CA 42056) and the Alfred P. Sloan Foundation.

Registry No. 1, 60935-21-9; 4-*Z*, 114995-75-4; 4-*E*, 114995-74-3; 5-*Z*, 114995-77-6; 5-*E*, 114995-76-5; 6-*cis*, 114995-79-8; 6-*trans*, 114995-78-7; 7-*cis*, 114995-81-2; 7-*trans*, 114995-80-1; 8a, 35234-88-9; 8b, 35234-87-8; 9a-*trans*, 114995-82-3; 9b-*trans*, 114995-83-4; 11, 114995-84-5; 12, 114995-86-7; 15, 19618-37-2; 16, 17665-72-4; 17, 114995-85-6; 19, 114995-87-8; 27, 114995-88-9; 28, 114995-91-4; 28 (dipole), 114995-90-3; 29, 114995-92-5; 30, 114995-89-0; A, 100-25-4; B, 2564-83-2; $PhCH_2O_2CCH_2CO_2CH_3$, 52267-39-7; PhCHO, 100-52-7; $(CH_3O)_3CH$, 149-73-5; $(CH_3)_3SiCH_2CH{=}NBu\text{-}t$, 73198-78-4; $(CH_3OC_6H_4\text{-}4)_2CO$, 90-96-0; $CH_2(CN)_2$, 109-77-3; $CH_3CH{=}NBu\text{-}t$, 7020-80-6; $(Me_2NC_6H_4\text{-}4)_2CO$, 90-94-8; cyclopropanecarboxaldehyde, 1489-69-6.

Supplementary Material Available: Full details of the attempted thermal isomerization (control studies) of 4-*E*, 4-*Z*, 5-*E*, 5-*Z*, 6-*cis*, 6-*trans*, 7-*cis*, and 7-*trans* and details of the attempted reaction of 1 with 1-cyanovinyl acetate are provided (3 pages). Ordering information is given on any current masthead page.

Oxidation of Thymines by Peroxosulfate Ions in Water

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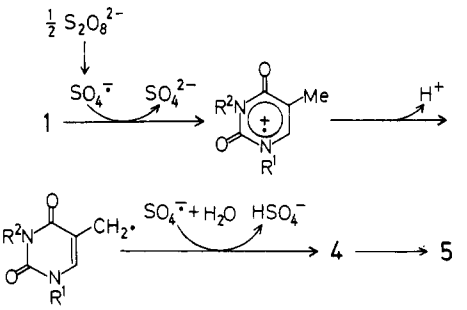
Oxidation of thymines by sodium peroxodisulfate in water at 85 °C gave the corresponding 5-(hydroxymethyl)uracils and 5-formyluracils. The reaction may proceed via thymine cation radicals. On the other hand, oxidation of thymines by potassium peroxomonosulfate in water gave the corresponding *cis*-5,6-dihydroxy-5,6-dihydrothymines and 5-hydroxy-5-methylbarbituric acids. Furthermore, treatment of thymine with both potassium peroxomonosulfate and hydrogen peroxide in water gave *cis*-6-hydroperoxy-5-hydroxy-5,6-dihydrothymine.

Many peroxides such as hydrogen peroxide,[1] hydroperoxythymines,[2] fatty acid hydroperoxides,[3] and benzoyl peroxide[4] are known to have mutagenic and carcinogenic activity. Therefore, damage of nucleic acids by peroxides is of interest. Oxidation of nucleic acid bases and their derivatives by peroxides such as hydrogen peroxide[5,6] and *m*-chloroperbenzoic acid[7] has been extensively investigated. Furthermore, reaction of them with peroxodisulfate ion ($S_2O_8^{2-}$) has been reported by several groups of workers.[8,9] However, little attention has been paid to isolation of products[10] of the oxidation by $S_2O_8^{2-}$ except for the reaction in alkaline solution.[8] This paper describes the oxidation of thymines (1) by sodium peroxodisulfate ($Na_2S_2O_8$) and potassium peroxomonosulfate ($KHSO_5$) in water. Treatment of 1 with $Na_2S_2O_8$ in water at 85 °C resulted in the selective oxidation of the 5-methyl group

Scheme I



of 1, whereas oxidation of 1 by $KHSO_5$ in water gave the corresponding *cis*-5,6-dihydroxy-5,6-dihydrothymines (8) and 5-hydroxy-5-methylbarbituric acids (9).

