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A novel synthesis of diethyl (*R*)-3-(*N*-benzyloxyamino)-2-hydroxypropylphosphonate, a precursor to hydroxylamine antibiotics FR-33289 and FR-33699

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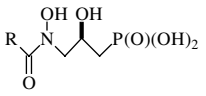
Abstract—Regioselective opening of the oxirane ring at C(3) of diethyl 2,3-epoxypropylphosphonate **6** with *N*- or *O*-benzylhydroxylamine led to 3-(*N*-benzyl-*N*-hydroxyamino)- or 3-(*N*-benzyloxyamino)-2-hydroxypropylphosphonates, **10** or **8**. From (*S*)-**6** (ee 94%), the phosphonate (*S*)-**10** (ee 98%) was prepared in 80% yield. Highly enantiomerically enriched (*R*)- and (*S*)-**8** (ee 97%) were obtained from (*R*)- and (*S*)-**6** (ee 88% and 94%), respectively.

1. Introduction

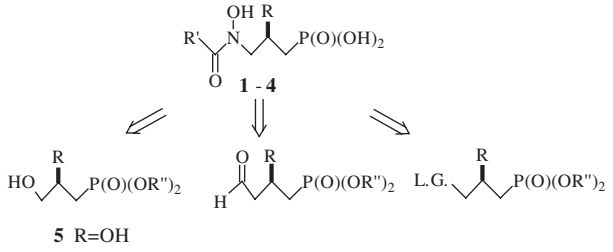
A series of propylphosphonates **1**–**4**, which contain an unusual *N*-acylated hydroxylamine substituent at C(3), has been isolated from broths of strains of *Streptomyces* over 25 years ago.[1–3] Their high antibacterial activity has been recognized first, but later on it appeared that **1** and **2** also exhibit antimalarial activity.[4] Several prodrugs of **1** and **2** have recently been reported.[5,6]

Structural assignments in the phosphonates **1**–**4** were based on spectroscopic studies[7] and finally proved by chemical synthesis.[8–10] The (*R*)-configuration in **3** and **4** was established using diethyl (*R*)-2,3-dihydroxypropylphosphonate[11] (*R*)-**5** as a starting material.[9,10] Analogues of **1**–**4** have also been prepared.[12] The key step in syntheses of the phosphonates **1**–**4** is the introduction of the hydroxylamino group at C(3) by nucleophilic displacement with a suitably protected hydroxylamine derivatives,[6,8–10] by the Mitsunobu reaction[12] or by the reductive amination[5] (Scheme 1).

R=H FR-31564 **1**
R=Me FR-900098 **2**



R=H FR-33699 (*R*)-**3**
R=Me FR-33289 (*R*)-**4**



Scheme 1. The known strategies to the phosphonates **1**–**4**; R = H, OH.

Recently, we have elaborated the efficient approach to highly enantiomerically enriched diethyl (*S*)-2,3-epoxypropylphosphonate, (*S*)-**6** by a hydrolytic kinetic resolution (HKR)[13] of the racemic epoxide **6**.[14,15] The phosphonate (*S*)-**6** has later been used in the synthesis of the enantiomerically pure phosphonate analogues of carnitine, (*S*)-**7a**[15] and GABOB, (*S*)-**7b**[16] (Scheme 2). Herein we present the application of the epoxide **6** in the synthesis of diethyl (*R*)-3-(*N*-benzyloxyamino)-2-hydroxypropylphosphonate **8**,[5] a precursor to (*R*)-**3** and (*R*)-**4**.

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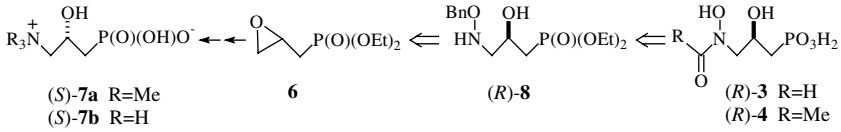
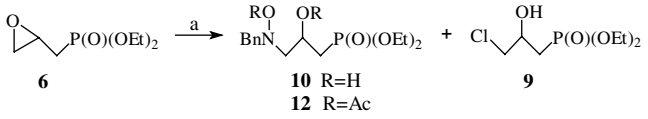


Scheme 2.

