

Electrophilic Heteroaromatic Reactions. 3.¹ The α -Side-Chain Bromination of Some Polysubstituted α -Methylpyrroles in the Dark. Evidence for the Formation of Intermediate σ Adducts

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The bromination of some ethyl 3,5-dimethyl-4-R-pyrrole-2-carboxylates (R = alkyl, Br, Cl, CO₂Et) with molecular bromine in dichloromethane solution, in the dark, occurs smoothly at room temperature to yield the corresponding 5-bromomethyl derivatives. The course of the reaction was followed by titrimetric, spectrophotometric, and NMR methods. The reaction can be regarded as an extreme case of behavior in the interaction of aromatic systems with electrophiles, as it consists of two separately observable processes. Upon addition of bromine to the solution of the pyrrole, a number of cationic σ adducts form as a result of attack on all carbon positions of the pyrrole ring to varying extents. The adducts then decompose relatively slowly to a single substitution product. Each of the 4-R groups appears to affect the rates of the two main steps in opposite ways. This is interpreted in terms of stabilization of the reaction intermediate.

Studies on nonconventional pathways for the electrophilic chlorination of alkyl aromatics leading to side-chain substitution³ have been extended to methyl-substituted 5-membered heteroaromatics⁴ and, more recently, to pyrrole derivatives.^{1b}

Dark bromination also gives rise to similar processes, but it may bring new kinetic features⁵ which help to broaden our knowledge on the scope of these reactions.

Like chlorination, the side-chain bromination of α -methylpyrroles has been known for a long time.⁶ No physical organic studies have ever been reported, however. We now wish to report on a kinetic and spectroscopic investigation of the dark bromination of a number of pyrrole derivatives (1-5). Although the kinetic information which has been obtained is not extensive, it has been made possible by the lower reactivity of electrophilic bromine as compared to chlorine. The special timing of the main stages of the reaction of the pyrrole substrates with bromine has enabled the spectral detection and, in favorable cases, isolation of σ adducts as true intermediates in an electrophilic aromatic substitution process.

Experimental Section

Melting points are uncorrected. Chromatographic separations were carried out on silica gel (Merck) and TLC analyses on Merck F₂₅₄ silica plates. The eluant was a mixture of benzene and ethyl acetate (9:1 v/v). ¹H NMR spectra were obtained in CDCl₃ or CD₂Cl₂ solution either on a JEOL JNM-C60 HL or on a Bruker WH-90 spectrometer with Me₄Si as internal standard and ESR spectra were obtained on a Varian E9 apparatus by using quartz tubes. Electronic spectra were taken on a Perkin-Elmer 402 spectrophotometer.

(1) (a) A preliminary account of this work was given by G. Illuminati at the Friedel-Crafts Centennial Symposium, New Orleans, LA, March 23-25, 1977. This work was then presented by G. Sleiter at the 2nd International Conference on the Mechanisms of Reactions in Solution, Canterbury (U.K.), July 9-13, 1979. (b) Part 2: Angelini, G.; Illuminati, G.; Monaci, A.; Sleiter, G.; Speranza, M. *J. Am. Chem. Soc.* **1980**, *102*, 1377.

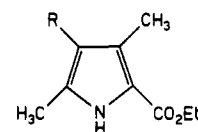
(2) Laboratorio CNR di Chimica Nucleare, I-00010 Montelibretti (Roma).

(3) Baciocchi, E.; Illuminati, G. *Prog. Phys. Org. Chem.* **1967**, *5*, 1.

(4) Baciocchi, E.; Clementi, S.; Sebastiani, G. V. *J. Chem. Soc., Perkin Trans. 2* **1976**, 266, and references therein.

(5) Baciocchi, E.; Casula, M.; Illuminati, G.; Mandolini, L. *Tetrahedron Lett.* **1969**, 1275.

(6) (a) Fischer, H.; Orth, H. "Die Chemie des Pyrrols"; Akademische Verlagsgesellschaft: Leipzig, 1934; Vol. I, pp 75 ff. Corwin, A. H.; Viohl, P. *J. Am. Chem. Soc.* **1944**, *66*, 1137. Gossauer, A. "Die Chemie der Pyrrole"; Springer-Verlag: Berlin, 1974; pp 326 ff. Jones, R. A.; Bean, G. P. "The Chemistry of Pyrroles"; Academic Press: London, 1976; pp 349 ff. (b) Fischer, H.; Scheyer, H. *Justus Liebigs Ann. Chem.* **1923**, *434*, 237. (c) Fischer, H.; Walach, B. *Ibid.* **1926**, *450*, 125.



