Monatshefte für Chemie 130, 1167–1173 (1999)

Monatshefte für Chemie
Chemical Monthly

Synthesis of Triazenopyrazole Derivatives as Potential Inhibitors of HIV-1

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Summary. Ethoxymethylenemalononitrile and *bis*(methylthio)methylenemalononitrile were condensed with hydrazine hydrate to yield 5-aminopyrazole-4-carbonitrile (**3a**) and 5-amino-3-methylthiopyrazole-4-carbonitrile (**3b**), respectively. These compounds were treated with nitrous acid and coupled with different secondary amines to yield the triazenopyrazoles **4a–j**. 5-(3,3-Diethyl-1-triazeno)pyrazole-4-carbonitrile (**4c**) was transferred into its two regioisomeric 2-deoxyribose nucleosides **5a**,**b** which were subsequently hydrolyzed with H_2O_2/OH^- to give the corresponding carboxamides **6a**,**b**. All synthesized compounds were tested for biological activity against HIV-1 and *herpes simplex* virus, but only **4c** showed moderate activity against HIV-1 with $ED_{50} = 32\mu M$.

Keywords. Triazenopyrazoles; Nucleosides, convergent synthesis of; Nucleosides, 1-(5-triazeno)-pyrazole; Nucleosides, 2-(5-triazeno)pyrazole; Human immunodeficiency virus; Herpes simplex virus.

Synthese von Triazenopyrazolderivaten als potentielle Inhibitoren von HIV-1

Zusammenfassung. Ethoxymethylenmalonitril und *Bis*(methlthio)methylenmalonitril wurden mit Hydrazinhydrat zu 5-Aminopyrazol-4-carbonitril (**3a**) und 5-Amino-3-methyltiopyrazol-4-carbonitril (**3b**) umgesetzt. Behandlung mit salpetriger Säure und Kupplung mit verschiedenen sekundären Aminen ergab die Triazenopyrazole **4a–j**. 5-(3,3-Diethyl-1-triazeno)pyrazol-4-carbonitril (**4c**) wurde in seine beiden regioisomeren 2-Deoxyribonucleoside **5a**,**b** übergeführt, welche anschließend mit H_2O_2/OH^- zu den entsprechenden Carboxamiden **6a**,**b** hydrolysiert wurden. Alle hergestellten Verbindungen wurden auf ihre biologische Aktivität gegenüber HIV-1 und *Herpes simplex* getestet. Nur **4c** zeigte geringfügige Aktivität gegenüber HIV-1 ($ED_{50} = 32\mu M$).

Introduction

In recent years, the interest in finding anti-HIV drugs has been exploding, and the field is still rapidly growing. Among the most active compounds today are the non-nucleoside reverse transcriptase inhibitors NNRTIs, MKC-442 [1], and HEPT [2], but the nucleoside analogues *AZT* [3], ddC [4], and ddI [5] are also very potent inhibitors of HIV-1. Triazenopyrazoles are new in HIV research but have been

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widely tested in the field of cancer research where these compounds showed activity against L1210 leukemia in mice with low cytotoxicity [6]. In this paper we present the synthesis and biological activity of several triazenopyrazoles and some nucleoside analogues thereof. The background for this work came from an observation during random screening that 5-(3,3-diethyl-1-triazeno)pyrazole-4-carbonitrile showed a moderate effect on a HIV-1 infected cell strain. It was therefore decided to synthesize analogues of this compound. Furthermore, 5-(3,3-diethyl-1-triazeno)-pyrazole-4-carbonitrile was also chosen for testing of the corresponding nucleoside.

