Cycloaddition Reaction of 2-Azadienes Derived from β-Amino Acids with Electron-Rich and Electron-Deficient Alkenes and Carbonyl Compounds. Synthesis of Pyridine and 1,3-Oxazine Derivatives

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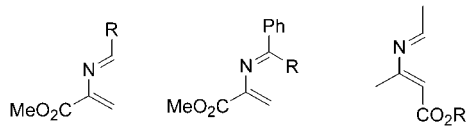
Functionalized keto-enamines **6** were obtained by nucleophilic addition of enol ethers to the imine moiety of 2-azadienes derived from dehydroaspartic esters **4**. Reactions of 2-azadiene **4c** containing three electron-withdrawing substituents (CO_2R) with enol ethers **5** in the presence of lithium perchlorate led to the formation of tetrahydropyridine derivatives **7** in a regio- and stereoselective fashion. 2*H*-[1,3]-oxazines **10** and pyridine derivatives **12** and **13** were obtained by heterocycloaddition reactions of electron-poor azadienes **4d**−**g** containing two electron-withdrawing substituents (4-$O_2N-C_6H_4$, CO_2R) in positions 1 and 4 with carbonyl derivatives (ethyl glyoxalate **9a** and diethyl ketomalonate **9b**) and the electron-deficient olefin tetracyanoethylene **11**.

Introduction

2-Azabutadiene systems have proved to be efficient Diels−Alder partners for dienophiles.[1] The great majority of 2-azadienes studied are substituted with strong electron-donating groups and are excellent reagents in *normal* Diels−Alder reactions with electron-deficient dienophiles.[1,2] Neutral azadienes have been used as heterodienes, not only in *inverse*-demand Diels−Alder reactions with electron-rich dienophiles[3] but also in normal Diels−Alder reactions with electron-poor dienophiles[1e] and with heterodienophiles[4,5] for the preparation of nitrogen heterocyclic compounds. Nevertheless, electron-poor 2-azadienes, despite their potential as heterodienes for Diels−Alder reactions, have received much less attention.[1]

Azadienes **1** (Scheme 1) undergo dimerization,[6] and these heterodienes **1** (R = C_6H_5, 4-$Me_2N-C_6H_4$) bearing one electron-withdrawing substituent (CO_2R) take part in the Diels Alder reaction both with electron-rich dienophiles such as enamines as well as with electron-deficient dienophiles.[7] However, azadienes **1** (R = 4-$O_2N-C_6H_4$, 4-pyridyl, COC_6H_5, CO_2Et) containing a second electron-withdrawing substituent participate only in inverse cycloaddition reactions with enamines,[7] whereas similar azadienes **2** (Scheme 1) containing a second substituent in position 1 (R = C_6H_5, OEt) are found to react only with strongly activated dienophiles.[8] None of these azadienes **1** react with enol ethers because the use of more activated electron-rich dienophiles is necessary, and in an excellent semiempirical molecular orbital study of the Diels−Alder reaction of acyclic 2-azadienes **1**, it has been suggested[9] that the introduction of a new electron-withdrawing substituent in azadienes **1** could favor the reaction of these heterodienes with enol ethers.

Scheme 1



1 **2** **3**

Given the above, we have been involved in the synthesis of neutral[5] and electron-poor azadienes derived

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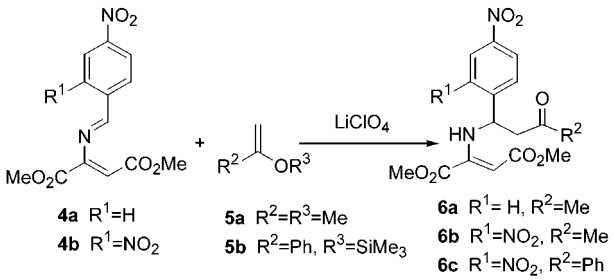
from aminophosphorus derivatives[10] and β-amino esters[11] **3** (Scheme 1) and in the preparation of nitrogen heterocyclic compounds.[12]As a continuation of our work on the [4 + 2] cycloaddition chemistry of 2-azadienes, here we aim to explore whether azadienes **3** could react not only with electron-deficient dienophiles such as tetracyanoethylene or carbonyl derivatives but also with electron-rich enol ethers, as well as study their use as key intermediates in the synthesis of pyridine and oxazine compounds.