2. Results and discussion

In preliminary experiments opening of the oxirane ring in the racemic phosphonate **6** with hydroxylamine hydrochloride was studied. In the presence of triethylamine or sodium bicarbonate in aqueous ethanol the opening was complete at room temperature, but complex reaction mixtures were formed. Trace amounts of diethyl 3-chloro-2-hydroxypropylphosphonate[15] **9** were separated by column chromatography from crude reaction mixtures. In the nonpolar solvent CH_2Cl_2 in the presence of triethylamine the reaction of the epoxyphosphonate **6** with hydroxylamine was incomplete even after 3 days at room temperature leaving an 82:18 mixture of **9** and **6**.

The epoxide ring opening in the phosphonate **6** with *N*-benzylhydroxylamine hydrochloride[17–19] occurred exclusively at C(3) leading to the formation of diethyl 3-(*N*-benzyl-*N*-hydroxyamino)-2-hydroxypropylphosphonate **10**. However, the expected product **10** was contaminated with various amounts of the chlorophosphonate **9** (Scheme 3).



Scheme 3. Reagents and conditions: (a) BnNHOH·HCl, NEt_3, ethanol/water, rt, 24 h.

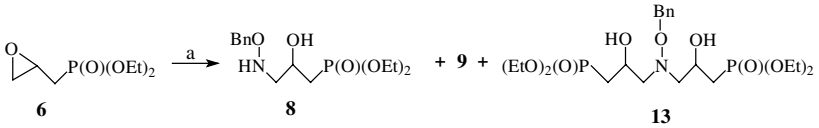
Depending on the reaction conditions ratios of **10** and **9** varied from 95:5 (NEt_3, ethanol/water, 24 h) to 91:9 ($NaHCO_3$, CH_2Cl_2, 48 h) and to 83:17 (NEt_3, CH_2Cl_2, 6 days). Chromatographic separation of the crude product obtained in aqueous ethanol gave pure phosphonates **10** and **9** in 74% and 4% yield, respectively. Final proof of the exclusive C(3) opening in the epoxyphosphonate **6** was achieved by transforming the phosphonate **10** into diacetate **12** and careful analysis of its ^1H NMR spectrum. When the epoxide (*S*)-**6** (ee 94%) was subjected to the reaction with *N*-benzylhydroxylamine, (*S*)-**10** (ee 98%) was obtained in 80% yield after column chromatography (Scheme 3).

On the other hand, when the racemic epoxyphosphonate **6** was reacted with *O*-benzylhydroxylamine hydrochloride in the presence of triethylamine in aqueous ethanol, a mixture of diethyl 3-(*N*-benzyloxyamino)-2-hydroxypropylphosphonate **8**, the chlorophosphonate **9** and bisphosphonates **13** (*dl* δ ^{31}P = 30.52 and *meso* 30.44 ppm) in a 76:5:12:7 ratio, respectively, was obtained (Scheme 4). Chromatographic purification gave the phosphonate **8** in 56% yield.