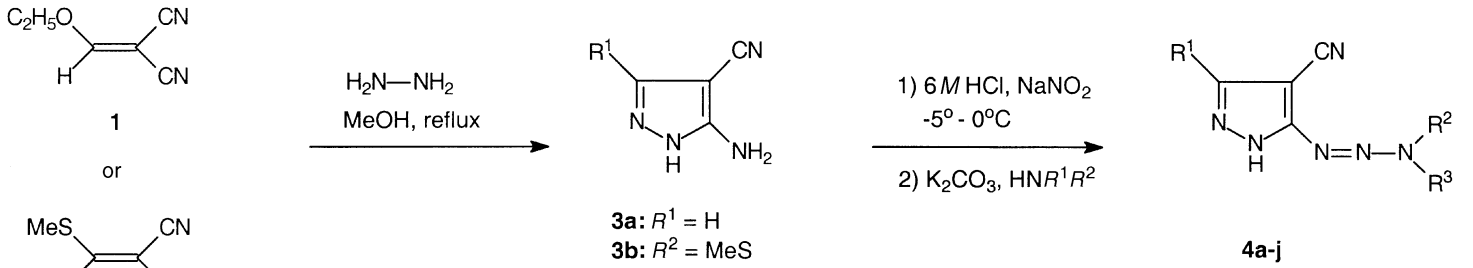
Results and Discussion

Ethoxymethylenemalononitrile (**1**) and hydrazinehydrate 85% were refluxed in methanol to give 5-aminopyrazole-4-carbonitrile (**3a**) [7] in 26% yield after recrystallization from water. Compound **3a** was then treated with HCl and $NaNO_2$ at 0°C to give the corresponding diazonium ion. After subsequent addition of a secondary amine dissolved in aqueous K_2CO_3, the products **4a–e** were obtained in 23–46% yield after extraction with chloroform.

Bis(methylthio)methylenemalononitrile (**2**) and hydrazinehydrate 85% were treated in the same manner to give 5-amino-3-methylthiopyrazole-4-carbonitrile (**3b**) [8] in 73% yield after recrystallization from methanol. Compound **3b** was then reacted with HCl and $NaNO_2$ at 0°C to give the intermediate diazonium ion which was not isolated but submitted directly to an excess of amine dissolved in aqueous K_2CO_3 to give **4f–j** in 42–70% yield. In the ^{13}C NMR spectra of all pyrazoles and triazenopyrazoles, a line broadening of C-3, C-4, and C-5 in the pyrazole ring is observed, indicating a tautomeric equilibrium between N1-H and N2-H.

