

Nonlinear Effects in Asymmetric Catalysis: Some Recent Aspects*

Henri B. Kagan,[†] Christian Girard, Denis Guillaneux, David Rainford, Odile Samuel, Sheng Yong Zhang and Shu Hai Zhao

Laboratoire de Synthèse Asymétrique, associé au CNRS, Institut de Chimie Moléculaire d'Orsay, Bâtiment 420, Université Paris-Sud, 91405 Orsay Cedex, France

Kagan, H. B., Girard, C., Guillaneux, D., Rainford, D., Samuel, O., Zhang, S. Y. and Zhao, S. H., 1996. Nonlinear Effects in Asymmetric Catalysis: Some Recent Aspects. – Acta Chem. Scand. 50: 345–352 © Acta Chemica Scandinavica 1996.

Some basic definitions and principles dealing with nonlinear effects are recalled. Examples of amplification or depression of the expected ee of the product are presented for some catalytic reactions involving organometallic complexes with chiral ligands. A mathematical model has been set up in order to analyze various situations and to make some predictions. The special case of mixtures of diastereomeric ligands having pseudo-enantiomeric relationships is discussed. Finally, an example of nonlinear effects in stoichiometric asymmetric synthesis is described in the case of the asymmetric reduction of acetophenone by Ipc_2BCl .

The properties of each single enantiomer often differ from the properties of a mixture of both enantiomers. It was Pasteur¹ who showed, in 1848, that solutions of natural or racemic tartaric acid had different abilities to rotate the plane of polarized light.

Since that time polarimetry remained the major way to obtain quantitative information on the relative amounts of each enantiomer in a sample, enantiomers giving the same contribution, but of opposite sign, to the overall rotation in the polarimetric cell. Horeau discovered, in 1969, that 1-ethyl-1-methylsuccinic acid failed to enter in the above category when its specific rotation was measured in chloroform.² The measured optical purity was significantly larger than the actual enantiomeric excess. This nonlinear property was interpreted as the consequence of diastereomeric autoassociations by hydrogen bonding in chloroform, while in water the solvation prevents aggregation allowing strict proportionality between ee and optical purity. The general case of the quantitative relationships between ee's and physical properties by diastereomeric interactions in solution have been discussed by Horeau and Guetté³ in 1974. Wynberg and Feringa in 1976 made the important comment, based on simple symmetry considerations, that the diastereomeric excess of some diastereoselective reactions should be influenced by the ee of the substrate.⁴

For example, they demonstrated that the lithium aluminum hydride reduction of racemic or natural camphor gave different relative amounts of isborneol and borneol. They also studied the asymmetric coupling of a chiral or racemic phenol and McMurry coupling of camphor.

These authors did not discuss the quantitative aspects connecting ee's of the starting material and the reaction stereoselectivities. In 1986, in a joint work with Professor Agami's group, we considered the case of asymmetric synthesis where the chiral auxiliary is not enantiomerically pure.⁵ We questioned the general assumption that the ee of the product (ee_{prod}) of an asymmetric synthesis is proportional to the ee of the chiral auxiliary (ee_{aux}). This allowed workers to make an estimation of the experimental ee (ee_{prod}) by a correction, knowing the maximum ee of the product (ee_0) being reached with enantiopure catalyst and using eqn. (1). This linear relationship is represented as curve A in Fig. 1.

$$ee_{\text{prod}} = ee_0 \cdot ee_{\text{aux}} \quad (1)$$

If the proportionality is not followed one can expect a plain curve above [curve B, positive nonlinear effect, abbreviated as (+)-NLE] or below [curve C, negative nonlinear effect or (–)-NLE] the straight line, respectively. These nonlinearities may in principle arise by autoassociation of the initial chiral species giving diastereomeric perturbations. We specifically studied asymmetric catalysis and will detail this subject in the next section.

* Contribution presented at the Nobel Symposium on *Catalytic Asymmetric Synthesis*, September 3–7, 1995 at Tammsvik, Bro, Sweden.

[†] To whom correspondence should be addressed.

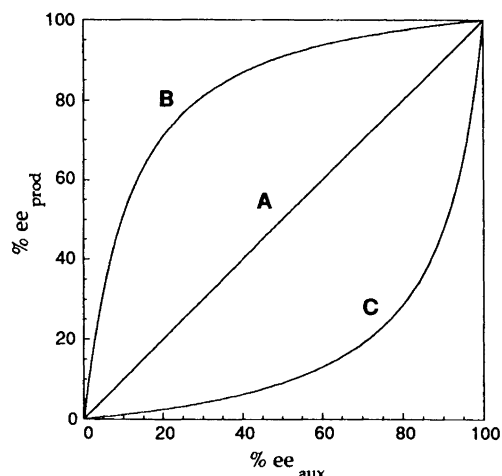


Fig. 1. Possible deviations from the (A) linear relationship between ee's of the auxiliary and the product: (B) positive and (C) negative nonlinear effects.