Under the same conditions, from (*S*)-**6** (ee 94%) a 68:11:4:17 mixture of (*S*)-**8**, (*R*)-**9** and (*S*,*S*)-**13** containing unreacted starting epoxyphosphonate was formed. After chromatographic purification (*S*)-**8** (ee 97%) was separated in 53% yield. Significant improvements in transforming the epoxyphosphonate **6** into the phosphonate **8** (Scheme 4) were achieved using freshly prepared *O*-benzylhydroxylamine.[20] Refluxing the ethanolic solution of highly enantiomerically enriched phosphonate (*R*)-**6** and *O*-benzylhydroxylamine for 24 h afforded mixtures consisting of (*R*)-**8**, (*R*,*R*)-**13** and (*R*,*S*)-**13**. No traces of the unreacted starting material or unwanted chlorophosphonate **9** were observed. Furthermore, phosphonates (*R*)-**8** were cleanly separated from the bisphosphonates **13** on a silica gel column in over 80% yield. When (*R*)-**6** (ee 52%) was used, the enantiomeric purity of (*R*)-**8** was not increased after chromatography on silica gel. However, from (*R*)-**6** (ee 88%) the phosphonate (*R*)-**8** (ee 97%) was obtained.

3. Conclusions

N- and *O*-Benzylhydroxylamines react with diethyl 2,3-epoxypropylphosphonate **6** regiospecifically at C(3) to produce diethyl 3-(*N*-benzyl-*N*-hydroxyamino)-2-hydroxypropylphosphonate **10** and 3-(*N*-benzyloxyamino)-2-hydroxypropylphosphonate **8**, respectively, as major products. Up to 15% of *meso*- and *dl*-bisphosphonates **13** was formed in the reaction of *O*-benzylhydroxylamine with **6**. When *N*- and *O*-benzylhydroxylamines were prepared in situ from their hydrochlorides, up to 5% of diethyl 3-chloro-2-hydroxypropylphosphonate **9** was found in the crude products. From (*S*)-**6** (ee 94%), the phosphonate (*S*)-**10** (ee 98%) was prepared in 80% yield. Highly enantiomerically enriched (*R*)- and (*S*)-**8** (ee 97%) were obtained from the epoxyphosphonates (*R*)- and (*S*)-**6** (ee 88% and 94%), respectively. The phosphonate (*R*)-**8** is a key intermediate in the synthesis of hydroxylamine antibiotics FR-33289 and FR-33699.



Scheme 4. Reagents and conditions: (a) $BnONH_2$·HCl, NEt_3, ethanol/water, rt, 48 h or $BnONH_2$, ethanol, reflux, 24 h.

4. Experimental

^{1}H NMR spectra were recorded with a Varian Mercury-300 spectrometer; chemical shifts δ in ppm with respect to TMS; coupling constants J in Hz. ^{13}C and ^{31}P NMR spectra were recorded on a Varian Mercury-300 machine at 75.5 and 121.5 MHz, respectively. IR spectral data were measured on an Infinity MI-60 FT-IR spectrometer. Elemental analyses were performed by the Microanalytical Laboratory of this Faculty on a Perkin Elmer PE 2400 CHNS analyzer. Polarimetric measurements were conducted on a Perkin Elmer 241 MC apparatus.

Diethyl (*R*)- and (*S*)-2,3-epoxypropylphosphonates **6** (ee 52% or 88% and 94%, respectively) were prepared according to the literature procedure.[15]

4.1. Reaction of the racemic epoxyphosphonate 6 with *N*-benzylhydroxylamine hydrochloride

4.1.1. In the presence of triethylamine in aqueous ethanol. A mixture of **6** (1.00 g, 5.15 mmol), *N*-benzylhydroxylamine hydrochloride (1.23 g, 7.73 mmol) and triethylamine (1.07 mL, 7.73 mmol) in ethanol/water (1:1, v/v, 4 mL) was stirred at room temperature for 24 h. The reaction mixture was extracted with CH_2Cl_2 (3×4 mL), the organic extracts were washed with water (1×3 mL), dried over $MgSO_4$ and concentrated in vacuo. The crude product was chromatographed on a silica gel column with methylene chloride/methanol (50:1, v/v) to give less polar phosphonate **10** (1.21 g, 74%) as a colourless oil and more polar chlorophosphonate **9**[15] (0.07 g, 4%).