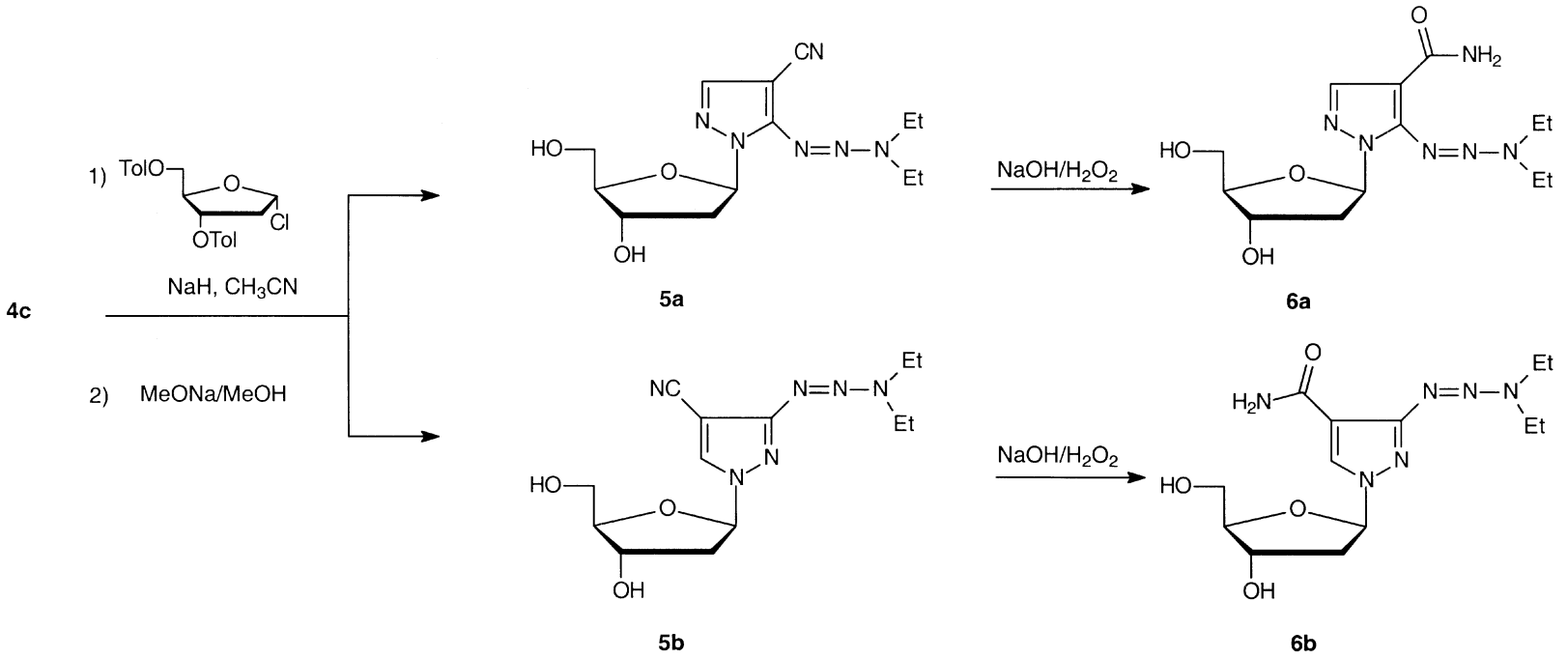
5-(3,3-Diethyl-1-triazeno)pyrazole-4-carbonitrile (**4c**) was glycosylated with 1-chloro-2-deoxy-3,5-di-O-*p*-tolyl-α-*D-erythro*-pentofuranose [9] using the sodium salt procedure [10] in which the sodium salt is generated *in situ* by treatment with sodium hydride in acetonitrile at room temperature. Deoxyribosylation of **4c** had occurred at both nitrogens of the pyrazole ring and produced a 1:1 mixture of the desired nucleoside products according to ^1H NMR. The mixture was not separated but treated with methanolic sodium methoxide at room temperature to give a mixture of the unprotected 2′-deoxy-β-*D*-ribofuranosides **5a** and **5b** which were separated using silica gel column chromatography. This gave **5a** in 23% and **5b** in 27% overall yield starting from **4c**. Assignment of the regioisomeric glycosylation and the anomeric configuration was performed by NOE and 2D NMR experiments. In an NOE experiment on **5a**, irradiation of H-2′α induced 6.6% NOE on H-1′ and 1.4% NOE on H-3′, whereas irradiation of H-2′β induced 2.4% NOE on H-1′ and 3.4% NOE on H-3′, thus confirming β-configuration. As expected, the 1-glycocylpyrazole **5a** did not show an NOE effect at H-3 upon irradiation of H-2′β. The assignments also agree with the shift differences of H-3 and H-1′ when compared with those previously reported for the corresponding riboside derivatives [11].

The nucleosides **5a**,**b** were subjected to alkaline hydrolysis in the presence of hydrogen peroxide according to the procedure reported by *Noller et al.* [12] to afford the corresponding 1-(2-deoxy-β-*D-erythro*-pentofuranosyl)-5-(3,3-diethyl-1-triazeno)-pyrazole-4-carboxamide (**6a**) and 2-(2-deoxy-β-*D-erythro*-pentofyranosyl)-5-(3,3-diethyl-1-triazeno)pyrazole-4-carboxamide (**6b**) in almost quantitative yields.