Results and Discussion

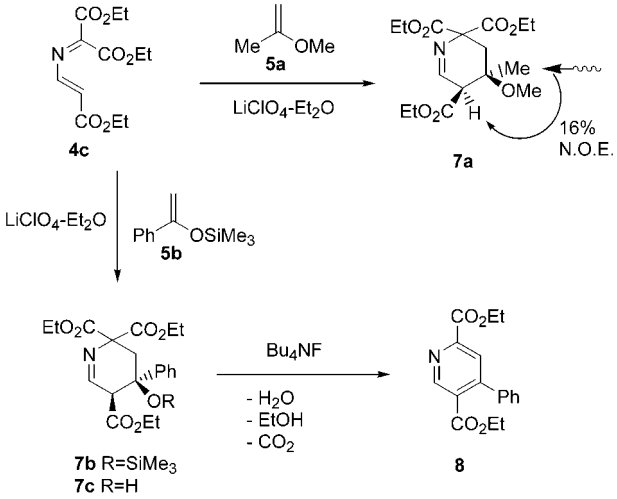
Reaction of 2-Azadienes 4a−c with Enol Ethers 5. "Ab initio" molecular orbital calculations (HF/3-21G* level)[13] of 2-aza-1,3-butadiene and vinyl alcohol have been reported before. But azadienes **1** (Scheme 1) have not reacted with enol ethers,[7,9] although molecular orbital calculations (AM1) of the energies of frontier orbitals (HOMO and LUMO) suggested[9] that with the introduction of new electron-withdrawing substituents in azadienes **1**, these heterodienes should then be reactive enough to participate in the Diels−Alder reaction with enol ethers. In addition, a recent report describes the cycloaddition reaction in the gas phase of N-protonated 2-azadienes with ethyl vinyl ether.[14] We thought that the complementary substitution of electron-withdrawing groups to azadienes **3** could accelerate its 4π-participation in LUMO-diene-controlled Diels−Alder Reactions.

First, we explored the reaction of 2-azadienes derived from dehydroaspartic esters **4a** (R^1 = H) and **4b** (R^1 = NO_2) containing three electron-withdrawing groups (one nitro-aryl group and two carboxylic esters) with methoxy propene **5a** (R^2 = R^3 = Me), but no reaction took place. Taking into account that Lewis acids such as lithium perchlorate can activate[5,11c,15] Diels−Alder reactions, we attempted the activation of the process with this catalyst. Adducts **6a**,**b** (R^2 = Me) were obtained in low yield (30−31%) when the reaction of azadienes **4a**,**b** with enol ether **5a** was performed in the presence of lithium perchlorate in nitromethane or ether (Scheme 2). Similarly, azadiene **4b** reacted with 1-trimethylsilyloxy-1-phenylethene **5b** (Scheme 2) to give functionalized enamine **6c** (61%). The formation of adducts **6** could be explained by nucleophilic addition of enol ethers **5** to the imine carbon of azadienes **4** in a manner similar to that observed for simple aldimines in the presence of Lewis acids.[16]

Scheme 2



Scheme 3



Substitution of azadienes **1** with electron-withdrawing groups makes these substrates more electron-deficient, lowering both HOMO and LUMO energies and favoring the cycloaddition reaction with electron-rich dienophiles.[9] For this reason, we thought that the addition of two electron-withdrawing groups (CO_2Et) to position 1 of azadienes **3** could accelerate its 4π-participation in LUMO-diene-controlled Diels−Alder reactions so that the corresponding azadiene **4c** could be sufficiently reactive to participate in hetero Diels−Alder reactions with enol ethers.

The treatment of 2-azadiene **4c** containing three electron-withdrawing groups with methoxy propene **5a** in the presence of lithium perchlorate in ether led to the formation of cycloadduct **7a** in a regio- and stereoselective fashion (Scheme 3) in good yield (70%). A similar result was obtained when azadiene **4c** reacted with 1-trimethylsilyloxy-1-phenylethene **5b** to give substituted tetrahydropyridine derivative **7b** (R = $SiMe_3$). NOE difference experiments were combined with spectral data to confirm the structures of tetrahydropyridine derivatives **7a**,**b**. The selective saturation of the singlet of the methyl group at 1.55 ppm in compound **7a** afforded positive NOE over the adjacent H-3 proton (see Scheme 3), suggesting a syn configuration between the methyl group and the position 3 proton and, therefore, the endo stereoselectivity of the cycloaddition with controlled stereochemistry of two stereocenters. A concerted reaction mechanism could explain these results in a manner similar to that observed

