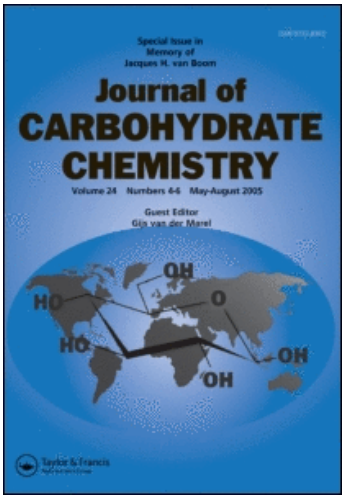



## Journal of Carbohydrate Chemistry

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

# Synthesis of C-Glycosyl α-Glycines

Sylvie Pochet[a]; Patrice Allard[a]; Tam Huynh-dinh[a]; J. Igolen[a]
[a] Unité de Chimie Organique, Département de BGM, Equipe de Recherche Associée au CNRS (ERA 927) INSTITUT PASTEUR 28, PARIS CEDEX 15, France

**To cite this Article** Pochet, Sylvie , Allard, Patrice , Huynh-dinh, Tam and Igolen, J.(1982) 'Synthesis of C-Glycosyl α-Glycines', Journal of Carbohydrate Chemistry, 1: 3, 277 — 288
**To link to this Article: DOI:** 10.1080/07328308208085100
**URL:** http://dx.doi.org/10.1080/07328308208085100

J. CARBOHYDRATE CHEMISTRY, 1(3), 277-288 (1982-83)

# SYNTHESIS OF C-GLYCOSYL α-GLYCINES

Sylvie Pochet[1], Patrice Allard, Tam Huynh-Dinh and J. Igolen*

Unité de Chimie Organique, Département de BGM
Equipe de Recherche Associée au CNRS (ERA 927) INSTITUT PASTEUR
28, rue du Docteur Roux, 75724 PARIS CEDEX 15 (France)

Received October 1, 1982



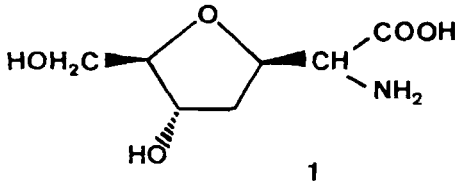
## ABSTRACT

A scheme of asymmetric synthesis of C-glycosyl α-glycines is described. Reductive hydrolysis of 2-deoxy-3,5-di-O-p-toluoyl-β D-erythropentofuranose 1-cyanide (4) in the presence of N,N-diphenylethylenediamine gave the imidazolidine 5, which was converted to 2,5-anhydro-3-deoxy-4,6-di-O-p-toluoyl-β-D-allose (3)by acid hydrolysis. The aldehyde (3), chiralamine, benzoic acid and t-butyl isocyanide four component condensation afforded in good yield two diastereomeric adducts (6a and 6b), which were separated by column chromatography and deblocked to furnish 2-deoxy-β-D-erythropentofuranosyl R and S-glycines (1a) and (1b).

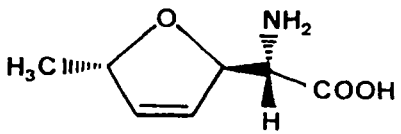
## INTRODUCTION

Our previous work on the synthesis of carbohydrate derivatives[2] led us to investigate the preparation of C-glycosyl-amino acids. In spite of the potential biological interest in these molecules, very few syntheses have been reported until recently. The majority of these have been carried out by Rosenthal and co-workers.[3,4,5]

We describe in this paper the synthesis of two 2-ribosyl glycines, 2-deoxy-β-D-erythropentofuranosyl R and S-glycines (1a) and (1b). These compounds are analogues of a natural antibiotic, (+)-furanomycin (2), whose synthesis and structure have been recently reviewed.[6]




