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ASYMMETRIC PAUSON-KHAND REACTIONS OF CHIRAL SULFINAMIDES: ASYMMETRIC SYNTHESIS OF 3-AZABICYCLO[3.3.0]OCT-5-EN-7-ONE DERIVATIVES

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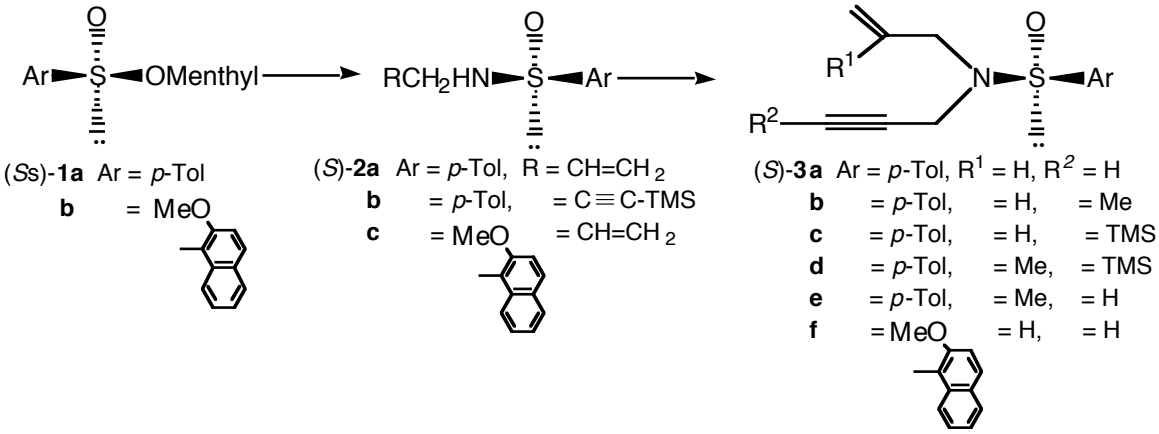
Abstract- Unprecedented asymmetric Pauson-Khand reactions of chiral sulfinamides are described. Cobalt-catalyzed reactions of chiral *N*-allyl-*N*-propargyl-*N*-arylsulfinamide derivatives were carried out in dichloromethane at -20°C ~ room temperature under carbon monoxide atmosphere in the presence of $Co_2(CO)_8$ to give chiral 3-azabicyclo[3.3.0]oct-5-en-7-one with moderate or low enantioselectivity.

A Pauson-Khand reaction is a useful and versatile method for the preparation of cyclic α,β-unsaturated ketones, especially 2-cyclopentenone derivatives. However, there have been published only a limited number of reports related to asymmetric Pauson-Khand reactions,[2] using substrates with chiral auxiliaries,[3] chiral ligands,[4] and others.[5] Currently, we are developing a new method for asymmetric Pauson-Khand reactions with (*S*)-methionine derivatives and disclosing the crucial participation of the organosulfur groups in the asymmetric induction.[6] Quite recently, unprecedentedly, we have successfully achieved very highly efficient catalytic asymmetric Pauson-Khand reactions with chiral phosphine ligands.[7] In the course of our research along this line, we have investigated so far the effects of a chiral organosulfinyl functionality in the Pauson-Khand reactions. We wish to communicate herein our recent work in asymmetric Pauson-Khand reactions using a chiral sulfinamide as a chiral source.

As chiral reaction substrates, optically pure sulfinamides ((*S*)-**3a-f**) were easily obtainable as follows. Allylamine was lithiated with *n*-butyllithium, followed by reaction with (-)-menthyl (*S*)-*p*-toluenesulfinate (**1a**) in THF at -78°C～room temperature, giving (*S*)-*N*-allyl-*p*-toluenesulfinamide (**2a**) in 95% yield.

