Azadiene Chemistry. 3. Polycyclic Amines from 2,3,4,5,5-Pentachloro-1-azacyclopentadiene in Diels–Alder Reaction[1]

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The title azadiene has been shown to undergo typical Diels–Alder reaction to yield polycyclic amine adducts. These cycloadducts include the bridgehead aza analogues of the commercial insecticides aldrin and dieldrin as well as several 5-substituted 1-azanorbornenes. Structural analysis of these polycyclic amine adducts is achieved via NMR spectral analyses using decoupling, shift reagent, and computer simulation techniques. Thus, azaaldrin is assigned structure **2**, azadieldrin **3**, and the equilibration of **2** with isomer **2b** via retrograde Diels–Alder reaction has been demonstrated. Reactions of the azadiene with monosubstituted olefins are both stereo- and regiospecific, yielding only the endo-5-substituted 1-azanorbornenes. The rates of the reactions of norbornadiene and styrene with the azadiene and hexachlorocyclopentadiene are compared and their relative reactivity discussed.

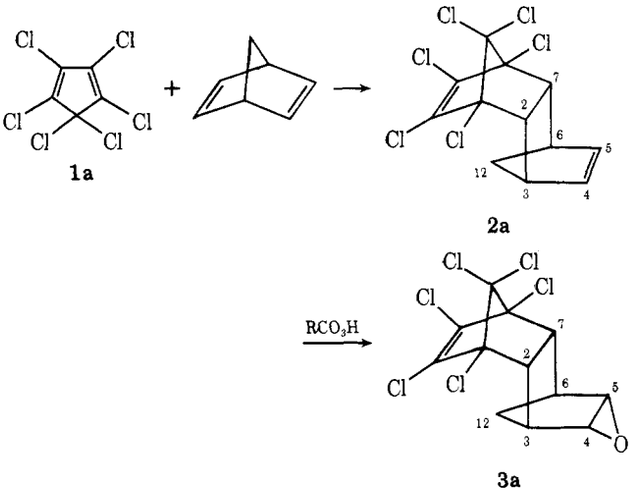
The enormous preparative importance of the Diels–Alder reaction is based on the range of variations of both the dienes and dienophiles. Dienes containing one heteroatom for the synthesis of heterocyclic compounds are uncommon, except for the 1-oxadienes such as acrolein.[2] The 1-azadiene, as a Diels–Alder diene, is conspicuously absent in the recent literature. The unreactive nature of this diene system was shown by Snyder et al.,[3] who reported that certain conjugated anils (–N=C–C=C–CH–) reacted with maleic anhydride via the enamine form (–NHC=C–C=C–) to yield an amino-substituted cyclohexane adduct, and that *N*-cinnamylideneaniline did not react since it has no γ hydrogen to tautomerize. In a review article[4] on the Diels–Alder synthesis with heteroatomic addends, there are ten references cited concerning the unsuccessful attempts to synthesize pyridine derivatives using anils as dienes. A few successful examples are also known where the azadiene is part of an extensive π system.[2] More recently, it has been observed that *N*-cinnamylideneaniline reacts with ketene to form the normal [4 + 2] dihydropyridone adduct.[5] However, reaction of *N*-cinnamylidenemethylamine with *N*-methylmaleimide was found to proceed in a non-Diels–Alder manner to yield a 1:2 adduct.[6] It therefore appears that the course of cycloaddition reactions with a 1-azadiene may be determined by the choice of diene, dienophile, and reaction conditions.

For a variety of synthetic goals to prepare polycyclic amines with bridgehead nitrogen, a one-step synthesis starting from cyclic 1-azadienes in Diels–Alder reaction would be particularly useful. As part of our continuing program[1] to study the reactivities and properties of α- and β-pyrrolenines (1- and 2-azadienes, respectively, in the cyclic form), we have discovered that 2,3,4,5,5-pentachloro-1-azacyclopentadiene (pentachloro-α-pyrrolenine, **1**)[7] reacts in typical Diels–Alder manner to yield polycyclic amine adducts. Thus, we have prepared polycyclic amines which are bridgehead aza analogues of the commercial insecticides aldrin and dieldrin as well as several 5-substituted 1-azanorbornenes. This paper describes the structural analysis of these polycyclic amines and the reactivity, stereospecificity, and regiospecificity of the cyclic azadiene **1** in the Diels–Alder reaction.

Results and Discussion

Synthesis and Structure of Azaaldrin (2) and Azadieldrin (3). An example of the preparative significance of the Diels–Alder reaction can be seen in the once popular insecticides aldrin (**2a**) and dieldrin (**3a**). Heating hexachlorocyclopentadiene (**1a**) in excess norbornadiene at 90 °C produces aldrin (**2a**)[8] in quantitative yield and peracid oxidation of **2a** forms the monoepoxide dieldrin (**3a**)[9] as shown in Scheme I. Structure **2a** was established for aldrin by a x-ray

