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CONTENTS

Contribution

From Asymmetric Catalyst to Asymmetric Autocatalyst

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1. Introduction

It is known that many physiologically active substances are chiral molecules containing asymmetric carbon atoms. Development of an asymmetric synthesis process to selectively synthesize an enantiomer with the desired absolute configuration is an important subject dealt with by organic chemists specializing in synthesis. In particular, asymmetric synthesis based on the use of a catalytic amount of an asymmetric catalyst is a very attractive research subject. The asymmetric alkylation of an aldehyde by dialkyl zinc using a chiral aminoalcohol as the asymmetric catalyst has become one of the mainstream reactions in the preparation of optically active secondary alcohols owing to the research carried out by many groups including the authors' group[1]. The authors have developed a process for the highly enantioselective asymmetric alkylation of aldehydes using a chiral aminoalcohol derived from proline, an *N,N*-dialkylnorephedrine derivatives or chiral piperazine as the asymmetric catalyst. In this reaction, there is substrate generality and many useful intermediates can be obtained in high yield.

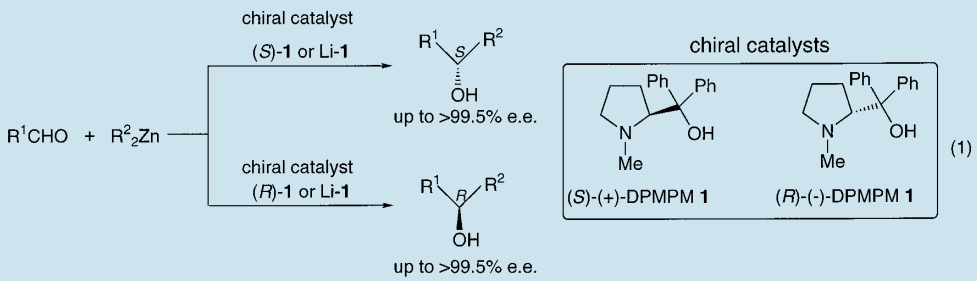
Formation of a substance with a new function by precise design of molecular structure is also interesting. Previously there were no known chiral molecules which are asymmetric autocatalysts capable of multiplying themselves. We have found that chiral pyrimidine and quinolyl alcohols are highly enantioselective asymmetric autocatalysts with the ability to self-proliferate and to give good optical purity[2].

In this article, we will introduce our study on asymmetric alkylation and asymmetric autocatalysis of aldehydes.

2. Asymmetric alkylation of an aldehyde using a chiral aminoalcohol

1) Asymmetric alkylation using diphenyl (1-methyl-pyrrolidin-2-yl) methanol (1, DPMPM)

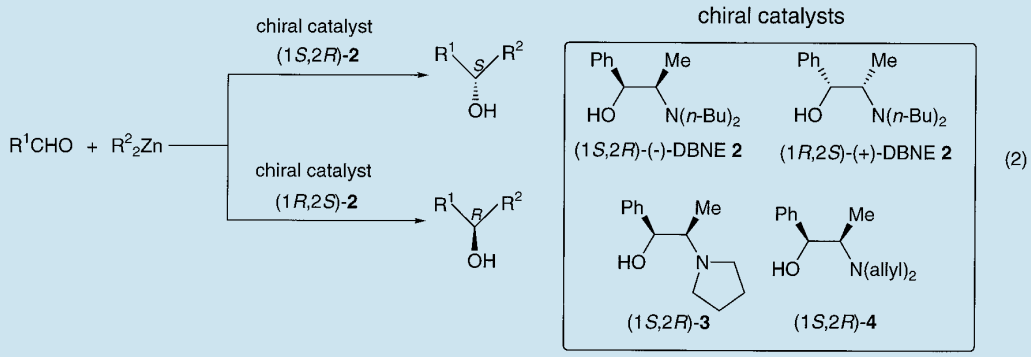
We have studied asymmetric alkylation with dialkyl zinc using a chiral aminoalcohol (DPMPM) prepared from proline and derivatives[3)4)]. As a result, in an asymmetric addition reaction to an aromatic aldehyde, the corresponding optically active secondary alcohol was produced in extremely high optical yield. Asymmetric ethylation, using the lithium alkoxide of DPMPM gave the highest enantioselectivity and almost optically-pure 1-phenyl-1-propanol was obtained. By selection of the absolute configuration of the asymmetric catalyst, *S*- and *R*- enantiomers of the product can be produced separately. That is, alcohols with *S*- and *R*- configurations can be obtained by use of (*S*)-(+)-DPMPM and (*R*)-(-)-DPMPM, respectively (Formula 1).



2) Asymmetric alkylation of an aldehyde using an *N,N*-dialkylnorephedrine

A chiral aminoalcohol, *N,N*-dialkylnorephedrine, is also an effective asymmetric catalyst for asymmetric alkylation of aldehydes[5]. Generally, the asymmetric alkylation of aliphatic aldehydes in high yield is more difficult than that of aromatic aldehydes. We have found that an *N,N*-dialkylnorephedrine can be a highly enantioselective catalyst not only for aromatic aldehydes but also for aliphatic aldehydes. *N,N*-

