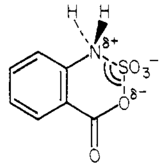
believe that the difference which will exist for these rate constants at the same temperature excludes the proposed mechanism as there are hydrogen bonding solvation differences which must be taken into account in the ground and transition states.[17] It can also be shown that the model for the proton-catalyzed hydrolysis of *N*-arylsulfamates, namely, the attack of water on pyridine-*N*-sulfonates, also reacts faster than the zwitterionic sulfamate. The energy difference between the model and the arylsulfamate is the difference in solvation energy between the transition and ground state in both water and acetate ion attack. This is likely to be less for the transition state where the aniline acidity is less than the acidity in the anilinium ion ground state.

The mechanistic difference demonstrated for inter- and intramolecular catalysis by the carboxyl group is in our opinion due to a stereoelectronic phenomenon. We believe that the intermolecular mechanism is the preferred one but that this is excluded in the intramolecular case by the stereoselectronic requirements of attack by nucleophiles on the sulfur which is collinear with entering and leaving atoms. The six-membered-ring transition state for eq 9 and 12 (6-endo-tet) requires a deviation of about 70° from collinearity (structure III). Similar constraints have been observed to suppress endocyclic $S_N$ reactions at saturated carbon[18,19] because the preferred backside attack is not possible in small rings.[20]



III

**Acknowledgment.** We thank SERC for a CASE maintenance grant (A.H.) and ICI, Organics Division, Blakely, for generous support.

**Registry No.** sodium *N*-1-Naphthyl sulfamate, 35525-93-0; disodium *N*-(2-carboxyphenyl)sulfamate, 81044-28-2; salicyl sulfate, 89-45-2; sodium *N*-[(2-methoxycarbonyl)phenyl]sulfamate, 81044-29-3.

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# Electrophilic Heteroaromatic Substitutions. 5.[1] Acid-Catalyzed Reaction of Ethyl 3,4,5-Trimethylpyrrole-2-carboxylate with Diazonium Salts in Aqueous Acetic Acid[2]

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The reaction with diazonium salts of the title compound, 1, has been examined in detail by chromatographic and spectroscopic methods. In the presence of a strong mineral acid, 1 reacts with *p*-nitrobenzenediazonium ions to give a red, chemically labile, azo dye, 4, in equilibrium with its orange conjugated base 3. Both 3 and 4 slowly undergo α-demethylation in the aqueous reaction medium, affording ethyl 3,4-dimethyl-5-[(*p*-nitrophenyl)azo]pyrrole-2-carboxylate (2), identified by comparison with an authentic specimen. Thus, for the first time, conclusive experimental evidence for α-dealkylation by diazonium ions in monopyrrole derivatives has been obtained. This dealkylation reaction seems to be especially favored by the electron-withdrawing ability of the *p*-nitro group. The red azo dye (analogous to 4) formed when 1 reacts with diazotized sulfanilic acid in the presence of strong acids reverts to the reactants on dilution of the reaction mixture with water. A structure for 4 is proposed, and possible reaction mechanisms are discussed.

The reaction of pyrrole derivatives with diazonium salts has received considerable attention. Besides conventional diazo coupling,[4] a few nonconventional processes have been reported, including α-side-chain substitution[5] and dealkylation reactions.[6-8] Dealkylations are well established in polypyrrolic chemistry (e.g., dipyrrylmethane derivatives), and mechanisms have also been proposed[6b,8] for

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(1) Part IV: Giardi, M. T.; Sleiter, G. *Gazz. Chim. Ital.* **1980**, *110*, 361.

(2) Presented at the 12th Convegno Nazionale di Chimica Organica, Ancona, Italy, Sept 14–19, 1980.

