Health is gratefully acknowledged. Matthey-Bishop is acknowledged for their generous loan of palladium chloride.

Registry No. 1 (R = H), 10604-59-8; 1 (R = M), 16885-94-2; 1 (R = Bu), 42951-62-2; 2 (R = Me), 16885-99-7; 2 (R = Bu), 76916-48-8; 3, 1557-08-0; 4, 76916-49-9; 4 free acid, 6639-06-1; 5, 76916-50-2; 6, 76916-51-3; 7, 1613-32-7; 8, 76916-52-4; 9, 13228-37-0; 10, 76916-53-5; 11, 76916-54-6; 12, 76916-55-7; 13, 76916-56-8; 14, 76927-69-0; 15, 76916-57-9; 16, 76916-58-0; indolyllithium, 18344-49-5; indolylsodium, 16982-67-5; indolylmagnesium bromide, 20356-50-7; indolylpotassium, 31163-74-3; bis(acetonitrile)palladium(II) chloride, 14592-56-4; ethylene, 74-85-1; propene, 115-07-1; 1-hexene, 592-41-6; tetrabutylammonium indole, 76916-59-1; *N*-(trimethylsilyl)indole, 17983-42-5; skatole, 83-34-1; 1-skatolepropionic acid, 57662-47-2; 2-allylskatole, 76916-60-4; 2-[acetoxymercury(II)]skatole, 76916-61-5; 2-[chloromercury(II)]skatole, 76916-62-6; allyl chloride, 107-05-1; 2-propylskatole, 1859-90-1; [1-(2-propenyl)-π-allyl]nickel bromide, 12012-90-7; 2-(2,5-hexadienyl)benzamide, 76916-63-7; 2-bromobenzamide, 4001-73-4; 2-bromoaniline, 615-36-1; 1-(2-nitrophenyl)-1,5-hexadiene, 76916-64-8; (*o*-nitrobenzyl)triphenylphosphonium bromide, 23308-83-0; 4-pentenal, 2100-17-6; 1-(2-nitrophenyl)-1,4-pentadiene, 76916-65-9; (3-butenyl)triphenylphosphonium bromide, 16958-42-2; *o*-nitrobenzaldehyde, 552-89-6; 1-(2-nitrophenyl)buta-1,3-diene, 76916-66-0; 2-(1,3-butadienyl)aniline, 76916-67-1; 5-(2-nitrophenyl)-1,3-pentadiene, 76916-68-2; allyltriphenylphosphonium bromide, 1560-54-9; (*o*-nitrophenyl)acetaldehyde, 1969-73-9; 3-butyl-3,4-dihydrocarbostyril, 76916-69-3.

Bromination and Chlorination of Pyrrole and Some Reactive 1-Substituted Pyrroles[1]

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Monobromination of pyrrole and 1-methyl-, 1-benzyl-, and 1-phenylpyrrole with 1 mol of *N*-bromosuccinimide in tetrahydrofuran results in the regiospecific formation of the 2-bromopyrroles. A little disubstitution is observed. Similarly, brominations with 2, 3, or 4 mol of NBS form primarily the di-, tri-, and tetrabromopyrroles, respectively. The thermodynamically more stable 3-bromopyrroles are the major monobrominated products observed when bromine is used as the brominating agent due to isomerization of the 2-bromopyrroles with hydrogen bromide. These reaction mixtures are further complicated because of disproportionation reactions. Chlorination with *N*-chlorosuccinimide gave results similar to those for the bromination with NBS, but the reaction is not as selective.

The exhaustive bromination or chlorination of pyrrole (1) with bromine or chlorine leads to the corresponding tetrahalopyrroles which are stable.[2] There are no reports of the formation of partially brominated or chlorinated pyrroles by electrophilic halogenation of pyrrole by bromine or chlorine. Other substitution procedures result in the formation of mixtures of partially halogenated pyrroles.[3-6]

Electrophilic bromination of 1-substituted pyrroles, of similar reactivity as 1, such as 1-methylpyrrole (2) and 1-benzylpyrrole (3) with 1 mol of bromine in CCl_4 gives complex reaction mixtures which contain starting material, 2-bromo-, 3-bromo-, di-, tri-, and tetrabromopyrroles.[5,7] Most electrophilic substitutions of pyrrole and its 1-substituted derivatives occur exclusively at the 2-position;[2] however, nitration of 1, 2,[8,9] 3,[1] and 1-phenylpyrrole (4)[10] and nitrosation of 4,[10] also give considerable amounts of 3-substituted pyrroles. Acid-catalyzed proton exchange also occurs at the 2- and 3-positions of pyrrole.[2] Large substituents at the 1-position of pyrrole will cause more substitution to occur at the 3-position.[11,12]

The bromination and chlorination of 1-4 were investigated in order (1) to get a better understanding of why such complex reaction mixtures are obtained when 2, 3, or 4 is brominated in CCl_4, (2) to find out why the increased amount of 3-substitution sometimes occurs, (3) to find conditions under which selectively halogenated pyrroles might be formed, and (4) to determine the regiospecific nature of these halogenations.

