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Substrate-selective catalysis in an aqueous biphasic system with per(2,6-di-*O*-methyl)-β-cyclodextrin

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Abstract

The biphasic palladium-catalysed cleavage of water-insoluble allylic substrates in the presence of methylated cyclodextrins has been investigated with the aim of performing substrate-selective catalytic reactions. While no substrate selectivity was observed in control experiments in which acetonitrile was used as mass transfer promoter, the use of DMCyD led in some cases to high substrate selectivities. For instance, a 97:3 product ratio was observed during the cleavage of a 50:50 mixture of *N*-dodecyl-*O*-allyl urethane and *N*,*N*-dihexyl-*O*-allyl urethane. The whole results demonstrate that the size-fit concept which postulates the highest reactivity for the best size-matched host–guest pair is limited to predict the substrate selectivity.

Keywords: Cyclodextrin; Two-phase catalysis; Substrate selectivity; Palladium; Carbonates; Urethanes

1. Introduction

During these last years, cyclodextrins which are cyclic oligosaccharides composed of glucopyranose units linked by an α-(1-4) glucosidic bond have greatly contributed to extend the scope of the aqueous organometallic catalysis [1]. The role played by cyclodextrins in this field is ascribed to their complexing properties and it is postulated that cyclodextrins operate like inverse phase transfer catalysts according to Scheme 1 [2].

In this mechanism, the cyclodextrin which is represented by a truncated cone forms a host/guest complex with the substrate at the liquid/liquid interface and transfers the water-insoluble substrate (S) into the aqueous phase where it reacts with the water-soluble organometallic catalyst. After reaction, the product (P) is released in the organic phase and the transfer cycle can go on.

Native cyclodextrins are effective inverse phase transfer catalysts for the epoxydation [3] or oxidation [4] of olefins, hydrogenation of α,β-unsaturated acids or α-keto ester [5], reduction of conjugated dienes [6], aryl alkyl ketones [7] or aromatic derivatives [8]. Interestingly, chemically modified cyclodextrins like the per(2,6-di-*O*-methyl)-β-cyclodextrin (DMCyD) show a better catalytic activity than native cyclodextrins in numerous reactions such as the Wacker oxidation [9,10], hydroformylation [11,12], hydrocarboxylation of olefins [13], and the hydrogenation of aldehydes [14].

As the principle of the inverse phase transfer catalysis with cyclodextrin is based on a subtle process of molecular recognition between the host cavity of the cyclodextrin and the substrate, we have envisaged to take advantages of this property to perform

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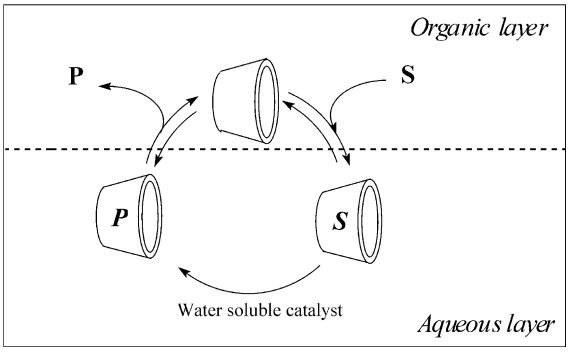


Scheme 1. Cyclodextrins as inverse phase transfer catalysts.

substrate-selective catalytic reactions in biphasic medium. Indeed, the water-soluble catalyst should react selectively with the substrate that is preferentially bound in the cyclodextrin cavity. Our wish to explore this field inaccessible nowadays with conventional transition metal catalysts was so far reinforced by recent reports on the substrate-selective behaviour of cyclodextrins bearing ethylenediamine [15,16], phosphinite [17,18] or phosphine [19] group in cleavage, hydroformylation and hydrogenation reactions.

The possibility to perform substrate-selective catalytic reactions in a biphasic system was investigated though a reaction which has been recently developed in our laboratory, i.e. the cleavage of water-insoluble allylic substrates in the presence of DMCyD (Scheme 2) [20].

