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cis and *trans* Configurations of the Peptide Bond in N-Monosubstituted Amides by Nuclear Magnetic Resonance

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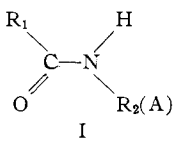
The n.m.r. spectra of thirteen N-monosubstituted aliphatic amides reveals that four of these, N-methylformamide, N-ethylformamide, N-isopropylformamide, and N-*t*-butylformamide, exist in both the *cis* and the *trans* configuration about the central C–N bond. Although the *trans* form predominates, the percentage of *cis* isomer increases as the nitrogen substituent becomes more bulky. Studies of the change in chemical shift of the nitrogen substituent upon dilution with benzene are in accord with the peak assignments. Spin coupling constants between the protons on carbon and nitrogen may be found for each isomer in sulfuric acid solutions of the substituted formamides. The remaining nine amides, where the carbonyl substituent was larger than hydrogen, showed the presence of only the *trans* configuration.

Introduction

Although the *trans* configuration of the amide bond in polypeptides has been accepted as the predominant configuration for protein structures,[3] the *cis* configuration has been proposed[4] for some of the residues of fibrous proteins. Since monosubstituted amides are the simplest structures which contain the peptide bond, they have often been the subject of investigations attempting to shed light upon the structures of the much more complex proteins.

The *trans* configuration (I) about the central C–N bond in N-monosubstituted amides has been shown to predominate over the *cis* (II) by dipole moment,[5–7]



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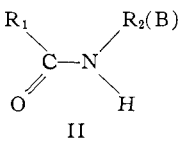

II

dielectric constant,[8] and vapor pressure[9] measurements and by ultraviolet,[5,6] infrared, and Raman spectroscopy studies.[10] Several bands in the infrared have been associated with the *cis* isomer,[11] but whether or not a predominantly *trans*-amide such an N-methylformamide contains any molecules with the *cis* configuration remains a point of controversy.[10a]

The small ring lactams are in the *cis* configuration,[11,12] but the *trans* form predominates in the larger rings. A few cyclic dimers of amides having the *cis* configuration have been reported, among them N-methylcarbamate[8] and N-methyltrichloroacetamide.[9] A transition from the *trans* to the *cis* configuration has been found in monolayers of N-*n*-octadecylacetamide.[13]

The purpose of the present investigation was to attempt to observe both *cis* and *trans* isomers of monosubstituted amides by n.m.r. The rotation about the central C–N bond of amides is hindered and the sites A (of I) and B (of II) are therefore magnetically nonequivalent.[14] If $\tau_A >> \sqrt{2}/2\pi\ (\nu_A - \nu_B)$, where τ_A is the mean lifetime at site A and ν_A is the resonance frequency of group A, the rotation is slow enough so that separate resonances are observed in the n.m.r. spectrum for nuclei at sites A and B. By associating a given site (A or B) with a given resonance peak, it is possible to determine whether a group is at site A or B, and thus, in the case of N-monosubstituted amides, it is possible to tell whether the configuration about the peptide bond is *trans* or *cis*.

Previous work[15–17] has shown that the resonance of an N-methyl group in dimethylamides or the methyl of an N-ethyl group in diethylamides to higher magnetic fields may be associated with the group at site A (*cis* to the carbonyl oxygen). Additional studies[17] of unsymmetrically disubstituted amides reveal that the set of resonances of the methyls of an N-isopropyl group which is in a position *cis* to the carbonyl oxygen occurs at higher magnetic field. However, the resonance of the methyls of a *t*-butyl group in this position is at lower magnetic field. By use of this criterion, we have assigned resonance peaks to the *cis* and *trans* isomers of the four formamides studied. These assignments are supported by n.m.r. studies of solutions of the N-monosubstituted formamides in benzene and in sulfuric acid.

