amine held at 45°. After 18 hr. at this temperature, the solvent was removed and the crystalline residue washed with ether and recrystallized. In the cases of secondary amines and mercaptans, approximately equivalent amounts of reactants were used and the methanol solutions heated at reflux for about 3 hr. Pertinent data are listed in Table III.

B. With Hydrogen Bromide.—To a solution of 14.4 g. (0.05 mole) of V in 75 ml. of methanol at 5° was added a solution of 4 g. (0.05 mole) of hydrogen bromide in 40 ml. of methanol. After 2 hr. at 25°, the solution was heated at reflux for 18 hr., neutralized with 0.1 g. of sodium bicarbonate, evaporated to dryness, and the residue recrystallized twice from acetone. The structure of the product (XVI) was confirmed by conversion to the known $C_6H_{13}SH$ adduct of V (see Table III) as follows: A solution of 1.4 g. of sodium *n*-hexylmercaptide and 3.7 g. of XVI in 75 ml. of methanol was heated at reflux for 7 hr. and left at 30° for 2 days. Then 2.7 g. of silver *p*-tosylate was added, the solution was boiled, filtered, and the filtrate evaporated to dryness. Recrystallization of the residue from acetone, using charcoal, gave an 86% yield of N-(2-hydroxy-4-thiadecyl)trimethylammonium *p*-tosylate; m.p. 119–121°. Its identity with the products prepared as indicated in Table III was confirmed by mixture melting points and infrared spectra.

C. With Water.—A solution of 5 g. of V in 15 ml. of water, heated at reflux for 18 hr., showed incomplete reaction. A similar solution containing 1 drop of 72% aqueous perchloric acid and allowed to stand for 3 days at 30° gave nearly complete recovery of V. When this latter solution was heated at reflux for 20 hr., evaporated to dryness, and converted to the perchlorate in acetonitrile solution with sodium perchlorate, 3.1 g. (75% yield) of diol XVII was obtained; m.p. 110–112.5° (from ethanol). A second recrystallization raised the melting point to 111.5–113.5°.

IV. Reactions of Tertiary Glycidyl Amines.—Most of the compounds prepared from the tertiary amines were involved in structure elucidations of the products derived from the quaternary salts. Reaction conditions and properties of the products are given in Table IV and in the following example.

3-Diethylamino-2-hydroxypropyl Mercaptan (IX).—A solution of 60 g. (1.5 moles) of sodium hydroxide in 500 ml. of water was saturated with hydrogen sulfide, with stirring and cooling in an ice bath. A slow stream of the gas was continued during the subsequent 2-hr. addition of 65 g. (0.5 mole) of 2,3-epoxypropyldiethylamine at a temperature of 4–10°. After 2 hr. at 10–20°, the solution was cooled to 5° and 123 ml. of concentrated (37.5%) hydrochloric acid added at less than 10°. The bulk of the water was removed on the steam bath at reduced pressure, and the residue extracted with 200-, 100-, and 100-ml. portions of ether. The combined ether solutions were dried over anhydrous magnesium sulfate and distilled through a 12-in. column packed with helices.

Essentially the same procedure was used to prepare XI from N,N-bis(2,3-epoxypropyl)ethylamine.

V. 3-(4-Pyridyl)propanethiol.—A solution of 346 g. (5.2 moles) of potassium hydroxide in 1600 ml. of 95% ethanol was treated with hydrogen sulfide until nydrogen sulfide was no longer absorbed. A slow stream of the gas was continued while the solution was heated to reflux and a solution of 288 g. (1.5 moles) of γ-3-chloropropylpyridine hydrochloride[11] in 400 ml. of ethanol was added during 0.5 hr. After an additional 2 hr. under reflux, the solution was cooled and the mercaptan liberated by the addition of 183 ml. (2.2 moles) of concentrated hydrochloric acid, *i.e.*, to the equivalence point of *ca.* pH 6.5. The solution was filtered, then concentrated to a volume of 700 ml., diluted with 500 ml. of brine, and the organic phase was extracted with chloroform. After drying over anhydrous magnesium sulfate, the solution was distilled rapidly through a short Vigreux column. The portion having a b.p. of 80–105° (0.1–0.3 mm.) was then fractionated to give 148 g. (65%) of colorless oil; b.p. 102–103.5° (1.2 mm.); $n^{25}D$ 1.5532.

Anal. Calcd. for $C_8H_{11}NS$: C, 62.8; H, 7.2; N, 9.15. Found: C, 62.8; H, 7.0; N, 8.9.

Acknowledgment.—The authors are indebted to Miss Thelma Davis for infrared spectra and to Miss Jane O. Fournier for preparation of a quantity of compound V.

(11) This was prepared according to the method of K. C. Kennard and D. M. Burness, *J. Org. Chem.*, **24**, 464 (1959). The crude hydrochloride was isolated after the reflux period by removing volatiles at reduced pressure, treating the residue with toluene and again stripping it at reduced pressure; the remaining hygroscopic solid was washed with ligroin (65–75°) and filtered.

Action of Base on Quaternary Salts of Nicotinamide[1-3]

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Received March 8, 1963

Treatment of 1-benzyl-3-carbamoylpyridinium chloride with sodium hydroxide in dilute ethanol yielded a new substance 11, believed to be a cyclic trimer. The structure of the new compound was based on its analysis, infrared spectrum, ultraviolet spectrum, fluorescence spectrum, proton magnetic resonance spectrum, molecular weight, and its chemical reactions. The compound is believed to have been formed by way of a pyridinium ylide. Several new pseudo base ethers of 1-substituted nicotinamide salts have been prepared.

Treatment of 1-substituted pyridinium salts and related compounds with hydroxide ions is reported to yield easily dissociated pseudo bases in which the hydroxide ion has become bound covalently to one of the carbon atoms of the heterocyclic ring.[6] In some cases the pyridinium ring is opened by alkali.[7]

This paper is about a new type of compound obtained by treatment of 1-benzyl-3-carbamoylpyridinium chloride with hydroxide ions or by treatment of pseudo base ethers with ethanol. Several new pseudo base ethers have been prepared also.

Results

When an aqueous solution of 1-benzyl-3-carbamoylpyridinium chloride was treated with sodium hydroxide in dilute ethanol, a white solid of empirical formula $(C_{13}H_{12}N_2O)_n$ precipitated; the empirical formula corresponds to the hypothetical ylide **1**.

If the treatment with base was done in aqueous solution, the dimolecular ether **2** precipitated. The ether is formulated as a 1,4-dihydro structure on the basis of its having only one ultraviolet absorption maximum at 330–335 mμ in the nonpolar solvents,

(1) This work was supported in part by grant 7582 from the National Science Foundation.

(2) For complete details see John M. Kolyer, Ph.D. thesis, University of Pennsylvania, 1960.

(3) Reported at the 139th National Meeting of the American Chemical Society, St. Louis, Mo., March, 1961.

