

Purines. XLVI.¹⁾ Preparation of 1-Ethyladenine from Adenosine

Tozo FUJII,* Taisuke ITAYA, Fumiko TANAKA, Tohru SAITO, and Hiromi HISATA

Faculty of Pharmaceutical Sciences, Kanazawa University, Takara-machi, Kanazawa 920, Japan. Received May 18, 1990

A detailed account is given of the synthesis and glycosidic cleavage of 1-ethyladenosine (**2b**), which established an alternative synthesis of 1-ethyladenine (**3b**). Ethylation of adenosine (**1**) with EtI in AcNMe₂ at 35–38 °C for 90 h gave **2b**·HI in 54% yield. The hydriodide **2b**·HI was readily converted into the perchlorate **2b**·HClO₄ and into the free nucleoside **2b**. Treatment of **2b**·HI with 0.5 N aqueous HCl at 92–94 °C for 30 min or that of **2b**·HClO₄ with boiling AcOH for 60 min produced the aglycone **3b** in good yield. The free base easily formed the hydrochloride **3b**·HCl, and the perchlorate **3b**·HClO₄ as well.

Keywords adenosine; ethylation; 1-ethyladenosine; acid hydrolysis; glycosidic cleavage; 1-ethyladenine; UV; ¹H-NMR; acid dissociation constant

In previous work by us²⁾ on the Dimroth rearrangement of 1,9-dialkyladenines, it was necessary to prepare 1-ethyladenine (**3b**) in quantity. Although a few methods for the synthesis of **3b** were available at that time,³⁾ we prepared it from adenosine (**1**) through 1-ethyladenosine (**2b**) according to the general, two-step procedure first described by Jones and Robins⁴⁾ for the preparation of 1-methyladenine (**3a**), and subsequently utilized for securing many other 1-alkyladenines (type **3**).⁵⁾ The ethylation of **1**^{2a,5b,g,j,k,6)} and acid hydrolysis of **2b**^{2a,5b,g,j,k,6b)} leading to **3b** have been reported by us and by other research groups, but without experimental details or full characterization of the products. We present herein a detailed account of our synthetic procedure, in response to many requests for it.

Ethylation of **1** with an excess of EtI was effected in AcNMe₂ at 35–38 °C for 90 h, and the crude product was triturated with AcOH. The crystalline material that formed was then recrystallized from 70% (v/v) aqueous EtOH, giving **2b**·HI in 54% yield. Separate treatments of **2b**·HI in H₂O with Amberlite IRA-402 (ClO₄[−]) and with Amberlite IRA-402 (HCO₃[−]) produced the perchlorate **2b**·HClO₄ and the free nucleoside **2b** in 95% and 87% yields, respectively. The correctness of the structures of **2b**·HI, **2b**·HClO₄, and **2b** was supported by the way in which they had been generated, microanalytical data, and comparison of their ultraviolet (UV) spectra with that^{2b,4)} of known 1-methyladenosine (**2a**).

On treatment with 0.5 N aqueous HCl at 92–94 °C for 30 min, the hydriodide **2b**·HI underwent glycosidic hydrolysis to give the desired aglycone **3b** in 76% yield. The aglycone **3b** was characterized by its UV spectrum and two pK_a's (7.08 and 11.40 at 40 °C), indicative of a 1-substituted

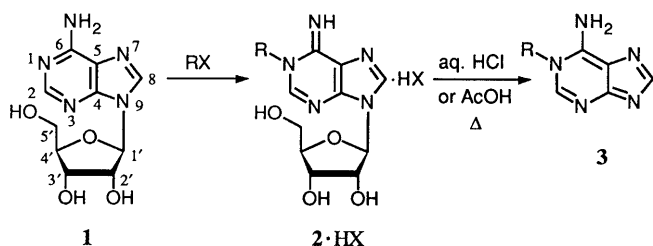
adenine.^{3a,4)} A similar hydrolysis of **2b**·HI in boiling 5% aqueous HBr for 10 min has been reported to give **3b**·HBr in 24% yield.^{5j)}