Experimental

Chemical shifts were measured in c.p.s. from internal tetramethylsilane using a Varian A-60 analytical spectrometer. The temperature of the probe was about 35°. N-Methylformamide, N-methylacetamide, N-methylpropionamide, N-ethylformamide, and N-ethylacetamide were obtained from Eastman Organic Chemicals, Rochester, N. Y., dried over anhydrous sodium sulfate, and fractionally distilled *in vacuo* using a packed column. The remaining amides were prepared in this laboratory.

N-Methylisobutyramide.—The reaction of methylamine hydrochloride with isobutyryl chloride[18] gave the desired product, b.p. 78.0–78.5° (2.5 mm.) (reported[18] 120–121° (27 mm.)).

N-Ethylpropionamide.—The reaction of ethylamine hydrochloride with propionamide[19] was used, b.p. 79.5–80.5° (1 mm.) (reported[20] 100° (10 mm.)).

N-Ethylisobutyramide was prepared by the addition of isobutyryl chloride to ethylamine hydrochloride[18] and recrystallized from hexane; m.p. 69.0–71.0° (reported[20] 68°).

N-Isopropylformamide.—The reaction of isopropylamine and formic acid[21] gave the desired product, b.p. 70.0° (1.5 mm.) [reported[22] 220° (1 atm. (?))].

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(2) National Institutes of Health Predoctoral Fellow, 1961–1963.

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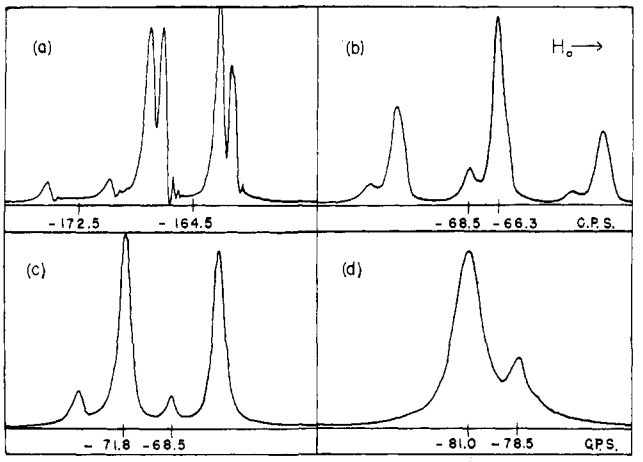

Fig. 1.—N.m.r. spectra (ν_0 = 60.0 Mc./sec.) of the methyl resonances of the N-alkyl group in the *cis* and *trans* isomers of (a) N-methylformamide (b) N-ethylformamide (c) N-isopropylformamide (d) N-*tert*-butylformamide. The chemical shifts of the centers of the multiplets belonging to the *cis* and *trans* isomers are marked on the horizontal axis; the less intense multiplet in each case belongs to the *cis* isomer.

N-Isopropylacetamide was prepared by the addition of isopropylamine to acetyl chloride[23]; b.p. 86.5–87.0° (4 mm.) (reported[24] 89–90° (9 mm.)).

N-Isopropylisobutyramide.—The addition of isopropylamine to isobutyryl chloride[23] gave the desired product, which was recrystallized from hexane; m.p. 102° (reported[25] 102°).

N-*t*-Butylformamide was prepared by the addition of a solution of sulfuric acid in acetic acid to a mixture of *t*-butyl alcohol, sodium cyanide, and acetic acid[26]; b.p. 67.0° (1.5 mm.) (reported[26] 202° cor.).

N-*t*-Butylacetamide.—Gaseous isobutene was led into a solution of acetonitrile, acetic acid, and sulfuric acid[27] to give the desired product, which was recrystallized from hexane; m.p. 98.5–98.8° (reported[27] 97–98°).

Results and Discussion

In four of the thirteen N-monosubstituted amides studied (the four formamides in Table I) two distinct sets of resonance peaks were found in the n.m.r. spectra, one from each planar configuration about the peptide bond (I and II). The spectra are shown in Fig. 1. From previous assignments,[15–17] the sets of resonance peaks at higher field may be associated with the N–CH_3 group of N-methylformamide, the N–CH_2–CH_3 group of N-ethylformamide, and the N–CH–(CH_3)$_2$ group of N-isopropylformamide at site A in I, and thus with the groups in the *trans* configuration. Similarly, the resonance peak at lower magnetic field in N-*t*-butylformamide may be associated with the N–C–(CH_3)$_3$ group at site A in I. As these are the more intense peaks (Fig. 1), the *trans* form predominates in these compounds.

