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A CATALYTIC ASYMMETRIC SYNTHESIS OF *cis*-DECALIN DERIVATIVES VIA π-ALLYLPALLADIUM INTERMEDIATES

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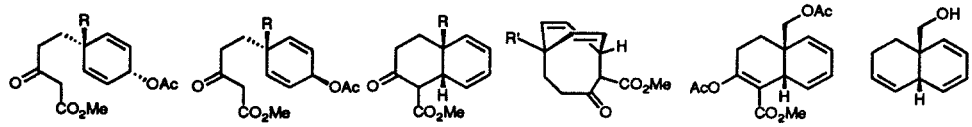
Abstract: The usefully functionalized *cis*-decalin derivative **6** has been synthesized in up to 83% ee through the π-allylpalladium intermediate starting with the prochiral allylic acetate **3**.

In the preceding paper we have shown that treatment of prochiral allylic acetates such as **1** with a catalytic amount of $Pd(PPh_3)_4$ and 1.2 equiv of NaH affords usefully functionalized *cis*-decalin derivatives such as **5** in high yields, which are efficiently converted to *trans*-decalin derivatives.[1] Herein, we report an application of the above-mentioned methodology to a catalytic asymmetric synthesis of *cis*-decalin derivatives.

First of all, a catalytic asymmetric synthesis of **5** utilizing **1** as a prochiral substrate was carefully investigated. Treatment of **1**[1] with Pd(0), generated in situ from $Pd(OAc)_2$ (10 mol %) and BuLi (20 mol %), (*R*)-(*S*)-BPPFA[2] (10 mol %) and NaH (1.2 equiv) in CH_3CN at 25 °C for 10 min gave **5** of 47% ee (62%) accompanied with **7** (19%).[3] Among several solvents examined, THF was found to afford the best result. That is, reaction of **1** in THF furnished **5** of 52% ee together with **7** (19%),[3] and use of DMSO and DMF provided **5** of 31% and 44% ees, respectively. Other representative bidentate ligands such as (*S, S*)-chiraphos and (*S*)-BINAP gave the less satisfactory results, furnishing **5** of 37% (chiraphos) and 30% (BINAP) ees, respectively.[4] Encouraged by these interesting results, a catalytic asymmetric synthesis utilizing **2** was also investigated. It was found that treatment of **2**[1] with Pd(0), generated in situ from $Pd(OAc)_2$ (10 mol %) and BuLi (20 mol %), (*R*)-(*S*)-BPPFA (10 mol %) and NaH (1.2 equiv) in THF at 25 °C afforded **5** of 37% ee (21%) together with **7** (35%).[5] The results are summarized in Table 1. The enantiomeric excess (ee) was unequivocally determined by the HPLC analysis (DAICEL CHIRALCEL OJ, hexane:2-propanol, 9:1) of the corresponding enol acetate **9** obtainable on treatment with acetic anhydride, triethylamine and 4-dimethylaminopyridine in CH_2Cl_2 (97%), and assignment of the absolute configuration was achieved by converting **5** to the known decalin derivative **10**.[6]

With the aim of synthesizing the *cis*-decalin derivative of higher ee, asymmetric cyclization of the prochiral allylic acetates **3** and **4** was next examined. After many experiments, it was found that treatment of **3** with Pd(0), generated in situ from $Pd(OAc)_2$ (10 mol %) and BuLi (20 mol %), (*R*)-(*S*)-BPPFA (10 mol %) and LiOAc (5 equiv) in THF at 20 °C for 2 hr gave the best result, providing **6** with 83% ee (34%) together with the 8-membered product **8** (51%).[7] Likewise, the prochiral β-acetate **4** was transformed into the *cis*-decalin derivative **6** with 46% ee (20%) and **8** (26%)[5] on treatment with Pd(0) (10 mol %), (*R*)-(*S*)-BPPFA (10 mol %) and K_2CO_3 (1 molar equiv) in THF at 40 °C for 33 hr. The results are summarized in Table 2. The *cis*-decalin derivative **6** was converted to **5** in 51% overall yield by treatment with NaH followed by chemoselective reduction with $LiAlH_4$ and subsequent acetylation.

In conclusion, we have developed a catalytic asymmetric synthesis of usefully functionalized *cis*-decalin derivatives. Further work is in progress on the probable mechanism of asymmetric induction.



1: R= CH_2OAc
3: R= CO_2Me
2: R= CH_2OAc
4: R= CO_2Me
5: R= CH_2OAc
6: R= CO_2Me
7: R'= CH_2OAc
8: R'= CO_2Me
9
10

Figure 1

Table 1. Catalytic Asymmetric Synthesis of 5[a]

run	substrate	ligand (10 mol %)	solvent	temp. (° C)	time (hr)	product 5 yield, % (ee, %)	product 7 yield, %
1	1	(*S*, *S*)-chiraphos	THF	0	3	32 (37)	41
2	1	(*S*)-BINAP	THF	25	2	47 (30)	48
3	1	(*R*)-(*S*)-BPPFA	THF	25	1	74 (52)	19
4	1	(*R*)-(*S*)-BPPFA	CH_3CN	25	0.2	62 (47)	19
5	2	(*R*)-(*S*)-BPPFA	THF	25	1	21 (37)	35

[a] Pd(0), generated from $Pd(OAc)_2$ (10 mol %) and BuLi (20 mol %), and NaH (1.2 equiv) were utilized.

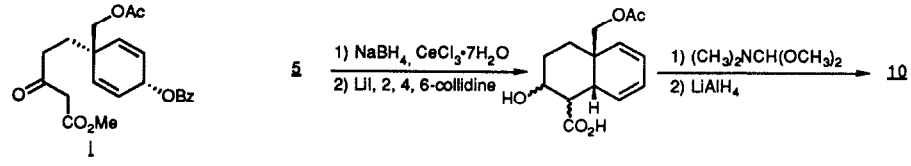
Table 2. Catalytic Asymmetric Synthesis of 6[a]

run	substrate	base (equiv)	temp. (° C)	time (hr)	product 6 yield, % (ee, %)	product 8 yield, %
1	3	LiOAc (5)	25	2	34 (83)	51
2	3	Bu_4NOAc (5)	25	2	23 (79)	43
3[b]	4	LiOAc (5)	20	42	15 (71)	36
4	4	K_2CO_3 (1)	40	33	20 (46)	26

[a] Pd(0), generated from $Pd(OAc)_2$ (10 mol %) and BuLi (20 mol %), (*R*)-(*S*)-BPPFA (10 mol %) and THF solvent were utilized.
[b] 4 was recovered (18%).

References and Notes

1. The preceding paper in this issue.
2. T. Hayashi, T. Mise, M. Fukushima, M. Kagotani, N. Nagashima, Y. Hamada, A. Matsumoto, S. Kawakami, M. Konishi, K. Yamamoto, and M. Kumada, *Bull. Chem. Soc. Jpn.*, **53**, 1138 (1980).
3. Use of LiOAc as a base afforded **5** of 45% ee (57%) together with **7** (34%).
4. Use of other prochiral substrates gave the less satisfactory results. For example, **i** was transformed into **5** of 49% ee (25%) and **7** (6%) [(*R*)-(*S*)-BPPFA-NaH].
5. The reason why the slightly lower ee was obtained is not clear at present.
6. Y. Sato, M. Sodeoka, and M. Shibasaki, *J. Org. Chem.*, **54**, 4738 (1989). Conversion to **10** is as follows.
7. Use of NaH as a base gave the less satisfactory result. The reason is not clear at present.



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