The reaction of 3-(trimethylsilyl)propargylamine with (*S*)-**1a** was carried out in a similar way to give (*S*)-**2b** in 47% yield. The reaction of allylamine with (-)-menthyl (*S*)-2-methoxy-1-

naphthalenesulfinate (**1b**) in THF at -78°C～room temperature gave (*S*)-*N*-allyl-2-methoxy-1-naphthalenesulfinamide (**2c**) in 70% yield. The reactions of (*S*)-**2a** with propargyl bromide or 1-bromo-2-butyne using *n*-butyllithium as a base in THF at room temperature for 2 h afforded (*S*)-**3a,b** in 90 or 79% yield, respectively. Similarly, the reactions of (*S*)-**2a,b** with 3-bromo-1-(trimethylsilyl)propyne or 3-bromo-2-methylpropene gave (*S*)-**3c,d** in 91 or 54% yield, respectively. Desilylation of (*S*)-**3d** by treating with tetrabutylammonium fluoride furnished (*S*)-**3e**. *N*-Propargylation of (*S*)-**2c** was carried out in a similar way to afford (*S*)-**3f** in 69% yield.

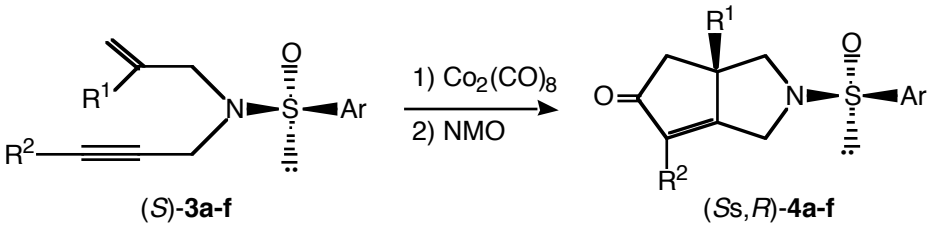


Scheme 1

The reaction of (*S*)-**3a** with $Co_2(CO)_8$ (1.2 equiv.) was carried out in dichloromethane at room temperature for 20 h in the presence of *N*-methylmorpholine *N*-oxide (NMO) (10 equiv.) to give (*Ss*,*R*)-**4a** in 79% yield with 38% diastereoselectivity. At lower reaction temperature (0 or -20°C), unexpectedly, decrease of the diastereoselectivity was observed; however, large decrease of the chemical yield was circumvented by extending the reaction time. The reactions of other substrates ((*S*)-**3b-e**) were carried out in dichloromethane at room temperature for 17-20 h to afford (*Ss*,*R*)-**4b-e** in good yields with rather low diastereoselectivity (10-18%).

Replacement of the *p*-tolyl group in (*Ss*)-**2a** with a sterically bulky substituent, a 2-methoxy-1-naphthyl group, could not improve the diastereoselectivity; the reaction of (*S*)-**3f** with $Co_2(CO)_8$ gave (*Ss*,*R*)-**4f** in 13% yield with 15% diastereoselectivity.

The diastereomeric excess (d.e.) of the products (**4a-f**) was determined by HPLC analysis



(*S*)-**3a-f** (*Ss*,*R*)-**4a-f**

Scheme 2

Table 1. The Intramolecular Asymmetric Pauson-Khand Reactions of (*S*)-**3a**-**f**[a)]

