

Interaction of Sodium Methoxide with 4-Nitropyridine *N*-Oxide in Benzene in the Presence of Surfactant Aggregates

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The rate constant for the interaction of 4-nitropyridine *N*-oxide with sodium methoxide in benzene in the presence of polyoxyethylene(6) nonylphenol aggregates is 1220 and 7-fold greater than that in neat benzene or in neat methanol. Conversely, this reaction does not proceed appreciably in benzene in the presence of dodecylammonium propionate and sodium bis-(2-ethylhexyl)sulphosuccinate aggregates. ¹H N.m.r. data indicate that 4-nitropyridine *N*-oxide interacts to differing extents with each charge type of surfactant aggregate. The rate effects and ¹H n.m.r. behaviour are discussed in terms of the interaction of both reactants with the surfactant and differential reaction rates in this media and that in the neat solvent.

SURFACTANT aggregates in nonpolar solvents provide a unique catalytic media for organic and inorganic reactions.¹⁻⁸ The observed rate enhancements have been rationalized in terms of substrate localization in the polar interiors of the surfactant aggregates, dynamically formed in the nonpolar solvents, where favourable orientation, proton transfer, and enhanced activity lower the overall free energy requirements for the reaction.¹⁻⁸ In a previous study we reported that the rate constant for the decomposition of sodium 1,1-dimethoxy-2,4,6-trinitrocyclohexadienylide (a Meisenheimer or σ -complex) in benzene in the presence of dodecylammonium benzoate aggregates is greater

by factors of 62,900 and 1800 than that in pure benzene or in pure water.² This reaction was chosen to represent a nucleophilic aromatic substitution in which the overall rate is governed by the decomposition of the intermediate σ -complex.⁹ Examination of the effects of surfactant aggregates in benzene on a nucleophilic aromatic substitution for which the rate-determining step is the formation of the intermediate would complement this previous study. The present paper reports the results of our investigations on the interaction of sodium methoxide with 4-nitropyridine *N*-oxide in benzene in the presence of dodecylammonium propionate, sodium bis-(2-ethylhexyl)sulphosuccinate, and polyoxyethylene(6) nonylphenol aggregates.

¹ J. H. Fendler, E. J. Fendler, R. T. Medary, and V. A. Woods, *J. Amer. Chem. Soc.*, 1972, **94**, 7288.

² J. H. Fendler, E. J. Fendler, and S. A. Chang, *J. Amer. Chem. Soc.*, 1973, **95**, 3273.

³ C. J. O'Connor, E. J. Fendler, and J. H. Fendler, *J. Org. Chem.*, 1973, **38**, 3371.

⁴ C. J. O'Connor, E. J. Fendler, and J. H. Fendler, *J.C.S. Dalton*, 1974, 625.

⁵ C. J. O'Connor, E. J. Fendler, and J. H. Fendler, *J. Amer. Chem. Soc.*, 1974, **96**, 370.

⁶ J. H. Fendler, F. Nome, and H. C. Van Woert, *J. Amer. Chem. Soc.*, 1974, **96**, 6745.

⁷ W. Hinze and J. H. Fendler, *J.C.S. Dalton*, 1975, in the press.

⁸ J. H. Fendler and L.-J. Liu, *J. Amer. Chem. Soc.*, 1974, **96**, 6745.

⁹ J. Miller, 'Aromatic Nucleophilic Substitution,' Elsevier, London, 1968; M. J. Strauss, *Chem. Rev.*, 1970, **70**, 667, and references cited therein.

EXPERIMENTAL

Materials.—Reagent grade methanol was dried and stored over Linde type 5A molecular sieve. Reagent grade benzene was distilled from sodium and stored identically to methanol. The molecular sieve was activated by baking at 375° for at least 2 h, followed by cooling in a desiccator under nitrogen prior to use. [²H₆] Benzene (99.5% isotopic purity; Aldrich) was dried and stored over Linde 5A molecular sieve.

