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Catalytic Chirally Self-replicating Molecule. Asymmetric Autocatalytic Reaction of a Zinc Alkoxide of Chiral 1-Ferrocenyl-2-methylpropan-1-ol

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Abstract: Isopropylzinc alkoxide of 1-ferrocenyl-2-methylpropan-1-ol was found to be a catalytic chirally self-replicating molecule which produces itself with the same configuration from ferrocenyl aldehyde and diisopropylzinc with 35-39% e.e. in good yields.

One of the most essential characteristic features of life is the ability of self-replication. On the other hand, another essential characteristic feature of life is that it is composed of a various kinds of chiral molecules. Meanwhile, von Neumann described the self-replicating *machines* which are considered to be a model of life.¹ Thus, a chiral *molecule* which has the ability of chiral self-replication might be called as the simple and primitive life of the molecular level, *i.e.*, molecular life. However, the number of chirally self-replicating molecules² so far known is very few (chiral pyridylalcohol^{3a} and chiral diol^{3b}).⁴

We now report that the alkylzinc alkoxide of a chiral ferrocenyl alcohol is a catalytic and chirally self-replicating molecule. When 0.20 mmol (20 mol%) of chiral (*S*)-(+)-1-ferrocenyl-2-methylpropan-1-ol **2** (97.3% e.e.)^{5a} was treated with *i*-Pr₂Zn (3 mmol) and ferrocenyl aldehyde **1** (1.0 mmol) in toluene at room temperature, 0.95 mmol of **2** which contains the newly synthesized **2** and the **2** (0.20 mmol) used as the catalyst was obtained (Table 1, entry 1). The result showed that the synthetic yield of the newly formed **2** was 75% (0.95 - 0.20 = 0.75 mmol). The HPLC analysis of the obtained **2** using a chiral column and the subsequent calculation [deduction of the amount of **2** (0.2 mmol) used as chiral catalyst] showed that the amount of **2** increased to 4.75 times and that the newly formed (*S*)-**2** possessed the enantiomeric purity of 29% e.e. with the same configuration as the asymmetric catalyst. The e.e. of the newly formed (*S*)-**2** increased to 35% e.e. in 69% yield, when 50 mol% of (*S*)-**2** (0.50 mmol) was employed as the chiral catalyst (entry 2). When the reaction was quenched after 2 h in the presence of the chiral catalyst (*S*)-**2** (20 mol%), (*S*)-**2** with 39% e.e. was newly formed (entry 3). The solvents didn't affect much on the enantiomeric purities of the newly formed (*S*)-**2** (entries 4-6). Because the treatment of (*S*)-**2** and *i*-Pr₂Zn afforded chiral (*S*)-isopropylzinc alkoxide **3** (satisfactory ¹H NMR and High

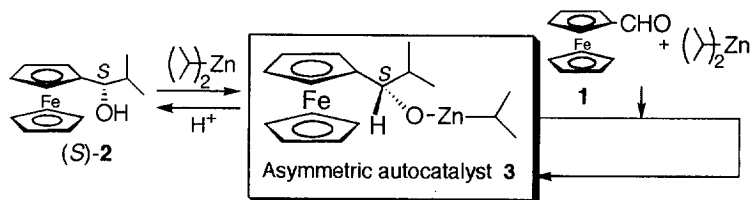


Table 1. Chiral Self-replicating Reaction of Zinc Alkoxide of Ferrocenyl Alcohol **2**

Entry	<i>i</i> -Pr ₂ Zn (eq.)	Catalyst (<i>S</i>)- 2 (% e.e., mol%)	Solvent	Time (h)	Recovered cat. 2 and product (%)	Newly formed (<i>S</i>)- 2 Yield (%) E.e.(%) ^a
1	(3)	97.3, 20	toluene	53	95	75 29
2	(3)	96.3, 50	toluene	46	119	69 35
3	(3)	96.3, 20	toluene	2	27.3	7.3 39
4	(3)	97.3, 20	tol.- hexane	40	94	74 28
5	(3)	97.3, 20	tol.- benzene	66	89	69 26
6	(3)	96.3, 20	tol.- Et ₂ O	67	82	62 27
7	(2.2)	96.3, 20	toluene	41	91	71 28
8	(3)	97.7, 10	toluene	53	82	72 24

^a Determined by HPLC analysis using a chiral column.

