Diels-Alder Reaction of 2-Cyano-1-aza Dienes. The Effect of Nitrogen Substituents

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The Diels-Alder reactions of 2-cyano-1-aza dienes with three nitrogen substituents possessing different electronic requirements (phenyl, $CO_2C_2H_5$, and OCH_3) were studied with three dienophiles with different electronic requirements (styrene, methyl acrylate, and ethyl vinyl ether). The *N*-phenyl substituent aza diene was equally reactive with all three dienophiles. The *N*-$CO_2C_2H_5$-substituted aza diene behaved as an electrophilic diene being more reactive with the electron-rich ethyl vinyl ether than styrene or methyl acrylate. The *N*-$CO_2C_2H_5$-substituted aza diene is more reactive with all three dienophiles, including methyl acrylate, than the *N*-phenyl substituent azadiene. The *N*-OCH_3-substituted aza diene was unreactive with all three dienophiles under the conditions investigated.

Introduction

Although the Diels-Alder reaction was first recognized as a general transformation over 60 years ago,[1] it still remains an active area of research in both mechanistic[2] and synthetic chemistry.[3] Few reactions can compete with the Diels-Alder reaction with respect to the degree of organic synthesis accomplished in one step. This reaction produces a six-membered ring, two new carbon-carbon single bonds, and potentially, four new stereocenters. The Diels-Alder reaction has been, arguably, called the most powerful construction process in organic synthesis.[3,4]

Six-membered rings containing nitrogen are common structural features in a number of goal compounds of interest to synthetic chemists. In principle, six-membered nitrogen heterocycles are accessible using 1-aza dienes as reactants in the Diels-Alder reaction. However, early attempts to develop the Diels-Alder reaction of 1-aza dienes as a useful synthetic method were not successful.[5] Although isolated reports of 1-aza diene Diels-Alder reactions appeared in the early literature,[5] activation of the aza diene was clearly necessary if the Diels-Alder reaction of 1-aza dienes was to be developed into a general synthetic method for the preparation of nitrogen heterocycles. A few years ago we demonstrated that an acyl function on the nitrogen atom of the aza diene was sufficient for Diels-Alder activation[6] and successfully applied this reaction to an efficient synthesis of (-)-deoxynupharidine.[7] The synthetic utility of this approach has recently been enhanced by the availability of new methods for the preparation of the requisite *N*-acyl-1-aza dienes.[8] Because of the potential importance of the Diels-Alder reaction for the preparation of six-membered nitrogen heterocycles, other methods for activating 1-aza dienes have been developed. Among these methods, the use of *N*,*N*-dialkylamino[9] and *N*-sulfonyl[10] substituents are particularly notable.

We have recently observed that a 2-cyano substituent is capable of activating 1-aza dienes with respect to the Diels-Alder reaction.[11,12] These observations led us to consider the role both the 2-cyano and nitrogen substituent are playing in the activation of 1-aza dienes with respect to the Diels-Alder reaction. Because of the potential synthetic utility of the 2-cyano substituent,[13] it is particularly attractive as an activating group for the Diels-Alder reaction of 1-aza dienes. For this reason we have performed studies on the reactivity and regiochemistry of 2-cyano-1-aza dienes as a function of an *N*-phenyl, electron-withdrawing (*N*-CO_2CH_3) and electron-donating substituents (OCH_3).

Results

For our comparative studies we chose to employ 1-aza dienes with a 4-phenyl substituent. An attractive synthetic method for the preparation of the required aza dienes

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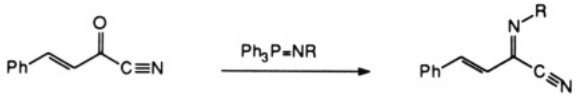
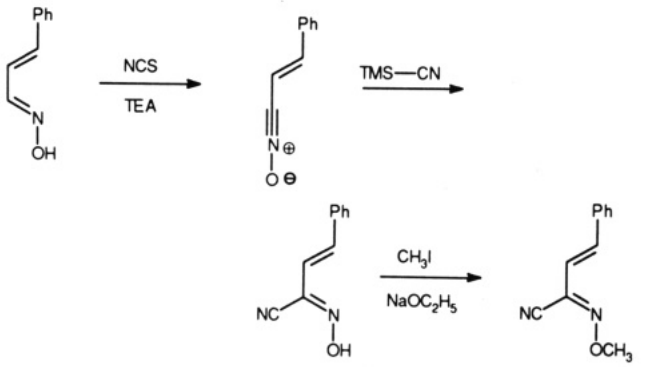
Scheme I. Preparation of *N*-Phenyl- and *N*-(Ethoxycarbonyl)-1-aza Dienes Using the Aza-Wittig Reaction



1 R = Ph (90%)
2 R = $CO_2C_2H_5$ (25%)

Scheme II. Preparation of *N*-Methoxy-1-aza Dienes



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proved to be the Staudinger or aza-Wittig reaction[14] of *N*-acyl cyanides.[15] This method was very successful for the preparation of the *N*-phenyl aza diene **1**, a compound that we had difficulty preparing using a previously reported method. However, application of the Staudinger reaction to the synthesis of aza diene **2** using *N*-(ethoxycarbonyl)-triphenylphosphinimine gave a somewhat lower yield of the desired aza diene, undoubtedly reflecting the differences in nucleophilicity of the nitrogen atom in these two reagents. The carbonyl group, by electron delocalization, stabilizes the nitrogen lone pair and suppresses its nucleophilicity.