4-Nitropyridine *N*-oxide (Aldrich) was recrystallized from acetone and dried overnight *in vacuo*, m.p. 159–160° (lit.,^{10,11} 159–160°); its absorption spectroscopic parameters in aqueous solutions, λ_{\max} 314 (ϵ 1.32×10^4 l mol⁻¹ cm⁻¹) and 216 nm (8.42×10^3), agreed well with those quoted in the literature.^{10,11} The preparation, purification, and characterization of dodecylammonium propionate (DAP) and sodium bis-(2-ethylhexyl)sulphosuccinate (Aerosol-OT) have been reported.¹⁻⁶ Polyoxyethylene(6) nonylphenol (Igepal CO-530) were used as received from General Aniline and Film Corporation. Critical concentrations for aggregation of DAP, Aerosol-OT, and Igepal CO-530 in benzene are 5×10^{-3} , 2×10^{-3} , and 1.0×10^{-3} M, respectively.¹⁻⁸

Solubility and Partitioning.—Saturated solutions of 4-nitropyridine *N*-oxide, in water, in methanol, in benzene, and in the surfactant solutions in benzene, containing an excess of crystalline compound, were shaken occasionally for 12 h. The concentration of 4-nitropyridine *N*-oxide was determined by absorption spectrophotometry in the supernatant liquids, using appropriate dilutions. Independent determinations established the validity of the Beer–Lambert Law in all systems. Information on the solubilities obtained was substantiated by partitioning of 4-nitropyridine *N*-oxide between water and cyclohexane and between water and benzene. The concentration of 4-nitropyridine *N*-oxide in each layer was determined spectrophotometrically.

Solubilities of methanolic sodium methoxide in benzene in the absence and in the presence of surfactants were qualitatively determined by observing the appearance of precipitates at a given sodium methoxide concentration. In all systems, the concentration of methanol was 0.10% (v/v).

Kinetics.—The reaction between sodium methoxide and 4-nitropyridine *N*-oxide in methanol and in surfactant solutions in benzene was followed spectrophotometrically, at 325 and 350 nm, respectively, in the thermostatted cell compartment of a Beckman Kintrac VII spectrophotometer. Stock solutions of the surfactant and 4-nitropyridine *N*-oxide in benzene were separately prepared and mixed prior to the initiation of the kinetic run. Kinetic runs were initiated by injecting a small volume (typically 5 μ l) of methanolic sodium methoxide to thermostatted benzene solutions of the substrate and surfactant (typically 2.00 ml). For reactions having half-lives >5 h reactants of desired concentrations were mixed in benzene and the solutions were kept in a constant temperature bath. At suitable time intervals portions were withdrawn for analysis. In all solutions, the concentration of 4-nitropyridine *N*-oxide was kept at *ca.* 5.0×10^{-5} M while the apparent sodium methoxide concentration varied over $(0.6\text{--}3.3) \times 10^{-3}$ M. Plots of $\log(A_\tau - A_\infty)$ against time gave good straight

lines, up to at least two half-lives, from the slopes of which the pseudo-first-order rate constants k_d were calculated. The second-order rate constants were obtained from linear plots of k_d against $[\text{NaOCH}_3]$.

¹H N.m.r.—The 100 MHz ¹H n.m.r. spectra were obtained on a modified Varian Associates HA-100 spectrometer with a Hewlett–Packard model 200-ABR audio oscillator and frequency counter. Each spectrum was recorded at least three times after equilibration to ambient probe temperature ($30 \pm 0.50^\circ$). All spectra were determined on freshly prepared solutions in benzene and were measured relative to neat tetramethylsilane which was contained in a Wilmad 520-2 internal coaxial capillary tube. No difference between a capillary and the coaxial tube containing the same reference could be detected. However, a downfield chemical shift difference of 47.5 Hz at 100 MHz was observed for the chloroform signal (10% v/v in CCl₄) between the 'external' neat TMS in the coaxial tube and the 'internal' 10% v/v TMS in the same solution. Chemical shifts were generally obtained from spectra recorded at 500 Hz sweep width and are given on the δ scale relative to the external TMS (δ 0). Individual measurements are accurate to ± 0.005 p.p.m.

