Acid-Catalyzed Intermolecular Rearrangement of *N*-Chlorocarbazole

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The chlorination of carbazole with sodium hypochlorite in CH_2Cl_2, $CHCl_3$, or CCl_4 gave *N*-chlorocarbazole in 63–95% yield. It rearranged in refluxing methanol to give carbazole, 3-chlorocarbazole, 1-chlorocarbazole, 3,6-dichlorocarbazole, and 1,6-dichlorocarbazole. These chlorocarbazoles were formed in an acid-catalyzed intermolecular reaction. In the presence of potassium carbonate dechlorination of *N*-chlorocarbazole was observed. No evidence for an intramolecular rearrangement was found.

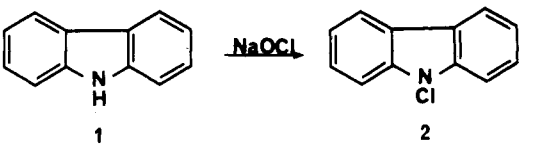
The chlorination of pyrrole[2] and indole[3] with aqueous sodium hypochlorite initially gives an *N*-chloro intermediate that subsequently rearranges in methanol to give *C*-chloro products. We have now extended this work to carbazole. Comparison of the results obtained in the three systems could indicate the effect of ring annelation on reactivity. To our best knowledge, only two previous studies of this series treat the effect of changes in aromatic character on reactivity.[4-6]

Reviews on carbazole chemistry[7] and halocarbazoles[8] have recently appeared. A number of different chlorinating agents[7-9] have been used, and 3-chlorocarbazole (major) and 1-chlorocarbazole (minor) are the products of monochlorination. Product studies have been limited by the difficulty of separating the products formed,[10,11] and in some cases it would appear that product ratios reflect the ease of separation of the products.[12]

This study reports on the formation and rearrangement of *N*-chlorocarbazole. Its behavior is compared to that of *N*-chloropyrrole[2] and *N*-chloroindole[3].

Formation of *N*-Chlorocarbazole. The chlorination of carbazole (1) with sodium hypochlorite, under homogeneous conditions and pH 7.0 and 5.3, has been reported.[9c] Carbazoles containing one to four chlorine atoms were detected, but their structures were not determined. In this study pure *N*-chlorocarbazole (2) was obtained in 63–95+% yield when a solution of carbazole (1) in CH_2Cl_2, $CHCl_3$, or CCl_4 was stirred vigorously for 48 h with an aqueous solution of sodium hypochlorite (pH ca. 12). Solutions of **2** oxidize iodide ion (Scheme I). The spectral evidence: IR (no NH); ^1H NMR consistent with N-substitution. Removal of solvent under reduced pressure gives a short-lived solid that decomposes with the evolution of HCl. Solutions of **2** at 0 °C and stored over K_2CO_3 are stable for 2–3 months.

Scheme I



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Scheme II

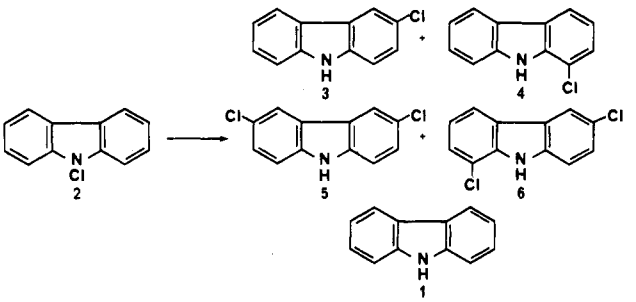

Table I. ^1H NMR Chemical Shifts of *N*-Methyl Groups in Product Mixture[a]

substituent(s)	authentic carbazoles[b]	components of reactn mixture[b]
H	2.67	3.05[c]
1-Cl	3.57	3.57
2-Cl	2.82	
3-Cl	2.88	2.88[c]
4-Cl	2.92	
3,6-Cl_2	2.75	2.73[c]
1,6-Cl_2	3.40[d]	3.42[c]

[a] Reaction run with 0.05 M **2** in CCl_4/CH_3OH (1:1) v/v. [b] C_6D_6. [c] Checked by adding authentic sample to reaction mixture. [d] Determined in a mixture containing 80% (^1H NMR) of component.