The percentage of *cis* isomer in the formamides, as determined from the relative peak areas, is given in Table I. It will be noted that the percentage of *cis* isomer increases as the alkyl substituent on the nitrogen becomes more bulky. This may be explained in terms of simple steric interactions between the alkyl substituent on the nitrogen and the carbonyl oxygen in the *trans* configuration (I).

For the remaining nine amides in Table I, only one isomer was found in the n.m.r. spectrum. This could mean that: (1) $\tau_A << \sqrt{2}/2\pi(\nu_A - \nu_B)$ so that only an average of chemical shifts is "seen"; (2) $\tau_A >> \sqrt{2}/2\pi \cdot (\nu_A - \nu_B)$ so that most of the amide molecules have assumed one of the two planar orientations; or (3) the chemical shifts of the *cis* and *trans* configurations are accidently equal. The third possibility is unlikely because of the nonequivalence of the chemical shifts in the monosubstituted formamides and in the symmetrically disubstituted amides. The presence of two rotational isomers in the formamides indicates that the barrier to internal rotation in the other monosubstituted amides is probably high enough so that condition (1) would not be fulfilled. The barrier has been estimated at 28.0–28.5 kcal./mole for N-methylformamide,[10a] which is certainly too high for rapid *cis–trans* conversion at 35°. Thus we are led to the conclusion that the amides containing R_1 > H are almost entirely in one configuration. That this is the *trans* configuration is supported by a comparison of chemical shifts of the nitrogen substituents (Table I) and by previous investigations.[5–10] When R_1 of I is methyl, ethyl, or isopropyl, the *trans* configuration is sterically preferred because it places the large alkyl groups *trans* to one another. However, there must be a second effect operating which keeps the molecule predominantly *trans* even when R_1 = H. Nyquist[28] claims that there may be weak hydrogen bonding between the α-substituent of R_1 (I) and the nitrogen proton which tends to keep the amide in the *trans* configuration. Clearly, this type of bonding is not possible in the formamides, which are also predominantly in the *trans* configuration. Mizushima[29] has suggested that the strength of an amide hydrogen bond increases as each monomer is added to the polymer chain. It may be energetically favorable for the N—H and C=O to occur in the

TABLE I

CHEMICAL SHIFTS IN N-MONOSUBSTITUTED AMIDES[a]

Amide	δN–CH_3 (A)[b]	δN–CH_3 (B)	δNH	δH–CO	Percentage of preferred configuration
N-Methylformamide	−164.5	−172.5	−474	−485	92
acetamide	−164.0	.....	−487	...	100
propionamide	−162.5	.....	−483	...	100
isobutyramide	−162.0	.....	−484	...	100
	δN–CH$_2$–CH_3(A)	δN–CH$_2$–CH_3(B)	δNH	δH–CO	
N-Ethylformamide	−66.3	−68.5	−476	−482	88
acetamide	−66.0	....	−489	...	100
propionamide	−66.2	....	−478	...	100
isobutyramide[c]	−66.0	....	−475	...	100
	δN–CH–(CH_3)$_2$(A)	δN–CH–(CH_3)$_2$(B)	δNH	δH–CO	
N-Isopropylformamide	−68.5	−71.8	?	−480	88
acetamide	−67.0	....	−484	...	100
isobutyramide[d]	−68.0	....	−449	...	100
	δN–C–(CH_3)$_3$(A)	δN–C–(CH_3)$_3$(B)	δNH	δH–CO	
N-*t*-Butylformamide	−81.0	−78.5	−462	−489 −475	82[f]
acetamide[e]	−76.6	....	−436	....	100

[a] Measured in c.p.s. (ν_0 = 60.0 Mc./sec.) from tetramethylsilane internal reference. [b] The isomer in which the nitrogen alkyl substituent is *cis* to the carbonyl oxygen (as in I) is referred to here as A. [c] A 0.60-mole fraction carbon tetrachloride solution. [d] A 0.21-mole fraction carbon tetrachloride solution. [e] A 0.20-mole fraction carbon tetrachloride solution. [f] Determined in dilute benzene solution. The resonance peaks from the *cis* and *trans* isomers were too close to be integrated in the pure amide.