Resolution mass spectra were obtained),⁶ the chiral (*S*)-isopropylzinc alkoxide **3** formed *in situ* was an asymmetric autocatalyst which replicates itself by the catalyzed addition of diisopropylzinc to ferrocenyl aldehyde from the *Si* face. The subsequent hydrolysis of (*S*)-**3** during the work-up procedure afforded (*S*)-**2**.^{7,8,9}

References and Notes

1. J. von Neumann, "Theory of Self-replicating Machines," Univ. Illinois Press, Urbana, 1966.
2. Reviews: H. Wynberg, *Chimia*, **1989**, 43, 150; cf. K. Soai and S. Niwa, *Chem. Rev.*, **1992**, 92, 833.
3. (a) K. Soai, S. Niwa and H. Hori, *J. Chem. Soc., Chem. Commun.*, **1990**, 982; (b) K. Soai, T. Hayase, C. Shimada and K. Isobe, *Tetrahedron: Asymmetry*, **1994**, 5, 789.
4. For the asymmetric autoinduction (not self-replication), see (a) A. M. Alberts and H. Wynberg, *J. Am. Chem. Soc.*, **1989**, 111, 7265; (b) H. Danda, H. Nishikawa and K. Otaka, *J. Org. Chem.*, **1991**, 56, 6740; (c) For the achiral amine mediated asymmetric autoinduction, L. Shengjian, J. Yaoshong, M. Aiqiao and Y. Guishu, *J. Chem. Soc., Perkin Trans. 1*, **1993**, 885. Although the induction of 14.3% e.e. is reported using 1-phenylpropanol in the ethylation of benzaldehyde, a contradictory result has been reported in ref. 4a. For the replication of a molecule which does not produce new chiralities, see L. E. Orgel, *Nature*, **1992**, 358, 203; E. A. Wintner, M. M. Conn and J. Rebek, Jr., *J. Am. Chem. Soc.*, **1994**, 116, 8877.
5. (a) K. Soai, T. Hayase, K. Takai and T. Sugiyama, *J. Org. Chem.*, in press. The configuration is tentatively assigned based on the results that (1*S*, 2*R*)-*N,N*-dialkylnorephedrine catalyze the addition of dialkylzinc from the *Si* face of the aldehydes. K. Soai, S. Yokoyama and T. Hayasaka, *J. Org. Chem.*, **1991**, 56, 4264. The direction of the optical rotation [(*S*)-(+)] was in good agreement with that [(*R*)-(-), tentatively assigned] described in ref. 5g. For the preparation of chiral ferrocenyl alcohols, see (b) G. Gokel and I. Ugi, *J. Chem. Educ.*, **1972**, 49, 294; (c) N. W. Boaz, *Tetrahedron Lett.*, **1989**, 30, 2061; (d) Y. Yamazaki and K. Hosono, *ibid.*, **1989**, 30, 5313; (e) R. Noyori, S. Suga, K. Kawai, S. Okada, M. Kitamura, N. Oguni, M. Hayashi, T. Kaneko and Y. Matsuda, *J. Organomet. Chem.*, **1990**, 382, 19; (f) Y. Matsumoto, A. Ohno, S. Lu, T. Hayashi, N. Oguni and M. Hayashi, *Tetrahedron: Asymmetry*, **1993**, 4, 1763; (g) J. Wright, L. Frambes and P. Reeves, *J. Organomet. Chem.*, **1994**, 476, 215.
6. cf. M. Ishimori and T. Tsuruta, *Makromol. Chem.*, **1963**, 64, 190.
7. A typical experimental procedure is as follows: A solution of **1** (0.2139g, 1.0 mmol) and (*S*)-**2** [0.0517g, 0.2 mmol, 20 mol%, 97.3% e.e., containing (*S*)-**2** (0.0510g) and (*R*)-**2** (0.0007g)] in toluene (3.0 ml) was stirred at room temperature for 20 min. The solution was cooled to 0 °C, and toluene solution (1 M) of *i*-Pr₂Zn (3.0 ml, 3.0 mmol) was added. The mixture was stirred at room temperature for 53 h, and the reaction was quenched by adding satd. aqueous ammonium chloride (10 ml). The precipitate was filtered off (celite), and the filtrate was extracted with EtOAc, dried (Na₂SO₄), evaporated under reduced pressure. The purification of the residue by silica gel TLC (eluent, hexane/EtOAc = 5/1) afforded a mixture of catalyst **2** (0.0517g) and the newly formed **2** in a total amount of 0.2462g. Thus the amount of the newly formed **2** was 0.1945g (0.75 mmol, 75%) (0.2462 - 0.0517 = 0.1945). HPLC analysis of the mixture of the catalyst **2** and the product **2** using a chiral column [DAICEL CHIRALCEL OD; 4 x 250 mm; 40 °C; eluent: 0.25% 2-propanol in hexane; UV detector (254 nm); retention time (min) 26.8 for the major (*S*)-**2**, 33.9 for the minor (*R*)-**2**] showed that the mixture contains (*S*)-**2** (0.1764g) and (*R*)-**2** (0.0698g). Therefore the newly formed (*S*)-**2** was 0.1254g (0.1764 - 0.0510 = 0.1254) and (*R*)-**2** was 0.0691g (0.0698 - 0.0007 = 0.0691). Thus the e.e. of the newly formed (*S*)-**2** was determined as 29% e.e.
8. Chiral (*S*)-**3** catalyzed the enantioselective isopropylation of benzaldehyde affording (*S*)-2-methyl-1-phenylpropan-1-ol with 9% e.e. in 31% yield. Reaction of **1** and *i*-Pr₂Zn without using chiral **3** afforded racemic **2** in 69% yield as the result of the formation of racemic autocatalyst **3**.
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