Scheme I



crystallographic analysis,[10] and the exo configuration of the epoxide ring in **3a** was assigned on the basis of NMR studies.[11,12] By patterning on Scheme I, 2,3,4,5,5-pentachloro-1-azacyclopentadiene (**1**) was heated in excess norbornadiene at 90 °C for 24 h to yield an adduct (~80% yield after recrystallization) which analyzed correctly for $C_{11}H_8NCl_5$ as azaaldrin. Its IR spectrum (KBr) ν_{C-H} 3050, 2990, 2900, δ_{C-H} 1475, 720, $\nu_{C=C}$ 1615, and ν_{C-N} 1150 cm^{-1}, is almost superimposable on that of aldrin (**2a**). Of the four structural candidates for azaaldrin shown in Scheme II, viz., endo-exo (2β,3β,6β,7β,8α) **2**, exo-endo (2α,3β,6β,7α,8α) **2b**, endo-endo (2β,3α,6α,7β,8α) **2c**, and exo-exo (2α,3α,6α,7α,8α) **2d**, the Diels–Alder "endo" adduct **2** is favored by analogy to aldrin.[10] Also shown in Scheme II is the exo epoxidation of **2** to yield azadieldrin **3** in a *m*-chloroperbenzoic acid–methylene chloride mixture at 25 °C. The structural assignments of **2** and **3** are substantiated by NMR studies. In Table IA are tabulated the ^1H NMR spectra of aldrin (**2a**), azaaldrin (**2**), dieldrin (**3a**), and azadieldrin (**3**), and Table IB shows the ^{13}C NMR spectra of the same. The spectral assignments for aldrin and dieldrin are in accordance with literature.[11,12] Similarly, the assigned proton and carbon chemical shifts for the aza analogues are compatible with structures **2** and **3**.

Confirmation of the above NMR assignments was sought by analyzing the characteristic patterns due to the two C-12 methylene protons of **2** and **3** (syn and anti relative to the 4,5 double bond or epoxide). It was reported by several groups[11] that in aldrin (**2a**) H-12 anti can be decoupled from the vinyl protons to resolve one of the pairs of broadened doublets into a doublet of triplets which are attributed to the coupling of H-12 anti to H-3 and H-6. Also, the broadened doublet of H-12

Table I. NMR Spectra of Azaaldrin, Azadieldrin, and the Carbocycle Analogues

Hydrogen or carbon	δ ($CDCl_3$, Me_4Si = 0), J Hz			
	Aldrin (2a)	Azaaldrin (2)	Dieldrin (3a)	Azadieldrin (3)
	A. ^1H NMR Spectra			
2	2.68 s	2.88 d, 8	2.67 m	2.88 d, 7
3	2.87 s[a]	3.12 s[a]	2.70 s[a]	2.87 s[a]
4	6.30 m	6.28 m	3.12 s[a]	3.14 d, 3.5
5	6.30 m	6.28 m	3.12 s[a]	3.09 d, 3.5
6	2.87 s[a]	2.90 s[a]	2.70 s[a]	2.66 s[a]
7	2.68 s	2.68 d, 8	2.67 m	2.67 d, 7
12 syn	1.28 d, 11	1.27 d, 12	1.14 d, 13	1.23 d, 12
12 anti	1.63 d, 11	2.02 d, 12	0.97 d, 13	1.48 d, 12
	B. ^{13}C NMR Spectra			
2	54.50 d, 150	54.19 d, 150	53.56 d, 140	53.31 d, 150
3	40.82 d, 150	41.34 d, 145	36.98 d, 145	37.30 d, 145
4	141.04 d, 175	140.81 d, 175	51.09 d, 195	50.89 d, 200
5	141.04 d, 175	140.81 d, 175	51.09 d, 195	50.49 d, 200
6	40.82 d, 150	40.81 d, 145	36.98 d, 145	36.90 d, 145
7	54.50 d, 150	53.30 d, 150	53.56 d, 140	52.04 d, 150
12	40.69 t, 130	41.50 t, 140	20.41 t, 140	21.00 t, 140

[a] Broad singlet.

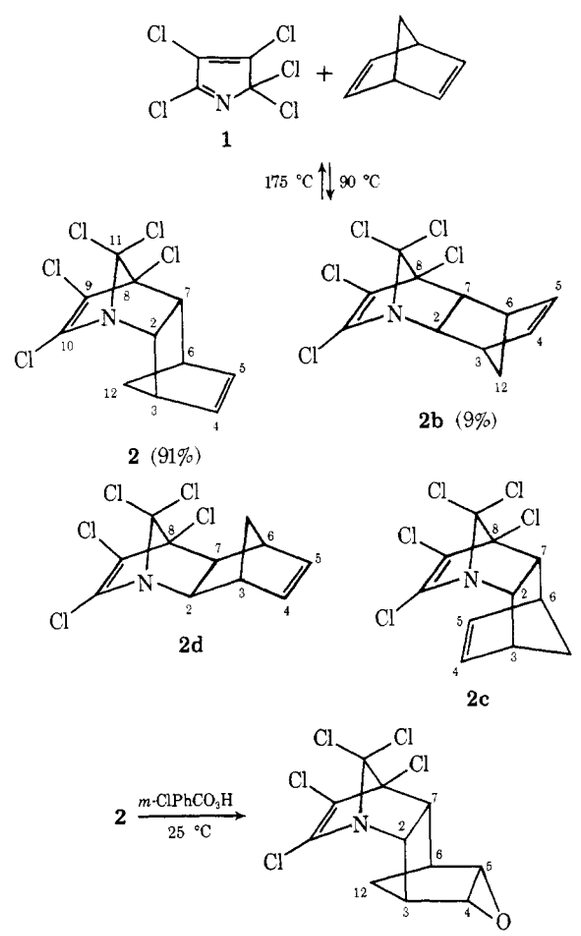
anti of dieldrin (**3a**) can be resolved by decoupling the long-range W-shape coupling between H-12 anti and H-4, H-5 of the epoxide ring.[11] The decoupled spectra clearly identify the H-12 anti doublet in each case. (See paragraph at end of paper regarding supplementary material.) The great resemblance of these decoupled partial spectra for **2** and **2a** as well as for **3** and **3a** gives support to the structural assignments of **2** and **3**. The apparent anomaly of H-12 anti of dieldrin (**3a**) appearing at higher field than H-12 syn, while the reverse is true in azadieldrin (**3**), is explained as follows. The upfield shift of the C-12 methylene hydrogens in **3a** compared to those in **2a**, Δδ anti 0.66 ppm and Δδ syn 0.14 ppm, can be attributed to steric compression of these hydrogens by the exo epoxide in **3a**.[11b] Similar upfield shifts in azadieldrin (**3**) are Δδ anti 0.55 ppm and Δδ syn 0.04 ppm. The apparent reversal of H-12 anti and H-12 syn in **3a** but not in **3** can be traced to the original separation of these two resonances in **2** of 0.75 ppm but only 0.35 ppm in **2a**.