4	a	b	c	d	e	f	g	h	i	j
R^1	H	H	H	H	H	MeS	MeS	MeS	MeS	MeS
R^2	Me	Me	Et	Pr	Me	Me	Me	Et	Pr	Me
R^3	Me	Et	Et	Pr	Ph	Me	Et	Et	Pr	Ph

Scheme 1



Scheme 2

Compounds **4a–j**, **5a**, **5b**, **6a**, and **6b** were tested for their activity aganist HIV-1 cells. Only **4c** showed moderate activity against HIV-1 with $ED_{50} = 32\ \mu M$ which is the effective dose achieving 50% inhibition of HIV-1 antigen production in MT-4 cultures. The cytotoxic dose CD_{50} is $>200\ \mu M$ for **4c**. For all other compounds, only the lipophilic derivatives **4d**,**i–j** showed cytotoxicity against MT-4 cells at $100\ \mu M$ but without showing activity against HIV-1 at subtoxic concentrations. Upon testing against herpes simplex (strain *McIntyre*, African green monkey kidney cell line *Vero*), no activity was found.

Experimental

NMR spectra were recorded at 250 MHz for ^{1}H and 63 MHz for ^{13}C on a Bruker AC-250 FT spectrometer; δ values are given in ppm relative to *TMS* as internal standard. EI mass spectra were recorded on a Varian MAT 311A spectometer. The silica gel (0.004–0.063 mm) used for column chromatography was purchased from Merck. Analytical TLC was performed on Merck precoated 60 F_{254} plates.

5-Aminopyrazole-4-carbonitrile (**3a**) [7]

Ethoxymethylenemalononitril (**1**; 20 g, 167 mmol) and hydrazine hydrate 85% (8.2 g, 167 mmol) was refluxed in 100 cm^3 of EtOH for 3 h. The solvent was removed *in vacuo*, and the solid compound was recrystallized from H_2O to give **3a** as a yellow solid.

Yield: 4.7 g (26%); m.p.: 167–169°C (Ref.: [7]; 172°C); ^{1}H NMR (*DMSO*-d_6): $\delta = 6.03$ (br s, 2H, NH_2), 7.72 (br s, 1H, CH), 12.09 (br s, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 73.64$ (C-4), 115.19 (CN), 138.77 (C-3), 154.41 (C-5) ppm.

5-Amino-3-methylthiopyrazole-4-carbonitrile (**2**) [8]

Bis(methylthio)methylenemalononitril (**2**; 17 g, 0.1 mol) and hydrazine hydrate 85% (6 g, 0.12 mol) were refluxed in 200 cm^3 of MeOH for 3 h. The solvent was removed *in vacuo*, and the yellow solid was recrystallized from MeOH to give **3b** as colourless crystals.

Yield: 11.31 g (73%); m.p.: 147°C (Ref. [8]: 152°C); 1H NMR (*DMSO*-d_6): $\delta = 2.44$ (s, 3H, S-CH3), 6.43 (s, 2H, NH2), 11.95 (s, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 13.72$ (S-CH_3), 72.18 (C-4), 114.64 (CN), 147.70 (C-3), 154.1 (C-5) ppm.

General procedure for the preparation of **4a–j**

To a mixture of 5-aminopyrazole-4-carbonitrile (**3a**; 1.0 g, 9.35 mmol) or 5-amino-3-methylthiopyrazole-4-carbonitrile (**3b**; 1.86 g, 12 mmol) in 3 cm^3 conc. HCl and 3 cm^3 H_2O cooled to 0°C, a solution of $NaNO_2$ (1.05 g, 15.2 mmol) in 10 cm^3 H_2O was added. After stirring for additional 30 min, a mixture of the approriate amine (12 mmol) and K_2CO_3 (2.5 g, 18.1 mmol) in 25 cm^3 of H_2O was added. The reaction mixture was stirred at room temperature until TLC showed that all diazonium salt had disappeared. The reaction mixture was extracted with 3×75 cm^3 $CHCl_3$. The combined organic phases were washed with 3×30 cm^3 H_2O, dried over Na_2SO_4, and evaporated *in vacuo* to give the crude product which was washed with Et_2O/petroleum ether (65–70°C) (1:1, v/v) to give **4a–j** in 23–70% yield.