2. Experimental

2.1. Materials

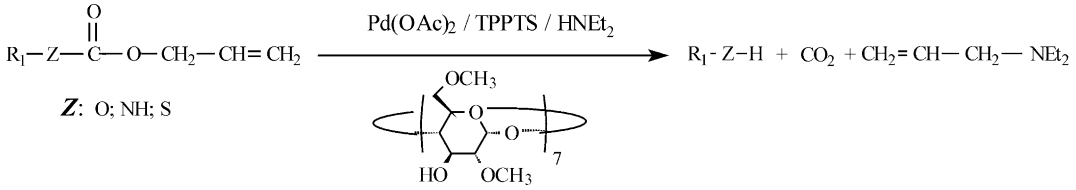
The per(2,6-di-*O*-methyl)-β-cyclodextrin were supplied by Aldrich Chemical and was used as received without further purification. This compound is a mixture of methylated β-cyclodextrins. Indeed, electrospray mass spectrum of this modified cyclodextrin exhibits signals at *m/z* 1311, 1325, 1339, 1353, 1367 and 1381 corresponding to different degrees of methylation. Palladium acetate and organic compounds were purchased from Strem Chemicals, Aldrich Chemical and Acros Organics in their highest purity and used without further purification. Trisodium tris(*m*-sulphonatophenyl)phosphine ($(P(C_6H_4SO_3Na)_3$; TPPTS)) was synthesized as reported by Gärtner et al. [21]. The purity of the TPPTS was carefully controlled. In particular, ^{31}P solution NMR indicated that the product was a mixture of TPPTS (ca. 98%) and its oxide (ca. 2%). Distilled deionized water was used in all experiments. All catalytic reactions were performed under nitrogen using standard Schlenk techniques. All solvents and liquid reagents were degassed by bubbling nitrogen for 15 min before each use or by two freeze-pump-thaw cycles before use.

2.2. Catalytic experiments

In a typical experiment, $Pd(OAc)_2$ (0.134 mmol, 30 mg), TPPTS (1.20 mmol, 0.68 g), DMCyD (0.94 mmol) and water (6 g) were introduced under nitrogen atmosphere into a Schlenk tube. After stirring with a magnetic bar for 1 h, the yellow solution was transferred into a mixture of allylic substrate (3.35 mmol), diethylamine (6.67 mmol, 0.49 g) and toluene (6 g). The medium was stirred at 1000 rpm at room temperature and the reaction was monitored by quantitative gas chromatographic analysis of the organic layer.

2.3. Molecular modelling

In order to determine the geometrical parameters of the phenylbenzyl allyl carbonate isomers and the



Scheme 2. Palladium-catalysed cleavage of allylic substrate in the presence of DMCyD.

biphenyl allyl carbonate isomers, we performed a full-restricted Hartree–Fock (RHF) optimization with an STO-3G basis set. The goal of the calculations was mainly qualitative, so we used this minimal basis set and did not taking into account the solvent (water) effects. The results were obtained with the Gaussian 98 A.7 version package.

3. Results and discussion

The possibility to perform substrate-selective reactions was investigated with different pairs of isomers. It was also carefully checked that each isomer exhibited the same reactivity in a biphasic medium in which a classical co-solvent (acetonitrile) was used as mass transfer promoter. [1] These control experiments were carried out to make sure that substrate selectivity was not due to a different reactivity of the palladium catalyst towards the substrate.

At first, different pairs of isomers of allylic carbonates were tested. As isomers have similar water solubilities, the ratio between the initial catalytic activities in the presence of DMCyD was used as a measure of substrate selectivity. In order to evaluate the efficiency of the DMCyD, experiments without DMCyD were also conducted. The ratio between the initial catalytic activity in the presence of DMCyD and the initial catalytic activity without DMCyD was determined for each allylic carbonate. The results are summarized in Table 1.