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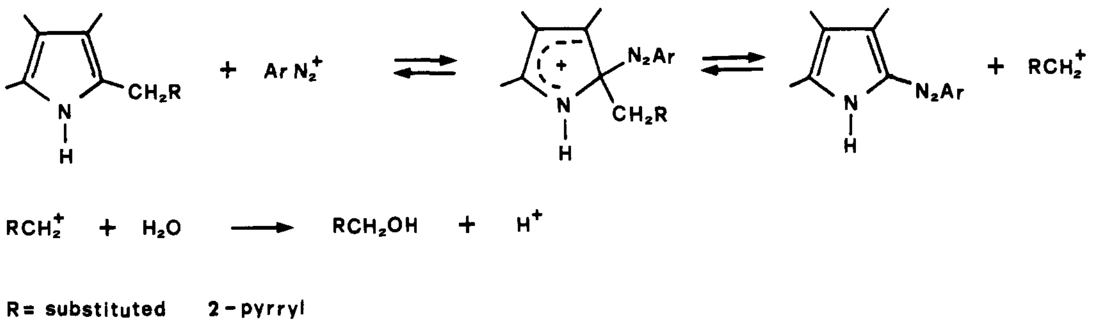
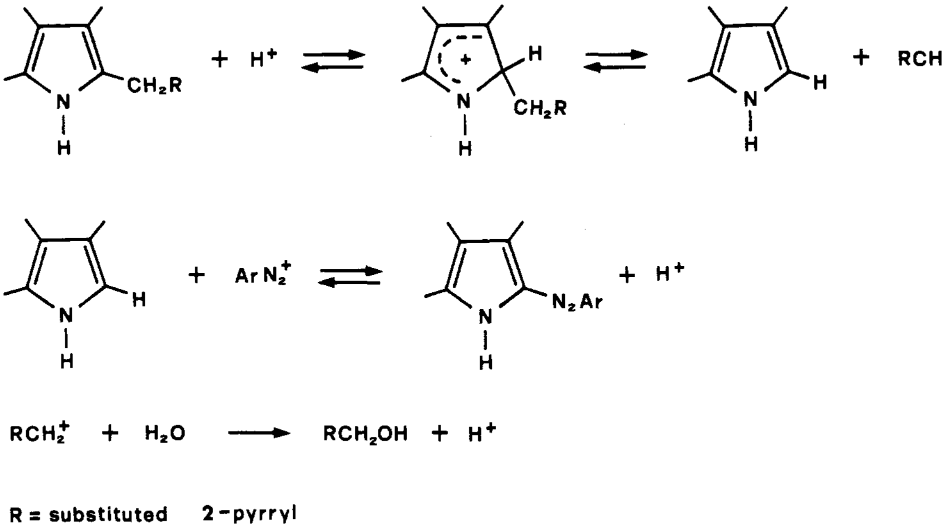
(7) Triebs, A.; Derra-Scherer, H. *Justus Liebigs Ann. Chem.* **1954**, *589*, 196.

(8) Butler, A. R.; Shepherd, P. T. *J. Chem. Soc., Perkin Trans. 2* **1980**, 115.

Scheme I



Scheme II



these processes (Schemes I and II). As to $\alpha$-methylpyrrole derivatives, virtually no experimental evidence exists about the possibility of demethylation by diazonium salts. Treibs and Derra-Scherer[7] reported on the reaction of 2,3,4,5-tetramethylpyrrole with diazotized sulfanilic acid, which they assumed to afford 2-[(*p*-sulfophenyl)azo]-3,4,5-trimethylpyrrole since the visible (VIS) spectrum of the reaction mixture was identical with that obtained when 2,3,4-trimethylpyrrole was coupled with diazotized sulfanilic acid. The reaction product of either reaction was, however, neither isolated nor otherwise characterized. It was also assumed[6b,7] that electron-withdrawing nuclear substituents prevent the $\alpha$-demethylation reaction.

In a previous paper[1] it was shown that in a hydroxylic solvent and in the presence of strong mineral acid ethyl 3,4,5-trimethylpyrrole-2-carboxylate (1) undergoes reversible N-substitution by formaldehyde rather than $\alpha$-side-chain substitution.[9] In order to ascertain whether other electrophilic reagents behave similarly under comparable conditions and to possibly gain experimental support for Treibs and Derra-Scherer's hypothesis, we examined the reaction of pyrrole 1 with diazotized sulfanilic acid and *p*-nitrobenzenediazonium salts in aqueous acetic acid. The structural features of pyrrole 1 are such as to avoid conventional diazo coupling, to assure, by the presence of the $\beta$-methyl groups, a conveniently high reactivity toward relatively weak electrophiles, and to slow down, by the presence of an electron-withdrawing $\alpha$ substituent, oxidation and polymerization processes, which are strongly favored in an acid medium. Among several possible electron-withdrawing substituents ($CO_2H$, CHO, COR, etc.), the ethoxycarbonyl group was chosen since it is known to be a very poor leaving group in electrophilic aromatic substitutions.

