Enantiospecific syntheses of (R)- and (S)-proline and some derivatives from D-glucono-1,5-lactone

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Carbohydrate-based enantiospecific syntheses of (R)-proline 1 and (S)-proline 2 from the previously reported d-erythro-hexonate ester 9 are described. Azide-substitution reactions on appropriately activated intermediates derived from ester 9, followed by reductive cyclization (H₂/Pd–C), gave the substituted pyrrolidines 14 and 22, which were converted into their corresponding N-Cbz derivatives 16 and 24 in conventional manner. Mild acidic hydrolysis of these, followed by oxidation (sodium metaperiodate), gave the protected prolinal 3 and 4, which on further oxidation (sodium chlorite), followed by catalytic hydrogenolysis, gave the prolines 1 and 2. The N-Cbz-prolinol derivatives 5 and 6 are also reported.

Introduction

The stereospecific syntheses of enantiomerically pure compounds, especially those of natural origin, is an active area of modern organic chemistry. The synthesis of prolines and their derivatives seems currently of interest, inter alia, in this respect. A simple route to (R)-proline 1, (S)-proline 2 and the related protected aldehydes 3, 4 and alcohols 5, 6, from D-glucono-1,5-lactone via the hexonate ester 9, became available during studies on pyrroline-2-1-carboxylic acid. Early syntheses of prolines 1 and 2 produced racemic mixtures which required resolution. Various asymmetric syntheses, including asymmetric transformations, have been reported, but with greater emphasis on the naturally occurring S-isomer 2. Compound 2 is responsible for conformational constraint in certain proteins and is obtained currently almost exclusively from protein hydrolysates or by fermentation. Recent interest has also centred on syntheses designed for the introduction of specific isotopic labelling into the products. The new route described here is noteworthy in its flexibility. Both enantiomers 1 and 2 and their related protected derivatives 3–6 are available, by choice, from an inexpensive source using simple reactions. Compound 3 has not been described previously and its enantiomer 4 is not obtained readily. The prolinal 5 and 6 are usually prepared by metal hydride reduction of suitably protected esters of prolines 1 and 2. Compounds 1 and 2 and derivatives thereof, including the alcohols 5 and 6, are useful chiral catalytic components or auxiliaries for inter alia, enantioselective catalytic reductions and asymmetric intramolecular aldolizations and asymmetric induction in conjugated additions, self-condensation of \( \alpha,\beta \)-unsaturated aldehydes, Robinson annelation reactions, and in the synthesis of some alkaldoids.

Results and discussion

Treatment of the toluene-p-sulphonate ester 10 of compound 9 with sodium azide in N,N-dimethylformamide (DMF) gave the corresponding \( \alpha \)-threo-azide 11 as a syrup (91%) which was characterized by catalytic (palladized charcoal, 10%) reductive amination to give the crystalline pyrrolidine-2-one derivative 12. Reduction of compound 11 in toluene with disobutylaluminium hydride (DIBAL) at 78°C yielded the pure, but unstable aldehyde 13. Attempts to form a stable crystalline phenylhydrazine, or semicarbazone, of compound 13 were unsuccessful. Catalytic hydrogenation of compound 13 over palladized charcoal (10%) proceeded with concomitant ring closure to produce the substituted pyrrolidine 14, which on treatment with toluene-p-sulphonyl chloride (TsCl)–triethylamine gave the crystalline N-toluene-p-sulphonate 15. Treatment of compound 14 in acq. ethanol with benzyl chloroformate in the presence of sodium hydrogen carbonate in the usual manner gave the corresponding N-benzoyloxy carbonyl (N-Cbz) derivative 16. Hydrolysis (80% acq. acetic acid) of compound 16 gave the diol 17, which on oxidation with acq. sodium metaperiodate in methanol gave the protected (R)-proline derivative 3. Reduction of aldehyde 3 with sodium borohydride in methanol produced the corresponding (R)-prolinol derivative 5.

