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Photolytic induction of the asymmetric catalytic complexation of prochiral cyclohexa-1,3-dienes by the tricarbonyliron fragment[1]

Hans-Joachim Knölker,* Holger Hermann and Daniela Herzberg

Institut für Organische Chemie, Universität Karlsruhe, Richard-Willstätter-Allee, 76131 Karlsruhe, Germany. E-mail: knoe@ochhades.chemie.uni-karlsruhe.de

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Photolytic induction of the asymmetric catalytic complexation of prochiral cyclohexa-1,3-dienes by the tricarbonyliron fragment using a camphor-derived azadiene catalyst provides the corresponding tricarbonyliron complexes quantitatively in up to 86% ee.

Asymmetric catalysis provides the most efficient access to enantiopure compounds for organic synthesis starting from achiral precursors because only catalytic amounts of the chiral auxiliary are required.[2] We recently reported a novel method of asymmetric catalysis which transforms prochiral dienes into their planar-chiral tricarbonyl(η⁴-diene)iron complexes. Tricarbonyl(η⁴-diene)iron complexes have found numerous applications to stereoselective organic synthesis.[3] Therefore, a simple and versatile access to the chiral complexes in enantiomerically pure form would open up new routes for enantioselective synthesis. We now report that the asymmetric catalytic complexation of prochiral cyclohexa-1,3-dienes proceeds much more efficiently by photolytic induction.

The reaction of dienes with tricarbonyliron transfer reagents provides a much better access to the corresponding iron complexes than direct complexation with pentacarbonyliron.[4] Enantioselective complexations of prochiral 1,3-dienes were achieved with moderate enantioselectivity using chiral tricarbonyl(η⁴-1-oxadiene)iron complexes as transfer reagents.[5] Recently we introduced (η⁴-1-azadiene)tricarbonyliron complexes as a novel class of tricarbonyliron transfer reagents.[6] Moreover, the 1-azadienes represent highly efficient catalysts for the catalytic complexation of dienes with pentacarbonyliron.[7] Most noteworthy using chiral 1-azadienes an asymmetric catalytic complexation of prochiral cyclohexa-1,3-dienes was achieved.[8] The highest asymmetric inductions were obtained by using chiral catalysts which have a fixed s-*cis* conformation of the 1-azadiene moiety. These 1-azadiene catalysts are easily prepared by aldol condensation of a chiral cyclic ketone with *p*-methoxybenzaldehyde and subsequent imine formation with *p*-anisidine. Thus, (1*R*)-(+)- and (1*S*)-(−)-camphor were transformed to (*R*)-**1** and (*S*)-**1**, (1*R*)-(+)-nopinone to (*R*)-**2**, and (+)-estrone methyl ether to (−)-**3** [$[\alpha]_D^{20}$ −318.1 (*c* 0.53, $CHCl_3$)]. The catalyst (*R*)-**4** was prepared by imine condensation of *o*-anisidine with (1*R*)-(−)-myrtenal.

Catalyst **1** showed the highest enantioselectivity in the asymmetric catalytic complexation of 1-methoxycyclohexa-1,3-diene **5a** which was performed in benzene at reflux with exposure to daylight. An extensive reinvestigation of the asymmetric catalytic complexation of **5a** using catalyst (*R*)-**1** revealed two important aspects (Table 1). First, the result is strongly dependent on the amount of catalyst applied. Higher turnovers and asymmetric inductions are obtained at higher concentrations of the catalyst (*R*)-**1**. Second, the asymmetric catalysis is influenced by light, perhaps due to a photolytically induced loss of a carbon monoxide ligand (compare our proposed mechanism).[7b,8c] In the dark the reaction proceeds much more slowly and using catalytic amounts of (*R*)-**1** also the ee of the product is lower in the absence of light. After reaction for 7 d with exclusion of light in the presence of 4 equiv. of (*R*)-**1** the asymmetric complexation of **5a** provides a result (99% yield, 88% ee of the *S* enantiomer) which is comparable with respect to yield and ee to the corresponding outcome obtained in the presence of daylight after 2 d.

