Alkaline Hydrolysis of Methylthiopurines Bearing Oxo Groups in the Ring

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The susceptibility of methylthiopurines, bearing also oxo groups, to alkaline hydrolysis was studied. Those derivatives which lack *N*-methyl substituents are refractory. The *N*-monomethyl derivatives of the series react as anions; attack is directed exclusively toward methylthio groups, placed in the same ring as the *N*-methyl substituent. *N,N'*-Dimethyl compounds undergo alkaline hydrolysis as neutral molecules. Here hydrolysis of a methylthio group in the pyrimidine ring is preferred over attack on a methylthio substituent in the imidazole moiety. In all cases, polarization of *N*-methyl groups creates a positive center which directs the attack by hydroxyl ion.

We have shown recently that methylthiopurines, which are able to form anions, are not hydrolyzed by alkali. On the other hand, *N*-methyl derivatives of methylthiopurines, which lack an ionizable NH group, are susceptible to nucleophilic attack, the direction of the reaction being determined by the position of the *N*-methyl substituent.[1]

The present study is concerned with the hydrolysis of methylthiopurines, bearing also an oxo group. The substrates used comprise mono-NMe derivatives, which still have a free NH group and therefore react with alkali as anions, and bis-*N*-methylpurines, which lack NH groups and thus are attacked as neutral molecules. We shall show that, here again, the position of the *N*-methyl substituent determines the feasibility and the course of the hydrolysis.

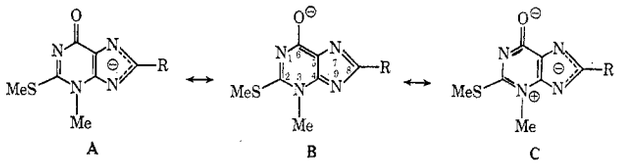
Attack of Hydroxyl Ion on Anionic Substrates.— All methylthiooxopurines, lacking *N*-methyl substituents, are resistant to weak (pH ~9) or strong bases (2 *N* NaOH), *i.e.*, neither the mono- nor the dianions are attacked. *E.g.*, 2,8-dimethylthiohypoxanthine shows p*K* values of 7.5 and 10.75. At pH 9, mainly the monoanion, formed by dissociation of the 1-NH group,[2] is present in aqueous solution. Although in this anion the negative charge is confined to the pyrimidine ring, the 8-SMe substituent is not replaced by OH^-.

The derivatives, bearing a single *N*-methyl group, can be divided into two classes. In class a, the *N*-methyl group facilitates hydrolysis of a neighboring *S*-methyl substituent (compounds **2**, **6**, **7**, and **12**, Table I). This effect is observed even if the second neighbor is a carbonyl group (as in **1**, **5**, and **8**). In class b, on the contrary, an *N*-methyl group in one moiety of the purine ring, whether adjacent to a C=N— double bond (**3**, **4**) or to a carbonyl group (**10**, **13**, **20**, **21**, **22**, and **23**), does not support hydrolysis of an S–Me substituent in the second moiety.

Table I also includes the p*K* values for anion formation in the substrates studied. It is evident that, at pH 14, both reactive and refractory purines are completely ionized. Therefore the presence of a negative charge as such is not sufficient to explain the resistance of certain derivatives to alkaline hydrolysis. However, the location of the NH groups, undergoing dissociation, relative to the methylthio substituents is of great importance.

The facilitatory influence of an *N*-methyl group is ascribed to its polar form. This is shown in Scheme I

SCHEME I

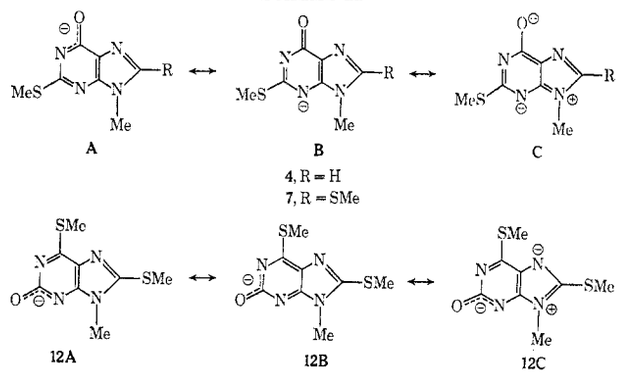


2, R = H
6, R = SMe

for the anions **2** and **6**, **A**–**C**. In the mesomeric form **C**, the pyrimidine ring possesses an aromatic structure; here, the positive charge at N-3 directs attack of OH^- to the 2–3 bond. In **6**, the 8-methylthio group is resistant to alkaline hydrolysis.