4.1.1.1. Diethyl 3-(*N*-benzyl-*N*-hydroxy)amino-2-hydroxypropylphosphonate 10. IR (film): $\nu = 3330$, 3063, 3030, 2983, 2932, 2908, 1454, 1393, 1221, 1047, 966, 750, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.32$ (t, $J = 7.1$ Hz, 6H), 1.98 (ddd, $J_{1a\text{-}P} = 17.4$ Hz, $J_{1a\text{-}1b} = 15.3$ Hz, $J_{1a\text{-}2} = 7.8$ Hz, 1H, H-1a), 2.04 (ddd, $J_{1b\text{-}P} = 8.6$ Hz, $J_{1a\text{-}1b} = 15.3$ Hz, $J_{1b\text{-}2} = 5.1$ Hz, 1H, H-1b), 2.82 and 2.83 (AB part of ABX system, $J_{3a\text{-}3b} = 12.9$ Hz, $J_{3a\text{-}2} = 6.3$ Hz, $J_{3b\text{-}2} = 5.4$ Hz, 2H, H-3ab), 3.88 and 3.89 (AB, $J_{AB} = 13.2$ Hz, 2H, H_2C-Ph), 3.83–3.93 (br s, 1H, OH), 4.03–4.16 (m, 4H), 4.34 (ddddd, $J_{2\text{-}P} = 11.1$ Hz, $J_{2\text{-}1a} = 7.8$ Hz, $J_{2\text{-}3a} = 6.3$ Hz, $J_{2\text{-}3b} = 5.4$ Hz, $J_{2\text{-}1b} = 5.1$ Hz, 1H, H-2), 5.86 (br s, 1H, OH), 7.25–7.37 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta = 16.7$ (d, $J = 6.0$ Hz), 31.8 (d, $J = 140.3$ Hz, C-1), 61.9 and 62.2 (2d, $J = 6.3$ Hz), 64.6 (d, $J = 3.4$ Hz, C-2), 65.3, 65.6 (d, $J = 16.0$ Hz, C-3), 127.5, 128.4, 129.6, 137.1; ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = 31.04$. Anal. Calcd for $C_{14}H_{24}NO_5P \cdot 1/5H_2O$: C, 52.40; H, 7.66; N, 4.37. Found: C, 52.49; H, 7.85; N, 4.42.

4.1.1.2. Diethyl (*S*)-3-(*N*-benzyl-*N*-hydroxy)amino-2-hydroxypropylphosphonate (*S*)-10. As described for the racemic compound (Section 4.1.1), from (*S*)-**6** (0.810 g, 4.17 mmol, ee 94%), *N*-benzylhydroxylamine hydrochloride (1.00 g, 6.26 mmol) and triethylamine (0.868 g, 6.26 mmol) in aqueous ethanol (8.0 mL, 1:1) (*S*)-**10** (1.09 g, 80%) was obtained as a colourless oil. $[\alpha]_D^{20} = -14.3$ (*c* 1.68, $CHCl_3$) (ee 98%). Anal. Calcd for $C^{14}H_{24}NO_5P \cdot 0.2H_2O$: C, 52.40; H, 7.66; N, 4.37. Found: C, 52.40; H, 7.76; N, 4.19.

4.1.2. In the presence of sodium bicarbonate in methylene chloride. To a solution of **6** (0.100 g, 0.515 mmol) in methylene chloride (2 mL), *N*-benzylhydroxylamine hydrochloride (0.120 g, 0.750 mmol) was added followed by sodium bicarbonate (0.063 g, 0.75 mmol) and the suspension was stirred at room temperature for 2 days. The reaction mixture was diluted with methylene chloride (10 mL), washed with water (3×2 mL) and the aqueous layer was extracted with methylene chloride (3 mL). Organic phases were dried over $MgSO_4$ and concentrated in vacuo. The crude product was chromatographed on a silica gel column with methylene chloride/methanol (50:1, v/v) to give the phosphonate **10** (0.099 g, 61%) as a colourless oil.