- 1: R = CO₂Et
- 2: R = Br
- 3: R = CH₃
- 4: R = C₂H₅
- 5: R = Cl

Materials. Dichloromethane was purified as described previously^{1b} and carbon tetrachloride was dried over P₄O₁₀ and fractionally distilled. Bromine was Merck Suprapur. Hydrogen bromide solutions were prepared shortly before use by bubbling anhydrous HBr⁷ into dry, oxygen-free CH₂Cl₂. Their HBr content was determined by potentiometric argentometry in water-methanol using a Radiometer P401 silver electrode and a K601 mercurous sulfate-potassium sulfate (saturated) reference electrode. Blank experiments showed that CH₂Cl₂ does not interfere with the HBr determination.

α -Methylpyrroles, including diethyl 3,5-dimethylpyrrole-2,4-dicarboxylate (1),⁸ ethyl 4-bromo-3,5-dimethylpyrrole-2-carboxylate (2),⁹ ethyl 3,4,5-trimethylpyrrole-2-carboxylate (3),¹¹ ethyl 4-ethyl-3,5-dimethylpyrrole-2-carboxylate (4),¹¹ and ethyl 4-chloro-3,5-dimethylpyrrole-2-carboxylate (5),¹² were recrystallized from the appropriate solvent to a constant melting point and their purity was checked by TLC.

Product Analysis. The bromination of pyrroles 1-4 in CCl₄ or CH₂Cl₂ solution, using equimolar quantities of Br₂ and pyrrole, affords the related α -bromomethyl derivatives 1a,^{6b} 2a,^{6b} 3a,^{6c} and 4a⁹ in yields no less than 90%. Their physical properties matched those reported in the given references.

Ethyl 5-bromomethyl-4-chloro-3-methylpyrrole-2-carboxylate (5a) was obtained in similar yield from 5 as oyster white crystals, which melted with partial decomposition at 140-141 °C. Anal. Calcd for C₉H₁₁BrClNO₂: C, 38.53; H, 3.95; Br, 28.48; Cl, 12.64; N, 4.99. Found: C, 38.28; H, 3.93; Br, 28.64; Cl, 12.70; N, 4.98.

¹H NMR spectroscopic examination of the crude bromination products revealed the presence of α -dibromomethyl derivatives

(7) Becker, H.; Berger, W.; Domschke, G.; Fanghänel, E.; Faust, J.; Fischer, M.; Gentz, F.; Gewalt, K.; Gluch, R.; Mayer, R.; Müller, K.; Pavel, D.; Schmidt, H.; Schollberg, K.; Schwetlick, K.; Seiler, E.; Zepfenfeld, G. "Organikum. Organisch-Chemisches Grundpraktikum", 7th ed.; VEB Deutscher Verlag der Wissenschaften: Berlin, 1967; p 620.

(8) Fischer, H.; Noller, C. R. "Organic Syntheses"; Wiley: New York, 1943; Collect. Vol. 2, p 202.

(9) Fischer, H.; Ernst, P. *Justus Liebigs Ann. Chem.* **1926**, *447*, 139.

(10) Gregorovich, B. V.; Liang, K. S. Y.; Clugston, D. M.; MacDonald, S. F. *Can. J. Chem.* **1968**, *46*, 3291.

(11) Rattini, G. A.; Sleiter, G. *Justus Liebigs Ann. Chem.* **1975**, 1977.

(12) Angelini, G.; Sleiter, G. *Gazz. Chim. Ital.* **1975**, *105*, 961.

as byproducts. The latter do not form in detectable amounts when the molar ratio Br_2 :pyrrole is ≤ 0.5 , whereas they become the only reaction product when the molar ratio Br_2 :pyrrole is ≥ 2 and the reaction is allowed to go to completion. Product composition and reaction yields were determined by a combination of chromatographic and electroanalytical methods according to the procedure described earlier.^{1b} α -Dibromomethylpyrroles are red oils sensitive to moisture and characterized by a singlet (1 H) at about δ 6.5 (CHBr_2) in the NMR spectrum and by their conversion into the corresponding aldehydes. The latter can be obtained in good yields as shown by the following experiment. Pyrrole 4 (161.5 mg, 0.83 mmol) was dissolved in 2.1 mL of CHCl_3 and treated with 90 μL (1.75 mmol) of Br_2 in the dark. After the solution was allowed to stand for 24 h, any volatile material was stripped off under reduced pressure at room temperature, and the residue was treated with a saturated solution of ammonium carbonate in aqueous methanol. After 20 min of stirring, the solution was concentrated at 40 °C under reduced pressure to yield, on cooling, the crude ethyl 4-ethyl-5-formyl-3-methylpyrrole-2-carboxylate, 121 mg (70%), mp 87–89 °C (lit.⁹ mp 90 °C).

