complicates the mechanistic interpretation.

Anion Effects. The effects of substitution of acetate for chloride on the kinetic behavior of the catalyzed reactions were examined with $Lau_{12}PEI$ and $Lau_{12}Im_{10}PEI$.[23] As for the catalytic constants, that of the hydroxide path (k_1'/K_c') was not affected significantly. The effects of acetate ion on k_w' have been attributed to the general base assistance by the bound acetate ion (see previous section).

In regard to the binding of **1**, K_m for $Lau_{12}Im_{10}PEI$ is lowered significantly when chloride is replaced by acetate, but binding to $Lau_{12}PEI$ is unaffected.[24] The different behavior of the two polymers is also seen in the ionization of the bound substrate. In $Lau_{12}PEI$, pK_a' is affected significantly. In $Lau_{12}Im_{10}PEI$, however, pK_a' is not changed appreciably, but the ionization behavior of CS becomes abnormal (α = 1.8) when chloride is substituted by acetate. These specific anion effects cannot be easily explained until more details are available on their disposition in the matrix of the poly(ethylenimines).

(23) Even when acetate ion (0.02 M) was used as the anion of the supporting electrolyte, a small amount of chloride ion (up to 5 mM) was present in the reaction mixture because of its inherent presence in the polymer preparations. However, the pH profile of k_{cat} illustrated (curve B of Figure 2 or curve B of Figure 3) was obtained in solutions with a fixed amount of chloride ion.

(24) Anion effects have been also studied in the decarboxylation of 6-nitrobenzisoxazole-3-carboxylate catalyzed by $Lau_{25}Me_6PEI$ or $Lau_{25}Et_6PEI$ (Suh, J.; Klotz, I. M. *Bioorg. Chem.* **1979**, *8*, 283). In this reaction, k_{cat} was not affected, but binding of the substrate was facilitated by the anion of the supporting electrolyte, in the order azide < chloride < acetate.

Conclusion

It is evident that poly(ethylenimine) polymers can accelerate hydrolysis in an activated amide such as **1**. The effects observed are largely due to increased local concentrations of hydroxide ion and of substrate. The intrinsic reactivity of the OH^- ion, however, does not appear to be changed, evidently because it is situated at the periphery of the hydrophobic domain rather than within the apolar cluster. It is possible, therefore, that if nonprotic, polar substituents could be built into the apolar cluster, a desolvated OH^- ion could more readily approximate the substrate to form the tetrahedral intermediate, T. This interpretation suggests alternative modifications of poly(ethylenimines) that might generate more effective catalysts of amide hydrolysis.

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Registry No. 1, 89165-27-5.

α-Nitrodiarylmethyl Cations[1]

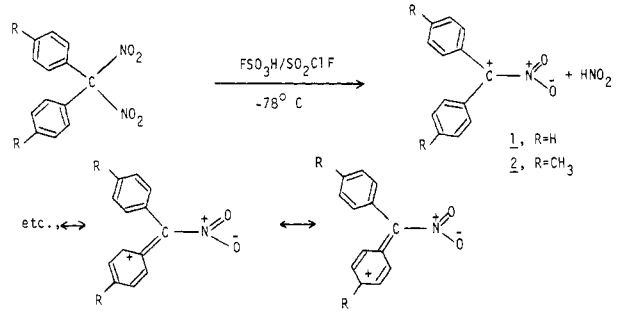
George A. Olah,* G. K. Surya Prakash, Massoud Arvanaghi, V. V. Krishnamurthy, and Subhash C. Narang

Contribution from the Hydrocarbon Research Institute and Department of Chemistry, University of Southern California, Los Angeles, California 90089. *Received October 11, 1983. Revised Manuscript Received December 8, 1983*

Abstract: The α-nitrodiphenylmethyl and the α-nitrodi-*p*-tolylmethyl cations **1** and **2**, the first α-nitro-substituted carbocations under long-lived conditions, have been prepared by the ionization of the corresponding α,α-dinitrodiarylmethanes in FSO_3H/SO_2ClF at −78 °C. ^1H, ^{13}C, and ^{15}N spectroscopic data are in accord with the assigned structures. The ^{13}C NMR chemical shift data of **1** are in good agreement with those observed for α-(trifluoromethyl)diphenylmethyl cation **3** and α-benzoyldiphenylmethyl cation **5**, indicating the similar electron-withdrawing nature of nitro, trifluoromethyl, and acyl groups adjacent to a carbocationic center. Ions **1** and **2** give their respective protonated ketones upon raising the temperature. Attempts to prepare the 9-nitro-9-fluorenyl cation from 9,9-dinitrofluorene gave instead directly the protonated fluorenone.