The first examples of nonlinear effects in asymmetric catalysis

We discovered, in 1986, three cases in which there is a significant nonlinear effect, thus validating the idea that eqn. (1) must be used with some caution.⁵ A weak (-)-NLE was observed in the asymmetric aldolization of triketone **1** in the presence of (*S*)-proline of various ee's (Fig. 2).⁶⁻⁸ This was interpreted by Agami *et al.* in terms of a kinetic model based on the fact that the reaction is second-order with respect to proline.⁹

A positive nonlinear effect was observed in the Sharpless epoxidation of geraniol **2** (Fig. 3, curve A). This is compatible with the Sharpless mechanism of asymmetric epoxidation, which indicates the intervention of a dimeric complex, introducing two tartrate units in the active species.¹⁰ The asymmetric sulfoxidation **5**→**6**

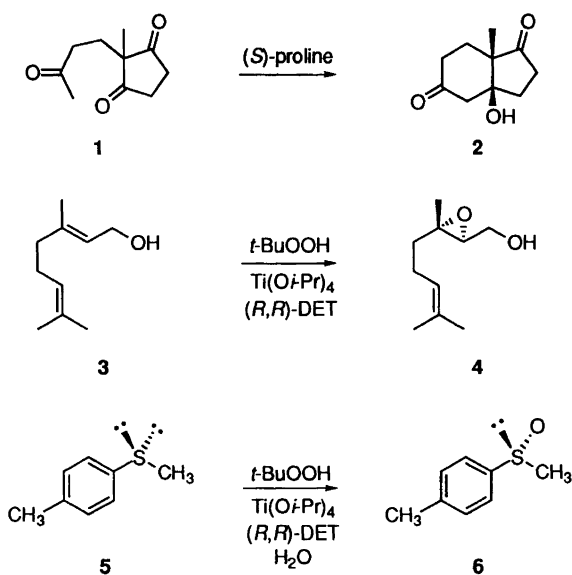


Fig. 2. Reactions in which the first NLEs were observed.

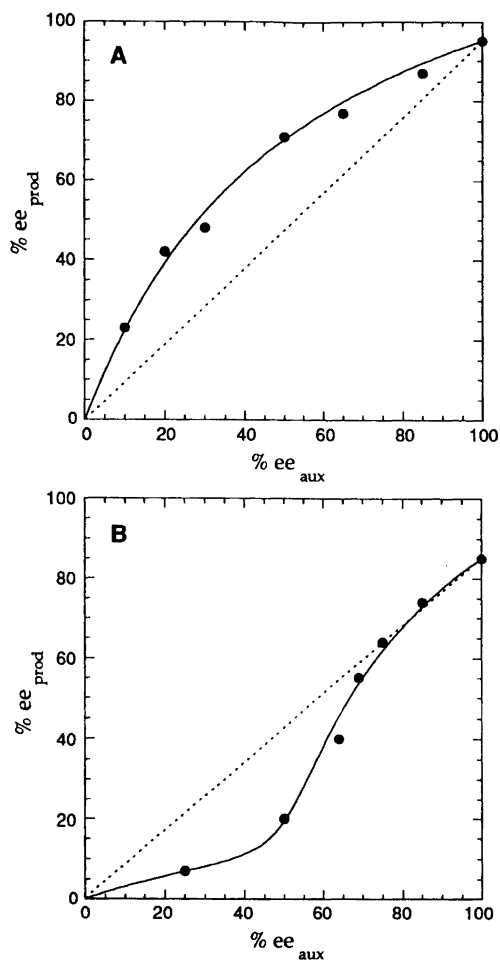


Fig. 3. Nonlinear effects in (A): asymmetric epoxidation of geraniol **2** and (B): oxidation of sulfide **5** (Ref. 5).

produced a (-)-NLE, until $ee_{aux} = 70\%$, then linearity was resumed (Fig. 3, curve B). This complex behavior is indicative of a complicated structure for the water-modified titanium complex,^{11,12} with the involvement of several diethyl tartrate molecules (DET) in the titanium complex.

In 1988, Oguni *et al.*¹³ produced an additional example of a nonlinear effect, specifically in the case of addition of Et_2Zn to benzaldehyde catalyzed by a chiral β -amino alcohol (Fig. 4). A strong (+)-NLE, for the formation of the carbinol **7**, was observed (called *amplification* by the authors). For example, **8** with 100% ee or 10% ee gave the alcohol **7** with 97% ee and 92% ee, respectively.

In 1989 Noyori *et al.*¹⁴ studied in great detail a similar reaction, using β -amino alcohol **9** as the catalyst (Fig. 5, curve A). The mechanistic investigation showed that the strong amplification originated mainly from the initial formation of a stable heterochiral dimer of the zinc alcoholate of **9**. This interesting reaction has been investigated in depth at the molecular level.^{15,16} In 1990 Mikami and Nakai¹⁷ disclosed a spectacular example of (+)-NLE in an enantioselective glyoxylate ene-reaction catalyzed by a chiral titanium complex **10** (Fig. 5, curve B).

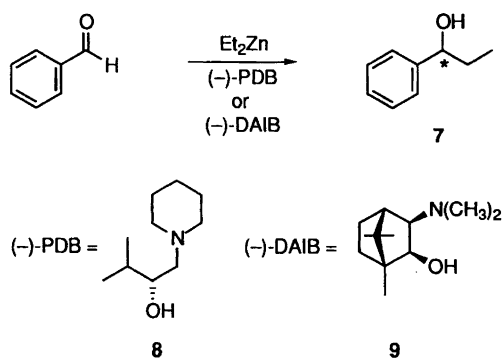


Fig. 4. Enantioselective diethylzinc addition to benzaldehyde catalyzed by **8** or **9** (Refs. 13 and 14).