The counterpart to these two cases is represented by **7** and **12**. Here the negative charge of the anion is confined to the pyrimidine ring (Scheme II). Attack of

SCHEME II



4, R = H
7, R = SMe

OH^- at position 8 is facilitated in the polar form **7C**. The analogous interpretation is assumed for the anion of **12** (Scheme II).

For the derivatives **1**, **5**, and **8**, in which the 1-methyl substituent is located between an SMe and a carbonyl group, Scheme III demonstrates that the "aromatic" resonance forms **1C**, **5C**, and **8C** facilitate attack at the carbon atom in the pyrimidine ring, bearing an SMe group. Again in **5**, the 8-methylthio substituent is refractory to alkaline hydrolysis.

By a similar way of reasoning, we may explain the resistance to hydrolysis of the members of class b. In the anions of **3** and **4**, the positive charge is confined to the imidazole ring; thus reaction at position 2 is not possible (see the polar forms of **4** in Scheme II). In the anion of **10**, structure C is assumed to make the greatest contribution (Scheme III). Here the imidazole ring is

(1) U. Reichman, F. Bergmann, D. Lichtenberg, and Z. Neiman, *J. Org. Chem.*, **38**, 2066 (1973).

(2) U. Reichman, F. Bergmann, and D. Lichtenberg, *J. Chem. Soc., Perkin Trans. 1*, in press.

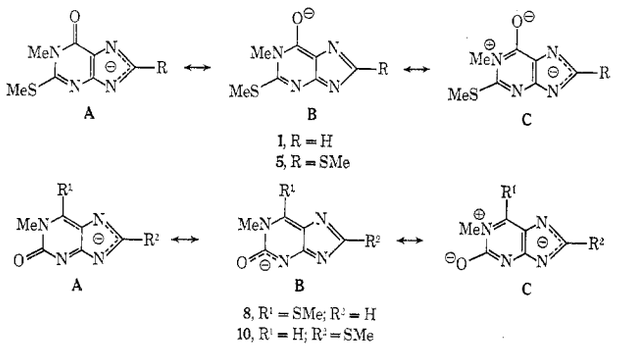
TABLE I

HYDROLYSIS OF METHYLTHIO GROUPS IN THE ANIONS OF OXOPURINES

No.	Compd	p*K* for anion formation	Position attacked[a]	Product formed
		A. Hypoxanthines		
1	1-Methyl-2-methylthio-	9.5	2	1-Methylxanthine (**18**)
2	3-Methyl-2-methylthio-	8.7	2	3-Methylxanthine (**19**)
3	7-Methyl-2-methylthio-	8.0		
4	9-Methyl-2-methylthio-	9.5		
5	1-Methyl-2,8-dimethylthio-	8.2	2	1-Methyl-8-methylthioxanthine (**20**)
6	3-Methyl-2,8-dimethylthio-	7.9	2	3-Methyl-8-methylthioxanthine (**21**)
7	9-Methyl-2,8-dimethylthio-	7.5	8	9-Methyl-2-methylthio-6,8-dioxopurine (**22**)
		B. 2-Oxopurines		
8	1-Methyl-6-methylthio-	8.8	6	1-Methylxanthine (**18**)
9	3-Methyl-6-methylthio-	7.7	6	3-Methylxanthine (**19**)
10	1-Methyl-8-methylthio-	7.1		
11	3-Methyl-6,8-dimethylthio-	6.6	6	3-Methyl-8-methylthioxanthine (**21**)
12	9-Methyl-6,8-dimethylthio-	6.2	8	9-Methyl-6-methylthio-2,8-dioxopurine (**23**)
		C. 8-Oxopurines		
13	9-Methyl-2,6-dimethylthio-	8.8		

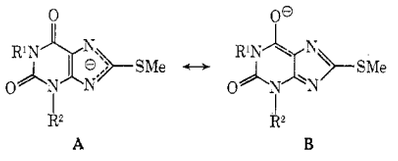
[a] All compounds were hydrolyzed by method A, with the exception of **3**, **4**, **10**, and **13** which were recovered unchanged after use of method C.

