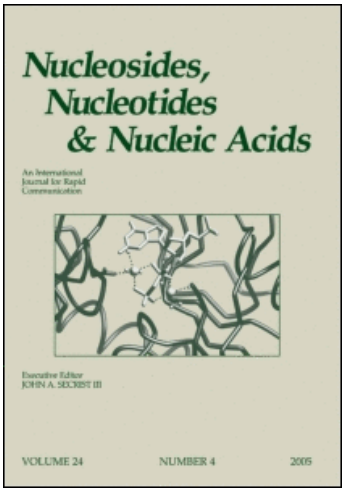
This article was downloaded by:
On: *27 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



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

Chemical Conversion of Some Ribonucleosides into the Corresponding β-D-Arabinofuranosyl Derivatives[1]

Nobuo Sakairi[a]; Ichiro Hirao[b]; Yoshiaki Zama[c]; Yoshiharu Ishido[b]
[a] School of Dental Medicine, Tsurumi University, Tsurumi, Tsurumi-ku, Yokohama, Japan [b] Department of Chemistry, Faculty of Science, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo, Japan [c] Central Research Laboratories, Kaken Chemical Co., Ltd., Honkomagome, Bunkyo-ku, Tokyo, Japan

To cite this Article Sakairi, Nobuo , Hirao, Ichiro , Zama, Yoshiaki and Ishido, Yoshiharu(1983) 'Chemical Conversion of Some Ribonucleosides into the Corresponding β-D-Arabinofuranosyl Derivatives[1]', Nucleosides, Nucleotides and Nucleic Acids, 2: 3, 221 — 229
To link to this Article: DOI: 10.1080/07328318308078856
URL: http://dx.doi.org/10.1080/07328318308078856

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

NUCLEOSIDES & NUCLEOTIDES, 2(3), 221-229 (1983)

CHEMICAL CONVERSION OF SOME RIBONUCLEOSIDES INTO THE CORRESPONDING β-D-ARABINOFURANOSYL DERIVATIVES[1]

Nobuo Sakairi,[†1] Ichiro Hirao,[†2] Yoshiaki Zama,[†3] and Yoshiharu Ishido*,[†2]

[†1]School of Dental Medicine, Tsurumi University, Tsurumi, Tsurumi-ku, Yokohama 230, Japan

[†2]Department of Chemistry, Faculty of Science, Tokyo Institute of Technology, O-okayama, Meguro-ku, Tokyo 152, Japan

[†3]Central Research Laboratories, Kaken Chemical Co., Ltd., Honkomagome, Bunkyo-ku, Tokyo 113, Japan

Downloaded At: 10:32 27 January 2011

Abstract: Five 3',5'-di-O-acylribonucleosides were converted into the corresponding β-D-arabinofuranosyl derivatives through DMSO-oxidation followed by $NaBH_4$-reduction and deacylation with NaOMe-MeOH.

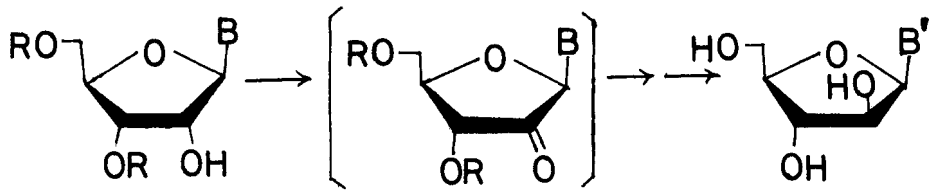
Some of arabinofuranosyl nucleosides, e.g., 9-β-D-arabinofuranosyladenine (Ara A) and 1-β-D-arabinofuranosylcytosine (Ara C) are known for their antiviral and antileukemic properties.[2] Typically, purine β-D-arabinonucleosides have been derived from 2',3'-anhydrolyxonucleosides by Reist et al.,[3] from 8,2'-cyclonucleosides by Ikehara and Ogiso,[4] by Sowa and Tsunoda,[5] and by Chattopadhyaya and Reese,[6] from condensation of arabinofuranose derivatives and purines by Glaudemans and Fletcher,[7] and by Keller et al.,[8] and from 2'-trifluoromethanesulfonate by Ranganathan and Larwood[9]; however, these procedures were tedious to perform and, in addition, the total yields were not so high.

