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Formation of σ and π or Charge-Transfer Complexes from Pyridinium Cations

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Complex formation was studied with the anions MeO^-, PhS^-, CN^-, $CH_2NO_2^-$, $CMe_2NO_2^-$, and c-$C_6H_{10}NO_2^-$. All formed σ complexes at the 4-position with 1,2,6-triphenylpyridinium cation and σ complexes at the 6-position with 1,2,4-triphenylpyridinium cation. With 1,2,4,6-tetraphenylpyridinium cation MeO^- formed a σ complex at the 2-position, CN^- a σ complex at the 4-position; the nitronate anions all formed π or charge-transfer (CT) complexes.

Extensive kinetic and mechanistic studies[1,2] of the preparatively useful C-alkylation of simple nitronate anions by the N-substituents of pyridinium and quinolinium salts[3,4] led us to propose a novel nonchain radicaloid pathway for this reaction, involving an intermediate charge-transfer complex (CTC) formed from the heterocyclic cation and the nitronate anion.

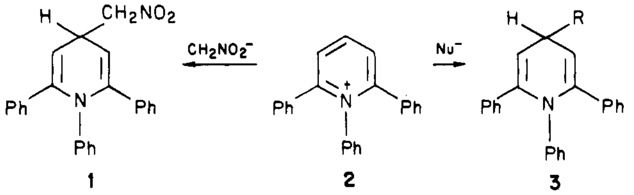
This work has prompted the present investigation of the reactions of selected nucleophiles with three pyridinium cations (see Table I), aimed at elucidation of the factors governing the formation of CTC's and/or covalent Meisenheimer-type σ adducts. The latter are intermediates in the nucleophilic substitution of pyridinium salts, and 2(6)- as well as 4-addition products, corresponding to 1,2- and 1,4-dihydropyridine systems, respectively, have been reported.[5,6] The orientation of nucleophilic attack has been correlated both with the possible intermediacy of a CTC preceding the attack,[7] and, in a more recent approach, with the "hard/soft" concept.[8]

To help elucidate the steric and electronic requirements for adduct formation, 1,2,6- (**2**) and 1,2,4-triphenylpyridinium cations (**4**) were studied (in each of which one of the three possible sites of attack remains unsubstituted), together with the 1,2,4,6-tetraphenyl analogue (**7**) (where all three sites are substituted). They were allowed to react with anions (MeO^-, PhS^-, CN^-, $CH_2NO_2^-$, $CMe_2NO_2^-$, c-$C_6H_{10}NO_2^-$) which included C, O, S, ambident C/O, hard and soft, small and bulky, nucleophiles. The products were characterized by ^1H NMR, ^{13}C NMR, ESR, and UV data (see Tables II and III for cation **4**).

Results and Discussion

The substitution pattern of the 1,2,6- and 1,2,4-triphenylpyridinium cations was expected to direct the nucleophiles into the remaining unsubstituted γ or α site, respectively, affording the corresponding 1,4- or 1,2-dihydropyridines (cf. Schemes I and II). In the case of the 1,2,4,6-tetraphenylpyridinium cation (**7**), where no steric factors were involved, the "hard/soft"-concept suggested hard bases should form 2- (**8**) and soft bases 4-adducts (**6**).[8] Bulky nucleophiles were expected to form π or charge-transfer complexes (**9**) rather than stable σ adducts with this cation (Scheme III).

