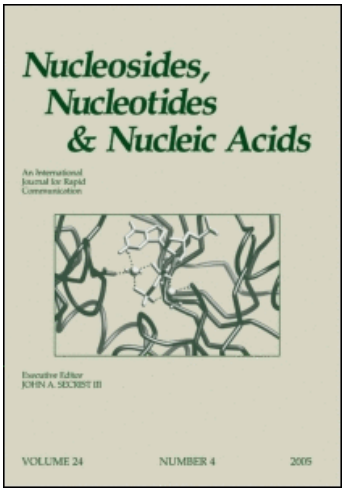


Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

Convenient Synthesis of 8-Amino-2'-deoxyadenosine

Miriam Frieden[a]; Anna Aviñó[a]; Ramon Eritja[ab]
[a] Instituto de Biología Molecular de Barcelona, Barcelona, Spain [b] Instituto de Biología Molecular de Barcelona, E-08034 Barcelona, Spain

Online publication date: 04 February 2003

To cite this Article Frieden, Miriam , Aviñó, Anna and Eritja, Ramon(2003) 'Convenient Synthesis of 8-Amino-2'-deoxyadenosine', Nucleosides, Nucleotides and Nucleic Acids, 22: 2, 193 — 202
To link to this Article: DOI: 10.1081/NCN-120019521
URL: http://dx.doi.org/10.1081/NCN-120019521

NUCLEOSIDES, NUCLEOTIDES & NUCLEIC ACIDS
Vol. 22, No. 2, pp. 193–202, 2003

Convenient Synthesis of 8-Amino-2′-deoxyadenosine

Miriam Frieden,[1,2] Anna Aviñó,[1] and Ramon Eritja[1,*]

[1]Instituto de Biología Molecular de Barcelona,
C.S.I.C. Jordi Girona, Barcelona, Spain
[2]Cureon A/S, Copenhagen, Denmark

ABSTRACT

We studied the behaviour of 8-azido-2′-deoxyadenosine and 8-bromo-2′-deoxyadenosine in aqueous solutions of ammonia and primary and secondary amines. Unexpectedly, 8-Azido-2′-deoxyadenosine is converted to 8-amino-2′-deoxyadenosine in excellent yields. The use of this reaction for the preparation of 8-aminoadenine derivatives needed for the preparation of oligonucleotides carrying 8-aminoadenine is discussed.

Key Words: 8-amino-2′-deoxyadenosine; Oligonucleotides; 8-azido-2′-deoxyadenosine; 8-aminopurine.

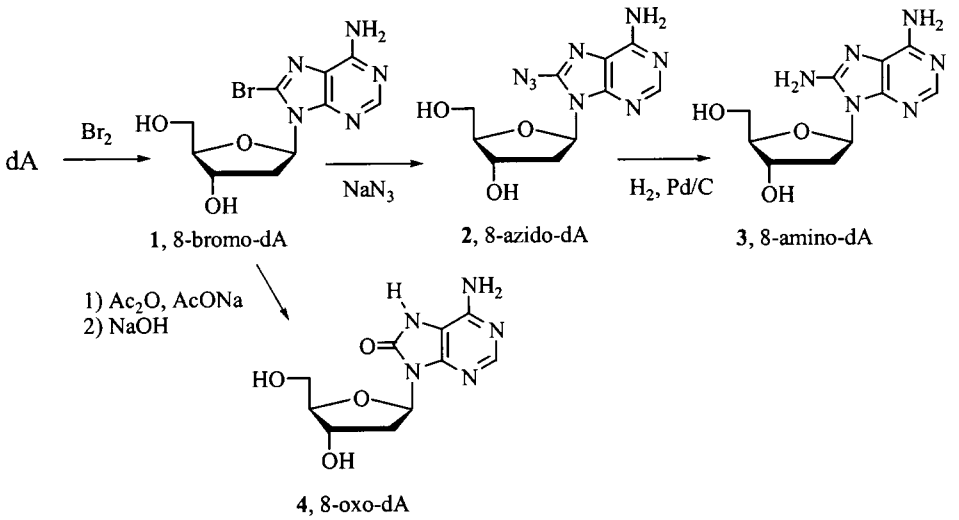
INTRODUCTION

Purine nucleosides carrying azido groups at the nucleobase are important intermediates for the preparation of photoreactive nucleotides used in the study of protein-nucleic acid interactions.[1] Moreover, they are useful intermediates in the synthesis of modified nucleosides such as purine nucleosides carrying amino groups.[2,3] For this purpose, a nucleoside carrying a halogen (Cl or Br) is treated with

*Correspondence: Ramon Eritja, Instituto de Biología Molecular de Barcelona, C.S.I.C. Jordi Girona 18-26, E-08034 Barcelona, Spain; Fax: 34-93-2045904; E-mail: recgma@cid.csic.es.

