change. We showed this by transfer of saturation (Forsen–Hoffman) experiments in which preirradiation was at the water NMR frequency rather than that of the indole proton. A delay of about 0.2 sec was used between preirradiation and observation; this delay is short compared to the water T_1 but long enough to substantially decrease interference from a water signal which is stimulated by the preirradiation pulse (this water signal was also suppressed by a spoil pulse). If chemical exchange dominates the indole proton's apparent relaxation, then its resonance should disappear because the saturation of H_2O will be transmitted via exchange.[5] Furthermore, the indole resonance should reappear when the preirradiation frequency is displaced slightly from exact H_2O resonance. This was indeed observed at pH 2.2, where the apparent rate is so fast that exchange dominates. At pH 4.7, however, the indole resonance decreased by only about 20% when the water resonance was presaturated in the same way.

The observed rate R_1, of about 0.7 sec^{-1} at pH 4.7, is the sum of several rates

$$R_1 = R_x + R_n + R_s \tag{1}$$

where the right-hand terms are, respectively, contributions from chemical exchange with water, nitrogen intramolecular relaxation, and solvent proton intermolecular relaxation. We neglect relaxation due to other tryptophan protons.

For the transfer of saturation experiment, if the solvent magnetization is assumed always to be zero because of its saturation by the preirradiation, the indole NH proton magnetization M has the time derivative

$$\mathrm{d}M/\mathrm{d}t = -(M - M_0)R_N - \mathrm{M}R_x - (M - 1.5M_0)R_s \tag{2}$$

Here M_0 is the equilibrium indole proton magnetization, and we assume that the Overhauser enhancement of indole NH by solvent saturation is 1.5 as expected[6] for like-nuclei in the fast correlation-time limit.

The experiment is performed by saturating the protons for a time long enough for the indole proton magnetization to reach a steady state value, for which $\mathrm{d}M/\mathrm{d}t = 0$. The magnitude of M shortly after such a pulse is monitored by the observation pulse and is $0.8M_0$ at pH 4.7, as mentioned above. If we set $M = 0.8M_0$ and $\mathrm{d}M/\mathrm{d}t = 0$ in eq 1 and 2, we obtain limits on the contribution of R_x to the total relaxation. If $R_s \ll R_N$ then $R_x \cong 0.2R_1$. If $R_s \ll R_N$ then $R_x \cong (7/15)R_1$.

A slightly better limit can be set by studying the apparent relaxation time as a function of solvent H/D ratio. If such effects as the influence of the solvent isotope ratio on either molecular tumbling or on the proton–proton exchange rate are neglected, then R_s is proportional to the H/D ratio whereas R_N is not. We compared the apparent rate R_1 in 40 and 80% H_2O at pH 5. There was no difference in R_1 within our accuracy limits (±10%), suggesting that R_1 is dominated by relaxation due to the nitrogen nucleus. This is also expected theoretically, based on reasonable estimates for internuclear distances and molecular tumbling rates. Therefore, the exchange rate at pH 4.7 is estimated to be 0.15–0.25 sec^{-1}. Of this, 0.05 sec^{-1} presumably comes from the sum of the acid and base catalyzed exchanges estimated earlier.

We hope to extend this work by studying modified tryptophan and peptides containing tryptophan in order to elucidate the mechanisms of the exchange. The present work was carried out on unbuffered solutions, but a survey of several buffers reveals no significant increase in catalysis up to 0.1 mM buffer concentration. None is expected on the basis of simple arguments based on diffusion-controlled rates of reaction and estimates of the ionization constants of the indole group. We postpone a discussion of these points to a later paper.

Acknowledgments. This research was supported by U.S. Public Health Service Grant GM20168 and by National Science Foundation Grants GU3852 and GP37156 for equipment. We thank Sara Kunz who built much of the specialized modification of the spectrometer.

References and Notes

(1) Contribution No. 993 from the Graduate Department of Biochemistry, Brandeis University, Waltham, Mass.

(2) See, for example, R. S. Molday and R. G. Kallen, *J. Am. Chem. Soc.*, **94**, 6739 (1972); B. McConnell and P. C. Seawell, *Biochemistry*, **12**, 4426 (1973), and reference therein.

(3) J. D. Glickson, W. D. Phillips, and J. A. Rupley, *J. Am. Chem. Soc.*, **93**, 4031 (1971).

(4) A. G. Redfield and R. K. Gupta, *Adv. Magn. Reson.*, **5**, 82 (1971).

(5) See, for example, A. G. Redfield and R. K. Gupta, *Cold Spring Harbor Symp., Quant. Biol.*, 405 (1971); J. D. Glickson, J. Dadok, G. R. Marshall, *Biochemistry*, **13**, 11 (1974).

(6) J. H. Noggle and R. E. Schirmer, "The Nuclear Overhauser Effect", Academic Press, New York, N.Y., 1971, p 16.

(7) Also at the Physics Department and the Rosenstiel Basic Medical Sciences Research Center, Brandeis University, Waltham, Mass.

