

This product reacted quickly with mercury to form O-nitrosobis(trifluoromethyl)hydroxylamine ((CF₃)₂-NONO), indicating the new compound to be O-nitrosobis(trifluoromethyl)hydroxylamine ((CF₃)₂NONO₂).

The radical material I was allowed to contact air, water, and 10% sodium hydroxide with no reaction

based on visual observation and infrared analysis. It has been found to be compatible with stainless steel, copper, and glass over long periods of time.

Acknowledgments. The authors are indebted to Dr. Stanley A. Francis for assistance with the e.s.r. measurements and interpretation.

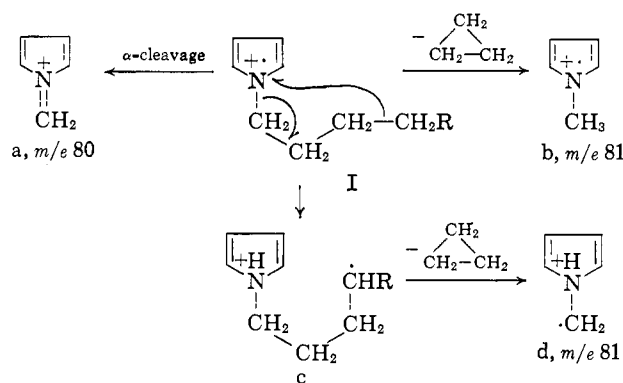
Mass Spectrometry in Structural and Stereochemical Problems. LXIII.¹ Hydrogen Rearrangements Induced by Electron Impact on N-n-Butyl- and N-n-Pentylpyrroles²

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A study of the mass spectra of deuterated analogs of N-n-butyl- and N-n-pentylpyrroles has uncovered and clarified the rather complex origin of the peaks at *m/e* 80 and 81 in the spectra of the parent compounds. High-resolution mass spectrometry established the composition of these species as C₅H₆N⁺ and C₅H₇N⁺. The former results from α-cleavage of the respective molecular ions and also from loss of a hydrogen radical from *m/e* 81 and is assigned structure a. The fragment of mass 81 is formed predominantly by transfer of hydrogen from C-3 of the alkyl chains through any one of three mechanisms. Anomalous quantitative shifts in *m/e* 81 observed in some of the deuterated analogs of N-n-butyl and N-n-pentylpyrroles can be explained by a process involving exchange of deuterium and hydrogen between C-3 of the alkyl chain and an α-carbon atom of the heterocyclic ring. The formation of the less abundant ions at *m/e* 67 and 53 is also rationalized.

butylpyrrole, and to be represented by a. This cleavage corresponds to that observed with alkyl amines (α-cleavage) as well as to the fission of benzylic bonds in alkyl-substituted aromatic systems.



Introduction

Systematic work on the mass spectrometric fragmentation of pyrroles has been performed only recently.^{4,5} In that connection relatively few N-alkylpyrroles have been studied and an analysis of the recorded^{6a} mass spectrum of N-n-butylpyrrole (I, R = H) has been attempted,⁵ especially as far as the major peaks at *m/e* 80 and 81 (see Figure 1) are concerned. The *m/e* 80 species was suggested⁵ to have its genesis from α-cleavage of the molecular ion (I, R = H) of N-n-

Two possibilities were suggested for the ion of mass 81 in the spectrum of N-n-butylpyrrole⁵: (1) transfer of the terminal methyl group of the side chain to nitrogen with concomitant homolysis of the nitrogen-carbon bond (I (R = H) → b) and elimination of cyclopropane, or (2) hydrogen transfer from the terminal methyl group via a six-membered intermediate to nitrogen (I (R = H) → c (R = H)) followed by α-cleavage and formation of d.

In view of our great interest^{6b} in demonstrating possible methyl migrations in mass spectrometric fragmentation processes, N-n-(butyl-4,4,4-*d*₃)pyrrole was prepared but no migration of the labeled methyl group was found to occur (Table I). The mass spectrum of this labeled analog showed the second possibility, I → c → d, to operate only to the extent of 8% as deduced from the shift of the *m/e* 81 peak to *m/e* 82. Consequently, we decided to prepare N-n-butylpyrroles labeled with deuterium in all positions of the alkyl chain in order to determine precisely the source of the hydrogen transferred in the formation of the ion of mass 81. It was observed that the spectra (Figures 1 and 2) of N-n-pentyl- and N-n-butylpyrroles were identical with

(1) Paper LXII: J. Karliner, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 580 (1965).

(2) We are indebted to the National Institutes of Health of the U. S. Public Health Service for financial assistance (Grants No. GM-11309 and AM-04257).

(3) (a) Postdoctoral Research Fellow 1963-1965; (b) recipient of a N.A.T.O. (Paris) travel grant; (c) N.S.F. Postdoctorate Fellow 1963-1964.

(4) H. Budzikiewicz, C. Djerassi, A. H. Jackson, G. W. Kenner, D. J. Newman, and J. M. Wilson, *J. Chem. Soc.*, 1949 (1964).