A different strategy was employed for the synthesis of the 2-cyano-1-aza dienes possessing electron-donating groups, **3** (OCH_3). The preparation of **3** was accomplished by generation of the required nitroxide in the presence of a slight excess of trimethylsilyl cyanide followed by selective oxygen alkylation with methyl iodide in the presence of sodium ethoxide.

The aza dienes **2** and **3** were further characterized using single-crystal X-ray diffractometry.[16] The molecular structures of these compounds are shown below. One interesting feature of these structures concerns the nitrogen atom of the imine. In compound **2**, the carbonyl group is oriented (88°) from the plane of the imine for an excellent interaction with the lone pair of electrons on nitrogen whereas the methoxyl substituent is oriented 2.8° from the plane of the imine for excellent conjugation of the oxygen lone pair with the aza diene π-system.

The above syntheses provided 2-cyano aza dienes with an electron-withdrawing ($CO_2C_2H_5$), an electron-donating

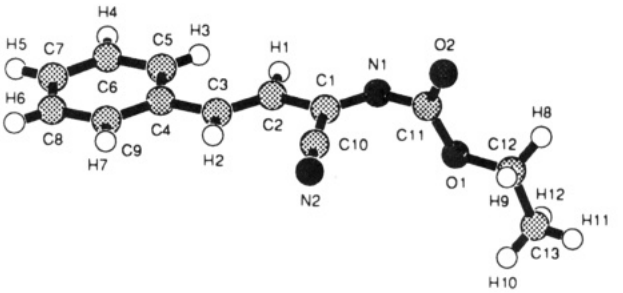

Figure 1. X-ray structure of compound **2**.

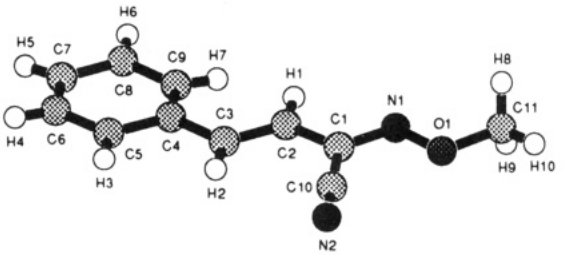

Figure 2. X-ray structure of compound **3**.

(OCH_3), and a phenyl substituent on the nitrogen atom. The Diels–Alder reactions of these aza dienes, with analogous dienophiles possessing an electron withdrawing (CO_2CH_3), an electron-donating (OC_2H_5), and a phenyl substituent, were investigated. The results of these studies are shown in Table I.

The regiochemistry of the Diels–Alder adducts was apparent from their NMR spectra. For example, in the ^{13}C-NMR spectrum of the Diels–Alder adducts, the chemical shift of the α and β carbon atoms are influenced by the substituent (Ph, CO_2CH_3, and OC_2H_5). The ratios of α to β regioisomers was determined by proton integration of the vinylic hydrogens. The stereochemistry of the Diels–Alder adducts could be determined from the coupling constant of the vinyl hydrogen. If the phenyl substituent at C-4 is axial then the coupling of the equatorial hydrogen to the vinyl hydrogen is relatively large (ca. 5 Hz). If the phenyl substituent at C-4 is equatorial then the coupling of the axial hydrogen to the vinyl hydrogen is relatively small (ca. 2.5 Hz).

The Diels–Alder adduct of styrene and ethyl vinyl ether with aza diene **1** gave products that demonstrated different conformational structures with respect to the ring substituents. The coupling constants of the vinyl hydrogen (2.7 Hz) and the proton α to the nitrogen atom (11 and 4.1 Hz) of the styrene Diels–Alder adduct clearly demonstrate that phenyl substituents on the ring carbons were in pseudoequatorial positions (see Figure 3), whereas the coupling constants of the vinyl hydrogen (4.2 Hz) and the proton α to the nitrogen atom (2.8 Hz) are consistent with both the 4-phenyl and ethoxyl substituent being axial. These observations are consistent with anomeric stabilization of the ethyl vinyl ether Diels–Alder adduct.

Discussion

Reactivity. All Diels–Alder reactions of 1-aza dienes suffer from a common problem. The stronger carbon–nitrogen π-bond, which is broken during the Diels–Alder reaction, causes the Diels–Alder reaction of 1-aza dienes to be *less* thermodynamically favorable than the all-carbon

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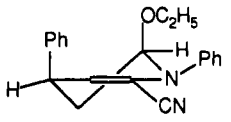
(16) The author has deposited atomic coordinates for these structures with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Campridge, CB2 1EZ, UK.

