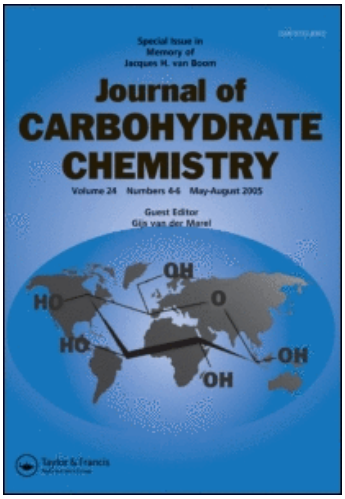


Journal of Carbohydrate Chemistry

Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Synthesis of the N,N''-Dibenzoyl Derivative of the Ornithine Decarboxylase Inhibitor (2R,5R)-Hept-6-Yne-2,5-Diamine from D-Glucosamine.

Ricardo José Alves; Joaquin Isac Garcia; Alain Olesker; Gabor Lukacs

To cite this Article Alves, Ricardo José , Garcia, Joaquin Isac , Olesker, Alain and Lukacs, Gabor(1991) 'Synthesis of the N,N''-Dibenzoyl Derivative of the Ornithine Decarboxylase Inhibitor (2R,5R)-Hept-6-Yne-2,5-Diamine from D-Glucosamine.', Journal of Carbohydrate Chemistry, 10: 6, 1049 — 1057

To link to this Article: DOI: 10.1080/07328309108543971

URL: http://dx.doi.org/10.1080/07328309108543971

J. CARBOHYDRATE CHEMISTRY, 10(6), 1049-1057 (1991)

SYNTHESIS OF THE N,N'-DIBENZOYL DERIVATIVE OF THE ORNITHINE DECARBOXYLASE INHIBITOR (2R,5R)-HEPT-6-YNE-2,5-DIAMINE FROM D-GLUCOSAMINE.

Ricardo José Alves*, Joaquin Isac Garcia, Alain Olesker and Gabor Lukacs*

Institut de Chimie des Substances Naturelles du C.N.R.S.,
91198 Gif-sur-Yvette Cedex, France.

January 7, 1991 - Final form September 4, 1991

ABSTRACT

The *N,N'*-dibenzoyl derivative of (2R,5R)-hept-6-yne-2,5-diamine, a very powerful inhibitor of the enzyme ornithine decarboxylase, was prepared from D-glucosamine in fourteen steps.

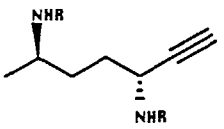
INTRODUCTION

Irreversible inhibitors of ornithine decarboxylase (O.D.C., E.C. 4.1.1.17) have been shown to have potential for treating diseases associated with rapid cell proliferation.[1] (2R,5R)-Hept-6-yne-2,5-diamine **1** is one of the most powerful inhibitors of O.D.C., a key-enzyme in the synthesis of the diamine putrescine and the polyamines spermidine and spermine. These amines are implicated in regulation of cellular growth, although the exact mechanism of this phenomenon is not well

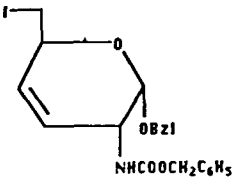
known.[2] Compound **1** was first synthesized by the Merrell group, along with the three other possible isomers, in a fourteen step convergent synthesis involving the alkylation of either (R) or (S)-*N*-*t*-butoxycarbonyl-4-iodo-2-aminobutane by the appropriately protected propargylamin.[3] Our strategy involved the preparation of a key intermediate, 2-benzamido-2,3,4,6-tetradeoxy-**D**-*erythro*-hexose-propylene dithioacetal **6** , in five steps (25 % overall yield) from **D**-glucosamine using well-established methodology.[4]