1



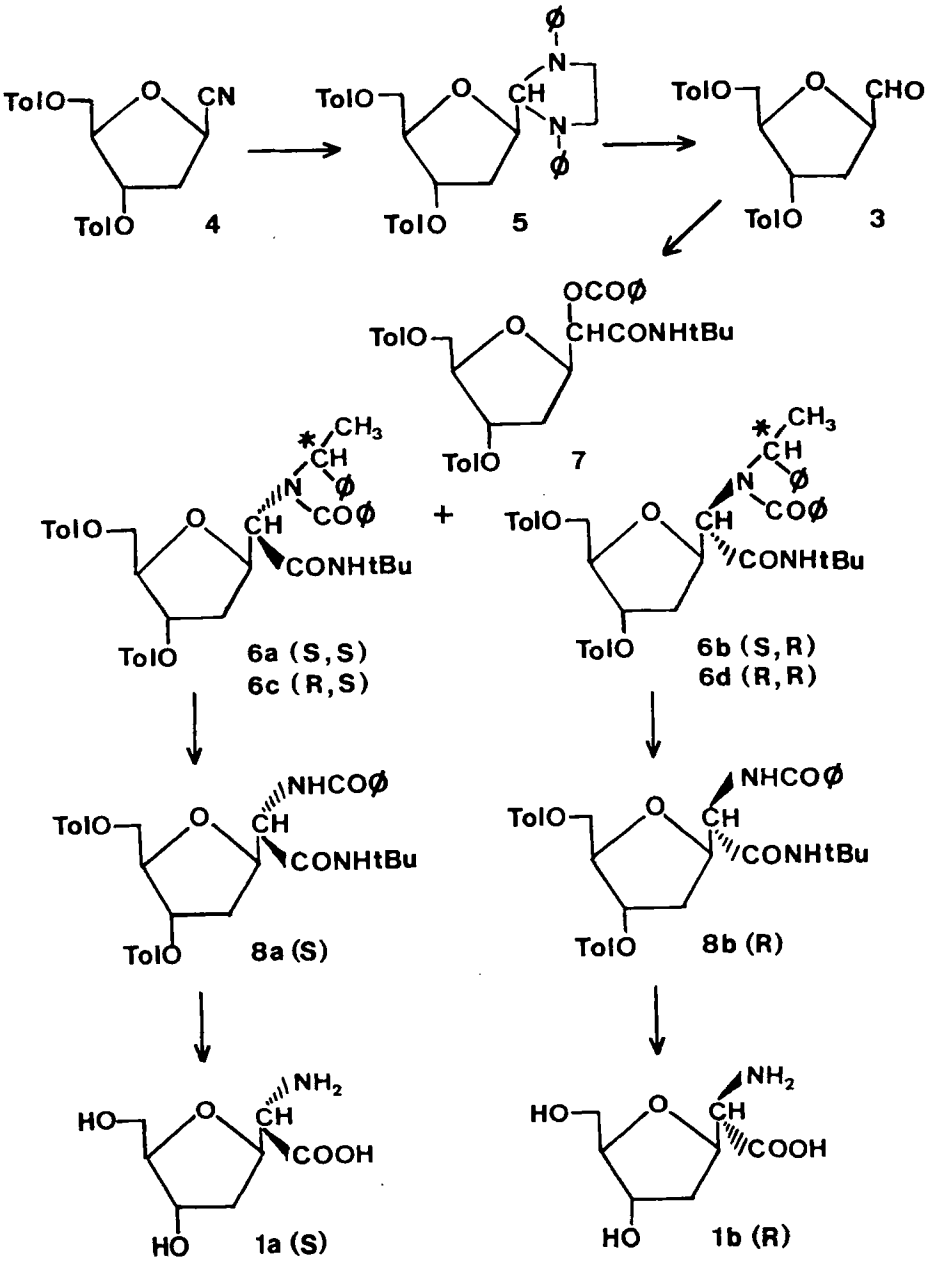

2(αS,2R,5S)

Our strategy for the preparation of 1 was based on the asymmetric synthesis of α-amino acids, according to the method described by Ugi and co-workers.[7] The four component condensation: aldehyde, chiral amine, benzoic acid, t-butyl isocyanide, has been recently used for the syntheses of (+)-furanomycin[6] and some analogues.[8] It was conceived that condensation of aldehyde 3, followed by two deblocking steps, should afford the two chiral forms of the glycine derivative 1 (Scheme).

Moffatt and co-workers[9] have reported in the D-ribose series the reductive hydrolysis, in two steps, of the cyano group into the corresponding aldehyde. The same treatment applied to cyanide 4[10] should permit easy access to aldehyde 3.

