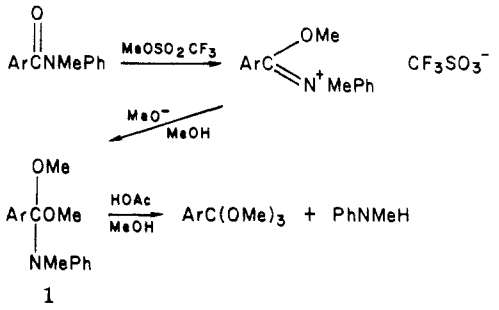
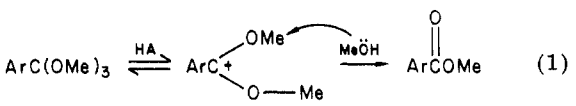
Scheme I

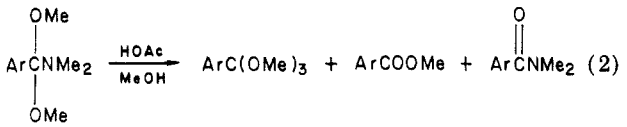


action times which are involved. This minimizes the possibility of the ortho ester reverting back to dialkoxycarbonium ion and eventually being dealkylated to form a simple benzoate ester[1] (eq 1).



(1)

Interestingly, attempts to prepare ortho esters by using amide acetals derived from dimethylamine lead to a mixture of products (eq 2). The difference here is that C–O



(2)

bond cleavage competes with C–N cleavage in acid.[5] The former reaction produces an imidatonium ion, the same type of species which is involved in the Pinner reaction.

Experimental Section

Trimethyl 4-Methylorthobenzoate. *N*,4-Dimethylbenzanilide (15.0 g, 0.067 mol) and methyl trifluoromethanesulfonate (13.0 g, 0.080 mol) were stirred in dry CH_2Cl_2 (30 mL) overnight. Dry ether (100 mL) was added, resulting in the precipitation of the imidatonium salt. This was filtered, washed with ether, redissolved in CH_2Cl_2 (30 mL) and added over a period of 30 min to a cooled (0 °C) stirred solution made by the addition of sodium (3.0 g) to dry methanol (50 mL). The solvents were removed on a rotary evaporator, and hexane (200 mL) was added. This dissolved the anilide acetal, and the remaining solid consisting of sodium trifluoromethanesulfonate and excess sodium methoxide was filtered. Evaporation of the hexane produced the crude anilide acetal.

This was taken up in dry methanol (50 mL) and 5 mL of glacial acetic acid added. After the mixture was stirred for 10 min, 10 g of potassium carbonate was added and the methanol removed on the rotary evaporator. Ether (100 mL) and water (50 mL) were added, the ether layer was dried (K_2CO_3), and the ether was removed. Fractional distillation at 0.1 mm produced *N*-methylaniline at 20–30 °C followed at 90 °C by the ortho ester: 8.8 g (67%, based on initial benzanilide); NMR ($CDCl_3$) δ 7.47 (d, 2 H), 7.13 (d, 2 H), 3.13 (s, 9 H), 2.35 (s, 3 H).

Trimethyl 4-methoxyorthobenzoate was prepared in a similar way by starting from 19.8 g of anilide; yield 10.1 g (58%).

Trimethyl 4-nitroorthobenzoate was prepared in a similar way by starting from 6.0 g of anilide. The majority of the *N*-methylaniline was removed by distillation at 0.1 mm, and the ortho ester recrystallized from ethanol–H_2O; yield 2.0 g (40%).

Reaction of Amide Acetal. *N*,*N*,4-Trimethylbenzamide dimethyl acetal (1.0 g) was stirred in dry MeOH (20 mL) containing acetic acid (1 mL) for 2 h. The solution was worked up as described above. The NMR of the crude product showed peaks attributable to the ortho ester, the benzamide, and the ester; no separation was attempted.

(5) McClelland, R. A. *J. Am. Chem. Soc.* **1978**, *100*, 1844.

Acknowledgment. Financial support of the Natural Sciences and Engineering Research Council of Canada and the J. P. Bickell Foundation is gratefully acknowledged.