Identification of Rearrangement Products. A solution containing **2** in CH_2Cl_2 was combined with an equal volume of methanol and refluxed. After 1–2 h no **2** could be detected iodometrically. An inseparable mixture of carbazole (1), 3-chlorocarbazole (3), 1-chlorocarbazole (4), 3,6-dichlorocarbazole (5), and 1,6-dichlorocarbazole (6) was obtained. The composition of the mixture was determined by ^1H NMR following N-methylation of the products (Scheme II).

All the monochlorocarbazoles were prepared[13] and methylated with CH_3I/KOH in THF. *N*-Methylcarbazole

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Table II. Effect of Reaction Conditions on Relative Product Yields

reactn conditions	time, h	% yields[a] 1-Cl	1,6-Cl_2	carbazole	3-Cl	3,6-Cl_2
0.05 M[b]	1–2	11	5	19	52	13
0.05 M; 1 g K_2CO_3[c]	8	3		86	11	
0.05 M; 0.1 M carbazole	0.25	16			84	
0.005 M	2	11	4	23	51	11
0.0005 M	2	12	5	18	53	12
0.05 M; 0.25 M NMP[d]	2			100		
0.005 M; 0.0025 M NMP[d]	2			100		
0.05M; 0.01 M HCl	0.25	8	3	20	56	13

[a] Determined by ^1H NMR. [b] Concentration of *N*-chlorocarbazole. [c] There are also present several small (5%) unidentified peaks whose chemical shifts do not correspond to any of those in Table I. [d] NMP = *N*-methylpyrrole.

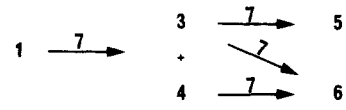
was also prepared. Spectra were taken in C_6D_6, and a large aromatic solvent-induced shift[14] was noted for the *N*-methyl derivatives of 2- and 3-chlorocarbazole. Also the chemical shift of the methyl group of *N*-methylcarbazole was at δ 2.67 in C_6D_6 but at δ 3.05 in the spectrum of the methylated reaction mixture taken in C_6D_6.[15] The presence of 1- and 3-chlorocarbazole was determined by comparison of the chemical shifts (Table I) of the *N*-methyl groups observed in the product mixtures with those of the authentic chloro-*N*-methylcarbazoles. Assignments were checked by adding authentic samples to the reaction mixture and noting the changes in the ^1H NMR spectrum. This method was also used to identify *N*-methylcarbazole. Two compounds were not identifiable by this method and were shown to be dichlorocarbazoles.

Carbazole reacts preferentially[17] at C-3 and C-1 with electrophiles. The most likely dichlorocarbazoles formed are 3,6-dichlorocarbazole (**5**) and 1,6-dichlorocarbazole (**6**). A sample of 3,6-dichloro-*N*-methylcarbazole was prepared by the chlorination of *N*-methylcarbazole with 2 mol of *N*-chlorobenzotriazole.[18] The *N*-methyl group at δ 2.73 was assigned to the 3,6-dichloro product. Chlorination of 1-chloro-*N*-methylcarbazole with 1 mol of *N*-chlorobenzotriazole[18] gave a three-component mixture (^1H NMR), and the compound formed in 80% yield was attributed to 1,6-dichloro-*N*-methylcarbazole. Its *N*-methyl group had the same chemical shift as the remaining unidentified peak at δ 3.42 (Table I). These two products disappeared when the reaction was run with added carbazole (Table II).

Mechanism of Rearrangement of *N*-Chlorocarbazole. Table II summarizes the relative yields of chlorocarbazoles obtained when acid (HCl), base (K_2CO_3), or a Cl^+ trap (carbazole, pyrrole) was added to the reaction. Comparison of these results with those obtained in CH_2Cl_2/CH_3OH strongly indicates that the products are formed in an intermolecular acid-catalyzed rearrangement analogous to that observed with *N*-chloropyrrole[2] or *N*-chloroanilines.[19]

Reactions run in the presence of K_2CO_3 resulted in the dechlorination of *N*-chlorocarbazole. This is analogous to the dechlorination of *N*-chloropyrrole under similar conditions.[2] Other *N*-chloro derivatives have also been reported to undergo dechlorination with methoxide[20,21] and other nucleophiles.[2,22,23] Nucleophilic attack on the chloro group is the most likely mechanism.[2,23]

Scheme III



Nitration of carbazoles has been shown to take place directly and also by the acid-catalyzed intramolecular rearrangement of an *N*-NO_2 intermediate.[24] The later resulted in a larger proportion of 1-NO_2 product relative to that obtained in direct nitration.