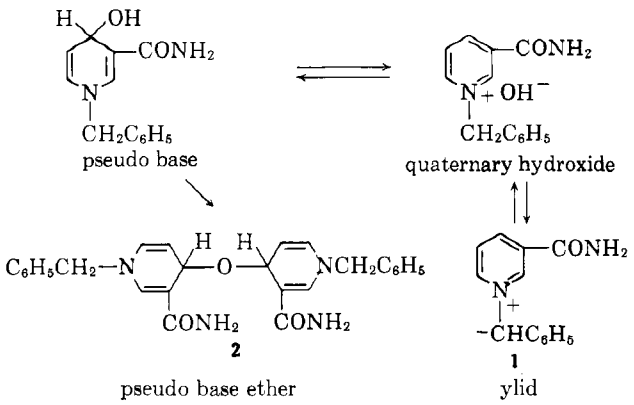
(4) Department of Chemistry, Syracuse University, Syracuse 10, N. Y.

(5) Walter T. Taggart Memorial Fellow, 1959-1960.

(6) A. Hantzsch and M. Kalb, *Ber.*, **32**, 3109 (1899).

(7) Reviewed by H. S. Mosher in R. C. Elderfield, "Heterocyclic Compounds," Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1950, pp. 424–433.

benzene or ether. A 1,6-isomer would be expected to have two maxima because of cross conjugation in excited states, and a 1,2-isomer would be expected to have a maximum at a longer wave length.[8] Anderson and Berkelhammer have reported the first isolation of a dimolecular ether of the pseudo base obtained by treatment of 1-benzyl-3-acetylpyridinium chloride with hydroxide ion.[9] They favored a structure in which the 2-positions of the pyridine rings were linked by the oxygen. When **2** was dissolved in chloroform, the solution became dark, and it was not possible to obtain a meaningful proton n.m.r. spectrum on the sample. In ethanol the dimolecular ethers exhibit two maxima which may imply a dissociation into pyridinium ions which have absorption around 260 mμ. In water there is only one maximum at 260 mμ. It is possible that the ether dissociates to a charge-transfer complex in some of the solvents and that the spectra observed are of this complex and not of the ether. The ultraviolet spectra of the dimolecular ethers in ethanol may not be accurate spectra because of a transformation of the ether: if the dimolecular ether **2** was dissolved in ethanol, the same white solid, $(C_{13}H_{12}N_2O)_n$, precipitated.



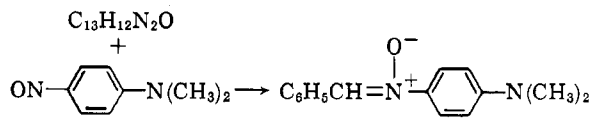
This new compound, $(C_{13}H_{12}N_2O)_n$, was soluble in dilute acids, chloroform, bromoform, and acetic acid but it was insoluble or only slightly soluble in water and in twenty-eight organic solvents. Potentiometric titration with perchloric acid in acetic acid indicated an equivalent weight of 212, the calculated molecular weight of **1**. Molecular weight determinations (cryoscopic in bromoform) gave an average value of 740 ± 30. Ultraviolet spectrum had an absorption maximum at 337 mμ (chloroform) and 340 mμ (ethanol).

Light, air, water, or heat cause decomposition of $(C_{13}H_{12}N_2O)_3$, but it was stable at room temperature for several days and was stable for months in the freezing compartment of a refrigerator. The compound on treatment with dry hydrogen chloride in chloroform or with hydrochloric acid gave 1-benzyl-3-carbamoylpyridinium chloride. With picric acid in chloroform it gave 1-benzyl-3-carbamoylpyridinium picrate. Treatment with hot sodium hydroxide yielded benzylamine indicating that the benzyl group was still attached to nitrogen. The only product isolated after treatment of the compound with malachite green oxalate was 1-benzyl-3-carbamoylpyridinium acid oxalate.

(8) K. Wallenfels and M. Gellrich, *Chem. Ber.*, **92**, 1406 (1959); K. Wallenfels, H. Schuly, and D. Hofmann, *Ann.*, **621**, 106 (1959).

(9) A. G. Anderson, Jr., and G. Berkelhammer, *J. Org. Chem.*, **23**, 1109 (1958).

The substance reduced aqueous silver nitrate, a property also of dihydronicotinamides,[10] and reduced nitrobenzene to aniline, another property of dihydronicotinamides.[11] Treatment of the compound with *p*-nitrosodimethylaniline gave the same nitrone as that obtained from the reaction of nicotinamide-1-benzylochloride and *p*-nitrosodimethylaniline with piperidine as catalyst.[11] The formation of nitrones from pyridinium ylides and nitroso compounds has been reported.[12]

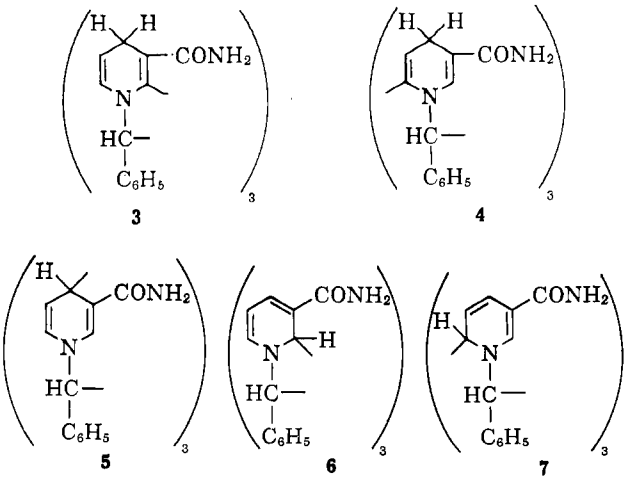


Hydrogenation of $(C_{13}H_{12}N_2O)_3$ over platinum in chloroform gave 1-benzyl-3-carbamoylpiperidine hydrochloride and hydrogenation in acetic acid gave 1-benzyl-3-carbamoylpiperidine. Hydrogenation in ethyl acetate or in dioxane over platinum or Raney nickel at various pressures gave a new product, $(C_{13}H_{14}N_2O)_3$, which had an ultraviolet absorption maximum at 305 mμ. Cryoscopic molecular weight determinations on this new substance in camphor and in bromoform gave values of 640 and 600, respectively.

The *p*-chloro-, *p*-bromo- and *p*-fluorobenzyl analogs of $(C_{13}H_{12}N_2O)_3$ were similar to the benzyl compound and reverted to quaternary salts on treatment with dry hydrogen chloride. It was not possible to convert 1-benzyl-3-acetylpyridinium chloride, 3-carbamoyl-1-(2,6-dichlorobenzyl)pyridinium bromide, 3-carbamoyl-1-(*p*-nitrobenzyl)pyridinium chloride, or 3-carbamoyl-1-(*p*-methoxybenzyl)pyridinium chloride to analogs of $(C_{13}H_{12}N_2O)_3$ under the same conditions which gave success in other cases.