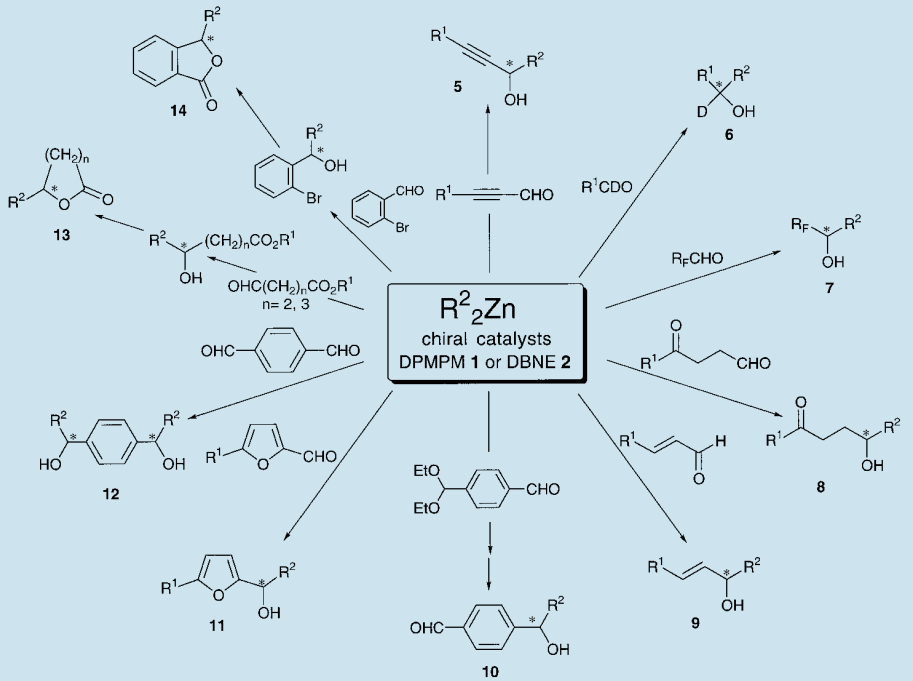
Dialkylnorephedrines show different enantioselectivities depending on the structure of the alkyl substituent on the nitrogen atoms. For example, in asymmetric ethylation of aliphatic aldehydes with diethyl zinc, *N,N*-dibutylnorephedrine (**2**, DBNE) exhibits a high enantioselectivity (93% *e.e.*)[5a]. Use of an *N,N*-dialkylnorephedrine as asymmetric catalyst also enables highly-selective asymmetric alkylation with diisopropyl or dibutyl zinc[6]. In addition, 1-phenyl-2-pyrrolidinyl-1- propanol **3** and *N,N*-diallyl norephedrine **4** are also effective asymmetric catalysts (Formula 2)[5b].



(2)

3) Enantioselective addition of diethyl zinc to an aldehyde containing a functional group

Use of the chiral aminoalcohols **1** and **2** enables asymmetric alkylation of various aldehydes (Scheme 1). For example, an alkynylaldehyde as substrate yields a chiral propargyl alcohol **5**[7a]. When deuterated and fluorine-containing aldehydes are employed, an optically-active heavy hydrogen-substituted alcohol **6**[7b] and a fluorine-containing alcohol **7**[7c] can be obtained, respectively, in high asymmetric yield. Ketoaldehydes yield chiral hydroxyketones **8** by chemo- and enantioselective addition of dialkyl zinc to the aldehyde[7d]. By asymmetric addition to an enone carbonyl an allyl alcohol **9** can be obtained in high asymmetric yield[4b,7e]. Furthermore, chiral hydroxyaldehyde **10**[7f] and heterocycle-containing alcohols **11**[7g] can also be prepared asymmetrically. The addition to dialdehyde proceeds highly enantioselectively and diastereoselectively, yielding a diol of high optical purity **12**[7h]. Alkylation of a compound with both anester and aldehyde group leads to an hydroxyester. The hydroxyester can be converted to chiral lactones such as chiral lactone **13**[7i]. Chiral phthalide **14**, a component of celery, can be obtained from the halogenated benzaldehyde by asymmetric alkylation of the aldehyde, conversion of the halogen group to an ester group, and the subsequent lactonization of the resulting hydroxyester[7j].

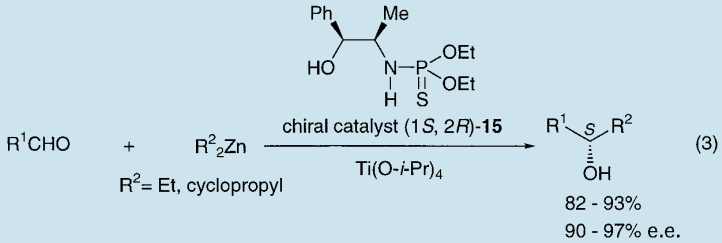


Scheme 1

The aminoalcohols (1*R*, 2*S*)-**3** have been used as asymmetric ligands in the key-step asymmetric synthesis of HIV reverse-transcriptase inhibitor (Efavirenz, DMP266, Merck), through asymmetric alkylation of a ketone[8].

4) Asymmetric alkylation using thiophosphoramidate

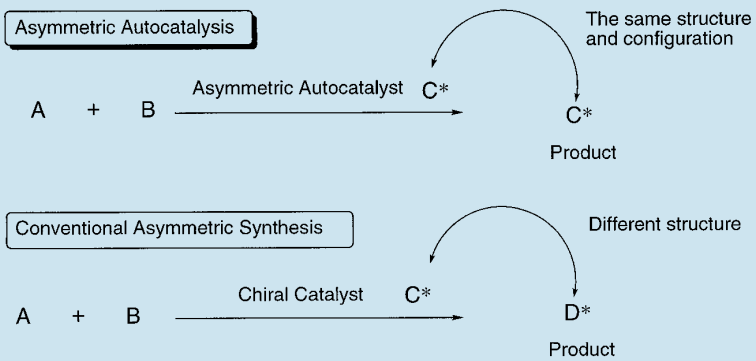
Examples of using chiral thiophosphoramidate in asymmetric reaction are rare. In this study, asymmetric alkylation of an aldehyde was carried out in the presence of tetraisopropoxy titanium using a thiophosphoramidate (**15**, PHONE) as the asymmetric catalyst[9]. The reaction progressed at a low temperature (-45°C), yielding the optically-active secondary alcohol in high asymmetric yield. This catalyst is also useful in asymmetric cyclopropylation of aldehydes with dicyclopropyl zinc to produce optically-active cyclopropyl alcohol with optical purity approaching 97% *e.e.* (Formula 3)[10].