DOI: 10.1081/NCN-120019521
1525-7770 (Print); 1532-2335 (Online)

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016



Scheme 1. Synthesis of the 8-substituted 2′-deoxyadenosine derivatives.

sodium or lithium azide yielding the azidopurine, which is reduced by catalytic hydrogenation[3] or reducing metals.[2,4] Oligonucleotides carrying 8-aminoadenine form very stable triple helices[5–8] and parallel-stranded structures.[8,9] The introduction of the amino group at position 8 increases the stability of Hoogsteen structures owing to the combined effect of the gain of one Hoogsteen purine-pyrimidine H-bond and the tendency of the amino group to be integrated into the 'spine of hydration' located in the minor-major groove of the triplex structure.[6] 8-Amino-2′-deoxyadenosine (**3**) was prepared using the following three-step protocol: bromination of dA, nucleophilic displacement to form the 8-azidonucleoside (**2**) and catalytic hydrogenation of 8-azido-2′-deoxyadenosine (**2**) (Sch. 1).[3]

Moreover, 8-azido-2′-deoxyadenosine (**2**) has been incorporated into oligonucleotides.[10,11] 8-Azido-2′-deoxyadenosine (**2**) is partially decomposed during the ammonia treatment used for the removal of protecting groups of oligonucleotides (conc. NH_3, room temperature and 55°C). Fàbrega et al. described the formation of one single side product, 8-amino-2′-deoxyadenosine (**3**)[10] and Liu et al. reported two possible side compounds: 8-amino-2′-deoxyadenosine (**3**) and 8-oxo-2′-deoxyadenosine (**4**).[11] These two products are also formed during the ammonia treatment of oligonucleotides carrying 8-bromo-2′-deoxyadenosine.[12]

We analysed the behaviour of 8-azido-2′deoxyadenosine (**2**) in ammonia solutions and in solutions of primary and secondary amines. We confirmed that only 8-amino-2′-deoxyadenosine (**3**) is formed and that the reaction of compound **2** with volatile primary amines is useful for the preparation of 8-amino-2′-deoxyadenosine without hydrogenation.

RESULTS AND DISCUSSION

8-Bromo-2′-deoxyadenosine (**1**, Sch. 1) was prepared by bromination of dA[13] (73% yield). Reaction of **1** with sodium azide[3,14] gave 8-azido-2′-deoxyadenosine

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

(**2**) in 75% yield. Hydrogenation[3] of compound **2** using Pd/ activated charcoal as the catalyst gave 8-amino-2′-deoxyadenosine (**3**) in 90% yield. Finally, starting from compound **1**, 8-oxo-2′-deoxyadenosine (**4**) was prepared as described elsewhere.[13] Reverse-phase HPLC using a diode-array detector allowed the separation and rapid identification of compounds **1**–**4**. The elution order from more polar to less polar was as follows: 8-amino-dA (**3**), 8-oxo-dA (**4**), 8-azido-dA (**2**) and 8-bromo-dA (**1**).

Aliquots of 8-azido-dA (**2**) and 8-bromo-dA (**1**) were treated with 3 mL of 30% aqueous ammonia and 5M methanolic ammonia at 55°C. The reaction of 8-azido-dA (**2**) with aqueous ammonia gave only 8-amino-dA (**3**). A 45% conversion was observed after 20 h, 62% after 3 days and 90% after 6 days (Table 1). The product was isolated and characterized by ^{1}H and ^{13}C-NMR. Compound **2** decomposed slowly in methanolic ammonia (< 50% after 6 days, Table 1). On the other hand, treatment of 8-bromo-dA (**1**) with 30% aqueous ammonia and 5M methanolic ammonia at 55°C gave small amounts of a mixture of 8-amino-dA (**3**) and 8-oxo-dA (**4**) (20% decomposition with aqueous ammonia after 16 h at 55°C, Table 1).

