Available online at www.sciencedirect.com
ScienceDirect
Carbohydrate Research 342 (2007) 254–258
Carbohydrate RESEARCH

Note

Enantioselective epoxidation of non-functionalized alkenes using carbohydrate based salen–Mn(III) complexes

Shanshan Zhao, Jiquan Zhao* and Dongmin Zhao

School of Chemical Engineering, Hebei University of Technology, Tianjin 300130, PR China

Received 25 June 2006; received in revised form 18 November 2006; accepted 29 November 2006
Available online 3 December 2006

Abstract—Three new salen ligands with carbohydrate moieties were prepared from a salicylaldehyde derivative obtained by reaction of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose with 3-*tert*-butyl-5-(chloro-methyl)-2-hydroxybenzaldehyde. These ligands were coordinated with Mn(III) to give three chiral salen–Mn(III) complexes. The complexes were characterized and employed in the asymmetric epoxidation of unfunctionalized alkenes. Catalytic results showed that although there are no chiral groups on the diimine bridge, these complexes had some enantioselectivity, which indicates the carbohydrate moiety has an asymmetric inducing effect in the epoxidation reaction.

Keywords: Salen–Mn(III) complexes; Carbohydrate; Glucofuranose; Asymmetric epoxidation; Salicylaldehyde derivative

During the last few years, salen–Mn(III) complexes have emerged as efficient and practical catalysts for the asymmetric epoxidation of various non-functionalized *cis*-di, tri-, and tetra-substituted alkenes. Much attention has been given to the design and synthesis of salen ligands and to the explanation of the chiral induction of the salen structure. It has been assumed that the two main structural features required to achieve good enantioselectivity are bulky substituents on C-3 (3′) of the salen ligand and an asymmetrical diimine bridge derived from a C_2-symmetric diamine.[1] However, how the substituents on C-5 (5′) influence catalytic results has not yet been identified.

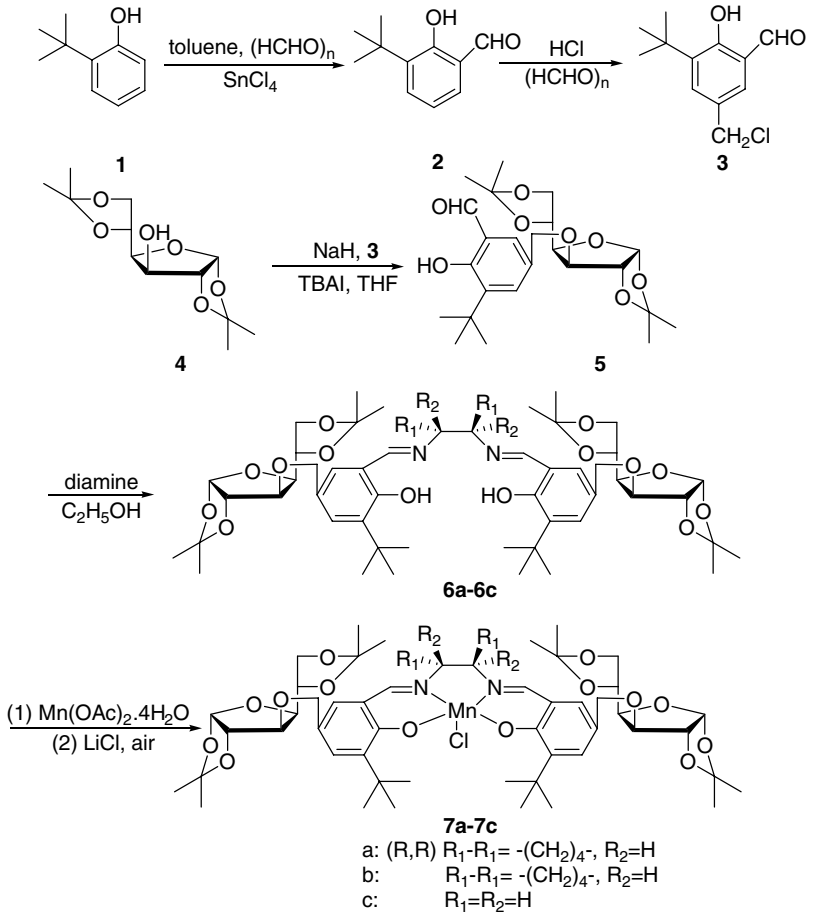
Carbohydrates are naturally occurring multifunctional products and inexpensive starting materials with chiral centers, which makes them ideal precursors for the introduction of chiral building blocks into catalysts. Previously it has been a challenge to incorporate carbohydrates into an asymmetric catalyst. But recently, Yan and Klemm reported the first carbohydrated-derived chiral Mn(III)–salen complex by incorporating a chiral carbohydrate into the diamine moiety.[2] Ruffo and co-workers also reported new chiral salen ligands derived from α-D-glucose and α-D-mannose by introducing appropriate functional groups at the C-2 and C-3 of the sugar ring, and they reported high enantiomeric excesses for epoxidation reactions.[3] In another work, Ruffo and co-workers prepared a supported salen–Mn(III) catalyst derived from D-glucose and the catalytic results showed that the complex had good reactivity and enantioselectivity.[4] These efforts have strengthened the prospects of utilizing natural products as templates for asymmetric epoxidative catalysts.

