An Unusually Easy Oxidative Dequaternization of *N*-Alkyl-1,2,4-triazinium Salts

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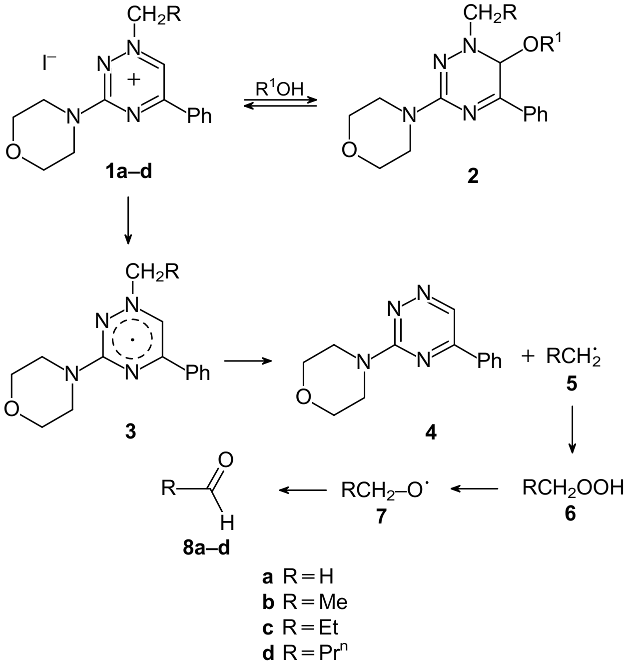
Unusually easy dequaternization has been found to occur on treatment of 1-alkyl-3-morpholino-5-phenyl-1,2,4-triazinium iodides with triethylamine in alcohol or acetone solutions at room temperature; a plausible reaction mechanism has been advanced on the basis of NMR and kinetic studies.

It used to be commonly felt that *N*-alkylation of azaaromatic compounds was an irreversible process.[1] Indeed, the overwhelming majority of quaternary *N*-alkylazinium salts are rather stable and, unlike their NH, *N*-acyl, *N*-cyano and *N*-fluoro analogues, they usually do not easily lose the *N*-substituent in reactions with a variety of nucleophilic reagents.[2]

During the last two decades a number of examples of dequaternization reactions have been found to occur in the series of 2-(6-)aryl- or 2,6-diaryl-substituted *N*-alkylpyridinium cations. It is noteworthy that conditions for such dequaternization reactions are rather severe (many hours of reflux in chlorobenzene) and the presence of a bulky *ortho*-substituent is necessary in most cases to facilitate elimination of the *N*-alkyl group.[3,4]

In the course of our studies on the reactivity of 1-alkyl-1,2,4-triazinium salts[5] we have discovered an example of an unusually easy conversion of *N*-alkylazinium cations into uncharged azines. 1-Alkyl-3-morpholino-5-phenyl-1,2,4-triazinium iodides **1a–d** were found to undergo the dequaternization reaction smoothly on treatment with triethylamine in methanol, ethanol or acetone solutions at room temperature to yield 3-morpholino-5-phenyl-1,2,4-triazine **4** together with the corresponding aldehydes **8**. The reaction discovered is even more challenging if one takes into account that *N*-alkylazinium substrates **1a–d** bear no *ortho*-substituents which could assist the dealkylation process.



Scheme 1

In order to get an insight into the mechanism of the reaction and estimate its rate constants in comparison with those for dequaternization of *N*-alkyl pyridinium cations a series of 1-alkyl-1,2,4-triazinium iodides **1a–d** has been obtained and NMR and kinetic studies on dequaternization of these substrates have been undertaken.

The present paper reports these rate measurements, together with NMR data on the structures of plausible intermediates.

1-Alkyl-3-morpholino-5-phenyl-1,2,4-triazinium iodides **1a–d** were prepared by alkylation of 3-morpholino-5-phenyl-1,2,4-triazine **4** with an excess of the corresponding alkyl iodides according to the procedure described earlier.[6,7] Evidence for their structure is based on comparison of their ^{1}H NMR spectral data with those reported in the literature.[6–8]

Since the absorption bands of triazinium salts **1** in the UV region overlap with those of triazine **4** and aldehydes **8**, those iodides **1a–d** which have an absorbance band in the visible region with a maximum at 470 nm have been chosen for kinetic measurements. Triazine **4** and aldehydes **8a–d** are transparent at 470 nm. Kinetic runs in ethanol at $25 \pm 0.1\,^\circ$C were followed by UV-VIS spectrophotometry (Specord M50) by monitoring the decrease of absorbance of triazinium salts at fixed wavelength (470 nm) under pseudo-first-order conditions. In all experiments the starting concentration of triazinium salts was 1.43×10^{-3} M. Concentrations of triethylamine were varied from 3.22×10^{-2} to 11.76×10^{-2} M.

