Synthesis and Diastereofacial Selectivity in Diels–Alder Reactions of Halogenated 2-Aza 1,3-Dienes

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The synthesis of mono- and trihalogenated derivatives of 2-aza 1,3-dienes 2 and 3 is described. The first example of diastereofacial selectivity in Diels–Alder reactions of heterodienes of type 2 with electron-poor dienophiles is reported, and a model for the explanation of the observed epimeric ratios, based on the interactions between diene and dienophile, is proposed.

Introduction

In recent years, there has been an increasing interest in the diastereofacial selectivity of Diels–Alder reactions.[1-3] However, only all-carbon dienes have been previously been employed, and as far as we are aware, no examples of diastereofacial selectivity in Diels–Alder reactions of heterodienes have been reported.

For several years our group has been intensively studying the chemistry of neutral 2-aza 1,3-dienes 1 (Schemes I and II), showing their ability to participate in Diels–Alder reactions.[4]

In the course of these studies, we thought that a simple procedure for the functionalization of compounds 1 could be by halogenation. This method would allow the creation of a chiral center in the molecule, enabling us to study the diastereofacial selectivity in the Diels–Alder reactions of these 2-aza diene derivatives. In addition, this functionalization reaction may be a useful extension of the synthetic utility of the neutral 2-aza 1,3-dienes 1 (Scheme I). Whereas the the halogenation of imino compounds has been extensively reviewed by De Kimpe,[5] very little is known about the halogenation of 2-aza 1,3-dienes. Very recently, the use of α-chloro imines in the synthesis of unactivated 2-aza 1,3-dienes and 3-aza 1,3,5-trienes has been reported.[6]

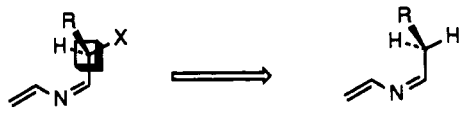
From a theoretical point of view, three different approaches to rationalizing the diastereofacial selectivity of Diels–Alder reactions have been described. These methods are usually based on electrostatic interactions of the reactants,[7] frontier molecular orbital theory,[2b,8] and direct calculations on the transition state of the cycloaddition reaction.[3] The attempts to rationalize the observed results do not have a broad validity, and no theoretical studies have been developed in the case of hetero-1,3-dienes.

We have recently described our preliminary results in the study of the synthesis and behavior of monohalogenated 2-aza 1,3-dienes 2 (Scheme I) in Diels–Alder reactions[9] and in heterocyclization reactions.[4] In this paper, we report our experimental results on the synthesis and diastereofacial selectivity in Diels–Alder reactions of halogenated 2-aza 1,3-dienes 2 and 3 with several dienophiles.

Results and Discussion

The preparation of monohalogenated 2-aza 1,3-dienes 2 was carried out by halogenation of 2-aza 1,3-dienes 1 with 1 equiv of *N*-halosuccinimide (NXS = Cl, Br, I) in toluene or carbon tetrachloride, overnight at room temperature (Scheme II, Table I).[9]

Scheme I



Scheme II

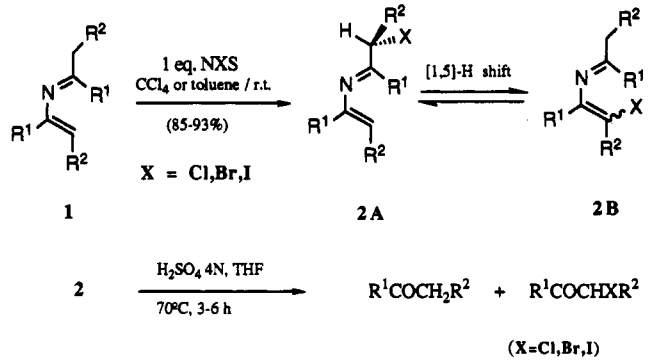


Table I. Halogenated 2-Aza 1,3-Dienes 2

2[a]	R^1	R^2	X	yield, %
a	Ph	Me	Cl	95
b	Ph	Et	Cl	97
c	Ph	Pr	Cl	90
d	*p*-MeC_6H_4	Me	Cl	95
e	Ph	Me	Br	90
f	Ph	Me	I	90

[a] All compounds 2 are isolated as yellow oils.

† X-ray analysis.

(1) (a) Tripathy, R.; Franck, R. W.; Onan, K. D. *J. Am. Chem. Soc.* **1988**, *110*, 3257. (b) Fisher, M. J.; Hehre, W. J.; Kahn, S. D.; Overman, L. E. *J. Am. Chem. Soc.* **1988**, *110*, 4625. (c) Tripathy, R.; Carroll, P. J.; Thornton, E. R. *J. Am. Chem. Soc.* **1990**, *112*, 6743.

(2) (a) Fleming, I.; Sarkar, A. K.; Doyle, M. J.; Raithby, P. R. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2023. (b) Kozikowski, A. P.; Jung, S. H.; Springer, J. P. *J. Chem. Soc., Chem. Commun.* **1988**, 167.

(3) (a) Kaila, N.; Franck, R. W.; Dannenberg, J. J. *J. Org. Chem.* **1989**, *54*, 4206. (b) Burnouf, C.; López, J. C.; Calvo-Flores, F. G.; Laborde, M.; Olesker, A.; Lukacs, G. *J. Chem. Soc., Chem. Commun.* **1990**, 823.

(4) Barluenga, J.; Joglar, J.; González, F. J.; Fustero, S. *Synlett* **1990**, 129 and references cited therein.

(5) See: De Kimpe, N.; Schamp, N. *Org. Prep. Proced. Int.* **1983**, *15*(1-2), 71 and references cited therein. De Kimpe, N.; Verhé, R. *The Chemistry of α-Haloketones, α-Haloaldehydes and α-Haloimines*; Patai, S., Ed.; Wiley: New York, 1988.