## RESULTS AND DISCUSSION

Reductive hydrolysis of 2-deoxy-3,5-di-O-p-toluoyl-β-D-erythropentofuranose 1-cyanide (4) in the presence of N,N'-diphenylethylenediamine according to a procedure reported by Moffatt and co-workers,[9] gave the crystalline diphenylimidazolidine derivative




Scheme

5 (75%). Acid hydrolysis of 5 in refluxing aqueous tetrahydrofuran afforded the unstable aldehyde 3, which was immediately used, without purification, in the next step.

The Ugi condensation of 3 in the presence of the chiral inducing amine, S(-)-α-methylbenzylamine (2 equiv.), benzoic acid (2 equiv.) and t-butyl isocyanide (1 equiv.) afforded the two expected diastereomeric adducts, 6a (S,S) and 6b (S,R), which were separated by sequential column and preparative thin-layer chromatography. The product ratio, as determined by HPLC was dependent on the solvent used for the condensation (Table).

Condensation in toluene (exp. 1) yielded 6a and 6b in a 3:7 ratio (27%). In methanol (exp. 3), the yield was increased (77%) to the detriment of reaction stereoselectivity (6a and 6b in a 4:6 ratio).



TABLE. Experimental yields obtained with different solvents

| Exp. n° | Solvent | Aldehyde 3 (mmol) | Yield (%) of 7 | Yield (%) of 6a+6b or 6c+6d | Stereoselectivity 6b/6a+6b or 6c/6c+6d (%) |
|---|---|---|---|---|---|
| 1 | Toluene | 0.73 | 22[a] | 27[a] | 74[a] |
| 2 | Toluene | 10.72 | 17[b] | 21[b] | 50[b] |
| 3 | Methanol | 0.08 | 1.5[a] | 77[a](53[c]) | 60[a](50[c]) |
| 4 | Dichloro-methane | 0.05 | 8[a] | 52[a] | 72[a] |
| 5[d] | Toluene | 0.05 | 16[a] | 42[a] | 50[a] |
| 6[d] | Methanol | 0.26 | nm | 88[a](62[c]) | 60[a](60[c]) |

a. The product ratios were determined by analytical HPLC.
b. Ratio of isolated products after column chromatography and preparative TLC plates.
c. Isolated by preparative HPLC.
d. Condensation was realized with the R-amine. The main product possesses then the (R,S) configuration.

Dichloromethane (exp. 4) appeared as a good compromise between yield (52%) and stereoselectivity (6a and 6b in a 3:7 ratio). Concentration and reaction temperature have little or no influence on either the yield or stereoselectivity of the reaction.

We observed also the presence of a secondary reaction product which was identified by spectroscopic means as an α-acyloxy-carboxamide 7 (22% yield in toluene, 1.5% in methanol). The chirality of the exocyclic α-carbon of 7 has not been determined. Formation of such compounds has been previously observed by Passerini.[7a,11]

The absolute configuration of 6a and 6b was determined from their $^1$H NMR spectra by the chemical shift of the t-butyl singlet.[7,8,12] Thus, products which present a resonance at δ 1.14 ppm have either the (S,S) or (R,R) configuration, while adducts which exhibit a singlet at δ 1.39 ppm have either the (S,R) or (R,S) configuration. The validity of these assignments was further supported by X-ray crystallographic studies in the norfuranomycin series.[8]

We have also studied the influence of the amine chirality on the reaction products : thus, condensation of 3 with R(+)-α-methyl-benzylamine in toluene (exp. 5) and in methanol (exp. 6) afforded two diastereomers 6c (R,S) and 6d (R,R) in better yield than with the S-amine. The absolute configuration of these compounds was determined from $^1$H NMR spectra and confirmed after their debenzylation into compounds 8a and 8b.

We observed that the main product was again the "negative" isomer[13]: with the S-amine, the major product was the (S,R) isomer (6b), while with the R-amine it was the (R,S) isomer (6c). Thus, the stereoselectivity was reversed according to the amine chirality. However it was lower with the R-amine than with the S-antipode.

Each of the diastereomers 6a and 6b was separately debenzylated with concentrated formic acid at 50-60 °C to afford, after separation by column chromatography, 8a (S) and 8b (R) in 53 and 82% yield respectively.