Registry No. Trimethyl 4-methylorthobenzoate, 22911-22-4; trimethyl 4-methoxyorthobenzoate, 4316-33-0; trimethyl 4-nitroorthobenzoate, 27689-97-0; *N*,4-dimethylbenzanilide, 40669-49-6; methyl trifluoromethanesulfonate, 333-27-7.

^1H and ^{13}C CIDNP Study of the Radical Rearrangement Involved in the Reaction of *tert*-Butylsulfinyl Chloride with *N*-Hydroxysulfonamides

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Received October 2, 1980

Alkyl- and arylsulfinyl chlorides have been found to react with several types of *N*-hydroxy compounds, including hydroxylamines,[1] *N*-hydroxyureas,[2] *N*-hydroxycarbamates,[3] *N*-phenylhydroxamic acids,[4] and oximes.[5] These reactions predominantly occur via the formation of O-sulfinylated intermediates which subsequently undergo thermal rearrangement involving radical cage processes. Herein we report a study of the reaction of *tert*-butylsulfinyl chloride (**1**) with *N*-hydroxymethane- (**2a**) and *N*-hydroxybenzenesulfonamide (**2c**) and their *N*-methyl-substituted derivatives (**2b** and **2d**, respectively) in the presence of at least 1 equiv of pyridine.[6] ^1H and ^{13}C CIDNP effects provide clear evidence for a homolytic rearrangement of a transient *N*-[(*tert*-butylsulfinyl)oxy]-sulfonamide intermediate via rather persistent sulfonamidyl radicals.

Results and Discussion

The products obtained from the reactions of **1** with **2a–d** are listed in Table I and their formation is rationalized in terms of the mechanism depicted in Scheme I. The first step involves nucleophilic displacement of chloride at the tricoordinate sulfur atom[7] of **1** by the hydroxyl oxygen atom of **2a–d** (α-effect nucleophile). This substitution is strongly accelerated by the presence of pyridine acting as a base.[6] Despite many attempts, the proposed intermediate *N*-[(*tert*-butylsulfinyl)oxy]sulfonamides (**3a–d**) could not be isolated or adequately characterized by NMR spectroscopy. However, their formation is quite plausible in view of the evidence discussed below. For several related reactions[2-4] the corresponding intermediates also decomposed rapidly; only *O*-sulfinylated oximes (formed from oximes with sulfinyl chlorides) were found to be sufficiently stable to allow their isolation before thermal rearrangement.[5,8]

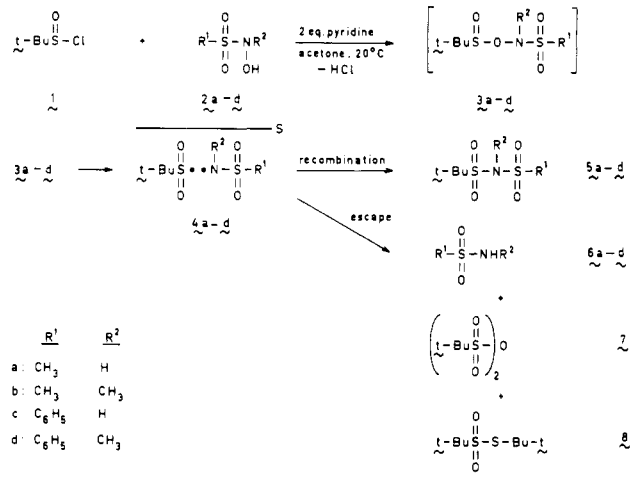
(1) Hovius, K., Engberts, J. B. F. N. *Tetrahedron Lett.* **1972**, 181.
(2) Bleeker, I. P.; Engberts, J. B. F. N. *Recl. Trav. Chim. Pays-Bas* **1979**, *98*, 120.
(3) Bouma, W. J.; Engberts, J. B. F. N. *J. Org. Chem.* **1976**, *41*, 143.
(4) Heesing, A.; Homann, W. K.; Müllers, W. *Chem. Ber.* **1980**, *113*, 152.
(5) Brown, C.; Hudson, R. F.; Record, K. A. F. *J. Chem. Soc., Perkin Trans. 2* **1978**, 822.
(6) The presence of pyridine is essential.[2,3] Since the pK_a of *N*-hydroxysulfonamides is ca. 10 (Brink, K.; Gombler, W.; Bliefert, C. *Z. Anorg. Allg. Chem.* **1977**, *429*, 255) and that of $pyrH^+$ 5.25, it is not likely that the reaction proceeds via the anions of **2a–d**.
(7) For a review of nucleophilic attack at tricoordinate sulfur, see: Tillett, J. G. *Chem. Rev.* **1976**, *76*, 747.

