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Asymmetric allylboration for the synthesis of β-hydroxy-δ-lactone unit of statin drug analogs☆

M. Venkat Ram Reddy, Herbert C. Brown* [1], P. Veeraraghavan Ramachandran* [2]

Herbert C. Brown Center for Borane Research, 1393 H. C. Brown Laboratories of Chemistry, Purdue University, West Lafayette, IN 47907-1393, USA

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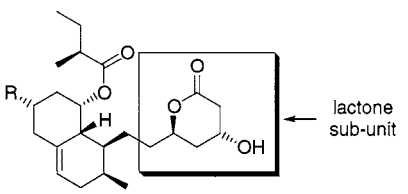
Abstract

Acrylic esters of homoallylic alcohols prepared in 92–96% ee via the asymmetric allylboration of appropriate aldehydes with *B*-allyldiisopinocampheylborane, upon ring-closing metathesis in the presence of 10 mol% of Grubbs' catalyst provided the corresponding 6-substituted dihydropyran-2-ones. These were diastereoselectively epoxidized and regioselectively reduced to furnish optically pure analogs of statin drugs. This procedure allows for the development of a combinatorial library of analogs of these drugs. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Asymmetric synthesis; Allylboration; Metathesis; Epoxidation; Reduction

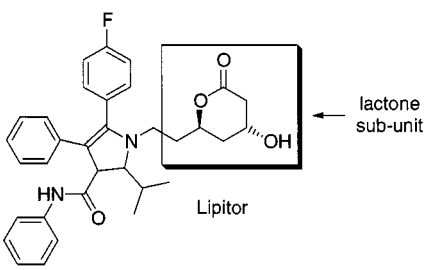
1. Introduction

The discovery of compactin [1] and mevinolin [2] (Fig. 1) as inhibitors of hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase a quarter of a century ago revolutionized research toward the treatment of hypercholesterolemia, a condition that leads to coronary artery disease (CAD), which is one of the leading causes of death all over the world. These are members of a series of drugs known as statin drugs available in the market for the lowering of LDL-cholesterol [3]. For example, mevinolin is also known as lovastatin, with a brand name of Mevacor® [4]. Other statin drugs currently marketed in the USA that are analogs of mevinolin include: simvastatin (velostatin, Zocor®) [5], pravastatin (eptastatin, Pravachol®) [6], atorvastatin (Lipitor®) [7], cerivastatin (Baycol®) [8], and fluvastatin (Lescol®) [9]. Of these, Lipitor® was second in the list of most sold drugs in the USA in 1999 with Zocor® in fifth place [10]. The enormous success of Lipitor® (Fig. 2) and Zocor® within a short time points to the poten-



R = H, compactin (**1a**)
R = Me, mevinolin (**1b**)

Fig. 1.



Lipitor

Fig. 2.

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[1] *Corresponding author. Tel.: +1-765-494-5316; fax: +1-765-494-0239; e-mail: hcbrown@purdue.edu

[2] *Corresponding author.

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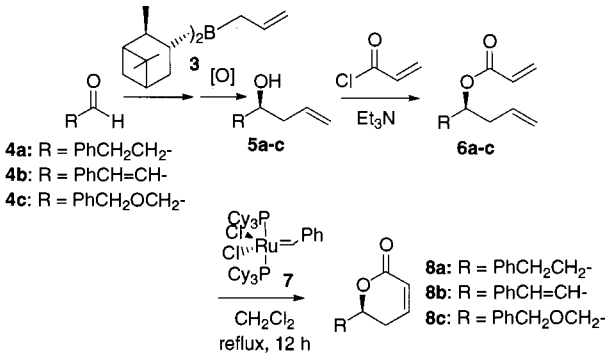
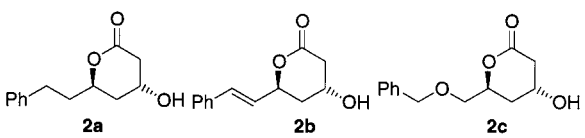


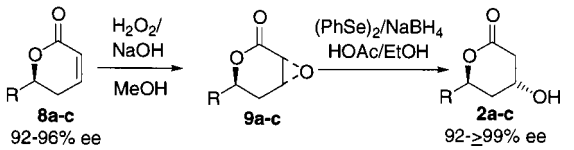
Scheme 1.

tial of statin drugs to become one of the most successful classes of pharmaceuticals ever developed. Accordingly, several more are under clinical investigation [3c].