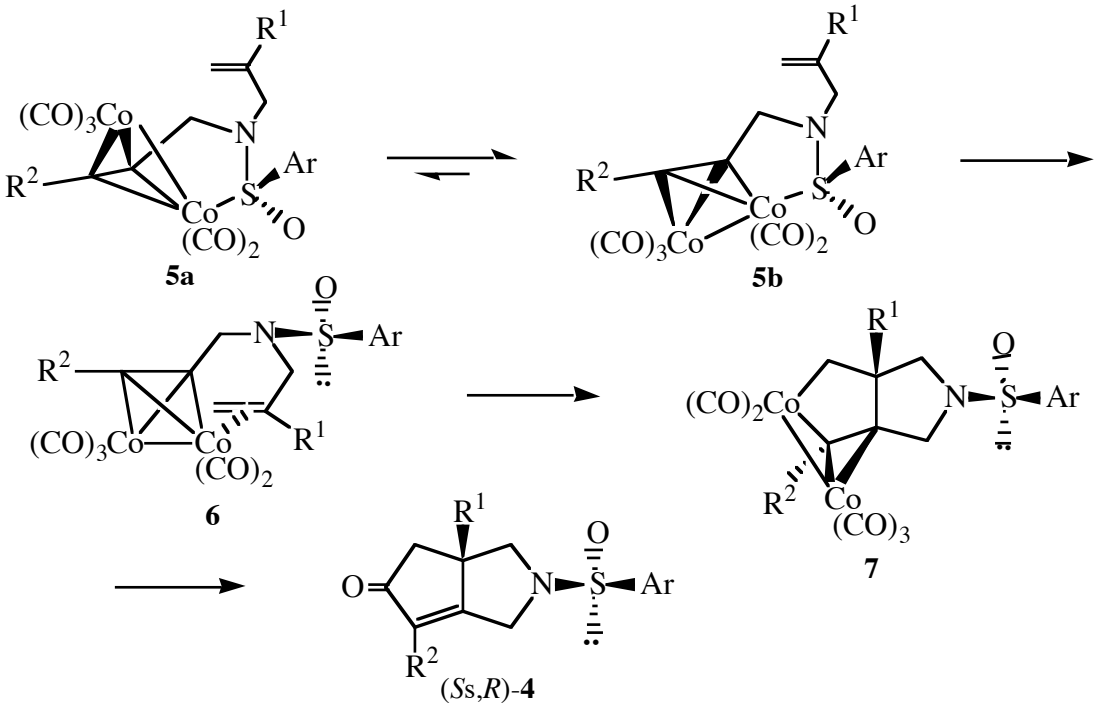
Substrate	Reaction temp. (℃)	Reaction time (h)	Yield (%) of (*S*s,*R*)-**4**	d.e. (%) of (*S*s,*R*)-**4**[b)]
3a	rt	20	79	38
3a	0	40	62	25
3a	-20	90	68	26
3b	rt	20	87	10
3c	rt	17	81	18
3d	rt	17	42	10
3e	rt	17	55	11
3f	rt	12	13	15

a) Each reaction was carried out in CH_2Cl_2 in the presence of $Co_2(CO)_8$ (1.2 equiv.), followed by treatment with NMO (10 equiv.).
b) The diastereomeric excess (d.e.) of the products (**4a-f**) was determined by the HPLC analysis with L-column ODS.

with L-column ODS. The results obtained are summarized in Table 1.

The absolute configuration of the products (**3a-f**) is deduced on the basis of the plausible mechanism of these cobalt-catalyzed reactions of the sulfinamides mentioned later.

The mechanism of the asymmetric induction with chiral sulfinamides is rationalized as follows. The sulfur atoms in the chiral sulfinamides would coordinate to the cobalt catalyst of the initially formed alkyne-cobalt complexes, forming five-membered chelates. In the conformational equilibrium of the diastereomeric alkyne-cobalt complexes (**5a,b**) coordinated by the sulfinyl sulfur atoms, **5b** would be preferentially formed in preference to **5a** because of the existence of steric hindrance between the aryl group and the alkyne-cobalt part in **5a**. Thus,the Pauson-Khand reaction would proceed through easy exchange of the



Scheme 3

ligand on the same coordination site of the cobalt catalyst from the sulfur atom (**5b**) of the sulfinamide to the olefin (**6**), giving (*S*s,*R*)-**4** *via* **7** with slightly low diastereoselectivity. Thus, conclusively, it should be noted that the chiral sulfinamide functionality involved in the substrates participated in Pauson-Khand reactions, achieving asymmetric carbon-carbon bond forming reactions to provide chiral 2-cyclopentenone derivatives. This work is the first example of the use of a chiral sulfinamide functionality in Pauson-Khand reactions.

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