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Chiral Synthons for CARBA- β -D-Ribonucleosides. Synthesis of CARBA-4-Deoxypyrazofurin and Isomeric CARBA-4-Deaza-oxoformycin Analogues

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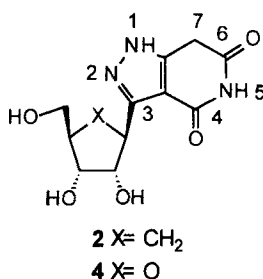
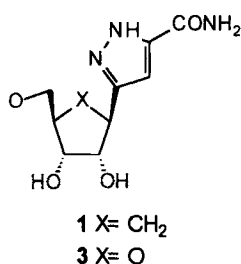
**CHIRAL SYNTHONS FOR *CARBA*- β -D-RIBONUCLEOSIDES.
SYNTHESIS OF *CARBA*-4-DEOXYPYRAZOFURIN AND ISOMERIC
CARBA-4-DEAZA-OXOFORMYCIN ANALOGUES**

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ABSTRACT: Multi-step transformation of enantiomerically pure synthons, (1*S*,2*S*,3*R*,4*R*)-(4-hydroxymethyl-2,3-isopropylidenedioxy-1-cyclopentyl) methyl butyrate {(-)-**5**} and (1*R*,5*R*,6*R*,7*S*)-6,7-(isopropylidenedioxy)-3-oxabicyclo[3.2.1]octane-2-one {(+)-**11**} into *carba*-4-deoxypyrazofurin **1** and isomeric *carba*-4-deaza-oxoformycin **2** analogues is presented.

Nucleoside analogues have long been prepared to act as potential antiviral agents and are now becoming increasingly important as building blocks in the synthesis of nucleic acids for use in antisense and antigene strategy.¹ In our continuing effort to synthesize *carba*-ribonucleoside analogues to be used as building blocks for nucleic acids, we introduced general approaches that allowed access to a diverse array of chiral synthons for *carba*-*N*- and *C*-ribonucleosides of both enantiomeric forms.²⁻⁵ Recently, we presented asymmetric syntheses of enantiomerically pure compounds **5** and **11** *via* enzymatic

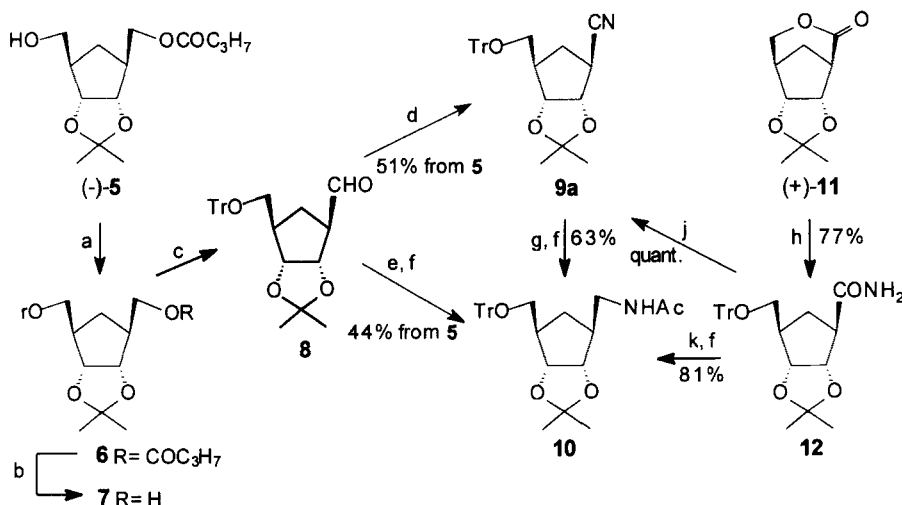


hydrolysis³ and asymmetric hydrosilylation reaction⁵ of the readily available *meso*-norbornane derivatives. Our approach was a rational extension of the use of Ohno's lactone (+)-**11**, which has been used⁶ as a key synthon for the preparation of natural (-)-aristeromycin through Hoffman degradation of the amide derivative of (+)-**11**. In this work we give the full account on the synthesis of *carba*-*C*-ribonucleosides (-)-**15** and (-)-**24**, congeners of *C*-ribonucleosides **37** and **48**, starting from (-)-**5** and (+)-**11**.

RESULTS AND DISCUSSION. *Preparation of carba-2,5-anhydro-3,4-O-isopropylidene-6-O-trityl-D-allonitrile (9a) and carba-1-acetamido-2,5-anhydro-3,4-O-isopropylidene-6-O-trityl-1-deoxy-D-allitol (10).* The results of previous synthetic efforts^{7,8} indicated that the construction of heterocycle moieties of our targeted compounds **1** and **2** could be efficiently accomplished from *N*-acetamide and nitrile functionality, respectively.

In the course of our studies, we have demonstrated the utility of monoester (-)-**5**³ and lactone (+)-**11**^{2,5} in the synthesis of the appropriate enantiomerically pure cyclopentane derivatives in which the hydroxymethyl group was protected as acetyl, pivaloyl, or benzoyl ester. Regarding our retrosynthetic scheme which requires the use of protecting group stable under alkaline conditions, a trityl protection was found to be a useful alternative. Another advantage of using this protection was formation of more crystalline, more readily separated derivatives. Indeed, all key compounds **9a**, **10**, and **12** either prepared from (-)-**5** or (+)-**11** (SCHEME 1) were successfully purified just by recrystallization. Thus, in the presence of trityl chloride, the alcohol (-)-**5** was protected into **6**. Further cleavage of the butyryl group with potassium carbonate in methanol gave **7** which was transformed to aldehyde **8** with pyridinium chlorochromate (PCC) in methylene chloride.⁹ The reaction was carried out in the presence of sodium acetate in order to avoid partial deprotection of trityl group. The unstable aldehyde **8** was directly converted into crystalline nitrile **9a**¹⁰ by reacting it first with *N,N*-dimethylhydrazine and then with magnesium monoperoxyphthalate (MMPP).¹¹ Alternatively, conversion of the intermediate **8** with hydroxylammonium chloride to oxime followed by reduction with lithium aluminum hydride afforded amine which was acetylated with acetic anhydride to give the crystalline *N*-acetamide **10**.¹²

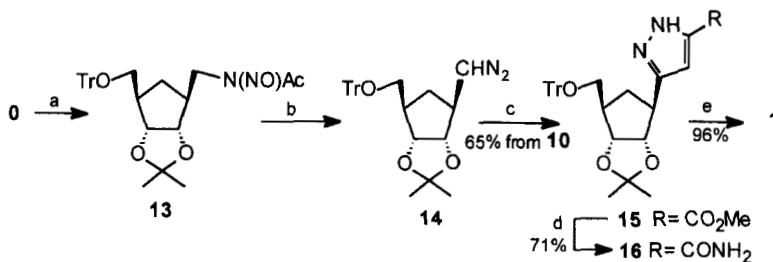
Treatment of lactone (+)-**11** with methanolic ammonia and further tritylation of hydroxymethyl group provided crystalline carboxamide **12**. This was smoothly