Oxidation of aldehyde 3 with sodium chlorite, in the presence of 2-methylbut-2-ene as a chlorine scavenger, was rapid and proceeded smoothly to give the protected (R)-proline derivative 7, which on catalytic hydrogenolysis provided pure (R)-proline 1 (Scheme 1). Treatment of the bromoester 18 with sodium azide in DMF did not proceed satisfactorily. Analysis (TLC and GLC) of the reaction mixture produced after 18 h indicated the presence of not only the expected azido derivative 19 but also its diastereomer 11 (vide supra), in the ratio 3:2, indicating that epimerization was occurring during the course of the substitution reaction. This was probably due to nucleophilic attack of bromide ions, produced during the initial phase of the displacement reaction, on remaining compound 18, with subsequent and concurrent replacement of both by azide ions (Scheme 2). The required compound 19 was obtained successfully by treatment of bromide 18 with a solution of lithium azide in DMF at room temp. for 7 days. Lithium azide is much more.

followed by reductive (Pd/C, H\(_2\)) cyclization of the resultant unstable aldehyde, which was characterized as the crystalline compound with the numerical values for their enantiomeric counterparts, good overall agreement with the values reported here, and also the observed optical rotations for these two derivatives were in value, \(\alpha\) and \(\beta\), of compound 4, derived from reduction of esters of (S)-proline. It had been implied that amino aldehydes derived from chiral amino acids could be difficult to obtain with high optical purity. Compound 3 has not been described hitherto. The two enantiomeric aldehydes 3 and 4 described here probably have very high optical purities in view of their mode of synthesis. These two compounds could be stored (0°C) for appreciable periods of time (2–3 months) without any obvious deterioration or racemization.

Further oxidation of aldehyde 4 with sodium chlorite in the same manner as described for its enantiomer 3 (vide supra) yielded the known, commercially available N-Cbz-(S)-proline 8, which on catalytic hydrogenation (palladized charcoal, 10%) yielded (S)-proline 2.

The syntheses described illustrate the useful application of the ester 9 as a chiral synthon. Further studies on the use of the aldehydes 4 and 5 as sources of novel chiral ligands is currently in progress.

### Experimental

Optical rotations were determined with a Perkin-Elmer model 241 automatic polarimeter on 1% solutions in chloroform at 25°C, unless indicated otherwise. TLC on pre-coated plates of silica gel (Merck) was performed with light petroleum-ethyl acetate (1:1). Detection was affected by spraying with 0.1 m K\(_2\)Cr\(_2\)O\(_7\) in 0.05 m H\(_2\)SO\(_4\) and heating at 140°C. Column chromatography and flash-column chromatography were performed on silica gel 60 and 60 H with the solvent mixtures indicated. GLC was performed with a Hewlett-Packard 5890 gas chromatograph; a fused-silica capillary column (25 m) coated with HP-1 cross-linked methyl silicone gumphase operating at 100–150°C \((t = 0 \text{ min}, 100^\circ\text{C isothermal}; t = 5 \text{ min}, 5^\circ\text{C min}^{-1})\) and nitrogen as the carrier gas at 2 ml min\(^{-1}\) was used. \(^1\)H NMR spectra were recorded with a Bruker AC 100 (100 MHz) or Bruker AC 300 (300 MHz) spectrometer on solutions in CDCl\(_3\) (internal Me\(_4\)Si) or D\(_2\)O or as indicated. J-Values are given in Hz. \(^1\)C NMR spectra were recorded with Bruker AC 100, AC 300 or AM 400 spectrometers operating at 25, 75 and 100.6 MHz respectively on solutions in CDCl\(_3\) (internal Me\(_4\)Si) or D\(_2\)O (external 1,4-dioxane at \(d_2\) 67.8). Mass spectra were recorded using a double-focusing VG 7070E.

### Scheme 1

Reagents and conditions: i, TsCl, pyridine; ii, NaN\(_3\), DMF; iii, Pd–C (10%), H\(_2\); iv, DIBAL, –78°C; v, PhCH\(_2\)OOC\(_2\)H, NaHCO\(_3\); vi, 80% HOAc–water; vii, NaIO\(_4\); viii, NaBH\(_4\); ix, NaClO\(_2\), 2-methylbut-2-ene; x, TsCl, Et\(_3\)N

### Scheme 2

Reagents and conditions: i, Ph\(_3\)P, CBr\(_4\); ii, NaN\(_3\), DMF, 100°C.
spectrometer or a Varian Saturn 2 GC-MS ion-trap system. IR spectra were determined on a Perkin-Elmer 298 spectrometer as indicated. DIBAL was purchased as a 1 M solution in hexane. Light petroleum is the fraction distilled between 60–80 °C.

