changes. The nitrobenzene reaction mixture was dumped into ice-H_2O and this mixture extracted with ether. The ether layer was extracted with aqueous NaOH, the NaOH extract acidified, and a solid product precipitated. The product (10.1 g, 20.2%) was recrystallized from cyclohexane: mp 109–110° (lit.[26] mp 109–110°); uv max 299 mμ (ε 1.12×10^4); ir (KBr disk) 1660 cm^{-1} (C=O).

Anal. Calcd for $C_{11}H_{14}O_4$: C, 62.84; H, 6.71. Found: C, 62.61; H, 6.88.

α-(2-Methoxyphenoxy)-4-hydroxy-3-methoxypropiophenone (20) was synthesized from the benzyl ether of **1** by a previously described method[27] then debenzylated by warming 2 g of the benzyl ether of **20** with 10 ml of HOAc and 5 ml of HCl for 20 min in the steam bath. The product was crystallized from EtOAc-hexane: mp 133–135°; uv max 308 mμ (ε 5.42×10^4) and 279.5 (6.29×10^4); ir (KBr disk) 1675 cm^{-1} (C=O).

Anal. Calcd for $C_{17}H_{18}O_5$: C, 67.53; H, 6.03. Found: C, 67.52; H, 6.19.

α-[(2-Methoxyphenoxy)-β-hydroxy]-4-hydroxy-3-methoxypropiophenone (21) was synthesized as the benzyl ether according to previously published report for the corresponding dimethoxy (veratryl) compound,[27] then debenzylated by hydrogenolysis over $PdCl_2$/C:[28] mp 80–82°; uv max 309.6 mμ (ε 1.2×10^5) and 279.6 (1.32×10^5); ir 1675 cm^{-1} (C=O).

Propionic Acid Determination.—The acid was obtained by steam distillation of an acidified saponification mixture from the dehydrogenation of **1**. The acid was extracted from the steam distillate with ether and identified by glpc on a 1.95×0.25 in. stainless steel column packed with 20% sebacic acid on acid-washed Chromosorb W.[6] The acid was also converted into the 5-methoxytripytamine salt, mp 114–115°, mp 114–115°, with a derivative from reagent propionic acid.

Registry No.—**1**, 1835-14-9; **10**, 18592-97-7; **11**, 16737-80-7; **12**, 18592-99-9; **13**, 18593-00-5; **14**, 16737-81-8; **15**, 18593-02-7; **19**, 5650-43-1; **20**, 7107-93-9.

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[26] M. J. Hunter, A. B. Cramer, and Harold Hibbert, *J. Amer. Chem. Soc.*, **61**, 516 (1939).

[27] E. Adler, B. O. Lindgren, and U. Saeden, *Svensk Papperstidn.*, **55**, 245 (1952).

[28] A. I. Vogel, "A Textbook of Practical Organic Chemistry," 3rd ed, John Wiley & Sons, Inc., New York, N. Y., 1962, p 950.

Hydrogen–Deuterium Exchange of the Thiapyrones, N-Methylpyridones, and N-Methylpyrimidones in Basic Media

PETER BEAK AND ELIZABETH MCLEISTER MONROE

Department of Chemistry and Chemical Engineering, University of Illinois, Urbana, Illinois 61801

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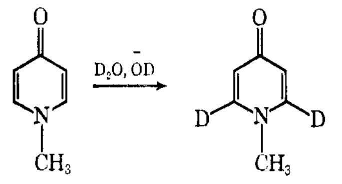
Base-catalyzed hydrogen–deuterium exchange occurs at the positions adjacent to the heteroatom for 4-thiapyrone (**3**), N-methyl-2-pyridone (**9**), 4-methoxy-N-methylpyridinium fluoroborate (**19**), and 1,3-dimethyl-4-pyrimidonium fluoroborate. The rates of exchange, relative to that of N-methyl-4-pyridone (**1**) in deuterium oxide at 100°, are for **3**, $10^{4.8}$ (deuterium oxide at 100°); **9**, $10^{-0.8}$ (deuterium oxide at 100°); and **19**, $10^{5.3}$ (deuteriomethanol at 40°). Attempts to observe isotopic exchange at the corresponding positions in 2-thiapyrone, 2-pyrone and 4-pyrone led to substrate decomposition. Hydrogen–deuterium exchange at the 2 position of 3-methyl-4-pyrimidone and 1-methyl-4-pyrimidone in deuterium oxide at 100° is zero order in base as previously reported.[6] These results are interpreted qualitatively in terms of ylide intermediates.

Following the discovery that N-methyl-4-pyridone (**1**) undergoes base-catalyzed hydrogen–deuterium exchange at 100° in deuterium oxide to give N-methyl-4-pyridone-2,6-d_2 (**2**) by an ylide mechanism,[1] a systematic study was undertaken of the effect of the position and type of heteroatom on exchange. The goals of this work were to determine the scope of the reaction and to compare the rates of exchange with analogous reactions of structurally related five-membered[2,3] and six-membered[4–6] heteroaromatics.[7] This information should provide a guide for the synthetic use of the ylide intermediates.



1 **2**

Studies of the six-membered mesoionic heteroaromatics containing one nitrogen, sulfur or oxygen atom, of the 4-pyrimidones, and of some pyridinium salts are reported herein. These results suggest that the formation of ylides is an important reaction pathway for six-membered mesoionic or cationic sulfur and nitrogen heteroaromatic.

Results

The positions and rates of hydrogen–deuterium exchange in the compounds studied were determined by

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[1] P. Beak and J. Bonham, *J. Amer. Chem. Soc.*, **87**, 3365 (1965).

[2] R. Breslow, *ibid.*, **80**, 3719 (1958); P. Haake and W. B. Miller, *ibid.*, **85**, 4044 (1963); H. A. Staab, H. Irngartinger, A. Mannschreck, and M. T. Wu, *Ann.*, **695**, 55 (1966); H. Prinzbach, E. Futterer, and A. Lüttringhaus, *Angew. Chem. Intern. Ed. Engl.*, **5**, 513 (1966), and references cited therein; W. W. Paudler and H. G. Shin, *J. Org. Chem.*, **33**, 1638 (1968).

[3] R. A. Olofson and J. M. Landesberg, *J. Amer. Chem. Soc.*, **88**, 426, (1966); R. A. Olofson, J. M. Landesberg, K. N. Houk, and J. S. Michelman, *ibid.*, **88**, 4265 (1966), and references cited therein.

[4] A. San Pietro, *J. Biol. Chem.*, **217**, 589 (1955); H. E. Dubb, M. Saunders, and J. H. Wang, *J. Amer. Chem. Soc.*, **80**, 1767 (1958); N. N. Zatsepina, I. F. Tupitsyn, and L. S. Efros, *J. Gen. Chem. USSR*, **34**, 4124 (1964); H. Igeta, M. Yamada, Y. Yoshioka, and Y. Kawazoe, *Chem. Pharm. Bull.* (Tokyo), **15**, 1411 (1967); R. K. Howe and K. W. Ratts, *Tetrahedron Lett.*, 4743 (1967); T. J. Curphey, *J. Amer. Chem. Soc.*, **87**, 2063 (1965); R. A. Abramovitch, G. M. Singer, and A. R. Vinutha, *Chem. Commun.*, 55 (1967), and references cited therein.

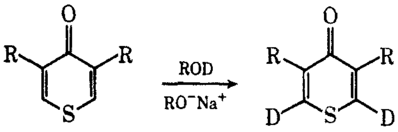
[5] J. A. Zoltewicz and C. L. Smith, *J. Amer. Chem. Soc.*, **89**, 3358 (1967), and references cited therein.

[6] G. E. Wright, L. Bauer, and C. L. Bell, *J. Heterocycl. Chem.*, **3**, 440 (1966).