Based on the experimental observations described above, we hoped to exploit the photolytic induction of the asymmetric complexation in order to achieve a quantitative reaction with high asymmetric induction (> 85% ee) by using only catalytic amounts of the chiral 1-azadienes with shorter reaction times. Therefore, we investigated the asymmetric catalytic complexation of **5a** with pentacarbonyliron in benzene at reflux on irradiation with a 10 W halogen lamp using the catalysts (*R*)-**1** to (*R*)-**4** (Scheme 1, Table 2). The ee values were determined accurately *via* separation of the two enantiomers by chiral HPLC on a cyclodextrin column.[9] To avoid the formation of hexacarbonyldiiron clusters,[7b,8c] the excess of pentacarbonyliron was reduced to 1.5 equiv. based on the diene. A blank experiment (complexation without catalyst) demonstrated that photolytic induction in contrast to the solely thermal conditions promotes also the uncatalyzed complexation, which leads to the formation of racemic product (compare also the two blank experiments in Table 1). However, the catalytic complexation proceeds much faster and therefore, this pathway predominates. The camphor-derived catalyst **1** proved to be the best for the photolytically induced asymmetric catalytic complexation and

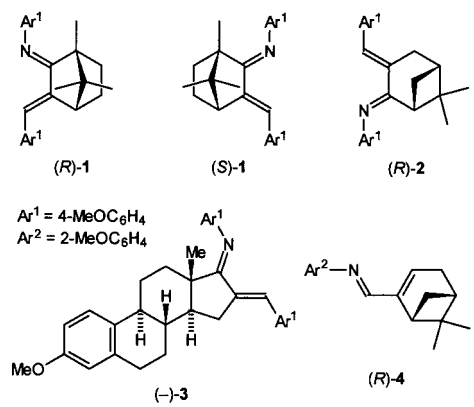
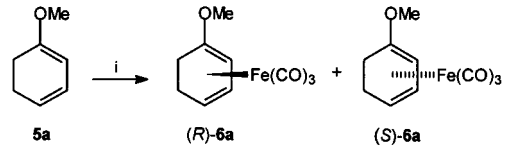


Table 1 Asymmetric catalytic complexation of **5a** with catalyst (*R*)-**1**: variation of the reaction conditions[a]

(*R*)-**1**/equiv.	$Fe(CO)_5$/ equiv.	Conditions	Yield (%)	Ee (%)[b]
0.0	4.0	2 d, daylight	26	—
0.125	4.0	2 d, daylight	62	56 (*S*)
0.25	4.0	2 d, daylight	66	73 (*S*)
0.25	4.0	12 d, daylight	99	73 (*S*)
0.50	4.0	2 d, daylight	87	80 (*S*)
1.0	4.0	2 d, daylight	94	83 (*S*)
2.0	4.0	2 d, daylight	98	86 (*S*)
4.0	4.0	2 d, daylight	96	89 (*S*)
0.0	4.0	9 d, dark	2	—
0.25	4.0	2 d, dark	3	53 (*S*)
0.25	4.0	14 d, dark	14	56 (*S*)
4.0	4.0	7 d, dark	99	88 (*S*)

[a] *Reaction conditions*: **5a**, (*R*)-**1**, $Fe(CO)_5$, C_6H_6, 80 °C. [b] Ee determined by chiral HPLC (absolute configuration) (ref. 9).



5a (*R*)-6a (*S*)-6a

Scheme 1 *Reagents and conditions*: i, $Fe(CO)_5$ (1.5 equiv.), catalyst (0.25 equiv.), benzene, 80 °C, *hν* (10 W halogen lamp, 12 V).

Table 2 Photolytically induced asymmetric catalytic complexation of **5a** with $Fe(CO)_5$ to give **6a**: variation of the catalyst[a]

Catalyst	*t*/d	Yield (%)	Ee (%)[b]	$[\alpha]_D^{20}(c)$[c]
—	1	20	0	—
(*R*)-**4**	2	98	39 (*R*)	−54.0 (1.02)
(−)-**3**	2	94	57 (*R*)	−83.5 (0.97)
(*R*)-**2**	5	92	59 (*S*)	+87.4 (0.96)
(*S*)-**1**	1	99	85 (*R*)	−127.3 (1.00)
(*R*)-**1**	1	97	86 (*S*)	+130.0 (1.09)

[a] All reactions were performed using 0.25 equiv. of catalyst, 1.5 equiv. of $Fe(CO)_5$ and a 10 W halogen lamp (12 V) in benzene at 80 °C. [b] Ee determined by chiral HPLC (absolute configuration) (ref. 9). [c] Specific rotation in $CHCl_3$ (concentration).

led to a quantitative complexation within only one day. Using the 1-azadiene (*R*)-**1** complex (*S*)-**6a** was obtained in 86% ee (Fig. 1) and (*S*)-**1** provided complex (*R*)-**6a** in 85% ee.† The previous procedure for asymmetric catalytic complexation using the same catalyst afforded complex **6a** quantitatively after a reaction time of 12 days and with 73% ee of either enantiomer.[8c] Also for the other catalysts application of the photolytic induction led to a significant increase of the asymmetric induction compared to the result of the thermally induced catalytic complexation.