RESULTS

Table 1 gives the solubilities of 4-nitropyridine *N*-oxide in the different solvents. These data are in good agreement with the partitioning experiments: the distribution ratio of 4-nitropyridine *N*-oxide in water–benzene is 3.6:1 and that in water–cyclohexane 57:1. Solubilities

TABLE 1
Solubility of 4-nitropyridine *N*-oxide at $23 \pm 1^\circ$

Solvent	Solubility (mol l ⁻¹)
Water	1.9×10^{-1}
Methanol	1.1×10^{-1}
Benzene	6.0×10^{-2}
0.10M-DAP in benzene	5.9×10^{-2}
0.10M-Aerosol-OT in benzene	6.8×10^{-2}
0.10M-Igepal CO-530 in benzene	6.5×10^{-2}

of sodium methoxide in benzene solutions containing 0.1% methanol (v/v) are estimated to be: 6.3×10^{-4} M in the absence of surfactant, and 1.1×10^{-3} , 2.7×10^{-3} , 1.1×10^{-3} , 3.4×10^{-3} , 1.1×10^{-3} , 3.1×10^{-3} , and 5.0×10^{-3} M in the presence of 0.01M-DAP, 0.10M-DAP, 0.01M-Aerosol OT, 0.10M-Aerosol OT, 0.01M-Igepal CO-530, 0.10M-Igepal CO-530, and 1.0M-Igepal CO-530, respectively.

Table 2 gives the rate constants, k_d and k_2 , for the interaction of sodium methoxide with 4-nitropyridine *N*-oxide in benzene in the absence and in the presence of Igepal CO-530. No detectable reaction occurred in benzene in the presence of 0.10M-DAP or 0.10M-Aerosol-OT over one month at 49.7°, using the highest possible sodium methoxide concentration.

¹H N.m.r. spectroscopy has been utilized for the determination of the extent and site of interaction of 4-nitropyridine *N*-oxide with the surfactants. In the absence of surfactants the spectrum of 4-nitropyridine *N*-oxide in benzene consists of two 2H doublets centred at δ 6.598 (H _{α}) and 6.951 (H _{β}) which are assigned to the protons *ortho* and *meta* to the *N*-oxide group, respectively.¹²

¹⁰ E. Oclirai, *J. Org. Chem.*, 1953, **18**, 534.

¹¹ R. M. Johnson, *J. Chem. Soc. (B)*, 1966, 1058.

¹² A. R. Katritzky and J. M. Lagowski, *J. Chem. Soc. (B)*, 1971, 43.

The spectrum of DAP in the presence and absence of 4-nitropyridine *N*-oxide consists of a single ammonium resonance, an apparent triplet for the methylene protons adjacent to the ammonium ion, a quartet for the propionate

pyridine *N*-oxide, in the concentration range 0.010–0.064M, to 0.50M-DAP results in significant observable shifts for only three of the surfactant protons at 100 MHz, the ammonium protons and the methylene protons

TABLE 2

Interaction of sodium methoxide with 4-nitropyridine *N*-oxide in benzene in the presence of Igepal CO-530 at 49.7°^a

10 ³ [Igepal CO-530]/M	10 ³ k _ψ /s ⁻¹						k ₂ /l mol ⁻¹ s ⁻¹
	0.605 × 10 ⁻³ M-NaOCH ₃	1.06 × 10 ⁻³ M-NaOCH ₃	1.50 × 10 ⁻³ M-NaOCH ₃	2.12 × 10 ⁻³ M-NaOCH ₃	2.68 × 10 ⁻³ M-NaOCH ₃	3.25 × 10 ⁻³ M-NaOCH ₃	
0	0.0013	0.0019	0.0026	0.0042	<i>b</i>	<i>b</i>	0.00187
1.00	1.06	1.29	1.92	2.84	2.75	<i>b</i>	0.90
2.00	0.792	2.29	2.01	3.26	3.77	<i>b</i>	1.12
4.00	1.51	2.36	3.89	4.59	5.50	6.39	1.75
6.00	0.795	1.85	2.66	4.59	5.74	6.65	2.17
7.00	0.679	1.51	2.60	4.05	5.41	6.85	2.28
8.00	0.615	1.62	2.38	3.99	4.87	6.55	2.17
9.00	0.465	1.13	2.01	3.16	4.23	5.20	1.85
10.0	0.511	1.26	2.02	3.12	3.94	3.04	1.67
15.0	0.308	1.39	1.67	2.56	2.81	3.61	1.14
20.0	0.242	0.598	1.01	2.02	2.21	2.88	0.96

