Synthesis of Aza Polycyclic Compounds Derived from Pyrrolidine, Indolizidine, and Indole via Intramolecular Diels−Alder Cycloadditions of Neutral 2-Azadienes

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A method for the preparation of novel oxaza and diaza polycyclic 9-oxa-4-azaphenanthrene, 5*H*-pyrido[2,3-*a*]pyrrolizine, 5*H*,6*H*-pyrido[3,2-*g*]indolizine, and 5*H*,6*H*-indeno[2,1-*a*]indole is described, based on tandem reactions: aza-Wittig reaction of *N*-vinylic phosphazenes with functionalized aldehydes and an intramolecular aza-Diels−Alder reaction.

Introduction

Isolation of aza polynuclear aromatic compounds from natural/environmental sources is sometimes very difficult, and in these cases biochemical studies have to rely on synthetic materials. A great deal of interest exists in the chemistry of these substances and in the study of their interaction with biomolecules. The development of efficient and mild methods of heterocyclic compound synthesis represents a broad area of organic chemistry.[1] In this context, nitrogen-containing rings are among the most useful heterocycles and their utility has been widely demonstrated.[2−4]

In the development of strategies for the preparation of heterocycles the Diels−Alder reaction has proved to be exceptionally useful.[5−7] Furthermore, the intramolecular Diels−Alder reaction (IMDA) has been extensively investigated,[8] and it requires efficient designing and linking of the two reacting moieties prior to the reaction.[9] Earlier studies from our group[10] have developed very efficient methods for the preparation and heterocycloaddition reaction of 2-azadienes. But the corresponding intramolecular version of the hetero Diels−Alder cycloaddition process related with azadiene compounds (IMADA, intramolecular aza-Diels−Alder) has hardly been investigated.[11,12] While some relevant examples

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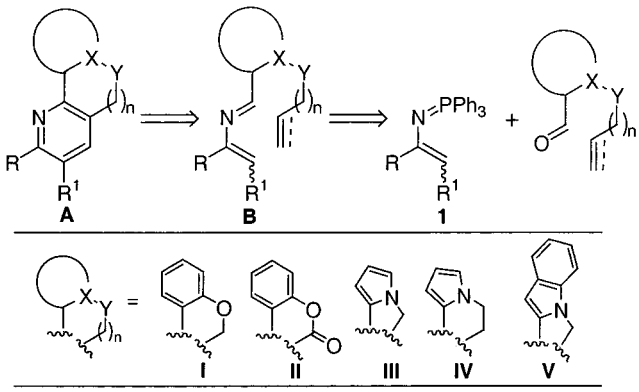
Scheme 1



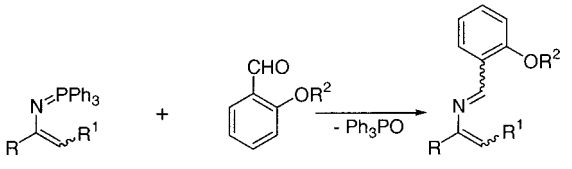
involving 1-azadienes have been reported,[5a,11] little information is available regarding 2-azadienes. To the best of our knowledge, one intramolecular Diels−Alder reaction involving 2-azadienes substituted with two electron-withdrawing groups[12a] and one example of Lewis acid-catalyzed IMADA of neutral 2-azadienes have been reported.[12b] Moreover, no intramolecular reaction was observed when a poor 2-azadiene bearing only one electron-withdrawing group in the diene double bond was used.[12c]

As a continuation of our work on the [4 + 2] cycloaddition chemistry of 2-azadienes,[13] we report here a new, general and effective strategy for the preparation of polyheterocyclic compounds **A** that relies on the IMADA cycloaddition of 2-azadienes **B** bearing a dienophile side chain (Scheme 1). We had thought that this strategy would be useful for the preparation of oxaza and diaza polycyclic derivatives (**I**−**V**) and could even afford an entry to new families, for example to the not previously reported 5*H*-pyrido[2,3-*a*]pyrrolizine **III**, 5*H*,6*H*-pyrido-[3,2-*g*]indolizine **IV**, and 5*H*,6*H*-indeno[2,1-*a*]indole **V** (Scheme 1).