Recently considerable effort has been expended[2-7] to understand the effects of strongly electron-withdrawing substituents on solvolytic reactions leading to electron-deficient intermediates. Substituents that have been experimentally[2-7] and theoretically[8] pursued include CF_3, CN, $-C(=O)-$, NO_2 and others. However, thus far the effect of a nitro group α to a carbocationic center under long-lived stable ion conditions has not been explored. More recently under stable ion conditions we have shown[9] that α-cya-

Scheme I



(1) Considered Stable Carbocation. 250. Arvanaghi, M.; Prakash, G. K. S.; Krishnamurthy, U. V.; Narang, S. C.; Olah, G. A. "Abstracts of Papers", 186th National Meeting of the American Chemical Society, Washington, DC, Aug 1983; American Chemical Society: Washington, DC, 1983; ORGN 97. Abstract No. 97. For part 249 see: Olah, G. A.; Prakash, G. K. S.; Saunders, M. *Acc. Chem. Res.* **1983**, *16*, 440.

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Table I. ^1H, ^{13}C, and ^{15}N NMR Data of Observed Carbocations

carbocation	^1H, δ[a]	^{13}C, δ[b]	^{15}N, δ[c]
1	H_p = 8.58 (1 H, t, J = 7.3 Hz)	$C^+\alpha$ = 189.1	363.6
		C_p = 152.2	
	H_o = 8.22 (2 H, br)	C_o = 145.3	
	H_m = 8.08 (2 H, br)	C_m = 133.3	
		C_i = 127.2	
2		$C^+\alpha$ = 186.0	
		C_p = 170.4	
		C_o = 144.3	
		C_m = 135.6	
		C_i = 126.1	
		CH_3 = 25.0	
6	H_p = 8.50 (1 H, t, J = 7.1 Hz)	$C^+\alpha$ = 198.6	
		C_p = 150.3	
	H_o = 8.23 (2 H, d, J = 6.9 Hz)	C_o = 143.4	
		C_m = 132.9	
	H_m = 8.02 (2 H, d-d)	C_i = 130.5	
3	H_p = 8.55 (1 H, t, J = 6.6 Hz)	$C^+\alpha$ = 189.6 ($^2J_{C-F}$ = 32.4 Hz)	
		C_p = 151.4	
	H_o & H_m = 8.12-7.98 (4 H, m)	C_o = 146.4	
		C_m = 131.8	
		C_i = 136.6	
		CH_3 = 120.5 ($^1J_{C-F}$ = 281.9 Hz)	

[a, b] Chemical shifts are in ppm from external capillary tetramethylsilane. [c] Chemical shifts are from anhydrous ammonia.

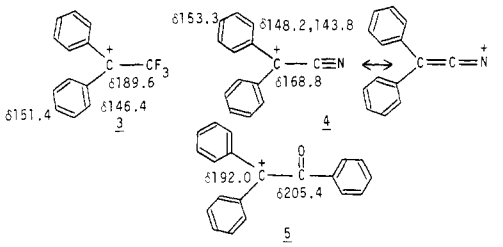
nodiarylmethyl cations do have significant mesomeric nitrenium ion character despite competitive aryl ring charge delocalization. The effect of an acyl group α- to a carbocationic center has been recently explored.[10,11] We now wish to report the preparation and ^1H, ^{13}C, and ^{15}N NMR spectroscopic characterization of α-nitrodiphenylmethyl and α-nitrodi-*p*-tolylmethyl cations **1** and **2**, the first stable long-lived α-nitro-substituted carbocations.