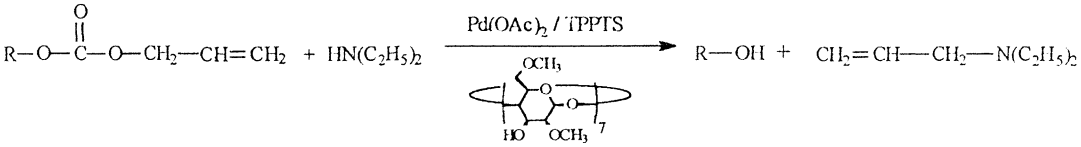
In all cases, DMCyD allows to increase significantly the reaction rate. For instance, the catalytic activities were up 100 times higher than those observed without DMCyD in the case of decyl allyl carbonates (entry 5 in Table 1). From substrate selectivity point of view, DMCyD is efficient for four pairs of isomers (entries 1–4 in Table 1). The best substrate selectivity was obtained with phenylbenzyl allyl carbonate isomers. Indeed, a substrate selectivity of 4 in favour of *p*-phenylbenzyl allyl carbonate was reached. It must be pointed out that the high substrate selectivity observed with phenylbenzyl allyl carbonate isomers was also confirmed with competitive experiments. [2] In these experiments, the deprotection of a 50/50 mixture of *o*-phenylbenzyl allyl carbonate and *p*-phenylbenzyl allyl carbonate was carried out with acetonitrile or with the DMCyD. The ratio of the products *p*-phenylbenzyl alcohol and *o*-phenylbenzyl alcohol, as determined by chromatography, was used as a measure for substrate selectivity. As expected, no substrate selectivity was observed in a control experiment in which acetonitrile was used as mass transfer promoter (50:50 product ratio). In contrast, the use of DMCyD as mass transfer promoter led to substantial substrate selectivity: a 79:21 product ratio was observed in the initial stages of the reaction.

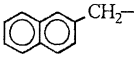
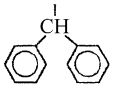
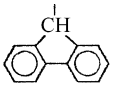
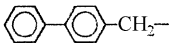
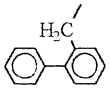
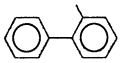
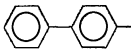
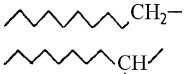
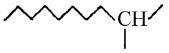
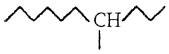
The substrate selectivity obtained in experiments 1–3 can be interpreted from a size-fit concept which predicts the highest reactivity for the best size-matched host–guest pair [22]. As a matter of fact, the β-naphthylmethyl allyl carbonate and *p*-phenylbenzyl allyl carbonate owing to the linear shape of these molecules fit better in the DMCyD cavity than the α-naphthylmethyl allyl carbonate and the *o*-phenylbenzyl allyl carbonate. Similar comments can be made with diphenylmethyl allyl carbonate and fluorenyl allyl carbonate (entry 2 in Table 1). In the case of biphenyl allyl carbonates (entry 4 in Table 1), the size-fit concept appears clearly inadequate to predict the substrate selectivity. Indeed, in comparison with phenylbenzyl allyl carbonate isomers, a complete reversal of the substrate selectivity was observed with biphenyl allyl carbonate isomers. The bulky *ortho*-isomer was the most reactive. Thus, the conversion of *o*-biphenyl allyl carbonate is 3.3 times faster than that of *p*-biphenyl allyl carbonate (entry 4 in Table 1). This reversal of selectivity cannot easily be explained by comparing the dimensions of biphenyl allyl carbonate isomers and phenylbenzyl allyl carbonate isomers with the size of the DMCyD cavity. Indeed, the shapes of *ortho*- or *para*-isomers are very similar (compare (a) with (b), and (c) with (d) of Fig. 1).

[1] The cleavage of allylic substrate in the presence of acetonitrile was conducted as described in Section 2 except that 6 g of acetonitrile was added to the reaction medium in the place of DMCyD. With such an amount of acetonitrile, the main limitation of the reaction rate was not related to the low water solubility of allylic substrate in the aqueous catalytic phase.

[2] The competitive experiments were conducted as described in Section 2 except that a mixture of *o*-phenylbenzyl allyl carbonate (1.68 mmol, 0.45 g) and *p*-phenylbenzyl allyl carbonate (1.68 mmol, 0.45 g) was used. In the control experiment, 1.2 g of acetonitrile was added to the reaction medium in the place of DMCyD.

Table 1
Cleavage of various allylic carbonates by diethylamine in the presence of DMCyD



Entry	R	Initial activity in the presence of DMCyD (h^{-1})[a]	Initial activity without DMCyD (h^{-1})[b]	Initial activities ratio[c]	Substrate selectivity[d]
1a		150	2	75	1.6
1b		96	3	32	
2a		54	1	54	2.2
2b		25	1	25	
3a		76	0.3	250	4
3b		19	0.3	63	
4a		210	3	70	3.3
4b		64	2	32	
5a		11	0.1	110	1.1
5b		10	0.1	100	
5c		11	0.1	110	

[a] The initial catalytic activities in the presence of DMCyD were calculated as the amount of converted substrate per hour per mole of palladium at 20% conversion.

