This article was downloaded by: [University of Toronto Libraries] On: 14 November 2014, At: 13:05 Publisher: Taylor & Francis Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



# Nucleosides, Nucleotides and Nucleic Acids

Publication details, including instructions for authors and subscription information: <u>http://www.tandfonline.com/loi/lncn20</u>

## A One-Pot Preparation of 1-Benzyl-2'deoxyinosine from ionized 2'-Deoxyinosine

Ki-Young Moon<sup>a</sup> & Yeong Shik Kim<sup>a</sup>

<sup>a</sup> Natural Products Research Institute, Seoul National University, 28 Yeonkun-Dong, Jongno-Ku, Seoul, 110-460, Korea E-mail: Published online: 05 Nov 2010.

To cite this article: Ki-Young Moon & Yeong Shik Kim (2000) A One-Pot Preparation of 1-Benzyl-2'deoxyinosine from ionized 2'-Deoxyinosine, Nucleosides, Nucleotides and Nucleic Acids, 19:7, 1135-1143, DOI: <u>10.1080/15257770008035036</u>

To link to this article: http://dx.doi.org/10.1080/15257770008035036

### PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the "Content") contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at <u>http://www.tandfonline.com/page/terms-and-conditions</u>

#### A ONE-POT PREPARATION OF 1-BENZYL-2'-DEOXYINOSINE FROM IONIZED 2'-DEOXYINOSINE

Ki-Young Moon\* and Yeong Shik Kim Natural Products Research Institute, Seoul National University, 28 Yeonkun-Dong, Jongno-Ku, Seoul 110-460, Korea. kmoon@yes.snu.ac.kr

**ABSTRACT:** A simple and one step synthetic method for the formation of 1-benzyl-2'deoxyinosine was developed by direct benzylation of ionized 2'-deoxyinosine. Treatment of 2'-deoxyinosine, in the presence of NaOH, with benzyl bromide in 2,2,2trifluoroethanol (TFE) or N,N-dimethylaetamide (DMA) gave 1-benzyl-2'-deoxyinosine in 35 % and 80 % yields, respectively.

#### **INTRODUCTION**

Nucleoside alkylation and aralkylation has been extensively studied to elucidate reactivity of nucleic acids.<sup>1,2</sup> Model studies of nucleoside reactions with benzylic electrophiles<sup>3-6</sup> have shown that site-selectivity is dependent on the reaction medium (solvent effect) and the leaving group of the electrophile. In dipolar aprotic solvents [e.g., N,N-dimethylacetamide (DMA) or N,N-dimethylformamide], benzylic electrophiles react predominantly with nucleoside pyrimidine-type ring-nitrogen sites. Solvent systems that can solubilize ions, such as aqueous based systems favour formation of aralkyl ions and these mainly modify exocyclic nucleoside sites.

Several studies have shown that the anionic form of guanosine is much more reactive than the neutral form of guanosine toward benzylic electrophiles.<sup>7,8</sup> Similar anionic forms and their altered reactivity of both uridine<sup>9</sup> and thymidine<sup>10</sup> and their reactivities have also been reported. We have previously reported that the reaction of the anion of 2'-deoxyguanosine with benzyl bromide in 2,2,2-trifluoroethanol (TFE) produced  $N^2$ -benzyl-2'-deoxyguanosine in high yield and with high selectivity. 7-

Benzylguanine was the only benzylated product formed in the reaction with the neutral nucleoside in TFE. However, the reaction of the anion of 2'-deoxyguanosine with benzyl bromide in DMA produced 1-and/or 7-position 2'-deoxyguanosine derivatives. These results indicated that the ionic state of 2'-deoxyguanosine and solvent polarity were the factors that determined the site of aralkylation with benzyl bromide.<sup>11</sup>

These studies have led us to extend these explorations to the nucleophilicity of the purine nucleoside, 2'-deoxyinosine (1), in various solvents with benzyl bromide. We report an efficient approach for the preparation of 1-benzyl-2'-deoxyinosine (4) from 1.