Although treatment of azaaldrin (**2**) with the europium shift reagent did not produce any shift in the ^1H NMR spectrum, addition of $Eu(fod)_3$ to azadieldrin (**3**) did. A plot of the proton chemical shifts of **3** vs. equivalents of $Eu(fod)_3$ gave the following slopes: H-12 syn (29.4), H-4,5 (16.2), H-3 (15.2), H-6 (15.0), H-12 anti (12.7), H-2 (10.8) and H-7 (10.5). (See paragraph at end of paper regarding supplementary material.) These data are compatible with structure **3** with the europium atom attached to the oxygen lone pair anti to H-4,5 which is sterically most accessible.

Equilibration of Azaaldrin (2) with Isoazaaldrin (2b). For many cyclopentadiene–cyclic dienophile combinations, the endo adduct is the kinetically controlled product, and the exo isomer sometimes the thermodynamically more stable one.[13] We have scrutinized the crude reaction mixture from which azaaldrin was isolated by means of GLC analysis. The chromatogram revealed two peaks (t_R 17.4 and 18.5 min) in a 91:9 ratio. Azaaldrin (**2**), after recrystallization from acetone–water, showed only the shorter retention time peak. Preparatory high-pressure liquid chromatography allowed the collection of the minor product, which analyzed correctly for $C_{11}H_8NCl_5$. This adduct is therefore isoazaaldrin, an isomer of azaaldrin (**2**). The same analytical techniques, when applied to the Diels–Alder reaction mixture of aldrin, showed no other products but aldrin itself.

Among the three theoretically possible adducts other than **2** shown in Scheme II, the exo-exo adduct **2d** is sterically unlikely, while the endo-endo adduct **2c** is the aza analogue of isodrin. The latter is not formed in the aldrin synthesis and is known to cyclize to a caged compound upon irradiation.[14] When isoazaaldrin was irradiated under conditions sufficient to cause cyclization of isodrin in <10 min (high-pressure

Scheme II

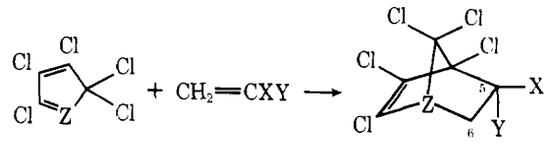


mercury lamp with Pyrex filter using acetone as medium), no reaction was observed even after 1 h. This leaves **2b** as the most plausible candidate for isoazaaldrin. The ^1H NMR spectrum, δ 1.38 (d, 2 H, J = 7 Hz, H-12), 2.71 (d, 1 H, J = 7 Hz, H-7), 2.85 (s, 1 H, H-6), 2.90 (d, 1 H, J = 7 Hz, H-2), 3.15 (s, 1 H, H-3), 6.38 (m, 2 H, H-4,5), is consistent with the assignment of **2b**. Particularly, the vinyl resonance is of diagnostic value. Comparing isodrin to aldrin, $\Delta\delta$ H-4,5 0.30 ppm upfield, the vinyl hydrogens in isodrin at δ 6.00[14] are shielded by the stacking dichlorovinyl moiety. However, the same comparison for isoazaaldrin and azaaldrin shows that H-4,5 in isoazaaldrin are deshielded by 0.1 ppm; hence the latter compound is incompatible with structure **2c**.