Table I. Diels–Alder Reactions of Aza Dienes 1, 2, and 3 with Styrene, Methyl Acrylate, and Ethyl Vinyl Ether

R_1	R_2	regio- and stereochemistry	yield (%)	reaction conditions
C_6H_5	C_6H_5	α cis only	50	110 °C, 8 days
C_6H_5	OC_2H_5	α cis:trans = 5:1	40	120 °C, 7 days
C_6H_5	CO_2CH_3	β cis:trans = 6:1	83	110 °C, 7 days
$C(=O)OCH_2CH_3$	C_6H_5	$\alpha:\beta$ = 2:1 α cis βcis:trans = 10:1	92	90 °C, 24 h
$C(=O)OCH_2CH_3$	OC_2H_5	α cis:trans = 14:1	92	25 °C, 27 h
$C(=O)OCH_2CH_3$	CO_2CH_3	β cis:trans = 10:1	91	81 °C, 25 h
OCH_3	C_6H_5		dienophile polymerization	110 °C, 24 h
OCH_3	OC_2H_5		NR	120 °C, 14 days
OCH_3	CO_2CH_3		dienophile polymerization	110 °C, 24 h



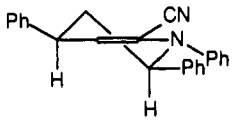


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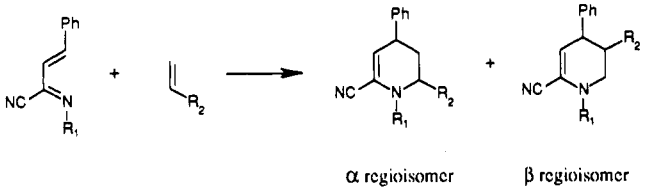
Figure 3. Predominant conformations of the endo Diels–Alder adducts of 1 with ethyl vinyl ether and styrene.

Scheme III. Diels–Alder Reaction 2-Cyano-1-aza Dienes



analog.[17] This thermodynamic factor should also play a role in the transition state causing 1-aza dienes to be less reactive than their all carbon analogs and probably plays an important role for the reported lack of Diels–Alder reactivity of simple aza dienes.

The presence of the electronegative nitrogen atom causes 1-aza dienes to be more electron deficient than their all carbon analogs in the Diels–Alder reaction. The placement of an electron-withdrawing cyano substituent further increases their electron-deficient character. However, the electron-deficient aza diene 1 is slightly *more* reactive with the electron-deficient methyl acrylate than either the electron-rich dienophile ethyl vinyl ether or styrene.[18] In spite of its electron-deficient character, aza diene 1 cannot be considered an "inverse electron demand" Diels–Alder diene. The addition of a cyano substituent to a 1-aza diene appears to accelerate its Diels–Alder reactions with all dienophiles.

It would be anticipated that the aza diene with the electron-withdrawing *N*-ethoxycarbonyl substituent (aza diene 2) would have more character of an inverse electron demand Diels–Alder reaction. Table I demonstrates that this is the case. Aza diene 2 is more reactive with ethyl vinyl ether than either styrene or methyl acrylate. What is unusual about aza diene 2 is that, qualitatively, it is equally reactive with both styrene and methyl acrylate. Also, the more electron-deficient diene 2 is *more* reactive with the electron-deficient dienophile, methyl acrylate, than aza diene 1. The greater reactivity of aza diene 2 with methyl acrylate, as well as all dienes studied, is probably reflecting a diminished activation energy due to the stabilization of the transition state by the developing amide functionality.

Given the behavior of the 2-cyano aza dienes 1 and 2, with an *N*-phenyl and the electron-withdrawing *N*-ethoxycarbonyl substituent, the Diels–Alder reactivity of the 2-cyano aza diene 3 with the electron-donating methoxyl substitution is of interest. Diels–Alder reactions of aza dienes with electron-donating substituents on the nitrogen are known.[9] Although less reactive, there are examples of the Diels–Alder reactions of conjugated oxime derivatives.[19] If aza diene 1 is displaying type II Diels–Alder reactivity, then an electron-donating group on nitrogen along with the electron-withdrawing cyano substituent could enhance this behavior. However, Table I demonstrates that *aza diene 3 was unreactive with styrene, methyl acrylate, and ethyl vinyl ether under the reaction conditions that were successful for aza dienes 1 and 2.*

We attribute this observation as due to a significant ground-state stabilization of the 2-cyano oxime.[20] Because this stabilizing electronic interaction is destroyed during the Diels–Alder reaction, it has the effect of increasing the activation energy.

(17) The π-bond strengths of ethylene and methylene imine have been calculated to be 59.4 and 74.3 kcal/mol, respectively (Shaw, R. In *The Chemistry of Double Bonded Functional Groups*; Patai, S., Ed.; Wiley: New York, 1977; p 131).

(18) Subjecting aza diene 1 to the three dienophiles at the same temperature (120 °C) until partial conversion to the Diels–Alder adduct was achieved allowed for an estimation of the half-lives of these three reaction (shown parenthetically in hours): Methyl acrylate (52), styrene (140), and ethyl vinyl ether (160).

(19) (a) Kusurkar, R. S.; Bhosale, D. K. *Tetrahedron Lett.* **1991**, *32*, 3199. (b) Boger, D. L.; Zhu, Y. *Tetrahedron Lett.* **1991**, *32*, 7643. (c) Wade, P. A.; Amin, N. B.; Yen, H.-K.; Price, D. T.; Huhn, G. F. *J. Am. Chem. Soc.* **1984**, *49*, 4595.