4.1.3. In the presence of NEt_3 in methylene chloride. The procedure described in the previous section replacing sodium bicarbonate with triethylamine (0.104 mL, 0.750 mmol) was followed. After 6 days the reaction mixture was worked up and the crude product was purified to afford the phosphonate **10** (0.083 g, 52%).

4.2. Diethyl 2-acetyloxy-3-(*N*-acetyloxy-*N*-benzyl)aminopropylphosphonate 12

Standard acetylation (acetic anhydride, NEt_3, DMAP) of the phosphonate **10** gave the diacetate **12** in 69% yield after chromatography on silica gel with methylene chloride/methanol (100:1, v/v). IR (film): $\nu = 2984$, 2933, 2909, 1743, 1443, 1369, 1240, 1028, 965, 750, 700 cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 1.30$ (t, $J = 7.0$ Hz, 6H), 1.91 (s, 3H), 2.04 (s, 3H), 2.16 (ddd, $J_{1a\text{-}P} = 18.3$ Hz, $J_{1a\text{-}1b} = 15.6$ Hz, $J_{1a\text{-}2} = 6.9$ Hz, 1H, H-1a), 2.42 (ddd, $J_{1b\text{-}P} = 18.6$ Hz, $J_{1a\text{-}1b} = 15.6$ Hz, $J_{1b\text{-}2} = 5.7$ Hz, 1H, H-1b), 3.09 (ddd, $J_{3a\text{-}3b} = 13.8$ Hz, $J_{3a\text{-}2} = 5.7$ Hz, $J_{3a\text{-}P} = 1.2$ Hz, 1H, H-3a), 3.15 (dd, $J_{3a\text{-}3b} = 13.8$ Hz, $J_{3b\text{-}2} = 5.7$ Hz, 1H, H-3b), 3.88 and 3.89 (AB, $J_{AB} = 13.2$ Hz, 2H, H_2C-Ph), 4.02–4.16 (m, 4H), 5.24 (ddddd, $J_{2\text{-}P} = 14.0$ Hz, $J_{2\text{-}1a} = 6.9$ Hz, $J_{2\text{-}3a} = 5.7$ Hz, $J_{2\text{-}3b} = 5.7$ Hz, $J_{2\text{-}1b} = 5.7$ Hz, 1H, H-2), 7.25–7.36 (m, 5H); ^{13}C NMR ($CDCl_3$): $\delta = 16.6$ (d, $J = 6.3$ Hz), 19.6, 21.3, 28.5 (d, $J = 140.9$ Hz, C-1), 60.2 (d, $J = 9.5$ Hz, C-3), 61.9 (d, $J = 6.6$ Hz), 63.8, 66.7 (d, $J = 2.9$ Hz, C-2), 127.9, 128.4, 129.6, 135.3, 169.2, 169.9; ^{31}P NMR (121.5 MHz, $CDCl_3$): $\delta = 28.04$. Anal. Calcd for $C_{18}H_{28}NO_7P$: C, 53.86; H, 7.03; N, 3.49. Found: C, 54.13; H, 6.87; N, 3.71.

4.3. Diethyl 3-(benzyloxyamino)-2-hydroxypropylphosphonate 8

A mixture of the epoxyphosphonate **6** (1.00 g, 5.15 mmol), *O*-benzylhydroxylamine hydrochloride (1.23 g, 7.72 mmol) and triethylamine (1.07 mL, 7.72 mmol) in aqueous ethanol (5 mL, 1:1) was stirred at room temperature for 48 h. Organic compounds were extracted with methylene chloride (5×5 mL), the combined organic layers were washed with water (5 mL),