Results and Discussion

α,α-Dinitrophenylmethane, α,α-dinitrodi-*p*-tolylmethane, and 9,9-dinitrofluorene were prepared by the oxidation of their corresponding oximes with dinitrogen tetraoxide following the procedure of Frojmovic and Just.[12] The 5% ^{15}N-enriched α,α-dinitrodiphenylmethane was prepared by the oxidation of 15% ^{15}N-enriched benzophenone oxime with N_2O_4. Ionizations of these precursors to the corresponding α-nitro carbocations were carried out in FSO_3H/SO_2ClF either at −78 °C or −120 °C (Scheme I). For comparison the α-(trifluoromethyl)diphenylmethyl cation **3** was also prepared by the ionization α-(trifluoromethyl)diphenylmethanol in $FSO_3H:SbF_5/SO_2ClF$ at −78 °C.[13] The chemical shift parameters of the observed carbocations are listed in Table I.

Dissolving α,α-dinitrodiphenylmethane in FSO_3H/SO_2ClF at −78 °C resulted in a deep red solution, whose 200-MHz ^1H NMR spectrum shows three sets of absorptions (Table I) in the ratio 1:2:2 at δ 8.58 (1 H, t, J = 7.3 Hz), 8.22 (2 H, broad), and 8.08 (2 H, broad).[14] The 20-MHz ^{13}C NMR spectrum at −80 °C showed absorptions at δ 189.1 (s), 152.2 (d), 145.3 (d), 133.3 (d), and 127.2 (s). The ^1H and ^{13}C NMR data show significant deshieldings and are in accord with the formation of the α-nitrodiphenylmethyl cation **1**.[15] There is substantial charge dispersal into the aromatic ring in cation **1** involving *o*- and *p*-quinoidal resonance forms.

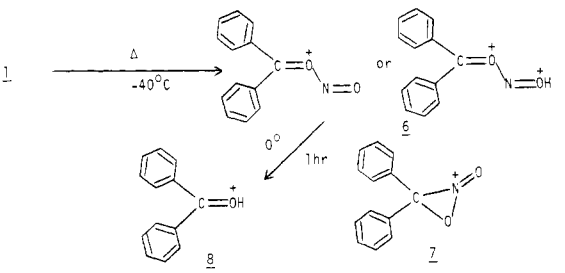
The observed ^{13}C NMR chemical shifts in **1** were also compared to those obtained for the α-(trifluoromethyl)diphenylmethyl cation **3** generated from α-(trifluoromethyl)diphenylmethanol[13] in $FSO_3H:SbF_5/SO_2ClF$ at −78 °C, indicating the similar electron-withdrawing nature of the substituents. In contrast, in the case of the previously reported[9] cyano analogue (i.e. α-cyanodiphenylmethyl cation **4**), the electron-withdrawing nature of the



cyano group is significantly diminished by the mesomeric nitrenium ion resonance, which is clearly indicated by the observed ^{13}C NMR chemical shift of the cationic center. The C^+ chemical shift of **1** is also comparable to that observed in α-benzoyldiphenylmethyl cation (**5**).[11]

To ascertain the nature of the nitro substituent in **1**, we prepared the ~5% ^{15}N-enriched ion from ^{15}N-enriched α,α-dinitrodiphenylmethane. In the ^{15}N NMR spectrum of **1** the nitro group was observed at δ 363.6, a chemical shift characteristic for a nitro group attached to a sp^2 center (as observed in nitroarenes).[16] In fact nitrobenzene shows that ^{15}N chemical shift at δ 370.3. The ^{15}N chemical shifts of the nitro group in **1** are shielded by 130 ppm from that observed in the progenitor. In the ionic solution of **1** along with the nitro peak, an absorption for the nitrosonium ion at δ −0.4 was also observed. The nitronium ion (NO^+) is formed during the ionization of the nitro group in the FSO_3H/SO_2ClF medium.

Raising the temperature of the solution of **1** to −40 °C for 30 min results in an irreversible rearrangement to a new species whose spectral properties are consistent with O-nitrosated benzophenone (or its protonated form) **6**. The rearrangement probably occurs



through the intermediacy of *N*-oxooxaziridine structure **7**.[17] Warming the solution further at 0 °C results, again, in an irreversible fragmentation via loss of NO^+ to protonated benzophenone **8**.[18a] Attempts to prepare **6** by nitrosating benzophenone with either NO^+BF_4 or NO^+PF_6 in SO_2 at various temperatures were, however, unsuccessful.