The glycosidic hydrolysis of 1-substituted adenosines (type **2**) with hot mineral acids sometimes encounters difficulties because it is accompanied with acid-catalyzed ring opening, although this is much slower,^{5d,e)} or dealkylation [as in the case of the 1-(3-methyl-2-butenyl) analogue **2e**]^{5c)} of the resulting aglycones (type **3**). Our previous, improved procedure using hot AcOH instead of hot aqueous HCl,⁵ⁱ⁾ as exemplified in the cases of the benzyl analogue **2c**·HBr and the allyl analogues **2d,e**·HBr, may overcome such difficulties. Thus, the effectiveness of the AcOH procedure was then tested in the glycosidic cleavage of the 1-ethylated nucleoside (**2b**) and its salts **2b**·HI and **2b**·HClO₄. It may be seen from Table I that the glycosidic cleavage of the free nucleoside **2b** in boiling AcOH proceeds to some extent, but slows down in aqueous AcOH. The presence of potassium halide causes the reaction to speed up to a certain extent, regardless of the kind of halide ion. The glycosidic cleavage of the perchlorate salt **2b**·HClO₄ proceeds much faster than that of the free nucleoside **2b**. Interestingly, it is accelerated in the presence of halide ion, and this salt effect increases in the order of KCl < KI < KBr. These results suggest that the glycosidic cleavage of **2** or

TABLE I. The Glycosidic Hydrolysis of 1-Ethyladenosine (**2b**) and Its Salts (**2b**·HI and **2b**·HClO₄) in AcOH

Substrate	Additive	Reaction conditions ^{a)}	Product (3b) Yield ^{b)} (%)
2b	Nil	A	17
	H ₂ O ^{c)}	A	5
	KCl (1 eq)	A	35
	KCl (2 eq)	A	49
	KBr (1 eq)	A	37
	KI (1 eq)	A	33
2b ·HI	Nil	A ^{d)}	— ^{e)}
	Nil	A	87
	KCl (1 eq)	B	37
	KBr (1 eq)	B	83
	KBr (2 eq)	B	98
	KI (1 eq)	B	51
2b ·HClO ₄	Nil	A	87
	KCl (1 eq)	B	37
	KBr (1 eq)	B	83
	KBr (2 eq)	B	98
	KI (1 eq)	B	51
	Nil	A	87

a) The letter A stands for refluxing a solution of the substrate (0.2 mmol) in AcOH (10 ml) with or without an additive for 30 min; B, heating a solution of the substrate (0.05 mmol) in AcOH (30 ml) with an additive at 110 °C for 30 min. b) Determined by UV spectrophotometry after paper electrophoretic separation. c) Contained in the solvent in the form of 50% (v/v) aqueous AcOH (10 ml). d) The hydriodide salt was sparingly soluble under these conditions. e) Unmeasurably low.



a: R = Me b: R = Et c: R = PhCH₂
 d: R = CH₂=CH-CH₂ e: R = Me₂C=CH-CH₂

Chart 1

2·HX in AcOH proceeds by a complex mechanism rather than a simple A-1 mechanism.^{5e,7)} In the case of the hydriodide salt 2b·HI, this AcOH procedure is not of practical value because of the extremely poor solubility of the substrate in boiling AcOH.

In a preparative run, 2b·HClO₄ was heated in AcOH under reflux for 60 min, producing 3b·HClO₄ in 71% yield. Alternatively, treatment of crude 2b·HI, obtained from the above ethylation of 1, with 0.5 N aqueous HCl at 95–100 °C for 45 min furnished, after basification, the free base 3b in 80% overall yield (from 1). The free base gave the hydrochloride (3b·HCl) and the perchlorate (3b·HClO₄) in the usual manner.

In conclusion, the AcOH procedure developed by us⁵ⁱ⁾ for the glycosidic cleavage of 2c→e·HBr has proved to be also effective for that of the 1-ethyl analogue 2b·HX. However, the conventional procedure using aqueous HCl may be recommended for preparation of 1-ethyladenine (3b) because of the overall simplicity of operation.

Experimental

General Notes All melting points were taken on a Yamato MP-1 capillary melting point apparatus and are corrected. UV spectra reported herein were recorded with a Hitachi EPS-2U or a Hitachi model 323 or 320 spectrophotometer on solutions in 95% (v/v) aqueous EtOH, 0.1 N aqueous HCl (pH 1), 0.005 M phosphate buffer (pH 7), and 0.1 N aqueous NaOH (pH 13). Spectrophotometric determinations were carried out with a Hitachi EPU-2A or a Hitachi model 320 spectrophotometer, and pH's were measured on a Toa HM-18ET pH meter. See ref. 1 for details of other instrumentation and measurements. Elemental analyses were performed by Mr. Y. Itatani and his associates at Kanazawa University. The following abbreviations are used: br=broad, d=doublet, m=multi-plet, q=quartet, s=singlet, sh=shoulder, t=triplet.