(6) De Kimpe, N.; Yao, Z.-P.; Boeyken, M.; Nagy, M. *Tetrahedron Lett.* **1990**, *31*, 2771.

(7) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 663.

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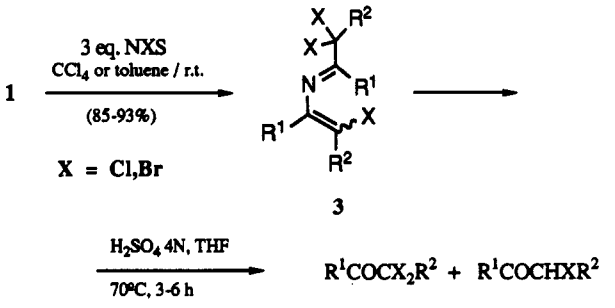
Table II. Trihalogenated 2-Aza 1,3-Dienes 3

3[a]	R^1	R^2	X	yield, %
a	Ph	Me	Cl	80
b	Ph	Me	Br	75
c	Ph	Et	Cl	80
d	p-MeC_6H_4	Me	Cl	80
e	Ph	Pr	Cl	70
f	p-MeC_6H_4	Me	Br	80
g	Ph	Et	Br	70
h	Ph	Pr	Br	70

[a] All compounds 3 are isolated as yellow oils.

Scheme III



As can be seen in Table I, the reaction is general with regard to the halogen and the substituent R^2, although in all cases R^1 is an aryl group. When this substituent R^1 was aliphatic, complex mixtures, probably containing polyhalogenation products, were obtained. These 2-aza diene derivatives 2 were isolated as mixtures of two tautomeric forms, 2A and 2B, as seen from NMR spectra (Scheme II).

Thus, in the case of compound 2a (R^1 = Ph, R^2 = Me, X = Cl), the ^1H NMR spectrum shows major signals at δ 0.8 (t, 3 H), 2.2 (s, 3 H), and 2.6 (q, 2 H) corresponding to CH_3CH_2, $CH_3(Cl)C{=}C$, and CH_2CH_3. This spectrum is in accord with the tautomeric form 2aB. In addition, other signals of low intensity (<10%), corresponding to the tautomer 2aA, can be seen.

In the case of halogeno derivatives 2 (X = Br, I), the ^1H NMR spectra are very complex due to the presence of *Z,E* stereoisomers.[5] For this reason, the structure of the halogeno derivatives 2 was also confirmed by chemical methods. Thus, acid hydrolysis of compounds 2 led in all cases to a 1:1 mixture of the corresponding ketones (Scheme II).

The transformation of 2A into 2B can be explained by a 1,5-sigmatropic hydrogen shift (Scheme II); the 2A:2B ratio strongly depends on the halogen atom. Thus, while the tautomer 2B is predominant (90%) when X = Cl, both tautomers are present in approximately a 1:1 ratio in the case where X = I.

In addition, we studied the polyhalogenation reactions of 2-aza 1,3-dienes 1. Thus, treatment of 1 with 3 equiv of NXS (X = Cl, Br) in CCl_4 at room temperature for 12 h gave rise to the trihalogenated derivatives 3 (Scheme III, Table II). In all cases, the reaction of 1 with NIS failed, probably due to the steric bulk of iodine. On the other hand, when we tried to prepare the dihalogenated derivatives of 2-aza 1,3-dienes 1 using 2 equiv of NXS, mixtures of trihalogenated 2-aza 1,3-dienes 3 and starting material were produced. The dihalogenated derivative was not detected in any case.

The structures of trihalogenated derivatives 3 were determined on the basis of spectroscopic data and were secured chemically. For example, compound 3b (R^1 = Ph, R^2 = Me, X = Br) shows only two methyl singlets, at δ 2.2 (3 H) and 2.9 (3 H). Acid hydrolysis of compounds 3 led to a 1:1 mixture of the α,α'-dihalogenated ketones and α-monohalogenated ketones (Scheme III).

Table III. 3-(1-Chloroethyl)-1,2,3,6-tetrahydro-1,2,4-triazines 4

4	R^1	R^2	R^3	X	epimer ratio[a]	yield, %
a	Ph	Me	Et	Cl	93:7	75
b	Ph	Me	^{i}Pr	Cl	94:6	80
c	Ph	Et	^{i}Pr	Cl	97:3	80

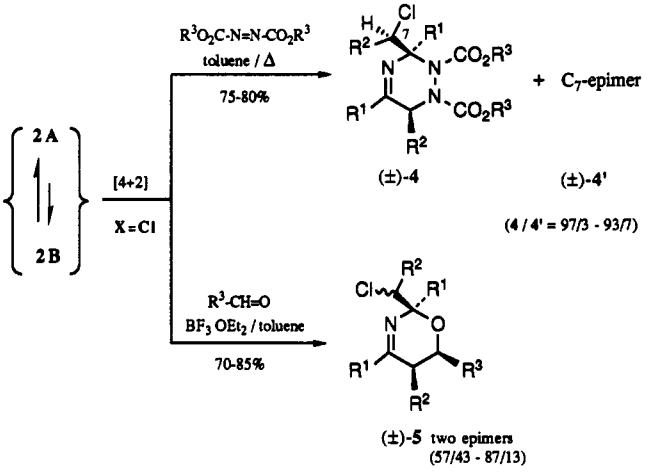
[a] Determined by ^1H NMR (300 MHz).

Table IV. 2-(1-Chloroalkyl)-5,6-dihydro-2*H*-1,3-oxazines 5

5	R^1	R^2	R^3	epimer ratio[a]	yield, %
a	Ph	Me	Ph	87:13	75
b	Ph	Et	Ph	86:14	80
c	Ph	Me	Ph(Me)CH	82:18	70
d	p-MeC_6H_4	Me	Ph	57:43	85
e	Ph	Me	p-$NO_2C_6H_4$	69:31	75

[a] Determined by ^1H NMR (300 MHz).