Discussion

The following possible structures of $(C_{13}H_{12}N_2O)_3$ have been considered: **1** and **3** through **7**.



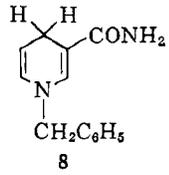
A possible structure has been deduced from the aforementioned data plus additional data from infrared, ultraviolet, fluorescence, and proton n.m.r. spectra.

(10) P. Karrer and F. J. Stare, *Helv. Chim. Acta*, **20**, 418 (1937).

(11) D. C. Dittmer and J. M. Kolyer, *J. Org. Chem.*, **27**, 56 (1962).

(12) F. Kröhnke, *Chem. Ber.*, **83**, 253 (1950); W. Ried and R. M. Gross, *ibid.*, **90**, 2646 (1957).

The ylide structure **1** explains most of the chemical reactions but the structure is untenable when other data are considered. The molecular weight of the parent substance and its partially hydrogenated derivative indicate that $(C_{13}H_{12}N_2O)_n$ is a trimer. The molecular weight eliminates monomeric structures and casts some doubt on the ylide structure **1** although such a polar substance might be associated. The possibility of association or charge-transfer complex formation[13] was investigated by determination of the extinction coefficients of a series of chloroform solutions of the *p*-chlorobenzyl compound [from 3-carbamoyl-1-(*p*-chlorobenzyl)pyridinium chloride and sodium hydroxide] ranging in concentration from 1.4×10^{-4} *M*. to 1.1×10^{-6} *M*. Beer's law was followed. The ultraviolet spectrum of the benzyl compound in bromoform was the same as the spectrum in chloroform, dioxane, benzene, and dimethylformamide. The infrared spectra of $(C_{13}H_{12}N_2O)_3$ in bromoform, chloroform, a potassium bromide disk, and in a Nujol mull were identical; the spectrum was very similar to that of 1-benzyl-1,4-dihydronicotinamide (**8**). The strongest



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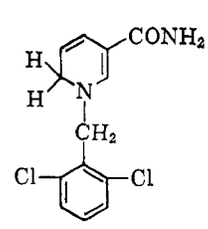
band in both spectra is near 1570 cm.$^{-1}$ which is attributed to a vinylogous amide group.[14] Bands in the spectra of both compounds for N—H stretching, carbonyl stretching, and N—H deformation are of approximately the same relative intensities and appear at the same place.

The ultraviolet absorption spectrum of $(C_{13}H_{12}N_2O)_3$ is like that of **8** [λ_{max} 350 mμ (ϵ 5100, benzene or ethanol)] although the absorption maximum of the trimer is at a lower wave length (337 mμ) and the intensity is greater (ϵ 6100, benzene). The ultraviolet absorption of 2,4,6-trimethyl-3,5-dicarboethoxy-1,4-dihydropyridine is at shorter wave length and is of greater intensity than is the absorption of the compound in which the 4-methyl group is absent. This behavior is attributed to nonbonded repulsions between the 4-methyl group and the carbonyl oxygen in an excited state.[15] The ultraviolet absorption spectrum of the supposed 1,6-dihydronicotinamide[8] (**9**) [λ_{max}^{MeOH} 355 mμ (ϵ 7450), 265 mμ (ϵ 9840)] is dissimilar to that of $(C_{13}H_{12}N_2O)_3$ whereas the spectrum of the analogous 1,4-dihydro compound **10** is similar [λ_{max}^{MeOH} 350 mμ (ϵ 7500)]. The ultraviolet and fluorescence spectra of $(C_{13}H_{12}N_2O)_3$ resemble that of **8** and **10** in that they have only one maximum; **9** has two maxima.

The structure of **9** is not absolutely certain but **8** is almost surely a 1,4-dihydropyridine by analogy to the 1-methyl compound.[16] The activation maxima for fluorescence of $(C_{13}H_{12}N_2O)_3$ and 1-benzyl-1,4-dihydronicotinamide (**8**) are both at 310 mμ while the activation maximum of **10** is at 400 mμ and of **9**, 470 mμ.



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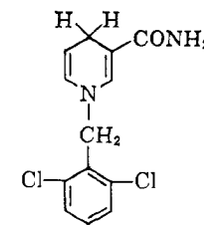


10

These data are not easily explained in terms of a structure which involves an aromatic pyridine ring. The spectroscopic data are more in line with those to be expected from a 1,4-dihydropyridine structure (**3, 4, 5**) rather than a 1,2- or 1,6-dihydro structure (**6** or **7**).[8]

The infrared spectrum of $(C_{13}H_{14}N_2O)_3$, obtained by hydrogenation of the trimer in neutral solvents, still showed the strong vinylogous amide band at 1570 cm.$^{-1}$. Its ultraviolet spectrum [λ_{max} 305 mμ (ϵ 6100)] resembled that of 1,4-dihydropyridine derivatives in which the 5,6- double bond presumably had been saturated.[14,17] The saturated compound, 1-benzyl-3-carbamoylpiperidine, absorbs below 220 mμ.

Open chain models with similar ultraviolet absorption maxima include *n*-propyl β-diethylaminovinyl ketone (λ_{max} 307 mμ)[18] and cinnamylidineacetamide (λ_{max} 302 mμ).

Apparently addition of one mole of hydrogen to the trimer leaves a conjugated double bond intact; *i.e.*, the system $-\overset{|}{N}-\overset{|}{C}=\overset{|}{C}-\overset{|}{C}=O$ is still present as it would be in **5** and **7**. Removal of the 5,6- double bond in **6** by hydrogenation would yield a substituted acrylamide whose ultraviolet absorption maximum is expected to be considerably lower than that found for the hydrogenated product.[19] The ring nitrogen would be removed from conjugation.

Structure **5** best accounts for the data. Why **3** and **4** should dissociate so readily to the pyridinium ion in acidic solutions is difficult to explain. The ready dissociation of **5** has parallels in the dissociation of addition compounds of cyanide ion[20] to pyridinium rings or of carbonyl compounds to pyridinium[21] or quinolinium[22] rings. Compounds **3** and **4** might have been expected to reduce malachite green oxalate as does 1-benzyl-1,4-dihydronicotinamide[23] rather than to be dissociated by the acid oxalate ion.

The precursor of the trimer, whose preferred structure is **5**, may be the ylide **1**. The carbanion may at-

(13) E. M. Kosower, "The Enzymes," Vol. 3, P. D. Boyer, H. Lardy, and K. Myrbäck, Ed., 2nd Ed., Academic Press, New York, N. Y., Chap. 13.

(14) A. G. Anderson and G. Berkelhammer, *J. Am. Chem. Soc.*, **80**, 992 (1958).

(15) D. Hofmann, E. M. Kosower, and K. Wallenfels, *ibid.*, **83**, 3314 (1961).