1-Ethyladenosine Hydriodide (2b·HI) A mixture of adenosine (1) (6.70 g, 25.1 mmol) and EtI (39.5 g, 253 mmol) in AcNMe₂ (75 ml) was stirred at 35–38 °C for 90 h. The resulting brown solution was concentrated *in vacuo*, and the residue was triturated with AcOH (50 ml). The crystals that resulted were collected by filtration, washed successively with EtOH (20 ml) and ether (10 ml), and dried *in vacuo* over KOH pellets to afford crude 2b·HI (10.5 g). This was recrystallized from 70% (v/v) aqueous EtOH to give 2b·HI (5.73 g, 54%) as colorless needles, mp 200–201 °C (dec.). Further recrystallization from the same solvent provided an analytical sample as colorless needles, mp 200–201 °C (dec.) (lit.^{5j)} mp 208–209 °C; $[\alpha]_D^{25} -33.8^\circ$ ($c=0.709$, MeOH); UV $\lambda_{\max}^{95\% \text{ EtOH}}$ 260 nm (ϵ 12600); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 1) 259 (13400); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 7) 259 (13400); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 13) 261 (13700), 267 (sh) (12300), 289 (sh) (4100); ¹H-NMR (Me₂SO-*d*₆) δ : 1.35 (3H, t, $J=7$ Hz, CH₂Me), 3.63 [2H, m, C(5')-H₂], 3.99 [1H, m, C(4')-H], 4.17 [1H, m, C(3')-H], 4.33 [2H, q, $J=7$ Hz, CH₂Me], 4.51 [1H, m, C(2')-H], 5.06 (1H, t, $J=5$ Hz, 5'-OH), 5.29 (1H, d, $J=5$ Hz, 3'-OH), 5.56 (1H, d, $J=6$ Hz, 2'-OH), 5.95 [1H, d, $J=5$ Hz, C(1')-H], 8.77 (2H, s, purine protons), 9.60 (2H, br, NH₂⁺).⁸⁾ Anal. Calcd for C₁₂H₁₇N₅O₄·HI: C, 34.06; H, 4.29; N, 16.55. Found: C, 34.11; H, 4.35; N, 16.59.

1-Ethyladenosine Perchlorate (2b·HClO₄) A solution of 2b·HI (1.69 g, 3.99 mmol) in H₂O (50 ml) was passed through a column packed with Amberlite IRA-402 (ClO₄[−]) (40 ml), and the column was eluted with H₂O (150 ml). The eluates were combined and concentrated *in vacuo* to leave a solid (1.50 g, 95%). Recrystallization of the solid from EtOH afforded an analytical sample of 2b·HClO₄ as colorless minute prisms, mp 158–159 °C (dec.); $[\alpha]_D^{25} -34.9^\circ$ ($c=0.929$, MeOH); UV $\lambda_{\max}^{95\% \text{ EtOH}}$ 260 nm (ϵ 13000); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 1) 259 (13100); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 7) 259 (13100); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 13) 261 (13500), 268 (sh) (12000), 290 (sh) (4000); ¹H-NMR (Me₂SO-*d*₆) δ : 1.35 (3H, t, $J=7$ Hz, CH₂Me), 3.63 [2H, m, C(5')-H₂], 3.99 [1H, m, C(4')-H], 4.17 [1H, m, C(3')-H], 4.32 [2H, q, $J=7$ Hz, CH₂Me], 4.51 [1H, m, C(2')-H], 5.06 (1H, t, $J=5$ Hz, 5'-OH), 5.29 (1H, d, $J=5$ Hz, 3'-OH), 5.56 (1H, d, $J=6$ Hz, 2'-OH), 5.95 [1H, d, $J=5$ Hz, C(1')-H], 8.75 and 8.76 (1H each, s, purine protons), 9.57 (2H, br, NH₂⁺). Anal. Calcd for C₁₂H₁₇N₅O₄·HClO₄: C, 36.42; H, 4.58; N, 17.70. Found: C, 36.47; H, 4.63; N, 17.64.