Azaaldrin (**2**) was found to be stable when heated at its melting point at 99 °C. However, pyrolysis of **2** in a sealed tube at 175 °C for 24 h led to 12% decomposition to nonvolatiles, and the remainder showed the same two peaks for **2** and **2b** on the gas chromatogram in the same 91:9 ratio as did the original reaction mixture. This indicates that an equilibrium was reached between the more stable endo-exo adduct **2** and its exo-endo isomer **2b**. This thermal conversion of **2** to **2b** is analogous to the isomerization of some strained endo Diels–Alder adducts to the exo isomers via a retrograde Diels–Alder reaction.[13] Thus, the dissociation of **2** to the azadiene **1** and norbornadiene was followed by forward Diels–Alder reaction to re-form **2** and **2b** in the same ratio. The remarkably low degree of polymerization when **2** was subjected to prolonged pyrolysis and the reversibility shown by the equilibration between **2** and **2b** indicate a normal diene character for the cyclic azadiene **1** in Diels–Alder reaction.

Synthesis of 5-Substituted 2,3,4,7,7-Pentachloro-1-azanorbornenes. Both regiospecificity and endo stereospecificity in the Diels–Alder reaction of 2,3,4,5,5-pentachloro-1-azacyclopentadiene (**1**) with unsymmetrical dienophiles are apparent from the reactions summarized in Scheme III. Thus, reactions of **1** with vinyl chloride, styrene, isobutylene, and α-methylstyrene led to the exclusive formation of the 5-substituted adducts, **4, 5, 6,** and **7**, respectively. Although the yields of these adducts are 9–62%, chromatographic analysis (gas–liquid phase and high-pressure liquid) of the reaction mixtures did not show other product peaks with reasonable retention times. Cycloaddition of **1** with ethylene itself to yield pentachloro-1-azanorbornene (**8**) was also carried out as a point of reference. The corresponding carbocyclic analogues **4a, 5a, 6a, 7a,** and **8a** as adducts of hexachlorocyclopentadiene are known,[15–18] and they were prepared for NMR comparisons. Comparison of the ^1H NMR spectra of the four 5-substituted norbornene pairs shows $\Delta\delta$ (N–CCl) range for H-5 exo −1.2 to −4.8 Hz, H-6 exo +7.2 to +10.2 Hz, and H-6 endo +11.4 to +12.6 Hz, and that the nitrogen atom induced shifts are consistently deshielding for the 6-methylene hydrogens but slightly shielding for the 5-methine hydrogen. (See paragraph at end of paper regarding supplementary material.) In order to ascertain that the 5 substituents are not contributing to these $\Delta\delta$ values, the proton spectra of the ethylene adducts **8** and **8a** are compared. The spectrum of the azanorbornene **8** showed a tightly coupled ABCD pattern, and was analyzed using the iterative computer program LAOCN3 executed on a DEC 1080 computer. (See paragraph at end of paper regarding supplementary material.) The average probable error of the parameter sets in this simulation is 0.061. The AA′BB′ spectrum of the carbocycle analogue **8a** was reported by Fay et al.[19] Thus, the $\Delta\delta$(N–CCl) values for **8** and **8a** are H-5 exo −0.96 Hz, H-5 endo, −2.76 Hz, H-6 exo +7.6 Hz, and H-6 endo +11.5 Hz, quite comparable to those of the 5-substituted pairs. It appears that the downfield shifts of the C-6 methylene protons may be attributable to the predominance of the inductive withdrawing effect of the bridgehead nitrogen, while the difference in induced shifts for H-6 exo and H-6 endo may be the result of changing anisotropies. It has been shown that the diamagnetic shielding by a nitrogen lone pair is the cause of chemical shift differences between certain axial and equatorial protons in a number of polycyclic amines.[20] Otherwise, bond rehybridizations due to shorter C–N bond compared to C–C bond[21] and electrostatic field effects of the lone pair are also perturbing factors in induced shifts. The small upfield shifts observed for the C-5 hydrogens may be due to a combination of these factors, although their relative contributions have not been sorted out. The consistent trend of these nitrogen-induced shifts therefore lends strong support to the structural assignments of the 5-substituted 1-azanorbornenes shown in Scheme III.

Scheme III



			Z = N	Z = CCl	
(i)	X = H; Y = Cl	110 °C, 53%	4	4a	(ref 15)
(ii)	X = H; Y = Ph	135 °C, 62%	5	5a	(ref 16)
(iii)	X = Y = Me	100 °C, 34%	6	6a	(ref 17)
(iv)	X = Me; Y = Ph	110 °C, 9%	7	7a	(ref 17)
(v)	X = Y = H	95 °C, 26%	8	8a	(ref 18)

A comparison of the methylene resonances of the isobutylene adduct **6** with those of the α-methylstyrene adduct **7** (cf. supplementary material) demonstrates the endo preference of the cycloadducts. While $\Delta\delta$ of H-6 exo is only 0.11 ppm, $\Delta\delta$ of H-6 endo is 1.18 ppm. The large downfield shift of H-6 endo of **7** is best accounted for by the endo benzene ring. Also, the methylene peaks of the exo-phenyl epimer of the carbocycle **7a** at δ 3.495 (H-6 exo) and 2.125 (H-6 endo) as reported by Mark[17] are drastically different from those of **7**, thereby confirming the endo phenyl configuration in **7**. Furthermore, the europium shift behavior of this 1-azanorbornene is worthy of note. While azaaldrin (**2**) was not shifted at all by several shift reagents, addition of 0.3 equiv of Eu(fod)$_3$ to **7** led to induced shifts of 7 and 5 Hz for H-6 endo and H-6 exo, respectively. The slopes of the linear curves relating induced shifts to equivalents of europium are 23 for the endo and 17 for the exo hydrogen. The greater change for the endo hydrogen seems to indicate that the steric bulk of Eu(fod)$_3$ and the norbornenyl bridgehead nitrogen require the shift reagent to approach **7** from the less hindered endo face of the molecule rather than along the axis of the nitrogen lone pair. Such behavior has been reported for other sterically hindered heteroatom–shift reagent complexes.[22] The small absolute magnitude of the induced shifts reflects weak complex formation due to the large steric requirement of both the shift reagent and the substrate.

