

Optically Active Cyclopentadienyl Ligands from the Chiral Pool, Part 1. The Synthetic Utility of a Camphor-Derived Pentafulvene

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Starting from (1*R*)-(+)-camphor, the reaction with cyclopentadienylmagnesium chloride gave the corresponding tertiary alcohol **1**, which was transformed into the optically active pentafulvene 5-(1,7,7-trimethylbicyclo[2.2.1]heptan-2-ylidene)cyclopentadiene (**2**) by acid-catalyzed water elimination. Deprotonation with *tert*-butyllithium yielded the corresponding lithium 5-[(1*R*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl]cyclopentadienide (**3**), which was converted into the non-racemic 1,1'-bis[(1*R*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl]ferrocene (**4**). **4** forms orthorhombic crystals of the space group $P2_12_12_1$ with $a = 7.7163(4)$, $b = 10.7381(6)$, and $c = 28.804(2)$ Å, which have been subjected to X-ray diffraction.

Introduction

Although the growing interest in optically active metallocene derivatives with titanium, zirconium, or lanthanide as central atoms spurred the development of procedures for the synthesis of non-racemic cyclopentadienyl ligands, there is still a shortage of facile routes to cyclopentadienes with optically active substituents originating from easily available starting compounds [1].

Pentafulvenes are easily accessible and versatile precursors of cyclopentadienyl anions and have been synthesized from cyclopentadiene derivatives and a large variety of organic oxo compounds [2]. The fulvene route works well even for very crowded molecules like pentaisopropylcyclopentadienide [3] or for the diastereoselective synthesis of optically active cyclopentadienyl ligands, *e.g.* from cholestanone [4].

The synthesis of cyclopentadiene fused to the bornane ring system [5,6] demonstrates the consideration camphor has received as a potential starting compound for optically active cyclopentadienes. Missing, however, are cyclopentadienes with non-fused camphor-derived substituents. Although menthol [7] and isopinocampheol [8] have been used to create non-racemic cyclopentadienyl or indenyl derivatives, we are not aware of borneol having been used successfully for this purpose.

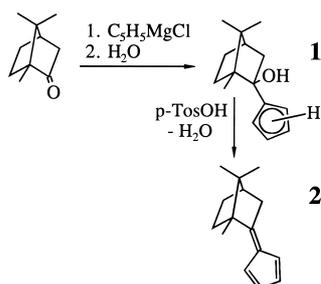
If the camphor molecule with its CMe₂ handle on top of a folded six-membered ring and one

methyl group sticking out on one side of that ring can be attached to a cyclopentadienyl ring or derivatives thereof with suitable substituent patterns, the unsymmetry of such arrangements should have interesting stereochemical consequences.

The work presented in this paper shows one way to utilize (1*R*)-(+)-camphor for the synthesis of pentafulvenes and optically active cyclopentadienides.

Results and Discussion

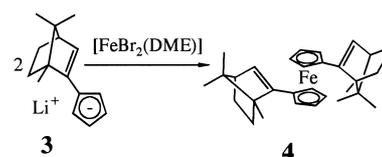
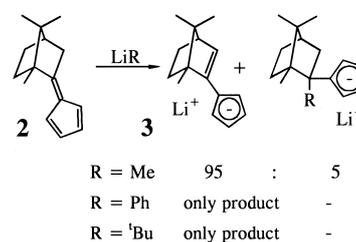
Several attempts to prepare a fulvene from cyclopentadiene and camphor, including the pyrrolidine method so successfully employed by Erker and coworkers [4], failed in our hands. The reaction of camphor with cyclopentadienylmagnesium chloride, however, resulted in formation of the corresponding tertiary alcohol **1**, as demonstrated by GC-MS methods. Treatment of **1** with *p*-toluenesulfonic acid resulted in water elimination and formation of the desired pentafulvene **2** (Scheme 1). Although the isolated yield of **2** is only 27% with respect to the amount of camphor used in the first step, the reaction utilizes cheap starting materials and is easily carried out without purification of intermediates. The main reaction during the first step is deprotonation of camphor in 3-position with formation of the corresponding enolate. The camphor regenerated during aqueous workup can be recycled.