Encouraged by these recent advances, we have focused on combining chiral carbohydrate derivatives with a salicylaldehyde moiety to attain new complexes. It was expected that the chiral centers of the carbohydrate derivatives would improve the enantiometric excesses. Therefore, we synthesized a new salicylaldehyde derivative with a sugar ring at C-5 (5′), and from this was prepared several asymmetric salen–Mn(III) complexes.

The synthetic route for these chiral complexes, **7a**–**c**, is shown in Scheme 1. First, 3-*tert*-butyl-2-hydroxybenzaldehyde **2** was prepared from 2-*tert*-butylphenol with

* Corresponding author. Tel.: +86 22 26564279; fax: +86 22 26564733; e-mail: zhaojq@hebut.edu.cn

0008-6215/$ - see front matter © 2006 Elsevier Ltd. All rights reserved.
doi:10.1016/j.carres.2006.11.026



Scheme 1. Synthetic route for the complexes.

a moderate yield. Chloromethylation of **2** produced a salicylaldehyde derivative **3**, 3-*tert*-butyl-5-(chloromethyl)-2-hydroxybenzaldehyde which has a chloromethyl group at C-5. Condensation of **3** and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **4** yielded **5**. Complexes **7a**–**c** were then prepared by condensing **5** with the desired diamine in a 2:1 molar ratio, followed by metalation with Mn(III) as Jacobsen's procedure.[5] These complexes were characterized by optical rotation, IR spectroscopy, elementary analysis, and MS.

Complexes **7a**–**c** were used as catalysts for the epoxidation of 1,2-dihydronaphthalene, styrene, α-methyl-styrene, and *cis*-β-methyl-styrene. Two different oxidative systems were used for the epoxidation reactions. The first was a binary media system, NaClO/PyNO/H_2O/CH_2Cl_2, and the second was a homogeneous system, *m*-CPBA/NMO/CH_2Cl_2, where PyNO is pyridine *N*-oxide and NMO is *N*-methylmorpholine *N*-oxide. The results of the asymmetric epoxidation catalyzed by the complexes are presented in Table 1.

7a showed moderate yields and good enantioselectivities for the asymmetric epoxidation of *cis*-β-methyl-styrene and 1,2-dihydronaphthalene (entries 3 and 23). The terminal-olefin styrene had good yields and lower ee's[†] (entries 8 and 10), whereas α-methyl-styrene afforded moderate ee's (entries 16 and 17). For all the substrates, except α-methyl-styrene, the *m*-CPBA system produced higher ee's with a shorter time than the NaClO system (entries 1, 2, 8, 11, 16, 17, 23 and 24). The *m*-CPBA results were achieved in less than 1.5 h, whereas the reaction time for the NaClO system extended to several hours at 0 °C. For the *m*-CPBA system, lowering the temperature from −20 to −78 °C increased the yields and the ee values of the epoxides (entries 9 and 10). For the NaClO system, increasing the amount of loaded catalyst markedly shortened the reaction time, but no obvious effects on the yields or enantioselectivities were observed (entries 2 and 3).

The catalytic properties of **7a**–**c** were compared. The latter two complexes, which have no asymmetrical diimine bridges, both had poor epoxidation results with ee's of 6% and 11%, when 1,2-dihydronaphthalene was used as the substrate (entries 4 and 6). This enantioselectivity is undoubtedly induced by the chiral sugar groups of the complexes. Thus, it can be concluded that the

[†] ee: enantiomeric excess.

