Table II. Dependence of the Values of ρ on the Concentration of Solubilized Water[a]

H_2O, M	ρ_X	ρ_Y[b]	ρ_Y/ρ_X
0	2.043	2.36	1.16
0.1	1.848	2.58	1.40
0.2	1.877	2.72	1.45
0.3	1.848	2.80	1.51
0.4	1.910	2.86	1.50
0.6	1.910	2.94	1.54
0.8	1.877	2.97	1.58

[a] [DAP] = 0.2 M, at 35 °C in cyclohexane. [b] Based on σ_p.

As expected, both ρ_X and ρ_Y were independent of the concentration of the surfactant since we have less than one ester molecule/DAP aggregate. Consequently, ester solubilization is not likely to change the nature of the reaction site, i.e., the micellar core (however, vide infra when water was solubilized). The fact that $\rho_Y > \rho_X$ shows that the reaction is more susceptible to the nature of the LG and is in agreement with eq 2 representing the rate limiting step. Two important differences exist, however, between the results of aminolysis by DA in cyclohexane and by DAP or by DA + DAP in the same solvent. First the values of ρ_X and ρ_Y are different, and the micellar ρ_Y/ρ_X ratios are, at a first glance, disappointingly small. The nature of the reaction "medium" is, however, very different in both cases. Unlike the nonpolar, aprotic cyclohexane, the micellar core is protic and highly polar.[2,13] As a consequence the ionic tetrahedral intermediates, and the incipient transition states, will most likely be H-bonded to the DAP headions.[14] In fact, only in cyclohexane is the aminolysis by DAP second order in the surfactant,[2,5] showing that the intermediate I of eq 1 is associated with a second molecule of the detergent. This H-bonding will stabilize the transition state and attenuate the dependence of k_{obsd} on the nature of the LG, i.e., decrease ρ_Y.

The preceding idea can be neatly verified by examining the behavior of ρ_X and ρ_Y when the H-bonding ability of DAP is progressively decreased. Solubilization of water is known to hydrate the $^+NH_3$ and CO_2^- groups of DAP and to decrease their tendency to form H-bonds.[1,2,13] We have studied the aminolysis of 3 esters (X/Y = H/NO_2; NO_2/H; NO_2/NO_2) by DAP in the presence of solubilized water and the results are given in Table II. The remarkable feature of this table is the constancy of ρ_X as a function of increasing the concentration of the solubilized water. On the other hand, ρ_Y (and hence ρ_Y/ρ_X) steadily increased. From this table it is clear that as the H-bonding ability of DAP decreases (due to its hydration), the reaction becomes more sensitive to the structure of the LG, as argued before. The fact that only ρ_Y showed a noticeable dependence on [H_2O] is in clear agreement with eq 2 being the slow step.[16] Compared to acyl transfer reactions in bulk organic solvents,[10,11] it seems, therefore, that the observed enhancement of the reaction rates by micellar alkylammonium carboxylates[2-6] is not due to changes either in the reaction mechanism or in the nature of the slow step.

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(16) It has been argued that the aggregation number of DAP reversed micelles increases as a function of increasing R.[17a] Evidence to the contrary is also available.[17b] It is not expected, however, that any changes in the micellar parameters due to water solubilization will affect the validity of the preceding discussion. The similarity of the structures of the series of esters used here guarantees that any additional perturbance (for example, that induced by water solubilization) will affect ρ_x, ρ_y, and hence their ratio, in a similar way.

Experimental Section

Cylohexane (Merck) was kept on activated 4-Å molecular sieves; DA (Merck) was distilled from CaH_2. DAP was prepared as given elsewhere[15] and dried to a constant weight in vacuo, over P_2O_5. The esters were prepared by refluxing the appropriate acyl chloride (from the acid and $SOCl_2$)[18] and sodium phenoxide (from the phenol and NaH)[18] in dichloroethane for 5 h. After filtration of the precipitated NaCl, and evaporation of the solvent, the crude esters were crystallized from ethanol–hexane. Their purity was established from their melting points[11,19] and ^1H NMR spectra.