[7] Comparison with thermodynamic acidities is also a matter of interest: D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, pp 1-47.

nmr measurements. For all but one of these compounds the chemical shift of the base-exchangeable proton is unique and structurally definitive.

The nmr spectrum of 4-thiapyrone (**3**) is of the AA'-XX' type. In deuterium oxide the multiplet due to the protons at positions 2 and 6 is centered at δ 8.69 ppm and an identical multiplet for the protons at positions 3 and 5 is centered at 7.49.[8] Base-promoted exchange of the 2 and 6 protons upon addition of base to the deuterium oxide solution at room temperature is indicated by the rapid disappearance of the multiplet at 8.69 and the transformation of the multiplet at 7.49 to a singlet. The product, 4-thiapyrone-2,6-d_2 (**4**), has been isolated in preparative runs in 57% yield and characterized by analytical and spectral methods.[9] Isolation of **4** from kinetic runs was achieved in 95 ± 4% yield. The reconversion of **4** to **3** occurs on treatment with aqueous base. The reaction of 3,5-dimethyl-4-thiapyrone (**5**) with sodium methoxide–methanol-*d* at 55–60° to give **6** provides another example of the base-promoted exchange of the 2 and 6 hydrogens of a 4-thiapyrone. In contrast, reaction of 2,6-dimethyl-4-thiapyrone (**7**) with sodium methoxide in methanol-*d* gives **8** by exchange of the methyl protons.



3, R = H
5, R = CH_3

4, R = H
6, R = CH_3

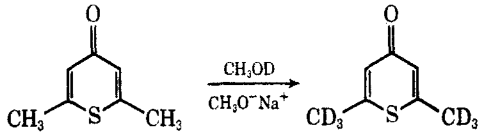


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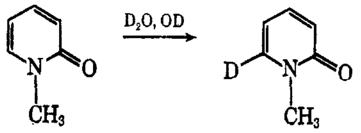
Table I

Rates of Deuteration of 4-Thiapyrone (3) and N-Methyl-2-pyridone (9) in Deuterium Oxide at 100°

[OD⁻], *M*	[**3**], *M*	[**9**], *M*	k_{obsd}, 10^4 sec^{-1}	k_{sp}, l. mol^{-1} sec^{-1}	k_{sp} (av), l. mol^{-1} sec^{-1}
0.193×10^{-5}	0.895		0.64 ± 0.01	33.0 ± 0.5	
0.196×10^{-5}	0.895		0.66 ± 0.01	33.5 ± 0.6	
1.43×10^{-5}	0.895		4.50 ± 0.12	31.5 ± 0.9	
18.85×10^{-5}	0.895		5.33 ± 0.06	28.9 ± 0.4	31.2 ± 1.4
2.02×10^{-5}	0.895		6.10 ± 0.07	30.2 ± 0.3	
2.02×10^{-5}	0.477		6.41 ± 0.15	31.7 ± 0.8	
2.38×10^{-5}	0.895		7.03 ± 0.10	29.5 ± 0.5	
0.510		1.50	0.361 ± 0.014	$7.08 \pm 0.20 \times 10^{-5}$	
1.015		1.00	0.796 ± 0.033	$7.85 \pm 0.33 \times 10^{-5}$	
1.015		1.50	0.731 ± 0.025	$7.20 \pm 0.25 \times 10^{-5}$	
1.015		1.50	0.755 ± 0.025	$7.44 \pm 0.25 \times 10^{-5}$	$7.36 \pm 0.24 \times 10^{-5}$
1.015		2.00	0.724 ± 0.021	$7.13 \pm 0.21 \times 10^{-5}$	
1.515		1.50	1.15 ± 0.062	$7.56 \pm 0.41 \times 10^{-5}$	

The rate of the conversion of **3** to **4** as followed by nmr in deuterium oxide at 100° using borate buffers is first order in **3** and first order in base from 2×10^{-5} to 2×10^{-6} *M* deuterioxide is summarized in Table I. The base concentration was found to change less than 0.1 pD unit over the course of a run. The second-order rate constant obtained from an average of the seven runs in Table I is 31.2 ± 1.4 l. mol^{-1} sec^{-1}. The second-order rate constant for the reverse reaction, **4** → **3**, was calculated from two runs to be 15.7 l. mol^{-1} sec^{-1}. This gives a combined solvent and kinetic isotope effect ratio k_H/k_D of *ca.* 2 in rough agreement with the value of 1.2 observed for the base-catalyzed exchange of the 2,6 protons of N-methyl-4-pyridone.[1] The change in the amounts of undeuterated, monodeuterated and dideuterated 4-thiapyrone, determined by mass spectrometry, as a function of time was analyzed with the aid of an analog computer and was found to fit the expected two-step consecutive first-order sequence with the rates of the first step twice that of the second[1] and a specific rate constant of 32.4 l. mol^{-1} sec^{-1}.

The base-catalyzed conversion of N-methyl-2-pyridone (**9**) to N-methyl-2-pyridone-6-*d* (**10**) has been reported as part of a synthetic sequence.[10,11] The location of the deuterium was established by the chemical shift of the proton replaced and the coupling constants of the protons in **10**, J_{34} = 9 Hz, J_{35} = 1.5 Hz, and J_{45} = 6.5 Hz. The kinetics of this reaction at 100° in deuterium oxide show reaction is first order in **9** and first order in base from 0.5 to 1.5 *M* deuterioxide (Table I). The second-order rate constant is $7.36 \pm 0.24 \times 10^{-5}$ l. mol^{-1} sec^{-1}.



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10

Attempted base-promoted deuterium exchange at the 2 and/or 6 positions of 2-thiapyrone (**11**), 2-pyrone (**12**), and 4-pyrone (**13**) in sodium deuterioxide–deuterium oxide at 100° or sodium methoxide–methanol-*d* at 60° for 2–48 hr failed because of decomposition of

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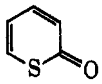
[8] (a) J. Jonas, W. Derbyshire, and H. S. Gutowsky [*J. Phys. Chem.*, **69**, 1 (1965)] have completely analyzed the spectra of the oxygen- and sulfur-containing 4-pyrones. (b) A comparison of the chemical shifts in deuteriochloroform for the ring protons of **3** (H-2 and H-6, δ 7.88 ppm; H-3 and H-5, 7.05) with those of **5** (H-2 and H-6, 7.58) and **7** (H-3 and H-5, 6.59) supports the critical chemical shift assignments.

[9] J. Bonham, E. McLeister, and P. Beak, *J. Org. Chem.*, **32**, 639 (1967).

[10] P. Beak, J. Bonham, and J. T. Lee, Jr., *J. Amer. Chem. Soc.*, **90**, 1569 (1968).

[11] Hydrogen–deuterium exchange of **9** has been reported by B. S. Thyagrarajan and K. Rajagopalen, *Tetrahedron*, **19**, 1483 (1963), and suggested to occur at the methyl group.

the pyrones.[12] The sensitivity of these compounds to basic reagents which can cause ring opening is well known[13] and is presumed to account for the decomposition. Thiophene (**14**) did not undergo exchange on heating in 1 *N* sodium methoxide–methanol-*d* at 60° for 68 hr.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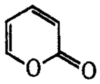
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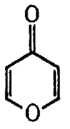
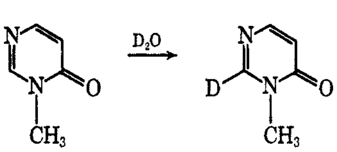

13


14

The exchange of hydrogen for deuterium at the 2 positions of 3-methyl-4-pyrimidone (**15**) and 1-methyl-4-pyrimidone (**17**) to give **16** and **18**, respectively, has been reported by Wright, Bauer, and Bell[6] and the rate of exchange has been found by them to be independent of base concentration over a wide range. We also find the rate of deuterium incorporation at the 2 position of **15** and **17** at 100° in deuterium oxide to be zero order in base from 2.3 × 10^{-5} to 2.7 × 10^{-10} *M* deuterioxide in substrate (Table II). The rate constants for the formation of **16** and **18** are 4.91 ± 0.43 ± 10^{-4} sec^{-1} and 15.22 ± 0.93 × 10^{-4} sec^{-1}, respectively.