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Scheme 4

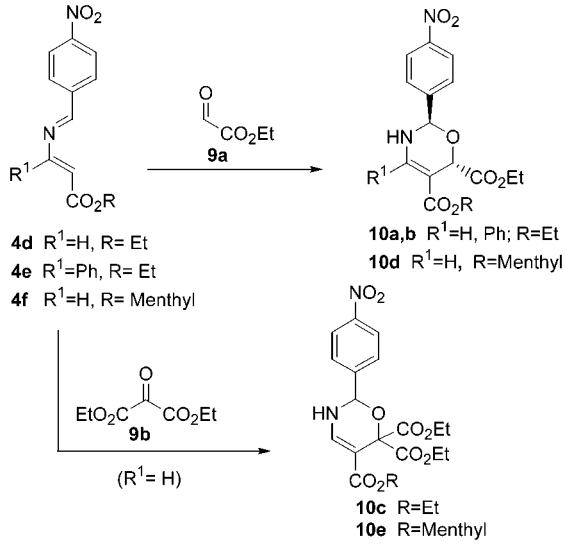

Table 1. Compounds Obtained by Reaction of 2-Azadienes 4d−g with Dienophiles 9 and 11

entry	compound	R^1	R	time (h)	yield (%)[a]
1	**10a**	H	Et	20[b]	92
2	**10b**	Ph	Et	16[b]	70
3	**10c**	H	Et	20[c]	86
4	**10d**	H	menthyl	20[b]	43
5	**10e**	H	menthyl	20[c]	52
6	**12**	H	Et	30[d]	30
7	**13a**	Ph	Et	16[d]	25
8	**13b**	Me	Me	13[d]	33

[a] Purified by chromatography. [b] At 60 °C in THF. [c] In refluxing $CHCl_3$. [d] In THF at room temperature.

for neutral azadienes with enol ethers in the presence of boron trifluoride,[3] although a stepwise process cannot be excluded. The treatment of silyloxy-tetrahydropyridine derivative **7b** with tetrabutylammonium fluoride did not give the deprotected cycloadduct **7c** (R = H), and the aromatic pyridine **8** was obtained instead, which could be explained by desilylation of compound **7b** and subsequent decarboxylation and loss of water from tetrahydropyridine **7c**.

Hetero Diels−Alder Reaction of 2-Azadienes 4d−f with Carbonyl Compounds 9. Some examples of Diels−Alder reaction of azadienes derived from α-amino acids **1** (R = C_6H_5, 4-Me_2N−C_6H_4)[7] and **2** (R = C_6H_5, OC_2H_5)[8] with very activated dienophiles such as electron-deficient alkenes or alkynes have been described. However, as far as we know, examples either of hetero Diels−Alder reaction of electron-poor 2-azadienes **1**−**3** with carbonyl compounds or of the normal Diels−Alder reaction of azadienes **3** with heterodienophiles and electron-deficient dienophiles have not been reported.

For this reason, the reaction of heterodienes **4d**,**e** with a reactive aldehyde such as ethyl glyoxalate **9a** was studied. Cycloaddition of azadienes **4d**,**e** (R^1 = H, Ph) with ethyl glyoxalate in refluxing $CHCl_3$ gave 2*H*-[1,3]-oxazines **10a**,**b** (Scheme 4, Table 1, entries 1 and 2) obtained as single isomers in a regio- and stereoselective fashion. 2*H*-[1,3]-Oxazines **10a**,**b**, in which two new stereogenic centers are created, proved to be single stereoisomers and were characterized on the basis of their spectroscopic data and X-ray diffraction analysis of **10a**, showing the trans configuration between H-6 and H-2 protons. The corresponding ORTEP drawing with the appropriate atom numbering is available in Supporting Information. Given that only the trans stereoisomers (C2−C6) were obtained, formation of 1,3-oxazines **10** can be explained by [4 + 2] cycloaddition reaction of heterodienes **4d**,**e** with ethyl glyoxalate with exo selectivity. This behavior seems to be consistent with previous results of our group[5] and of others[4] when neutral 2-azadienes were used. Diethyl ketomalonate **9b** also reacted with azadiene **4d** to give the corresponding substituted 1,3-oxazine **10c** in very good yield (Table 1, entry 3).

