Stable Carbocations. CXXIII.[1] Relating to the Reported N Protonation of *N,N*-(Diisopropyl)carbamates. Evidence for O Protonation Followed by Rearrangement

GEORGE A. OLAH,* ANTHONY M. WHITE,[2] AND ALICE T. KU[3]

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106

Received March 10, 1971

Alkyl carbamates in FSO_3H–SO_2ClF solutions at low temperature (−80°) are exclusively O protonated. O-Protonated methyl and ethyl *N,N*-(diisopropyl)carbamates are shown to slowly rearrange upon raising the temperature to the thermodynamically more stable N-protonated species. It is suggested that the previous observation by Moodie of N protonation of ethyl *N,N*-(diisopropyl)carbamate was due to $=\overset{+}{O}H \rightarrow \overset{+}{N}H$ rearrangement following usual O protonation of the carbamate.

Protonated amides[4] and carbamates[5] have been observed in superacid solutions. The position of protonation has always been shown to be on the carbonyl oxygen atom. Armstrong, Farlow, and Moodie[6] found that ethyl *N,N*-(diisopropyl)carbamate, when dissolved in 90–98% sulfuric acid, or fluorosulfuric acid, gave an nmr spectrum at temperatures below 0° indicating N protonation through the presence of one nitrogen-bound proton. They, however, also found[6] that *N,N*-diisopropylacetamide and *N,N*-diisopropylbenzamide in 98% sulfuric acid gave no nmr peaks attributable to a nitrogen-bound proton. In both cases[6] separate methyl resonances for the two isopropyl groups were observed which were thought to be due to restricted rotation about the carbonyl carbon–nitrogen bond owing to protonation on oxygen. In both cases, however, no proton on oxygen was observed under the experimental conditions.

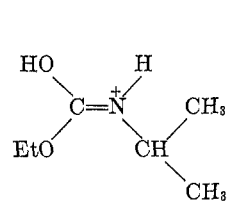
It was suggested by Moodie that the interesting and unexpected N protonation of ethyl *N,N*-(diisopropyl)-carbamate was due to steric reasons, the bulky substituents interfering with O protonation.

Due to our continuing study of protonation of heteroorganic compounds, we felt it of interest to reexamine the protonation of alkyl carbamates with bulky substituents on the nitrogen atom (such as isopropyl, *tert*-butyl) in the strong acid systems, FSO_3H–SO_2 and FSO_3H–SO_2ClF. It was also hoped that the increased acidity of the system would result in sufficiently slowing down proton exchange with the solvent at obtainable low temperatures to allow direct observation of protons (if any) on oxygen as well as on nitrogen atoms by pmr spectroscopy. The use of SO_2ClF as solvent in the FSO_3H acid system allows the temperatures of the solution to be lowered to as low as −120°. At this low temperature we found that protonation of methyl and ethyl *N,N*-(diisopropyl)carbamates takes place on the carbonyl oxygen atom. Upon slowly raising the temperature to −30°, rearrangement to the nitrogen-protonated carbamate takes place. For comparison, we have also studied ethyl *N*-(isopropyl)carbamate and ethyl *N*-(*tert*-butyl)carbamate.

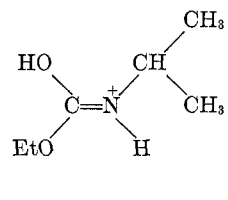
(1) Part CXXII: G. A. Olah, A. T. Ku, and J. A. Olah, *J. Org. Chem.*, **36**, 3582 (1971).
(2) National Institute of Health Postdoctoral Research Investigator, 1968–1969.
(3) National Institute of Health Predoctoral Research Investigator, 1967–1970.
(4) R. J. Gillespie and T. Birchall, *Can. J. Chem.*, **41**, 1481, 2642 (1963).
(5) G. A. Olah and M. Calin, *J. Amer. Chem. Soc.*, **90**, 401 (1968).
(6) V. C. Armstrong, D. W. Farlow, and R. B. Moodie, *Chem. Commun.*, 1362 (1968).

