uct was obtained on elution with petroleum ether, b.p. 60–70°. The chromatographed product was distilled again to prepare an analytical sample, b.p. 119–126° (0.4 mm.), n_D^{20} 1.5748.

Anal. Calcd. for $C_{14}H_{18}S$: C, 77.06; H, 8.25; S, 14.67. Found: C, 76.71; H, 8.52; S, 14.99.

The palladium chloride complex, m.p. 98–99.5°, was prepared as described above.

3-Cyclohexenylmethanol (XI). Ten grams (0.0649 mole) of 3-acetoxymethylcyclohexene,[6] was heated at reflux with an ethanolic solution of sodium hydroxide for 2 hr. Most of the ethanol was distilled under reduced pressure and the residue was diluted with 100 ml. of water. The organic layer was separated and the aqueous layer was extracted with two 50-ml. portions of ether. The combined organic solution was dried over anhydrous magnesium sulfate, the ether was evaporated and the residue distilled under vacuum to yield 4.74 g. (65%) of XI, b.p. 94–96° (15 mm.), n_D^{20} 1.4857.

3-Cyclohexenylmethyl p-tolyl thioether (VI). 3-Cyclohexenylmethanol (2.22 g., 0.0198 mole) was treated with an equivalent quantity of methanesulfonyl chloride to give 1.85 g. (49%) of the crude methanesulfonate. This was treated with sodium *p*-thiocresoxide as above to yield 1.5 g. (70%) of VI, b.p. 110–113° (0.15 mm.), n_D^{20} 1.5781.

Anal. Calcd. for $C_{14}H_{18}S$: C, 77.06; H, 8.25; S, 14.67. Found: C, 77.09; H, 8.25; S, 14.89.

Palladous chloride complex of 3-cyclohexenylmethyl p-tolyl thioether (VI). One hundred milligrams of the thioether VI was shaken with an aqueous solution of palladous chloride to give 129 mg. (45%) of the complex, m.p. 112–114°. Two crystallizations from acetone and water gave an analytical sample, m.p. 117–118°.

Anal. Calcd. for $C_{28}H_{36}S_2PdCl_2$: C, 54.75; H, 5.86. Found: C, 54.73; H, 5.80.

Acknowledgment. The authors are indebted to the National Science Foundation for support of this work.

BOULDER, COLO.

[CONTRIBUTION FROM THE BIOCHEMICAL RESEARCH DIVISION, CHEMICAL WARFARE LABORATORIES]

Quaternary Heterocyclic Aldehydes and Hemiacetals

G. M. STEINBERG, E. J. POZIOMEK, AND B. E. HACKLEY, JR.

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1-Methyl-2- and 4-formylpyridinium and 2-formylquinolinium iodides can be obtained as crystals having characteristic and reproducible properties by separation from alcoholic solution. Elemental analyses correspond to 1:1 adducts with alcohol; the infrared spectra indicate that the products obtained are hemiacetals. 1-Methyl-2-formylpyridinium iodide accelerates the hydrolysis of isopropyl methylphosphonofluoridate in near neutral aqueous solution.

In connection with the investigation of pyridinium carboxaldoximes as potential therapeutics in the treatment of poisoning by organophosphorus anticholinesterase compounds,[1] a number of quaternary carboxaldehydes were prepared by methylation of the corresponding tertiary aldehydes (Table I). These compounds had been prepared by earlier workers by what is normally a simple and straightforward reaction and it seemed curious to find that their reported physical properties were subject to great variation. For example, one of the compounds (1-methyl-2 formylpyridinium iodide) had been reported as a liquid,[2] and as a high melting crystalline solid.[3] In most cases elemental analyses were not reported. As the substances are hygroscopic and in each case reacted in a manner consistent with the assumed structure, it seemed probable that the variations in physical properties resulted from the adsorption of moisture. We, too, initially obtained products with nonreproducible melting points; however, by careful operation under anhydrous conditions, the desired products could be obtained as crystalline solids with constant and reproducible melting points and proper elemental analyses (Table I).

It was also observed that crystalline light yellow solids having reproducible physical properties could be conveniently prepared by treatment of the 2- or 4-formylpyridinium and 2-formylquinolinium aldehydes with methyl or ethyl alcohol. Elemental analyses of these compounds, which were not the original aldehydes, correspond with 1:1 adducts of aldehyde and alcohol (Table II).