SCHEME III



protected by its negative charge against nucleophilic attack at position 8. This applies also to **20** and **21** (Scheme IV).

SCHEME IV



In the 3-methyl-2-oxo derivatives **9** and **11**, the *N*-methyl substituent facilitates hydrolysis of the remote 6-SMe group. Here the anion can be represented by the polar structures **A**–**C** (Scheme V). It appears that the 6-SMe group can acquire a formal positive charge *via* the polar form **C**, which facilitates attack by OH^- at the 1–6 bond. It is also evident that the 8-SMe group in **11** is protected by the negative charge of the imidazole ring.

Attack of Hydroxyl Ion on Uncharged Substrates.— The oxo derivatives in Table II bear two *N*-methyl substituents and thus are unable to form anions. In the members of this group, hydrolysis in the pyrimidine ring is preferred over attack at the 8-SMe group. Scheme VI shows the mesomeric forms of

SCHEME V

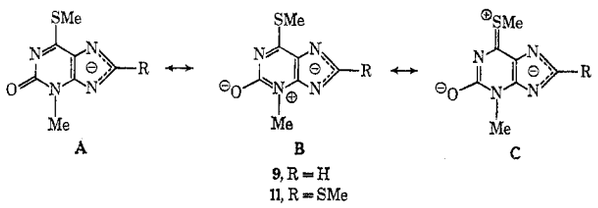


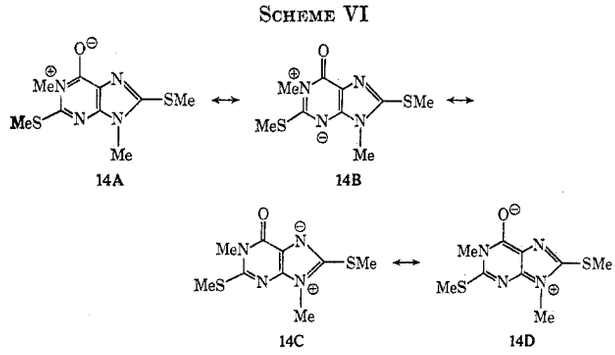
TABLE II

ALKALINE HYDROLYSIS OF METHYLTHIO GROUPS IN NEUTRAL MOLECULES OF OXOPURINES

No.	Compd	Position[a] attacked	Product formed
14	1,9-Dimethyl-2,8-dimethylthiohypoxanthine	2	1,9-Dimethyl-8-methylthioxanthine (**24**)
15	3,7-Dimethyl-6-methylthio-2-oxopurine	6	Theobromine (**25**)
16	3,7-Dimethyl-2,8-dimethylthiohypoxanthine	2	3,7-Dimethyl-8-methylthioxanthine (**26**)
17	3,7-Dimethyl-6,8-dimethylthio-2-oxopurine	6	**26**

[a] All purines in Table II were hydrolyzed by method B.

SCHEME VI

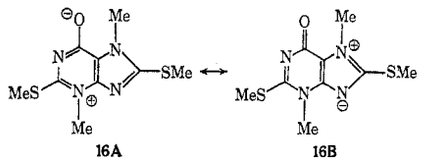


the 1,9-dimethyl derivative **14**. In the polar structures **A** and **B**, the positive charge at N-1 is close to the 2-SMe group. Form **A** is assumed to make the greatest contribution, in view of the aromatic struc-

ture of its pyrimidine ring. In order to explain the preference of position 2 over 8 for attack by OH^-, we may assume that forms **14C** and **D** are less important than **14A**, presumably because of the lack of aromatic structure.

In analogy, we describe 3,7-dimethyl-2,8-dimethylthiohypoxanthine (**16**) by the resonance forms **A–B** in Scheme VII. In **16A**, the pyrimidine ring exhibits aro-

SCHEME VII

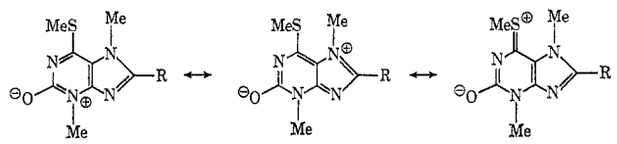


16A **16B**

matic character; this may be responsible for attack at C-2 rather than at C-8 to give 1,9-dimethyl-8-methylthioxanthine (**24**).