Kinetic Measurements. The kinetics were usually followed in the presence of an excess of the pyrrole (variable from 2- to 19-fold), by measuring the bromine consumption either by titrimetry or spectrophotometry. By the former method, the procedure was as described in previous papers,^{13,14} except for quenching which was effected with 2-mL samples and 10 mL of a 1.5% KI solution in aqueous methanol (MeOH/ H_2O 9:1). Blank experiments showed that losses of volatile iodine and oxidation of iodide ions by atmospheric oxygen were negligible. All the kinetic experiments were carried out in a dark room (red lamp). The spectral method was based on the decrease in absorbance at the second absorption band of bromine, λ_{max} 412 nm (ϵ_{412} (CH_2Cl_2) 186.4 $\text{M}^{-1} \text{cm}^{-1}$). A Beckman DB-GT spectrophotometer equipped with a thermostatted cell compartment and a Kontron W+W 1100 recorder was used. The reaction was started by adding in the dark an appropriate volume of a stock solution of bromine to the prethermostatted solution of the pyrrole contained in a 10-mm glass cuvette, which was tightly stoppered, shaken, and placed in the cell compartment of the spectrophotometer. Blank experiments showed that losses of volatile bromine were negligible even after 6 h at 25 °C.

Pseudo-first-order rate coefficients were calculated as usual either from plots of $\ln(c_0/c_t)$ (titrimetric method) or $\ln(A_t - A_{t_{\infty}})$ (spectrophotometric method) vs. time and converted to second-order rate coefficients, k_2 , to take the concentration of the substrate into account. Second-order rate coefficients were also obtained from plots of $\ln(a_t/b_t)$ vs. time (a_t and b_t are the concentrations of Br_2 and pyrrole, respectively, at time t).

The order of the reaction in bromine was determined by the tangent method,¹⁵ and the one in the pyrrole by the application of the second-order integrated rate expression.

The effect of illumination on the reaction was studied in CCl_4 solution by measuring times at 10% reaction¹³ in rate experiments performed in the dark or in the sunlight by using nearly equimolar quantities of pyrrole and bromine.

NMR and ESR Experiments. For the NMR experiments, stock solutions (0.06–0.09 M) of the pyrroles under investigation were prepared in the deuterated solvent (CDCl_3 , CD_2Cl_2). To 0.5 mL of these solutions contained in the NMR tube was added in the dark by means of a microsyringe the quantity of Br_2 (neat) necessary to have a final concentration of 0.04–0.06 M. The spectra were recorded before the addition of bromine and after at convenient time intervals up to reaction completion. Some experiments were performed at varying temperatures (from –10 to +40 °C).

In the ESR experiments the concentrations of bromine and pyrrole 2 (CCl_4 solution) were varied between ca. 2×10^{-2} and ca. 1×10^{-3} M; their ratio was varied from ca. 1:5 to ca. 5:1. Spectra were taken both at room and at liquid-nitrogen temperature. At the former temperature, the samples were either exposed to

Table I. Effect of Light on the Rate of Bromination of Pyrroles 1, 2, 3, and 5 in CCl_4 at 30.0 ± 0.1 °C^a

pyrrole	4-substituent	t_{10} , s ^{b,c}	t_{10}' , s ^{b,d}	t_{10}/t_{10}'
1	CO_2Et	57 900	440	131.6
2	Br	840	88	9.5
3	CH_3	<<1	<<1	ca. 1
5	Cl	730	68	10.7

^a $[\text{Br}_2]_0 = 7.1 \times 10^{-3}$ M; $[\text{pyrrole}]_0 = 5.5 \times 10^{-3}$ M.
^b Time at 10% reaction. ^c In the dark. ^d In the light.

sunlight or irradiated for a few seconds with a high-pressure mercury lamp. At the latter temperature, the frozen samples were irradiated for 2 h or more both with UV and visible light. In no case could pyrroly radicals be detected.