The 3-formyl-1-methylpyridinium iodide proved to be quite different from the others. It forms a relatively weakly hygroscopic, easily crystallized solid which upon treatment with methyl or ethyl alcohol gives a gum. Atmospheric drying or even repeated washing with ether results in recovery of the original aldehyde.

It is well known that carbonyl compounds form hydrates and hemiacetals when dissolved in water of alcohols.[4,5] Usually they are too unstable to be isolated. However, when the carbonyl function is attached to electron withdrawing groups, stable hydrates are frequently formed,[6] *e.g.*, chloral, glyoxal. It might be predicted that the electron withdrawing activity of the quaternary

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(1) E. J. Poziomek, B. E. Hackley, Jr., and G. M. Steinberg, *J. Org. Chem.*, **23**, 714 (1958).

(2) G. Lenart, *Ber.*, **47**, 808 (1914).

(3) S. Ginsburg and I. B. Wilson, *J. Am. Chem. Soc.*, **79**, 481 (1957).

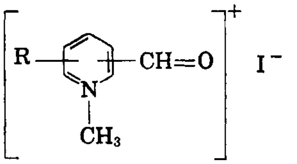
(4) A. Ashdown and T. A. Kletz, *J. Chem. Soc.*, 1454 (1948).

(5) J. Tirouflet and E. Laviron, *Compt. rend.*, **246**, 217 (1958).

(6) (a) Schimmel and Co., *Ann. Rept.*, **1933**, 71. (b) D. M. Anderson, L. J. Bellamy, and R. L. Williams, *Spectrochem. Acta*, **12**, 233 (1958).

TABLE I

QUATERNARY HETEROCYCLIC ALDEHYDES

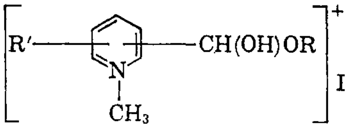


Substituent					Carbon, %		Hydrogen, %		Nitrogen, %	
—CH=O	R	Yield, %	Color	M.P.	Calcd.	Found	Calcd.	Found	Calcd.	Found
2	—	85	Bright orange	180–183[a] dec.	33.6	33.6	3.2	3.3	5.6	5.8
2	5,6-C_4H_4	26	Dull red	220–221[b] dec.	44.3	44.1	3.4	3.4	4.7	5.1
3	—	90	Bright orange	173–175[c] dec.	33.6	33.4	3.2	3.5	—	—
									Oxygen	
4	—	65	Bright orange-red	105–106[d] dec.	33.7	33.3	3.2	3.3	6.42	6.7

[a] Reported m.p. 174° (ref. 3); liquid (ref. 2). [b] Quinoline; m.p. 177–178° dec. (ref. 9). [c] Reported, m.p. 173° (ref. 3). [d] Low melting impure solid (ref. 3); we found that upon exposure to the air a stable higher melting crystalline solid was formed, m.p. 114–116°. *Anal.* Calcd. for the hydrate, $2C_7H_8ONI \cdot H_2O$: C, 32.6; H, 3.5; N, 5.4. Found: C, 32.5; H, 3.5; N, 5.7.

TABLE II

QUATERNARY HETEROCYCLIC HEMIACETALS



Substituent			Carbon, %		Hydrogen, %		Nitrogen, %	
—CH(OH)(OC_2H_5)	R′	M.P.[a]	Calcd.	Found	Calcd.	Found	Calcd.	Found
2	—	62–70	36.6	36.8	4.8	4.8	4.8	5.0
2	5,6-C_4H_4[b]	209–210	45.1	45.2	4.7	4.8	4.1	4.7
—CH(OH)(CH_3)								
2	—	—[c]	34.2	34.1	4.3	4.3	—	—
							Oxygen	
4	—	93–97	34.2	34.0	4.3	4.3	11.1	11.3

[a] M.p. uncorrected. [b] Quinoline. [c] With rapid heating on the Fisher Hot Plate sample melted at 104°, than resolidified and melted at 180°. With slow heating there was a color change to deep orange without melting near 100° followed by melting at 180°.

nitrogen atom when coupled by resonance interaction with the carbonyl group substituted in the 2- or 4- position of the pyridine ring would lead to increased polarization of the carbonyl group with resultant hydrate of hemiacetal stabilization. However, even simple quaternary ammonium salts are frequently hygroscopic and form crystalline hydrates and alcoholates so that it was of interest to learn whether the 1:1 aldehydealcohol adducts were true hemiacetals or simply "alcoholates of crystallization"—*i.e.*, where in alcohol is bound into the crystalline lattice by electrostatic forces. The alternatives could readily be resolved by study of infrared absorption spectra.