3. Asymmetric autocatalysis

In the investigation of the reaction of pyridine-3-carboxaldehyde to determine the generality of asymmetric alkylation with aminoalcohols **1** and **2** as asymmetric catalysts, the authors observed that the reaction rate was higher than for other aldehydes (reaction time: approximately three hours, reaction time for benzaldehyde: approximately 20 hours)[11]. This suggests that the compound produced by the reaction may function as an asymmetric autocatalyst.

In conventional asymmetric catalysis, the structures of asymmetric catalyst C and product D are generally quite different. In asymmetric autocatalysis, however, the structure and absolute configuration of asymmetric catalyst C is identical with that of product C (Scheme 2).



Scheme 2

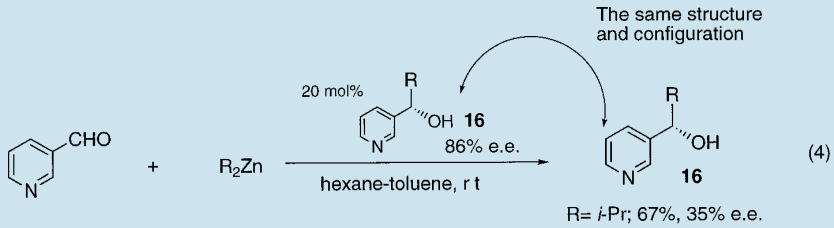
Asymmetric autocatalysis has the following three advantages:

(i.) **High reaction efficiency** In asymmetric autocatalysis, the asymmetric catalyst in the reaction system increases as the reaction proceeds; and therefore, the reaction efficiency is very high and the reaction rapidly goes to completion.

(ii.) **Simple reaction procedure** Separation of the reaction product from the asymmetric catalyst, required in the conventional process, is unnecessary since they have the same structure.

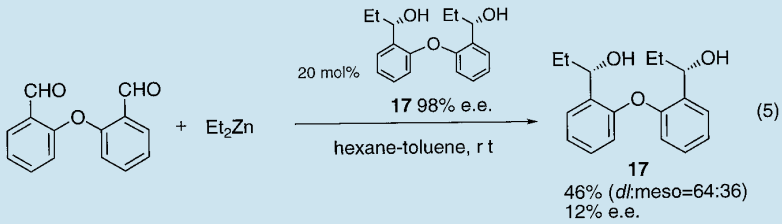
(iii.) **Consecutive reaction is possible** The product obtained can be employed repeatedly as catalyst for the asymmetric autocatalysis since the product acts as an asymmetric catalyst. A trace amount of asymmetric autocatalyst enables synthesis of a chiral compounds in large quantities.

As described above, asymmetric autocatalysis may be regarded as an energy-saving next-generation asymmetric synthesis with the advantages that conventional processes do not have. No experimental report has been written on asymmetric autocatalysis, although Wynberg has described the implication of the reaction[12]. In 1990, we reported for the first time an asymmetric autocatalysis in which a catalytic amount of chiral 3-pyridyl alcohol acted as an asymmetric autocatalyst in the alkylation of 3-pyridine carboxaldehyde to give 3-pyridyl alcohols having the same structure and absolute configuration as that of the catalyst[13]. The asymmetric isopropylation of 3-pyridine carboxaldehyde with diisopropyl zinc using 86% *e.e.* (*S*)-2-methyl-1-(3-pyridyl)-1-propanol **16** as asymmetric autocatalyst gave (*S*)-3-pyridyl alcohol with the same absolute configuration as that of the autocatalyst in 67% yield and 35% *e.e.* (Formula 4).



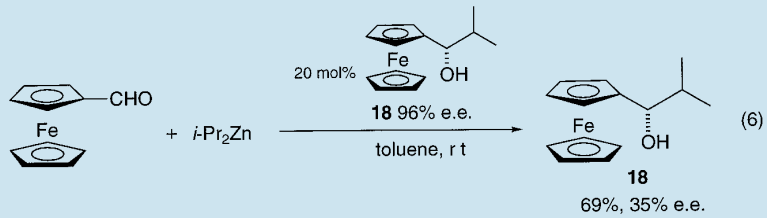
(4)

Then we synthesized a chiral diol and employed it as an asymmetric autocatalyst[14]. We found that the chiral diol **17** (98% *e.e.*) with a diphenyl ether skeleton acts as an asymmetric autocatalyst in the diethylation of the corresponding dialdehyde with diethyl zinc to produce diol **17** with 12% *e.e* (Formula 5).



(5)

We have furthermore demonstrated that chiral ferrocenyl alcohol **18** (96% *e.e.*) used as asymmetric autocatalyst also gave alcohol **18** in 69% yield and 35% asymmetric yield in the reaction of ferrocene carboxaldehyde with diisopropyl zinc (Formula 6)[15].