**Methyl 4-azido-2,3,4-trideoxy-5,6-O-isopropylidene-D-threo-manonate (4R,5S)-methyl 4-azido-5,6-O-isopropylidenedioxy-hexan-1-one**

A stirred mixture of compound 10 (2.4 g, 6.65 mmol) and sodium azide (1.28 g, 19.7 mmol) in DMF (50 ml) was heated for 12 h at 100 °C, cooled and then treated with ice-water (200 ml). The mixture was extracted with diethyl ether (2 × 150 ml) and the combined extracts were washed successively with saturated aq. sodium chloride (2 × 20 ml) and water (2 × 20 ml), dried (MgSO₄), and concentrated in vacuo. Column chromatography (ethyl acetate-light petroleum, 3:1) of the residue yielded compound 11 (1.43 g, 91%) as a pure (TLC and GLC) syrup.

**Scheme 3 Reagents and conditions:** i, LiN₃, DMF, 20 °C; ii, DIBAL, –78 °C; iii, Pd–C (10%), H₂; iv, TsCl, KOH; v, PhCH₂OCOCI, NaHCO₃; vi, 80% HOAc–water; vii, NaIO₄, viii, NaBH₄; ix, NaClO₂, 2-methylbut-2-ene.

**(5R,4'S)-5-(2',2'-Dimethyl-1',3'-dioxolan-4'-yl)pyrrolidin-2-one**

A solution of compound 11 (0.604 g, 2.49 mmol) in methanol (20 ml) was treated with palladized charcoal (10%; 60 mg) and was then hydrogenated (1 atm) at room temp. The inorganic material was removed by filtration and washed with methanol (20 ml), and the combined filtrate and washings were concentrated in vacuo to give an oil which crystallized on storage (48 h). Recrystallization (diisopropyl ether–dichloromethane) gave pure lactam 12 (0.23 g, 63%), mp 102–104 °C; [α]D +54 (Found: C, 58.27; H, 8.11; N, 7.45. C₄H₅NO₃ requires C, 58.36; H, 8.16; N, 7.56%). δ(CHCl₃) 6.48 (br s, 1 H, NH), 4.03–3.67 (m, 4 H, H-4', -5 and H-5'), 2.3–1.95 (m, 4 H, H-3' and -4') and 1.42 and 1.33 (2 s, each 3 H, CMe₂); νmax(KBr)/cm⁻¹ 3260, 1690 and 1650.

**(4R,5S)-4-Azido-5,6-(isopropylidenedioxy)hexan-1-one**

A solution of DIBAL (7.1 ml) was added dropwise to a stirred, cooled (–78 °C) solution of compound 11 (1.44 g, 5.9 mmol) in light petroleum–toluene (25 ml; 1:1) maintained under nitrogen. The mixture was stirred for a further 1 h at the same temperature, treated with sodium sulfite decarboxylate (1.5 g), diluted with dichloromethane (25 ml) and stirred at room temp. for 1 h. The mixture was then treated with anhydrous sodium sulfate, and filtered, the inorganic material was washed with dichloromethane, and the combined filtrate and washings were washed with water (2 × 20 ml), dried (NaSO₄), and concentrated *in vacuo*. Column chromatography (light petroleum-ethyl acetate, 1:1) of the resultant material gave aldehyde 13 (1.04 g, 82%) as an oil; [α]D +10.4; δ(CHCl₃) 9.81 (s, 1 H, CHO), 4.10 (m, 2 H, H-5, H-6'), 3.82 (dd, J 6 and 8, 1 H, H-6'), 3.27 (m, 1 H, H-4), 2.68 (m, 2 H, H-2'), 1.84–1.70 (m, 2 H, H-3) and 1.47 and 1.38 (2 s, each 3 H, CMe₂); δ(CHCl₃) 200.73, 110.12, 78.53, 66.33, 62.71, 40.22, 26.32, 25.13 and 23.01; νmax 186 (M⁺ + 1 – 28, 2.8%), 101 (100), 82 (44), 55 (12) and 43 (97); νmax(neat)/cm⁻¹ 2880, 2710, 2100 and 1710.