If an acid-catalyzed (pseudo-first-order)[24] or a neutral (first-order)[2] intramolecular rearrangement was competing with the observed pseudo-second-order process, it would be favored by dilution. No change was noted in the product distribution when the concentration of **2** was varied 100-fold (Table II). The possibility of an intramolecular process analogous to that observed in *N*-nitrocarbazole (acid-catalyzed) or *N*-chloropyrrole (neutral) can be eliminated.

Carbazoles protonate on nitrogen.[25] In this reaction, the most likely source of Cl^+ was the conjugate acid of *N*-chlorocarbazole (**7**). It is proposed that traces of carbazole present in solutions containing *N*-chlorocarbazole or formed by dechlorination reacted with the conjugate acid of *N*-chlorocarbazole to give the monochlorocarbazoles, which in turn gave the dichloro products (Scheme III).

No evidence was detected for an intramolecular rearrangement of *N*-chlorocarbazole (**2**). In contrast, the intramolecular rearrangement of *N*-chloropyrrole gave 2-chloropyrrole.[2] This implies the intermediacy of a 2-chloro-2*H*-pyrrole, which tautomerizes to the final product. An analogous 3-chloro-3*H*-indole intermediate was detected kinetically and by UV during the base-promoted rearrangement of *N*-chloroindole to 3-chloroindole.[3] The intramolecular rearrangement of *N*-chlorocarbazole would lead initially to 3-chloro-3*H*-carbazole. There is a greater loss of aromaticity (two rings) in the transition state, leading to 3-chloro-3*H*-carbazole than in that leading to 2-chloro-2*H*-pyrrole or 3-chloro-3*H*-indole. The result is that an intramolecular rearrangement cannot compete with

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either the acid-catalyzed intermolecular rearrangement or dechlorination.

Experimental Section

Infrared spectra were taken on a Perkin-Elmer 735 B. A Varian T-60 was used for recording ^1H NMR spectra and a Varian XL-100 for ^{13}C NMR spectra. Solutions of sodium hypochlorite were prepared by passing Cl_2 through a solution of NaOH, and the resulting solutions were ca. 1 M and pH 13.

N-Chlorination of Carbazole. To a vigorously stirred solution containing 1.716 g (10.3 mmol) of carbazole (1) in 250 mL of methylene chloride were added 25 mL of ca. 1 M solution of freshly prepared sodium hypochlorite and 25 mL of water. The mixture was stirred for 48 h. The organic layer was separated, dried by passing it through a short column of anhydrous potassium carbonate, and analyzed iodometrically. Solutions were thus obtained that contained 63–95+% of *N*-chlorocarbazole (2): IR (CCl_4) no NH, 3065, 1610, 1485, 1450, 1440, 1315, 1225, 725 cm^{-1}; ^1H NMR (CCl_4) δ 7.03–7.57 (6 H, m), 7.80–8.07 (2 H, m).

Preparation of Chlorocarbazoles. Carbazole (Merck) was used without further purification. The chlorocarbazoles were prepared[13] by the *p*-chloroanil dehydrogenation of the appropriate chlorotetrahydrocarbazole. **3-Chlorocarbazole (3)**: mp 198 °C (lit.[13] mp 199–200 °C). **1-Chlorocarbazole (4)**: mp 107–108 °C (lit.[13] mp 109–110 °C). **4-Chlorocarbazole**: mp 95 °C (lit.[13] mp 96 °C). **2-Chlorocarbazole**: mp 241 °C (lit.[13] mp 242 °C). The reaction of (*m*-chlorophenyl)hydrazine with cyclohexanone gave a mixture of 7-chloro- and 5-chlorotetrahydrocarbazole. In the original procedure[13] they were separated by repeated recrystallizations. It was found that if the mixture was washed with *n*-hexane, the filtrate contained 5-chlorotetrahydrocarbazole [purified by distillation bp 216 °C (4 mm)] and the remaining solid was 7-chlorotetrahydrocarbazole (recrystallized from methanol).