#### **EXPERIMENTAL SECTION**

Ultraviolet absorption spectra were determined on a Milton Roy SLM-AMINCO 3000 diode array spectrophotometer. <sup>1</sup>H NMR spectra were recorded on a Varian VXR 500S spectrometer equipped with Sun 4/110 data stations or a Varian XL200 instrument interfaced to an Advanced data system. Samples were dissolved in dimethyl- $d_6$  sulfoxide, and chemical shifts are reported as  $\delta$  values (ppm) downfield from tetramethylsilane (TMS) as an internal standard. Positive ion (+ve) fast atom bombardment (FAB) and high-resolution FAB mass spectra (MS) were obtained with a reversed-geometry VG Micromass ZAB-2F spectrometer interfaced to a VG 2035 data system. A mixture of dithiothreitol and dithioerythritol (1:1) was used as the FAB matrix. Sephadex LH-20 was purchased from Pharmacia, Biotechnology AB, Uppsala, Sweden. 2'-Deoxyinosine, most reagents and solvents were purchased from Aldrich Chemical Co., Inc., Milwaukee, WI, U.S.A.

#### Benzylation of 2'-deoxyinosine (1) in TFE.

To a stirred suspension of 2'-deoxyinosine (650 mg, 2.58 mmol) in 13 mL of TFE was added benzyl bromide (0.31 mL, 2.6 mmol) over 1 min. The reaction mixture was stirred at room temperature for 72 h. The resulting white suspension was evaporated *in vacuo* to give a white solid. The solid was dissolved in 60 mL of MeOH/H<sub>2</sub>O (1:1) and was loaded on a Sephadex LH-20 column (2.8 x 80 cm) eluted with MeOH/H<sub>2</sub>O (1:1) at 1 mL/min. UV absorption was checked continuously at 280 nm, and fractions (10 mL) were collected. 3,7-Dibenzylhypoxanthine (3) eluted in fractions 73-79 (35 mg, yield 4.3 %): UV pH 6.9  $\lambda_{min}$  239 nm,  $\lambda_{max}$  268 nm, pH 13  $\lambda_{max}$  268 nm; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>)

δ 8.75 (1H, s, 8-H), 8.44 (1H, s, 2-H), 7.26-7.44 (10H, m, 2C<sub>6</sub>H<sub>5</sub>), 5.58 (2H, s, 7-C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 5.42 (2H, s, 3-C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>); FAB<sup>+</sup>-MS *m/z* 317 ([C<sub>19</sub>H<sub>16</sub>N<sub>4</sub>O + H]<sup>+</sup>), 227 ([C<sub>12</sub>H<sub>10</sub>N<sub>4</sub>O + H]<sup>+</sup>); HRFAB<sup>+</sup>-MS calcd for C<sub>19</sub>H<sub>17</sub>N<sub>4</sub>O 317.1403, found 317.1425. Fractions 30-70 were pooled and evaporated to give a white solid. This solid was dissolved in 50 mL of MeOH/H<sub>2</sub>O (10:90) and was loaded on a Sephadex LH-20 column (2.8 x 80 cm) eluted with MeOH/H<sub>2</sub>O (10:90) at 1 mL/min. Under these chromatographic conditions, unreacted 2'-deoxyinosine eluted in fractions 30-66 (580 mg, yield 90 %). 7-Benzylhypoxanthine (**2**) eluted in 92-119 (30 mg, yield 5 %): UV pH  $6.9 \lambda_{min} 231 \text{ nm}, \lambda_{max} 253 \text{ nm}, pH 13 \lambda_{max} 261; ^{1}H NMR (DMSO-d<sub>6</sub>) \delta 12.31 (1H, br s, 1-$ H, exchanges with D<sub>2</sub>O), 8.38 (1H, s, 8-H), 7.96 (1H, s, 2-H), 7.26-7.36 (5H, m, C<sub>6</sub>H<sub>5</sub>), $<math>5.56 (2H, s, 7-C_6H_5CH_2); FAB<sup>+</sup>-MS m/z 227 ([C<sub>12</sub>H<sub>10</sub>N<sub>4</sub>O + H]<sup>+</sup>); HRFAB<sup>+</sup>-MS calcd$ for C<sub>12</sub>H<sub>11</sub>N<sub>4</sub>O 227.0930, found 227.0900.