SCHEME 1. Reagents and conditions: (a) TrCl/Et₃N/DMAP/(CH₂Cl)₂, 60 °C; (b) K₂CO₃/MeOH; (c) PCC/NaOAc/CH₂Cl₂; (d) i, NH₂NMe₂/MeOH; ii, MMPP·6H₂O/MeOH, 0 °C; (e) i, NH₂OH·HCl/MeOH, Δ ; ii, LiAlH₄/Et₂O, Δ ; (f) Ac₂O/Et₃N/DMAP/MeCN; (g) NaBH₃(O₂CCF₃)/THF; (h) i, 27% NH₃/MeOH; ii, TrCl/Et₃N/DMAP/MeCN; (j) (CF₃CO)₂O/py/THF, 0 °C \rightarrow r.t.; (k) 1 M BH₃/THF, Δ .

dehydrated¹³ with trifluoroacetic anhydride into nitrile **9a** or reduced with borane¹⁴ to the amine which upon acetylation afforded **10**.

Synthesis of 3-[(1S,2S,3R,4R)-2,3-dihydroxy-4-(hydroxymethyl)cyclopentyl]-1H-pyrazole-5-carboxamide (carba-4-deoxypyrazofurin) (1). The tetrazole to pyrazole transformations of 2-N-alkenyl intermediates do not provide the natural positional isomer⁸, that's why the approach *via* diazo dipole **14** was considered. Such a route has already been used for the preparation of the nucleoside congener **3**.⁷ Thus, conversion of **10** using the method of Acton *et al*¹⁵ with dinitrogen tetroxide into the *N*-nitrosamide **13** followed by exposure to aqueous potassium hydroxide furnished diazoalkane **14**. 1,3-Dipolar cycloaddition of diazo dipole **14** to methyl propiolate gave the expected pyrazole regioisomer **15** which was ammonolysed at 60 °C in a sealed tube to yield pure **16**. Deprotection of **16** using 60% aqueous acetic acid resulted in the title compound **1** (SCHEME 2). ¹H and ¹³C NMR data of the pyrazole moiety of **1** were similar with those of **3**.⁸



SCHEME 2. Reagents and conditions: (a) i, $\text{N}_2\text{O}_4/\text{NaOAc}/\text{AcOH}/\text{CCl}_4$, 0 °C; ii, aq. $\text{KOH}/\text{Et}_2\text{O}$, 0 °C; iii, $\text{HC}\equiv\text{CCO}_2\text{Me}$; (b) 27% NH_3/MeOH , 60 °C; (c) 60% aq. AcOH .

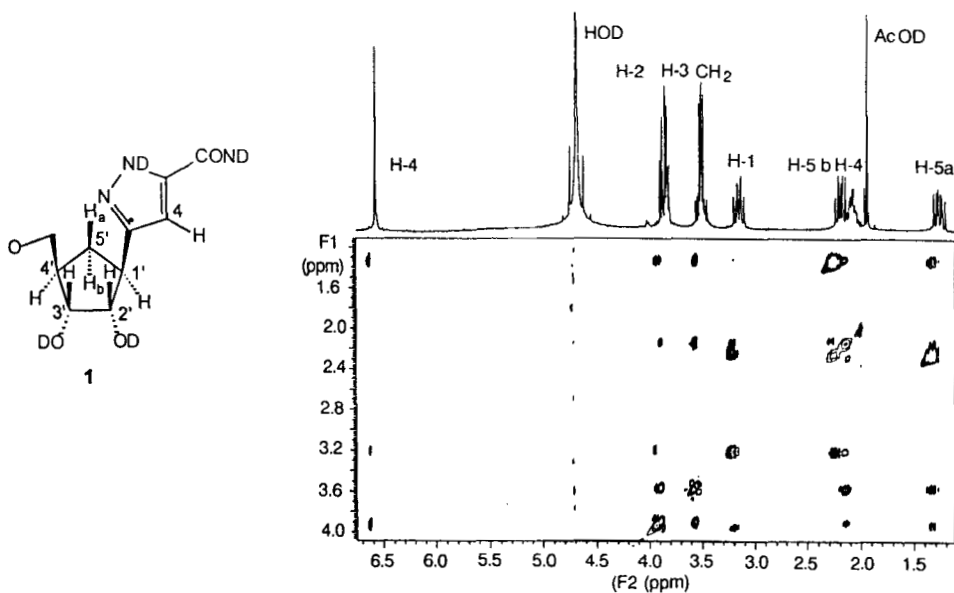
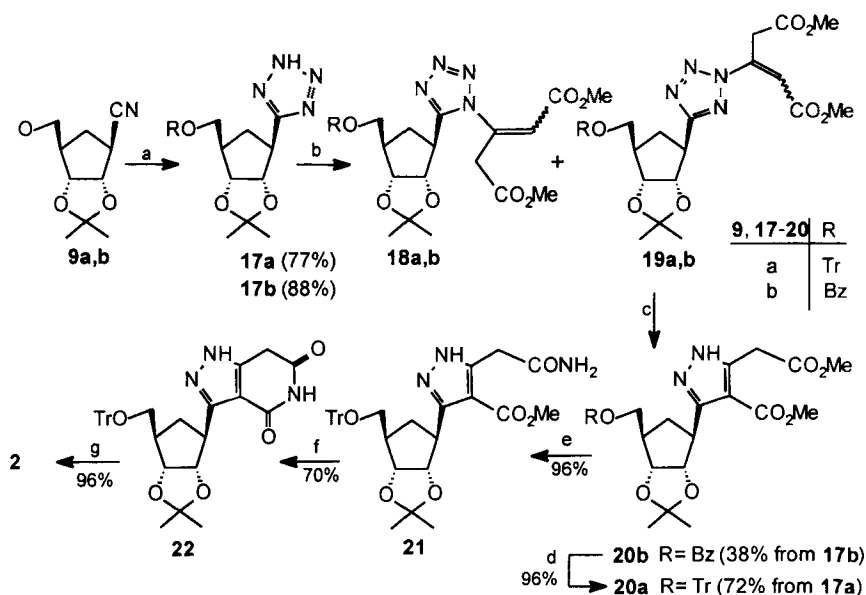


FIGURE 1. 300 MHz NOESY spectrum of **1** in D_2O with a mixing time of 400 ms at 25 °C.

A NOESY analysis of **1** in D_2O was performed to prove its relative stereochemistry (FIGURE 1). The pyrazole H-4 displayed medium NOE cross peaks to H-2' and H-5a' and a weak one to H-1'. Furthermore, stronger NOE cross peaks were observed between H-5b', H-1', and H-4' and between H-5a', H-2', and H-3'. This data prove conclusively that H-2', H-3', and H-5a' are located on the β -face of the cyclopentane ring, while H-1', H-4', and H-5b' are located on the α -face.