(16) R. F. Hutton and F. H. Westheimer, *Tetrahedron*, **3**, 73 (1958); H. E. Dubb, M. Saunders, and J. H. Wang, *J. Am. Chem. Soc.*, **80**, 1767 (1958).

(17) (a) K. Wallenfels and H. Schüly, *Angew. Chem.*, **69**, 505 (1957); (b) M. Marti, M. Viscontini, and P. Karrer, *Helv. Chim. Acta*, **39**, 1451 (1956).

(18) K. Bowden, E. A. Braude, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 45 (1946).

(19) Arecaidinamide (1-methyl-1,2,5,6-tetrahydronicotinamide) shows only end absorption (ref. 17b). Crotonamide has no pronounced absorption maximum and the intensity of absorption decreases from 230 to 280 mμ. [G. Tsatsas, *Bull. soc. chim. France*, 1011 (1947)].

(20) M. R. Lamborg, R. M. Burton, and N. O. Kaplan, *J. Am. Chem. Soc.*, **79**, 6173 (1957).

(21) W. v. E. Doering and W. E. McEwen, *ibid.*, **73**, 2104 (1951); R. M. Burton and N. O. Kaplan, *J. Biol. Chem.*, **206**, 283 (1954).

(22) F. Kröhnke and I. Vogt, *Ann.*, **600**, 211 (1956).

(23) D. Mauzerall and F. H. Westheimer, *J. Am. Chem. Soc.*, **77**, 2261 (1958).

TABLE I

COMPARISON OF PROTON MAGNETIC RESONANCE SPECTRA OF TRIMER AND OF 1-BENZYL-1,4-DIHYDRONICOTINAMIDE

Trimer				1-Benzyl-1,4-dihydronicotinamide			
Signal, p.p.m.[a]	Assignment	Relative area[b]	Multiplicity[d]	Signal, p.p.m.	Assignment	Relative area[c]	Multiplicity[d]
7.22	C_6H_5,7-H,2-H	7.0	Complex	7.28	C_6H_5	5.1	1
6.00	6-H,4-H	2.0	4 (complex)	7.13	2-H	1.1	1
4.85	5-H	1.0	4	5.72	6-H	.9	2
4.05	$-NH_2$	2.0	1	5.55	NH_2[e]	1.9	(broad)
				4.75	5-H	1.0	6
				4.27	7-H	2.1	1
				3.18	4-H	1.9	2

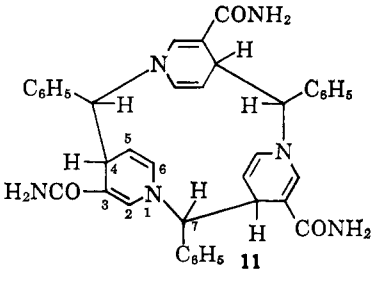
[a] Downfield from tetramethylsilane at 60 Mc. [b] Total area corresponds to 12 protons. [c] Total area corresponds to 14 protons. [d] Does not include peaks separated by less than 2 c.p.s. [e] The position of the signal originating with the amide protons is variable, depending presumably on the purity of the chloroform in which the spectrum was run and on the relative dryness of the compound.

tack the 4-position[24] of the pyridinium ring of another molecule of ylide and addition of one more molecule with cyclization would yield the trimeric structure. Trimerization may occur in one step since no intermediates were isolated. A pyridinium ylide in which the negative charge is borne by a nitrogen atom attached to the positive nitrogen of the pyridine ring adds to the double bond of acrylonitrile.[25] N-Cyclopentylpyridinium ylides have been isolated but are unstable.[26]

Models of **5** could be constructed by means of Stuart–Briegleb atom models, but models of a dimer or tetramer could not be made.

The proton magnetic resonance spectrum (Table I) of $(C_{13}H_{12}N_2O)_3$ was consistent with structure **5**, the spectrum having points of similarity with the spectra of 1-benzyl-1,4-dihydronicotinamide and 1-methyl-1,4-dihydronicotinamide.[16]

A possible interpretation of the proton n.m.r. spectrum on the basis of a trimeric structure **11** is given in Table I.[27] Although several conformations of **11** could be constructed by means of Stuart–Briegleb models, only two were symmetrical (*i.e.*, in which all three 7-protons were equivalent). The two models differed



11

in the relative positions of the carboxamide groups; the amide groups could be either in "inside" or "outside" positions in **11**.

It is clear that there is no analogous absorption in the spectrum of the trimer in the region where the 4-proton absorbed in 1-benzyl-1,4-dihydronicotinamide. The absorption of the 5- and 6-protons in the trimer (δ 4.85, 6.00 p.p.m.) is similar to that in 1-benzyl-1,4-dihydronicotinamide (δ 4.75, 5.72 p.p.m.). The environment of the 4- and 7-protons in the trimer are different from their environments in the model dihydro compound.

The considerable shift (2.95 p.p.m.) of the absorption of the 7-protons to low field may reflect the unusual environment in which the proton is found in the trimer. These three protons are located in the center of the cup-shaped molecule, the sides of which are the three dihydropyridine rings. The protons are in or near the plane of the phenyl rings whose rotation is restricted; and, thus, these protons ought to be deshielded by diamagnetic circulations of the π-electrons of the benzene rings.[28] Further deshielding may be attributed to the diamagnetic anisotropy of the olefinic bonds[29] and to the added inductive effect of another allylic system. The downfield shift of the absorption attributed to the 4-protons may have its origin in part in the restricted rotation of the phenyl groups and in inductive effects of the β-phenyl group and β-nitrogen. In the Stuart–Briegleb model of the trimer, the amide protons can spend considerable time above the plane of the phenyl rings because of hindrance to free rotation. This positional restriction may account for the increased shielding of these protons.[30] The assignments in Table I may be incorrect, but it seemed reasonable to attribute the largest changes in chemical shift to those protons (**4** and **7**) whose environment had changed most, and small changes to those protons (**2**, **5**, and **6**) whose environment had changed least.

The trimeric substance obtained by hydrogenation of $(C_{13}H_{12}N_2O)_3$ in neutral solvents had a proton n.m.r. spectrum which showed considerable absorption in the aliphatic region (1.27, 1.77, and 3.21 p.p.m.) and further absorption at 4.30, 5.15, 6.85, 7.33, and 7.58 p.p.m. The concentration of the substance was too small to yield a good spectrum and it was not possible to determine accurately the areas of the absorption peaks, many of which were broad and complex.

Experimental

All melting points are uncorrected. High resolution proton magnetic resonance spectra were obtained by Varian Associates, Palo Alto, Calif.

(24) This position may be less hindered sterically than the 2- or 6-positions.

(25) H. Beyer, K. Leverenz, and H. Schilling, *Angew. Chem.*, **73**, 272 (1961).