Copyright © 1983 by Marcel Dekker, Inc. 0732-8311/83/0203-0221$3.50/0

On the other hand, Moffatt et al.[10] reported the synthesis of 1-β-D-arabinofuranosyl uracil and cytosine through DMSO-oxidation and subsequent stereoselective reduction with sodium borohydride of the corresponding 3',5'-di-O-trityl derivatives. We have recently established regioselective 2'-O-deacylation of fully acylated purine and pyrimidine ribonucleosides by treatment with hydrazine hydrate in acetic acid-pyridine (1:4 v/v) and/or hydroxylaminium acetate in pyridine, giving the corresponding 2'-OH derivatives in high yields.[11] Thus, we tried to covert the 3',5'-diacylates to the corresponding β-D-arabinofuranosyl derivatives by the method reported by Moffatt et al.[10]

In addition to 3',5'-di-O-benzoyladenosine[11] (1), 3',5'-di-O-benzoyl-N^6-benzyladenosine[11] (2), and 3',5'-di-O-acetyl-N^2-benzoylguanosine[11] (3), 9-(3,5-di-O-benzoyl-β-D-ribofuranosyl)-6-methylthiopurine (4) and 4-amino-7-(3,5-di-O-benzoyl-β-D-ribofuranosyl)pyrrolo[2,3-d]pyrimidine (5) were prepared from 9-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-6-methylthiopurine (6) and 4-dibenzoylamino-7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)pyrrolo[2,3-d]pyrimidine (7), respectively by the hydrazinolysis procedure. Oxidation of 1, 2, 3, and 4 with DMSO-trifluoroacetic anhydride at -78°C,[12] and of 5 with DMSO-acetic anhydride[13] gave the corresponding pentofuran-2'-uloside derivatives. Thin layer chromatography of these reaction mixtures showed that they contained more than three components, which might be the starting material, the corresponding pentofuran-2'-ulosides, and their hydrates; Separation of the mixture with silica gel-column chromatography (chloroform-methanol system) was unsuccessful due to undesirable decomposition of the furan-2'-ulosides on silica gel. Therefore, we directly treated the oxidation mixture with sodium borohydride at 0°C in benzene-ethanol (1:1 v/v) and with sodium methoxide in methanol for deacylation, and purified the objective products —— 9-β-D-arabinofuranosyladenine (8), 9-β-D-arabinofuranosyl-N^6-benzyladenine (9), 9-β-D-arabinofuranosylguanine (10), 9-β-D-arabinofuranosyl-6-methylthiopurine (11), and 4-amino-7-β-D-arabinofuranosylpyrrolo[2,3-

Downloaded At: 10:32 27 January 2011



1: B=Adenine-9, R=Bz
2: B=N^6-Benzyladenine-9, R=Bz
3: B=N^2-Benzoylguanine-9, R=Ac
4: B=6-Methylthiopurine-9, R=Bz
5: B=7-Deazaadenine-9, R=Bz

8: B'=Adenine-9
9: B'=N^6-Benzyladenine-9
10: B'=Guanine-9
11: B'=6-Methylthiopurine-9
12: B'=7-Deazaadenine-9

TABLE Synthesis of Arabinofuranosides [a]

Entry	B	Method	Yield (%)
1	Adenine-9 (1)	DMSO-TFAA	66[b]
2	N^6-Benzyladenine-9 (2)	DMSO-TFAA	70
3	N^2-Benzoylguanine-9 (3)	DMSO-TFAA	38
4	6-Methylthiopurine-9 (4)	DMSO-TFAA	51
5	7-Deazaadenine-9 (5)	DMSO-AA	40

[a] Oxidation reactions were performed by the use of dimethyl sulfoxide (DMSO)-trifluoroacetic anhydride (TFAA) at -78°C, or DMSO-acetic anhydride (AA) at room temperature, and the products were isolated after reduction with $NaBH_4$ at 0°C, followed by deacylation.
[b] The yield was 63% on oxidation with DMSO-AA in place of TFAA (ref. 10).

d]pyrimidine (12) —— through column chromatography on Dowex 1 x 2 [OH^- form], reported by Dekker,[14] or on silica gel. The results thus obtained are summarized in the TABLE.