Results and Discussion

Under appropriate experimental conditions (see Experimental Section), the reaction of α -methylpyrroles 1–5 with bromine affords the related α -monobromomethyl derivatives in quantitative yield; in no case were β -bromomethylpyrroles detected among the reaction products. In contrast to previous reports,¹⁶ dibromination of the α side chain may occur, the extent of this reaction depending on the pyrrole:bromine molar ratio, substituent effects, and temperature.

It has been shown^{1b} that the side-chain chlorination of α -methylpyrroles is electrophilic in nature. This appears to be true for the analogous bromination reaction as suggested by the fact that the reaction takes place even in complete exclusion of light and by the electronic effects of the 4 substituents (Table I). Furthermore, neither NMR nor ESR experiments provided any evidence for the formation of paramagnetic species or free-radical intermediates, respectively, and induction periods were never observed in nondegassed solutions. Light speeds up the reaction (Table I), but the acceleration effect decreases as the reactivity of the pyrroles toward electrophilic attack increases. Also, the electronic effect of the 4 substituent is qualitatively the same both in the dark and in the light. We interpret this behavior by assuming that a nonradical component of the process is also present in the experiments performed in the presence of light.

Rate Studies. Rate measurements for the determination of the rate law of the reaction were carried out with 2 ($R = \text{Br}$). They were based on the consumption of bromine and obtained by titrimetric and visible spectrophotometric methods (Table II). The reaction of the alkyl derivatives ($R = \text{Me}, \text{Et}$) was too fast to be followed under the conditions used. With 1 ($R = \text{CO}_2\text{Et}$), although the reaction goes smoothly to completion in preparative batches, it did not progress any further beyond 20% in the kinetic runs, probably because of a specific inhibiting effect of the HBr formed during the reaction and remaining in the closed vessel system.

Bromine is used up by 2 according to a second-order process, first order in each reactant. The simple rate law, $v = k[\text{Br}_2][\text{substrate}]$, is consistent with the observation that Br_2 and Br^- do not associate in CH_2Cl_2 solution.¹⁷ The absence of higher order terms with respect to Br_2 in the bromine concentration range investigated (from ca. 5×10^{-3} to ca. 5×10^{-2} M), as observed in noncatalyzed

(13) Illuminati, G.; Marino, G. *J. Am. Chem. Soc.* 1956, 78, 4975.

(14) Illuminati, G.; Mandolini, L.; Arnett, E. M.; Smoyer, R. *J. Chem. Soc. B* 1971, 2206.

(15) Margerison, D. In "Comprehensive Chemical Kinetics"; Bamford, C. H., Tipper, C. F. H., Eds.; Elsevier: Amsterdam, 1969; Vol. 1, p 356.

(16) Treibs, A.; Bader, H. *Justus Liebigs Ann. Chem.* 1959, 627, 182.

(17) The electronic spectra in the region $350 \leq \lambda \leq 530$ nm of a solution prepared by adding 1 mL of CH_2Cl_2 to 2 mL of 2.83×10^{-3} M Br_2 in CH_2Cl_2 and of a solution prepared by adding 1 mL of 3.03×10^{-3} M HBr in CH_2Cl_2 to 2 mL of a 2.83×10^{-3} M Br_2 in the same solvent were found to be superimposable.

Table II. Kinetic Data for the Reaction of Pyrrole 2 with Br₂ in CH₂Cl₂

<i>T</i> , °C	[Br ₂] ₀ × 10 ³ , M	[2] ₀ × 10 ² , M	<i>k</i> _{obsd} × 10 ⁴ , ^a s ⁻¹	<i>k</i> ₂ × 10 ² , ^a M ⁻¹ s ⁻¹	<i>k</i> _{obsd} × 10 ³ , ^b s ⁻¹	<i>k</i> ₂ × 10 ² , ^b M ⁻¹ s ⁻¹
8.3 ± 0.05	2.26	2.67	2.98	1.12		
	2.20	2.44	2.78	1.14		
	4.64	1.02		1.14		
15.1 ± 0.05	2.10	2.85	5.33	1.87		
	2.10	3.91	7.45	1.90		
	2.10	2.75	5.08	1.85		
24.1 ± 0.1	3.0	5.34			1.59	2.98
	3.0	5.34		3.80 ^c	1.54	2.86
	3.0	6.70			1.92	2.86
25.0 ± 0.05	2.16	2.54	1.02	4.01		

^a Bromine consumption followed by titrimetry. ^b Bromine consumption followed by spectrophotometry (at λ 412 nm).
^c Calculated from the activation parameters (Δ*H*[‡] = 12.3 kcal mol⁻¹, Δ*S*[‡] = -22 eu) derived from the rate constant data measured at 8.3, 15.1, and 25.0 °C.

