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Kurzmitteilungen / Short Communications

An Easy Access to (*S*)- and (*R*)-Hydroxycyclohexenone[1)]

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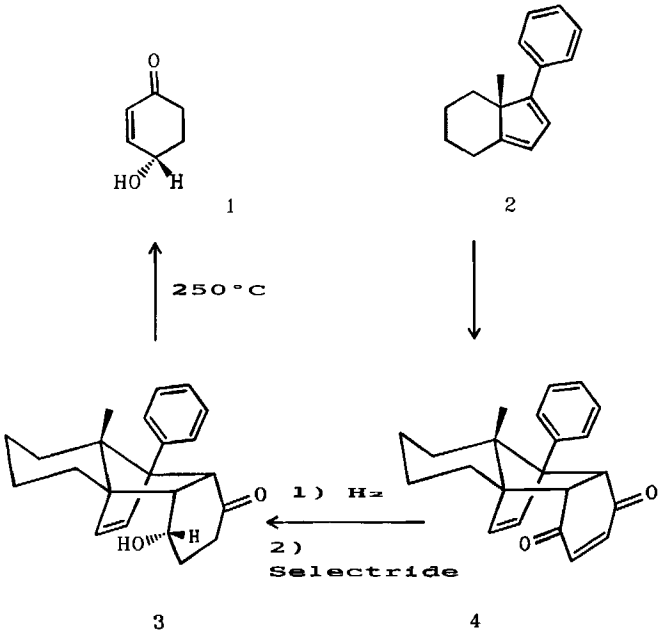
The Diels-Alder adduct obtained by addition of quinone to the chiral cyclopentadiene **2** undergoes regioselective and stereoselective reduction after hydrogenation. The 4-hydroxy ketone **3** thus formed yields the title compound **1** in a thermal retro Diels-Alder process.

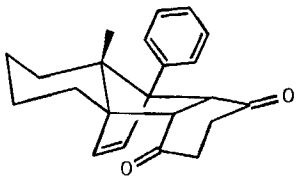
The title compound **1** is considered a very useful chiral starting material since inter- as well as intramolecular conjugate additions can be performed with excellent diastereoselectivity. This has triggered synthetic work aiming at the preparation of this compound in various laboratories. While Danishefsky[2)] developed a multistep procedure starting from quinic acid as a homochiral natural product, Solladié[3)] applied a chiral sulfoxide as an auxilliary, which was eliminated in the final step to form the conjugated double bond[4)].

We present here a very simple approach to this compound which makes use of the configurationally well-defined cyclopentadiene **2** as a chiral template[5)]. Dienes such as **2** were originally mainly devised to induce diastereoselectivity in adducts formed with nonsymmetric dienophiles, since with the symmetric ones regioselectivity poses an additional problem.



1 2 3 4

Since our recent investigations on maleic anhydride adducts had provided convincing proof for high regioselectivity[6)], even in these cases, we prepared and studied Diels-Alder adducts generated from quinone as another symmetric dienophile. High-pressure cycloaddition (6.5 kbar) at room temperature provided a nearly quantitative yield of adduct **4** which turned out to be thermally comparatively labile, showing a high tendency to reform quinone in a retro Diels-Alder process even at room temperature and particularly on recrystallization. Hydrogenation stabilized the molecule, and the subsequent Selectride reduction proved again to be a highly regioselective and stereoselective process. While high diastereoselectivity was of course expected (cage-type molecule) the excellent regioselectivity is probably due to the very typical boat-like conformation of a 1,4-cyclohexanedione (see **5**), indicating steric hindrance of one carbonyl group by the phenyl residue.



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As in the anhydride series the regioselectivity changed completely on changing from the hydrindane series to the steroid series[6)] (additional ring attached to the hydrindane system) it will be necessary to compare these results with corresponding reductions of polycyclic adducts prepared from dienes derived from steroids.

On heating **3** in a kugelrohr apparatus to 250°C, the retro Diels-Alder process provides a high yield of ketone **1** and the corresponding diene which can easily be separated by flash chromatography. HPLC analysis with chiral columns as well as NMR investigations on the Mosher ester proved the hydroxy ketone to be more than 98% optically pure although a comparison of the rotation values with the data cited by Dansihefsky[2)] indicated a lower purity (86%), but exactly the same observation was communicated by Solladié[3)].

Since the enantiomer of **2** may be prepared and used exactly in the same way, this route also provides access to (*R*)-**1**.

Experimental

IR: In chloroform, Perkin-Elmer 580. – ^{1}H NMR: Bruker WH-90, WP-200, AM-300. – MS: Finnigan MAT-312, ionization potential 70 eV. – Elemental analyses: Heraeus CHN rapid ana-

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lyzer. – TLC: Merck plates with silica gel 60 F/254. – Flash chromatography: Baker silica gel 30–60 μ.