These results were in agreement with the behaviour of compounds **1** and **2** in oligonucleotides,[10–12] except that 8-oxo-dA (**4**) was not formed in the treatment of compound **2** with aqueous ammonia. Unexpectedly, the formation of 8-amino-dA (**3**) from compound **2** was clean and faster than the formation of compound **3** from compound **1**. To gain more information on this reaction, compound **2** was also treated with an aqueous solution of several amines.

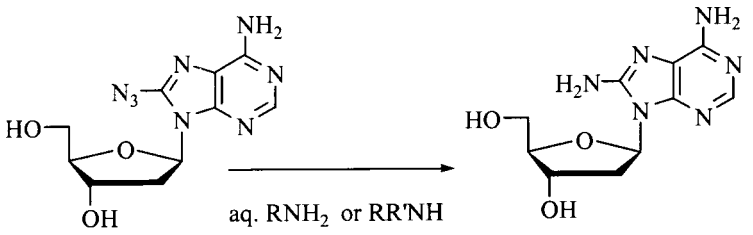
Aliquots of 8-azido-dA (**2**) were treated with solutions of amines (Sch. 2) at 55°C. The reaction of 8-azido-dA (**2**) with 40% aqueous methylamine gave complete conversion to 8-amino-dA (**3**) in less than 5 h. Reaction with a 30% aqueous solution of dimethylamine gave 70% conversion to 8-amino-dA (**3**) after 16 h. Treatment of

Table 1. Composition of the reaction mixtures obtained after the treatment of compounds **1** and **2** with amine solutions at 55°C.

			Composition of the reaction mixture (%)				
Compound	Treatment	Time	**2**	**3**	**1**	**4**	**5**
2	30% aq.NH_3	16 h	55	45	–	–	–
		3 days	38	62	–	–	–
		6 days	10	90	–	–	–
2	5M NH_3/MeOH	16 h	96	4	–	–	–
		3 days	65	35	–	–	–
		6 days	53	47	–	–	–
1	30% *aq*NH_3	5 h	–	7	80	13	–
1	5M NH_3/MeOH	16 h	–	9[#]	80[#]	7[#]	–
2	40% *aq*CH_3NH_2	5 h	0	100	–	–	–
2	30% *aq* dimethylamine	16 h	30	70	–	–	–
2	1M *aq* piperidine	16 h	0	100	–	–	–
2	1M *aq* hexane-1,6-diamine	5 h	0	100	–	–	–
1	1M *aq* hexane-1,6-diamine	16 h	–	–	0	20	80

[#]In addition 4% of a product eluting at 9.8 min (UV max 260 nm) was observed. Most probably the product was 8-methoxy-2′-deoxyadenosine.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016



RNH_2 = 40% aq. CH_3NH_2, 1M aq. NH_2-$(CH_2)_6$-NH_2,
1M aq. NH_2-$[(CH_2)_2$-$O]_2$-$(CH_2)_2$-NH_2, 1M aq. NH_2-$(CH_2)_2$-S-S-$(CH_2)_2$-NH_2

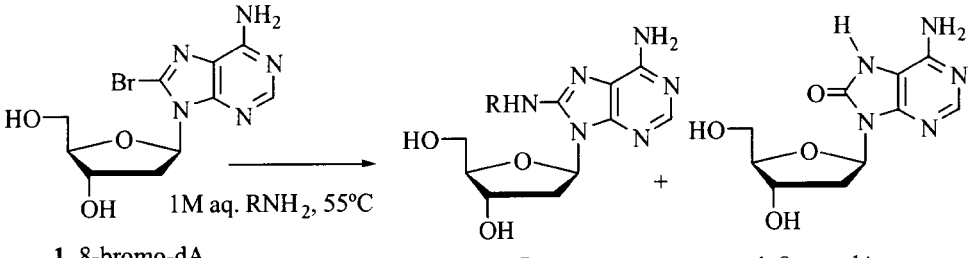
RR'NH = 40% $(CH_3)_2NH$, 1M aq. piperidine

Scheme 2. Treatment of 8-azido-2′-deoxyadenosine with amines.

compound **2** with 1M aqueous solutions of piperidine and hexane-1,6-diamine gave 8-amino-dA (**3**) after 16 and 5 h at 55°C , respectively. The identity of the product was confirmed by HPLC analysis and by isolation of the products resulting from the reactions and analysis of their ^1H and ^{13}C-NMR spectra.