Results and Discussion

Ethyl *N*-(isopropyl)carbamate in FSO_3H–SO_2 at −80° gave an pmr spectrum showing an OH singlet at δ 9.73 indicating oxygen protonation. The N–H proton appeared as two sets of doublets at δ 6.90 and 6.60. This indicates two isomers (**1a** and **1b**) of the O-protonated



1a



1b

species to be present due to restricted rotation about the carbon–nitrogen bond. The pmr spectrum showed no changes even then solutions were heated up to −20° No indication for N protonation was obtained.

Methyl *N,N*-(diisopropyl)carbamate in FSO_3H–SO_2 at −80° gave a pmr spectrum (Figure 1) indicating about 50% oxygen protonation and 50% nitrogen protonation. Both the OH and NH protons are observed (OH at δ 9.25, NH at δ 7.30) at this temperature. The pmr spectrum also showed a singlet at δ 4.26 for the CH_3O protons and multiplets at δ 4.23 for the methine proton and two doublets for the isopropyl methyls in the nitrogen- and oxygen-protonated species respectively at δ 1.50 and 1.40. At −50°, the CH_3O peaks are shown to be two singlets, one each, for nitrogen- and oxygen-protonated species. At this temperature the oxygen-protonated species gradually rearranges to the nitrogen-protonated species. This is evident by the increase of the peak areas of the nitrogen-protonated species at δ 4.20 and 1.46 and the decrease of the peak intensity of the oxygen-protonated species at δ 4.25 and 1.36 (Figure 2). At −30°, the rearrangement goes to completion showing only the N-protonated species.

Ethyl *N,N*-(diisopropyl)carbamate, when dissolved in FSO_3H–SO_2 solution at −80°, gave an nmr spectrum (Figure 3 A) showing an OH proton at δ 9.20 and giving no indication for a nitrogen-bounded proton at this temperature. At −100°, the proton exchange is slow and the OH resonance sharpens. At −60°, the oxygen-protonated species, however, slowly rearranges to the nitrogen-protonated species. This process goes faster and even to completion at higher temperature, such as −30°. At −30°, the methylene quartet appears at δ 4.66, the methine multiplet at δ 4.10, the methyl triplet at δ 1.46, and the methyl doublet of the isopropyl

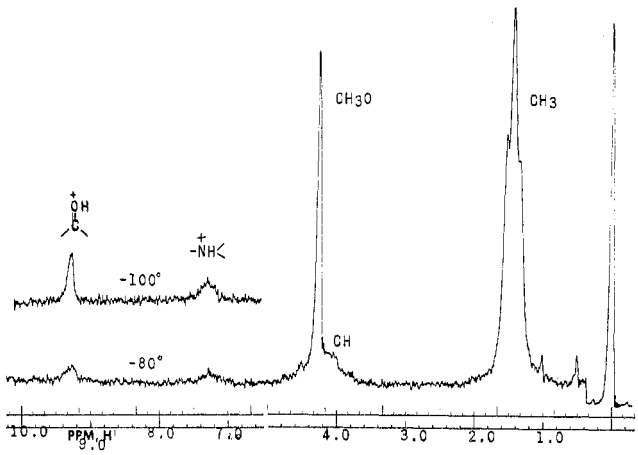


Figure 1.—Protonation of methyl *N,N*-(diisopropyl)carbamate in FSO_3H–SO_2 at −80°.