RESULTS AND DISCUSSION

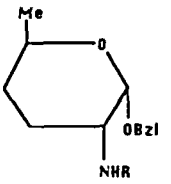
According to Garegg's procedure,[4] benzyl-2-(benzoyloxycarbonyl)amino-2,3,4,6-tetradeoxy-6-iodo-α-**D**-*erythro*-hex-3-enopyranoside **2** was obtained in large scale. Catalytic hydrogenation of **2** in the presence of Raney nickel gave benzyl 2-(benzoyloxycarbonyl)amino-2,3,4,6-tetradeoxy-α-**D**-*erythro*-hexopyranoside **3** in 80 % yield. The benzoyloxycarbonyl protecting group of the nitrogen atom of **3** was replaced by a benzoate group using sequential hydrogenation in the presence of Pd/C 5% catalyst and benzoic anhydride treatment of the resulting free amine. These two steps afforded benzyl 2-benzamido-2,3,4,6-tetradeoxy-α-**D**-*erythro*-hexopyranoside **4** with an overall yield of 81%. Catalytic hydrogenolysis of **4** in acetic acid solution and in the presence of Pd/C 5% gave a mixture of 2-benzamido-2,3,4,6-tetradeoxy-α- and -β-**D**-*erythro*-hexopyranose **5** in 78% yield. Treatment of **5** with propanedithiol afforded **6** (85%). Mitsunobu reaction[5] from **6** permitted the configurational inversion[6] at C-5 furnishing 2-benzamido-5-*O*-benzoyl-2,3,4,6-tetradeoxy-**L**-*threo*-hexose-propylene dithioacetal **7** (75%). The latter was accompanied by the formation of the elimination product (2-R)-2-benzamido-hex-4-enal-propylene dithioacetal **8** (10%). Mild alkaline treatment of **7** was followed first by mesylation and then by azide ion induced configurational inversion giving (2R,5R)-5-azido-2-benzamido-hexanal-propylene dithioacetal **11** in nearly quantitative yield. The azide group of **11** was transformed into the corresponding benzamide by the Staudinger methodology[7] using triphenylphosphine and the resulting primary amine was allowed to react with benzoyl chloride giving (2R,5R)-2,5-dibenzamido-hexanal-propylene dithioacetal **12** in an overall yield of 75% from **11**.



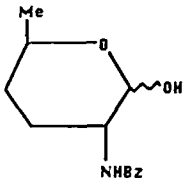
1 R = H
15 R = Bz



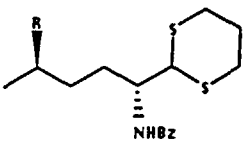
2



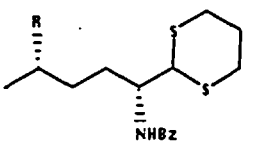
3 R = $COOCH_2C_6H_5$
4 R = Bz



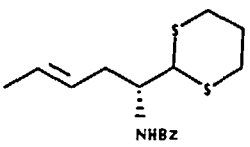
5



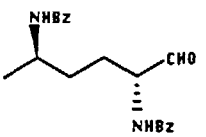
6 R = OH
11 R = N_3
12 R = NHBz



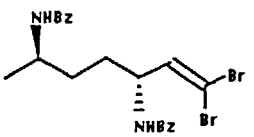
7 R = OBz
9 R = OH
10 R = OMs



8



13



14

Liberation of the aldehyde function in **13** was accomplished with mercuric chloride/mercuric oxide in quantitative yield. The crude aldehyde **13** was immediately used in the next step to obtain the dibromo-olefin **14** (50%) according to the methodology of Corey and Fuchs.[8] Finally, treatment of **14** with butyllithium in tetrahydrofuran and quenching with water gave the title compound **15** (40%). Compound **15** was identical with the *N,N'*-dibenzoyl derivative prepared from **1**.

EXPERIMENTAL

General procedures. Melting points were determined with a Buchi apparatus and are uncorrected. A Perkin-Elmer Model 141 MC polarimeter and 1

dm tubes were used for measurement of specific rotations. ^1H NMR spectra were recorded in chloroform-*d* solution at 400 MHz. The ^{13}C NMR spectra were measured in chloroform-*d* solution at 50.31 MHz with a Bruker WP-200 spectrometer. Chemical shifts are given in parts per million, and tetramethylsilane was the internal standard (δ 0.000). Carbon-13 chemical shifts for aromatic carbons are not given. Microanalyses were performed by the Service Central de Microanalyse du CNRS. Silica gel 60 PF_{254} (Merck) activated at 120 °C was the support for TLC and for column chromatography. The term "standard workup" means that the organic layer was washed with water, dried over Na_2SO_4, and filtered and the solvent was removed at reduced pressure.