(26) E. M. Kosower and B. G. Ramsey, *J. Am. Chem. Soc.*, **81**, 856 (1959); D. Lloyd and J. S. Sneezum, *Chem. Ind.* (London), 1221 (1955); *Tetrahedron*, **3**, 334 (1958).

(27) We wish to thank Dr. LeRoy Johnson of Varian Associates, Palo Alto, Calif., for assistance with the interpretation.

(28) C. E. Johnson, Jr., and F. A. Bovey, *J. Chem. Phys.*, **29**, 1012 (1958).

(29) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press Ltd., London, 1959, p. 129; R. R. Fraser, *Can. J. Chem.*, **40**, 78 (1962).

(30) J. S. Waugh and R. W. Fessenden, *J. Am. Chem. Soc.*, **79**, 846 (1957).

Fluorescence spectra were obtained with a recording Farrand spectrofluorometer, Model 104244.[31]

1-Substituted Nicotinamide Salts.—These were prepared by treatment of nicotinamide with a substituted benzyl chloride. The products were recrystallized from ethanol or ethanol–water mixtures. 1-Benzyl-3-carbamoylpyridinium chloride[32] and 3-carbamoyl-1-(2,6-dichlorobenzyl)pyridinium bromide[33] were prepared according to previously published procedures.

Analyses and melting points of new salts are summarized in Table II.

TABLE II

1-SUBSTITUTED NICOTINAMIDE CHLORIDES

1-Substituent	M.p., °C.	—Calcd.— C	H	—Found— C	H
p-Chlorobenzyl	266–268 dec.	55.14	4.27	55.11	4.14
p-Fluorobenzyl	260–262	58.54	4.54	58.64	4.54
p-Methoxybenzyl	229–231	60.32	5.42	60.32	5.51
p-Nitrobenzyl[a]	213–214 dec.	53.16	4.12	53.19	4.29
2,4-Dinitrobenzyl	249–250 dec.	46.10	3.27	46.06	3.28

[a] The bromide has been prepared [K. Wallenfels and H. Schüly, *Ann.*, **621**, 126 (1959)].

1-(*p*-Bromobenzyl)-3-carbamoylpyridinium chloride, m.p 256–259°, did not give a satisfactory analysis. Its infrared spectrum was similar to that of 3-carbamoyl-1-(*p*-chlorobenzyl)pyridinium chloride. However, the crude material when treated with base gave the desired product.

1-Benzyl-3-carbamoylpyridinium Picrate.—A solution of 1-benzyl-3-carbamoylpyridinium chloride and picric acid in 95% ethanol was refluxed for 30 min. When the solution was chilled, the product separated as a yellow solid. Recrystallization from 95% ethanol gave glistening yellow plates, m.p. 165–168°.

Anal. Calcd. for $C_{19}H_{15}N_5O_8$: C, 51.70; H, 3.43. Found: C, 51.47; H, 3.62.

Intense infrared bands (KBr disk) occurred at 3450, 1680, 1625, 1570 and 1270 cm.$^{-1}$.

1-Benzyl-1,4-dihydronicotinamide was prepared according to Mauzerall and Westheimer.[23]

Infrared absorption (with per cent transmission in parentheses) occurred at 3440 (81), 3000 (75), 2830 (81), 1688 (32), 1648 (39), 1565 (14), 1496 (81), 1450 (72), 1423 (73), 1400 (52), 1378 (53), 1345 (31), 1298 (44), 1210 (64), 1173 (32), 1074 (58), 1027 (84), 995 (72), 692 (72) cm.$^{-1}$ (KBr disk).

The ultraviolet maximum was at 350 mμ in alcohol or in benzene (ϵ 5.1 × 10^3) [lit.[23] λ_{max} 355 mμ (ϵ 7.2 × 10^3)]. The dihydro compound fluoresced bright yellow-white under ultraviolet illumination. The fluorescence spectrum of a 2.8 × 10^{-3} *M* solution in chloroform showed maximum activation at 310 mμ and maximum fluorescence at 420 mμ.

1-(*p*-Fluorobenzyl)-1,4-dihydronicotinamide.—3-Carbamoyl-1-(*p*-fluorobenzyl)pyridinium chloride (5.0 g., 0.019 mole) was added slowly with stirring to a solution of sodium carbonate monohydrate (7.5 g.) and sodium dithionite (90% pure) (13.0 g., 0.056 mole) in 100 ml. of distilled water at 45°. The mixture was stirred at 45° for 10 min. The product separated as an orange oil which solidified on trituration with ice–water. It was recrystallized by dissolution in 40 ml. of ethanol and addition of water to the cloud point followed by chilling. The fine, yellow crystals (3.0 g., 68%), m.p. 112–114.5°, were dried over phosphorus pentoxide at reduced pressure.

Anal. Calcd. for $C_{13}H_{13}N_2OF$: C, 67.22; H, 5.64. Found: C, 67.15; H, 5.74.

Intense infrared bands (KBr disk) occurred at 3400, 3210, 1680, 1650, 1605, 1550, 1510, 1395, 1360, 1220, and 1170 cm.$^{-1}$.

The ultraviolet maximum was at 350 mμ in ethanol (ϵ 5.3 × 10^3).

1-(2,6-Dichlorobenzyl)-1,4-dihydronicotinamide was prepared by the method of Wallenfels and Schüly.[34] Intense infrared bands (KBr disk) occurred at 3400, 1680, 1640, 1575, 1440, 1380, 1360, 1340, 1210, and 1160 cm.$^{-1}$.

The ultraviolet maximum was at 345 mμ in ethanol (ϵ 4.5 × 10^3), (lit.[34] λ_{max} 350 mμ). The fluorescence spectrum of a chloroform solution showed maximum activation at 400 mμ and maximum fluorescence at 480 mμ.

1-(2,6-Dichlorobenzyl)-1,6-dihydronicotinamide was prepared by reduction of 3-carbamoyl-1-(2,6-dichlorobenzyl)pyridinium bromide with sodium borohydride in water.[35]

Intense infrared bands (KBr disk) occurred at 3400, 3190, 1640, 1600, 1580, 1562, 1430, 1380, 1360, 1315, 1280, and 777 cm.$^{-1}$.

Ultraviolet maxima were at 354 mμ (ϵ 4.2 × 10^3) and 263 mμ (ϵ 4.3 × 10^3) in ethanol (lit.[35] λ_{max} 355, 265 mμ). The fluorescence spectrum of a chloroform solution showed maximum activation at 470 mμ and maximum fluorescence at 515 mμ with a less intense maximum at 487 mμ.

1-Benzyl-3-carbamoylpiperidine.—Hydrogenation of 1-benzyl-3-carbamoylpyridinium chloride (0.59 g.) at 1 atm. for 2 hr. over platinum oxide (0.09 g.) in 25 ml. of water gave white crystals of product, m.p. 122–125° (lit.[36] m.p. 122–123°). The picrate was prepared by addition of a saturated solution of picric acid in ethanol to a solution of 1-benzyl-3-carbamoylpiperidine in ethanol. Recrystallization from ethanol–water gave fine yellow needles, m.p. 218–221.5°.