Quinone Adduct **4**: 483 mg (2.297 mmol) of diene **2** and 273 mg (2.56 mmol) of quinone were dissolved in 10 ml of dichloromethane and pressurized in a Teflon® tube at 6.5 kbar for three days at room temperature. After evaporation of the solvent, the residue crystallized from ether/petroleum ether, yield 520 mg (71%), m.p. 151 °C (decomp.). – IR (KBr): $\tilde{\nu}$ = 2934 cm^{-1}, 1663, 1607, 1497, 751. – ^1H NMR (200 MHz, $CDCl_3$): δ = 0.47–2.31 (m, 8H), 0.81 (d, *J* = 1 Hz), 3H), 3.16 (d, *J* = 8 Hz, 1H), 4.08 (d, *J* = 8 Hz, 1H), 5.98 (d, *J* = 6 Hz, 1H), 6.13 (d, *J* = 6 Hz, 1H), 6.53 (ABq, *J* = 10 Hz, 2H), 7.37–7.44 (m, 5H). – MS (70 eV, 20 °C): *m/z* (%) = 318 (17) [M^+], 259 (11), 227 (12), 210 (100), 167 (80), 108 (49), 91 (70).

$C_{22}H_{22}O_2$ (318.2)
Calcd. C 82.53 H 7.56 Found C 82.28 H 7.44
Calcd. 318.16198 Found 318.16195 (MS)

Hydroxy Ketone **3**: 580 mg (1.82 mmol) of adducts **4** was dissolved in THF (40 ml). After the addition of palladium catalyst (10% Pd on activated carbon) the hydrogenation was performed at 2.5 bar for 2.5 h until TLC (ether/petroleum ether, 1:1) indicated complete conversion of the starting material. The solution was filtered through Celite and concentrated to yield the crude dihydro ketone which was immediately dissolved in dry toluene (150 ml). The mixture was cooled to –78 °C and then treated with 1.5 mmol of L-Selectride (THF solution). After 2.5 h, saturated ammonium chloride solution was added at –78 °C and the temperature raised to room temperature. The organic material was dissolved in dichloromethane, this solution was washed with saturated sodium hydrogen carbonate solution and dried with magnesium sulfate. After evaporation of the solvent in vacuo the residue was purified by flash chromatography (ether/petroleum ether, 1:1) to yield 524 mg (90%) of hydroxy ketone **3**, m.p. 176 °C. – IR($CHCl_3$): $\tilde{\nu}$ = 3421 cm^{-1}, 1693, 1496, 770, 702. – ^1H NMR: δ = 0.51–2.34 (m, 16H), 0.78 (d, *J* = 1 Hz, 3H), 2.78 (dd, *J* = 11 Hz, *J* = 4 Hz, 1H), 3.81 (d, *J* = 11 Hz, 1H), 4.33 (m, 1H), 6.16 (d, *J* = 6 Hz, 1H), 6.34 (d, *J* = 6 Hz, 1H), 7.87–7.36 (m, 5H). – MS (70 eV, 160 °C): *m/z* (%) = 392 (13) [M^+], 237 (8), 236 (13), 221 (14), 210 (100), 167 (22).

$C_{22}H_{26}O_2$ (322.2)
Calcd. C 82.01 H 8.13 Found C 82.52 H 8.01
Calcd. 322.19328 Found 322.19330 (MS)

(4S)-4-Hydroxy-2-cyclohexen-1-one (**1**): 134 mg (0.416 mmol) of hydroxy ketone **3** was quickly heated in a kugelrohr apparatus to 250 °C in vacuo. The distilled material was additionally purified by flash chromatography to yield 25 mg (54%) of (*S*)-**1**. IR and NMR spectral data are identical with the data given in the literature[2,3]. – $[\alpha]_D$ = –95 (*c* = 0.06, $CHCl_3$); NMR data (Mosher's ester) and HPLC investigation indicate an optical purity of >98%. This proves that the rotation value reported[2] is obviously too high.

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[1] Part 4 of a series on cyclopentadienes as chiral templates. – For part 3 see ref.[6].
[2] J. E. Audia, L. Boisvert, A. D. Patten, A. Villabos, S. J. Danishefsky, *J. Org. Chem.* **54** (1989) 3738.
[3] M. C. Garreno, J. L. Garcia Ruano, M. Garrido, M. P. Ruiz, G. Solladié, *Tetrahedron Lett.* **31** (1990) 6653.
[4] *Note added in proof* (June 5, 1991): A very interesting vitamin-B_{12}-catalyzed epiperoxide isomerization was reported by S. Essig, R. Scheffold, *Chimia* **45** (1991) 30.
[5] K. Matcheva, M. Beckmann, D. Schomburg, E. Winterfeldt, *Synthesis* **1989**, 814.
[6] M. Beckmann, H. Hildebrandt, E. Winterfeldt, *Tetrahedron Asymmetry* **1** (1990) 335.

[114/91]