## Experimental Section

Melting points are uncorrected. $^1H$ NMR spectra were obtained on a JEOL JNM-C60HL apparatus and mass spectra on an AEI MS 12 spectrometer (70 eV). Electronic spectra were registered on a Beckman DB-GT spectrophotometer equipped with a Kontron W + W 1100 recorder, and IR spectra (Nujol mulls) were obtained on a Perkin-Elmer Infracord instrument. Microanalyses were carried out at the Laboratorio di Microanalisi of the Istituto Superiore di Sanità, Rome. Chromatographic separations were carried out on pretreated[10] silica gel (Merck, reinst); for the thin-layer chromatographic analyses, Merck $F_{254}$ silica plates were used. Unless otherwise noted, the eluant was a mixture of benzene and ethyl acetate (9:1 v/v). The solvents used were purified and, when necessary, dried as usual.

**Arenediazonium Salts. 4-Diazobenzenesulfonic acid** was a commercial product (Fluka).

***p*-Nitrobenzenediazonium chloride solutions** were prepared by the following procedure. *p*-Nitroaniline[11] (0.1 mol) was dissolved in hot (80–90 °C) concentrated HCl[15] (104 mL). The solution was chilled to −10 °C with vigorous stirring, and to the resulting slurry was added an ice-cold solution of $NaNO_2$ (0.1 mol in 182 mL of water) under the surface of the liquid at such a rate as to prevent temperature from rising above 0 °C. After the addition was complete, stirring was continued for ca. 30 min before testing for the presence of unreacted $HNO_2$, which was eventually destroyed with urea. The titer of the diazonium salt solution, which proved spectrophotometrically ($\lambda_{max}$ 259 nm) to be stable for at least 36 h if stored at 5 °C in the dark, was determined

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[9] Angelini, G.; Giancaspro, C.; Illuminati, G.; Sleiter, G. *J. Org. Chem.* **1980**, *45*, 1786.

[10] Rattini, G. A.; Sleiter, G. *Justus Liebigs Ann. Chem.* **1975**, 1677.

[11] The commercial product was purified by repeated crystallizations from aqueous ethanol to a constant melting point.

colorimetrically against a standard of Chromotrop 2B (Fluka, p.a.) after coupling with alkaline disodium chromotropate (Erba, RPE).

***p*-Nitrobenzenediazonium Tetrafluoroborate.** To a solution of *p*-nitrobenzenediazonium chloride[12] (from 5 g of *p*-nitroaniline) was added the required amount of ice-cold 40% tetrafluoroboric acid dropwise with stirring. The precipitate was collected, washed with ice-cold water, and purified by repeated low-temperature crystallizations from acetone–petroleum ether (bp 30–50 °C). Yields were always better than 95%. Anal. Calcd for $C_6H_4BF_4N_3O_2$: C, 30.41; H, 1.69; N, 17.74. Found: C, 30.15; H, 1.69; N, 17.67.

**Pyrrole Derivatives.** Ethyl 3,4,5-trimethylpyrrole-2-carboxylate (1)[1] and ethyl-5-formyl-3,4-dimethylpyrrole-2-carboxylate (9)[13] were prepared as described in the references given. Ethyl 3,4-dimethylpyrrole-2-carboxylate (8) was obtained from 3,4-dimethylpyrrole[14] by the usual procedure;[15] mp 94–95 °C (lit.[16] mp 95–96 °C).

**(*p*-Nitrophenyl)hydrazone of 9 (7).** To a stirred solution of 0.4 g (2.6 mmol) of (*p*-nitrophenyl)hydrazine in 2 mL of 96% sulfuric acid were cautiously added 2 mL of water and 10 mL of 95% ethanol in that order. The resulting mixture was filtered, and a solution of 9 (0.126 g, 0.65 mmol) in 4.2 mL of 95% ethanol was added to 12.6 mL of the filtrate. After the mixture had been allowed to stand a few minutes, a little water was dropped in; the red precipitate formed was collected (nearly quantitative yield) and recrystallized from aqueous ethanol; mp 192–193 °C. Anal. Calcd for $C_{16}H_{18}N_4O_4$: C, 58.17; H, 5.49; N, 16.96. Found: C, 57.98; H, 5.47; N, 16.66.