The hydrolysis of the debenzylated products was carried out with 6N hydrochloric acid in dioxane at 80 °C. The crude amino acid was purified by elution through a weakly basic ion-exchange resin. The aqueous fractions were analyzed by TLC using ninhydrin, and anisaldehyde-sulfuric acid spray reagents. Appropriate fractions were combined and evaporated to yield the deprotected α-amino-acids 1a and 1b. The structure and the configuration of these compounds have been assigned from their mass and $^1$H NMR spectra. The coupling constants $J_{1,2} + J_{1,2'}$ allowed us to etablish the β configuration of the proton H-1.[2,15] The predominance of S conformation for the furanose ring was determined by the coupling constants $J_{1,2}$ and $J_{3,4}$.[2,16]

No antibiotic activity has been detected for these compounds up to 100 µg/mL when tested against *Staphylococcus aureus* (209P) and *Escherichia coli* (EK12, DC2[17]).

In spite of the low yield of 1a and 1b obtained, which may be explained by the cleavage of the furanose ring under acidic conditions, further studies will be of interest since unusual amino acids or C-analogues of glycoproteins may be prepared by the reported reaction sequence.



## EXPERIMENTAL

General Procedures. Melting points were determined on a Thomas-Hoover Unimelt capillary melting point apparatus. All reported values are uncorrected. Optical rotations were determined on a Perkin-Elmer 241-MC polarimeter. Microanalyses were carried out in our laboratories. Nuclear magnetic resonance spectra were obtained on a Varian EM-360 (60 MHz) and/or a Cameca (250 MHz) instrument. Low-resolution mass spectra were obtained on a VG-Micromass spectrometer (70 70F). Analytical thin-layer chromatography (TLC) was performed on precoated silica gel plates (Merck $60F_{254}$), visualized under UV light (254 nm), and sprayed with a sugar reagent (anisaldehyde/sulfuric acid + heating), "aldehyde-ketone" reagent,[18] Reindel-Hoppe reagent,[18] or ninhydrin.[18] Column chromatography utilized Merck SG-60 (70-230 mesh) silica gel.

HPLC conditions: a series 3B chromatograph and a LC 75 spectrometer (Perkin-Elmer) were used. Peak areas were calculated by a Hewlett-Packard 3390A integrator. For the analytical runs (HS-5 C18 Perkin-Elmer 5 μm, 12.5 cm long), the crude products were dissolved in acetonitrile and eluted with a linear gradient of acetonitrile in water (70% initial to 100% $CH_3CN$ in 16 min.) at a flow rate of 1.8 mL/min. and detected at 254 nm. For preparative work, we used a Zorbax ODS 9.3 mm internal diameter column (Du Pont Instruments). The conditions were as above except for the flow rate (5.5 mL/min.).

1,3-Diphenyl 2-(2-deoxy-3,5-di-O-p-toluoyl-β-D-erythropento-furanosyl) imidazolidine (5). To a solution of cyanide 4 (5.9 g, 15.5 mmol) in a mixture of pyridine (150 mL), water (75 mL) and acetic acid (75 mL) was added under vigorously stirring, monosodium hypophosphite (15 g), N,N'-diphenylethylenediamine (4 g) and an excess of Raney nickel. The mixture was stirred at room temperature for 1.5 h and then filtered. The precipitate was washed with water, then thoroughly with dichloromethane. The organic layers were washed with water, dried on sodium sulfate and evaporated to dryness. After column chromatography, we isolated 6.3 g (72%) of crystalline imidazolidine 5: mp 50-55 °C (methanol); Rf 0.69 (dichloromethane); $^1H$ NMR ($CDCl_3$) δ 2.20 (s, 6, $2CH_3$ aro.), 2.10-2.50 (m, 2, H-2 and H-2'), 3.40 (m, 4, $2CH_2N$), 4.10 (s, 3, H-4, H-5 and H-5'), 4.40 (m, 1, H-1), 5.30 (m, 1, H-3), 5.50 (d, 1,H-α) $J_{1-\alpha}$ = 2 Hz, 6.30-7.10 (m, 14, H aro.), 7.55 (m, 4, H aro.); Anal. Calcd for $C_{36}H_{36}N_2O_5$ (564.65): C 74.44; H 6.43; N 4.96. Found: C 74.90; H 6.65; N 5.37.