(23) N. L. Drake, C. M. Eaken, and W. Shenk, *J. Am. Chem. Soc.*, **70**, 677 (1948).
(24) K. G. Wyness, *J. Chem. Soc.*, 2934 (1958).
(25) V. Meyer and A. Warrington, *Ber.*, **20**, 505 (1887).
(26) J. J. Ritter and J. Kalish, *J. Am. Chem. Soc.*, **70**, 4048 (1948).
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(29) S. I. Mizushima, "Structure of Molecules and Internal Rotation," Academic Press, Inc., New York, N. Y., 1954, p. 134.

trans configuration so that the amides can associate in linear (open-chain) hydrogen-bonded polymers.

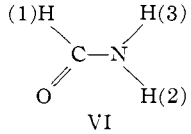
A study of the n.m.r. spectra of the formamides upon dilution with benzene provides further evidence that the less intense peaks are associated with the *cis* isomer. Hatton and Richards[16] have proposed a specific interaction between the benzene ring and N,N-disubstituted amides, whereby the ring is attracted by the partial positive charge on the nitrogen, but repelled by the negative charge of the carbonyl oxygen. The same type of association is expected for monosubstituted amides. Resonance structures for each rotational isomer of the formamides are shown in III and IV with the benzene ring in a plane parallel to the amide. The proximity of the benzene ring and R (B) in the expected benzene complex with the *cis* isomer IV would cause a large high-field shift of the n.m.r. resonance peak associated with R (B) due to the large diamagnetic anisotropy of the benzene ring. One would therefore predict that the resonance peaks for

III IV

the R groups in the *cis* isomer IV would shift to higher field more rapidly than the peaks from the R groups in the *trans* isomer III on dilution with benzene. As shown in Fig. 2, the less intense pair of peaks shifts to high field most rapidly and would therefore be assigned to the R (B) groups of the *cis* isomer in each case. Thus the spectra of dilute benzene solutions provide a confirmation of the assignment made previously and support the conclusion that in each case the *trans* isomer predominates.

Because of the considerable broadening of the N–H resonance peak by the quadrupole relaxation of the N-14 nucleus, it was not possible to observe the N–H proton in both the *cis* and *trans* configurations. Only a combined resonance was found. This problem has been overcome in the case of formamide by N-15 substitution[30] and by decoupling the N-14 nuclear spin.[31] The chemical shift between the two nitrogen protons was found to be 12.0 c.p.s.[30] (ν_0 = 60.0 Mc./sec.)

Greater success was obtained in finding the two formyl hydrogens of the *cis* and *trans* isomers of the formamides. Two formyl hydrogen peaks are clearly evident in the n.m.r. spectrum of pure N-*t*-butylformamide. As mentioned previously, the more intense resonance may be assigned to the *trans* (I) isomer. The more intense formyl resonance, at −475 c.p.s., is split into a doublet by the nitrogen proton with a coupling constant of 2.0 c.p.s. This is quite close to the value of the *cis* (J_{13} in VI) coupling constant in formamide[30] (2.1 c.p.s.) and in N-methylformamide (1.8 c.p.s.[32]). Splitting of the formyl hydrogen resonance of *cis*-N-*t*-butylformamide (II) at −489 c.p.s. would be expected to be on the order of the *trans*



VI

(J_{12} in VI) coupling constant in formamide[30] of 12.9 c.p.s.; however, only a single resonance peak is observed in the formyl proton region of the n.m.r. spectrum of the *cis* isomer. The integrated intensity of this peak was 18% of the total formyl hydrogen peak area (Table I).

