $J = 6$ Hz, 1 H), 6.20 (d, $J = 6$ Hz, 2 H), 6.84−6.96 (m, 2 H), 7.22−7.32 (m, 2 H). − MS (120°C); *m/z* (%): 390 (3) [M$^+$], 349 (2), 240 (100), 225 (43), 197 (38). − $C_{26}H_{30}O_3$ (390.52): calcd. 390.2195; found 390.2202.

11c: IR ($CHCl_3$): $\tilde{\nu} = 3308$ cm^{-1}, 2932, 2860, 1712, 1516, 1252, 1180, 908. − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.77 (s, 3 H), 3.1 (d, $J = 9$ Hz, 1 H), 3.80 (s, 3 H), 4.05 (d, $J = 9$ Hz, 1 H), 6.14 (d, $J = 6$ Hz, 1 H), 6.22 (d, $J = 6$ Hz, 1 H), 6.83−6.92 (m, 2 H), 7.10−7.24 (m, 2 H). − MS (130°C); *m/z* (%): 388 (2) [M$^+$], 348 (2), 240 (100), 225 (24), 197 (22). − $C_{26}H_{28}O_3$ (388.51): calcd. 388.2030; found 388.2038 (MS).

11d: IR ($CHCl_3$): $\tilde{\nu} = 2932$ cm^{-1}, 2864, 1700, 1516, 1252, 1180. − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.76 (s, 3 H), 1.05 (d, $J = 6$ Hz, 1 H), 3.08 (d, $J = 9$ Hz, 1 H), 3.81 (s, 3 H), 4.02 (d, $J = 9$ Hz, 1 H), 6.14 (d, $J = 6$ Hz, 1 H), 6.18 (d, $J = 6$ Hz, 1 H), 6.86−6.94 (m, 2 H), 7.14−7.33 (m, 2 H). − MS (110°C); *m/z* (%): 364 (2) [M$^+$], 240 (100), 225 (21), 197 (17), 124 (14).

12a: IR ($CHCl_3$): $\tilde{\nu} = 2940$ cm^{-1}, 2864, 1700, 1516, 1252, 1180, 1036, 908. − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.73 (s, 3 H), 3.16 (d, $J = 9$ Hz, 1 H), 3.80 (s, 3 H), 3.95 (d, $J = 9$ Hz, 1 H), 6.00 (d, $J = 6$ Hz, 1 H), 6.28 (d, $J = 6$ Hz, 1 H), 6.84−6.94 (m, 2 H), 7.03−7.14 (m, 2 H), 7.18−7.33 (m, 5 H). − MS (230°C); *m/z* (%): 439 (1.92) [M$^+$], 240 (100), 225 (39), 197 (34), 91 (75). − $C_{30}H_{32}O_3$ (440.58): calcd. 440.2351; found 440.2339 (MS).

12b: IR ($CHCl_3$): $\tilde{\nu} = 2928$ cm^{-1}, 2860, 1700, 1612, 1516, 1252, 1180. − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.78 (s, 3 H), 3.16 (d, $J = 9$ Hz, 1 H), 3.81 (s, 3 H), 3.97 (d, $J = 9$ Hz, 1 H), 4.97−5.05 (m, 1 H), 5.08 (s, 1 H), 5.54−5.76 (m, 1 H), 5.98 (d, $J = 6$ Hz, 1 H), 6.30 (d, $J = 6$ Hz, 1 H), 6.84−6.96 (m, 2 H), 7.22−7.32 (m, 2 H). − MS (120°C); *m/z* (%): 390 (3) [M$^+$], 349 (2), 240 (100), 225 (43), 197 (38). − $C_{26}H_{30}O_3$ (390.52): calcd. 390.2195; found 390.2202 (MS).

12c: IR ($CHCl_3$): $\tilde{\nu} = 3308$ cm^{-1}, 2932, 2860, 1712, 1516, 1252, 1180, 908. − ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 0.77 (s, 3 H), 3.22 (d, $J = 9$ Hz, 1 H), 3.82 (s, 3 H), 4.01 (d, $J = 9$ Hz, 1 H), 5.94 (d, $J = 6$ Hz, 1 H), 6.34 (d, $J = 6$ Hz, 1 H), 6.83−6.92 (m, 2 H), 7.10−7.24 (m, 2 H). − MS (130°C); *m/z* (%): 388 (2) [M$^+$], 348 (2), 240 (100), 225 (24), 197 (22). − $C_{26}H_{28}O_3$ (388.51): calcd. 388.2030; found 388.2038 (MS).