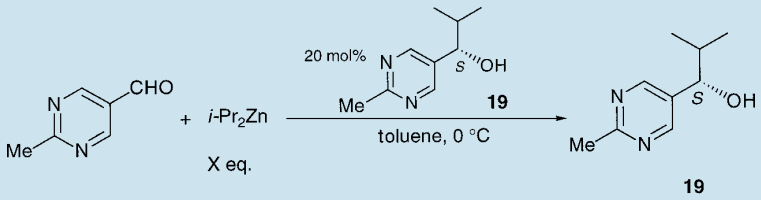


(6)

1) Highly-enantioselective asymmetric autocatalysis

As described above, we have engaged in the development of an asymmetric autocatalysis process since our first report on asymmetric autocatalysis[13]. However, the fact that the optical purity of the product was lower than that of the catalyst remained an unsolved problem. We conducted further investigations to make a highly enantioselective asymmetric autocatalysts, taking into consideration the molecular symmetry and reactivity of aldehyde. As a result, we found that a 5-pyrimidyl alcohol containing two nitrogen atoms was an excellent asymmetric autocatalyst. We investigated the reaction conditions in detail and found that chiral 5-pyrimidyl alcohol to be an effective asymmetric autocatalyst. Asymmetric isopropylation of 5-pyrimidine carboxaldehyde with diisopropyl zinc produced chiral 5-pyrimidyl alcohol with the same absolute configuration as that of the autocatalyst in high enantiomeric yield (90% *e.e.* or more) (Table 1)[16]. When (*S*)-5-pyrimidyl alcohol **19** (94% *e.e.*) was used as asymmetric autocatalyst, the optical purity of the newly produced (*S*)-5-pyrimidyl alcohol **19** was 95.7% *e.e.*, which meant that the chiral compound had self-

multiplied without losing its optical purity (Entry 1). When almost optically pure pyrimidyl alcohol **19** was employed, the optical purity of the newly produced compound **19** reached 98.2% *e.e.* (Entry 3).

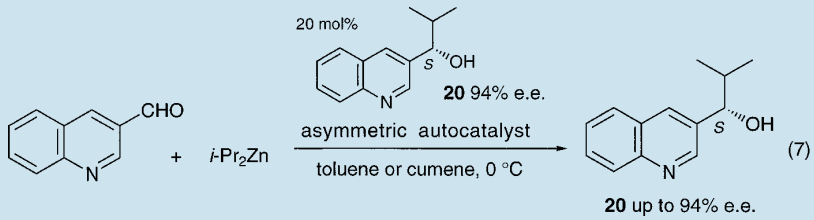


19

Table 1. Highly Enantioselecitve Autocatalytic Reaction using **19**

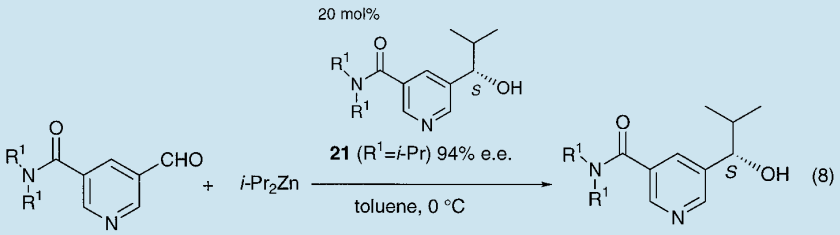
Entry	Asym. Autocat. e.e. (%)	X eq.	Product Yield (%)	Product e.e. (%)
1	94.8	1.2	48	95.7
2	94.8	3.2	80	93.5
3	>99.5	1.2	38	98.2
4	>99.5	3.2	80	95.0

The 3-quinolyl alcohols, containing only one nitrogen atom also proved to be highly effective asymmetric autocatalysts[7]. Specifically, asymmetric isopropylation of 3-quinoline carboxaldehyde using 3-quinolyl alcohol **20** (94% *e.e.*) as asymmetric autocatalyst gave quinolyl alcohol **20** of extremely high optical purity (94% *e.e.*) (Formula 7).



20 up to 94% e.e.

We also found that 3-pyridyl alcohols containing a carbamoyl group in the 5-position were much better asymmetric autocatalysts when compared with catalysts containing no substituent group at the 5-position (Formula 4, **16**)[18]. The asymmetric yield varies depending on the nature of the alkyl group on the nitrogen atom in the carbamoyl group. When 3-pyridyl alcohol **21**, in which R^1 is an isopropyl group, is employed, the asymmetric yield of the product reached 86% *e.e.* (Formula 8).



21 (R^1=*i*-Pr) 86% e.e.

2) Asymmetric autocatalysis with improvement of optical purity

Kagan, *et al.* first reported on the non-linear phenomenon in asymmetric oxidation where the optical purity of the product is higher than that of the asymmetric catalyst used[19a] .Oguni[19b], Noyori, *et al.*[19c] have also made further studies on the asymmetric alkylation of an aldehyde[19d]. However, all of the reactions were non-autocatalytic and the structure of the asymmetric catalyst was entirely different from that of the product. Although a product with 50% *e.e.* could be obtained from a catalyst with 10% *e.e.*, further

improvement of the optical purity of the product was impossible.

On the other hand, we have found that pyrimidyl alcohols are effective asymmetric autocatalysts. Consecutive asymmetric autocatalytic reaction were attempted, making the most of the fact that the reaction is autocatalytic. First, asymmetric autocatalysis was carried out using (*S*)-pyrimidyl alcohol **22** with only 2% *e.e.* As a result, the optical purity of the new pyrimidyl alcohol **22** obtained (total of the product and the asymmetric autocatalyst employed) was amplified to 10% *e.e.* Use of the compound with 10% *e.e.* as the asymmetric autocatalyst for the next reaction further increased the optical purity, yielding pyrimidyl alcohol **22** with 57% *e.e.* The optical purity was amplified to 81% *e.e.* and further to 88% *e.e.* by successively using the alcohol obtained in the subsequent asymmetric autocatalysis (Table 2)[20]. The *S*-configuration which was present slightly in excess at first in the alcohol self-multiplied 238 times in the four reactions carried out successively and *R*-configuration of the alcohol self-multiplied only 16 times. As a result, the optical purity was amplified from 2% *e.e.* to 88% *e.e.* (Figure 1).