TABLE III

INFRARED ABSORPTION SPECTRA OF 2-FORMYL-1-METHYLPYRIDINIUM IODIDE[a]

Spectral Region, μ	Aldehyde	Adduct[b]
2–5	Medium—3.31, 3.36 Shoulders—3.26, 3.42	Strong—3.12, 3.32 Shoulders—3.36, 3.43
5–6	Strong—5.89	Very weak—5.00, 5.30, 5.90
6–7	Strong—6.18 Medium—6.63, 6.82 Weak—6.35, 6.92	Strong—6.15, 6.63, 6.83, 6.88, 6.95 Medium—6.35
9–10	None	Very strong wide bands with maxima at 9.17, 9.68. Strong sharp peaks at 9.35, 9.51

[a] Potassium bromide disc. [b] 1:1 Methanol adduct of 2-formyl-1-methylpyridinium iodide.

Infrared absorption. In Table III the pertinent infrared absorption maxima of crystalline 2-formyl-1-methylpyridinium iodide and its 1:1 methanol adduct (in potassium bromide) are compared. The aldehyde absorbs strongly at 5.89 μ (C=O) and does not absorb significantly at 3.12 μ (OH) or in the 9–10 μ (C—O—C) region, whereas in the methanol adduct the 5.89 μ peak has virtually disappeared and strong absorption has de-

TABLE IV

ULTRAVIOLET ABSORPTION MAXIMA OF 2-FORMYL-1-METHYLPYRIDINIUM IODIDE AND ITS METHANOL ADDUCT

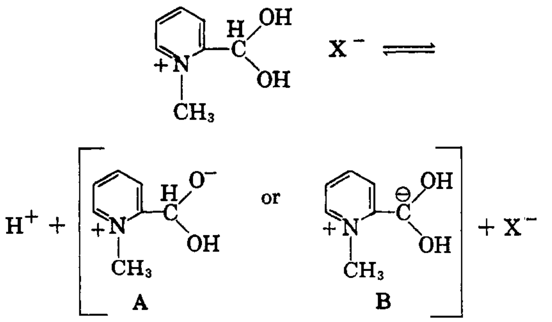
Solvent	pH	Aldehyde		Adduct	
H_2O[a]		λ_{max}(mμ)	$\epsilon_{max} \times 10^{-4}$	λ_{max} (mμ)	$\epsilon_{max} \times 10^{-4}$
	6.5 (within 3 min.)	264	0.662	264	0.664
	6.5 (after 5 hr.)	264	0.668	264	0.652
	12	267	0.511	267	0.514
Methanol		264	0.670	265	0.670

[a] The ultraviolet absorption of the aldehyde in aqueous acidic and alkaline solution was reported recently, R. I. Ellin and A. A. Kondritzer, *Anal. Chem.*, **31**, 200 (1959). In 0.1N sodium hydroxide solution they reported λ_{max} at 258 mμ.

veloped at 3.12 μ and in the 9–10 μ region. No major differences appear in the 6–7 μ region. Hence, the methanol adduct is a true hemiacetal.

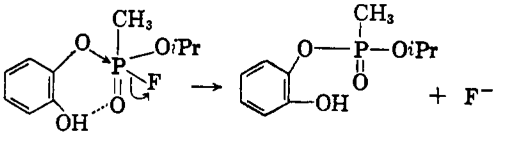
Ultraviolet absorption. 2-Formylpyridinium iodide and its methanol adduct gave identical ultraviolet absorption maxima in both aqueous and methanolic solutions (Table IV). Addition of solvent to the carbonyl group in aqueous solution at autogenous pH (6.5) appears to occur very rapidly, as no differences in absorption maxima were observed between measurements made within three minutes after solution and those made several hours later.