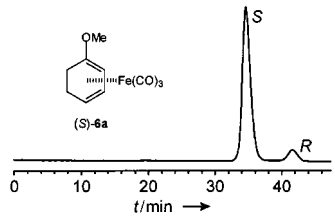
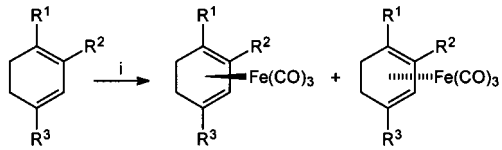


Fig. 1 Chiral HPLC on a permethylated β-cyclodextrin column of complex **6a** with 86% ee of the (*S*)-(+) enantiomer.

We investigated the photolytic induction of the asymmetric catalytic complexation for a series of prochiral cyclohexa-1,3-dienes **5** using the chiral catalysts (*R*)-**1** and (*S*)-**1** (Scheme 2, Table 3). Quantitative yields should be available in all cases simply by extension of the reaction time. However, further optimization was not executed because at this stage of our studies we were primarily interested in the enantioselectivity of the reaction. The asymmetric induction for the catalytic complexation of **5b**,**c** and **e** was in the range of 70–80% ee. Complex **6d**, a potential precursor for discorhabdin alkaloids,[10] was obtained in 50% ee for either enantiomer. The photolytically induced asymmetric catalytic complexation of **5f** with pentacarbonyliron using the catalysts (*R*)-**1** and (*S*)-**1** provided only 42% ee for either enantiomer of the corresponding tricarbonyliron complex. In this case however, the estrone-



5a–e 5f (*R*)-6a–e (*S*)-6f (*S*)-6a–e (*R*)-6f

Scheme 2 *Reagents and conditions*: i, $Fe(CO)_5$ (1.5 equiv.), (*R*)-**1** or (*S*)-**1** (0.25 equiv.) respectively, C_6H_6, 80 °C, *hν* (10 W halogen lamp, 12 V).

Table 3 Photolytically induced asymmetric catalytic complexation of the prochiral cyclohexa-1,3-dienes **5** with $Fe(CO)_5$ to give **6** using the camphor-derived azadiene catalysts (*R*)-**1** and (*S*)-**1** [a]

					(*R*)-**1**/(*S*)-**1**	
5	R^1	R^2	R^3	*t*/d	Yield (%)	Ee (%)[b]
a	OMe	H	H	1	97/99	86 (*S*)/85 (*R*)
b	OPr^i	H	H	3	78/82	79 (+)/81 (−)
c	OMe	H	Me	2	86/81	72 (*S*)/73 (*R*)
d	OMe	H	CH_2CO_2Me	2	93/89	50 (*S*)/50 (*R*)
e	H	CO_2Me	H	1	90/87	76 (−)/74 (+)
f	CO_2Me	H	H	1	81/77	42 (−)/42 (+)

[a] All reactions were performed using 0.25 equiv. of catalyst, 1.5 equiv. of $Fe(CO)_5$ and a 10 W halogen lamp (12 V) in benzene at 80 °C. [b] Ee determined by chiral HPLC (absolute configuration or, respectively, direction for rotation of the plane of polarized light) (ref. 9).

derived catalyst (−)-**3** was superior and afforded after 2 d complex **6f** in 87% yield and 57% ee of the (+)-enantiomer.

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Notes and references

† Photolytically induced asymmetric catalytic complexation of **5a**: The 1-azadiene (*R*)-**1** or (*S*)-**1** (188 mg, 0.50 mmol) was added to a solution of 1-methoxycyclohexa-1,3-diene **5a** (220 mg, 2.00 mmol) and pentacarbonyliron (395 μl, 588 mg, 3.00 mmol) in anhydrous, degassed benzene (30 ml) under an argon atmosphere. The solution was heated at reflux for 24 h and irradiated with a 10 W halogen lamp (Osram 64415S, 12 V) positioned about 20 cm from the flask. Evaporation of the solvent and flash chromatography (pentane) of the residue on silica gel afforded (*S*)-**6a** (484 mg, 97%) [$[\alpha]_D^{20}$ +130.0 (*c* 1.09, $CHCl_3$)], or respectively, (*R*)-**6a** (497 mg, 99%) [$[\alpha]_D^{20}$ −127.3 (*c* 1.00, $CHCl_3$)] as yellow oils.

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