Systematic study of the statin drugs has revealed that the key pharmacophore necessary for the drug action is the β-hydroxy-δ-lactone unit [11]. Of the several analogs that have been studied, δ-2-phenylethyl-β-hydroxy-δ-lactone (**2a**) [12], δ-benzylidenemethyl-β-hydroxy-δ-lactone (**2b**) [13], and δ-benzyloxymethyl-β-hydroxy-δ-lactone (**2c**) [14](Figure 3) have received most attention. Accordingly, various syntheses for **2a**–**c** have been reported in the literature [12–14]. One of the most utilized procedures for the synthesis of the hydroxylactones is via the ring closing of 3,5-dihydroxy esters that are obtained via the diastereoselective syn-reduction of optically pure 5-hydroxy-3-ketoesters via a boron-mediated intramolecular reduction with $NaBH_4$ [15].

As an extension of our ongoing program involving the synthesis of α-pyranone-containing molecules via an asymmetric allylboration-ring-closing metathesis strategy [16], we envisaged the synthesis of the hydroxylactone moiety of statin drug analogs via a diastereoselective epoxidation and 1,3-reduction (Scheme 1). Our successful results are described below.





Scheme 2.

2. Results and discussion

Allylboration of 3-phenylpropionaldehyde (**4a**) with (−)-*B*-allyldiisopinocampheylborane [17] ((−)-**3**) in Et_2O–pentane mixture at −100°C for 1 h, followed by oxidation, provided a 76% yield [18] of (*S*)-1-phenyl-hex-5-en-3-ol (**5a**) in 96% ee, as determined by HPLC analysis using a Chiralcel® OD-H™ [19] column (Table 1). We used this product for further reactions without rigorous purification. Since the additional product from oxidation, isopinocampheol, did not interfere with our reaction, we did not separate it until after the ring-closing metathesis reaction. Esterification of the product mixture with acryloyl chloride provided an 80% yield [18] of the corresponding acryloyl ester **6a**, along with isopinocampheyl acrylate. Treatment of the mixture of esters with 10% of Grubbs' ruthenium catalyst (**7**) [20] in refluxing CH_2Cl_2 for 12 h provided, after column chromatography, **8a** in 84% isolated yield (Scheme 1). The enantiomeric excess of **8a** was not affected during these processes.

Epoxidation of **8a** with H_2O_2/NaOH in methanol provided the corresponding *trans*-epoxide **9a** in diastereomerically pure form and 86% yield. High diastereoselectivities in these types of epoxidations are known [14b]. The regioselective 1,3-reduction of the epoxide using diphenyldiselenide–sodium borohydride in ethanol, in the presence of acetic acid, provided an 87% yield of the required β-hydroxy-δ-lactone (Scheme 2). It is believed that this reduction proceeds via the formation of PhSeH [21]. Crystallization of this product provided optically pure material, as was determined by comparison of the optical rotation with that reported in the literature [12a].