[b] The initial catalytic activities without DMCyD were calculated as the amount of converted substrate per hour per mole of palladium at 10–20% conversion.

[c] Initial activity ratio is defined as the ratio between the initial catalytic activity in the presence of DMCyD and the initial catalytic activity without DMCyD.

[d] Substrate selectivity was the ratio between the initial catalytic activity observed with substrate 'a' in the presence of DMCyD and the initial catalytic activity observed with substrate 'b' in the presence of DMCyD.

Results obtained with the decyl allyl carbonate isomers illustrate also clearly the limit of the size-fit concept. Indeed, whereas the alkyl groups of the decyl allyl carbonate isomers are relatively different, no selectivity was observed during the cleavage of these compounds (entry 5 in Table 1). The lack of selectivity seems indicate that the discrimination power of the DMCyD is weak when alkyl groups are involved in the molecular recognition process [23].

The cleavage of various pairs of *O*-allylic urethane isomers was investigated in a second time. The results are presented in Table 2.

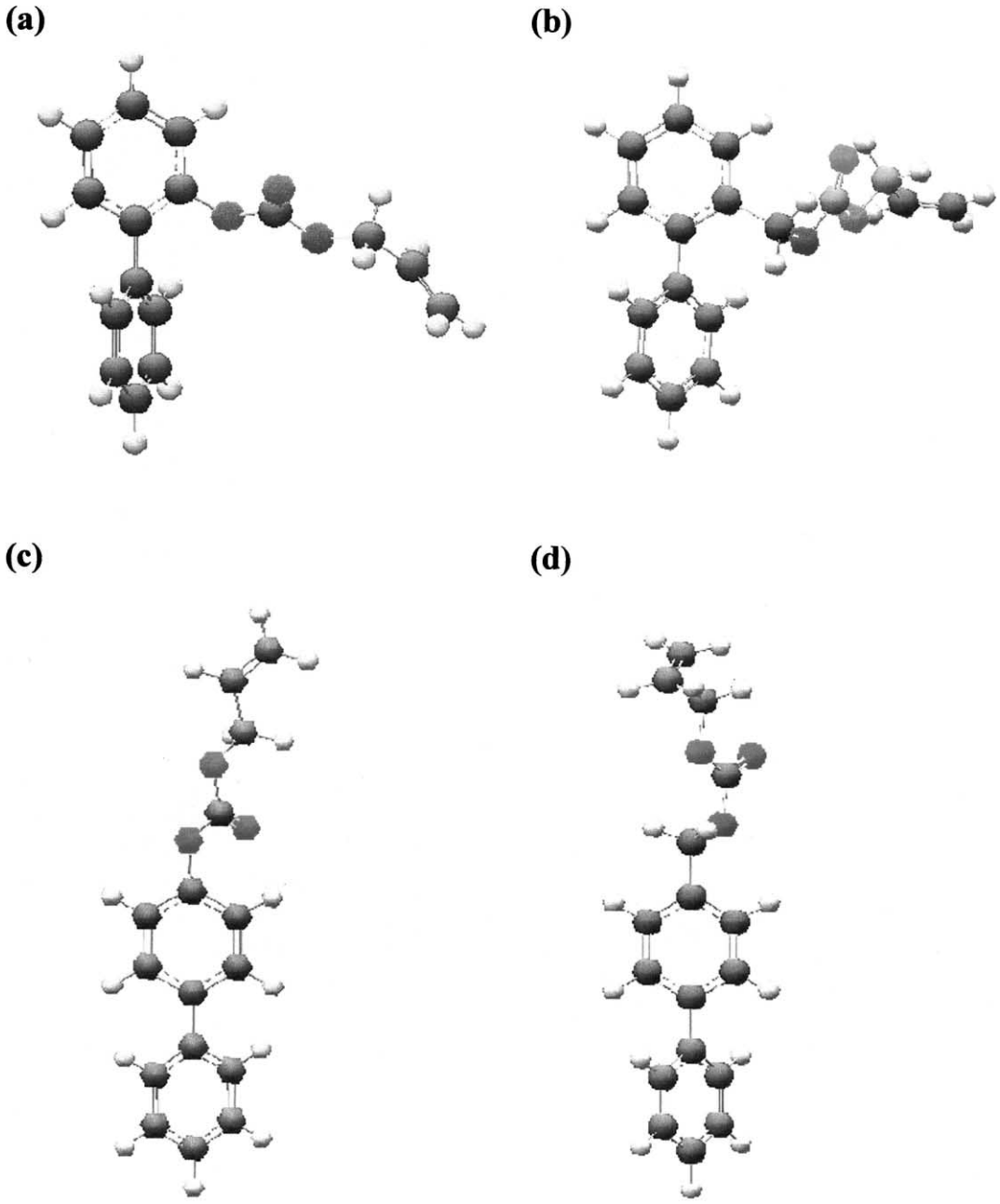
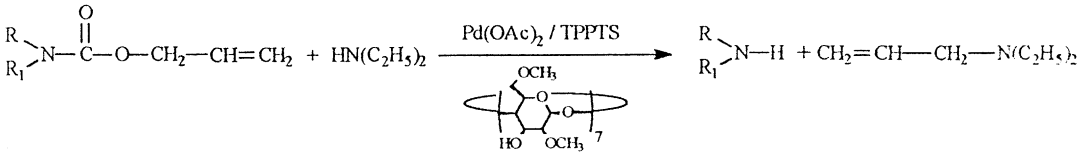
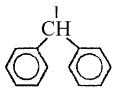
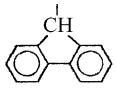
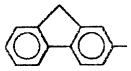
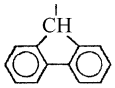


