*Anal.* Calcd for $C_9H_{18}ClNO_4S$: C, 39.88; H, 6.84; S, 11.40; mol wt, 272. Found: C, 39.98; H, 6.70; S, 11.58; mol wt (in benzene), 269.

**1-Chloro-2-hydroxy-2-phenylethanesulfonmorpholide (8).**—Chloromethanesulfonmorpholide (1.99 g, 0.01 mol), *n*-butyllithium (0.01 mol), and benzaldehyde (1.17 g, 0.011 mol) afforded a yellow oil which upon crystallization and recrystallization from 95% ethanol gave 1.19 g (39%) of diastereomeric **8**, mp 138–155°, nmr $\delta$ 3.65 (m, 9), 4.90–5.80 (m, 2), 7.50 (s, 5).

*Anal.* Calcd for $C_{12}H_{16}ClNO_4S$: C, 47.12; H, 5.24; Cl, 11.61. Found: C, 46.72; H, 5.34; Cl, 11.52.

Repeated fractional crystallization from 95% ethanol gave 0.62 g (20%) of one pure diastereomer, mp 156.5–158°, which was assigned the erythro configuration (see Table I) on the basis of the nmr spectrum: $\delta$ 3.21 (d, 1, $J$ = 4.0 Hz, –OH), 3.70 (m, 8), 4.87 d, 1, $J$ = 1.6 Hz, >CHCl), 5.67 (m, 1, >CHOH). This isomer also gave a satisfactory analysis for $C_{12}H_{16}ClNO_4S$.

**1-Chloro-2-hydroxy-2-(*o*-chlorophenyl)ethanesulfonmorpholide (9).**—Chloromethanesulfonmorpholide (1.99 g, 0.01 mol) and *o*-chlorobenzaldehyde (1.55 g, 0.011 mol) gave, after recrystallization of the crude product from 95% ethanol, 3.16 g (93%) of diastereomeric **9**, mp 108–141°, nmr $\delta$ 3.62 (m, 10), 5.30 (m, 1), 7.60 (m, 4).

*Anal.* Calcd for $C_{12}H_{15}Cl_2NO_4S$: C, 42.50; H, 4.41; Cl, 20.82. Found: C, 42.46; H, 4.56; Cl, 21.01.

**1-Chloro-2-hydroxy-2-(*m*-methoxyphenyl)ethanesulfonmorpholide (10).**—Chloromethanesulfonmorpholide (2.20 g, 0.011 mol), *n*-butyllithium (0.011 mol), and *m*-methoxybenzaldehyde (1.53 g, 0.0112 mol) afforded a yellow oil which was recrystallized from 90% ethanol to give a white solid, which was further recrystallized from benzene–hexane to yield 3.00 g (81%) of **10**, tentatively assigned the threo configuration (see Table I), mp 110–111.50°, nmr $\delta$ 3.50 (m, 5), 3.72 (m, 4), 3.82 (s, 3), 4.82 (d, 2, $J$ = 9.0 Hz), 5.14 (d, 2, $J$ = 9.0 Hz), 7.12 (m, 4).

*Anal.* Calcd for $C_{13}H_{18}ClNO_5S$: C, 46.50; H, 5.49; Cl, 10.59; S, 9.56. Found: C, 46.47; H, 5.61; Cl, 10.81; S, 9.27.

**General Procedure for Cyclopropane Formation from α-Chloromethyllithium Sulfonamides and Activated Olefins.**—To chloromethanesulfonmorpholide (0.020 mol) in 50 ml of dry THF at −75° under $N_2$ was added *n*-butyllithium (0.020 mol in hexane) while maintaining the temperature below −60°. The olefin (0.021 mol) was then added in THF and the reaction mixture was stirred for 10–15 min and quenched with 150 ml of 3% aqueous $NH_4Cl$. The resultant mixture was extracted with 5 × 40 ml of chloroform, and the combined chloroform extracts were dried over $Na_2SO_4$ and then evaporated *in vacuo*, yielding the cyclopropane as a white solid which was recrystallized from ethanol.

**Reaction of α-Chloromethyllithiumsulfonmorpholide with *trans*-1-Phenylsulfonyl-2-phenylethene.**—Chloromethanesulfonmorpholide (1.99 g, 0.01 mol), *n*-butyllithium (0.01 mol), and *trans*-1-phenylsulfonyl-2-phenylethene (2.68 g, 0.011 mol) afforded 2.92 g (73%) of **12**, mp 175–176.5° (geometric stereochemistry was undefined). In addition 0.45 g (12%) of a second cis–trans configurational isomer was obtained, mp 142–143°. The minor component was much more soluble in 95% ethanol than the major component, nmr of which showed $\delta$ 3.10 (m, 4), 3.38 (m, 2), 3.63 (m, 5), 7.28 (s, 5), 7.82 (m, 5).

