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AN EASY SYNTHESIS OF METHYL 4-(2,3:5,6-DI-*O*-ISOPROPYLIDENE-α- AND -β-D-MANNOFURANOSYL)-3-OXOBUTANOATE: A NEW APPROACH TO PYRAZOFURINS*

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ABSTRACT

The reaction of 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose with (3-methoxycarbonyl-2-oxopropylidene)triphenylphosphorane, catalysed by benzoic acid in dry benzene, gives methyl 4-(2,3:5,6-di-*O*-isopropylidene-α- and -β-D-mannofuranosyl)-3-oxobutanoate in good yield. These compounds are easily transformed into 4-hydroxy-3-(α- and β-D-mannofuranosyl)pyrazole-5-carboxamide, which are the mannofuranosyl analogues of pyrazofurins. The anomeric configurations of the products were assigned on the basis of ^{1}H-n.m.r. data.

INTRODUCTION

The chemistry of *C*-nucleosides has received considerable attention due to the biological action of naturally occurring compounds such as pyrazofurin, formycin, oxazinomycin, and showdomycin[1]. There has been much work on the synthesis of these compounds and their analogues[2]. The most general synthetic approach involves the elaboration of the heterocycles from suitably functionalised anhydroalditols and has been applied to pyrazofurin[3] (**1**), pyrazofurin B (**2**), showdomycin[4], formycin B[5], *etc.* Suitable anhydroalditol derivatives have been synthesised by the Wittig reaction of variously protected reducing-sugars with stabilised phosphoranes[6,7].

We have been interested in the preparation of *C*-nucleosides[8] and in the application of the Wittig reaction in their synthesis[9], for example, the reaction of protected furanoses with a highly functionalised ylid such as (3-methoxycarbonyl-2-oxopropylidene)triphenylphosphorane (**4**), as a direct route to protected 4-furanosylacetoacetates. These *C*-glycosides contain all the carbon atoms needed to build up the heterocyclic moiety, *inter alia,* in pyrazofurin, formycin, and oxoformycin. We now report the synthesis of methyl 4-(2,3:5,6-di-*O*-isopropylidene-α- and -β-D-mannofuranosyl)-3-oxobutanoates (**5α** and **5β**) by the reaction of 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**3**) with **4**, and its use in a first approach

*Synthesis of *C*-Glycosides and *C*-Nucleosides, Part II.

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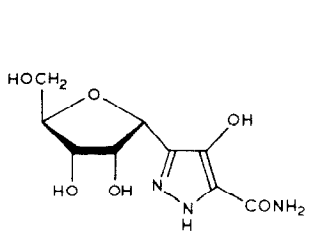

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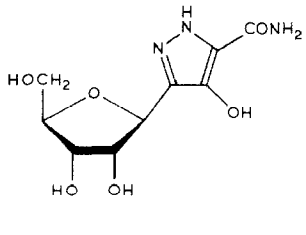

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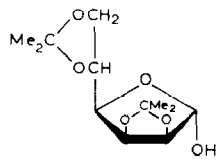

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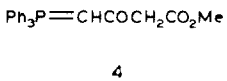

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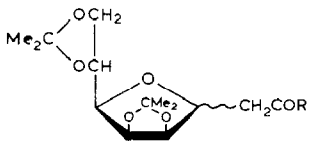
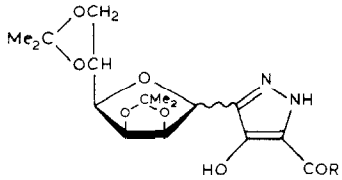


5α,β R = CH_2CO_2Me
6 R = Me
7α,β R = CN_2CO_2Me



8α,β R = OMe
9α,β R = NH_2

to a general synthetic method for pyrazofurin. Four different syntheses of pyrazofurin[10,11] have been reported, one of which[11] is closely related to our approach.

RESULTS AND DISCUSSION

The ylid **4** was prepared from the corresponding phosphonium salt by a method similar to that described for the ethyl ester[12] and its structure was confirmed by spectroscopic data. The λ_{max} at 267, 215, and 202 nm accord with the ylid structure. The i.r. spectrum of **4**, when compared with that of the corresponding phosphonium salt, shows a higher displacement of $\nu_{C=O}$ for the ketone group (1745 cm^{-1}) than for the ester group (1720 cm^{-1}), as would be expected from the high carbanionic character of C-4 in **4**. The ^1H-n.m.r. spectrum of **4** contained a broad signal at 3 p.p.m. for a proton exchangeable by D_2O, which was assigned to H-4. On the addition of basic alumina, a change to a sharp singlet was produced, in agreement with previous observations[13].