Anal. Calcd. for $C_{19}H_{21}N_5O_7$: C, 51.00; H, 4.73. Found: C, 51.00; H, 4.82.

Formation of Dimolecular Ethers. A. From 1-Benzyl-3-carbamoylpyridinium Chloride.—To 1-benzyl-3-carbamoylpyridinium chloride (10.0 g., 0.0402 mole) in 50 ml. of distilled water was added 70 ml. of 10% aqueous sodium hydroxide. The yellow precipitate which formed was washed with water and dried over phosphorus pentoxide at *ca.* 10 mm. for 2.5 hr. The yield was 6.36 g. (72%). Another sample was dried over phosphorus pentoxide at less than 1 mm. for 2 hr. This sample sintered and contracted at 100° and melted with decomposition at 135–137°.

Anal. Calcd. for $C_{26}H_{26}N_4O_3$: C, 70.57; H, 5.92; N, 12.66. Found: C, 70.84; H, 5.60; N, 12.70.

Intense infrared bands (KBr disk) occurred at 1680, 1640, 1610, 1560, 1535, 1500, and 1178 cm.$^{-1}$.

Ultraviolet maxima were at 260 mμ (water), 330 mμ (benzene), 335 and 270 mμ (dioxane),[37] 321 mμ (chloroform), 365 (weak) and 263 mμ (10% ethanol), 320 (weak) and 260 mμ (ethanol), and 335 mμ (ether).

The ether is unstable in air and in solution and was stored at 0°.

B. From 3-Carbamoyl-1-(2,6-dichlorobenzyl)pyridinium Bromide.—The dimolecular ether was prepared in the previous manner by addition of aqueous sodium hydroxide to an aqueous solution of 3-carbamoyl-1-(2,6-dichlorobenzyl)pyridinium bromide. The yield was 63%, m.p. 145–146° dec. (evacuated capillary).

Anal. Calcd. for $C_{26}H_{22}N_4O_3Cl_4$: C, 53.81; H, 3.82; N, 9.66. Found: C, 53.83; H, 4.03; N, 9.66.

Intense infrared bands (KBr disk) occurred at 3410, 1650, 1565, 1525, 1435, and 1170 cm.$^{-1}$.

The ultraviolet absorption maxima were at 372 (very weak), 320 (very weak), and 265 mμ in ethanol (ϵ_{265} 1.6 × 10^3). This ether may be dissociated to a great extent.

C. From 3-Carbamoyl-1-(*p*-fluorobenzyl)pyridinium Chloride.—The dimolecular ether was prepared in a similar manner by treatment of 3-carbamoyl-1-(*p*-fluorobenzyl)pyridinium chloride with aqueous sodium hydroxide. Yield of pale yellow material was 17%; it contracted at 119° and melted with decomposition at 134–145°. In an evacuated capillary the compound softened at 121° and decomposed at 132°.

Anal. Calcd. for $C_{26}H_{24}N_4O_3F_2$: C, 65.26; H, 5.06; N, 11.71. Found: C, 65.44; H, 5.10; N, 11.59.

Intense infrared bands (KBr disk) occurred at 3410, 1675, 1640, 1605, 1565, 1515, 1220, 1180, and 1160 cm.$^{-1}$.

Ultraviolet absorption maxima were at 360 (ϵ 7.2 × 10^2) and 262 mμ (ϵ 1.6 × 10^3) in ethanol, at 368 and 262 mμ in 40% ethanol, and at 330 and 260 mμ in ether.

D. From 3-Carbamoyl-1-(*p*-nitrobenzyl)pyridinium Chloride.—A solution of 3-carbamoyl-1-(*p*-nitrobenzyl)pyridinium chloride (1.06 g., 0.00360 mole) in 100 ml. of distilled water was chilled in an ice bath, and 2 ml. of 6 *N* aqueous sodium hydroxide was added. The yellow precipitate which formed was washed with water and dried over phosphorus pentoxide at less than 1-mm. pressure for 4 hr. The yield of compound was 0.640 g.

(31) We are greatly indebted to Dr. J. C. Touchstone of the Hospital of the University of Pennsylvania for assistance in obtaining the spectra.

(32) P. Karrer and F. J. Stare, *Helv. Chim. Acta*, **20**, 418 (1937).

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(34) K. Wallenfels, H. Schüly, and D. Hofmann, *ibid.*, **621**, 128 (1959).

(35) Ref. 34, p. 129.

(36) K. Wallenfels and M. Gellrich, *Chem. Ber.*, **92**, 1415 (1959).

(37) The absorption at 335 mμ decreased and that at 270 mμ increased with time.

(67%), m.p. 142–143° dec. and 144–145° dec. (evacuated capillary).

Anal. Calcd. for $C_{26}H_{24}N_6O_7$: C, 58.64; H, 4.54; N, 15.78. Found: C, 58.88; H, 4.62; N, 15.31.

Intense infrared bands (KBr disk) occurred at 3400, 1680, 1640, 1600, 1565, 1515, 1350, and 1180 cm.$^{-1}$.

The ultraviolet absorption maxima in chloroform were at 320 and 262 mμ.

Reaction of 1-Substituted Nicotinamide Salts with Ethanolic Sodium Hydroxide.—Sodium hydroxide (2.8 g.) in 4 ml. of distilled water and 36 ml. of 95% ethanol were added with stirring to a solution of 1-benzyl-3 carbamoylpyridinium chloride (10.0 g., 0.00402 mole) in 20 ml. of distilled water. The resulting slurry was stirred for 2 min., and 40 ml. of 95% ethanol was added. The reaction mixture was stirred for 30 min.; the pale yellow precipitate was collected and washed with water (to remove sodium chloride) and with absolute ethanol. The material obtained was recrystallized by dissolving it in the minimum amount of chloroform (4 to 5 ml.) followed by addition of 250 ml. of 95% ethanol and chilling in an ice bath for 1 hr. The fine, almost white crystals (0.31 g., 3.6%) melted at 185–186° dec. In an evacuated capillary the melting point was 1° higher. Yields in other runs varied from 3 to 10%.

Anal. Calcd. for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70; N, 13.20; mol. wt., 212 (monomer), 424 (dimer), 636 (trimer), 848 (tetramer). Found: C, 73.58; H, 5.73; N, 13.14; mol. wt., 714, 739, 774 (cryoscopic in bromoform).

Infrared absorption (with per cent transmission in parentheses) occurred at 3300 (79), 2970 (83), 1675 (36), 1618 (43), 1568 (16), 1540 (28), 1425 (53), 1359 (69), 1332 (50), 1306 (74), 1267 (67), 1175 (28), 1102 (76), 1040 (69), 1022 (67), 692 (70) cm.$^{-1}$ (KBr disk).