Scheme IV



According to our previous studies on Diels–Alder reactions of 2-aza 1,3-dienes,[4] we considered that the halogenated 2-aza 1,3-dienes could undergo [4 + 2] cycloaddition reactions and that the presence of a stereogenic center attached to the diene system would make compounds 2 suitable for the study of the diasterofacial selectivity. The participation of compounds 2 in Diels–Alder reactions was tested by using different types of dienophiles,[10] e.g., dialkyl azodicarboxylates and aldehydes (Scheme IV, Tables III and IV). Thus, the reaction of 2 (X = Cl) in toluene with dialkyl azodicarboxylates (12–24 h, 80 °C) or aldehydes (20–24 h, 25 °C, 0.15 equiv of BF_3OEt_2) afforded the corresponding Diels–Alder adducts (±)-4(4'), and (±)-5, in yields above 70% (Scheme IV, Tables III and IV). In all cases, the reaction was found to occur through the more reactive trisubstituted tautomer 2A, as expected.

We found that cycloadducts 4 and 5 were formed as a mixture of epimers in different ratios, the cycloaddition reaction showing in most cases good diastereofacial selectivity. The epimeric ratios for the reactions of 2 with

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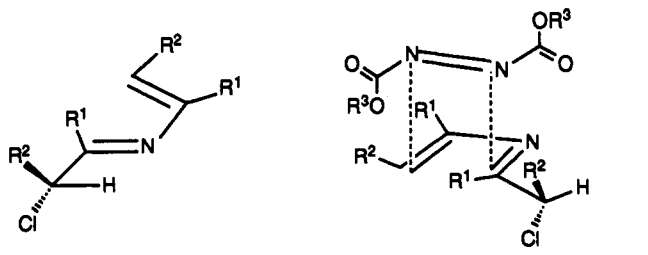
(9) Barluenga, J.; González, F. J.; Fustero, S. *Tetrahedron Lett.* **1990**, *31*, 397.
(10) When tetracyanoethylene (TCNE) was used as dienophile, a very different result was found. The reaction between 2 and TCNE did not lead to the expected Diels–Alder adduct, as in our previous studies with 2-aza 1,3-dienes, but other compounds, identified as 4,6-diazasemibullvalene derivatives, were isolated: Barluenga, J.; González, F. J.; Fustero, S.; Solans, X.; Domenech, M. V. *J. Chem. Soc., Chem. Commun.* **1990**, 1057. Reference 4.



syncoplanar conformation *Like* Approach Diene-Dienophile

Figure 1.

dialkyl azodicarboxylates and aldehydes are collected in Tables III and IV.

As shown in Table III, the best diastereofacial selectivity was observed for dialkyl azodicarboxylates with an epimeric ratio of adducts 4:4' ranging from 93:7 to 97:3. The structural assigment of adducts 4 (Scheme IV) was made on the basis of their spectral and analytical data and of our results obtained previously in the cycloaddition of 1 with the same dienophiles.[11] However, it was necessary to perform an X-ray diffraction analysis in order to establish the configuration at the exocyclic carbon bearing the chlorine atom (Scheme IV). The result of this study (see Experimental Section), performed on the major epimer of compound **4a** (R^1 = Ph, R^2 = Me, R^3 = Et), reveals that the cycloaddition of 2-aza 1,3-diene **2a** with diethyl azodicarboxylate takes place through the face bearing the R^2 group (Figure 1).

In order to explain these experimental results, a theoretical study of the reaction of halogenated derivatives **2** (X = Cl) with dialkyl azodicarboxylates using the AM1 method is being developed.[12] Preliminary calculations indicate that the syn-coplanar conformation between the hydrogen attached to the carbon atom supporting the chlorine and the C=N double bond, in compounds **2**, is the more stable by 1.6 kcal (Figure 1). In this situation, the approach of the dialkyl azodicarboxylate to **2** takes place preferentially through the face opposite the chlorine in order to avoid the electronic repulsions between the carboxylate group of the dienophile and the chlorine atom. Thus, the major cycloadduct obtained could arise from a *like* transition state,[13] as shown in Figure 1.

In the case of the reaction of **2** with aldehydes (Scheme IV and Table IV), the presence of catalytic amounts of $BF_3{\cdot}OEt_2$ was necessary. In the absence of this catalyst, the yield of **5** was very low. The molar ratio of aldehyde:$BF_3{\cdot}OEt_2$ was found to have an optimum value of 7:1; when other ratios were used, the ratio of Diels–Alder adducts **5** was lowered. The influence of temperature was also studied, and the best results were obtained at room temperature. On the other hand, when we tried Lewis acids other than $BF_3{\cdot}OEt_2$ (e.g., $MgBr_2OEt_2$, $ZnCl_2$, or $TiCl_4$) in order to improve the diastereofacial selectivity, the reaction failed in all cases. Additionally, we found that the use of other boron compounds like BCl_3 did not lead to higher selectivity.

The origin of the diastereofacial selectivity in the reaction of **2** with aldehydes can be understood by assuming that the reaction proceeds primarily through a *like* transition state in the same way as the reaction of **2** and dialkyl azodicarboxylates. The interaction between the chlorine atom in diene **2** and the BF_3 moiety coordinated to oxygen in the aldehyde causes the preferential approach of the dienophile to **2** through the face opposite the chlorine. In this case, minor repulsions between BF_3 and chlorine could explain the presence of the epimer coming from an *unlike* transition state in larger amounts than in the reaction of **2** with dialkyl azodicarboxylates.

