4-(dimethylamino)benzophenone-sensitized irradiations or at 334 nm for xanthone-sensitized irradiations. Concentrations of the sensitizers were such that greater than 98% of the incident light was absorbed by the sensitizer. Analyses were performed by 270-MHz NMR with added standards as described for the direct runs. The data are reported in Table V.

Control Experiment. Direct Irradiation of 3-(2,2-Diphenylvinyl)indene. A solution of 101 mg (0.34 mmol) of 3-(2,2-diphenylvinyl)indene in benzene was irradiated for 3 h on the immersion apparatus through Pyrex. Concentration in vacuo gave 98 mg (97%) of recovered indene, identical with starting material by NMR.

Control Experiment. Direct Irradiation of 1,4,5-Triphenylcyclopentadiene. A solution of 10 mg (0.034 mmol) of 1,4,5-triphenylcyclopentadiene in 10 mL of benzene was irradiated for 35 min on the immersion apparatus through Pyrex. Concentration in vacuo gave 8 mg (80%) of recovered 1,4,5-triphenylcyclopentadiene as nearly colorless needles (mp 129–131 °C), identical with starting material.

Control Experiment. Direct Irradiation of 1,2-Diphenylcyclopentadiene. A solution of 15 mg of 1,2-diphenylcyclopentadiene in 15 mL of cyclohexane was irradiated for 30 min on the immersion apparatus through Corex. Concentration in vacuo gave 14 mg (93%) of recovered cyclopentadiene. The spectral data were identical with those of starting material.

Control Experiment. Direct Irradiation of 3-(1-Phenylvinyl)indene. A solution of 20 mg (0.092 mmol) of 3-(1-phenylvinyl)indene in 15 mL of cyclohexane was irradiated for 0.5 h on the immersion apparatus through Corex. Concentration in vacuo gave 20 mg (100%) of recovered indene, identical with starting material by NMR.

Control Experiment. Test for Singlet Energy Transfer from Xanthone to 3-Phenyl-3-(1-phenylvinyl)cyclopropene. The fluorescence of a degassed 3.18×10^{-2} M solution of xanthone in benzene was unquenched by addition of 5.0×10^{-3} M 3-phenyl-3-(1-phenylvinyl)cyclopropene, indicating that no singlet energy transfer was occurring.

Control Experiment. Direct Irradiation of 3-Phenyl-3-(2,2-diphenylvinyl)cyclopropene in Tetrahydrofuran. A solution of 100 mg (0.34 mmol) of 3-phenyl-3-(2,2-diphenylvinyl)cyclopropene in 250 mL of tetrahydrofuran was irradiated for 2.5 h on the black box apparatus through filter A (1.7 mEinsteins). Concentration in vacuo gave 112 mg of a yellow oil containing, in addition to recovered starting material, 2,5,5- and 1,4,5-triphenylcyclopentadiene and a trace of 3-(2,2-diphenylvinyl)indene by NMR. No increase in the amount of indene relative to cyclopentadiene photoproducts was apparent by NMR, when compared with amounts of products from similar runs carried out in cyclohexane.

Acknowledgment. Support of this research by National Institutes of Health Grant GM07487 and by the National Science Foundation is gratefully acknowledged. The synthetic aspects were supported by the NIH while mechanistic studies were supported by the NSF.

Registry No. 1, 81245-47-8; 1(1'd), 81245-48-9; 2, 81245-49-0; 3, 81245-50-3; 3(2d), 81245-51-4; 4, 81245-52-5; 4(1d), 81245-53-6; *cis*-5(1'd), 81255-40-5; *trans*-5(1'd), 81245-54-7; 6, 5074-28-2; 12, 81245-55-8; 12(1d), 81245-56-9; 12(4d), 81245-57-0; 13, 81245-58-1; 15, 81245-59-2; 16, 81245-60-5; 16(2d), 81245-61-6; 16(5d), 81245-62-7; 17, 24102-68-9; 18, 81245-63-8; 19, 17792-17-5; 19(2d), 78522-52-8; 20, 81245-64-9; 21, 81245-65-0; 22, 81245-66-1; (*E*)-27, 81245-67-2; (*Z*)-27, 81245-68-3; (E)-28, 81245-69-4; (E)-29, 81245-70-7; 1-bromo-2-phenyl-2-(2,2-diphenylvinyl)cyclopropene (isomer 1), 81245-71-8; 1-bromo-2-phenyl-2(2,2-diphenylvinyl)cyclopropene (isomer 2), 81245-72-9; 1,1-dibromo-2-phenyl-2(1-phenylvinyl)cyclopropane, 81245-73-0; 2,3-diphenyl-1,3-butadiene, 2548-47-2; 1-bromo-2-phenyl-2-(1-phenylvinyl)cyclopropane, 81245-74-1; 1,4,4-triphenylcyclopent-2-en-1-ol, 81245-75-2; 4,4-diphenylcyclopent-2-en-1-one, 38464-75-4; 1-bromo-2,2-diphenylethylene, 13249-58-6; 1-indanone, 83-33-0; 1-bromostyrene, 98-81-7; 2-deuterio-1,1,3,3-tetraphenylprop-2-en-1-ol, 81245-76-3; 5,5-dideuterio-4,4-diphenylcyclopent-2-en-1-one, 81245-77-4; 5,5-dideuterio-1,4,4-triphenylcyclopent-2-en-1-ol, 81255-41-6; 2,2-diphenylcyclopentan-1-one, 15324-42-2; 1-deuterio-2,2-diphenylcyclopentan-1-ol, 81245-78-5; 2-deuterio-3,3-diphenylcyclopentene, 81245-79-6; 3-deuterio-4,4-diphenylcyclopent-2-en-1-one, 81245-80-9; 3-deuterio-1,4,4-triphenylcyclopent-2-en-1-ol, 81245-81-0; 1,4,7,10-tetraphenyl-2,4,6-triazatricyclo-[5.2.1.$3^{2,6}$]dec-8-en-3,5-dione, 81245-82-1; 2,3-bis(carbomethoxy)-1,6-diphenyl-2,3-diazabicyclo[2.2.1]hept-5-ene, 81245-83-2.