Table 1. Epoxidation of 1,2-dihydronaphthalene, styrene, α-methyl-styrene and *cis*-β-methyl-styrene using catalysts **7a**–**c**

Entry	Substrate[a]	Catalyst[b]	Oxidant[c]	Temperature (°C)	Time	Yield[d] (%)	ee[e] (%)
1	A	**7a** (1.0)	*m*-CPBA	−78	75 min	44	78
2	A	**7a** (1.0)	NaClO	0	9.5 h	66	67
3	A	**7a** (3.0)	NaClO	0	2.0 h	67	70
4	A	**7b** (2.0)	*m*-CPBA	−78	50 min	59	6
5	A	**7b** (1.0)	NaClO	0	12 h	63	6
6	A	**7c** (2.0)	*m*-CPBA	−78	30 min	40	11
7	A	**7c** (2.0)	NaClO	0	5.5 h	57	4
8	B	**7a** (0.5)	*m*-CPBA	−78	25 min	95	38
9	B	**7a** (1.0)	*m*-CPBA	−20	5 min	67	22
10	B	**7a** (1.0)	*m*-CPBA	−78	20 min	99	37
11	B	**7a** (0.5)	NaClO	0	7 h	44	20
12	B	**7b** (2.0)	*m*-CPBA	−78	10 min	>99	1
13	B	**7b** (2.0)	NaClO	0	5 h	97	2
14	B	**7c** (1.0)	*m*-CPBA	−78	15 min	93	<1
15	B	**7c** (2.0)	NaClO	0	1 h	34	7
16	C	**7a** (2.0)	*m*-CPBA	−78	20 min	93	51
17	C	**7a** (1.0)	NaClO	0	10 h	78	60
18	C	**7b** (2.0)	*m*-CPBA	−78	10 min	87	6
19	C	**7b** (2.0)	NaClO	0	10 h	87	9
20	C	**7c** (1.0)	*m*-CPBA	−78	15 min	82	10
21	C	**7c** (2.0)	NaClO	0	10.5 h	91	6
22	D	**7a** (0.5)	*m*-CPBA	−78	50 min	47	83
23	D	**7a** (1.0)	*m*-CPBA	−78	50 min	74	84
24	D	**7a** (1.0)	NaClO	0	10.5 h	41	82
25	D	**7b** (2.0)	*m*-CPBA	−78	15 min	91	5
26	D	**7b** (2.0)	NaClO	0	5 h	54	3
27	D	**7c** (1.0)	*m*-CPBA	−78	15 min	80	2
28	D	**7c** (2.0)	NaClO	0	5 h	28	2

[a] A: 1,2-dihydronaphthalene; B: styrene; C: α-methyl-styrene; D: *cis*-β-methyl-styrene.
[b] The number in parentheses is the molar percentage of catalyst used as compared to the amount of substrate.
[c] Reactions were carried out in CH_2Cl_2. For the *m*-CPBA oxidative system the substrate:oxidant:NMO molar ratios were 1:2:5. For the NaClO system the substrate:oxidant:PyNO molar ratios were 1:2:0.2.
[d] Determined by GC.
[e] Determined by GC with a chiral Cyclodex-β column.

chiral centers on C-5 (5′) of the salicylaldehyde moiety has an influence on enantioselectivity but only a weak one. This weak effect may be explained due to the chiral centers are not being in the vicinity of Mn metal.[5]

1. Experimental

1.1. Methods and materials

^{1}H NMR and ^{13}C NMR spectra were obtained in $CDCl_3$ or DMSO using a Bruker AC 300/75 spectrometer. IR spectra in KBr pellets were recorded on a Bruker Vector-22 spectrophotometer. Melting points were determined on a Perkin XT-4 microscopic analyzer. Elemental analyses were acquired using an Elementary vario El instrument. Optical rotations were measured on a Shanghai WZZ-2S/2SS digital rotation analyzer, at ambient temperature using a 100 mm sample tube. Fast atom bombardment mass spectrometry was performed on a VG ZAB-HS Mass Spectrometer. Reaction products were analyzed on a Shandong Lunan Ruihong Gas Chromatograph, SP-6800A, equipped with a Cyclodex-β capillary column (30 m × 250 μm i.d.) using an FID detector. 2-*tert*-Butylphenol, 1,2-dihydronaphthalene, α-methyl-styrene, *cis*-β-methyl-styrene, *N*-methylmorpholine *N*-oxide, and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose were purchased from Acros. (*R*,*R*)-1,2-Cyclohexanediamine was prepared according to the literature.[6] Solvents were redistilled prior to use. Other chemicals were purchased from commercial sources and used as received.