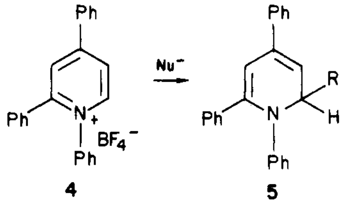
Scheme I



1 2 3

R=CMe_2NO_2, CN, *c*-$C_6H_{10}NO_2$, OMe, SPh

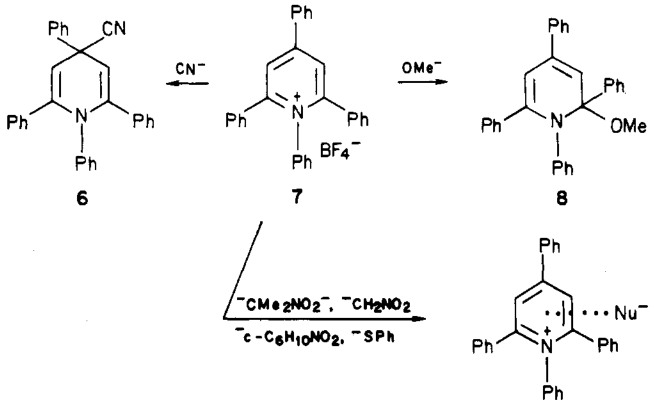
Scheme II



4 5

R=CMe_2NO_2, CH_2NO_2, CN, *cyclo*-$C_6H_{10}NO_2$, OMe, SPh

Scheme III



6 7 8 9

The ^1H NMR spectra of the symmetrical 4-adducts (**3**) derived from the 1,2,6-triphenylpyridinium cation (**2**) display the triplet of the 4-proton (a multiplet for $CH_2NO_2^-$ as the 4-substituent, confirming the expected bonding via carbon) at 3.82-4.22 ppm, coupled (J = ca. 5 Hz) with the doublet for the equivalent olefinic 3- and 5-protons at 4.83-5.45 ppm (Table IV).

The unsymmetrical 6-adducts (**5**) obtained from the 1,2,4-triphenylpyridinium cation show the olefinic 3-proton as a singlet (Table II). The 5-protons resonate as a doublet coupled (J = 5-6 Hz) with the doublet of the 6-protons. the 6-proton appears as a multiplet for $CH_2NO_2^-$ as 6-substituent, indicating bonding via carbon in this position.

Depending on the hardness/softness of the nucleophile, the 1,2,4,6-tetraphenylpyridinium cation forms both σ and

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Table I. $^1H^a$ and $^{13}C^b$ Chemical Shifts (ppm) of the Pyridinium Cations

	^1H						^{13}C					
pyridinium	pyridinium ring				other phenyl rings		pyridinium ring					other phenyl rings
cation	C_3H	C_4H	C_5H	C_6H			C_2	C_3	C_4	C_5	C_6	
1,2,4-triphenyl	8.30^c		8.38^d	8.90^e	7.18	7.65 (m)	156.0	126.7	149.4	125.1	155.2	123.0–145.5
1,2,6-triphenyl	8.43^f	9.03^g	8.43^f		7.15	7.80 (m)	156.1	128.1	146.4	128.1	156.1	123.2–138.2
1,2,4,6-tetraphenyl	8.74^h		8.74^h		6.47	8.60 (m)	156.2	125.1	155.5	125.1	156.2	127.7–145.8

[a] Relative to Me_4Si. [b] Relative to Me_2SO-d_6. [c] d, J = 2 Hz. [d] dd, J^o = 7 Hz; J^m = 2 Hz. [e] d, J^o = 7 Hz. [f] d, J = 8 Hz. [g] t, J = 8 Hz. [h] s.

Table II. Proton Chemical Shifts (ppm)^a from Tetramethylsilane of the 6-Position Anion Adducts of 1,2,4-Triphenylpyridinium Tetrafluoroborate

anion	3 H	5 H	6 H	phenyl substit	hydrogen of anion unit
OMe	6.02 (s)	6.38 (d, J = 6)^b	5.17 (d, J = 6)	7.1–7.9 (m)	3.40 (s)
CN	5.85 (s)	6.25 (d, J = 5.5)	4.35 (d, J = 5.5)	6.8–7.9 (m)	
CMe_2NO_2	5.83 (s)	6.21 (d, J = 6)	4.84 (d, J = 6)	6.8–7.9 (m)	1.57 (s) 1.72 (s)
CH_2NO_2	5.80 (s)	5.86 (d, J = 6)	4.73 (m)	6.6–7.9 (m)	4.45 (m)
c-$C_6H_{10}NO_2$	5.91 (s)	6.30 (d, J = 6)	4.81 (d, J = 6)	6.9–7.8 (m)	0.83–2.25 (m)
PhS	5.76 (s)	6.17 (d, J = 5.5)	4.72 (d, J = 5.5)	6.9–7.9 (m)	6.55–7.10 (m)

[a] In Me_2SO-d_6. [b] J = coupling constant in hertz.