Effect of Neighboring Alkyl Groups on the Rate of Proton Loss in Methylpyrimidine Derivatives

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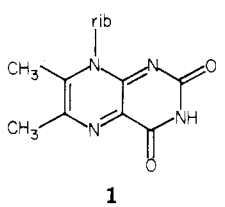
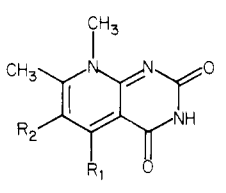
A number of alkyl-substituted 2-iminopyrimidines, 2-pyrimidones, and 2-pyridonium quaternary salts have been prepared and measurements made of the rates of proton loss from an activated methyl group in these compounds (aqueous solution, acetate ion as base). In all cases the presence of a methyl group at next-but-one position of the ring (in most cases the 4-position) causes a decrease in the rate of reaction of the reactive methyl group (in most cases located at the 6-position), the deactivating effect being in the range 4–40. With only one exception an alkyl group at an *adjacent* position (position 5) to the reactive methyl group produces an increase in the rate of reaction, the effects being in the range 2–4. The size of the adjacent alkyl group does not seem to be significant, at least in the iminopyrimidine series. This effect could not be evaluated in the other two series because of spontaneous dealkylation of groups larger than methyl during synthesis. These results duplicate those recently reported in other heterocyclic systems, though the cause of the activating effect of an adjacent alkyl group remains obscure.

Proton loss from the 7-methyl group in 6,7-dimethyl-8-ribityllumazine (1) is a key step in its conversion to riboflavin in nature.[1] We have observed that proton loss from the 7-position in the 8-methyl analogue of 1 is slower in the absence of the 6-methyl group, and this effect is duplicated in the series of 5-deazalumazines (2) which we have also examined.[2] In this series the rate constants for



1

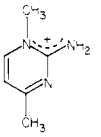
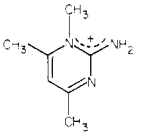
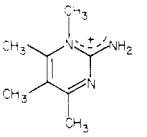
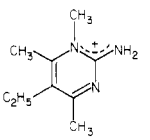
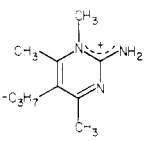


2

(1) (a) Beach, R. L.; Aogaichi, T. *Biochemistry* **1970**, *9*, 771. (b) Beach, R. L.; Plaut, C. W. E. *Ibid.* **1970**, *9*, 760. (c) Paterson, T.; Wood, H. C. S. *J. Chem. Soc., Perkin Trans. 1*, **1972**, 1051.

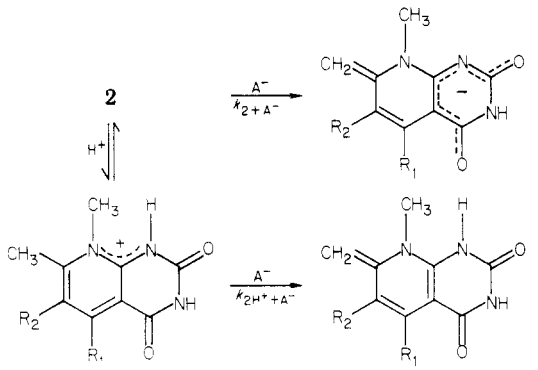
0022-3263/82/1947-2075$01.25/0

Table I. Rate Constants for the Exchange of the 4- and 6-Methyl Groups of 2-Iminopyrimidinium Salts in D_2O–Acetate Buffer[a]