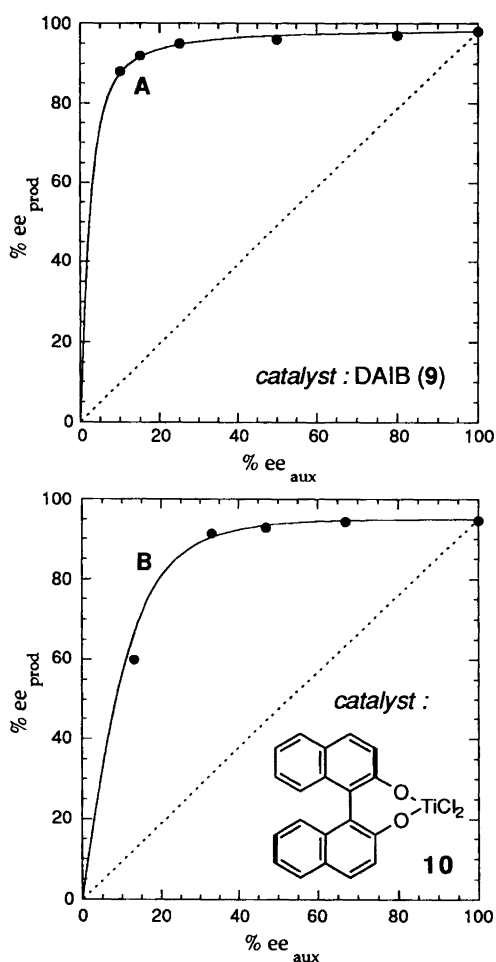


Fig. 5. NLEs in (A) the formation of **7** (Fig. 4 and Ref. 14) and (B) the ene-reaction between methyl glyoxylate and 1-methylstyrene (Ref. 17).

In 1991 nonlinear effects observed in various asymmetric catalytic reactions were described, for example in the conjugated addition of diethylzinc to chalcone catalyzed by a chiral nickel complex,¹⁸ to cite only one. The present article will not cover all the reports on nonlinear effects, which will appear in a separate review article.¹⁹

Some models for nonlinear effects

Usually asymmetric catalytic reactions are performed by adding a chiral ligand to a metal complex, giving rise to an *in situ* catalytically active complex. This procedure applies, for example, in asymmetric hydrogenation with phosphines–rhodium systems or to Sharpless epoxidation of allylic alcohols. In a recent paper,²⁰ we classified the nonlinear effects into two broad classes, called model 1 and model 2. Here we will describe briefly those two situations.

Model 1. We considered first a fast ligand exchange between reactive species involving two chiral ligands (L_R , L_S), for example around a metallic center M , giving an ML_2 complex [the discussion is identical for the $(ML)_2$ system or even for dimeric species symbolized by L_2]. We assumed an equilibrium between complexes ML_RL_R , ML_SL_S and ML_RL_S , in amounts of x , y , and z respectively, and a last irreversible step with pseudo-first order constants k_{RR} , k_{SS} and k_{RS} ; these apparent rate constants include absolute rates and equilibrium constants. Enantiomeric products (of $ee = EE_0$) are obtained from the two homochiral catalysts, while the *meso* catalyst generates a racemic product (Fig. 6).

Simple calculations allowed us to express the ee of the product (EE_{prod}) as a function of ee_0 , ee_{aux} , g and β [eqn. (2)].²⁰

$$ee_{\text{prod}} = ee_0 ee_{\text{aux}} \frac{1 + \beta}{1 + g\beta} \quad (2)$$

When $\beta = 0$ (no *meso* complex) or if $g = 0$ (unreactive *meso* complex) eqn. (2) reverts to eqn. (1), which means that there is a linear correlation. If $g < 1$ (*meso* complex less reactive than the homochiral complexes) there is an amplification effect which is maximum for $g = 0$ (with an amplification factor of $1 + \beta$). If $g > 1$ there is a depressing effect [with a factor $(1 + \beta)/(1 + g\beta) < 1$]. In order to use eqn. (2), to compute the curves $ee_{\text{prod}} = f(ee_{\text{aux}}, ee_0, K)$, it is necessary to express β as a function of ee_{aux} and K . The analytical expression has been calculated,²⁰ and will be not detailed here. In the case where there is a statistical distribution of ligands between the three complexes the equilibrium constant K becomes equal to 4. The corresponding curve $ee_{\text{prod}} = f(ee_{\text{aux}})$ is indicated in Fig. 7.

The maximum amplification is obtained for $g = 0$ (*meso*

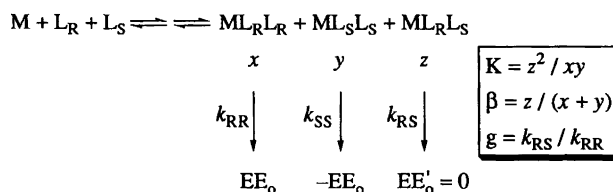


Fig. 6. Simplified model for the ML_2 system with the catalytic complexes in equilibrium (in respective concentrations of x , y and z).