When a dry solution of **3** and **4** (in anhydrous form) in benzene was boiled, no reaction occurred. However, the addition of a catalytic amount of benzoic yielded, after 50 h, **5αβ** (58% overall yield). The αβ-ratio was 4.2:1 as determined by g.l.c. The α and β anomers could be isolated by flash column chromatography. Small quantities of 1-(2,3:5,6-di-*O*-isopropylidene-α- and -β-D-mannofuranosyl)-2-oxopropane (**6α** and **6β**) were isolated when the time of reaction was prolonged to 100 h (molar ratio of ylid/benzoic acid increased to 19:1). Traces of water might be responsible for the formation of **6α** and **6β**; when the reaction was repeated with the hydrate of **4**, **6α** and **6β** were formed in almost quantitative yield.

TABLE I

^{1}H-NMR DATA

Compound	*Solvent*	*H-1'*	*H-2'*	*H-3'*	*H-4'*	*H-5'*	*H-6'*	*H-6''*	*H-2a,2b*	*H-4a,4b*	*CMe$_2$*	*Others*
5α[a,c]	$CDCl_3$	4.8 t	4.53 d	4.78 dd	3.78 dd	4.35 dt	4.0 d		3.5 s	2.76 d	1.28, 1.30 1.39, 1.46	3.7 s (OMe)
5β[a,c]	$CDCl_3$	4.1 m	4.6 m		3.55 m	4.4 dt	4.05 d		3.5 s	3.0 d	1.30, 1.35 1.42, 1.44	3.75 s (OMe)
5β[b,c]	C_6D_6	3.8 dd	4.5 m		3.4 m	4.50 m	4.12 d		3.22 s	2.95 d	1.20, 1.38 1.40, 1.50	3.45 s (OMe)
7α[a,c]	$CDCl_3$	4.35 dd	4.6 d	4.8 dd	3.9 m	4.3 m	4.0 m			2.98 d 3.16 d	1.34, 1.36 1.45, 1.50	3.82 s (OMe)
7β[a,c]	$CDCl_3$	4.0 m	4.74 m		3.5 dd	4.3 m	4.0 d			3.25 d	1.20, 1.28 1.34, 1.37	3.8 s (OMe)
8α[a,d]	$CDCl_3$	5.20 s	5.26 d	4.98 dd	3.94 dd	4.42 dt	4.05 dd	4.02 dd			1.34, 1.35 1.39, 1.51	7–6.5 (NH) 3.93 s (OMe)
8β[a,d]	$CDCl_3$	4.70 d	4.87–4.83 m		3.58 dd	4.40 dt	4.05 d				1.32, 1.33 1.41, 1.54	7.8–7.2 (NH) 3.9 s (OMe)
9α[a,d]	$CDCl_3$	5.23 s	5.34 d	4.81 dd	3.87 dd	4.44 ddd	4.08 d				1.35, 1.41 1.50	7.8, 6.7, 5.9 (NH)
9β[a,d]	$CDCl_3$	4.71 d	4.9–4.86 m		3.59 dd	4.42 dt	4.07 d				1.27, 1.35 1.43, 1.59	8.1, 6.8, 6.15 (NH)

[a]Internal Me_4Si. [b]Internal C_6H_6. [c]60 MHz. [d]200 MHz.

TABLE II

COUPLING CONSTANTS (Hz)

Compound	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'}$	$J_{5',6''}$	$J_{4,1'}$
5α	0	6	4	2	6	6	8
5β ($CDCl_3$)				6	5		7
5β (C_6D_6	2				5	5	6
7α	0	6	4				6.5, 8
7β			2 and 6			5	6
8α	0	6	3.7	7	5.6	5.6	
8β	2.5	—	3	7.76	5.18	5.18	
9α	0	6	3.7	5.6	6	6	
9β	1.2	—	2.4	7.6	4.9	4.9	

Treatment of the most polar isomer with methanolic 0.1M sodium methoxide caused rapid anomerisation (**5β/5α** ~4.2:1) to the thermodynamically more stable, less polar isomer. This conversion was readily followed by g.l.c.