To show the generality of our reaction sequence for the synthesis of hydroxylactones, we prepared two

Table 1
Preparation of homoallylic alcohols

RCHO		$RCH(OH)CH_2CH{=}CH_2$			
No.	R	No.	Yield (%)	% ee[a]	Configuration[b]
4a	$PhCH_2CH_2$	**5a**	76	96	*R*
4b	PhCH=CH	**5b**	71	92	*S*
4c	$PhCH_2OCH_2$	**5c**	74	92	*S*

[a] % ee determined by the HPLC analysis of the alcohol on a Chiralcel OD-H™ column.
[b] Configuration is based on analogy of allylborations with **3**.

other frequently prepared statin analogs, **2b** and **2c**, starting from cinnamaldehyde (**4b**) and bezyloxyacetaldehyde (**4c**) respectively. In both of these cases, the corresponding homoallylic alcohols were obtained in 92% ee. Since **2b** is a solid, it was upgraded to $\geq 99\%$ ee by crystallization. The yields for each step are presented in Table 2. The physical data of both of the compounds matched with those reported in the literature [13,14].

3. Conclusion

In conclusion, we have described a general asymmetric synthesis of β-hydroxy-δ-lactones via an asymmetric allylboration-ring-closing metathesis–diastereoselective epoxidation–regioselective 1,3-reduction strategy. All of these sequences can be carried out within a short time on a large scale. The ready availability of both isomers of α-pinene for the preparation of either enantiomer of the allylborating agent makes this procedure especially attractive. With the availability of several types of 'allylborating' agents that have been developed using α-pinene as chiral auxiliary [22], several different analogs of **2a**–**c** can be readily accessed. Moreover, such a general synthesis can be readily adopted for the preparation of a library of statin drug analogs via combinatorial synthesis.

4. Experimental

4.1. General methods

All operations were carried out under a nitrogen atmosphere. Techniques for handling air-sensitive compounds have been previously described [23]. Enantiomeric excesses were determined by analysis of the products on a Chiralcel® OD–H™ column using a Rainin HPLC. Optical purities were determined by comparing the rotations of the products measured using a Rudolph Autopol III polarimeter with that reported in the literature. The ^{1}H, ^{11}B and ^{13}C-NMR spectra were plotted on a Varian Gemini-300 spectrometer with a Nalorac-Quad probe.

4.2. Materials.

Anhydrous ethyl ether and dichloromethane were purchased from Mallinckrodt, Inc. and was used as received. THF was distilled from sodium benzophenone ketyl. DIP-Chloride™, allylmagnesium bromide, acryloyl chloride, sodium borohydride, diphenyl diselenide, benzyloxyacetaldehyde and cinnamaldehyde, were all obtained from the Aldrich Chemical Co. 3-phenyl-1-propanal was prepared by Swern oxidation of the corresponding alcohol (Aldrich). Grubbs' ruthenium catalyst was purchased from Strem Chemicals.

4.3. Methods

4.3.1. Allylboration of aldehydes

General procedure. The synthesis of **5a** is representative. To a stirred solution of (−)-*B*-allyldiisopinocampheylborane (prepared from DIP-Chloride™) was added, at −100°C, 3-phenylpropionaldehyde (**4a**) (1.34 g, 10 mmol) in 5 ml of Et_2O. The mixture was stirred at this temperature for 1 h, 1 ml of methanol was added, warmed to room temperature (r.t.), and worked up as usual with NaOH and H_2O_2. The product was extracted with Et_2O, washed with brine, and dried over anhydrous $MgSO_4$. Removal of the solvent and partial purification by silica gel column chromatography provided 2.6 g of a liquid mixture, which contained 1.34 g (76%) of (*S*)-(+)-1-phenyl-hex-5-en-3-ol (**5a**) along with isopinocampheol [18].

