lithium in ethylamine, the reaction is obviously limited to saturated carboxylic acids unless reduction of other functional groups is intended. Additional efforts to increase the yield of aldehyde by the use of other solvents such as ethylenediamine were relatively unsuccessful unless a considerable amount of ethylamine also was present.

Experimental

The general procedure for the reduction of acids to aldehydes with lithium in ethylamine is illustrated by the reduction of undecanoic acid.

Finely divided lithium shot[8] (0.75 g., 0.11 g.-atom) was added to a magnetically stirred solution of undecanoic acid (1.86 g., 0.01 mole) in anhydrous, redistilled ethylamine (35 g., 50 ml.) in a 100-ml. three-necked flask fitted with a soda-lime drying tube, a dewar-type reflux condenser,[9] and a flexible-necked addition flask[10] containing (40 g., 0.9 mole) of anhydrous ammonium chloride. After 4 hr. the deep blue color of the mixture was discharged by careful addition of the ammonium chloride. The condenser then was removed, and after partial evaporation of the solvent for 1 hr. at room temperature the residue was added to a mixture of 65 g. of cracked ice and 35 ml. of concentrated hydrochloric acid. The resulting acidic solution was extracted with 100 ml. of ether, and the ether layer was washed with cold 1 N sodium hydroxide solution to yield 90 mg. (5% recovery) of unchanged undecanoic acid. The ether layer then was dried and evaporated to give a mixture of undecanol and undecanal from which the aldehyde was isolated and identified as its 2,4-dinitrophenylhydrazone (1.05 g., 30% yield), m.p. 102.5–103.5°.[11] For further identification the aldehyde from another run was converted into the semicarbazone, m.p. 104–106°.[11]

(8) P. D. Bartlett and E. B. Lefferts, *J. Am. Chem. Soc.*, **77**, 2804 (1955).
(9) A. I. Vogel, "Practical Organic Chemistry," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1962, pp. 48–49.
(10) L. F. Fieser, "Experiments in Organic Chemistry," 3rd Ed., D. C. Heath and Co., Boston, Mass., 1957, p. 265.
(11) "Tables for Identification of Organic Compounds," C. D. Hodgman, Ed., Chemical Rubber Publishing Co., Cleveland, Ohio, 1960, p. 73.

The Structures of Methazonic Acid and Its Anions[1]

S. BROWNSTEIN

Division of Applied Chemistry, National Research Council, Ottawa, Canada

The reaction of nitromethane with base first yields the nitromethane anion, then the methazonate ion.[2] The rates of these reactions have been determined and some suggestions made about mechanism.[3–5] However, the structures of methazonic acid and its anion have not been definitely established. Since proton resonance spectroscopy has been very useful in determining structures of mobile species in solution, an

(1) Issued as National Research Council No. 7591.
(2) C. M. Drew, J. R. Mc Nesby and A. S. Gordon, *J. Am. Chem. Soc.*, **77**, 2622 (1955).
(3) P. J. Elving and J. Lakritz, *ibid.*, **77**, 3217 (1955).
(4) D. J. Morgan, *J. Org. Chem.*, **23**, 1069 (1958).
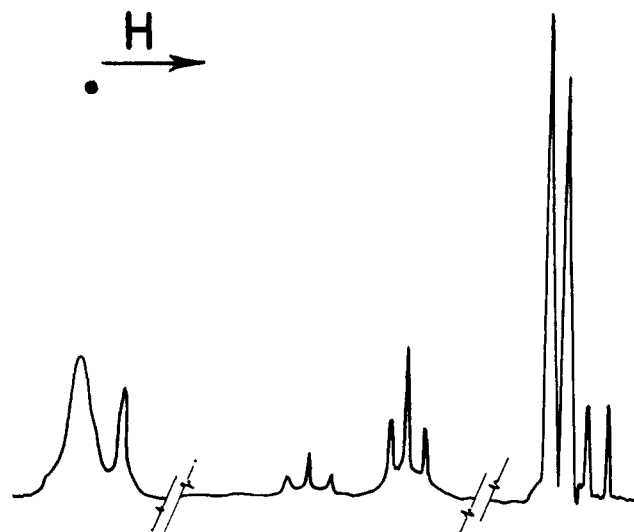(5) D. J. Morgan, *ibid.*, **27**, 4646 (1962).