Pseudo-first-order rate constants (Table 1) were calculated from the slope of conventional plots of $\ln[(A - A_2)/(A_1 - A_2)]$ *vs.* time, where A is current absorbance, A_1 is absorbance at $\tau = 0$ and A_2 is absorbance at the ten half-life point ($\tau = \infty$). Such plots were linear to at least 80% completion. Plots of k_{obs} *vs.* concentration of triethylamine are straight lines; however, these plots do not pass through the origin thus indicating that the reaction mechanism is more complicated than to obey the kinetic dependence expected for S_N2 reactions.

The reaction course was followed by ^{1}H NMR spectroscopy which provided unequivocal evidence for the formation of triazine **4** and aldehydes **8**. Treatment of 1-ethyl-3-morpholino-5-phenyl-1,2,4-triazinium iodide **1b** with 1 equiv. of triethylamine in [^{2}H$_6$]acetone immediately resulted in the appearance of a number of very indicative ^{1}H NMR signals instead of those of the starting 1-ethyl-1,2,4-triazinium salt **1b**, Fig. 1(*a*)–(*c*). A low-field singlet at 9.24 ppm was unambiguously assigned to the H-6 resonance of 3-morpholino-5-phenyl-1,2,4-triazine **4**. Another singlet at 5.34 ppm is characteristic of the resonance of a proton

Table 1 Pseudo-first-order rate constants for dequaternization of 1-alkyl-3-morpholino-5-phenyl-1,2,4-triazinium iodides **1a–d** in ethanol at 25 °C.

Triazinium salt		$k_{\text{obs}}/10^{-3}$ s^{-1}, depending on concentrations of triethylamine (10^2 M)			
Compound	R¹	3.22	6.25	9.09	11.76
1a	H	1.16 ± 0.08	1.36 ± 0.08	1.26 ± 0.07	1.41 ± 0.09
1b	Me	2.75 ± 0.07	3.25 ± 0.07	4.00 ± 0.07	4.34 ± 0.08
1c	Et	1.76 ± 0.08	1.93 ± 0.12	2.20 ± 0.28	2.66 ± 0.20
1d	Prⁿ	1.93 ± 0.08	2.36 ± 0.09	2.89 ± 0.08	3.15 ± 0.10