On the other hand, when 2-phenylpropanal was used as dienophile (see Table IV), only the Cram adduct was obtained, in close agreement with previous results.[14]

A theoretical study[12] with the AM1 method does not allow one to correlate the conformation of **2** with the energy of the HOMO of the diene system, as in the case described by Fleming et al.;[2a] thus, the model proposed by Fleming cannot be used in the understanding of the origin of the diastereofacial selectivity in the Diels–Alder reactions of **2**.

On the other hand, the trihalogenated 2-aza 1,3-dienes **3** do not undergo the Diels–Alder reactions, probably due to the steric hindrance and deactivating effect of the halogen atoms.

Experimental Section

Melting points are uncorrected. 2-Aza 1,3-dienes **1** were prepared according to the previously described method.[14] Tetrahydrofuran (THF), toluene, and carbon tetrachloride were dried, distilled, and stored under argon prior to use.[15] Hexane was distilled prior to use. The *N*-iodosuccinimide was prepared according to a literature method.[16] All other reagents were commercially available and were used as received. All reactions were run under argon.

General Preparative Procedure for Halogenated 2-Aza 1,3-Dienes 2 and 3 from 1. A solution of the 2-aza 1,3-diene **1** (10 mmol) and 1 equiv of *N*-halosuccinimide, in dry toluene or carbon tetrachloride, was stirred overnight at room temperature and filtered. The solvent was removed at reduced pressure, and the resulting residue was dissolved in hexane, stirred for 20 min, and filtered. After the solvent was removed, the residue was purified by flash chromatography (Florisil, 100–200 mesh, hexane as eluent) to give **2** as a yellow oil (yield higher than 90%, based on **1**). The trihalogenated 2-aza 1,3-dienes **3** were prepared by using the same procedure, but 3 equiv of NCS or NBS was used in the halogenation reaction. The compounds **3** were isolated as yellow oils (70–80% yield based on **1**) after flash chromatography (Florisil, 100–200 mesh, hexane as eluent). Reaction yields are listed in Tables I and II.

6-Chloro-3,5-diphenyl-4-aza-3,5-heptadiene (2a): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 0.8 (t, 3 H, J = 6.9 Hz), 2.2 (s, 3 H), 2.6 (q, 2 H, J = 6.9 Hz), 6.8–7.9 (m, 10 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 172.45, 143.82, 138.09, 131.09–124.73, 110.73, 24.18, 21.64, 10.18; MS m/z 283 (M^+). Anal. Calcd for $C_{18}H_{18}NCl$: C, 76.19; H, 6.35; N, 4.94. Found: C, 76.05; H, 6.37; N, 4.82.

7-Chloro-4,6-diphenyl-5-aza-4,6-nonadiene (2b): ^{1}H NMR ($CDCl_3$, 80 MHz) δ_H 0.8 (t, 3 *H*, J = 7.0 Hz), 1.2 (m, 2 H), 1.25 (t, 3 H, J = 7.0 Hz), 2.6 (m, 4 H), 7.0–7.9 (m, 10 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 172.16, 144.64, 138.88, 131.2–125.44, 118.4, 32.64, 26.88, 19.2, 12.8, 11.52; MS, m/z 311 (M^+). Anal. Calcd for $C_{20}H_{22}NCl$: C, 77.04; H, 7.06; N, 4.49, Found: C, 76.85; H, 7.17; N, 4.42.

8-Chloro-5,7-diphenyl-6-aza-5,7-undecadiene (2c): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 0.7 (t, 3 H, J = 7.0 Hz), 0.9 (t, 3 H, J = 7.0 Hz), 1.2 (m, 4 H), 1.5–1.8 (m, 2 H), 2.4 (m, 2 H), 2.6 (m, 2 H), 6.8–7.9 (m, 10 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 169.13, 143.73, 137.72, 137.50, 129.53–127.06, 115.57, 35.89, 31.02, 28.15, 22.47, 21.28, 13.17, 12.75; MS, m/z 339 (M^+). Anal. Calcd for $C_{22}H_{26}NCl$:

(11) See, for example: Barluenga, J.; Gonzalez, F. J.; Fustero, S.; Foces-Foces, M. C.; Hernández Cano, F.; San Feliciano, A. *J. Chem. Res. Synop.* **1989**, 66 and references cited therein.

(12) Sordo, T. L.; Sordo, J. A., work in progress.

(13) The terms *like* and *unlike* describe the topicity of the approach of the diene and dienophile, according the Seebach–Prelog convention: Seebach, D.; Prelog, V. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 654.

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(15) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. In *Purification of Laboratory Chemicals*, 2nd ed.; Pergamon: New York, 1980.

(16) Benson; McBee; and Rand, *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, p 663.

C, 77.76; H, 7.66; N, 4.12. Found: C, 77.75; H, 7.57; N, 4.22.

6-Chloro-3,5-bis(4-methylphenyl)-4-aza-3,5-heptadiene (2d): ^{1}H NMR ($CDCl_3$, 80 MNz) δ_H 0.9 (t, 3 H, J = 7.0 Hz), 2.3 (s, 3 H), 2.40 (s, 3 H), 2.45 (s, 3 H), 2.8 (q, 2 H, J = 7.1 Hz), 7.1–8.0 (m, 8 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 171.52, 144.0, 142.08, 137.60, 135.04, 133.12, 130.56–124.16, 110.08, 23.04, 21.12, 19.84, 9.6; MS, m/z 311 (M^+). Anal. Calcd for $C_{20}H_{22}NCl$: C, 77.04; H, 7.06; N, 4.49. Found: C, 76.95; H, 7.17; N, 4.54.