Table III. ^{13}C Chemical Shifts (ppm) from Me_2SO-d_6 of the σ Adducts of 1,2,4-Triphenylpyridinium Tetrafluoroborate

	dihydropyridine ring carbons^a					carbons^b of anion
anion	2	3	4	5	6	unit C_α
OMe	145.9	107.1	138.1	109.0	87.6	47.5
CN	141.3	109.2	137.5	110.5	67.5	118.1
CMe_2NO_2	147.4	110.4	137.7	112.4	69.3	93.7^c
CH_2NO_2	144.1	106.5	135.9	108.9	71.3	79.1
c-$C_6H_{10}NO_2$	141.2	108.5	137.6	107.8	68.9	98.2^d
PhS	143.6	107.2	136.0	108.0	73.4	124.7^e

[a] The carbons of the phenyl substituents appeared in the range 120.5–143.8 ppm. [b] C_α is nearest to the pyridine ring. [c] β = 19.7; β' = 22.8. [d] β = 27.4; β' = 30.2; δ = 21.8; δ' = 23.9; δ = 21.5. [e] β, γ, δ at 122.1–128.8 ppm.

π adducts. The equivalent 3- and 5-protons of the symmetrical 4-adduct (**6**) appear as a singlet at 5.20 ppm in the ^1H NMR spectrum, and the cyanide carbon resonates at 117.5 ppm in the ^{13}C NMR spectrum. The unsymmetrical 2(6)-adduct (**8**) shows the expected resonances in both the ^{13}C and ^1H NMR spectra.

The σ adducts formed from all three pyridinium cations show proton chemical shifts due to olefinic protons and protons adjacent to the nucleophilic substituents, as well as coupling constants, all of which are comparable with those observed in similar dihydropyridine systems.[9] The protons of the nucleophilic substituents in the the 4- and 6-positions of the σ adducts appear in all cases at typical values.[10]

The ^{13}C NMR spectra of the 4-adducts (**3**) obtained from the 1,2,6-triphenylpyridinium cation display the C-4 carbons at 43.9–81.3 ppm (Table V). The equivalence of C-2 and C-6 and of C-3 and C-5 confirms the 1,4-dihydropyridine structure.

The 6-adducts (**5**) derived from the 1,2,4-triphenylpyridinium cation show the C-6 carbons between 67.5 and 87.6 ppm (Table III). The similar chemical shifts of C-6 substituted by the CN, CMe_2NO_2, and CH_2NO_2 groups (67.5–71.3 ppm) indicate an attachment of the nitronate anions via their nucleophilic carbon atom. The remaining 1,2-dihydropyridine ring carbons resonate in the expected ranges.

The 4-adduct (**6**) obtained from addition of cyanide anion to the 1,2,4,6-tetraphenylpyridinium cation (**7**) displays a line for C-4 at 71.3 ppm. The equivalent C-2 and C-6 appear at 137.0 ppm, and C-3 and C-5 at 108.1 ppm. The 2-adduct (**8**) shows a line for C-2 at 92.3 ppm. The remaining carbon atoms resonate in the expected ranges.

The ^{13}C NMR resonances of carbon atoms of the nucleophilic substituents in the 2(6)- and 4-positions of all the σ adducts are little affected by the remaining substitution pattern and appear in the ^{13}C NMR spectra at typical values (ppm): MeO (47.5–50.0 ppm), CMe_2NO_2 (19.7–22.8 ppm and 92.3–93.7 ppm), CH_2NO_2 (79.1–79.5 ppm), and CN (116.3–118.1 ppm).