(5) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964, p. 237.

(6) (a) "Catalog of Mass Spectral Data," American Petroleum Institute Project 44, Carnegie Institute of Technology, Pittsburgh, Pa., spectrum no. 624; b) F. Komitsky, J. E. Gurst, and C. Djerassi, in press.

Table I. Principal Mass Spectral Peaks of N-n-Butyl- (I, R = H) and N-n-Pentylpyrroles (I, R = CH₃) in the Mass Range *m/e* 80 → *m/e* 86

Compound	Isotopic purity	Relative abundance, <i>m/e</i>							Transfer <i>m/e</i> 81 → <i>m/e</i> 82
		80	81	82	83	84	85	86	
N-n-Butylpyrrole	...	63	100	8	
N-n-(Butyl-1,1- <i>d</i> ₂)-pyrrole	98% <i>d</i> ₂	8	12	60	100	7	100% to <i>m/e</i> 83
N-n-(Butyl-2,2- <i>d</i> ₂)-pyrrole	98% <i>d</i> ₂	54	100	23	11	2	6	...	15%
N-n-(Butyl-3,3- <i>d</i> ₂)-pyrrole	95% <i>d</i> ₂ 5% <i>d</i> ₁	65	32	100	25	2	1	...	78%
N-n-(Butyl-4,4- <i>d</i> ₃)-pyrrole	97% <i>d</i> ₃	58	100	14	2	8%
N-n-Butyl-2',3',4',5'- <i>d</i> ₄ -pyrrole	90% <i>d</i> ₄ 7% <i>d</i> ₃ 3% <i>d</i> ₂	2	4	6	27	90	100	8	
N-n-(Butyl-3,3- <i>d</i> ₂)-2',3',4',5'- <i>d</i> ₄ -pyrrole	88% <i>d</i> ₃ 7% <i>d</i> ₅ 5% <i>d</i> ₄	3	5	7	17	66	36	100	
N-n-Pentylpyrrole	...	62	100	10	3	1	2	...	
N-n-(Pentyl-3,3- <i>d</i> ₂)-pyrrole	98% <i>d</i> ₂	65	35	100	30	4	4	1	76%
N-n-(Pentyl-4,4- <i>d</i> ₂)-pyrrole	95% <i>d</i> ₂ 5% <i>d</i> ₁	58	100	33	7	1	1	...	22%
N-n-Pentyl-2',3',4',5'- <i>d</i> ₄ -pyrrole	90% <i>d</i> ₄ 7% <i>d</i> ₃ 3% <i>d</i> ₂	4	10	34	80	100	86	12	

respect to the ions at mass numbers 80 and 81 and the problem was expanded to include both substances.

Synthesis of alkyl chains containing deuterium in selected positions can be achieved using diethyl alkylmalonic esters as starting material.⁷ Exchange of the

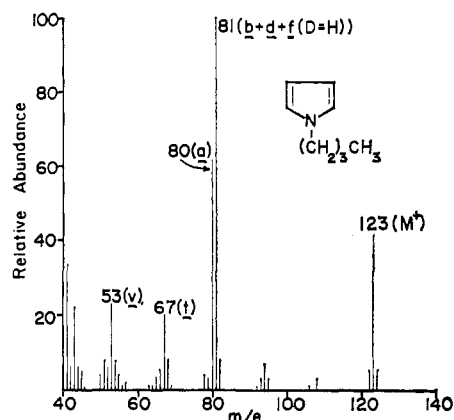
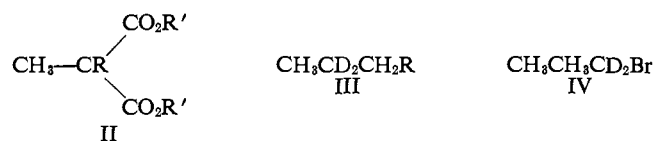


Figure 1. Mass spectrum of N-n-butylpyrrole (I, R = H).

enolic proton of diethyl methylmalonate (II, R = H, R' = Et) with sodium in deuterium oxide followed by saponification and acidification yielded the trideuterated methylmalonic acid (II, R = D, R' = D) which on decarboxylation yielded propionic-2,2-*d*₂ acid. Lithium aluminum hydride reduction afforded propanol-2,2-*d*₂ (III (R = OH)) which on bromination gave

(7) For a review of the available methods for introducing deuterium into organic molecules, see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Mass Spectrometry of Natural Products," Vol. I, Holden-Day, Inc., San Francisco, Calif., 1964, Chapter 2.



bromopropane-2,2-*d*₂ (III (R = Br)) of 95% isotopic purity. Lithium aluminum deuteride reduction of propionic acid and bromination of the product yielded bromopropane-1,1-*d*₂ (IV). Chain elongation of III

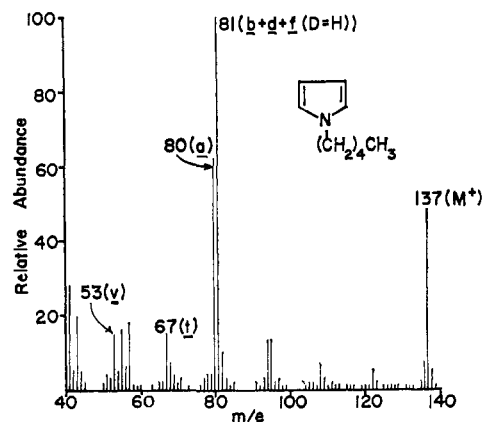


Figure 2. Mass spectrum of N-n-pentylpyrrole (I, R = CH₃).