Results and Discussion

IMADA of Functionalized Azadienes. Synthesis of Oxaza Polycyclic Compounds. We first investigated the readily available 2-allyloxybenzaldehyde[14] **2** for aza-Wittig reaction as a model system. It was found that reaction of this aldehyde with *N*-vinylic phosphazenes **1a** (R = 2-furyl, R^1 = Ph) and **1b** (R = 2-thienyl, R^1 = Ph)[13b] in refluxing chloroform gave good yields of electronically neutral azadienes **3a**, **3b** (Scheme 2, Table 1, entries 1, 2). Compounds **3a**, **3b** were characterized on the basis of their spectroscopic data and mass spectrometry, which

Scheme 2



1a R= 2-fur, R^1= Ph (E)
1b R= 2-thi, R^1= Ph (E)
1c R= R^1= Ph (E)
1d R= 3-pyr, R^1= Ph (E)
1e R= H, R^1= Ph (E,Z)
1f R= H, R^1= CH_3 (E,Z)

2 R^2= allyl **4** R^2= propargyl **3** R^2= allyl **5** R^2= propargyl

Table 1. Azadienes 3 and 5 and Oxaza Polycyclic Compounds 6 Obtained

				reaction conditions		
entry	compd	R	R^1	*T* (°C)	time (h)	yield (%)[a]
1	**3a**	2-furyl	phenyl	61	72	42[b]
2	**3b**	2-thienyl	phenyl	61	24	48[b]
3	**3c**	phenyl	phenyl	61	48	57[c]
4	**5a**	2-furyl	phenyl	61	9	73[b]
5	**5b**	2-thienyl	phenyl	61	20	64[b]
6	**5c**	phenyl	phenyl	61	72	70[b]
7	**5d**	3-pyridyl	phenyl	61	20	72[b]
8	**5e**	H	phenyl	61	24	*d*, *e*
9	**5f**	H	CH_3	61	6	*d*, *f*
10	**6a**	2-furyl	phenyl	140	72[g]/31[h]	40[g]/60[h]
11	**6b**	2-thienyl	phenyl	140	144[g]/48[h]	45[g]/68[h]
12	**6c**	phenyl	phenyl	140	96[g]/72[h]	60[g]/64[h]
13	**6d**	3-pyridyl	phenyl	140	16[h]	69[h]
14	**6e**	H	phenyl	140	60[h]	60[h]
15	**6f**	H	CH_3	140	36[h]	56[h]

[a] Yields are for isolated compounds. [b] Isomer 1*E*,3*Z*. [c] Mixture of 1*E*,3*Z*/1*Z*,3*Z* (40/60) isomers. [d] Not isolated, was used in situ in a posterior IMADA reaction. [e] Isomer 1*E*,3*E*. [f] Mixture of 1*E*,3*Z*/1*E*,3*E* isomers (30/70). [g] Obtained from 2-azadiene **3**. [h] Obtained from 2-azadiene **5**.

indicated that only the 1*E*,3*Z*-isomers were obtained. However, when (*E*)-*N*-vinylic phosphazene **1c** (R= R^1 = Ph) was used, a mixture of 1*E*,3*Z*-isomer/1*Z*,3*Z*-isomer (40/60) functionalized azadiene **3c** (Table 1, entry 3) was obtained, in a way similar to that reported for phosphazene **1c** and simple aldehydes.[13b] Nevertheless, the separation of both isomers is not necessary for subsequent reactions. The characteristic spectroscopic data (^{1}H resonance) of compounds **3** are the representative signals for 2-azadiene systems. For instance, the vinylic proton of **3a** showed absorption at δ 6.60 ppm as a singlet and the iminic proton at δ 8.97 ppm also as a singlet.