6-Bromo-3,5-diphenyl-4-aza-3,5-heptadiene (2e): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 0.9 (t, 3 H, J = 6.9 Hz), 1.2–1.4 (m), 1.6 (d, 3 H, J = 6.9 Hz), 1.9–2.1 (m), 2.4 (m, 2 H), 2.6 (m, 2 H), 4.9 (m, 1 H), 5.1 (m, 1 H), 5.5 (q, 1 H, J = 6.8 Hz), 6.8–8.0 (m, 10 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 170.57, 146.95, 138.01, 137.59, 129.78–124.42, 103.57, 103.02, 49.31, 23.33, 12.59, 11.11; MS, m/z 328 (M^+). Anal. Calcd for $C_{18}H_{18}NBr$: C, 65.85; H, 5.49; N, 4.27. Found: C, 66.01; H, 5.45; N, 4.24.

6-Iodo-3,5-diphenyl-4-aza-3,5-heptadiene (2f): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 0.8 (t, 3 H, J = 7.0 Hz), 1.3 (d, 3 H, J = 6.9 Hz), 1.5–1.7 (m, 2 H), 2.1 (m, 2 H), 2.2 (d, 3 H, J = 6.9 Hz), 2.4 (s, 3 H), 2.58 (m, 2 H), 2.6 (s, 3 H), 5.0 (m, 1 H), 5.1 (m, 1 H), 5.4 (m, 1 H), 6.8–8.0 (m, 10 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 170.61, 146.01, 138.46, 136.07, 132.50, 130.01–124.4, 103.62, 103.14, 28.70, 27.25, 24.74, 24.44, 12.68, 10.68, 7.98; MS, m/z 375 (M^+). Anal. Calcd for $C_{18}H_{18}NI$: C, 57.60; H, 4.80; N, 3.73. Found: C, 57.51; H, 4.85; N, 3.74.

2,2,6-Trichloro-3,5-diphenyl-4-aza-3,5-heptadiene (3a): ^{1}H NMR ($CDCl_3$, 80 MHz) δ_H 2.0 (s, 3 H), 2.6 (s, 3 H), 6.8–7.5 (m, 10 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 170.88, 142.72, 137.6, 135.04, 133.76, 129.92–125.44, 114.56, 83.84, 34.56, 21.12; MS, m/z 351 (M^+). Anal. Calcd for $C_{18}H_{16}NCl_3$: C, 61.27; H, 4.54; N, 3.97. Found: C, 61.41; H, 4.45; N, 3.84.

2,2,4-Tribromo-3,5-diphenyl-4-aza-3,5-heptadiene (3b): ^{1}H NMR ($CDCl_3$, 80 MHz) δ_H 2.2 (s, 3 H), 2.9 (s, 3 H), 6.7–7.8 (m, 10 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 169.97, 143.57, 136.62, 134.84, 131.12–125.10, 108.02, 63.46, 38.64, 24.31; MS, m/z 486 (M^+). Anal. Calcd for $C_{18}H_{16}NBr_3$: C, 44.44; H, 3.29; N, 2.88. Found: C, 44.41; H, 3.40; N, 2.84.

3,3,7-Trichloro-4,6-diphenyl-5-aza-4,6-nonadiene (3c): ^{1}H NMR ($CDCl_3$, 80 MHz) δ_H 0.9 (t, 3 H, J = 7.1 Hz), 1.2 (t, 3 H, J = 7.1 Hz), 2.1 (q, 2 H, J = 7.1 Hz), 2.7 (q, 2 H, J = 7.1 Hz), 6.8–7.6 (m, 10 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 172.80, 143.64, 139.52, 137.61, 131.84–127.36, 123.52, 94.08, 40.32, 29.44, 14.08, 10.88; MS, m/z 379 (M^+). Anal. Calcd for $C_{20}H_{20}NCl_3$: C, 63.07; H, 5.25; N, 3.68. Found: C, 62.91; H, 5.30; N, 3.64.

2,2,6-Trichloro-3,5-bis(4-methylphenyl)-4-aza-3,5-heptadiene (3d): ^{1}H NMR ($CDCl_3$, 80 MHz) δ_H 1.9 (s, 3 H), 2.2 (s, 3 H), 2.3 (s, 3 H), 2.5 (s, 3 H), 6.8–7.3 (m, 8 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 169.10, 141.86, 138.55, 137.26, 133.77, 131.24, 128.41–127.64, 113.24, 87.21, 35.11, 21.82, 21.12, 20.97; MS, m/z 379 (M^+). Anal. Calcd for $C_{20}H_{20}NCl_3$: C, 63.07; H, 5.25; N, 3.68. Found: C, 63.11; H, 5.20; N, 3.59.

4,4,8-Trichloro-5,7-diphenyl-6-aza-5,7-undecadiene (3e): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 0.7 (t, 3 H, J = 6.9 Hz), 1.0 (t, 3 H, J = 6.9 Hz), 1.4 (m, 2 H), 1.7 (m, 2 H), 2.1 (t, 2 H, J = 7.0 Hz), 2.6 (t, 2 H, J = 6.9 Hz), 6.6–7.4 (m, 10 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 169.05, 142.36, 136.62, 134.58, 128.77–126.97, 119.54, 91.32, 47.15, 35.72, 21.11, 18.88, 13.55, 12.87; MS, m/z 407 (M^+). Anal. Calcd for $C_{22}H_{24}NCl_3$: C, 64.63; H, 5.87; N, 3.43. Found: C, 64.61; H, 5.80; N, 3.34.

2,2,6-Trichloro-3,5-bis(4-methylphenyl)-4-aza-3,5-heptadiene (3f): ^{1}H NMR ($CDCl_3$, 80 MHz) δ_H 2.2 (s, 3 H), 2.3 (s, 3 H), 2.35 (s, 3 H), 2.9 (s, 3 H), 6.6–7.4 (m, 8 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 174.08, 147.84, 142.08, 140.08, 137.60, 135.68, 133.12, 109.44, 65.92, 40.32, 25.6, 22.4; MS, m/z 514 (M^+). Anal. Calcd for $C_{20}H_{20}NBr_3$: C, 46.69; H, 3.89; N, 2.72. Found: C, 46.61; H, 3.80; N, 2.82.