0022-3263/81/1946-1012$01.00/0

Table I. Reaction Products from the Reaction of 1 with 2a–d in Acetone at 20 °C

substrate	recombination product $R^1SO_2N(R^2)SO_2Bu$-*t* (5), % yield	escape products, % yield: $R^1SO_2NHR^2$ (6)	$(t\text{-}BuSO_2)_2O$ (7)	*t*-$BuSO_2SBu$-*t* (8)
2a	15	80	22	13
2b	16	81	25	12
2c	20	50	32	14
2d	24	65	30	16

Scheme I



Homolytic dissociation of the N–O bond in **3a–d** then gives a solvent-caged radical pair (**4a–d**) from which both recombination products (**5a–d**) and escape products (**6a–d**, **7**, **8**) can be formed. The escaped sulfonamidyl radicals will readily abstract hydrogen from the solvent molecules[9] to yield the sulfonamides **6a–d**. It is most likely that *tert*-butylsulfonic anhydride (**7**)[10] and *tert*-butyl *tert*-butylthiolsulfonate (**8**) originate from disproportionation[11] of *tert*-butylsulfonyl radicals after escape from the cage.

The relatively large yield of escape products is consistent with the persistence of sulfonamidyl radicals noted previously.[12,13] The structurally related, but far less persistent, carbamoylaminyl (ureyl) radicals afford in a similar process a lower yield of escape products and much more complicated reaction mixtures.[2]

In order to obtain further evidence for the pathway shown in Scheme I, several reactions were followed by ^1H and ^{13}C NMR spectroscopy. Figure 1 portrays the course of the reaction of **1** with **2b** monitored by ^1H NMR in the δ 2.5–3.5 range. The observation of polarized signals provides strong evidence for the proposed radical cage process. For example, the polarized absorption at δ 3.3 represents the *N*-methyl signal of the recombination

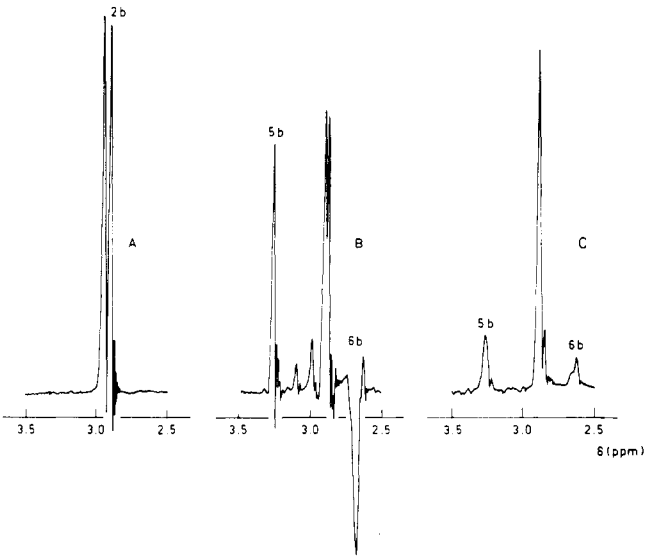


Figure 1. Reaction of **1** with **2b**. (A) ^1H NMR spectrum of **2b** in acetone-d_6 in the presence of 2 equiv of pyridine. (B) Spectrum taken 30 s after addition of **1**. (C) Spectrum taken after 10 min (complete reaction).

product **5b**. Application of Kaptein's rule[14] in terms of the radical-pair mechanism[15,16] predicts an enhanced absorption ($A^H_{N\text{-}Me}$ will be positive,[17] $g_{RSO_2\dot{N}Me}$ = 2.0045,[12] and $g_{t\text{-}BuSO_2\cdot}$ = 2.0054[16]) as is borne out by experiment. The signal at δ 2.7 is due to the *N*-methyl group of the escape product **6b**. Again, the sign of the polarization (emission in this case) is in accord with that predicted by Kaptein's rule.[14] No polarization is observed for the methylsulfonyl signal in **5b** (δ 2.9), consistent with the notion that there is no spin delocalization through the sulfonyl moiety.[12] Previous work has shown that only in rare cases such as in sulfamoylaminyl radicals ($Me_2NSO_2\dot{N}R$) a small amount of spin density is delocalized through the sulfonyl group to the second nitrogen atom and one of the *N*-methyl groups.[19]