Scheme 1. Reaction of (1*R*)-camphor with cyclopentadienylmagnesium chloride.

The reaction of **2** with methyllithium according to a GC-MS investigation of the hydrolyzed reaction mixture results in approximately 5% addition and 95% proton abstraction (Scheme 2). With *tert*-butyllithium or phenyllithium the same procedure gives {(1*R*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl}cyclopentadienyllithium (**3**), a *tert*-butyl or phenyl addition product has not been encountered. Compound **3** was reacted in a 2:1 ratio with [FeBr₂(DME)] to yield the corresponding ferrocene **4** with two (1*R*)-born-2-en-2-yl substituents in 1,1' position (Scheme 2). Complex **4** shows 15

signals in the ¹³C NMR spectra as expected (see Experimental Part for peak listing and assignment).



Scheme 2. Proton abstraction from pentafulvene **2** and formation of ferrocene **4**.

The interpretation of the ¹³C NMR spectra is straightforward, the singlet at 146.5 ppm for the olefinic α carbon atom of the bornenyl substituent and the doublet at 130.3 ppm for the olefinic CH moiety may serve as examples.

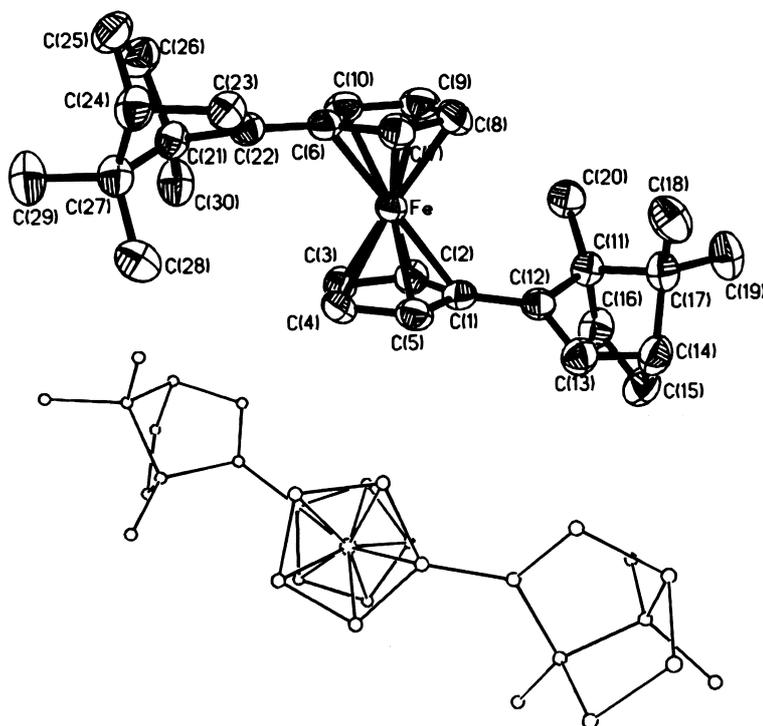


Fig. 1. Molecular structure of ferrocene **4** in the crystalline state. Two views of the molecule are shown. Selected bond lengths [Å] and angles [°]: Fe-C 2.032(2)–2.079(2), av. 2.049, Fe-Cp_{cent.} 1.655 (C1–C5), 1.654 (C6–C10), intra ring C-C 1.407(3)–1.436(2), av. 1.419, interplanar angle of the cyclopentadienyl rings 2.0°.

Apart from the four methylene protons of the ABCDKX spin system of the six-membered ring protons, the ^1H NMR spectra are also easily assigned (see Experimental Part).

The anisotropy effect of the double bond shifts the signal of one methyl group to low field (1.26 ppm), the resonance of the geminal partner is located at 1.01 ppm. EI mass spectra show the molecular ion as the signal of highest intensity.