^a Benzene solutions containing 0.10% methanol; [4-nitropyridine *N*-oxide] = 5 × 10⁵M; concentration of NaOCH₃ expressed stoichiometrically, *i.e.* as that in benzene-surfactant-methanol; in neat methanol *k*₂ at 49.7° = 0.32 l mol⁻¹ s⁻¹ (obtained from *k*_ψ values of 4.40 × 10⁻³, 7.70 × 10⁻³, 10.1 × 10⁻³, 14.4 × 10⁻³, and 17.9 × 10⁻³ s⁻¹ using 1.21 × 10⁻², 2.12 × 10⁻², 3.00 × 10⁻², 4.24 × 10⁻², and 5.35 × 10⁻²M-NaOCH₃, respectively). ^b Precipitation occurs.

methylene protons, a broad resonance for the intermediate methylene protons of the ammonium ion, and fairly sharp

adjacent to the ammonium ion and to the carboxy-group. For purposes of comparison the data can be described by equation (1)¹³ where δ and δ₀ are the observed and limiting

$$\delta = \delta_0 + a[S] \quad (1)$$

chemical shifts, respectively, and S is the solubilize or substrate. A minor discontinuity has been observed at *ca.* 0.02M concentration of 4-nitropyridine *N*-oxide in the plots of the former two protons (the slope *a* changes from negative to positive) while the plot of δ_{CH₂CO₂} shows no discontinuity (Figure 1). These breaks may be interpreted in terms of changes in the solubilization site of the substrate in DAP aggregates.¹⁴ It is likely that the orientation of 4-nitropyridine *N*-oxide involves interactions between the nitrogen and oxygen atoms of the nitro and *N*-oxide groups and the headgroups of DAP, *i.e.* the carboxylate and ammonium ions. From the *a* values (*a* 0.64 for H_α and 0.57 for H_β), it is apparent that the α-protons, *ortho* to the *N*-oxide group, are affected to a slightly greater extent than the protons *meta* to the *N*-oxide group. Although a variety of factors could contribute to this observed behaviour, some interactions between the headgroups of DAP and aromatic protons of the 4-nitropyridine *N*-oxide substrate is clearly indicated.

The ¹H n.m.r. spectra of Aerosol-OT show a fairly sharp

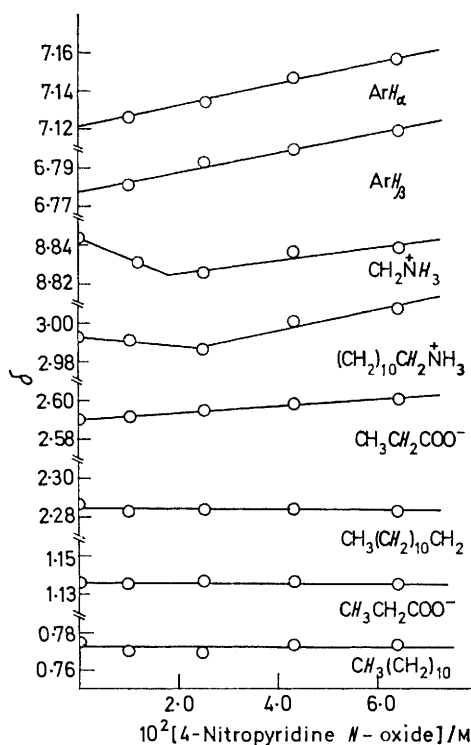


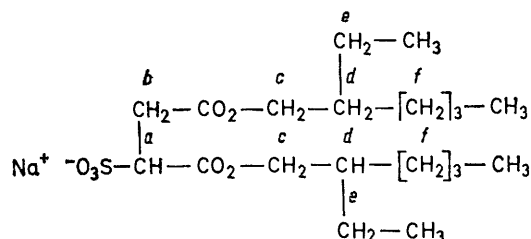
FIGURE 1 Plots of the observed chemical shifts (δ) of 0.50M-DAP and of 4-nitropyridine *N*-oxide at 100 Hz as a function of 4-nitropyridine *N*-oxide concentration

triplets for the terminal methyl protons of the propionate ions and of the alkyl ammonium ion. Addition of 4-nitro-