Relative Reactivity of Pentachloro-1-azacyclopentadiene (1) and Hexachlorocyclopentadiene (1a). Alder[23] classified hexachlorocyclopentadiene (**1a**) as "the diene with the highest possible addition ability", implying an inverse electron demand on the dienophile. Mark[24] reported that reactions of **1a** with a number of electron-deficient trans-1,2-disubstituted ethylene derivatives gave appreciable amounts of the cis adducts via stepwise reactions, while

Table II. Rates of Diels–Alder Reaction of 1 and 1a at 90 °C[a]

Diene	Dienophile	k, s^{-1}	Rel rates
1a	Norbornadiene	1.04×10^{-4}	2.16
1	Norbornadiene	4.82×10^{-5}	1
1a	Styrene	4.36×10^{-4}	7.87
1	Styrene	5.54×10^{-5}	1

[a] Diene:dienophile 1:4; disappearance of dienes and formation of products were followed by GLC and peak areas plotted as ln A^0/A vs. time. The pseudo-first-order rate constants were determined by a least-squares curve fit program.

electron-rich trans-1,2-disubstituted dienophiles, such as *trans*-2-butene, added stereospecifically and concertedly. However, attempted reactions of **1** with a variety of trans-disubstituted dienophiles such as *trans*-β-methylstyrene, methyl crotonate, and *trans*-1,2-dichloroethylene gave no adducts, indicating the decreased reactivity of **1** relative to **1a**. No reaction was observed for **1** with either maleic anhydride or *N*-phenylmaleimide at temperatures to 175 °C. More electron-rich cis-disubstituted olefins such as norbornadiene or monosubstituted olefins as shown in Scheme III reacted with **1** to yield Diels–Alder adducts, albeit slower than the corresponding reactions with **1a**. Using norbornadiene and styrene as the dienophiles, these two diene systems are compared quantitatively as shown in Table II. Given the assumption that these reactions are frontier orbital controlled,[25] it can be inferred from the rate ratios of 2.16 and 7.87 (**1a**:**1**) that either the LUMO of **1** is of higher energy than the LUMO of **1a** or that the atomic coefficients in the LUMO of **1** are uniformly smaller than those in the LUMO of **1a**.

Experimental Section

^{1}H NMR spectra were obtained using a Varian A-60A spectrometer or a Perkin-Elmer R-12 spectrometer. The 100-MHz proton spectrum of **8** was obtained on a JEOL FX-100 spectrometer, courtesy of JEOL Analytical Instruments, Inc., Cranford, N.J. ^{13}C NMR spectra were determined on a Varian CFT-20 spectrometer, courtesy of University of Kentucky, Lexington, Ky. NMR samples were prepared as 0.5 M solutions in $CDCl_3$ containing 1% tetramethylsilane [δ (Me_4Si = 0)]. IR spectra were run on a Beckman IR-12. GLC analyses were performed on a Hewlett-Packard 5750 B chromatograph with dual flame ionization detector. All analyses were done on a 6 ft × 0.25 in. aluminum column packed with 20% SE-30 on Chromosorb W AW DMCS and at 30 ml/min of nitrogen, T_I = 270 °C, T_D = 240 °C, T_C = 170 °C (unless otherwise noted). High-pressure liquid chromatography was done on a Waters Associates instrument (M6000 pump, U6K injector) using a μ-porasil column, chloroform as solvent, and 254-nm UV detector. Melting points are uncorrected. Combustion analyses were performed by either Midwest Microlab, Ltd., Indianapolis, Ind., or M-H-W Laboratories, Garden City, Mich.

(2β,3β,6β,7β,8α)-8,9,10,11,11-Pentachloro-1-azatetracyclo-[6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene (Azaaldrin, 2). To 6.5 g (27 mmol) of pentachloro-1-azacyclopentadiene (**1**)[7] was added 9.1 g (108 mmol, 4 equiv) of bicyclo[2.2.1]hepta-2,5-diene, and the mixture was refluxed for 24 h. The dark brown reaction mixture containing the product, T_R 17.5 min, 91%, and an isomer, T_R 18.5 min, 9%, was evaporated, and the residue chromatographed on 100 g of silica gel in hexane. The eluent was evaporated, and the light orange residue was recrystallized from acetone–water to yield 6.83 g (76.3%) of white, crystalline product: mp 97–99 °C; NMR as shown in Table I.

Anal. Calcd for $C_{11}H_8NCl_5$: C, 39.81; H, 2.41; N, 4.22. Found: C, 39.99; H, 2.22; N, 4.06.