**Ethyl 3,4-Dimethyl-5-[(*p*-nitrophenyl)azo]pyrrole-2-carboxylate (2).**[17] To a solution of *p*-nitrobenzenediazonium chloride (0.55 mmol) was added an equimolar amount of 8 (92 mg) dissolved in 15 mL of glacial acetic acid at 5 °C. After 30 min, the precipitate was collected, thoroughly washed with ice-cold water, and taken up in methyl formate. Drying (anhydrous $Na_2SO_4$) and removal of the solvent in vacuo afforded 0.19 g (98.8%) of orange crystals: mp 111–113 °C dec; $^1H$ NMR ($CDCl_3$) $\delta$ 1.4 (t, 3 H, $CO_2CH_2CH_3$), 2.3 (s, 3 H, $\beta$-$CH_3$), 2.4 (s, 3 H, $\beta$-$CH_3$), 4.4 (q, 2 H, $CO_2CH_2CH_3$), 8.05 (AA'XX' q, 4 H, para-disubstituted $C_6H_4$), 9.03 (br s, 1 H, NH); IR $\nu_{max}$ 3250 (NH), 1700 (CO), 1530 ($NO_2$), 1350 cm$^{-1}$ ($NO_2$); VIS (94% aqueous AcOH) $\lambda_{max}$ 420 nm ($\epsilon$ 3.3 × 10$^4$ M$^{-1}$ cm$^{-1}$); upon addition of HCl, $\lambda_{max}$ 480 nm; mass spectrum, *m/z* 316 (M), 166 ($C_9H_{12}NO_2$), 150 ($C_6H_4N_3O_2$). Anal.[18] Calcd for $C_{15}H_{16}N_4O_4$: C, 56.96; H, 5.10; N, 17.71. Found: C, 56.96; H, 5.53; N, 16.97.

**Ethyl 1,3,4,5-Tetramethylpyrrole-2-carboxylate (10).** The procedure described by Anderson et al.[19] was adopted, with slight modifications. The preparation was carried out in an argon atmosphere with degassed solvents. To an ice-cold solution of 1 (1.8 g, 10 mmol) and $Me_2SO_4$ (1.05 mL, 11 mmol) in $CH_2Cl_2$ (15 mL) containing 0.4 g of Aliquat 336 (Fluka) was added 50% aqueous NaOH (5 mL) with stirring. After being refluxed 20 h, the reaction mixture was diluted with water, and the layers were separated. The aqueous phase was extracted with two 2-mL portions of $CH_2Cl_2$. The combined extracts were washed with dilute HCl and with brine and finally dried over anhydrous $Na_2SO_4$. The solvent was removed in an argon flow, and the residue (1.7 g) was purified by low-temperature recrystallization from aqueous ethanol: yield 1.6 g (81%); mp 39–40 °C (lit.[20] mp 39–40 °C); $^1H$ NMR ($CCl_4$) $\delta$ 1.4 (t, 3 H, $CO_2CH_2CH_3$), 1.8 (s, 3 H, 4-$CH_3$), 2.10 and 2.12 (2 s, 6 H, 3- and 5-$CH_3$), 3.65 (s, 3 H, 1-$CH_3$), 4.2 (q, 2 H, $CO_2CH_2CH_3$).

**Reactions of 1 with Diazonium Salts. With *p*-Nitrobenzenediazonium Tetrafluoroborate in the Presence of HCl.** To 5 mL of a 0.0423 M solution of the diazonium salt in 86% aqueous AcOH containing 6 mmol of HCl was added 1 (0.21 mmol, 38 mg) at 5 °C. Upon addition of the pyrrole, the solution became brownish. After ca. 5 min, the color changed first to yellow and then to ruby red. At this point, neutralization (AcONa) of the HCl in a portion of the reaction mixture caused the color to change from red to orange. The progress of the reaction was followed by TLC: a few drops of the reaction mixture were brought to dryness in vacuo, and the residue was taken up in ether for the analysis. Solutions of 1, 2, and 7 were also applied on the plate for comparison. After 1 h, four spots appeared on the chromatogram: (1) $R_f$ ca. 0, *p*-nitrobenzenediazonium salt; (2) ruby red, $R_f$ 0.13, compound 4;[21] (3) orange, $R_f$ 0.21, compound 3; (4) $R_f$ 0.40, starting 1. After ca. 7 h, a fifth spot (orange) was apparent on the plate, the color and the $R_f$ (0.55) of which were the same as those of 2. It should be noted that, if the HCl present was neutralized with AcONa prior to the TLC analysis, the red spot with $R_f$ 0.13 did not appear on the chromatogram. Up to 24 h at 5 °C and in the dark the analyses gave the same results, qualitatively. Thereafter, the reaction mixture started to blacken, and the number of the spots on the chromatograms increased. Therefore, it was decided to not prolong the reaction time over 20–22 h.

In the absence of mineral acid, a very complex mixture of products formed, among which none of the compounds 2–4 were present (TLC).