SCHEME 3. Reagents and conditions: (a) $\text{LiN}_3/\text{py}\cdot\text{CF}_3\text{CO}_2\text{H}/\text{py}$, 120 °C; (b) DMCP/ $\text{Et}_3\text{N}/\text{THF}$, -5 °C; (c) xylene, Δ ; (d) i, NaOMe/MeOH ; ii, $\text{TrCl}/\text{Et}_3\text{N}/\text{DMAP}/(\text{CH}_2\text{Cl})_2$, 50 °C; (e) 27% NH_3/MeOH ; (f) NaOEt/EtOH , Δ ; (f) 60% aq. $\text{CH}_3\text{CO}_2\text{H}$.

Synthesis of 3-[(1S,2S,3R,4R)-2,3-dihydroxy-4-(hydroxymethyl)cyclopentyl]-1H-pyrazolo[4,3-c]pyridine-4,6(5H,7H)-dione (isomeric carba-4-deaza-oxoformycin analogue) (**2**). The synthesis of pyrazolo[4,3-c]pyridine ribonucleosides as **4** was introduced in our group via regioselective conjugate addition of β-D-ribofuranosyltetrazole to dimethyl 1,3-allenedicarboxylate (DMAL) and further rearrangement into the corresponding pyrazole.⁸ We extended the use of this approach to carba-ribonucleoside analogues and reported on the conversion of the nitrile **9b** to tetrazole **17b** employing modified reaction conditions by using lithium azide and pyridinium trifluoroacetate in pyridine at 120 °C.² With **17b** available, conjugate addition with DMAL prepared *in situ* from dimethyl 3-chloro-2-pentenedioate (DMCP) at -5 °C regioselectively provided the *N*-2 alkenyltetrazole **19b** (SCHEME 3). Thermolysis of **19b** in boiling xylene resulted in pyrazole **20b**. Since the benzoyl protecting group was not expected to withstand further ammonolytic conditions it was removed by treatment with sodium methylate and resulting hydroxymethyl group reprotected with trityl chloride to give **20a**.

In order to avoid deprotection/reprotection steps in the synthesis of **20a** the trityl protected derivative **9a** was preferentially utilized instead of **9b**. Treatment of **9a** with lithium azide gave crystalline tetrazole **17a**. Further alkylation with DMAL at -5 °C gave *N*-1 and *N*-2 alkenyltetrazoles **18a** and **19a** in a ratio of 20/80. Slightly better ratio resulted at -10 °C at the expense of longer reaction time. Thermolysis of **18a+19a** in boiling xylene affected **19a** only resulting in pyrazole **20a** which was easily separated from unchanged **18a** by chromatography.

Attempts to convert diester **20a** into the cyclic imide **22** using urea in boiling sodium ethylate solution¹⁶ failed. However, the ammonolysis of diester **20a** in a sealed tube furnished monoamide **21** in quantitative yield, which cyclized readily in boiling sodium ethylate solution to give the cyclic imide **22**. ¹H NMR spectrum (CDCl₃) of **22** showed characteristic signals for the imide broad singlet due to NH at δ 8.4¹⁷ and singlet at δ 3.83 due to two protons at C-7. In infrared spectrum two carbonyl bands overlapped at ν 1705 cm⁻¹. Deprotection of **22** with 60% aqueous acetic acid gave the desired isomer of *carba*-4-deaza-oxoformycin **2**. The latter was further studied for its pseudorotational equilibrium of the cyclopentane ring.¹⁸

In summary, the readily available compounds (-)-**5** and (+)-**11** were used as versatile intermediates for preparing *carba-N-ribonucleosides* via Hoffman rearrangement⁶ as well as for the generation of variety of *carba-C-ribonucleosides* like **1** and **2**. We are continuing our work by incorporation of the latter into modified nucleic acid analogues.

EXPERIMENTAL. General. Operations were carried out in an oven-dried glassware assembled under nitrogen atmosphere when necessary. Solvents were dried according to known methods. Lithium azide was prepared as described previously¹⁹ and dried at 100 °C *in vacuo* over P₄O₁₀. Dimethyl 3-chloro-2-pentenedioate (DMCP) was prepared by literature procedure.¹⁹ Flash chromatography was carried out on Silica gel 60 (40-63 μm, Merck) and thin-layer chromatography on precoated plates Silica gel 60 F₂₄₅ (Merck). The spots were visualised by irradiation with UV light (254 nm) or by spraying with 10% H₂SO₄ in ethanol, and heating. Optical rotations were measured on a Perkin-Elmer 241MC polarimeter. Melting points (m.p.) were determined on a Kofler apparatus and are uncorrected. Infrared spectra were obtained using a Bio-Rad FTS 15/80 spectrophotometer. ¹H (299.94 MHz, internal Me₄Si), ¹³C NMR (75.43 MHz, internal CDCl₃), and NOESY spectra were recorded on Varian UNITY+300 instrument for solutions in CDCl₃ if not stated otherwise. Chemical shifts and coupling constants were obtained from first order analysis of the spectra. The spectra were assigned by means of the corresponding ¹H-¹H and ¹³C-¹H chemical correlated spectra. Mass spectra were recorded on a VG Autospec Q spectrometer.

[(1*R*,2*S*,3*R*,4*R*)-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)cyclopentyl]methanol (7). A mixture of monobutyrate (-)-**5** (88.70 g, 0.326 mol), trityl chloride (95.33 g, 0.342 mol), Et₃N (55 mL, 0.392 mol), and DMAP (1.50 g) in dry 1,2-dichloroethane (500 mL) was stirred at 60 °C for 4 h and then cooled to r.t. After washing with water (3 \times 800 mL) and concentration, the residue was treated with K₂CO₃ (45.01 g, 0.326 mol) in methanol (500 mL) for 5 h. The insoluble material was filtered off and the filtrate concentrated. The residue was partitioned between Et₂O (800 mL) and water (400 mL). The organic layer was dried (MgSO₄) and concentrated to afford **7** as an amber coloured stiff syrup in a quantitative yield (149.25 g, 103%). An analytical sample was purified by flash chromatography (petrolether/EtOAc 2:1) to give **7** as a colourless syrup. $[\alpha]_{\text{D}}^{25} = +16.0$ (*c* 3.0, CHCl₃). ¹H NMR δ 1.27 (m, 1H, H-5a), 1.26 and 1.48 (2s, 6H, CMe₂), 2.06 (br s, 1H, OH), 2.15 (m, 1H, H-5b), 2.19 (m, H, H-4), 2.38 (m, 1H, H-1), 3.01 and 3.23 (2dd, *J* = 8.9, 7.4, 5.7 Hz, 2H, CH_aH_bOTr), 3.50 and 3.57 (2dd, *J* = 10.6, 6.7, 5.7 Hz, 2H, CH_aH_bOH), 4.27 (m, 2H, H-2,3), 7.21 and 7.43 (2m, 15H, CPh₃). ¹³C NMR δ 25.11 and 27.57 (CMe₂), 31.51 (C-5), 45.40 (C-4), 47.78 (C-1), 64.74 and 64.94 (CH₂OH, CH₂OCO), 83.20 and 83.38 (C-2,3), 86.34 (CPh₃), 112.45 (CMe₂), 126.90, 127.72, 128.67 and 144.06 (CPh₃). *Anal.* Calcd for C₂₉H₃₂O₄ (444.576): C, 78.35; H, 7.26. Found: C, 78.12; H, 7.37.