Susan Waelder, Lana Lee, Alfred G. Redfield*[7]
Department of Biochemistry, Brandeis University
Waltham, Massachusetts 02154

Received January 8, 1975

Electrophilic Reactions at Single Bonds. XVIII.[1] Indication of Protosolvated de facto Substituting Agents in the Reactions of Alkanes with Acetylium and Nitronium Ions in Superacidic Media

Sir:

Brouwer and Kiffen recently reported on hydride abstraction by the acetyl cation (acetylium ion)[2] and also by protonated aldehydes and ketones,[3] from alkanes including isobutane. These reactions are of substantial interest as far as mechanistic aspects of hydrogen transfer from alkanes to electrophiles are concerned but also raise some puzzling questions.

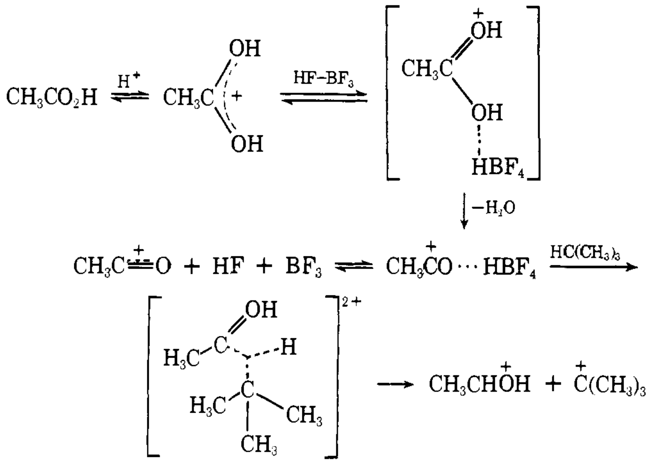
Brouwer and Kiffen carried out their studies always using strongly acidic solvent media, generally $HF\text{-}BF_3$, with acetic acid serving as the source of the acetyl cation. In control experiments they proved that the alkanes studied, such as isobutane, show no reactivity with the acid solvent, which thus is not responsible for the observed hydrogen transfer. However, the reported reaction

$$\begin{array}{ll} \underset{152}{CH_3CO^+} + \underset{-31.3}{(CH_3)_3CH} \longrightarrow & \\ & \underset{-39.8}{CH_3CHO} + \underset{169}{(CH_3)_3C^+} \quad \Delta\Delta H^\circ = 8.5\ \text{kcal/mol} \end{array}$$

is endothermic by 8.5 kcal/mol (in the gas phase[4]) and thus is energetically unfavorable. Furthermore, Brouwer never observed acetaldehyde, only secondary products derived from protonated acetaldehyde, such as ethyl acetate (indicating hydride abstraction from isobutane to protonated acetaldehyde giving ethyl alcohol and esterification).

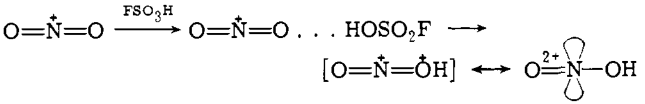
We would like to report that in our hands stable acetylium salts in aprotic media (as well as other related acylium salts, which were prepared and studied extensively in our work since 1954[5]) showed no ability to abstract hydrogen from any of the studied alkanes, including isobutane. Extensive studies were carried out with solutions of stable acyl salts, particularly acetylium hexafluoroantimonate in a variety of aprotic solvents such as SO_2, SO_2ClF, AsF_3, and methylene chloride. We also tried reactions in an excess of the alkanes themselves and other hydrocarbon media, such as cyclohexane, with no success. Thus we must face the question of how to explain the experimental observation of the absence of any reaction with stable acetyl salts in aprotic media in our work, in contrast to the hydride transfer to acetyl cation reported by Brouwer and Kiffen.

Our previous studies relating to the formyl cation, CHO^+, led to the rather surprising observation that it gives very rapid hydrogen exchange involving the methine hydrogen.[6] Under no experimental conditions could the static ion be observed, even in solutions where the presence of the equilibrating ion is indicated by both ^{13}C NMR studies and chemical reactivity. Our conclusion was that the nonbonded electron pairs on oxygen in the formyl cation interact further with the superacidic solvent system, leading to a highly active dipositive species which then eliminates the methine proton. This observation suggests an explanation for the rather unusual behavior of the acetylium ion in superacidic media, as contrasted with its behavior in aprotic solvents, that the de facto reactive species is not the acetylium ion itself but its protosolvated form. The acetylium ion is considered to be hydrogen bonded in the superacidic solvent through the nonbonded oxygen electron pairs. Hydrogen bonding helps to polarize the -C≡O bond and thus increases the electrophilic reactivity of the acetylium ion. In the limiting case, the hydrogen bonded species can lead toward the formation of a protosolvated, highly reactive, dicationic species, which is not considered stable itself, but would form only in interaction with the hydrocarbon substrate (isobutane) via the usual front side σ-bond attack



In this reaction the immediate product formed is protonated acetaldehyde and not acetaldehyde itself (which could be subsequently protonated). We consider this the only thermodynamically feasible reaction and conclude that there is no simple hydride transfer between the acetyl cation or other acyl cations and alkanes, such as isobutane. These reactions take place only in acidic media by complexing of the carbonyl oxygen of the acylium ions by either a Lewis or Brønsted acid.