12d: IR ($CHCl_3$): $\tilde{\nu}$ = 2932 cm^{-1}, 2864, 1700, 1516, 1252, 1180. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.75 (s, 3 H), 1.09 (d, J = 6 Hz, 1 H), 3.19 (d, J = 9 Hz, 1 H), 3.80 (s, 3 H), 3.97 (d, J = 9 Hz, 1 H), 5.96 (d, J = 6 Hz, 1 H), 6.31 (d, J = 6 Hz, 1 H), 6.86−6.94 (m, 2 H), 7.14−7.33 (m, 2 H). − MS (110°C); *m/z* (%): 364 (2) [M^+], 240 (100), 225 (21), 197 (17), 124 (14).

14: 1.0 g (4.16 mmol) of diene **1** and 633 mg (4.16 mmol) of *p*-benzoquinone monoketal were dissolved in 3 ml of dichloromethane. The resulting solution was sealed in a Teflon tube, which was pressurized at 6.5 bar for 48 h. After evaporation of the solvent and purification of the residue by flash chromatography (diethyl ether/petroleum ether, 2:1), 1.41 g (86%) of white crystals was obtained. − M.p. 132°C. − $[\alpha]_D$ = −128.4 (c = 0.395, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2952 cm^{-1}, 2928, 2892, 2864, 1668, 1516, 1248, 1180, 1116, 964, 948, 824. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.46 (br. d, J = 12 Hz, 1 H), 0.80 (s, 3 H), 2.34 (br. d, J = 12 Hz, 1 H), 2.83 (dd, J_1 = 9 Hz, J_2 = 1 Hz, 1 H), 3.80 (s, 3 H), 3.91−4.17 (m, 5 H), 5.89 (d, J = 6 Hz, 1 H), 5.90 (d, J = 10 Hz, 1 H), 6.03 (d, J = 6 Hz, 1 H), 6.32 (d, J = 10 Hz, 1 H), 6.83−6.91 (m, 2 H), 7.26−7.34 (m, 2 H). − MS (110°C); *m/z* = 392 (2) [M^+], 312 (2), 240 (100), 197 (7), 152 (6), 82 (4). − $C_{25}H_{28}O_4$ (392.49): calcd. 392.1988; found 392.1987 (MS).

16a: A suspension of 500 mg (1.27 mmol) of the monoketal adduct **14**, 375 mg (1.85 mmol) of $NiCl_2 \cdot 6\ H_2O$ and 625 mg (9.47 mmol) of zinc dust in 20 ml of glycol monoethyl ether and 2 ml of water was subjected to ultrasonification for 3 h. The inorganic residue was then filtered off and the filtrate was extracted with diethyl ether. The organic phase was dried with $MgSO_4$ and the solvent was evaporated. The remaining oil was purified by flash chromatography (diethyl ether/petroleum ether, 1:2) to yield 340 mg (67%) of a colourless solid. − M.p. 144°C. − $[\alpha]_D$ = −36.1 (c = 0.415, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 2928 cm^{-1}, 1709, 1615, 1515, 1230, 1182. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.49 (br. d, J = 13 Hz, 1 H), 0.76 (s, 3 H), 2.87 (d, J = 10 Hz, 1 H), 3.78 (d, J = 10 Hz, 1 H), 3.79 (s, 3 H), 3.90−4.07 (m, 4 H), 6.08 (d, J = 6 Hz, 1 H), 6.12 (d, J = 6 Hz, 1 H), 6.81−6.89 (m, 2 H), 7.16−7.24 (m, 2 H). − MS (100°C); *m/z* (%): 394 (3) [M^+], 240 (100), 225 (13). − $C_{25}H_{30}O_4$ (394.51): calcd. 394.2144; found 394.2143 (MS).

16b: To a solution of 100 mg (0.25 mmol) of the monoketal adduct **14** in 3 ml of THF, 2 equiv. of ethylmagnesium bromide in diethyl ether was added dropwise at 0°C. The mixture was stirred for 4 h at this temperature, then diluted with an aqueous ammonium chloride solution, and extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. The remaining oil was purified by flash chromatography (diethyl ether/petroleum ether, 2:1) to yield 28 mg (26%) of a colourless oil. − IR (KBr): $\tilde{\nu}$ = 2932 cm^{-1}, 1704, 1614, 1516, 1251, 1181. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.47 (br. d, J = 13 Hz, 1 H), 0.75 (s, 3 H), 2.80 (d, J = 10 Hz, 1 H), 3.71 (d, J = 10 Hz, 1 H), 3.79 (s, 3 H), 3.90−4.06 (m, 4 H), 6.06 (d, J = 6 Hz, 1 H), 6.16 (d, J = 6 Hz, 1 H), 6.81−6.90 (m, 2 H), 7.15−7.25 (m, 2 H). − MS (95°C); *m/z* (%): 422 (2) [M^+], 395 (1), 241 (100), 225 (12), 198 (10), 165 (6). − $C_{27}H_{34}O_4$ (422.56): calcd. 422.2457; found 422.2464 (MS).