(1*S*,2*S*,3*R*,4*R*)-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)cyclopentanecarbonitrile (9a). *Method A:* To a mixture of PCC (6.27 g, 0.03 mol) in dry CH₂Cl₂ (40 mL) was added a solution of **7** (9.00 g, 20 mol) in CH₂Cl₂ (15 mL). The reaction mixture was stirred for 4 hours at r.t., diluted with Et₂O (200 mL) and filtered through Florisil. The concentrated residue was dissolved in MeOH (65 mL) and stirred with *N,N*-dimethylhydrazine (2.13 mL, 0.028 mol) for 2 h. The solution of hydrazone was then added dropwise to magnesium monoperoxyphthalate hexahydrate (37 g, approx. 0.064 mol) suspended in MeOH (65 mL) at 0 °C; stirring was continued at this temperature for 10 min. Et₂O (500 mL) and water (500 mL) were added, and the organic layer was separated and washed with water (260 mL) and brine (160 mL). The dried organic layer was evaporated and crystallized from MeOH to yield colourless crystals (4.54 g, 51%). M.p. 141–143 °C. $[\alpha]_{\text{D}}^{22} = -21.0$ (*c* 0.4, CHCl₃). IR (KBr) 2243 (CN) cm⁻¹. ¹H NMR δ 1.26 and 1.46 (2s, 6H, CMe₂), 1.90 (m, 1H, H-5a), 2.43 (m, 2H, H-5b,4), 2.85 (dt, *J* = 7.8, 4.4 Hz, 1H, H-1), 3.17 and 3.23 (2dd, *J* = 9.5, 6.6, 6.2 Hz, 2H, CH_aH_bOTr), 4.38 (dd, *J* = 6.1, 2.4 Hz, 1H, H-3), 4.62 (dd, *J* = 6.1, 4.4 Hz, 1H, H-2), 7.28 and 7.43 (2m, 15H, CPh₃). ¹³C NMR δ 24.64 and 27.04 (CMe₂), 31.89 (C-5), 35.01 (C-1), 45.46 (C-4), 63.26 (CH₂OTr), 82.72 (C-3), 83.52 (C-2), 86.71 (CPh₃), 112.58 (CMe₂), 120.65, 127.06, 128.57 and 143.69 (CPh₃). *Anal.* Calcd for C₂₉H₂₉NO₃ (439.558): C, 79.24; H, 6.65; N, 3.19. Found: C, 79.39; H, 6.79; N, 2.88.

Method B: Trifluoroacetic anhydride (22 mL, 0.156 mol) was added dropwise to a stirred solution of **12** (62.00 g, 0.135 mol) and pyridine (22 mL, 0.271 mol) in THF (190 mL) at a temperature below 0 °C. The mixture was stirred at r.t. for 2 h, concentrated, and partitioned between EtOAc (500 mL) and sat. aq. NaHCO₃ (300 mL). Organic phase was washed with water (300 mL), brine (500 mL), and dried (Na₂SO₄). Concentration

gave a crude product (60.01 g) which was crystallised from cold MeOH (-15 °C) to give **9a** (59.38 g, 99.5%) as colourless crystals identical to that prepared by method A.

***N*-{[(1*S*,2*S*,3*R*,4*R*)-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)cyclopentyl]methyl} acetamide (10).** *Method A:* A mixture of **7** (74.62 g, 0.168 mol), NaOAc (4.13 g), and PCC (54.27 g, 0.252 mol) in dry CH₂Cl₂ (420 mL) was stirred for 4 h, diluted with Et₂O (1 L), the solvent decanted, and the black solid washed with Et₂O (500 mL). After filtration through Florisil and concentration, the residue was boiled under reflux in methanol (500 mL) with hydroxylammonium chloride (16.93 g, 0.244 mol) for 1 h. The concentrated residue was partitioned between Et₂O (2 L) and water (1.5 L), organic layer dried (MgSO₄) and concentrated to 1/3 of its volume. This solution was added to a mixture of Et₂O (250 mL) and LiAlH₄ (8.50 g) at such a rate that the reaction mixture boiled gently (1 h) and then stirred for additional 3 h. The excess LiAlH₄ was decomposed by careful addition of 1 M NaOH (25 mL) and water (10 mL). The white precipitate was removed by filtration and washed with CH₂Cl₂ (200 mL). The combined filtrates were dried (MgSO₄) and concentrated. The residue was stirred with Ac₂O (15.8 mL, 0.168 mol), Et₃N (23.4 mL, 0.168 mol), and DMAP (0.30 g) in dry MeCN (350 mL) for 3.5 h. The mixture was concentrated and partitioned between CH₂Cl₂ (1.5 L) and sat. aq. NaHCO₃ (1 L). The organic layer was washed with water (1 L), brine (1 L), and dried (Na₂SO₄). The crude **10** was purified by a short-path chromatography (Et₂O, then CH₂Cl₂/MeOH 10:1), and crystallised from Et₂O to give pure **10** (35.95 g, 44%) as white crystals. M.p. 174–175 °C. $[\alpha]_D^{25} = -0.85$ (*c* 2.0, CHCl₃). IR (KBr) 3426 (NH), 1675 (CO) cm⁻¹. ¹H NMR (CDCl₃) δ 1.23 (m, 1H, H-5a), 1.27 and 1.49 (2s, 6H, CMe₂), 1.97 (s, 3H, COCH₃), 2.00 (m, 1H, H-5b), 2.14 (m, 1H, H-4), 2.37 (m, 1H, H-1), 3.05 and 3.22 (2dd, *J* = 9.0, 7.1, 5.7 Hz, 2H, CH_aH_bOTr), 3.14 (ddd, *J* = 13.2, 9.0, 4.6 Hz, 1H, CH_aH_bNH), 3.37 (dt, *J* 13.2, 5.4 Hz, 1H, CH_aH_bNH) 4.16 (dd, *J* = 7.1, 6.1 Hz, 1H, H-3), 4.28 (dd, *J* = 7.1, 4.8 Hz, 1H, H-2), 5.78 (m, 1H, NH), 7.26 and 7.42 (2m, 15H, CPh₃). ¹³C NMR δ 23.22 (COCH₃), 25.16 and 27.61 (CMe₂), 32.82 (C-5), 42.75 (CH₂NH), 44.99 (C-1), 45.27 (C-4), 64.76 (CH₂OTr), 83.18 (C-3), 84.70 (C-4), 86.36 (CPh₃), 112.71 (CMe₂), 126.92, 127.72, 128.63 and 143.97 (CPh₃), 170.16 (CO). *Anal.* Calcd for C₃₁H₃₅NO₄ (485.630): C, 76.67; H, 7.26; N, 2.88. Found C, 76.39; H, 7.34; N, 2.81.