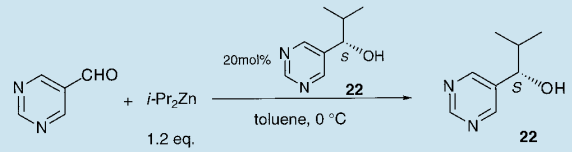
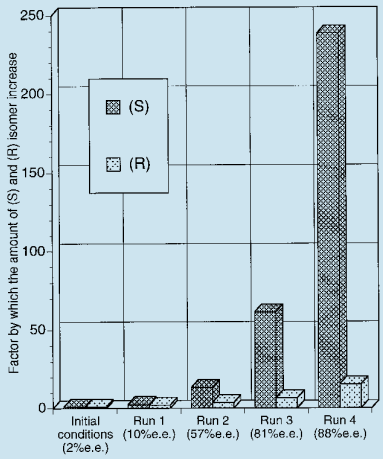
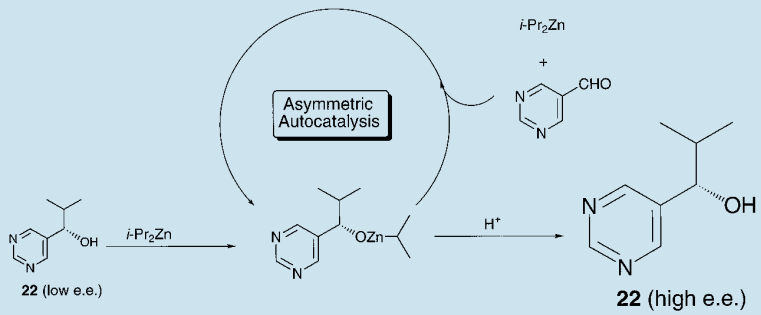


Table 2. Consecutive Asymmetric Autocatalysis of (*S*)-**22** with an Amplification of e.e.

Entry	Asym. autocat. **22**	Catalyst and product **22**	
	e.e. (%)	Yield (%)	e.e (%)
1	2	38	10
2	10	63	57
3	57	67	81
4	81	63	88
5	88	66	88



We hypothesize as follows: The zinc alkoxide of pyrimidyl alcohol **22** was the real asymmetric autocatalyst. Addition of an aldehyde and diisopropyl zinc allowed the asymmetric autocatalysis to proceed with the optical purity being improved. Treatment of the reaction product with acid after the completion of the reaction gave pyrimidyl alcohol **22** of high optical purity (Scheme 3).



Scheme 3

In the above reactions, the reaction product was treated with acid after each reaction in order to isolate pyrimidyl alcohol and subsequently used in the next reaction. An attempt was made to successively add diisopropyl zinc and an aldehyde in one container without stopping the reaction after each cycle. The results proved to be practical and the optical purity of pyrimidyl alcohol was greatly amplified[21]. For example, reaction of dialkylzinc and aldehyde with catalyst of low optical purity 0.2% *e.e.*, produced products of approximately 90% *e.e.* (Table 3).

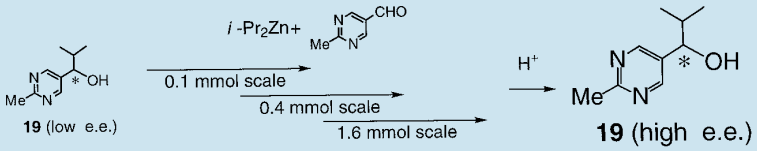


Table 3. One-pot Asymmetric Autocatalysis of **19** with an Amplification of e.e.

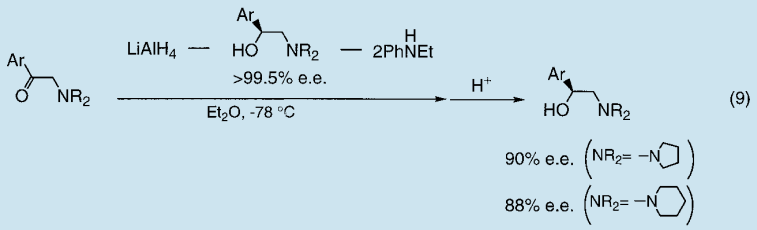
Run	Asym. autocat. **19**		Obtained alcohol **19**		
	Amount (mg)	e.e. (%)	Amount (mg)	Yield (%)	e.e. (%)
1	3.2	0.28 (*S*)	323.5	92	87.0 (*S*)
2	3.3	0.18 (*R*)	297.4	84	83.9 (*R*)

Molar ratio. Aldehyde : Catalyst : *i*-Pr_2Zn = 1.0 : 0.009 :1.77.