Results and Discussion

The N-methylated thymines **1b–d** were prepared by treatment of sodium salts of thymine (**1a**) with methyl iodide in dimethylformamide. Droplet countercurrent chromatography was used for preparative separation of a mixture of 1-methylthymine (**1b**), 3-methylthymine (**1c**), and 1,3-dimethylthymine (**1d**). Separation with $CHCl_3$–MeOH–H_2O (5:5:3) by the descending method resulted in the isolation of them. However, **1c** was obtained only in very low yield. Therefore, synthesis of **1c** according to the method for preparation of 3-methyluracil[11] was attempted. Treatment of the sodium salt of 2-thiothymine (**2**) with methyl iodide in dimethylformamide gave 2-(methylthio)pyrimidine (**3**), which was reacted with hydrochloric acid to give **1c**.

Treatment of thymines **1a–d** with $Na_2S_2O_8$ in water at 85 °C under nitrogen or in air gave the corresponding 5-(hydroxymethyl)uracils **4a–d** and 5-formyluracils **5a–d**

(1) (a) Ames, B. N. *Science (Washington, D.C.)* **1983**, *221*, 1256. (b) Halliwell, B.; Gutteridge, J. M. C. *Biochem. J.* **1984**, *219*, 1. (c) Cerutti, P. A. *Science (Washington, D.C.)* **1985**, *227*, 375. (d) Sies, H. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1058.
(2) (a) Thomas, H. F.; Herriott, R. M.; Hahn, B. S.; Wang, S. Y. *Nature (London)* **1976**, *259*, 341. (b) Wang, S. Y.; Hahn, B. S.; Batzinger, R. P.; Bueding, E. *Biochem. Biophys. Res. Commun.* **1979**, *89*, 259.
(3) (a) Yamaguchi, T.; Yamashita, Y. *Agric. Biol. Chem.* **1979**, *43*, 2225. (b) *Ibid.* **1980**, *44*, 1675.
(4) Slaga, J. T.; Klein-Szanto, A. J. P.; Triplett, L. L.; Yotti, L. P.; Trosko, J. E. *Science (Washington, D.C.)* **1981**, *213*, 1023.
(5) (a) Priess, H.; Zillig, W. *Z. Physiol. Chem.* **1965**, *342*, 73. (b) Subbaraman, L. R.; Subbaraman, J.; Behrman, E. J. *J. Org. Chem.* **1971**, *36*, 1256. (c) Itahara, T. *Chem. Lett.* **1987**, 841.
(6) Hahn, B. S.; Wang, S. Y. *Biochem. Biophys. Res. Commun.* **1977**, *77*, 947.
(7) (a) Harnden, M. R.; Brown, A. G.; Hodge, R. A. V. *J. Chem. Soc., Perkin Trans. 1* **1973**, 333. (b) Harayama, T.; Kotoji, K.; Yanada, R.; Yoneda, F.; Taga, T.; Osaki, K.; Nagamatsu, T. *Chem. Pharm. Bull.* **1986**, *34*, 2354.
(8) Moschel, R. C.; Behrman, E. J. *J. Org. Chem.* **1974**, *39*, 1983, 2699.
(9) (a) Bansal, K. M.; Fessenden, R. W. *Radiat. Res.* **1978**, *75*, 497. (b) Fujita, S.; Steenken, S. *J. Am. Chem. Soc.* **1981**, *103*, 2540. (c) Hazra, D. K.; Steenken, S. *Ibid.* **1983**, *105*, 4380.
(10) A part of this work was published as a preliminary report: Itahara, T.; Ebihara, R.; Fujii, Y.; Tada, M. *Chem. Lett.* **1986**, 1319.
(11) Brown, D. J.; Hoerger, E.; Mason, S. F. *J. Chem. Soc.* **1955**, 211.

0022-3263/88/1953-3421$01.50/0

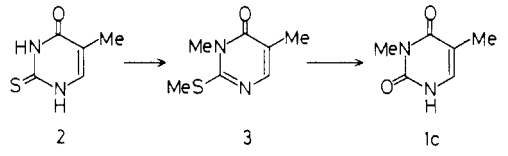


Figure 1.