Method B: A solution of **9a** (1.00 g, 2.27 mmol) in dry THF (2 mL) was slowly added to a mixture of trifluoroacetoxyborohydride prepared *in situ* from CF₃CO₂H (0.25 mL, 3.18 mmol) and NaBH₄ (1.13 g, 3.40 mmol) in THF (0.5 mL) at 0 °C. After addition the mixture was stirred at r.t. for 1 day and then cooled to 0 °C. The reaction was quenched with water (0.1 mL). The concentrated residue was partitioned between Et₂O (15 mL) and water (15 mL). Organic phase was washed with sat. aq. NH₄Cl (10 mL), dried (Na₂SO₄), and concentrated. The residue was treated with Ac₂O (0.26 mL, 2.8 mmol), Et₃N (0.39 mL, 2.8 mmol), and DMAP (8 mg) in dry MeCN (6 mL) at r.t. for 20 h and then partitioned between Et₂O (30 mL) and sat. aq. NH₄Cl (20 mL). Organic phase was washed with water (2 × 20 mL), brine (20 mL), and dried (Na₂SO₄). The concentrated product was crystallised from Et₂O to give **10** (0.69 g, 63%) as colourless crystals identical to that prepared by method A.

Method C: To a solution of BH_3 in THF (1 M, 46 mL) was added the amide **12** (6.00 g, 13.1 mmol) at 0 °C. The solution was boiled under reflux overnight, cooled to 0 °C and treated with 3 M HCl (10 mL). 2 M NaOH was added to neutralise the solution and the organic layer was separated. The aqueous layer was extracted with Et_2O (50 mL). After drying (Na_2SO_4), the solvent was concentrated. The residue was treated with Ac_2O (1.6 mL, 17.0 mmol), Et_3N (2.4 mL, 17.0 mmol) and DMAP (25 mg) in dry MeCN (30 mL) at r.t. for 6 h and then partitioned between Et_2O (160 mL) and sat. aq. NH_4Cl (100 mL). Organic phase was washed with water (2×100 mL), brine (100 mL), and dried (Na_2SO_4). Flash chromatography of the concentrated residue (Et_2O , then EtOAc/MeOH 10:1) furnished **10** (5.16 g, 81%) as colourless crystals identical to that prepared by method A.

(1*R*,2*S*,3*R*,4*R*)-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)cyclopentane-carboxamide (12). Lactone (+)-**11** (34.53 g, 0.174 mol) was treated with methanolic NH_3 (27%, 300 mL) at r.t. overnight and the solution was concentrated. Trityl chloride (53.42 g, 0.192 mol), Et_3N (34.0 mL, 0.244 mol), and DMAP (0.80 g) were added to the residue in dry MeCN (270 mL). After stirring at r.t. for 4 h the mixture was filtered, concentrated, and partitioned between EtOAc (600 mL) and water (400 mL). Organic phase was washed with brine (350 mL) and dried (Na_2SO_4). Concentration afforded a crude product which was crystallised from cyclohexane to give **12** (64.50 g, 71%) as colourless needles. M.p. 154–155 °C. The mother liquid was concentrated and purified by flash chromatography (petroleum ether/ EtOAc 3:1, then EtOAc) to yield another portion of **12** (5.31 g, 6%); total yield 69.81 g, 77%. $[\alpha]_{\text{D}}^{22} = -11.8$ (c 0.4, CHCl_3). IR (KBr) 1690 (CO) cm^{-1} . ^1H NMR (CDCl_3) 1.28 and 1.51 (2s, 6H, CMe_2), 1.83 (dt, $J = 13.3, 11.4$ Hz, 1H, H-5a), 2.29 (dt, $J = 13.3, 6.8$ Hz, 1H, H-5b), 2.40 (m, H, H-4), 2.73 (dt, $J = 11.6, 6.7$ Hz, 1H, H-1), 3.06 and 3.24 (dd, $J = 9.0, 7.2, 5.9$ Hz, 2H, $\text{CH}_a\text{H}_b\text{OTr}$), 4.29 (dd, $J = 6.8, 4.4$ Hz, 1H, H-3), 4.59 (t, $J = 6.7$, 1H, H-2), 5.30 and 5.63 (2 br s, 2H, CONH_aH_b), 7.22, 7.29 and 7.42 (3m, 15H, CPh_3). ^{13}C NMR δ 25.06 and 27.61 (CMe_2), 31.64 (C-5), 45.04 (C-4), 51.04 (C-1), 64.51 (CH_2OTr), 82.82 (C-3), 83.12 (C-2), 86.44 (CPh_3), 113.00 (CMe_2), 126.96, 127.78, 128.68 and 143.97 (CPh_3), 175.04 (CO). *Anal.* Calcd for $\text{C}_{29}\text{H}_{31}\text{NO}_4$ (457.575): C, 76.12; H, 6.83; N, 3.06. Found: C, 76.07; H, 6.91; N, 3.06.

Methyl 3-[(1*S*,2*S*,3*R*,4*R*)-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)cyclopentyl]-1*H*-pyrazole-5-carboxylate (15). A mixture of **10** (44.70 g, 9.68 mmol), anhydrous NaOAc (4.66 g), and $\text{CCl}_4/\text{glacial AcOH}$ (1:1, 60 mL) was cooled on an ice-bath, treated with N_2O_4 (8.5 mL), and stirred for 2 h at 0 °C. Then it was poured over ice-water (150 g)/6 M NaOH (100 mL). The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (2×80 mL). The combined organic layers were washed with sat. aq. NaHCO_3 (80 mL), dried (Na_2SO_4), filtered, and the filtrate concentrated to yield the *N*-nitrosoacetamide derivative **13** as a light green syrup: IR (neat) 1732 (CO), 1505 (NO) cm^{-1} .

The above compound was dissolved in Et_2O (40 mL) and mixed with an ice-cold solution of KOH (7.7 g) in water (16 mL). The mixture was vigorously stirred at 0 °C for

2 h, after which the IR spectrum of the Et₂O layer showed the absence of the band at 1505 cm⁻¹, replacing it by a strong band at 2055 cm⁻¹ (CHN₂). The mixture was diluted with Et₂O (50 mL), washed with water (100 mL, then 50 mL), and dried rapidly first over KOH pellets followed by decantation onto MgSO₄.