(20) The presence of electronic stabilization indicated in Figure 4 is supported by the X-ray determined molecular structure (Figure 2) which showed the N–O bond to be within 2.8° of the plane defining the oxime functionality. This structure allows for maximum electronic delocalization shown in Figure 4. Similar stabilization is probably also responsible for the enhanced acidity of cyano oximes compared to the unsubstituted derivatives. (a) Rutkovskii, G. V.; Bequuov, A. V.; Kuznetsov, S. G. *J. Org. Chem. USSR* **1983**, *19*, 696. (b) Przybylski, J.; Jeschkeit, H.; Kupryszewski, G. *Rocz. Chem.* **1977**, *51*, 939.

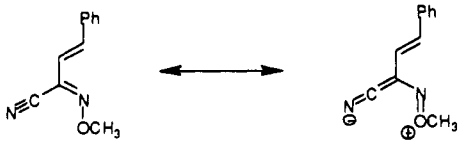


Figure 4. Ground-state electronic stabilization of 1-aza diene 3.

Thus, it is concluded from the lack of reactivity of 3 that any stabilization of the Diels–Alder transition state due to the *N*-methoxyl substituent is more than compensated by the ground state stabilization shown above in Figure 4.

Regiochemistry. The origin of the regiochemical patterns observed in various Diels–Alder reactions remains an active area of discussion in the literature.[21] Common structural features present in both aza dienes 1 and 2, that can play a role determining their regiochemistry, are the 2-cyano, 4-phenyl substituent and the nitrogen atom with its lone pair of electrons. The variable in these studies is the nitrogen substituent, *N*-$CO_2C_2H_5$ or *N*-Ph. There are two interesting regiochemical trends for the Diels–Alder reactions of aza dienes 1 and 2. The first is that the only regioisomer observed for the reaction of both aza dienes with methyl acrylate has the carboxyl group β to the nitrogen atom and the reaction of ethyl vinyl ether has the ethoxyl group α to the nitrogen atom. The second trend is that the Diels–Alder reaction of styrene with aza diene 2 (*N*-$CO_2C_2H_5$) produces an increase of the β-isomer compared to the reaction of styrene with aza diene 1 (*N*-Ph).

The regiochemistries of Diels–Alder reactions of acrylate derivatives with 1- and 2-substituted dienes are known.[21,22] Interestingly, the carboxyl group prefers to be oriented "ortho" (1-substituted dienes) or "para" (2-substituted dienes) to either a phenyl or an electron-withdrawing *or* an electron-donating substituent. That is, the regiochemical pattern observed with the Diels–Alder reaction of acrylate derivatives is independent of the electronic nature of the diene substituent. Thus, all three of the substituents of aza dienes 1 and 2 would prefer to have the carboxyl group oriented "ortho" or "para". The major regioisomer observed has the carboxyl group of methyl acrylate oriented favorably with respect to *two* of these substituents, the phenyl and cyano groups, and an unfavorable orientation with respect to the nitrogen substituents (*N*-$CO_2C_2H_5$ or *N*-Ph). The α orientation of the electron-donating ethoxyl substituent with respect to the powerful *N*-$CO_2C_2H_5$ electron-stabilizing group is consistent with the literature and a simple polarity model for the regiochemistry of the Diels–Alder reaction. The ability of a substituent at the 1-position of a diene to orient the substituent on the dienophile is known to be greater with phenyl than carboxyl.[21] Thus, the increase of the α-isomer in the reaction of aza diene 1 (*N*-Ph) with styrene is probably reflecting the greater "ortho" orienting ability of the *N*-Ph compared to the *N*-$CO_2C_2H_5$ substituent.[21]

Stereochemistry. The endo and exo pathways of a given diene determine the relative stereochemistry on the ring substituents in the Diels–Alder reaction. The Alder endo rule has been extremely successful in predicting the major stereoisomer of a wide range of Diels–Alder reactions. The present case is no exception. The endo stereochemical pathway is preferred in the Diels–Alder reactions of both aza dienes 1 and 2 with styrene, methyl acrylate, and ethyl vinyl ether. Although many factors for the endo transition state being more stable have been given, secondary orbital interactions have proven to be the most common explanation for this observation.

In summary, the 2-cyano-4-phenyl-1-aza dienes with *N*-$CO_2C_2H_5$ or *N*-Ph are reactive partners in the Diels–Alder reaction. Remarkably, they show significant reactivity with dienophiles that are relatively unactivated (styrene) or with dienophiles that are activated with an electron-withdrawing group (methyl acrylate) and an electron-donating group (ethyl vinyl ether). This wide range of reactivity holds particular promise for the application of these aza dienes to synthetic problems related to the preparation of six-membered heterocyclic rings.

