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An Efficient Method for the Kinetic Resolution of Cyclic dl-Dicarboxylic Anhydrides Catalyzed by Diphenylboryl Triflate

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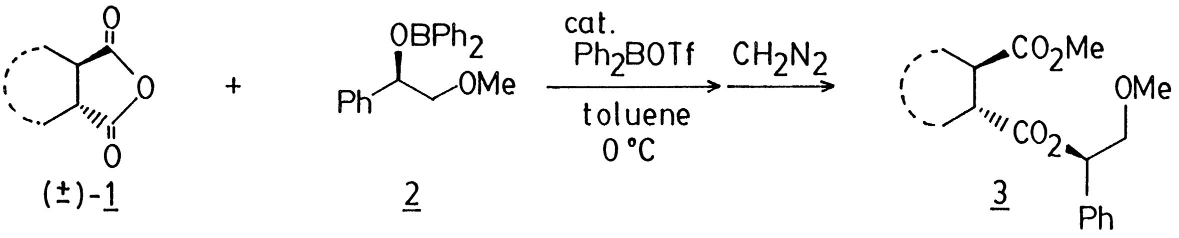
In the presence of a catalytic amount of diphenylboryl triflate, the kinetic resolution of cyclic dl-dicarboxylic anhydrides is effectively achieved by the use of diphenylboric ester of (R)-2-methoxy-1-phenylethanol as the chiral source.

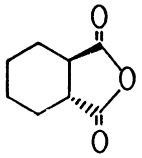
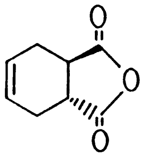
The kinetic resolution of racemic dicarboxylic acid derivatives is a promising method for the preparation of optically active dicarboxylic acid derivatives, useful intermediates for natural products syntheses. However, this method has largely been overlooked from the standpoint of organic synthesis, and there are only a few reports on the kinetic resolution of racemic dicarboxylic acid derivatives, that is, the selective hydrolysis of the racemic diester by enzyme or microorganism1) and the selective amidation of the racemic dicarboxylic anhydrides with the chiral binaphthyldiamine derivative.2-4) In the above-mentioned chemical method, both the chemical yield and the stereoselectivity were not satisfactory, although a fivefold excess of the anhydride was used per one mole of the chiral source. Therefore, an efficient method for the kinetic resolution of racemic dicarboxylic anhydrides by the chemical procedure is a challenging goal of great interest in synthetic chemistry.

In the previous paper,5) it has been reported that, in the presence of a catalytic amount of diphenylboryl triflate, cyclic meso-dicarboxylic anhydrides are esterified with diphenylboric ester of (R)-2-methoxy-1-phenylethanol in a highly stereoselective manner. In this reaction, discrimination between two enantiotopic carbonyl groups in symmetrical dicarboxylic anhydrides is effectively achieved by the chiral diphenylboric ester with the formation of the rigid five-membered ring structure. It is assumed that this asymmetric esterification can be applied to the kinetic resolution of cyclic dl-dicarboxylic anhydrides, because the chiral diphenylboric ester differentiates enantiomers of racemic dicarboxylic anhydrides, and the reaction rates of both enantiomers for the esterification must be different from each other.



Scheme 1.

Table 1. The kinetic resolution of cyclic dl-dicarboxylic anhydrides

Entry	Anhydride	Molar ratio of 1 per 2	Yield/%[a)]	Diastereomer excess/%[b)]	Absolute configuration[c)]
1		2.0	73	90	1R,2R
2		2.8	81	90	1R,2R
3		5.0	76	92	1R,2R
4		2.0	71	80	1R,2R

a) Yields are based on 2.

b) Determined by HPLC.

c) Determined by comparison of the optical rotation value of dimethyl trans-1,2-cyclohexanedicarboxylate in Ref.6, after the removal of the chiral source by catalytic hydrogenation and the treatment with diazomethane.

Based on this consideration, an initial probe of the reaction was attempted. Namely, in the presence of a catalytic amount of diphenylboryl triflate (0.31 mmol), dl-trans-1,2-cyclohexanedicarboxylic anhydride (1.57 mmol) was treated with diphenylboric ester of (R)-2-methoxy-1-phenylethanol (0.79 mmol) in toluene (16 ml) at 0 °C for 118 h. After usual work-up and the treatment with diazomethane, the desired diester was obtained [0.58 mmol, 73% based on the chiral source, $[\alpha]_D^{21}$ -87.6° (c 0.96, CH_2Cl_2)]. It was shown that, by the HPLC analysis of the diester, the reaction proceeded with high stereoselectivity (90% d.e.). In contrast to the conventional kinetic resolution, the increase of the substrate (anhydride) did not have a significant effect on the stereoselectivity (entries 2,3).

It was proved that the efficient kinetic resolution of the racemic dicarboxylic anhydride became possible by the use of theoretical amount of the reagent, a twofold excess of the anhydride to the chiral source. Then the application of this method to other cyclic dl-dicarboxylic anhydride was examined and proved to be sucessful (entry 4).

It should be pointed out that the diesters thus obtained have absolute configuration of (1R, 2R). This result indicates that the distinction between enantiomers of the racemic anhydrides was effectively realized. That is, in the case of the enantiomer with absolute configuration of (1S, 2S), the approaoch of the chiral diphenylboric ester (2) to the anhydride (1) is limited by the steric repulsion between phenyl group of 2 and α-hydrogen atom of 1 as illustrated in Fig. 1. On the other hand, the enantiomer with absolute configuration of (1R, 2R) does not cause such repulsion, therefore this enantiomer is preferentially esterified with the chiral diphenylboric ester (2).

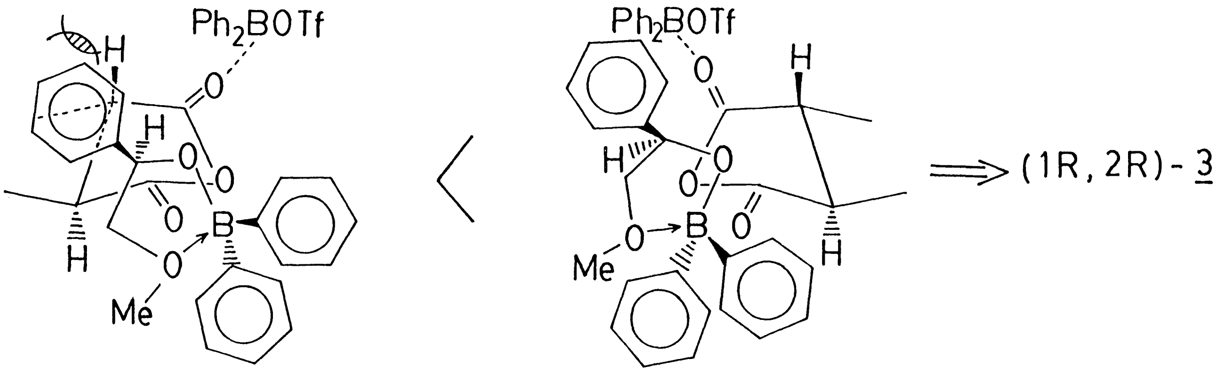


Fig. 1.

Thus, the present method has a characteristic feature of synthetic usefulness as follows; 1) the kinetic resolution of cyclic dl-dicarboxylic anhydrides was effectively achieved by the use of a twofold excess of the anhydrides; 2) the chiral source was readily synthesized from commercially available methyl mandelate; 3) after the reaction, the chiral source was easily removed by catalytic hydrogenation under mild conditions to afford the optically active half-esters in high yields.

References

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