Bromination of 2-4 with 1 mol of bromine in CCl_4 was reinvestigated by using procedures similar to those in the literature.[5,7] The results given in Table I are typical percentages because the ratio of products is dependent on experimental conditions such as the rate of addition of bromine, the length of time the reaction mixture is stirred after the addition of bromine is complete, the rate of stirring, etc. Only representative values are reported.

From a combination of GC and mass and ^1H NMR spectrometric techniques it was determined that, under these acidic conditions, some starting material always remains, and varying amounts of 2- and 3-substitution occur. Two dibromopyrroles were observed in the bromination of 2 and 4, and three dibromopyrroles were observed in

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Table I. Bromination of Some 1-Substituted Pyrroles with 1 mol of Bromine in Carbon Tetrachloride

		% brominated pyrroles					
substr	% starting matl	2-	3-	2,5-	2,4- and/or 3,4-	2,3,5-	2,3,4,5-
2[a]	9	19	8	24[b]	4[b]	23[c]	12
3[d]	2	10	28	1[e]	37[e]	20	2
4[d]	18	10	36	21[f]	4[f]	7	

[a] The procedure of G. A. Cordell, *J. Org. Chem.*, **40**, 3166 (1975), was used. [b] Two different retention times were observed for the dibromo-1-methylpyrroles. The compound with a shorter retention time is in agreement with the retention time of 2,5-dibromo-1-methylpyrrole and is calculated to be 24% of the product. At least one more brominated product with a longer retention time was observed (4%) and assumed to be the 2,4- or 3,4-dibrominated product. It is not known whether either one of these peaks is only due to one isomer. [c] A small amount of another tribromopyrrole was observed with a somewhat longer retention time which is assumed to be the 2,3,4-tribrominated isomer. [d] The procedure of H. J. Anderson and S. J. Griffiths, *Can. J. Chem.*, **45**, 2231 (1967), was used. [e] Three different retention times were observed for the dibromo-1-benzylpyrroles. The one with the shortest retention time is known to be 2,5-dibromo-1-benzylpyrrole (1%), and the other two compounds are assumed to be 2,4- and 3,4-dibromo-1-benzylpyrrole. [f] Two different retention times were observed for the dibromo-1-phenylpyrroles. The compound with the shorter retention time is known to be 2,5-dibromo-1-phenylpyrrole, and the other peak is assumed to be 2,4- or 3,4-dibromo-1-phenylpyrrole.

Table II. Bromination of Some Pyrroles with NBS in THF

		% bromopyrroles									
		1 mol of NBS			2 mol of NBS			3 mol of NBS			4 mol of NBS	
substr	% starting matl	2-	3-	2,5-	2-	2,5-	2,3,5-	2,5-	2,3,5-	2,3,4,5-	2,3,5-	2,3,4,5-
1	9	91		<1	<1	98	2	33	66			
2	1	99	<1	<1	1	99	<1	10	90		<1	100
3	1	99	<1	<1	1	99	<1	8	92		<1	100
4	37	49	<1	14	<1	100	<1	1	96	3	<1	100
4[a]	13[a]	81	<1	6								

[a] DMF was the solvent used.

Table III. Chlorination of Some Pyrroles with NCS in THF

		% chloropyrroles									
		1 mol of NCS		2 mol of NCS		3 mol of NCS			4 mol of NCS		
substr	% starting matl	2-	2,5-	2-	2,5-	2,5-	2,3,5-	2,3,4,5-	2,5-	2,3,5-	2,3,4,5-
1	5	86	9	25	75						
2	1	89	11	1	100	44	56		7	33	60
3	8	86	6	12	88	48	52			79	21
4[a]	26	69	5	1	100		83	17		1	100

[a] DMF was the solvent used.

the bromination of **3**. In each case the 2,5-dibromopyrrole was identified. It was assumed that the 2,3-dibromopyrroles would be least likely to form, and therefore the other dibromopyrroles were considered to be the 2,4- and/or 3,4-dibromopyrroles. The major tribrominated pyrroles were the 2,3,5-tribromopyrroles while in the bromination of **2** and **3** small amounts of the 2,3,4-tribromopyrroles were also observed. Hence, in each case, all possible ring-substitution products probably form.

The bromination and chlorination of **4** with NBS and *N*-chlorosuccinimide (NCS) in dioxane have been reported to give mixtures of the corresponding 2-halo- and 2,5-dihalo-1-phenylpyrroles.[13] The ratios of the products or yields were not reported. Mitchell et al. have reported that NBS in dimethylformide (DMF) is a mild and selective electrophilic nuclear brominating reagent for reactive aromatic systems.[14] Bromination of **1** and **2** with NBS in DMF does result in selective bromination. However, the solutions become dark, suggesting that oxidation of the pyrrole is also occurring. In addition, it is difficult to separate the DMF from some of the bromopyrroles. When NBS in tetrahydrofuran (THF) is used as the brominating reagent, there is little or no oxidation, substitution occurs only in the pyrrole nucleus, the reaction is selective for mono-, di-, tri-, or tetrasubstitution, the reaction is regiospecific for the 2-position, and the solvent is readily removed from the brominated pyrroles.