Benzyl 2-(benzyloxycarbonyl)amino-2,3,4,6-tetradeoxy-α-D-erythro- hexopyranoside (3) To a solution of **2** (4 g, 8.35 mmol) in dioxane (50 mL) was added triethylamine (2 mL) and Raney nickel (2 g) and the mixture was hydrogenated at 75 psi for 48 h. After filtration and the usual workup, crystalline **3** (2.37 g, 80%) was obtained; mp 128-130 °C, $[\alpha]_D$ = - 65° (*c* 1.07, chloroform) ; mass spectrum (chemical ionization) (M^+ + H) 356; ^1H NMR δ 7.23-7.40 (m, 10H, 2Ph); 5.1O (s, 2H, $PhC\underline{H}_2$), 4.90 (d, 1H, J_{gem} = 12Hz, $PhC\underline{H}$), 4.60 (s, 1H, H-1), 4.56 (d, 1H, J_{gem} = 12Hz, PhCH), 4.26 (d, 1H, $J_{NH,2}$ = 7Hz, NH), 3.53 (m, 2H, H-2 and H-5), 2.23 (m, 1H, H-4e), 1.63 (m, 1H, H-4a), 1.42 (m, 2H, H-3a and H-3e), 1.25 (d, 3H, $J_{5,6}$ = 6Hz, H-6)

Anal. Calcd for $C_{21}H_{25}NO_4$: C, 70.98 ; H, 7.04 ; N, 3.94 ; O, 18.04. Found : C, 71.21 ; H, 7.27 ; N, 3.90.

Benzyl 2-benzamido-2,3,4,6-tetradeoxy-α-D-erythro-hexopyranoside (4). To a solution of **3** (3 g, 8.45 mmol) in methanol (50 mL) was added Pd/C 5% (1.5 g) and the mixture was hydrogenated at 75 psi for three days. After filtration, benzoic anhydride (3 g) was added to the solution and the mixture was stirred for 48 h. The usual workup afforded crystalline **4** (2.22 g, 81%); mp 112-115 °C; $[\alpha]_D$ = +97° (c 1.28, chloroform); mass spectrum (chemical ionization) (M^+ + H) 326; ^1H NMR δ 7.27-7.67 (m, 10H, 2Ph), 6.30 (d, 1H, $J_{NH,2}$ = 7Hz, NH), 4.92 (d, 1H, $J_{1,2}$ = 3Hz, H-1), 4.80 (d, 1H, J_{gem} = 12Hz, $PhC\underline{H}$), 4.53 (d, 1H, J_{gem}=12 Hz, $PhC\underline{H}$), 4.28 (m, 1H, H-5), 3.93 (m, 1H, H-2), 1.47-2.03 (m, 4H, H-3a, H-3e, H-4a and H-4e), 1.20 (d, 3H, $J_{5,6}$ = 7Hz, H-6).

Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73,85 ; H, 7.07 ; N, 4.31 ; O, 14.77. Found : C, 73.61 ; H, 7.27 ; N, 4.37.

2-Benzamido-2,3,4,6-tetradeoxy-D-erythro-hexose Propylene Dithioacetal (6). To a solution of **4** (2 g, 6.15 mmol) in acetic acid (75 mL) containing 20% water was added Pd/C 5% (2 g). The mixture was hydrogenolysed at 125 psi for 48 h. After the usual workup **5** was obtained (1.13 g, 78%); mass spectrum (chemical ionization) ($M^+ + H$) 236. To a solution of crude **5** (0.86 g, 3.66 mmol) in anhydrous chloroform (15 mL) was added slowly propanedithiol (0.97 g, 7.8 mmol) and the mixture was kept at room temperature for 24 h. After the usual workup crystalline **6** was obtained (1.01 g, 85%); mp 194 °C; $[\alpha]_D$ = - 15° (*c* 1.0, methanol); mass spectrum (chemical ionization) ($M^+ + H$) 326; ^1H NMR δ 7.33-7.83 (m, 5H, Ph), 6.53 (d, 1H, $J_{NH,5}$ = 7 Hz, NH), 4.50 (m, 1H, H-2), 4.40(d, 1H, $J_{5,6}$ = 4Hz, H-1), 3.83 (m, 1H, H-5), 2.81-2.93(m, 4H, 2 C$\underline{H}_2$S), 1.38-2.17 (m, 6H, H-3, H-3', H-4, H-4' and C$\underline{H}_2$ dithiane), 1.20 (d, 3H, $J_{5,6}$ = 7Hz, H-6); ^{13}C NMR δ : 167.5 (NH$\underline{C}$OPh), 67.8 (C-5), 53.1 and 52.5 (C-1 and C-2), 35.0 (C-4), 30.2 (2 $\underline{C}H_2$S), 28.7 (C-3), 26.1 ($\underline{C}H_2$ dithiane), 23.8 (C-6).