16c: To a stirred slurry of 22.7 mg (0.25 mmol) copper(I) cyanide in 1 ml of diethyl ether at −20°C, 0.32 ml (0.25 mmol) of a methyllithium solution was added slowly until the suspension became homogeneous and colourless. The resulting dimethylcuprate solution was stirred at −30°C for 20 min and then added dropwise to a solution of 50 mg (0.12 mmol) monoketal adduct **14** and 48 µl (0.38 mmol) of trimethylsilyl chloride in 1 ml of diethyl ether and 1 ml of THF at −30°C. After 5 min, the reaction mixture was diluted with aqueous ammonium chloride solution and extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. The remaining oil was dissolved in 1.5 ml of acetic acid and stirred at room temperature for 30 min. Subsequently, the mixture was diluted with saturated sodium hydrogen carbonate solution, extracted with diethyl ether, and the combined extracts were dried with $MgSO_4$. The solvent was evaporated under reduced pressure and the remaining oil was purified by flash chromatography (diethyl ether/petroleum ether, 5:1) to yield 44.4 mg (86%) of a colourless oil. − $[\alpha]_D$ = −54.1 (c = 0.425, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2932 cm^{-1}, 2860, 1696, 1612, 1516, 1464, 1252, 1196, 1180. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.42 (br. d, J = 12 Hz, 1 H), 0.75 (s, 3 H), 0.96 (d, J = 6 Hz, 1 H), 2.78 (d, J = 10 Hz, 1 H), 3.73 (d, J = 10 Hz, 1 H), 3.79 (s, 3 H), 3.95−4.07 (m, 4 H), 6.07 (d, J = 6 Hz, 1 H), 6.17 (d, J = 6 Hz, 1 H), 6.80−6.89 (m, 2 H), 7.17−7.25 (m, 2 H). − MS (100°C); *m/z* (%): 408 (2) [M^+], 240 (100), 225 (12), 197 (12), 165 (6), 85 (24). − $C_{28}H_{32}O_4$ (408.54): calcd. 408.2301; found 408.2312 (MS).

19a−d. − *General Procedure:* A solution of 0.506 ml (0.76 mmol) of *n*-butyllithium (1.6 M in toluene) and 0.107 ml (0.76 mmol) of diisopropylamine in 1.5 ml of THF was stirred for 30 min at 0°C. A precooled solution of 150 mg (0.38 mmol) of the reduced monoketal adduct **16a** in 3 ml of HF was then added dropwise at −30°C. After stirring for 15 min, 2 equiv. of the alkylating reagent was added. The reaction mixture was slowly allowed to warm to 0°C over a period of 2 h, and then poured into an aqueous ammonium chloride solution. The phases were separated and the aqueous phase was extracted with diethyl ether. The organic phase was washed with brine, dried with $MgSO_4$, and the solvent was evaporated under reduced pressure. The remaining oil was purified by flash chromatography (diethyl ether/petroleum ether, 1:1) to yield 50−84% of the products **19a−d**.

19a: $[\alpha]_D$ = −9 (c = 0.21, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2932 cm^{-1}, 2892, 2856, 1704, 1516, 1248, 1180. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.50 (d, J = 13 Hz, 1 H), 0.77 (s, 3 H), 1.05 (d, J = 7 Hz, 3 H), 3.02 (d, J = 10 Hz, 1 H), 3.80 (s, 3 H), 3.82 (d, J = 10 Hz, 1 H), 3.92−4.04 (m, 4 H), 6.03 (d, J = 6 Hz, 1 H), 6.12 (d, J = 6 Hz, 1 H), 6.81−6.90 (m, 2 H), 7.16−7.26 (m, 2 H). − MS (135°C); *m/z* (%): 408 (2) [M^+], 240 (100), 225 (14), 197 (12). − $C_{26}H_{32}O_4$ (408.54): calcd. 408.2301; found 408.2290 (MS).