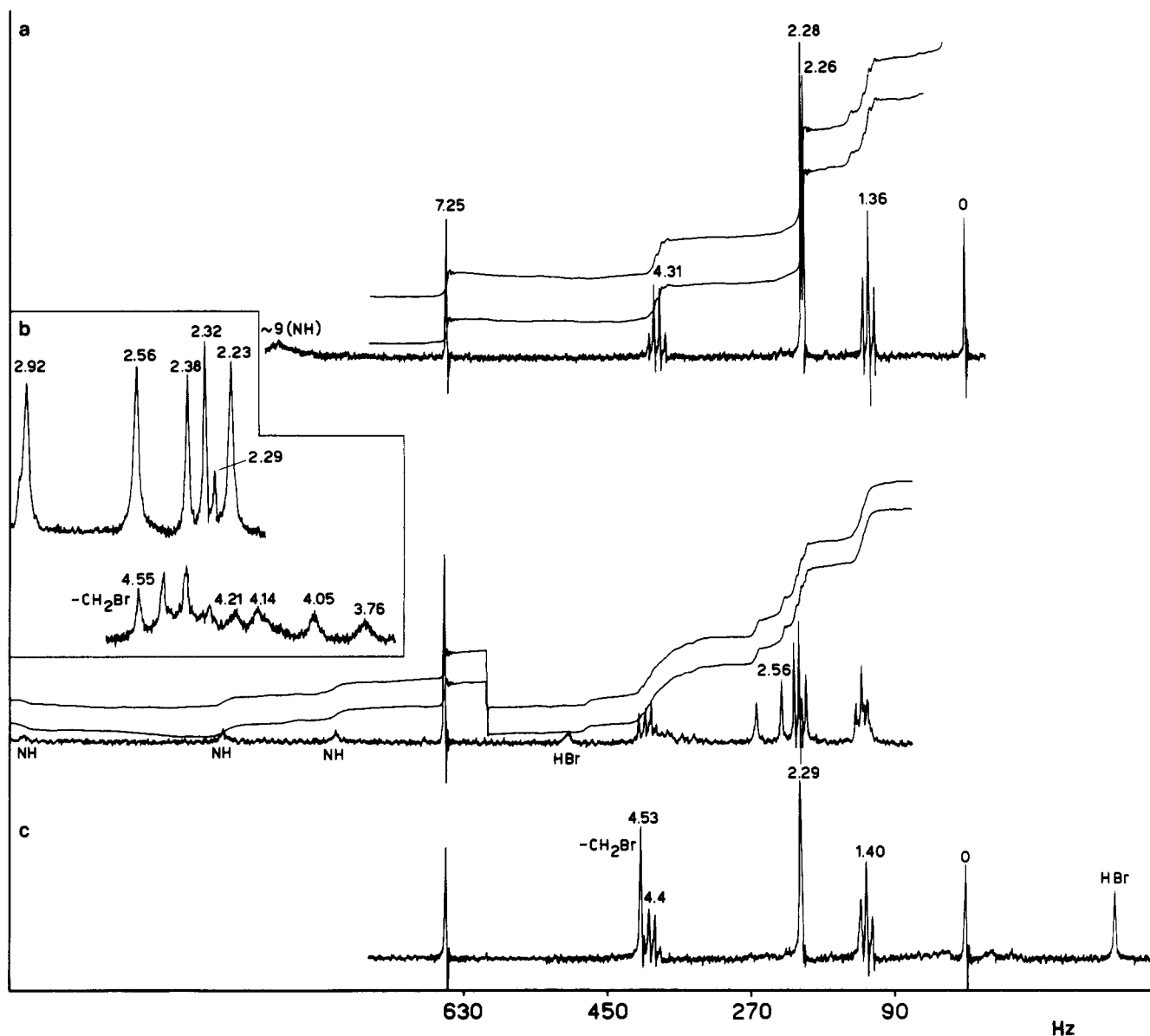


Figure 1. ¹H NMR study of the reaction of pyrrole 2 with bromine at room temperature (ca. 25 °C): (a) 90-MHz spectrum of 2 in CDCl₃ solution ([2] = 0.06 M); (b) spectrum of the reaction mixture 10 min after the addition of bromine ([Br₂] = 0.04 M) (the inset shows the enlarged portion of the spectrum between δ 2.1 and 3.0 (top) and between δ 3.7 and 4.7 (bottom)); (c) spectrum of the reaction mixture near the end of the reaction (ca. 30 min after the addition of Br₂).