Next, we extended the process to the optically active azadiene containing the (1*R*,2*S*,5*R*)-(−)-menthyl group. Electron-deficient 2-azadiene derived from (1*R*,2*S*,5*R*)-(−)-menthyl ester **4f** could be obtained by means of an Aza−Wittig reaction of the correspondent functionalized phosphazene with *p*-nitrobenzaldehyde in a manner similar to that reported for simple azadienes.[11c,17] The reaction of optically active azadiene **4f** with ethyl glyoxalate **9a** in refluxing THF was studied, and 2*H*-[1,3]-oxazine **10d** (R = menthyl) (Scheme 4, Table 1, entry 4) was obtained with an enantiomeric excess of 30%. However, when diethyl ketomalonate **9b** was treated with azadiene **4f**, 2*H*-[1,3]-oxazine **10e** (R = menthyl) (Scheme 4, Table 1, entry 5) was obtained in a regioselective fashion but without enantiomeric excess. Hetero Diels−Alder reactions have a great potential for the efficient construction of heterocycles[1a,22] and natural products,[23a,b] as well as for asymmetric synthesis.[23b−e] In our case, the reaction led to a new approach to the formation of dihydro-2*H*-[1,3]-oxazines **10** with controlled stereochemistry of two stereocenters. In this context, it is notewortly that 2*H*-[1,3]-oxazines are known intermediates in organic synthesis.[24]

Reaction of 2-Azadienes 4d,e,g with Tetracyanoethylene 11. Finally, the Diels−Alder reaction of 2-azadienes **4d**,**e**,**g** with some electron-deficient alkenes and alkynes was explored. No cycloaddition was observed when azadiene **4d** reacted with *N*-phenyl maleinimide, maleic anhydride, or dimethyl acetylendicarboxylate.

(17) Required N-vinylic phosphazene was prepared as follows: optically active (1*R*,2*S*,5*R*)-(−)-menthyl propiolate was prepared by titanium-catalyzed transesterification of ethyl propiolate with (1*R*,2*S*,5*R*)-(−)-menthol in the presence of titanium(IV) ethoxide.[18] The addition of tetramethylguanidinium azide (TMGA) to (1*R*,2*S*,5*R*)-(−)-menthyl propiolate in chloroform at room temperature led to the formation of the corresponding vinyl azide, which was isolated as a mixture of the *E*/*Z* isomers (40:60). The preparation of phosphazene was accomplished very easily through the classic Staudinger reaction[19] of the former vinyl azide and methyldiphenylphosphine to give only the trans isomer of the N-vinylic phosphazene (see Supporting Information).[20]

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(20) Synthesis of the trans isomer of conjugated phosphazenes from a mixture of *E*/*Z* vinyl azide and phosphines has been previously observed by our group[11c] and by others.[21]

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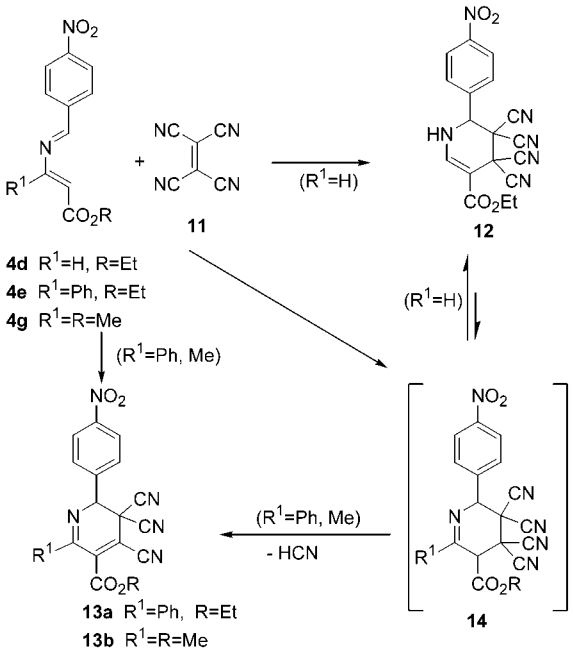
Scheme 5



However, azadiene **4d** (R^1 = H) underwent a hetero Diels−Alder reaction with tetracyanoethylene **11**, leading to the formation of the polysubstituted tetrahydropyridine **12** (Scheme 5, Table 1, entry 6). 3-Substituted azadienes **4e** (R^1 = Ph) and **4g** (R^1 = Me) also reacted with this dienophile **11**, but in this case, polysubstituted dihydropyridines **13a**,**b** were obtained (Scheme 5, Table 1, entries 7 and 8). The formation of pyridine derivatives **12** and **13** could be explained through a [4 + 2] hetero cyclization of the azadienes and the alkene to give the cycloadduct **14**. Subsequent tautomerization of azadiene **4d** (R^1 = H) could afford the tetrahydropyridine **12**, while the loss of cyanide acid from cycloadduct **14** could give the dihydropyridines **13** when substituted azadienes **4e** (R^1 = Ph) and **4g** (R^1 = Me) are used.