A solution of diazo compound **14** was directly decanted in a solution of methyl propiolate (0.8 mL, 9.57 mmol) in Et₂O (8 mL). The mixture was stirred at r.t. overnight. Flash chromatography of the concentrated residue (CH₂Cl₂, then EtOAc) furnished **15** (3.37 g, 65 %) as a white foam. $[\alpha]_D^{21} = -28.8$ (*c* 0.6, CHCl₃). IR (film) 1729 (CO) cm⁻¹. ¹H NMR (CDCl₃) δ 1.30 and 1.55 (2s, 6H, CMe₂), 1.78 (m, 1H, H-5a'), 2.51 (m, 2H, H-5b', 4'), 3.05 and 3.20 (2dd, *J* = 9.0, 6.8, 5.6 Hz, 2H, CH_aH_bOTr), 3.29 (dt, *J* = 6.4, 11.2 Hz, 1H, H-1'), 3.90 (s, 3H, CO₂Me), 4.39 (dd, *J* = 6.7, 6.8 Hz, 1H, H-3'), 4.57 (dd, *J* = 6.6, 6.3 Hz, 1H, H-2'), 6.64 (s, 1H, H-4), 7.25 and 7.41 (2m, 15H, CPh₃), 10.90 (br s, 1H, NH). ¹³C NMR δ 25.06 and 27.54 (CMe₂), 34.22 (C-5'), 43.50 (C-1'), 45.40 (C-4'), 52.03 (CO₂Me), 64.59 (CH₂OTr), 82.89 (C-3'), 85.54 (C-2'), 86.43 (CPh₃), 105.96 (C-4), 112.88 (CMe₂), 126.93, 127.75, 128.63 and 143.96 (CPh₃), 139.19 and 150.35 (C-3,5), 161.40 (CO₂Me). HRMS: *m/z* M⁺ calcd for C₃₃H₃₄N₂O₅ 538.247, found 538.247. *Anal.* Calcd for C₃₃H₃₄N₂O₅ (538.65): C, 73.59; H, 6.36; N, 5.20. Found: C, 73.57; H, 6.52; N, 5.11.

3-[(1*S*,2*S*,3*R*,4*R*)-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)cyclopentyl]-1*H*-pyrazole-5-carboxamide (16**).** Ester **15** (0.50 g, 0.93 mmol) was treated with methanolic NH₃ (25%, 5 mL) in a sealed tube at 60 °C overnight. Flash chromatography of the concentrated residue (petrolether/EtOAc 2:1, then CH₂Cl₂/MeOH 10:1) furnished **16** (0.346 g, 71%) as a white foam. $[\alpha]_D^{22} = -31.5$ (*c* 0.6, CHCl₃). IR (KBr) 1667 (CO) cm⁻¹. ¹H NMR (CDCl₃) δ 1.29 and 1.54 (2s, 6H, CMe₂), 1.77 (m, 1H, H-5a'), 2.47 (m, 2H, H-5b', 4'), 3.08 and 3.22 (2dd, *J* = 9.0, 6.6, 5.4 Hz, 2H, CH_aH_bOTr), 3.25 (m, 1H, H-1'), 4.38 (dd, *J* = 6.9, 3.7 Hz, 1H, H-3'), 4.46 (t, *J* = 6.6 Hz, 1H, H-2'), 5.91 and 6.84 (2br s, 2H, CONH_aH_b), 6.60 (s, 1H, H-4), 7.25 and 7.43 (2m, 15H, CPh₃), 11.37 (br s, 1H, NH). ¹³C NMR δ 25.12 and 27.58 (CMe₂), 33.77 (C-5'), 42.77 (C-1'), 45.14 (C-4'), 64.42 (CH₂OTr), 82.84 (C-3'), 85.64 (C-2'), 86.51 (CPh₃), 103.42 (C-4), 113.18 (CMe₂), 127.00, 127.79, 128.60 and 143.89 (CPh₃), 145.47 and 147.18 (C-3,5), 164.05 (CO). HRMS: *m/z* M⁺ calcd for C₃₂H₃₃N₃O₄ 523.247. Found 523.248. *Anal.* Calcd for C₃₂H₃₃N₃O₄ (523.63): C, 73.40; H, 6.35; N, 8.02. Found C, 73.53; H, 6.42; N, 7.79.

3-[(1*S*,2*S*,3*R*,4*R*)-2,3-(Dihydroxy)-4-(hydroxymethyl)cyclopentyl]-1*H*-pyrazole-5-carboxamide (1**).** A mixture of **16** (0.110 g, 0.21 mmol) in 60% aq. AcOH (8 mL) was stirred at r.t. overnight, diluted with water (8 mL) and filtered to remove TrOH. The filtrate was freeze dried to yield fluffy compound **1** (0.048 g, 96%). $[\alpha]_D^{22} = -63.6$ (*c* 0.55, H₂O). IR (KBr) 1657 (CO) cm⁻¹. ¹H-NMR (D₂O) δ 1.40 (ddd, *J* = 12.7, 11.2, 8.2, 1H, H-5a'), 2.21 (m, 1H, H-4'), 2.33 (dt, *J* = 12.7, 8.2 Hz, 1H, H-5b'), 3.28 (dt, *J* = 11.0, 8.4 Hz, 1H, H-1'), 3.61 (2dd, *J* = 11.2, 6.4, 6.4 Hz, 2H, CH₂OH), 3.86 (dd, *J* = 5.5, 3.3 Hz, 1H,

H-3'), 4.01 (dd, $J = 8.8, 5.5$ Hz, 1H, H-2'), 6.71 (s, 1H, H-4). ^{13}C NMR δ 29.03 (C-5'), 39.43 (C-1'), 45.37 (C-4'), 62.70 (CH_2OH), 72.86 (C-3'), 76.75 (C-4'), 102.56 (C-4), 143.96 and 147.51 (C-3,5), 165.74 (CO). *Anal.* Calcd for $\text{C}_{10}\text{H}_{13}\text{N}_3\text{O}_4 \cdot 0.3 \text{H}_2\text{O} \cdot 0.15 \text{CH}_3\text{CO}_2\text{H}$ (255.65): C, 48.39; H, 6.39; N, 16.44. Found C, 48.24; H, 6.30; N, 16.56.