Fig. 1.—Proton resonance spectrum of methazonic acid in acetone (solvent not shown).

attempt was made to obtain the spectra of methazonic acid and its anion.

The proton resonance spectrum of methazonic acid in acetone solution is shown in Fig. 1. A similar spectrum is observed in aqueous solution except for the absence of the two low field peaks, attributed to the oxime protons, which are presumably exchanging rapidly with the solvent. Chemical shifts and spin-coupling constants are listed in Table I. The doublet, triplet, and single peaks observed for methazonic acid may be most readily explained if the compound has the structure $O_2NCH_2CH:NOH$. The two groups of peaks can be attributed to syn–anti isomerism about the carbon–nitrogen bond. The aldehydic proton in aldoximes has been found to occur at lowest magnetic field in the syn isomer.[6] Although no effect of syn–anti isomerism was observed on the β-hydrogens in aldoximes it has been observed in 2,4-dinitrophenylhydrazones and ketoximes.[7,8] It is, therefore, concluded that the lowest field triplet, highest field doublet, and highest field singlet can be assigned to the syn isomer of methazonic acid. As with the 2,4-dinitrophenylhydrazones the shielding effect of the carbon–nitrogen double bond is opposite for the α- and β-hydrogens, and smaller for the β- than the α-hydrogens.

An AX_2 spectrum for the protons on the carbon chain in both isomers of methazonic acid indicates either free rotation about the carbon–carbon bond or a fixed conformation in which the two CH_2 protons are equivalent. Since the average coupling constants are different for the two isomers, it is likely that there is free rotation about the carbon–carbon bond, with different populations in the various conformations for each isomer.

The spectrum of a freshly prepared acetone solution of methazonic acid shows only those peaks attributed to the anti form. With time, peaks due to the syn isomer appear, and at equilibrium it is the more abundant by 1.29:1.00. When methazonic acid is dissolved in water the equilibrium concentrations of syn

(6) W. D. Phillips, *Ann. N. Y. Acad. Sci.*, **70**, 817 (1958).
(7) G. J. Karabatsos, J. D. Graham, and F. M. Vane, *J. Am. Chem. Soc.*, **84**, 753 (1962).
(8) E. Lustig, *J. Phys. Chem.*, **65**, 491 (1961).

TABLE I

CHEMICAL SHIFTS AND SPIN-COUPLING CONSTANTS OF SOME NITRO DERIVATIVES

Compound		$\delta_1(H_2O)^a$	δ_1(acetone)	$\delta_1(CH_3OH)$	$\delta_2(H_2O)$	δ_2(acetone)	$\delta_2(CH_3OH)$	δ_3(acetone)	$J_{1-2}{}^b$
$O_2NCH_2CH:NOH$	syn	0.48	3.17		2.90	5.56		8.78	6.0
1 2 3	anti	0.67	3.35		2.46	5.08		8.90	4.7
$O_2N:CHCH:NO^c$	syn	1.99		3.38^d	3.19		4.71		9.0
1 2	anti	2.33		3.82	2.83		4.26		8.8
$CH_2:NO_2{}^-$		1.00		2.32					
1									
$CH_3CH:NO_2{}^-$				3.14^e			1.39		6.2
1 2									
$(CH_3)_2C:NO_2{}^-$				1.39^e					
1									