Anal. Calcd for $C_{16}H_{23}NO_2S_2$: C, 59.07 ; H, 7.07 ; N, 4.31 ; O, 9.86 ; S, 19.69. Found : C, 59.14 ; H, 7.16 ; N, 4.03 ; S, 19.87.

2-Benzamido-5-O-benzoyl-2,3,4,6-tetradeoxy-L-threo-hexose Propylene Dithioacetal (7) and (2-R)-2-Benzamido-hex-4-enal Propylene Dithioacetal (8). To a solution of triphenylphosphine (800 mg, 3.05 mmol) in tetrahydrofuran (50 mL) in an argon atmosphere and at -78 °C was added drop by drop diethyl azodicarboxylate (0.51 mL, 3.23 mmol). The temperature was allowed to rise to -20 °C and after 30 minutes benzoic acid (380 mg, 3.11 mmol) in tetrahydrofuran (5 mL) was added to it. After the solution was stirred 15 minutes, compound **6** (500 mg, 1.54 mmol) in tetrahydrofuran (2 mL) was added. The reaction was allowed to proceed at room temperature for 24 h and then the usual workup furnished a residue which was chromatographed (toluene/ethyl acetate, 8:2) affording **7** (495 mg, 75 %) and **8** (65 mg, 10 %). Crystalline **7** had mp 145-148 °C; $[\alpha]_D$ = + 9°(*c* 1.2, chloroform); mass spectrum (chemical ionization) ($M^+ + H$) 430; ^1H NMR δ 7.45-8.20 (m, 10H, 2 Ph), 6.58 (d, 1H, $J_{NH,2}$ = 9Hz, NH), 5.20 (m, 1H, H-2), 4.58 (m, 1H, H-5), 4.42 (d, 1H, $J_{1,2}$ = 4Hz, H-1), 2.91 (m, 4H, 2 C$\underline{H}_2$S), 1.70-2.18 (m, 6H, H-3, H-3', H-4, H-4' and C$\underline{H}_2$ dithiane), 1.37 (d, 3H, $J_{5,6}$ =6 Hz, H-6); ^{13}C NMR δ 170.5 (C=O), 166.2 (C=O), 71.3 (C-5), 52.8 and 52.2 (C-1 and C-2), 32.8 (C-4), 30.0 and 29.8 (2 $\underline{C}H_2$S), 28.3 (C-3), 25.8 ($\underline{C}H_2$ dithiane), 20.0 (C-6).

Anal. Calcd for $C_{23}H_{27}NO_3S_2$: C, 64.34 ; H, 6.29 ; N, 3.26 ; O,11.19 ; S, 14.92. Found : C, 64.10 ; H, 6.32 ; N, 3.30 ; S, 14.78.

Crystalline **8** had mp 101-103 °C, ; $[\alpha]_D$ = + 14° (*c* 1, chloroform); mass spectrum (chemical ionization) (M^+ + H) 308; ^1H NMR δ 7.40-8.10 (m, 5H, Ph), 6.42 (m, 1H, NH), 5.56 (m, 2H, H-4 and H-5), 4.53 (m, 1H, H-2), 4.37 (d, 1H, $J_{1,2}$ = 3,5Hz, H-1), 2.88 (m, 4H, 2 $C\underline{H}_2S$), 2.55 (m, 2H, H-3 and H-3'), 1.77-2.23 (m, 2H, $\underline{C}H_2$ dithiane), 1.67 (d, 3H, $J_{5,6}$ = 7Hz, H-6).