2,5-Anhydro-3-deoxy-4,6-di-O-p-toluoyl-β-D-allose (3). A solution of 5 (6.3 g, 11.16 mmol) with an excess of Dowex 50 ($H^+$) resin (50 g) was stirred under reflux in a mixture of tetrahydrofuran (100 mL) and water (50 mL) for 2 h (reaction being monitored by TLC). The mixture was then filtered, the resin was washed with tetrahydrofuran. The filtrate was evaporated to dryness to give 4.1 g (96%) of aldehyde 3 as a yellow-brown foam: Rf 0.50 (dichloromethane-methanol, 98:2); $^1H$ NMR ($CDCl_3$) δ 2.20-2.60. (m, 8, $2CH_3$ aro., H-2 and H-2'), 4.30-4.60 (m, 3, H-4, H-5 and

H-5'), 5.00 (m, 1, H-1), 5.50 (m, 1, H-3), 7.20 (m, 4, H aro.), 7.90 (m, 4, H aro.), 9.8 (s large, 1, H ald.).

Four component condensation. General procedure. Exp. 2: To a stirred solution of crude aldehyde (4.1 g, 10.7 mmol) in 30 mL of toluene was added at ambient temperature, 1 equivalent of S(-)-α-methylbenzylamine (1.36 mL). After 30 min., a second equivalent of amine was added. After 30 min., 2 equivalents of benzoic acid (2.62 g) and 1 equivalent of t-butyl isocyanide[14] were added. The reaction mixture was then stirred for 15 h. After removing the solvent in vacuo, the residue was dissolved in 50 mL of dichloromethane. The organic layer was washed with 1N hydrochloric acid, 1N sodium hydroxide, water, dried over sodium sulfate and evaporated to dryness to give 5 g of crude product.

Separation by column chromatography (dichloromethane) yielded 0.84 g (17%) of the α-benzoyloxy carboxamide 7, then 0.45 g of the (S,S) isomer 6a, 0.95 g of mixture 6a + 6b, and finally 0.27 g of 6b (S,R). The mixture was rechromatographed on a column, or preparative TLC plates to yield 21% of diastereomers in 1:1 ratio.

The same procedure applied to 0.73 mmol of 3 in toluene (exp.1) or 0.05 mmol of 3 in dichloromethane (exp. 4) afforded 27% of 6a and 6b in a 27:74 ratio and 52% of 6a and 6b in a 28:72 ratio respectively.

Exp. 3: The same procedure applied to 0.08 mmol (28 mg) of 3 in 3 mL of methanol afforded, after HPLC separation on Zorbax ODS, 13 mg of 6a (S,S) and 14 mg of 6b (S,R) (53% yield). The purity of the two compounds was over 99% as determined by the integrator. Retention times were respectively 14.4 and 15.1 minutes.

Exp. 6: Condensation of aldehyde 3 (0.1 g, 0.26 mmol) with R(+)-α-methylbenzylamine in methanol according to the general procedure, afforded after HPLC separation 45 mg of the (R,R) isomer 6d and 65 mg of the (R,S) isomer 6c in 62% overall yield. (Retention times: 13.8 and 14.7 - Zorbax ODS).

6d: Rf 0.31 (petroleum ether-ethyl acetate, 5:2); $^1$H NMR ($CDCl_3$)

δ 1.15 (s, 9, tBu), 1.55 (d, 3, $\underline{CH_3}$-CH), 2.50 (m, 8, $2CH_3$ aro., H-2 and H-2'), 3.75 (d, 1, H-α), 4.60 (m, 3, H-4, H-5 and H-5'), 5.15 (m, 2, H-1 and $\underline{HC}$-$CH_3$), 5.55 (m, 1, H-3), 7.40 (m, 14, H aro.), 8.00 (m, 4, H aro.). 6c: Rf 0.64 (petroleum ether-ethyl acetate, 5:2); $^1$H NMR ($CDCl_3$) identical with those of 6b.

Exp. 5: The same procedure applied to 0.05 mmol of 3 in toluene yield 6c and 6d in a 1:1 ratio (42%).