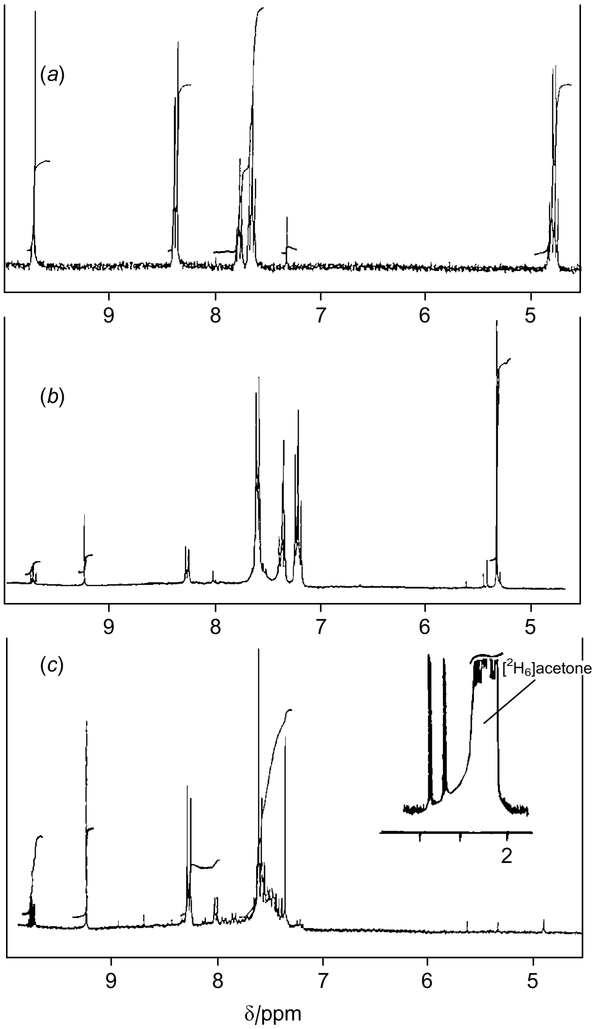


Fig. 1 ^{1}H NMR spectra of 1-ethyl-3-morpholino-5-phenyl-1,2,4-triazinium iodide **1b** in [$^2H_6$]acetone (*a*) and its reaction mixture with triethylamine: (*b*) immediately after mixing with 1 equiv. of triethylamine; (*c*) after 3 days at 20 °C.

attached to an sp^3-hybridized carbon atom[8] and it proved to belong to H-6 of the hydroxy adduct **2**[†] derived from the addition of the hydroxide ion to the cation **1b**, Fig. 1(*b*). Besides these singlets, there are a quartet and doublet at 9.73 and 2.13 ppm with $^3J = 1.8$ Hz which were identified as absorptions of the COH and Me groups of acetaldehyde **8b**, respectively,[‡] Fig. 1(*b*,*c*).

Observing changes in the ^{1}H NMR spectra in the course of the reaction one can see that the intensity of the singlet at 9.24 ppm increases gradually at the expense of a simultaneous decrease of the hydroxy adduct **2** (singlet at 5.34 ppm). Since it is unlikely that the *N*-ethyl group is eliminated directly from the hydroxy adduct **2** (R = Me , R^1 = H), we therefore suggest that the conversion of **1b** into **4** occurs *via* the intermediacy of **3** which is present in the reaction mixture in a small equilibrium concentration. After 3 days the ^{1}H NMR spectra are characterized by a full conversion of the salt **1b** into triazine **4**, Fig. 1(*c*), which was isolated from the reaction mixture and identified by comparison of its physical characteristics (melting point, IR and ^{1}H NMR data as well as elemental analyses) with those of the authentic sample. A similar picture is observed in the ^{1}H NMR spectra of other 1-alkyl-1,2,4-triazinium salts (**1a**,**c**,**d**). In all cases yields of aldehyde were *ca.* 90%.

On consideration of the results presented in this paper one has to note two features of the dequaternization of 1-alkyl-1,2,4-triazinium salts.

It follows from the kinetic data that the reaction is very fast in comparison with dequaternization of *N*-alkylpyridinium cations. Indeed, the observed pseudo first-order rate constants k_{obs} are *ca.* 10^{-3} s^{-1} at 25 °C (Table 1), while *N*-alkylpyridinium salts are dequaternized much more slowly ($k_{obs} \sim 10^{-5}$ s^{-1} at 100 °C). Another trait concerns the reaction mechanism. Since dequaternization of 1-alkyl-1,2,4-triazinium salts is not accompanied by the formation of olefinic products *via* carbocation intermediates we propose Scheme 1 involving participation of the triazinyl radical as a plausible reaction mechanism. Indeed, recently reported data[9] on recording of the EPR spectra of the radicals **3** obtained on treatment of 3-substituted 1-alkyl-5-phenyl-1,2,4-triazinium salts with triethylamine in an ethanolic solution free of oxygen (under vacuum $\sim 10^{-5}$ mmHg) provide substantial experimental support for the occurrence of this mechanistic pathway. Further steps involve the cleavage of the C–N bond, interaction of the alkyl radicals **5** with oxygen followed by the known chain of transformations $\mathbf{5} \rightarrow \mathbf{6} \rightarrow \mathbf{7}$ which finally results in aldehydes **8**. The radical nature of the photochemical dequaternization of 1-alkyl-2-azidocarbonylpyridinium cations induced by UV irradiation, which is somewhat similar in that it results in the formation of the same aldehydes,[10] can also be considered as an argument in favour of the radical mechanism shown in Scheme 1.

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[†] Usual (not dry) [$^2H_6$]acetone was used in the ^{1}H NMR experiments. A similar methoxy adduct **2** (R = R^1 = Me) with an H-6 resonance signal at 5.14 ppm is formed on dissolving the triazinium salt **1b** in methanol in the presence of triethylamine.[9]

[‡] The sample was spiked with acetaldehyde to prove beyond doubt the formation of the latter.