Crystals of the orthorhombic space group $P2_12_12_1$ were grown from pentane solution and have been subjected to X-ray diffraction (Fig. 1). The molecule has no crystallographic symmetry and is slightly bent with an interplanar angle between the two five-membered rings of 2.0° . The conformation of the two rings is almost staggered with an 8.8° torsion angle. The optically active alkyl substituents are rotated into a position with the bridgehead methyl groups (C20 and C30) pointing toward the iron atom. The C...Fe distances are 3.99 and 4.00 Å, which is not indicative of any significant interaction. The configuration of the (1*R*)-1,1,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl substituent is derived from that of the (1*R*)-camphor precursor as expected and has been verified by a Van Vleck parameter of $-0.015(13)$.

The same compound can be synthesized by acid-catalyzed water elimination (see Experimental Part) from 1,1'-bis[(1*R*,2*S*)-2-exo-hydroxy-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl]ferrocene (**5**) obtained by Dimitrov and coworkers from 1,1'-dithioferrocene and camphor [9].

Conclusion

The reaction of (1*R*)-camphor with cyclopentadienylmagnesium chloride with subsequent hydrolysis and dehydration offers a convenient way to obtain the camphor-derived pentafulvene **2**, which can be converted to optically active {(1*R*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl}cyclopentadienyllithium by proton abstraction.

Experimental Section

General procedures

All manipulations were carried out under argon or nitrogen using standard Schlenk techniques or a glove box (MBraun) and carefully dried solvents. NMR spectra were recorded on a Bruker AMX 400 spectrometer with the protiosolvent signal (^1H

NMR) or solvent signals (^{13}C NMR) used as a reference; chemical shifts are quoted on the δ scale (downfield shifts are positive) relative to tetramethylsilane. Elemental analyses were performed with an Elemental Analyser 240 (Perkin Elmer).

(1*R*)-Camphor (Merck-Schuchardt) was recrystallized from petroleum ether prior to use.

5-(1,7,7-Trimethylbicyclo[2.2.1]heptan-2-ylidene)cyclopentadiene (**2**)

To a solution of 2-propylmagnesium chloride, freshly prepared from 7.85 g (0.100 mol) of 2-chloropropane and 2.9 g (0.120 mol) of magnesium turnings in 90 ml of diethyl ether, a solution of 6.94 g (0.105 mol) of cyclopentadiene in 20 ml of diethyl ether was added dropwise. The resulting suspension was stirred under reflux for 2 h. At room temperature a solution of 15.2 g (0.100 mol) of (1*R*)-(+)-camphor in 30 ml of diethyl ether was added dropwise with stirring. Reflux started during the ketone addition and was maintained by external heating for another 2 h.

Addition of ca. 80 ml of 3% aqueous hydrochloric acid and 50 ml of diethyl ether, followed by phase separation and extraction of the aqueous phase with another 30 ml of diethyl ether gave a combined organic extract which was stirred for 2 h at room temperature with 1.2 g of *p*-toluenesulfonic acid. The solution was washed with 50 ml portions of water, saturated sodium hydrogencarbonate solution and again with water, then evaporated to leave a brown oil and distilled at 0.01 mbar. First camphor was sublimed off, then in a boiling range of 95–115 °C 5.83 g (0.027 mol, 27%) of a yellow, oily liquid was collected which was shown by GC/MS to consist of the desired fulvene **2** and small amounts of camphor and the tertiary alcohol **1**. – ^1H NMR (400.13 MHz, C_6D_6): δ = 6.76 (m, 1 olefin-H), 6.49 (m, 1 olefin-H), 6.45 (m, 2 olefin-H), 2.78 (d, $^3J_{\text{H,H}}$ = 18.2, 1H, CH_2 (endo-H)), 2.25 (d, $^3J_{\text{H,H}}$ = 18.1, 1H, CH_2 (exo-H)), 1.67–1.55 (m, 3H), 1.35–1.27 (m, 1H), 1.06–0.99 (m, 1H, CH_2), 1.20 (s, CH_3), 0.72 (s, CH_3), 0.67 (s, CH_3). – ^{13}C NMR (100.61 MHz, C_6D_6): δ = 165.5 (s, $\text{sp}^2\text{-C}$ (bornylidene)), 137.7 (s, C), 130.3 (d, $^1J_{\text{C,H}}$ = 165 Hz, CH), 128.7 (d, $^1J_{\text{C,H}}$ = 165 Hz, CH), 122.5 (d, $^1J_{\text{C,H}}$ = 168 Hz, CH), 120.3 (d, $^1J_{\text{C,H}}$ = 169 Hz, CH), 55.5 (s, CMe_2), 49.4 (s, CMe), 44.6 (d, $^1J_{\text{C,H}}$ = 140 Hz, $\text{sp}^3\text{-CH}$), 38.8 (t, $^1J_{\text{C,H}}$ = 137 Hz, CH_2), 35.2 (t, $^1J_{\text{C,H}}$ = 131 Hz, CH_2), 28.0 (t, $^1J_{\text{C,H}}$ = 132 Hz, CH_2), 20.3 (q, $^1J_{\text{C,H}}$ = 125 Hz, CH_3), 19.2 (q, $^1J_{\text{C,H}}$ = 124 Hz, CH_3), 15.6 (q, $^1J_{\text{C,H}}$ = 125 Hz, CH_3). – MS (EI, 70 eV): m/z (%) = 200 (100) [M^+], 185 (69) [$\text{M}^+ - \text{CH}_3$], 171