Acidity and the acceleration of the hydrolysis of isopropyl methylphosphonofluoridate. Potentiometric titration of 2-formyl-1-methylpyridinium iodide with aqueous alkali gave a smooth titration curve corresponding to that of a weak acid of pK_a 9.8–10.0. The curve obtained upon back-titration with acid was identical (no hysteresis) which eliminated the possibility that the inflection point might have been an artifact resulting from decomposition of the aldehyde in alkaline solution. The compound presumably dissociates according to equation 1, with the anion either in form A or B or possibly a mixture of the two (the slight shift in ultraviolet maximum in alkali, Table IV, can be accommodated by either A or B).



(1)

The catecholate anion has been shown to accelerate the decomposition of isopropyl methylphosphonate (GB) in aqueous solution by a concerted nucleophilic attack as indicated in Equation 2.[7] The structural similarity between form A of



(2)

the aldehyde hydrate anion and that of catechol together with their comparable acidity prompted a determination of its effect on the rate of hydrolysis of GB in near neutral aqueous solution. At pH 7.6 in sodium bicarbonate–carbon dioxide buffer, 30°, 2.27 × $10^{-3}M$ aldehyde and 2.27 × $10^{-3}M$ GB, the decomposition of the phosphonofluoridate, as measured manometrically by the evolution of carbon dioxide in a Warburg apparatus,[8] was kinetically first order with a half-time of 14.5 minutes. Acid liberation corresponded to 2.3 moles per mole of GB, which is within reasonable range of the theoretical value of 2.0, calculated for complete hydrolysis of the phosphonofluoridate. In the absence of aldehyde the half-time of hydrolysis of GB under the stated conditions is 250 minutes. A detailed kinetic study of the pyridinium aldehyde accelerated decomposition of GB is in progress and will be reported elsewhere.

EXPERIMENTAL

Melting points are uncorrected.

Quarternary carboxaldehydes. 2-Formyl-1-methylpyridinium iodide. A mixture of 10.7 g. (0.1 mole) of 2-pyridinecarboxaldehyde (Aldrich Chem. Co., freshly distilled) and 42.3 g. (0.3 mole) of methyl iodide in 25 ml. of anhydrous acetone was stored overnight in a pressure bottle at 60°. The orange solid which separated was washed with acetone and vacuum-dried. The yield varied between 80 and 95% depending upon the purity of the original aldehyde.

The corresponding 3- and 4-formylpyridinium compounds were prepared in an identical fashion. An alternative procedure which was found in one case to yield a somewhat more satisfactory product was to mix the aldehyde and methyl iodide in cold dry ether in the proportions given above and to store the solution at room temperature for 2 weeks. The quinoline derivative was prepared by storing a mixture of methyl iodide and 2-quinolinecarboxaldehyde (10:1 molar ratio) for 50 days in a pressure bottle at 60°.

Quaternary hemiacetals. These were prepared from the corresponding quaternary aldehydes by precipitation of the light yellow solids from alcoholic solution with a 3:1 ether-acetone mixture. For this purpose the quaternary aldehyde could be prepared as described above or simply by reaction

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[7] For studies of the reaction between catechols and GB, see (a) B. J. Jandorf, T. Wagner-Jauregg, J. J. O'Neill, and M. A. Stolberg, *J. Am. Chem. Soc.*, **73**, 5202 (1951); (b) J. Epstein, D. H. Rosenblatt, and M. M. Demek, *J. Am. Chem. Soc.*, **78**, 341 (1956).

[8] For a description of the method see, T. Wagner-Jauregg and B. E. Hackley, Jr., *J. Am. Chem. Soc.*, **75**, 2125 (1952).

of methyl iodide with the pyridinecarboxaldehyde in alcoholic solution under the conditions described. The solid products obtained were air dried.

Physical measurements. Infrared spectra were determined on a Perkin-Elmer 1R 21. The ultraviolet determinations were performed with a Beckman model DU spectrophotometer; concn. 5 × 10^{-5} *M*, temp. 23.5°, slit width 0.82 mm. The Beckman Model G pH meter was employed for potentiometric titration.