1.2. Synthesis of 3-*tert*-butyl-2-hydroxybenzaldehyde (2)

Compound **2** was synthesized according to reported procedures.[7] Light yellow liquid. Yield 37%. ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 9H), 6.93 (t, $J = 7.5$, 7.5 Hz, 1H), 7.39 (q, $J = 1.8$, 5.7, 1.8 Hz, 1H), 7.52 (q, $J = 1.8$, 6.0, 1.5 Hz, 1H), 9.88 (s, 1H), 11.79 (s, 1H).

1.3. Synthesis of 3-*tert*-butyl-5-(chloro-methyl)-2-hydroxybenzaldehyde (3)

3 was prepared using the procedure reported in the literature.[8,9] Light yellow crystalline solid. Yield 87%, mp

61–63 °C, lit.[9] 63–65 °C; ^{1}H NMR (DMSO): δ 1.39 (s, 9H), 4.81 (s, 2H), 7.63 (d, $J = 2.2$ Hz, 1H), 7.75 (d, $J = 2.2$ Hz, 1H), 9.98 (s, 1H), 11.91 (s, 1H).

1.4. Synthesis of 1,2:5,6-di-*O*-isopropylidene-3-*O*-methylene-[5-(3-*tert*-butyl-2-hydroxy benzaldehyde)]-α-D-glucofuranose (5)

Oil-free NaH[10] (0.10 g, 4 mmol) was suspended in dry THF (10 mL) under nitrogen at 0 °C. A solution of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **4** (0.52 g, 2 mmol) in THF (10 mL) was added dropwise using a dropping funnel and the mixture was stirred at room temperature for 3 h. Then a solution of **3** (0.57 g, 2.5 mmol) in THF (10 mL) was added very slowly at 0 °C followed by the addition of tetrabutylammonium iodide (TBAI, 0.02 g, 0.06 mmol).[11] The reaction mixture was heated under reflux for 11 h. After destroying excess NaH by adding a few drops of water at 0 °C the solvent was evaporated in vacuo. The resulting mass was extracted with $CHCl_3$. The $CHCl_3$ phase was washed with brine, dried over Na_2SO_4 and concentrated to obtain a crude residue. The product was purified by silica gel column chromatography, eluting with a 1:3 (V:V) EtOAc–petroleum ether mixture to give compound **5**, a light yellow solid (0.60 g, yield 67%): mp 96–98 °C; $[\alpha]_D^{20}$ −34.1 (*c* 0.80, EtOH); IR (KBr): *v* 3423, 2992, 2969, 2936, 2862, 1655, 1617, 1456, 1440, 1384, 1374, 1321, 1265, 1226, 1212, 1167, 1152, 1081, 1024, 847, 771, 759 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.38 (s, 9H), 1.42 (s, 12H), 4.01–4.68 (m, 8H), 5.90 (d, $J = 3.9$ Hz, 1H), 7.41 (d, $J = 2.4$ Hz, 1H), 7.48 (d, $J = 1.8$ Hz, 1H), 9.87 (s, 1H), 11.80 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 197.0, 161.0, 138.6, 133.9, 131.0, 128.3, 120.3, 111.9, 109.1, 105.3, 82.6, 81.6, 81.3, 77.7, 76.7, 72.4, 71.8, 67.5, 34.9, 29.1, 26.9, 26.8, 26.7, 26.2; FABMS: *m*/*z* 450 $[M]^+$. Anal. Calcd for $C_{24}H_{34}O_8$: C, 63.98; H, 7.61. Found: C, 63.71; H, 7.83.