The isomer (isoazaaldrin, **2b**) was isolated from the reaction mixture by high-pressure liquid chromatography using two 18 × 0.25 in. preparative columns packed with 14 g each of Porasil A (35–75 μ) in series, eluted with chloroform at 6 mL/min. The eluent was evaporated and the residue crystallized from ethanol–water yielding a white, crystalline product: mp 105–107 °C; NMR described in text.

Anal. Calcd for $C_{11}H_8NCl_5$: C, 39.81; H, 2.41; N, 4.22. Found: C, 40.22; H, 2.37; N, 4.37.

(2β,3β,6β,7β,8α)-*exo*-4,5-Epoxy-8,9,10,11,11-pentachloro-1-azatetracyclo[6.2.1.1^{3,6}.0^{2,7}]dodec-9-ene (3). To 6 g (18 mmol) of (2β,3β,6β,7β,8α)-8,9,10,11,11-pentachloro-1-azatetracyclo[6.2.1.1^{3,6}.0^{2,7}]-dodeca-4,9-diene (azaaldrin, **2**) in 50 mL of methylene chloride was added 3.90 g (21 mmol, 1.25 equiv) of *m*-chloroperbenzoic acid. The homogeneous solution was allowed to stand for 5 days at 22–24 °C. The solution was extracted with 3 × 50 mL of 5% $NaHSO_3$, 6 × 50 mL of 5% $NaHCO_3$, and 2 × 50 mL of water. The methylene chloride layer was dried and evaporated, and the solid residue recrystallized from ethanol–water to yield 5.9 g (94.4%) of white, crystalline **3**: mp 158.5–160 °C; IR (KBr) 2990, 2960, 2900 (C–H stretch), 1475 (C–H bend), 1575 (Cl–C=C–Cl stretch), 1150 cm^{-1} (C–N stretch); NMR as shown in Table I.

Anal. Calcd for $C_{11}H_8NOCl_5$: C, 37.98; H, 2.30; N, 4.02. Found: C, 38.24; H, 2.21; N, 3.82.

2,3,4,5-*endo*,7,7-Hexachloro-1-azabicyclo[2.2 1]hept-2-ene (4). Pentachloro-1-azacyclopentadiene (1,[7] 1.17 g, 4.9 mmol) and vinyl chloride (0.62 g, 9.9 mmol) were dissolved in 5.6 mL of toluene and the solution was heated under nitrogen in a sealed tube at 110 °C for 96 h. The brown reaction mixture was decolorized and the toluene removed in vacuo. The yellow residue was recrystallized from ethanol–water to yield 0.78 g (53%) of white, crystalline **4**: mp 88–90 °C; NMR as shown in Table II.

Anal. Calcd for $C_6H_3NCl_6$: C, 23.84; H, 0.99; N, 4.64. Found: C, 23.80; H, 1.02; N, 4.56.

***endo*-5-Phenyl-2,3,4,7,7-pentachloro-1-azabicyclo[2.2.1]hept-2-ene (5).** A mixture of 4.92 g of pentachloro-1-azacyclopentadiene (1, 20.5 mmol) and 2.14 g (20.5 mmol) of styrene was heated at 135 °C for 24 h. The dark brown reaction mixture was molecularly distilled at 130 °C (2 mmHg) to afford 4.403 g (62%) of a clear, pale yellow liquid which solidified on standing overnight at −20 °C: mp 56–60 °C; NMR δ 2.68 (q, 1 H, J_{AB} = −14 Hz), 3.02 (q, 1 H, J_{BX} = 9.4 Hz), 3.90 (q, 1 H, J_{AX} = 4.6 Hz), 7.10–7.50 (m, 5 H).

Anal. Calcd for $C_{12}H_8NCl_5$: C, 41.96; H, 2.35; N, 4.08. Found: C, 41.78; H, 2.56; N, 3.95.

5,5-Dimethyl-2,3,4,7,7-pentachloro-1-azabicyclo[2.2.1]hept-2-ene (6). To an excess (~0.5 g, 9 mmol) of isobutylene condensed at −78 °C in an 8-mm i.d. heavy-walled glass tube was added 0.492 g (2.05 mmol) of pentachloro-1-azacyclopentadiene (**1**).[7] The tube was sealed under reduced pressure and heated at 100 °C for 72 h. The tube was opened and evaporated, and the liquid which remained was dissolved in 1 mL of a 19:1 isooctane–chloroform mixture and chromatographed on 50 g of silica gel in the above solvent system. The 50:50 isooctane–chloroform eluent containing the product was decolorized, filtered, and evaporated to provide 0.206 g (34%) of a white solid: mp 95–99 °C; NMR δ 1.12 (s, 3 H), 1.51 (s, 3 H), 2.17 (d, 1 H, J = −14.0 Hz), 2.68 (d, 1 H, J = −14.0 Hz).

Anal. Calcd for $C_8H_8NCl_5$: C, 32.53; H, 2.73; N, 4.74. Found: C, 32.71; H, 2.73; N, 4.67.