^{a} Chemical shifts are listed in p.p.m. to low field of the solvent resonance (the CH_3 resonance in the case of methanol). ^{b} Spin-coupling constants are in cycles per second. ^{c} The n.m.r. evidence cannot distinguish between the monoanion with a rapidly exchanging hydrogen and the dianion. ^{d} Spectra in methanol are for lithium salts only. ^{e} To high field of solvent.
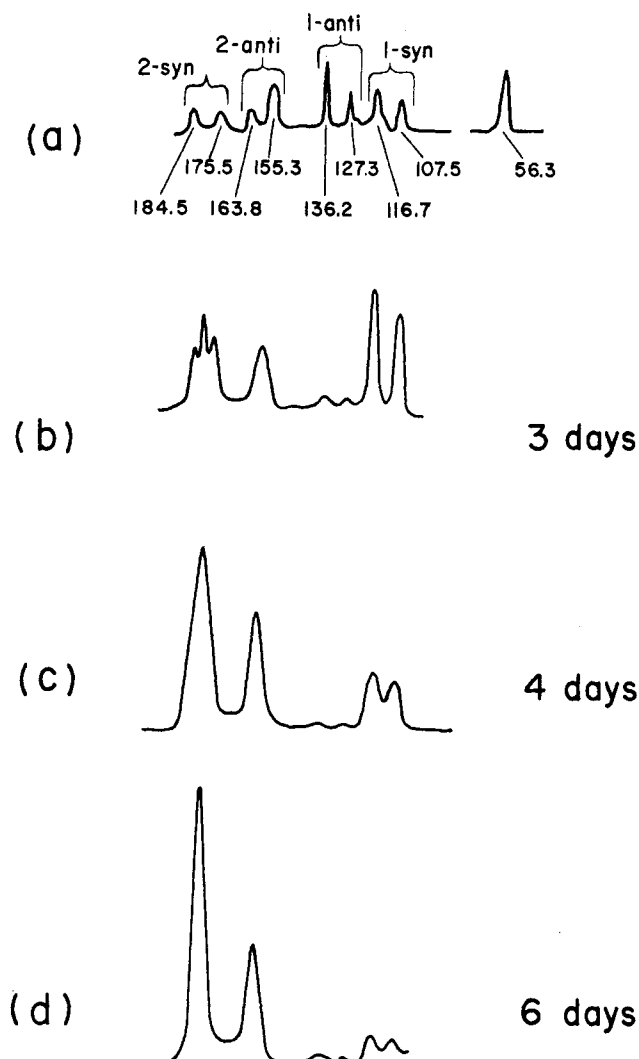

Fig. 2.—(a) Proton resonance spectrum of $CH_2NO_2{}^-$ and $^-{}^2O_2NCHCHNO$; (b), (c), and (d) progressive deuteration of $^-{}^2O_2NCHCHNO$. Peak positions are in c.p.s. to low field of water.

and anti isomers are observed immediately. The syn isomer is favored by 2.53:1.00. One may conclude that crystalline methazonic acid occurs as the anti isomer and goes into solution in that form. This also agrees with the observations of Phillips,[6] who found that those aldoximes which were isolated after recrystallization were exclusively in the anti form.

The reaction of nitromethane with base in water or methanol yields, after a short time, an eight-line spectrum whose spacing and intensity is consistent with two AB pairs. A similar spectrum is also obtained when methazonic acid is dissolved in water containing one equivalent of base. The chemical shifts and spin coupling constants for these species, the syn and anti isomers of methazonate ion, are listed in Table I. A typical spectrum is illustrated in Fig. 2(a). These spectra may be explained by the structure $O_2N:$-$CHCH:NO^{-2}$ for the methazonate ion. It is not possible to distinguish, from the proton resonance spectra, between the dianion and the monoanion with a rapidly exchanging hydrogen on one of the oxygen atoms. The retention of configuration about the oxime anion has also been observed with ketoximes.[8] Since the spectrum is the same with either one equivalent of base (methazonic acid in aqueous alkali) or two equivalents (nitromethane anion in water) it seems likely that the oxime proton is the last to ionize. This is consistent with the ultraviolet spectral data on the mono- and disodium salts.[5]

The proton resonance peaks centered at 2.83 and 3.19 p.p.m. to low field of water are assigned to the hydrogen adjacent to the oxime group since they are at lowest field as in methazonic acid. Therefore, the peaks centered at 1.99 and 2.33 p.p.m. are assigned to the hydrogen adjacent to the nitro group. The peaks at 2.33 and 2.83 p.p.m. are assigned to the anti isomer since they have the same position relative to the syn protons as in methazonic acid. The variation of intensity with time, described later, is also similar to that of methazonic acid for this peak assignment.