#### Benzylation of 2'-deoxyinosine (1) in TFE containing NaOH.

To a stirred suspension of 2'-deoxyinosine (650 mg, 2.58 mmol) in 13 mL of TFE was added NaOH (103.2 mg, 2.58 mmol) at room temperature. When all NaOH was dissolved, the reaction was changed into the solution. Then, benzyl bromide (0.31 mL, 2.6 mmol) was added dropwise over 1 min. The reaction mixture was stirred at room temperature for 72 h (as the reaction was going on, the reaction mixture was changed into the white suspension). The resulting white suspension was evaporated in vacuo to give a crude solid. This solid was dissolved in 50 mL of MeOH/H<sub>2</sub>O (1:1) and was loaded on a Sephadex LH-20 column (2.8 x 80 cm) eluted with MeOH/H2O (1:1) at 1 mL/min. UV absorption was monitored continuously at 280 nm, and fractions (10 mL) were collected. Fractions 52-77 contained a mixture of 2'-deoxyinosine and 7-benzylhypoxanthine (2) were pooled and evaporated to give a white solid. 1-Benzyl-2'-deoxyinosine (4) eluted in fractions 83-136 (310 mg, yield 35 %): UV pH 1 λ<sub>max</sub> 252 nm, pH 6.9 λ<sub>max</sub> 252 nm, 271 nm (sh), pH 13  $\lambda_{min}$  233 nm,  $\lambda_{max}$  252 nm, 271 nm (sh); <sup>1</sup>H NMR (DMSO- $d_6$ )  $\delta$  8.61 (1H, s, 8-H), 8.33 (1H, s, 2-H), 7.26-7.36 (5H, m,  $C_6H_5$ ), 6.31 (1H, t, J = 6.80 Hz, H-1'), 5.33 (1H, s, OH-3', exchanges with D<sub>2</sub>O), 5.23 (2H, s, 1-C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 4.96 (1H, s, OH-5', exchanges with D<sub>2</sub>O), 4.39 (1H, m, H-3'), 3.86 (1H, m, H-4'), 3.55 (2H, m, H-5'), 2.63 (1H, m, H-2'b), 2.30 (1H, m, H-2'a); FAB<sup>+</sup>-MS *m/z* 343 ([C<sub>17</sub>H<sub>18</sub>N<sub>4</sub>O<sub>4</sub> + H]<sup>+</sup>), 253

([ $C_{10}H_{12}N_4O_4 + H$ ]<sup>+</sup>); HRFAB<sup>+</sup>-MS calcd for  $C_{17}H_{19}N_4O_4$  343.1406, found 343.1390. 1,7-Dibenzylhypoxanthine (5) eluted in fractions 139-158 (25 mg, yield 3 %): UV pH 6.9  $\lambda_{min}$  237 nm,  $\lambda_{max}$  258 nm, pH 13  $\lambda_{max}$  258 nm; <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>)  $\delta$  8.50 (1H, s, 8-H), 8.43 (1H, s, 2-H), 7.26-7.36 (10H, m, 2C<sub>6</sub>H<sub>5</sub>), 5.57 (2H, s, 7-C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 5.20 (2H, s, 1-C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>); FAB<sup>+</sup>-MS *m/z* 317 ([C<sub>19</sub>H<sub>16</sub>N<sub>4</sub>O + H]<sup>+</sup>), 227 ([C<sub>12</sub>H<sub>10</sub>N<sub>4</sub>O + H]<sup>+</sup>); HRFAB<sup>+</sup>-MS calcd for C<sub>19</sub>H<sub>17</sub>N<sub>4</sub>O 317.1390, found 317.1358. The white solid recovered from the evaporation of fractions 52-77 was dissolved in 50 mL of MeOH/H<sub>2</sub>O (3:7) and was loaded on a 2.8 x 80 cm Sephadex LH-20 column eluted with MeOH/H<sub>2</sub>O (3:7) at 1 mL/min. Under these chromatographic conditions, unreacted 2'-deoxyinosine eluted in fraction 70-83 (380 mg, yield 59 %). 7-Benzylhypoxanthine (2) eluted in fractions 112-118 (15 mg, yield 2.6 %).