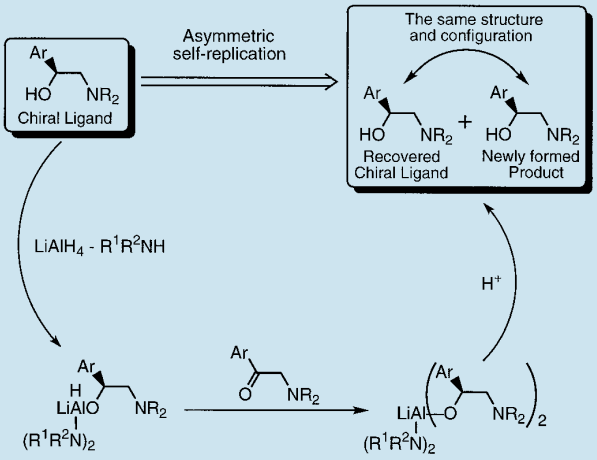
3) Self-replication type asymmetric reduction

As described above, we found that asymmetric autocatalysis occurs in several asymmetric alkylations of an aldehyde with dialkyl zinc. On the other hand, could this concept of "self-replication type reaction" where the asymmetric source and the product are of the same structure and absolute configuration be applicable to other reactions?

We considered hydride reduction of aminoketones using chiral aminoalcohols as asymmetric ligands to give aminoalcohols of the same structure and absolute configuration as those of the ligands. We found that asymmetric reduction of α-aminoketone using lithium aluminium hydride was possible. An assymetric β-aminoalcohol catalyst and an achiral amine ligand were used to produce an aminoalcohol of the same structure and absolute configuration as that of the asymmetric ligand [22]. The reaction may be regarded as a self-replication type asymmetric reduction. Aminoalcohols containing a cyclic substituent group on the nitrogen atom, in particular, were even more effective, raising the optical purity to 90% *e.e.* (Formula 9).



These aminoalcohols can be recrystallized to improve optical purity. Combining the self-replication type asymmetric reduction with recrystallization creates a complete loop in the self-replication of the chiral aminoalcohol (Scheme 4). Many of the chiral amino alcohols, such as the compounds **1** and **2** described above, act as highly enantioselective asymmetric catalysts. Other known examples are compounds with useful pharmacological and physiological activities. This makes the self-replication type asymmetric reduction of a chiral amino alcohols a valuable synthetic process.



4. Conclusion

Chiral aminoalcohols, such as DPMPM **1** and DBNE **2**, act as asymmetric catalysts in asymmetric alkylation of aldehydes and give optically active secondary alcohols in high asymmetric yield. Chiral pyrimidyl, quinolyl, and pyridyl alcohols act as asymmetric autocatalysts and are asymmetrically self-multipliable. Furthermore, pyrimidyl alcohols are sensitive to very minute asymmetry of the chiral molecules[23]. This leads to amplification of optical purity.

It is expected that other substances with interesting functions will be created in the future.

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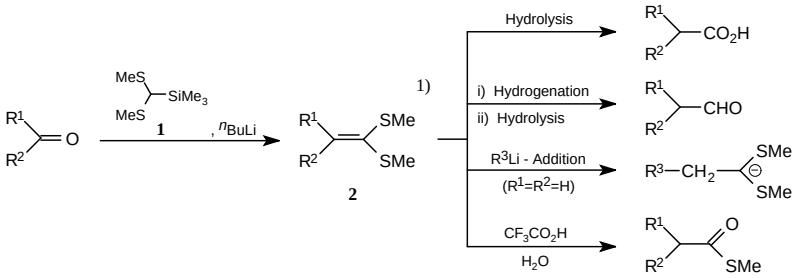
References