Similar behavior to the protosolvated acetylium is also observed in the case of the nitronium ion in superacidic media. We have previously found[7] that nitronium salts (such as $NO_2^+BF_4^-$ or $NO_2^+PF_6^-$) show no (or minimal) reactivity toward methane, in strictly aprotic media. However, in fluorosulfuric acid or HF-BF_3 solution nitration takes place giving nitromethane. The effect of the superacidic solvents seems to be to protosolvate the nitronium ion. The protonitronium ion (NO_2H^{2+}), if completely formed, would be a dicationic, unstable, and consequently highly reactive species. Simonetta,[8] indeed, carried out calculations on this dication and found no energy minimum comparable to the nitronium ion (although in the gas phase dications are generally more unfavorable, due to charge-charge repulsion, than in the condensed state, where solvation can help to remove excess charge).



$$O{=}\overset{+}{N}{=}O \xrightarrow{FSO_3H} O{=}\overset{+}{N}{=}O\ .\ .\ .\ HOSO_2F \longrightarrow [O{=}\overset{+}{N}{=}\overset{+}{O}H] \longleftrightarrow O\overset{2+}{=}N{-}OH$$

An indication that the nitronium ion is hydrogen bonded by fluorosulfuric acid is obtained from ir spectra in arsenic trifluoride solution (a suitable solvent for these studies). The HO stretching frequency of the acid in AsF_3 is shifted from about 3300 to 3265 cm^{-1} and is also broadened upon addition of about 10% $NO_2^+PF_6^-$ to the system. At the same time the N-O stretching frequency at 2380 cm^{-1} remains practically unchanged, indicating no change in the force constant for the NO bond.

Finally it should be emphasized that the stability of intermediates and their reactivity are not parallel, but opposing properties. It was previously assumed, according to Ingold,[9] that the existence of a reactive intermediate is convincingly established only if it can be directly observed or even isolated (such as nitronium, nitrosonium, or acylium salts). With stable, isolable intermediates the question must be raised, however, whether these are indeed the reactive forms involved in reactions in solution. Acylium and nitronium salts themselves may be only of relatively limited electrophilic reactivity as polarizable electrophiles. They will readily react with relatively strong electron donors such as n- and π-donors, which can polarize and eventually displace a bonding π-electron pair onto oxygen, but apparently are not capable of reacting with pure σ-donors, such as methane and higher alkanes. In the latter case, it is suggested that acid solvated, highly reactive species are the de facto reagents.

Acknowledgment. Support of our work by the National Institutes of Health, the National Science Foundation (relating to acylation), and the US Army Office of Research and the Picattiny Arsenal (relating to nitration) is gratefully acknowledged. We also thank Professor E. M. Arnett and Dr. D. M. Brouwer for stimulating discussions.

References and Notes

(1) Part XVII. G. A. Olah, R. Renner, P. Schilling, and Y. K. Mo, *J. Am. Chem. Soc.*, **95**, 7686 (1973).

(2) D. M. Brouwer and A. A. Kiffen, *Recl. Trav. Chim. Pays-Bas*, **92**, 689 (1973).

(3) D. M. Brouwer and A. A. Kiffen, *Recl. Trav. Chim. Pays-Bas*, **92**, 809, 906 (1973).

(4) (a) Based on heats of formation data from "Ionization Potentials, Appearance Potentials, and Heats of Formation of Gaseous Positive Ions", National Bureau of Standards, NSRDS-NBS 26 (1969), and, in the case of $(CH_3)_3C^+$, W. Tsung, *J. Phys. Chem.*, **76**, 143 (1972), as well as F. P. Lossing and G. P. Semeluk, *Can. J. Chem.*, **48**, 955 (1970). (b) Since submission of our manuscript, Professor J. L. Beauchamp informed us about improved heats of formation for CH_3CO^+ (159 kcal/mol) and $C^+(CH_3)_3$ (167 kcal/mol). These data would make the reaction more thermoneutral (in the gas phase) but will not affect the overall argument outlined.

(5) For a review, see G. A. Olah, A. Germain, and A. M. White in "Carbonium Ions", Vol. V., G. A. Olah and P. v. R. Schleyer, Ed., Wiley-Interscience, New York, N.Y., in press, and references given therein.

(6) G. A. Olah, K. Dunne, Y. K. Mo, and P. Szilagyi, *J. Am. Chem. Soc.*, **94**, 4200 (1972).

(7) G. A. Olah and H. C. Lin, *J. Am. Chem. Soc.*, **93**, 1259 (1971).

(8) P. Cremaschin and M. Simonetta, *Theor Chim. Acta*, **34**, 175 (1974).

(9) C. K. Ingold in "Structure and Mechanism in Organic Chemistry," 2nd ed, Cornell University Press, Ithaca, N.Y., 1969.

George A. Olah,* Alain Germain
Henry C. Lin, David A. Forsyth
Department of Chemistry, Case Western Reserve University
Cleveland, Ohio 44106

Received January 6, 1975