5-(3,3-Dimethyl-1-triazeno)pyrazole-4-carbonitrile (**4a**)

Yield: 603 mg (39%); light yellow solid; m.p.: 152–154°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 3.20$ (s, 3H, NCH_3), 3.54 (s, 3H, N-CH_3), 7.87 (br s, 1H, CH), 8.37 (br s, 1H, CH), 13.38 (br s, 1H, NH) ppm; ^{13}C

NMR (*DMSO*-d_6): $\delta = 36.20$ (N-CH_3), 43.30 (N-CH_3), 79.45 (C-4), 115.07 (CN), 136.59 (C-3), 142.60 (C-5) ppm; MS: $m/z = 164$ (M^+).

5-(3-Ethyl-3-methyl-1-triazeno)pyrazole-4-carbonitrile (**4b**)

Yield: 716 mg (43%); orange solid; m.p.: 112–116°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.31$ (t, 3H, $J = 7.0$ Hz, CH_3), 3.21 (s, 3H, N-CH_3), 3.84 (q, 2H, $J = 7.0$ Hz, CH_2), 7.92 (br s, 1H, CH), 8.41 (br s, 1H, CH), 13.40 (br s, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 13.19$ (CH_3), 34.45 (N-CH_3), 50.96 (CH_2), 80.01 (C-4), 115.11 (CN), 136.5 (C-3), 142.71 (C-5) ppm; MS: $m/z = 178$ (M^+).

5-(3,3-Diethyl-1-triazeno)pyrazole-4-carbonitrile (**4c**)

Yield: 825 mg (46%); ^{1}H NMR ($CDCl_3$): $\delta = 1.25$ (t, 3H, $J = 7.5$ Hz, CH_3), 1.39 (t, 3H, $J = 7.5$ Hz, CH_3), 3.81 (q, 4H, $J = 7.5$ Hz, 2 × NCH_2), 7.78 (s, 1H, H-3), 11.70 (br s, 1H, NH) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 10.55$ (CH_3), 13.75 (CH_3), 42.10 (NCH_2), 49.84 (NCH_2), 80.43 (C-4), 114.64 (CN), 140.21 (C-3), 157.63 (C-5) ppm.

5-(3,3-Dipropyl-1-triazeno)pyrazole-4-carbonitrile (**4d**)

Yield: 730 mg (36%); yellow solid; m.p.: 104–106°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 0.90$ (t, 6H, $J = 7.4$ Hz, 2 × CH_3), 1.65 (q, 2H, $J = 7.3$ Hz, CH_2), 1.76 (q, 2H, $J = 7.1$ Hz, CH_2), 3.70 (m, 4H, 2×N-CH_2), 13.39 (br s, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 10.95$ (CH_3), 11.39 (CH_3), 18.29 (CH_2), 21.25 (CH_2), 48.66 (N-CH_2), 56.37 (N-CH_2), 79.19 (C-4), 115.17 (CN), 136.50 (C-3), 142.10 (C-5) ppm; MS: $m/z = 220$ (M^+); $C_{10}H_{16}N_6$; calcd.: C 54.53, H 7.32, N 38.15; found: C 54.57, H 7.50, N 37.85.

5-(3-Methyl-3-phenyl-1-triazeno)pyrazole-4-carbonitrile (**4e**)

Yield: 485 mg (23%); red solid; m.p.: 158–162°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 3.69$ (s, 2H, N-CH_3), 7.23 (t, 1H, $J = 7.2$ Hz, H_{arom}), 7.46 (t, 2H, $J = 7.6$ Hz, H_{arom}), 7.68 (d, 2H, $J = 8.2$ Hz, H_{arom}) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 32.82$ (N-CH_3), 79.59 (C-4), 115.28 (CN), 117.25, 124.60, 129.22 (C_{arom}), 138.48 (C-3), 143.72 (C-5), 159.00 (C_{arom}) ppm; MS: $m/z = 226$ (M^+).

3-Methylthio-5-(3,3-dimethyl-1-triazeno)pyrazole-4-carbonitrile (**4f**)

Yield: 1.44 g (57%); yellow solid; m.p.: 152–154°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 2.54$ (s, 3H, S-CH_3), 3.23 (s, 3H, N-CH_3), 3.57 (s, 3H, N-CH_3), 13.48 (br s,1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 14.19$ (S-CH_3), 36.35 (N-CH_3), 43.56 (N-CH_3), 78.48 (C-4), 114.31 (CN), 148.78 (C-3), 156.79 (C-5) ppm; MS: $m/z = 210$ (M^+).