Experimental Section

***N*,4-Diphenyl-2-cyano-1-azabutadiene (1).** To a solution of 3.5 g (10 mmol) of *N*-(triphenylphosphoranylidene)aniline in 150 mL of anhydrous CH_2Cl_2 was added 1.6 g (10 mmol) of cinnamoyl cyanide.[23] The mixture was refluxed for 5 h. After concentration in vacuo, the residue was dissolved in ether and triphenylphosphine oxide was removed by filtration. After concentration in vacuo, the reaction mixture was purified by flash chromatography on silica gel (ether/hexanes, 1/6) to afford 2.0 g (85%) of bright yellow crystals: mp 70–71 °C; ^{1}H NMR (benzene-d_6) δ 6.81–6.85 (m, 5 H), 7.0–7.03 (m, 6 H), 7.32–7.38 (d, J = 16.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 110.3, 120.57, 126.6, 127.4, 128.1, 129.1, 129.2, 130.65, 134.4, 140.2, 144.4, 149; IR (KBr) 2220 cm^{-1} (C≡N); MS *m/z* 232 (M^+), 231 (base peak), 204, 128, 103, 77, 51.

Anal. Calcd for $C_{16}H_{14}N_2$: C, 82.73; H, 5.21; N, 12.06. Found: C, 83.03; H, 4.96; N, 11.99.

Reaction of *N*,4-Diphenyl-2-cyano-1-azabutadiene (1) with Methyl Acrylate. A solution of 300 mg (1.24 mmol) of aza diene 1 in 6 mL (66 mmol, 50 equiv) of freshly distilled methyl acrylate was heated in a sealed tube at 110 °C for 1 week. The cooled reaction mixture was concentrated in vacuo and purified by column chromatography (1/6 ether/hexanes) to give 100 mg (66% conversion) of the aza diene 1 and 230 mg (83%) of a mixture of the two stereoisomers in a 6/1 ratio (NMR integration of vinyl hydrogen) as a yellow oil. The major stereoisomer, methyl *N*,4-diphenyl-1,2,3,4-tetrahydro(3*S**,4*S**)-6-cyanonicotinate (90 mg), was separated from the mixture by recrystallization from ethyl acetate/hexane: mp 136–137 °C; ^{1}H NMR ($CDCl_3$) δ 3–3.1 (m, 1 H, C3-H), 3.4 (s, 3 H, CH_3O), 3.65–3.68 (m, 2 H, C2-H), 3.98–4 (t, J = 6 Hz, 1 H, C4-H), 5.78–5.79 (d, J = 5.2 Hz, 1 H, C5-H), 7.1–7.4 (m, 10 H, aromatic); ^{13}C NMR ($CDCl_3$) δ 41 (C4), 43 (C3), 47.1 (C2), 51.3 (CH_3O), 115.2 (CN), 119.2, 119.8, 122.9, 124.8, 127.6, 128.4, 129.1, 129.3, 139.1, 145.3, 170.7; IR (KBr) 2225 (C≡N), 1725 cm^{-1} (C=O); MS *m/z* 318 (M^+), 257, 231, 181, 129, 91, 77, 51.

Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.7; N, 8.8. Found: C, 75.15; H, 5.91; N, 8.7.

Reaction of Aza Diene 1 with Ethyl Vinyl Ether. A solution of 150 mg (0.65 mmol) of the aza diene 1 in 6.2 mL (64 mmol, 100 equiv) of freshly distilled ethyl vinyl ether was heated in a sealed tube at 120 °C for 1 week. The cooled reaction mixture was concentrated in vacuo and purified by column chromatography (1/5 ether/hexanes) to give 75 mg of the aza diene 1 and 40 mg (40%) of a mixture of the two stereoisomers in a 5/1 ratio (NMR integration of the vinyl hydrogens) which showed only one spot by thin-layer chromatography. The major isomer, *N*,4-diphenyl-1,2,3,4-tetrahydro(2*R**,4*S**)-2-ethoxy-6-cyanopyridine, was separated from the minor one by recrystallization from

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a 1/7 mixture of ether/hexanes: mp 87–88 °C; ^{1}H NMR ($CDCl_3$) δ 0.95–1 (t, J = 7 Hz, 3 H, CH_3), 2.11–2.2 (ddd, J_1 = 2.7 Hz, J_2 = 8.4 Hz, J_3 = 15 Hz, 1 H, C3-H), 2.28–2.33 (bd, J = 15 Hz, 1 H, C3-H), 3.19–3.29 (m, 1 H, C4-H), 3.55–3.70 (m, 2 H, OCH_2), 4.8–4.82 (t, J = 2.8 Hz, 1 H, C2-H), 6.15–6.16 (d, J = 4.2 Hz, 1 H, C5-H), 7.1–7.38 (m, 10 H, aromatic); ^{13}C NMR ($CDCl_3$) δ 14.8 (CH_3), 33.4 (C3), 36.2 (C4), 62.6 (OCH_2), 87.9 (C2), 116 (CN), 122.9, 124.7, 126.2, 126.4, 128.1, 128.3, 129.4, 143.6, 144.3; IR (KBr) 2222 cm^{-1} (C≡N); MS m/z 304 (M^+), 257, 231, 181, 91, 77.

Anal. Calcd for $C_{20}H_{20}N_2O$: C, 78.92; H, 6.62; N, 9.2. Found: C, 78.7; H, 6.46; N, 9.01.