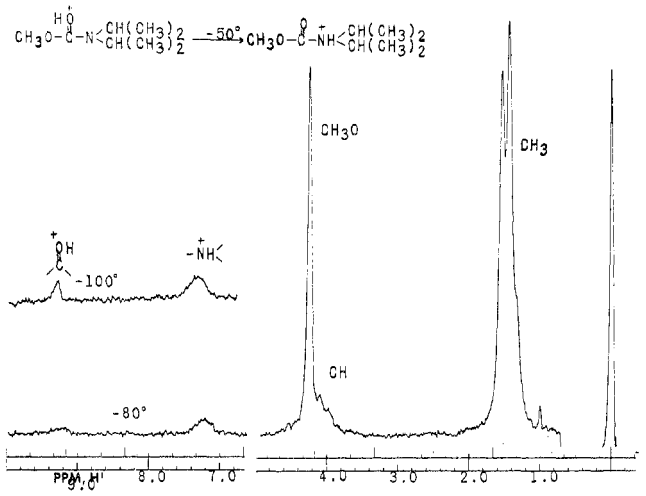


Figure 2.—Heating the solution shown in Figure 1 to −50° and recording the spectra by cooling to −80 and −100°, respectively, showed isomerization of O-protonated species to the more stable N-protonated carbamate.

group at δ 1.46. The proton on nitrogen is observed at this temperature. However, on cooling the solution back to −80° or below, the nmr spectrum (Figure 3 B) showed a broad N–H singlet at δ 7.20, and no OH absorption could be observed, indicating the oxygen-protonated species went completely to the N-protonated species and the process is not reversible.

Protonated ethyl *N*-(*tert*-butyl)carbamate in FSO_3H–SO_2 solution could not be observed. Cleavage reaction occurs even at temperatures as low as −80° to give the *tert*-butyl cation and protonated ethyl carbamate (which had previously been reported).[5] In FSO_3H–SbF_5 solution, the formed *tert*-butyl cation reacts slowly with the system to give unidentified products. In 1:1 *M* FSO_3H–SbF_5–SO_2 solution, the *tert*-butyl cation formed is stable and the nmr spectrum gave resonances for the carbonyl oxygen of the protonated ethyl carbamate and the *tert*-butyl cation.

Conclusion

In strong acid solutions at low temperature, carbonyl oxygen atoms of carbamic acid esters are kinetically first protonated. However, carbamates with two iso-

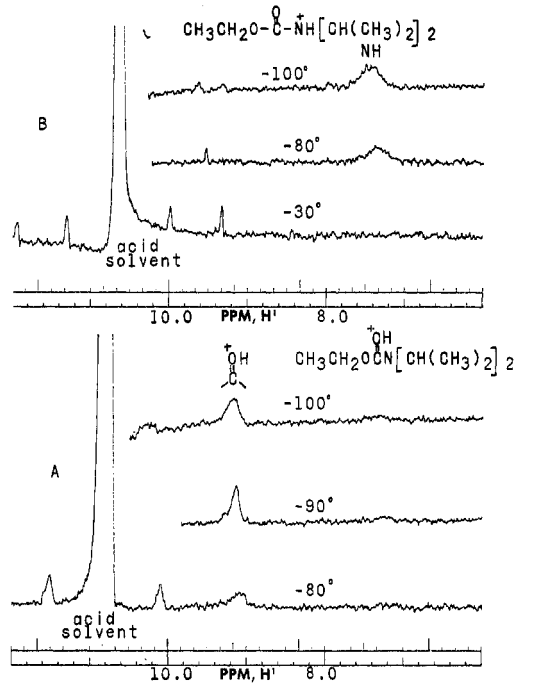
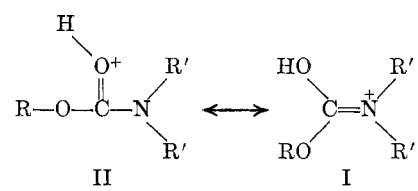


Figure 3.—(A) The OH and NH absorptions of the pmr spectrum of protonated ethyl *N,N*-(diisopropyl)carbamate at −80 to −100° showing O protonation. (B) The OH and NH absorptions of the pmr spectrum of protonated ethyl *N,N*-(diisopropyl)-carbamate after the sample has been treated to −30° indicating $=\overset{+}{O}H \rightarrow -\overset{+}{N}H<$ isomerization.

propyl groups substituted on nitrogen, such as methyl *N,N*-(diisopropyl)carbamate and ethyl *N,N*-(diisopropyl)carbamate, rearrange slowly to the N-protonated species, upon raising the temperature. It is evident that in protonated carbamic acid esters with bulky substituents on nitrogen the stabilization due to the contribution of I is very small. Hence they rearrange to the thermodynamically more stable N-protonated species.