#### Benzylation of 2'-deoxyinosine (1) in DMA.

To a stirred solution of 2'-deoxyinosine (650 mg, 2.58 mmol) in 13 mL of DMA was added benzyl bromide (0.31 mL, 2.6 mmol) over 1 min. The reaction mixture was stirred at room temperature for 72 h. The resulting clear solution was diluted with MeOH/H<sub>2</sub>O (2:8) to a final volume of 50 mL and was loaded on a Sephadex LH-20 column (2.8 x 80 cm). The column was eluted with MeOH/H<sub>2</sub>O (2:8) at 1 mL/min. UV absorption was checked continuously at 280 nm, and fractions (10 mL) were collected. Unreacted 2'-deoxyinosine eluted in fractions 34-64 (440 mg, yield 69 %). 7-Benzylhypoxanthine (2) eluted in fractions 96-123 (145 mg, yield 24.8 %). 3,7-Dibenzylhypoxanthine (3) eluted in 141-178 (50 mg, yield 6.1 %).

#### Benzylation of 2'-deoxyinosine (1) in DMA containing NaOH.

To a stirred solution of 2'-deoxyinosine (650 mg, 2.58 mmol) in 13 mL of DMA was added NaOH (103.2 mg, 2.58 mmol) at room temperature. After stirring for 30 min, benzyl bromide (0.31 mL, 2.6 mmol) was added dropwise over 1 min. The reaction mixture was stirred at room temperature for 72 h. The resulting pale yellow solution was diluted with MeOH/H<sub>2</sub>O (2:8) to a final volume of 50 mL and was loaded on a Sephadex LH-20 column (2.8 x 80 cm). The column was eluted with MeOH/H<sub>2</sub>O (2:8) at 1mL/min. UV absorption was continuously monitored at 280 nm. Unreacted 2'-deoxyinosine eluted in fractions 35-44 (110 mg, yield 17 %). 1-Benzyl-2'-deoxyinosine

(4) eluted in fractions 59-90 (710 mg, yield 80 %). 1,7-Dibenzyl-2'-deoxyinosine (6) eluted in fractions 145-167 (34 mg, yield 3 %): UV pH 6.9  $\lambda_{min}$  232 nm,  $\lambda_{max}$  252 nm, 270 nm (sh), pH 13  $\lambda_{min}$  233 nm,  $\lambda_{max}$  252 nm, 270 nm (sh); <sup>1</sup>H NMR  $\delta$  8.62 (1H, s, 8-H), 8.36 (1H, s, 2-H), 7.28-7.39 (10H, m, 2C<sub>6</sub>H<sub>5</sub>), 6.31 (1H, t, *J* = 6.84 Hz, H-1'), 5.24 (3H, s, OH-3' and 7-C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>, changes to a 2H on addition of D<sub>2</sub>O), 5.09 (1H, s, OH-5', exchanges with D<sub>2</sub>O), 4.58 ( 2H, s, 1-C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>), 4.34 (1H, m, H-3'), 4.12 (1H, m, H-4'), 3.57 (2H, m, H-5'), 2.75 (1H, m, H-2'b), 2.56 (1H, m, H-2'a); HRFAB<sup>+</sup>-MS calcd for C<sub>24</sub>H<sub>26</sub>N<sub>4</sub>O<sub>4</sub> 450.3211, found 450.3192.