Similar ionization of the α,α-dinitrodi-*p*-tolylmethane in FSO_3H/SO_2ClF at −78 °C gave a dark red solution whose ^{13}C NMR spectrum showed six absorptions indicating the formation of the α-nitro cation **2**. The observation of the cationic center

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(17) We propose that ketone formation from the α-nitro cation **1** occurs by oxygen insertion reaction. In principle this mechanism can be proven by ^{17}O labeling of the nitro group but because of the difficulty and expense of such labeling this experiment was not yet possible to carry out.
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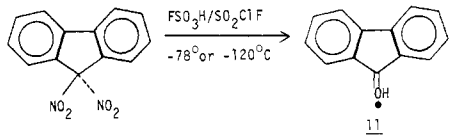
at δ ^{13}C 186.0 and the para carbon at δ ^{13}C 170.4 indicates extensive charge delocalization into the aromatic ring. The complete assignment is shown in Table I. Upon warming of the solution to −40 °C for several hours the cation **2** completely, and irreversibly fragments to the O-protonated 4,4′-dimethylbenzophenone (**9**).[18b] The intermediate O-nitrosated 4,4′-dimethylbenzophenone (or its protonated form) was not observed in this case.

Attempts to prepare 9-nitro-9-fluorenyl cation (**10**) by the ionization of 9,9-dinitrofluorene in FSO_3H/SO_2ClF either at −78 or −120 °C was not successful. Only protonated fluorenone **11**[18a]



11

was observed in the media, indicating the instability of 9-nitro-9-fluorenyl cation (**10**). This can be readily rationalized by the similar failure to observe the parent 9-fluorenyl cation under stable ion conditions.[18a] Only 9-fluorenyl cations with strongly stabilizing substituents were observed.

We were also unsuccessful in preparing α-nitrodialkylmethyl cations under stable ion conditions. Therefore, it appears that to counteract the electron-withdrawing effect of the nitro group strongly positive charge stabilizing substituents are needed to obtain long-lived α-nitromethyl cations. We are continuing our study of nitro carbocations.

Experimental Section

The starting α,α-dinitro compounds were prepared by the oxidation of the corresponding ketoximes with N_2O_4 following the procedure of Frojmovic and Just.[12]

General Procedure. To a N_2O_4-saturated stirred solution of dry dichloromethane (50 mL) in a 250-mL round bottom flask at 0 °C is rapidly added the corresponding ketoxime (20 mmol) in 15 mL of dichloromethane. The resulting mixture is brought to room temperature and stirred for a period of 10 min. Subsequently the mixture is evaporated to dryness in a Rotavap at ambient temperature in a well-ventilated hood. The resulting residue is chromatographed on silica gel (50 g) with hexane–benzene (7:3) as eluant. The collected eluant is evaporated to obtain the gem dinitro compound.

α,α-Dinitrodiphenylmethane: mp 80.4 °C (lit.[12] 79–79.5 °C); ^{13}C NMR ($CDCl_3$, ambient), δ 131.6 (d), 131.1 (s), 129.8 (d), 128.6 (d), 126.6 (s).

α,α-Dinitroditolylmethane: Viscous yellow oil; ^{13}C NMR ($CDCl_3$, ambient), δ 142.1 (s), 129.6 (d), 129.1 (d), 128.9 (s), 128.2 (s).

9,9-Dinitrofluorene: mp 134.2 °C (lit.[12] 131–133 °C); ^{13}C NMR ($CDCl_3$, ambient), δ 142.1 (s), 133.7 (d), 132.8 (s), 129.3 (d), 127.2 (d), 120.9 (d), 119.5 (s).

The ~5% ^{15}N-enriched α,α-dinitrodiphenylmethane was prepared by using 15% ^{15}N-enriched benzophenone oxime and N_2O_4. There was loss of enrichment during the oxidation. This can be rationalized by a radical-type reaction. ^{15}N-enriched benzophenone oxime (15%) was prepared from 15% ^{15}N-enriched hydroxylamine hydrochloride and benzophenone; 99% ^{15}N-enriched hydroxylamine hydrochloride was purchased from MSD Isotopes, Canada.