**With *p*-Nitrobenzenediazonium Chloride.** To a solution containing 0.55 mmol of the diazonium salt and 5.7 mmol of HCl[22] was added 1 (100 mg, 0.55 mmol) dissolved in 15 mL of glacial AcOH at 5 °C. The chromatic changes and the course of the reaction (as ascertained by TLC) were the same as described above. After 20 h, the isolation of the products was attempted. The mixture was poured in ice-cold water and extracted with four 20-mL portions of cold ether. The extracts were washed with ice-cold 5% aqueous ammonia and with ice-cold water, dried ($Na_2SO_4$), and brought to dryness in vacuo at 5 °C. The residue was applied onto a refrigerated column of silica gel (2-cm i.d., length 37 cm) and eluted. Examination (TLC) of the fractions collected showed that extensive decomposition of the reaction products had occurred. In another experiment, instead of extracting the reaction products into ether, the reaction mixture was poured onto 300 g of crushed ice: an orange precipitate formed slowly, which was collected, thoroughly washed with ice-cold water, and taken up in pentane. The dried pentane solution was brought to dryness in vacuo; the residue (0.34 g starting from 0.30 g of 1) proved (TLC) to be a mixture of 1 and of the compound with $R_f$ 0.55. Compounds 3 and 4 were absent. For separation of the two components, the mixture was applied onto silica gel (refrigerated column) and eluted with 9:1 (v/v) pentane–methyl formate. A first group of fractions contained only the colored substance, a second group pyrrole 1 in admixture with the orange compound, and a third group only the starting 1. Complete separation was achieved by rechromatographing the second group of fractions. The solvent was removed at 5 °C under vacuum; 0.115 g (20%) of the orange compound with $R_f$ 0.55 and 0.22 g (76%) of 1 were obtained. The physical properties of the orange product were the same as those reported above for compound 2. Anal.[18] Calcd for $C_{15}H_{16}N_4O_4$: C, 56.96; H, 5.10; N, 17.71. Found: C, 57.46; H, 5.53;, N, 17.07.

An increase of the molar ratio diazonium salt/pyrrole 1 from 1:1 up to 10:1 did not appreciably affect the yield of 2. Pyrrole 1 was always recovered in about 75% yield. No 2 was formed at all if the HCl used in the diazotization of *p*-nitroaniline was neutralized with AcONa before addition of the pyrrole.

**With Diazotized Sulfanilic Acid.** To a solution of diazotized sulfanilic acid (1.5 g, 8 mmol) and 1 (0.5 g, 2.7 mmol) in 10 mL

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(12) Fierz-David, H. E.; Blangey, L. "Grundlegende Operationen der Farbenchemie", 5th ed.; Springer-Verlag: Vienna, 1943; p 235.

(13) Paine, J. B., III; Dolphin, D. *Can. J. Chem.* **1976**, *54*, 411.

(14) Ichimura, K.; Ichikawa, S.; Imamura, K. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1157.

(15) Fischer, H.; Orth, H. "Die Chemie des Pyrrols"; Akademische Verlagsgesellschaft: Leipzig, 1934; Vol. I, p 234.

(16) Fischer, H.; Höfelmann, H. *Justus Liebigs Ann. Chem.* **1938**, *533*, 216.

(17) The coupling of 8 with *p*-nitrobenzenediazonium salts has been reported by Badger et al.[4b] However, they did neither isolate nor characterize the reaction product.

(18) An entirely satisfactory analysis could not be obtained for this compound due to its thermal and chemical lability which prevented its purification.[5]

(19) Wang, N.-C.; Teo, K.-E.; Anderson, H. J. *Can. J. Chem.* **1977**, *55*, 4112.

(20) Booth, H.; Johnson, A. W.; Johnson, F.; Langdale-Smith, R. A. *J. Chem. Soc.* **1963**, 650.

(21) Compound 7 has the same $R_f$ as 4. The color of the spot is, however, very different.