In conclusion, Swern-oxidation of ribonucleoside 3',5'-diacylates, followed by $NaBH_4$-reduction, is effective for the conversion to the corresponding β-D-arabinonucleosides.

EXPERIMENTAL SECTION

Melting points were determined with a Yanagimoto Micro Melting Point Apparatus and are uncorrected. Specific

Downloaded At: 10:32 27 January 2011

rotational values were determined with a JASCO DIP-4 apparatus. U.v. spectra were recorded with a Hitachi EPS 3T spectrometer for solution in ethanol. ^{1}H-n.m.r. spectra were recorded with a Varian T-60 instrument (Tetramethylsilane as the internal standard). T.l.c. was performed on Merck 60 F_{254} silica gel precoated plates (thickness 0.25 mm) employing chloroform-methanol (9:1 v/v) as eluent. Column chromatography was performed on Wakogel C-300. Elementary analysis was performed with a Perkin-Elmer 240-002 instrument by Miss Mikiko Aoki, Laboratory of Organic Analysis, Department of Chemistry, Tokyo Institute of Technology.

9-β-D-Arabinofuranosyladenine (8).

To a stirred solution of dimethyl sulfoxide (0.43 mL, 6 mmol) in dichloromethane (6 mL) in a dry ice-acetone bath, trifluoroacetic anhydride (0.19 mL, 9 mmol) in dichloromethane (6 mL) was added dropwise, and stirred for 10 min. To the resulting mixture 3',5'-di-O-benzoyladenosine[11] (1) (1.43 g, 3 mmol) in dichloromethane-dimethyl sulfoxide (1:1 v/v, 20 mL) was added dropwise, and stirred for 30 min, after which triethylamine (4 mL) was added dropwise, followed by warming to room temperature. The reaction mixture was then poured into ice-water, and the solution was extracted with dichloromethane (100 mL). The organic layer was washed successively with 1 M hydrochloric acid, aqueous saturated sodium hydrogen carbonate, and water, and dried over anhydrous magnesium sulfate. A syrup obtained by evaporation of the organic solution was then dissolved in benzene-ethanol (1:1 v/v, 50 mL) and the resulting solution was treated with sodium borohydride (150 mg) at 0°C. After stirring the mixture at 0°C for 2 h, it was then evaporated to dryness, and the residue was dissolved in anhydrous methanol (20 mL), to which several drops of 2 M methanolic sodium methoxide was added, and the solution was stirred overnight at room temperature. The syrup obtained by evaporation of the resulting solution was subjected to chromatographic purification on a column of Dowex 1 x 2 [OH^- form] ion-exchange resin, eluting successively with 60% aqueous

Downloaded At: 10:32 27 January 2011

methanol and 0.1 M aqueous ammonium hydrogen carbonate. The fraction eluted by the latter was evaporated to dryness and the residue was recrystallized from water to give 8 (0.64 g, 66% yield), identical to an authentic sample.[11]

9-β-D-Arabinofuranosyl-N^6-benzyladenosine (9).

Treatment of 3',5'-di-O-benzoyl-N^6-benzyladenosine[11] (2) (1.0 g, 1.7 mmol) with trifluoroacetic anhydride-dimethyl sulfoxide, followed by sodium borohydride and methanolic sodium methoxide in the same way as above, and chromatographic purification on a column of silica gel (elution with chloroform-methanol (9:1 v/v)], gave 9 (0.42 g, 70% yield); m.p. 195-197°C (from ethanol), $[\alpha]_D^{23}$ -5°, N,N-dimethylformamide), ^{1}H-n.m.r. [dimethyl sulfoxide-d_6 – chloroform-d (1:1 v/v)] δ 6.40 (d, 1, $J_{1',2'}$ 4.0 Hz, H-1'), 7.35 (m, 5, Ph), 8.30 (s, 1, H-2), and 8.33 (s, 1, H-8).