15 **16**

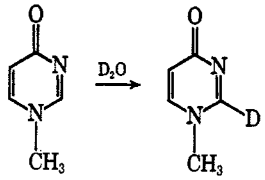

17 **18**

TABLE II

RATES OF DEUTERATION OF 3-METHYL-4-PYRIMIDONE (15) AND 1-METHYL-4-PYRIMIDONE (17) IN DEUTERIUM OXIDE AT 100°

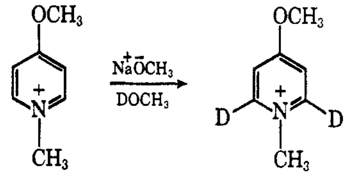
$[OD^-]$, *M*	[**15**], *M*	[**17**], *M*	k_{obsd}, 10^4 sec^{-1}	k_{obsd} (av), 10^4 sec^{-1}
2.9 × 10^{-10}	1.00		5.54 ± 0.09	
5.9 × 10^{-10}	2.00		4.41 ± 0.03	
4.7 × 10^{-8}	1.00		5.17 ± 0.10	4.91 ± 0.43
7.0 × 10^{-8}	2.00		4.65 ± 0.04	
1.5 × 10^{-5}	1.00		5.37 ± 0.09	
2.3 × 10^{-5}	2.00		4.47 ± 0.04	
2.7 × 10^{-10}		1.00	16.37 ± 0.21	
6.5 × 10^{-10}		2.00	14.12 ± 0.12	
4.9 × 10^{-8}		1.00	15.28 ± 0.32	15.22 ± 0.93
8.6 × 10^{-8}		2.00	14.17 ± 0.10	
1.5 × 10^{-5}		1.00	16.76 ± 0.36	
2.3 × 10^{-5}		2.00	14.57 ± 0.14	

The base-promoted hydrogen–deuterium exchange at the 2 and 6 positions of 4-methoxy-N-methylpyridinium fluoroborate (**19**) to give **20** has been reported,[1] and related reactions are known.[4-6] The exchange of **19** is first order in sodium methoxide from 0.01 to 0.04 *M* in methanol-*d* at *ca.* 40° with a specific rate constant of exchange of 19.6 ± 0.6 × 10^{-3} l. mol^{-1} sec^{-1} (Table III). The data show considerable scatter due to the lack of precision in the nmr area measurements in dilute solutions used and to concurrent side reactions. The initial base concentration was used to calculate the specific rate constants. The exchange could not be carried out in deuterium oxide because of the hydrolysis of the salt. The rate of deuterium exchange of 4-thiapyrone (**3**) to give **4** was also studied at *ca.* 40° in sodium methoxide-methanol-*d* and found to exchange with a specific rate constant of 5.76 ± 0.46 × 10^{-3} l. mol^{-1} sec^{-1}. The rate of exchange of N-methyl-4-pyridone was not directly compared under these conditions; 86% exchange of **1** to give **2** did occur at 60° in sodium methoxide–methanol-*d* after 2 hr.

TABLE III

RATES OF DEUTERATION OF 4-METHOXY-N-METHYLPYRIDINIUM FLUOROBORATE (19) AND 4-THIAPYRONE (3) IN METHANOL-*d* AT *Ca.* 40°

Initial $[CH_3ONa]$, *M*	[**19**], *M*	[**3**], *M*	k_{obsd}, 10^4 sec^{-1}	k_{sp}, 10^3 l. mol^{-1} sec^{-1}	k_{sp} (av), 10^3 l. mol^{-1} sec^{-1}
0.01	0.2		1.92	19.2	19.6 ± 0.6
0.02	0.2		3.82	19.1	
0.04	0.2		8.26	20.6	
0.01		0.2	0.675	6.75	
0.02		0.2	1.08	5.40	5.76 ± 0.46
0.04		0.2	2.32	5.80	


19 **20**

The base-catalyzed hydrogen–deuterium exchange of the 1,3-dimethyl-4-pyrimidonium iodide at position 2 has been reported.[6] This reaction has been studied with the 1,3-dimethyl-4-pyrimidonium fluoroborate (**21**) in acetate-buffered deuterium oxide at *ca.* 40° and is roughly first order in base over a range of 1.25 × 10^{-10} to 5.57 × 10^{-10} *M* base with a specific rate constant of 5.38 ± 0.85 × 10^6 l. $mole^{-1}$ sec^{-1} (Table IV).

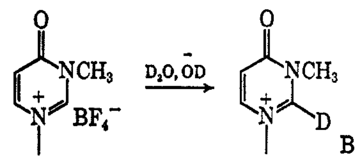

21 **22**

TABLE IV

RATES OF DEUTERIUM EXCHANGE OF 1 *M* 1,3-DIMETHYL-4-PYRIMIDONIUM FLUOROBORATE IN ACETATE-BUFFERED DEUTERIUM OXIDE SOLUTIONS AT *Ca.* 40°

Initial $[OD^-]$, *M* × 10^{10}	k_{obsd}, 10^3 sec^{-1}	k_{sp}, 10^{-6} l. mol^{-1} sec^{-1}	k_{sp} (av), l. mol^{-1} sec^{-1}
1.25	0.815	6.52	5.38[a] ± 0.82 × 10^6
2.61	1.48	5.67	
5.57	2.37	4.25	

[a] This rate is based on the debatable assumption that only deuterioxide can act as the base for proton removal from **21** in order to provide a maximum rate for assessing the mechanism of exchange of **15** and **17** (*vide infra*).

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[12] In most cases precipitates formed. In some cases the nmr spectrum of the solution indicated small amounts of undeuterated starting material. The reaction of 4-pyrone with sodium methoxide in methanol showed some deuterium substitution at H-5 although extensive decomposition occurred.

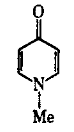
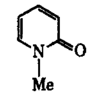
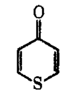
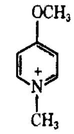
[13] J. Fried, "Heterocyclic Compounds," I, R. C. Elderfield, Ed., John Wiley & Sons, New York, N. Y., 1950, pp 354–396.

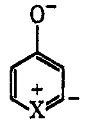
Discussion

The positions of deuterium exchange of pyridones **1** and **9**, 4-thiapyrones **3** and **5**, onium fluoroborates **19** and **21**, and pyrimidones **15** and **17**, are as expected if the ylide species **23**, **24**, and **25** are important in product determining stages of the reactions. The relative reaction rates of four substrates, which are first order in base, are shown in Table V. The order observed is in qualitative agreement with the rate-limiting removal of a proton from the appropriate substrate to give an intermediate ylide. For example the rate increase for hydrogen–deuterium exchange of **3** relative to **1** is consistent with the stabilization of the developing negative charge by d–σ overlap with sulfur[3,14] in the transition state leading to **23b**. The increase in rate of exchange for **19** relative to **1** fits the expectation[2-6] that a positive charge should lower the energy of activation for formation of **24b** from **19** relative to that for formation of **23a** from **1**.[15,16] No large disparity in rates would be expected for **1** and **9** and the observed difference of $10^{0.8}$ is relatively small.