Ultraviolet absorption maxima were observed at 337 (ϵ 8.2 × 10^3, dioxane), 337 (ϵ 6.0 × 10^3, chloroform), 337 (ϵ 6.1 × 10^3, benzene), 337 (ϵ 6.0 × 10^3, dimethylformamide), 341 (bromoform), and 265 mμ (acetic acid).

The fluorescence spectrum of a 2.7 × 10^{-3} *M* solution in chloroform showed maximum activation at 310 mμ and maximum fluorescence at 395 mμ. The solid fluoresced blue under ultraviolet illumination.

In chloroform the intensity of the absorption maximum at 337 mμ decreased slightly with time. In one run ϵ 6.04 × 10^3 after 7 min. and 5.54 × 10^3 after 247 min. The compound decomposed on standing in ethanol for 2 days; ultraviolet absorption maxima for this orange solution were at 360 (weak) and 270 mμ.

The trimer was soluble in 1 *N* hydrochloric acid, chloroform, bromoform, and acetic acid. Decomposition occurred during an attempted ebullioscopic determination of the molecular weight in chloroform.

The compound (0.0616 g.) in 30 ml. of chloroform was titrated with 0.101 *N* perchloric acid in acetic acid. The titration was followed by means of a Beckman Model H-2 pH meter with a glass electrode and a Beckman 4919-V6D silver–silver chloride electrode. The curve obtained by plotting milliliters *vs.* millivolts had a sharp inflection at 2.88 ml. corresponding to an equivalent weight of 212. No strong inflection was observed in the titration of 1-benzyl-1,4-dihydronicotinamide.

A slurry in 3% silver nitrate was inert at room temperature, but a black precipitate of silver was formed when the mixture was heated on a steam bath for 5 min.[38]

The melting points for the *p*-chlorobenzyl, *p*-bromobenzyl, and *p*-fluorobenzyl substituted products, obtained from the quaternary salts and ethanolic sodium hydroxide, are, respectively, 188–189° dec., 187.5–188° dec., and 183° dec. All of these compounds had an ultraviolet absorption maximum in chloroform at 337 mμ.

Anal. Calcd. for $C_{13}H_{11}N_2OCl$: C, 63.29; H, 4.50; N, 11.36. Found: C, 63.04; H, 4.64; N, 11.30.

Anal. Calcd. for $C_{13}H_{11}N_2OBr$: C, 53.62; H, 3.81; N, 9.62. Found: C, 53.57; H, 3.98; N, 9.54.

Anal. Calcd. for $C_{13}H_{11}N_2OF$: C, 67.81; H, 4.82; N, 12.17. Found: C, 67.89; H, 4.98; N, 12.20.

Successive dilutions of a 1.4 × 10^{-4} *M* solution of the *p*-chlorobenzyl compound were carried out to 1.1 × 10^{-6} *M*. A plot of the optical densities *vs.* concentration was linear.

(38) It is possible that the silver was formed *via* silver oxide which is derived from the quaternary pyridinium hydroxide resulting from ring opening of the trimer.

Reaction of the Dimolecular Ether in Ethanol.—The dimolecular ether was prepared from 1-benzyl-3-carbamoylpyridinium chloride (10.0 g., 0.0402 mole) and aqueous hydroxide as described previously. The ether was dissolved in 100 ml. of 95% ethanol. After 30 min. a pale yellow powder (1.06 g., 12%) m.p. 180–182° dec., was removed by filtration and washed successively with water, alcohol, and ether. In other runs the yield was 10–18%. The crude product was air dried and recrystallized three times from chloroform (2–3 ml.)–ethanol (200 ml.) to give fine white crystals, m.p. 184–185° dec.

Anal. Calcd. for $C_{13}H_{12}N_2O$: C, 73.56; H, 5.70. Found: C, 73.61; H, 5.41.

The infrared spectrum of this compound was identical with that of the product obtained by treatment of 1-benzyl-3-carbamoylpyridinium chloride with ethanolic sodium hydroxide.

Reactions of $(C_{13}H_{12}N_2O)_3$. With Hydrogen Chloride.—Anhydrous hydrogen chloride was passed through a solution of the compound (4.0 g., 0.019 equiv.) in 30 ml. of chloroform. The precipitate (2.0 g., 43%) was identified after recrystallization from ethanol–water as 1-benzyl-3-carbamoylpyridinium chloride by a mixture melting point (239°) with an authentic sample. Its infrared spectrum was identical with that of an authentic sample.

When the compound was treated with refluxing 10% aqueous hydrochloric acid, 1-benzyl-3-carboxypyridinium chloride, m.p. 198–198.5° dec., was obtained.

The substances with substituted benzyl groups also reverted to the quaternary nicotinamide salts on treatment with hydrogen chloride.

With Picric Acid.—Addition of a saturated solution of picric acid in chloroform to a solution of $(C_{13}H_{12}N_2O)_3$ in chloroform gave 1-benzyl-3-carbamoylpyridinium picrate which was recrystallized from 95% alcohol, m.p. 165–168°. A mixture melting point with an authentic sample was 168°, and infrared spectra of this compound and an authentic sample were identical.

With Malachite Green Oxalate.—The compound (0.385 g., 0.00182 equiv.) was added to 50 ml. of chloroform saturated with malachite green oxalate, and the mixture was stirred for 3 hr. Filtration gave an off-white powder (0.300 g., 55%) which was very hygroscopic; it was washed successively with chloroform and ether and dried in a nitrogen-filled drybox.

Anal. Calcd. for $C_{15}H_{14}N_2O_5$: C, 59.60; H, 4.67; N, 9.27. Found: C, 59.31; H, 4.80; N, 9.53.

The compound decolorized a very dilute solution of malachite green in chloroform in 10 min. while 1-benzyl-1,4-dihydronicotinamide decolorized a similar solution immediately.

With *p*-Nitrosodimethylaniline.—*p*-Nitroso-N,N-dimethylaniline (0.41 g., 0.0027 mole) and $(C_{13}H_{12}N_2O)_3$ (0.42 g., 0.0020 equiv.) were dissolved in 40 ml. of hot ethanol. The solution was concentrated to 30 ml. by heating and was cooled in an ice bath. Water (100 ml.) was added and a tan solid precipitated. After two recrystallizations from ethanol with decolorization by charcoal, the benzal nitrone of *p*-nitroso-N,N-dimethylaniline was obtained as yellow plates, m.p. 141–143°. Its infrared spectrum was identical with that of an authentic sample prepared by treating 1-benzyl-3-carbamoylpyridinium chloride with *p*-nitroso-N,N-dimethylaniline (m.p. of authentic material 143°).[11]

In another run with $(C_{13}H_{12}N_2O)_3$ and *p*-nitroso-N,N-dimethylaniline, the yield of nitrone was estimated by addition of 2,4-dinitrophenylhydrazine–sulfuric acid reagent to the reaction mixture. Benzaldehyde (85%), representing the nitrone, was isolated as its 2,4-dinitrophenylhydrazone, m.p. 237–240°, identified by a mixture melting point (240°) with an authentic sample.