1-[α-Benzoyloxy-N-t-butylacetamido]-2-deoxy-3,5-di-O-p-toluoyl-β-D-erythropentofuranose (7): mp 132 °C; $[\alpha]_D^{25}$ - 6.7° (c 0.70, $CHCl_3$); Rf 0.57 (dichloromethane-methanol, 98:2); m/e 466 (60.4, M-OCOØ), 353 (7.3, M-$CHOR_1R_2$, $R_1$ = COØ, $R_2$ = CONHtBu), 330 (20.5), 235 (63.4, M-$CHOR_1R_2$ - Tol), 193 (100), 137 (78.8, TolOH + H), 121 (100), 119 (100, Tol), 105 (100, $R_1$), 94 (100), 91 (100, $C_7H_7$), 81 (100, $CH_2$ = dihydrofuran); $^1$H NMR ($CDCl_3$) δ 1.40 (s, 9, tBu), 2.45 (s, 8, $2CH_3$ aro., H-2 and H-2'), 4.40 (m, 3, H-4, H-5 and H-5'), 4.80 (m, 1, H-1), 5.50 (m, 2, H-3 and H-α), 6.10 (m, 1, NH), 7.30 (m, 7, H aro.), 7.95 (m, 6, H aro.); Anal. Calcd for $C_{34}H_{37}NO_8$ (587.64): C 69.49; H 6.35; N 2.38. Found: C 69.42; H 6.59; N 2.84.

1-[α-S-[N-[(S)-α-methylbenzyl]benzamido]]-N-t-butylacetamido-2-deoxy-3,5-di-O-p-toluoyl-β-D-erythropentofuranose (6a): mp 82-86 °C; $[\alpha]_D^{25}$ + 39.0° (c 0.70, $CHCl_3$); Rf 0.50 (dichloromethane-methanol, 98:2, white spot with Reindel-Hoppe reagent); m/e 590 (11.7, M-CONHtBu), 467 (11.6, M-CONHtBu-$NR_1R_2$, $R_1$ = COØ, $R_2$ = $CH\text{Ø}CH_3$), 215 (13.6), 214 (85.1), 193 (23.1), 119 (100, Tol), 105 (100, $R_1$ and $R_2$), 91 (20.9, $C_7H_7$), 81 (100, $CH_2$ = dihydrofuran); $^1$H NMR ($CDCl_3$) δ 1.15 (s, 9, tBu), 1.50 (d, 3, $\underline{CH_3}$-CH) $J_{H\text{-}CH_3}$ = 7 Hz, 2.45 (m, 8, $2CH_3$ aro., H-2 and H-2'), 3.55 (d, 1, H-α) $J_{1\text{-}\alpha}$ = 8.5 Hz, 4.35-4.65 (m, 3, H-4, H-5 and H-5'), 4.75-5.25 (m, 2, H-1 and $\underline{HC}$-$CH_3$), 5.50 (m, 1, H-3), 6.95-7.55 (m, 14, H aro.), 7.95 (m, 4, H aro.); Anal. Calcd for $C_{42}H_{46}N_2O_7$ (690.8): C 73.02; H 6.71; N 4.06. Found: C 72.75; H 6.88; N 4.35.

1-[α-R-[N-[(S)-α-methylbenzyl]benzamido]]-N-t-butylacetamido 2-deoxy-3,5-di-O-p-toluoyl-β-D-erythropentofuranose (6b): mp 79-82 °C; $[\alpha]_D^{25}$ - 44.3° (c 0.17, $CHCl_3$); Rf 0.40 (dichloromethane-

methanol, 98:2, white spot with Reindel-Hoppe reagent); m/e 590 (18.8, M-CONHtBu), 467 (11.9, M-CONHtBu-$NR_1R_2$), 215 (15.4), 214 (98.9), 119 (100, Tol), 105 (100, $R_1$ and $R_2$), 91 (75.5, $C_7H_7$), 81 (100, $CH_2$ = dihydrofuran); $^1H$ NMR ($CDCl_3$) δ 1.40 (s, 9, tBu), 1.65 (d, 3, $\underline{CH_3}$-CH) $J_{H-CH}$ = 7 Hz, 2.45 (m, 8, $2CH_3$ aro., H-2 and H-2'), 3.70 (d, 1, H-α) $J_{1-\alpha}$ = 8.5 Hz, 4.20-5.20 (m, 5, H-4, H-5, H-5', H-1 and $\underline{HC}$-$CH_3$), 5.55 (m, 1, H-3), 7.10-7.75 (m, 14, H aro.), 8.00 (m, 4, H aro.); Anal. Calcd for $C_{42}H_{46}N_2O_7$ (690.80): C 73.02; H 6.71; N 4.06. Found: C 72.73; H 6.74; N 3.78.