(6) [C₁₃H₁₅], 157 (69) [C₁₂H₁₃], 143 (54) [C₁₁H₁₁], 129 (86) [C₁₀H₉], 115 (42) [C₉H₇].

1,1'-Bis[(1R)-1,7,7-trimethylbicyclo[2.2.1]hept-2-en-2-yl]ferrocene (4)

To a magnetically stirred solution of 0.80 g (4.0 mmol) **2** in 10 ml of petroleum ether a solution of *tert*-butyllithium in petroleum ether (8 ml, 4.0 mmol) was added at room temperature and stirring was continued for 24 h. The supernatant solution was decanted from the white precipitate of the lithium salt **3**, which was dried *in vacuo* and dissolved in 10 ml of tetrahydrofuran. 0.61 g (2.0 mmol) of solid FeBr₂(DME) was added and the mixture was stirred magnetically for 14 h. The solvent was evaporated, the residue was extracted with petroleum ether and the crude product was isolated by evaporation. Recrystallization from diethyl ether/acetonitrile gave 0.35 g of analytically pure ferrocene **3**. The mother liquor was evaporated to dryness, the waxy residue was dissolved in a minimum amount of petroleum ether and subjected to column chromatography (silica gel in petroleum ether, column length 20 cm, inner diameter 1.5 cm). From the orange main fraction another 0.10 g of **3** could be isolated. Total yield 0.45 g (0.99 mmol, 49.5%). Crystallization from pentane at ambient temperature gave single crystals suitable for X-ray diffraction – ¹H-NMR (400.13 MHz, C₆D₆): δ = 5.98 (d, ³J_{H,H} = 3.1, olefin-H), 4.28 (m, 1H, ring H), 4.23 (m, 1H, ring H), 4.14 (m, 2H, ring H), 2.25 (t, 1H, ³J_{H,H} = 7.0, allyl-H), 1.86 (m, 2H, CH₂), 1.55 (m, 2H, CH₂), 1.26 (s, 3H, CH₃), 1.01 (s, 3H, CH₃), 0.77 (s, 3H, CH₃). – ¹³C-NMR (100.61 MHz, C₆D₆, 363 K): δ = 146.5 (s, olefin C), 130.3 (d, ¹J_{C,H} = 165, olefin CH), 83.6 (s, ring C), 69.8 (dm, ¹J_{C,H} = 174 Hz, ring CH), 69.7 (dq, ¹J_{C,H} = 174 Hz, ring CH), 68.3 (dq, ¹J_{C,H} = 175/6.3, ring CH), 67.5 (dq, ¹J_{C,H} = 175/6.3, ring CH), 57.0 (s, CMe₂), 55.7 (s, CMe), 52.4 (d, ¹J_{C,H} = 144 Hz, sp³-CH), 32.5 (t, ¹J_{C,H} = 131 Hz, CH₂), 26.2 (t, ¹J_{C,H} = 131 Hz, CH₂), 20.4 (qq, ¹J_{C,H} = 125/4.0, propylidene CH₃), 19.9 (qq, ¹J_{C,H} = 125/4.0, propylidene CH₃), 13.3 (q, ¹J_{C,H} = 125 Hz, CH₃). – MS (EI, 70 eV): *m/z* (%) = 453.9 (100) [M⁺], 425.9