Reaction of Aza Diene 1 with Styrene. A solution of aza diene 1 (200 mg, 0.86 mmol) and freshly distilled styrene (5 mL, 43 mmol, 50 equiv) was heated in a sealed tube at 110 °C for 8 d. After concentration in vacuo, the reaction mixture was purified by column chromatography (ether/hexanes, 1/6) to yield 60 mg of the aza diene 1 and 100 mg (50%) of *N*,2,4-triphenyl-1,2,3,4-tetrahydro(2*S**,4*S**)-6-cyanopyridine as a thick orange oil that showed a single spot on TLC: ^{1}H NMR ($CDCl_3$) δ 2.35–2.38 (m, 2 H, C3-H), 3.78–3.84 (td, J = 2.9, 8.9 Hz, 1 H, C4-H), 4.66–4.7 (dd, J = 4.1, 11 Hz, 1 H, C2-H), 5.79–5.8 (d, J = 2.7 Hz, 1 H, C5-H), 7–7.38 (m, 10 H, aromatic); ^{13}C NMR ($CDCl_3$) δ 39.7 (C3), 40.7 (C4), 64 (C2), 115.8 (CN), 121.9, 122.1, 125.8, 125.9, 126.7, 127.5, 128.1, 128.3, 128.6, 129, 140.2, 143.2, 144.8; IR (CH_2Cl_2) 2228 cm^{-1} (C≡N); MS m/z 336 (M^+), 257, 245, 231, 165, 128, 104, 91, 91, 77, 65; HRMS calcd for $C_{24}H_{20}N_2$ 336.1626, found 336.1621.

***N*-(Ethoxycarbonyl)triphenylphosphinimine.** To a solution of 3.1 g (23 mmol) of azidotrimethylsilane and 1.6 mL (16 mmol) of ethyl chloroformate in 25 mL of benzene was added a few drops of pyridine. The mixture was refluxed for 30 min and cooled an an ice bath. To the ice-cold mixture was added 4.35 g (16 mmol) of triphenylphosphine, and stirring was continued at room temperature for 30 min until the evolution of nitrogen was complete. After concentration in vacuo, the crude solid was recrystallized from a mixture of ethyl acetate/hexanes (1/5) to yield 4.5 g (80%) of *N*-(ethoxycarbonyl)triphenylphosphinimine as colorless crystals: mp 136.5–137 °C (lit. mp 136–137 °C); ^{1}H NMR ($CDCl_3$) δ 1.2–1.25 (t, J = 7.1 Hz, 3 H), 4.02–4.09 (q, J = 7.1 Hz, 2 H), 7.27–7.8 (m, 15 H).

***N*-(Ethoxycarbonyl)-2-cyano-4-phenyl-1-azabutadiene (2).** To a solution of 13.2 g (38 mmol) of iminophosphorane *N*-(ethoxycarbonyl)triphenylphosphinimine in 70 mL of anhydrous benzene was added 5.4 g (35 mmol) of cinnamoyl cyanide. The mixture was refluxed for 22 h, concentrated in vacuo, and purified by column chromatography (1/10 ether/hexanes) to afford 1.6 g (25%) of aza diene 2: mp 67–69 °C; ^{1}H NMR ($CDCl_3$) δ 1.30–1.36 (t, J = 7.2 Hz, 3 H, CH_3), 4.29–4.36 (q, J = 7.2 Hz, 2 H, CH_2), 6.85–6.90 (d, J = 16.2 Hz, 1 H, vinylic H), 7.36–7.51 (m, 5 H, aromatic H), 7.60–7.66 (d, J = 16.2 Hz, 1 H, vinylic H); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3), 63.9 (CH_2), 109.3 (CN), 124.4, 128.7, 129, 129.1, 129.3, 131.9, 133.5, 149.7 (CO); IR (KBr) 2228 (C≡N), 1729 (C=O), 1688 (C=C) cm^{-1}; MS m/z 228 (M^+), 183, 155, 129, 115, 102, 77.

Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41: H, 5.3; N, 12.27. Found: C, 68.41; H, 5.37; N, 12.29.

Reaction of *N*-(Ethoxycarbonyl)-2-cyano-4-phenyl-1-azabutadiene (2) with Methyl Acrylate. A solution of 100 mg (0.43 mmol) of aza diene 2 in 1.18 mL (13 mmol) of freshly distilled methyl acrylate was refluxed for 25 h, concentrated in vacuo, and purified by column chromatography on silica gel (ether/hexanes, 1/3) to give 125 mg (91%) of a mixture of the two stereoisomers (10 to 1 ratio NMR integration of the vinyl hydrogens). The major isomer methyl *N*-(ethoxycarbonyl)-1,2,3,4-tetrahydro(3*S**,4*S**)-4-phenyl-6-cyanonicotinate was isolated from the mixture by recrystallization using ethyl acetate/hexanes: mp 87–88 °C; ^{1}H NMR ($CDCl_3$) δ 1.28–1.32 (t, J = 7.1 Hz, 3 H, CH_3CH_2), 2.98–3.04 (m, 1 H, C3-H), 3.38 (s, 3 H, CH_3O), 3.41–3.49 (dd, J = 10.5, 13.8 Hz, 1 H, C2-H), 3.93–3.96 (t, J = 5.5 Hz, 1 H, C4-H), 4.11–4.16 (dd, J = 3, 13.8 Hz, 1 H, C2-H), 4.22–4.29 (q, J = 7.1 Hz, 2 H, CH_2O), 5.98–5.99 (d, J = 4.64 Hz, 1 H, C5-H), 7.03–7.25 (m, 5 H, aromatic); ^{13}C NMR ($CDCl_3$) δ 14.2 (CH_3CH_2), 40.4 (C4), 41.4 (C2), 43.6 (C3), 51.5 (CH_3O), 63.5 (OCH_2), 114.6 (CN), 127.68, 128.1, 128.6, 128.7, 128.8, 137.4, 152.5 (COOEt), 170.1 (COOMe); IR (KBr) 2236 (C≡N), 1734, and 1716 cm^{-1} (C=O); MS m/z 314 (M^+), 285, 241, 209, 181, 149, 115, 91, 77.