Ester aminolysis was studied with a Zeiss PM6KS spectrophotometer under pseudo-first-order conditions as given before.[4,5] The values of k_{obsd} were obtained from the absorbance–time data with a Burroughs 6900-B computer. The percentage relative standard deviation of k_{obsd} (i.e., the standard deviation × 100/k_{obsd}) was <2%.

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Registry No. DA, 124-22-1; DAP, 17448-65-6; $O_2NC_6H_4$-*p*-$CO_2C_6H_4$-*p*-NO_2, 1037-31-6; ClC_6H_4-*p*-$CO_2C_6H_4$-*p*-NO_2, 6264-29-5; $PhCO_2C_6H_4$-*p*-NO_2, 959-22-8; $H_3CC_6H_4$-*p*-$CO_2C_6H_4$-*p*-NO_2, 15023-67-3; $H_3COC_6H_4$-*p*-$CO_2C_6H_4$-*p*-NO_2, 7464-46-2; $O_2NC_6H_4$-*p*-$CO_2C_6H_4$-*p*-CN, 32792-81-7; $O_2NC_6H_4$-*p*-$CO_2C_6H_4$-*p*-Cl, 7511-31-1; $O_2NC_6H_4$-*p*-CO_2Ph, 1429-05-6; $O_2NC_6H_4$-*p*-$CO_2C_6H_4$-*p*-CH_3, 15024-11-0.

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Nucleophilic Aromatic Substitution in the Pyrrole Ring: Leaving Group Effect

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In nucleophilic aromatic substitutions the leaving group order $NO_2 \gg Cl > Br$ is commonly observed when anionic nonpolarizable nucleophilic reagents such as methoxide ion react with activated aromatic derivatives such as 1-X-2,4-dinitrobenzenes[1] or 1-X-4-nitrobenzenes.[2] The greater reactivity of the nitro group reflects a two-step addition–elimination mechanism, in which the attachment of the nucleophile to the aromatic ring is the rate-determining step. The high rate of attachment to the NO_2-bearing position can thus be explained on the basis of the ipso effect: the highly electronegative nitro group favors the formation of a bond between the anionic nucleophile and the ipso carbon atom, which has a relatively low electron density.[1]

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Table I. Second-Order Rate Constants, Activation Parameters, and Reactivity Ratios of the Substitution Reactions of Compounds 1a–c and 2a–c with MeO^- Ion, in MeOH at 25 °C

compd	X	k, M^{-1} s^{-1}	$\Delta H^{\ddagger}$,[a] kcal mol^{-1}	$-\Delta S^{\ddagger}$,[a] cal $°C^{-1}$ mol^{-1}	k_{NO_2}/k_X
1a[b]	Br	6.97×10^{-5}	20.6 (0.6)	8.4 (1.7)	20
1b[c]	Cl	1.22×10^{-4}	19.3 (0.4)	11.8 (1.2)	11
1c[d,e]	NO_2	1.36×10^{-3}	20.4 (0.2)	3.4 (0.7)	1
2a[f]	Br	2.67×10^{-7}	24.0 (0.25)	7.6 (0.7)	633
2b[f]	Cl	3.78×10^{-7}	23.2 (0.2)	9.8 (0.5)	447
2c[e,g]	NO_2	1.69×10^{-4}	21.8 (0.1)	2.5 (0.4)	1

[a] Standard deviation in parentheses. [b] $k \times 10^7$, M^{-1} s^{-1} (°C): 3.1 (38.3), 7.4 (45.9), 17.0 (53.7), 33.7 (61.6). [c] $k \times 10^4$, M^{-1} s^{-1} (°C): 4.9 (38.2), 11.3 (45.8), 23.8 (53.9), 46.5 (61.5). [d] Reference 3. [e] Corrected for the statistical factor. [f] Calculated from data reported in ref 4. [g] Calculated from data reported in ref 5.

We have been interested in comparing the relative reactivities of nitro, bromo, and chloro groups in pyrroles with those in benzenes. With this aim we have measured the rate of substitution of 1-methyl-2-X-5-nitropyrroles (**1a,b**; X = Br, Cl) with methoxide ion in methanol. Kinetic and activation data have been compared with our previous data on the related reaction of 1-methyl-2,5-dinitropyrrole[3] (**1c**) and the literature data on the reaction of 1-X-4-nitrobenzenes **2a–c** (X = Br,[4] Cl,[4] NO_2[5]) under the same conditions.