aromatic brominations,¹⁸ may be explained by the very high reactivity of the pyrrole,¹⁹ which would render the

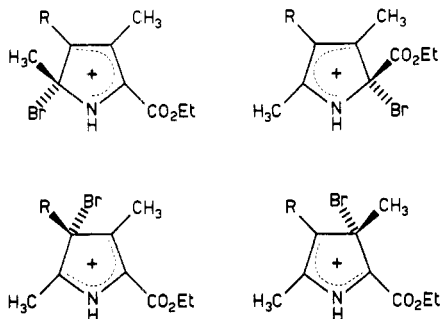
assistance by a second molecule of Br₂ unimportant. First order in bromine has also been explained⁵ as a consequence of a special timing of the process whereby decomposition of the σ adduct becomes the rate-limiting step, as suggested

(18) De la Mare, P. B. D.; Ridd, J. H. "Aromatic Substitution"; Butterworths: London, 1959. Norman, R. O. C.; Taylor, R. "Electrophilic Substitution in Benzenoid Compounds"; Elsevier: Amsterdam, 1965.

(19) Marino, G. *Adv. Heterocycl. Chem.* 1971, 13, 235.

for the side-chain bromination of hexamethylbenzene in acetic acid (vide infra).

Spectroscopic Study of the Reaction. Evidence for σ Adducts as Reaction Intermediates. The ^1H NMR spectra of the CDCl_3 solutions of the alkyl-substituted pyrroles 3 and 4, as recorded at room temperature immediately after the extremely fast bromine consumption, instead of showing the features of the side-chain substituted product, exhibited a very complex pattern. A decrease in the intensity of the signals (at δ 1.9–2.25) related to the α - and β -alkyl groups of the starting substrates was observed along with the formation of 12 new signals at δ values between 1.9 and 4.0. The downfield shift of some of these newly formed signals is quite large for nonring protons and is consistent with the formation of cationic species. Comparable shifts are observed in the formation of σ adducts from methylbenzene substrates.²⁰ The number of newly formed alkyl proton signals and that found for N protons (only two, rather than three, new signals at δ 10.15 and 12.64, respectively) would support the view that the electrophile attacks all nuclear positions except nitrogen to form four, i.e., two α and two β , different σ adducts. Furthermore, since the signals differ from each other in intensity, there are preferential positions for attack.



If the temperature of the reaction mixture is lowered to -10°C or below after bromine has been added, the NMR spectrum remains unchanged for a long period of time and precipitation of the σ adducts as orange-red crystals eventually occurs. The NMR spectrum of the redissolved crystals was superimposable on that recorded in solution. At room temperature, the NMR spectrum of the adducts slowly changes into that of the side-chain substituted product; the intensity of the signals related to the adducts decreases and singlets corresponding to the α - CH_2Br group (δ 4.5) and to the HBr formed start to appear. The change requires ca. 100 h to be complete. A single product is formed.

A similar pattern is observed with the halogeno-substituted pyrroles 2 and 5. The ^1H NMR spectral behavior of 2 is illustrated in Figure 1. What changes is the relative rates of the two processes, i.e., the formation and decomposition of the adducts. Here the former process, which is marked by the appearance of eight new CH_3 signals and two new NH signals, is appreciably slower, and the latter process faster, than for pyrroles 3 and 4. This is because the stabilization of the adduct by any given substituent will be rate enhancing for its formation (transition-state stabilization) and rate depressing for its decomposition (ground-state stabilization), in the assumption that the transition state for formation resembles the configuration of the adduct. The hypothesis that the intermediates are covalent, neutral adducts seems to be ruled out by their observed properties, i.e., intense color, low solubility in