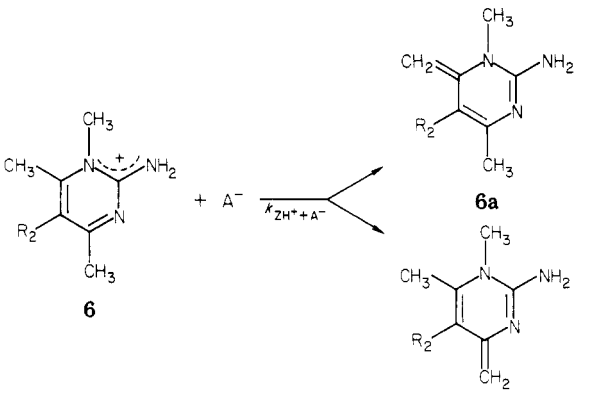
	10^6k_2,[b] M^{-1} s^{-1}				
					
reaction conditions	**7**	**8**	**9**	**10**	**11**
pD 6.35, [AcO^-] = 1.108		1.89 (6), 0.29 (4)	4.38 (6), 0.31 (4)	4.50 (6), 0.30 (4)	4.85 (6), 0.32 (4)
pD 6.62, [AcO^-] = 0.454	0.99 (4)				
pD 6.82, [AcO^-] = 0.691	0.98 (4)	1.85 (6), 0.30 (4)	4.21 (6), 0.29 (4)		
pD 6.89, [AcO^-] = 0.926	0.98 (4)	1.73 (6), 0.30 (4)	3.87 (6), 0.28 (4)		
pD 6.97, [AcO^-] = 0.882				4.49 (6), 0.31 (4)	4.64 (6), 0.31 (4)
pD 7.24, [AcO^-] = 1.187		1.67 (6)	4.35 (6)		

[a] The temperature = 33 °C; ionic strength = 1.20; salts were added as iodides. [b] The numbers in parentheses indicates the 4- or 6-methyl group.

Scheme I

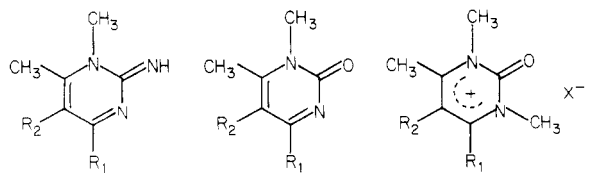


Scheme II



proton loss from the 7-methyl group (to general bases such as acetate ion) is decreased by methyl substitution at position 5 (**2**; $R_1 = CH_3$, $R_2 = H$) but increased by methyl substitution at position 6 (**2**; $R_1 = H$, $R_2 = CH_3$), in agreement with the lumazine work, and this is so both for the general-acid and general-base-catalyzed processes (Scheme I).

In order to learn the basis for this unusual proximity effect, we have examined a series of 2-iminopyrimidines, **3**, and 2-pyrimidones, **4**, and the latter's quaternary salts, **5**, that contain some of the structural features of the lumazine and deazalumazine molecules.



3 **4** **5**

We were also interested in observing the effect of larger alkyl groups at position 5 in these compounds (R_2 in **3–5**) on the reaction of methyl groups at position 6 (CH_3 in **3–5**) and position 4 ($R_1 = CH_3$ in **3–5**). Previous work has shown the 6-position to be more reactive than the 4-position in 1,4,6-trimethyl-2-pyrimidone and 1,4,5,6-tetramethyl-2-pyrimidone.[3,4]

Results

Iminopyrimidines. The rates of proton loss from the activated 4-methyl and 6-methyl positions of these compounds were measured in acetate buffers in D_2O in the pH range 6.6–7.2. Since these compounds have pK values near pD 11,[3a] they are completely in the cationic form and the reaction being followed is that between the cation (ZH^+) and acetate ion (A^-) (Scheme II).

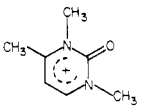
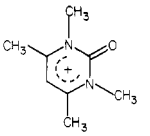
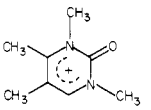
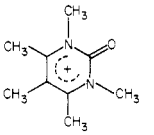
Table I lists the rate constants obtained at 33 °C and constant ionic strength for a number of iminopyrimidines. Four conclusions can be drawn from the results shown therein. (a) Comparison of the rate constants for reaction of the 4-methyl group in **7** and **8** shows that a methyl group on the next-but-one carbon hinders the reaction, though only by a factor of about 3, rather less than for the case with deazalumazines. (b) Comparing **8** and **9** shows that an adjacent methyl group has an activating effect (some

(2) (a) Stewart, R.; Gumbley, S. J.; Srinivasan, R. *J. Am. Chem. Soc.* **1980**, *102*, 6168. (b) Stewart, R.; Srinivasan, R.; Gumbley, S. J. *Can. J. Chem.* **1981**, *59*, 2755.