Similar polarized ^1H NMR spectra were observed in the reaction of **1** with **2d**. Thus, an enhanced absorption for the *N*-methyl group of **5d** and an emissive *N*-methyl absorption for **6d** again substantiate the radical cage process. However, the half-life of the intermediate **3d** was now significantly longer (2–3 min at the temperature of the probe), providing the possibility to monitor the reaction by ^{13}C NMR. The results are shown in Figure 2. The spectrum, recorded 3 min after initiation of the reaction, exhibits for **5d** an emissive signal at 37 ppm for the *N*-methyl group and a strong emission at 65 ppm for the quaternary carbon. The complete agreement between the observed polarization signs and the theoretically predicted signs based on application of Kaptein's rule[14,20] further supports the radical cage process indicated in Scheme I. We note that no pronounced polarizations are observed for the escape product **6d**, probably as a result of nuclear spin-lattice relaxation effects in the persistent sulfonamidyl

(8) Hudson, R. F.; Record, K. A. F. *J. Chem. Soc., Chem. Commun.* **1976**, 831.
(9) This is a well-known reaction for this type of radical: Neale, R. S. *Synthesis* **1971**, 1.
(10) After workup of the reaction mixture, the anhydride is isolated as pyridinium *tert*-butylsulfonate. The ^1H NMR spectrum taken immediately after completion of the reaction exhibits an absorption at δ 1.60 (s) which we ascribe to the *tert*-butyl group of **7**. Within a few hours, this signal is gradually replaced by a singlet at 1.40 ppm due to $pyrH^+$ *t*-$BuSO_3^-$.
(11) da Silva Correa, C. M. M.; Waters, W. A. *J. Chem. Soc. C* **1968**, 1874.
(12) Zomer, G.; Engberts, J. B. F. N. *Tetrahedron Lett.* **1977**, 3901.
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(15) "Chemically Induced Dynamic Nuclear Polarization"; Lepley, A. R., Closs, G. L., Eds.; Wiley: New York, 1973.
(16) Kaptein, R. *Adv. Free Rad. Chem.* **1975**, *5*, 319.
(17) Compare the positive sign of $A^H_{N\text{-}Me}$ in RCONMe; see: Brown, C.; Hudson, R. F.; Lawson, A. J. *J. Am. Chem. Soc.* **1973**, *95*, 6500.
(18) Davies, A. G.; Roberts, B. P.; Sanderson, B. R. *J. Chem. Soc., Perkin Trans. 2* **1973**, 626.
(19) Teeninga, H.; Zomer, B.; Engberts, J. B. F. N. *J. Org. Chem.* **1979**, *44*, 4717.
(20) (a) The sign of $A_{\alpha\text{-}^{13}C}$ in $\dot{N}\text{–}C_\alpha$ is negative; see: Brown, C.; Lawson, A. J. *Tetrahedron Lett.* **1975**, 191. (b) The sign of $A_{\alpha\text{-}^{13}C}$ in $C_\alpha\text{–}SO_2\cdot$ is positive; see ref 5.