Bromination of **1**–**3** with 1 mol of NBS in THF selectively forms the 2-bromopyrroles as shown in Table II. In each case only very small amounts of starting material remain. The amounts of 3-substitution and 2,5-disubstitution are too small to measure by the gas chromatographic techniques available. Bromination of **4** under similar conditions was not as selective as that for the other pyrroles, but the selectivity was improved by using DMF as the solvent, from which the product can be easily separated.

Bromination of **1**–**4** with 2 mol of NBS in THF selectively forms the 2,5-dibromopyrroles with only very small amounts of 2-bromo- or 2,3,5-tribromopyrroles forming. Selective bromination of **2**–**4** with 3 and 4 mol of NBS to form the 2,3,5-tribromopyrroles and tetrabromopyrroles, respectively, has also been accomplished. Treatment of **1** with 3 and 4 mol of NBS results in mostly oxidation and therefore is not a suitable procedure for forming good yields of 2,3,5-tribromo- and tetrabromopyrroles.

Chlorination of **1**–**4** with NCS gives results (Table III) which are similar to the bromination results except that chlorination is not as selective as bromination. When **1** is reacted with an equimolar amount of NCS, a small amount of oxidation occurs. As the molar amount of NCS is increased, more oxidation is observed. Therefore, it is

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Table IV. Yields of Some Brominated Pyrroles

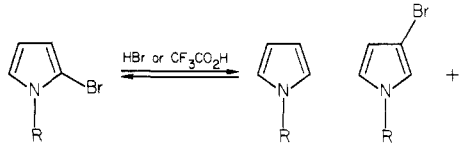
substr	moles of NBS	product	yield,[a] %
1	1	2-bromopyrrole	82[b]
1	2	2,5-dibromopyrrole	93[b]
2	1	2-bromo-1-methylpyrrole	90[b]
2	4	2,3,4,5-tetrabromo-1-methylpyrrole	91 (85)
3	1	2-bromo-1-benzylpyrrole	90
3	2	2,5-dibromo-1-benzylpyrrole	92 (87)
4	2	2,5-dibromo-1-phenylpyrrole	90
4	3	2,3,5-tribromo-1-phenylpyrrole	93

[a] Yields reported are of unpurified product. The yield in parentheses is of isolated crystalline product once crystallized from hexane. [b] Decomposes very rapidly shortly after isolation but can be stabilized by the addition of a trisubstituted amine (tributylamine).

not practical to prepare tri- and tetrachloropyrrole with this technique although some of the halogenated products are formed in each case.

These halogenation techniques can be used as very simple methods of obtaining relatively pure samples of the halogenated pyrroles. When halogenation is complete, the solution is eluted with hexane by using a short alumina column. Evaporation of the solvent gives good yields of some representative halopyrroles as shown in Table IV. All of the tetrahalopyrroles are stable; however, the partially halogenated pyrroles are not. Partially brominated and chlorinated **1** and brominated **2** are especially unstable and when purified must be stabilized with a base such as tributylamine.[5] Partially chlorinated **2** and partially halogenated **3** and **4** are stable but slowly decompose on standing. It was found convenient to store solutions of these halogenated pyrroles in a refrigerator over sodium sulfite.

1-Methyl-, 1-benzyl-, and 1-phenyl-2-bromopyrrole undergo isomerization and disproportionation when treated with hydrogen bromide gas or trifluoroacetic in CCl_4 as shown in eq 1. The above reaction is accompanied by



dibromopyrroles + tribromopyrroles (1)

R = CH_3, CH_2Ph, Ph

considerable decomposition similar to the reaction of bromine and **2**, **3**, or **4** in CCl_4. After the ratio of products does not appear to be changing, the ratio of 2- to 3-bromopyrroles is about 1 to 3 or 4 with considerable amounts of the disporportionation products. The reduction of iodopyrroles with hydrogen iodide has been reported by Doak and Corwin,[15] but the formation of polyiodopyrroles under these conditions has not be reported. The conversion of 2-bromo- to 3-bromopyrroles may be similar to the rearrangement of 2-acyl- to 3-acylpyrroles[16] and 2-sulfinyl- to 3-sulfinylpyrroles[17] under acidic conditions. The 2,5-dibromopyrroles also undergo similar isomerization and disproportionation in the presence of hydrogen bromide or trifluoroacetic acid.

The usual procedure for the bromination of pyrroles with molecular bromine[2,5,7] does not completely remove all of the hydrogen bromide formed. The complex reaction mixtures observed in these brominations are, therefore, not only the result of electrophilic substitution of the pyrrole nucleus but also of the isomerization and disproportionation of the various bromopyrroles by the hydrogen bromide formed. This accounts for why considerable starting material as well as polybrominated pyrroles is among the products of the reaction mixture. This is further verified by the fact that the bromination of **2** with an equimolar amount of bromine in CCl_4 in the presence of pyridine forms only 2-bromo- and 2,5-dibromo-1-methylpyrrole. The reaction is not as selective as the NBS–THF system.