Anal. Calcd for $C_{17}H_{18}N_2O_4$: C, 64.96; H, 5.77; N, 8.91. Found: C, 64.96; H, 5.53; N, 9.20.

Reaction of Aza Diene 2 with Ethyl Vinyl Ether. A solution of 100 mg (0.44 mmol) of aza diene 2 in 1.4 mL (14.4 mmol) of freshly distilled ethyl vinyl ether was stirred at room temperature for 27 h. After concentration in vacuo, the mixture was purified by column chromatography (1/4 ether/hexanes) to afford 121 mg (92%) of a mixture of two stereoisomers in a 14 to 1 ratio (by NMR integration of the vinyl hydrogens). The major isomer, *N*-(ethoxycarbonyl)-1,2,3,4-tetrahydro(2*R**,4*S**)-2-ethoxy-4-phenyl-6 cyanopyridine, was separated from the mixture by recrystallization from ethyl acetate/hexanes: mp 78–79 °C; ^{1}H NMR ($CDCl_3$) δ 1.02–1.06 (t, J = 6.9 Hz, 3 H, OCH_2), 1.3–1.35 (t, J = 6.9 Hz, 3 H, $CO_2CH_2CH_3$), 2.26–2.29 (m, 2 H, C3-H), 3.3–3.4 (m, 1 H, C4-H), 3.44–3.56 (m, 2 H, OCH_2), 4.22–4.3 (q, J = 6.9 Hz, 2 H, CO_2CH_2), 5.59–5.61 (t, J = 3 Hz, 1 H, C2-H), 6.27–6.28 (d, J = 3.6 Hz, 1 H, C5-H), 7.16–7.26 (m, 5 H, aromatic); ^{13}C NMR ($CDCl_3$) δ 14.2, 14.8, 35.7 (C3), 37 (C4), 63.2 (CO_2CH_2), 63.3 (OCH_2), 79.5 (C2), 111, 116 (CN), 126.8, 128, 128.33, 133.86, 143, 153; IR (KBr) 2224 (C≡N), 1709 cm^{-1} (C=O); MS m/z 300 (M^+), 254, 209, 182, 181, 155, 140, 115, 91, 77.

Anal. Calcd for $C_{17}H_{20}N_2O_3$: C, 67.98; H, 6.71; N, 9.33. Found: C, 68.11; H, 6.73; N, 9.61.

Reaction of Aza Diene 2 with Styrene. A solution of 150 mg (0.65 mmol) of aza diene 2 in 3 mL (26 mmol, 40 equiv) of freshly distilled styrene was heated at 90 °C under nitrogen for 1 d. After concentration in vacuo to remove the excess of styrene, the crude mixture was purified by column chromatography (1/10 ether/hexanes) to afford 48.4 mg (22%) of a mixture of two stereoisomers in a 10 to 1 ratio (*N*-(ethoxycarbonyl)-1,2,3,4-tetrahydro(3*S**,4*S**)-2,4-diphenyl-6-cyanopyridine and *N*-(ethoxycarbonyl)-1,2,3,4-tetrahydro(3*R**,4*S**)-3,4-diphenyl-6-cyanopyridine) and 37.6 mg (17%) of the other regioisomer as an orange thick oil (overall yield: 92% including 114 mg of a mixture of the 3 adducts). From ^{1}H NMR measurement, the ratio of the two stereoisomers to the minor regioisomer is 1:2. The mixture of the two stereoisomers was further purified by recrystallization from ethyl acetate/hexanes to give pure *N*-(ethoxycarbonyl)-1,2,3,4-tetrahydro(3*S**,4*S**)-3,4-diphenyl-6-cyanopyridine as colorless crystals: mp 123–124 °C; ^{1}H NMR ($CDCl_3$) δ 1.27–1.31 (t, J = 7.2 Hz, 3 H, CH_3), 3.29–3.36 (ddd, J_1 = 3.0, 5.7, 14.7 Hz, 1 H, C3-H), 3.43–3.55 (t, J = 12 Hz, 1 H, C2-H), 3.76–3.79 (t, J = 5.4 Hz, 1 H, C4-H), 4.14–4.19 (dd, J = 2.7, 12.9 Hz, 1 H, C2-H), 4.22–4.29 (q, J = 7.2 Hz, 2 H, CH_2O), 6.12–6.14 (d, J = 5.1 Hz, 1 H, C5-H), 6.6–7.3 (m, 10 H, aromatic); ^{13}C NMR ($CDCl_3$) δ 14.3 (CH_3), 43.3 (C3), 43.5 (C4), 45.6 (C2), 63.3 (CH_2O), 114.6 (CN), 115.1, 127.1, 127.2, 127.3, 127.8, 128.1, 129, 129.6, 137.3, 138.5, 152.6; IR (KBr) 2223 cm^{-1} (C≡N); MS m/z 332 (M^+), 181, 155, 128, 104 (base peak), 91, 77, 71, 57, 55.