Preparation of Chloro-*N*-methylcarbazoles. In 10–15 mL of anhydrous tetrahydrofuran was dissolved 1.00 g (4.86 mmol) of chlorocarbazole, and the solution was cooled in an ice bath. There was then added ca. 2 g of powdered potassium hydroxide: the mixture was stirred vigorously for 15 min and excess methyl iodide (3–5×) added. The mixture was stirred for 30 min and warmed to room temperature and 90 mL of benzene added. The mixture was filtered and dried over anhydrous sodium sulfate and the solvent removed under reduced pressure. The ^1H NMR of the crude material indicated essentially pure product. **3-Chloro-*N*-methylcarbazole**: mp 38–40 °C [lit.[26] bp 238 °C (6 mm)]. **1-Chloro-*N*-methylcarbazole**: mp 70–71 °C; IR (KBr) 1330, 1080, 735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.83 (3 H, s), 6.80–7.43 (4 H, m), 7.66–8.03 (2 H, m). Anal. Calcd for $C_{13}H_{10}NCl$: C, 72.40; H, 4.67; N, 6.49. Found: C, 72.35; H, 4.49; N, 6.81. **2-Chloro-*N*-methylcarbazole**: mp 78–79 °C; IR (KBr) 1320, 815, 750, 725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.73 (3 H, s), 6.85–7.58 (5 H, m), 7.68–8.15 (2 H, m). Anal. Calcd for $C_{13}H_{10}NCl$: C, 72.40; H, 4.67; N, 6.49. Found: C, 72.27; H, 4.75; N, 6.11. **4-Chloro-*N*-methylcarbazole** was obtained as a yellow oil which was unstable in air. A brown solid was obtained by column chromatography on silica gel G using xylene as the eluent: mp 30–37 °C; ^1H NMR (CCl_4) δ 3.32 (3 H, s), 6.89–7.60 (7 H, m).

3,6-Dichloro-*N*-methylcarbazole.[18] To 29.9 mg (0.165 mmol) of *N*-methylcarbazole dissolved in 5.0 mL of methylene chloride was added 52.8 mg (0.33 mmol) of *N*-chlorobenzotriazole.[27] The mixture was allowed to stand overnight and 40 mL of chloroform was added. This solution was extracted three times with 30-mL portions of 3% sodium hydroxide solution and dried with anhydrous potassium carbonate and the solvent removed by distillation at reduced pressure. The solid was recrystallized from ethanol: mp 154–157 °C (lit.[26] mp 158–159 °C).

1,6-Dichloro-*N*-methylcarbazole.[18] In a similar manner as above, 34.4 mg (0.16 mmol) of 1-chloro-*N*-methylcarbazole was reacted with 25.2 mg (0.164 mmol) of *N*-chlorobenzotriazole.[27] The ^1H NMR spectrum (C_6D_6) indicated the presence of three components, and the compound formed in 80% yield was attributed to 1,6-dichloro-*N*-methylcarbazole (NCH_3 at δ 3.40).

Rearrangement of *N*-Chlorocarbazole (2). To 5.0 mL of a 0.1 M solution of *N*-chlorocarbazole (2) was added 5.0 mL of methanol and the solution heated to reflux for 1–2 h (solution gave negative KI test). Solvent was removed by evaporative distillation. The residue dissolved in 10 mL of anhydrous tetrahydrofuran and cooled in an ice bath. There was then added ca. 1 g of powdered potassium hydroxide. The mixture was stirred for 10 min and 62 μL (1.0 mmol) of methyl iodide added. After 30 min, 40 mL of benzene was added, the mixture was filtered, washed twice with an equal volume of water saturated with sodium chloride, washed once with water, and dried with anhydrous potassium carbonate, and the solvent was removed by evaporative distillation. The IR ($CHCl_3$) spectrum of the mixture indicated the complete disappearance of the NH band at 3490 cm^{-1}, which was present in the spectrum of the unmethylated mixture. In the ^1H NMR spectrum (C_6D_6) of the methylated mixture, there were five *N*-methyl signals present. They were identified (Table I) by comparison with samples of authentic chloro-*N*-methylcarbazoles prepared as described above. Their relative yields were determined by integration of the ^1H NMR spectrum (Table II).

Registry No. 1, 86-74-8; 2, 105598-33-2.

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