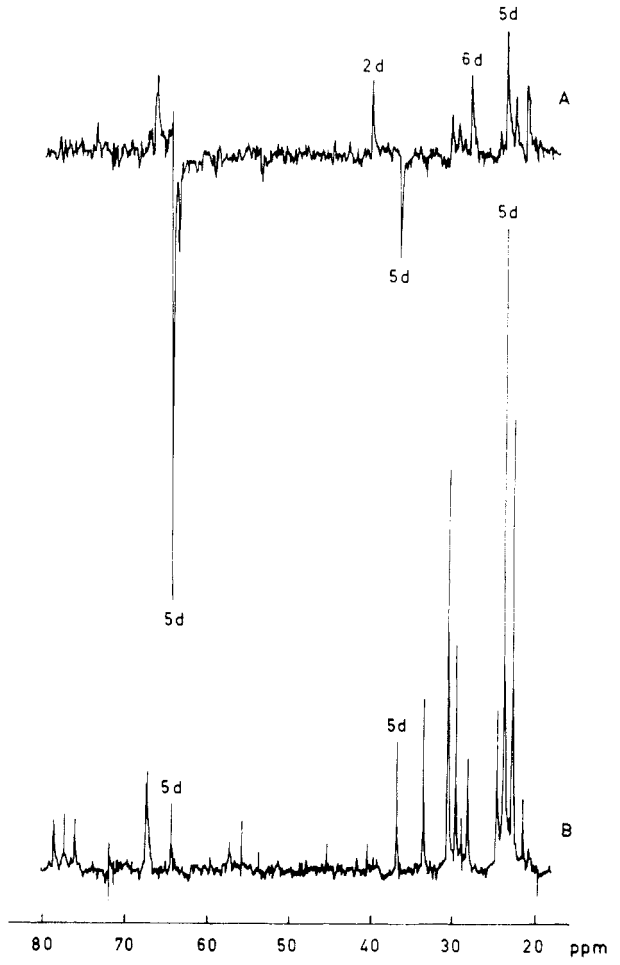

Figure 2. Reaction of 1 with **2d**. (A) ^{13}C NMR spectrum taken 3 min after initiation of the reaction in $CDCl_3$ in the presence of pyridine. (B) Spectrum taken after 10 min (complete reaction).

radical prior to reaction in chloroform as the solvent.[16]

Experimental Section

Melting points were determined on a Mettler FP-2 apparatus. ^1H NMR spectra were run on a Varian A-60 instrument. Chemical shifts (δ) are downfield from Me_4Si. ^{13}C NMR spectra were recorded on a Varian XL-100 spectrometer, chemical shifts (δ) are relative to the solvent $CDCl_3$ (δ = 77.0 ppm). Infrared spectra were recorded on a Unicam SP200 spectrophotometer.

Materials. The solvents were purified and dried by standard methods. *tert*-Butylsulfinyl chloride[21] [1: pale yellow oil; bp 58 °C (15 mm); NMR ($CDCl_3$) δ 1.40 (s)] and the *N*-hydroxysulfonamides **2a**,[6] **2b**,[22] **2c**,[23] and **2d**[22] were prepared according to literature procedures.

General Procedure for Reaction of 1 with 2a-d. A solution of 1 (0.007 mol) in acetone (40 mL) was added dropwise under N_2 to a stirred solution of **2a-d** (0.007 mol) and pyridine (0.014 mol) in acetone (40 mL) at 20 °C. After the solution was stirred for 2 h the acetone was evaporated (20 mm; 30 °C). The residue was dissolved in chloroform (150 mL), extracted once with 150 mL of water, and dried over Na_2SO_4. After removal of the solvent, the organic material was resolved into its components by column chromatography (silica gel, 60-120 mesh; $CHCl_3$). The components were identified by comparison of their boiling point or melting point and their NMR and infrared spectra with authentic samples. The aqueous layer contained pyridinium chloride, pyridinium *tert*-butylsulfonate,[10] and the water-soluble sulfonamides. The sulfonamides were obtained after extraction of the aqueous layer with three 150-mL portions of ethyl acetate and subsequent evaporation of the organic solvent in vacuo.

Sulfonimides 5b and 5d were prepared by adding a solution of the appropriate sulfonyl chloride (0.010 mol) in 50 mL of dry dimethoxyethane (DME) to a stirred solution of *N*-methyl-*tert*-butylsulfonamide (0.010 mol) and *n*-butyllithium (0.010 mol) in 50 mL of dry DME under N_2 at 20 °C. After evaporation of the solvent (20 mm; 50 °C), the crude reaction mixture was dissolved in CCl_4 (150 mL) and extracted twice with 150 mL of water. Removal of CCl_4 in vacuo afforded almost pure **5b** and **5d**. Crystallization from CCl_4 gave pure **5b** [mp 75-76 °C; IR (CCl_4) 1135, 1165, 1345, 1370 cm^{-1}; ^1H NMR (CCl_4) δ 1.49 (s, 9 H), 3.20 (s, 3 H), 3.28 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 24.0, 37.0, 40.9, 64.3. Anal. Calcd for $C_6H_{15}NO_4S_2$: C, 31.42; H, 6.59; N, 6.11; S, 27.96. Found: C, 31.19; H, 6.42; N, 6.02; S, 27.58] and pure **5d** [mp 97-98 °C; IR (CCl_4) 1140, 1175, 1350, 1380 cm^{-1}; ^1H NMR δ 1.50 (s, 9 H), 3.18 (s, 3 H), 7.4-8.1 (m, 5 H); ^{13}C NMR δ 24.2, 37.2, 64.6, 128.7, 128.8, 133.5, 137.9. Anal. Calcd for $C_{11}H_{17}NO_4S_2$: C, 45.34; H, 5.88; N, 4.81; S, 22.01. Found: C, 45.21; H, 5.80; N, 4.90; S, 21.79].