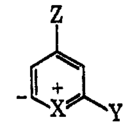
Table V

Relative Rates of Deuterium Incorporation at the 2 and 6 Positions for the Reactions First Order in Base

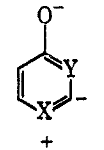
Compound	Relative rate/4	Base solvent
 1	1	OD^-–D_2O
 9	$10^{-0.8}$	OD^-–D_2O
 3	$10^{4.8}$	OD^-–D_2O OCH_3^-–CH_3OD
 19	$10^{5.8}$	OCH_3^-–CH_3OD



23a, X = NCH_3
b, X = S



24a, X = NCH_3; Y = O^-; Z = H
b, X = NCH_3; Y = H; Z = OCH_3



25a, X = $\overset{+}{N}CH_3$; Y = N
b, X = N; Y = $\overset{+}{N}CH_3$
c, X = Y = $\overset{+}{N}CH_3$

It would be of interest to dissect these relative rates quantitatively in terms of the inductive, coulombic resonance, d- orbital and s-character effects usually considered for related cases.[2-6,17] Such an analysis requires that the contribution of each effect be independent in the series of reactions compared. Although previous studies suggest that generalized structure–reactivity relationships exist for hydrogen–deuterium exchange of closely similar compounds[2-7,18,19] anomalies have been noted and attributed to differences in mechanism,[5] in exact geometry, or to a special multiatom overlap effect.[3]

A number of complications exist for even a semiquantitative analysis of the limited series in Table V. The charge distributions for the substrates or intermediate ylides are not known. The rates of exchange could be low due to the equilibrium formation of addition compounds with methoxide[20,21] which would reduce the base level and give kinetics including unknown equilibrium constants. The reactions could suffer to different degrees from "internal return" in a ylide solvent complex[22] such that the rates compared in Table V would not reflect quantitatively the relative stabilities of the intermediate ylides. Finally the required quantitative independence of related effects on the rates of exchange of **1**, **3**, **9**, and **19** does not seem likely.

Circumspection concerning the choice of model compounds for assessing different effects on the relative rates of exchange reactions is suggested by the kinetics of hydrogen–deuterium exchange of 3-methyl-4-pyrimidone (**15**) and 1-methyl-4-pyrimidone (**17**). The exchanges observed at the 2 position for **15** and **17** are consistent with the intermediacy of ylides **25a** and **25b**; however, the rates of exchange are zero order in base. This stands in sharp contrast to the first-order dependence on base observed for N-methyl-2-pyridone (**9**) and N-methyl-4-pyridone (**1**), compounds which would seem to be suitable models for **15** and **17**. Wright, Bauer, and Bell,[6] the first to observe this result, proposed a four-center mechanism, **26**, to explain the lack of base dependence.

The kinetics could be mechanistically deceptive.

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[14] (a) W. von E. Doering and A. K. Hoffmann, *J. Amer. Chem. Soc.*, **77**, 521 (1955); (b) G. Cilento, *Chem. Rev.*, **60**, 147 (1960); (c) ref 7, pp 71–84; (d) A. W. Johnson, "Ylid Chemistry," Academic Press, New York, N. Y., pp 304–319; (e) S. Oae, W. Tagaki, and A. Ohno, *Tetrahedron*, **20**, 417 (1964).

[15] This comparison is based on the assumption that the relative rates of exchange of **1** and **3** would be the same in deuterium oxide and deuteriomethanol. Only a small difference was found in the relative rates of exchange of the protons of thiazole[1] and imidazo[1,2-*a*]pyrimidine[16] in deuterium oxide–deuterioxide and methanol-*d*–methoxide. Acidities in methanol and water appear to be parallel. (a) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, pp 43–51; (b) C. D. Ritchie and P. D. Heffley, *J. Amer. Chem. Soc.*, **87**, 5402 (1965).

[16] W. W. Paudler and L. S. Helmick, *J. Org. Chem.*, **33**, 1087 (1968).

[17] Reference 7, pp 48–84.

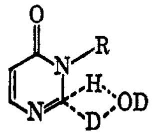
[18] M. Saunders and E. H. Gold, *J. Amer. Chem. Soc.*, **88**, 3376 (1966).

[19] Kinetic and thermodynamic acidities[7] appear to be parallel for structurally similar carbon acids over limited acidity ranges: D. J. Cram and W. D. Kollmeyer, *ibid.*, **90**, 1791 (1968).

[20] E. N. Shaw, "Pyridine and Its Derivative," Part II, E. Klingsberg, Ed., Interscience Publishers, New York, N. Y., 1961.

[21] A. Albert, *Angew. Chem. Intern. Ed. Engl.*, **6**, 919 (1967).

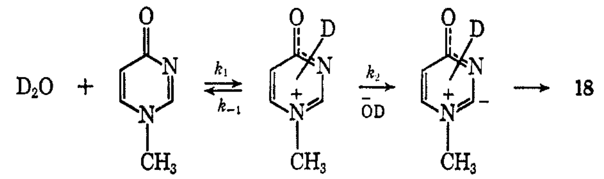
[22] D. J. Cram, C. A. Kingsbury, and B. Rickborn, *J. Amer. Chem. Soc.*, **83**, 3688 (1961); A. Streitwieser, Jr., and H. F. Koch, *ibid.*, **86**, 404 (1964); Y. E. Hofman, A. Schriesheim, and R. E. Nichols, *Tetrahedron Lett.*, 1745 (1965).



26

It is possible that reaction proceeds by deuteration prior to hydrogen exchange[23] as shown for **17** in Scheme I. Steady-state treatment leads to a kinetic expression

SCHEME I



17 **27** **28**

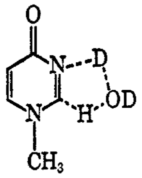
for the formation of **18** which is zero order in base. A rough evaluation of this mechanism with $k_2 \ll k_{-1}$

$$\frac{d[\mathbf{18}]}{dt} = \frac{k_2k_1}{k_{-1} + k_2}[D_2O][\mathbf{17}] = k'[\mathbf{17}]$$

may be obtained by taking the rate of deuterium exchange of 1,3-dimethyl-4-pyrimidonium fluoroborate (**21**) as equal to that of **27**, approximating the ratio k_1/k_{-1} from the pK of **17**[24] and the ion product of deuterium oxide ($xk_1/k_{-1} = (K_{D_2O}/K_{a[D_2O]})$ and calculating a $k'_{calcd} = k_2(k_1/k_{-1})[D_2O] = 8.5 \times 10^{-7}$ sec^{-1}. This is 2×10^3 different from the k'_{obsd} of 1.5×10^{-3} sec^{-1} for **17** (Table II) and approximations in the models might account for such a difference.[25,26] Although this mechanism rationalizes the position and the lack of base dependence of exchange of **15** and **17**, it would not necessarily be expected that **1** and **9** would exchange by a different process.[24,27]

Another possible base independent route could involve the deuteration of the unsubstituted nitrogen accompanied or closely followed by transfer of H-2 to the oxygen atom of the same solvent molecule. The process could be considered to initiate in a hydrogen-bonded species, giving a transition state corresponding to **29** which would lead to **28**. A variation on this would have **29** proceed to an ion pair which is particularly reactive because of the juxtaposition the base and the C-2 proton. This type of mechanism at least rationalizes the differences in mechanism for **15** and **17** as opposed to **1** and **9**. Further work will be necessary to distinguish the possibilities.

A third base independent route for the exchanges of the pyrimidones could involve the essentially complete formation of an addition compound from the substrate and base (*e.g.*, **30** from **17**) so that the nmr measurements are really following the disappearance of this adduct *via* a small equilibrium concentration of the



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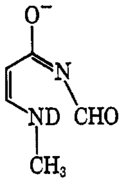
pyrimidone which, in turn, exchanges through an ylide. The failure of the ultraviolet spectrum of **17** to change in basic solution and the observation of a 2 Hz coupling between H-2 and H-6 throughout the exchange suggests this mechanism is not operating.