1.5. Synthesis of Schiff-base ligands (6a–c)

A solution of **5** (1.00 g, 2.2 mmol) and (*R*,*R*)-1,2-cyclohexanediamine (0.13 g, 1.1 mmol) in dry EtOH (25 mL) was refluxed for 2 h under nitrogen atmosphere.[12] The ethanol was evaporated under reduced pressure and the residue was purified by chromatography (EtOAc–petroleum ether 1:2, V:V) to give the Schiff base **6a**, a yellow foam solid (0.78 g, yield 72%): mp 85–87 °C; $[\alpha]_D^{20}$ −164.0 (*c* 0.14, EtOH); IR (KBr): *v* 3442, 2986, 2935, 2865, 1631, 1598, 1444, 1373, 1322, 1265, 1214, 1164, 1077, 1027, 849, 800, 776 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.27 (s, 9H), 1.39 (s, 12H), 1.42–1.48 (m, 2H), 1.88–1.98 (m, 2H), 3.31 (d, $J = 9.9$ Hz, 1H), 3.96–4.55 (m, 8H), 5.84 (d, $J = 3.6$ Hz, 1H), 6.99 (d, $J = 1.8$ Hz, 1H), 7.20 (d, $J = 1.8$ Hz, 1H), 8.28 (s, 1H), 13.91 (s,1H); ^{13}C NMR ($CDCl_3$): δ 165.4, 160.5, 137.6, 129.7, 126.7, 118.4, 112.0, 109.2, 105.5, 82.9, 81.6, 77.7, 77.2, 76.8, 72.7, 67.5, 35.0, 33.4, 29.5, 27.1, 26.5, 25.7, 24.5; FABMS: *m*/*z* 979 $[M+H]^+$. Anal. Calcd for $C_{54}H_{78}O_{14}N_2$: C, 66.24; H, 8.03; N, 2.86. Found: C, 66.39; H, 8.03; N, 2.64.

6b was prepared from **5** and 1,2-cyclohexanediamine, yellow foam solid: yield 53%; mp 66–68 °C; $[\alpha]_D^{20}$ −57.8 (*c* 0.08, EtOH); ^{1}H NMR and IR data were in agreement with those of **6a**; FABMS: *m*/*z* 979 $[M+H]^+$. Anal. Calcd for $C_{54}H_{78}O_{14}N_2$: C, 66.24; H, 8.03; N, 2.86. Found: C, 66.52; H, 8.02; N, 2.71.

6c was synthesized from **5** and ethylenediamine, yellow foam solid: yield 60%; mp 81–83 °C; $[\alpha]_D^{20}$ −56.0 (*c* 0.20, EtOH); IR (KBr): *v* 3442, 2987, 2932, 1633, 1444, 1373, 1341, 1268, 1215, 1164, 1077, 1026, 848, 798, 776 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.31 (s, 9H), 1.42 (s, 12H), 3.95 (s, 2H), 4.00–4.34 (m, 5H), 4.55–4.58 (m, 3H), 5.87 (d, $J = 3.6$ Hz, 1H), 7.10 (s, 1H), 7.26 (s, 1H), 8.38 (s, 1H), 13.87 (s, 1H); ^{13}C NMR ($CDCl_3$): δ 202.8, 167.2, 160.5, 137.9, 129.8, 129.5, 126.9, 118.4, 112.0, 109.2, 105.5, 83.0, 81.7, 77.6, 76.8, 72.7, 67.6, 60.8, 59.8, 48.9, 35.1, 29.5, 27.1, 26.5, 25.7; FABMS: *m*/*z* 925 $[M+H]^+$. Anal. Calcd for $C_{50}H_{72}O_{14}N_2$: C, 64.92; H, 7.84; N, 3.03. Found: C, 64.89; H, 8.04; N, 3.10.

1.6. Synthesis of salen–Mn(III) complexes (7a–c)

A mixture of **6a** (0.33 g, 0.34 mmol) and $Mn(OAc)_2 \cdot 4H_2O$ (0.17 g, 0.68 mmol) in EtOH (30 mL) was refluxed with stirring under an atmosphere of nitrogen for 4 h. Then solid LiCl (0.04 g, 1.02 mmol) was added and the mixture was further heated for 3 h while exposed to air.[12] The solvent was removed and the residue was extracted with CH_2Cl_2. The extract was washed with brine, dried over Na_2SO_4, and concentrated to obtain a dark brown powder **7a** (0.27 g, yield 75%): mp 140–142 °C; $[\alpha]_D^{20}$ −789 (*c* 0.07, CH_2Cl_2); IR (KBr): *v* 2986, 2938, 2869, 1613, 1543, 1455, 1438, 1422, 1383, 1340, 1310, 1263, 1234, 1210, 1166, 1076, 1027, 848, 828, 784, 567, 512 cm^{-1}; FABMS: *m*/*z* 1031 $[M-Cl]^+$. Anal. Calcd for $C_{54}H_{76}O_{14}N_2MnCl$: C, 60.75; H, 7.18; N, 2.62. Found: C, 60.47; H, 7.21; N, 2.43.