19b: M.p. 157°C. − $[\alpha]_D$ = 32.4 (c = 0.105, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 2930 cm^{-1}, 1708, 1515, 1248, 1182. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.50 (br. d, J = 13 Hz, 1 H), 0.77 (s, 3 H), 3.00 (d, J = 10 Hz, 1 H), 3.75 (d, J = 10 Hz, 1 H), 3.79 (s, 3 H), 3.90−4.02 (m, 4 H), 4.99 (dd, J_1 = 7 Hz, J_2 = 1 Hz, 1 H), 5.06 (s, 1 H), 5.59−5.78 (m, 1 H), 6.04 (d, J = 6 Hz, 1 H), 6.10 (d, J = 6 Hz, 1 H), 6.80−6.88 (m, 2 H), 7.14−7.22 (m, 2 H). − MS (140°C); *m/z* (%): 434 (5) [M^+], 406 (3), 377 (2), 240 (100), 225 (69), 197 (71). − $C_{28}H_{34}O_4$ (434.57): calcd. 434.2457; found 434.2454 (MS).

19c: M.p. 145°C. − $[\alpha]_D$ = 64 (c = 0.5, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2924 cm^{-1}, 2856, 1704, 1516, 1248, 1180. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.49 (br. d, J = 13 Hz, 1 H), 0.69 (s, 3 H), 2.32−2.50 (m, 1 H), 2.68 (dd, J_1 = 14 Hz, J_2 = 9 Hz, 1 H), 2.92 (d, J = 11 Hz, 1 H), 2.97 (dd, J_1 = 14 Hz, J_2 = 4 Hz, 1 H), 3.55 (d, J = 11 Hz, 1 H), 3.81 (s, 3 H), 3.87−3.98 (m, 4 H), 6.04 (d, J = 6 Hz, 1 H), 6.09 (d, J = 6 Hz, 1 H), 6.82−6.92 (m, 2 H), 7.05−7.32 (m, 7 H). − MS (130°C); *m/z* (%): 484 (3) [M^+], 467 (2), 406 (3), 240 (100), 225 (22), 197 (19). − $C_{32}H_{36}O_4$ (484.63): calcd. 484.2614; found 484.2615 (MS).

19d: $[\alpha]_D$ = 34 (c = 1.07, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2932 cm^{-1}, 2856, 1704, 1612, 1516, 1248, 1180. − ^1H NMR ($CDCl_3$,

400 MHz): δ = 0.52 (br. d, *J* = 13 Hz, 1 H), 0.76 (s, 3 H), 1.55 (s, 3 H), 1.60 (s, 3 H), 1.69 (s, 3 H), 1.85−2.30 (m, 6 H), 3.00 (d, *J* = 11 Hz, 1 H), 3.75 (d, *J* = 11 Hz, 1 H), 3.78 (s, 3 H), 3.88−4.02 (m, 4 H), 5.02−5.12 (m, 2 H), 6.05 (s, 2 H), 6.80−6.87 (m, 2 H), 7.11−7.19 (m, 2 H). − MS (130°C); *m/z* (%): 530 (3) [M^+], 502 (1), 290 (36), 240 (100), 225 (39), 197 (38). − $C_{35}H_{46}O_4$ (530.75): calcd. 530.3408; found 530.3396 (MS).

20: An excess of $LiAlH_4$ was refluxed in 3 ml of dry diethyl ether. The suspension was then cooled to −40°C and a solution of 550 mg (1.27 mmol) of the adduct **18b** in diethyl ether was added dropwise. After 15 min, the reaction mixture was diluted with an aqueous ammonium chloride solution and extracted with diethyl ether. The organic phase was washed with brine and dried with $MgSO_4$. The solvent was evaporated to yield 550 mg (99%) of a colourless oil. − $[\alpha]_D$ = −44.6 (*c* = 0.56, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3492 cm^{-1}, 2928, 2856, 1512, 1248, 1224, 1180. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.45 (br. d, *J* = 12 Hz, 1 H), 0.82 (s, 3 H), 2.50 (d, *J* = 10 Hz, 1 H), 3.41 (dd, J_1 = 10 Hz, J_2 = 5 Hz, 1 H), 3.80 (s, 3 H), 3.87−4.02 (m, 4 H), 3.94−5.13 (m, 2 H), 5.63−5.87 (m, 1 H), 5.93 (d, *J* = 6 Hz, 1 H), 6.20 (d, *J* = 6 Hz, 1 H), 6.83−6.91 (m, 2 H), 7.21−7.31 (m, 2 H). − MS (110°C); *m/z* (%): 436 (1) [M^+], 240 (100), 225 (8), 197 (8). − $C_{28}H_{36}O_4$ (436.59): calcd. 436.2614; found 436.2603 (MS).