The two 3,7-dimethyl-2-oxo derivatives **15** and **17** are attacked at position 6. This shows that among the three mesomers **A–C** (Scheme VIII), form **C** in which a

SCHEME VIII



A **B** **C**

15, R = H
17, R = SMe

positive charge is placed at the 6-SMe group, similar to **11C**, is responsible for directing nucleophilic attack towards position 6. However, it is difficult to see why in mesomer **17B** reaction at position 8 should not be facilitated. Careful analysis of the reaction mixture revealed only the presence of 3,7-dimethyl-8-methylthioxanthine (**26**), no traces of the isomeric 3,7-dimethyl-6-methylthio-2,8-dioxopurine being detected.

We have sought an explanation for the predominant participation of **14A** and **17C** by theoretical considerations. Following Fukui's method,[3] we have determined the sequence of susceptibility to nucleophilic attack for purines **14**, **16**, and **17** (Table III). For the first two

TABLE III
SUPERDELOCALIZABILITIES FOR NUCLEOPHILIC ATTACK

		Superdelocalizability of position			
No.	Compd	2	6	8	Sequence
14	1,9-Dimethyl-2,8-dimethylthiohypoxanthine	0.874		0.766	2 > 8
16	3,7-Dimethyl-2,8-dimethylthiohypoxanthine	0.894		0.827	2 > 8
17	3,7-Dimethyl-6,8-dimethylthio-2-oxopurine		0.819	0.847	8 > 6

compounds, calculation of superdelocalizabilities for nucleophilic attack shows preference of C-2 over C-8, in agreement with our experimental results. However, for **17** we calculate the sequence 8 → 6, while the reverse has been found experimentally (Table II).

A tentative explanation for this discrepancy may be based on Scheme VIII by assuming that attack of OH^- between 6-SMe and 7-NMe in **17B** or **C** is less obstructed than approach of OH^- to the $C^8{=}N^7$ double bond in **17B**. This is suggested by FMM models[4] which show that rotation of the 6-SMe group is less hindered by the 7-alkyl substituent than is that of the 8-SMe group in **17**. Considerations of steric hindrance do not enter into Fukui's calculations.

Evidence for the Structure of the Dioxo Products, Obtained by Alkaline Hydrolysis.—The xanthines **18**,[5] **19**, and **25** were identified by comparison with authentic samples (uv and nmr spectra; R_F values). Compounds **20**, **21**, and **24** were synthesized independently from the corresponding *N*-methyl-8-thiouric acids.[6,7] Among the latter, the 1-methyl derivative **28** is new (see Experimental Section). In addition, the structure of 3-methyl-8-methylthioxanthine **21** follows from the fact that the same product results from hydrolysis of either **6** or **11** (see Table I). Likewise, **26** is obtained by hydrolysis of either **16** or **17** (Table II).

22 differed in all its properties from the alternative product that would result from attack at position 2, *viz.* 9-methyl-8-methylthioxanthine **27**, which was prepared by an independent route (Table IV). In **22**, the 9-methyl substituent is adjacent to an 8-oxo group. The $\delta_{9\text{-Me}}$ value (3.47 ppm) is shifted upfield by 0.39 ppm, relative to the corresponding signal in **27** ($\delta_{9\text{-Me}}$ 3.86).

Compound **23** proved identical with an authentic sample, obtained by S-methylation of the new 9-methyl-6-thiouric acid **29** (see Experimental Section).

Experimental Section

All melting points are uncorrected; analyses were performed by F. Strauss, Oxford, England. For chromatography on Whatman No. 1 paper by the descending method, the following solvents were used: solvent A, 1-butanol–acetic acid–water (12:3:5, v/v); solvent B, ethanol–DMF–water (3:1:1, v/v). Spots were detected by their fluorescence under a Mineralight uv lamp (λ ~254 nm). Uv spectra were measured on a Hitachi Perkin-Elmer Model 124 spectrophotometer and nmr spectra on a Jeol MH-100 instrument, using TSP (sodium 3-trimethylsilylpropionate-*2,2,3,3-d*$_4$ of Merck Sharp and Dohme, Canada), as internal standard. p*K* values were determined by the spectrophotometric method, plotting λ_{max} as function of pH.

I. Alkaline Hydrolysis. General Procedures.—In all experiments, 1 mmol of substrate and 10 ml of 2 *N* NaOH were used. The pH during and after the reaction was above 14.