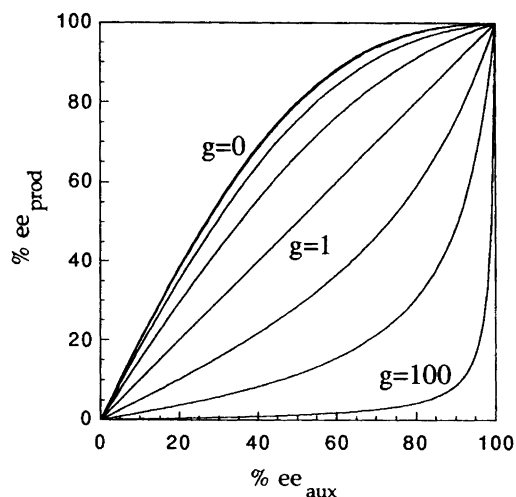


Fig. 7. Computer simulation of NLEs for the ML_2 system (statistical distribution of L_R and L_S ligands, $K=4$) for $ee_o=100\%$ and $g=0, 0.01, 0.1, 0.33, 1, 3, 10$ and 100 (redrawn from Ref. 20).

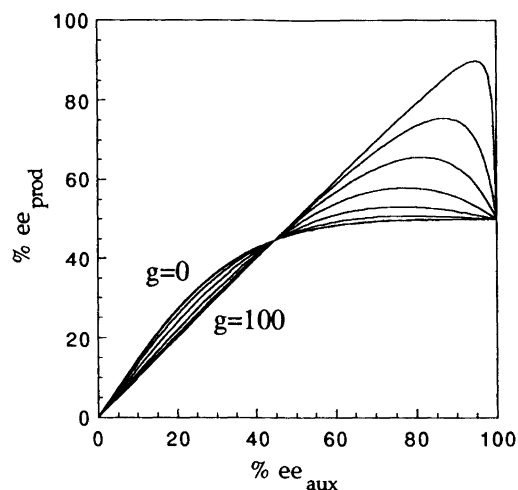


Fig. 8. Computer simulation of NLEs for the ML_3 system (statistical distribution of L_R and L_S ligands) for $ee_o=50\%$, $ee'_o=100\%$ and $g=0, 0.01, 0.1, 0.33, 1, 3, 10$ and 100 (redrawn from Ref. 20).

complex unreactive), while depression can be very important if one can reach high reactivities for the *meso* complex (large values for g). The (+)-NLE is substantially increased if K is large (>4); for more details and curves see Ref. 20.

Model 1 (Fig. 6) was extended to complexes having three or four ligands (ML_3 and ML_4 cases) and generalized to ML_n species.²⁰ Additional parameters were needed to define the relative amounts and catalytic activities of these complexes. The family of curves often have the same general features as the set of curves in Fig. 7. However, we discovered very unexpected cases. For example, the ML_3 can give rise to a homochiral complex ($ML_R L_R L_R$, $ML_S L_S L_S$) and an heterochiral complex ($ML_R L_R L_S$, $ML_S L_S L_R$). This last one is not a *meso* compound and will generate a product with $ee'_o \neq 0$. For a given set of parameters expressing a superior reactivity and enantioselectivity of the heterochiral complex (with respect to the homochiral complex), one finds that the product has a higher ee when the chiral auxiliary is not enantiopure (see an example in Fig. 8).

Finally, ML_n systems with $n \geq 4$ give rise to curves with very complicated shapes. Some curves cross the straight line of the linear correlation several times or are multi-shaped above or below the straight line. A triple-shaped curve has recently been found experimentally by Pfaltz *et al.*²¹

The equations developed for catalysis by stereoisomeric ML_n complexes allowed us to reproduce many experimental curves by selecting the appropriate choice of n , g and K values.²⁰ For example ML_2 [equivalent to $(ML)_2$] applied well to curve A of Fig. 3, while ML_4 model was used to simulate curve B of Fig. 3. The ML_4 model [equivalent to $(ML)_4$] was also useful to give a curve which fits well with the experimental case of asymmetric 1,4-cuprate addition in a muscone syn-

thesis.²² In this experiment, a double-shaped curve [(−)-NLE at low ee_{aux} , (+)-NLE at high ee_{aux}] has been observed.

Model 2. Part of the chiral auxiliary (of initial enantiomeric excess ee_{aux}) may be diverted from the catalytically active ML_n complexes through the prior or competitive formation of catalytically inactive species $M'L_n$. The chiral auxiliary may be stored with an enantiomeric excess different from the initial ee (ee_{aux}). As a consequence, the effective ee of the chiral auxiliary entering in the catalytically active complexes will be changed. We named this phenomenon the *reservoir effect*. We called ee_{res} and ee_{eff} the enantiomeric excesses of the chiral auxiliary which is in the reservoir and distributed in the catalytically active species, respectively. If one starts from 1 mol of chiral auxiliary ($L_R + L_S$), it is easy to establish that ee_{eff} is given by eqn. (3).

$$ee_{eff} = \frac{ee_{aux} - \alpha ee_{res}}{1 - \alpha} \quad (3)$$

In this equation, α is the mole fraction of chiral auxiliary which is stored in the reservoir. For example one calculates that if a reservoir diverts in a racemic composition 40% of the chiral auxiliary initially present with an $ee_{aux}=50\%$, then 60% of the catalyst is left for catalysis with $ee_{eff}=83\%$. Here is a substantial amplification. If $ee_{res} < ee_{aux}$ there will be a (−)-NLE (depressing effect).