Anal. Calcd for $C_{21}H_{20}N_2O_2$: C, 75.88; H, 6.06; N, 8.43. Found: C, 75.69; H, 5.97; N, 8.36.

***N*-(Ethoxycarbonyl)-1,2,3,4-tetrahydro(2*S**,4*S**)-2,4-diphenyl-6-cyanopyridine**: ^{1}H NMR ($CDCl_3$) δ 1.18–1.23 (t, J = 7.2 Hz, 3 H, CH_3), 2.15–2.25 (dt, J = 8, 16.2 Hz, 1 H, C3-H), 2.5–2.6 (dt, J = 6, 13.5 Hz, 1 H, C3-H), 3.52–3.56 (m, 1 H, C4-H), 4.13–4.2 (m, 2 H, CH_2O), 5.26–5.31 (t, J = 7.2 Hz, 1 H, C2-H), 6.37–6.39 (d, J = 3.6 Hz, 1 H, C5-H), 6.8–7.3 (m, 10 H, aromatic); ^{13}C NMR ($CDCl_3$) δ 14.1 (CH_3), 38.9 (C3), 41 (C4), 57.2 (C2), 63.15 (CH_2O), 114.3 (CN), 115, 125, 126.8, 127.1, 127.2, 128.4, 128.5, 135.2, 140.4, 141.5, 152.9; IR (CH_2Cl_2) 2223 (C≡N), 1707 cm^{-1} (C=O); MS m/z 332 (M^+), 181, 155, 128, 104 (base peak), 91, 77, 71, 57, 55; HRMS calcd for $C_{21}H_{20}N_2O_4$ 332.1525, found 332.1514.

***N*-Methoxy-2-cyano-4-phenyl-1-azabutadiene (3).** *N*-Hydroxy-2-cyano-4-phenyl-1-azabutadiene was prepared according to a procedure adapted from the literature.[24] To a solution of phenylacryloaldoxime[25] (7.35 g, 0.05 mol) in anhydrous CH_2Cl_2 (200 mL) was added *N*-chlorosuccinimide (6.67 g, 0.05 mol). The mixture was refluxed under nitrogen for 3 h. The mixture was cooled to in an ice bath, and trimethylsilyl cyanide (5.95 g, 0.06 mol) was added. A mixture of triethylamine (5.05 g, 0.05 mol) in CH_2Cl_2 (20 mL) was added dropwise over a period of 20 min. The reaction mixture was allowed to warm to room temperature and stir for a further 2–3 h. The solvent was removed in vacuo,

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and the residue was purified by column chromatography (ethyl acetate/hexanes, 1/6) to yield a beige solid. Beige needles of good quality for X-ray crystallography[26] were obtained by slow evaporation from the same solvent system (7.20 g, 84%): mp 130–131 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.82–6.87 (d, J = 16.5 Hz, 1 H), 7.16–7.22 (d, J = 16.5 Hz, 1 H), 7.32–7.48 (m, 5 H), 9.55 (b, 1 H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 108.5, 119.1, 127.6, 129.1, 130.0, 134.8, 135.1, 139.6; IR (KBr) 2252 cm^{-1} (C≡N); MS (EI) m/z 172 (M^+), 155 (base peak), 140, 128, 115, 77.

The above *N*-hydroxy-2-cyano-4-phenyl-1-azabutadiene was converted into the aza diene 3 according to a procedure adapted from the literature.[27] To a solution of 0.23 g (0.01 mol) of sodium was added 1.72 g (0.01 mol) of the oxime in 20 mL of absolute ethanol. To the magnetically stirred solution was added in one portion methyl iodide (1.56 g, 0.011 mol), and the reaction mixture was heated in an oil bath (80–85 °C) until the pH was just below 7. The solvent was evaporated in vacuo, and the residue was treated twice with 15-mL portions of $CHCl_3$, and the inorganic material was removed by filtration. The remaining oil was first purified by column chromatography (ethyl acetate/hexanes, 1/10) followed by recrystallization from the same solvent system to yield colorless needles (1.24 g, 67%): mp 78–79 °C; 1H NMR ($CDCl_3$) δ 4.12 (s, 3 H), 6.82–6.88 (d, J = 16.5 Hz, 1 H), 7.17–7.22 (d, J = 16.5 Hz, 1 H), 7.36–7.49 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 64.0 (CH_3), 108.7 (CN), 119.1, 127.3, 128.9, 129.7, 132.8, 134.8, 138.7; IR (KBr) 2232 cm^{-1} (C≡N); MS (EI) m/z 186 (M^+) 155 (base peak), 140, 128, 114, 102, 77.

(26) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

(27) Taylor, E. C.; Ray, P. S. *J. Org. Chem.* **1991**, *56*, 1812.

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