1. a) K. Soai, S. Niwa, *Chem. Rev.*, **92**, 833 (1992)
   b) R. Noyori, M. Kitamura, *Angew. Chem. Int. Ed. Engl.*, **30**, 49 (1991)
   c) K. Soai, T. Hayase, *Yuki Gosei Kagaku Kyokaishi (J. Synth. Org. Chem. Jpn.)*, **53**, 138 (1995)
   d) Aminoalcohols promote the ethylation of benzaldehyde by diethyl zinc.
   T. Mukaiyama, K. Soai, T. Sato, H. Shimizu, K. Suzuki, *J. Am. Chem. Soc.*, **101**, 1455 (1979)
2. K. Soai, T. Shibata, *Yuki Gosei Kagaku Kyokaishi (J. Synth. Org. Chem. Jpn.)*, **55**, 994 (1997)
3. a) K. Soai, A. Ookawa, *J. Chem. Soc., Chem. Commun.*, **1986**, 412
   b) A. Ookawa, K. Soai, *J. Chem. Soc., Perkin Trans. 1*, **1987**, 1465
4. a) K. Soai, A. Ookawa, K. Ogawa, T. Kaba, *J. Chem. Soc., Chem. Commun.*, **1987**, 467
   b) K. Soai, A. Ookawa, T. Kaba, K. Ogawa, *J. Am. Chem. Soc.*, **109**, 7111 (1987)
5. a) K. Soai, S. Yokoyama, K. Ebihara, T. Hayasaka, *J. Chem. Soc., Chem. Commun.*, **1987**, 1690
   b) K. Soai, S. Yokoyama, T. Hayasaka, *J. Org. Chem.*, **56**, 4264 (1991)
6. K. Soai, T. Hayase, K. Takai, T. Sugiyama, *J. Org. Chem.*, **59**, 7908 (1994)
7. a) S. Niwa, K. Soai, *J. Chem. Soc., Perkin Trans. 1*, **1990**, 937
   K. Soai, S. Niwa, *Chem. Lett.*, **1989**, 481
   b) K. Soai, Y. Hirose, S. Sakata, *Bull. Chem. Soc. Jpn.*, **65**, 1734 (1992)
   c) K. Soai, Y. Hirose, S. Niwa, *J. Fluorine Chem.*, **59**, 5 (1992)
   T. Hayase, T. Sugiyama, M. Suzuki, T. Shibata, K. Soai, *J. Fluorine Chem.*, **84**, 1 (1997)
   d) K. Soai, M. Watanabe, M. Koyano, *Bull. Chem. Soc. Jpn.*, **62**, 2124 (1989)
   K. Soai, M. Watanabe, M. Koyano, *J. Chem. Soc., Chem. Commun.*, **1989**, 534
   M. Watanabe, K. Soai, *J. Chem. Soc., Perkin Trans. 1*, **1994**, 3125
   e) K. Soai, Y. Kawase, A. Oshio, *J. Chem. Soc., Perkin Trans. 1*, **1991**, 1613
   f) K. Soai, H. Hori, M. Kawahara, *Tetrahedron : Asymmetry*, **1**, 769 (1990)
   g) K. Soai, Y. Kawase, S. Niwa, *Heterocycles*, **29**, 2219 (1989)
   h) K. Soai, H. Hori, M. Kawahara, *J. Chem. Soc., Chem. Commun.*, **1992**, 106
   i) K. Soai, S. Yokoyama, T. Hayasaka, *Chem. Lett.*, **1988**, 843
   j) K. Soai, H. Hori, M. Kawahara, *Tetrahedron : Asymmetry*, **2**, 253 (1991)
8. A. S. Thompson, E. G. Corley, M. F. Huntington, E. J. J. Grabowski, *Tetrahedron Lett.*, **36**, 8937 (1995)
   A. S. Thompson, E. G. Corley, M. F. Huntington, E. J. J. Grabowski, J. F. Remenar, D. B. Collum, *J. Am. Chem. Soc.*,
   120, 2028 (1998)
9. K. Soai, Y. Hirose, Y. Ohno, *Tetrahedron : Asymmetry*, **4**, 1473 (1993)
   K. Soai, Y. Ohno, Y. Inoue, T. Tsuruoka, Y. Hirose, *Rec. Trav. Chim. Pays-Bas*, **114**, 145 (1995)
10. T. Shibata, H. Tabira, K. Soai, *J. Chem. Soc., Perkin Trans. 1*, **1998**, 177
11. K. Soai, S. Hori, S. Niwa, *Heterocycles*, **29**, 2965 (1989)
12. H. Wynberg, *J. Macromol. Sci. Chem., Sect. A*, **26**, 1033 (1989)
13. K. Soai, S. Niwa, H. Hori, *J. Chem. Soc., Chem. Commun.*, **1990**, 982
14. K. Soai, T. Hayase, C. Shimada, K. Isobe, *Tetrahedron : Asymmetry*, **5**, 789 (1994)
15. K. Soai, T. Hayase, K. Takai, *Tetrahedron : Asymmetry*, **6**, 637 (1995)
16. T. Shibata, H. Morioka, T. Hayase, K. Choji, K. Soai, *J. Am. Chem. Soc.*, **118**, 471 (1996)
17. T. Shibata, K. Choji, H. Morioka, T. Hayase, K. Soai, *Chem. Commun.*, **1996**, 751
18. T. Shibata, H. Morioka, S. Tanji, T. Hayase, Y. Kodaka, K. Soai, *Tetrahedron Lett.*, **37**, 8783 (1996)
19. a) C. Puchot, O. Samuel, E. Duñach, S. Zhao, C. Agami, H. B. Kagan, *J. Am. Chem. Soc.*, **108**, 2353 (1986)
   b) N. Oguni, Y. Matsuda, T. Kaneko, *J. Am. Chem. Soc.*, **110**, 7877 (1988)
   c) M. Kitamura, S. Okada, S. Suga, R. Noyori, *J. Am. Chem. Soc.*, **111**, 4028 (1989)
   d) C. Girard, H. B. Kagan, *Angew. Chem. Int. Ed.*, **37**, 2922 (1998)
20. K. Soai, T. Shibata, H. Morioka, K. Choji, *Nature (London)*, **378**, 767 (1995)

FOR PETERSON OLEFINATION

B2004 Bis(methylthio)(trimethylsilyl)methane 1g JPYen 10,300



The lithio product of the present reagent 1, i.e. α-silylcarbaninon, reacts with a ketone or an aldehyde to give ketenethioacetal 2 in high yield. The ketenethioacetal 2 is a useful intermediate convertible to various compounds. The carbanion 1 is used in the synthesis of cyclopropane from oxirane[2a], diastereoselective alkylation of an α, β-unsaturated ester[2b], etc. The present reagent is so versatile ones that it can be employed not only in conversion of ketone and aldehyde but also in many other fields.

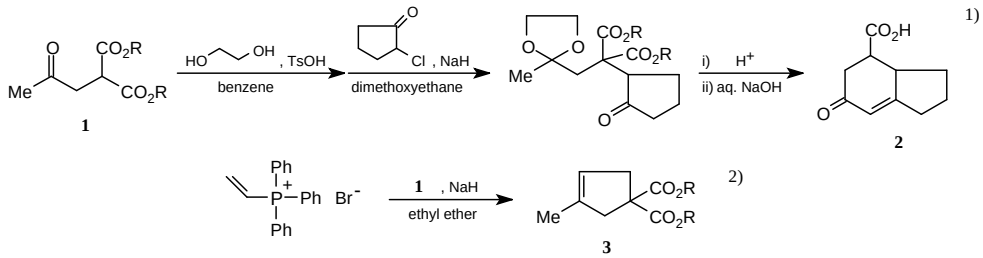
references

1) Synthesis of ketene thioacetals
D. Seebach, B.-Th. Gröbel, A. K. Beck, M. Braun, K.-H. Geiss, *Angew. Chem. Int. Ed. Engl.*, **11**, 443 (1972)
D. Seebach, R. Bürstinghaus, *Synthesis*, **1975**, 461
2) Other applications
a) E. Schaumann, C. Friese, *Tetrahedron Lett.*, **30**, 7033 (1989)
b) H. Kawasaki, K. Tomioka, K. Koga, *Tetrahedron Lett.*, **26**, 3031 (1985)
c) D. Seebach, R. Bürstinghaus, *Angew. Chem. Int. Ed. Engl.*, **14**, 57 (1975)