1-Ethyladenosine (2b) A solution of 2b·HI (2.96 g, 6.99 mmol) in H₂O (100 ml) was passed through a column packed with Amberlite IRA-402 (HCO₃[−]) (22 ml), and the column was eluted with H₂O (250 ml). The

eluates were combined and concentrated *in vacuo* below 45 °C, leaving an oil. The oily residue was dissolved in MeOH (10 ml), and the solution was kept in a refrigerator for several hours. The precipitate that resulted was collected by filtration and dried to give 2b (1.80 g, 87%). Recrystallization from MeOH afforded an analytical sample as colorless prisms, mp 198–200 °C (dec.); $[\alpha]_D^{25} -60^\circ$ ($c=0.149$, MeOH); UV $\lambda_{\max}^{95\% \text{ EtOH}}$ 254 nm (sh) (ϵ 11000), 260 (13300), 268 (11000), 288 (sh) (3900); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 1) 259 (13700); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 7) 259 (13700); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 13) 261 (14300), 268 (sh) (12800); 290 (sh) (4300); ¹H-NMR (Me₂SO-*d*₆) δ : 1.27 (3H, t, $J=7$ Hz, CH₂Me), 3.59 [2H, m, C(5')-H₂], 3.92 [1H, m, C(4')-H], 4.05 [2H, q, $J=7$ Hz, overlapped with a one-proton m [C(3')-H], CH₂Me], 4.47 [1H, m, C(2')-H], 5.09 (1H, t, $J=5$ Hz, 5'-OH), 5.16 (1H, d, $J=5$ Hz, 3'-OH), 5.43 (1H, d, $J=6$ Hz, 2'-OH), 5.75 [1H, d, $J=6$ Hz, C(1')-H], 7.03 (1H, br, NH), 8.09 and 8.14 (1H each, s, purine protons).⁹⁾ Anal. Calcd for C₁₂H₁₇N₅O₄: C, 48.81; H, 5.80; N, 23.72. Found: C, 48.73; H, 5.84; N, 23.53.

1-Ethyladenine (3b) i) A solution of 2b·HI (3.18 g, 7.51 mmol) in 0.5 N aqueous HCl (150 ml) was heated at 92–94 °C for 30 min. The reaction mixture was concentrated *in vacuo*, and the residue was dissolved in H₂O (100 ml). The resulting aqueous solution was passed through a column of Amberlite IRA-402 (HCO₃[−]) (100 ml), and the column was eluted with H₂O (200 ml). The eluates were combined and concentrated *in vacuo* to a volume of ca. 15 ml and kept in a refrigerator to complete crystallization. The precipitate that resulted was collected by filtration and dried to give 3b·1/2H₂O (985 mg, 76%) as a colorless solid, mp ca. 250 °C (dec.). Recrystallization from MeOH and drying over P₂O₅ at 2 mmHg and 50 °C for 21 h afforded an analytical sample of 3b·1/2H₂O as colorless prisms, mp 252–254 °C (dec.)¹⁰⁾ (lit.^{3c)} mp 265–266 °C; UV $\lambda_{\max}^{95\% \text{ EtOH}}$ 227 nm (ϵ 22100), 274 (12300); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 1) 261 (11800); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 7) 267 (11400); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 13) 272 (14700); ¹H-NMR (Me₂SO-*d*₆) δ : 1.30 (3H, t, $J=7$ Hz, CH₂Me), 3.46 (br, NH₂ and H₂O), 4.21 (2H, q, $J=7$ Hz, CH₂Me), 7.85 and 8.18 (1H each, s, purine protons). Anal. Calcd for C₇H₉N₅·1/2H₂O: C, 48.83; H, 5.85; N, 40.67. Found: C, 48.75; H, 6.01; N, 40.58.

ii) A mixture of adenosine (1) (40.0 g, 0.15 mol) and EtI (53 ml, 0.66 mol) in AcNMe₂ (500 ml) was stirred at room temperature for 5.5 h and then at 30 °C for 163 h. The reaction mixture was concentrated *in vacuo* to leave a yellowish brown oil, which was washed with ether and then dissolved in 0.5 N aqueous HCl (450 ml). The resulting solution was heated at 95–100 °C (bath temperature) for 45 min, concentrated *in vacuo* to a volume of ca. 150 ml, brought to pH 8.5 by addition of concentrated aqueous NH₃, and kept in a refrigerator overnight. The yellowish brown precipitate that resulted was filtered off and dried to give 3b·1/2H₂O (20.5 g, 80%). Recrystallization from MeOH and drying over P₂O₅ at 2 mmHg and 55 °C for 16 h yielded a pure sample as colorless prisms, mp 252–253 °C (dec.). This sample was identical [by comparison of the thin-layer chromatographic (TLC) mobility] with the one prepared by method (i).