(R = Br) and IV by either one or two carbon atoms was accomplished by standard procedures,⁸ while bromobutane-4,4-*d*₃ was prepared from the corresponding trideuteriobutanol.⁹

(8) C. Beard, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 269 (1964).

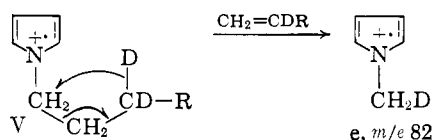
(9) D. H. Williams, H. Budzikiewicz, and C. Djerassi, *ibid.*, **86**, 284 (1964).

N-*n*-Alkylpyrroles were synthesized by condensing the alkyl bromide with pyrrole in tetrahydrofuran solution in the presence of sodium hydride. Under these conditions no C-alkylation occurred, as could be demonstrated from the n.m.r. spectrum of the resulting N-*n*-pentylpyrrole. The spectrum was determined in deuteriochloroform solution at 60 Mc. and the four vinylic protons were visible as two triplets ($J = 4$ c.p.s.) centered around 6.12 and 6.62 p.p.m., while the methylene group adjacent to nitrogen appeared as a triplet centered around 3.82 p.p.m. ($J = 14$ c.p.s.).

Discussion of Mass Spectra

The mass spectra of N-*n*-butyl- and N-*n*-pentylpyrrole (Figures 1 and 2) are dominated by the peaks at m/e 80 and 81. High-resolution mass spectrometry¹⁰ established that the ion of mass 80 in both compounds consisted entirely of the $C_5H_6N^+$ species. This peak shifted completely to m/e 82 in the spectrum of N-*n*-(butyl-1,1- d_2)pyrrole which is consistent with its formation by α -cleavage in I and with its representation as a. By analogy, the ion at m/e 80 in the N-*n*-pentylpyrrole spectrum is also assigned the same structure a.

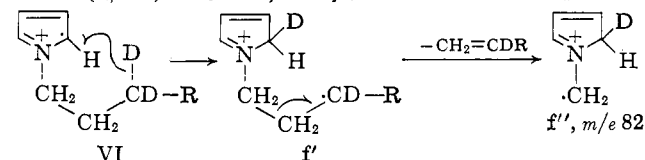
The base peak (m/e 81) in the spectra of N-*n*-butyl- and N-*n*-pentylpyrrole was shown by high-resolution mass spectrometry¹⁰ to contain only the $C_5H_7N^+$ ion. As has already been discussed, transfer of the terminal methyl, or hydrogen therefrom, in N-*n*-butylpyrrole according to mechanisms $I \rightarrow b$ or $I \rightarrow c \rightarrow d$ does not account for the genesis of this ion. In the spectrum of N-*n*-(butyl-1,1- d_2)pyrrole, m/e 81 shifted completely to m/e 83 (see Table I), necessitating retention of C-1 of the alkyl chain in the charged species. In the spectra (Table I) of N-*n*-(butyl-2,2- d_2)- and N-*n*-(butyl-3,3- d_2)pyrrole m/e 81 was displaced to the extent of 15 and 78% to m/e 82, while transfers of 76 and 22% were noted in N-*n*-(pentyl-3,3- d_2)- and N-*n*-(pentyl-4,4- d_2)pyrrole. A mechanism utilizing transfer of deuterium in N-*n*-(butyl-3,3- d_2)- and N-*n*-(pentyl-3,3- d_2)pyrroles [V (R = CH₃) and V (R = C₂H₅)] to the α -carbon atom of the aliphatic chain with synchronous fission of the α,β -carbon bond rationalizes these results in terms of structure e (m/e 82).