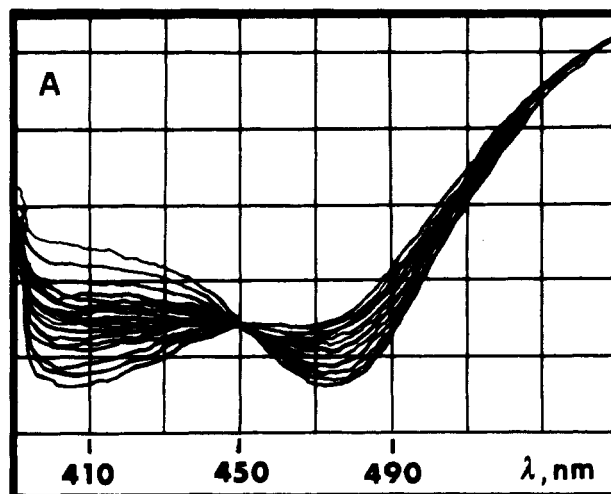


Figure 2. Repetitive-scan visible spectrum of a CH_2Cl_2 solution containing 2 and Br_2 . $[2] = 5.3 \times 10^{-2}$ M, $[\text{Br}_2] = 3.0 \times 10^{-3}$ M.

solvents of low polarity, and N–H resonances at $\delta > 10$.

A confirmation of the preceding results and further information were obtained by a spectrophotometric study of the reaction. In the case of pyrroles 3 and 4, as expected, bromine consumption is so fast that it cannot be followed by conventional spectrophotometry; the visible spectrum of the reaction mixture recorded immediately after bromine addition lacks the characteristic absorption of the molecular halogen at 412 nm and only a band at 510 nm is observed, which eventually disappears slowly. The latter band can be attributed to σ adducts by analogy with the spectral behavior of benzenium cations.²¹ 2 and 5 behave in a similar manner. In fact, for the latter it is possible to follow σ -adduct formation by repetitive scans of the spectrum between 390 and 550 nm. The spectrum reported in Figure 2 shows the increasing absorbance of a band at 475 nm at the expense of the molecular bromine absorption and the appearance of a well-defined isobestic point at 450 nm. These results indicate that σ -adduct formation is a simple process involving no intermediate along the reaction path and that the kinetic data obtained by spectrophotometric measurements (Table II) refer to formation of the adducts rather than to that of the final bromomethyl derivative. Furthermore, since there is agreement between spectrophotometric and titrimetric kinetic data (Table II), it must be inferred that also by titrimetry *only* the rate of σ -adduct formation is measured. The subsequent decomposition (and, presumably, the mutual interconversion) of the adducts is so much slower than their formation that it could not possibly enter the kinetics of bromine consumption as a rate-limiting step (see previous section). There is no evidence that the adducts revert to the reactants rapidly and to any appreciable extent since iodine was never detected in the bromination mixtures of 3 and 4 when quenched with potassium iodide immediately after the addition of bromine.

Concluding Remarks. The reaction of pyrroles 2–5 with bromine is an extreme case of behavior in the interaction of aromatic systems with electrophiles in that it consists of two *distinct* and *separately observable* processes. The first process is the (irreversible) formation of relatively stable σ adducts and the second is the (spontaneous) decomposition of the adducts into the α -bromomethyl product. Both processes are influenced, as expected, by the electronic effect of the 4 substituent, but

(20) Olah, G. A.; Lin, H.; Mo, Y. K. *J. Am. Chem. Soc.* 1972, 94, 3667.

(21) Olah, G. A.; Pittman, C. U., Jr.; Symons, M. C. R. *Carbonium Ions*, 1968, 1, 153.

clearly in opposite ways. Eventually all possible σ adducts deriving from attack on α and β ring carbon atoms decompose into a single, well-defined, side-chain-substituted product. The results do not indicate the structure of the adduct(s) through which the final product is formed. Furthermore, the mechanism of migration is still to be elucidated in further studies.

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Registry No. 1, 2436-79-5; **1a**, 57745-26-3; **2**, 5408-07-1; **2a**, 73018-12-9; **3**, 2199-46-4; **3a**, 73018-13-0; **4**, 2199-47-5; **4a**, 4789-44-0; **5**, 58921-31-6; **5a**, 73018-14-1; ethyl 4-ethyl-5-formyl-3-methylpyrrole-2-carboxylate, 4391-87-1.