1-Ethyladenine Hydrochloride (3b·HCl) The free base 3b·1/2H₂O (1.53 g, 8.89 mmol) was dissolved in 5% aqueous HCl (26 ml), and the resulting solution was concentrated to dryness *in vacuo*. The residue was then recrystallized from EtOH to furnish 3b·HCl·1/5H₂O (1.45 g, 80%) as colorless needles, mp 259.5–261 °C (dec.). Further recrystallization from EtOH and drying over P₂O₅ at 2 mmHg and 75 °C for 14 h provided an analytical sample as colorless needles, mp 260–261 °C (dec.). Anal. Calcd for C₇H₉N₅·HCl·1/5H₂O: C, 41.37; H, 5.16; N, 34.46. Found: C, 41.61; H, 5.22; N, 34.54.

1-Ethyladenine Perchlorate (3b·HClO₄) i) The hydrochloride 3b·HCl·1/5H₂O (201 mg, 0.98 mmol) was dissolved in a small amount of H₂O, and a solution of NaClO₄ (185 mg, 1.51 mmol) in H₂O (0.2 ml) was added. The resulting mixture was concentrated *in vacuo* to a volume of ca. 1 ml and then kept in a refrigerator overnight. The colorless precipitate that deposited was filtered off, washed with a little H₂O, and dried to afford 3b·HClO₄ (195 mg, 75%). Recrystallization from H₂O yielded an analytical sample as colorless prisms, mp 277.5–278.5 °C (dec.); pK_a 7.08 ± 0.06 and 11.40 ± 0.06 (at 40 °C and ionic strength 1.0)¹¹⁾ (lit.^{3a)} pK_a 6.9 and 11.4; UV $\lambda_{\max}^{95\% \text{ EtOH}}$ 225 nm (sh) (ϵ 8700), 265 (11500); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 1) 259 (12900); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 7) 265 (12000); $\lambda_{\max}^{\text{H}_2\text{O}}$ (pH 13) 271 (16100); ¹H-NMR (Me₂SO-*d*₆) δ : 1.34 (3H, t, $J=7$ Hz, CH₂Me), 4.30 (2H, q, $J=7$ Hz, CH₂Me), 8.48 and 8.65 (1H each, s, purine protons), 8.8–10.0 (2H, br, NH₂), 13.7–14.3 (1H, br, NH). Anal. Calcd for C₇H₉N₅·HClO₄: C, 31.89; H, 3.82; N, 26.56. Found: C, 31.77; H, 3.79; N, 26.55.

ii) A mixture of adenosine (1) (10.0 g, 37.4 mmol) and EtI (58.3 g, 374 mmol) in AcNMe₂ (125 ml) was stirred at 35 °C for 98 h. The reaction mixture was worked up as described above for 3b under item (ii), giving crude 3b as a colorless solid. The total amount of the solid was dissolved

in aqueous HClO_4 , which had been prepared by diluting 70% aqueous HClO_4 (6.44 g, 44.9 mmol) with H_2O (30 ml). The resulting solution was kept in a refrigerator for 2 h, and the colorless prisms that resulted were filtered off and dried to provide $3b \cdot \text{HClO}_4$ (4.49 g, 46% overall yield from **1**). Recrystallization from H_2O yielded a pure sample as colorless prisms, mp 277.5–278.5 °C (dec.). This sample was identical [by comparison of the infrared (IR) spectrum] with the one obtained by method (i).

iii) A mixture of $2b \cdot \text{HClO}_4$ (158 mg, 0.4 mmol) and AcOH (1.2 ml) was heated under reflux for 60 min. After cooling, the reaction mixture deposited a colorless precipitate, which was collected by filtration, washed successively with a little AcOH and ether, and dried to give $3b \cdot \text{HClO}_4$ (75 mg, 71%), mp 275–276 °C (dec.). This sample was identical (by comparison of the IR spectrum and TLC mobility) with the one prepared by method (i). Recrystallization from H_2O formed colorless prisms, mp 277.5–278.5 °C (dec.).

Determination of 1-Ethyladenine (3b) in Glycosidic Cleavage Study The glycosidic cleavage reactions of **2b**, $2b \cdot \text{HI}$, and $2b \cdot \text{HClO}_4$ were carried out as specified in Table I. After cooling, an aliquot (0.2 ml) of each reaction mixture was applied along a 13-cm line on Toyo Roshi No. 51A filter paper. Paper electrophoresis was then conducted with a Toyo Kagaku EP-2 apparatus at 500 V for 3 h using 0.01 M KH_2PO_4 – Na_2HPO_4 buffer (pH 8.09 at 18 °C). A zone whose mobility corresponded to that of authentic **3b** was detected on the filter paper under UV light (254 nm), excised, and extracted with 0.01 N aqueous HCl (5 ml). The optical density of the extract at 258 nm was then read against a blank extract, and the concentration of **3b** in the extract was estimated from a calibration curve which had been obtained by applying a similar process to AcOH solutions containing known amounts of pure samples of **3b** and **2b**. The results are listed in Table I.