dried over $MgSO_4$ and concentrated in vacuo. The crude product was chromatographed on a silica gel column with chloroform/methanol (100:1, v/v) to give the phosphonate **8** (0.930 g, 56%) as a colourless oil. IR (film): ν = 3357, 3063, 3031, 2982, 2910, 2869, 1454, 1224, 1020, 966, 835, 746, 699 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.32 and 1.34 (2t, J = 7.0 Hz, 6H), 1.92 (ddAB, $J_{1a\text{-}P}$ = 16.9 Hz, $J_{1a\text{-}1b}$ = 15.2 Hz, $J_{1a\text{-}2}$ = 8.1 Hz, 1H, H-1a), 1.94 (ddAB, $J_{1b\text{-}P}$ = 18.6 Hz, $J_{1a\text{-}1b}$ = 15.2 Hz, $J_{1b\text{-}2}$ = 4.4 Hz, 1H, H-1b), 2.89 (dAB, $J_{3a\text{-}3b}$ = 13.5 Hz, $J_{3a\text{-}2}$ = 8.1 Hz, 1H, H-3a), 3.08 (dAB, $J_{3a\text{-}3b}$ = 13.5 Hz, $J_{3b\text{-}2}$ = 3.6 Hz, 1H, H-3b), 3.58 (d, J = 2.8 Hz, 1H, OH), 4.06–4.19 (m, 4H), 4.20–4.30 (m, 1H, H-2), 4.70 (s, 2H, H_2C-Ph), 5.97 (br s, 1H, NH), 7.27–7.37 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 16.7 and 16.7 (2d, J = 6.0 Hz), 31.8 (d, J = 139.3 Hz, C-1), 58.2 (d, J = 16.6 Hz, C-3), 62.1 and 62.2 (2d, J = 6.3 Hz), 64.0 (d, J = 4.6 Hz, C-2), 76.4, 128.1, 128.5, 128.5, 137.7; ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 30.75. Anal. Calcd for $C_{14}H_{24}NO_5P{\cdot}1/3H_2O$: C, 52.01; H, 7.69; N, 4.33. Found: C, 51.99; H, 7.71; N, 4.55.

4.3.1. Diethyl (*S*)-3-(benzyloxyamino)-2-hydroxypropylphosphonate, (*S*)-8. As described for the racemic compound (Section 4.3), from (*S*)-**6** (0.380 g, 1.97 mmol, ee 94%), *O*-benzylhydroxylamine hydrochloride (0.469 g, 2.94 mmol) and triethylamine (0,408 mL, 2.94 mmol) in aqueous ethanol (4.0 mL) (*S*)-**8** (0.329 g, 53%) was obtained as a colourless oil. $[\alpha]_D^{20} = -12.8$ (*c* 1.79, $CHCl_3$) (ee 97%). Anal. Calcd for $C_{14}H_{24}NO_5P{\cdot}1/3H_2O$: C, 52.01; H, 7.69; N, 4.33. Found: C, 51.95; H, 7.77; N, 4.81.

4.3.2. Diethyl (*R*)-3-(benzyloxyamino)-2-hydroxypropylphosphonate, (*R*)-8. *O*-Benzylhydroxylamine hydrochloride (0.554 g, 3.47 mmol) was stirred with 6 N NaOH (1.2 mL) for 15 min. After addition of water (5 mL) containing ice, the mixture was extracted with ether (5 × 5 mL), combined extracts were dried over $MgSO_4$ and concentrated. To the oily residue (*R*)-**6** (0.337 g, 1.74 mmol, ee 52%) was added followed by ethanol (ca. 2 mL) to get a homogeneous solution, which was refluxed under argon atmosphere for 24 h. Volatiles were removed in vacuo to leave a crude product (0.544 g), which was purified on a silica gel column with chloroform/methanol (50:1, v/v) to give (*R*)-**8** (0.463 g, 84%, ee 57%) as a colourless oil and *dl*- and *meso*-**13** (0.039 g, 9%) as a viscous colourless oil.