Fig. 1. Optimized conformation for *o*-biphenyl allyl carbonate (a), *o*-phenylbenzyl allyl carbonate (b), *p*-biphenyl allyl carbonate (c), and *p*-phenylbenzyl allyl carbonate (d).

Table 2
Cleavage of various allylic urethanes by diethylamine in the presence of DMCyD[a]



Entry	R	R_1	Initial activity in the presence of DMCyD (h^{-1})[b]	Initial activity without DMCyD (h^{-1})[c]	Initial activities ratio[d]	Substrate selectivity[e]
1a		H	37	4	9	2.3
1b		H	16	4	4	
2a		H	25	5	5	1.6
2b		H	16	4	4	
3a	n-$C_{12}H_{23}$	H	19	0.03	630	47
3b	n-C_6H_{11}	n-C_6H_{11}	0.4	0.03	13	

[a] The entries 1 and 2, dimethylformamide (3 g) was added to the reaction mixture to solubilize the substrate and benzonitrile (24 g) was used instead of toluene. The amount of water was 12 g.

[b] The initial catalytic activities in the presence of DMCyD were calculated as the amount of converted substrate per hour per mole of palladium at 20% conversion.

[c] The Initial catalytic activities without DMCyD were calculated as the amount of converted substrate per hour per mole of palladium at 10–20% conversion.

[d] Initial activities ratio is defined as the ratio between the initial catalytic activity in the presence of DMCyD and the initial catalytic activity without DMCyD.

[e] Substrate selectivity was the ratio between the initial catalytic activity observed with substrate 'a' in the presence of DMCyD and the initial catalytic activity observed with substrate 'b' in the presence of DMCyD.

In all cases, rate enhancement and substrate selectivity phenomenon were observed. The substrate selectivity obtained with the *N*-alkyl-*O*-allyl urethane is outstanding (entry 3 in Table 2). Indeed, a substrate selectivity of 47 in favour of *N*-dodecyl-*O*-allyl urethane can be reached. As this high value contrasts with the precedent values included between 1 and 4, competitive experiments were also conducted to confirm this value.[3] In these experiments, the deprotection of a 50/50 mixture of *N*,*N*-dihexyl-*O*-allyl urethane and *N*-dodecyl-*O*-allyl urethane was carried out with acetonitrile or with the DMCyD. The ratio of the products dodecylamine and *N*,*N*-dihexylamine was used as a measure for substrate selectivity. As expected, no substrate selectivity was observed in the control experiment. In other terms, the two substrates are converted with the same rate ($0.4\,h^{-1}$). In contrast, the use of DMCyD led to substantial substrate selectivity: a 97:3 product ratio was observed in the initial stages of the reaction. Although the value of the substrate selectivity was lower in the competitive experiment than in the experiments where urethanes were tested alone (32 against 47), these experiments confirm the high discrimination power of the DMCyD in the case of *N*-alkyl-*O*-allyl urethanes.