With Nitrobenzene.—The trimer (1.85 g., 0.00874 equiv.) and nitrobenzene (0.895 ml., 0.00874 mole) were heated under nitrogen at 245° for 35 min. The reaction mixture was extracted with 30 ml. of 1:5 sulfuric acid. The extract was washed with three 15-ml. portions of ether, made basic with 10% sodium hydroxide solution, saturated with salt, and extracted with two 20-ml. portions of ether. Evaporation of the ether left aniline (1.2%) identified as the phenylthiourea, m.p. 155°, and by a mixture melting point (156°) with an authentic sample.

Hydrogenation of $(C_{13}H_{12}N_2O)_3$. A.—Ethyl acetate (300 ml.) was saturated with 0.0707 g. of trimer. Platinum oxide catalyst (0.205 g.) was added and the solution was hydrogenated in a Parr apparatus at 49 p.s.i. for 13 hr. The catalyst was removed by filtration, and the solution was evaporated to about 5 ml. When the solution was cooled, a white solid (0.0085 g., 12%) crystallized, m.p. 260–261° dec.

Anal. Calcd. for $C_{13}H_{14}N_2O$: C, 72.87; H, 6.59; N, 13.08; mol. wt., 214 (monomer), 428 (dimer), 642 (trimer), and 856 (tetramer). Found: C, 73.03; H, 6.75; N, 13.11. mol. wt., 640 (cryoscopic, camphor), 600 (cryoscopic, bromoform).

Intense infrared absorption (KBr disk) occurred at 3350, 1635, 1570, 1460, 1435, 1350, 1320, 1200, and 1170 cm.$^{-1}$.

The compound had an ultraviolet absorption maximum at 305 mμ in ethanol (ϵ 6.1 × 10^3).

B.—The compound (0.685 g.) with 2 g. of Raney nickel W-2 catalyst in 200 ml. of dioxane was hydrogenated at 1500 lb. in.$^{-2}$ for 5 hr. The catalyst was removed by filtration, and the solvent was removed under reduced pressure. A light brown solid (0.357 g., 51%) remained which was recrystallized from dioxane to give white crystals, m.p. 261–262° dec. This substance was identical (mixture melting point and infrared spectrum) with that obtained in the low pressure hydrogenation in ethyl acetate.

C.—Hydrogenation of the compound (0.4 g.) with 0.09 g. of platinum oxide catalyst in 75 ml. of chloroform at atmospheric pressure for 4 hr. gave a white solid, m.p. 248–249° dec., which was identified as 1-benzyl-3-carbamoylpiperidine hydrochloride by a mixture melting point (249–250°) and comparison of its infrared spectrum with that of an authentic sample.

D.—Hydrogenation of the compound (0.30 g.) with 0.10 g. of platinum oxide catalyst in 25 ml. of acetic acid at atmospheric pressure for 1.5 hr. gave 1-benzyl-3-carbamoylpiperidine, m.p. 124–125.5° (lit.[36] m.p. 123°). It was identified as a picrate, m.p. 218–221.5°, and by a mixture melting point and comparison of its infrared spectrum with that of an authentic sample.

N-Nitrobenzamides. I. Synthesis, Spectra, and Structure[1]

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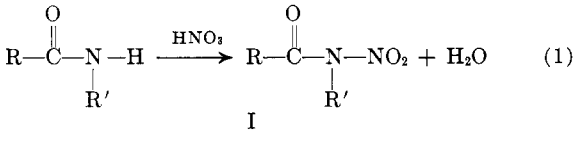
Received March 12, 1963

A series of monosubstituted N-nitro-N-methylbenzamides has been prepared by controlled direct nitration. Infrared and ultraviolet spectra are reported and discussed. Hydrolysis of the N-nitro-N-methylbenzamides yielded benzoic acids. The nitrobenzamides were converted readily to benzamides by reductive cleavage. Various similar nitration conditions applied to benzamide failed to yield N-nitrobenzamide, except as an unstable intermediate.

Two general synthetic methods can be expected to yield N-nitroamides: direct substitution of the nitro group on the amide nitrogen atom (equation 1) or



(1)

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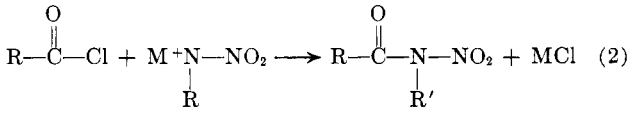
acylation of the nitramine by the action of an acid halide upon the metal salt of the nitramine (equation 2).



(2)

Due to the thermal instability of the N-nitroamides[2] the reaction conditions for either of these methods must be necessarily mild. Acylation of nitramines has been reported employing the silver salt of the nitramine. Either N- or O-acylation can occur. The evidence for the latter is indirect, and the O-acyl product is thermally unstable, preventing isolation and characterization.[2,3] The N-acyl product is formed in small yields,[3] and is stable at room temperature, permitting isolation in most cases. O-Alkylation is reported[4] to occur in the reaction of silver nitramide with alkyl iodides.

The direct nitration of amides has been effective if R′ is aliphatic, usually methyl, and R is aliphatic,[2] amino,[5,6] or alkoxyl.[2,7–9] If R is aromatic, substitution usually occurs on the benzene nucleus, with[10–13] or without[2,11,13] substitution on nitrogen. Three cases of exclusive N-nitration are found in which the benzene ring is strongly deactivated. Thus, two nitro groups[2] or three halogen atoms[13] were sufficiently deactivating to preclude nitration on the benzene ring. Thus, N-methyl-3,5-dinitrobenzamide[2] undergoes nitration at the amide function with 100% nitric acid and sulfur trioxide and only incomplete nitration with acetyl nitrate reagents. Nitration of the amide function occurred when concentrated nitric acid was used with N-methyl-2,4,6-trichlorobenzamide and with the trinitro analog.[13] The treatment of N-methyl-3-chlorobenzamide and the 4-isomer with 100% nitric acid[10] at ice temperature resulted in substitution on the ring and on the amide nitrogen.

Extrapolation of this series of reactions for the purpose of predicting the position of nitration in other monosubstituted and unsubstituted N-methylbenzamides leads to conclusions: (a) ring nitration is expected to occur under conditions favoring nitryl ion (NO_2^+) formation, *viz.*, nitric and sulfuric acids[14]; (b) N-nitration can be expected only if the absence of deactivating groups on the ring renders the amide nitrogen sufficiently more electron rich to permit nitration employing fuming nitric acid and acetic anhydride[15] or copper nitrate and acetic anhydride.[16] Under these conditions acetyl nitrate is the nitrating species and is considered milder than the nitric acid–sulfuric acid mixture.

Nitration of Monosubstituted N-Methylbenzamides.—N-Methylbenzamides were chosen for nitration due

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