#### **RESULTS AND DISCUSSION**

The product distributions from benzylations of 2'-deoxyinosine in the presence and absence of NaOH in TFE and DMA are shown in Scheme I. All the products were separated by column chromatography on Sephadex LH-20 (Experimental Section) and their yields were measured. The overall yield of products from the benzylation of neutral 2'-deoxyinosine in TFE was very low giving 7-benzylhypoxanthine (2) in 5 % and 3,7dibenzylhypoxanthine (3) in 4 % yields, respectively. The benzylation of neutral 2'deoxyinosine in DMA also produced similar product yields as reactions in TFE with the exception of a 5-fold increased yield of 2 (25 % yield). No 1-, 3- or O<sup>6</sup>-benzylated derivatives were detected in these reactions, indicating that the most reactive modification site of 2'-deoxyinosine under these reaction conditions was the 7-position. The chromatographic and spectroscopic properties of 2 were identical to those of an authentic sample published previously.<sup>12</sup> Compound 3 was assigned to be 3.7dibenzylhypoxanthine on the basis of its <sup>1</sup>H NMR, MS, and UV spectra. The mass spectral properties of product 3 showed that this compound was a dibenzylated hypoxanthine exhibiting a molecular ion at m/z 317. The UV absorption spectrum of 3 agreed well with that for 3,7-dibenzylhypoxanthine described previously.<sup>13</sup> The <sup>1</sup>H NMR spectrum of **3** showed a singlet for one pair of benzylic hydrogens at  $\delta$  5.58 (assignable to benzylic attachment to the 7-position) and a singlet for the second pair of benzylic hydrogens at  $\delta$  5.42 (assignable to benzylic attachment to the 3-position) which consistent with a previous report.12

In contrast, the reaction of the anion of 2'-deoxyinosine with benzyl bromide in TFE and DMA produced 1-benzyl-2'-deoxyinosine (4) as the major product with yields





of 35 % and 80 %, respectively. 1,7-Dibenzylhypoxanthine (5), 1,7-dibenzyl-2'deoxyinosine (6) and 2 were also detected as minor products under these reaction conditions (Scheme I). The mass spectrum for 4 indicated this compound was a monobenzylated nucleoside. Spectral shifts in wavelength under alkaline condition were not observed with 4 indicating that the dissociable proton at the 1-position is absent as the site was benzylated. The UV absorption spectra also agreed with reported previously.<sup>14</sup> The <sup>1</sup>H NMR spectrum for 4 was confirmatory of structure since it showed a singlet for the benzylic hydrogens of 4 at  $\delta$  5.23 and no resonance for an exchangeable 1-proton in the  $\delta$  12-13 range where the resonance for the 1-proton on 2'-deoxyinosine appears. The mass spectrum for compound 5 indicated that the molecule was a dibenzylated

#### 1-BENZYL-2'-DEOXYINOSINE

hypoxanthine derivative. The similarity of the UV spectra for neutral 2 and neutral 5 suggested that one benzyl group was attached to the 7-position. Its UV spectra in neutral and alkaline solutions were very similar indicating that the second benzyl group was attached to the 1-position in place of the dissociable 1-proton in a molecule. The <sup>1</sup>H NMR data showed a peak for one set of benzylic hydrogens at  $\delta$  5.57 assignable to benzyl group attachment at the 7-position and a second set of benzylic hydrogens at  $\delta$  5.20 resulting from attachment of the benzyl group to the 1-position. The mass spectral properties of 6 indicated that this product was a dibenzylated deoxyribonucleoside. The UV absorption spectra of 6 showed that the molecule could not dissociate in alkaline solution suggesting that the 1-position was substituted. In addition, the UV spectra were not consistent with benzylation at the O<sup>6</sup>-position. This data suggested that the two benzyl groups were attached to the 1- and 7-positions on 2'-deoxyinosine. The <sup>1</sup>H NMR data showed a singlet for one pair of benzylic hydrogens at  $\delta$  5.24 (assignable to attachment of the benzyl carbon to the 7-position) and a single for one pair of benzylic hydrogens at  $\delta$  4.58 attachment of the benzyl group to the 1-position. Production of 4 in significant yields, indicating that the reactivity of 1-position on 2'-deoxyinosine was markedly increased toward the benzylic electrophiles when 2'-deoxyinosine was in the anionic state. It has been reported that the methylation of neutral inosine in dimethyl sulfoxide was shown to react primarily at the 7-position, while the methylation of anionic inosine in DMA primarily reacted at the 1-position.<sup>2</sup> Therefore, these data indicate the similarity of the site selectivity for methylation of inosine and benzylation of 2'deoxyinosine.