[3] The competitive experiments were conducted as described in Section 2 except that a mixture of *N*-dodecyl-*O*-allyl urethane (1.68 mmol, 0.45 g) and *N*,*N*-dihexyl-*O*-allyl urethane (1.68 mmol, 0.45 g) was used. In the control experiment, 6 g of acetonitrile was added to the reaction medium in the place of DMCyD.

As no selectivity was observed in the case of decyl allyl carbonates isomers (entry 5 in Table 1), the high value of the substrate selectivity observed with the *N*-alkyl-*O*-allyl urethane isomers is difficult to explain; in the two cases, the lipophilic groups which are recognized by the host cavity are alkyl groups. This unexpected result could be rationalized by hypothesizing that the DMCyD assists or participates directly in the catalytic cleavage process of the *N*-decyl-*O*-allyl urethane. Further studies are currently under way in our laboratory to investigate more deeply this last possibility.

4. Conclusion

The whole results established unequivocally that substrate-selective catalytic reactions can be performed with the DMCyD. However, the substrate selectivity remains difficult to foretell. Indeed, the size-fit concept alone cannot explain the different reactivity observed with some isomers and the direct participation of the DMCyD in the catalytic cleavage process cannot be totally left out.

References

[1] T. Okano, in: B. Cornils, W.A. Hermann (Eds.), Aqueous-phase Organometallic Catalysis, Wiley–VCH, Weinheim, 1998, pp. 221–233.
[2] S. Tilloy, F. Bertoux, A. Mortreux, E. Monflier, Catal. Today 48 (1999) 245.
[3] P.A. Ganeshpure, S. Satish, J. Chem. Soc. Chem., Commun. (1988) 981.
[4] A. Harada, Y. Hu, S. Takahashi, Chem. Lett. (1986) 2083.
[5] R. Ravichandran, S. Divakar, Ind. J. Chem. B 35 (1996) 1167.
[6] J.T. Lee, H. Alper, J. Org. Chem. 55 (1990) 1854.
[7] H. Zahalka, H. Alper, Organometallics 5 (1986) 1909.
[8] S. Shimizu, Y. Sasaki, C. Hirai, Bull. Chem. Soc. Jpn. 63 (1990) 176.
[9] E. Monflier, E. Blouet, Y. Barbaux, A. Mortreux, Angew. Chem. Int. Ed. Engl. 33 (1994) 2100.
[10] E. Monflier, S. Tilloy, E. Blouet, Y. Barbaux, A. Mortreux, J. Mol. Catal. A 109 (1996) 27.
[11] E. Monflier, G. Fremy, Y. Castanet, A. Mortreux, Angew. Chem. Int. Ed. Engl. 34 (1995) 2269.
[12] E. Monflier, S. Tilloy, G. Fremy, Y. Castanet, A. Mortreux, Tetrahedron Lett. 52 (1995) 9481.
[13] E. Monflier, S. Tilloy, F. Bertoux, Y. Castanet, A. Mortreux, New J. Chem. 21 (1997) 857.
[14] E. Monflier, S. Tilloy, Y. Castanet, A. Mortreux, Tetrahedron Lett. 39 (1998) 2959.
[15] H.J. Schneider, F. Xiao, J. Chem. Soc., Perkin Trans. 2 (1992) 387.
[16] M. Komiyama, Y. Matsumoto, Chem. Lett. (1989) 719.
[17] M.T. Reetz, Topics Catal. 4 (1997) 187.
[18] M.T. Reetz, S.R. Waldvogel, Angew. Chem. Int. Ed. Engl. 36 (1997) 865.
[19] R.M. Deshpande, A. Fukuoka, M. Ichikawa, Chem. Lett. (1999) 13.
[20] T. Lacroix, H. Bricout, S. Tilloy, E. Monflier, Eur. J. Org. Chem. (1999) 3127.
[21] R. Gärtner, B. Cornils, H. Springer, P. Lappe, 1982, DE Patent 3235030.
[22] E. Fenyvesi, L. Szente, N.R. Russell, M. McNamara, in: J.L. Atwood, J.E.D. Davies, D.D. MacNicol, F. Vögtle (Eds.), Comprehensive Supramolecular Chemistry, Vol. 3, Pergamon Press, Oxford, 1996, pp. 305–366.
[23] M.V. Rekharsky, Y. Inoue, Chem. Rev. 98 (1998) 1875.