(3) (a) Stewart, R.; Gumbley, S. J.; Srinivasan, R. *Can. J. Chem.* **1979**, *35*, 2783. (b) Stewart, R.; Gumbley, S. J.; Srinivasan, R. *Tetrahedron* **1979**, *35*, 1257.

(4) Picquenard, E.; Dizabo, P. *Can. J. Chem.* **1981**, *59*, 1270. See also Krueger, S. A.; Paudler, W. P. *J. Org. Chem.* **1972**, *37*, 4188.

Table II. Rate Constants for the Exchange of the 4-Methyl Groups[a] of 2-Pyrimidonium Quaternary Salts in D_2O-Acetate Buffer[b]

	10^2k, M^{-1} s^{-1}			
				
[AcO^-], M	12	13	14	15
0.036			15.7	
0.099	5.3	0.47	15.0	0.73
0.21	5.2	0.47		0.71
0.29	5.2	0.45		0.72
0.37		0.42		0.72
0.45		0.43		0.60
average k	5.2	0.45	15.4	0.70
rel rate/reactive methyl group[a]	23	1	69	1.6

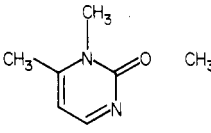
[a] Compounds 13 and 15 have two equivalent reactive groups. [b] The temperature = 33 °C; ionic strength = 1.20; pD range 4.97-6.62.

2.5 times) on the 6-methyl group but very little effect on the 4-methyl group; the latter is the only example of nonactivation by an adjacent methyl that we have found. (c) Increasing the size of the alkyl group at the 5-position has very little effect on the rate constants for proton loss from a methyl group at either C-4 or C-6, the small increase in the rate constants for the 5-ethyl and 5-isopropyl compounds being within experimental error. (d) The methyl group at the 6-position in 8 is more reactive than that at the 4-position, in agreement with the effect observed earlier with the pyrimidines.[3] That is, full conjugation in the product (**6a**) is more effective than cross conjugation (**6b**) in promoting reaction.

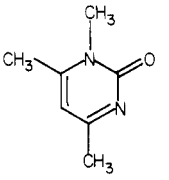
Pyrimidonium Salts. Four methyl quaternary iodides, **12–15**, of pyrimidone were studied in acetate buffer at constant ionic strength in the region pD 5.0–6.6. Only one reaction path is available for these compounds (cation reacting with acetate ion), and the purpose of the pD variance was to adjust the acetate concentration in order that rates could be conveniently measured.

The effects considered in the previous section will be considered here in the same order, the following conclusions being drawn from the rate constants given in Table II. (a) Comparison of **12** and **13** or **14** and **15** shows that a methyl on the next-but-one carbon has a large deactivating effect on the exchanging methyl group.[5] Alkylation renders positions 4 and 6 equivalent, and so a statistical correction of 2 needs to be made to the rate constant for exchange; the rate constants for **12** and **13** differ by a factor just over 11, but this corresponds to a difference of 23 per methyl group. That is, a methyl on the next-but-one carbon decreases the rate of reaction of the exchanging methyl group by a factor of 23. The effect is even larger for **14** and **15**. (b) Comparison of **12** and **14** shows that addition of a methyl group at an adjacent (unreactive) position to a reactive methyl group increases the rate of reaction by a factor of 3. Compounds **13** and **15** show a similar, though somewhat smaller, effect. (c) We have been unable to examine the effect of larger alkyl groups at positions 5 in this series because of the loss of such groups from the intermediate compounds in the synthetic routes available. An elimination reaction takes place with all alkyl groups but methyl during the condensation process (See Experimental Section). (d) No comparison of the 4- and 6-positions is possible in this series, since they are equivalent.

Pyrimidones. We have determined the rate of proton abstraction by acetate ion from the 6-position of the four pyrimidones **16–19**. (The rates for the less reactive 4-position in **17** and **19** were not determined.)

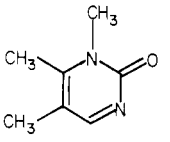


16

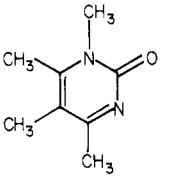


17

k_{AcO^-} (30 °C), M^{-1} s^{-1} 8.5×10^{-6} 2.2×10^{-6}



18



19

k_{AcO^-} (30 °C), M^{-1} s^{-1} 7.2×10^{-5} 5.6×10^{-6}

The acetate rates were measured at the minimum in the pH rate profile for these compounds (approximately pH 9.5, pD 9.9) by varying the concentration of acetate at constant ionic strength at this pD. By this means contributions from acetic acid catalysis and from hydroxide ion catalysis are minimized, though pD control in these virtually unbuffered solutions was difficult to achieve. The results are shown in Figure 1. The rate constants for reaction of the neutral substrates with acetate ion (plus a very small contribution from acetic acid catalysis) are given by the slopes of the lines, and the intercepts give the combined water and hydroxide catalyzed rates. The hydroxide ion contribution in 1 M acetate appears to be less than 10%, at least for **18**, as shown by experiments conducted in the absence of acetate but in the presence of small amounts of NaOD.