1-(S)-[α-N-benzamido]-N-t-butylacetamido-2-deoxy-3,5-di-O-p-toluoyl-β-D-erythropentofuranose (8a). A solution of 6a (0.28 g, 4 mmol) in 4 mL of 98% formic acid was stirred at 60 °C for 3 h (reaction monitoring by TLC). The mixture was then diluted in dichloromethane and washed with water. The organic layer was dried with sodium sulfate and evaporated to dryness. Column chromatography (dichloromethane-methanol) afforded 0.12 g (52%) of 8a: mp 95-98 °C; $[\alpha]_D^{25}$ - 12.5° (c 0.46, $CHCl_3$); Rf 0.17 (petroleum ether-ethyl acetate, 5.2); m/e 486 (18.8, M-CONHtBu), 353 (20.3, M-$CHR_1R_2$, $R_1$ = CONHtBu, $R_2$ = NHCOØ), 234 (37.5, $CHR_1R_2$ and M-$CHR_1R_2$-Tol), 214 (100), 202 (21.9), 193 (37.5), 136 (25.0, TolOH), 119 (100, Tol), 105 (100, COØ), 94 (100), 91 (62.5), 81 (100, $CH_2$ = dihydrofuran); $^1H$ NMR ($CDCl_3$) δ 1.40 (s, 9, tBu), 2.40 (m, 8, $2CH_3$ aro., H-2 and H-2'), 4.55 (m, 4, H-4, H-5, H-5' and H-1), 5.15-5.60 (m, 2, H-α and H-3), 6.20 (m, 1, NH), 7.30 (m, 9, H aro.), 7.80 (m, 4, H aro.); Anal. Calcd for $C_{34}H_{38}N_2O_7$ (586.66): C 69.90; H 6.53; N 4.78. Found: C 69.44; H 6.69; N 5.08.

1-(R)-[α-N-benzamido]-N-t-butylacetamido-2-deoxy-3,5-di-O-p-toluoyl-β-D-erythropentofuranose (8b). The same treatment applied to 6b afforded 0.51 g (82%) of debenzylated product 8b: mp 82 °C; $[\alpha]_D^{25}$ - 10.8° (c 0.43, $CHCl_3$); Rf 0.20 (petroleum ether-ethyl acetate, 5:2); m/e 486 (12.5, M-CONHtBu), 353 (70.7, M-$CHR_1R_2$), 234 (100, M-$CHR_1R_2$-Tol and $CHR_1R_2$ ), 214 (100), 202 (33.2), 193 (25.0), 136 (25.0, TolOH), 119 (100, Tol), 105 (100, COØ), 94 (100), 91 (80.6), 81 (100, $CH_2$ = dihydrofuran); $^1H$ NMR ($CDCl_3$) identical with those of 8a. Anal. Calcd for $C_{34}H_{38}N_2O_7$ (586.66): C 69.60; H 6.53; N 4.78. Found: C 69.38; H 6.65; N 4.82.

General procedure for the synthesis of α-amino-acids. The debenzylated product was stirred at 80 °C in 6N hydrochloric acid-dioxane (15 mL/mmol) for 2-3 h (TLC monitoring). The mixture was then evaporated in vacuo. The residue was evaporated with small portions of methanol-water (1:1) to remove excess hydrochloric acid and applied to a weakly basic ion-exchange column (Amberlite IR-45, 2 x 6 cm, slow elution with water). The aqueous fractions revealed with ninhydrin and sugar reagent were evaporated in vacuo.

(S)[2-deoxy-β-D-erythropentofuranosyl] glycine (1a). 0.43 g (0.73 mmol) of 8a gave 5 mg (4%) of the α-amino acid 1a. $[\alpha]_D^{25}$ + 12.5° (c 0.37, methanol); Rf 0.57 (methanol); m/e 146 (100, M-COOH), 130 (68.3, M-COOH-$NH_2$); $^1$H NMR (250 MHz, $D_2O$) δ 2.06 (m, 2, H-2 and H-2'), 3.50-3.70 (m, 3, H-α, H-5 and H-5'), 3.97 (m, 1, H-4), 4.37 (m, 2, H-1 and H-3), $J_{3-4}$ = 2 Hz, $J_{4-5}$ = 4 Hz, $J_{4-5'}$ = 5.5 Hz, $J_{5-5'}$ = 13 Hz.