¹³ E. J. Fendler, C. L. Day, and J. H. Fendler, *J. Phys. Chem.*, 1972, **76**, 1460; J. H. Fendler, E. J. Fendler, G. A. Infante, P.-S. Sheih, and L. K. Patterson, *J. Amer. Chem. Soc.*, 1975, **97**, 89.

triplet for the methine proton (*a*) next to sulphonate group (δ 4.697), and the methylene protons of the succinate

¹⁴ J. C. Eriksson and G. Gillberg, *Surface Chem.*, 1965, 148.



system (b) appear as one singlet at δ 3.508. The broad apparent doublet which is centred at δ 4.126 is assigned to the methylene proton attached to the ester oxygen atom (c) based on the characteristic resonance frequencies of methylene protons bonded to the oxygen atom of carboxylic esters.¹⁵ The four terminal methyl groups of the hydrocarbon chain and the ethyl group appear as one broad singlet (δ 0.885). All the other protons of the hydrocarbon chain appear as a poorly resolved broad singlet centred at σ 1.281, *i.e.*, the methine protons (d) and the methylene protons (e and f). The methine protons may comprise the observed downfield shoulder of this

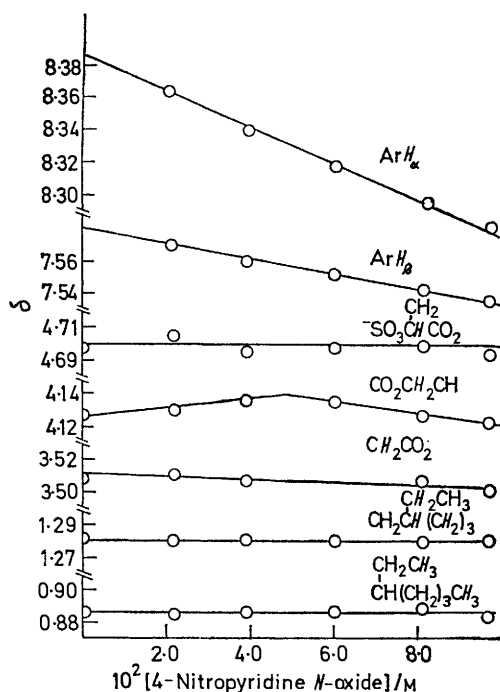
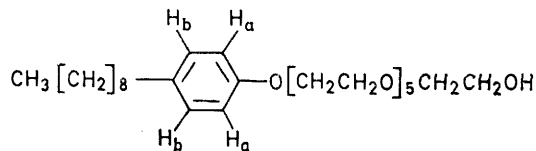


FIGURE 2 Plots of the observed chemical shifts (δ) of 0.50M-Aerosol-OT and of 4-nitropyridine *N*-oxide at 100 Hz as a function of 4-nitropyridine *N*-oxide concentration

resonance while the main portion of the peak is due to the methylene protons (e and f). The data for 0.50M-Aerosol-OT in the presence and absence of 4-nitropyridine *N*-oxide are illustrated in Figure 2. It is notable that with increasing concentration of 4-nitropyridine *N*-oxide the only surfactant protons which are significantly affected are the methylene protons of the succinate system and the methylene protons attached to the ester oxygen atom. However the H_α and H_β protons of 4-nitropyridine *N*-oxide shift upfield to a considerable extent (0.03 and 0.08 p.p.m., respectively) in the concentration range 0.022–0.097M (Figure 2). The dependence is linear and gives values of -1.09 and -0.44 for the protons *ortho* and *meta* to the *N*-oxide group, respectively. The upfield shift suggests that the aromatic protons of 4-nitropyridine *N*-oxide are increasingly shielded with increasing substrate concentration. These results again indicate a substrate-surfactant interaction, the precise site(s) of which is not discernible

¹⁵ R. M. Silverstein and G. S. Bassler, 'Spectrometric Identification of Organic Compounds,' Wiley, New York, 1967, 2nd edn., pp. 136–137.

from these results. However, the observation that the protons *ortho* to the *N*-oxide group are affected to a greater extent than those *ortho* to the nitro-group by aggregated



Aerosol-OT suggests at least some degree of specific orientation of the substrate.