*Anal.* Calcd for $C_{19}H_{21}NO_5S_2$: C, 56.28; H, 5.19; N, 3.43; S, 15.69; mol wt, 409. Found: C, 56.10; H, 5.28, N, 3.28; S, 15.55; mol wt (in acetone), 410.

**Reaction of α-Chloromethyllithiumsulfonmorpholide with *trans*-Cinnamonitrile.**—Chloromethanesulfonmorpholide (2.00 g, 0.01 mol), *n*-butyllithium (0.01 mol), and *trans*-cinnamonitrile (1.42 g, 0.011 mol) gave 2.06 g (70%) of a mixture of geometrical isomers of **13**, mp 143–148 and 165–169°, nmr $\delta$ 2.58 (q. 1, $J$ = 5.0 Hz), 3.38 (m, 5), 3.78 (m, 4), 7.40 (s, 5).

*Anal.* Calcd for $C_{14}H_{16}N_2O_3S$: C, 57.55; H, 5.48; N, 9.58; S, 10.95; mol wt, 292. Found: C, 57.63; H, 5.67; N, 9.88; S, 10.91; mol wt (in benzene), 297.

**Reaction of α-Chloromethyllithiumsulfonmorpholide with β-Nitrostyrene.**—Chloromethanesulfonmorpholide (1.99 g, 0.01 mol), *n*-butyllithium (0.01 mol), and β-nitrostyrene (1.53 g, 0.011 mol) gave 0.72 g (21%) of geometric isomers of **14**, mp 162–171°, nmr $\delta$ 4.26 (q, 1), 3.38 (m, 5), 3.80 (m, 4), 7.40 (s, 5).

*Anal.* Calcd for $C_{13}H_{18}N_2O_5S$: C, 50.01; H, 5.14; S, 10.22. Found: C, 49.87; H, 5.26; S, 10.25.

**Reaction of α-Chloromethyllithiumsulfonmorpholide with *N*-Benzylideneaniline.**—Chloromethanesulfonmorpholide (1.99 g, 0.01 mol), *n*-butyllithium (0.01 mol), and *N*-benzylideneaniline (1.99 g, 0.011 mol) gave 2.36 g (69%) of **11**, nmr $\delta$ 3.60 (m, 8), 5.20 (m, 2), 7.50 (m, 10).

*Anal.* Calcd for $C_{18}H_{20}N_2O_3S$: C, 62.95; H, 5.82. Found: C, 62.80; H, 5.96.

**Registry No.**—**1**, 23917-17-1; (*R**,*R**)-**6**, 39542-15-9; (*R**,*S**)-**6**, 39542-16-0; (*R**,*R**)-**7**, 39542-17-1; (*R**,*S**)-**7**, 39542-18-2; *erythro*-**8**, 39542-19-3; (*R**,*R**)-**9**, 39542-20-6; (*R**,*S**)-**9**, 39542-21-7; *threo*-**10**, 39542-22-8; **11**, 39542-23-9; **12**, 39542-24-0; **13**, 39542-25-1; **14**, 39542-26-2; chloromethanesulfonmorpholide, 39542-27-3; triethylamine, 121-44-8; morpholine, 110-91-8; chloromethanesulfonyl chloride, 3518-65-8; *n*-butyllithium, 109-72-8.

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## A Stereospecific Synthesis of (±)-(*E*)-Nuciferol *via* the [2,3]-Sigmatropic Rearrangement of Allylic Sulfoxides

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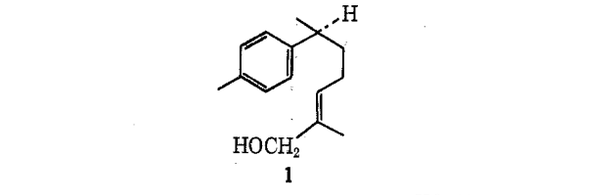
We wish to report a convenient four-step synthesis of racemic (*E*)-nuciferol (**1**)[1] utilizing the concerted nature of the [2,3]-sigmatropic rearrangement[2] of allylic sulfoxides to allylic sulfenate esters (eq 1).