On the other hand, treatment of 8-bromo-dA (**1**) with 1M aqueous hexane-1,6-diamine gave the expected mixture of the products resulting from the attack of both nucleophiles present in the mixture: 8-oxo-dA (**4**) and 8-(6-aminohexyl) amino-dA (**5**) (Sch. 3), in agreement with the results obtained during the preparation of 8-N-aminosubstituted dA derivatives.[3,15]

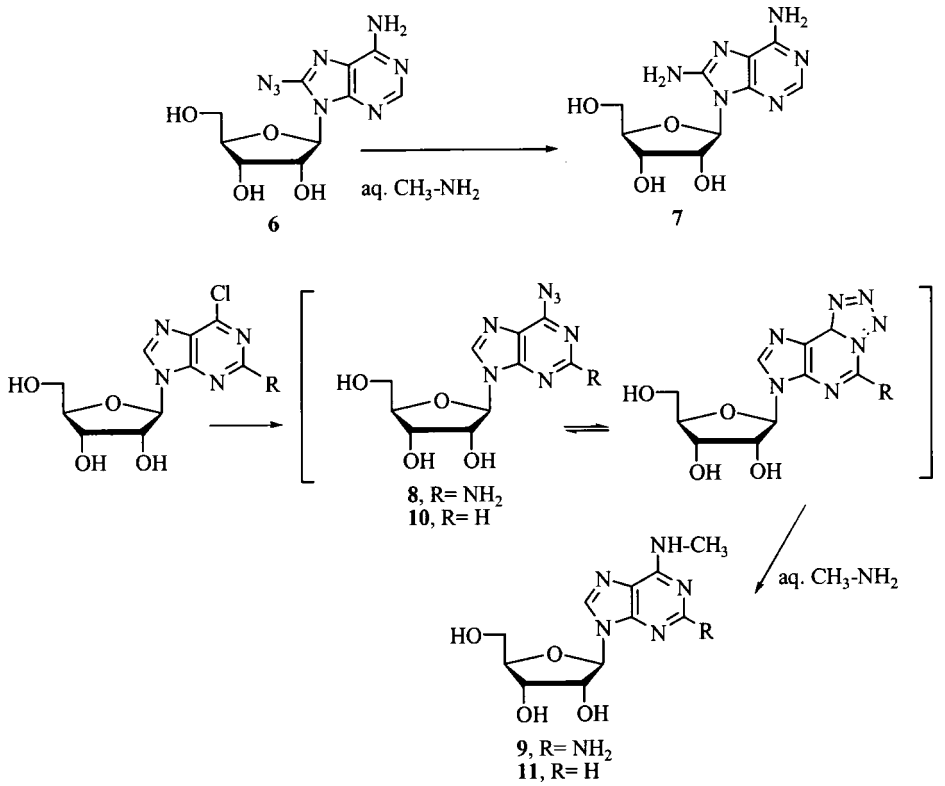
These data reveal a distinct behaviour of compounds **1** and **2** towards aqueous amine solutions. The bromo derivative suffers a nucleophilic displacement by the amine and water, while the azido derivative is converted to the amino derivative (**3**) regardless of the amine present in the reaction and without interference with water. The reaction in the presence of primary amines is faster than in the presence of secondary amines, which is faster than in the presence of ammonia. This suggests



R= NH_2-$(CH_2)_2$-

Scheme 3. Products obtained from the treatment of 8-bromo-2′-deoxyadenosine with hexane-1,6-diamine.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016



Scheme 4. Products obtained from the treatment of the ribonucleosides carrying azido groups with methylamine.

the involvement of the amine in the thermal decomposition of the azido group to the nitrene intermediate, which later abstracts hydrogen from the environment to give the 8-aminopurine.[16] The scope of this reaction was assayed with several purine ribonucleosides carrying azido groups. As expected the treatment of ribonucleoside-8-azidoadenosine (**6**) with 40% aqueous methylamine gave 8-aminoadenosine (**7**) (Sch. 4). However, treatment of 6-azido-2-aminopurine riboside (**8**) and 6-azidopurine riboside (**10**) resulted in the addition of methylamine at position 6 of the purine with the subsequent displacement of the azido group (compounds **9** and **11**) together with some decomposition products. In these cases, the azido group is in the tetrazolo tautomeric form (absence of an IR band in the region of 2000–2200 cm^{-1} and presence of an intense band in the 1700–1500 cm^{-1} region)[17,18] and a nitrene is not formed. The reaction observed with compound **2** is only possible when the azido group is at position 8.