Mechanisms involving carbanionic species different from those suggested can be imagined. For example, intermediates formed by nucleophilic addition of base adjacent to the carbonyl[28] of **3** (**31**) or to the sulfur of the ring[29] (**32**) have formal precedent. The character of such intermediates is, at best, uncertain and can



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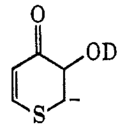

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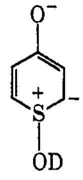

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at present only be evaluated by analogy to the pyridone case where such species do not seem necessary.[30]

On the basis of the present results and previous reports[1-5] the positions of many hydrogen–deuterium exchanges of mesoionic and cationic heteroaromatic compounds appear to be satisfactorily rationalized by ylide intermediates. The detailed mechanisms of these reactions may vary from case to case and will require individual investigation.

Experimental Section[31]

4-Thiapyrone (**3**) was prepared in approximately 40% yield by the method of Arndt and Bekir.[32] Purification by sublimation

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[23] Mechanisms involving prior protonations have been established for hydrogen–deuterium exchange of imidazole [T. M. Harris and J. C. Randall, *Chem. Ind.* (London), 1728 (1965)] and thiazole in intermediate pH ranges (R. A. Olofson, private communication).

[24] The pK_a's of interest are **17**, 2.02; **15**, 1.74; **1**, 3.33; and **9**, 0.32: A. Albert, "Physical Methods in Heterocyclic Chemistry," Vol. 1, A. R. Katritzky, Ed., Academic Press, London, 1963, pp 79, 81.

[25] The rate of reaction of **27** would probably be slower than that of **21** at the same temperature but the difference in temperature of 40° for the exchange of **21** and 100° for the presumed reaction of **27** should tend to counterbalance this difference.

[26] The ratio of k_1/k_{-1} in water is probably different from that in deuterium oxide by a factor of 2-4 (ref 15a, pp 187-188).

[27] N-Methyl-4-pyridone (**1**) does not exchange at pD 8.5 and for 6 hr at 100° in deuterium oxide.[1]

[28] W. von E. Doering and K. C. Schreiber, *J. Amer. Chem. Soc.*, **77**, 514 (1955); L. A. Paquette and L. D. Wise, *ibid.*, **90**, 807 (1968); R. H. Schlessinger and A. G. Schultz, *ibid.*, **90**, 1676 (1968).

[29] G. Suld and C. C. Price, *ibid.*, **84**, 2094 (1962).

[30] Reaction of N-methyl-4-pyridone **1** *via* a species analogous to **31** can probably be ruled out by the fact that deuteration of 3,5-dibromo-N-methyl-4-pyridone occurs in deuterium oxide–deuterioxide at 100° without replacement of the bromine by deuterioxide. If an intermediate such as **31** were formed, substitution of the bromine whould be expected. Attempts to prepare 3,5-dibromo-4-thiapyrone, a case where reaction *via* **31** is more likely than for **1**, was abandoned due to the potent vesicant properties of the intermediates.

[31] Melting points were determined in open capillaries on a Büchi or a Thomas-Hoover melting point apparatus and are corrected. Boiling points are uncorrected. Infrared spectra were determined on a Perkin-Elmer Infracord, Model 137, or Model 521 spectrometer using 10% chloroform solutions, unless otherwise indicated. The ultraviolet spectra were measured on a Perkin-Elmer 202 ultraviolet-visible spectrophotometer using 95% ethanol solutions unless otherwise noted. The proton magnetic resonance spectra, reported in δ (parts per million), were determined on a Varian Associates Model A-60, A-60A, or A-56/60 high-resolution spectrometer; unless otherwise indicated, chloroform-*d* solutions were used with tetramethylsilane as an internal standard. Mass spectra were determined by Mr. J. Wrona on an Atlas CH4 mass spectrometer using a vac lock inlet system. Molecular ions for the determination of molecular weights were measured at an ionization potential of 11–15 eV. Microanalyses were done by Mr. Joseph Nemeth and associates. The deuterium oxide used for the preparation of any stock solutions and in the reactions was in all cases at least 99.5% pure.

[32] F. Arndt and N. Bekir, *Ber.*, **63**, 2393 (1930).

(90°, 0.5 mm) and recrystallization from carbon tetrachloride gave a product with mp 110.5-112° (lit.[32] mp 110°). The ultraviolet,[33] infrared,[34] and nmr[8] spectra were consistent with the established structure.

2,6-Dimethyl-4-thiapyrone (**7**) was prepared as described by Arndt, *et al.*,[35] and purified by sublimation (110°, 1.0 mm), mp 102–103° (lit.[35] mp 104°). Strong infrared absorptions appeared at 3000, 1615, 1580, 875 cm^{-1}. The nmr spectrum had resonances at δ 6.59 ppm (2 **H** singlet, **H**-3 and **H**-5) and 2.32 (6 **H** singlet, CH_3). The ultraviolet maxima were in agreement with the reported values.[33]

3,5-Dimethyl-4-pyrathione.—To a solution of 1.60 g of 3,5-dimethyl-4-pyrone[36] in 25 ml of benzene was added 2.75 g of phosphorus pentasulfide. The mixture was heated under reflux for 70 min, then filtered while still hot. The residue was extracted several times with hot benzene, and the combined extracts were evaporated *in vacuo* to give 1.9 g of yellow solid. Recrystallization from methanol, including a filtration to remove elemental sulfur, gave 1.52 g (84%) of yellow needles, mp 147–148°. The ultraviolet spectrum showed λ_{max} at 251 mμ (ϵ 6600) 342 (19,000). The infrared spectrum had absorptions at 2900, 1556, 1422, 1335, 1190, 1124, 1016, 870, and 840 cm^{-1}. The nmr spectrum had resonances at δ 7.72 ppm (2 **H** singlet, **H**-2 and **H**-6) and 2.20 (6 **H** singlet, CH_3).

Anal. Calcd for C_7H_8OS: C, 60.00; H, 5.71; S, 22.86. Found: C, 60.05; H, 5.66; S, 22.94.

3,5-Dimethyl-4-thiapyrathione.—A solution of 20 g of potassium hydroxide in 20 ml of water was saturated with hydrogen sulfide and the resulting solution was added to a refluxing solution of 1.50 g of 3,5-dimethyl-4-pyrathione in 15 ml of 95% ethanol. The mixture was boiled for 15 min, chilled in an ice bath, then filtered to give 1.09 g of a red solid. The crude product was recrystallized from petroleum ether (bp 68°) to yield 1.02 g (61%) of red needles, mp 125–126°. The ultraviolet spectrum had λ_{max} at 262 mμ (ϵ 3700) and 383 (25,000). The infrared spectrum had absorptions at 2900, 1556, 1335, 1124, 1016, 870 and 840 cm^{-1}. The nmr spectrum showed resonances at δ 7.72 (2 **H** singlet, **H**-2 and **H**-6) and 2.50 (6 **H** singlet, CH_3).

Anal. Calcd for $C_7H_8S_2$: C, 53.85; H, 5.13; S, 41.02. Found: C, 53.94; H, 5.02; S, 41.48.

3,5-Dimethyl-4-thiapyrone (**5**).—A slurry of 1.20 g of mercuric acetate in 2.5 ml of acetic acid was added to a solution of 0.157 g of 3,5-dimethyl-4-thiapyrathione in 5 ml of chloroform. The mixture was stirred at ambient temperature for 43 hr. The solid obtained by filtration of this solution was washed with 10 ml of chloroform. The combined filtrate and washings were diluted with 30 ml of chloroform and this solution was washed with water, dried over sodium sulfate, and evaporated *in vacuo* to give an orange oil which solidified upon scratching. Sublimation of the crude solid (40°, 0.3 mm) yielded 0.120 g of pale yellow solid, mp 57–59°. Recrystallization from petroleum ether (bp 68°) gave 66 mg (47%) of white needles, mp 58–60°. The ultraviolet spectrum had λ_{max} 227 mμ (ϵ 7800), 299 (17,600) and 305 (17,600). The infrared spectrum had absorptions at 3000, 1598, 1580 (sh), 1382, 1332, 1023, 872 and 857 cm^{-1}. The nmr spectrum showed resonances at δ 7.58 ppm (2 **H** singlet, **H**-2 and **H**-6), and 2.18 (6 **H** singlet, CH_3).