(22) It was ascertained that solutions of *p*-nitrobenzenediazonium chloride are stable for at least 36 h if kept at 5 °C in the dark.

of 94% aqueous AcOH was added 1 mL of 65% sulfuric acid (ca. 10 mmol) at 0 °C. After 24 h at 15 °C, the deep red reaction mixture was divided in two portions. The first was poured into water. To the second was added the amount of aqueous AcONa sufficient to neutralize the sulfuric acid, causing the color to change from red to green. Shortly after, both colors started to fade, and an off-white solid began to precipitate from both solutions upon addition of more water. Both precipitates were collected and analyzed by TLC: only 1 (which could be recovered in nearly quantitative yield) and the reagent were present. Attempts to isolate the green substance by extraction into an organic solvent were unsuccessful. The $^1$H NMR of a ca. 2:1 (mole/mole) mixture of 1 and diazotized sulfanilic acid in trifluoroacetic acid (internal standard $CH_2Cl_2$) immediately after mixing showed the signals of the pyrrole at $\delta$ 1.2 (t, $CO_2CH_2CH_3$), 1.95 (s, $CH_3$), 2.2 (s, $CH_3$), 2.5 (s, $CH_3$), and 4.3 (q, $CO_2\mathbf{CH_2}CH_3$) and that of the AA′XX′ system of the *p*-diazobenzenesulfonic acid at $\delta$ 8.45 (q). After 70 h, the AA′XX′ quartet appeared at $\delta$ 7.65, whereas all the signals due to the pyrrole were doubled, the new ones being shifted to lower field.

**Reaction of 10 with *p*-Nitrobenzenediazonium Tetrafluoroborate.** To 5 mL of a 0.0423 M solution of the diazonium salt in 86% aqueous AcOH containing 6 mmol of HCl was added 10 (0.2 mmol, 39 mg) at 5 °C. After being stirred 20 h, the nearly colorless reaction mixture was poured into water. The creamy white precipitate was collected and analyzed by TLC; no 2 had been formed.

**Attempt To Isolate Compounds 3 and 4.** The reaction of 1 with *p*-nitrobenzenediazonium chloride was carried out under the same conditions described above for the preparative experiment. After 20 h, the unreacted diazonium salt was precipitated by adding the stoichiometric amount of ammonium hexafluorophosphate. The diazonium hexafluorophosphate was filtered and washed with a minimum of cold, aqueous AcOH. The filtrate was examined spectrophotometrically ($\lambda_{max}$ 360, 420, and 504 nm) and then brought to dryness under vacuum (no heat was applied). A red powder was obtained, the VIS spectrum of which (94% aqueous AcOH) still showed maxima at 360, 420, and 504 nm. The powder was applied onto silica gel (refrigerated column) and eluted with 10:1 benzene–ethyl acetate. A first group of fractions contained (TLC) 2 alone, a second group 2 in admixture with 1, a third group a mixture of 1–3, and a fourth group a mixture of 2 and 3. The red substance (4) remained absorbed on the column. On further elution, 4 gradually turned black; the eluate first contained only 2 and 3 and, later on, several unidentified decomposition products. The fractions containing substance 3 were chromatographed again, but separation could not be achieved; 3, which eventually disappeared completely, was always accompanied by 2. It is therefore evident that chromatography causes both 3 and 4 to transform into 2.

**Spectrophotometric Study of the Reaction of 1 with *p*-Nitrobenzenediazonium Chloride.** Two kinds of experiments were performed. In the first, to 2 mL of a ca. $10^{-4}$ M solution of 1 in 94% aqueous AcOH ($\lambda_{max}$ 285 nm) was added 37% HCl (ca. 80 $\mu$L). A new absorption maximum appeared at 360 nm, indicating the formation of the conjugated acids of 1. Treatment of this solution with an equivalent amount of *p*-nitrobenzenediazonium chloride ($\lambda_{max}$ 259 nm) caused the appearance of an absorption band at 504 nm (the intensity of which increased gradually) and, later on, of a further absorption at 420 nm. The latter increased at the expense of that at 504 nm if the HCl was neutralized with AcONa. On addition of HCl again, the process reversed. In the second, two 1-mL samples of the reaction mixture of pyrrole 1 and *p*-nitrobenzenediazonium chloride obtained as described in the preparative experiments were transferred into 100-mL volumetric flasks. The first sample was diluted to the mark with 94% aqueous AcOH (solution A) and the VIS spectrum of the solution registered immediately thereafter. The spectrum showed a weak absorption at 420 nm and a strong one at 504 nm. Solution A was then set aside in the refrigerator. To the second sample was added the volume (0.15 mL) of a 2.35 M solution of AcONa in 94% aqueous AcOH required to neutralize the excess of HCl. After dilution to the mark with 94% aqueous AcOH, the VIS spectrum of the solution (B) was registered: Only an absorption maximum at 420 nm was present. This absorption shifted to 504 nm upon addition of 1 drop of concentrated HCl into the cell. Also solution B was then set aside in the refrigerator.