Finally, we tested the reaction of compound **2** with amines for preparative purposes. We selected the inexpensive 40% aqueous methylamine solution because the formation of the desired compound **3** was very fast, and the amine was volatile. Several reactions on a 1–5 gram scale gave the desired compound in quantitative yields. The product resulting from the evaporation of methylamine was pure enough

to perform the protection of the amino groups with the dimethylformamidine[19,20] groups needed for the preparation of oligonucleotides carrying 8-amino-2′-deoxyadenosine. The DMT-protected phosphoramidite derivative as well as oligonucleotides carrying 8-amino-2′-deoxyadenosine were prepared as described elsewhere.[5,6]

EXPERIMENTAL SECTION

General Methods

Solvents, including those of HPLC grade, were from SDS and E. Merck. Reagents were from Aldrich and Fluka and were used without further purification. Analytical TLC was run on aluminium sheets coated with silica gel 60 F_{254} from Merck. Silica gel column chromatography was performed with Chromatogel 60 A C.C. (40–60 microns, 230–400 mesh, SDS). 8-Bromo-2′-deoxyadenosine (**1**),[13] 8-azido-2′-deoxyadenosine (**2**),[3,14] 8-amino-2′-deoxyadenosine (**3**)[3] and 8-oxo-2′-deoxyadenosine (**4**)[13] were prepared as described. 8-Bromoadenosine, 2-amino-6-chloro-9-β-D-ribofuranosylpurine, and 6-chloro-9-β-D-ribofuranosylpurine were obtained from Pharma-Waldhof GmbH (Düsseldorf, Germany). N^6-methyladenosine (**11**) was purchased from Sigma.

Instrumental

^{1}H-NMR (250 MHz) and ^{13}C-NMR (63 MHz) spectra were recorded on a Brüker AM-250. HPLC chromatography was performed on an HPLC Shimadzu equipped with a diode array detector.

Treatment of 8-Azido-2′-deoxyadenosine and 8-Bromo-2′-deoxyadenosine with Ammonia and Amine Aqueous Solutions. To 50 mg aliquots of 8-azido-2′-deoxyadenosine or 8-bromo-2′-deoxyadenosine in screw-cap tubes was added 3 mL of the appropriate ammonia or amine solutions. The mixtures were heated to 55°C for a period of time between 5 h and 6 days, allowed to cool to room temperature and evaporated to dryness. The residues were analysed by HPLC. HPLC conditions were as follows: Solution A, 0.1 M aqueous triethylammonium acetate pH 6.5/acetonitrile (95 : 5); solution B, 0.1 M aqueous triethylammonium acetate pH 6.5/acetonitrile (3 : 7); Column PRP-1 (Hamilton, 10 μm) 250 × 10 mm; flow rate, 3 mL/min; 20 min linear gradient from 0% B to 50% B. Retention time for 8-amino-dA: 7.4 min; for 8-oxo-dA: 8.1 min; for 8-azido-dA: 11.3 min and for 8-bromo-dA: 11.4 min. UV maximum for 8-amino-dA: 276 nm; for 8-oxo-dA 272 nm; for 8-azido-dA 284 nm and for 8-bromo-dA 267 nm. Reaction products were also identified by comparison of the chemical shift of C-8 in ^{13}C-NMR spectra with published spectra.[10,13]

8-Azidoadenosine (6). Compound **6** was prepared as described in Ref.[14] with minor modifications. 8-Bromoadenosine (250 mg, 0.72 mmol) was treated with 148 mg (2.17 mmol) of sodium azide in 5 mL of dimethylformamide (DMF) at

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

60°C for 16 h. The solution was cooled and evaporated to dryness. The resulting product was crystallized from water-methanol giving 130 mg (59% yield) of a white solid. UV (max, pH 6.5) 284 nm. IR (KBr, cm^{-1}): intense bands at 2154 and 2043. ^{1}H-NMR (DMSO-d_6): 8.05 (s, 1H, H-2), 7.31 (br s, 2H, amino), 5.60 (d, 1H, OH), 5.38 (m, 2H, OH and H-1′), 5.15 (d, 1H, OH), 4.84 (m, 1H, H-2′), 4.18 (m, 1H, H-3′), 3.9 (m, 1H, H-4′), 3.58 (m, 2H, H-5′). ^{13}C-NMR (DMSO-d_6): 154.7 (C-6), 156.8 (C-2), 149.6 (C-4), 144.6 (C-8), 117.5 (C-5), 87.8 (C-1′), 86.5 (C-4′), 71.5 (C-3′), 71.0 (C-2′), 62.3 (C-5′). MS (electrospray) calculated for $C_{10}H_{12}N_8O_4$ 308.3. Found: 309.8 ($M + H^+$).