3,3,7-Tribromo-4,6-diphenyl-5-aza-4,6-nonadiene (3g): ^{1}H NMR ($CDCl_3$, 80 MHz) δ_H 0.8 (t, 3 H, J = 7.1 Hz), 1.3 (t, 3 H, J = 7.1 Hz), 2.4 (q, 2 H, J = 7.1 Hz), 2.9 (q, 2 H, J = 7.1 Hz), 6.5–8.0 (m, 10 H): ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 169.81, 143.54, 136.83, 135.37, 130.94, 128.88–125.16, 116.46, 73.26, 40.93, 29.62, 14.08, 12.73; MS, m/z 514 NM^+). Anal. Calcd for $C_{20}H_{20}NBr_3$: C, 46.69; H, 3.89; N, 2.72. Found: C, 46.58; H, 3.78; N, 2.73.

4,4,8-Tribromo-5,7-diphenyl-6-aza-5,7-undecadiene (3h): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 0.6 (t, 3 H, J = 7.0 Hz), 1.0 (t, 3 H J = 7.0 Hz), 1.3 (m, 4 H), 1.8 (m, 2 H), 3.8 (m, 2 H), 6.5–7.4 (m, 10 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 169.58, 144.52, 137.28, 135.89, 133.34, 131.34, 129.10–125.50, 114.59, 96.39, 49.89, 37.92, 22.59, 21.97, 13.93, 13.30; MS, m/z 542 (M^+). Anal. Calcd for $C_{22}H_{24}NBr_3$: C, 48.71; H, 4.43; N, 2.58. Found: C, 48.61; H, 4.38; N, 2.52.

General Preparative Procedure for 3-(1-Chloroethyl)-1,2,3,6-tetrahydro-1,2,4-triazines 4 from 2. To a toluene solution (5 mL) of halogenated 2-aza 1,3-diene 2 (X = Cl) (2 mmol) was added the dialkyl azodicarboxylate (2.1 mmol). The reaction mixture was stirred at 80 °C for 12–24 h. The solvents were removed (0.1 mmHg), and the resulting oil was triturated with methanol, giving 4 + 4′ as a white solid. The solid was recrystallized from hot hexane–chloroform (5:2) to give colorless crystals of 4. Reaction yields and epimer ratios are given in Table III.

3-(1-Chloroethyl)-1,2-bis(ethoxycarbonyl)-3,5-diphenyl-1,2,3,6-tetrahydro-6-methyl-1,2,4-triazine (4a): mp 155–7 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 0.73 (t, 3 H, J = 6.9 Hz), 1.2 (t, 3 H, J = 6.9 Hz), 1.5 (d, 3 H, J = 7.1 Hz), 1.55 (d, 3 H, J = 7.1 Hz), 3.26 (m, 1 H), 3.7 (m, 1 H), 4.2 (m, 2 H), 5.47 (q, 1 H, J = 7.0 Hz), 6.14 (q, 1 H, J = 7.1 Hz), 7.2–7.8 (m, 10 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 167.0, 154.43, 139.65, 135.33, 131.03, 128.75–127.41, 61.83; 61.65, 49.55, 20.13, 16.56, 14.45, 13.79; MS, m/z 457 (M^+). Anal. Calcd for $C_{24}H_{28}N_3O_4Cl$: C, 63.02; H, 6.13; N, 9.19. Found: C, 63.18; H, 6.05; N, 9.23.

4′a:[17] ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 0.71 (t, 3 H, J = 6.9 Hz), 1.04 (t, 3 H, J = 6.9 Hz), 1.40 (d, 3 H, J = 7.0 Hz), 1.46 (d, 3 H, J = 7.0 Hz), 3.11 (m, 1 H), 5.55 (q, 1 H, J = 7.0 Hz), 6.10 (q, 1 H, J = 7.1 Hz), 7.2–8.0 (m, 10 H).

3-(1-Chloroethyl)-3,5-diphenyl-1,2-bis(isopropoxycarbonyl)-1,2,3,6-tetrahydro-6-methyl-1,2,4-triazine (4b): mp 170–3 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 0.4 (d, 3 H, J = 7.0 Hz), 1.02 (d, 3 H, J = 7.0 Hz), 1.25 (d, 3 H J = 5.2 Hz), 1.27 (d, 3 H, J = 5.2 Hz), 1.5 (d, 6 H, J = 7.0 Hz), 4.5 (m, 1 H), 5.0 (m, 1 H), 5.5 (q, 1 H, J = 7.0 Hz), 6.15 (q, 1 H, J = 7.0 Hz), 7.2–7.9 (m, 10 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 166.90, 154.01, 153.77, 140.12, 135.38, 130.98, 128.73–127.41 (m), 82.96, 69.91, 69.51, 62.03, 49.20, 21.97, 21.70, 20.72, 20.14, 16.49; MS, m/z 485 (M^+). Anal. Calcd for $C_{28}H_{32}N_3O_4Cl$: C, 64.50; H, 6.50; N, 8.60. Found: C, 64.33; H, 6.60; N, 8.66.

4′b:[17] ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 1.01 (d, 3 H, J = 7.0 Hz), 1.45 (d, 6 H, J = 7.0 Hz), 4.4 (m, 1 H), 5.58 (q, 1 H, J = 7.0 Hz), 6.08 (q, 1 H, J = 7.0 Hz), 7.2–8.0 (m, 10 H).