The completely stereospecific nature of the allylic sulfoxide–sulfenate interconversion resulting in the synthesis of trisubstituted olefins of type **5** was recently reported by one of us.[3]

Reduction[4] of β-methyl-4-methylcinnamic acid with excess lithium in liquid ammonia proceeded cleanly to give a 98% yield of the crystalline saturated acid **2a**, mp 90–90.5° (lit.[5] mp 91°). Further reduction of acid **2a** with lithium aluminum hydride afforded a nearly quantitative yield of alcohol **2b**. Standard

(1) T. Sakai, K. Nishimura, and Y. Hirose, *Bull. Chem. Soc. Jap.*, **38**, 381 (1965).

(2) P. Bickart, F. W. Carson, J. Jacobus, E. G. Miller, and K. Mislow, *J. Amer. Chem. Soc.*, **90**, 4869 (1968); R. Tang and K. Mislow, *ibid.*, **92**, 2100 (1970); D. A. Evans, G. C. Andrews, and C. L. Sims, *ibid.*, **93**, 4956 (1971).

(3) P. A. Grieco, *J. Chem. Soc., Chem. Commun.*, 702 (1972).

(4) J. E. Shaw and K. K. Knutson, *J. Org. Chem.*, **36**, 1151 (1971).

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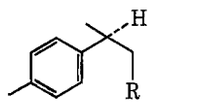
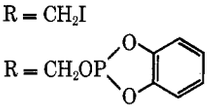
methods for the preparation of iodide **2c** from **2b** were not satisfactory. However, reaction of alcohol **2b** with *o*-phenylene phosphorochloridite[6] in ether in the presence of pyridine afforded a quantitative yield of the corresponding phosphite **2d**, which was subsequently treated with iodine in methylene chloride.[7] The desired iodide **2c** was thus obtained in 91% yield.



**2a**, R = COOH
**b**, R = $CH_2OH$
**c**, R = $CH_2I$



**d**, R = $CH_2OP$

Treatment of methallyl alcohol **5** (R = H) with *n*-butyllithium (−20°, THF) followed by addition of *p*-toluenesulfenyl chloride[8] produced the corresponding sulfenate **4** (R = H), which was smoothly transformed into sulfoxide **3** (R = H) in 92% yield. Addition of *n*-butyllithium (−50°) to a THF solution of sulfoxide **3** (R = H) followed by addition of iodide afforded the alkylated allylic sulfoxide **3** (R = 3-*p*-tolylbutyl), which upon subsequent treatment with thiophenoxide[9] in methanol produced the trans allylic alcohol, (±)-(*E*)-nuciferol (**1**), in 58% yield whose infrared and nuclear magnetic resonance spectra were in agreement with those of (±)-(*E*)-nuciferol obtained from natural nuciferal.[1] The chemical shift of the olefinic methyl protons in the nuclear magnetic resonance spectrum of synthetic nuciferol (δ 1.50, $CCl_4$) is in good agreement with those of other trans (*E*) olefinic methyl protons of type **5**.[10] In contrast, the nuclear magnetic resonance spectrum of natural (*Z*)-nuciferol exhibited the olefinic methyl signal at δ 1.71 ($CCl_4$).[1] In addition, the protons α to the hydroxyl group appeared as a singlet at δ 3.82, clearly in agreement with the trans (*E*) assignment. The synthesis of racemic (*E*)-nuciferol in *ca.* 50% overall yield from β-methyl-4-methylcinnamic acid is in agreement with and thus confirms the earlier work[1] which established that (*E*)-nuciferol is obtained by reduction of natural nuciferal and that natural nuciferol possesses the *Z* (cis) configuration.

## Experimental Section

Microanalyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn. Boiling and melting points are uncorrected. Gas–liquid chromatography was performed on a Varian Aerograph Model 90-P instrument, using silicone rubber gum SE-30. Pre-coated PLC silica gel F-254 Merck plates were used for preparative tlc. The following spectrometers were used: nmr, Varian A-60D and T-60; ir, Perkin-Elmer Model 247; mass spectrum, LKB-9.