4.3.2. Preparation of acryloyl ester

General procedure. The synthesis of **6a** is representative. The above mixture was dissolved in 10 ml of CH_2Cl_2, cooled to 0°C, and 1.92 ml (23.7 mmol) of acryloyl chloride and 6.6 ml (47.4 mmol) of Et_3N were

Table 2
Synthesis of β-hydroxy-δ-lactones[a]

Alcohol no.	Acryloyl ester		Lactenone			Epoxy lactone			Hydroxy lactone		
	No.	Yield (%)	No.	Yield (%)	$[\alpha]_D$	No.	Yield (%)	$[\alpha]_D$	No.	Yield (%)	$[\alpha]_D$
5a	**6a**	80	**8a**	84	−46.09 (*c* 0.64)	**9a**	86	115.08 (*c* 1.53)	**2a**	87	69.21 (*c* 1.45)
5b	**6b**	75	**8b**	78	−170.12 (*c* 1.2)	**9b**	70	53.15 (*c* 0.5)	**2b**	89	9.89 (*c* 0.99)
5c	**6c**	76	**8c**	82	−110.22 (*c* 0.45)	**9c**	78		**2c**	81	6.85 (0.7)

[a] All of the rotations were measured in $CHCl_3$.

added, warmed to r.t. and stirred for 4 h. The resulting mixture was filtered through a short pad of Celite to remove solid $Et_3N{\cdot}HCl$, poured into water and the product was extracted with CH_2Cl_2. The crude product was partially purified by silica gel column chromatography (hexane:ethyl acetate: 99:1) and concentrated to obtain 2.2 g of a mixture, which contained 1.4 g (80%) of **6a** along with isopinocampheyl acrylate [18].

4.3.3. Ring-closing metathesis reaction

General procedure. The synthesis of **8a** is representative. Grubbs' catalyst (0.5 g, 0.6 mmol, 10 mol%) was dissolved in 25 ml of CH_2Cl_2 and was added dropwise to a refluxing solution of the above mixture of **6a** and isopinocampheyl acrylate in 1 l of CH_2Cl_2. Refluxing was continued for 12 h, by which time all of **6a** was consumed (TLC). The solvent was removed under aspirator vacuum and the crude product was purified by silica gel column chromatography (hexane:ethylacetate: 75:25) to obtain 1.02 g (84%) of pure **8a**.

4.3.4. Preparation of epoxylactone

General procedure. The synthesis of **9a** is representative. Lactenone **8a** (0.79 g, 3.9 mmol) in methanol was treated with 1.33 ml (13.2 mmol) of H_2O_2 and 0.39 ml of 6 N NaOH at 0°C. The reaction mixture was stirred for 1 h, diluted with Et_2O and water, acidified with concentrated HCl, and extracted with Et_2O (3×50 ml). The solvents were removed under aspirator and the crude product was cyclized with PPTS in refluxing toluene using a Dean–Stark apparatus and purified by column chromatography (EtOAc:hexane: 1:4) to obtain 0.73 g (86%) of the epoxy lactone **9a**.

4.3.5. Preparation of hydroxylactone

General procedure. The synthesis of **2a** is representative. Sodium borohydride (0.057 g, 1.5 mmol) was added, in small portions, to a stirred solution of diphenyldiselenide (0.234 g, 0.75 mmol) in ethanol at r.t. and cooled to 0°C. Acetic acid (120 μl) was then added, followed by the addition 0.109 g (0.5 mmol) of **9a** dissolved in 2 ml of THF–ethanol (1:1) and stirred for 20 min. The product was extracted with ethyl acetate, washed with brine, and dried over $MgSO_4$. Evaporation of the solvents, followed by column chromatography over silica (ethyl acetate:hexane: 3:2 as eluent) provided 0.096 g (87%) of the hydroxylactone **2a**.

Compound **8a**: ^{1}H-NMR (300 MHz) δ ($CDCl_3$) (ppm) 1.94 (1H, m), 2.15 (1H, m), 2.35 (2H, m), 2.84 (2H, m), 4.42 (1H, m), 6.03 (1H, dt, $J = 9.78$, 1.8 Hz), 6.87(1H, m), 7.26(5H, m); ^{13}C-NMR ($CDCl_3$) δ (ppm) 29.49, 30.99, 36.55, 76.96, 121.43, 126.20, 128.53, 128.59, 140.93, 145.15, 164.51; MS EI m/z 202 (M^+), 184, 117 (100%), 91; CI m/z 203 $(M + H)^+$ (100%).