3-(1-Chloropropyl)-6-ethyl-3,5-diphenyl-1,2-bis(isopropoxycarbonyl)-1,2,3,6-tetrahydro-1,2,4-triazine (4c): mp 143–5 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 0.4 (d, 3 H, J = 6.1 Hz), 1.0 (d, 6 H, J = 6.5 Hz), 1.2 (t, 3 H, J = 7.1 Hz), 1.3 (dd, 6 H, J = 6.3 and 6.5 Hz), 1.7 (m, 2 H), 2.0 (m, 2 H), 4.5 (m, 1 H), 5.0 (m, 1 H), 5.3 (dd, 1 H, J = 1.8 and 11.4 Hz), 5.9 (dd, 1 H J = 1.8 and 11.4 Hz), 7.2–7.9 (m, 10 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 165.88, 154.32, 153.65, 140.22, 135.34, 130.54, 128.22–126.84, 82.45, 69.46, 69.06, 55.40, 26.07, 23.76, 21.71, 21.61, 21.26, 20.29, 11.79, 11.18; MS, m/z 513 (M^+). Anal. Calcd for $C_{28}H_{36}N_3O_4Cl$: C, 65.49; H, 7.02; N, 8.19. Found: C, 65.76; H, 6.95; N, 8.02.

General Preparative Procedure for 2-(1-Chloroalkyl)-5,6-dihydro-2*H*-1,3-oxazines 5 from 2. A toluene solution (15 mL) of the aldehyde (9.0 mmol) and $BF_3{\cdot}OEt_2$ (1.27 mmol) was stirred at room temperature for 20 min. Then, the halogenated 2-aza 1,3-diene 2 (X = Cl) (9.0 mmol) was added, and the reaction mixture was stirred at room temperature for 20–24 h. Then the solvents were removed (0.1 mmHg), and the resulting residue was triturated with methanol, giving 5 as a white solid. The solid was recrystallized from hot hexane–chloroform (6:1) to give colorless crystals of the epimer mixture. Reaction yields and epimer ratios are given in Table IV.

2-(1-Chloroethyl)-2,4,6-triphenyl-5,6-dihydro-5-methyl-2*H*-1,3-oxazine (5a): major epimer ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 0.97 (d, 3 H, J = 7.2 Hz), 1.57 (d, 3 H, J = 6.7 Hz), 3.06 (dq, 1 H, J = 3.0 and 6.7 Hz), 4.51 (q, 1 H, J = 6.7 Hz), 4.75 (d, 1 H, J = 3.0 Hz), 7.2–8.0 (m, 15 H); minor epimer[17] ^{1}H NMR ($CDCl_3$, 300 MHz δ_H 0.79 (d, 3 H, J = 7.2 Hz) 1.47 (d, 3 H, J = 6.7 Hz), 4.57 (q, 1 H, J = 6.8 Hz), 4.87 (d, 1 H, J = 3.0 Hz); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 169.6, 167.68, 147.72, 141.44, 140.16, 137.6, 130.56–126.08, 99.84, 70.4, 64.64, 33.28, 19.2, 10.88; MS, m/z 326

(17) Characteristic signals taken from the crude mixture. Other signals are missing because of overlapping.

(M^+ – 63). Anal. Calcd for $C_{25}H_{24}NOCl$: C, 77.12; H, 6.17; N, 3.6. Found: C, 77.06; H, 6.21; N, 3.45.

2-(1-Chloropropyl)-5-ethyl-2,4,6-triphenyl-5,6-dihydro-2*H*-1,3-oxazine (5b): major epimer ^1H NMR ($CDCl_3$, 80 MHz) δ_H 0.4 (t, 3 H, J = 7.1 Hz), 1.0 (t, 3 H, J = 7.0 Hz), 1.7 (m, 4 H), 2.8 (m, 1 H), 4.2 (dd, 2 H, J = 8.0 Hz), 4.8 (d, 1 H, J = 3.0 Hz), 7.1–8.0 (m, 15 H); minor epimer[17] ^1H NMR ($CDCl_3$, 300 MHz δ_H 4.9 (d, 1 H, J = 3.0 Hz); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 168.96, 143.36, 140.8, 138.88, 131.2–125.44, 94.08, 71.68, 70.4, 40.32, 24.32, 19.84, 12.8, 10.24; MS, m/z 417 (M^+). Anal. Calcd for $C_{27}H_{28}N_8OCl$: C, 77.70; H, 6.71; N, 3.36. Found: C, 77.58; H, 6.8; N, 3.4.

2-(1-Chloroethyl)-2,4-diphenyl-6-(1-phenylethyl)-5,6-dihydro-5-methyl-2*H*-1,3-oxazine (5c): major epimer ^1H NMR ($CDCl_3$, 300 MHz) δ_H 1.1 (d, 3 H, J = 7.0 Hz), 1.26 (d, 3 H, J = 6.7 Hz), 1.40 (d, 3 H, J = 6.7 Hz), 2.37 (dq, 1 H, J = 2.5 and 7.0 Hz), 2.95 (m, 1 H), 3.53 (dd, 1 H, J = 2.5 and 10.5 Hz), 4.39 (q, 1 H, J = 6.7 Hz), 6.8–7.9 (m, 15 H); minor epimer[17] ^1H NMR ($CDCl_3$, 300 MHz) δ_H 1.03 (d, 3 H, J = 7.0 Hz), 3.72 (d, 1 H, J = 2.5 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ_C 168.72, 143.28, 142.35, 137.06, 130.16–126.46, 94.11, 74.30, 65.01, 41.39, 31.17, 20.90, 20.54, 11.87; MS, m/z 354 (M^+ – 63). Anal. Calcd for $C_{27}H_{28}NOCl$: C, 77.70; H, 6.71; N, 3.36. Found: C, 77.48; H, 6.8; N, 3.44.