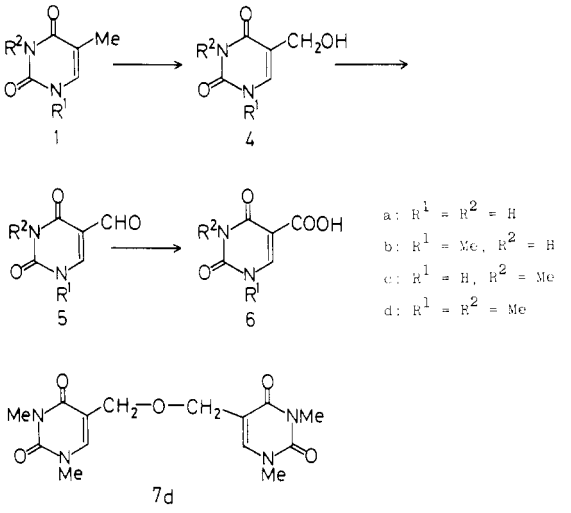


Figure 2.

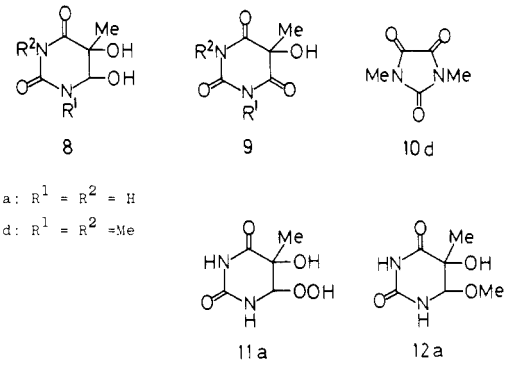


Figure 3.

Table I. Oxidation of Thymines by Potassium Peroxomonosulfate in Water[a]

substrate (1 mmol)	$KHSO_5$, mmol	temp, °C	reacn time, h	products (isol yield, %)
1a	2	36–40	24	**8a** (35), **9a** (20)
1a	2	75–80	7	**8a** (40), **9a** (12)
1a[b]	2	75–80	7	**8a** (43), **9a** (12)
1a[c]	2	24–26	24	**9a** (20), **11a** (35)
1a[b,c]	2	24–26	24	**9a** (30), **11a** (24)
1d	1	24–26	24	**1d** (45), **8d** (30), **9d** (5)
1d	1	75–80	4	**1d** (36), **8d** (48), **9d** (3), **10d** (1), **5d** (2)
1d	2	75–80	4	**8d** (65), **9d** (5), **10d** (5), **5d** (2)
8a	2	75–80	7	**8a** (20), **9a** (55)

[a] The reaction was performed in water (50 mL) in air. [b] The reaction was performed under a nitrogen atmosphere. [c] The reaction was performed in the presence of H_2O_2 (4 mmol).

together with a dimeric compound (**7d**) in the case of the oxidation of **1d**.[10] Reaction of **4d** with $Na_2S_2O_8$ gave **5d** in good yield. However, compared with the ready conversion of both **1d** to **4d** and **4d** to **5d**, the formation of **6d** from **5d** occurred only to an extent of 11%. On the other hand, attempted selective oxidation of methyl groups of 6-methyluracil, 1,3,6-trimethyluracil, 6-azathymine, and 5-methylpyrimidine failed under similar conditions.

The oxidation of the 5-methyl group of thymines by thymine 2-oxoglutarate dioxygenase (EC 1.14.11.6) is known,[12] and **4a** exists in DNA as a minor base.[13] However, no reports concerned selective oxidation of the 5-methyl group have been published except for the photooxidation of **1a**,[14] **1d**,[14] and thymidine[15] and ionizing radiation of [methyl-^{3}H]thymidine.[16] Therefore, the mechanism of the oxidation of **1** by $Na_2S_2O_8$ is of interest. The oxidation of a methyl group attached to aromatic compounds by $S_2O_8^{2-}$ has been reported to proceed via cation radical intermediates.[17] Furthermore, reaction of **1** with radicals such as hydroxy radical[18–21] and carbon radicals[22] in aqueous solutions is known to result in an addition reaction at the 5,6-double bond but a formation of only a small amount of **4**. The observations of cation radicals of nucleic acid bases is also known.[23] In view of these reported facts, the selective oxidation of the methyl group of **1** by $Na_2S_2O_8$ is reasonably explained in terms of formation of thymine cation radical intermediates (Scheme I).

When **1a** was reacted with $KHSO_5$ in water, 5,6-dihydroxy-5,6-dihydrothymine (**8a**) and 5-hydroxy-5-methylbarbituric acid (**9a**) were obtained. The stereochemistry of **8a** was assigned the cis configuration by direct comparison with an authentic sample prepared from the oxidation of **1a** with $KMnO_4$.[24] The trans isomer of **8a** was not isolated. A similar oxidation of **1d** gave **8d** and **9d** together with a small amount of 1,3-dimethylparabanic acid (**10d**) and **5d**. The stereochemistry of **8d** was assumed by comparing its ^{1}H NMR data with those reported for *cis*- and *trans*-5,6-dihydroxy-1,3-dimethyl-5,6-dihydrothymines[6] and the fact that **8a** had the cis configuration. Furthermore, treatment of **8a** with $KHSO_5$ in water gave **9a**. These results are summarized in Table I.