The ^1H n.m.r. spectrum of 0.50M-Igepal CO-530 in [$^2\text{H}_6$]benzene consists of 2H doublets for the aromatic protons, and two sets of multiplets in the range δ 0.4–1.6 which correspond to the methyl and methylene protons of the long chain hydrocarbon system and the protons of the oxyethylene portion of the surfactant, respectively.¹⁶ Chemical shifts of the surfactant protons are insensitive to the addition of 4-nitropyridine *N*-oxide in the concentration range 0.022–0.094M with the exception of the H_α protons of the aromatic ring (Figure 3). Likewise the

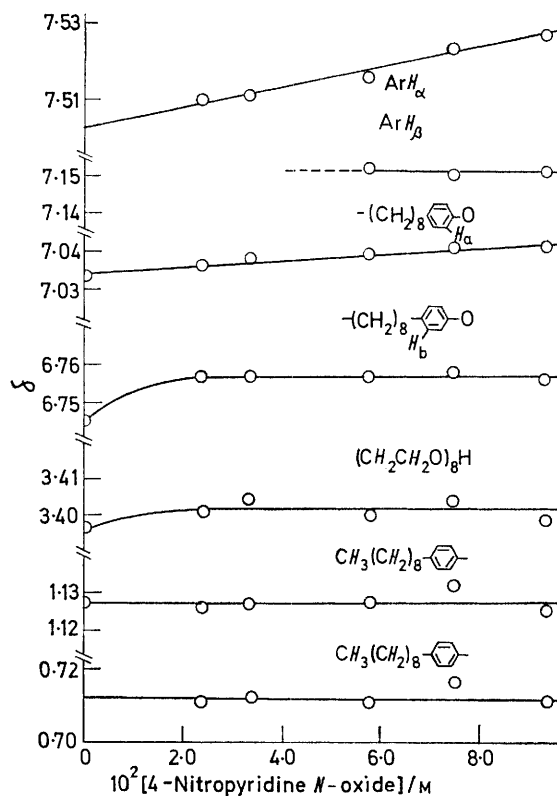


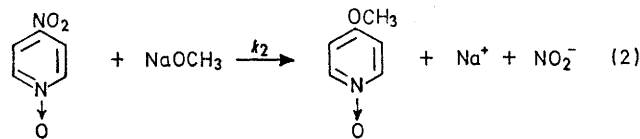
FIGURE 3 Plots of the observed chemical shifts (δ) of 0.50M-Igepal CO-530 and of 4-nitropyridine *N*-oxide at 100 Hz as a function of 4-nitropyridine *N*-oxide concentration

H_α protons of 4-nitropyridine *N*-oxide shift downfield only very slightly with increasing concentration thus indicating little if any interaction between the substrate and the non-ionic surfactant.

¹⁶ P-S. Sheih and J. H. Fendler, *J. Phys. Chem.*, 1975, **79**, in the press.

DISCUSSION

The observed rate constants for the reaction (2) of sodium methoxide with 4-nitropyridine *N*-oxide must



be discussed in terms of differential reactivities in bulk benzene and that in the environment of surfactant aggregates in addition to considering interactions of *both* reactants with the surfactants. The separation of these parameters is not an easy problem, since a knowledge of effective reagent concentration in both pseudo-phases is required. Indeed, the reported rate enhancements by aqueous micelles for second-order reactions are often merely the consequence of preferential concentration of the reagent into (or onto) the micelles.¹⁷⁻²⁰ Although the data obtained for reaction (2) in benzene in the presence of surfactant aggregates are also expressed as apparent rate constants (*i.e.*, they are calculated on the basis of methoxide ion concentrations in the total system), they can be fruitfully compared not only to that in neat benzene but to that in a polar reference solvent such as methanol.