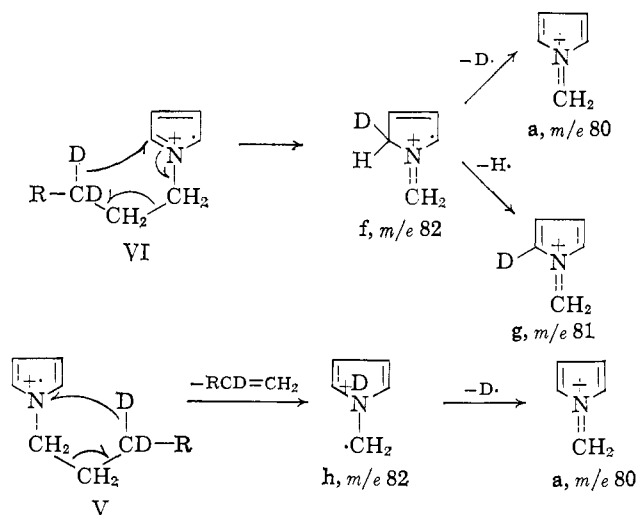
A second mechanism consistent with the observed shift of m/e 81 to 82 in the alkylpyrroles-3,3- d_2 can be written if the molecular ion V is visualized in the resonance form VI. Transfer of deuterium through a six-membered cyclic intermediate would yield the resonance-stabilized ion radical f (m/e 82).¹¹

(10) Determined on an A.E.I. MS-9 double focussing mass spectrometer.

(11) This process can also be written as a stepwise mechanism $VI \rightarrow f' \rightarrow f''$ (m/e 82). However, an objection to this formulation is that a



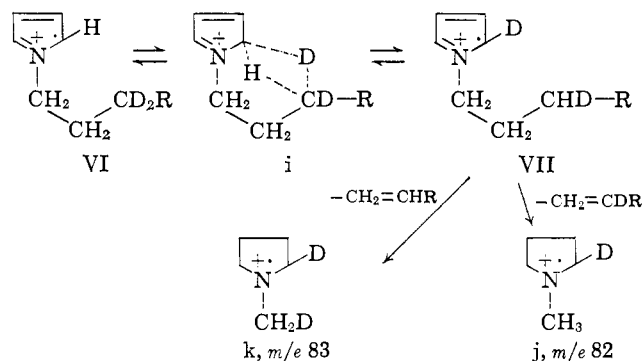
resonance stabilized radical (VI) is converted to a secondary radical (f'), a transfer which would not be favored on the basis of ground-state theory.



An alternate rationalization may be transfer of deuterium in V to nitrogen with concomitant α -cleavage to afford h (m/e 82).

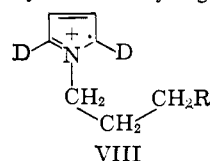
Elimination of either hydrogen or deuterium from f would form g (m/e 81) and a (m/e 80), while loss of deuterium from h would yield a. The presence of a metastable ion at m/e 79.2 in the spectrum of I (R = H) definitely established the occurrence of the transition m/e 81 \rightarrow 80.

The spectra of N-*n*-(butyl-3,3- d_2)- and N-*n*-(pentyl-3,3- d_2)pyrrole contain peaks (see Table I) at m/e 83 of more than 20% of the intensity of the base peak, thus requiring the transfer of two deuterium atoms from the alkyl chain to the charged species. Models demonstrate that in the resonance form (VI) of the molecular ion of these compounds one of the deuterium atoms is in close proximity to an α -carbon of the heterocyclic ring such that formation of the intermediate (i) should be favored. The latter would then be in equilibrium with both VI and VII.



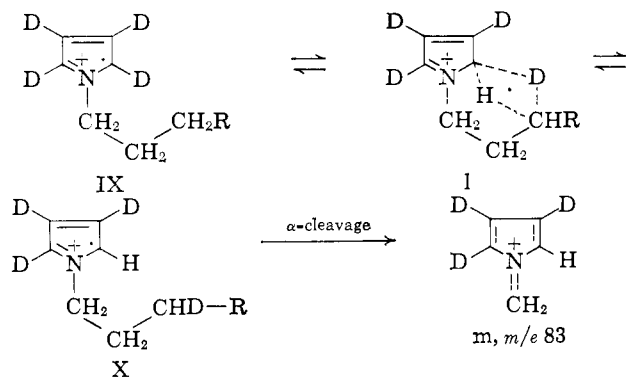
Transfer of either hydrogen or deuterium from the γ -carbon atom of the alkyl chain in VII with concomitant α,β -bond fission would yield m/e 82 and 83, respectively,¹² which are represented arbitrarily (see e vs. f vs. h) by j and k.

(12) Another explanation for the formation of m/e 83 in both N-*n*-(butyl-3,3- d_2)- and N-*n*-(pentyl-3,3- d_2)pyrrole would be repetition of the exchange process $VI \rightarrow i \rightarrow VII$ at the alternate α -position of the heterocyclic ring in VII with formation of VIII. This could then afford an m/e 83 species by transfer of hydrogen.