The structure of **5α** was established on the basis of ^{1}H-n.m.r. data. Spin-decoupling studies showed $J_{1',2'}$ to be ~0 Hz, indicating H-1′,2′ to be *trans*-diequatorial. The $J_{1',2'}$ value for **5β** was 2 Hz, which falls in an ambiguous range for configurational assignment. These results accord with those reported for analogous mannofuranosyl acetates[7,14].

Compounds **5α** and **5β** were transformed quantitatively into the diazo derivatives **7α** and **7β**, respectively, by reaction with equimolecular amounts of tosyl azide and triethylamine in acetonitrile[15] at room temperature. No anomerisation occurred under these conditions, as shown by g.l.c. The configuration of **7α** was established by comparison of the ^{1}H-n.m.r. data with those of **5α** and **5β**.

Treatment of **7α** with sodium hydride in dry 1,4-dioxane (1 h, 100°) caused cyclisation and anomerisation, giving a mixture of the pyrazole derivatives **8α** and **8β** (αβ-ratio ~3:2) which was fractionated readily by flash column chromatography. Similarly, **7β** gave a mixture of **8α** and **8β** (αβ-ratio ~1.1:1), proving that **8α** is thermodynamically the most stable isomer. The configurational assignment of these anomers was straightforward, because the ^{1}H-n.m.r. (200 MHz) spectrum of **8α** contained a sharp singlet for H-1′ (*i.e.*, $J_{1',2'}$ 0 Hz), indicating the α configuration, whereas the signal for H-1′ in **8β** was a doublet ($J_{1',2'}$ ~2.5 Hz).

The reactions of **8α** and **8β** with dry, saturated methanolic ammonia involved partial anomerisation to give mixtures of **9α** and **9β**. Since the former preponderated, it was thermodynamically the most stable isomer. Treatment of **9α** and **9β** with aqueous 10% trifluoracetic acid caused anomerisation, as was proved by the ^{13}C-n.m.r. data for the products **10** and **11** (Tables III and IV). Assignments were made by selective proton-decoupling experiments. The greater values of the chemical shifts for the signals for C-4′ (δ 82.56 in **10** and 83.02 in **11**) show[16] that both are furanosides. The chemical shift of the signal for C-1 has been used to distinguish between α- and β-furanosides in glycosides[17], nucleosides[18], and *C*-

TABLE III

^{1}H-N.M.R. DATA [a] FOR **10** AND **11** (200 MHz)

	Chemical shifts (δ)						
Compound	*H-1'*	*H-2'*	*H-3'*	*H-4'*	*H-5'*	*H-6'*	*H-6''*
10	5.00 d	4.08 dd	4.47 dd	4.26 dd	4.02 ddd	3.82 ddd	3.65 ddd
11	5.28 d	4.80 dd	4.49 dd	3.95 dd	4.07 ddd	3.85 ddd	3.76 ddd
	Coupling constants (Hz)						
Compound	$J_{1',2'}$	$J_{2',3'}$	$J_{3',4'}$	$J_{4',5'}$	$J_{5',6'}$	$J_{5',6''}$	$J_{6',6''}$
10	9.2	4.0	3.1	8.9	2.9	5.8	12.1
11	8.2	4.2	3.0	8.2	3.0	5.8	12.0

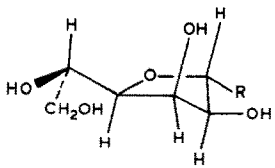
[a]In D_2O (internal DSS).

TABLE IV

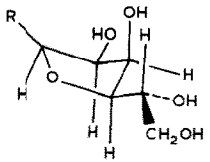
^{13}C-N.M.R. CHEMICAL SHIFTS (δ)[a] FOR **10** AND **11** (50 MHz)

Compound	*C-1'*	*C-2'*	*C-3'*	*C-4'*	*C-5'*	*C-6'*	*C-1*	*C-2*	*C-3*	*C-4*
10	76.17	78.15	74.27	82.56	72.09	65.70	167.02	131.02	142.59	136.20
11	75.62	73.51	76.28	83.02	69.60	64.00	168.00	131.00	141.00	135.50

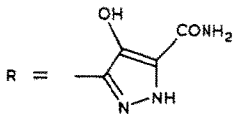
[a]In D_2O (internal DSS).