Anal. Calcd for $C_{17}H_{19}N_5O_4$: C, 57.14; H, 5.36; N, 19.60. Found: C, 56.82; H, 5.45; N, 19.33.

9-β-D-Arabinofuranosylguanine (10).

Treatment of 3',5'-di-O-acetyl-N^2-benzoylguanosine[11] (3) (0.47 g, 1.0 mmol) with trifluoroacetic anhydride-dimethyl sulfoxide, followed by sodium borohydride and methanolic sodium methoxide in the same way as above, and chromatographic purification on a column of Dowex 1 x 2 [OH^- form], eluting successively with 60% aqueous methanol and 0.1 M and 0.2 M aqueous ammonium hydrogen carbonate, gave 10 (0.11 g, 38% yield); m.p. 262-266°C (decomp.) (from water) [lit.[15] m.p. 265°C (decomp.)], ^{1}H-n.m.r. (dimethyl sulfoxide-d_6) δ 6.40 (d, 1, $J_{1',2'}$ 3.5 Hz, H-1').

9-(3,5-Di-O-benzoyl-β-D-ribofuranosyl)-6-methylthiopurine (4).

9-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-6-methylthiopurine (6) (6.10 g, 10 mmol) and hydroxylaminium acetate (3.70 g, 40 mmol) were stirred in pyridine (50 mL) at room temperature for 2 d. After quenching the resulting solution with acetone (ca. 10 mL) with stirring, the reaction

Downloaded At: 10:32 27 January 2011

mixture was evaporated to a syrup, which was then chromatographed on a column of silica gel [chloroform-methanol (97:3 v/v)] to give 4 (2.7 g, 53% yield); m.p. 116-117.5°C (from ethanol), $[\alpha]_D^{20}$ -76.4° (c 1.0, N,N-dimethylformamide), λ_{max}(EtOH) 283 nm (ε 18500) and $\lambda_{shoulder}$(EtOH) 289 nm (ε 17900), ^{1}H-n.m.r. (chloroform-d) δ 2.60 (s, 3, SMe), 4.40-4.96 (m, 3, H-4', 5', and 5"), 5.17-5147 (m, 1, H-2'), 5.72-5.93 (m, 1, H-3'), 6.18 (d, 1, $J_{1',2'}$ 5.4 Hz, H-1'), and 7.07-8.60 (m, 12, H-2, 8, and Ph x 2).

Anal. Calcd for $C_{25}H_{26}N_4O_6S$: C, 59.28; H, 4.38; N, 11.06; S, 6.33. Found: C, 59.05; H, 4.40; N, 10.81; S, 6.37.

9-β-D-Arabinofuranosyl-6-methylthiopurine (11).

Treatment of 4 (1.52 g, 3 mmol) with trifluoroacetic anhydride-dimethyl sulfoxide, followed by sodium borohydride and methanolic sodium methoxide in the same way as described above, and chromatographic purification on silica gel, gave 11 (0.46 g, 51% yield); m.p. 182-192°C, $[\alpha]_D^{20}$ -2.2° (c 1.0, N,N-dimethylforamide), λ_{max}(EtOH) 283 nm (ε 18500) and $\lambda_{shoulder}$(EtOH) 289 nm (ε 17900), ^{1}H-n.m.r. (dimethyl sulfoxide-d_6) δ 2.70 (sm 3, SMe), 3.55-4.05 (m, 3, H-4', 5', and 5"), 4.05-4.49 (m, 2, H-2' and 3'), 5.02-5.31 (m, 1, 5'-OH), 5.53-5.77 (m, 2, 2'- and 3'-OH), 6.43 (d, 1, $J_{1',2'}$ 4.2 Hz, H-1'), 8.55 (s, 1, H-2), and 8.75 (s, 1, H-8).

Anal. Calcd for $C_{11}H_{14}N_4O_4S$: C, 44.29; H, 4.73; N, 18.78; S, 10.75. Found: C, 44.56; H, 4.71; N, 18.79; S, 10.49.

4-Amino-7-(3,5-di-O-benzoyl-β-D-ribofuranosyl)pyrrolo[2,3-d]pyrimidine (5).