6-Azido-2-amino-9-β-D-ribofuranosylpurine (8). 6-Chloro-2-amino-9-β-D-ribofuranosylpurine (300 mg, 1 mmol) was treated with 211 mg (3 mmol) of sodium azide in 7 mL of DMF at 60°C for 16 h. The solution was cooled and evaporated to dryness. The resulting product was crystallized from water-methanol giving 200 mg (65% yield) of a white solid. UV (max, pH 6.5) 270, 300 nm. IR (KBr, cm^{-1}): absence of bands in the region 2200–2000, intense band at 1694. ^{1}H-NMR (DMSO-d_6): 8.4 (m, 3H, H-8 and amino), 5.91 (d, 1H, H-1′), 5.45 (d, 1H, OH), 5.20 (d, 1H, OH), 5.02 (t, 1H, OH), 4.5 (m, 1H, H-2′), 4.18 (m, 1H, H-3′), 3.9 (m, 1H, H-4′), 3.6 (m, 2H, H-5′). ^{13}C-NMR (DMSO-d_6): 146.3 (C-6), 145.1 (C-2), 144.1 (C-4), 138.5 (C-8), 112.4 (C-5), 87.3 (C-1′), 85.7 (C-4′), 74.3 (C-3′), 70.2 (C-2′), 61.4 (C-5′). MS (electrospray) calculated for $C_{10}H_{12}N_8O_4$ 308.3. Found: 309.0 ($M + H^+$).

6-Azido-9-β-D-ribofuranosylpurine (10). 6-Chloro-9-β-D-ribofuranosylpurine (500 mg, 1.75 mmol) was treated with 357 mg (5.2 mmol) of sodium azide in 10 mL of DMF at 60°C for 16 h. The solution was cooled and concentrated to dryness. The resulting product was crystallized from water-methanol giving 110 mg (21% yield) of a white solid. UV (max, pH 6.5) 290 nm. IR (KBr, cm^{-1}): absence of bands in the region 2200–2000, intense band at 1645. ^{1}H-NMR (DMSO-d_6): 10.1 (s 1H), 8.9 (s, 1H), 6.11 (d, 1H, H-1′), 5.62 (d, 1H, OH), 5.29 (d, 1H, OH), 5.1 (t, 1H, OH), 4.53 (m, 1H, H-2′), 4.15 (m, 1H, H-3′), 3.98 (m, 1H, H-4′), 3.64 (m, 2H, H-5′). ^{13}C-NMR (DMSO-d_6): 145.6 (C-6), 142.8 (C-2), 142.1 (C-4), 136.3 (C-8), 121 (C-5), 88.5 (C-1′), 85.9 (C-4′), 74.8 (C-3′), 70.2 (C-2′), 61.1 (C-5′). MS (electrospray) calculated for $C_{10}H_{11}N_7O_4$ 293.2. Found: 293.9 ($M + H^+$).

Treatment of Ribonucleosides Carrying Azido Groups with Methylamine. To 50 mg aliquots of azido-ribonucleosides (**6**, **8**, **10**) in screw-cap tubes was added 3 mL of 40% *aqueous* methylamine. The mixtures were heated to 60°C for a period of time between 16 and 48 h, allowed to cool to room temperature and evaporated to dryness. The residues were analysed by HPLC as described above. Retention time (UV maxima) for compound **6**: 9.6 min (284 nm); for compound **7**: 6.4 min (272 nm); for compound **8**: 7.5 min (270, 300 nm); for compound **9**: 2.7 min (242 nm); for compound **10**: 8.2 min (290 nm) and for compound **11**: 3.8 min (250 nm).

The reaction with compound **6** was completed after 16 h, giving one single product that was characterized as 8-aminoadenosine (**7**)[14]. ^{1}H-NMR (DMSO-d_6): 7.89 (s, 1H, H-2), 6.54 (m, 2H, amino), 5.82 (d, 1H, H-1′), 4.64 (m, 1H, H-2′), 4.12 (m, 1H, H-3′), 3.9 (m, 1H, H-4′), 3.58 (m, 2H, H-5′). ^{13}C-NMR (DMSO-d_6): 152.6

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

(C-6), 151.8 (C-2), 149.5 (C-4), 148.5 (C-8), 117.4 (C-5), 86.8 (C-1′), 86.0 (C-4′), 71.1 (C-3′ and C-2′), 62.0 (C-5′). MS (electrospray) calculated for $C_{10}H_{14}N_6O_4$ 282.2. Found: 283.4 ($M + H^+$).