Conclusion

We conclude that electron-poor azadienes derived from *β*-amino acids **4c** containing three electron-withdrawing substituents (CO_2R) are suitable 4*π* systems in inverse-demand Diels−Alder reactions with enol ethers **5** in the presence of lithium perchlorate. However, azadienes **4d**−**g** containing two electron-withdrawing substituents (4-O_2N−C_6H_4, CO_2R) in positions 1 and 4 can be used as heterodienes in normal Diels−Alder reactions with carbonyl derivatives (ethyl glyoxalate **9a** and ethyl ketomalonate **9b**) and with the electron-deficient olefin tetracyanoethylene **11**. These processes provide a useful route to new oxazine and pyridine compounds derived from *β*-amino acids. It is worth noting that pyridine compounds derived from *β*-amino acids are useful heterocycles not only for their biological activities[25] but also because the pyridine nucleus is a structural unit appearing in many natural products.[26]

Experimental Section

General. All reactions were carried out under nitrogen. Ethyl ether and tetrahydrofuran were distilled from benzophenone ketyl and sodium, while $CHCl_3$ was distilled from P_2O_5. 2-Azadienes **4c**−**e**,**g** were synthesized according to literature procedures.[11]

General Procedure for the Preparation of 2-Azadienes 4a,b. Aldehyde (4 mmol) was added to a 0−10 °C solution of phosphazene 3,4-bis(methoxycarbonyl)-1-methyl-1,1-diphenyl-2-aza-1λ^5-phosphabuta-1,3-diene[11c] (1.430 g, 4 mmol) in $CHCl_3$ (15 mL) under N_2, and the mixture was stirred at room temperature or warmed at 60 °C until TLC indicated the disappearance of phosphazene.

(1*E*,3*Z*)-3,4-Dimethoxycarbonyl-1-(4-nitrophenyl)-2-azabuta-1,3-diene (4a). The general procedure was followed using 4-nitrobenzaldehyde (0.604 g, 4 mmol) and warming for 15 h. Evaporation of solvent under reduced pressure and chromatography on silica gel (5:1 hexane/AcOEt) gave 0.584 g (50%) of **4a** as a yellow solid: mp 83−84 °C (recrystallized from AcOEt/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.62 (s, 3H), 3.80 (s, 3H), 6.28 (s, 1H), 7.99 (d, $^3J_{HH}$ = 9.0 Hz, 2H), 8.26 (d, $^3J_{HH}$ = 9.0 Hz, 2H), 8.29 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 51.7, 53.2, 109.6, 123.9, 129.9, 140.1, 149.9, 151.1, 162.2, 163.4, 165.1; IR (KBr) 1720, 1712, 1526; EIMS *m*/*z* 292 (M^+, 2). Anal. Calcd for $C_{13}H_{12}N_2O_6$: C, 53.43; H, 4.14; N, 9.59. Found: C, 53.47; H, 4.13; N, 9.60.

(1*E*,3*E*)-4-[(1*R*,2*S*,5*R*)-(−)-Menthyl]-1-(4-nitrophenyl)-2-azabuta-1,3-diene (4f). 4-Nitrobenzaldehyde (0.604 g, 4 mmol) was added to a solution of 1.964 g (4 mmol) of phosphazene (see Supporting Information) in $CHCl_3$ (10 mL) at 0 °C under N_2. The mixture was stirred for 2 h, and the crude oil was chromatographed on silica gel (20:1 hexane/AcOEt) to give 1.200 g (67%) of **4f** as a yellow solid: mp 100−101 °C (recrystallized from AcOEt/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.70−2.01 (m, 18H), 4.75 (dt, $^3J_{HH}$ = 4.4 MHz, $^3J_{HH}$ = 10.8 Hz, 1H), 6.22 (d, $^3J_{HH}$ = 13.1 Hz, 1H), 7.87 (d, $^3J_{HH}$ = 13.1 Hz, 1H), 7.97 (d, $^3J_{HH}$ = 8.9 Hz, 2H), 8.24 (d, $^3J_{HH}$ = 8.9 Hz, 2H), 8.45 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.5, 20.7, 21.9, 23.6, 26.4, 31.4, 34.2, 40.9, 47.1, 74.0, 121.6, 124.0, 129.9, 140.5, 149.8, 153.8, 164.4, 166.1; IR (KBr) 1679, 1527; $[\alpha]_D^{20}$ −48.0° (*c* 1.02, CH_2Cl_2); M/S (EI) *m*/*z* 358 (M^+, 5). Anal. Calcd for $C_{20}H_{26}N_2O_4$: C, 67.05; H, 7.32; N, 7.82. Found: C, 67.02; H, 7.31; N, 7.81.