The total energies of 2-bromo- and 3-bromo-1-methylpyrrole were determined by using the extended Hückel molecular orbital method of Hoffman.[18,19] 3-Bromo-1-methylpyrrole was found to be 8.8 kcal more stable than 2-bromo-1-methylpyrrole.[20] Under strongly acidic conditions, where near-equillibrium conditions exist, the 3-bromopyrroles would therefore be expected to increase in concentration. This is the case when **2** and **3** are brominated with bromine in CCl_4 in the presence of hydrogen bromide and when 2-bromo-1-methylpyrrole, 2-bromo-1-benzylpyrrole, or 2-bromo-1-phenylpyrrole are reacted with hydrogen bromide or trifluoroacetic acid in CCl_4. This is consistent with the reports that 3,4-dichloropyrrole is a stable white crystalline solid[21-23] and that 2,5-dichloropyrrole is an unstable oil.[5]

Experimental Section

All melting points are uncorrected and were determined on a Thomas-Hoover unimelt apparatus. The gas chromatographic–mass spectroscopic data were obtained by using a Hewlett-Packard 5700A gas chromatograph equipped with a 6-ft glass column packed with 2% OV-101 on Chromosorb G and a Hewlett-Packard 5930 A mass spectrometer. Gas chromatographs were obtained by using a Hewlett-Packard Model 700 instrument equipped with a flame detector and a 10 ft × $^1/_8$ in., 10% SE-30 on 80/100-mesh Chromosorb W-HP column. Column temperatures ranged from 120 °C for the bromopyrroles to 230 °C for the 1-benzylbromopyrroles. ^1H NMR spectra were obtained by using a Varian EM360A instrument, tetramethylsilane as an internal standard, and carbon tetrachloride as solvent. Thin-layer chromatographs were done with precoated sheets of silica gel 60 F_{254} (0.2 mm thickness) obtained from Matheson Coleman and Bell with hexane as a solvent unless otherwise noted. Column chromatography was done on a 12 × $^3/_4$ in. column packed with chromatographic grade activated alumina obtained from Matheson Coleman and Bell and with hexane as the eluant.

Materials. All chemicals were purchased from Aldrich Chemical Co. unless otherwise noted. Pyrrole (**1**) and 1-methylpyrrole (**2**) were distilled just before use. (Only colorless liquids were used.) 1-Phenylpyrrole (**4**) was sublimed before use. 1-Benzylpyrrole (**3**) was prepared by the method of Hobbs et al.,[24] by using tetrahydrofuran as solvent. *N*-Bromosuccinimide and *N*-chlorosuccinimide were stored in a refrigerator and then placed in a vacuum desiccator connected to a water aspirator for 1 h just before use. Tetrahydrofuran (99.5%) was dried over $LiAlH_4$ and then distilled.

Bromination of 2–4 with Bromine. A solution of bromine (2.40 g, 0.015 mol) in 50 mL of carbon tetrachloride was added dropwise during 30 min to a stirred mixture of 1.20 g of **2**, 3.0

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g of magnesium oxide, and 100 mL of carbon tetrachloride at 0 °C (similar to the procedure in ref 3). Stirring was continued for 30 min after the addition of bromine was complete. The mixture was filtered, washed with 10% sodium sulfate, and dried over anhydrous sodium sulfate. Most of the solvent was evaporated by using a rotary evaporator. The residue was stored over sodium sulfite in a refrigerator and analyzed by GC and GC/MS [compound, retention time, m/e (relative intensity)]: 2-bromo-1-methylpyrrole, 1.0 min, 161 (M^+, 97), 159 (M^+, 100), 80 (17), 78 (20), 53 (21), 39 (25); 3-bromo-1-methylpyrrole, 1.6 min, 161 (M^+, 95), 159 (M^+, 100), 80 (12), 79 (17) 78 (11), 53 (12), 42 (12), 39 (11); 2,5-dibromo-1-methylpyrrole, 3.0 min, 241 (M^+, 48), 239 (M^+, 100), 237 (M^+, 52), 222 (10), 224 (20), 226 (11), 119 (12), 117 (12); 2,4- and/or 3,4-dibromo-1-methylpyrrole, 3.7 min, 241 (M^+, 49), 239 (M^+, 100), 237 (M^+, 53), 119 (10), 117 (9), 79 (12); 2,3,5-tribromo-1-methylpyrrole, 5.5 min, 321 (M^+, 32), 319 (M^+, 96), 317 (M^+, 100), 315 (M^+, 34), 306 (9), 304 (15), 302 (15), 300 (10), 199 (10), 197 (22), 195 (10); 2,3,4-tribromo-1-methylpyrrole, 6.1 min, 321 (M^+, 29), 319 (M^+, 100), 317 (M^+, 99), 315 (M^+, 34), 240 (10), 238 (23), 236 (9); 2,3,4,5-tetrabromo-1-methylpyrrole, 7.8 min, 401 (M^+, 18), 399 (M^+, 66), 397 (M^+, 100), 395 (M^+, 68), 393 (M^+, 19), 386 (4), 384 (13), 382 (21), 380 (14), 378 (4), 279 (8), 277 (19), 275 (20), 273 (9). The relative amounts of bromopyrroles found by GC analysis are given in Table I.