3-Methylthio-5-(3-ethyl-3-methyl-1-triazeno)pyrazole-4-carbonitrile (**4g**)

Yield: 1.80 g (67%); yellow powder; m.p.: 107–109°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.31$ (t, 3H, $J = 7.0$ Hz, CH_3), 2.54 (s, 3H, S-CH_3), 3.23 (s, 3H, N-CH_3), 3.87 (q, 2H, $J = 7.0$ Hz, CH_2), 13.52 (br s, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 9.44$ (CH_3), 13.11 (S-CH_3), 34.96 (N-CH_3), 51.33 (CH_2), 77.76 (C-4), 114.37 (CN), 149.44 (C-3), 156.47 (C-5) ppm; MS: $m/z = 224$ (M^+); $C_8H_{12}N_6S$; calcd.: C 42.84, H 5.39, N 37.47; found: C 43.05, H 5.02, N 37.44.

3-Methylthio-5-(3,3-diethyl-1-triazeno)pyrazole-4-carbonitrile (**4h**)

Yield: 1.20 g (42%); brown crystals; m.p.: 99–100°C; ^{1}H NMR (*DMSO*-d_6): $\delta = 1.19$ (t, 3H, $J = 7.0$ Hz, CH_3), 1.34 (t, 3H, $J = 7.0$ Hz, CH_3), 2.54 (s, 3H, S-CH_3), 3.82 (t, 4H, $J = 7.0$ Hz, 2

$\times NCH_2$), 13.51 (s, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 10.27$ (CH_3), 13.49 (CH_3), 13.90 (S-CH_3), 42.31 (CH_2), 49.65 (CH_2), 77.70 (C-4), 114.44 (CN), 149.48 (C-3), 156.69 (C-5) ppm; MS: $m/z = 238$ (M^+); $C_9H_{14}N_6S$; calcd.: C 45.36, H 5.92, N 35.26, S 13.45; found: C 45.32, H 6.04, N 35.44, S 13.43.

3-Methylthio-5-(3,3-dipropyl-1-triazeno)pyrazole-4-carbonitrile (**4i**)

Yield: 1.90 g (61%); light yellow crystals; m.p.: 108–110°C; ^1H NMR (*DMSO*-d_6): $\delta = 0.90$ (t, 6H, $J = 7.0$ Hz, 2 × CH_3), 1.66 (q, 2H, $J = 7.0$ Hz, CH_2), 1.78 (q, 2H, $J = 7.0$ Hz, CH_2), 2.52 (s, 3H, S-CH_3), 3.73 (m, 4H, 2 ×NCH_2), 13.49 (s, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 10.88$ (CH_3), 11.34 (CH_3), 13.89 (S-CH_3), 18.20 (CH_2), 21.11 (CH_2), 49.17 (N-CH_2), 56.80 (N-CH_2), 77.63 (C-4), 114.36 (CN), 149.50 (C-3), 156.57 (C-5) ppm; MS: $m/z = 266$ (M^+); $C_{11}H_{18}N_6S$; calcd.: C 49.60, H 6.81, N 31.55, S 12.04; found: C 49.56, H 6.93, N 31.66, S 11.77.

3-Methylthio-5-(3-methyl-3-phenyl-1-triazeno)pyrazole-4-carbonitrile (**4j**)

Yield: 2.30 g (70%); orange crystals; m.p.: 168–169°C; ^1H NMR (*DMSO*-d_6): $\delta = 2.61$ (s, 3H, S-CH_3), 3.70 (s, 3 H, N-CH_3), 7.26 (t, 1H, $J = 7.0$ Hz, H_{arom}), 7.47 (t, 2H, $J = 7.0$ Hz, H_{arom}), 7.67 (d, 2H, $J = 7.0$ Hz, H_{arom}), 13.93 (br s, 1H, NH) ppm; ^{13}C NMR (*DMSO*-d_6): $\delta = 14.67$ (S-CH_3), 33.18 (N-CH_3), 79.50 (C-4), 114.36 (CN), 117.52, 125.05, 129.16, 143.38 (C_{arom}), 147.94 (C-3), 157.43 (C-5) ppm; MS: $m/z = 272$ (M^+); $C_{12}H_{12}N_6S$; calcd.: C 52.06, H 4.55, N 30.36, S 11.58; found: C 52.23, H 4.52, N 30.79, S 11.44.