Dimethyl 2-[1-(4-Nitrophenyl)-3-oxo-butylamino]-fumarate (6a). $LiClO_4$ (1.28 g, 3 mmol) and 2-methoxypropene (0.14 mL, 1.5 mmol) were added to a solution of 2-azadiene **4a** (0.877 g, 3 mmol) in nitromethane (3 mL) under N_2. The mixture was stirred at room temperature for 19 h. The reaction mixture was poured onto CH_2Cl_2 (20 mL), washed with a saturated solution of $NaHCO_3$, and dried ($MgSO_4$). Evaporation of the solvent under reduced pressure afforded an oil that was chromatographed on silica gel (5:1 hexane/AcOEt) to give 0.158 g (30%) of **6a** as a yellow oil (R_f = 0.21, 2:1 hexane/AcOEt): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.87 (dd, $^3J_{HH}$ = 5.6 Hz, $^3J_{HH}$ = 17.2 Hz, 1H), 3.00 (dd, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 17.2 Hz, 1H), 3.64 (s, 3H), 3.66 (s, 3H), 5.23 (s, 1H), 5.50 (td, $^3J_{HH}$ = 5.6 Hz, $^3J_{HH}$ = 7.2 Hz, $^3J_{HH}$ = 8.9 Hz, 1H), 7.41 (d, $^3J_{HH}$ = 8.7 Hz, 2H), 8.11 (d, $^3J_{HH}$ = 8.7 Hz, 2H), 8.55 (d, $^3J_{HH}$ = 8.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.6, 50.8, 51.0, 52.7, 53.4, 91.0, 123.9, 127.3, 147.2, 149.7, 149.8, 163.6, 170.5, 204.6; IR (NaCl disks) 3325, 2930, 1732, 1600, 1527; M/S (EI) *m*/*z* 350 (M^+, 2). Anal. Calcd for $C_{16}H_{18}N_2O_7$: C, 54.86; H, 5.18; N, 8.00. Found: C, 54.90; H, 5.19; N, 7.99.

General Procedure for the Preparation of Compounds 7a,b. To a solution of 2-azadiene **4c**[11c] (0.406 g, 1.5 mmol) in Et_2O (5 mL) were added 1.5 mmol of enol ether and 2.66 g (25 mmol) of $LiClO_4$, and the mixture was stirred at room temperature under N_2. The reaction mixture was poured onto CH_2Cl_2 (20 mL), washed with a saturated solution of $NaHCO_3$,

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and dried ($MgSO_4$). The solvent was evaporated under reduced pressure, and the resulting oil was purified by silica gel column chromatography.

Triethyl 4-Trimethylsilanyloxy-4-phenyl-2,3,4,5-tetrahydropyridinecarboxylate (7b). The general procedure was followed using 0.285 g (1.5 mmol) of 1-trimethylsilyloxy-1-phenylethene for 5 h. The crude oil was chromatographed on silica gel (hexane) to give 0.486 g (70%) of **7b** as a colorless oil (R_f = 0.7, 1:2 AcOEt/hexane): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.2 (s, 9H), 1.29−1.35 (m, 4H), 3.08 (d, $^2J_{HH}$ = 12.0 Hz, 1H), 3.23 (d, $^2J_{HH}$ = 12 Hz, 1H), 4.08 (m, 2H), 4.26−4.39 (m, 4H), 4.80 (d, $^3J_{HH}$ = 14 Hz, 1H), 7.26−7.34 (m, 3H), 7.38 (d, $^3J_{HH}$ =14 Hz, 1H), 7.48−7.52 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 1.5, 13.9, 14.4, 45.9, 59.0, 59.1, 62.5, 67.9, 92.5, 93.8, 125.8, 128.4, 141.5, 142.6, 167.5, 167.7, 168.9; IR (NaCl disks) 1755, 1709, 1624; M/S (EI) *m*/*z* 463 (M^+, 5). Anal. Calcd for $C_{23}H_{33}NO_7Si$: C, 59.59; H, 7.17; N, 3.02. Found: C, 59.64; H, 7.12; N, 3.01.