**3-*p*-Tolylbutanoic Acid (2a).**—A solution of β-methyl-4-methylcinnamic acid (4.07 g, 23.1 mmol) in 75 ml of anhydrous ether was rapidly added to a dark blue solution of lithium (660 mg, 0.095 g-atom) in 200 ml of anhydrous liquid ammonia. After stirring for 30 min at −33°, the reaction mixture was quenched by slow addition of ammonium chloride (20.8 g) and the ammonia was allowed to evaporate. The resulting residue was dissolved in water and extracted with ether. The remaining aqueous layer was acidified with 6 *N* hydrochloric acid and extracted twice with ether and the combined ethereal extracts (250 ml) were washed with saturated sodium chloride solution and dried over anhydrous magnesium sulfate. Evaporation of the solvent *in vacuo* afforded the crude crystalline saturated acid **2a** in quantitative yield. Recrystallization from ethanol gave 4.02 g (98%) of pure acid: mp 90–90.5° (lit.[5] mp 91°); ir ($CHCl_3$) 1705 $cm^{-1}$ (C=O); nmr ($CDCl_3$) δ 1.28 (d, 3 H), 2.28 (s, 3 H), 2.30–2.70 (m, 2 H), 3.25 (m, 1 H), 7.08 (s, 4 H), 11.51 (s, 1 H); mass spectrum *m/e* 178.

**3-*p*-Tolyl-1-butanol (2b).**—To a suspension of lithium aluminum hydride (1.0 g, 26 mmol) in 125 ml of anhydrous ether was added dropwise over 15 min 4.0 g (23 mmol) of acid **2a** dissolved in 10 ml of THF and diluted with 50 ml of ether. After stirring for a total of 30 min, the reaction was quenched by the dropwise addition of water. Usual work-up afforded 3.7 g (99%) of alcohol **2b**: bp 80° (0.1 mm) [homogeneous on glc analysis (SE-30 column)]; ir (film) 3350 $cm^{-1}$; nmr ($CCl_4$) δ 1.18 (d, 3 H), 1.50–3.00 (m, 2 H), 2.22 (s, 3 H), 2.78 (m, 1 H), 3.38 (t, 2 H), 4.00 (s, 1 H), 6.98 (s, 4 H); mass spectrum *m/e* 164.

*Anal.* Calcd for $C_{11}H_{16}O$: C, 80.93; H, 9.26. Found: C, 80.74; H, 9.40.

**1-Iodo-3-*p*-tolylbutane (2c).**—To a mixture of 1.15 g (6.60 mmol) of *o*-phenylene phosphorochloridite[6] and 0.51 g of pyridine in 22 ml of anhydrous ether cooled to 0° was added with stirring 1.02 g (6.20 mmol) of alcohol **2b** in 22 ml of anhydrous ether. After the addition was complete, the reaction was warmed to room temperature. After a total of 15 hr, the pyridine hydrochloride was filtered off. The solvent was removed *in vacuo* to give an oily residue (quantitative yield) which was dissolved in 18 ml of methylene chloride. To the resultant solution was added 1.60 g (6.25 mmol) of iodine. After stirring for 7 hr at 25°, the reaction was diluted with ether and was extracted with 25 ml of 5% sodium hydroxide solution, 25 ml of 5% sodium bisulfite solution, and 10 ml of saturated sodium chloride solution. After drying over anhydrous sodium sulfate, the solvent was removed under reduced pressure. Distillation afforded 1.55 g (91%) of pure iodide **2c** which was homogeneous on glc (SE-30): bp 72° (0.05 mm); nmr ($CCl_4$) δ 1.22 (d, 3 H), 1.80–2.20 (m, 2 H), 2.28 (s, 3 H), 2.50–3.15 (m, 3 H), 7.01 (s, 4 H); mass spectrum *m/e* 274.

*Anal.* Calcd for $C_{11}H_{15}I$: C, 48.19; H, 5.52. Found: C, 48.42; H, 5.50.

**Methallyl *p*-Tolyl Sulfoxide (3, R = H).**—To a solution of anhydrous THF (90 ml) containing 3.24 g (45 mmol) of methallyl alcohol at −20° under an atmosphere of nitrogen was added dropwise 18 ml (45 mmol) of 2.5 *M* *n*-butyllithium in hexane. After addition was complete, 5.56 g (35 mmol) of *p*-toluenesulfenyl chloride[8] in 10 ml of THF was added dropwise and the reaction was warmed to room temperature. The intense orange color of the sulfenyl chloride was discharged immediately upon addition. After 15 min the solvent was removed under reduced pressure and the product was taken up in ether. The resulting ethereal solution was washed with saturated sodium chloride solution and dried (magnesium sulfate). Distillation of the crude product obtained upon removal of the solvents *in vacuo* afforded 6.25 g (92%) of **3** (R = H): bp 107–109° (0.15 mm); ir (film) 1050 (sulfoxide), 898 $cm^{-1}$ (=$CH_2$); nmr ($CCl_4$) δ 1.76 (s, 3 H), 2.37 (s, 3 H), 3.32 (s, 2 H), 4.82 (d, 2 H), 7.35 (q, 4 H); mass spectrum *m/e* 194.