Method A.—A solution of the substrate in 2 *N* NaOH was refluxed for 3 hr. The pH was brought to 6 by addition of glacial acetic acid. The precipitate was filtered, washed with cold water, and purified as described in Table IV.

Method B.—A suspension of the substrate in 2 *N* NaOH was stirred and refluxed for 5 min. The clear solution was rapidly cooled and acidified.

Method C.—A suspension of the substrate in 2 *N* NaOH was stirred and refluxed until a clear solution was obtained, but in any case not less than 5 hr. Acidification and further treatment followed method A.

(3) K. Fukui, T. Yonezawa, and H. Shingu, *J. Chem. Phys.*, **20**, 722 (1952).

(4) Framework Molecular Models, Nutley, N. J.

(5) G. B. Elion, *J. Org. Chem.*, **27**, 2478 (1962).

(6) F. Bergmann, H. Kwietny-Govrin, H. Ungar-Waron, A. Kalmus, and M. Tamari, *Biochem. J.*, **86**, 567 (1963).

(7) H. Biltz, K. Strufe, E. Topp, M. Heyn, and R. Roll, *Justus Liebigs Ann. Chem.*, **423**, 200 (1921).

TABLE IV

PHYSICAL PROPERTIES OF NEW OXOPURINES

Compd	λ_{max}, nm,[a] at pH 1	λ_{max}, nm,[a] at pH 6	λ_{max}, nm,[a] at pH 12	Mp, °C	Method of preparation[b]	Solvent for crystallization	Crystal form and color	R_f in solvent[c] A	R_f in solvent[c] B	Fluorescence[d]
I. *N*-Methylthiouric Acids										
28[e] 1-Methyl-8-thiouric acid	243 (4.07) 295 (4.42)	253 (4.30)[f] 299 (4.30)		>300	See Experimental Section	NH_3–acetic acid	Yellow microcrystals	0.41	0.62	Greenish
29[e] 9-Methyl-6-thiouric acid	259 (3.84) 356 (4.18)	349 (4.43)[f]		>300	See Experimental Section	NH_3–acetic acid	Yellow microcrystals	0.38	0.57	Greenish
II. Derivatives of 2,8-Dimethylthiohypoxanthine										
6[e] 3-Methyl-	297.5 (4.30)	297.5 (4.30)	303 (4.30)	298–299	II[g]	1-Butanol	Colorless plates	0.79	0.55	Bright violet
14[e] 1,9-Dimethyl-	283 (4.42)	279 (4.32)		210–212	See Experimental Section	Ethyl acetate	Colorless needles	0.89	0.74	Dark violet
16[e] 3,7-Dimethyl-	297.5 (4.30)	297.5 (4.30)		190	From **6** (see Experimental Section)	Ethyl acetate	Colorless needles	1.0	0.9	Blue
III. Derivatives of 8-Methylthioxanthine										
20[e] 1-Methyl-	289 (4.17)	293 (4.14)	295 (4.16)	>300	II (from **28**); hydrolysis of **5**	Ethanol	Colorless plates	0.87	0.74	Dark violet
21[e] 3-Methyl-	291 (4.25)	295 (4.15)	294 (4.43)	>300	II; hydrolysis of **6** and **11**	Ethanol	Colorless rods	0.87	0.74	Dark violet
27[e] 9-Methyl-	285	287	291	>300	II[h]	Dil acetic acid	Colorless plates	0.90	0.79	Dark violet
24[e] 1,9-Dimethyl-	285 (4.20)	287 (4.20)	291 (4.17)	>300	See Experimental Section; hydrolysis of **14**	1-Butanol	Colorless boats	0.83	0.71	Dark violet
26[e] 3,7-Dimethyl-	294 (4.23)	295 (4.23)	295 (4.12)	268	Hydrolysis of **16** and **17**	Ethanol	Colorless needles	0.86	0.75	Dark violet
IV. Other 9-Methyl Derivatives										
22[e] 2-Methylthio-6,8-dioxopurine	278 (4.12)	281 (4.14)	287 (4.14)	>300	Hydrolysis of **7**	1-Butanol	Colorless microcrystals	0.83	0.70	Dark violet
23[e] 6-Methylthio-2,8-dioxopurine	341 (4.20)	335 (4.20)	329 (4.23)	>300	II (from **29**); hydrolysis of **12**	Ethanol	Colorless microcrystals	0.75	0.69	Blue