The reaction with compound **8** was completed after 48 h, giving one major product that was characterized as 2-amino-N^6-methyladenosine (**9**)[21] together with some minor products that were not characterized. ^{1}H-NMR (DMSO-d_6): 7.9 (s, 1H, H-8), 5.49 (d, 1H, H-1′), 4.32 (m, 1H, H-2′), 4.12 (m, 1H, H-3′), 3.86 (m, 1H, H-4′), 3.58 (m, 2H, H-5′), 2.7 (s, 3H, CH_3). ^{13}C-NMR (DMSO-d_6): 156.5 (C-6), 155.6 (C-2), 150.7 (C-4), 133.7 (C-8), 112.7 (C-5), 87.6 (C-1′), 84.4 (C-4′), 74.6 (C-3′), 69.6 (C-2′), 60.6 (C-5′), 27.9 (CH_3). MS (electrospray) calculated for $C_{11}H_{16}N_6O_4$ 296.3. Found: 297.5 ($M + H^+$).

The reaction with compound **10** was completed after 16 h, giving several products. One of the products was characterized as N^6-methyladenosine (**11**) by comparison with the commercially available product and mass spectrometry. MS (electrospray) calculated for $C_{11}H_{15}N_5O_4$ 281.2. Found 284.5 ($M + H^+$).

Synthesis of 8-Amino-N,N-bis(dimethylaminomethylidene)-2′-deoxyadenosine. In a screw-cap tube, 4.62 g of 8-azido-2′-deoxyadenosine[3,14] was dissolved in 20 mL of 40% aqueous methylamine solution and 2 mL of dioxane. The solution was heated overnight to 55°C. It was then cooled to room temperature and evaporated to dryness, yielding an oil that was used in the following step without purification. Purity assessed by HPLC (< 95%).

The product described above (approx. 17.5 mmol) was dissolved in 250 mL of DMF and treated with 12.1 mL of DMF dimethyl acetal. The solution was stirred overnight at room temperature and then evaporated to dryness. The resulting product was purified by silica gel chromatography (0–20% methanol in dichloromethane), yielding 5.4 g of the desired compound (82% yield). Physical and spectral data were as described elsewhere.[5,6]

ACKNOWLEDGMENTS

We thank the Dirección General de Investigación Científica y Técnica (grants BQU2000-0649 and CAL01-058-C2-2), the Generalitat de Catalunya (2000-SGR-0018 and 2001-SGR-0049), and Cygene Inc. for financial support.

REFERENCES

1. Sylvers, L.A.; Wower, J. Nucleic acid-incorporated azidonucleotides: probes for studying the interaction of RNA or DNA with proteins and other nucleic acids. Bioconjugate Chem. **1993**, *4*, 411–418.
2. Sproat, B.S.; Iribaren, A.M.; Güimil García, R.; Beijer, B. New synthetic routes to synthons suitable for 2′-*O*-allyloligoribonucleotide assembly. Nucleic Acids Res. **1991**, *19*, 733–738.
3. Long, R.A.; Robins, R.K.; Townsed, L.B. Purine nucleosides. XV. The synthesis of 8-amino- and 8-substituted aminopurine nucleosides. J. Org. Chem. **1967**, *32*, 2751–2756.