In the most general situation the reservoir effect (model 2) may superimpose model 1. The enantiomeric excess of the product is then given by the general equation of model 2 such as eqn. (2) related to ML_2 case, where ee_{aux} is replaced by ee_{res} , which is the actual ee involved in the production of the various stereoisomeric catalytic

complexes. The reservoir effect with storage of racemic composition seems to be an important feature of many (+)-NLE described in literature.¹³⁻¹⁸ Formation of an inactive *meso* complex such as $ML_R L_S$ or $ML_R L_R L_S L_S$ is a particular case of a reservoir involving complexes directly related to the catalytic species.

Pseudo-enantiomeric chiral auxiliaries

It is known that some diastereomeric chiral auxiliaries sometimes induce the formation of products of opposite configuration with ee's which can be similar or different. This is particularly well established for many asymmetric reactions (catalytic or stoichiometric) using alkaloids as chiral auxiliaries. It is then usually considered that quinine and quinidine have pseudo-enantiomeric relationships for the C2 and C9 configurations (Fig. 9).

We were interested to check whether some of the features connected to the presence of a mixture of enantiomers could be found when the chiral auxiliary used to produce the catalyst was a mixture of pseudo-enantiomers. If some interactions occur between the two one-ligand complexes, if ligands are competitors towards a metal center or if complexes bearing two different ligands are produced, one can expect some deviations to the calculated curve $ee_{\text{prod}} = f(\%$ of the two chiral auxiliaries) which should give a linear correlation. For that purpose, and as an example, we investigated the Sharpless dihydroxylation²³ of 2,2'-dibromostilbene (**11**) using OsO_4 (1 mol%), a chiral auxiliary (10 mol%) and a stoichiometric reoxidant [$K_3Fe(CN)_6$, 3 equiv.] as illustrated in Fig. 10.

We found that mixtures of $(DHQ)_2$ PHAL and $(DHQD)_2$ PHAL (giving *R,R*-diol **12** in 98% ee) provided an almost linear correlation. For mixtures of DHQ-PCB (giving the *S,S*-diol **12** in 91% ee) and $(DHQD)_2$ PHAL, a strong (+)-NLE was observed,²⁴ as expected from the previous mechanistic studies of asymmetric dihydroxylation²³ (Fig. 11). A similar study has recently been published by Noyori, in which a mixture of diastereomeric

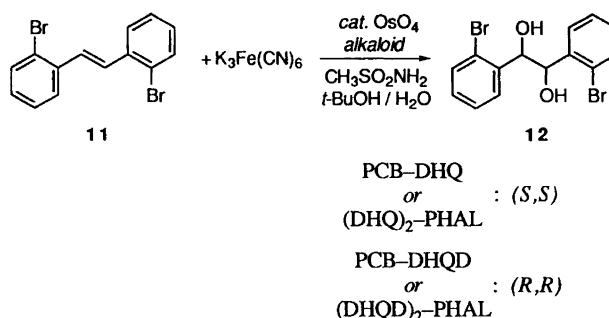


Fig. 10. Asymmetric dihydroxylation of 2,2'-dibromostilbene (**11**) with pseudo-enantiomeric chiral catalysts.

eric β -amino alcohols was used as the catalyst in the addition of Et_2Zn to benzaldehyde. A detailed mechanistic investigation clarified the origin of the observed nonlinear effects.¹⁶

Nonlinear effects in stoichiometric asymmetric synthesis

The main trend observed above for catalytic reactions apply also to stoichiometric asymmetric synthesis. Let us assume that a chiral auxiliary L_R , L_S is part of a chiral reagent abbreviated as ML_n . If the reagent has an ML_2 structure one deals with model 1 of asymmetric catalysis (Fig. 6) in which the initial composition $ML_R L_R$, $ML_S L_S$ and $ML_R L_S$ is defined by x , y , z (or by parameters β and K , where K is no longer an equilibrium constant). It is not necessary to consider the relative reactivity g if we assume the full use of 1 mol equiv. of the reagent for the transformation of the achiral substrate into the mixture of enantiomeric products. The product will be formed by the two homochiral reagents and the *meso* reagent. It is easy to calculate ee_{prod} since it appears in eqn. (1) and there is no NLE. As in the catalytic reaction if there is no *meso* complex ($\beta=0$) the same linearity will be observed in all cases.

However, the presence of a very large excess of ligands will cause retention of the relative concentrations of the three complexes at relatively the same levels during the entire course of the reaction. In this case the calculations are equivalent to those of the catalytic reaction, ending up with eqn. (2). If the heterochiral reagent generated is very unreactive, then one can expect that the maximum (+)-NLE will be reached for $k_{RS} \rightarrow 0$, giving $g \rightarrow 0$, and eqn. (4) will describe this particular situation.

$$ee_{\text{prod}} = ee_o ee_{\text{aux}} (1 + \beta) \quad (4)$$

If the conversion of the chiral reagent is not complete, or if there is an excess of the reagent, then a more complicated equation is needed in order to take into account the relative reactivity g of the *meso* isomer with respect to the homochiral reagents.