[a] Figures in brackets designate log ϵ_{max}. [b] Methods of preparation; see Experimental Section. All compounds prepared by methylation according to method II were obtained in nearly quantitative yield. [c] For solvents A and B, see Experimental Section. [d] Under a Mineralight uv lamp (λ ~254 nm). [e] Satisfactory combustion analytical data for C, H, N, S were reported for these compounds: Ed. [f] At pH 8.0. [g] From 3-methyl-2,8-dithiouric acid [U. Reichman, F. Bergmann, D. Lichtenberg, and Z. Neiman, *J. Chem. Soc., Perkin Trans. 1*, 793 (1973)]. [h] By methylation of 9-methyl-8-thiouric acid.[7]

II. S-Methylation.—Solutions of the thio compounds in 2 *N* NaOH were stirred at room temperature with 2 equiv of methyl iodide. The precipitate, obtained after acidification, was purified as shown in Table IV.

The following compounds were synthesized by known procedures: **3**, **4**, **5**, **7**, **9**, **10**, **11**, **12**, and **13**;[1] **1**;[5] **2** and **8**;[8] 3-methyl-8-thiouric acid;[6] 9-methyl- and 1,9-dimethyl-8-thiouric acid;[7] 3,7-dimethyl-6-methylthio-2-oxopurine (**15**);[9] 1- (**18**)[5] and 3-methylxanthine (**19**).[10] Synthesis of 3,7-dimethyl-6,8-dimethylthio-2-oxopurine (**17**) will be published elsewhere.

New Purines. 3,7-Dimethyl-2,8-dimethylthiohypoxanthine (16).—A solution of 3-methyl-2,8-dimethylthiohypoxanthine (**6**) (0.5 g) in acetonitrile (400 ml) and methyl iodide (2 ml) was refluxed for 4 hr. The solvent was removed *in vacuo* and the residue shaken with cold 2 *N* NaOH. The insoluble portion crystallized from ethyl acetate, mp 190° (see Table IV).

1-Methyl-8-thiouric Acid (29).—A solution of 1-methyl-4,5-diaminouracil[11] (2 g) in dry pyridine (150 ml) and carbon disulfide (10 ml) was refluxed for 5 hr. The solvent was removed *in vacuo*, the residue dissolved in ammonia (charcoal), and the solution filtered and acidified, mp >300° (see Table IV).

9-Methyl-6-thiouric Acid (28).—A mixture of 4,5-diamino-6-thiouracil[12] (4 g) and methyl isocyanate (2.5 g) in pyridine (100 ml) was stirred and refluxed for 3 hr. The solvent was distilled *in vacuo* and the residue stirred with acetone. The insoluble portion was stirred and heated during 5 hr with concentrated HCl (100 ml). The product was dissolved in concentrated ammonia (charcoal) and reprecipitated with glacial acetic acid, mp >300°.

1,9-Dimethyl-2,8-dimethylthiohypoxanthine (14).—A solution of 1-methyl-2,8-dimethylthio-6-thiopurine[1] (1 g) in 2 *N* NaOH (7.5 ml) was stirred at room temperature with methyl iodide (2 ml) for 15 min. The precipitate formed was filtered; yield of **14**, 60%.

From the filtrate, the second product (**5**) separated after addition of glacial acetic acid.

Calculation of Superdelocalizabilities for 14, 16, and 17.—π-Electronic Hückel-type calculations were performed with the use of Pullman's[13] parametrization, to construct the Hückel topological matrices. After diagonalization (Jacobi's method), the coefficients of the wave functions were subjected to a "frontier" analysis according to Fukui.[3] All computations were performed on a CDC 6400 digital computing machine using a Fortran program.

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(11) W. Pfleiderer, *Chem. Ber.*, **90**, 2272 (1957).
(12) G. Levin, A. Kalmus, and F. Bergmann, *J. Org. Chem.*, **25**, 1752 (1960).
(13) A. Pullman and B. Pullman, "Quantum Biochemistry," Interscience, New York, N. Y., 1963, p 108.

Acknowledgment.—This research was supported in part by a grant (to U. R.) of the California Foundation for Biochemical Research.