4. Bartra, M.; Urpí, F.; Vilarrasa, J. New synthetic tricks. Two useful reagents for the reduction of azides to amines. Tetrahedron Lett. **1987**, *28*, 5941–5944.
5. Kawai, K.; Saito, I.; Sugiyama, H. Stabilization of Hoogsteen base pairing by introduction of amino group at the C8 position of adenine. Tetrahedron Lett. **1998**, *39*, 5221–5224.
6. Güimil García, R.; Ferrer, E.; Macias, M.J.; Eritja, R.; Orozco, M. Theoretical calculations, synthesis and base-pairing properties of oligonucleotides containing 8-amino-2′-deoxyadenosine. Nucleic Acids Res. **1999**, *27*, 1991–1998.
7. Aviñó, A.; Frieden, M.; Morales, J.C.; de la Torre, B.G.; Güimil García, R.; Azorín, F.; Gelpí, J.L.; Orozco, M.; González, C.; Eritja, R. Properties of triple helices formed by parallel-stranded hairpins containing 8-aminopurines. Nucleic Acids Res. **2002**, *30*, 2609–2619.
8. Aviñó, A.; Morales, J.C.; Frieden, M.; de la Torre, B.G.; Güimil García, R.; Cubero, E.; Luque, F.J.; Orozco, M.; Azorín, F.; Eritja, R. Parallel-stranded hairpins containing 8-aminopurines. Novel efficient probes for triple-helix formation. Bioorg. Med. Chem. Lett. **2001**, *11*, 1761–1763.
9. Cubero, E.; Aviñó, A.; de la Torre, B.G.; Frieden, M.; Eritja, R.; Luque, F.J.; Gonzalez, C.; Orozco, M. Hoogsteen-based parallel-stranded duplexes of DNA. The effect of 8-aminoderivatives. J. Am. Chem. Soc. **2002**, *124*, 3133–3142.
10. Fàbrega, C.; Güimil García, R.; Díaz, A.R.; Eritja, R. Studies on the synthesis of oligonucleotides containing photoreactive nucleosides: 2-azido-2′-deoxyinosine and 8-azido-2′-deoxyadenosine. Biol. Chem. **1998**, *379*, 527–533.
11. Liu, J.; Fan, Q.R.; Sodeoka, M.; Lane, W.S.; Verdine, G.L. DNA bending by an amino acid residue in the C-terminal half of the ReI homology region. Chem. Biol. **1994**, *1*, 47–55.
12. Liu, J.; Verdine, G.L. Synthesis of photoactive DNA: incorporation of 8-bromo-2′-deoxyadenosine into synthetic oligodeoxynucleotides. Tetrahedron Lett. **1992**, *33*, 4265–4268.
13. Wood, M.L.; Esteve, A.; Morningstar, M.L.; Kuziemko, G.M.; Essigmann, J.M. Genetic effects of oxidative DNA damage: comparative mutagenesis of 7,8-dihydro-8-oxoguanine and 7,8-dihydro-8-oxoadenine in *Escherichia coli*. Nucleic Acids Res. **1992**, *20*, 6023–6032.
14. Holmes, R.E.; Robins, R.K. Purine nucleosides. IX. The synthesis of 9-β-D-ribofuranosyl uric acid and other related 8-substituted purine ribonucleosides. J. Am. Chem. Soc. **1965**, *87*, 1772–1776.
15. Sarfati, S.R.; Naname, A. Synthesis of fluoresceinylated 2′-deoxyadenosine. Mono, di and triphosphate derivatives. Tetrahedron Lett. **1990**, *31*, 2581–2584.
16. Sheradsky, T. Azides as synthetic starting materials. In *The Chemistry of the Azido Group*; Patai, S., Ed.; Interscience Publishers: London, 1971, 339–340.
17. Johnson, J.A.; Thomas, H.J.; Schaeffer, H.J. Synthesis of potential anticancer agents. XIII. Ribosides of 6-substituted purines. J. Am. Chem. Soc. **1958**, *80* 699–702.
18. Mathé, C.; Lioux, T.; Gosselin, G. Synthesis and biological evaluation of (β-D-pentofuranonucleoside derivatives of 2-azidoadenine. Abstracts of papers. 15th International Round Table on Nucleosides, Nucleotides and Nucleic Acids, Leuven, Belgium, Sept. 10–14, 2002.

MARCEL DEKKER, INC.
270 Madison Avenue, New York, New York 10016

19. MacBride, L.J.; Kierzek, R.; Beaucage, S.L.; Caruthers, M.H. Amidine protecting groups for oligonucleotide synthesis. J. Am. Chem. Soc. **1986**, *108*, 2040–2048.
20. Vu, H.; Mc Collum, A.; Jacobson, K.; Thiesen, P. Fast oligonucleotide deprotection phosphoramidite chemistry for DNA synthesis. Tetrahedron Lett. **1990**, *31*, 7269–7272.
21. Saladino, R.; Mincione, E.; Crestini, C.; Mezzetti, M. Transformations of thiopyrimidine and thiopurine nucleosides following oxidation with dimethyldioxirane. Tetrahedron **1996**, *52*, 6759–6780.

Received October 8, 2002
Accepted December 23, 2002

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016