1-(2-Deoxy-β-D-erythro-pentofuranosyl)-5-(3,3-diethyl-1-triazeno)pyrazole-4-carbonitrile (**5a**) and *2-(2-deoxy-β-D-erythro-pentofuranosyl)-5-(3,3-diethyl-1-triazeno)pyrazole-4-carbonitrile* (**5b**)

To a stirred solution of **4c** (4.65 g, 24.3 mmol) in MeCN (150 cm^3), NaH (990 mg, 55–65% dispersed in mineral oil) was added under nitrogen at room temperature. After 4 h, 2-deoxy-3,5-di-O-*p*-tolyl-α-*D-erythro*-pentofuranosyl chloride (9.45 g, 24.3 mmol) was added in one portion, and stirring was continued for 2 h. The mixture was filtered through celite and evaporated to dryness. The residue was purified on a silica gel column using 10–40% Et_2O in petroleum ether (65–70°C) to afford a 1:1 mixture of the protected nucleosides as an hygroscopic pale yellow foam in 65% yield. To a solution of the protected nucleosides (8.60 g, 15.80 mmol) in dry MeOH (100 cm^3), NaOMe (2.16 g, 40 mmol) in 10 cm^3 dry MeOH was added, and the mixture was stirred at room temperature for 30 min. The reaction mixture was then neutralized with Dowex-50^+ resin and filtered. The filtrate was evaporated to dryness. The residual semisolid was chromatographed on a silica gel column using 1–2% MeOH in $CHCl_3$ to give **5a** in 27% and **5b** in 23% yield, respectively.

1-(2-Deoxy-β-D-erythro-pentofuranosyl)-5-(3,3-diethyl-1-triazeno)pyrazole-4-carbonitrile (**5a**)

Yield: 1.10 g (23%); faint yellow oil; ^1H NMR ($CDCl_3$): $\delta = 1.25$ (t, 3H, $J = 7.5$ Hz, CH_3), 1.41 (t, 3H, $J = 7.5$ Hz, CH_3), 2.42 (m, 1H, H-2′α), 2.79 (m, 1H, H-2′β), 3.76 (m, 2H, H-5′), 3.85 (m, 4H, 2 × NCH_2), 4.13 (m, 1H, H-4′), 4.25 (br s, 1H, OH-5′), 4.74 (m, 1H, H-3′), 6.66 (t, 1H, $J = 7.5$ Hz, H-1′), 7.70 (s, 1H, H-3) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 10.43$ (CH_3), 13.54 (CH_3), 40.44 (C-2′), 42.78 (NCH_2), 50.28 (NCH_2), 63.14 (C-5′), 72.04 (C-3′), 77.41 (C-4), 85.11 (C-4′), 88.57 (C-1′), 114.89 (CN), 142.65 (C-3), 154.59 (C-5) ppm; FAB MS (3-nitrobenzylalcohol): $m/z = 309$ (M^+H^+).