Registry No.—1, 33867-98-0; 2, 40959-21-5; 5, 39013-76-8; 6, 40959-22-6; 7, 39062-23-2; 8, 38759-23-8; 9, 38759-24-9; 11, 39013-78-0; 12, 40848-20-2; 14, 40848-21-3; 15, 38759-27-2; 16, 40848-23-5; 17, 40848-24-6; 20, 34617-98-6; 21, 40848-26-8; 22, 40848-27-9; 23, 40848-28-0; 24, 40848-29-1; 26, 40959-23-7; 27, 40848-30-4; 28, 40848-31-5; 29, 40848-32-6; 1-methyl-4,5-diaminouracil, 40959-24-8; 4,5-diamino-6-thiouracil, 40848-33-7; carbon disulfide, 75-15-0; acetone, 67-64-1; 1-methyl-2,8-dimethylthio-6-thiopurine, 39008-25-8.

Hydrolysis of 2,4-Dinitrophenyl Sulfate in Benzene in the Presence of Alkylammonium Carboxylate Surfactants

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Alkylammonium carboxylates markedly enhance the hydrolysis of 2,4-dinitrophenyl sulfate in benzene. The observed rate constants increase sigmoidally with increasing surfactant concentration in the region of the critical micelle concentration and linearly at higher surfactant concentrations. Rate constants are analyzed in terms of micellar and composite general-acid and general-base catalysis. The micellar catalyzed rates in benzene in the presence of alkylammonium carboxylates are factors of 21- to 70-fold greater than that obtained for the hydrolysis of 2,4-dinitrophenyl sulfate in water. The observed micellar catalysis is discussed in terms of solubilization of 2,4-dinitrophenyl sulfate in the polar micellar cavity where it is held fairly rigidly (as indicated by the remarkably large decrease in the entropy of activation with respect to that in water) and enhanced water activity and proton transfer assist the rate-determining S–O bond fission. Linear dependencies have been observed between the logarithms of rate constants for micellar and combined general-acid and -base catalysis and the number of carbon atoms in both the carboxyl and ammonium groups of the alkylammonium carboxylates. Changes in the chain length of the carboxyl and ammonium groups affect the micellar catalysis to the same extent, but general-acid catalysis depends on the chain length to a greater extent than general-base catalysis.

Rate constants for the mutarotation of 2,3,4,6-tetramethyl-α-D-glucose,[1] for the decomposition of σ complexes,[2] for the aquation of chromium(III) and cobalt(III) complexes,[3] and for the trans–cis isomerization of bis(oxalato)diaquochromate(III) anion[4] are enhanced remarkably by alkylammonium carboxylate surfactants in nonpolar solvents. These rate enhancements have been rationalized in terms of favorable substrate partitioning in the polar cavities of reversed micelles, dynamically formed from alkylammonium carboxylates,[5–8] where specific interactions, proton transfer, and enhanced water activity provide the driving force for the catalysis. Rate constants for these reactions in the reversed micellar environment in nonpolar solvents are orders of magnitude greater than those in the pure nonpolar solvents and in water.[1–5] Simple partitioning by itself is clearly an inadequate explanation for rate enhancements of this magnitude. It is likely that substrates are being held more rigidly in the polar cavities of reversed micelles than they are in aqueous "normal" micelles. This factor and the presence of a polar interior render, we believe, reversed micelles not only an inherently unique reaction media but a potentially fruitful model for biomembranes and enzymatic interactions.

Investigations of aquation and isomerization of chromium(III) complexes[3,4] indicated that, other factors being the same, alkylammonium carboxylate micelles enhance the rates of acid-catalyzed reactions to the greatest extent when the neutral rate is relatively small. In order to probe this contention further and to extent the range of reversed micellar interactions to hydrolyses, we have examined the hydrolysis of 2,4-dinitrophenyl sulfate in benzene in the presence of micelle-forming alkylammonium carboxylates. Our selection was somewhat governed by the availability of information on the mechanisms of 2,4-dinitrophenyl sulfate hydrolyses in water[9,10] and in aqueous micellar solutions in the absence[11] and presence[12] of nucleophilic reagents. Additionally, ^{1}H nmr investigations indicated that in aqueous zwitterionic 3-(dimethyldodecylammonio)propane-1-sulfonate micelles the environment of 2,4-dinitrophenyl sulfate is somewhat hydrophobic but its *in situ* hydrolysis products interact to a greater extent with the polar head groups of the micelle than the substrate.[13]

Experimental Section

The preparation and purification of 2,4-dinitrophenyl sulfate has been described.[10]

Reagent-grade benzene (<0.02% water) was distilled from

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