(20) [M⁺ – C₂H₄], 397.9 (15) [M⁺ – C₄H₈]. – C₃₀H₃₈Fe (454.483), calcd. C 79.28, H 8.43; found C 79.36, H 8.44.

Alternative procedure for the preparation of 4

1,1'-Bis[(1R,2S)-2-exo-hydroxy-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl]ferrocene was prepared as starting compound according to lit. [9]. To a solution of 3.84 g (7.83 mmol) of this compound in 100 ml of diethyl ether 1.49 g (7.83 mmol) of *p*-toluenesulfonic acid was added and the mixture was stirred at room temperature for 4 h. Then 40 ml of distilled water was added, the organic phase was washed with 20 ml of saturated sodium carbonate solution and dried with sodium sulfate. Removal of the solvent *in vacuo* gave 3.23 g of complex **4** as a red, microcrystalline powder (91%).

Crystal structure determination of 4

IPDS diffractometer with imaging system (Stoe), Mo-K_α radiation, λ = 71.073 pm, 2θ_{max} = 52.0°, T = 293(2) K, crystal dimensions 0.60 × 0.40 × 0.20 mm³, orthorhombic, space group P2₁2₁2₁ (no. 19), lattice parameters: a = 7.7163(4), b = 10.7381(6), c = 28.804(2) Å, V = 2386.7(3) Å³, Z = 4, ρ_{calc.} = 1.265 g cm⁻³, μ(Mo-K_α) = 6.47 cm⁻¹, empirical absorption correction (MULABS/PLATON 98), transmission factors 0.7105 to 0.6461. Structure solution: direct methods (SHELXS-97), full-matrix least-squares refinement based on F_o² (SHELXL-97), 33347 reflections, 4659 unique reflections, 286 parameters, no restraints, R1(F_o>2σ(F_o)) = 0.0270, wR2 = 0.0707, R1 (all data) = 0.0284, wR2 = 0.0717, residual electron density +0.213 to -0.197 eÅ⁻³. Hydrogen atoms have been localized using the riding model provided with SHELXL-97.

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- [1] a) E. Winterfeldt, *Chem. Rev.* **93**, 827 (1993); b) R. L. Halterman in A. Togni, R. L. Halterman (eds): *Metallocenes*, vol. 1, p. 455–544, Wiley-VCH, Weinheim (1998).
- [2] K.-P. Zeller, Pentafulvene, in H. Kropf (ed.): *Houben-Weyl, Methoden der Organischen Chemie*, 4. ed., vol. V/2c, p. 504–684, Georg Thieme Verlag, Stuttgart (1985).
- [3] T. Dezember, H. Sitzmann, *Z. Naturforsch.* **52b**, 911 (1997).
- [4] G. Erker, C. Mollenkopf, *J. Organomet. Chem.* **483**, 173 (1994).
- [5] L. A. Paquette, K. J. Moriarty, J. A. McKinney, R. D. Rogers, *Organometallics* **8**, 1707 (1989).
- [6] a) R. L. Halterman, K. P. C. Vollhardt, *Tetrahedron Lett.* **27**, 1461 (1986); b) R. L. Halterman, K. P. C. Vollhardt, *Organometallics* **7**, 883 (1988).
- [7] E. Cesarotti, H. B. Kagan, R. Goddard, C. Krüger, *J. Organomet. Chem.* **162**, 297 (1978).
- [8] G. Erker, M. Aulbach, C. Krüger, S. Werner, *J. Organomet. Chem.* **450**, 1 (1993).
- [9] V. Dimitrov, M. Genov, S. Simova, A. Linden, *J. Organomet. Chem.* **525**, 213 (1995).