A portion of the above material (98.4 mg, 0.575 mmol) in methanol (2 ml) was treated with TsCl (134 mg, 0.702 mmol), set aside at room temp. for 4 h, and processed in the usual manner. A solution of compound 13 (0.442 g, 2.07 mmol) in methanol (20 ml) was treated with palladized charcoal (10%; 60 mg) and was then hydrogenated (1 atm) at room temp. for 7 h. The inorganic material was removed by filtration and washed with methanol (10 ml). The combined filtrate and washings were concentrated *in vacuo* to give pure compound 14 (30 mg, 76%); [α]D +9 (Found: C, 62.84; H, 10.41; N, 7.36. C₇H₁₀NO₃ requires C, 63.12; H, 10.01%; N, 8.18%). δ(CHCl₃) 3.99 (m, 2 H, H-5'), 3.64 (m, 1 H, H-4'), 3.09–2.89 (m, 3 H), 2.10 (br s, 1 H, NH), 1.85–1.67 (m, 3 H) and 1.42 and 1.36 (2 s, each 3 H, CMe₂); δ(CHCl₃) 109.13, 79.40, 67.11, 60.95, 46.30, 27.43, 26.77, 25.37 and 25.24; νmax 172 (M⁺ + 1, 8.4%), 156 (3,3), 70 (100) and 43 (31); νmax(film)/cm⁻¹ 3330, 2940, 2850 and 1690.

A portion of the above material (98.4 mg, 0.575 mmol) in methanol (2 ml) containing trimethylamine (0.163 ml, 1.17 mmol) was treated with TsCl (134 mg, 0.702 mmol), set aside at room temp. for 4 h, and processed in the usual manner. Recrystallization (light petroleum) of the resultant crude crystalline material (151 mg) gave the N-toluene-p-sulfonate 15 (125 mg, 67%); mp 95–97 °C; [α]D –68 (Found: C, 58.67; H, 6.83; N, 4.31; S, 9.78. C₇H₁₀NO₃S requires C, 59.05; H, 7.12; N, 4.30; S, 9.85%). δ(CHCl₃) 77.2 and 73.2 (2 d, each J 8.2, each 2 H, ArH), 4.21 (q, J 6.3, 1 H, H-4'), 4.13 (dd, J 8.5 and 6.3, 1 H, H₂-5'), 3.98 (dd, J 8.5 and 6.3, 1 H, H₂-5'), 3.72 (m, 1 H, H-2'), 3.41 (m, 1 H, H-5'), 3.18 (m, 1 H, H₆-5'), 2.43 (s, 3 H, C₃H₆Me), 1.90

† 1 bar = 10⁵ Pa.
A solution of compound (2.16 g, 5.19 mmol) was treated with Dibal (6.23 ml) and processed as described above. Column chromatography (light petroleum–ethyl acetate, 3:1) of the resulting material gave the aldehyde (0.85 g, 77%), [α]D +46, as an oil; δH(CDC1) 9.81 (s, 1 H, CHO), 4.08 (400 MHz, 3), 2.65 (2 H, H-2), 1.97 (1 H, Me-3), 1.60 (4, H-5), 2.14 and 1.36 (2 s, each 3 H, Me-C); δC(CDC1) 200.76, 109.85, 77.69, 65.86, 62.70, 40.29, 26.19, 25.07 and 23.24; m/z 186 (M+1), 184 (m/z 186 + 2, 0.44%), 101 (44.49), 82 (16.35), 55 (11.06) and 43 (100); νmax (film) cm⁻¹ 3490, 3020, 2450 and 1700.