*Anal.* Calcd for $C_{11}H_{14}OS$: C, 67.99; H, 7.26. Found: C, 68.21; H, 7.45.

**(±)-(*E*)-Nuciferol (1).**—To a solution of 195 mg (1.00 mmol) of allylic sulfoxide **3** (R = H) in 10 ml of freshly distilled THF (from $LiAlH_4$) cooled to −50° under an atmosphere of nitrogen was added dropwise 0.65 ml (1.08 mmol) of 1.66 *M* *n*-butyllithium in hexane. After 15 min, 548 mg of iodide **2c** in 1.0 ml of THF was added dropwise over a 10-min period. After stirring at −50° for 1 hr, the reaction mixture was slowly warmed over a period of 1 hr to room temperature and stirred at room temperature for 2 hr. The reaction contents were poured into a solution of brine and the product was extracted with ether–hexane (3:1) mixture (three times). The crude alkylated sulfoxide was dissolved in 1.5 ml of methanol and added to a solution of 660 mg of benzenethiol in 20 ml of methanol to which had been added

(6) P. C. Crofts, J. H. H. Markes, and H. N. Rydon, *J. Chem. Soc.*, 4250 (1958).
(7) E. J. Corey and J. E. Anderson, *J. Org. Chem.*, **32**, 4160 (1967).
(8) F. Kurzer and J. R. Powell, "Organic Syntheses," Collect. Vol. IV, N. Rabjohn, Ed., Wiley, New York, N. Y., 1962, p 934.
(9) D. J. Abbott and C. J. M. Stirling, *J. Chem. Soc. C*, 818 (1969).
(10) K. C. Chan, R. A. Jewell, W. H. Nutting, and H. Rapoport, *J. Org. Chem.*, **33**, 3382 (1968).

0.70 ml of 1.66 *M* *n*-butyllithium in hexane under nitrogen. The reaction mixture was heated at *ca.* 65° for 7 hr and then left for 10 hr at room temperature. After removal of methanol under reduced pressure, the product was isolated by addition of water and extraction with ether. The combined ethereal extracts were washed with 2% sodium hydroxide solution and saturated sodium chloride solution and dried over magnesium sulfate. Removal of the solvents *in vacuo* produced the crude product. Purification by preparative tlc on silica gel plates using ether–hexane (2:1) afforded 127 mg (58%) of racemic (*E*)-nuciferol which was homogeneous by glc (SE-30): ir (film) 3340 $cm^{-1}$; nmr ($CCl_4$) δ 1.21 (d, 3 H), 1.50 (s, 3 H), 1.60–2.15 (m, 5 H), 2.30 (s, 3 H), 2.60 (m, 1 H), 3.82 (s, 2 H), 5.28 (b t, 1 H), 6.98 (s, 4 H); mass spectrum *m/e* 218.

*Anal.* Calcd for $C_{15}H_{22}O$: C, 82.51; H, 10.16. Found: C, 82.73; H, 10.15.

**Registry No.**—**1**, 39599-18-3; **2a**, 39533-45-4; **2b**, 39533-46-5; **2c**, 39533-47-6; **3** (R = H), 37616-05-0; **5** (R = H), 513-42-8; β-methyl-4-methylcinnamic acid, 14271-34-2; *p*-toluenesulfenyl chloride, 933-00-6.