Compound **8b**: ^{1}H-NMR (300 MHz) δ ($CDCl_3$) (ppm) 2.54 (2H, m), 5.10 (1H, m), 6.09 (1H, dt, $J = 9.8$, 1.8 Hz), 6.28 (1H, dd, $J = 15.99$, 6.33 Hz), 6.73 (1H, d, $J = 15.93$ Hz), 6.93 (1H, dt, $J = 9.8$, 4.2 Hz), 7.34 (5H, m); ^{13}C-NMR ($CDCl_3$) δ (ppm) 29.93, 78.00, 121.68, 125.70, 126.75, 128.41, 128.74, 133.16, 135.80, 144.74, 163.94; MS EI m/z 200 (M^+), 172, 104, 68 (100%); CI m/z 201 $(M + H)^+$ (100%).

Compound **8c**: ^{1}H-NMR (300 MHz) δ ($CDCl_3$) (ppm) 2.43 (2H, m), 3.66 (2H, d, $J = 4.68$ Hz), 4.56 (3H, m), 5.97 (1H, ddd, $J = 9.72$, 2.64, 1.02 Hz), 6.86 (1H, ddd, $J = 9.72$, 5.91, 2.58 Hz), 7.32 (5H, m); ^{13}C-NMR ($CDCl_3$) δ (ppm) 26.14, 70.86, 73.59, 76.70, 121.04, 127.75, 127.87, 128.50, 137.75, 145.31, 163.82; MS EI m/z 218 (M^+), 127, 112, 97 (100%); CI m/z 219 $(M + H)^+$ (100%).

Compound **9a**: ^{1}H-NMR (300 MHz) δ ($CDCl_3$) (ppm) 1.92 (3H, m), 2.35 (1H, dt, $J = 9.93$, 3.00 Hz), 2.71 (1H, m), 2.86 (1H, m), 3.59 (1H, d, $J = 3.84$ Hz), 3.66 (1H, m), 4.53 (1H, m), 7.25 (5H, m); ^{13}C-NMR ($CDCl_3$) δ (ppm) 29.49, 31.13, 36.46, 49.14, 52.11, 72.97, 126.24, 128.47, 128.61, 140.78, 167.73; MS EI m/z 218 (M^+), 155, 143, 91 (100%); CI m/z 219 $(M + H)^+$ (100%).

Compound **9b**: ^{1}H-NMR (300 MHz) δ ($CDCl_3$) (ppm) 2.16 (1H, dd, $J = 15.12$, 11.8 Hz), 2.37 (1H, dt, $J = 15.12$, 3.03 Hz), 3.65 (1H, d, $J = 4.05$ Hz), 3.74 (1H, m), 5.17 (1H, m), 6.13 (1H, dd, $J = 15.87$, 6.84 Hz), 6.69 (1H, d, $J = 15.93$ Hz), 7.34 (5H, m); ^{13}C-NMR ($CDCl_3$) δ (ppm) 30.17, 49.16, 52.09, 74.17, 125.00, 126.78, 128.51, 128.75, 133.42, 135.62, 167.33; MS EI m/z 216 (M^+), 171, 131 (100%), 104; CI m/z 217 $(M + H)^+$ (100%), 199, 173.

Compound **9c**: ^{1}H-NMR (300 MHz) δ ($CDCl_3$) (ppm) 2.21 (1H, m), 2.36 (1H, m), 3.62 (4H, m), 4.61 (3H, m), 7.32 (5H, m); ^{13}C-NMR ($CDCl_3$) δ (ppm) 26.01, 49.10, 52.14, 70.68, 73.04, 73.61, 127.76, 127.92, 128.52, 137.63, 167.29.