Preparation of Carbocations. To a cooled solution of FSO_3H in SO_2ClF at −78 °C (dry ice/acetone bath) or −120 °C (ethanol/liquid N_2 slush) is added a SO_2ClF slurry of dinitro compound in small portions with stirring so as to obtain ~15% of the ionic solution.

The ^1H NMR spectra were recorded by using a Varian Associates XL-200 NMR spectrometer equipped with a variable temperature probe. ^{15}N and ^{13}C NMR spectra were obtained on a Varian Associates Model FT-80 NMR spectrometer equipped with a variable temperature probe. The ^1H and ^{13}C NMR chemical shifts are referenced to those of external capillary Me_4Si. The ^{15}N shifts are with respect to that of anhydrous NH_3.

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Registry No. 1, 89196-81-6; **2**, 89196-82-7; **3**, 89196-84-9; **5**, 87963-52-8; **6**, 89196-86-1; **6** (deprotonated), 89196-85-0; **7**, 89196-87-2; **8**, 25721-22-6; **10**, 89196-80-5; **11**, 25721-28-2; ^{15}N, 14390-96-6; N_2O_4, 10544-72-6; α,α-dinitrodiphenylmethane, 21160-03-2; α,α-dinitrodi-*p*-tolylmethane, 89196-83-8; 9,9-dinitrofluorene, 21159-97-7; ^{15}N-enriched α,α-dinitrodiphenylmethane, 89196-88-3; ^{15}N-enriched benzophenone oxime, 89196-89-4; ^{15}N-enriched hydroxylamine hydrochloride, 40711-48-6; benzophenone, 119-61-9.

Mechanistic Investigation of Reduction of Daunomycin and 7-Deoxydaunomycinone with Bi(3,5,5-trimethyl-2-oxomorpholin-3-yl)

Don L. Kleyer and Tad H. Koch*

Contribution from the Department of Chemistry, University of Colorado, Boulder, Colorado 80309. *Received August 15, 1983*

Abstract: The mechanisms of reduction of 7-deoxydaunomycinone (**3**) and daunomycin (**1**) by 3,5,5-trimethyl-2-oxomorpholin-3-yl (**5**), the one-electron reducing agent formed from bond homolysis of *dl*-bi(3,5,5-trimethyl-2-oxomorpholin-3-yl) (**4**), are described. Reaction of **3** with **5** in buffered methanol gave the semiquinone **9** of 7-deoxydaunomycinone characterized by EPR spectroscopy. The semiquinone was further reduced to the hydroquinone **8** characterized by a transient absorption maximum at 420 nm (ϵ 12000) in the visible spectrum. The hydroquinone **8** subsequently reacted in a single step with 1 equiv of 5,6-dihydro-3,5,5-trimethyl-1,4-oxazin-2-one (**6**), the product of oxidation of **5**, to give 3,5,5-trimethyl-2-oxomorpholine (**7**) with a rate constant of 2 M^{-1} s^{-1} at 25 °C and a deuterium kinetic isotope effect of 3. The reduction of **6** is proposed to occur by hydride transfer. The overall reaction, disproportionation of **5**, was facilitated by the creation of a two-electron reducing agent from a one-electron reducing agent. Reduction of **1** with **5** in buffered methanol gave the semiquinone **12**, which was further reduced to the hydroquinone **10** also characterized by a very transient absorption at 420 nm. The hydroquinone rapidly eliminated daunosamine to give the tautomer **11** of 7-deoxydaunomycinone. Tautomer **11** showed transient absorption at 380 and 608 nm (ϵ 9400). Protonation of **11** by methanol gave 7-deoxydaunomycinone (**3**) and occurred with a pseudounimolecular rate constant of 0.013 s^{-1} and a deuterium kinetic isotope effect of 9. Tautomer **11** reacted as a nucleophile with benzaldehyde to give the aldol adduct **19** with a rate constant of 0.09 M^{-1} s^{-1}. This work represents the first spectroscopic observation and chemical trapping of **11**, proposed as a biologically active form of daunomycin.

Daunomycin (**1**) is an anthracycline antitumor drug produced by a mutant strain of *Streptomyces peucetius*.[1] Because of its value in the treatment of acute leukemia and the value of the structurally related anthracycline, adriamycin (**2**), as a broad

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