Heating 2-azadienes **3a**−**c** at xylene reflux temperature afforded polyheterocyclic compounds **6** (Scheme 3, Table 1, entries 10−12) through simultaneous double formation of two rings. Compounds **6** showed a characteristic signal for the methylene attached directly to the oxygen atom at approximately 5.3 ppm in ^{1}H NMR spectra and at approximately 68 ppm in ^{13}C NMR spectra. Their formation can be explained by intramolecular [4 + 2] cycloaddition reaction of heterodienes **3**, followed by subsequent aromatization of compound **7**. Tricyclic pyridine **6a** has been previously obtained from triazines.[9e]

Next, we tried to extend the above reaction to the use of terminal alkyne in the side chain. In a way similar to that reported in the aza-Wittig reaction of aldehyde **2** (Scheme 2), an analogous set of products **5a**−**d** was obtained in good yields (Table 1, entries 4−7) under

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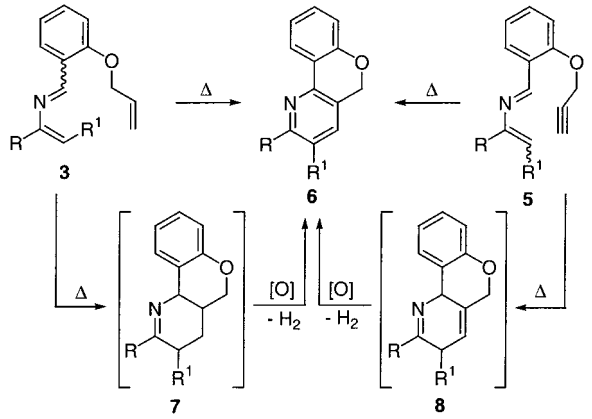
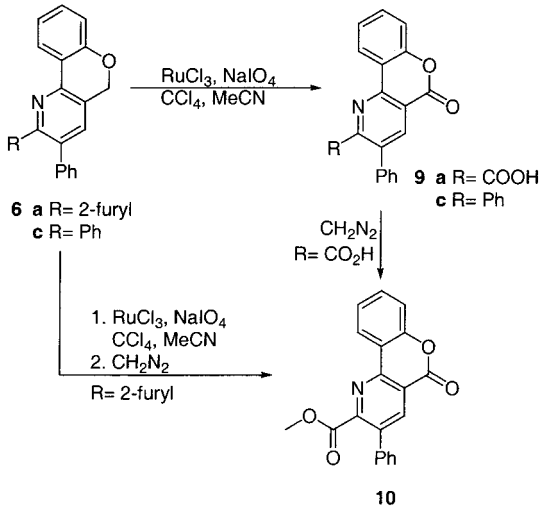
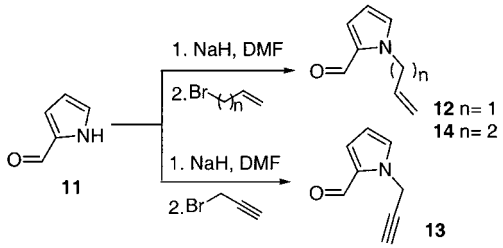
Scheme 3



Scheme 4



Scheme 5



similar reaction conditions when *N*-vinylic phosphazenes **1a**−**d** reacted with propargyloxybenzaldehyde[14] **4** (Scheme 2). Azadienes **5a**−**d**, with aromatic and heteroaromatic substituents in the 3-position, were isolated and obtained as only the *1E*,*3Z*-isomer, maintaining the starting phosphazene configuration in the vinylic double bond. The reaction can also be extended to conjugated phosphazenes bearing a proton in the 3-position **1e** (R = H, R^1 = Ph) and **1f** (R = H, R^1 = Me),[3d] but azadienes **5e** and **5f** could not be isolated by distillation or by column chromatography, although their presence was determined by ^{1}H NMR in crude mixtures and so they were subsequently used in situ without further isolation or purification. In addition, the formation of azadiene **5e** showed an unexpected result (Table 1, entry 8). The starting phosphazene being a mixture of isomers *3E*/*3Z* (70/30),[3d] only evidence of (1*E*,3*E*)-azadiene **5e** was detected (J = 7 Hz). This observation could be explained by an isomerization of the vinylic double bond through an ionic intermediate.[15] However, azadiene **5f** containing a methyl group in the 4-position and obtained from a mixture of isomers 3*E*/3*Z* of phosphazene **1f**[3d] delivered one isomer corresponding to each isomer of the starting material, affording a mixture of 1*E*,3*Z*/1*E*,3*E* azadienes **5f** in proportion similar to those presented in the precursor phosphazene **1f** (Table 1, entry 9). Polycyclic compounds **6a**−**f** were obtained when azadienes **5a**−**f** were heated at xylene reflux temperature (Table 1, entries 10−15) and were compared with those corresponding to the polyheterocycles **6a**−**c** obtained from 2-allyloxybenzaldehyde **2** (Table 1, entries 10−12). Formation of compounds **6** can be explained, as before, by intramolecular [4 + 2] cycloaddition reaction of heterodienes **5**, followed by subsequent aromatization of compounds **8** (Scheme 3).