E_2-10



^3E-11



glycosides[7]; the signal for the isomer having the aglycon and HO-2 *cis* appears at higher field. Thus, the signals for C-1' and C-2' of **11** occur at 0.55 and 2.64 p.p.m., respectively, which are upfield of the corresponding signals in **10**, strongly suggesting that **10** is α and **11** is β. Moreover, the coupling constants for **10** and **11** accord with those expected for the conformers E_2-**10** and ^3E-**11**, respectively.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Evaporations were conducted *in vacuo* at <40° (bath). Elemental analyses were carried out by the microanalysis service of the University of Granada. Specific rotations were measured with a Perkin–Elmer 141 or 241 polarimeter (10-cm cell). I.r. spectra were recorded with a Beckman Aculab IV spectrophotometer. ^{1}H-n.m.r. spectra (internal Me_4Si) were recorded with a Perkin–Elmer–Hitachi R-24B (60 MHz) or Bruker WP 200 SY (200 MHz) spectrometer. Coupling constants were measured directly from the spectra. U.v. spectra were recorded with a Beckman DB-GT spectrophotometer.

G.l.c. was carried out on a Hewlett–Packard 5710A chromatograph equipped with a flame-ionisation detector. The injection-port and the detector temperatures were 250 and 350°, respectively, and the nitrogen flow-rate was 30 mL/min. A stainless-steel column (2.00 m × 3.00 mm i.d.) packed with 3% of diethyleneglycol succinate on 80–100 Chromosorb was used. Retention times (T) are given in min. T.l.c. was performed on Kieselgel 60 F_{254} (Merck) and detection was effected by u.v. light. Flash column chromatography was performed on Kieselgel 60 (Merck, 230–400 mesh).

(3-Methoxycarbonyl-2-oxopropyl)triphenylphosphonium bromide. — This compound, prepared (83%) by a procedure[12] similar to that used for the ethyl ester, had m.p. 177° (from ethanol–ether); λ_{max}^{MeOH} 280 (ε 250), 228 (ε 5600), and 210 nm (ε 8000); ν_{max}^{KBr} 3100–2950, 2900–2700, 1745, 1720, 750, and 700 cm^{-1}.

Anal. Calc. for $C_{23}H_{22}BrO_3P$: C, 60.40; H, 4.48. Found: C, 60.23; H, 4.62.

(3-Methoxycarbonyl-2-oxopropylidene)triphenylphosphorane (**4**). — Compound **4**, prepared (82%) by a method[12] similar to that used for the ethyl ester, had m.p. 126° (from benzene); λ_{max}^{MeOH} 267 (ε 5600), 215 (ε 2500), and 202 nm (ε 30,000); ν_{max}^{KBr} 3100–2990, 1720, and 1540 cm^{-1}. ^{1}H-N.m.r. data (CCl_4): δ 7.8–7.3 (m, 15 H, 3 Ph), 3.65 (s, 3 H, MeO), 3.35 (2 s, 2 H, -CH_2-), and 2.3 (bs, 1 H, CH=; became a sharp s after the addition of basic aluminum oxide).

Anal. Calc. for $C_{23}H_{22}O_3P$: C, 73.39; H, 5.62. Found: C, 73.09; H, 5.48.

*Methyl 4-(2,3:5,6-di-O-*isopropylidene-*α- and -β-*D*-mannofuranosyl)-3-oxobutanoate* (**5α** *and* **5β**). — A solution of 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose[19] (**3**; 8 g, 30.7 mmol), **4** (23.1 g, 61.4 mmol), and benzoic acid (0.4 g, 3.2 mmol) in anhydrous benzene (200 mL) was boiled under reflux until **3** was absent (~50 h; t.l.c., hexane–ether, 1:2). The solvent was evaporated and to a solution of the residue in ethyl acetate (100 mL) was added hexane (300 mL), causing the separation of an oil which was separated and treated twice in the same manner. The three resulting solutions were combined and cooled, triphenylphosphine was removed, the filtrate was concentrated, and the residue was purified by flash chromatography (hexane–ethyl acetate, 4:1) to yield **5β** (4.67 g, 47%) and **5α** (1.22 g, 11%).

Compound **5α** had $[\alpha]_D^{20}$ +10° (*c* 1, methanol), R_F 0.35 (ethyl ether–hexane,

3:1), *T* 5.9 min (175°); ν_{max}^{film} 3000–2860, 1755, 1730, and 1385 cm^{-1}; λ_{max}^{MeOH} 270 nm (ε 2200).

Anal. Calc. for $C_{17}H_{26}O_8$: C, 72.43; H, 6.45. Found: C, 72.31; H, 6.41.