Both ^1H and ^{13}C NMR spectra provide evidence for the formation of π or charge-transfer complexes rather than σ adducts between nitronate anions ($CMe_2NO_2^-$, $CH_2NO_2^-$, c-$C_6H_{10}NO_2^-$, or PhS^-), and the 1,2,4,6-tetraphenylpyridinium cation. The signals in the ^1H NMR spectra were considerably more broad than those in the spectra of the σ adducts, although the chemical shifts for hydrogen derived from the anionic unit were similar: CMe_2NO_2, 1.80 (s); CH_2NO_2, 4.50 (s); c-$C_6H_{10}NO_2$, 0.95–2.20 (m); SPh, 6.41–7.30 (m). In addition, whereas the ^{13}C NMR of the σ adducts contained well-defined and well-spaced lines, the ^{13}C NMR of the adducts from pyridinium cation (**7**) and nitronate anions showed a collapse of many of the expected signals to a broad line around 125 ppm, and no signals in the olefinic region. Thus the ^{13}C NMR of the complex formed from cation (**7**) and thiophenoxide showed an envelope of lines in the region 123.2–126.5 ppm. Solutions of these π or CT complexes were red, whereas those of the σ adducts were invariably deep brown. Further analysis of the ^{13}C NMR data (Table VI) is given below.

Compared to the neutral nitroalkanes,[11] the corresponding nitronate anions show the α-C signal at lower field, (vide Table VI) which could be due to contributions from the canonical form $R_2C{:}N^+(O^-)_2$ and/or paramagnetic contributions.

The small but significant difference of C-α of the π or CT complexes from the corresponding neutral Me_2CHNO_2 and $C_6H_{11}NO_2$ molecules is further evidence of formation of distinct species. Further evidence for the formation of

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Table IV. Proton Chemical Shifts (ppm)[a] from Tetramethylsilane of the 4-Position Anion Adducts of 1,2,6-Triphenylpyridinium Tetrafluoroborate

anion	3,5 H	4-H	phenyl substit	hydrogen of anion unit
OMe[b]	5.45 (d, J = 6)[c]	4.22 (t, J = 6)	6.6–7.6 (m)	3.85 (s)
CN	5.07 (d, J = 5.5)	4.09 (t, J = 5.5)	6.5–7.8 (m)	
CMe_2NO_2	4.95 (d, J = 5)	4.01 (t, J = 5)	6.5–7.8 (m)	1.73 (s)
CH_2NO_2	5.18 (d, J = 4)	4.11 (m)	6.7–7.9 (m)	4.46 (d)
c-$C_6H_{10}NO_2$	4.87 (d, J = 5)	3.97 (t, J = 5)	6.6–7.7 (m)	0.90–2.15 (m)
PhS	4.83 (d, J = 4.5)	3.82 (t, J = 4.5)	6.5–7.7 (m)	6.63–7.18 (m)

[a] In Me_2SO-d_6. [b] With excess of nucleophile, ring-opening occurred via 2-adduct. [c] J = coupling constant in hertz.

Table V. ^{13}C Chemical Shifts (ppm) from Me_2SO-d_6 of the Anion Adducts of 1,2,6-Triphenylpyridinium Tetrafluoroborate

	dihydropyridine ring carbons[a]			carbons[b] of anion unit
anion	2,6	3,5	4	C_α
OMe	145.9	113.9	81.3	50.0
CN	139.1	107.7	45.1	116.3
CMe_2NO_2	146.6	102.3	44.6	92.3[c]
CH_2NO_2	139.2	108.7	43.9	79.5
c-$C_6H_{10}NO_2$	138.6	101.8	44.8	96.5[d]
PhS	140.3	104.5	52.4	123.8[e]

[a] The carbons of the phenyl substituents appeared in the range 126.1–138.9 ppm. [b] C_α is nearest to the pyridine ring. [c] β = 22.4. [d] α = 30.6; β = 24.2; γ = 22.0. [e] β, γ, δ = 120.4–127.3 ppm.