(R) [2-deoxy-β-D-erythropentofuranosyl] glycine (1b). 0.51 g (0.87 mmol) of 8b gave 4 mg (3%) of 1b. $[\alpha]_D^{23}$ + 8.1° (c 0.31, methanol); Rf 0.57 (methanol); m/e identical fragmentations with those of 1a; $^1$H NMR (250 MHz, $D_2O$) δ 1.89 (m, 2, H-2 and H-2'), 3.51 (dd, 1, H-5), 3.60 (dd, 1, H-5'), 3.77 (d, 1, H-α), 3.87 (m, 1, H-4), 4.25 (m, 1, H-3), 4.34 (m, 1, H-1); $J_{1-\alpha}$ = 5.5 Hz, $J_{1-2}$ + $J_{1-2'}$ = 15.5 Hz, $J_{3-4}$ = 2 Hz, $J_{4-5}$ = 4.0 Hz, $J_{4-5'}$ = 5.5 Hz, $J_{5-5'}$ = 12.0 Hz.

ACKNOWLEDGEMENTS

We thank Professor F. Le Goffic, University of Paris VI, for the biological tests and Dr. D. Shire for a careful reading of this manuscript.

REFERENCES AND FOOTNOTES

1. Taken in part from the Thèse de Docteur Ingénieur, E.N.S.C.P., University of Paris, Feb. 1982. Presented at the XIth International Carbohydrate Symposium, Vancouver, Canada, August 1982.

2. S. Pochet and T. Huynh-Dinh, J. Org. Chem., 47, 193 (1982).

3. A. Rosenthal and C. M. Richards, Carbohyd. Res., 31, 331 (1973).

4. A. Rosenthal and A. J. Brink, J. Carbohydrates. Nucleosides Nucleotides, 2, 343 (1975).

5. A. Rosenthal and A. J. Brink, J. Carbohyd. Res., 47, 332 (1976).

6. J. C. Semple, P. C. Wang, Z. Lysenko and M. M. Joullié, J. Am. Chem. Soc., 92, 7505 (1980).

7. (a) D. Marquanding, P. Hoffmann, H. Heitzer and I. Ugi, J. Am. Chem. Soc., 92, 1969 (1970) and references cited therein.

(b) I. Ugi, "Isonitrile Chemistry", Academic Press, New York, N.Y., 1971, p. 196.

8. H. R. Divanfard, Z. Lysenko, J. E. Semple, P. C. Wang and M. M. Joullié, Heterocycles, 16(11), 1975 (1981).

9. (a) H. P. Albrecht, D. B. Repke and J. G. Moffatt, J. Org. Chem., 38, 1836 (1973).

(b) G. Trummlitz, J. G. Moffatt, J. Org. Chem., 38, 1841 (1973).

10. A. Kolb, C. Gouyette, T. Huynh-Dinh and J. Igolen, Tetrahedron, 31, 2914 (1975).

11. (a) M. Passerini, Gazz. Chim. Ital., 51(II), 126 (1921).

(b) I. Ugi, Angew. Chem., 74, 9 (1962).

12. W. Klyne and J. Buckingham, "Atlas of Stereochemistry. Absolute Configurations of Organic Molecules". Oxford University Press, New York, N.Y., 1974, p. 23.

13. The positive nomenclature refers to (R,R) or (S,S) isomers while negative refers to (R,S) or (S,R) isomers.[7]

14. t-Butyl isocyanide was prepared according to a modification of the procedure of I. Ugi. We thank Prof. M. M. Joullié for this private communication.

15. M. J. Robins and R. K. Robins, J. Am. Chem. Soc., 87, 4934 (1965).

16. D. B. Davies and S. S. Danyluk, Biochemistry, 13, 4417 (1975) and references cited therein.

17. B. C. Clark, Antimicrob. Agents Chemoth., 19, 369 (1981).

18. E. Stahl, "Thin-layer Chromatography", 2nd Ed., New York, N.Y., 1969.