The isolation of **8a** and its deoxyribonucleoside in human and rat urine is known.[25] Compound **8a** has been

(12) (a) Abbot, M. T.; Schandl, E. K.; Lee, R. F.; Parker, T. S.; Midgett, R. T. *Biochim. Biophys. Acta* **1967**, *132*, 525. (b) Abbott, M. T.; Dragila, T. A.; McCroskey, R. P. *Ibid.* **1968**, *169*, 1. (c) Watanabe, M. S.; McCroskey, R. P.; Abbott, M. T. *J. Biol. Chem.* **1970**, *245*, 2023.

(13) Kallen, R. G.; Simon, M.; Marmur, J. *J. Mol. Biol.* **1962**, *5*, 248.

(14) Alcantara, R.; Wang, S. Y. *Photochem. Photobiol.* **1965**, *4*, 465, 473.

(15) Decarroz, C.; Wagner, J. R.; Van Lier, J. E.; Murali Krishina, C.; Riesz, P.; Cadet, J. *Int. J. Radiat. Biol.* **1986**, *50*, 491.

(16) Teebor, G. W.; Frenkel, K. Goldstein, M. S. *Proc. Natl. Acad. Sci. U.S.A.* **1984**, *81*, 318.

(17) (a) Minisci, F.; Citterio, A.; Giordano, C. *Acc. Chem. Res.* **1983**, *16*, 27. (b) Walling, C.; Zhao, C.; El-Taliawi, G. M. *J. Org. Chem.* **1983**, *48*, 4910. (c) Walling, C.; El-Taliawi, G. M.; Zhao, C. *Ibid.* **1983**, *48*, 4914. (d) Walling, C.; El-Taliwai, G. M.; Amarnath, K. *J. Am. Chem. Soc.* **1984**, *106*, 7573. (e) Camaioni, D. M.; Franz, J. A. *J. Org. Chem.* **1984**, *49*, 1607. (f) Minisci, F.; Vismara, E.; Giampiero, M.; Francesca, F.; Silvio, L.; Marco, S. *J. Org. Chem.* **1986**, *51*, 476 and references therein.

(18) (a) Hariharan, P. V.; Cerutti, P. A. *J. Mol. Biol.* **1972**, *66*, 65. (b) Frenkel, K.; Goldstein, M. S.; Teebor, G. M. *Biochemistry* **1981**, *20*, 7566. (c) Wada, T.; Ide, H.; Nishimoto, S.; Kagiya, T. *Chem. Lett.* **1982**, 1041.

(19) Mead, E. L.; Sutherland, R. G.; Verrall, R. E. *Can. J. Chem.* **1976**, *53*, 2394.

(20) (a) Scholes, G.; Weiss, J.; Wheeler, C. M. *Nature (London)* **1956**, 178, 157. (b) Ekert, B.; Monier, R. *Ibid.* **1959**, *184*, B.A. 58. (c) Scholes, G.; Weiss, J. *Ibid.* **1960**, *185*, 305. (d) Cadet, J.; Teoule, R. *Biochim. Biophys. Acta* **1971**, *238*, 8. (e) Cadet, J.; Teoule, R. *Biochem. Biophys. Res. Commun.* **1974**, *59*, 1047.

(21) Hahn, B. S.; Wang, S. Y. *Biochem. Biophys. Res. Commun.* **1973**, *54*, 1224.

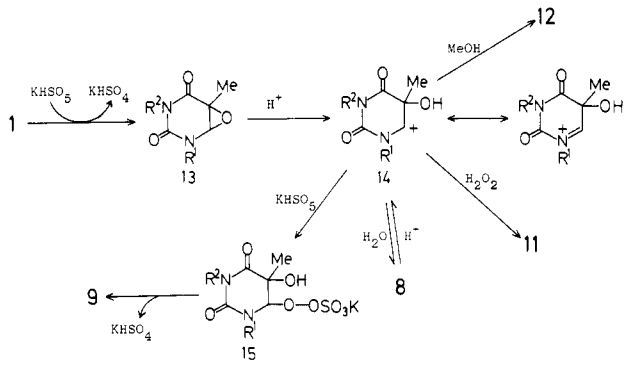
(22) Itahara, T. *Chem. Lett.* **1985**, 1442.