***exo*-5-Methyl-*endo*-5-phenyl-2,3,4,7,7-pentachloro-1-azabicyclo[2.2.1]hept-2-ene (7).** A solution of pentachloro-1-azacyclopentadiene (1, 2.46 g, 10.3 mmol) and α-methylstyrene (1.21 g, 10.3 mmol) in 20 mL of freshly distilled toluene was heated at reflux for 42 h. The solvent was evaporated, the residue dissolved in 1 mL of distilled hexane, and the solution chromatographed on 50 g of silica gel. The eluent containing the product was filtered and evaporated to provide 0.341 g (9.3%) of a white solid: mp 75–79 °C; NMR δ 1.96 (s, 3 H), 3.35 (d, 1 H, J = −14 Hz), 2.79 (d, 1 H, J = −14 Hz), and 7.20–7.60 (m, 5 H).

Anal. Calcd for $C_{13}H_{10}NCl_5$: C, 43.72; H, 2.82; N, 3.91. Found: C, 43.71; H, 2.91; N, 3.92.

2,3,4,7,7-Pentachloro-1-azabicyclo[2.2.1]hept-2-ene (8). To 12 mmol of freshly distilled 1,2-dimethoxyethane saturated with ethylene was added 2.13 g (89 mmol) of pentachloro-1-azacyclopentadiene (1).[7] The solution was sealed in a heavy-walled glass tube, and the mixture was heated at 95 °C for 70 h. The tube was opened and evaporated, and the brown residual liquid was chromatographed on 50 g of silica gel. Elution with chloroform–hexane (7:3) afforded a fraction containing the product. This was decolorized, filtered, and evaporated to provide a white solid (0.672 g, 26%). Sublimation of this material provided an analytical sample of the adduct: mp 66–71 °C; NMR as shown in Table II.

Anal. Calcd for $C_6H_4NCl_5$: C, 26.95; H, 1.51; N, 5.24. Found: C, 26.82; H, 1.96; N, 5.10.

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Registry No.—**1**, 57802-40-1; **2**, 61473-88-9; **2b**, 61473-89-0; **3**, 61473-90-3; **4**, 61394-83-0; **5**, 61394-84-1; **6**, 61394-85-2; **7**, 61394-86-3; **8**, 61394-87-4; bicyclo[2.2.1]hepta-2,5-diene, 121-46-0; *m*-chloroperbenzoic acid, 937-14-4; vinyl chloride, 75-01-4; styrene, 100-42-5; isobutylene, 115-11-7; α-methylstyrene, 98-83-9; ethylene, 74-85-1.

Supplementary Material Available. Normal and decoupled ^1H NMR spectra of **2**, **2a**, **3**, and **3a** in the C-12 methylene region, a plot of chemical shift of **3** protons vs. equivalents of $Eu(fod)_3$, the 100-Hz ^1H NMR of 8 and the simulated spectrum of 8, and ^1H NMR data for the compounds 4–8 and **4a**–**8a** (4 pages). Ordering information is given on any current masthead page.

References and Notes

(1) (a) Part 1: J. L. Wong and M. H. Ritchie, *J. Chem. Soc. D.*, 142 (1970). (b) Part 2: J. L. Wong, M. H. Ritchie, and C. M. Gladstone, *ibid.*, 1093 (1971).
(2) J. Hamer, Ed., "1,4-Cycloaddition Reactions", Academic Press, New York, N.Y., 1967.
(3) H. R. Snyder and J. C. Robinson, Jr., *J. Am. Chem. Soc.*, **63**, 3279 (1941), and previous papers in this series.
(4) S. B. Needleman and M. C. Chang Kuo, *Chem. Rev.*, **62**, 405 (1962).
(5) R. Pfleger and A. Jager, *Chem. Ber.*, **90**, 2460 (1957).
(6) M. Sakamoto, Y. Tomimatsu, T. Momose, C. Iwata, and M. Hanaoka, *Yakugaku Zasshi*, **92**, 1431 (1972).
(7) R. Anshutz and G. Schroeter, *Justus Liebigs Ann. Chem.*, **295**, 82 (1896).
(8) (a) H. E. Ungnade and E. T. McBee, *Chem. Rev.*, **58**, 249 (1958); (b) R. E. Lidov, U.S. Patent 2 635 977; *Chem. Abstr.*, **48**, 2769 (1954).
(9) R. E. Lidov and S. B. Soloway, U.S. Patent 2 676 131; *Chem. Abstr.*, **48**, 8473 (1954).
(10) T. P. DeLacy and C. H. L. Kennard, *J. Chem. Soc., Perkin Trans. 2*, 2153 (1972).
(11) (a) L. H. Keith, *Tetrahedron Lett.*, 3 (1971); (b) B. Franzus, W. C. Baird, Jr., N. F. Chamberlain, T. Hines, and E. I. Snyder, *J. Am. Chem. Soc.*, **90**, 3721 (1968); (c) A. P. Marchand and J. E. Rose, *ibid.*, **90**, 3721 (1968); (d) R. W. McCullock, A. R. Rye, and D. Wege, *Tetrahedron Lett.*, 5163 (1969).
(12) R. L. Roberts and G. L. Blackner, *J. Agric. Food Chem.*, **22**, 542 (1974).
(13) J. Sauer, *Angew. Chem., Int. Ed. Engl.*, **6**, 16 (1967).
(14) (a) R. E. Lidov and H. Bluestone, U. S. Patent 2 714 617; *Chem. Abstr.*, **50**, 5756 (1956); (b) J. A. Bukowski and A. Cisak, *Rocz. Chem.*, **42**, 1339 (1968).
(15) H. Bluestone, U.S. Patent 2 676 132; *Chem. Abstr.*, **48**, 8474 (1954).
(16) S. H. Herzfeld, R. E. Lidov, and H. Bluestone, U.S. Patent 2 606 910; *Chem. Abstr.*, **47**, 8775 (1953).
(17) V. Mark, *J. Org. Chem.*, **39**, 3181 (1974).
(18) L. Schmerling, U.S. Patent 2 881 223; *Chem. Abstr.*, **53**, 17013*c* (1959).
(19) C. K. Fay, J. B. Grutzner, L. F. Johnson, S. Sternhell, and P. W. Westerman, *J. Org. Chem.*, **38**, 3122 (1973).
(20) (a) I. D. Blackburne and A. R. Katritsky, *Acc. Chem. Res.*, **8**, 300 (1975), and pertinent references therein; (b) I. Morishima, K. Yoshikawa, and K. Okada, *J. Am. Chem. Soc.*, **98**, 3787 (1976).
(21) P. Bruesch, *Spectrochim. Acta*, **22**, 867 (1966).
(22) (a) S. Farid, A. Ateya, and M. Maggio, *J. Chem. Soc. D*, 1285 (1971); (b) J. Briggs, F. A. Hart, and G. P. Moss, *ibid.*, 1506 (1970).
(23) K. Alder, *Experientia, Suppl. II*, 86 (1955).
(24) V. Mark, *J. Org. Chem.*, **39**, 3179 (1974).
(25) K. N. Houk, *Acc. Chem. Res.*, **8**, 361 (1975).