Results and Discussion

1-Methyl-2-nitropyrrole[6] was brominated with Br_2 in AcOH, giving low yields of both 2-bromo-1-methyl-5-nitropyrrole (**1a**, 3.7%) and 3-bromo-1-methyl-5-nitropyrrole (12.6%). This bromination procedure was not very reproducible: in some experiments we obtained only polybromo derivatives or 3-bromo-1-methylmaleimide. Attempted brominations with Br_2 in CF_3COOH or CCl_4 were unsuccessful. A mixture of the two bromonitro derivatives was also obtained by bromination with *N*-bromosuccinimide in tetrahydrofuran,[7] but the somewhat higher yield of **1a** was accompanied by an even larger amount of the 3-bromo isomer, making the separation more difficult. The reaction of 1-methyl-2-nitropyrrole with Cl_2, SO_2Cl_2, or *N*-chlorosuccinimide did not yield the desired chloronitro derivative **1b**. However, we were able to prepare **1b** by the reverse sequence of nitrating 2-chloro-1-methylpyrrole, which was prepared according to a literature method.[8] No attempt was made to prepare **1a** by this sequence because 2-bromo-1-methylpyrrole is reported to decompose more easily than 2-chloro-1-methylpyrrole.[8,9]

Kinetic data for the methoxy denitration of **1c** were available from our previous work[3] and for the methoxy substitution of the benzene derivatives **2a–c** from the literature.[4,5] Activation enthalpy and entropy data for the benzene compounds were calculated by using Eyring's equation. Kinetic measurements were carried out on the methoxy dehalogenation of **1a** and **1b**. Rate constants and activation parameters for the reactions of **1a–c** and **2a–c** are reported in Table I, together with the calculated k_{NO_2}/k_X ratios at 25 °C.

The pyrrole ring affects markedly the relative rate of substitution, as shown by the k_{NO_2}/k_X ratios, whereas the relative rates of the bromo and chloro compounds are not very different. The reactivity order in the pyrrole series (NO_2 > Cl > Br) is qualitatively similar to that observed in the benzene series. However, the increased reactivity of the nitro compounds **1c** and **2c**, compared with their halogenated analogues, is much higher in the benzene derivative than in the pyrrole.

Some interesting information can also be obtained from the activation parameters. The denitration reaction in the benzene derivative requires an activation enthalpy lower by nearly 2 kcal mol^{-1} than that of the dehalogenation reactions, whereas the activation enthalpy for each reaction in the pyrrole ring is virtually the same. As for the activation entropy, the change in the calculated $\Delta S^{\ddagger}$ between denitration and dehalogenation is nearly the same in both the benzenes and the pyrroles. Therefore the difference in the activation enthalpy is the factor that seems to be mainly responsible for the fact that denitration of the benzene derivative occurs more rapidly than the dehalogenation reactions. The formation of a new bond at the reaction center and the change of sp^2 to sp^3 hybridization require a major reorganization of the π and σ electron systems. Thus the departure of the nitro group from the aromatic ring plane because of the attachment of the nucleophile occurs with an interruption of the conjugation between the nitro group and the rest of the molecule. Therefore the formation of the anionic intermediate from the pyrrole substrate should be disfavored with respect to the corresponding step in the benzene ring because more energy is required to interrupt the conjugation between the nitro group and the heteroatom, which is stronger than that between the nitro group and the benzene ring. For the same reason the reactions of nucleophilic reagents with 2-acylpyrroles occur less easily than those with acylbenzenes.[10]

The problem can be examined from another point of view. Even if the primary driving force for the nucleophilic attachment is provided by the electrostatic interaction between the nucleophile and the reaction center, the electronegativity factor may be counterbalanced because the electron density of the nitro group may repel the incoming nucleophilic reagent.[1] Increased conjugation of the nitro group should increase the electron density at the nitro group and decrease reactivity because of the increased repulsion between the nucleophile and the reaction site. ^{17}O NMR chemical shift measurements indicate that the electron density at the oxygen atoms of the nitro group in 1-methyl-2-nitropyrrole is higher than that in nitrobenzene because the conjugation in the former is significantly higher.[11]

In contrast to the pyrroles, the conjugation in 4-halopyridines is higher than that in 4-nitropyridine, leading to an increase in the k_{NO_2}/k_X. The relative ratio for reaction of methoxide ion with these pyridines, calculated from literature rate constants,[12,13] is 1.1×10^4 at 25 °C.

