Pergamon

Tetrahedron Letters, Vol. 35, No. 26, pp. 4543-4546, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $7.00+0.00

0040-4039(94)00871-X

An Approach to Chiral η^4-Butadiene-Fe(CO)$_3$ Complexes *via* Diastereoselective Complexation of Nonracemic 2-Alkoxy-4-vinyl-2,5-dihydrofuran Derivatives

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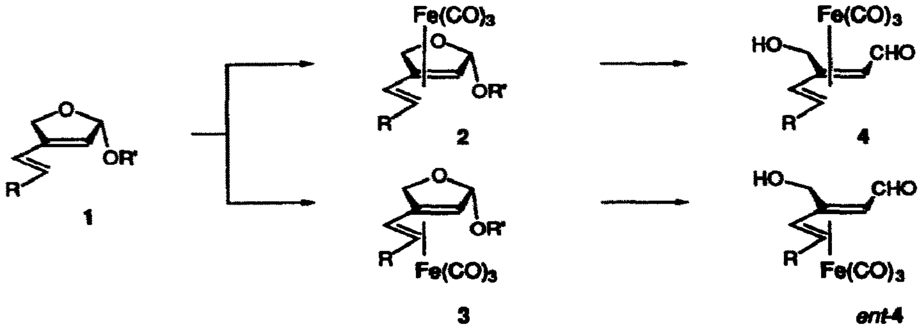
Abstract: Complexation of (+)-*L*-arabinose-derived 2-benzyloxy-4-vinyl-2,5-dihydrofuran derivatives (8) with $Fe_2(CO)_9$ in ether proceeds diastereoselectively providing a (separable) mixture of the corresponding *exo*- and *endo*- η^4-diene-Fe(CO)$_3$ complexes 9 and 10 in a ratio of about 1 : 3. The relative (and absolute) configuration of the complexation products was determined by a combination of analytical methods (CD, NMR, X-ray).

Due to their interesting chemical and stereochemical properties, chiral η^4-1,3-butadiene-Fe(CO)$_3$ complexes of both cyclic[1] and acyclic[2] diene ligands offer as synthetic building blocks new strategies for the total synthesis of biologically active compounds[3]. If in the course of a synthesis, new, permanent chirality centers are generated diastereoselectively under the influence of the chiral metal-complex substructure, the competitiveness of such syntheses depends to a large extent on the accessibility of the starting complexes in optically active form.

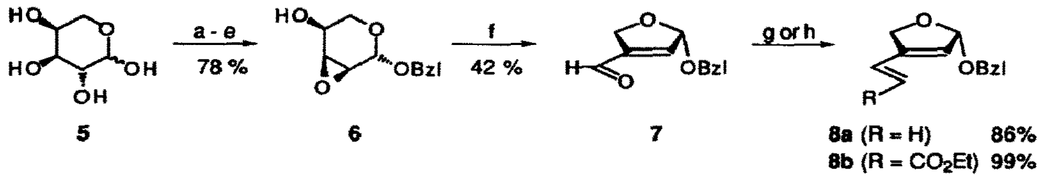
The techniques reported in the literature for the preparation of nonracemic η^4-Fe(CO)$_3$ complexes of prochiral diene ligands[2,4] are almost exclusively grounded on the resolution of racemic mixtures[5]. In contrast, we here describe an approach to such compounds, which is based on the diastereoselective complexation of enantiomerically pure diene ligands containing an easily removable (disposable) chirality center (Scheme 1).



Scheme 1

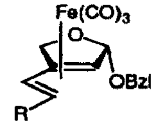
As chiral ligands, we decided to investigate 2-alkoxy-4-vinyl-2,5-dihydrofuran derivatives of type **1**. These compounds possess a removable chirality center (acetal carbon) close to the diene unit. Furthermore, the orientation of the alkoxy (OR') substituent is conformationally restricted due to the presence of the five-membered ring. Thus, complexation should more or less selectively furnish the diastereomeric products **2** or **3**, which (after separation) should be, for instance, hydrolizable to the optically active aldehyde complexes of type **4** (or *ent*-**4**, respectively).

The synthesis of the chiral diene ligands[6] was carried out according to Scheme 2. First, the epoxide **6** was prepared from (+)-*L*-arabinose (**5**) in 78% overall yield using modified literature procedures[7]. By employing the method of Magnusson[8], **6** was transformed to the aldehyde **7**, which was then converted to the dienes **8a** and **8b**, respectively, under standard Wittig conditions.

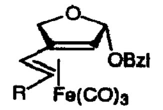


Scheme 2: a) BzlOH, $HCl_{(g)}$, 0 °C → r.t., 12 h; b) 2,2-dimethoxypropane, p-TsOH, reflux, 2 h; c) p-TsCl, pyridine, r.t., 2 d; d) 1 N HCl, THF, r.t. → 50 °C, 12 h; e) NaOMe, MeOH, 0 °C → r.t., 12 h; f) 4.1 eq. LiBr, 4.1 eq. TMU, toluene, reflux, slow addition of **6**, 90 min; g) $Ph_3P{=}CH_2$, THF, -90 °C → 0 °C, 3 h; h) $Ph_3P{=}CHCO_2Et$, THF, 50 °C, 4 h;

Complexation of these ligands (**8**) with $Fe_2(CO)_9$ (2.0 eq., 4 - 5 h reflux) furnished a mixture of the *exo*- and *endo*- diastereomers **9** and **10** in varying ratios dependent on the solvent used (Table 1)[9]. The highest yields and selectivities were obtained in ether. The prevailing formation of the (sterically less favored) *endo*-isomers **10** under these conditions can presumably be rationalized in terms of a primary coordination of the $Fe(CO)_x$ species to the oxygen of the benzyloxy substituent[10]. Thus, an *endo*-η²-complex of type **11** might be formed as an intermediate which in turn could directly pass into the observed major product **10**.