Taking the above into account, we were interested in determining whether aza-heteroaromatic systems **6** could be oxidized, and in the case of **6a**, containing a furyl substituent (R = 2-furyl), whether this compound could afford the corresponding aza-polycyclic system derivatized from α-amino acids **10**, given that furan derivatives could be considered as synthetic equivalents of carboxylic groups.[16] A ruthenium tetraoxide catalyzed oxidation[17] appeared suitable to achieve this purpose. However, it had to be previously considered if the methylene group attached to an oxygen atom of heterocycles **6** could be oxidized by these reaction conditions. The Sharpless procedure[18] was used for compound **6c**, and the corresponding lactone **9c** (Scheme 4) was obtained with an 83% yield. Nevertheless, in the case of compound **6a**, a simultaneous oxidation of the furan ring and of the methylene group was observed. Furthermore, in situ transformation of oxidation product **9a** (R = CO_2H) into the corresponding methyl ester **10** was performed with diazomethane in Et_2O (Scheme 4). Comparison of the ^{1}H NMR spectra of compounds **6a** and **10** revealed that the oxidation step had taken place, since both the disappearance of the $-CH_2-$ signal at 5.26 ppm and the disappearance of signals of the 2-furyl substituent of compound **6a** could be observed. The structure could be also confirmed by mass spectroscopy which gave the molecular ion M^+ of 331 for compound **10**. Some 5-oxo-5*H*[1]-benzopyrano[4,3-*b*]pyridine derivatives[19] present antiallergic activity.[20] But, as far as we know, 5-oxo-5*H*[1]benzopyrano[4,3-*b*]pyridine derived from α-amino acids has not been reported until now.

IMADA of Functionalized Azadienes. Synthesis of Cyclic Fused Pyridines. The results observed with 2-allyloxy- **2** and 2-propargyloxybenzaldehyde **4** described successful applications of the tandem aza-