Compound **5β** had $[\alpha]_D^{20}$ +1.4° (*c* 0.79, methanol), R_F 0.62 (ethyl ether–hexane, 3:1), *T* 3.8 min; ν_{max}^{film} 3000–2850, 1745, 1715, and 1370 cm^{-1}; λ_{max}^{MeOH} 275 nm (ε 1600).

Anal. Found: C, 72.29; H, 6.72.

*Methyl 2-diazo-4-(2,3:5,6-di-*O*-isopropylidene-β-*D*-mannofuranosyl)-3-oxobutanoate* (**7β**). — Triethylamine (0.847 g, 8.36 mmol) was added to a well-stirred solution of **5β** (3.0 g, 8.38 mmol) in acetonitrile (13.34 mL, 8.36 mmol). The temperature of the mixture was adjusted to 15° and tosyl azide (1.65 g, 12.4 mmol) was added dropwise. The mixture was allowed to attain room temperature; stirring was continued for ~3 h until **5β** disappeared (t.l.c.; hexane–ethyl acetate, 4:1). Solvents were evaporated, the residue was triturated with ethyl ether (40 mL), and the ethereal solution was washed successively with aqueous KOH (0.5 g in 40 mL, 0.08 g in 25 mL) and water (25 mL), dried (Na_2SO_4), filtered, and concentrated, yielding **7β** (3.98 g, 79.6%). Crystallisation from hexane–ethyl acetate (2:1) gave material having m.p. 110°, $[\alpha]_D^{20}$ +21° (*c* 0.79, methanol), R_F 0.42 (hexane–ethyl acetate, 3:1), *T* 3.9 min (190°); ν_{max}^{KBr} 2990, 2960, 2860, 2150, 1715, 1650, and 1390 cm^{-1}; λ_{max}^{MeOH} 255 (ε 8300) and 226 nm (ε 8600).

Anal. Calc. for $C_{17}H_{24}N_2O_8$: C, 53.12; H, 6.29; N, 7.28. Found: C, 53.25; H, 6.36; N, 7.31.

*Methyl 2-diazo-4-(2,3:5,6-di-*O*-isopropylidene-α-*D*-mannofuranosyl)-3-oxobutanoate* (**7α**). — Following the same procedure for **7β**, **5α** (0.38 g, 1.07 mmol) yielded **7α** (0.265 g, 69.68%), which, after purification by column chromatography (hexane–ethyl acetate, 3:1), had m.p. 75° (from hexane–ethyl acetate), $[\alpha]_D^{20}$ +25° (*c* 0.96, methanol), R_F 0.4 (hexane–ethyl acetate, 3:1), *T* 3.5 min (190°); ν_{max}^{KBr} 2940, 2910, 2120, 1745, and 1375 cm^{-1}; λ_{max}^{MeOH} 262 (ε 1460) and 225 nm (ε 1990).

Anal. Calc. for $C_{17}H_{24}N_2O_8$: C, 53.12; H, 6.29; N, 7.28. Found: C, 53.09; H, 6.20; N, 7.26.

*3-(2,3:5,6-Di-*O*-isopropylidene-α-* and *-β-*D*-mannofuranosyl)-4-hydroxypyrazole-5-carboxylic acid methyl ester* (**8α** *and* **8β**). — NaH (0.37 g, 12.3 mmol) was added to a well-stirred solution of **7β** (2.36 g, 6.15 mmol) in anhydrous 1,4-dioxane (30 mL). The resulting solution was boiled under reflux for 1 h, the excess of NaH was decomposed with MeOH, and the mixture was neutralised with dilute HCl. The solvents were evaporated, and the residue was purified by column chromatography (hexane–ethyl acetate, 3:2) to yield, first, **8α** (1.01 g, 42.79%), m.p. 206° (from hexane–ethyl acetate), $[\alpha]_D^{20}$ +19° (*c* 0.79, ethanol); R_F 0.66 (ethyl acetate–hexane, 2:1); ν_{max}^{KBr} 3500, 3380, 2980–2900, 1710, 1575, and 1380 cm^{-1}; λ_{max}^{MeOH} 267 (ε 5400) and 227 nm (ε 6800).

Anal. Calc. for $C_{17}H_{24}N_2O_8$: C, 53.12; H, 6.29; N, 7.28. Found: C, 53.21; H, 6.50; N, 7.19.