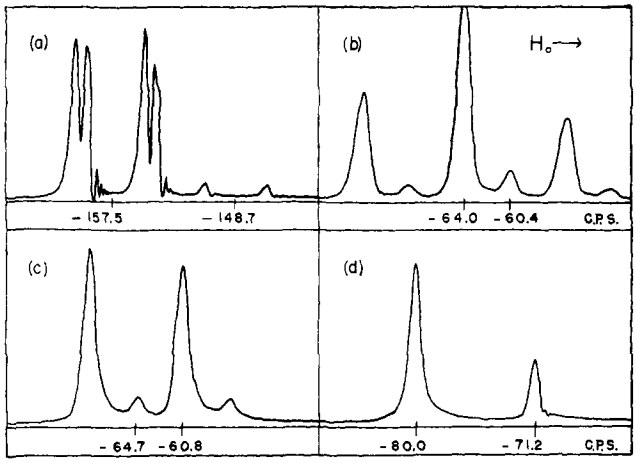
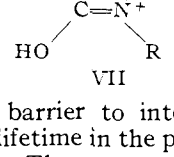


Fig. 2.—N.m.r. spectra (ν_0 = 60.0 Mc./sec.) of the methyl resonances of the N-alkyl group in the *cis* and *trans* isomers of (a) N-methylformamide (b) N-ethylformamide (c) N-isopropylformamide (d) N-*tert*-butylformamide. All are in benzene solutions and show (by comparison with Fig. 1) how the resonance peaks of the *cis* isomer have moved to high field faster than the more intense resonance peaks from the *trans* isomer.

Coupling constants of interest in the pure amides are given in Table II. It will be noted that J_{34} (VIII) is 0.5 c.p.s. larger than J_{25} (IX). A similar anomaly has been observed in the n.m.r. spectrum of N-15 formamide[30] (VI) where $J_{NH(3)}$ is 4.0 c.p.s. larger than $J_{NH(2)}$. However, microwave studies of formamide[33] reveal that the N–H(3) bond is 0.012 Å. shorter than the N–H(2) bond, which could result in a larger coupling constant.[34] A second explanation[30] is that the C–N–H(3) bond angle is larger than the C–N–H(2) angle which could lead to greater s-character in the N–H(3) bond, thus a larger $J_{NH(3)}$.[34] Both primary[35] and secondary[11] amides absorb in the infrared at two different N–H stretching frequencies, believed due to whether the bond is oriented *cis* or *trans* to the carbonyl oxygen. Similar differences in the N–H bond of the *cis* and *trans* isomers of N-methylformamide may be responsible for the two values found for J_{34} and J_{25} (VIII and IX). The same difference in this coupling constant would be expected in N-ethylformamide and N-isopropylformamide; however, the N–CH_2 and N–CH resonance peaks from the *cis* isomer partially overlap those of the *trans* isomer and therefore J_{25} cannot be accurately determined.

Because of the smaller percentage of *cis* isomer in the other formamides, it is more convenient to study these amides in 100% sulfuric acid solution. Protonation of the amides on the carbonyl oxygen[36,37] tends to stabilize resonance form VII. This has the effect of



VII

raising the energy barrier to internal rotation[36] and thus increasing the lifetime in the planar configurations, both *cis* and *trans*. The protonation of the carbonyl oxygen increases its size, and thus the R group (VII)

(30) B. Sunners, L. H. Piette, and W. G. Schneider, *Can. J. Chem.*, **38**, 681 (1960).
(31) L. H. Piette, J. D. Ray, and R. A. Ogg, *J. Mol. Spectry.*, **2**, 66 (1958).
(32) E. W. Randall and J. D. Baldeschwieler, *ibid.*, **8**, 365 (1962).
(33) C. C. Costain and J. M. Dowling, *J. Chem. Phys.*, **32**, 158 (1960).
(34) N. Muller and D. E. Pritchard, *ibid.*, **31**, 768, 1471 (1959).
(35) A. G. Moritz, *Nature*, **195**, 800 (1962).
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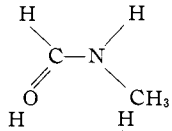
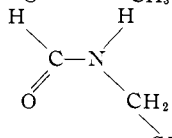
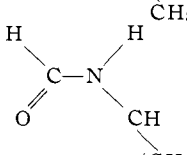
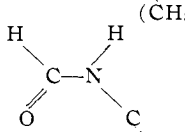
(37) R. J. Gillespie and T. Birchall, *Can. J. Chem.*, **41**, 148 (1963).