(2,4',S)-N-Benzoylcarboxyl-2-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)pyridine 22

A solution of compound (0.64 g, 3.0 mmol) in methanol (20 ml) was hydrogenated (1 atm) in the presence of palladium charcoal (10%; 60 mg) for 6 h and was then processed as described above. Distillation in vacuo (Kügelrohr, 80 °C/0.5 mbar) of the material gave pure compound (232 mg, 62.5%), [α]D +16 (Found: C, 63.4; H, 9.86; N, 8.01. C16H16NO3 requires C, 63.12; H, 10.01; N, 8.18%); δH(CDC1) 4.04 (400 MHz, 2 H, H-5'), 3.76 (dd, δJ 8 and 6, 1 H, H-4'), 3.15 (1 H, H-2), 2.92 (2 H, H-2'), 1.96 (br s, 4 H, NH), 1.95–1.54 (4, H, H-3 and -4) and 1.42 and 1.35 (2 s, each 3 H, CMe2); δC(CDC1) 108.97, 78.86, 67.59, 60.53, 46.98, 28.19, 26.65, 25.71 and 25.26; m/z 172 (M+1, 3.25%), 156 (4.08), 96 (15.37), 70 (100) and 43 (32.51); νmax(film) cm⁻¹ 3340, 2920 and 1690.

Treatment of a portion (100 mg) of compound 22 in the manner described above for compound 14 gave the N-toluenep-sulfonate (109 mg, 57%), mp 71–72.5 °C (from light petroleum); [α]D +95.3 (Found: C, 59.23; H, 7.04; N, 4.33; S, 9.90. C16H16NO3S requires C, 59.05; H, 7.12; N, 4.30; S, 9.85%); δH(CDC1) 7.73 and 7.32 (2, δJ 8.5 and 6.3, each 1 H, ArH), 4.54 (dt, δJ 6.0 and 1 H, H-4'), 4.10 (dd, δJ 9.9 and 6.1, 1 H, H-5'), 3.98 (dd, δJ 9.9 and 6.1, 1 H, H-5'), 3.82 (quintet, J=4.2 Hz, 2), 3.35 (3, H, H-5'), 2.43 (4, 3 H, CMe3), 1.89–1.60 (3, H, 1), 1.42 and 1.35 (2 s, each 3 H, CMe3) and 1.33 (1 H, =CH); δC(CDC1) 143.66, 134.10, 129.71, 127.70, 109.26, 77.51, 65.61, 50.24, 27.29, 26.17, 24.99, 24.44 and 21.53.

(2,4',S)-N-Benzoylcarboxyl-2-(2',2'-dimethyl-1',3'-dioxolan-4'-yl)pyridine 24

Treatment of a portion of compound 22 (260 mg, 1.52 mmol) with benzyl chloroformate (0.23 ml, 1.52 mmol) followed by processing in the usual manner, and column chromatography (hexane–ethyl acetate, 3:1) gave compound 24 (302 mg, 65%), [α]D -39; δH(400 MHz, 61 °C; CDC1) 7.52 (5 H, Ph), 5.13 (q, δJ 16.9 and 12.5, 2 H, PhCH2), 4.26 (2 H, 1), 3.99 (1 H, 3, 1 H, 3.49 (2 H, 1), 2.02 (2 H, 1), 1.85 (1 H, 1), 1.40 and 1.31 (2 s, each 3 H, CMe2); δC(CDC1) 61.6 °C; CDC1) 155.29, 137.00, 128.50 and 127.91 (2s), 127.56, 109.10, 76.67, 67.69, 66.86, 55.54, 47.06, 26.36 (2s), 25.20 and 23.82; m/z 306 (M+1, 0.18%), 290 (1.5), 160 (35.34), 91 (100) and 43 (16.49); νmax(film) cm⁻¹ 3430, 3020, 2960, 2800 and 1690.

(2,1'S)-N-Benzoylcarboxyl-2-(1,2-dihydroxyethyl)pyrroline 17

A solution of compound 16 (491 mg) in 80% aq. acetic acid (10 ml) was set aside for 4 days and was then concentrated in vacuo. Water (5 ml) followed by toluene (3 × 10 ml) was distilled in vacuo from the residue to give diol 17 (403 mg, 95%) as an oil; [α]D +66; δH(CDC1) 7.36 (5, 3 H, Ph), 5.15 (s, 2 H, PhCH2), 4.05 (400 MHz, 3), 2.98 (1 H, 2), 3.37 (1 H, 1) and 2.09–1.73 (4, H, H-3 and -4); δC(CDC1) 157.90, 136.15, 128.14, 128.14, 128.13, 70.65, 67.45, 64.04, 59.99, 47.31, 28.48 and 24.12; m/z 266 (M+1, 0.16%), 204 (40.24), 160 (45.83), 114 (7.79), 91 (100), 70 (17.04), 65 (14.85), 43 (10.32), 41 (15.28), 39 (13.27), 31 (8.33) and 28 (19.73); νmax(KBr) cm⁻¹ 3430, 3030, 2940 and 1665.