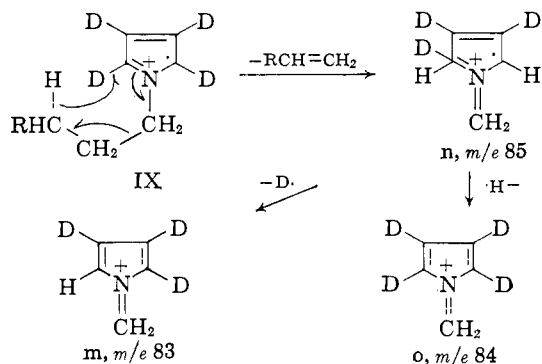


It is important to note that from the three mechanisms used to account for the shift of m/e 81 to 82 and 83 in both N-*n*-(alkyl-3,3- d_2)pyrroles that m/e 81 will contain g if mechanisms VI \rightarrow f or VI \rightarrow VII operate, but not in the case of V \rightarrow h. High-resolution mass spectrometry¹⁰ (apparent resolution 1 in 20,000) indicated that, in both dideuterated alkylpyrroles, m/e 81 contained at least 80% of the $C_5H_5ND^+$ species, the remainder being $C_5H_7N^+$.¹³ Hence the 20% $C_5H_7N^+$ ion must arise from hydrogen transfers from the unlabeled C-2 or C-4 positions of the side chain.

Further evidence for the exchange of deuterium and hydrogen as depicted in VI \rightleftharpoons i \rightleftharpoons VII was obtained from the spectra (see Table I) of N-*n*-butyl- and N-*n*-pentylpyrroles labeled in the ring (2',3',4',5'- d_4) positions. These compounds were prepared by equilibration of pyrrole with deuterium oxide using a palladium on charcoal catalyst^{7,14} followed by N-alkylation of the tetradeuterated pyrrole and were shown by mass spectrometry to consist of 90% d_4 , 7% d_3 , and 3% d_2 species. The spectra of these N-*n*-alkylpyrroles- d_4 had peaks at m/e 83, 84, and 85 (see Table I). The first of these peaks can arise from the molecular ion via the equilibrium IX \rightleftharpoons I \rightleftharpoons X. α -Cleavage of the latter would then afford m (m/e 83).



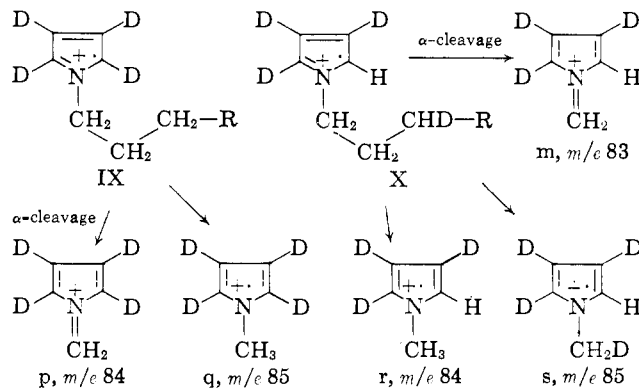
An alternative genesis of m/e 83 in the spectra of both compounds can be transfer of hydrogen from C-3 of the alkyl chain via a six-membered transition state to an α -carbon atom of the heterocycle as shown in IX \rightarrow n (m/e 85). The latter could then lose either deuterium or hydrogen and yield m (m/e 83) or o (m/e 84).



(13) The species corresponding to $C_5H_7N^+$ appeared as a shoulder of variable intensity superimposed on the predominant deuterium-containing ion. The presence of the former could be demonstrated by admitting the unlabeled N-*n*-alkylpyrrole on the mass spectrometer containing N-*n*-(alkyl-3,3- d_2)pyrrole when the shoulder corresponding to $C_5H_7N^+$ was seen to increase markedly.

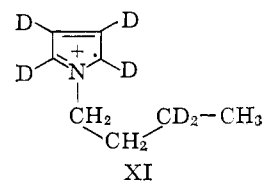
(14) C. G. MacDonald and J. S. Shannon, *Tetrahedron Letters*, 1349 (1963).

In the spectra of N-*n*-butyl- and N-*n*-pentylpyrroles-2',3',4',5'- d_4 the ratio of the relative abundances of m/e 83 plus 84 to m/e 85 is 1.17 and 2.09, while in the parent unlabeled compounds (Figures 1 and 2) this ratio (m/e 80: m/e 81) was 0.63 and 0.62, respectively. This anomaly can be explained by the exchange process IX \rightleftharpoons I \rightleftharpoons X. α -Cleavage of IX would yield p (m/e 84), while transfer of a γ -hydrogen atom to the α -carbon of the alkyl chain with synchronous α,β -carbon bond fission would yield q (m/e 85).¹⁵ Similar processes when applied to the "exchanged molecular ion" (X) would yield m (m/e 83) by α -cleavage, and either r (m/e 84) or s (m/e 85) depending on whether hydrogen or deuterium was transferred from the γ -carbon atom.¹⁵



The formation of the rearrangement ion (r) will increase the abundance of m/e 84 (α -cleavage) thereby causing the observed change in the ratio of α -cleavage to rearrangement ions found in the spectra (Table I) of N-*n*-alkylpyrroles-2',3',4',5'- d_4 . This result is compatible with the equilibrium depicted by IX \rightleftharpoons I \rightleftharpoons X but does not eliminate the possibility of the cooccurrence of the mechanism IX \rightarrow n \rightarrow o + m.