Compound **2a**: ^{1}H-NMR (300 MHz) δ ($CDCl_3$) (ppm) 1.91 (4H, m), 2.22 (1H, s, br), 2.76 (4H, m), 4.38 (1H, quintet, $J = 4.00$ Hz), 4.72 (1H, m), 7.25 (5H, m); ^{13}C-NMR ($CDCl_3$) δ (ppm) 31.17, 35.97, 37.35, 38.66, 62.63, 75.24, 126.16, 128.50, 128.58, 141.10, 170.92; MS EI m/z 220 (M^+), 202, 142, 91 (100%); CI m/z 221 $(M + H)^+$ (100%), 203.

Compound **2b**: ^{1}H-NMR (300 MHz) δ ($CDCl_3$) (ppm) 1.96 (1H, m), 2.14 (1H, m), 2.32 (1H, s, br), 2.73 (2H, m), 4.45 (1H, quintet, $J = 3.98$ Hz), 5.38 (1H, m), 6.21 (1H, dd, $J = 15.93$, 6.48 Hz), 6.71 (1H, d, $J = 15.93$ Hz), 7.33 (5H, m); ^{13}C-NMR ($CDCl_3$) δ (ppm) 36.30, 38.71, 62.56, 76.43, 126.56, 126.73, 128.30, 128.73, 132.58, 135.89, 170.56; MS EI m/z 218 (M^+), 200, 104 (100%), 91; CI m/z 219 $(M + H)^+$, 201 (100%).

Compound **2c**: ^{1}H-NMR (300 MHz) δ ($CDCl_3$) (ppm) 1.92 (2H, m), 2.61 (2H, m), 3.58 (1H, dd, $J = 10.71$, 4.32 Hz), 3.67 (1H, dd, $J = 10.7$, 3.81 Hz), 4.35

(1H, m), 4.56 (2H, d, $J = 1.98$ Hz), 4.84 (1H, m), 7.31 (5H, m); ^{13}C-NMR ($CDCl_3$) δ (ppm) 31.98, 38.58, 62.34, 71.68, 73.57, 75.28, 127.78, 127.89, 128.51, 137.75, 170.87; MS EI m/z 189, 107 (100%), 91; CI m/z 237 $(M + H)^+$ (100%), 219.