Cyclophanes. 10.[1] Synthesis and Conformational Behavior of [2.2](2,5)Pyrrolophanes[2]

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Attempted synthesis of [2.2](2,5)pyrrolophanes by 1,6-Hofmann elimination proved unsuccessful and led only to dipyrrolmethanes. [2.2](2,5)Pyrroloparacyclophane (**11a**), [2.2](2,5)pyrrolo(1,4)naphthalenophane (**12a**), and [2.2](2,5)pyrrolo(2,5)furanophane (**13a**) were prepared by Paal–Knorr cyclization of 3,6-diketo[8]paracyclophane (**10a**), 3,6-diketo[8](1,4)naphthalenophane (**10b**), and 3,6-diketo[8](2,5)furanophane (**10c**), respectively, with ammonia. Preparation of the analogous *N*-methyl derivatives **11b**, **12b**, and **13b** by Paal–Knorr cyclization using methylamine was successful only for the synthesis of *N*-methyl[2.2](2,5)pyrroloparacyclophane (**11b**). *N*-Methyl-[2.2](2,5)pyrrolophane (**17a**) and *N*-benzyl[2.2](2,5)pyrrolophane (**17b**) were also synthesized by Paal–Knorr cyclization of 1,4,7,10-cyclododecatetraone by successive treatment with the appropriate alkylamine and ammonia. Reductive cleavage of the benzyl group in **17b** with sodium afforded the parent [2.2](2,5)pyrrolophane (**1**). The spectral properties and structural assignment of the above pyrrolophanes are discussed. Variable temperature NMR studies on the above pyrrolophanes indicated that all aromatic rings in the above phanes are conformationally rigid on the NMR time scale with the exception of the pyrrole ring in **11a**. In this pyrrolophane the barrier to pyrrole ring rotation is 17 kcal/mol.

In the past two and one-half decades a substantial literature has accumulated concerning the synthesis and properties of cyclophanes.[4] The syntheses of [2.2]cyclophanes containing heteroaromatic nuclei have been extensively recorded and among some of the common heteroaromatic groups which have been incorporated into the cyclophane macrocycle are furan,[5] thiophene,[5a,6] pyridine,[7] and pyridazine.[7a,8] However, conspicuously absent from these ranks are those containing the pyrrole moiety.[9] Indeed, except for the recent synthesis of *N,N'*-dimethyl[2.2](2,5)pyrrolophane (**2**)[10] the literature is devoid of reports concerning [2.2]pyrrolophanes. Of special interest is the parent phane, [2.2](2,5)pyrrolophane (**1**). On the basis of relative properties, general chemical behavior, and stability,[11] pyrrole, like the analogous furan and thiophene ring systems, ought to exist as a stable aromatic entity within a [2.2]cyclophane macrocycle. Additionally, in view of the contemporary interest in rotational behavior of aromatic moieties within [2.2]cyclophanes,[12] the dynamic behavior of [2.2](2,5)pyrrolophanes, as compared with [2.2](2,5)furanophanes, [2.2](2,5)thiophenophanes, [2.2](2,6)pyridinophanes, and other [2.2]metaphanes, would prove of interest in defining the relative stéric bulk and intramolecular interactions of an N–H and N^- grouping as compared with O:, S:, N:, and C–H groupings during the rotational process in which these groups pass through the cavity of the cyclophane macrocycle. In view of the above we undertook the synthesis of a number of pyrrolophanes.

Hofmann Pyrolytic Route. Previous successful use of a 1,6-Hofmann elimination reaction on the appropriate quaternary ammonium hydroxide for the synthesis of **3**[5a] and **4**[5a] (see Scheme I) prompted us to attempt the synthesis of **2** by this method. A procedure quite analogous to that traditionally