Additional support for the exchange mechanism was forthcoming from the spectrum of N-*n*-(butyl-3,3- d_2)pyrrole-2',3',4',5'- d_4 . In this case the exchange process will not result in any alteration of the molecular ion XI and no distortion of the ratio of α -cleavage to rearrangement ions should be observed. This in fact is seen from Table I in which the relative abundances of the peaks at m/e 84, 85, and 86 are almost identical to those at m/e 80, 81, and 82 in the spectrum of N-*n*-(butyl-3,3- d_2)pyrrole.



The ion of mass 67 in the spectrum (Figure 1) of N-*n*-butylpyrrole is virtually homogeneous¹⁰ (see Table II), corresponding to $C_4H_5N^+$, and its genesis has been suggested⁵ to be loss of two moles of ethylene from the molecular ion according to I \rightarrow t. Deuterium

(15) The alternative mode of formation utilizing transfer of a γ -hydrogen atom through either a six-membered transition state to an α -carbon atom of the ring (VI \rightarrow f) or via a five-membered intermediate to nitrogen (e.g., V \rightarrow h) would yield ions of the same mass number; these possibilities are not excluded and, according to our present state of knowledge, they must be considered as equally plausible.

Table II. High-Resolution^a Mass Spectrum of Some Ions of N-*n*-Butylpyrrole

Found	Calcd.	Compn.	%
81.05761	81.05785	C ₈ H ₇ N ⁺	100
53.03871	53.03912	C ₄ H ₅ ⁺	100
67.04160	67.04220	C ₄ H ₅ N ⁺	90
67.05427	67.05477	C ₆ H ₇ ⁺	10
68.04967	68.05002	C ₄ H ₅ N ⁺	100
93.05775	93.05785	C ₈ H ₇ N ⁺	86
93.07040	93.07042	C ₇ H ₆ ⁺	14
95.07373	95.07350	C ₈ H ₉ N ⁺	80
95.08654	95.08607	C ₇ H ₁₁ ⁺	20
106.06468	106.06567	C ₇ H ₈ N ⁺	100

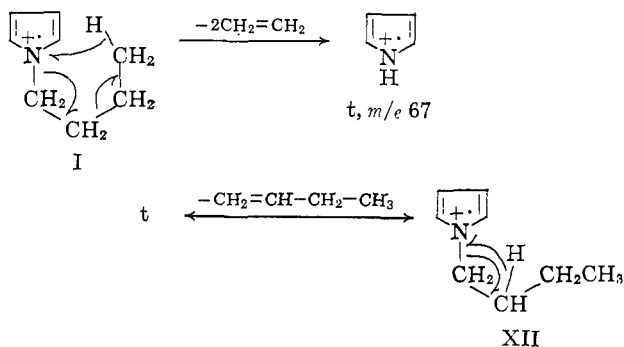
^a Apparent resolution 1 in 15,000.

Table III.^a Shifts in the Ions at *m/e* 67 and *m/e* 53 in the Spectra of Deuterated N-*n*-Butyl- and N-*n*-Pentylpyrroles

Compound	<i>m/e</i>	<i>m/e</i>
R-CH ₂ CH ₂ CH ₂ CH ₃	67	53
R-CD ₂ CH ₂ CH ₂ CH ₃	67 (q)	55 (q)
R-CH ₂ CD ₂ CH ₂ CH ₃	68 (50%)	53 (q)
R-CH ₂ CH ₂ CD ₂ CH ₃	68 (15%)	53 (q)
R-CH ₂ CH ₂ CH ₂ CD ₃	68 (40%)	53 (q)
R'-CH ₂ CH ₂ CH ₂ CH ₂	71 (q)	56 (q)
R-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂	67	53
R-CH ₂ CH ₂ CD ₂ CH ₂ CH ₃	67 (q)	53 (q)
R-CH ₂ CH ₂ CH ₂ CD ₂ CH ₃	68 (30%)	53 (q)
R'-CH ₂ CH ₂ CH ₂ CH ₂ CH ₂	71 (q)	56 (q)

^a R = pyrrol; R' = pyrrol-2',3',4',5'-*d*₄, q = quantitative transfer (>95%); isotopic purities for the deuterated analogs are given in Table I.

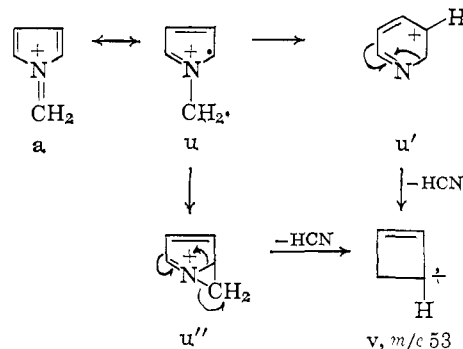
labeling (Table III) established that a substantial portion (40%) of this ion arose *via* transfer from the methyl group. The remaining sources of transfer (Table III) were from C-2 (50%) for which mechanism XII → t can be written with the expulsion in this instance of butene, with a smaller contribution (15%) from C-3. In harmony with these mechanisms *m/e* 67 shifted quantitatively to *m/e* 71 in the spectrum of N-*n*-butylpyrrole-2',3',4',5'-*d*₄.