**Acknowledgments.**—Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society.

## Isotopic Labeling Studies of the Base-Catalyzed Conversion of 1-Methyladenosine to $N^6$-Methyladenosine

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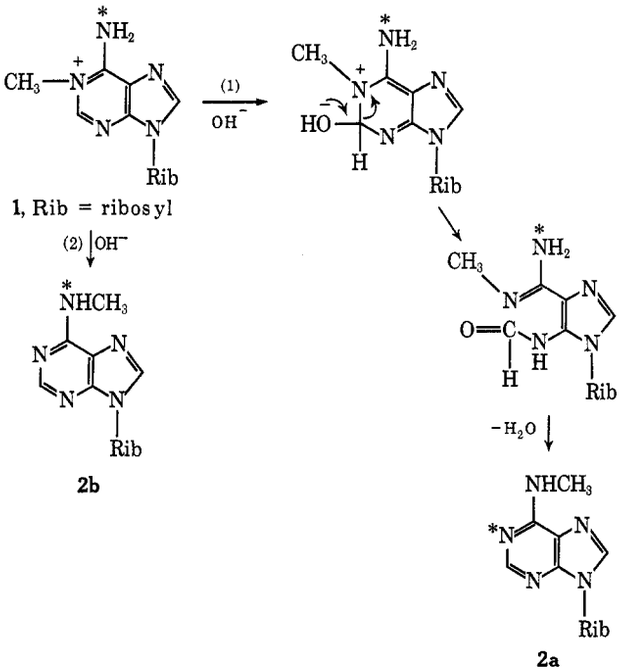
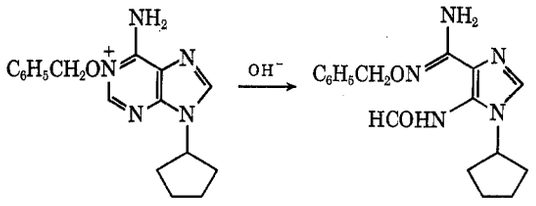
The observation that certain derivatives of 1-methylpurine rearrange in base to $N^6$-methyladenine was reported over a decade ago,[1,2] and has since been shown to occur for a variety of purine derivatives and has often been the basis for synthesis of $N^6$-substituted derivatives of adenine.[3] Following the proposal of Taylor and Loeffler, who studied the structurally similar pyrazolo[3,4-*d*]pyrimidine system,[4] the mechanism has been generally presumed to follow that of the Dimroth rearrangement,[5] involving ring opening and recyclization (eq 1) rather than simple methyl migration (eq 2).

In related work, Windmueller and Kaplan studied the ring opening of 1,6-bis(2-hydroxyethylamino)-9-(β-D-ribofuranosyl)purine in base.[6] An intermediate ring-opened product, which does not undergo recyclization




in dilute alkali, was isolated as a diazo derivative, but did not have a structure analogous to the intermediate shown in eq 1. The most detailed study to date is that of Macon and Wolfenden, who failed to detect or trap an intermediate species in the conversion of **1** to **2** but found that the reaction occurs at room temperature from ~pH 7 to 13 and follows pseudo-first-order kinetics.[7] Their data were interpreted in terms of an initial ring opening (eq 1) brought about by attack of hydroxide on the neutral or protonated form of 1-methyladenosine. In more recent work, Montgomery and Thomas have isolated the intermediate formamide derivative **4** derived from 1-benzyloxy-9-cyclopentyladenine (**3**), which was then converted with ring closure




to the $N^6$-benzyloxy derivative.[8] From these and other less relevant data[9,10] it has been reasonably assumed[7–10] that rearrangement of 1-substituted purines in base follows the Dimroth mechanism, in analogy to the pyrimidines, for which the overall mechanism has been clearly established.[5,11–13]

The present study of the conversion of 1-methyl-6-amino-9-(β-D-ribofuranosyl)purine (**1**) to 6-methylamino-9-(β-D-ribofuranosyl)purine (**2**) was undertaken to directly test the mechanism in eq 1 by use of $^{15}N$ and

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(3) For example, (a) A. Codington, *Biochem. Biophys. Acta*, **59**, 472 (1962); (b) G. B. Elion, *J. Org. Chem.*, **27**, 2478 (1962); (c) J. W. Jones and R. K. Robins, *J. Amer. Chem. Soc.*, **85**, 193 (1963); (d) P. D. Lawley and P. Brookes, *Biochem. J.*, **89**, 127 (1963); (e) W. Grimm, T. Fuji, and N. J. Leonard in "Synthetic Procedures in Nucleic Acid Chemistry," Vol. 1, W. W. Zorbach and R. S. Tipson, Ed., Wiley-Interscience, New York, N. Y., 1968, p 212; (f) H. T. Nagasawa, P. S. Fraser, and J. A. Elberling, *J. Org. Chem.*, **37**, 516 (1972).

(4) E. C. Taylor and P. K. Loeffler, *J. Amer. Chem. Soc.*, **82**, 3147 (1960).

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(7) J. B. Macon and R. Wolfenden, *Biochemistry*, **7**, 3453 (1968).

(8) J. A. Montgomery and H. J. Thomas, *J. Med. Chem.*, **15**, 182 (1972).

(9) J. H. Lister, "Fused Pyrimidines. Part II. Purines," D. J. Brown, Ed., Wiley-Interscience, New York, N. Y., 1971, p 313.

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