5-[(1*S*,2*S*,3*R*,4*R*)-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)cyclopentyl]-1*H*-tetrazole (17a). A mixture of **9a** (40.00 g, 91.0 mmol), LiN_3 (13.37 g, 273.0 mmol), and $\text{CF}_3\text{CO}_2\text{H}$ (13.9 mL, 182.0 mmol) in pyridine (160 mL) was boiled under reflux for 4 h and concentrated. The residue was partitioned between EtOAc (500 mL) and 1% HCl (500 mL). Organic phase was washed with brine (400 mL) and dried (Na_2SO_4). Concentration yielded a mixture of nitrile **9a** and tetrazole **17a** (43.73 g). Crystallization from ether gave **17a** (22.50 g, 51%) as a light pinky coloured solid. The concentrated mother liquid was purified by flash chromatography (petrolether/EtOAc 4:1, then EtOAc) to give **9a** (4.47 g, 11%) and **17a** (11.31 g, 26%); 77% overall yield of **17a**. An analytical sample (m.p. 142–143 °C) was obtained by crystallization from MeCN. $[\alpha]_{\text{D}}^{22} = -21.0$ (c 1.0, CHCl_3). ^1H NMR (CDCl_3) δ 1.27 and 1.52 (2s, 6H, CMe_2), 2.05 (m, 1H, H-5a'), 2.60 (m, 2H, H-5b',4'), 3.05 and 3.25 (2dd, $J = 9.0, 7.1, 5.6$ Hz, 2H, $\text{CH}_a\text{H}_b\text{OTr}$), 3.53 (m, 1H, H-1'), 4.42 (dd, $J = 6.6, 3.5$ Hz, 1H, H-3'), 4.74 (t, $J = 6.5$ Hz, 1H, H-2'), 7.24 and 7.34 (2m, 15H, CPh_3). ^{13}C NMR δ 24.97 and 27.42 (CMe_2), 33.32 (C-5'), 41.11 (C-1'), 45.30 (C-4'), 64.20 (CH_2OTr), 82.79 (C-3'), 84.46 (C-2'), 86.68 (CPh_3), 113.42 (CMe_2), 127.07, 127.85, 128.57 and 143.73 (CPh_3), 157.81 (C-5). *Anal.* Calcd for $\text{C}_{29}\text{H}_{30}\text{N}_4\text{O}_3$ (482.587): C, 72.18; H, 6.27; N, 11.61. Found: C, 72.13; H, 6.32; N, 11.70.

Methyl {5-[(1*S*,2*S*,3*R*,4*R*)-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)cyclopentyl]-4-methoxycarbonyl-1*H*-pyrazolyl-3}acetate (20a). A mixture of tetrazole **17a** (25.00 g, 51.8 mmol), Et_3N (10.1 mL, 72.5 mmol), and DMCP (11.97 g, 61.2 mmol) in dry THF (150 mL) was stirred at -5 °C for 1 day, filtered, and concentrated. The residue was partitioned between EtOAc, washed with water (450 mL), brine (450 mL), dried (MgSO_4), and concentrated. The obtained mixture (**18a/19a** 20:80; determined with ^1H NMR from the ratio of respective olefine protons in CDCl_3) was boiled under reflux in xylene (250 mL) for 4 h and then concentrated. Flash chromatography (gradient of petrolether (75–0%) in EtOAc) gave **20a** (22.79 g, 72%) as a light brown coloured foam. $[\alpha]_{\text{D}}^{21} = -23.5$ (c 1.0, CHCl_3). ^1H NMR (CDCl_3) δ 1.27 and 1.52 (2s, 6H, CMe_2), 2.05 (m, 1H, H-5a'), 2.51 (m, 2H, H-5b',4'), 3.01 and 3.23 (2dd, $J = 8.8, 7.1, 5.5$ Hz, 2H, $\text{CH}_a\text{H}_b\text{OTr}$), 3.53 (m, 1H, H-1'), 4.44 (dd, $J = 6.6, 4.0$ Hz, 1H, H-3'), 4.93 (t, $J = 6.1$ Hz, 1H, H-2'), 7.24 and 7.34 (2m, 15H, CPh_3). ^{13}C NMR δ 24.97 and 27.42 (CMe_2), 33.32 (C-5'), 41.11 (C-1'), 45.30 (C-4'), 64.20 (CH_2OTr), 82.79 (C-3'), 84.46 (C-2'), 86.68 (CPh_3), 113.42 (CMe_2), 127.07, 127.85, 128.57 and 143.73 (CPh_3), 157.81 (C-5). *Anal.* Calcd for $\text{C}_{29}\text{H}_{30}\text{N}_4\text{O}_3$ (482.587): C, 72.18; H, 6.27; N, 11.61. Found: C, 72.13; H, 6.32; N, 11.70.

2-{5-[(1*S*,2*S*,3*R*,4*R*)-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)cyclopentyl]-4-methoxycarbonyl-1*H*-pyrazolyl-3}acetamide (21). Pyrazolyl acetate **20a** (6.44 g, 10.5 mmol) was treated with methanolic NH₃ (27%, 80 mL) at r.t. overnight. The solution was concentrated and the residue partly decolourized by boiling with charcoal in EtOH and filtering the solution hot. Evaporation gave **21** as a yellow coloured foam (6.04 g, 96%). $[\alpha]_D^{21} = -25.6$ (*c* 1.6, CHCl₃). IR (KBr) 1712, 1682 (CO) cm⁻¹. ¹H NMR (CDCl₃) δ 1.27 and 1.53 (2s, 6H, CMe₂), 1.79 (m, 1H, H-5a'), 2.49 (m, 2H, H-5b',4'), 3.02 and 3.22 (2dd, *J* = 8.9, 7.2, 5.7 Hz, 2H, CH_aH_bOTr), 3.77 (dt, *J* = 6.2, 10.2 Hz, 1H, H-1'), 3.84 (s, 1H, CO₂Me), 3.85 and 3.91 (2d, *J* 15.2 Hz, 2H, CH_aH_bCONH₂), 4.42 (dd, *J* = 6.8, 4.2 Hz, 1H, H-3'), 4.94 (t, *J* 6.3 Hz, 1H, H-2'), 5.76 and 6.74 (2br s, 2H, CONH₄H₆), 7.23 and 7.41 (2m, 15H, CPh₃). ¹³C NMR δ 25.13 and 27.55 (CMe₂), 33.84 (CH₂CO), 35.56 (C-5'), 43.93 (C-1'), 45.96 (C-4'), 51.35 (CO₂Me), 64.87 (CH₂OTr), 82.94 (C-3'), 84.50 (C-2'), 86.34 (CPh₃), 108.70 (C-4), 112.33 (CMe₂), 126.87, 127.70, 128.66 and 144.06 (CPh₃), 144.06 and 153.44 (C-3,5), 165.19 (CO₂Me), 171.76 (CONH₂). HRMS: *m/z* M⁺ calcd for C₃₅H₃₇N₃O₆ 595.270. Found 595.268. *Anal.* Calcd for C₃₅H₃₇N₃O₆ (595.701): C, 70.57; H, 6.26; N, 7.05. Found C, 70.47; H, 6.29; N, 6.94.