1-Benzylpyrrole (**3**; 1.43 g, 0.009 mol) was brominated by the addition of 1.44 g (0.009 mol) of bromine in carbon tetrachloride using the procedure found in ref 4. After evaporation of most of the solvent, the sample was stored in a refrigerator over sodium sulfite and analyzed by GC and GC/MS [compound, retention time, m/e (relative intensity)]: 2-bromo-1-benzylpyrrole, 2.8 min, 237 (M^+, 29), 235 (M^+, 29), 91 (100), 65 (12); 3-bromo-1-benzylpyrrole, 3.6 min, 237 (M^+, 28), 235 (M^+, 27), 91 (100), 65 (14); 2,5-dibromo-1-benzylpyrrole, 4.2 min, 317 (M^+, 13), 315 (M^+, 28), 313 (M^+, 14), 91 (100), 65 (12); 3,4- or 2,4-dibromo-1-benzylpyrrole, 4.9 min, 317 (M^+, 11), 315 (M^+, 22), 313 (M^+, 11), 90 (100), 65 (10); 3,4- or 2,4-dibromo-1-benzylpyrrole, 5.6 min, 317 (M^+, 17), 315 (M^+, 34), 313 (M^+, 17), 91 (100), 65 (11); 2,3,5-tribromo-1-benzylpyrrole, 6.0 min, 397 (M^+, 5), 395 (M^+, 13), 393 (M^+, 13), 391 (M^+, 5), 91 (100), 65 (9); 2,3,4-tribromo-1-benzylpyrrole, 6.7 min, 395 (M^+, 12), 393 (M^+, 12), 391 (M^+, 4), 91 (100), 65 (10); 2,3,4,5-tetrabromo-1-benzylpyrrole, 7.7 min, 477 (M^+, 2), 475 (M^+, 6), 473 (M^+, 9), 471 (M^+, 6), 469 (M^+, 2), 92 (7), 91 (100), 65 (10). The relative amounts of bromopyrroles found by GC analysis are given in Table I.

1-Phenylpyrrole (**4**; 0.72 g, 0.005 mol) was brominated by the addition of 0.90 g (0.005 mol) of bromine in carbon tetrachloride using the procedure found in ref 4. After evaporation of most of the solvent, the sample was stored in a refrigerator over sodium sulfite and analyzed by GC and GC/MS [compound, retention time, m/e (relative intensity)]: 2-bromo-1-phenylpyrrole, 2.1 min, 223 (M^+, 94), 221 (M^+, 100), 142 (55), 115 (80), 77 (22), 51 (26); 3-bromo-1-phenylpyrrole, 3.2 min, 223 (M^+, 100), 221 (M^+, 100), 151 (24), 142 (43), 115 (46), 85 (18), 77 (25), 39 (22); 2,5-dibromo-1-phenylpyrrole, 3.5 min, 303 (M^+, 49), 301 (M^+, 100), 299 (M^+, 51), 222 (34), 220 (35), 140 (26), 141 (26), 77 (15), 51 (20); 2,3,5-tribromo-1-phenylpyrrole, 5.6 min, 383 (M^+, 30), 381 (M^+, 95), 379 (M^+, 100), 377 (M^+, 34), 302 (55), 300 (91), 298 (45), 221 (38), 220 (33), 219 (38), 218 (30), 140 (28), 77 (35), 51 (34); 2,3,4,5-tetrabromo-1-phenylpyrrole, 7.4 min, 463 (M^+, 16), 461 (M^+, 59), 459 (M^+, 93), 457 (M^+, 62), 455 (M^+, 18), 382 (41), 380 (100), 378 (95), 376 (32), 301 (35), 300 (45), 299 (63), 298 (80), 297 (32), 296 (39), 220 (46), 218 (41), 77 (53), 51 (48). The relative amounts of bromopyrroles found by GC analysis are given in Table I.

Procedure for the Bromination of 1–4 with *N*-Bromosuccinimide. Freshly purified pyrrole (**1**; 0.34 g, 0.005 mol) was dissolved in 20 mL of tetrahydrofuran and cooled in a dry ice–2-propanol bath. *N*-Bromosuccinimide (0.89 g, 0.005 mol) was added and the mixture swirled for a short time, after removal from the dry ice bath, until all the NBS was in solution. The solution was allowed to stand in a freezer (−10 °C) for 2 h during which the solutions became light green. Sodium sulfite (1 g) was added to the solution, and the solvent was removed on a rotary evaporator at room temperature. Carbon tetrachloride (3 mL) was added to the residue and the mixture stored in a refrigerator. GC analysis of the resulting solutions gave the results in Table II. ^{1}H NMR analysis of the carbon tetrachloride solutions was in agreement with the published spectra of 2-bromopyrrole:[5] GC/MS [retention time, m/e (relative intensity)] 5 min, 147 (M^+, 100), 145 (M^+, 97), 66 (22), 39 (36), 38 (20).