Finally a *reservoir effect* may also operate if the chiral

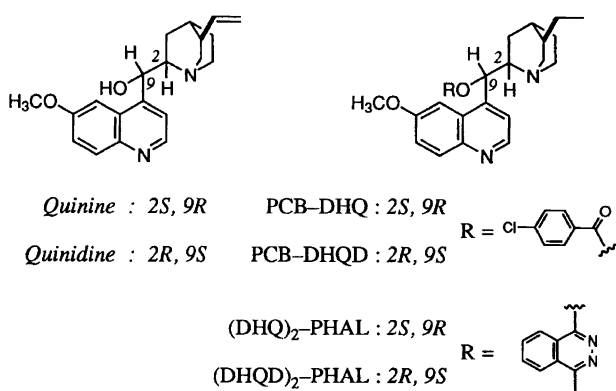


Fig. 9. Pseudo-enantiomeric chiral auxiliaries.

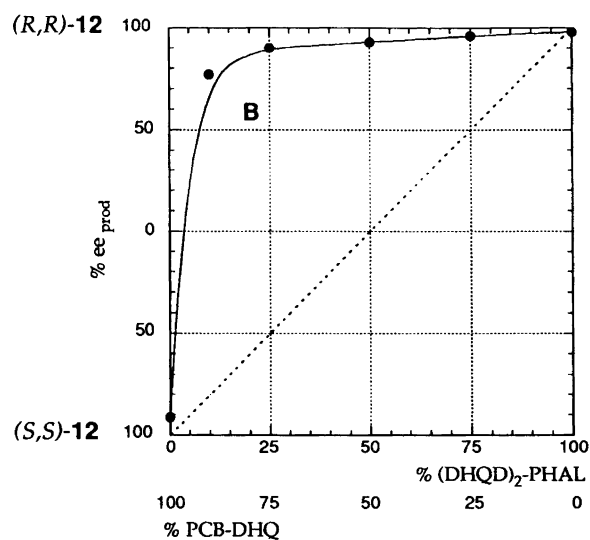
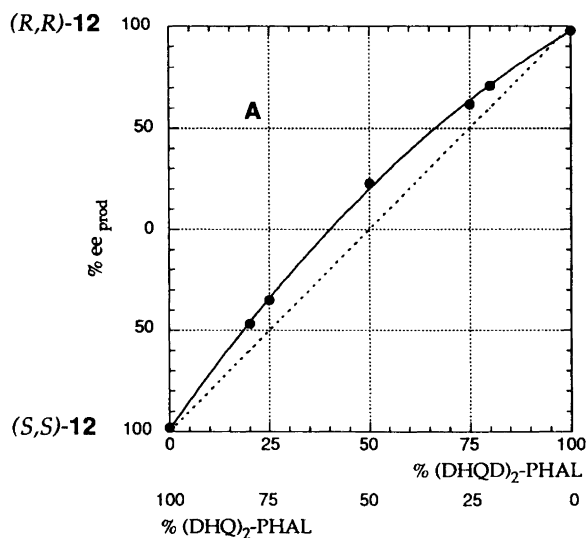


Fig. 11. Sharpless asymmetric dihydroxylation of **11** (Fig. 10) using (A) (DHQD)₂-PHAL/(DHQ)₂-PHAL and (B) (DHQD)₂-PHAL/PCB-DHQ as mixtures of pseudo-enantiomeric catalysts (Ref. 24).

auxiliary competitively generates inactive multiligand species. In this case ee_{aux} has to be replaced by ee_{eff} [eqn. (3)] in the calculations of ee_{prod} .

An example of a nonlinear effect was recently described by Shinkai *et al.* during the reduction of an aromatic ketone, by the Brown reagent Ip_2BCl , produced from α -pinene and BH_2Cl .²⁵ Starting with 70% ee α -pinene they obtained an alcohol of 95% ee. We also studied the asymmetric reduction of acetophenone by Ip_2BCl .²⁶ We prepared the reagent from (–)- α -pinene by the Brown procedure, i.e. formation of Ip_2BH and its further transformation by HCl into Ip_2BCl .^{27,28} We performed two sets of preparations (Fig. 12). The reagent was first prepared from (–)- α -pinene of various ee (reagent 1). In another approach (+)- or (–)- α -pinene of very high ee was used to prepare separately the two enantiomerically

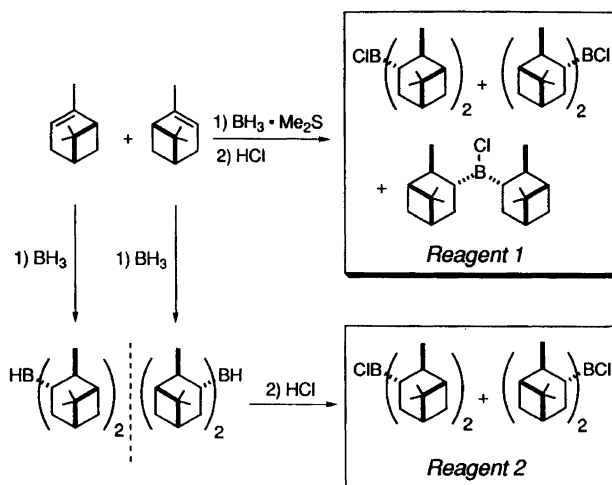


Fig. 12. Preparation of chloroboranes as reagent 1 and reagent 2 starting with α -pinenes.