TABLE II

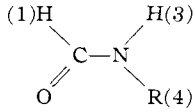
EFFECT OF SOLVENT ON SPIN COUPLING CONSTANTS (C.P.S.) IN MONOSUBSTITUTED FORMAMIDES

Amide	Solvent	J_{12}[a]	J_{13}[b]	J_{14}[b]	J_{15}[a]	J_{34}[b]	J_{25}[a]	Reference
	Neat	?	1.8	0.9	?	5.0	4.5	c
	33% (vol.) in H_2O	?	2.3	0.8	?	5.0	?	d
	1.0 M in H_2SO_4	?	5.0	1.3	0.9	5.6	?	e
	Neat	?	?	≈0.7	?	6.0	?	f
	1.0 M in H_2SO_4	14.0	5.1	≈1.0	?	≈6.0	?	f
	Neat	?	?	≈1.0	?	7.7	?	g
	1.0 M in H_2SO_4	13.8	5.1	≈0.9	?	≈7.7	?	g
	Neat	?	2.0	...	...	...	...	
		(14.0	5.5)					
	1.0 M in H_2SO_4	(14.4	5.0)	...	...	...	...	h

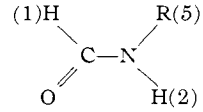
[a] Refers to the *cis* isomer IX. [b] Refers to the *trans* isomer VIII. [c] This work. See text for the discussion of the nonequivalence of J_{34} and J_{25} in N-methylformamide. [d] See ref. 32. [e] This work; J_{15} was obtained in a 1.0 M D_2SO_4 solution. [f] This work; $J_{CH_2\text{-}CH_3}$ = 7.6 c.p.s. [g] This work; $J_{CH(CH_3)_2}$ = 6.8 c.p.s.; $J_{14} \cong 0.9$ c.p.s. was obtained in a 1.0 M D_2SO_4 solution. [h] This work.

will interact sterically with an OH more strongly than with a carbonyl oxygen. This has an observable effect upon the isomer ratio, causing an increase in the percentage of *cis* isomers. The most striking example is N-*t*-butylformamide, where the percentage of *cis* isomer is about 18% in benzene solution, but increases to about 63% in sulfuric acid. The isomer ratios are difficult to measure in sulfuric acid because the isomer peaks partially overlap, just as they do in the pure amide (Fig. 1).

In 1.0 M solution of the amides in sulfuric acid, it is possible to observe the coupling of the formyl proton of both the *cis* and the *trans* isomers with the nitrogen proton. The coupling constants across the C–N bond are expected to be larger in sulfuric acid solution than in the pure amide[36] due to the increase in π-electron density in the C–N bond of the protonated amide VII through which coupling occurs. Thus, in sulfuric acid, the H–C–N–H dihedral angle in the formamides is probably close to 0° in the *cis* form and 180° in the *trans* form, leading to larger coupling constants[38] than observed in the pure amides, where rotation about the C–N bond was not as restricted. The increase in coupling constant upon an increase in amide planarity is evident in the data of Table II. Randall and Baldeschwieler[32] have explained the increase in J_{13} (Fig. VIII) in N-methylformamide upon addition of water



VIII, *trans*

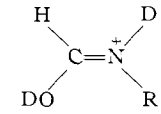


IX, *cis*

by postulating that water favors the ionic resonance form (as III or IV). The effect is even more pronounced in sulfuric acid because of protonation on the oxygen (VII), and allows resolution of the coupling constants of the other formamides in Table II.