1-Methylpyrrole (**2**; 0.41 g, 0.005 mol) was brominated with NBS–THF (0.89 g, 0.005 mol) as described above. The reaction mixture remained colorless. GC data are found in Table II. The ^{1}H NMR analysis agrees with published spectrum for 2-bromo-1-benzylpyrrole.[5]

1-Benzylpyrrole (**3**; 0.79 g, 0.005 mol) was brominated with NBS–THF (0.89 g, 0.005 mol) as described above. The reaction mixture remained colorless. GC data are found in Table II. The ^{1}H NMR analysis agrees with published spectra for 2-bromo-1-benzylpyrrole.[5]

1-Phenylpyrrole (**4**; 0.80 g, 0.005 mol) was brominated with NBS–THF (0.89 g, 0.005 mol) as described above. When the reagents are first mixed, a fleeting rusty color forms, but on being allowed to stand, the mixture becomes light yellow. GC data are found in Table II: ^{1}H NMR (CCl_4) δ 6.20 (m, 2, C_3H and C_4H), 6.98 (t, 1, C_5H), 7.32 (m, 5, C_6H_5). Compound **4** was also brominated with NBS by using *N*,*N*-dimethylformamide as the solvent. The bromination procedure was the same as that already given except that the DMF solution of the reaction mixture was analyzed directly by GC without evaporation of the solvent. Results are given in Table II.

Compounds **1–4** (0.005 mol) were brominated with 2 mol of NBS (1.78 g, 0.010 mol), 3 mol of NBS (2.67 g, 0.015 mol), and 4 mol of NBS (3.56 g, 0.020 mol) in 20 mL of THF by using the procedure described above except that the reaction mixtures were allowed to stand in a freezer (−10 °C) overnight. In all cases, as the solutions are swirled to dissolve all of the NBS, succinimide begins to separate from solution. Results of GC analysis are given in Table II. ^{1}H NMR analysis of the reaction obtained from 1 mol of **1** and 2 mol of NBS agrees with the published spectrum of 2,5-dibromopyrrole:[5] GC–MS [retention time, m/e (relative intensity)] 1.6 min, 227 (M^+, 49), 225 (M^+, 100), 223 (M^+, 51), 146 (18), 144 (18), 119 (19), 117 (18), 64 (27), 38 (38), 37 (33).

Analysis of 2,3,5-tribromopyrrole obtained from the reaction of 1 mol of **1** and 3 mol of NBS in CCl_4 gave the following: ^{1}H NMR (CCl_4) δ 6.10 (d, 2 J = 2.5 Hz, C_3H and C_4H), NH not observed; GC/MS [retention time, m/e (relative intensity) 3.9 min, 307 (M^+, 33), 305 (M^+, 95), 303 (M^+, 100), 301 (M^+, 34), 226 (17), 224 (35), 222 (18), 199 (13), 197 (27), 195 (12), 118 (11), 116 (11), 79 (8), 81 (8), 37 (12). Considerable oxidation is also observed.

GC/MS analysis of 2,3,4,5-tetrabromopyrrole obtained from the reaction of 1 mol of **1** and 4 mol of NBS gave the following [retention time, m/e (relative intensity)]: 6.0 min, 387 (M^+, 18), 385 (M^+, 66), 383 (M^+, 100), 381 (M^+, 71), 379 (M^+, 21), 306 (12), 304 (40), 302 (42), 300 (13), 279 (11), 277 (32), 275 (34), 273 (12), 198 (9), 196 (19), 194 (9), 117 (16), 115 (17). Considerable oxidation is also observed.

^{1}H NMR analysis of the reaction mixture obtained from 1 mol of **2** and 2, 3, and 4 mol of NBS agreed with the published spectra of 2,5-dibromo-, 2,3,5-tribromo-, and 2,3,4,5-tetrabromo-1-methylpyrrole, respectively.[5] GC/MS analysis of these bromo-1-methylpyrroles showed good agreement with the data for the isomers reported under the bromination of **2** with bromine. GC results are given in Table II. The ^{1}H NMR (CCl_4) analysis of the reaction mixture obtained from 1 mol of **3** and 2 mol of NBS was consistent with 2,5-dibromo-1-benzylpyrrole: δ 5.19 (s, 2, CH_2), 6.20 (s, 2, C_3H and C_4H), 6.80–7.40 (m, 5, C_6H_5). GC/MS of 2,5-dibromo-1-benzylpyrrole showed good agreement with that reported under the bromination of **3** with bromine. Evaporation of the solvent left a white crystalline solid which was crystallized from hexane; mp 80–80.5 °C.[7] The ^{1}H NMR (CCl_4) analysis of the reaction mixture obtained from 1 mol of **3** and 3 mol of NBS was consistent with 2,3,5-tribromo-1-benzylpyrrole: δ 5.20 (s, 2, CH_2), 6.33 (s, 1, C_4H), 6.80–7.40 (m, 5, C_6H_5). GC/MS spectrometry of 2,3,5-tribromo-1-benzylpyrrole showed good agreement with that reported under the bromination of **3** with bromine. Evaporation of the solvent left a white crystalline solid which was crystallized from hexane; mp 66–66.5 °C. ^{1}H NMR analysis of the reaction mixture obtained from 1 mol of **3** and 4 mol of NBS and its melting point (105–105.5 °C) were identical with those reported for 2,3,4,5-tetrabromo-1-benzylpyrrole.[7] GC/MS of 2,3,4,5-tetrabromo-1-benzylpyrrole showed good agreement with

that reported under the bromination of 3 with bromine. GC results for all of these brominations are given in Table II.