References and Notes

- 1) Paper XLV in this series, T. Fujii, M. Ohba, M. Sakari, and S. Matsubara, *Chem. Pharm. Bull.*, **38**, 2702 (1990).
- 2) a) T. Itaya, F. Tanaka, and T. Fujii, *Tetrahedron*, **28**, 535 (1972); b) T. Fujii, T. Itaya, and T. Saito, *Chem. Pharm. Bull.*, **23**, 54 (1975).
- 3) a) B. C. Pal, *Biochemistry*, **1**, 558 (1962); b) K. Suzuki and I. Kumashiro, Brit. Patent 1134974 (1968) [*Chem. Abstr.*, **70**, 58231n (1969)]; c) R. Denayer, *Ind. Chim. Belge*, **32**, 215 (1967) [*Chem. Abstr.*, **70**, 68314f (1969)].
- 4) J. W. Jones and R. K. Robins, *J. Am. Chem. Soc.*, **85**, 193 (1963).
- 5) See, for instance, a) N. J. Leonard and T. Fujii, *Proc. Natl. Acad. Sci. U.S.A.*, **51**, 73 (1964); b) L. Rosen, *Biochem. Biophys. Res. Commun.*, **33**, 546 (1968) [*Chem. Abstr.*, **70**, 26918a (1969)]; c) D. M. G. Martin and C. B. Reese, *J. Chem. Soc. (C)*, **1968**, 1731; d) P. Brookes, A. Dipple, and P. D. Lawley, *ibid.*, **1968**, 2026; e) E. R. Garrett and P. J. Mehta, *J. Am. Chem. Soc.*, **94**, 8532 (1972); f) P. D. Lawley, D. J. Orr, and M. Jarman, *Biochem. J.*, **145**, 73 (1975); g) M. Dorée, P. Guerrier, and N. J. Leonard, *Proc. Natl. Acad. Sci. U. S. A.*, **73**, 1669 (1976); h) M. Dreyfus, G. Dodin, O. Bensaude, and J. E. Dubois, *J. Am. Chem. Soc.*, **99**, 7027 (1977); i) T. Itaya, F. Tanaka, T. Fujii, and N. J. Leonard, *Chem. Pharm. Bull.*, **25**, 1449 (1977); j) J. A. Montgomery and H. J. Thomas, *J. Heterocycl. Chem.*, **17**, 583 (1980); k) D. B. Ludlum, *Biochim. Biophys. Acta*, **174**, 773 (1969).
- 6) a) F. J.-M. Rajabalee and S. Hanessian, *Can. J. Chem.*, **49**, 1981 (1971); b) B. Singer, L. Sun, and H. Fraenkel-Conrat, *Biochemistry*, **13**, 1913 (1974); c) T. Shimidzu, T. Kanou, A. Murakami, K. Yamana, H. Inagaki, and N. Donkai, *J. Chem. Res., Synop.*, **1980**, 376 [*Idem*, *J. Chem. Res. (M)*, **1980**, 4668]; d) H. C. Box, K. T. Lilga, J. B. French, G. Potienko, and J. L. Alderfer, *J. Carbohydr., Nucleosides, Nucleotides*, **8**, 189 (1981).
- 7) a) J. A. Zoltewicz, D. F. Clark, T. W. Sharpless, and G. Grahe, *J. Am. Chem. Soc.*, **92**, 1741 (1970); b) J. L. York, *J. Org. Chem.*, **46**, 2171 (1981), and references cited therein.
- 8) For the ^{13}C -NMR spectral data for $2b \cdot \text{HI}$, see ref. 6d.
- 9) For the ^{13}C -NMR spectral data for **2b**, see refs. 6c and 6d.
- 10) For the anodic peak potential (E_{pa}) data for **3b**, see T. Sato, K. Fukuzaki, and T. Fujii, *Bull. Chem. Soc. Jpn.*, **59**, 1599 (1986).
- 11) Determined by UV spectrophotometry in a manner similar to that described previously.^{2b)}