2-(2-Deoxy-β-D-erythro-pentofuranosyl)-5-(3,3-diethyl-1-triazeno)pyrazole-4-carbonitrile (**5b**)

Yield: 1.32 g (27%); foam; ^1H NMR ($CDCl_3$): $\delta = 1.21$ (t, 3H, $J = 7.5$ Hz, CH_3), 1.37 (t, 3H, $J = 7.5$ Hz, CH_3), 2.42 (m, 1H, H-2′α), 2.77 (m, 1H, H-2′β), 3.64 (m, 2H, H-5′), 3.80 (m, 4H, 2 ×

NCH_2), 4.08 (m, 1H, H-3′), 4.17 (br s, 1H, OH-5′), 4.63 (m, 1H, H-3′), 6.04 (t, 1H, $J = 6.0$ Hz, H-1′), 8.05 (s, 1H, H-3) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 10.48$ (CH_3), 13.59 (CH_3), 40.49 (C-2′), 41.55 (NCH_2), 49.29 (NCH_2), 62.36 (C-5′), 71.16 (C-3′), 81.64 (C-4), 88.15 (C-4′), 90.10 (C-1′), 114.14 (CN), 135.76 (C-3), 161.78 (C-5) ppm; FAB MS (3-nitrobenzylalchohol): $m/z = 309$ (M^+H).

5-(3,3-Diethyl-1-triazeno)pyrazole-4-carboxamide nucleosides **6a** and **6b**; *general procedure*

To a solution of **5a** or **5b** (1.0 g, 3.24 mmol) and NaOH (0.38 g, 9.72 mmol) in EtOH (95%, 30 cm^3) H_2O_2 (35%, 4 cm^3) was added. The mixture was stirred at 40–50°C for 3 days and then filtered. The filtrate was evaporated *in vacuo*, and the residue was purified on a silica gel using 0–3% MeOH in $CHCl_3$ to yield 0.92 g (87%) as an oil.

1-(2-Deoxy-β-D-erythro-pentofuranosyl)-5-(3,3-diethyl-1-triazeno)pyrazole-4-carboxamide (**6a**)

^{1}H NMR ($CDCl_3$): $\delta = 1.24$ (t, 3H, $J = 7.5$ Hz, CH_3), 1.36 (t, 3H, $J = 7.5$ Hz, CH_3), 2.39 (m, 1H, H-2′β), 2.80 (m, 1H, H-2′α), 3.80 (m, 6H, 2 × NCH_2, 2×H-5′), 4.11 (m, 1H, H-4′), 4.78 (m, 1H, H-3′), 6.00 (m, 1H, NH), 6.56 (t, 1H, $J = 6.2$ Hz, H-1′), 7.60 (br s, 1H, NH), 7.97 (s, 1H, H-3) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 10.37$ (CH_3), 14.11 (CH_3), 41.66 (C-2′), 42.45 (NCH_2), 50.02 (NCH_2), 63.30 (C-5′), 72.30 (C-3′), 87.03 (C-4′), 89.11 (C-1′), 106.84 (C-4), 142.27 (C-3), 147.09 (C-5), 164.89 (C=O) ppm; FAB MS (3-nitrobenzylalcohol): $m/z = 327$ ($M+H^+$).

2-(2-Deoxy-β-D-erythro-pentofyranosyl)-5-(3,3-diethyl-1-triazeno)pyrazole-4-carboxamide (**6b**)

^{1}H NMR ($CDCl_3$): $\delta = 1.21$ (m, 3H, CH_3), 1.33 (m, 3H, CH_3), 2.45 (m, 1H, H-2′), 2.74 (m, 1H, H-2′), 3.79 (m, 6H, 2 × NCH_2, H-5′), 4.13 (m, 1H, H-4′), 4.69 (m, 1H, H-3′), 5.24 (br s, 2H, OH-3′,OH-5′), 6.11 (m, 1H, H-1′), 6.55, 7.83 (2×s, 1H, NH_2), 8.23 (s, 1H, H-3) ppm; ^{13}C NMR ($CDCl_3$): $\delta = 10.18$ (CH_3), 13.92 (CH_3), 41.58 (C-2′, NCH_2), 49.81 (NCH_2), 62.89 (C-5′), 71.77 (C-3′), 88.95 (C-4′), 90.54 (C-1′), 109.09 (C-4), 133.04 (C-3), 155.99 (C-5), 165.52 (C=O) ppm; FAB MS (3-nitrobenzyl-alcohol): $m/z = 327$ ($M+H^+$).

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Received November 27, 1998. Accepted (revised) March 4, 1999