Discussion

The results described above show, in general, the same effects of substitution at adjacent and next-but-one carbon

(5) Previous measurements of the rates of these compounds under somewhat different conditions[3b] gave rate constants that were much closer together than those reported here. We believe that the present results, obtained at several acidities, are the more reliable.

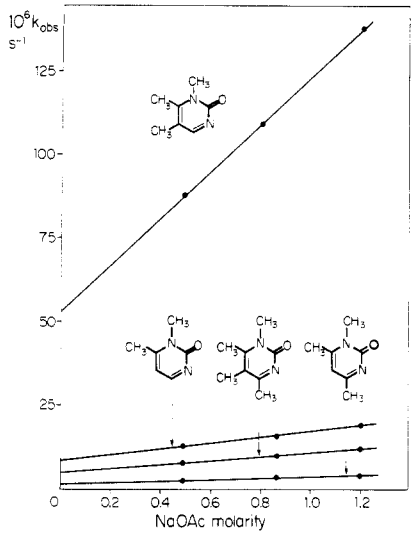


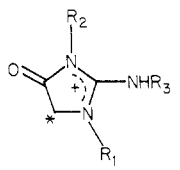
Figure 1. Observed rate constant for exchange at the 6-position of **16–19** as a function of sodium acetate concentration in D_2O (pD 9.81–9.90, ionic strength 1.2).

atoms of the ring that we had observed in the lumazine and 5-deazalumazine series.[2] The effect of adding a methyl group to a next-but-one position with respect to an exchanging methyl group has now been measured in nine systems. (This number would be larger if one included the rate constants for both protonated and unprotonated substrates, that is, both the general-acid-catalyzed and general-base-catalyzed results; since the same general effects are observed in both routes, we confine ourselves to the reaction of acetate ion with the principal form of the substrate under the reaction conditions employed.) The nine systems involve the pairs of compounds **7/8**, **12/13**, **14/15**, **16/17**, and **18/19**, one pair of lumazines, and three pairs of 5-deazalumazines, previously described.[2] In most of these cases substitution of methyl at a next-but-one position deactivates the reactive methyl group by roughly 1 order of magnitude. The largest effect, a factor of 40, is seen with the cations **14** and **15**, and the smallest effect, a factor of 4, is seen with the pyrimidones **16** and **17**.

The results described above are in line with the expected electronic effect of alkyl groups, that is, they decrease the ease of proton loss from an acidic site elsewhere in the molecule.

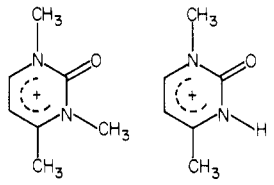
The effect of an *adjacent* methyl has now been observed in 11 systems: **8/9** (both 4- and 6-positions), **12/14**, **13/15**, **16/18**, **17/19**, one pair of lumazines,[2] and three pairs of 5-deazalumazines.[2] For most of these the activating effect is in the range 2–4. (In one case the effect is smaller and in two it is larger.) Although the effects are not large in themselves, they are remarkable in that the substantial electronic effect of a next-but-one methyl group has been overcome, as has the steric hindrance that would be expected to be observed in a bimolecular process such as this.

An examination of results reported earlier shows that the effect of an adjacent methyl is also present when the methyl is attached to a nitrogen atom of the ring and also when the ring is five membered. Thus the active methylene group in N-methylated glycocyamidine ions **20** (exchanging protons labeled with an asterisk) is consistently more reactive than that in the hydrogen analogues when methyl is attached to the adjacent ring nitrogen (R_1) but not when it is attached to the exocyclic position (R_3).[6] (The R_2 group is also activating in this system.)



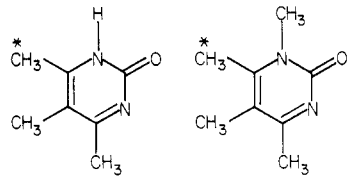
20

Similarly, the 4-methyl group in the quaternary ion **21** is more reactive than that in the protonated ion **22**.[2b] (Whereas methylation at either ring nitrogen is rate-accelerating for **20**, only the nitrogen adjacent to the reactive group shows this effect in the pyrimidone case.)



21 **22**

A further example from the literature is the work of Piquenard and Dizabo,[4] from whose results the relative rates of exchange of the active methyl groups in compounds **23** and **19** can be obtained. They found that the



23 **19**

6-position in **19** (marked by an asterisk) is more than 15 times more reactive than the 4-position, in satisfactory agreement with our earlier work on closely related compounds, and that it is 3.6 times more reactive than the corresponding position(s) in **23**. Because of tautomerism there are two degenerate methyl groups in **23**; however, because of the results obtained with **19** one can assume that, at any time, the one marked with the asterisk is responsible for most of the exchange. Thus a direct comparison is possible between the marked positions in **19** and **23**, the former being the more reactive by roughly a factor of 3.