R′ = isopropyl

We are presently studying the question of O *vs.* N protonation of amides in solvents of varying acid strength and will report our results separately.

Experimental Section

Materials.—All the carbamates used in this study were prepared[7] by reacting the related alkyl chloroformates with amines.

Nmr Spectra.—Varian Associates Model A-56/60A spectrometer with a variable-temperature probe was used for all spectra.

Preparation of Solutions.—Samples of protonated carbamates were prepared by dissolving approximately 1.5 ml of HSO_3F in an equal volume of SO_2 (or SO_2ClF) and cooling to −78°. The carbamate (approximately 0.2 ml) was dissolved in 1 ml of SO_2

(7) R. H. McKee, *Amer. Chem. J.*, **42**, 22 (1909).

(SO_2ClF) cooled to −78° and with vigorous agitation was slowly added to the acid solution. The acid was always in large excess as indicated by the large acid peak at δ 10.6–10.9.

Registry No.—Methyl *N,N*-(diisopropyl)carbamate, 31603-49-3, 31585-09-8 (protonated derivative); ethyl *N,N*-(diisopropyl)carbamate, 20652-39-5, 31585-10-1 (protonated derivative).

Acknowledgment.—Support of this work by a grant from the National Institutes of Health is gratefully acknowledged.

A Kinetic Study of the Nitrogen-15 Exchange of Para-Substituted Benzamides with Ammonia[1a]

CHARLES R. EVERLY[1b] AND ARTHUR FRY*

Department of Chemistry, University of Arkansas, Fayetteville, Arkansas 72701

Received January 20, 1971

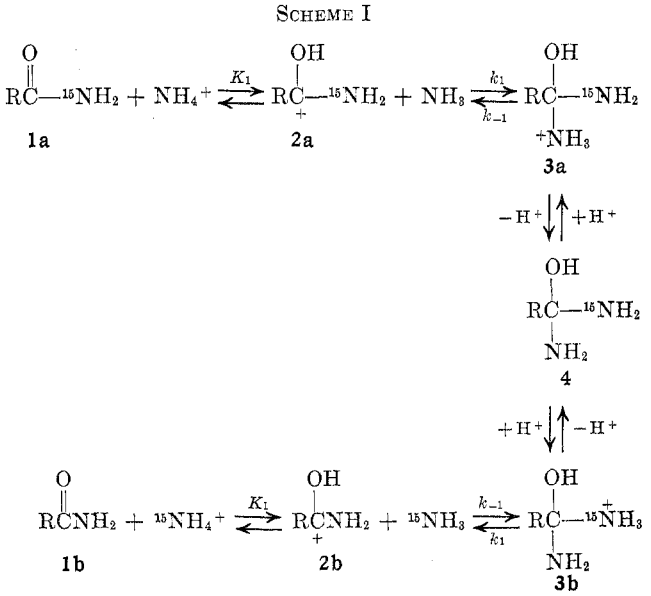
A kinetic study has been carried out on the nitrogen-15 exchange of para-substituted benzamides-^{15}N with liquid ammonia as a function of temperature and catalyst concentration. Neither a neutral nor a base-catalyzed exchange pathway is detectable under the conditions employed. The relative rates for the acid-catalyzed (ammonium chloride catalyzed) exchange of the para-substituted benzamides at 40° in the presence of 3 *M* ammonium chloride are NO_2:Cl:H:CH_3:CH_3O = 8.78:2.13:1.00:0.55:0.44. Hammett plots are linear with $\rho = +1.25$. The kinetic data indicate a first-order dependence of the exchange rate on the ammonium ion concentration. All of the reactions exhibit pseudo-first-order kinetics. The trends in the kinetic data are what would be expected for an exchange mechanism involving a rapid preequilibrium protonation of the amide followed by a slow rate-determining addition of ammonia to form a tetrahedral intermediate, which can revert to reactants or decompose to products depending upon which nitrogen is lost.