3-[(1*S*,2*S*,3*R*,4*R*)-2,3-(Isopropylidenedioxy)-4-(trityloxymethyl)cyclopentyl]-1*H*-pyrazolo[4,3-*c*]pyridine-4,6(5*H*,7*H*)-dione (22). A mixture of monoamide **21** (400 mg, 0.67 mmol) in ethanolic sodium ethylate (1 M, 10 mL) was boiled under reflux for 1 h 45 min. The cold solution was diluted with water (10 mL), neutralised with AcOH (0.45 mL), and the precipitated product filtered to yield light gray coloured imide **22** (266 mg, 70%). An analytical sample (m.p. 230-231°C) was obtained by recrystallization from MeCN. $[\alpha]_D^{21} = -21.0$ (*c* 0.5, MeOH). IR (film) 1705 (CO) cm⁻¹. ¹H NMR (CDCl₃) δ 1.29 and 1.54 (2s, 6H, CMe₂), 2.15 (m, 1H, H-5a'), 2.51 (m, 2H, H-5b',4'), 3.11 and 3.32 (2dd, *J* = 9.0, 7.3, 5.1 Hz, 2H, CH_aH_bOTr), 3.60 (m, 1H, H-1'), 3.83 (s, 2H, CH₂), 4.53 (dd, *J* = 6.8, 4.1 Hz, 1H, H-3'), 4.93 (t, *J* = 6.8 Hz, 1H, H-2'), 7.25 and 7.43 (2m, 15H, CPh₃), 8.37 (br s, 1H, imide NH), 11.01 (br s, 1H, pyrazole NH). ¹³C NMR δ 25.47 and 27.93 (CMe₂), 32.08 (C-7), 35.62 (C-5'), 44.38 (C-1'), 47.09 (C-4'), 65.42 (CH₂OTr), 83.86 (C-3'), 85.40 (C-2'), 87.17 (CPh₃), 107.55 (C-3a), 113.48 (CMe₂), 128.01, 128.79, 129.51 and 145.19 (CPh₃), 148.55 (C-3), 151.11 (C-7a), 162.48 (C-4), 171.12 (C-6). *Anal.* Calcd for. C₃₄H₃₃N₃O₅ (563.599): C, 72.46; H, 5.89; N, 7.46. Found: C, 72.33; H, 6.02; N, 7.27.

3-[(1*S*,2*S*,3*R*,4*R*)-2,3-Dihydroxy-4-(hydroxymethyl)cyclopentyl]-1*H*-pyrazolo[4,3-*c*]pyridine-4,6(5*H*,7*H*)-dione (2). A mixture of **22** (50 mg, 0.08 mmol) in 60% aq. AcOH (2 mL) was stirred at r.t. overnight, diluted with water (2 mL), and filtered to remove TrOH. The filtrate was freeze dried to yield **2** (24 mg, 96%) as a fluffy compound. M.p. 214-215 °C (abs. EtOH). $[\alpha]_D^{21} = -48.6$ (*c* 0.5, H₂O). IR (KBr) 1704 (CO) cm⁻¹. ¹H-NMR (D₂O) δ 1.69 (m, 1H, H-5a'), 2.34 (m, 2H, H-5b',4'), 3.70 (m, 1H, H-1'), 3.72 and 3.84 (2dd, *J* = 11.2, 6.4, 6.4 Hz, 2H, CH_aH_bOH), 4.10 (dd, *J* = 5.4, 3.4

Hz, 1H, H-3'), 4.48 (dd, J 9.3, 5.6 Hz, 1H, H-2'). ^{13}C NMR ($\text{Me}_2\text{SO}_4\text{-}d_6$) δ 30.07 (C-5'), 32.031.86 (br C-7), 40.57 (br C-1'), 46.89 (C-4'), 63.28 (CH_2OH), 73.18 (C-3'), 75.55 (C-2'), 106.23 (C-3a), 148.60 and 149.33 (br C-3, C-7a) 162.18 (C-4), 171.33 (br C-6). FABMS m/z 282 (MH^+). *Anal.* Calcd for. $\text{C}_{34}\text{H}_{33}\text{N}_3\text{O}_5$ (563.599): C, 72.46; H, 5.89; N, 7.46. Found: C, 72.33; H, 6.02; N, 7.27.

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REFERENCES AND NOTES

1. Moser, H.E.; Hurley, H.H.; Sun, D.; Fox, K.R. Drugs Acting on Nucleic Acids and Nucleic Acid Processing Enzymes. In *Perspectives in Medicinal Chemistry*; Testa, B.; Kyburz, E.; Fuhrer, W.; Giger, R., Eds.; VHCA: Basel, 1993; pp. 275-297.
2. Mohar, B.; Štimac, A.; Kobe, J. *Nucleosides & Nucleotides* **1993**, *12*, 793.
3. Mohar, B.; Štimac, A.; Kobe, J. *Tetrahedron: Asymmetry* **1994**, *5*, 863.
4. Mohar, B.; Kobe, J. *Nucleosides & Nucleotides* **1997**, *16*, 1427.
5. Mohar, B.; Koomen, G.-J.; Kobe, J. *Synlett*, **1997**, 1467.
6. (a) Arita, M.; Adachi, K.; Ito, Y.; Sawai, H.; Ohno, M. *J. Am. Chem. Soc.* **1983**, *105*, 4049. (b) Arai, Y.; Hayashi, Y.; Yamamoto, M.; Takayama, H.; Koizumi, T. *J. Chem. Soc. Perkin Trans. I* **1988**, 3133. (c) Takayama, H.; Iyobe, A.; Koizumi, T. *J. Chem. Soc., Chem. Commun.* **1986**, 771. (d) Katagiri, N.; Haneda, T.; Watanabe, N.; Hayasaka, E.; Kaneko, C. *Chem. Pharm. Bull.* **1988**, *36*, 3867.
7. Sauer, D.R.; Schneller, S.W. *Synthesis* **1991**, 747.
8. Prhavic, M.; Kobe, J. *Nucleosides & Nucleotides* **1996**, *15*, 1779.
9. Corey, E.J.; Suggs, J. *Tetrahedron Lett.* **1975**, 2647.
10. Synthesis of racemic nitrile **9a**: Just, G.; Reader, G. *Tetrahedron Lett.* **1973**, *17*, 1525.
11. Fernández, R.; Gasch, C.; Lassaletta, J.-M.; Llera, J.-M. Vázquez, J. *Tetrahedron Lett.* **1993**, *34*, 141.
12. Synthesis of *O*-benzyl protected acetamide **10**: Boyer, S.; Leahy, J. *J. Org. Chem.* **1997**, *62*, 3976.
13. Carotti, A.; Campagna, F.; Ballini, R. *Synthesis*, **1979**, 56.
14. Brown, H.; Heim, P. *J. Org. Chem.* **1973**, *38*, 912.
15. Acton, E.M.; Ryan, K.J. In *Nucleic Acid Chemistry, Improved and New Synthetic Procedures, Methods, and Techniques*; Townsend, L.B.; Tipson, R.S., Eds.; Wiley: New York, 1978; Part 1, pp. 475-480.

16. Roeder, G. *Chem. Ber.* **1913**, *46*, 2563.
17. Hargreaves, M.K.; Pritchard, J.G.; Dave, H.R. *Chem. Rev.* **1970**, *70*, 439.
18. Polak, M.; Mohar, B.; Kobe, J.; Plavec J. *J. Am. Chem. Soc.* **1998**, *120*, 2508.
19. Hofman-Bang, N. *Acta Chem. Scand.* **1957**, *11*, 581.
20. Bryson, T.A.; Dolak, T.M. *Org. Synth. Coll.* vol. 6., 505.

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