Table VI. $^{13}C^a$ Chemical Shifts (ppm) of Nitronates

	$MeNO_2$	Me_2HCNO_2		$C_6H_{11}NO_2$	
	C	C_α	C_β	C_α	C_β
neutral	62.8	86.9	20.0	83.8	30.3
anion[b]	92.0	106.3	18.8	94.9	28.3
CTC[b,c]	87.0	78.4	20.3	81.2	30.8

[a] Relative to Me_4Si; in Me_2SO-d_6. [b] 18-Crown-6 added to increase solubility of components. [c] CTC formed from nitronate anion and 1,2,4,6-tetraphenylpyridinium tetrafluoroborate.

new and distinct species is seen in C-β of the complexes (**9**) of Me_2CHNO_2 and $C_6H_{11}NO_2$, which resonate at slightly different positions from the corresponding neutral and anionic nitroalkanes (Table VI).

An ESR study was carried out on the products obtained from the reaction of 1,2,4,6-tetraphenylpyridinium cation with the nitronate anions or PhS^-. In all those cases, simple unresolved ESR signals were observed with band widths of 15 G, centered around g = 2.00525 to 2.00589. However, since ESR signals were obtained when 1,2,4,6-tetraphenylpyridinium tetrafluoroborate was treated with methoxide anion alone, these ESR studies are not evidence for or against the formation of a CT complex.

UV spectroscopy has been a valuable diagnostic tool for the identification of the isomers formed by nucleophilic attack on pyridinium cations in either the 2(6)- or the 4-position. Three UV absorption bands of dihydropyridines have been reported:[5] band I (λ_{max} 200–240 nm, both isomers), band II (λ_{max} 250–300 nm, cross-conjugated 1,2-systems, and band III (λ_{max} 300–400 nm, both isomers). Using Me_2SO as solvent, only the latter could be monitored. The UV absorptions of all dihydropyridines were shifted to longer wavelength compared with the pyridinium cations (Table VII: average bathochromic shift for MeO adducts, 32 nm). In accordance with previous results, the 1,2-adducts (**5**) and (**8**) showed a bathochromic shift relative to the corresponding 1,4-adducts (**3**) and (**6**)[5,10,12] (for the MeO adducts in the triphenylpyridinium series, the difference is 13 nm). Excess MeO^- or traces of water caused ring-opening, giving the divinylogous amide (absorption at λ_{max} 470–500 nm).[13]

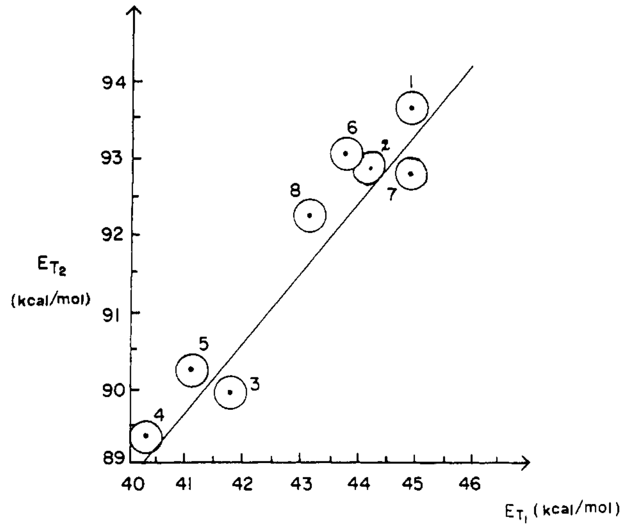

Figure 1. Plot of charge-transfer transition energies (E_T) of 1,2,4,6-tetraphenylpyridinium tetrafluoroborate (E_{T_2}) vs. 1-ethyl-4-(methoxycarbonyl)pyridinium iodide (E_{T_1}) as a function of solvent polarity.