21: To a solution of 550 mg (1.25 mmol) of the carbinol **20** in 10 ml of acetone, 2 ml of 6 N HCl was added dropwise. The solution was stirred at room temperature for 10 min, then diluted with water, and extracted with dichloromethane. The organic phase was washed with a saturated sodium hydrogen carbonate solution and dried with $MgSO_4$. The solvent was evaporated and the remaining oil was purified by flash chromatography (diethyl ether) to yield 283 mg (57%) of a colourless solid. − M.p. 53°C. − $[\alpha]_D$ = −76.4 (*c* = 0.56, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3576 cm^{-1}, 2928, 2860, 1696, 1512, 1248, 1180. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.45 (br. d, *J* = 13 Hz, 1 H), 0.80 (s, 3 H), 2.76 (d, *J* = 10 Hz, 1 H), 3.70 (dd, J_1 = 10 Hz, J_2 = 5 Hz, 1 H), 3.82 (s, 3 H), 4.16 (dd, J_1 = 11 Hz, J_2 = 5 Hz, 1 H), 5.08 (s, 1 H), 5.15 (dd, J_1 = 4 Hz, J_2 = 1 Hz, 1 H), 5.67−5.90 (m, 1 H), 6.13 (d, *J* = 6 Hz, 1 H), 6.27 (d, *J* = 6 Hz, 1 H), 6.86−6.96 (m, 2 H), 7.21−7.30 (m, 2 H). − MS (100°C); *m/z* (%): 392 (1) [M^+], 296 (10), 240 (100), 226 (14), 197 (15). − $C_{26}H_{32}O_3$ (392.54): calcd. 392.2351; found 392.2340 (MS).

22a: 88 mg (0.3 mmol) of **20** was heated to 200°C under high-vacuum conditions and vapour-pyrolyzed at 350°C. The products were eluted from the cold-trap with dichloromethane and subsequently separated by flash chromatography (diethyl ether/petroleum ether, 1:4) to yield 34 mg (97%) of a colourless oil. − $[\alpha]_D$ = 46.6 (*c* = 0.15, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3616 cm^{-1}, 3592, 2980, 2908, 2848, 1680, 1228, 1160. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 2.09−2.30 (m, 3 H), 2.62−3.41 (m, 2 H), 4.31 (br. s, 1 H), 5.11 (s, 1 H), 5.14−5.22 (m, 1 H), 5.72−5.91 (m, 1 H), 5.98 (ddd, J_1 = 10 Hz, J_2 = 2 Hz, J_3 = 1 Hz, 1 H), 6.90 (dd, J_1 = 10 Hz, J_2 = 2 Hz, 1 H). − MS (room temperature); *m/z* (%): 152 (1) [M^+], 134 (5), 110 (51), 150 (3).

22b: A mixture of 30 mg (0.20 mmol) of **22a**, 35.6 mg (0.24 mmol) of *tert*-butyldimethylsilyl chloride and 30 mg (0.433 mmol) of imidazole in 2 ml of dry DMF was stirred for 2 d at room temperature. The reaction mixture was then diluted with water and extracted with a mixture of diethyl ether and petroleum ether. The organic phase was washed with water and brine, and dried with $MgSO_4$. The solvent was evaporated to yield 42 mg (80%) of a colourless oil. − $[\alpha]_D$ = 232.5° (*c* = 0.15, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2956 cm^{-1}, 2932, 2856, 1680, 1256, 1100. − ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.13 (s, 3 H), 0.14 (s, 3 H), 0.93 (s, 9 H), 1.90−2.20 (m, 3 H), 2.50−2.65 (m, 2 H), 4.19−4.22 (m, 1 H), 5.04−5.10 (m, 2 H), 5.65−5.70 (m, 1 H), 5.91 (ddd, J_1 = 10 Hz, J_2 = 2 Hz, J_3 = 1 Hz, 1 H), 6.78 (dd, J_1 = 10 Hz, J_2 = 2 Hz, 1 H). − MS (room temperature); *m/z* (%): 267 (2) [M^+ + 1], 266 (2) [M^+], 209 (90), 167 (80), 135 (27). − $C_{15}H_{26}O_2Si$ (266.46): calcd. 266.1702; found 266.1689 (MS).

11b: To a solution of 50 mg (0.127 mmol) of **20** in 2 ml of dry dichloromethane, a solution of 41 mg (0.19 mmol) of PCC and 3 mg (0.04 mmol) of sodium acetate in 5 ml of dichloromethane was added dropwise. The reaction mixture was stirred for 1.5 h at room temperature, and then filtered through silica gel to yield 25 mg (50%) of a colourless oil. For spectroscopic data, see above.