4.3.2.1. *meso*- and *dl*-Bis-*N*,*N*-[3-(diethoxyphosphoryl)-2-hydroxypropyl]-*N*-benzyloxyamine 13. ^1H NMR ($CDCl_3$): δ = 1.32 (t, J = 6.9 Hz, 12H), 1.94 (ddAB, $J_{1a\text{-}P}$ = 17.1 Hz, $J_{1a\text{-}1b}$ = 15.3 Hz, $J_{1a\text{-}2}$ = 8.1 Hz, 2H, H-1a), 2.05 (ddAB, $J_{1b\text{-}P}$ = 18.9 Hz, $J_{1a\text{-}1b}$ = 15.3 Hz, $J_{1b\text{-}2}$ = 4.5 Hz, 2H, H-1b), 2.4–3.3 (br s, 2H, OH), 2.94 (dAB, $J_{3a\text{-}3b}$ = 13.5 Hz, $J_{3a\text{-}2}$ = 4.2 Hz, 2H, H-3a), 3.02 (dAB, $J_{3a\text{-}3b}$ = 13.5 Hz, $J_{3b\text{-}2}$ = 7.8 Hz, 2H, H-3b), 4.03–4.18 (m, 8H), 4.23 (ddddd, $J_{2\text{-}P}$ = 12.3 Hz, $J_{1a\text{-}2}$ = 8.1 Hz, $J_{2\text{-}3b}$ = 7.8 Hz, $J_{1b\text{-}2}$ = 4.5 Hz, $J_{2\text{-}3a}$ = 4.2 Hz, 2H, H-2), 4.77 (AB, J_{AB} = 11.0 Hz, 2H, H_2C-Ph), 7.3–7.4 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 16.7 (d, J = 6.0 Hz), 31.9 (d, J = 140.3 Hz, C-1), 62.0 and 62.1 (2d, J = 6.8 Hz), 64.2 (d, J = 3.8 Hz, C-2, *dl*), 64.4 (d, J = 3.0 Hz, C-2), 65.4 (d, J = 15.1 Hz, C-3, *dl*), 65.6 (d, J = 15.0 Hz, C-3, *meso*), 75.7 (C_2Ph, *dl*), 76.1 (C_2Ph, *meso*), 128.3, 128.5, 129.0, 136.6; ^{31}P NMR (121.5 MHz, $CDCl_3$): δ = 30.52 (*dl*), 30.44 (*meso*). Anal. Calcd for $C_{21}H_{39}NO_9P_2$: C, 49.31; H, 7.69; N, 2.74. Found: C, 49.12; H, 7.43; N, 3.02.

In a similar manner, from (*R*)-**6** (0.500 g, 2.58 mmol, ee 88%) and *O*-benzylhydroxylamine prepared from the hydrochloride (0.822 g, 5.15 mmol) (*R*)-**8** (0.663 g, 81%) was obtained as a colourless oil. $[\alpha]_D^{20} = +12.0$ (*c* 1.20, $CHCl_3$) (ee 97%).

4.4. General procedures for the estimation of ee's[21,22]

4.4.1. Diethyl (*R*)-3-(benzyloxyamino)-2-hydroxypropylphosphonate, (*R*)-8. ^{31}P NMR spectrum was taken for a solution of (*S*)-**8** (0.010 g, 0.032 mmol) and quinine (0.005 g, 0,015 mmol) in chloroform-*d* (0.7 mL); δ = 30.80 [(*S*)-**8**] and 30.68 ppm [(*R*)-**8**].

4.4.2. Diethyl (*S*)-3-(*N*-benzyl-*N*-hydroxy)amino-2-hydroxypropylphosphonate, (*S*)-10. ^{31}P NMR spectrum was taken for a solution of (*S*)-**10** (0.030 g, 0.095 mmol) and quinine (0.015 g, 0,046 mmol) in chloroform-*d* (0.7 mL); δ = 31.14 [(*S*)-**10**] and 30.39 ppm [(*R*)-**10**].

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