In the labeled N-*n*-pentylpyrroles (Table III) the *m/e* 67 peak shifted to the extent of 30% to *m/e* 68 in the 4,4-*d*₂ analog and was unaffected in the 3,3-*d*₂ compound. The anticipated quantitative transfer to *m/e* 71 was again found in N-*n*-pentylpyrrole-2',3',4',5'-*d*₄.

The ion of mass 53 in the spectrum (Figure 1) of N-*n*-butylpyrrole was homogeneous, having the composition C₄H₅⁺ (Table II), and was unaffected in the spectra of the β-, γ-, or δ-deuterated derivatives (Table III), but was transferred to *m/e* 55 in the spectra of the α-dideuterated compound and to *m/e* 56 in N-*n*-

butylpyrrole-2',3',4',5'-*d*₄. The shifts in the spectra of the deuterated compounds are compatible with the expulsion of the elements of HCN from the ion a, *m/e* 80,¹⁶ the hydrogen and carbon originating from the α-position of the pyrrole ring. The process can be visualized as either of two alternatives proceeding through resonance form u of a with bond fissions as indicated in u' and u'', the driving force in both cases being the expulsion⁴ of the stable hydrogen cyanide molecule and the formation of the cyclobutenyl cation v (*m/e* 53). The same sequence also applies to the homologous N-*n*-pentylpyrrole (Figure 2), where the observed shifts (Table III) in the deuterated species are again consistent with the postulated mechanism.



Experimental¹⁷

n-Bromobutane-4,4,4-*d*₃. This compound was prepared according to a published procedure.⁹

n-Bromobutane-3,3-*d*₂. Sodium (20 g.) was added in small pieces during 2 hr. to deuterium oxide (100 ml.) cooled to 0° and mechanically stirred. The solution was heated under reflux and diethyl methylmalonate (25 g.) added dropwise during 30 min. and refluxing continued for 2.5 hr. The ethanol liberated in the saponification was removed by distillation until the vapor temperature was 100°. The reactants were cooled to 0° and treated cautiously with phosphorus trichloride (64 g.) by dropwise addition over a period of 4 hr. with efficient mechanical stirring. The resultant acidic solution was refluxed for a period of 18 hr. and then distilled almost to dryness when deuterium oxide (20 ml.) was added and the process repeated. The combined distillate was continuously extracted with ether overnight and the organic phase dried (MgSO₄). The ether solution was added dropwise during 2 hr. to a slurry of lithium aluminum hydride (8 g.) in anhydrous ether (400 ml.), heated under reflux for 1 hr., and worked up in the usual manner affording propanol-2,2-*d*₂ (8 g.). Bromination using 48% hydrobromic

(16) The intermediacy of the *m/e* 80 species is indicated by the recognition⁶ of a metastable peak at *m/e* 35 (53²/80 = 35.1).

(17) All mass spectra, other than high-resolution spectra¹⁰ (see also Table II), were obtained with a Consolidated Electroynamics Corp. Model No. 21-103C mass spectrometer using an all-glass inlet system heated to 200°. The ionizing energy was maintained at 70 e.v. and the ionizing current at 50 μa. The labeled *n*-butyl and *n*-pentyl bromides were assayed for homogeneity by vapor phase chromatography (Wilkins Hy-Fi instrument) using 20% polydiethylene glycol succinate as the stationary phase at a temperature of 36° and nitrogen pressure of 2 p.s.i. Under these conditions *n*-butyl bromide had a retention time of 4 min. and *n*-pentyl bromide 6 min. The N-alkylated pyrroles were isolated by preparative vapor phase chromatography using a Wilkins Aerograph instrument at a temperature of 75° and helium pressure of 8 p.s.i. using phenyldiethylamine succinate as the stationary phase. Under these conditions N-*n*-butylpyrrole had a retention time of 12 min., N-*n*-pentylpyrrole 39 min., and pyrrole 16 min.

acid (20 ml.) containing concentrated sulfuric acid (6 ml.) and distillation of the product from the reaction mixture into water afforded bromopropane-2,2- d_2 (9 g.) after isolation with ether. Mass spectrometry indicated the presence of 95% d_2 and 5% d_1 species.

The Grignard reagent, prepared from bromopropane-2,2- d_2 (4 g.) and magnesium turnings (0.7 g.) in ether (25 ml.), was poured onto crushed Dry Ice (30 g.). After evaporation of the excess Dry Ice 2 *N* hydrochloric acid (25 ml.) was added and *n*-butyric-3,3- d_2 acid (1.5 g.) isolated with ether. Reduction with lithium aluminum hydride afforded butanol-3,3- d_2 (0.95 g.) which was converted to bromobutane-3,3- d_2 (600 mg.) as described above.