Acknowledgements

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References

[1] A. Endo, M. Kuroda, Y. Tsujita, J. Antibiot. 29 (1976) 1346.
[2] A.G. Brown, T.C. Smale, T.J. King, R. Hasenkamp, R.H. Thompson, J. Chem. Soc. Perkin Trans. I (1976) 1165.
[3] (a) A.W. Alberts, T.C. Smale, Proc. Natl. Acad. Sci. U. S. A. 77 (1980) 3957. (b) P.R. Hebert, J.M. Gaziano, K.S. Chan, C.H. Hennekens, JAMA 278 (1997) 4. (c) http://www.pharminfo.com/pubs/msb/statins.html.
[4] Mevacor® is a trademark of Merck & Co.
[5] Launched in the market (Merck & Co.) in 1988. FDA approved new dose ranges for Zocor® in 1998.
[6] Pravachol is a trademark of Bristol–Myers Squibb. FDA approved in 1996.
[7] FDA approved in 1996, Lipitor® is a trademark of Pfizer (Parke–Davis).
[8] Launched in the market in 1995. Baycol® is a trademark of Bayer in the USA.
[9] Lescol is a trademark of Novartis Pharma AG.
[10] Statin drugs constituted $\sim 6\%$ of the total annual sale of the top 200 drugs in 1999, worth $125 billion in the USA. Lipitor, $3.0b; Zocor, $2.3b; Pravacol, $1.18b; Mevacor, $389.5m; and Lescol, $268.1m. For a listing of the top 200 prescription drugs, see: http://www.rxlist.com and a listing of the top 200 drugs in sales, see: http://www.pharmacyline.com.
[11] (a) S.Y. Sit, R.A. Parker, I. Motoc, W. Han, N. Balasubramanian, J.D. Catt, P.J. Brown, W.E. Harte, M.D. Thompson, J.J. Wright, J. Med. Chem. 33 (1990) 2982. (b) G.E Stokker, W.F. Hoffman, A.W. Alberts, E.J. Cragoe Jr, A.A. Deana, J.L. Gilfillan, J.W. Huff, F.C. Novello, J.D. Purgh, R.L Smith, A.K. Willard, J. Med. Chem. 28 (1985) 347.
[12] (a) T. Honda, S. Ono, H. Mizutani, K.O. Hallinan, Tetrahedron Asymm. 8 (1997) 181. (b) M. Majewski, D.L.J. Clive, P.C. Anderson, Tetrahedron Lett. 25 (1984) 2101. (c) C. Bonini, R. Racioppi, L. Viggiani, G. Righi, L. Rossi, Tetrahedron: Asymm. 4 (1993) 793. (d) C. Bonini, R. Racioppi, G. Righi, L. Viggiani, J. Org. Chem. 58 (1993) 802. (d) B.D. Roth, W.H. Roark, Tetrahedron Lett. 29 (1988) 1255. (e) Y.L. Yang, J.R. Flack, Tetrahedron Lett. 23 (1982) 4305. (f) A.D. Mico, G. Piancatelli, S. Cacurri, S. Lappa, Gazz. Chim. Ital. 122 (1992) 415. (g) S.D. Rychnovsky, G. Griesgraber, S. Zeller, D.J. Skalitzky, J. Org. Chem. 56 (1991) 5161. (h) C.R. Johnson, C.H. Senanayake, J. Org. Chem. 54 (1989) 736. (i) F. Bonadies, R.D. Fabio, A. Gubbiotti, S. Melozzi, C. Bonini, Tetrahedron Lett. 28 (1987) 703. (j) G. Solladie, C. Bauder, L. Rossi, J. Org. Chem. 60 (1995) 7774. (k) V. Yadav, K.K. Kapoor, Ind. J. Chem. Sect. B. 34 (1995) 1026.
[13] (a) S. Takano, T. Kamikubo, T. Sugihara, K. Ogasawara, Tetrahedron Asymm. 3 (1992) 853. (b) H. Urabe, T. Matsuka, F. Sato, Tetrahedron Lett. 33 (1992) 4183. (c) T. Hiyama, G.B. Reddy, T. Minami, T. Hanamoto, Bull. Chem. Soc. Jpn. 68 (1995) 350. (d) T. Hiyama, T. Minami, K. Takahashi, Bull. Chem. Soc. Jpn. 68 (1995) 364. (e) B. Henkel, A. Kunath, H. Schick, Tetrahedron: Asymm. 