Diethyl 4-Phenyl-2,5-pyridinedicarboxylate (8). Tetrabutylammonium fluoride (1.4 mL, 11 M in THF) was added to a solution of **7b** (0.710 g, 1.54 mmol) in THF (5 mL) under N_2. The reaction mixture was stirred for 30 min. Evaporation of the solvent under reduced pressure afforded an oil that was chromatographed on silica gel (1:1 CH_2Cl_2/hexane) to give 0.451 g (98%) of **8** as a pale yellow solid: mp 98−99 °C (recrystallized from AcOEt/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04 (t, $^3J_{HH}$ = 7 Hz, 3H), 1.43 (t, $^3J_{HH}$ = 7 Hz, 3H), 4.16 (q, $^3J_{HH}$ = 7 Hz, 2H), 4.48 (q, $^3J_{HH}$ = 7 Hz, 2H), 7.26−7.45 (m, 5H), 8.13 (s, 1H), 9.07 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 14.2, 61.6, 62.2, 126.1, 127.9, 128.5, 128.8, 129.4, 137.7, 149.7, 150.6, 150.9, 164.4, 166.3; IR (KBr) 1749, 1723; M/S (EI) *m*/*z* 299 (M^+, 5). Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.20; H, 5.73; N, 4.68. Found: C, 68.15; H, 5.71; N, 4.66.

General Procedure for the Preparation of Compounds 10. Ethyl glyoxalate **9a** or diethyl ketomalonate **9b** (2 mmol) was added to a solution of 2-azadiene **4d**−**f** (2 mmol) in THF or $CHCl_3$ under N_2. The mixture was refluxed until TLC indicated the disappearance of azadiene. Evaporation of solvent under reduced pressure afforded an oil that was chromatographed on silica gel to give the compounds **10**.

5,6-Diethoxycarbonyl-2-(4-nitrophenyl)-3,6-dihydro-2*H*-[1,3]-oxazine (10a). The general procedure was followed using **9a** (0.204 g) and 2-azadiene **4d**[11b] (0.496 g, 2 mmol) in THF (5 mL) for 20 h. The crude oil was chromatographed on silica gel (5:1 hexane/AcOEt) to give 0.644 g (92%) of **10a** as a white solid: mp 110−111 °C (recrystallized from AcOEt/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18−1.26 (m, 6H), 4.08−4.21 (m, 4H), 4.99 (s, 1H), 5.13 (s, 1H), 5.92 (s, 1H), 7.56 (d, $^3J_{HH}$ = 5.8 Hz, 1H), 7.63 (d, $^3J_{HH}$ = 8.7 Hz, 2H), 8.20 (d, $^3J_{HH}$ = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 14.4, 59.8, 61.5, 71.8, 78.4, 97.8, 123.9, 127.9, 140.6, 143.6, 148.7, 165.5, 171.0; IR (KBr) 3283, 1732, 1659, 1527; M/S (EI) *m*/*z* 350 (M^+, 8). Anal. Calcd for $C_{16}H_{18}N_2O_7$: C, 54.86; H, 5.18; N, 8.00. Found: C, 54.89; H, 5.19; N, 7.99.

General Procedure for the Preparation of Compounds 12 and 13. Tetracyanoethylene (0.256 g, 2 mmol) was added to a solution of 2-azadiene **4d**,**e** or **4g** in THF (6 mL) at 0 °C under N_2. The mixture was stirred until TLC indicated the disappearance of 2-azadiene. Evaporation of solvent under reduced pressure afforded an oil that was chromatographed on silica gel to give the compounds **12** or **13**.