Nitrogen-15 labeled benzamide and other amides are known[2-4] to undergo isotopic exchange with ammonia in liquid ammonia solution catalyzed by ammonium ion. No exchange is observed in the absence of a catalyst except at very high temperatures.[2,3] At 20° in the presence of 3.33 molar ammonium chloride, Heyns, Brockmann, and Roggenbuck[2] observed that *p*-nitrobenzamide, benzamide, and *p*-methoxybenzamide underwent 29.7 ± 2.0, 4.2 ± 2.0, and 1.8 ± 2.0% exchange, respectively, after 7 days. They determined the rate constant for exchange of *p*-nitrobenzamide at 20° in the presence of 3.33 *M* ammonium chloride as 1.27×10^{-8} sec^{-1}. In a related study Heyns, Grutzmacher, and Roggenbuck[3] determined the activation energy for the liquid ammonia ammonolysis of *p*-nitrobenzamide to be 17.0 ± 0.5 kcal/mol.[5] They also noted a continual increase in exchange rate with increased ammonium chloride concentration up to about 12 mol/l.

Brodskii and coworkers[4] have also made a study of the nitrogen exchange between ammonia enriched with nitrogen-15 and various compounds dissolved in the ammonia. The exchange proceeds (at 180°)[6] in $-C(=X)-NH_2$ (X = O, S, NH), amino acids, and urea. According to these workers, the relative rates of exchange in a series of amides are proportional to the electrophilicites of the carbon atoms to which the nitrogen is attached. Electron donor groups in meta and para positions in aromatic amides hinder the exchange, while electron acceptor groups accelerate it.

Information about nitrogen exchange reactions of aromatic amides is, at best, qualitative and incomplete. We now wish to present the results of a kinetic study of the effect of para substituents on the rate of the acid- and base-catalyzed isotopic exchange between benzamides-^{15}N and liquid ammonia. If the aminolysis of benzamides with an acid catalyst is analogous to the acidic hydrolysis of amides, as suggested by Heyns and coworkers,[2,3] then a similar mechanism may be postulated involving attack by an ammonia molecule on the conjugate acid of the amide as the rate-determining step, shown in Scheme I. The tetrahedral intermediate

SCHEME I



(1) (a) Supported by U. S. Atomic Energy Commission Contract AT-(40-1)-3234; from the Ph.D. Dissertation of C. R. E., University of Arkansas, Fayetteville, Ark., 1970; presented in part at the Combined Southeast-Southwest Regional Meeting of the American Chemical Society, New Orleans, La., Dec 1970. (b) NSF Trainee, 1966–1969.

(2) K. Heyns, R. Brockmann, and A. Roggenbuck, *Justus Liebigs Ann. Chem.*, **614**, 97 (1958).

(3) K. Heyns, H. F. Grutzmacher, and A. Roggenbuck, *Chem. Ber.*, **93**, 1488 (1960).

(4) A. I. Brodskii, N. A. Vysotskaya, I. I. Kukhtenko, G. P. Miklukhin, L. L. Strizhak, and L. V. Sulima, *Izotopy Izluch. Khim., Tr. Vses. Nauch. Tekh. Konf. Primen. Radioaktiv. Stabil. Izotop. Izluch. Nar. Khoz. Nauke, 2nd*, 20 (1957); L. L. Gordienko and A. I. Brodskii, *Dokl. Akad. Nauk SSSR*, **134**, 595 (1960); L. L. Strizhak, S. G. Demidenko, and A. I. Brodskii, *ibid.*, **124**, 1089 (1959).

(5) Instead of determining the extents of exchange at a series of times and calculating the rate constants from the best straight lines, they calculated rate constants from the amount of exchange only at 120 hr for each temperature or catalyst concentration studied.

(6) Ammonia has a critical temperature of 132°; hence reactions above 132° are not liquid ammonia ammonolyses but vapor phase reactions.