A solution of 4-dibenzoylamino-7-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)pyrrolo[2,3-d]pyrimidine[16] (7) (3.13 g, 4 mmol) and hydrazine hydrate (1.4 mL, 28 mmol) in acetic acid-pyridine (1:19 v/v, 30 mL) was stirred at room temperature for 2 d, at which time further hydrazine hydrate (0.6 mL, 12 mmol) was added, and stirring continued for 2 d.

Downloaded At: 10:32 27 January 2011

After quenching the resulting solution with acetone (ca. 10 mL) with stirring, it was evaporated to a syrup, which was then chromatographed on a column of silica gel; elution with chloroform-methanol (97:3 v/v) gave a syrupy mixture of dibenzoates (1.34 g, 70% yield) and crystallization of the suryp from methanol gave 5 (1.06 g, 56% yield), and elution with chloroform-methanol (95:5 v/v) gave 4-amino-7-(5-O-benzoyl-β-D-ribofuranosyl)pyrrolo[2,3-d]pyrimidine (13) (0.18 g, 12% yield).

Compound 5 had m.p. 178-179°C, $[\alpha]_D^{22}$ -51° (c 1,5, N,N-dimethylformamide), λ_{max}(EtOH) 270 nm (ε 13600) and 227 nm (ε 30000), λ_{min}(EtOH) 249 nm (ε 7900), ^{1}H-n.m.r. [dimethyl sulfoxide-d_6 – acetone-d_6 (1:1 v/v)] δ 4.60-4.95 (m, 3, H-4', 5', and 5"), 5.05 (t, 1, $J_{1',2'} = J_{2',3'}$ 6.0 Hz, H-2'), 5.65-5.85 (m, 1, H-3'), 6.40 (d, 1, H-1'), 6.63 (d, 1, $J_{5,6}$ 3.5 Hz, H-5), 6.7 (broad s, 2, NH_2), 7.36 (d, 1, H-6), and 7.20-8.40 (m, 11, H-2 and Ph x 2).

Anal. Calcd for $C_{25}H_{22}N_4O_6$: C, 63.28; H, 4.67; N, 11.81. Found: C, 63.32; H, 4.69; N, 11.82.

Compound 13 had m.p. 205-205.5°C, $[\alpha]_D^{22}$ -37° (c 1.5, N,N-dimethylformamide), λ_{max}(EtOH) 271 nm (ε 18000), λ_{min} (EtOH) 248 nm (ε 7400), ^{1}H-n.m.r. (dimethyl sulfoxide-d_6) δ 4.20-4.47 (m, 5, H-2', 3', 4', 5', and 5"), 6.17 (d, 1, $J_{1',2'}$ 4.5 Hz, H-1'), 6.63 (d, 1, $J_{5,6}$ 3.5 Hz, H-5), 6.9 (broad s, 2, NH_2), 7.20 (d, 1, H-6), and 7.25-8.20 (m, 6, H-2 and Ph).

Anal. Calcd for $C_{18}H_{18}N_4O_5 \cdot H_2O$: C, 56.98; H, 5.05; N, 14.77. Found: C, 57.02; H, 4.87; N, 14.69.

4-Amino-7-β-D-arabinofuranosylpyrrolo[2,3-d]pyrimidine (12).

A solution of 5 (1.42 g, 3 mmol) in dimethyl sulfoxide (20 mL) and acetic anhydride (10 mL) was stirred at room temperature for 14 h. The resulting mixture was poured into ice-water, and the mixture was extracted with ethyl acetate (250 mL), and the extract was washed with aqueous saturated sodium hydrogen carbonate and with water. After drying the organic solution over sodium sulfate, it was evaporated to give a syrup, which was dissolved in benzene-

Downloaded At: 10:32 27 January 2011

ethanol (1:1 v/v, 50 mL), treated with sodium borohydride (200 mg), and allowed to stand at 0°C with stirring for 2 h. The reaction mixture was evaporated, the residue was distributed in a 1:1 mixture of ethyl acetate and water, and the organic layer was dried over sodium sulfate after washing with water. The organic solution, after filtering the dessicant off, was evaporated, and the syrup thus obtained was subjected to chromatographic purification on a column of silica gel [carbon tetrachloride-acetone (2:1 v/v)] to give a mixture of dibenzoates (700 mg). This mixture was dissolved in methanol (5 mL) to which was added 0.5 M methanolic sodium methoxide (0.5 mL), and the mixture was heated under reflux for 3 h. Evaporation of the resulting mixture left a syrup which gave 12 (320 mg, 40% yield) by chromatographic purification on a column of Dowex 1 x 2 [OH^- form] (elution with 60% aqueous methanol).