(2,1'S)-N-Benzoylcarboxyl-2-(1,2-dihydroxyethyl)pyrroline 25

Treatment of compound 24 (302 mg) with 80% aq. acetic acid (15 ml) followed by processing in the above manner, yielded compound 25 (235 mg, 90%), [α]D -20; δH(CDC1) 7.35 (5, 3 H, Ph), 5.14 (q, δJ 12.7 and 12.7, 2 H, 3.92 (1 H, m, H-2), 3.59 (br s, 1 H, H-4'), 3.46 (3, 3 H, 2.09 (1 H, m, 1 H, 1.91 (3 H, 3 H); δC(CDC1) 158.8, 136.3, 128.51, 128.71, 72.62, 67.41, 62.73, 59.32, 47.18, 27.62 and 23.31; m/z 266 (M+1, 0.16%), 204 (40.24), 160 (45.83), 114 (34.34), 91 (100), 70 (13.74), 65 (27.77), 43 (28.04), 41 (21.55), 39 (18.89), 31 (19.97) and 28 (13.94); νmax(KBr) cm⁻¹ 3380, 3020, 2980 and 1660.
(2R)-N-Benzoyloxy carbonyl)pyrrolidine-2-carbaldehyde 3
A stirred solution of compound 17 (405 mg, 1.52 mmol) in a mixture of water (12 ml) and methanol (6 ml) was treated with sodium metaperiodate (325 mg, 1.52 mmol) and sodium chlorite (0.5 g, 5.33 mmol) in vacuo. Column chromatography (light petroleum–ethyl acetate, 3:1) of the residue gave the aldehyde 3 (280 mg, 79%), \(\delta_H^{1H} = 83; \delta_C^{13C}(CDCl_3) 9.59 (d, 0.5 H, J = 1.6, CHO), 9.49 (d, J = 2.3, 0.5 H, CHO), 7.32 (m, 5 H, Ph), 5.16 (m, 2 H, PhCH_2), 4.30 (m, 0.5 H, H-2), 4.20 (m, 0.5 H, H-2), 3.56 (m, 2 H, H-5), 2.05 (m, 2 H, H-3) and 1.92 (m, 2 H, H-4); \(\delta_H^{1H}(CDCl_3) 199.98, 155.23, 154.37 (1 C), 136.35 + 136.12 (1 C), 128.85, 128.39, 127.99, 67.13, 65.15 + 64.76 (1 C), 47.12 + 46.59 (1 C), 27.67 + 26.47 (1 C) and 24.37 + 23.60 (1 C); m/z 204 (M^+ – 29, 3.15%), 160 (18.92), 91 (100) and 65 (12.60); \nu_{\text{max}}(neat)/cm^{-1} 2978, 2880, 1735 and 1694.

(2S)-N-Benzoyloxy carbonyl-2-(hydroxymethyl)pyrrolidine (R)-N-arylbenzoyl oxycarbonyl]proline 5
A stirred solution of compound 3 (148 mg, 0.63 mmol) in methanol (10 ml) was treated portionwise with sodium borohydride (60 mg, 1.19 mmol), and then was stirred for a further 30 min when analysis (TLC) indicated complete reaction. The stirred mixture was treated cautiously with water (50 ml), extracted with dichloromethane (2 x 20 ml) and the combined extracts were dried (Na_2SO_4), and concentrated in vacuo. Column chromatography (hexane–ethyl acetate, 1:1) of the residue gave compound 5 (130 mg, 88%), \(\delta_H^{1H} = 83.4, \delta_C^{13C}(CDCl_3) 7.34 (m, 5 H, Ph), 5.13 \text{(arom. J = 12.5 and 14.2, 2 H, PhCH_2)}, 4.46 (m, 1 H, H-3, 3.63 (m, 1 H, H-2), 3.63 (m, 1 H, H-3) and 3.51 – 3.38 (m, 2 H, H-5)) and 2.04 – 1.58 (m, 4 H, H-3 and -4); \(\delta_H^{1H}(CDCl_3) 156.71, 136.34, 128.30, 127.84, 66.97, 66.18, 60.35, 47.08, 28.26 and 23.78; \nu_{\text{max}}(KBr)/cm^{-1} 235 (M^+ , 0.5%), 204 (26.65), 160 (23.87), 91 (100), 65 (12.32) and 41 (9.42); \nu_{\text{max}}(KBr)/cm^{-1} 2960, 2885 and 1690.