In an aqueous solution of methazonate ion, freshly prepared from methazonic acid or from the anion of nitromethane, the anti isomer is in excess by 1.41:1.00. At equilibrium the syn isomer is favored by 2.02:1.00. The variation in intensity of the two groups of four peaks is good evidence in favor of the assignment to two AB pairs. Additional evidence comes from the change of the spectrum when the sodium salt of nitromethane is dissolved in deuterium oxide. Methazonate ion is first produced and exchange occurs in the order 1-anti > 1-syn > 2-anti > 2-syn. This behavior is illustrated in Fig. 2.

The logarithm of the rate constant for the reaction

$$2CH_2NO_2{}^- \longrightarrow {}^-{}^2O_2N:CHCH:NO \cdot H_2O$$
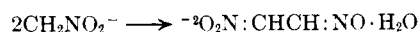
has been calculated as log k_2 = 1.79 moles^{-1} l. min.$^{-1}$ at 25°.[2] From the rate of disappearance of the peak due to the nitromethane anion a value of 1.75 moles^{-1}

1. min.$^{-1}$ was obtained in the present study. Since concentrations of nitromethane anion were one thousand times greater in the present study, the agreement is excellent.

Since deuterium exchange at the 1-position is faster than *syn-anti* equilibration the exchange cannot involve loss of configuration about the oxime double bond. Methazonate ion, produced from nitromethane anion in deuterium oxide as solvent, does not contain any deuterium. Therefore, the dimerization of nitromethane anion to methazonate ion occurs more rapidly than hydrogen exchange between water and nitromethane anion.

Experimental

The proton resonance spectra were obtained as described previously.[9] Two molar solutions were prepared by dissolving the appropriate amount of solid in 0.25 ml. of solvent. Despite care to introduce the salts of nitromethane slowly into solution excessive reaction sometimes occurred.[10] Methazonic acid was prepared by an established method.[11]

(9) S. Brownstein, *Can. J. Chem.*, **40**, 870 (1962).

(10) J. Heuberger, *Svensk Kem. Tidskr.*, **38**, 29 (1926).

(11) W. Steinkopf, *Ber.*, **42**, 2026 (1909).

Syntheses Based on 2-Methyl-5-nitrogramine. Preparation of 2-Methyl-5-nitroindole-3-acetic Acid

Wayland E. Noland and Kent R. Rush[1]

School of Chemistry, University of Minnesota, Minneapolis 14, Minnesota

Nitration of 2-methylgramine with nitric acid in acetic acid has been reported to yield 2-methyl-5-nitrogramine, m.p. 158–160°.[2] The product was subsequently proved, however, to be 2-methyl-6-nitrogramine.[3] In a recent paper from this laboratory[4] the preparation of authentic 2-methyl-5-nitrogramine, m.p. 173–175°, has been described, by a Mannich reaction with 2-methyl-5-nitroindole (I), the nitration product of 2-methylindole in concentrated sulfuric acid. Absence of a well defined NH band in the Nujol infrared spectrum of the gramine derivative suggested the possibility that the Mannich reaction might have occurred at the 1-position. Equilibration with deuterium oxide, however, produced a series of weak ND bands,[5] thus showing that the NH group is still present in the gramine derivative.[4]

The structure of 2-methyl-5-nitrogramine (II) has now been proved by chemical means. Catalytic hydrogenolysis of II, with concomitant hydrogenation of the nitro group, gave the known 5-amino-2,3-dimethylindole (III),[6–9] identical with a sample pre-

(1) National Science Foundation Graduate Fellow, June, 1961–June, 1963.

(2) V. Colo, B. Asero, and A. Vercellone, *Farmaco (Pavia), Ed. Sci.*, **9**, 611 (1954).

(3) G. Berti and A. Da Settimo, *Gazz. chim. ital.*, **90**, 525 (1960).

(4) W. E. Noland, L. R. Smith, and D. C. Johnson, *J. Org. Chem.*, **28**, 2262 (1963).

(5) The ND bands, unlike the NH bands, do not overlap with the CH region.

(6) H. Bauer and E. Strauss, *Ber.*, **65**, 308 (1932).