Compound 12 had m.p. 203-2-6°C (determined with a YAZAWA Micro Melting Point Apparatus), different from m.p. 125-126°C of an authentic sample,[17] although its ^{1}H-n.m.r. data [(dimethyl sulfoxide-d_6) δ 3.58-3.80 (m, 3, H-4', 5', and 5"), 3.98-4.20 (m, 2, H-2' and 3'), 6.42 (d, 1, $J_{1',2'}$ 4.0 Hz, H-1'), 6.50 (d, 1, $J_{5,6}$ 4.0 Hz, H-5), 6.9 (broad s, 2, NH_2), 7.30 (d, 1, H-6), and 8.03 (s, 1, H-2)] and behavior in TLC under the conditions used were identical with those[17] reported.

Anal. Calcd for $C_{11}H_{14}N_4O_4 \cdot 0.4\ H_2O$: C, 48.31; H, 5.46; N, 20.49. Found: C, 48.37; H, 5.48; N, 20.21.

ACKNOWLEDGMENT

This work was supported in part by a Grant-in-aid for Cancer Research (No. 53-11) from the Ministry of Health and Welfare, Japan.

REFERENCES

1. Partial Protection of Carbohydrate Derivatives. Part 12. For Part 11, see H. Tsutsumi and Y. Ishido,

Downloaded At: 10:32 27 January 2011

Carbohydr. Res., 111, 75-84 (1982).
2. S. S. Cohen, " Progress in Nucleic Acid Research and Molecular Biology," Vol. 5, Academic Press, New York and London, 1966.
3. E. J. Reist, A. Benitez, L. Goodman, B. R. Baker, and W. W. Lee, J. Org. Chem., 27, 3274-3279 (1962).
4. M. Ikehara and Y. Ogiso, Tetrahedron, 28, 3659-3704 (1972).
5. T. Sowa and K. Tsunoda, Bull. Chem. Soc. Jpn., 48, 3243-3245 (1975).
6. J. B. Chattopadhyaya and C. B. Reese, J. Chem. Soc., Chem. Commun., 414-415 (1977).
7. C. P. J. Glaudemans and H. G. Fletcher, Jr., J. Org. Chem., 28, 3004-3006 (1963).
8. F. Keller, J. J. Botvinick, and J. E. Bunker, J. Org. Chem., 32, 1644-1646 (1967).
9. R. Ranganathan and D. Larwood, Tetrahedron Lett., 4341-4344 (1978).
10. U. Brodbeck and J. G. Moffatt, J. Org. Chem., 35, 3552-3558 (1970).
11. Y. Ishido, N. Nakazaki, and N. Sakairi, J. Chem. Soc., Perkin Trans. 1, 2088-2098 (1979).
Y. Ishido, N. Sakairi, K. Okazaki, and N. Nakazaki, ibid., 563-573 (1980).
12. K. Omura, A. K. Sharma, and D. Swern, J. Org. Chem., 41, 975-962 (1976).
S. L. Juang, K. Omura, and D. Swern, ibid., 41, 3329-3331 (1976).
13. J. D. Albright and L. Goodman, J. Am. Chem. Soc., 87, 4241-4216 (1965).
14. C. A. Dekker, J. Am. Chem. Soc., 87, 4027-4029 (1965).
15. E. J. Reist and L. Goodman, Biochem., 3, 15-18 (1963).
16. A. R. Hanze, Biochem., 7, 932-939 (1968).
17. M. J. Robins, Y. Fouron, and W. H. Muhs, Can. J. Chem., 55, 1260-1267 (1977).

Received May 5, 1983

Downloaded At: 10:32 27 January 2011