Anal. Calcd for C_7H_8OS: C, 60.00; H, 5.71; S, 22.86. Found: C, 60.15; H, 5.71; S, 22.81.

N-Methyl-2-pyridone (**9**) was prepared from 2-methoxypyridine as previously described[10] and redistilled immediately before use.

4-Pyrone (**13**) was prepared by the decarboxylation of chelidonic acid according to the method of Willstatter and Pummerer[37] and was purified by vacuum distillation, bp 42° (0.2 mm) [lit.[37] bp 97° (13 mm)]. Its infrared[38] and nmr[8] spectral data were in agreement with the reported values.

2-Pyrone (**12**) was prepared by the decarboxylation of coumalic acid as described by Zimmerman, Grunewald, and Paufler,[39] and purified by vacuum distillation: bp 45° (0.5 mm) [lit. bp 130° (30 mm),[40] 103–105° (21 mm)[40]]; $n^{23}\mathrm{D}$ 1.5288 (lit.[36] $n^{24}\mathrm{D}$ 1.5285). The infrared,[38,39] ultraviolet,[41] and nmr spectra were consistent with the assigned structure.

2-Thiapyrone (**11**), prepared as described by Mayer, *et al.*,[42] was obtained in 76% yield as a pale yellow liquid: bp 52–55° (0.5 mm) [lit.[42] bp 50–55° (0.2 mm)]; $n^{30}\mathrm{D}$ 1.6133; ν_{max} 3010, 1640, 1595, 1580, 1516, 635 cm^{-1}. Its nmr spectrum consisted of a complex multiplet at δ 7.78–6.30; its ultraviolet maxima were as reported.[42]

1,3-Dimethyl-4-pyrimidonium Fluoroborate (**21**).—A solution of 2.68 g of silver fluoroborate (13.7 mmol) in 35 ml of ethylene dichloride was added to a solution of 1.51 g of 3-methyl-4-pyrimidone (13.7 mmol) followed by methyl iodide (8.5 ml, 19.4 g, 137 mmol). The mixture was stirred at ambient temperature (25°) for 5 days; the solid material was separated by filtration, then washed with methylene chloride and methanol. The product, isolated by addition of diethyl ether and purified in the usual manner, was 736 mg of a white salt, mp 92–109°. Reprecipitation with diethyl ether from methanol gave 600 mg of fluffy white solid, mp 114–117°. Extraction of the silver iodide residue with 150 ml of additional methanol and the same purification procedure gave 1.46 g of fluffy white solid, mp 116–118°. The total combined yield was 2.05 g (70%). The salt was purified further by recrystallization from absolute ethanol. The ultraviolet spectrum in methanol had λ_{max} 229 mμ (ϵ 8800) and 272 (3360). The infrared spectrum (Nujol) showed absorptions at 1730, 1120–1000 cm^{-1} (Nujol). The nmr spectrum consisted of an ABX pattern (δ 9.50, 1 **H**, **H**-2; δ 8.06, 1 **H**, **H**-6; δ 6.86, 1 **H**, **H**-5; $J_{2,6} = 2$ Hz; $J_{5,6} = 8$ Hz) plus two singlets at δ 3.98 (3 **H**, CH_3) and 3.70 (3 **H**, CH_3). The spectrum, measured in D_2O–0.1 *N* HCl–0.1 *N* KCl buffer, was consistent with that reported for 1,3-dimethyl-4-pyrimidonium iodide.[6]

Anal. Calcd for $C_6H_9N_2OBF_4$: C, 34.00; H, 4.28; N, 13.22. Found: C, 33.98; H, 4.19; N, 13.04.

This compound was also prepared in 10% yield by the alkylation of 1-methyl-4-pyrimidone in a similar manner. The preparation of **21** by methylation of **15** and **17** establishes its structure.

1-Methyl-4-pyrimidone (**17**), mp 158–160° (lit.[43] mp 156–158°), and **3-methyl-4-pyrimidone** (**15**), mp 126–128° (lit.[43] mp 124–126°), were prepared as described by Bauer, *et al.*[43] The infrared[44a] and nmr[43,44] spectral properties were as reported.

N-Methyl-4-pyridone 1 and **4-methoxy-N-methylpyridinium fluoroborate** (**19**) were prepared as reported.[1]

Deuterium Substitution in 4-Thiapyrone (**3**).—A 20% solution of 4-thiapyrone in deuterium oxide showed nmr absorptions of an AA′BB′ pattern with multiplets centered at δ 8.69 ppm and 7.49 (external TMS). The nmr spectrum of a 10% solution in 1.07 *N* sodium deuterioxide in deuterium oxide showed the multiplet at δ 8.69 decreased to 20% of the area of the δ 7.49 peak, with the signal at δ 7.49 collapsing to a singlet within 20 min of mixing. No exchange was observed for 4-thiapyrone in deuterium oxide heated at 98° for 14 hr or in concentrated deuterium chloride in deuterium oxide heated at 95–98° for 75 hr.

A preliminary kinetic run in 0.535 *N* sodium deuterioxide in deuterium oxide indicated that the exchange of the 2,6 protons of 4-thiapyrone was first order in substrate with a half-life of approximately 18 min at nmr probe temperature. Ultraviolet analysis of a solution of 4-thiapyrone in 0.50 *N* sodium hydroxide in water showed that the chromophore decreased less than 5% after 40 min at room temperature. Although the strongly basic aqueous solutions of **3** were deep red, the compound could be recovered almost quantitatively as a white solid of mp 110–112° (mp 110–112° of undeuterated) by extraction with ether.

4-Thiapyrone-2,6-d_2 (**4**) was prepared in 57% yield as reported.[9]

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(33) P. Franzosini, G. Traverso, and M. Sanesi, *Ann. Chim.* (Rome), **45**, 128 (1955).

(34) D. S. Tarbell and P. Hoffmann, *J. Amer. Chem. Soc.*, **76**, 2451 (1954).

(35) F. Arndt, R. Sehwarz, C. Martius, and E. Aron, *Rev. Fac. Sci. Univ. Istanbul*, **A13**, 57 (1948).

(36) P. Beak and G. A. Carls, *J. Org. Chem.*, **29**, 2678 (1964).

(37) R. Willstatter and R. Pummerer, *Ber.*, **37**, 3745 (1904).

(38) R. M. Jones, C. L. Angell, T. Ito, and R. J. D. Smith, *Can. J. Chem.*, **37**, 2007 (1959); A. R. Katritzky and R. A. Jones, *Spectrochim. Acta*, **17**, 64 (1961).

(39) H. E. Zimmerman, G. L. Grunewald, and R. M. Paufler, *Org. Syn.*, **46**, 101 (1966).

(40) H. von Pechmann, *Ann.*, **264**, 261 (1891); K. von Auwers, *ibid.*, **422**, 133 (1921).

(41) A. Mangini and R. Passerini, *Gazz. Chim. Ital.*, **87**, 243 (1957).

(42) R. Mayer, G. Laban, and M. Wirth, *Ann.*, **703**, 140 (1967).

(43) L. Bauer, G. E. Wright, B. A. Mikrut, and C. L. Bell, *J. Heterocycl. Chem.*, **2**, 447 (1965).

(44) (a) D. J. Brown, E. Hoerger, and S. F. Mason, *J. Chem. Soc.*, 211 (1965); (b) Y. Inoue, N. Furutachi, and K. Nakanishi, *J. Org. Chem.*, **31**, 175 (1966).