23a: A mixture of 255 mg (6.3 mmol) NaOH and 0.65 ml (6.3 mmol) of H_2O_2 (35% aqueous solution) was added to a solution of 500 mg (1.27 mmol) of adduct **14** in 10 ml of THF at 0°C. On completion of the reaction (TLC control), the mixture was extracted with dichloromethane. The organic phase was washed with a 5% aqueous solution of $FeSO_4$ and dried with $MgSO_4$. The solvent was evaporated under reduced pressure and the remaining oil was purified by flash chromatography (diethyl ether/petroleum ether, 5:1) to yield 415 mg (80%) of a colourless solid. − M.p. 194°C. − $[\alpha]_D$ = −12.9 (*c* = 0.155). − IR ($CHCl_3$): $\tilde{\nu}$ = 3392 cm^{-1}, 2932, 1716, 1516, 1248, 948, 824. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.55 (br. d, *J* = 13 Hz, 1 H), 0.75 (s, 3 H), 3.15 (d, *J* = 11 Hz, 1 H), 3.29 (d, *J* = 4 Hz, 1 H), 3.33 (d, *J* = 4 Hz, 1 H), 3.79 (s, 3 H), 3.93−4.23 (m, 5 H), 6.01 (d, *J* = 6 Hz, 1 H), 6.11 (d, *J* = 6 Hz, 1 H), 6.81−6.89 (m, 2 H), 7.08−7.17 (m, 2 H). − MS (80°C); *m/z* (%): 408 (16) [M^+], 380 (10), 240 (100), 225 (11), 197 (10). − $C_{25}H_{28}O_5$ (408.49): calcd. 408.1937; found 408.1935 (MS).

23b: A solution of 150 mg (0.37 mmol) of epoxide **23a** in 7 ml of dry toluene was treated with 1.04 ml (0.73 mmol) of a solution of L-Selectride in toluene at 0°C. The reaction mixture was allowed to warm to room temperature over a period of 3 h, diluted with aqueous ammonium chloride solution, and extracted with diethyl ether. The combined organic phases were washed with brine, and the solvent was evaporated under reduced pressure. The remaining oil was purified by flash chromatography (diethyl ether/petroleum ether, 5:1) to yield 145 mg (96%) of a colourless oil. − $[\alpha]_D$ = −65 (*c* = 0.415, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 3418 cm^{-1}, 2927, 2859, 1515, 1251, 1181. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.51 (br. d, *J* = 13 Hz, 1 H), 0.81 (s, 3 H), 2.47 (d, *J* = 2 Hz, 1 H), 2.64 (d, *J* = 10 Hz, 1 H), 3.17−3.26 (m, 2 H), 3.60 (dd, J_1 = 10 Hz, J_2 = 2 Hz, 2 H), 3.81 (s, 3 H), 3.89−4.20 (m, 4 H), 6.05 (d, *J* = 6 Hz, 1 H), 6.17 (d, *J* = 6 Hz, 1 H), 6.85−6.95 (m, 2 H), 7.23−7.34 (m, 2 H). − MS (120°C); *m/z* (%): 410 (3) [M^+], 392 (1), 381 (2), 365 (2), 240 (100), 225 (99), 197 (10). − $C_{25}H_{30}O_5$ (410.51): calcd. 410.2093; found 410.2095 (MS).

23c: To a mixture of 55 mg (0.134 mmol) of **23b** and 33 mg (0.27 mmol) of DMAP, dissolved in 3 ml of dichloromethane, 0.02 ml (0.205 mmol) of acetic anhydride was added dropwise. After stirring for 1 h at room temperature, the reaction mixture was diluted with water and extracted with diethyl ether. The organic phase was washed with aqueous citric acid solution and then with aqueous sodium hydrogen carbonate solution. The ethereal solution was dried with $MgSO_4$ and the solvent was evaporated under reduced pressure to yield 62 mg (100%) of a colourless oil. − $[\alpha]_D$ = −45.8 (*c* = 0.325, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2928 cm^{-1}, 2856, 1736, 1512, 1228, 1180. − ^1H NMR (200 MHz, $CDCl_3$): δ = 0.52 (br. d, *J* = 13 Hz, 1 H), 0.83 (s, 3 H), 2.17 (s, 3 H), 2.62 (d, *J* = 9 Hz, 1 H), 3.31−3.13 (m, 1 H), 3.59 (dd, J_1 = 9 Hz, J_2 = 2 Hz, 1 H), 3.82 (s, 3 H), 3.84−4.19 (m, 4 H), 5.19 (d, *J* = 4 Hz, 1 H), 6.06 (d, *J* = 6 Hz, 1 H), 6.17 (d, *J* = 6 Hz, 1 H), 6.87−6.96 (m, 2 H),

7.25−7.36 (m, 2 H). − MS (150°C); *m/z* (%) 452 (2) [M^+], 437 (1), 410 (1), 392 (2), 240 (100), 225 (6), 197 (4).