The one case in which there is little effect of adjacent methyl is for exchange at the 4-position of **8** and **9**. (The 6-position in these compounds shows the usual effect.) Compound **8** is the only system in which the exchanging methyl group is not flanked by at least one group other than hydrogen, but whether this is significant we do not know. It raises the question of buttressing,[7] but there is little evidence to support buttressing as a significant factor in our other results. For example, the ethyl and isopropyl groups in **10** and **11** have virtually the same effect as the methyl group in **9**. Furthermore, the phenomenon does not appear to become significantly more pronounced in the more highly substituted pyrimidine, lumazine, and glycocyamidine derivatives that have been examined.

The combination of activating and deactivating effects produced by substituting methyl groups at adjacent and next-but-one positions results in a consistent pattern for disubstitution in the pyrimidine and lumazine series. The

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deactivating effect predominates, and in all cases the dimethyl derivative reacts more slowly than the parent compound. With regard to isomeric compounds having adjacent or nonadjacent methyl groups, the effect is also uniform. The isomer with adjacent methyl groups reacts much faster than the isomer with nonadjacent methyl groups, despite the latter always having two reactive sites and the former only one.

Origin of the Anomolous Effect of Adjacent Methyl. We have earlier speculated on the origins of this effect in the lumazine series and wondered if relief of steric strain[7c] accompanies proton loss from an activated methyl group as the conversion of an essentially aromatic system (requiring planarity) to an aliphatic conjugated system (with little need for planarity in the region of the molecule under consideration) takes place.[2] This possibility is still open, though it seems surprising that the same effect should be present, and to about the same degree, in all the pyrimidines and lumazines and, indeed, in the glycocyamidines, which are nonaromatic to begin with and become mesoionic as the reaction proceeds.

We are now attempting to determine the crystal structure of suitable pairs of compounds that exhibit the effect described herein to see if the degree of ring planarity in the starting materials is significant.

Experimental Section

Kinetic Measurements. The exchange of the methyl proton in **7–19** in D_2O was followed by NMR, the extent of exchange being determined from the ratio of the areas of the *C*-methyl and *N*-methyl peaks. All kinetic runs were followed to 70–80% completion, with the reproducibility being ±5% and the exchange reactions all being first order. The observed first-order rate constant, k_{obsd}, was obtained by plotting ln (R_t/S_t) against time according to the equation ln $(R_t/S_t) = k_{obsd}t$, where R_t and S_t are the respective areas of the *N*-methyl and *C*-methyl peaks at time *t*. The NMR tubes were thermostated at the temperature of the probe and, for most runs, were removed to a constant-temperature bath between readings.

2-Aminoalkylpyrimidines. Those compounds that were not commercially available were prepared by condensing guanidine carbonate with the appropriate 2,4-pentanedione by the procedure of Brown and England.[8] The 3-methyl, 3-ethyl, and 3-isopropyl derivatives of 2,4-pentanedione were prepared essentially by the method of Johnson, Markham, and Price.[9]

2-Amino-4,5,6-trimethylpyrimidine. This compound was recrystallized from ethyl acetate to give colorless needles: mp 208 °C; NMR ($CDCl_3$) δ 4.80 (NH_2, br), 2.32 (6 H, s), 2.10 (3 H, s). Anal. Calcd for $C_7H_{11}N_3$: C, 61.29; H, 8.08; N, 30.63. Found: C, 61.54; H, 8,15; N, 30.69.

2-Amino-5-ethyl-4,6-dimethylpyrimidine. The crude product, containing about 40% of the 5-deethylated compound, was purified on a silica gel column and then recrystallized from benzene–ether (1:1) to give white crystals: mp 148–149 °C; NMR ($CDCl_3$) δ 4.90 (NH_2, br), 2.34 (2 H, q), 2.30 (6 H, s), 1.04 (3 H, t). Anal. Calcd for $C_8H_{13}N_3$: C, 63.54; H, 8.67; N, 27.79. Found: C, 63.53; H, 8.63; N, 27.95.

2-Amino-5-isopropyl-4,6-dimethylpyrimidine. This product, which also contained the 5-dealkylated compound, was purified as for the previous compound: mp 139 °C; NMR ($CDCl_3$) δ 5.40 (NH_2, br), 3.20 (1 H, m), 2.30 (6 H, s), 1.24 (6 H, d). Anal. Calcd for $C_9H_{15}N_3$: C, 65.42; H, 9.15; N, 25.43. Found: C, 65.19; H, 9.02; N, 25.34.

1,2-Dihydro-2-imino-1,4-dimethylpyrimidine Hydroiodide (7). This compound was obtained by methylating 2-amino-4-methylpyrimidine in 2-methoxyethanol with methyl iodide; mp 258–259 °C (lit.[3a] mp 257 °C dec). A nuclear Overhauser effect was observed for the proton doublet at δ 8.15 upon irradiation of the *N*-CH_3 group at δ 3.80, indicating that the C-6 position does not carry a methyl group.