9a (R = H)
9b (R = CO_2Et)



10a (R = H)
10b (R = CO_2Et)

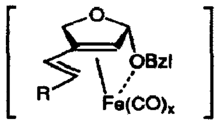


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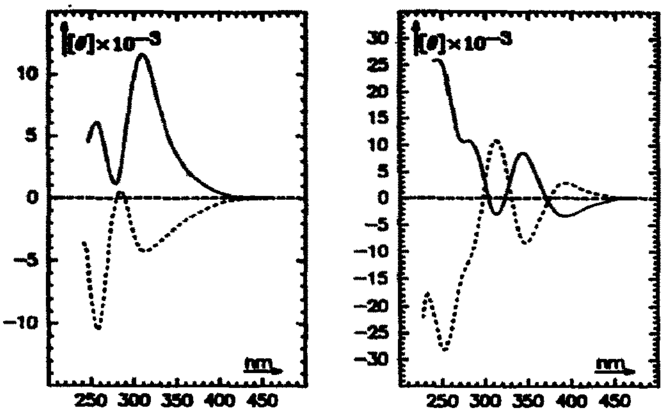
Table 1: Complexation of dienes **8a/b** with $Fe_2(CO)_9$:

entry	diene	solvent	yield (%)	**9** : **10**[a)]	separated products[b)] yields (%)	
1	**8a**	Et_2O	77	32 : 68	**9a**: 24	**10a**: 52
2	**8a**	*n*-heptane	85	59 : 41	**9a**: 48	**10a**: 35
3	**8a**	toluene	75	43 : 57	----	----
4	**8b**	Et_2O	90	25 : 75	**9b**: 20	**10b**: 59

a) ratio determined from the ¹H NMR spectra of the purified diastereomer mixture; b) isolated after flash chromatography.



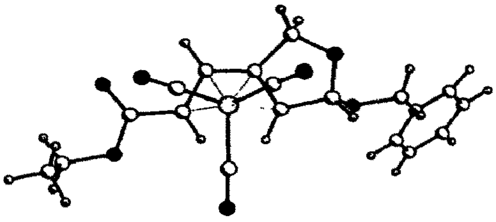


Figure 1: CD spectra in MeOH : left: **9a** (——), and **10a** (----); right: **9b** (——), and **10b** (----)

Figure 2: Structure of **9b** in the solid state[12]

The mixtures of diastereomeric complexes (**9a**/**10a** and **9b**/**10b**, respectively) were found to be easily separable by flash chromatography. The CD spectra of the pure complexes (Figure 1) displayed a pseudo-enantiomorphic behaviour for each pair of diastereomers. The relative configuration of the ester complexes **9b** and **10b** was (primarily) assigned by correlating the Cotton effects at about 400 nm with the data of Grée[11], and later confirmed by a single crystal X-ray analysis of **9b** (Figure 2)[12]. The configuration of **9a** and **10a** could then be assigned by comparison of their ^{1}H NMR spectra (270 MHz, $CDCl_3$) with those of **9b** and **10b**. In particular, the signal of the acetal hydrogen exhibited a characteristic pattern: In the case of the *exo*-isomers **9a** and **9b** this signal appeared as a pseudo-singlet at ca. 5.2 ppm, while for the *endo*-isomers **10a** and **10b** it showed up as a doublet (J = 2-3 Hz) at about 5.5 ppm in both cases.

In conclusion, we have elaborated a new entry to chiral butadiene-$Fe(CO)_3$ complexes of type **2** and **3** of known absolute and relative configuration in enantiomerically pure form. These compounds (especially the *endo*-complexes **3**) are now accessible in sufficient quantities to allow further investigations. Some synthetic transformations, e.g. the preparation of complexes **4** and *ent*-**4**, respectively, by acetal hydrolysis, are described in the accompanying paper[13].

Acknowledgement. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We also thank Prof. Dr. G. Quinkert, Frankfurt, for generous support.

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12. X-ray crystal structure analysis of **9b**: Enraf-Nonius CAD4 diffractometer, $Cu_{k\alpha}$ radiation, quadrant: $2 < 2\Theta < 60$ °, octant: $60 < 2\Theta < 120$ °; empirical absorption correction based on ψ-scans; structure determination with direct methods (SHELXS 86); the positions of the non-H atoms were determined by difference syntheses, and the hydrogen atoms in calculated positions were not refined. $C_{19}H_{18}FeO_7$, orthorhombic, space group $P2_1P2_1P2_1$ (no. 19), a = 8.030(3) Å, b = 8.063(3) Å, c = 59.314(11) Å, V = 3840(4) Å^3, Z = 8 (two independent molecules), ρ_{calc} = 1.433 g/cm^3; 3476 independent reflections, of which 3208 with $I > 0$ were used, R = 0.107, R_ω = 0.067. The residual density was less than 0.68 e/Å^3. The enantiomorphic structure gave R = 0.148 and R_ω = 0.126 and could thus be excluded. Further details of the crystal structure investigation may be obtained from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, Germany on quoting the depository number CSD-55895.
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(*Received in Germany* 29 *March* 1994; *accepted* 5 *May* 1994)