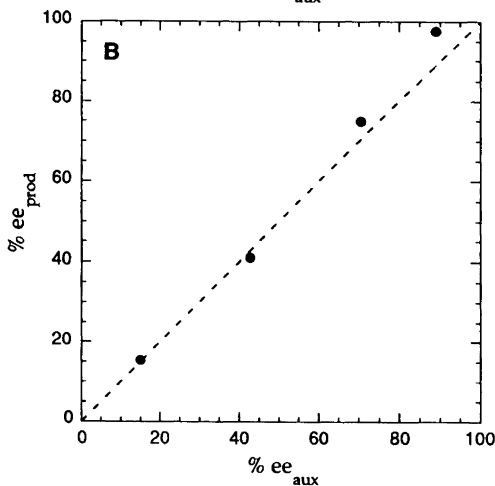
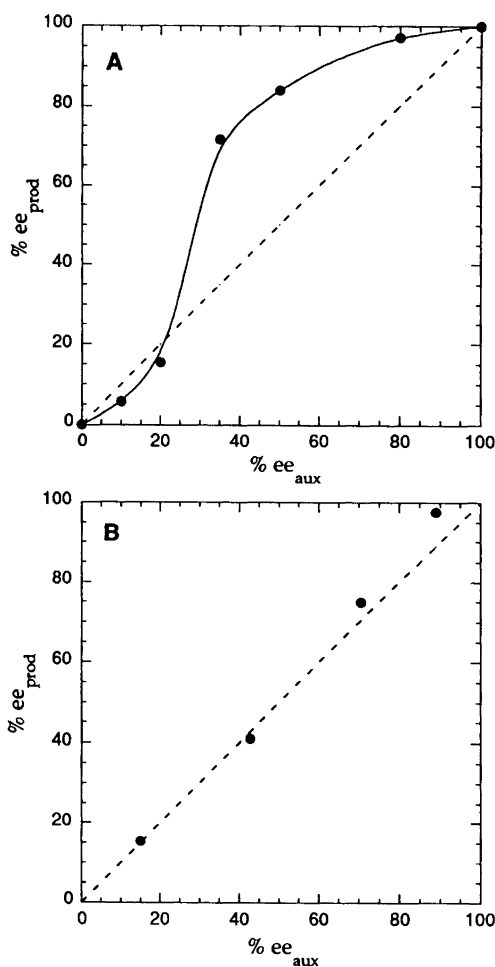


Fig. 13. Nonlinear effects in the reduction of acetophenone by Ip_2BCl using (A) reagent 1 and (B) reagent 2 (Ref. 26).

pure reagents; the reagent 2 of intermediate ee was then obtained by mixing the two enantiopure boranes before reacting them with HCl.

In the first case, Ipc_2BCl gave a strong (+)-NLE while in the second case very good linearity was observed (Fig. 13). These facts are well explained (Fig. 12) by considering that diastereomeric Ipc_2BCl reagents (reagent 1) are formed when one starts from (–)- α -pinene, the *meso* reagent being of very low reactivity with respect to the homochiral reagents. A *reservoir effect* is operating here, with storage of $ee_{\text{res}}=0$ giving $ee_{\text{eff}}>ee_{\text{aux}}$. Reagent 2 contains no *meso*-chloroborane reagent and therefore cannot give rise to an NLE. The reaction was performed with 4 equiv. of Ipc_2BCl in order to obtain a good conversion of acetophenone into alcohol.

The mode of preparation of the chiral reagent from the chiral auxiliary is very important and will determine the presence or the absence of a nonlinear effect. A similar observation was made recently by Mikami in a catalytic asymmetric Diels–Alder reaction.²⁹ The chiral Lewis acid catalyst $(\text{RO})_2\text{TiCl}_2$ was prepared from BINOL and $\text{Ti}(\text{O}i\text{-Pr})_2\text{Cl}_2$. A strong (+)-NLE was observed when the catalyst was prepared from BINOL of various ee. Enantiopure (*R*) or (*S*)-BINOL was used for the synthesis of the two enantiopure catalysts, subsequently mixed in various amounts to give the catalysts of intermediate ee. With the latter catalysts, the reaction showed a perfect linearity (no NLE). The experimental facts were explained by the presence of dimeric complexes (associated by a Cl bridge) which do not interconvert under the reaction conditions.

Conclusion

The existence of nonlinear effects in catalytic or stoichiometric asymmetric reactions may have some important consequences, which are summarized below.

If a chiral auxiliary is not enantiomerically pure and is used to prepare a catalyst, it is dangerous to extrapolate, to estimate the ee of the product, from experiments where $ee_{\text{aux}} \neq 100\%$. It is wise to make assays with intermediate values of ee_{aux} in order to check the absence of an NLE.

A strong amplification may be useful for synthetic operations where the chiral auxiliary is difficult to obtain as an enantiomerically pure material.