MALONIC ACID DERIVATIVE

A1487 Acetonylmalonic Acid Dimethyl Ester

5g JPYen 19,000 1g JPYen 6,750



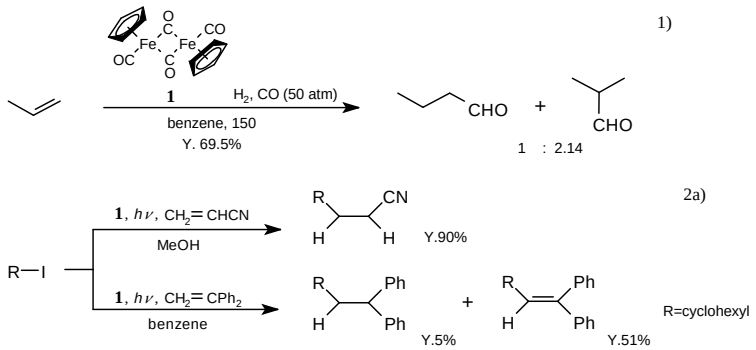
The present reagent 1 is a malonic acid derivative containing a carbonyl group and employed in the synthesis of a cyclic compound as a bifunctional building block. C. Mercier, *et al* . have reported the usefulness of 1 in the synthesis of a cyclic enone 2 *via* condensation between the cyclic ketal of 1 and α-chlorocyclopentanone in the presence of a base, followed by hydrolysis and ring-closing reaction. E. E. Schweizer, *et al* . also have reported usefulness of 1 by synthesis of cyclopentene 3 from the reaction of 1 with a vinyl phosphonium salt.

references

1) Reaction with α-chloro carbonyl compound
C. Mercier, A. R. Addas, P. Deslongchamps, *Can. J. Chem.*, **50**, 1882 (1972)
2) Reactions with phosphonium salts
E. E. Schweizer, G. J. O'Neill, *J. Org. Chem.*, **30**, 2082 (1965)
A. G. Cameron, A. T. Hewson, *J. Chem. Soc., Perkin Trans. 1*, **1983**, 2979
Y. Okada, T. Minami, S. Yahiro, K. Akinaga, *J. Org. Chem.*, **54**, 974 (1989)

FOR CARBON-CARBON BOND FORMING REACTIONS

C1592 Cyclopentadienyliron Dicarbonyl Dimer 5g JPYen 4,900



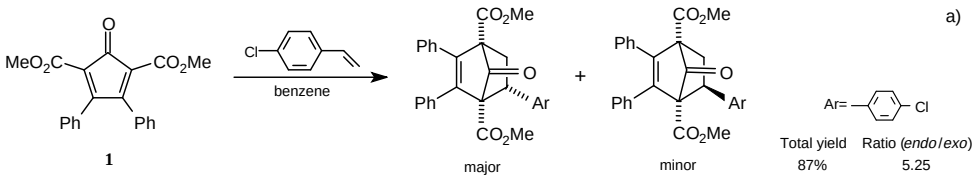
The present reagent 1 is a binuclear metal carbonyl complex containing cyclopentadienyl ligands and employed as catalyst in carbon-carbon bond forming reactions, such as hydroformylation. Unlike the cobalt carbonyl conventionally employed in so called oxo synthesis, this catalyst is so mild as to yield saturated aldehydes without accompanying alcohols, aldol condensates, etc., as by-products. This reagent 1 is also known as a radical mediator to catalyze the photochemical alkyl addition reactions to some alkenes[2a)] .

references

1) Oxo reaction catalyzed by cyclopentadienyliron dicarbonyl dimer
J. Tsuji, Y. Mori, *Bull. Chem. Soc. Jpn.*, **42**, 527 (1969)
2) Other applications
a) Dimeric metal complexes as mediators for radical C-C bond forming reactions
B. Giese, G. Thoma, *Helv. Chim. Acta*, **74**, 1135 (1991)
b) Stereochemistry of oxidative carboxylation
K. M. Nicholas, M. Rosenblum, *J. Am. Chem. Soc.*, **95**, 4449 (1973)

FOR DIELS-ALDER REACTION

B1962 2,5-Bis(methoxycarbonyl)-3,4-diphenylcyclopentadienone 1g JPYen 11,100



The present reagent 1 is a highly reactive dienone and reacts rapidly with various dienophiles to give the cyclic adducts. This reaction proceeds stereoselectively. For example, the reaction with *p* -substituted styrene produces preferentially an *endo* -oriented adduct. In the reaction with an electrone deficient, such as maleic anhydride, only an *endo* -oriented adduct is produced. Since the present dienone is colored intense orange while the adduct is faded, the progress of reaction can be monitored by observation of the color change.

references

Cycloaddition reaction of cyclopentadienones
a) M. Mori, A. Hayamizu, K. Kanematsu, *J. Chem. Soc., Perkin Trans. 1*, **1981**, 1259
b) H. Hart, D. Ok, *J. Org. Chem.*, **51**, 979 (1986)
c) T. Ban, Y. Wakita, K. Kanematsu, *J. Am. Chem. Soc.*, **102**, 5415 (1980)
d) N. G. Argyropoulos, N. E. Alexandrou, *J. Heterocycl. Chem.*, **16**, 731 (1979)

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