The increase in J_{13} from pure amide to sulfuric acid solution is much larger than the increase in the other coupling constants. This may be explained if it is assumed that the structure of the amide bond of the N-monosubstituted formamides is similar to that of formamide.[33] In formamide, the *cis*-H–C–N–H dihedral angle is 12 ± 5° and the *trans* dihedral angle is 7 ± 5°. Thus the larger change in J_{13} from the pure amide to the protonated form may be due to the larger change in dihedral angle required to achieve planarity in the sulfuric acid solution.

In 1.0 M deuterated sulfuric acid solutions, the amides exist as the deuterated species **X**. J_{12} and J_{13} collapse, and only a single broad resonance is observed for the formyl proton, except for N-*t*-butylformamide, in which



X

the chemical shift between the formyl proton of the *cis* and *trans* isomers is large enough so that both resonances may be seen.

A comparison of the relative intensities of the two formyl hydrogen resonance peaks, together with J_{13} (VIII) and J_{12}(IX), allows a check on the assignments made previously. In 1.0 M solutions of N-methylformamide, N-ethylformamide, and N-isopropylformamide in 100% sulfuric acid (Table II) it is the more intense formyl resonance which is coupled to the N–H by 5.0–5.1 c.p.s. and the less intense by 13.8–14.4 c.p.s. Since we have already assigned the smaller coupling to the isomer which has the hydrogens *cis* (VIII), the *trans* configuration predominates for these three formamides in sulfuric acid, although the percentage of *cis* isomer has increased from what it was in benzene. However, in N-*t*-butylformamide, the more intense formyl proton resonance is coupled to the N–H by 14.4 c.p.s. and the less intense by 5.0 c.p.s. The larger coupling is due to the configuration which has the hydrogens *trans* (IX). Thus the interaction between the *t*-butyl group and the OH of the protonated carbonyl oxygen must be great enough to change the preferred configuration from *trans* to *cis*.

It should be kept in mind that amides are highly associated and that the isomer that we refer to as *cis* probably exists as a cyclic dimer and the *trans* isomer as an open chain hydrogen-bonded polymer.

The significance of the occurrence of the *cis* configura-

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tion in certain amides is threefold: (1) it indicates that only one isomer is observed for most monosubstituted amides in the n.m.r. spectrum not because of rapid rotation about the C–N bond, but because of the preference for the *trans* configuration; (2) it shows that structural considerations, including nonbonded interactions, play a part in determining the configuration about the peptide bond (this may also be important for polypeptide structures); and (3) it confirms the extensive infrared studies of N-methylformamide[10] which indicate that a small percentage of the molecules may possess the *cis* configuration.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF BOSTON UNIVERSITY, BOSTON 15, MASS.]

Reactions of Active Nitrogen with Organic Substrates. II. Molecular Origins of Products of Reaction with Propene[1]

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The molecular origins of HCN, C_2H_2, C_2H_4, C_2H_6, C_3H_8, and CH_3CN formed by the reaction of active nitrogen with propene have been investigated by determining the relative molar radioactivities of these products when formed from propene-1-^{14}C, propene-2-^{14}C, and propene-3-^{14}C, respectively. The result establishes that none of these products arises by random utilization of the carbon atoms of the reactant. HCN originates more extensively in C-1 and C-3 than in C-2. Ethylene and CH_3CN appear to have the same precursor or precursors and are derived from C-2 plus C-1 and C-3 in the approximate ratio 2:1. Acetylene is derived from C-2 plus approximately equal proportions of C_1 and C_3. Ethane appears to be derived principally from C_1 and C_3. Propane is largely or solely formed by addition of hydrogen to propene. Mechanistic speculations are offered.

Introduction

Although the reactions of active nitrogen with organic molecules have, in recent years, been the subject of numerous investigations,[2-22] particularly in C. A. Winkler's laboratory at McGill University, there has been no report of studies directed toward identifying the chemical fate of individual atoms of a substrate molecule. This paper records our initial approach to securing such information by determining the molar radioactivities of the products of attack of active nitrogen on substrates suitably labeled with ^{14}C. Because each of its carbon atoms is structurally unique, propene is a convenient simple substrate and its three isomerically labeled forms were, accordingly, employed.