2-Benzamido-2,3,4,6-tetradeoxy-L-threo-hexose Propylene Dithioacetal (9). To a solution of sodium methanolate in methanol (3%, 20 mL) was added **7** (600 mg, 1.39 mmol) and the mixture was stirred at room temperature for 24 h. After treatment with Amberlite IRC 50 (H^+) and the usual workup, crystalline **9** was obtained (387 mg, 85%); mp 178-180 °C ; $[\alpha]_D$ = -7° (*c* 1.0, methanol); mass spectrum (chemical ionization) (M^+ + H) 326; ^1H NMR δ 7.40-7.83 (m, 5H, Ph), 6.60 (d, 1H, $J_{NH,2}$ = 8Hz, NH), 4.50 (m, 1H, H-2), 4.42 (d, 1H, $J_{1,2}$ = 4Hz, H-1), 3.87 (m, 1H, H-5), 2.90 (m, 4H, 2$C\underline{H}_2S$), 1.52-2.17 (m, 6H, H-3, H-3', H-4, H-4' and $C\underline{H}_2$ dithiane), 1.20 (d, 3H, $J_{5,6}$ = 7Hz, H-6); ^{13}C NMR δ 167.5 (C=O), 66.8 (C-5), 52.7 and 51.9 (C-1 and C-2), 35.1 (C-4), 29.5 and 29.3 (2 $\underline{C}H_2S$), 27.8 (C-3), 25.6 ($\underline{C}H_2$ dithiane), 22.8 (C-6).

Anal. Calcd for $C_{16}H_{23}NO_2S_2$: C, 59.07 ; H, 7.07 ; N, 4.31 ; O, 9.86 ; S, 19.69. Found : C, 58.99 ; H, 7.11 ; N, 4.05 ; S, 19.84.

2-Benzamido-5-O-methanesulfonyl-2,3,4,6-tetradeoxy-L-threo-hexose Propylene Dithioacetal (10). To a solution of **9** (325 mg, 1.03 mmol) in anhydrous pyridine (15 mL) was added mesyl chloride (0.17 mL) and the mixture was left overnight at 4 °C. After the usual workup, crystalline **10** was obtained (400 mg, 96%); mp 118-120 °C, $[\alpha]_D$ = + 6° (*c* 0.8, chloroform) : mass spectrum (chemical ionization) (M^+ + H) 404; ^1H NMR δ 7.43-7.83 (m, 5H, Ph), 6.48 (d, 1H, $J_{NH,2}$ = 7Hz, NH), 4.93 (m, 1H, H-5), 4.45 (m, 1H, H-2), 4.35 (d, 1H, $J_{1,2}$ = 3Hz, H-1), 3.02 (s, 3H, $C\underline{H}_3SO_2$), 2.93 (m, 4H, 2 $C\underline{H}_2S$), 1.60-2.16 (m, 6H, H-3, H-3', H-4, H-4' and $C\underline{H}_2$ dithiane), 1.43 (d, 3H, $J_{5,6}$ = 7Hz, H-6).

Anal. Calcd for $C_{17}H_{25}NO_4S_3$: C, 50.62 ; H, 6.20 ; N, 3.47 ; O, 15.89 ; S, 23.82. Found : C, 50.49 ; H, 6.26 ; N, 3.61 ; S, 24.00.

(2R,5R)-5-Azido-2-benzamidohexanal Propylene Dithioacetal (11). To a solution of **10** (383 mg, 0.95 mmol) in a mixture of *N,N'*-

dimethylformamide (8 mL) and hexamethylphosphorous triamide (4 mL) was added sodium azide (186 mg, 2.86 mmol) and the solution was kept at 80 °C for 12 h. The usual workup gave syrupy **11** (324 mg, 97%); $[\alpha]_D$ = -15° (*c* 0.85, chloroform); mass spectrum (chemical ionization) (M^+ + H) 351; ^{1}H NMR δ 7.47-7.97 (m, 5H, Ph), 6.50 (d, 1H, $J_{NH,2}$ = 8Hz, NH), 4.53 (m, 1H, H-2), 4.42 (d, 1H, $J_{1,2}$ = 4Hz, H-1), 3.53 (m, 1H, H-5), 2.95 (m, 4H, 2 C$\underline{H}_2$S), 1.53-2.23 (m, 6H, H-3, H-3', H-4, H-4' and C$\underline{H}_2$ dithiane), 1.30 (d, 3H, $J_{5,6}$ = 6Hz, H-6); ^{13}C NMR δ 167.4 (C=O), 57.7 (C-5), 52.9 and 52.6 (C-1 and C-2), 33.1 (C-4), 30.3 and 30.2 (2 $\underline{C}H_2$S), 28.0 (C-3), 25.6 ($\underline{C}H_2$ dithiane), 19.4 (C-6).