The ultraviolet, infrared, and nmr spectral data were consistent with those of undeuterated material. Recovery from kinetic runs was achieved in 95 ± 4% yield by ether extraction.

N-Methyl-2-pyridone-6-*d* (10) has been reported in a previous study.[10]

1-Methyl-4-pyrimidone-2-*d* (18).—A solution of 0.502 g of 1-methyl-4-pyrimidone in 3 ml of deuterium oxide was heated at 110° for 45 min. Continuous extraction of the cooled solution with methylene chloride gave a solid which was sublimed (150°, 0.5 mm) to give 0.237 g (47%) of 1-methyl-4-pyrimidone-2-*d*, mp 158–160° (melting point of undeuterated compound 158–160°). The infrared spectrum had absorptions at 2995, 1650, 1505, 845, 730 and 665 cm^{-1}. The nmr spectrum showed an AB quartet δ 7.92 ppm (1 **H**, J = 7 Hz, **H**-6), 6.46 (1 **H**, J = 7 Hz, **H**-5), 3.87 (3 **H** singlet, CH_3) (D_2O relative to TPS). Mass spectral molecular weight determination at 11 eV indicated the product consisted of 1% $C_5H_6N_2O$, 98% $C_5H_5DN_2O$, and 1% $C_5H_4D_2N_2O$.

3-Methyl-4-pyrimidone-2-*d* (16).—A solution of 0.517 g of 3-methyl-4-pyrimidone was heated in 3 ml of deuterium oxide at 110° for 3 hr. The white solid isolated by chloroform extraction was sublimed (55°, 0.5 mm) to give 0.467 g of 3-methyl-4-pyrimidone-2-*d* (90%), mp 126–128° (melting point of undeuterated compound 126–128°). The infrared spectrum had absorptions at 2995, 1685, 1535, 882, and 850 cm^{-1}. The nmr spectrum consisted of an AB quartet δ 8.15 ppm (1 **H**, J = 7 Hz, **H**-6), 6.67 (1 **H**, J = 7 Hz, **H**-5), 3.67 (3 **H**, singlet, CH_3) (D_2O relative to TPS). Mass spectral molecular weight determined at 13 eV indicated that the product was a mixture of 11% $C_5H_6N_2O$, 84% $C_5H_5DN_2O$, and 5% $C_5H_3D_2N_2O$.

Deuterium Substitution in 3,5-Dimethyl-4-thiapyrone (5).—A sample of **5** (0.52 g) in 0.5 ml of 1 *N* sodium methoxide in methanol-*d* showed nmr absorptions at δ 8.03 ppm (singlet, **H**-2 and **H**-6) and 2.18 (singlet, CH_3); the relative areas could not be determined because of the proximity of the δ 2.18 singlet to solvent peaks. After the solution was heated at 55–60° for 68 hr, the signal at 8.03 had almost completely disappeared, indicating exchange of the 2,6 protons. Evaporation of the sample to dryness, addition of methanol, and heating caused the reappearance of the singlet at 8.03. The singlet at 2.18 was unchanged throughout this cycle.

Deuterium Substitution in 2,6-Dimethyl-4-thiapyrone (7).—The nmr spectrum of **7** in methanol-*d* showed peaks at δ 6.79 ppm (1 **H**, singlet, **H**-3 and **H**-5) and 2.43 (3 **H** singlet, CH_3). When 0.030 g of 2,6-dimethyl-4-thiapyrone was dissolved in 0.5 ml of 1 *N* sodium methoxide in methanol-*d*, the nmr absorption at 2.43 decreased to 14% of its original area within 15 min, indicating exchange at the methyl groups as expected. The signal at 6.79 was unchanged.

Kinetics of Deuterium Exchange for 3, 9, 15 and 17 and the General Procedure.—A weighed sample of substate was added to a measured volume of the appropriate deuterium oxide solution. The resulting solution was divided among 11 nmr tubes, which were then sealed. One tube was kept at room temperature as a control sample; the others were placed simultaneously in a thermostated bath maintained at 100 ± 0.1°. At timed intervals, tubes were removed and quenched in cold water. Deuterium incorporation in the quenched samples was determined by nmr by measuring the ratio of the integral peak area of the exchanging proton(s) to the integral peak area of the nonexchanging proton(s). At least five peak ratios were determined for each quenched sample. A weighted, least-squares program for the calculation of first-order rate constants[45] was used to calculate the observed rate constants. Specific rate constants were calculated by dividing the observed rate constants by the concentration of deuterioxide ion.

Kinetics for the deuterium exchange of 3 were run in borate buffer solutions (0.2 *M* boric acid, 0.1 *M* sodium deuterioxide) for a pD range 9–10. The rate was followed for approximately 2 half-lives. After each run, pH measurements were made on the nmr samples using a Beckmann one-drop pH electrode assembly with a Corning Model 12 pH meter. The change in pD was less than 0.1 unit for each run; the average pD was used to calculate the specific rate constant for each run. Deuterioxide ion concentrations were calculated using the relationships

$$\text{pD} = \text{``pH''} + 0.40$$

$$K_{D_2O} = [D_3O^+][OD^-] = 0.15 \times 10^{-14}$$

where "pH" is the pH meter reading obtained using a glass electrode in deuterium oxide solutions, and K_{D_2O} is the ion product of deuterium oxide.[46]

The reverse reaction was followed in a similar manner using 4-thiapyrone-2,6-d_2 and aqueous borate buffer.

N-Methyl-2-pyridone (9) deuterium-exchange kinetics were run in 0.5–1.5 *N* sodium deuterioxide solutions prepared by diluting a 5 *N* sodium deuterioxide solution made by adding sodium to deuterium oxide. Exact base concentrations were determined by titration with standard hydrochloric acid to a phenolphthalein end point. The disappearance of H-6 was followed by measuring the quantity $2x - 1$, where x is the ratio of the area of the multiplet at δ 7.6 ppm (**H**-4 and **H**-6) to the area of the multiplet at δ 6.6 (**H**-3 and **H**-5). The reaction was followed only for the first half-life because the plot of ln $(2x - 1)$ deviated from linearity and a precipitate formed after longer reaction times. The initial concentrations of deuterioxide ion were used to calculate specific rate constants.

N-Methyl-4-pyrimidone (17) deuterium-exchange kinetics were measured in buffered deuterium oxide solutions that were 0.2 *M* in *t*-butyl alcohol as an internal standard. The buffer solutions used were acetate (0.1 *M* acetic acid, 0.1 *M* sodium acetate), phosphate (0.2 *M* potassium dihydrogen phosphate, 0.1 *M* sodium deuterioxide) and borate (0.2 *M* boric acid, 0.1 *M* sodium deuterioxide). The exchange was followed by measuring the ratio of **H**-2 to **H**-6 for 2 half-lives; comparison of **H**-5 and **H**-6 with the *t*-butyl peak indicated that no appreciable exchange of **H**-5 or **H**-6 had occurred. pH measurements on the nmr samples indicated that the pD had changed less than 0.02 pD unit during each run.

Kinetics of deuterium incorporation into 4-methoxy-1-methylpyridinium fluoroborate (19) and 4-thiapyrone (3) were followed in 0.01–0.04 *M* solutions of sodium methoxide in methanol-*d* at nmr probe temperatures of 39 ± 3°. Timing was begun when a measured volume of methanol-*d* solution was added to a weighed sample of substrate. The resulting solution was transferred to an nmr tube which was capped and placed in the nmr probe within 2 min of mixing. The ratio of the 2,6 protons to the 3,5 protons was measured every 2–3 min for 90 min. Plots of ln ([**H**-6 + **H**-2]/[**H**-3 + **H**-5) *vs.* time showed considerable scatter, ascribed in large part to the difficulty of making precise measurements in these dilute solutions, but the plots were nevertheless linear. A slight curvature during the first 5 min of the run is probably due to the sample warming from room temperature to probe temperature. The best straight line for each run was estimated visually and the first-order rate constant determined from the slope. The initial concentration of methoxide ion was used to calculate specific rate constants.