Small hypsochromic shifts were observed from the mixtures of 1,2,4,6-tetraphenylpyridinium with $CMe_2NO_2^-$, $CH_2NO_2^-$, c-$C_6H_{10}NO_2^-$, or PhS^- (cation, λ_{max} 310 nm; mixtures with nucleophiles, λ_{max} 305, 308, 309, and 308 nm, respectively). The difference in wavelength of this molecular association from the δ_{max} values of the corresponding pyridinium cation, σ adduct, and pyridine is tentative evidence for the formation of π or CT complexes. More substantial evidence comes from the extinction coefficients of the CT complex band for the 1,2,4,6-tetraphenylpyridinium cation in admixture with nitropropanide anion. The extinction coefficients of Me_2SO, sodium 2-nitropropanide, and 2,4,6-triphenylpyridine were insignificant at 305 nm. We found that ϵ_{max} decreases from 43 900 for a pure pyridinium salt to 24 000 when 1 equiv of nitropropanide anion is added: ϵ_{max} decreases further on raising the concentration of nitropropanide. This is prima facie evidence of a strong molecular association. Furthermore, at higher concentrations of nitropropanide, the solutions do not obey the Beer–Lambert Law, a fact which is commonly characteristic of a CT complex.[14]

The UV spectral maxima of the complex of 1,2,4,6-tetraphenylpyridinium tetrafluoroborate (5×10^{-5} M) with sodium 2-nitropropanide (5×10^{-4} M) in different solvents are given in Table VIII. CT transition energies values (E_T) were calculated[15] from $E_T = 2.859/\lambda \times 10^5$, where λ is the wavelength (A°) of the CT band; Figure 1 shows that a plot

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Table VII. UV Absorption Spectra in Me_2SO[a]

series	pyridinium cation		adduct with: OMe		CN		CMe_2NO_2		CH_2NO_2		c-$C_6H_{10}NO_2$		PhS		vinylogous[b] amide	
	λ_{max}	$10^{-3}\epsilon$	λ_{max}	$10^{-3}\epsilon$	λ_{max}	$10^{-3}\epsilon$	λ_{max}	$10^{-3}\epsilon$	λ_{max}	$10^{-3}\epsilon$	λ_{max}	$10^{-3}\epsilon$	λ_{max}	$10^{-3}\epsilon$	λ_{max}	$10^{-3}\epsilon$
1,2,6-triphenyl	300	10.7	323	10.0	319	8.9	331	3.1	326[c]	11.8	329	8.9	335	7.6	470	8.6
1,2,4-triphenyl	306	22.4	336	13.7	323	12.5	355	10.0	328	14.1	337	11.2	340	13.5	480	21.1
1,2,4,6-tetraphenyl	310	43.9	354	18.9	327	14.6	305[d]	17.3	308	16.7	309[d]	15.4	308[d]	16.9	500	29.7

[a] λ_{max} in nm, ϵ in cm^2 mol^{-1}. [b] Ring-opening was observed with excess of MeO^-. [c] This absorption, corresponding to the 4-adduct, decreased gradually while a new absorption appeared at 520 nm (oxidation, see Scheme I). [d] Assigned to the CTC.

Table VIII. Charge-Transfer Transition Energies (E_T) of 1-Ethyl-4-(methoxycarbonyl)pyridinium Iodide[a] (E_{T1}) and 1,2,4,6-Tetraphenylpyridinium Tetrafluoroborate[b] (E_{T2}) as a Function of Solvent

	solvent	E_{T1}	λ_{max}	E_{T2}
1.	dimethyl sulfoxide	45.0	305	93.7
2.	sulfolane	44.0	308	92.8
3.	1,2-dichloroethane	41.9	318	89.9
4.	pyridine	40.2	320	89.3
5.	dichloromethane	41.1	317	90.2
6.	dimethylformamide	43.8	307	93.1
7.	trimethylphosphite	45.0	308	92.8
8.	butyronitrile	43.1	309	92.5

[a] Taken from ref 15. [b] Calculated from λ_{max} values given in the table.

of E_T for 1,2,4,6-tetraphenylpyridinium tetrafluoroborate (E_{T2}) vs. E_T for 1-ethyl-4-(methoxycarbonyl)pyridinium iodide[16] (E_{T1}) is linear with a gradient of 0.82 and a correlation coefficient of 0.94. Similar linear plots have been reported for CT spectra of both 1-methylpyridinium iodide[17] and 1-ethyl-4-cyanopyridinium iodide[17] vs. 1-ethyl-4-(methoxycarbonyl)pyridinium iodide.