Finally, we note that the reactivity ratio of the structurally related pyrrole and benzene compounds is strongly affected by the nature of the leaving group: at 25 °C the ratio is 261 in the debromination, 322 in the dechlorination,

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and 8.0 in the denitration reaction.

Experimental Section

Melting points are uncorrected. UV spectra were recorded on a Cary Model 219 instrument. ^1H NMR spectra were obtained with a JEOL C60-HL apparatus. Low-resolution mass spectra were obtained with an AEI MS 12 spectrometer, high-resolution mass spectra with a Kratos MS 80 spectrometer.

2-Bromo-1-methyl-5-nitropyrrole (1a). A solution of bromine (420 mg, 2.63 mmol) in 5 mL of AcOH was rapidly added at room temperature to a solution of 340 mg of 1-methyl-2-nitropyrrole (2.70 mmol) in 5 mL of AcOH. After 1 h the reaction mixture was poured into water and kept overnight in a refrigerator. The petroleum ether extract (10 × 80 mL) was washed with a $NaHCO_3$ solution and water and dried (Na_2SO_4). After removal of the solvent the residue was subjected to column chromatography on silica gel. The first eluent was benzene, which was progressively enriched with CH_2Cl_2 up to a 1:1 ratio (vol). Four fractions were collected. The first and fourth were not further examined because their ^1H NMR spectra were not consistent with the presence of any simple bromination product. The second fraction (125 mg) showed (TLC) the presence of two compounds. Its ^1H NMR spectrum in CCl_4 was consistent with the presence of two monobromo derivatives of the starting compound. The third fraction (80 mg) was 3,4-dibromo-1-methylmaleimide, identified through its mp (119–120 °C, lit.[14] mp 121 °C) and MS spectrum (*m/e* 267, 269, 271 (M^+)). The second fraction was again subjected to column chromatography (silica gel, CCl_4). Two subfractions were obtained. The first (20 mg) was identified as 2-bromo-1-methyl-5-nitropyrrole (**1a**): mp (petroleum ether, 40–70 °C) 93.5–94.5 °C; ^1H NMR (CCl_4) δ 4.02 (s, 3 H, N-Me), 6.25 (d, 1 H, J = 4.5 Hz, H-3), 7.10 (d, 1 H, J = 4.5 Hz, H-4); UV (MeOH) λ_{max} 343 nm (ϵ 1.3 × 10^4); mass spectrum, calcd for $C_5H_5N_2O_2Br$ (M^+) *m/e* 203.9534, 205.9514, .9514, found 203.9520, 205.9503; yield 3.7%. The second subfraction (70 mg) was identified as the isomeric 3-bromo-1-methyl-5-nitropyrrole: mp 62–63 °C; ^1H NMR ($CDCl_3$) δ 3.99 (s, 3 H, N-Me), 6.80 (d, 1 H, J = 2.25 Hz, H-β), 7.17 (d, 1 H, J = 2.25 Hz, H-α); mass spectrum, *m/e* 205, 207 (M^+); yield 12.6%.