For **7b** and **7c**, the above procedure was followed but **6b** and **6c** were used in place of **6a**. **7b**: dark brown powder, yield 70%; mp 194–196 °C; $[\alpha]_D^{20}$ −92.6 (*c* 0.07, CH_2Cl_2); IR data were in accordance with that of **7a**. FABMS: *m*/*z* 1031 $[M-Cl]^+$. Anal. Calcd for $C_{54}H_{76}O_{14}N_2MnCl$: C, 60.75; H, 7.18; N, 2.62. Found: C, 60.52; H, 7.24; N, 2.48.

7c: dark brown powder, yield 65%; mp 135–137 °C; $[\alpha]_D^{20}$ −156.3 (*c* 0.02, CH_2Cl_2); IR (KBr): *v* 2957, 1615, 1544, 1440, 1383, 1339, 1302, 1264, 1210, 1165, 1076, 1026, 848, 823, 584, 537 cm^{-1}; FABMS: *m*/*z* 978 $[M-Cl]^+$. Anal. Calcd for $C_{50}H_{70}O_{14}N_2MnCl$: C,

59.25; H, 6.96; N, 2.76. Found: C, 59.46; H, 7.10; N, 2.47.

1.7. General procedures in epoxidation reactions

For the *m*-CPBA system: A solution containing catalyst (**7a**–**c**), alkene (0.5 mmol), and NMO (2.5 mmol) in dichloromethane was cooled to the desired temperature. The solid *m*-CPBA (1.0 mmol) was added with stirring. The reaction process was monitored by GC.

For the NaClO system: To a cooled (0 °C) solution of catalyst (**7a**–**c**), substrate (1 mmol) and PyNO (0.2 mmol) in dichloromethane, a pre-cooled solution of 13% NaClO (2 mmol, pH = 11.3) was added in portions. The reaction process was monitored by GC.

Acknowledgement

Financial assistance from the National Natural Science Foundation of China (Grant No. 20376017) is gratefully acknowledged.

References

1. Jacobsen, H.; Cavallo, L. *Chem. Eur. J.* **2001**, *7*, 800–807.
2. Yan, S.; Klemm, D. *Tetrahedron* **2002**, *58*, 10065–10071.
3. Borriello, C.; Litto, R. D.; Panunzi, A.; Ruffo, F. *Tetrahedron: Asymmetry* **2004**, *15*, 681–686.
4. Borriello, C.; Litto, R. D.; Panunzi, A.; Ruffo, F. *Inorg. Chem. Commun.* **2005**, *8*, 717–721.
5. Zhang, W.; Loebach, J. L.; Wilson, S. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1990**, *112*, 2801–2803.
6. Schanz, H. J.; Linseis, M. A.; Gilheany, D. *Tetrahedron: Asymmetry* **2003**, *14*, 2763–2769.
7. Casiraghi, G.; Casnati, G.; Puglia, G.; Sartori, G.; Terenghi, G. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1862–1865.
8. Minutolo, F.; Pini, D.; Petri, A.; Salvadori, P. *Tetrahedron: Asymmetry* **1996**, *7*, 2293–2302.
9. Kureshy, R. I.; Khan, N. H.; Abdi, S. H. R.; Patel, S. T.; Iyer, P. K.; Subramanian, P. S. *J. Catal.* **2002**, *209*, 99–104.
10. Tripathi, S.; Maity, J. K.; Achari, B.; Mandal, S. B. *Carbohydr. Res.* **2005**, *340*, 1081–1087.
11. Karche, N. P.; Jachak, S. M.; Dhavale, D. D. *J. Org. Chem.* **2003**, *68*, 4531–4534.
12. Liu, X. W.; Tang, N.; Liu, W. S.; Tan, M. Y. *J. Mol. Catal. A: Chem.* **2004**, *212*, 353–358.