4 (1993) 153. (f) B. Henkel, A. Kunath, H. Schick, Liebigs Ann. Chem. (1992) 809. (g) F. Bennet, D.W. Knight, Tetrahedron Lett. 29 (1988) 4625. (h) F. Bonadies, R.D. Fabio, A. Gubbiotti, S. Mecozzi, C. Bonini, Tetrahedron Lett. 28 (1987) 703. (i) K. Prasad, R. Oljan, Tetrahedron Lett. 25 (1984) 2435. (j) M. Sato, S. Sunami, Y. Sugita, C. Kaneko, Chem. Pharm. Bull. 42 (1994) 839. (k) G.B. Reddy, T. Minami, T. Hanamoto, T. Hiyama, J. Org. Chem. 56 (1991) 5752. (l) B. O'Connor, G. Just, Tetrahedron Lett. 27 (1986), 5201. (m) K. Prasad, O. Repic, Tetrahedron Lett. 25 (1984) 2435. (n) W.F. Hoffman, A.W. Alberts, E.J. Cragoe Jr, A.A. Deana, B.E. Evans, J.C. Gifillan, N.P. Gould, J.W. Huff, F.C. Novello, J.D. Prugh, K.E. Rittle, R.I. Smith, G.E. Stokker, A.K. Willard, J. Med. Chem. 29 (1986) 159.
[14] (a) R. Ballini, E. Marcantoni, M. Petrini, J. Chem. Soc. Perkin Trans I (1991) 490. (b) S. Takano, Y. Shimazaki, Y. Sekiguchi, K. Ogasawara, Synthesis (1989) 539. (c) J.M. Escudier, M. Baltas, L. Gorrichon, Tetrahedron Lett. 32 (1991) 5345. (d) J.M. Escudier, M. Baltas, L. Gorrichon, Tetrahedron 49 (1993) 5253. (e) S. Hatakeyama, K. Satoh, S. Takano, Tetrahedron Lett. 34 (1993) 7425. (f) M. Oizumi, M. Takahashi, K. Ogasiwara, Synlett 9 (1997) 1111. (g) S. Schabbert, R. Tiedemann, E. Schaumann, Liebigs Ann. Recl. (1977) 879. (h) G. Dujardin, S. Rossignol, E. Brown, Synthesis (1998), 763. (i) M. Miyazawa, E. Matsuoka, S. Sasaki, S. Oonuma, K. Maruyama, M. Miyashita, Chem Lett. (1998) 109. (j) K. Prasad, O. Repic, Tetrahedron Lett. 25 (1984) 3391. (k) A.K. Ghosh, H. Lei, J. Org. Chem. 65 (2000) 4779.
[15] (a) K. Narasaka, F.C. Pai, Tetrahedron 40 (1984) 2233. (b) K.M. Chen, G.E. Hardmann, K. Prasad, O. Repic, M.J. Shapiro, Tetrahedron Lett. 28 (1987) 155.
[16] (a) P.V. Ramachandran, M.V.R. Reddy, H.C. Brown, Tetrahedron Lett. 41 (2000) 853. (b) P.V. Ramachandran, M.V.R. Reddy, H.C. Brown, J. Ind. Chem. Soc. 75 (1999) 789.
[17] H.C. Brown, P.K. Jadhav, J. Am. Chem. Soc. 105 (1983) 2092.
[18] Yield based on ^{1}H-NMR spectroscopy.
[19] Chiralcel® OD-H™ is a product of Chiral Technologies, Inc. Exton, PA.
[20] R.H. Grubbs, S. Chang, Tetrahedron 54 (1998) 4413. (b) Wright, D.L. Current Org. Chem. 3 (1999) 211 and references cited therein.
[21] M. Miyashita, T. Suzuki, M. Hoshino, A. Yoshikoshi, Tetrahedron 53 (1997) 12469.
[22] (a) H.C. Brown, K.S. Bhat, J. Am. Chem. Soc. 108 (1986) 5919. (b) H.C. Brown, P.K. Jadhav, P.T. Perumal, Tetrahedron Lett. 25 (1984) 5111. (c) H.C. Brown, P.K. Jadhav, Tetrahedron Lett. 25 (1984) 1215. (d) H.C. Brown, R.S. Randad, Tetrahedron 46 (1990) 4463. (e) H.C. Brown, P.K. Jadhav, K.S. Bhat, J. Am. Chem. Soc. 110 (1988) 1535. (f) H.C. Brown, G. Narla, J. Org. Chem. 60 (1995) 4686. (g) H.C. Brown, P.K. Jadhav, K.S. Bhat, J. Am. Chem. Soc. 107 (1985) 2564. (h) A.G.M. Barrett, M.A. Seefeld, Tetrahedron 49 (1993) 7857. (i) S. Hu, S. Jayaraman, A.C. Oehlschlager, J. Org. Chem. 61 (1996) 7513.
[23] H.C. Brown, G.W. Kramer, A.B. Levy, M.M. Midland, Organic Syntheses via Boranes, Wiley–Interscience, New York, 1975 Reprinted edition, vol. 1. Aldrich Chemical Co. Inc., Milwaukee, WI, 1997, Chapter 9.