The structure assignments for these isomers were based upon their J values, by taking into account the fact that in the presence of nitro groups the J values are generally higher than those in other pyrrole derivatives.[15]

2-Chloro-1-methyl-5-nitropyrrole (1b). A solution of SO_2Cl_2 (850 mg, 6 mmol) in 2 mL of Et_2O was slowly added to a solution of 1-methylpyrrole (500 mg, 6 mmol) in 2 mL of Et_2O at 0 °C. The reaction mixture was kept at 10 °C for 1 h. A 10% K_2CO_3 solution (7 mL) was added, and the ether layer was separated and washed with water, and dried (Na_2SO_4). The solvent was cautiously removed at room temperature at nearly 300 mmHg, and the crude residue containing presumably 2-chloro-1-methylpyrrole was dissolved in 30 mL of Ac_2O for nitration. A nitrating mixture, made up from 100% HNO_3 (290 mg, 4.6 mmol) and Ac_2O (10 mL), was slowly added (1 h) under stirring to the Ac_2O solution of the chloro derivative at −10 °C. After 15 min the reaction mixture was poured on ice. The resulting black solution was repeatedly extracted with Et_2O, and the ether extracts were washed with $NaHCO_3$ and water, dried, and concentrated. The residue was subjected to column chromatography (silica gel, benzene–1:1 benzene/ethyl acetate). Seven fractions were collected. The first one (50 mg) was identified through its ^1H NMR spectrum as 2,5-dichloro-1-methylpyrrole.[8] The second fraction (50 mg) was identified as 2-chloro-1-methyl-5-nitropyrrole (**1b**): mp (petroleum ether, 40–70 °C) 72–72.5 °C; ^1H NMR (CCl_4) δ 4.00 (s, 3 H, N-Me), 6.15 (d, 1 H, J = 4.5 Hz, H-3), 7.11 (d, 1 H, J = 4.5 Hz, H-4); UV (MeOH) λ_{max} 340 nm (ϵ 1.2 × 10^4); mass spectrum, calcd for $C_5H_5N_2O_2Cl$ (M^+) *m/e* 160.0040, found 160.0035; yield 5%. The third fraction (40 mg) had a ^1H NMR spectrum consistent with the presence of **1b** and 1-methyl-2-nitropyrrole. The other fractions were not further examined.

Substitution Products. 2-Halogeno-1-methyl-5-nitropyrroles **1a,b** were kept with the equivalent amount of sodium methoxide in methanol at 40 °C for 4–5 days. 2-Methoxy-1-methyl-5-nitropyrrole[3] was obtained in good yields from both substrates. However, the yields were not quantitative because under the reaction conditions the methoxy derivative decomposes slowly. A similar behavior can be observed during the substitution of 2-bromo-5-nitrofuran with piperidine or benzenethiolate ion.[16] It must be observed that during the methoxy denitration of **1c** the decomposition reaction of the product does not interfere with the kinetic experiments because the denitration reaction occurs more rapidly than the dehalogenation reactions of **1a** or **1b**.

Kinetic Measurements. The kinetics were followed spectrophotometrically in the thermostated compartment of a Cary 219 instrument, under pseudo-first-order conditions in the presence of an excess of sodium methoxide. Kinetic experiments were carried out at the absorbance maximum of the product (375 nm). Rate constants were corrected for the thermal dilatation of methanol. The substrate concentrations were in the range 3–5 × 10^{-5} M, the MeO^- ion concentration in the range 0.03–0.25 M. The reactions were second order, first order in both substrate and nucleophile. Because of the instability of the reaction product under the reaction conditions, absorbance values at infinite time were calculated by Mangelsdorf's method.[17] The rate constants at 25 °C and the activation parameters were calculated with Eyring's equation.

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Registry No. **1a**, 91606-34-7; **1b**, 91606-35-8.

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Intramolecular Photochemistry of a Vinylogous Amide and Some Transformations of the Photoproduct

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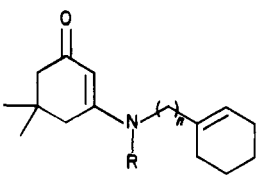
In connection with our interest in the intramolecular photochemistry of vinylogous imides we decided to investigate the similar reaction of a secondary vinylogous amide. Previously we had found that irradiation of vinylogous imide **1a** produced the expected photocyclo-



1a, R = Ac; *n* = 1
1b, R = Ac; *n* = 2
1c, R = Ac, *n* = 3
1d, R = H; *n* = 2

addition product[1] while irradiation of vinylogous imides **1b** and **1c** provided major photoproducts formally arising via an ene-type reaction.[2] We now report on the photochemistry of the nonacetylated vinylogous amide **1d** and

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