Investigation of the formation of complexes by infrared spectroscopy supported the supposition that, depending on the pyridinium cation and the nucleophile, either a σ adduct or some other type of complex could be formed. Thus, the 1,2,6-triphenylpyridinium perchlorate adducts with both methoxide and nitropropanide anions were characterized by very broad and fairly *weak* bands in the region 1630–1600 cm^{-1}. However, whereas the 1,2,4,6-tetraphenylpyridinium adducts with methoxide anion gave broad and *weak* absorptions in the IR (1660, 1610 cm^{-1}), the corresponding adduct with nitropropanide anion displayed a broad and very *strong* band (unchanged during 3 h) in the region 1620 cm^{-1}. All comparisons were made at a 1:1 pyridinium salt to nucleophile concentration of 0.85 M in Me_2SO. These differences in band intensities support the formation of two distinct types of complex.

The possibility of what we have described as π/CT adducts being equilibrating mixtures of the corresponding nitronate anion and σ adduct has been excluded. Thus the UV spectrum (Table VII) should in this case show peaks for a σ adduct and for the pyridinium cation: if the peaks observed were actually from the pyridinium cation, then the much reduced intensity would indicate considerable σ adduct formation at UV concentration. If this were the case the equilibrium should be almost completely displaced toward σ adduct at the much higher concentrations used for the NMR determinations: clearly they are not. Again the observed NMR spectra are not compatible with such an equilibrating mixture.

Conclusions

The 1,2,6- and 1,2,4-triphenylpyridinium cations undergo substitution by nucleophiles in the remaining unsubstituted α or γ position, affording stable Meisenheimer-type adducts. Thus, steric hindrance caused by a phenyl substituent overrides any electronic preference suggested by the "hard/soft" concept; for example, the "soft" nucleophilic carbon of the substituent anions $CH_2NO_2^-$ and $CMe_2NO_2^-$ was shown to attack the "hard" 6-position of the 1,2,4-triphenylpyridinium cation.

In accordance with the suggestions provided by Klopman,[8] the hard nucleophile MeO^- added to the 1,2,4,6-tetraphenylpyridinium cation in the 2(6)-position, whereas

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the soft nucleophile CN$^-$ afforded the 4-substituted adduct. The ambident nitronate anions do not form stable σ adducts with 1,2,4,6-tetraphenylpyridinium cation; interaction remained at the stage of π complex or CTC formation. The steric effect of the phenyl group is sufficient in the case of the nitronate anions to shift the equilibrium π to σ complex in favor of the former. Although we believe this to be a thermodynamic effect, it should be noted that the *kinetic* carbon basicities of nitronate ions appear to be very low;[18] cf. their low kinetic proton basicity in contrast to the nearly equal thermodynamic proton basicity of PhS$^-$ and Me$_2$CNO$_2^-$.

Experimental Section

^{1}H NMR spectra were obtained on a Varian EM360L spectrometer and ^{13}C NMR spectra on a JEOL JNM FX-100 spectrometer; chemical shifts in ppm from tetramethylsilane are reported from spectra taken in Me$_2$SO-d_6. UV spectra were obtained on a Perkin-Elmer 330 spectrophotometer, and the ESR studies were carried out on a BRUKER ER 200D-SRC spectrometer.

The following compounds were prepared by the literature method quoted: 1,2,6-triphenylpyridinium perchlorate, mp 197–199 °C (lit.[19] mp 198–199 °C); 1,2,4-triphenylpyridinium tetrafluoroborate, mp 235 °C (lit.[20] mp 235 °C), 1,2,4,6-tetraphenylpyridinium tetrafluoroborate, mp 251–252 °C (lit.[21] mp 251 °C). The nucleophiles were either commercially available (NaCN) or prepared by standard methods: NaOMe from NaH and dry MeOH, all others by reacting the appropriate nitroalkane or thiophenol with 1 equiv of NaOMe in MeOH. Me$_2$SO was dried by distillation in vacuo from CaO.