***N*-Methyl-*tert*-butylsulfonamide** was obtained by oxidation of *N*-methyl-*tert*-butylsulfinamide (prepared by passing 2 equiv of gaseous methylamine through a solution of 1 in ether) with 1 equiv of *m*-chloroperbenzoic acid in CH_2Cl_2 at 0 °C. Recrystallization of the crude product gave the pure sulfonamide: yield 50%; mp 83-84 °C; IR (CCl_4) 3410, 3300, 1320, 1130 cm^{-1}; ^1H NMR δ 1.40 (s, 9 H), 2.86 (d, J = 6 Hz, 3 H), 4.5 (br m, 1 H); ^{13}C NMR δ 23.7, 30.1, 59.3. Anal. Calcd for $C_5H_{13}NO_2S$: C, 39.71; H, 8.66; N, 9.26; S, 21.20. Found: C, 39.36; H, 8.56; N, 9.22; S, 21.23.

Sulfonimides 5a and 5c were prepared by a procedure similar to that for **5b** and **5d** by adding a solution of *tert*-butylsulfonamide and 1 equiv of *n*-BuLi in DME to a solution of the sulfonyl chloride in DME. The products obtained after removal of the inorganic material by filtration and evaporation of the DME were sufficiently pure to serve as reference compounds and were characterized by ^1H NMR. **5a**: NMR ($CDCl_3$) δ 1.45 (s, 9 H), 3.08 (s, 3 H). **5c**: NMR ($CDCl_3$) δ 1.47 (s, 9 H), 7.3-8.1 (m, 5 H).

***tert*-Butylsulfonamide** was prepared via a similar procedure as employed for the *N*-methyl derivative, mp 163-165 °C (lit.[2] mp 162-165 °C).

CIDNP Experiments. The ^1H CIDNP experiments (35 °C) were carried out by using solutions of **2a-d** (0.1 g) and 2 equiv of pyridine in 0.6 mL of acetone-d_6. The NMR spectrum was recorded immediately after initiating the reaction with 1 equiv of 1 and subsequently at suitable time intervals. For the ^{13}C CIDNP experiments solutions of **2d** (0.50 g) together with 2 equiv of pyridine in $CDCl_3$ (2 mL) were used. After the spectrometer was locked on $CDCl_3$, and equimolar amount of 1 was added carefully. CIDNP was observed after 7 times 27 pulses (acquisition time 0.8 s; 35 °C).

Acknowledgment. We thank Professor R. Kaptein for valuable discussions.

Registry No. 1, 31562-43-3; **2a**, 50695-55-1; **2b**, 66110-38-1; **2c**, 599-71-3; **2d**, 7340-20-7; **5a**, 75975-41-6; **5b**, 75975-42-7; **5c**, 75975-43-8; **5d**, 75975-44-9; **6a**, 3144-09-0; **6b**, 1184-85-6; **6c**, 98-10-2; **6d**, 5183-78-8; 7, 75975-45-0; 8, 31562-41-1.

(21) Asakawa, H.; Kamiya, K.; Takei, S. *Takeda Kenkyusho Ho* **1970**, *29*, 610; *Chem. Abstr.* **1971**, *74*, 125603.
(22) Backhaus, M.; Bliefert, C. *Z. Naturforsch., B* **1978**, *23*, 125.
(23) Piloty, O. *Chem. Ber.* **1896**, *29*, 1559.

Nitrogen-15 Nuclear Magnetic Resonance Spectroscopy of 5-Azacytidine[1]

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Received September 3, 1980

5-Azacytidine (4-amino-1-β-D-ribofuranosyl-1,3,5-triazin-2(1*H*)-one, 1)[3,4] has been investigated for its potential

0022-3263/81/1946-1014$01.00/0