(7) E. Shaw and D. W. Woolley, *J. Am. Chem. Soc.*, **75**, 1877 (1953).

pared by catalytic hydrogenation of 2,3-dimethyl-5-nitroindole (IV),[6,9–11] the nitration product of 2,3-dimethylindole in concentrated sulfuric acid. Other evidence that II is 3-substituted is provided by its
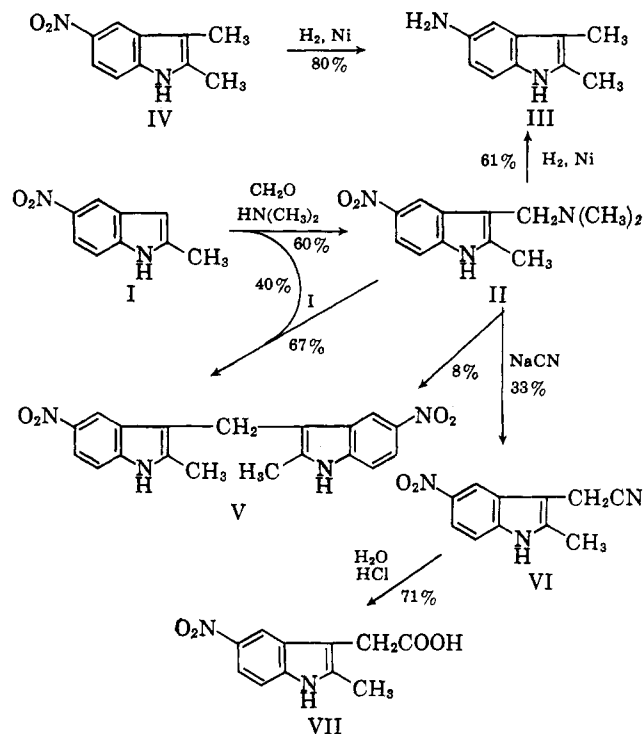
reaction with I in acetic acid, which gave 3,3'-methylenebis(2-methyl-5-nitroindole) (V). This nucleophilic replacement of the dimethylamino group of II by I is analogous to the formation[4] of V as a coproduct with II during the Mannich reaction. The presence of an NH band in the infrared spectrum of V is consistent with the formulation of V and of its precursor II as 3-substituted indole derivatives. Nucleophilic replacement of the dimethylamino group of II with cyanide ion gave 2-methyl-5-nitroindole-3-acetonitrile (VI) as well as a small amount of V. The presence of a well defined NH band in VI provides additional evidence that its precursor II is not a 1-substituted indole derivative.

Acid hydrolysis of VI provides a convenient synthesis of 2-methyl-5-nitroindole-3-acetic acid (VII).

Experimental

Melting points were determined on a calibrated Fisher-Johns hot stage.

2-Methyl-5-nitrogramine (3-Dimethylaminomethyl-2-methyl-5-nitroindole[12]) (II).—By increasing the mole ratio of formaldehyde and dimethylamine relative to 2-methyl-5-nitroindole the yield of 2-methyl-5-nitrogramine has been increased to 60% from the 18% previously reported.[4]

A solution of 2-methyl-5-nitroindole[4] (4.20 g., 0.0238 mole) in acetic acid (500 ml.) was added dropwise, with stirring, to a solution of formalin (2.50 g. of 37% formaldehyde, 0.031 mole) and dimethylamine (6.00 g. of aqueous 25% solution, 0.033 mole) in acetic acid (150 ml.) at 5°. Stirring was continued at 5° for an additional 1.5 hr., at room temperature for 1 hr., and at steam

(8) Z. J. Vejdělek, *Chem. Listy*, **51**, 1338 (1957); *Chem. Abstr.*, **51**, 17875 (1957).

(9) S. N. Nagaraja and S. V. Sunthankar, *J. Sci. Ind. Res.* (India), **17B**, 457 (1958); *Chem. Abstr.*, **53**, 11340 (1959).

(10) S. G. P. Plant and M. L. Tomlinson, *J. Chem. Soc.*, 955 (1933).

(11) C. M. Atkinson, J. C. E. Simpson, and A. Taylor, *ibid.*, 165 (1954).

(12) *Chemical Abstracts* name.