Bromobutane-2,2- d_2 . Reduction of propionic acid (3 g.) with lithium aluminum deuteride (1.3 g.) in anhydrous ether (50 ml.) afforded propanol-1,1- d_2 (2.5 g.) which yielded bromopropane-1,1- d_2 (3.0 g.) on bromination. The Grignard reagent, prepared from magnesium turnings (0.7 g.) in ether (25 ml.), was poured onto crushed Dry Ice (20 g.). The reaction was processed as described for the preparation of bromobutane-3,3- d_2 yielding *n*-butyric-2,2- d_2 acid (1.3 g.) which, after reduction with lithium aluminum hydride and bromination, gave bromobutane-2,2- d_2 (0.5 g.).

Bromobutane-1,1- d_2 . Lithium aluminum deuteride reduction of *n*-butyric acid and bromination of the product afforded bromobutane-1,1- d_2 .

Bromopentane-4,4- d_2 . The Grignard reagent, prepared from bromopropane-2,2- d_2 (4.5 g.) and magnesium turnings (0.7 g.) in dry ether (20 ml.), was cooled to 0°, and ethylene oxide (6 g.) in dry ether (5 ml., cooled to -10°) was added. The reactants were stirred and slowly allowed to attain room temperature over a period of 6 hr., after which time they were heated under reflux for 30 min. Benzene (10 ml.) was added and solvent was removed by distillation until the temperature of the liquid remaining in the flask was 65°. After heating under reflux for a further 30 min. water (10 ml.) was added followed by 15% sulfuric acid (10 ml.). Isolation with ether and distillation afforded a

clear liquid (3.5 g.) which was heated under reflux during 10 min. with 20% aqueous sodium hydroxide solution (10 ml.), and pentanol-4,4- d_2 (1.4 g.) isolated with ether. Bromination afforded bromopentane-4,4- d_2 (1.1 g.), shown by mass spectrometry to consist of 95% d_2 and 5% d_1 species.

Bromopentane-3,3- d_2 . The Grignard reagent, prepared from bromopropane-1,1- d_2 (2 g.), was treated with ethylene oxide (3 g.) as described for the preparation of bromopentane-4,4- d_2 , yielding after bromination bromopentane-3,3- d_2 (225 mg.).

N-Alkylation of Pyrrole. Pyrrole (200 mg.) was added to a suspension of sodium hydride (150 mg.) in tetrahydrofuran (2 ml., distilled from lithium aluminum hydride) under a nitrogen atmosphere. The reactants were stirred at room temperature for 30 min. when the labeled alkyl bromide (100 mg.) in dry tetrahydrofuran (1 ml.) was added and stirring under a nitrogen atmosphere continued overnight. Water (20 ml.) was added, the products were isolated with ether, and the desired *N*-alkylpyrrole was separated from unreacted pyrrole by vapor phase chromatography.¹⁷

Pyrrole-2,3,4,5- d_4 . 30% Palladium on charcoal was stirred under deuterium gas in ethyl acetate during 1 hr. and collected by filtration. This catalyst (100 mg.), pyrrole (200 mg.), and deuterium oxide (3 ml.) were sealed in an evacuated tube (water pump) and heated at 100° for a period of 18 hr. The product was isolated with ether and distilled. Mass spectrometry indicated the presence of 80% d_4 , 15% d_3 , and 5% d_2 species. Repetition of this process raised the isotopic composition to 90% d_4 , 7% d_3 , and 3% d_2 species.

N-n-Butyl- and N-n-Pentylpyrrole-2',3',4',5'- d_4 . These compounds were prepared from pyrrole-2,3,4,5- d_4 following the general procedure described for *N*-alkylation of pyrrole.

N-n-(Butyl-3,3- d_2)pyrrole-2',3',4',5'- d_4 . Condensation of bromobutane-3,3- d_2 with pyrrole-2,3,4,5- d_4 using the general procedure described for *N*-alkylation of pyrrole yielded *N-n*-(butyl-3,3- d_2)pyrrole-2',3',4',5'- d_4 of 88% d_6 , 7% d_5 , and 5% d_4 species.

Mass Spectrometry in Structural and Stereochemical Problems. LXIV.¹ A Study of the Fragmentation Processes of Some Cyclic Amines²

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Plausible mechanistic interpretations of the principal ions formed in the mass spectrometric fragmentation of pyrrolidine, N-methylpyrrolidine, piperidine, and N-

(1) Paper LXIII: A. M. Duffield, R. Beugelmans, H. Budzikiewicz, D. A. Lightner, D. H. Williams, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 805 (1965).

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methylpiperidine are presented. Deuterium labeling established the sources of hydrogen transfer in many of the rearrangement ions and which atoms were implicated in each of the ions studied. High-resolution mass spectrometry was used to determine the composition of many of the ions studied.

(3) Postdoctoral Research Fellow, 1963-1965.