

Optically Active Transition-Metal Complexes. 102¹. Enantioselective Synthesis of 3-Oxabicyclo[3.3.0]oct-7-en-7-phenyl-6-on via Khand-Pauson Reaction

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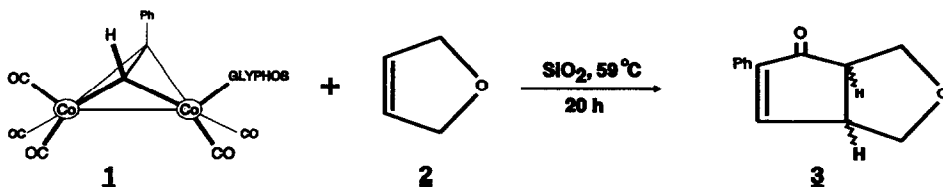
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Abstract: 3-Oxabicyclo[3.3.0]oct-7-en-7-phenyl-6-on is obtained in the enantioselective Khand-Pauson reaction of $(-)_546\text{-Co}_2(\text{CO})_5(\text{PhC}_2\text{H})$ - (GLYPHOS), GLYPHOS = (R)-(+)-2,3-O-isopropylidenglycerol-1-diphenylphosphane with 2,5-dihydrofuran. Complete resolution of the enantiomers can be achieved either by HPLC on tribenzoylcellulose or by fractional crystallization of an enantiomerically enriched sample from petroleum ether.

The Khand-Pauson reaction provides cyclopentenones by a single-step reaction of alkenes with binuclear alkynecobalt complexes. The product contains the alkyne unit and one carbonyl group of the complex as the olefinic ring fragment and the keto group. The olefin ends up as the saturated part of the cyclopentenone². In a previous study the use of $(-)_546\text{-Co}_2(\text{CO})_5(\text{PhC}_2\text{H})$ (GLYPHOS) **1**, containing (R)-(+)-2,3-O-isopropylidenglycerol-1-diphenylphosphane = GLYPHOS and a diastereomerically pure Co_2C_2 unit, enabled us to apply the Khand-Pauson reaction to asymmetric synthesis. The reaction of **1** with norbornene gave the corresponding optically pure cyclopentenone³. In order to extend the use of this asymmetric reaction type, we describe the enantioselective synthesis of the title compound **3** from **1** on SiO_2 and 2,5-dihydrofuran **2** (Scheme 1).

Scheme 1



High optical yields can be achieved if the epimerization of complex **1** is avoided, which proceeds in toluene at 60 °C with a half life of approximately 170 min³. As in the solid state epimerization is not observed, a solid state reaction with **1** on SiO₂ is the best choice to attain high optical inductions in the reaction of Scheme I⁴. Complex **1** is dissolved in CHCl₃ and mixed with dried silicagel. After removal of the solvent the reaction is started by adding 2,5-dihydrofuran. The results of the asymmetric Khand-Pauson reaction are summarized in Table 1.

Table 1

Solid state reaction of **1 on SiO₂ with 2,5-dihydrofuran at various temperatures.**

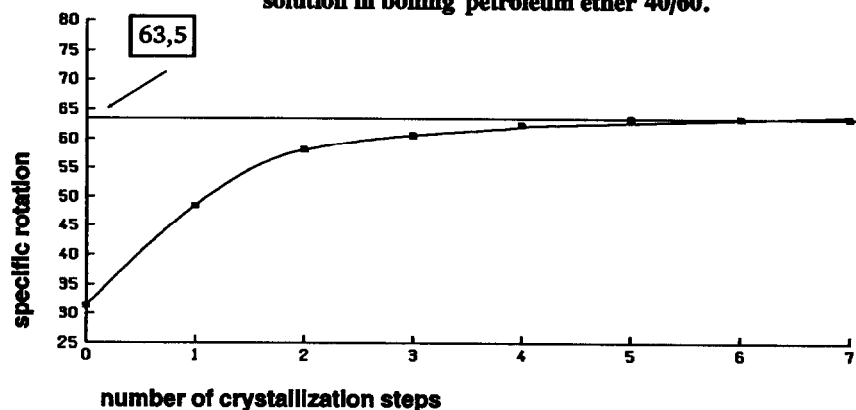
time [h]	temperature [°C]	chem. yield [%]	specific rotation *	ee %
175	37	22	+ 32,4	50,7
93	41	33	+ 33,6	62,4
68	45	42	+ 30,2	47,3
70	50	50	+ 35,4	55,4
20	59	35	+ 37,8	59,1
20	59	41	+ 37,6	58,8

* Measured at 589 nm, 25 °C (c 1, benzene).

Rate and enantiomeric excess increase with increasing temperature, the highest enantioselectivity with 59 %ee being observed at 59 °C. The boiling point of 2,5-dihydrofuran at 67 °C limits investigations at higher temperatures. The optical purities of the samples obtained in the asymmetric Khand-Pauson reactions were determined by comparison of the $[\alpha]_D$ values with that of an enantiomerically pure sample of **3**.