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Scheme 6

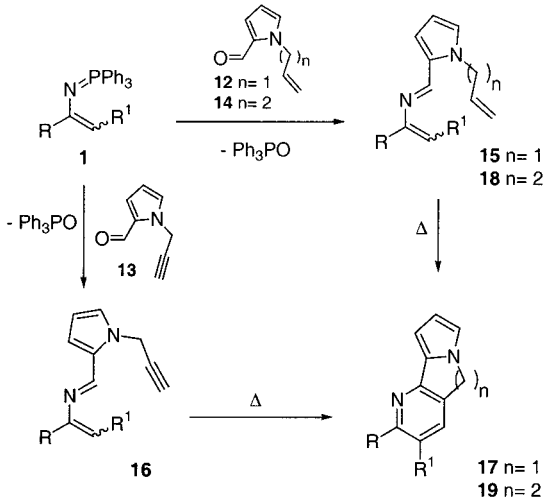


Table 2. Compounds 15−25 Obtained

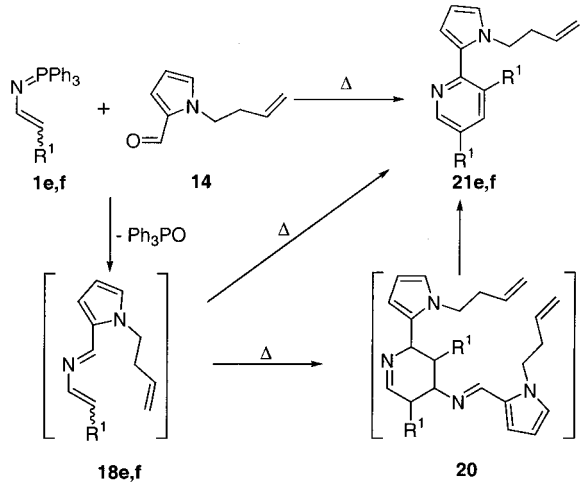
entry	compd	R	R^1	*T* (°C)	time (h)	yield (%)[a]
1	**15**	2-furyl	phenyl	111	152	48[b]
2	**16a**	2-furyl	phenyl	111	98	52[b]
3	**16c**	phenyl	phenyl	111	120	66[b]
4	**16e**	H	phenyl	61	72	50[c]
5	**16f**	H	CH_3	61	7	58[d]
6	**17a**	2-furyl	phenyl	140	120[e]/93[f]	50[e]/70[f]
7	**17c**	phenyl	phenyl	140	96[f]	71[f]
8	**18a**	2-furyl	phenyl	111	118	40[b]
9	**18b**	2-thienyl	phenyl	111	152	42[b]
10	**18e**	H	phenyl	61	72	*g*
11	**18f**	H	CH_3	61	24	*g*
12	**19a**	2-furyl	phenyl	140	96	60
13	**19b**	2-thienyl	phenyl	140	120	68
14	**21e**	H	phenyl	140	48	60
15	**21f**	H	CH_3	140	24	66
16	**24**	2-thienyl	phenyl	111	168	51
17	**25**	2-thienyl	phenyl	140	120	71

[a] Yields are for isolated compounds. [b] Isomer 1*E*,3*Z*. [c] Isomer 1*E*,3*E* (30/70). [d] Mixture of 1*E*,3*Z*/1*E*,3*E* isomers (30/70). [e] Obtained from 2-azadiene **15**. [f] Obtained from 2-azadiene **16**. [g] Not isolated, was used in situ in a later D−A reaction.

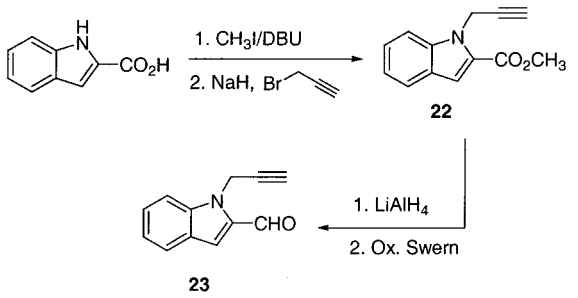
Wittig/intramolecular aza-Diels−Alder reactions. Therefore, we tried to extend this strategy to the preparation of various cyclic fused pyridines from appropriately substituted azadienes. Functionalized aldehydes **12**−**14** were prepared starting from pyrrole-2-carboxaldehyde **11**, and attaching the dienophile side chain to the nitrogen atom of the pyrrole ring, using *N*-alkylation reaction with allyl, homoallyl, or propargyl halides, respectively[14] (Scheme 5).

A new set of functionalized azadienes were obtained by heating *N*-vinylic phosphazenes **1** and aldehydes **12**, **13** in refluxing chloroform or toluene yielding heterodiene compounds **15**, **16** (Scheme 6, Table 2, entries 1−5). Characteristic spectroscopic signals for the vinylic and iminic protons, as well as the corresponding signals of allyl or propargyl substituents of the dienophilic side chain, support the formation of only the 1*E*-isomers of azadienes **15** and **16**. Heating in refluxing xylenes not only heterodiene **15** (R ≠ H) containing a terminal alkene in the side chain but also the heterodienes **16a**, **c** (R ≠ H) containing a propargyl group in the side chain led to the three-ring heterocycles **17a**, **c** (Table 2, entries 6, 7) through IMADA cyclization. However, when 2-azadienes **16e**, **f** (R = H) were heated under the same reaction conditions, no intramolecular Diels−Alder adduct was obtained, and the starting azadienes were recovered.