(23) Sevilla, M. D.; Suryanarayana, D.; Morehouse, K. M. *J. Phys. Chem.* **1981**, *85*, 1027 and references therein.

(24) Iida, S.; Hayatsu, H. *Biochim. Biophys. Acta* **1970**, *213*, 1.

(25) Cathcart, R.; Schwiers, E.; Saul, R. L.; Ames, B. N. *Proc. Natl. Acad. Sci. U.S.A.* **1984**, *81*, 5633.

Scheme II



reported to be obtained from oxidation of **1a** in aqueous solutions by ionizing radiation,[18] ultrasonication,[19] and near-UV irradiation in the presence of H_2O_2[6] and with OsO_4[26] and $KMnO_4$.[24] However, no reports concerning the formation of **8** by direct oxidation of **1** by peroxides have been published. The ionizing radiation in aerated aqueous solutions gives thymine hydroperoxides such as *cis*-6-hydroperoxy-5-hydroxy-5,6-dihydrothymine (**11a**), suggesting that it is a radical reaction with hydroxy radical.[19-21] On the other hand, oxidation of **1a** by $KHSO_5$ in water under an oxygen atmosphere gave no thymine hydroperoxides such as **11a**.

Recent papers concerning oxidation with $KHSO_5$[27] suggest that an intermediate of the reaction of **1** with $KHSO_5$ may be a thymine epoxide (**13**). Therefore, it is of interest that the products isolated from the oxidation of **1** by $KHSO_5$ in water had the cis configuration because reaction of epoxides with water usually gives *trans*-glycols. Similar results were already reported by Wang et al.[28] They reported that thymine epoxides (**13**), which were formed from the reaction of *trans*-5-bromo-6-hydroxy-5,6-dihydrothymines with bases, further reacted with water to give **8** in quantitative yields but with none of the trans isomers.

In order to elucidate the mechanism for the formation of **8** from **1**, we further investigated oxidation of **1** by $KHSO_5$ in the presence of nucleophiles. Treatment of **1a** with $KHSO_5$ in the presence of H_2O_2 gave **11a**, while reaction of **1a** with $KHSO_5$ in the presence of amines or *tert*-butyl hydroperoxide in water was unsuccessful. Treatment of **8a** with H_2O_2 in 0.1 M HCl also gave **11a** although both **8a** and the trans isomer of **8a** are known to be converted to **11a** by oxidation with H_2O_2 in acidic condition.[21] The stereochemistry of **11a** was determined by its ^1H NMR data and formation of **8a** by reduction of **11a** with dimethyl sulfoxide.[21] When the reaction mixture from **1a** with $KHSO_5$ in water was treated with methanol, 5-hydroxy-6-methoxy-5,6-dihydrothymine (**12a**) was obtained, though the stereochemistry was not clear.

Scheme II may be derived for the oxidation of **1** by $KHSO_5$ in water. The formation of **8**, **11**, and **12** may be explained as reaction of a cation (**14**) with nucleophiles such as water, H_2O_2, and methanol. Futher Wang et al.[28] explained the reason why the reaction of **14** with water gave **8** but not the trans isomers in terms of an energetically favorable gauche stereochemistry.[29] Compounds **9** may be formed via **15** by further oxidation of **14**.

Experimental Section

Melting points were determined on a Yanagimoto micro melting point apparatus and are uncorrected. Proton magnetic resonance spectra were obtained with a JEOL PMX60A spectrometer using tetramethylsilane as an internal standard. Infrared spectra were measured with a JASCO IRA-1 spectrometer. Mass spectra were obtained with a JEOL JMS-D300 spectrometer. The elemental analyses were performed by the Analytical Center of Kyoto University. Preparative thin-layer chromatography was performed with Wako silica gel B-5F. Thymine (**1a**) was obtained commercially.