Figure 1

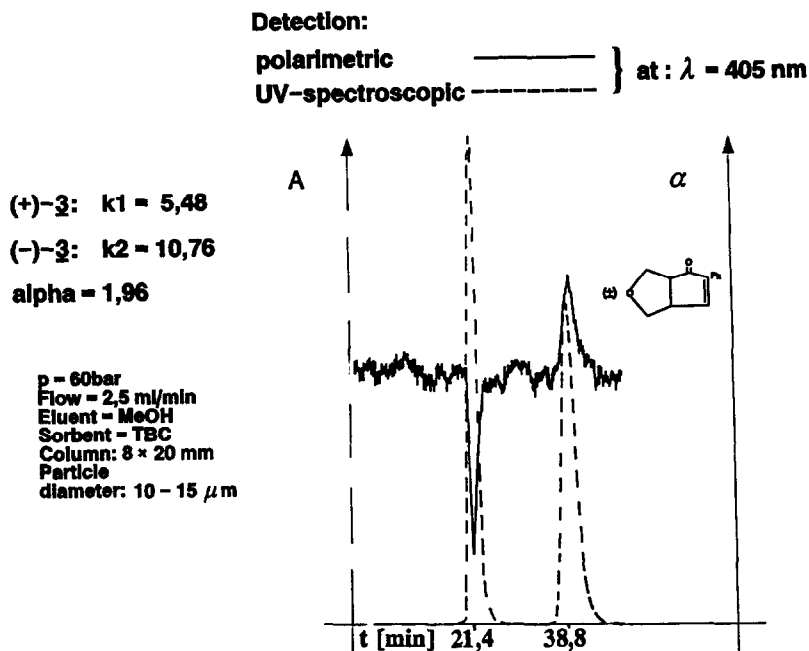
Optical resolution of **3 by repeated crystallization from a saturated solution in boiling petroleum ether 40/60.**



Optically pure **3** is obtained in (i) the resolution of an enantiomerically enriched sample of **3** by fractional crystallization from petroleum ether (Figure 1) and (ii) the chromatographic resolution of a racemic mixture of **3** by HPLC on tribenzoylcellulose as stationary phase (Figure 2)⁵. The melting points of racemic **3** (64–65 °C) and enantiomerically pure **3** (100–101 °C) differ by 36 °C.

Figure 2

Chromatogram of a racemate of **3.**



(-)₅₄₆-Co₂(CO)₅(PhC₂H)(GLYPHOS) (1**)**

(±)₅₄₆-Co₂(CO)₅(PhC₂H)(GLYPHOS) was prepared as described³. To improve the chromatographic separation from Co₂(CO)₄(PhC₂H)(GLYPHOS)₂, the eluent given in ref. 3 is replaced by petroleum ether/ethylacetate 4:1. Yield: 66 %.

1 was obtained by fractional crystallization. 19,1 g of (±)₅₄₆-Co₂(CO)₅(PhC₂H)(GLYPHOS) is dissolved in 100 ml of petroleum ether. The solution is kept 4 days at -25 °C. The precipitate is filtered off and recrystallized again from 50 ml of petroleum ether. The yield of diastereomerically pure **1** is 4,58 g. Optical rotation: $[\alpha]_{546}^{25} -175$ (c 0.35, benzene). At 589 nm the optical rotation of **1** is positive and not negative as erroneously given in ref 3.

Enantioselective Khand-Pauson reaction of **1 on SiO₂ with 2,5-dihydrofuran**

At room temperature, 1,11 g (1,68 mmol) of **1** was dissolved in 10 ml of CHCl₃ under N₂ protection. 20 ml of dried silicagel Si 60 (< 63 μm) was added and the solvent was removed while stirring. After addition of 2 ml (27,1 mmol) of 2,5-dihydrofuran the reaction mixture was stirred for 20 hours at 59 °C. Then the reaction mixture was poured into 100 ml of ethylacetate and filtered. The residue was washed with another 100 ml of ethylacetate. From the combined filtrates the solvent was evaporated. The residue was dissolved in 10 ml of petroleum ether/ethylacetate 3:1 and chromatographed with this eluent (column 30 x 3 cm, silicagel Si 60 (63 - 200 μm)). Kugelrohr distillation at 100-110 °C/10⁻³ Torr gave pure **3**. Yield: 116,5 mg, (35 %). Optical rotation: [α]_D²⁵ = 64, [α]₅₇₈²⁵ = 67, [α]₅₄₆²⁵ = 75, [α]₄₃₆²⁵ = 132 (c 0.46, benzene). IR (KBr): 1680 cm⁻¹ (C=O). ¹H-NMR (CDCl₃): δ = 3,12 (m, 1 H, C-H), 3,55 (m, 1H, C-H), 3,68 - 4,26 (m, 4H, 2 x CH₂), 7,25 - 7,42 (m, 3H, C-H olefin and 2 x Ar-H), 7,65 - 7,71 (m, 3H, Ar-H).

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References

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