Acknowledgment. We wish to thank Mr. Omer O. Owens for having determined the rate of GB hydrolysis and Mr. Jacob Hanker for his assistance in the interpretation of the infrared spectra.

ARMY CHEMICAL CENTER, MD.

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(9) J. B. Adams, J. Cymerman Craig, C. Ralph, and D. Willis, *Austr. J. Chem.*, 8, 392 (1955).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

ortho-Substitution Rearrangement of Certain Substituted Dibenzyldimethylammonium Ions by Sodium Amide in Liquid Ammonia[1]

WILLIAM Q. BEARD, JR.,[2] AND CHARLES R. HAUSER

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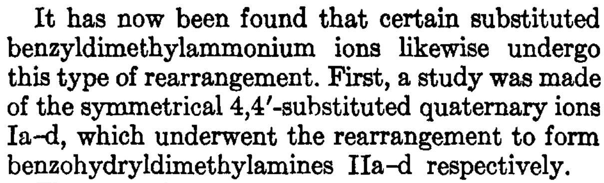
Several substituted dibenzyldimethylammonium ions were shown to undergo the *ortho*-substitution rearrangement with sodium amide in liquid ammonia to form substituted benzohydryldimethylamines. Each of the four 4,4′-disubstituted quaternary ions studied produced single rearranged amines, but each of the two unsymmetrical 4-substituted quaternary ions gave a mixture of rearranged amines. The unsymmetrical 2-chlorobenzylbenzyldimethylammonium ion yielded a single rearranged amine as the only isolated product. The structures of most of the rearranged amines were established.

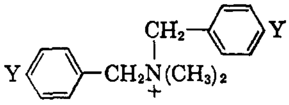
It has previously been observed[3] that the dibenzyldimethylammonium ion undergoes the *ortho*-substitution rearrangement with sodium amide in liquid ammonia to form 2,*N*,*N*-trimethylbenzohydrylamine in 95% yield. The mechanism has been assumed to involve the intermediate formation of the benzyl carbanion and the *exo*-methyleneamine (Equation 1).

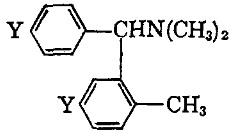


(1)

It has now been found that certain substituted benzyldimethylammonium ions likewise undergo this type of rearrangement. First, a study was made of the symmetrical 4,4′-substituted quaternary ions Ia–d, which underwent the rearrangement to form benzohydryldimethylamines IIa–d respectively.

These products presumably arose through the intermediate formation of the corresponding benzyl-type carbanions (see Equation 1). None of the possible *ortho*-substitution rearrangement products involving the intermediate formation of methyl carbanions or the Steven's 1,2-shift products were detected.





Ia. Y = CH_3
Ib. Y = OCH_3
Ic. Y = Cl
Id. Y = CN

IIa. Y = CH_3
IIb. Y = OCH_3
IIc. Y = Cl
IId. Y = CN

In Table I are summarized the results of the preparations of quaternary ions Ia–d, in Table II the results of the rearrangements of these ions to form rearranged amines IIa–d, and in Table III some infrared data on the rearranged amines. It can be seen from Table I that the yields of quaternary ions Ia–d from the appropriate 4-substituted benzyldimethylamines and benzyl halides were almost quantitative. It can be seen from Table II that the yields of the tertiary amines IIa–d from the rearrangements of the corresponding quaternary ions Ia–d were 89, 75, 21, and 11% respectively. The reaction with the chloro quaternary ion Ic was carried out by the inverse addition procedure in order to minimize the possible benzyne type of reaction of the rearranged tertiary amine with the alkali amide.[4] Even then there was obtained a considerable amount of amorphous, amine material, which apparently arose from the latter type of reaction. The reaction with the cyano quaternary ion Id appeared to be accompanied by a side reaction, since the recovered ether-insoluble organic salts could not be purified. Thus, the yield was not improved by a longer reaction time.

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(1) Supported in part by the National Science Foundation.

(2) Union Carbide Chemicals Company Fellow, 1956–58.

(3) S. W. Kantor and C. R. Hauser, *J. Am. Chem. Soc.*, 73, 4122 (1951).

(4) See J. D. Roberts, H. Simmons, Jr., L. Carlsmith, and C. Vaughan, *J. Am. Chem. Soc.*, 75, 3290 (1953).