On the basis of site-selectivity studies, benzylation predominantly occurs at the ring nitrogen sites on nucleosides in dipolar aprotic solvents, i.e., DMA whereas benzylation mainly occurs at exocyclic sites in solvents with the ability to solubilize ions, i.e., TFE. We would expect that benzylation of anion 2'-deoxyinosine in TFE would produce O<sup>6</sup>-benzylated derivatives. However, both the benzylation of the neutral and the anion of 2'-deoxyinosine in TFE did not produce any benzylated exocyclic oxygen derivatives. Thus, reactions with neutral or anionic 2'-deoxyinosine to prepare O<sup>6</sup>-benzylated derivatives remain to be investigated.

1-Substituted 2'-deoxyinosine products have been reported in reactions between epoxides and 2'-deoxyadenosine<sup>15</sup> and 2'-deoxyadenosine in DNA.<sup>16</sup> In such reactions,

1-substituted 2'-deoxyadenosine products are initially formed. However, these products are unstable and subsequently undergo either Dimroth rearrangement to give N<sup>6</sup>- substituted 2'-deoxyadenosines or deamination to produce 1-substituted 2'-deoxyinosine adducts. The structure and mutagenic potential of 1-substituted 2'-deoxyinosine adducts have not been reported. This is possibly due to the lack of a suitable high yielding method to prepare 1-substituted 2'-deoxyinosines.

A simple one step preparation of 1-benzyl-2'-deoxyinosine was developed by benzylation of the anion of 2'-deoxyinosine in TFE and DMA. These results further support the hypothesis that both the ionic state and solvent system are factors that determine site of reaction on purines. This synthetic approach is a useful method for the preparation of quantitative amounts of various 1-substituted aralkyl modified 2'deoxyinosine nucleotides and extends the information on the reactivity of electrophilic mutagens with purine nucleosides.

ACKNOWLEDGMENTS: We thank Dr. Thomas Barlow at the Chemical Safety & Toxicology Division, Food Standards Agency, London, UK for helpful discussions. This research was supported by the Brain Korea 21 project.

#### REFERENCES

- 1. Dipple, A.; Moschel, R. C.; Hudgins, W. R. Drug Metab. Rev., 1982 13, 249-268.
- 2. Jones, J. W.; Robins, R. K. J. Am. Chem. Soc., 1963 85, 193-201.
- 3. Moschel, R. C.; Hudgins, W. R.; Dipple, A. J. Org. Chem., 1979 44, 3324-3328.
- 4. Moschel, R. C.; Hudgins, W. R.; Dipple, A. J. Org. Chem., 1980 45, 533-535.
- 5. Moschel, R. C.; Hudgins, W. R.; Dipple, A. J. Org. Chem., 1986 51, 4180-4185.
- 6. Pei, G. K.; Moschel, R. C. Chem. Res. Toxicol., 1990 3, 292-295.
- 7. Moschel, R. C.; Hudgins, W. R.; Dipple, A. J. Am. Chem. Soc., 1981 103, 5489-5494.
- 8. Moschel, R. C.; Hudgins, W. R.; Dipple, A. J. Org. Chem., 1984 49, 363-372.
- 9. Barlow, T.; Dipple, A. Chem. Res. Toxicol., 1999 12, 883-886.
- 10. Selzer, R. R.; Elfarra, A. A. Carcinogenesis, 1997 18, 1993-1998.
- 11. Moon, K.-Y.; Moschel, R. C. Chem. Res. Toxicol., 1998 11, 696-702.
- 12. Montgomery, J. A.; Hewson, K., Clayton, S. J.; Thomas, H. J. J. Org. Chem., 1966 31, 2202-2210.

#### 1-BENZYL-2'-DEOXYINOSINE

- 13. Montgomery, J. A.; Thomas, H. J. J. Org. Chem., 1963 28, 2304-2310.
- 14. De Napoli, L.; Messere, A.; Montesarchio, D.; Piccialli, G.; Santacroce, C.; Varra, M. J. Chem. Soc., Perkin Trans. 1, **1994**, 923-925.
- 15. Barlow, T.; Takeshita, J.; Dipple, A. Chem. Res. Toxicol., 1998 11, 838-845.
- 16. Selzer, R. R.; Elfarra, A. A. Carcinogenesis, 1999 20, 285-292.

Received 3/16/00 Accepted 6/1/00