ASYMMETRIC MICHAEL ADDITION REACTION OF METHYL PHENYLTHIOACETATE TO 2-CYCLOPENTENONE CATALYZED BY CHIRAL CROWN - KO*t*Bu COMPLEXES[1]

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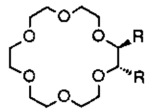
Abstract Asymmetric Michael addition reaction of methyl phenylthioacetate (**12**) to 2-cyclopentenone (**11**) using chiral crown ether - KO*t*Bu complexes as catalysts is reported. Crown (**7**) has been found to give **14** of 71%ee (enantiomeric excess).

The design of efficient catalysts for asymmetric induction has been a recent focus in synthetic organic chemistry. Crown ethers have been used as asymmetric catalysts by several groups.[3~5] We have previously reported the simple chiral crown (*S*,*S*)-**1** • KO*t*Bu complex which efficiently catalyzes 1,4-addition of methyl phenylacetates (**8**) to methyl acrylate (**9**) to give (*S*)-**10** (95% yield, 79%ee , Eq. 1).[6]



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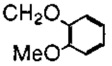
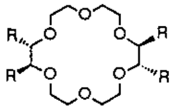
2 : R= CH$_2$O





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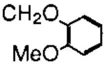

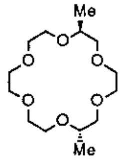

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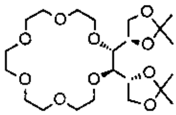

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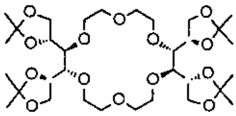

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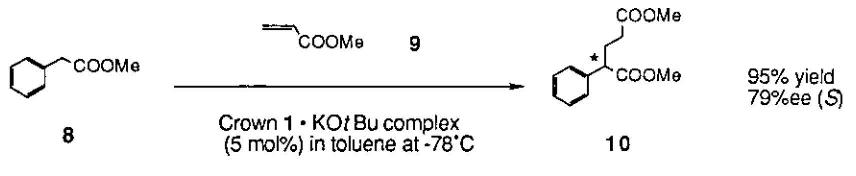


(1)

In 1988 Yamamoto *et al.* have developed Michael addition reactions of active methylene compounds stabilized by phenylthio group to cycloalkenones catalyzed by KO*t*Bu • chiral crown complexes, and succeeded in enantiofacial discrimination of the Michael acceptor.[7]

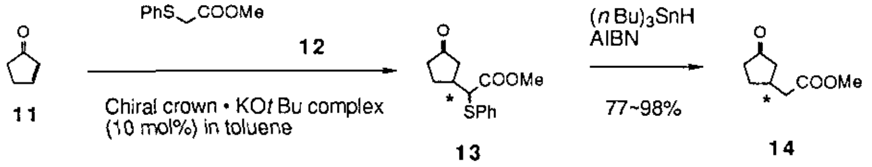
We report here the results of 1,4-addition reaction of methyl phenylthioacetate (**12**) to 2-cyclopentenone (**11**) catalyzed by several chiral crowns complexed with KO*t*Bu (Eq. 2).

The Michael reaction of **12** to **11** was carried out in the presence of 10 mol% of crown•KO*t* Bu complexes and the results are summarized in Table 1. The product (**13**) was converted to δ-keto ester (**14**) in good yields with methods described by Gutierrez's and Yamamoto's groups ; desulfurization with $(n\mathrm{Bu})_3\mathrm{SnH}$ in the presence of AIBN.[7,8]

The highest enantioselectivity was obtained in toluene, a less polar solvent. We have expected that chiral crown (*S,S*)-**1** and (*S,S,S,S*)-**3** would give **14** with relatively high optical yields, because methyl groups of **1** and **3** are in axial position in the complexes to affect the enantioselectivity.[6] But both gave the 1,4-adduct of rather low optical purity. (*S,S*)-**5**, in which two methyl groups are supposed to be equatrial in the complex, indicated no enantiofacial discrimination (entry 5).

We therefore prepared **2**, **4**, **6** and **7** bearing bulky substituents. Among them, **2** and **7** were found to induce relatively high enantioselectivity with 68%ee (*R*) and 71%ee (*S*), respectively (entries 2 and 7). It also should be mentioned that crowns having same chiral units exhibit the same sense of asymmetric induction (**1** and **3** for (R)-14, **2** and **4** for (*R*)-**14**, **6** and **7** for (*S*)-**14**).[13]

Mechanistic studies are now in progress.



(2)

Table 1. Asymmetric Michael Additions Catalyzed by Chiral Crown Ethers (Eq. 2)[a]

entry	crown	conditions	yield of **13** (%)	ee(%) of[b] **14**	confg.[b] of **14**
1	**1**[6,9a]	-78°C 1 h + 0°C 10 min	30	21	*R*
2	**2**[6]	-78°C 2 day	46	68	*R*
3	**3**[6,9b]	-78°C 1 h	97	15	*R*
4	**4**	-78°C 1 h + 0°C 10 min	82	26	*R*
5	**5**[6]	-78°C 1 h + 0°C 10 min	48	1	*S*
6	**6**	-78°C 1 day	62	36	*S*
7	**7**[10]	-78°C 1 h + 0°C 10 min	86	71	*S*

a) Ester : enone : crown•KO*t* Bu = 2 : 1 : 0.1. For procedure, see ref.11.

b) Determined by optical rotations according to ref.12. Maximum rotations were calculated to be $[\alpha]_D$ -121.0° ($\mathrm{CHCl_3}$) for (*S*) - **14**.

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REFERENCES AND NOTES

1. This paper is dedicated to Dr. Masatomo Hamana, Professor Emeritus of Kyushu University, on the occasion of his 75th birthday.
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11. A typical experiment (entry 7) : A solution of **11** (264 mg, 3.2 mmol) in toluene (11 ml) was added to a solution of **12** (1.17 g, 6.4 mmol), KO*t*Bu (38.0 mg, 0.34 mmol) and **7** (213.8 mg, 0.32 mmol) in toluene (21 ml) at -78°C. After stirring for 1 h at -78°C and 10 min at 0°C, the reaction mixture was quenched with aq. NH_4Cl and extracted with ethyl acetate. The organic layer was dried over $MgSO_4$ and concentrated to give a crude product. Purification by column chromatography (SiO_2, ether - hexane) gave **13** (734 mg, 86% yield) as a pale yellow oil (1:1 mixture of two diasteromers). A solution of **13** (238.7 mg, 0.93 mmol), $(n\mathrm{Bu})_3SnH$ (0.49 ml, 1.8 mmol), and AIBN (8.3mg, 0.05mmol) in benzene (3 ml) was heated under reflux for 1 h and cooled down. The resulting solution was directly subjected to column chromatography (SiO_2, ether-benzene). After bulb-to-bulb distillation, **14** (113 mg, 80% yield) was obtained as a colorless liquid of $[\alpha]_D$ -86° (c 2.2, $CHCl_3$).
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13. a) Satisfactory analytical and spectroscopic data were obtained for all new compounds.
    b) Crown ethers (1~7) were prepared by the conventional methods. Details will be published in due course.

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