Eluted second was **8β** (1.11 g, 47.24%), m.p. 83° (from hexane–ethyl

acetate), $[\alpha]_D^{20}$ +67° (*c* 0.79, methanol), R_F 0.48 (ethyl acetate–hexane, 2:1); ν_{max}^{KBr} 3380, 3320, 2990–2940, 1710, and 1380 cm^{-1}; λ_{max}^{MeOH} 267 (ε 4900) and 225 nm (ε 5900).

Anal. Found: C, 53.16; H, 6.19; N, 7.21.

In another reaction (1 h), **7α** yielded a mixture of **8α** and **8β** (~3:1).

*3-(2,3:5,6-Di-O-isopropylidene-α- and -β-D-mannofuranosyl)-4-hydroxypyrazole-5-carboxamide (**9α** and **9β**).* — A solution of **8β** (0.885 g, 2.22 mmol) in dry MeOH (15 mL) was saturated with anhydrous ammonia at 15° and heated in a sealed tube for 13 h at 85–90°. After removal of the solvent under reduced pressure, the residue was subjected to column chromatography (hexane–ethyl acetate, 4:3) to give, first, **9α** (0.479 g, 58.36%), m.p. 234° (dec.), $[\alpha]_D^{20}$ +24° (*c* 0.79, methanol), R_F 0.48 (ethyl acetate–hexane, 3:1); ν_{max}^{KBr} 3480, 3370, 3200, 2980–2960, 1650, 1610, and 1375 cm^{-1}; λ_{max}^{MeOH} 263 (ε 6200) and 227 nm (ε 7300).

Anal. Calc. for $C_{16}H_{23}N_3O_7$: C, 52.02; H, 6.27; N, 11.37. Found: C, 52.03; H, 6.04; N, 11.17.

Eluted second was **9β** (0.228 g, 27.82%), m.p. 214° (dec.), $[\alpha]_D^{20}$ +55° (*c* 0.79, methanol), R_F 0.44 (ethyl acetate–hexane, 3:1); ν_{max}^{KBr} 3430–3050, 2990–2940, 1670, 1615, and 1380 cm^{-1}; λ_{max}^{MeOH} 265 (ε 4700) and 226 nm (ε 6200).

Anal. Found: C, 52.00; H, 6.15; N, 11.27.

When a solution of **8α** (0.75 g, 1.95 mmol) in dry MeOH (15 mL) was treated with anhydrous ammonia as described above, **9α** and **9β** were obtained in the ratio ~4:3.

4-Hydroxy-3-(α- and β-D-mannofuranosyl)pyrazole-5-carboxamide (**10** *and* **11**). — A solution of **9α** (0.299 g, 0.8 mmol) in aqueous 10% CF_3COOH was left at room temperature for 3 h, neutralised, filtered, and concentrated. The residue was subjected to column chromatography (ethyl acetate–acetone–methanol–water, 6:1:1:1) to give, first, **11** (0.056 g, 28.3%), $[\alpha]_D^{20}$ +16° (*c* 0.51, methanol), R_F 0.22 (ethyl acetate–acetone–methanol–water, 6:1:1:1); ν_{max}^{film} 3600–3100, 1650, and 1610 cm^{-1}; λ_{max}^{MeOH} 266 (ε 2940) and 227 nm (ε 4100).

Anal. Calc. for $C_{10}H_{15}N_3O_7 \cdot H_2O$: C, 39.09; H, 5.57; N, 13.67. Found: C, 38.86; H, 5.37; N, 13.50.

Eluted second was **10** (0.113 g, 56.6%), $[\alpha]_D^{20}$ +24° (*c* 0.79, methanol), R_F 0.26 (ethyl acetate–acetone–methanol–water, 6:1:1:1); ν_{max}^{film} 3600–3100, 1650, 1610, and 1080 cm^{-1}; λ_{max}^{MeOH} 267 (ε 3100) and 224 nm (ε 4000).

Anal. Found: C, 38.79; H, 5.42; N, 13.39.

Similar treatment of **9β** yielded a 1:2.5 mixture of **10** and **11**.