Ethyl 3,3,4,4-Tetracyano-2-(4-nitrophenyl)-1,2,3,4-tetrahydro-4-pyridinecarboxylate (12). The general procedure was followed using 2-azadiene **4d**[11b] (0.496 g, 2 mmol) for 30 h. The crude oil was chromatographed on silica gel (6:1 hexane/AcOEt) to give 0.226 g (30%) of **23** as a brown oil (R_f = 0.37, 1:2 AcOEt/hexane): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (t, $^3J_{HH}$ = 7.2 Hz, 3H), 4.26 (q, $^3J_{HH}$ = 7.2 Hz, 2H), 5.02 (s, 1H), 7.30 (s, 1H), 7.79 (d, $^3J_{HH}$ = 8.7 Hz, 2H), 7.85 (d, $^3J_{HH}$ = 4.1 Hz, 1H), 8.31 (d, $^3J_{HH}$ = 8.7 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.1, 40.2, 45.6, 58.1, 62.0, 88.6, 107.7, 108.9, 109.9, 111.0, 124.7, 129.7, 136.3, 145.1, 149.9, 162.7; IR (NaCl) 3356, 2919, 1692, 1520; M/S (EI) *m*/*z* 376 (M^+, 5). Anal. Calcd For $C_{18}H_{12}N_6O_4$: C, 57.45; H, 3.21; N, 22.33. Found: C, 57.50; H, 3.20; N, 22.30.

Methyl 3,3,4-Tricyano-6-methyl-2-(4-nitrophenyl)-2,3-dihydro-5-pyridinecarboxylate (13b). The general procedure was followed using 2-azadiene **4g**[11a] (0.496 g, 2 mmol) for 13 h. The crude oil was chromatographed on silica gel (5:1 hexane/AcOEt) to give 0.230 g (33%) of **13b** as a brown solid: mp 193−194 °C (recrystallized from AcOEt/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.73 (s, 3H), 5.91 (s, 1H), 7.67 (d, $^3J_{HH}$ = 8.4 Hz, 2H), 8.22 (d, $^3J_{HH}$ = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 51.6, 55.9, 81.7, 99.9, 108.4, 110.2, 110.3, 123.9, 128.3, 140.6, 148.7, 161.4, 166.4, 167.5; IR (KBr) 2370, 2350, 1699, 1527; M/S (EI) *m*/*z* 349 (M^+, 5). Anal. Calcd for $C_{17}H_{11}N_5O_4$: C, 58.45; H, 3.17; N, 20.05. Found: C, 58.50; H, 3.19; N, 20.08.

X-ray Crystallography. Single-crystal X-ray diffraction experiments were carried out on a STOE IPDS diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.7173 Å). A prismatic crystal of dimensions 0.26 × 0.18 × 0.12 mm was used for data collection. Crystal data: orthorhombic (space group $P2_12_12_1$), a = 4.6620(10), b = 12.888(5), c = 28.008(14) Å, V = 1682.8(11) Å^3, ρ_{cal} = 1.383 g/cm^3. Data collection was performed at 293 K, with $2\theta_{max}$ = 52°. Intensities were measured on an image plate with oscillating crystal geometry. The total number of measured reflections was 9095, of which 2973 were independent. The criterion for observed reflections was $I > 2\sigma(I)$. Lorentzian polarization correction was applied using STOE software,[27] but no absorption correction (μ = 0.110 mm^{-1}) was made. The structure was solved by direct methods using the SIR97 program.[28] The structure was refined by full-matrix least-squares against $|F|^2$, and all reflections were considered (SHELXL-97 software).[29] The total number of parameters was 229, and all H atoms were generated using geometrical criteria and refined isotropically. Final values for *R*-indices: R_w(all) = 0.1269, R_w(obs) = 0.0972, R(all) = 0.1030, and R(obs) = 0.0405. Residual electron density: min = −0.140 and max = 0.163. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-173076. Copies of the data can be obtained free of charge upon application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax, (+44) 1223-336-033; e-mail, deposit@ccdc.cam.ac.uk).

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Supporting Information Available: Preparation, elemental analysis, and spectral data (^{1}H NMR, ^{13}C NMR, IR, and MS) for compounds **4b**, **6b**, **6c**, **7a**, **10b**−**e**, and **13a**; preparation, elemental analysis, and spectral data (^{1}H NMR, ^{13}C NMR, IR, and MS) for (1*R*,2*S*,5*R*)-(−)-menthylpropiolate and (1*R*,2*S*,5*R*)-(−)-menthyl 3-azidoacrylate; preparation, elemental analysis, and spectral data (^{1}H NMR, ^{13}C NMR, ^{31}P, IR, and MS) for (3*E*)-4-[(1*R*,2*S*,5*R*)-(−)-menthyl]-1-methyl-1,1-diphenyl-2-aza-1λ^5-phosphabuta-1,3-diene required for preparation of **4f**; and supplementary tables, an ORTEP drawing, and X-ray crystallography data for **10a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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