24a: 48.8 mg (1.02 mmol) of an NaH dispersion was washed with petroleum ether and dried under reduced pressure. 121 mg (1.02 mmol) of trimethyloxosulfonium chloride and 4 ml of DMSO were then added. After stirring for 20 min at room temperature, a solution of 200 mg (0.51 mmol) of adduct **14** in 10 ml of DMSO was added dropwise and stirring was continued for a further 2 h at room temperature. The reaction mixture was then diluted with water, the aqueous phase was extracted with diethyl ether, and the combined organic phases were washed with water. The ethereal solution was dried with $MgSO_4$ and the solvent was evaporated under reduced pressure to yield 185 mg (89%) of a colourless solid. − M.p. 192°C. − $[\alpha]_D = -12.2$ (c = 0.45, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3052 cm^{-1}, 2932, 2892, 1692, 1612, 1516, 1248, 1180, 1120, 1040. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.53 (br. d, J = 13 Hz, 1 H), 0.72 (s, 3 H), 3.02 (d, J = 11 Hz, 1 H), 3.82 (d, J = 11 Hz, 1 H), 3.88 (s, 3 H), 4.01−4.12 (m, 4 H), 6.06 (d, J = 6 Hz, 1 H), 6.11 (d, J = 6 Hz, 1 H), 6.78−6.87 (m, 2 H), 7.07−7.15 (m, 2 H). − MS (80°C); *m/z* (%): 406 (4) [M^+], 240 (100), 225 (23), 165 (17), 86 (34). − $C_{26}H_{30}O_4$ (406.52): calcd. 406.2144; found 406.2105 (MS).

24b: An excess of $LiAlH_4$ was refluxed for 30 min in 2 ml of dry diethyl ether. The suspension was then cooled to −40°C and a solution of 50 mg (0.123 mmol) of **24a** in 2 ml of a 1:1 mixture of diethyl ether and THF was added dropwise. After 10 min, the reaction mixture was diluted with an aqueous ammonium chloride solution and extracted with diethyl ether. The organic phase was washed with brine and dried with $MgSO_4$. The solvent was evaporated to yield 43 mg (85%) of a colourless solid. − M.p. 181°C. − $[\alpha]_D = -62.6$ (c = 0.225, $CHCl_3$). − IR (KBr): $\tilde{\nu}$ = 3527 cm^{-1}, 2932, 2862, 1618, 1516, 1259, 1241, 1180, 1129. − ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.48 (br. d, J = 13 Hz, 1 H), 0.77 (s, 3 H), 1.91 (br. d, J = 13 Hz, 1 H), 2.05 (ddd, J_1 = 13 Hz, J_2 = 13 Hz, J_3 = 4 Hz, 1 H), 2.35 (dd, J_1 = 13 Hz, J_2 = 13 Hz, 2 H), 2.89 (dd, J_1 = 11 Hz, J_2 = 5 Hz, 1 H), 3.80 (s, 3 H), 3.92 (d, J = 11 Hz, 1 H), 4.00−4.31 (m, 4 H), 4.20−4.30 (m, 1 H), 5.89 (d, J = 6 Hz, 1 H), 6.16 (d, J = 6 Hz, 1 H), 6.83−6.88 (m, 2 H), 7.17−7.24 (m, 2 H). − MS (100°C); *m/z* (%): 408 (3) [M^+], 392 (2), 374 (1), 240 (100), 225 (18), 197 (15). − $C_{26}H_{32}O_4$ (408.54): calcd. 408.2301; found 408.2298 (MS).

25: 185 mg (0.45 mmol) of **24** was heated to 250°C under high-vacuum conditions and vapour-pyrolyzed at 350°C. The products were eluted from the cold-trap with dichloromethane and subsequently separated by flash chromatography (diethyl ether/petroleum ether, 1:4) to yield 47 mg (62%) of a colourless oil. − $[\alpha]_D$ = −40 (c = 0.06, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 2988 cm^{-1}, 2960, 2628, 1696, 1512, 1264, 908, 816. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 3.49 (dd, J_1 = 4 Hz, J_2 = 2 Hz, 1 H), 3.59 (dd, J_1 = 4 Hz, J_2 = 3 Hz, 1 H), 4.11−4.27 (m, 4 H), 5.99 (dd, J_1 = 10 Hz, J_2 = 2 Hz, 1 H), 6.33 (dd, J_1 = 10 Hz, J_2 = 3 Hz, 1 H). − MS (100°C); *m/z* (%): 169 (57) [M^+ + 1], 168 (11) [M^+], 139 (20), 126 (76). − $C_8H_8O_4$ (168.15): calcd. 168.0423; found 168.0419 (MS).