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REFERENCES

1 R. J. SUHADOLNIK, *Nucleoside Antibiotics*, Wiley–Interscience, New York, 1970.
2 S. HANESSIAN AND A. G. PERNET, *Adv. Carbohydr. Chem. Biochem.*, 33 (1976) 111–188.
3 K. GERZON, D. C. DE LONG, AND J. C. CLINE, *Pure Appl. Chem.*, 28 (1971) 489–497; G. E. GUTOWSKI, M. O. CHANEY, N. D. JONES, R. L. HAMMILL, F. A. DAVIS, AND R. D. MILLER, *Biochem. Biophys. Res. Commun.*, 51 (1973) 312–317.
4 N. NISHIMURA, M. MAYMA, Y. KOMATSU, F. KATO, N. SHIMAOKA, AND Y. TANAKA, *J. Antibiot., Ser. A*, 17 (1966) 148–155.
5 G. KOYAMA AND H. UMEZAWA, *J. Antibiot., Ser. A*, 18 (1965) 175–177; G. KOYAMA, K. MAEDA, H. UMEZAWA, AND Y. IITAKA, *Tetrahedron Lett.*, (1966) 597–602.
6 Y. A. ZHDANOV, Y. E. ALEXEEV, AND V. G. ALEXEEVA, *Adv. Carbohydr. Chem. Biochem.*, 27 (1972) 227–299.
7 H. OHRUI, G. H. JONES, J. G. MOFFATT, M. L. MADDOX, A. T. CHRISTENSEN, AND S. K. BYRAM, *J. Am. Chem. Soc.*, 97 (1975) 4602–4613; H. OHRUI AND S. EMOTO, *J. Org. Chem.*, 42 (1977) 1951–1957.
8 F. J. LOPEZ APARICIO, F. J. LOPEZ HERRERA, AND M. VALPUESTA FERNANDEZ, *Carbohydr. Res.*, 69 (1979) 235–242; F. J. LOPEZ APARICIO, J. A. LOPEZ SASTRE, J. MOLINA MOLINA, AND F. J. LOPEZ HERRERA, *An. Quim., Ser. C*, 77 (1981) 147–149.
9 F. J. LOPEZ APARICIO AND F. J. LOPEZ HERRERA, *Carbohydr. Res.*, 80 (1980) c4–c7; F. J. LOPEZ HERRERA AND J. M. MORON DOMINGUEZ, Sintesis de manofuranosil acetoacetato de metilo, un intermedio en la preparación de análogos de antibióticos *C*-nucleósidos, Universidad de Málaga, 1981.
10 J. FARKAS, Z. FLEGELOVA, AND F. SORM, *Tetrahedron Lett.*, 22 (1972) 2279–2280; S. DE BERNARDO AND M. WEIGELE, *J. Org. Chem.*, 41 (1976) 287–290; J. G. BUCHANAN, A. STOBIE, AND R. H. WIGHTMAN, *J. Chem. Soc. Chem. Commun.*, (1981) 2267–2271.
11 N. KATAGIRI, K. TAKASHIMA, AND T. KATO, *J. Chem. Soc. Chem. Commun.*, (1982) 664–665.
12 F. SERRATOSA AND E. SOLE, *An. R. Soc. Esp. Fis. Quim., Ser. B*, 62 (1966) 431–440; H. MUXFELD, G. GRETHE, K. UHLING, AND H. ZEUGNER, *Chem. Ber.*, 96 (1963) 2943–2949.
13 P. CREWS, *J. Am. Chem. Soc.*, 90 (1968) 2961–2962; H. J. BESTMAN, H. G. LIBERDA, AND J. P. SNYDER, *ibid.*, 90 (1968) 2963–2964.
14 H. MAEHR, T. WILLIAMS, M. LEACH, AND A. STEMPEL, *Helv. Chim. Acta*, 57 (1974) 212–213.
15 M. REGITZ, J. HOCKER, AND A. LIEDHEGERNER, *Org. Synth.*, 5 (1973) 179–183; M. REGITZ, *Angew. Chem. Int. Ed. Engl.*, 6 (1967) 733–749.
16 *Atlas of Carbon-13 N.m.r. Data*, Heyden, London, 1975.
17 T. USUI, S. TSUSHIMA, N. YAMAOKA, K. MATSUDA, K. TUZIMURA, H. SUGIYAMA, S. SETO, K. FUJIEDA, AND G. MIYAJIMA, *Agric. Biol. Chem.*, 38 (1974) 1409–1410.
18 H. SUGIYAMA, N. YAMAOKA, B. SHIMIZU, Y. ISHIDO, AND S. SETO, *Bull. Chem. Soc. Jpn.*, 47 (1974) 1815–1816.
19 O. TH. SCHMIDT, *Methods Carbohydr. Chem.*, 2 (1962) 318–325.