After ca. 3 h, the VIS spectra of both solutions were recorded again. That of solution A showed the nearly complete disappearance of the absorption at 504 nm, which was replaced by a maximum at 480 nm (the absorption maximum of the conjugated acid of pyrrole 2), whereas no change was apparent in the spectrum of solution B. However, upon addition of 1 drop of concentrated HCl into the cell, the absorption maximum of solution B did not shift to 504 nm but, instead, to 480 nm, which is the wavelength of maximum absorption of the protonated form of 2.

## Results and Discussion

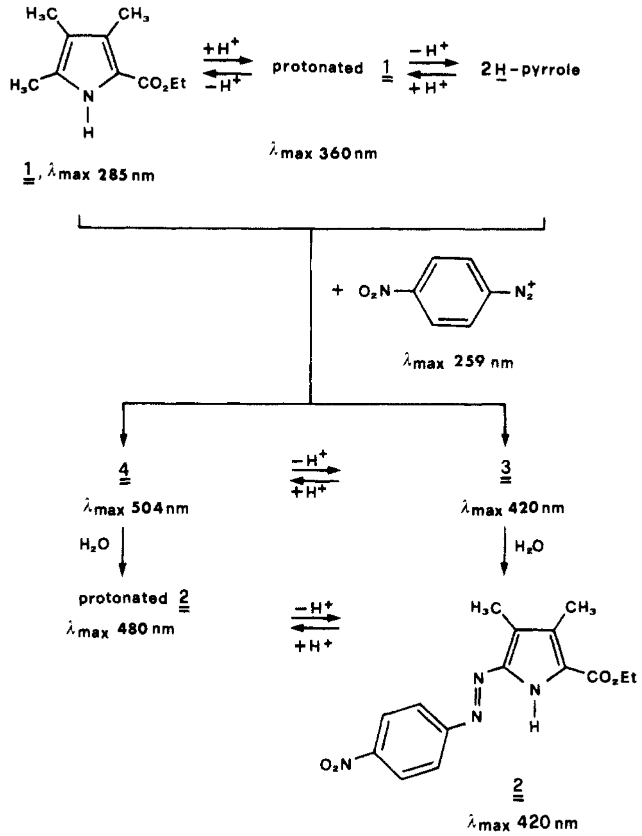
Contrary to previous statements,[6b,7] pyrrole 1 reacts in aqueous acetic acid with diazonium salts despite the presence of an electron-withdrawing substituent. The outcome of the reaction, however, depends on the nature of the diazonium salt and the reaction conditions. In the absence of strong acids, very complex mixtures of products formed, from which no definite substance could be isolated, whereas a simpler picture resulted when the reaction was carried out in the presence of a strong acid. Under the latter condition, 1 reacted with *p*-nitrobenzenediazonium salts to give a red substance (4) accompanied by minor amounts of two other orange compounds (2 and 3), as shown by TLC analysis. Neutralization (AcONa) of the reaction mixture caused 4 to disappear completely and the amounts of 2 and 3 to increase; 4 was therefore thought to be the protonated form of either 2 or 3. On dilution of the reaction mixture with water, an orange-yellow precipitate formed, which did not contain compounds 3 and 4 but only 2 and unreacted 1.

Pyrrole 2 proved to have the structure of ethyl 3,4-dimethyl-5-[(*p*-nitrophenyl)azo]pyrrole-2-carboxylate by its spectroscopic properties and by comparison with an authentic specimen (see the Experimental Section). Thus, for the first time conclusive experimental proof for $\alpha$-demethylation of monopyrrole derivatives by diazonium ions has been obtained.

However, $\alpha$-demethylation is by no means a general process, and as the present experimental data show, it can be neither the consequence of electrophilic attack of the diazonium ion on the methyl-substituted $\alpha$-position nor of a protiodemethylation, although processes of this kind have been proposed[6b,8] for the cleavage of dipyrrylmethane derivatives by diazonium ions in neutral (Scheme I) or acid solution (Scheme II), respectively.

Both the results of the TLC analysis of the reaction mixture of 1 and *p*-nitrobenzenediazonium salts at various times and of the attempted chromatographic separation of compounds 3 and 4 suggested that 2 might be the product of further transformation of both 3 and 4. Support for this suggestion was obtained by a spectrophotometric study of the reaction. The observed sequence of spectral changes (Scheme III) clearly showed that on electrophilic attack by the *p*-nitrobenzenediazonium ion on pyrrole 1 (or tautomers thereof) species 3 and 4 are formed first and that 2 (and its conjugated acid) is the product of a subsequent, slow reaction of 3 and 4 with the aqueous reaction medium. Spectral changes similar to those depicted in Scheme III (from pale yellow to red and, on neutralization of the mineral acid, from red to green) were also observed when 1 was reacted with diazotized sulfanilic acid. However, 1 was recovered unchanged upon dilution of the reaction mixture with water, and no color developed at all when the *N*-methyl derivative of 1 (10) was treated with *p*-nitrobenzenediazonium tetrafluoroborate. The mechanisms of Schemes I and II can be excluded for $\alpha$-methylpyrrole derivatives since dealkylation should also occur when an *N*-methyl substituent is present, in the absence

Scheme III



of an acid catalyst and independently of the nature of the diazonium ion.