26: To a solution of 22 mg (0.05 mmol) of **25** in 6 ml of acetone, 1 ml of 6 N HCl was added dropwise. The mixture was stirred at room temperature for 1.5 h, diluted with water, and extracted with dichloromethane. The organic phase was washed with a saturated sodium hydrogen carbonate solution and dried with $MgSO_4$. The solvent was evaporated and the remaining oil was purified by flash chromatography (diethyl ether) to yield 17.5 mg (89%) of a colourless solid. − M.p. 176°C. − $[\alpha]_D = -45.2$ (c = 0.155, $CHCl_3$). − IR ($CHCl_3$): $\tilde{\nu}$ = 3000 cm^{-1}, 2928, 2860, 1692, 1612, 1516, 1248, 1228, 1180. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 0.50 (d, J = 13 Hz, 1 H), 0.72 (s, 3 H), 2.03 (dd, J_1 = 10 Hz, J_2 = 5 Hz, 1 H), 2.18 (dd, J_1 = 10 Hz, J_2 = 5 Hz, 2 H), 3.10 (d, J = 10 Hz, 1 H), 3.80 (s, 3 H), 4.01 (d, J = 10 Hz, 1 H), 6.05 (d, J = 6 Hz, 1 H), 6.10 (d, J = 6 Hz, 1 H), 6.82−6.92 (m, 2 H), 7.08−7.21 (m, 2 H). − MS (150°C); *m/z* (%): 362 (1) [M^+], 240 (100), 225 (20), 197 (22), 165 (11). − $C_{24}H_{26}O_3$ (362.47): calcd. 362.1882; found 362.1880 (MS).

27: 100 mg (0.246 mmol) of **24** was heated to 225°C under high-vacuum conditions. Vapour pyrolysis took place at 350°C. The products were eluted from the cold-trap with dichloromethane and subsequently separated by flash chromatography (diethyl ether/petroleum ether, 1:2) to yield 37 mg (90%) of a colourless oil. − $[\alpha]_D = -97$ (c = 0.17, $CHCl_3$) − IR ($CHCl_3$): $\tilde{\nu}$ = 3000 cm^{-1}, 2956, 2928, 2892, 1680, 1604, 1508, 1192, 1152, 1120. − ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.07−1.17 (m, 1 H), 1.29−1.38 (m, 1 H), 1.92−2.11 (m, 2 H), 4.05−4.22 (m, 4 H), 5.84 (dd, J_1 = 10 Hz, J_2 = 1.5 Hz, 1 H), 6.20 (dd, J_1 = 10 Hz, J_2 = 2 Hz, 1 H). − MS (room temperature); *m/z* (%): 166 (85) [M^+], 138 (82), 112 (97), 78 (95), 66 (100). − $C_9H_{10}O_3$ (166.18): calcd. 166.0630; found 166.0633 (MS).

[1] R. Brünjes, U. Tilstam, E. Winterfeldt, *Chem. Ber.* **1991**, *124*, 1677−1678.
[2] M. Beckmann, H. Hildebrandt, E. Winterfeldt, *Chem. Ber.* **1991**, *124*, 2505−2509.
[3] M. Dockner, T.Meyer, P. Nemes, M. G. Otten, E. Winterfeldt, *Bull. Soc. Chem. Belg.* **1994**, *103*, 379−387.
[4] A. Mauvais, E. Winterfeldt, *Tetrahedron* **1993**, *49*, 5817−5822.
[5] P. Rivière, A. Mauvais, E. Winterfeldt, *Tetrahedron Asymm.* **1994**, *5*, 1831−1846.
[6] T. M. Kamenecka, L. E. Overman, *Tetrahedron Lett.* **1994**, *35*, 4279−4282.
[7] E. J. Corey, M. Chaykowsky, *J. Am. Chem. Soc.* **1965**, *87*, 1353−1364.
[8] Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as no. CCDC-101024. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: (int. code) + 44(1223)336-033, e-mail: deposit@ccdc.cam.ac.uk].

[97306]