Kinetics of deuterium incorporation into 21 were measured on 1.0 *M* solutions in deuterium oxide acetate buffers at nmr probe temperatures for 20–50 min.[21] Exchange was followed by determining the ratio of **H**-2 to **H**-6 every 2–3 min; plots of ln (**H**-2/**H**-6) were relatively linear except for some curvature during the first 5–10 min. The pD of each sample was determined at the end of each run; initial pD values were measured on freshly prepared solutions of identical composition. The pD decreased approximately 0.2 unit during each run. First-order rate constants were determined from the slope of a straight line estimated visually. Initial pD values were used to calculate specific rate constants. Rates are summarized in Table IV.

Mass Spectral Analysis of a Kinetic Run of 4-Thiapyrone.—To determine the percentages of undeuterated, monodeuterated, and dideuterated thiapyrone *vs.* time, partially deuterated samples were isolated from a kinetic run and analyzed by mass spectral molecular weight determination at 12.5 eV. These values were analyzed with the aid of an analog computer as heretofore.[1] Consistency of this data with consecutive second-order reactions with $k_1 = 2k_2$ was observed.

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[45] John Petrovich, Ph.D. Thesis, University of Illinois, 1964, p 91. We are grateful to Professor S. G. Smith and Dr. J. P. Petrovich for use of this program.

[46] P. K. Glasoe and F. A. Long, *J. Phys. Chem.*, **74**, 188 (1960).

Registry No.—**3**, 1003-41-4; **5**, 18542-89-7; **7**, 1073-80-9; **9**, 694-85-9; **15**, 6104-45-6; **16**, 18542-92-2; **17**, 2228-30-0; **18**, 18542-94-4; **19**, 2701-45-3; **21**, 18661-77-3; 3,5-dimethyl-4-pyrathione, 18542-95-5; 3,5-dimethyl-4-thiapyrathione, 18542-87-5.

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Mobile Keto Allyl Systems. VIII.[1a] Properties of 2-(α-Aminobenzyl)-1-indenones

Georges Maury and Norman H. Cromwell[1b]

Department of Chemistry, University of Nebraska, Lincoln, Nebraska 68508

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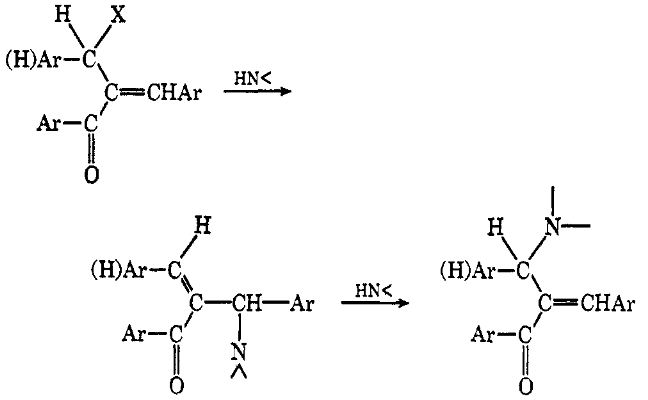
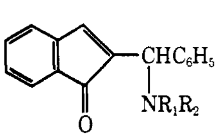
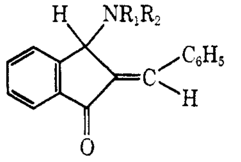
2-(α-Isopropylaminobenzyl)-1-indenone (**1a**) rearranges to the allylic isomer **2a** in the absence of added amine. Evidence supporting the intermolecularity of the rearrangement is presented; the results of kinetic studies support the occurrence of a chain reaction initiated by released amine. The aminoindenones **1b** and **1c** have specific properties associated with steric hindrance in the molecule; for instance, in contrast to the other indenones **1**, the hydrohalides of **1b** and **1c** rearrange to the corresponding 3-halo-2-benzal-1-indanones.

The ability of β-keto allyl systems to rearrange has been illustrated in the course of several studies involving the substitution of allyl halides by amines[2,3] or in the amine exchange reaction of allylamines.[1a,3] These investigations showed the occurrence of a variant of an S_N2' mechanism with a transition state in which bond making is running slightly ahead of bond breaking. The orientation and the ease of the rearrangements have been attributed to the combined electron-withdrawing effects of the carbonyl and the halogen (or the amino) groups.



It has now been found that the presence of added amine is not necessary to induce the allylic rearrangement of the indenone **1** to the indanone **2**. Initial results in this series showed that the behavior of the aminoindenones **1** was apparently different from that of the aminobenzylacrylophenones;[3] therefore, the new rearrangement **1** → **2** was extensively studied. Another important item of interest in the chemistry of 2-(α-aminobenzyl)-1-indenones is the special properties of compounds **1** when the amino groups are very bulky; these effects have been associated with steric hindrance and are consistent with previous kinetic results[1a] as well as conclusions drawn from the study of the nmr spectra of **1** and **2**.





1a, R_1 = H; R_2 = *i*-Pr
b, R_1 = R_2 = *i*-Pr
c, R_1 = *iso*-Pr; R_2 = cyclohexyl
d, R_1 = H; R_2 = *t*-But
e, R_1 = Me; R_2 = *i*-Pr
g, R_1 = H; R_2 = benzyl

2a, R_1 = H; R_2 = *i*-Pr
d, R_1 = H; R_2 = *t*-But
e, R_1 = Me; R_2 = *i*-Pr
f, R_1 = H; R_2 = *sec*-But
g, R_1 = H; R_2 = benzyl
h, R_1 = C_6H_5; R_2 = *i*-Pr

Results and Discussion

Rearrangement of 2-(α-Aminobenzyl)-1-indenones in the Absence of Added Amine.—2-(α-Isopropylaminobenzyl)-1-indenone rearranged slowly in chloroform at room temperature to give the isomeric 3-isopropylamino-2-benzal-1-indanone. The indanone **2a** was the only product detected by nmr or thin layer chromatographic analysis. The same reaction occurred, at different rates at room temperature, in dry acetonitrile, benzene, and *n*-hexane, and no other product than **2a** was found.

To investigate the mechanisms of the rearrangement, the kinetics of the preceeding reactions were followed in different solvents and at different concentrations. Nmr and uv spectroscopies were used in these studies because of the wide differences in the absorptivities of the compounds **1a** and **2a**.[1a] Characteristic kinetic curves are shown in Figure 1.

Each curve begins with an "induction period," the length of which depends upon the solvent and the starting concentration of **1a**; the middle part of the curves is very nearly a straight line, whereas the end approaches asymptotically the value of the initial concentration of **1a**. The addition of small amounts of dibenzoyl peroxide increases the rate of the rearrangement in chloroform or in acetonitrile, but no decrease in rate was observed upon addition of a radical inhibitor ruling out the possibility of a radical reaction; it is possible that the decomposition products of dibenzoyl peroxide initiate parallel nucleophilic reactions. The addition of small quantities of water has no effect on the rate within the experimental error.

The question first to be discussed is whether the

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[1] (a) For paper VII in this series see G. Maury, E.-M. Wu, and N. H. Cromwell, *J. Org. Chem.*, **33**, 1907 (1968). (b) The author to whom all correspondence concerning this article should be addressed.

[2] G. Maury, E.-M. Wu, and N. H. Cromwell, *ibid.*, **33**, 1900 (1968).

[3] R. P. Rebman and N. H. Cromwell, *Tetrahedron Lett.*, 4833 (1965); N. H. Cromwell and R. P. Rebman, *J. Org. Chem.*, **32**, 3830 (1967).