^{1}H NMR (CCl_4) analysis of the reaction mixture obtained from 1 mol of 4 and 2, 3, and 4 mol of NBS agrees with the expected ^{1}H NMR (CCl_4) of 2,5-dibromo-1-phenylpyrrole [δ 6.28 (s, 2, C_3H and C_4H), 7.1–7.5 (m, 5, C_6H_5)], 2,3,5-tribromo-1-phenylpyrrole [δ 6.40 (s, 1, C_4H), 7.0–7.6 (m, 5, C_6H_5)], and 2,3,4,5-tetrabromo-1-phenylpyrrole [δ 7.0–7.6 (m, 5, C_6H_5)], respectively. GC/MS data for these bromo-1-phenylpyrroles are in good agreement with those reported under the bromination of 4 with bromine. The GC results are given in Table II.

Procedure for the Chlorination of 1–4 with *N*-Chlorosuccinimide. Chlorinations of 1–4 (0.0050 mol) were accomplished by treatment each with 1 mol (0.67 g, 0.0050 mol), 2 mol (1.34 g, 0.010 mol), 3 mol (2.01 g, 0.015 mol), and 4 mol of NCS (2.68 g, 0.020 mol), respectively, in 40 mL of tetrahydrofuran as described for the bromination with NBS. GC analyses of these reaction mixtures are given in Table III.

^{1}H NMR analyses of the reaction mixtures obtained from the reaction of 1 with 1 and 2 mol of NCS are identical with those reported for 2-chloro- and 2,5-dichloropyrrole, respectively.[5] In each case a small amount of oxidation also occurs. Attempted chlorination of 1 with 3 and 4 mol of NCS formed only small amounts of the desired trichloro- and tetrachloropyrrole, respectively. Compounds resulting from the oxidation of 1 were the major products observed.

^{1}H NMR analyses of the reaction mixtures of 2 with 1 and 2 mol of NCS are identical with those reported for 2-chloro- and 2,5-dichloro-1-methylpyrrole, respectively:[5] ^{1}H NMR spectrum of 2,3,5-trichloro-1-methylpyrrole (CCl_4) δ 3.59 (s, 3, CH_3), 6.25 (s, 1, C_3H); ^{1}H NMR spectrum of 2,3,4,5-tetrachloro-1-methylpyrrole (CCl_4) δ 3.59 (s, 3, CH_3).

^{1}H NMR analysis of the reaction mixture of 3 with 1 mol of NCS is identical with that reported for 2-chloro-1-benzylpyrrole.[5] ^{1}H NMR spectra (CCl_4) were obtained for the following: 2,5-dichloro-1-benzylpyrrole, δ 5.15 (s, 2, CH_2), 6.10 (s, 2, C_3H and C_4H), 6.8–7.3 (m, 5, C_6H_5); 2,3,5-trichloro-1-benzylpyrrole, δ 5.15 (s, 2, CH_2), 6.25 (s, 1, C_4H), 6.8–7.3 (m, 5, C_6H_5); 2,3,4,5-tetrachloro-1-benzylpyrrole, δ 5.15 (s, 2, CH_2), 6.8–7.3 (m, 5, C_6H_5).

The chlorination of 4 was carried out in 30 mL of *N*,*N*-dimethylformamide. ^{1}H NMR spectra (CCl_4) were obtained for the following: 2-chloro-1-phenylpyrrole, δ 6.20 (m, 2, C_3H and C_4H), 6.97 (m, 1, C_5H), 7.1–7.6 (m, 5, C_6H_5); 2,5-dichloro-1-phenylpyrrole, δ 6.10 (s, 2, C_3H and C_4H), 7.1–7.6 (m, 5, C_6H_5); 2,3,5-trichloro-1-phenylpyrrole, δ 6.19 (s, 1, C_4H), 7.1–7.6 (m, 5, C_6H_5); 2,3,4,5-tetrachloro-1-phenylpyrrole, δ 7.1–7.6 (m, 5, C_6H_5).[25]

Preparation of Some Bromopyrroles. Freshly distilled pyrrole (0.68 g, 0.010 mol) was dissolved in 20 mL of THF and cooled in a dry ice–2-propanol bath, and NBS (1.78 g, 0.010 mol) was added to the solution with swirling after removal from the dry ice bath. After the NBS had dissolved, the solution was allowed to stand in a freezer overnight, 3 drops of pyridine were added, and the reaction mixture was added to an alumina column (12 × 1.5 in.) and eluted with 400 mL of hexane. The hexane was collected in a flask containing 0.65 g of tributylamine and anhydrous sodium sulfate. This mixture was filtered into a weighed 500 mL, round-bottomed flask, the hexane was removed in a rotary evaporator at 40 °C, and air was aspirated through the flask for a few minutes to remove the last traces of solvent. The difference in weight of the flask was due to 1.21 g (0.0082 mol, 82% yield) of crude 2-bromopyrrole and 0.65 g of tributylamine added to stabilize the product. The crude yields of product listed in Table IV were obtained by using 0.010 mol of the appropriate pyrrole and the calculated amount of NBS. 2,5-Dibromo- and 2,3,5-tribromo-1-phenylpyrrole were prepared by using the same procedure except that the solution was allowed to stand overnight at room temperature rather than in a freezer. It is not necessary to stabilize the bromo-1-benzyl- or bromo-1-phenylpyrroles with a trisubstituted amine. The solid bromopyrroles, 2,3,4,5-tetrabromo-1-methylpyrrole and 2,5-dibromo-1-benzylpyrrole, were crystallized from hexane. The yields of solid products obtained are listed in parentheses in Table IV.

