

Asymmetric Phase Transfer Catalysis Utilizing the Quaternary Ammonium Salts derived from Cinchona Alkaloids

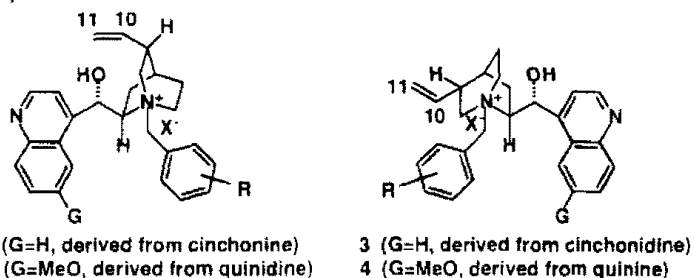
Takayuki Shioiri

*Graduate School of Pharmaceutical Sciences, Nagoya City University Tanabe-dori, Mizuho-ku,
Nagoya 467-8603, Japan*

Phase transfer catalysis (PTC) has now been recognized as a practical methodology for organic synthesis due to its operational simplicity, high yield processes, mild reaction conditions, use of safe and inexpensive reagents and solvents, safety considerations, environmental concerns, and possibility to conduct reactions on large scale. Furthermore, since phase transfer catalysis will increase the reaction rate and replace, reduce or eliminate solvents, it has a wide industrial application especially in pharmaceutical and agrochemical manufacturing as well as perfumes, flavors and dyes industry. Thus, phase transfer catalysis in general has now become a standard method in synthesis.

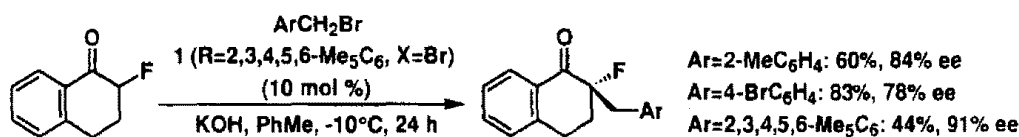
In contrast, the progress of asymmetric synthesis by use of chiral non-racemic phase transfer catalysts has been slow compared to the ordinary phase transfer catalysis. However, recent achievements in this particular area are noteworthy and efficient asymmetric phase transfer catalysis has been increasingly explored.¹ Especially, the quaternary ammonium salt derived from cinchona alkaloids now occupy the central position in designing the chiral non-racemic phase transfer catalysts because they have various functional groups easily derivatized and are commercially available with cheap price. As shown in Fig. 1, the exact relationship between the onium salts derived from cinchonine (or quinine) and cinchonidine (or quinidine) is diastereomeric, but their amino alcohol parts, the key parts for asymmetric induction, are enantiomeric. Thus, the relationship between 1 and 3 (2 and 4) is called "pseudoenantiomeric". Typically, if one family of catalysts gives (S)-enantiomer as the major product, the other family yields the antipodal (R)-enantiomer in excess.

Fig. 1

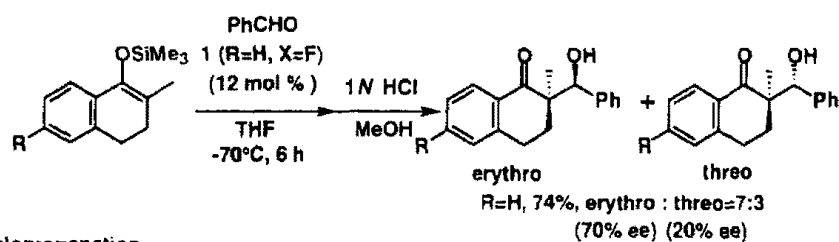


Utilizing these salts as catalysts, we have developed the following asymmetric phase transfer reactions: asymmetric alkylation of α -fluorotetralone, asymmetric aldol reaction of silyl enol ethers, asymmetric cyclopropanation, asymmetric Darzens reaction, asymmetric epoxidation, asymmetric α -hydroxylation of cyclic ketones, and asymmetric isomerization of alkynes to allenes. Some representative examples are shown in the following. In this talk, the recent results developed by our group in this area will be presented.

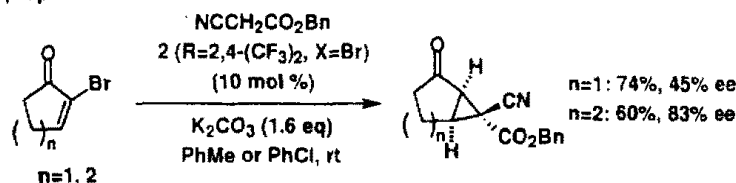
1. C-Alkylation



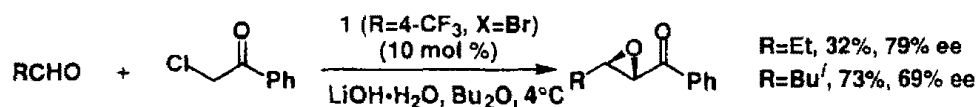
2. Silyl-Aldol Reaction: The First Preparation and Use of Chiral Ammonium Fluorides



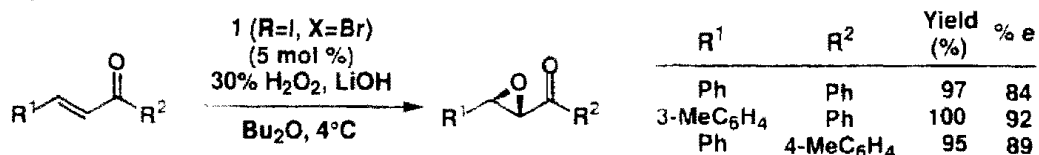
3. Cyclopropanation



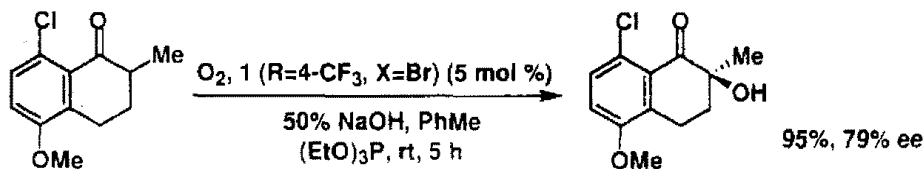
4. Darzens Reaction



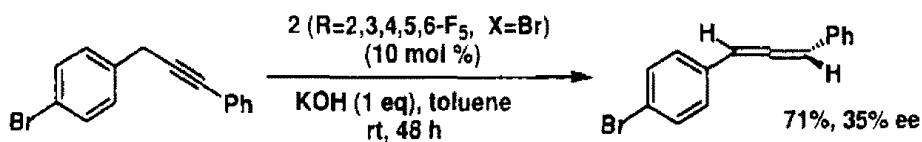
5. Epoxydation



6. Hydroxylation



7. Isomerization of Alkynes to Allenes



References

1. T. Shioiri and S. Arai, Asymmetric Phase Transfer Catalysis in "Stimulating Concepts in Chemistry" ed. M. Shibasaki, J.F. Stoddart, F. Vogtle, WILEY-VCH, Weinheim, 123-143 (2000).