Our choice of this aromatic substrate was somewhat dictated by its expected favourable partitioning into the polar interior of surfactant aggregates. Unfortunately, this expectation was not realized. None of the surfactants significantly solubilize 4-nitropyridine *N*-oxide (Table 1). The ¹H n.m.r. investigations also indicate relatively modest interactions between the aromatic substrate and the surfactant systems (Figures 1-3). The order of these interactions is DAP ~ Aerosol-OT > Igepal CO-530. Based on ¹H n.m.r. data, effects of surfactant aggregates on reaction (2) should therefore be more pronounced for DAP and Aerosol-OT than for Igepal CO-530. Experimental data are, however, just the opposite (see Results section and Table 2). Clearly interaction and hence apparent concentration of the other reactant, sodium methoxide, also need to be considered.

Since methanol is a weak acid ($K 10^{-16}$) compared to the dodecylammonium ion ($K 10^{-10.36}$),²¹ methoxide ion may be neutralized as in reaction (3). At the



highest methoxide ion concentration used, $3.25 \times 10^{-2}\text{M}$,

¹⁷ E. J. Fendler and J. H. Fendler, *Adv. Phys. Org. Chem.*, 1970, **8**, 271.

¹⁸ E. H. Cordes and C. Gitler, *Progr. Bioorg. Chem.*, 1973, **2**, 1.

in 0.10M-DAP in benzene containing 0.10% (*i.e.*, $2.47 \times 10^{-2}\text{M}$) methanol, equilibrium (3) could lie completely to the right, with $K 10^{5.6}$, thereby leaving no free methoxide ion available to attack 4-nitropyridine *N*-oxide.

Lack of reactivity in Aerosol-OT can be rationalized in terms of the sulphosuccinate group, which in the interior of the cavity of the aggregate is at least partially ionic. Electrostatic interaction will not only hinder the approach of the nucleophile but will lower the electron-withdrawing ability of the *N*-oxide group in 4-nitropyridine *N*-oxide. ¹H N.m.r. evidence substantiates the latter postulate (Figure 2).

Reaction (2) in benzene is considerably enhanced by Igepal CO-530 (Table 2). The second-order rate constant k_2 increases exponentially with increasing surfactant concentration up to a maximum, after which it slightly decreases. This type of kinetic rate profile has often been observed previously for micellar catalysis.¹⁷⁻²⁰ At maximum catalysis, the rate constant for reaction (2) in benzene in the presence of $7.0 \times 10^{-2}\text{M}$ -Igepal CO-530 is 1220 times greater than that in neat benzene. More significantly it is 7-fold greater than that in neat methanol. The origin of this rate enhancement is not entirely understood. It may not be the consequence of substrate-surfactant interactions, since the n.m.r. shifts of both the surfactant and the substrate protons are altered the least by Igepal CO-530. However, since the observed changes in chemical shifts depend upon the mole fraction of substrate in the 'free' and 'bound' form and the chemical shift of each species, more substrate may interact with Igepal CO-530, *i.e.* the percentage in the 'bound' form is higher, while DAP and Aerosol-OT exhibit larger changes in apparent chemical shifts with a much lower percentage in the 'bound' form. Similarly, the solubility of sodium methoxide in benzene is only some 5-6-fold greater in the presence of 0.10M-Igepal CO-530 than that in its absence. Conceivably, strong interactions between the methanol cosolvent and the polyoxyethylene units of Igepal CO-530 desolvate the incipient methoxide ion, thereby enhancing its nucleophilicity.

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¹⁹ I. V. Berezin, K. Martinek, and A. K. Yatsimirskii, *Russ. Chem. Rev.*, 1973, **42**, 787.

²⁰ J. H. Fendler and E. J. Fendler, 'Catalysis in Micellar and Macromolecular Chemistry,' Academic Press, New York, 1975.

²¹ 'Handbook of Chemistry and Physics,' Chemical Rubber Co., Cleveland, 1969, 50th edn., p. 501.