Another conceivable mechanism is the one involving $\alpha$-side-chain substitution, acid-catalyzed elimination of the substituted side chain, and subsequent reaction of the diazonium ion with the $\alpha$-alkyl-free pyrrole derivative. However, if this were the case, the yield of **2** should be dependent on the molar ratio of $ArN_2^+/1$ used, and the *p*-nitrophenylhydrazone of ethyl 5-formyl-3,4-dimethylpyrrole-2-carboxylate (**7**),[21] which may be considered the first side-chain substituted intermediate, should afford **2** when treated with *p*-nitrobenzenediazonium salts under the same conditions as for **1**. Actually, the yield of **2** is independent of the mole ratio $ArN_2^+/1$ in the range 1:1 to 10:1, and no **2** was formed when **7** was reacted with *p*-nitrobenzenediazonium salts.

The experimental data seem to be compatible with a primary electrophilic attack of the arenediazonium ion at the pyrrole nitrogen. In solution, such an attack can occur only if the NH group is deprotonated. Deprotonation from the pyrrole nitrogen can be achieved either in the presence of sufficiently strong bases or through an acid-catalyzed 1*H*-pyrrole $\rightleftarrows$ 2*H*-pyrrole equilibrium.[1] Electrophilic attack to the nitrogen atom of the 2*H*-pyrrole species thus formed would yield tautomeric pyrroleninium cations (**4**) in equilibrium with their conjugated base (**3**). Experimental support for this proposal is given by the following facts: the VIS spectra of **2** and **3** (Scheme III) are practically coincident (thus indicating similar conjugation of the (*p*-nitrophenyl)azo group with the pyrrole nucleus in both compounds); pyrrole **10** is not dealkylated by *p*-nitrobenzenediazonium ions; the $^1H$ NMR spectrum of the reaction mixture of **1** and diazotized sulfanilic acid only showed a downfield shift of the signals due to the methyl protons (which is consistent with the attachment of an electron-attracting group to the pyrrole nitrogen) instead of the extensive splitting which would have been observed[9] if electrophilic attack at the C-nuclear positions had occurred.

In the aqueous reaction medium, both **3** and **4** slowly convert into **2**. The formation of **2** may be explained by assuming nucleophilic attack by water on the $\alpha$-methyl group (which would be eliminated as methanol) and concerted migration of the (*p*-nitrophenyl)azo group to the $\alpha$-position.

As to the scope of this unusual reaction, only the absence of easily replaceable groups and of an N substituent seems to be required in the pyrrole, while the presence of strong electron-withdrawing substituents (such as $NO_2$) in the aromatic nucleus of the arenediazonium salt appears to be necessary for demethylation to take place.

Since under comparable conditions, the reactions of **1** with either formaldehyde[1] or diazotized sulfanilic acid only give N-substituted products which revert to the reactants when treated with dilute aqueous mineral acids, it appears unlikely that the reactions of 2,3,4,5-tetramethylpyrrole with diazotized sulfanilic acid[7] or with Ehrlich's reagent[7,23] result in $\alpha$-demethylation, as proposed[7,23] without any experimental evidence.

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**Registry No.** 1, 2199-46-4; 1 (conjugate acid), 38415-04-2; 2, 80975-84-4; 2 (conjugate acid), 80975-85-5; 3, 80975-87-7; 4, 80997-14-4; 7, 80975-86-6; 8, 938-75-0; 9, 4391-99-5; 10, 55770-80-4; *p*-nitroaniline, 100-01-6; *p*-nitrobenzenediazonium chloride, 100-05-0; *p*-nitrobenzenediazonium tetrafluoroborate, 456-27-9; *p*-nitrophenylhydrazine, 100-16-3; diazotized sulfanilic acid, 2154-66-7.

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[23] Alexander, R. S.; Butler, A. R. *J. Chem. Soc., Perkin Trans. 2* 1976, 696.