1,2-Dihydro-2-imino-1,4,6-trimethylpyrimidine Hydroiodide (8). 2-Amino-4,6-dimethylpyrimidine was treated with methyl iodide to give, after recrystallization from ethanol, an 81% yield of **8**: mp 286 °C dec; NMR (D_2O) δ 6.95 (1 H, s), 3.68 (3 H, s), 2.58 and 2.46 (each 3 H, s). Assignment of the signal at δ 2.58 to the C-6 methyl group was made by means of the nuclear Overhauser effect. Anal. Calcd for $C_7H_{12}N_3I$: C, 31.72; H, 4.56; N, 15.85. Found: C, 31.85; H, 4.62; N, 15.70.

1,2-Dihydro-2-imino-1,4,5,6-tetramethylpyrimidine Hydroiodide (9). 2-Amino-4,5,6-trimethylpyrimidine was treated with methyl iodide to give, after recrystallization from ethyl acetate, a 68% yield of **9**: mp 224–225 °C dec; NMR (D_2O) δ 3.70, 2.52, 2.46, and 2.20 (each 3 H, s). For purposes of analysis the iodide was exchanged for chloride by using Dowex 1-X8 (Cl^-) resin. Anal. Calcd for $C_8H_{14}N_3Cl$: C, 51.20; H, 7.52; N, 22.39. Found: C, 50.62; H, 7.49; N, 22.13.

1,2-Dihydro-2-imino-5-ethyl-1,4,6-trimethylpyrimidine Hydroiodide (10). 2-Amino-4,6-dimethyl-5-ethylpyrimidine was methylated as described before and the product recrystallized from ethanol–ethyl acetate: 45% yield, mp 203–204 °C dec; NMR (D_2O) δ 3.70, 2.60, and 2.52 (each 3 H, s), 2.66 (2 H, q), 1.10 (3 H, t). Anal. Calcd for $C_9H_{16}N_3I$: C, 36.88; H, 5.50; N, 14.33. Found: C, 36.46; H, 5.38; N, 14.44.

1,2-Dihydro-2-imino-5-isopropyl-1,4,6-trimethylpyrimidine Hydroiodide (11). Methylation and recrystallization as in the preceding case gave 33% of **11**: mp 232 °C dec; NMR (D_2O) δ 3.70, 2.62, 2.56 (each 3 H, s), 2.60 (1 H, m), 1.30 (6 H, d). Anal. Calcd for $C_{10}H_{18}N_3I$: C, 39.10; H, 5.91; N, 13.68. Found: C, 38.66; H, 5.54; N, 13.71.

1,3,5,6-Tetramethyl-2-pyrimidone Iodide (14). Compound **18** was treated with methyl iodide and the solution allowed to stand overnight. Recrystallization of the salt from methanol–ethyl acetate gave an 83% yield of **14**: mp 211 °C; NMR (D_2O) δ 3.76, 3.72, and 2.26 (each 3 H, s). Anal. Calcd for $C_8H_{13}N_2OI$: C, 34.30; H, 4.68; N, 10.00. Found: C, 34.33; H, 4.71; N, 10.00.

1,3,4,5,6-Pentamethyl-2-pyrimidone Iodide (15). Methylation of **19** as for the previous compound gave a 90% yield of **15**: mp 208–209 °C; NMR (D_2O) δ 3.80 (6 H, s), 2.30 (each 3 H, s), 2.70 (gradual exchange of H for D). Anal. Calcd for $C_9H_{15}N_2OI$: C, 36.75; H, 5.14; N, 9.52. Found: C, 36.68; H, 5.14, N, 9.44.

1,5,6-Trimethyl-2-pyrimidone (18). The procedure of Brown and Paddon-Row[10] was used to prepare this compound from methylurea and 4,4-dimethoxy-3-methyl-2-butanone: mp 128–129 °C; NMR ($CDCl_3$) δ 3.56, 2.32, and 2.02 (each 3 H, s). Anal. Calcd for $C_7H_{10}N_2O$: C, 60.85; H, 7.29; N, 20.28. Found: C, 60.58; H, 7.24; N, 20.14.

1,4,5,6-Tetramethyl-2-pyrimidone (19). Methylurea and 3-methyl-2,4-pentanedione were condensed as for the preceding compound: mp 94–95 °C; NMR ($CDCl_3$) δ 3.64, 2.34, 2.32, and 2.04 (each 3 H, s). Anal. Calcd for $C_8H_{12}N_2O{\cdot}H_2O$: C, 56.45; H, 8.30; N, 16.46. Found: C, 56.78; H, 8.41; N, 16.42.