Acid-Catalyzed Isomerization of Some Bromopyrroles. To 2 mL of a carbon tetrachloride solution of 2-bromo-1-methylpyrrole, obtained from the reaction of NBS–THF and 2, were added 2 drops of trifluoroacetic acid, or a small amount of HBr gas was passed through the solution. These solutions were monitored by GC which indicated the decreased concentration of 2-bromo-1-methylpyrrole and the appearance of 3-bromo-1-methylpyrrole, 1-methylpyrrole, and various dibromo- and tribromo-1-methylpyrroles. A typical GC analysis after 2 h indicates 20% 1-methylpyrrole and 13% 2-bromo-, 41% 3-bromo, 20% dibromo-, and 5% tribromo-1-methylpyrrole.

2-Bromo-1-benzylpyrrole treated similarly overnight gave the following results: 7% 1-benzylpyrrole and 11% 2-bromo-, 66% 3-bromo-, and 11% 2,5-dibromo-1-benzylpyrrole.

2,5-Dibromo-1-benzylpyrrole treated similarly for 1 h gave the following results: 2% 2-bromo-, 16% 3-bromo-, 4% 2,5-dibromo-, 49% 3,4- and 2,4-dibromo-, and 29% tribromo-1-benzylpyrrole.

2,5-Dibromo-1-phenylpyrrole treated simiarly for 1 h gave the following results: 13% 3-bromo-, 8% 2,5-dibromo-, 31% 2,4- and/or 3,4-dibromo-, and 48% tribromo-1-phenylpyrrole.

Registry No. 1, 109-97-7; 2, 96-54-8; 3, 2051-97-0; 4, 635-90-5; 2-bromo-1-methylpyrrole, 56454-27-4; 3-bromo-1-methylpyrrole, 77123-94-5; 2,5-dibromo-1-methylpyrrole, 56454-30-9; 2,4-dibromo-1-methylpyrrole, 77123-95-6; 3,4-dibromo-1-methylpyrrole, 77123-96-7; 2,3,5-tribromo-1-methylpyrrole, 77123-97-8; 2,3,4-tribromo-1-methylpyrrole, 77123-98-9; 2,3,4,5-tetrabromo-1-methylpyrrole, 56454-29-6; 2-bromo-1-benzylpyrrole, 56454-00-3; 3-bromo-1-benzylpyrrole, 18159-13-2; 2,5-dibromo-1-benzylpyrrole, 18159-14-3; 3,4-dibromo-1-benzylpyrrole, 77123-99-0; 2,4-dibromo-1-benzylpyrrole, 77124-00-6; 2,3,5-tribromo-1-benzylpyrrole, 18159-15-4; 2,3,4-tribromo-1-benzylpyrrole, 77124-01-7; 2,3,4,5-tetrabromo-1-benzylpyrrole, 18159-16-5; 2-bromo-1-phenylpyrrole, 30068-53-2; 3-bromo-1-phenylpyrrole, 77124-02-8; 2,5-dibromo-1-phenylpyrrole, 30068-54-3; 2,3,5-tribromo-1-phenylpyrrole, 77124-03-9; 2,3,4,5-tetrabromo-1-phenylpyrrole, 77124-04-0; 2,3,4,5-tetrabromopyrrole, 54705-14-5; 2,4-dibromo-1-phenylpyrrole, 77124-05-1; 3,4-dibromo-1-phenylpyrrole, 77124-06-2; 2-bromopyrrole, 38480-28-3; 2,5-dibromopyrrole, 56454-25-2; 2,3,5-tribromopyrrole, 77124-07-3; 2-chloropyrrole, 56454-22-9; 2,5-dichloropyrrole, 56454-23-0; 2-chloro-1-methylpyrrole, 56454-26-3; 2,5-dichloro-1-methylpyrrole, 56454-28-5; 2,3,5-trichloro-1-methylpyrrole, 77124-08-4; 2,3,4,5-tetrachloro-1-methylpyrrole, 77124-09-5; 2-chloro-1-benzylpyrrole, 56454-01-4; 2,5-dichloro-1-benzylpyrrole, 77124-10-8; 2,3,5-trichloro-1-benzylpyrrole, 77124-11-9; 2,3,4,5-tetrachloro-1-benzylpyrrole, 77124-12-0; 2-chloro-1-phenylpyrrole, 30068-55-4; 2,5-dichloro-1-phenylpyrrole, 30068-56-5; 2,3,5-trichloro-1-phenylpyrrole, 77124-13-1; 2,3,4,5-tetrachloro-1-phenylpyrrole, 77124-14-2.

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