Methylation of Thymine (1a). Methyl iodide (60 mmol) was added dropwise to a stirred solution of **1a** (2.52 g, 20 mmol) and sodium hydride (40 mmol) in dimethylformamide (300 mL). Then the mixture was stirred at room temperature for 16 h and evaporated to give a brown residue that was extracted with chloroform. The extract was evaporated and dissolved in 20 mL of an upper layer of $CHCl_3$–MeOH–H_2O (5:5:3). The resulting solution was subjected to droplet countercurrent chromatography (Tokyo Rikakikai Co., DCC-300-G2). Separation with $CHCl_3$–MeOH–H_2O (5:5:3) by the descending method resulted in the isolation of 1,3-dimethylthymine (**1d**) (1887 mg, 12.4 mmol) [mp 151–153 °C (lit.[30] mp 153 °C)], 3-methylthymine (**1c**) (51 mg, 0.8 mmol) [dec 205–209 °C (lit.[30] 202–205 °C)], and 1-methylthymine (**1b**) (298 mg, 4.2 mmol) [mp 288–290 °C (lit.[30] mp 280–282 °C)].

1,6-Dihydro-1,5-dimethyl-2-(methylthio)-6-oxopyrimidine (3). Compound **3** was prepared by treatment of 2-thiothymine (**2**) (1.42 g, 10 mmol), sodium hydride (20 mmol), and methyl iodide (30 mmol) in dimethylformamide (150 mL) according to the method of methylation of **1a**: yield 0.82 g (5.8 mmol); mp 99–100 °C; NMR ($CDCl_3$) δ 2.01 (d, 3 H, J = 0.5 Hz), 2.53 (s, 3 H), 3.50 (s, 3 H), 7.61 (q, 1 H, J = 0.5 Hz); IR (Nujol) 1665, 1650 (sh) cm^{-1}; mass spectrum, m/e (relative intensity) 170 (85), 126 (16), 125 (100), 124 (42), 123 (41). Anal. Calcd for $C_7H_{10}N_2OS$: C, 49.39; H, 5.92; N, 16.46. Found: C, 49.55; H, 5.92; N, 16.29.

3-Methylthymine (1c). A solution of **3** (1 mmol) in 1 M HCl (50 mL) was heated at 80 °C for 1 h and then evaporated to give a white solid mass that was triturated with chloroform to give **1c** (0.77 mmol).

Oxidation of Thymine (1a) by Sodium Peroxodisulfate. A solution (pH 2.1) of **1a** (1 mmol) and $Na_2S_2O_8$ (2 mmol) in water (50 mL) was heated at 85 °C under nitrogen for 7 h. The reaction mixture (pH 1.7) was evaporated to give a residue that was submitted to rotation locular countercurrent chromatography (Tokyo Rikakikai Co., RLCC). Separation with $CHCl_3$–MeOH–H_2O (5:5:3) by the descending method resulted in the isolation of 5-formyluracil (**5a**) (0.41 mmol) [dec 300–306 °C (lit.[31] 304–306 °C)] and 5-(hydroxymethyl)uracil (**4a**) (0.05 mmol). Compound **4a** was identified by direct comparison with an authentic sample obtained from Sigma Chemical Co.

Oxidation of N-Methylated Thymines 1b,c,d, 1,3-Dimethyl-5-(hydroxymethyl)uracil (4d), and 1,3-Dimethyl-5-formyluracil (5d) by Sodium Peroxodisulfate. A solution of thymines **1b,c,d** (1 mmol) and $Na_2S_2O_8$ (1 or 2 mmol) in water (50 mL) was heated at 85 °C for 7 h. The reaction mixture was evaporated to give a residue that was then chromatographed (silica gel TLC, developed with ethyl acetate or a mixture of ethyl acetate and methanol (10:1 or 20:3) to give 5-(hydroxymethyl)-1-methyluracil (**4b**) [mp 239–242 °C (lit.[32] mp 239–242 °C)], 5-(hydroxymethyl)-3-methyluracil (**4c**) [mp 167–170 °C (lit.[33] mp 170–171 °C)], 1,3-dimethyl-5-(hydroxymethyl)uracil (**4d**) [mp 136–138 °C (lit.[33] mp 136–138 °C)], 5-formyl-1-methyluracil (**5b**) [mp 227–230 °C (lit.[32] mp 227–229 °C)], 5-formyl-3-methyluracil