Attempts to prepare 5-ethyl-1,4,6-trimethyl-2-pyrimidone and 5-isopropyl-1,4,6-trimethyl-2-pyrimidone were unsuccessful. In each case, the C-5-dealkylated compound 1,4,6-trimethyl-2-pyrimidone was the sole product obtained. For example, reaction of methylurea and 3-ethyl-2,4-pentanedione yielded only 1,4,6-trimethyl-2-pyrimidone. No trace of 5-ethyl-1,4,6-trimethyl-2-pyrimidone was detected in the crude product. This reaction was also found to produce ethyl chloride (collected as brown liquid at −40 °C and verified by a mass spectral parent peak at *m/e* 64) during the course of reaction. It is likely that, in the presence of strong acid, the 3-alkyl-2,4-pentanedione was dealkylated before condensing with methylurea. 3-*tert*-Butyl-2,4-pentanedione has been reported to be dealkylated easily in the presence of acid at room temperature.[11]

Compounds **12**, **13**, **16**, and **17** were prepared by published procedures (ref 3b,b, 10, and 12, respectively).

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Cycloaddition and Polymerization Reactions of Methyl α-Cyanoacrylate with Electron-Rich Olefins

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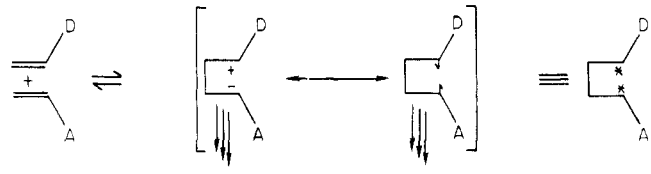
Methyl α-cyanoacrylate reacts with isobutyl vinyl ether to form a zwitterionic tetramethylene intermediate which can cyclize in a [4 + 2] fashion to 2-isobutoxy-5-cyano-6-methoxy-3,4-dihydro-2*H*-pyran. This cycloadduct isomerizes to methyl 2-cyano-5-isobutoxypent-4-enoate at 70 °C. The zwitterionic intermediate can be trapped with methanol. When methyl α-cyanoacrylate reacts with *p*-methoxystyrene and styrene, the tetramethylene intermediates now display biradical character because of resonance stabilization. They initiate alternating 1:1 copolymerizations of the reaction components. Under appropriate conditions *p*-methoxystyrene and methyl α-cyanoacrylate also undergo two consecutive Diels–Alder reactions to a Wagner–Jauregg adduct. β-Bromostyrene is not reactive enough to form a tetramethylene at room temperature. At 110 °C a Diels–Alder reaction occurs, followed by hydrogen bromide elimination to form methyl 1-cyano-1,2-dihydronaphthalene-1-carboxylate.

The reactions of electron-rich olefins with electron-poor olefins form a remarkable variety of polymeric and small-molecule products.[1-6] Polymeric products include homopolymers of either or both monomers and alternating copolymers of both monomers. Small-molecule addition products include cyclobutanes, 1-butenes, 1,3-butadienes, cyclohexanes, etc. These reactions involve bond formation between the respective β-positions of the double bonds, generating a tetramethylene intermediate which behaves as a resonance hybrid of a zwitterion and singlet biradical.[7-9] If derived from polymerizable olefins, the tetramethylene intermediate can then initiate cationic or anionic homopolymerization of, respectively, the electron-rich or electron-poor olefin or can initiate free-radical alternating copolymerization, depending on which character is predominant in the hybrid[4,10] (Scheme I).

The small molecules formed by cyclization of the tetramethylenes, on the other hand, are not diagnostic for the nature of the tetramethylene intermediate. However, substituent and solvent effects as well as trapping experiments[8,10] have been used to distinguish both mechanisms.

If further double bonds are present in either of the olefins, [4 + 2] cycloadditions will compete with the tetramethylene-type reactions. For example, in the presence of inhibitor, styrene reacts with maleic anhydride with participation of ring unsaturation to yield the "Wagner–Jauregg-type" 2:1 adduct[11] (two consecutive Diels–Alder reactions). The presence of an ester group in the electrophile can cause an inverse-electron-demand Diels–Alder reaction to occur. 6-Alkoxy-3,4-dihydro-2*H*-pyrans have been suggested in the dimerization and cycloaddition of acrylates.[12-15] Recently, dihydropyrans were isolated in the reaction of carboxylic ester containing electron-poor olefins with electron-rich vinyl compounds.[10,16]

Scheme I



Methyl α-cyanoacrylate is an extremely reactive monomer in anionic polymerization.[17] In the presence of amines, Pepper reports that methyl α-cyanoacrylate polymerizes via a macrozwitterionic mechanism.[18] It has also been widely studied in radically initiated homopolymerization and in copolymerizations with various vinyl compounds.[19-22] Snider and Phillips report the formation of cyclobutane adduct and dihydropyran in the presence of alkenes when catalyzed by dimethylaluminum chloride.[23]

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