Calculations on very simple models³⁰ allow various predictions to be made on the shape of the curves $ee_{\text{prod}} = f(ee_{\text{aux}})$. One interesting prediction is that higher ee for the product could occur in some cases when the chiral auxiliary is not enantiomerically pure.

Nonlinear effects are a good indication of the formation of diastereomeric species. They can be a tool for some mechanistic studies of stoichiometric or catalytic asymmetric syntheses.

Finally positive NLEs (amplification) should be of interest in the construction of self-replicating systems using a chiral auxiliary of low ee. If the catalyzed reaction produces the chiral auxiliary, and if there is fast exchange of ligands of the catalyst, a large amount of material of high ee will be generated, thanks to the amplification.^{31–33}

Acknowledgments. We thank CNRS for its financial support. C. Girard is grateful to the Ministère des Affaires Étrangères de France for the North American Chateaubriand postdoctoral fellowship. D. Rainford and S. Y. Zhang acknowledge postdoctoral fellowships from CNRS and CNRS–K. C. Wong, respectively. D. Guillaneux thanks DRET for a fellowship.

References

1. Pasteur, L. *C. R. Acad. Sci. Paris* 26 (1848) 535.
2. Horeau, A. *Tetrahedron Lett.* (1969) 3121.
3. Horeau, A. and Guetté, J. P. *Tetrahedron* 30 (1974) 1923.
4. Wynberg, H. and Feringa, B. *Tetrahedron* 32 (1976) 2831.
5. Puchot, C., Samuel, O., Duñach, E., Zhao, S. H., Agami, C. and Kagan, H. B. *J. Am. Chem. Soc.* 108 (1986) 2353.
6. Eder, U., Sauer, G. and Wiechert, R. *Angew. Chem. Int. Ed. Engl.* 10 (1971) 496.
7. Hajos, S. Z. and Parrish, D. *J. Org. Chem.* 39 (1974) 1615.
8. Agami, C. *Bull. Soc. Chim. Fr.* (1988) 499 and references quoted therein.
9. Agami, C. and Puchot, C. *J. Mol. Catal.* 38 (1986) 341.
10. Finn, M. G. and Sharpless, K. B. *J. Am. Chem. Soc.* 113 (1991) 113.
11. Pitchen, P., Duñach, E., Deshmukh, M. N. and Kagan, H. B. *J. Am. Chem. Soc.* 106 (1984) 8188.
12. Kagan, H. B. and Rebière, F. *Synlett.* (1990) 643.
13. Oguni, N., Matsuda, Y. and Kaneko, T. *J. Am. Chem. Soc.* 110 (1988) 7877.
14. Kitamura, M., Okada, S., Suga, S. and Noyori, R. *J. Am. Chem. Soc.* 111 (1989) 4028.
15. Noyori, R. and Matsuda, M. *Angew. Chem., Int. Ed. Engl.* 30 (1991) 49.
16. Kitamura, M., Suga, S., Niwa, M. and Noyori, R. *J. Am. Chem. Soc.* 117 (1995) 4832.
17. Terada, M., Mikami, K. and Nakai, T. *J. Chem. Soc., Chem. Commun.* (1990) 1623.
18. Bolm, C. *Tetrahedron: Asymmetry* 2 (1991) 701.
19. Kagan, H. B., Girard, C. and Guillaneux, D. *In preparation.*
20. Guillaneux, D., Zhao, S. H., Samuel, O., Rainford, D. and Kagan, H. B. *J. Am. Chem. Soc.* 116 (1994) 9430.
21. Zhou, Q. L. and Pfaltz, A. *Tetrahedron* 50 (1994) 4467.
22. Tanaka, K., Matsui, J., Kawabata, Y., Suzuki, H. and Watanabe, A. *J. Chem. Soc., Chem. Commun.* (1991) 1632.
23. Kolb, H. C., Anderson, P. G., Bennani, Y. L., Crispino, G. A., Jeong, K. S., Kwong, H. L. and Sharpless, K. B. *J. Am. Chem. Soc.* 115 (1993) 12226.
24. Zhang, S. Y., Girard, C. and Kagan, H. B. *Tetrahedron: Asymmetry* 6 (1995) 2637.
25. Shinkai, I., King, A. O. and Larsen, R. D. *Pure Appl. Chem.* 66 (1994) 1551.
26. Girard, C. and Kagan, H. B. *Tetrahedron: Asymmetry* 6 (1995) 1881.
27. Brown, H. C. and Joshi, N. N. *J. Org. Chem.* 53 (1988) 4059.
28. Chandrasekharan, J., Ramachandran, P. V. and Brown, H. C. *J. Org. Chem.* 50 (1985) 5448.

29. Mikami, K., Motoyama, Y. and Terada, M. *J. Am. Chem. Soc.* *116* (1994) 2812.
30. For the various approximations involved in these models see notes 31 and 39 of Ref. 20. One did not consider the catalyst which may arise by interaction with the product.³¹
31. Alberts, A. H. and Wynberg, H. *J. Chem. Soc., Chem. Commun.* (1990) 453.
32. Soai, K., Hayase, T. and Takai, K. *Tetrahedron: Asymmetry* *6* (1995) 637.
33. Bailey, P. D. *J. Chem. Soc., Chem. Commun.* (1995) 1797.

Received October 3, 1995.