(26) Beer, M.; Stern, S.; Carmalt, D.; Mohlhenrich, K. *Biochemistry* **1966**, *5*, 2283.
(27) (a) Curci, R.; Fiorentino, M.; Troisi, L. *J. Org. Chem.* **1980**, *45*, 4758. (b) Bloch, R.; Abecassis, J.; Hasan, D. *Ibid.* **1985**, *50*, 1544. (c) Corey, P. F.; Ward, F. E. *Ibid.* **1986**, *51*, 1925.
(28) (a) Ryang, H.; Wang, S. Y. *J. Am. Chem. Soc.* **1978**, *100*, 1302. (b) *J. Org. Chem.* **1979**, *44*, 1191. (c) Burrows, E. P.; Ryang, H.; Wang, S. Y.; Flippen-Anderson, J. L. *Ibid.* **1979**, *44*, 3736.
(29) Robins, M. J.; MacCoss, M.; Naik, S. R.; Ramani, G. *J. Am. Chem. Soc.* **1976**, *98*, 7381 and references therein.
(30) Johnson, T. B.; Clapp, S. H. *J. Biol. Chem.* **1908**, *5*, 49.
(31) Ressner, E. C.; Kampf, A.; Mertes, M. P. In *Nucleic Acid Chemistry*; Townsend, L. B., Tipson, R. S., Eds.; Wiley: New York, 1978; p 89.
(32) Sakai, T. T.; Pogolotti, A. L., Jr.; Santi, D. V. *J. Heterocycl. Chem.* **1968**, *5*, 849.
(33) Santi, D. V.; Pogolotti, A. L., Jr. *J. Heterocycl. Chem.* **1971**, *8*, 265.

(5c), and 1,3-dimethyl-5-formyluracil (5d) [mp 125–126 °C (lit.[14] mp 126–127 °C)]. A small amount of 5,5′-[oxybis(methylene)]-bis(1,3-dimethyluracil) (7d) was further obtained from the reaction of 1d. The spectral and analytical data of 5c and 7d are given below.

5c: mp 202–205 °C; NMR (DMSO-d_6) δ 3.20 (s, 3 H), 8.17 (s, 1 H), 9.87 (s, 1 H), 12.16 (broad, 1 H); IR (Nujol) 3130, 1730 (sh), 1685, 1610, 1590 cm^{-1}; mass spectrum, m/e (relative intensity) 154 (12), 126 (100), 69 (62). Anal. Calcd for $C_6H_6N_2O_3$: C, 46.76; H, 3.92; N, 18.18. Found: C, 46.61; H, 3.95; N, 17.95.

7d: mp 182–184 °C; NMR ($CDCl_3$) δ 3.34 (s, 6 H), 3.42 (s, 6 H), 4.35 (d, 4 H, J = 1 Hz), 7.39 (t, 2 H, J = 1 Hz); IR (Nujol) 1700, 1660, 1640 cm^{-1}; mass spectrum, m/e (relative intensity) 323 (0.1), 170 (9), 169 (100), 154 (22), 153 (46). Anal. Calcd for $C_{14}H_{18}N_4O_5$: C, 52.17; H, 5.63; N, 17.38. Found: C, 52.64; H, 5.67; N, 17.14.

Treatment of 4d (1 mmol) with $Na_2S_2O_8$ (1 mmol) was also carried out according to the procedure described above to give 4d (0.20 mmol) and 5d (0.72 mmol). Reaction of 5d (1 mmol) with $Na_2S_2O_8$ (1 mmol) gave 5d (0.53 mmol) and 1,3-dimethyluracil-5-carboxylic acid (6d)[34] (0.11 mmol).

Oxidation of Thymines 1a,d by Potassium Peroxomonosulfate. Oxone, which is a mixture of $KHSO_5$, $KHSO_4$, and K_2SO_4 (2:1:1), obtained from DuPont was used as potassium peroxomonosulfate. A solution (pH 2.4) of 1a (1 mmol) and $KHSO_5$ (2 mmol) in water (50 mL) was heated or stirred at room temperature. The reaction mixture (pH 2.0) was evaporated to give a residue that was extracted with acetone. The extract was evaporated and chromatographed (silica gel TLC, developed with ethyl acetate) to give 5-hydroxy-5-methylbarbituric acid (9a) [dec 225–227 °C (lit.[24] 226–227 °C)] and *cis*-5,6-dihydroxy-5,6-dihydrothymine (8a) [dec 212–216 °C (lit.[24] 215–216 °C)]: NMR (DMSO-d_6) δ 1.28 (s, 3 H), 4.35 (t, 1 H, J = 5 Hz), 5.23 (s, 1 H), 5.98 (d, 1 H, J = 5 Hz), 8.1 (broad, d, 1 H, J = 5 Hz), 10.05 (broad, 1 H).

(34) Itahara, T. *Chem. Lett.* **1983**, 127.