General Procedure for the Reaction of the Pyridinium Cations with the Nucleophiles. In a typical experiment, 1 equiv of nucleophile was added to the pyridinium cation in Me$_2$SO-d_6 (0.30 M) for the ^{1}H NMR and ^{13}C NMR measurements. A lower concentration of the pyridinium salt (4.50×10^{-5} M) and a fivefold excess of nucleophile was used for the UV studies.

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Registry No. **2**·BF$_4^-$, 102107-74-4; **3** (R = OMe), 102107-80-2; **3** (R = CN), 102107-81-3; **3** (R = CMe$_2$NO$_2$), 102107-82-4; **3** (R = CH$_2$NO$_2$), 102107-83-5; **3** (R = c-C$_6$H$_{10}$NO$_2$), 102072-54-8; **3** (R = PhS), 102107-84-6; **4**·BF$_4^-$, 80576-32-5; **5** (R = OMe), 102107-75-5; **5** (R = CN), 102107-76-6; **5** (R = CMe$_2$NO$_2$), 102107-77-7; **5** (R = CH$_2$NO$_2$), 102107-78-8; **5** (R = c-C$_6$H$_{10}$NO$_2$), 102072-53-7; **5** (R = PhS), 102107-79-9; **7**·BF$_4^-$, 59834-94-5; **8**, 75102-76-0; **9** (Nu$^-$ = NO$_2$CMe$_2^-$), 102107-86-8; **9** (Nu$^-$ = NO$_2$CH$_2^-$), 102107-87-9; **9** (Nu$^-$ = c-C$_6$H$_{10}$NO$_2^-$), 102107-88-0; 4-cyano-1,2,4,6-tetraphenyl-1,4-dihydropyridine, 102107-85-7.

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Synthesis of Anatoxin-*a*

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A short efficient synthesis of (±)-anatoxin-*a*, the alkaloidal toxin from *Anabaena flos-aquae*, is described. Bromination of 9-methyl-9-azabicyclo[3.3.1]nonan-1-ol (**3b**) provides the key intermediate 9-methyl-9-azabicyclo[4.2.1]nonan-2-one (**6**). Reaction of **6** with diethyl (1-cyanoethyl)phosphonate gives 2-(1-cyano-1-ethylidene)-9-methyl-9-azabicyclo[4.2.1]nonane (**8**). Oxygenation of **8**, followed by reduction and hydrolysis, gives *N*-methylanatoxin-*a* (**1b**) which has been earlier converted into anatoxin-*a*.

Anatoxin-*a* (**1**) is a powerful alkaloidal toxin isolated from the filamentous freshwater cyanophyte *Anabaena flos-aquae*.[1a] This toxin, also designated as "very fast death factor", VFDF,[1b] is responsible for the death of livestock, waterfowl, and other wildlife following ingestion of toxic blooms of the alga in freshwater lakes of midwestern United States and Canada.[1c] The structure and the absolute configuration of (+)-anatoxin-*a* has been established as (1*R*,6*R*)-2-acetyl-9-azabicyclo[4.2.1]non-2-ene by X-ray crystallography in 1972[2a] and was in full agreement with the spectroscopic studies obtained by Edwards and his co-workers.[1a] The stereospecific synthesis of (+)-anatoxin-*a* from (2*R*,3*S*)-cocaine by Campbell, Edwards, and Kolt in 1976 further confirmed the absolute configuration of this toxin.[2b]

Pharmacological studies have shown (+)-anatoxin-*a* (**1**) to be a powerful nicotinic agonist with a long duration of action.[3] Since (+)-anatoxin-*a* is a naturally occurring alkaloid that has the 9-azabicyclo[4.2.1]nonane ring system, its unusual bicyclic ring structure has stimulated the interest of many synthetic organic chemists. Syntheses of (+)-anatoxin-*a* have been reported by Campbell, Edwards, Elder, and Kolt in 1979[4] and Rapoport and Bates in 1979.[5]

Recently, Tufariello, Meckler, and Senaratne have reported a nitrone based entry to the reacemic natural

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