2-(1-Chloroethyl)-6-phenyl-5,6-dihydro-5-methyl-2,4-bis(4-methylphenyl)-2*H*-1,3-oxazine (5d): major epimer ^1H NMR ($CDCl_3$, 300 MHz) δ_H 0.95 (d, 3 H, J = 7.0 Hz), 1.56 (d, 3 H, J = 6.7 Hz), 2.3 (s, 3 H), 2.4 (s, 3 H), 3.02 (m, 1 H), 4.49 (q, 1 H, J = 6.7 Hz), 4.74 (d, 1 H, J = 2.5 Hz), 7.0–7.9 (m, 13 H); minor epimer[17] ^1H NMR ($CDCl_3$, 300 MHz) δ_H 2.38 (s, 3 H), 4.52 (q, 1 H, J = 6.7 Hz), 4.85 (d, 1 H, J = 2.5 Hz); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 172.16, 170.24, 144.8–144.0, 137.6, 133.12–128.0, 96.0, 73.6, 72.96, 67.2, 65.56, 35.84, 35.20, 22.4, 21.76, 21.12, 19.84, 13.44, 12.80; MS, m/z 354 (M^+ – 63). Anal. Calcd for $C_{27}H_{28}NOCl$: C, 77.70; H, 6.71; N, 3.36. Found: C, 77.53; H, 6.81; N, 3.40.

2-(1-Chloroethyl)-2,4-diphenyl-5,6-dihydro-5-methyl-6-(4-nitrophenyl)-2*H*-1,3-oxazine (5e): major epimer ^1H NMR ($CDCl_3$, 300 MHz) δ_H 0.97 (d, 3 H, J = 6.8 Hz), 1.57 (d, 3 H, J = 6.7 Hz), 3.12 (m, 1 H), 4.55 (q, 1 H, J = 6.7 Hz), 4.82 (d, 1 H, J = 2.5 Hz), 7.2–8.3 (m, 14 H); minor epimer[17] ^1H NMR ($CDCl_3$, 300 MHz) δ_H 4.95 (d, 1 H, J = 2.5 Hz); ^{13}C NMR ($CDCl_3$, 20 MHz) δ_C 169.6, 167.68, 148.48, 147.84, 147.2, 142.72, 141.44, 137.6, 131.2–126.08, 124.16, 94.08, 70.4, 69.76, 64.64, 33.28, 32.64, 19.2, 18.56, 11.52; MS, m/z 371 (M^+ – 63). Anal. Calcd for $C_{25}H_{23}N_2O_3Cl$: C, 69.12; H, 5.30; N, 6.45. Found: C, 69.01; H, 5.20; N, 6.42.

Crystal Data for 4a. A colorless triclinic crystal (0.40 × 0.36 × 0.33 mm) from chloroform saturated with hexane had space group symmetry of $P\bar{1}$ and cell constants of a = 8.9372 (1) Å, b = 10.1995 (1) Å, c = 13.2285 (1) Å, α = 87.515 (1)°, β = 82.716 (1)°, γ = 83.383 (1)°, V = 1187.13 (5) Å^3, Z = 2, and ρ(calcd) = 1.28 Mg m^{-3}; λ = 0.71073 Å; μ(Mo Kα) = 1.91 cm^{-1}; T = 293 K; 7200 reflections measured on an Enraf-Nonius CAD4 instrument (ω–2θ scan technique), range $0 < \theta < 30$ and $-12 < h < 12$, $-14 < k < 14$, $0 < l < 18$, 6920 unique reflections (R_{int} = 0.018, averaging some double measured) and 4000 observed ($I > 3\sigma(I)$). Semiempirical and empirical absorption corrections were applied. The structure was solved by direct methods, using the program SHELX86, and we anisotropically refined (SHELX76) all non-hydrogen atoms, except for C25, which was found in two disordered positions, namely C25 and C25′, with refined occupation factors of 0.575 (7) and 0.425 (7), respectively, to R = 0.062 and R_w = 0.071 (299 parameters). Maximum shift/error = 0.60 ρ_{max} = 0.41 e/Å^3.

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Supplementary Material Available: List of fractional positional and thermal parameters, bond lengths and angles, anisotropic temperature factors, fractional positional parameters of the hydrogen atoms, bond lengths and angles involving hydrogen atoms, angles between least-squares planes, and principal torsion angles for **4a** (15 pages); observed and calculated structure factors for **4a** (29 pages). Ordering information is given on any current masthead page.

Aryl Azide–Allene Cycloaddition. The Contrasting Behavior of Two Simple Allenes, 1,2-Cyclononadiene and 1,2-Propadiene

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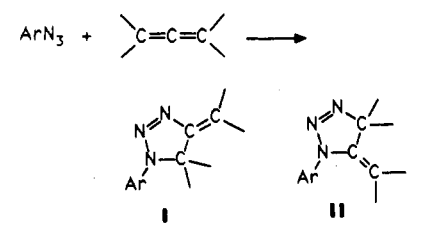
1,2-Cyclononadiene (**1**) reacts with phenyl azide (**2a**) and 4-bromophenyl azide (**2b**) to give conjugated triazoline adducts **3a** and **3b**, respectively. (*R*)-(+)-**1** and **2a** react to give (*S*)-(+)-**3a**, which is consistent with a concerted cycloaddition mechanism. The reaction of 1,2-propadiene (**6**) and **2a** gives triazoles **8** and **10** plus compound **18** in nearly equal amounts. The formation of these products is rationalized by a scheme involving initial formation of triazolines **7** and **9**. Triazoline **3a** is slowly isomerized by sodium ethoxide or *N*,*N*-dimethylaniline to triazole **20**.

The mechanism of the addition of aryl azides to simple alkenes has been extensively studied.[1] The relative insensitivity of the reaction to changes in solvent polarity, the stereospecificity of the addition, the large negative entropy of this kinetically second-order process, and the enhancement of the reaction rate by electron-withdrawing substituents on the aryl azide are consistent with a concerted formation of the 1,2,3-Δ^2-triazoline adduct by way of an unsymmetrical transition state in which the nitrogen

Scheme I



α to the aromatic ring is negative relative to the alkene carbon to which it is bonding. This concerted process is

(1) Huisgen, R. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; p 1. Lwowski, W. Ibid. p 559.

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