Oxidation of 1d (1 mmol) by $KHSO_5$ (1 or 2 mmol) in water (50 mL) was also carried out according to the procedure described above to give 1,3-dimethylparabanic acid (10d) [mp 151–153 °C (lit.[35] mp 151–153 °C)], 1,3-dimethyl-5-hydroxy-5-methylbarbituric acid (9d) [mp 106–107 °C (lit.[36] mp 107 °C)], 5d, and *cis*-5,6-dihydroxy-1,3-dimethyl-5,6-dihydrothymine (8d)[6] (oil): NMR (DMSO-d_6) δ 1.25 (s, 3 H), 2.95 (s, 3 H), 3.00 (s, 3 H), 4.50 (s, 1 H), 5.6 (broad, 1 H), 6.5 (broad, 1 H).

***cis*-6-Hydroperoxy-5-hydroxy-5,6-dihydrothymine (11a).** A solution of 1a (1 mmol), $KHSO_5$ (2 mmol), and H_2O_2 (4 mmol) in water (50 mL) was stirred at room temperature for 24 h. The reaction mixture was evaporated and chromatographed (silica gel TLC, developed with ethyl acetate) to give 11a (0.34 mmol): NMR (DMSO-d_6) δ 1.34 (s, 3 H), 4.60 (d, 1 H, J = 5 Hz), 5.28 (s, 1 H), 8.27 (broad, d, 1 H, J = 5 Hz), 9.99 (broad, 1 H), 11.58 (s, 1 H); (acetone-d_6) δ 1.50 (s, 3 H), 4.28 (s, 1 H), 4.88 (d, 1 H, J = 5 Hz), 7.6 (broad, d, 1 H, J = 5 Hz), 9.1 (broad, 1 H), 10.98 (s, 1 H). Treatment of 11a with DMSO-d_6 in a NMR tube led to the formation of 8a. Compound 11a was also prepared in 40% yield by treatment of 8a (1 mmol) with H_2O_2 (4 mmol) in 0.1 M HCl (50 mL) at room temperature for 24 h according to the method reported by Hahn and Wang.[21]

5-Hydroxy-6-methoxy-5,6-dihydrothymine (12a). A solution of 1a (1 mmol) and $KHSO_5$ (2 mmol) in water (50 mL) was heated at 80 °C for 7 h. The reaction mixture was evaporated to give a residue that was treated with methanol (20 mL) at room temperature for 24 h. The solution was evaporated and chromatographed (silica gel TLC, developed with ethyl acetate) to give 12a (0.47 mmol): mp 190–194 °C (lit.[28] mp 195 °C).

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(35) Hoyano, Y.; Bacon, V.; Summons, R. E.; Pereira, W. E.; Halpern, B.; Duffield, A. M. *Biochem. Biophys. Res. Commun.* **1973**, *53*, 1195.
(36) Clark-Lewis, J. W.; Thompson, M. J. *J. Chem. Soc.* **1959**, 3401.

Estimations of the Heats of Vaporization of Simple Hydrocarbon Derivatives at 298 K

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A simple method of estimating the enthalpies of vaporization of monofunctional hydrocarbon derivatives within 5% of literature values is described. The technique utilizes the analytical expression previously developed to estimate vaporization enthalpies of hydrocarbons, $\Delta H_v = 1.12\tilde{n}_c + 0.31n_Q + 0.71$, where n_Q and $\tilde{n}_c$ refer to the number of quaternary and nonquaternary carbon atoms, respectively, modified by introducing an additional parameter, b, that is characteristic of the functional group in question. Values of b for 21 different functional groups are derived from 433 critically reviewed vaporization enthalpies. They range from a low value of 1.19 kcal/mol for ethers to a high value of 12.74 kcal/mol for sulfones. Results obtained by other estimation techniques are compared. Advantages of this method include the ease with which estimations can be made, the general applicability of the method to compounds of diverse structure, and the overall accuracy of the estimations. In addition, the magnitude of b, a characteristic of the attractive interactions of a functional group, can be correlated to E_T values that are often used as a measure of solvent polarity.

Many studies of organic systems reference the gas phase as a standard state. Evaporation enthalpies[1] are an important physical property of the condensed phase, and some reliable measure of this quantity is a necessary requirement for such studies.[2] The large number of new

(1) The term "evaporation enthalpies" is used here to denote both enthalpies of vaporization (liquids) and enthalpies of sublimation (solids).

(2) See, for example: Benson, S. W. *Thermochemical Kinetics: Methods for the Estimation of Thermochemical Data and Rate Parameters*, 2nd ed.; Wiley: New York, 1976. Greenberg, A.; Liebman, J. F. *Strained Organic Molecules*; Academic: New York, 1978.

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