Anal. Calcd for $C_{16}H_{22}N_4OS_2$: C, 54.86 ; H, 6.29 ; N, 16.00 ; O, 4.56 ; S, 18.29. Found : C, 54.61 ; H, 6.32 ; N, 16.33 ; S, 18.50.

(2R,5R)-2,5-Dibenzamidohexanal Propylene Dithioacetal (12). To a solution of **11** (145 mg, 0.414 mmol) in tetrahydrofuran (10 mL) was added triphenylphosphine (165 mg, 0.063 mmol). The mixture was allowed to react at 50 °C in an argon atmosphere for 24 h, water (1 mL) was added to it and heating was continued for another 24 h. After the usual workup the residue was dissolved in pyridine (8 mL), cooled to 0 °C and benzoyl chloride (0.2 mL) was added to it drop by drop. The mixture was maintained at 4 °C for 18 h and workup as usual giving crystalline **12** (133 mg, 75%), mp 291-293 °C; $[\alpha]_D$ = -15° (*c* 0.69, chloroform); mass spectrum (chemical ionization) (M^+ + H) 429; ^{1}H NMR δ 7.40-8.20 (m, 10H, 2 Ph), 6.50 (d, 1H, $J_{NH,2}$ = 7Hz, NH), 4.63 (m, 1H, H-2), 4.40 (d, 1H, $J_{1,2}$ = 4Hz, H-1), 4.33 (m, 1H, H-5), 2.90 (m, 4H, 2 C$\underline{H}_2$S), 1.53-2.27 (m, 6H, H-3, H-3', H-4, H-4', and C$\underline{H}_2$ dithiane), 1.23 (d, 3H, $J_{5,6}$ = 6Hz, H-6).

Anal. Calcd for $C_{23}H_{28}N_2O_2S_2$: C, 64.49 ; H, 6.54 ; N, 6.54 ; O, 7.48 ; S, 14.95. Found : C, 64.51 ; H, 6.67 ; N, 6.47 ; S, 14.77.

(2R,5R)-2,5-Dibenzamidohexanal (13). To a solution of mercury chloride (60 mg, 0.22 mmol) in a mixture of acetonitrile (5 mL) and water (1 mL) was added mercury oxide (26 mg) and **12** (50 mg, 0.112 mmol) and the solution was heated to 75 °C for 5 h. After the usual workup the crude **13** was used for the preparation of **14**.

(2R,5R)-2,5-Dibenzamido-7,7-dibromohept-6-yne (14). To a solution of triphenylphosphine (115 mg, 0.44 mmol) in dichloromethane (2 mL) was added, in an argon atmosphere zinc powder (29 mg, 0.44 mmol). To this mixture was then added carbon tetrabromide (145 mg, 0.44 mmol) in dichloromethane (3 mL) and stirring was continued at room temperature for 24 h.

Then compound **13** (34 mg, 0.1 mmol) in dichloromethane (3 mL) was added to the mixture. The reaction was stopped after 3 h and after the usual workup the residue was chromatographed (toluene / ethyl acetate, 8 : 2) to afford pure syrupy **14** (24.5 mg, 50%) ; $[\alpha]_D$ = - 20°(*c* 0.32, chloroform); mass spectrum (FAB) : m/z 493, 495, 497 ; ^{1}H NMR δ 7.40-8.06 (m, 10H, 2Ph), 6.46 (d, 1H, $J_{5,6}$ = 6Hz, H-6), 6.30 (d, 1H, $J_{NH,5}$ = 7Hz, NH), 4.90 (m, 1H, H-5), 4.33 (m, 1H, H-2), 1.43-1.80 (m, 4H, H-3, H-3', H-4 and H-4'); 1.23 (d, 3H, $J_{1,2}$ = 7Hz, H-1).