Experimental

General Procedures.—Reactions were carried out in an unpoisoned Pyrex flow system at ambient temperature and 4.2 mm. pressure. Purified molecular nitrogen, pumped at a rate of 149 ± 2 μmoles sec.$^{-1}$, corresponding to a linear flow rate of 232 cm. sec.$^{-1}$, was irradiated with 2450 Mc. microwaves to yield a nitrogen atom flow rate of 1.3 μmoles sec.$^{-1}$, as determined by the nitric oxide emission titration method.[23] Whether this method accurately measures nitrogen atom concentration has been questioned[20,24] but, under the fixed conditions of the present work, there is little question that the procedure provides a reliable relative measure. If, as Winkler and his co-workers suggest,[24] NO is also decomposed by $N_2(A^3\Sigma_u^+)$, then our application of the NO titration established that the sum and ratio of nitrogen atoms and $A^3\Sigma_u^+$ molecular nitrogen were constant throughout this work.

Propene was introduced at various flow rates with its direction of flow opposed to that of the nitrogen stream (*cf.* Fig. 1). The latter procedure gives a small sharply defined flame represented by F in Fig. 1. Products were trapped at liquid nitrogen temperature and separated by vapor phase chromatography. Yields were determined, rather roughly, by a combination of manometric data with chromatogram peak areas and area factors determined with authentic materials in this work. Products were identified by their infrared spectra.

The molar radioactivity of each product was determined, after its isolation and purification, by counting a known quantity in a sandwich type flow counter by the method of Christman and his co-workers.[25,26]

Materials of Research.—Nitrogen was Matheson "prepurified" grade and was further purified as described below. Propene-1-^{14}C and -3-^{14}C were supplied by Research Specialties Co. while the 2-^{14}C isomer was from Nuclear Research Chemicals, Inc. Phillips Research Grade propene, which had been freed of air and water and which contained no other impurities detectable by gas chromatography, was used to dilute propene-1-^{14}C, -2-^{14}C, and -3-^{14}C to 0.25 μc./m*M*, 1.28 μc./m*M*, and 0.13 μc./m*M*, respectively. Undiluted propene-1-^{14}C and -2-^{14}C were analyzed for radioactive impurities by the methods used in analyzing reaction products. Propane and ethylene were the principal radioactive impurities, but their amounts and specific activities were too low to affect the results significantly. Nitric oxide (Matheson) was subjected to low temperature bulb-to-bulb distillation until no color was detectable in the gas phase.

Procedural Details.—Nitrogen, maintained at approximately atmospheric pressure by a mercury trap, was freed of O_2, H_2O, and CO_2 by passing it over copper turnings at 500°, cooling it in a water-jacketed tube, and trapping the condensables at liquid N_2 temperature. Flow rate was controlled at a capillary flow meter and measured at the exhaust side of the pump by means of a soap-bubble flow meter.

Active nitrogen was produced in a glow discharge generated with the full output of a Raytheon Model 10 microwave generator with a Type A medical antenna. Constancy of active nitrogen production in the unpoisoned system was achieved by pumping the system continuously when it was not in use and by conditioning the walls immediately before a run by passing active nitrogen until the afterglow intensities measured by photometers at P_1 and P_2 of Fig. 1 had fallen to constant values. The photometer at P_1 employed an A1P21 photomultiplier with a First Electronics Model 710-PR power supply and an RCA WV-84C d.c. microammeter. That at P_2 was an Eldorado Electronics Co. Model PH-200 equipped with a Model 200C 316 detector. It was established that interruption of the discharge for up to 1 min. did not

(1) Research supported by the Geophysics Research Directorate, Air Force Cambridge Research Laboratories, U. S. Air Force, under Contracts AF 19(604)5695 and AF 19(604)7272.

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