(2S)-N-Benzoyloxy carbonyl-2-(hydroxymethyl)pyrrolidine [(L)-N-arlbzoxycarbonyl]proline 6
Treatment of compound 4 (100 mg) in the above given compound gave compound 6 (77 mg, 89%), \(\delta_H^{1H} = 83.4, \delta_C^{13C}(CDCl_3) 7.36 (m, 5 H, Ph, ArH), 7.54 (arom. J = 12.5 and 13.9, 2 H, PhCH_2), 4.43 (br s, 1 H, OH), 3.99 (m, 1 H, H-2), 3.64 (d, 2 H, J = 6.3, H-1), 3.54 (m, 1 H, H-2), 3.39 (m, 1 H, H-4), 2.05 – 1.58 (m, 4 H, H-3 and -4); \(\delta_H^{1H}(CDCl_3) 156, 154, 136, 138, 123, 124, 127, 78, 67, 60, 56, 47, 48, 28, 23 and 21; m/z 235 (M^+ , 0.81%), 204 (36.59), 160 (32.53), 91 (100), 65 (18.65) and 41 (15.10); \nu_{\text{max}}(KBr)/cm^{-1} 3030, 2970, 2880 and 1680.

(2R)-N-Benzoyloxy carbonyl]proline 7
A stirred solution of the aldehyde 3 (140 mg) in a mixture of 2-methylprop-2-ol (12.5 ml) and 2-methylbut-2-ene (3 ml) was treated dropwise over a period of 10 min with a solution of sodium chlorite (0.5 g, 5.33 mmol) and sodium dihydrogen phosphate (0.5 g, 4.15 mmol) in water (6 ml), and then was set aside at room temperature for a further 1 h. The mixture was concentrated in vacuo, the residue was dissolved in water (10 ml), the pH was adjusted to 7–8 with dil. aq. sodium hydroxide, and the mixture was extracted with hexane (2 x 20 ml). The aqueous phase was then adjusted to pH 3 by addition of 10% aq. t-tartaric acid, extracted with diethyl ether (3 x 10 ml) and the combined extracts were dried (Na_2SO_4), and concentrated in vacuo to give compound 7 (131 mg, 88%), mp 74–75 °C; \([\alpha]_D^{176} + 69.7 \text{ (lit.} 77 – 76°C; [\alpha]_D^{176} = 61.2 (AcOH); \delta_H^{1H}(CDCl_3) 9.10 (br s, 1 H, CO:H), 7.34 (m, 5 H, Ph), 5.16 (m, 2 H, PhCH_2), 4.42 (m, 1 H, H-2), 3.52 (m, 2 H, H-5), 2.19 (m, 2 H, H-3) and 1.96 (m, 2 H, H-4); \(\delta_H^{1H}(CDCl_3) 178.01 + 175.59 (1 C), 156.15 + 154.34 (1 C), 136.46 + 136.17 (1 C), 128.51, 128.39, 128.17, 127.96, 127.89 + 127.67 (1 C), 67.64 + 67.10 (1 C), 59.37 + 58.56 (1 C), 46.90 + 46.71 (1 C), 31.94 + 29.04 (C), 24.30 and 23.45 + 23.1 (C); m/z 249 (M^+ , 1.84%), 160 (13.82), 114 (32.49), 91 (100), 70 (12.45), 65 (12.40) and 39 (5.19); \nu_{\text{max}}(KBr)/cm^{-1} 3010, 2980, 2885 and 1750.

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References


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