Anal. Calcd for $C_{22}H_{21}N_2O_2Br_2$: C, 52.28 ; H, 4,16 ; N, 5.54 ; O, 6.34 ; Br, 31.68. Found : C, 52.13 ; H, 4.24 ; N, 5.70 ; Br, 31.89.

(2R,5R)-2,5-Dibenzamidohept-6-yne (15) a. (from **14**) To a solution of **14** (15 mg, 0.03 mmol) in tetrahydrofuran (1 mL) was added at -78 °C and in an argon atmosphere, a solution of butyllithium (90 µL, 0.15 mmol) in hexane (1.6 M). The temperature was allowed to raise to + 25 °C and then water (1 mL) was added. After the usual workup and chromatography (toluene / ethyl acetate, 8 : 2) pure crystalline **15** (4.1 mg, 40 %) was obtained; mp 209-212 °C; $[\alpha]_D$ = + 9° (*c* 0.63, pyridine); mass spectrum (chemical ionization) (M^+ + H) 335; ^{1}H NMR δ 7.37-788 (m, 10H, 2Ph), 6.82 (d, 1H, $J_{NH,5}$ = 8Hz, NH), 6.20 (d, 1H, $J_{NH,2}$ = 8Hz, NH), 4.98 (m, 1H, H-5), 4.31 (m, 1H, H-2), 2.29 (d, 1H, $J_{5,7}$ = 3Hz, H-7), 1.93 (m, 2H, H-4 and H-4'), 1.77 (m, 2H, H-3 and H-3'), 1.26 (d, 3H, $J_{1,2}$ = 7Hz, H-1).

Anal. Calcd for $C_{21}H_{22}N_2O_2$: C, 75.45 ; H, 6.59 ; N, 8.38 ; O, 9.58. Found : C, 75.55 ; H, 6.97 ; N, 8.53.

b. (From **1**) To a solution of **1** (10 mg, 0.08 mmol) in pyridine (2 mL) was added at 0 °C benzoyl chloride (2 drops) and the mixture was stirred overnight. After the usual workup the resulting **15** (23 mg, 92 %) exhibited mp 211-213 °C; $[\alpha]_D$ = + 11° (*c* 0.5, pyridine), mass spectrum (chemical ionization) (M^+ + H) 335.

Acknowledgment

One of us (R.J.A.) thanks the Universidade Federal de Minas Gerais (Brasil) and CNPq (Brasil) for a predoctoral fellowship. The authors are grateful to Dr. P. Casara (Merrell Dow Research Institute, Strasbourg Center, France), for a generous gift of **1**.

REFERENCES

1. P. Mamont, M. Siat, A. M. Joder-Ohlenbush, A. Bernhardt and P. Casara, *Eur. J. Biochem.*, **142**, 457 (1984) and references therein.

2. S. A. Dredar, J. W. Blankenship, P. E. Marchant, V. Manneh and D. S. Fries, *J. Med. Chem.*, **32**, 984 (1989).

3. P. Casara, C. Danzin, B. Metcalf and M. Jung, *J. Chem. Soc., Perkin Trans. I*., 2201 (1985).

4. a- P. J. Garegg, R. Johansson and B. Sammuelsson, *J. Carbohydr. Chem.*, **3**, 189 (1984).
b-D. Seebach and E. J. Corey, *J. Org. Chem.*, **40**, 231 (1975).

5. O. Mitsunobu, *Synthesis*, 1 (1981).

6. The inverted benzoate **7** showed different physical properties (mp 145-148 °C,$[\alpha]_D$ = +9°, *c* 1.2, chloroform) from those of the benzoate prepared from **6** (mp 155-158 °C, $[\alpha]_D$ = -25°, *c* 1.3, chloroform). We also performed the inversion of the configuration of the hydroxyl group in **6** by sodium benzoate displacement of the corresponding mesylate. The resulting benzoate was identical with that obtained in the Mitsunobu reaction.

7. a-H. Staudinger and J. Meyer, *Helv. Chem. Acta*, **2**, 635 (1919).
b- M. Vaultier, N. Knouzi and R. Carrié, *Tetrahedron Lett.*, 763 (1983).

8. E. J. Corey and P. L. Fuchs, *Tetrahedron Lett.*, 3769 (1972).