Electrophilic Aromatic Substitution in Cyclopropenium Ions

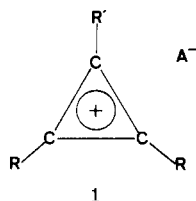
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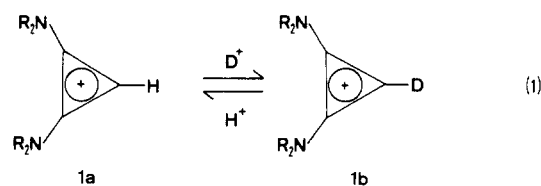
Electrophilic attack by a proton on the cyclopropenium ion is shown by ab initio molecular orbital theory to involve a planar tetracoordinate carbon atom. The process is, however, strongly endothermic, and the protonated cyclopropenium ion ring opens without activation energy. The diaminocyclopropenium ion, on the other hand, can be either C or N protonated exothermically. C protonation can account for the observed H/D exchange in derivatives of the diaminocyclopropenium ion. In this case the protonated ion has a normal tetrahedral carbon atom and is highly stabilized by charge delocalization to nitrogen.

Since the pioneering work of West et al.¹ substitution reactions on cyclopropenium systems of the general form **1** ($R = R' = \text{halogen}$) have gained an ever increasing im-



portance. Until very recently only substitution reactions on **1** of the classical addition-elimination type were known. The observation of the following reaction types has, however, revealed a complete spectrum of mechanistic possibilities: (a) four-center exchange reactions ($R = R' = \text{halogen}$),³ (b) elimination-addition reactions ($R = \text{NR}_2$, $R' = \text{halogen}$),⁴ (c) electrophilic substitutions ($R = \text{NR}_2$, $R' = \text{H}$).⁵ In addition the important influence of the counterion, A^- , on many such substitution reactions has been recognized and exploited synthetically.⁶

This paper is concerned with the theory of reaction type c. It was stimulated by our observation that donor-stabilized C_3^+ systems are capable of undergoing H/D exchange in strongly acidic media⁵ (eq 1).



This report has aroused considerable interest in electrophilic substitution of positively charged aromatic species.⁷ We have chosen to investigate protonation of the parent cyclopropenium ion as a model for this type of reaction. The nature and stability of protonated $C_3H_3^+$ is of particular interest since the resulting dication is isoelectronic with the "anti van't Hoff" BBC ring.⁸

Of all the Hückel aromatic systems, the cyclopropenium ion occupies a special position with respect to electrophilic substitution. This arises because the proximity of high-lying σ (Walsh type) orbitals to the occupied π orbital of cyclopropenium⁹ leads to additional possible modes of protonation, one of which involves a planar tetracoordinate carbon atom. Interaction of the proton with the σ system can lead to either in-plane corner or edge attack, whereas out-of-plane corner or face protonation results when the π system acts as the donor.

In this respect electrophilic substitution in the cyclopropenium ion resembles the protonation of cyclo-

(1) For a review see R. West, *Acc. Chem. Res.*, **3**, 130 (1970).

(2) For a review see Z. Yoshida, *Top. Curr. Chem.*, **40**, 47 (1973).

(3) R. Weiss, *Tetrahedron Lett.*, in press; R. Weiss and P. Maroldt, *Synthesis*, in press.

(4) R. Weiss, C. Priesner, and H. Wolf, *Angew. Chem., Int. Ed. Engl.*, **18**, 472 (1979); R. Weiss, M. Hertel, and H. Wolf, *ibid.*, **18**, 473 (1979).

(5) R. Weiss and C. Priesner, *Angew. Chem., Int. Ed. Engl.*, **17**, 445 (1978).

(6) R. Weiss, H. Kölbl, and C. Schlierf, *J. Org. Chem.*, **41**, 2258 (1976); see also ref 3.

(7) R. M. Pagni and R. J. Smith, *J. Am. Chem. Soc.*, **101**, 506 (1979).

(8) K. Krogh-Jespersen, D. Cremer, D. Poppinger, J. A. Pople, P. v. R. Schleyer, and J. Chandrasekhar, *J. Am. Chem. Soc.*, **101**, 4843 (1979).

(9) The molecular orbitals of the cyclopropenium ion are shown in W. L. Jorgensen and L. Salem, "The Organic Chemist's Book of Orbitals", Academic Press, New York, 1973. With the 6-31G** basis set (split valence with d functions for carbon and p functions for hydrogen) and the 4-31G optimum geometry for cyclopropenium, the $1a_2'$ orbital is the HOMO at -0.764652 au, with the $3e'$ set lying slightly lower in energy (-0.787644 au).