Scheme 7



Scheme 8

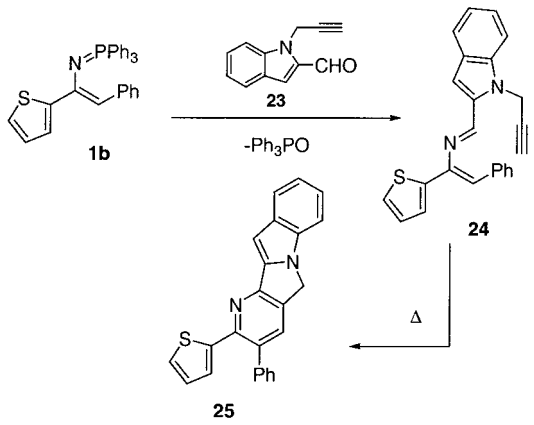


Similar results were obtained when the functionalized dienophile tether was lengthened by one methylene unit as illustrated in Scheme 6 for the preparation of compound **18** (Scheme 6, Table 2, entries 8−11) from aza-Wittig reaction of phosphazenes **1** with substituted pyrrolecarbaldehyde **14**. Azadiene compounds **18** were fully characterized by spectroscopic analyses. In a way similar to that observed for *N*-propargylpyrrole-2-carboxaldehyde derivatives **16**, subsequent heating of functionalized heterodienes **18a**,**b** (R ≠ H) afforded the three-ring heterocycles **19** (Scheme 6, Table 2, entries 12, 13) with the simultaneous formation of two six-membered rings. The two triplets (J = 6.6 Hz) at 3.10 and 4.14 ppm in the ^{1}H NMR spectrum of compound **19b**, corresponding to the two methylene groups of the side chain from the precursor aldehyde **14**, were of diagnostic value. However, pyridine products **21** were isolated when heterodienes **18e**,**f** generated in situ from phosphazenes **1e**,**f** and aldehyde **14** were used (Scheme 7, Table 2, entries 14, 15), as we had previously observed for neutral[13a] and electron-poor 2-azadienes.[10a]

Formation of compounds **21** can be explained in terms of a [4 + 2] cycloaddition of azadienes **18e**,**f** in which one molecule acts as the dienophile and the other as the heterodiene with subsequent aromatization of dimers **20** (Scheme 7).

This strategy can be extended to functionalized indole derivatives to obtain tetracyclic diaza heterocycles. *N*-Propargyl-7-indolecarboxaldehyde **23** was prepared from indole-2-carboxylic acid according to the procedure shown in Scheme 8.

Scheme 9



Treatment of conjugated phosphazene **1b** (R = 2-thienyl, R^1 = Ph) and the aldehyde derived from indole **23** in refluxing toluene yielded functionalized heterodiene **24** (Scheme 9, Table 2, entry 16). Intramolecular aza-Diels–Alder cyclization of azadiene **24** led to the tetracyclic compound **25** (Table 2, entry 17).

Conclusion

In conclusion, we report in this paper applications of this strategy based on tandem reactions: an aza-Wittig reaction of *N*-vinylic phosphazenes with functionalized aldehydes and an IMADA reaction, both of which provide convenient routes to a variety of tricyclic and tetracyclic condensed pyridines. Interestingly, no methods for the synthesis of skeletons of compounds **17**, **19**, and **25** have been previously reported, the synthesis here reported being the first for these types of compounds. These results significantly expand the scope and potential for polyheterocyclic compound synthesis based on intramolecular Diels–Alder reactions. This suggests that the IMADA reaction of these functionalized azadienes may be considered as one of the strategies for the highly efficient multistep synthesis of structurally complex heterocycles possessing useful and interesting properties.

Experimental Section

General Methods. All melting points are uncorrected. Analytical TLC was performed on 0.25 mm silica gel plates. Visualization was accomplished by UV light and iodine. Solvents for extraction and chromatography were technical grade and distilled from the indicated drying agents: CH_2Cl_2 (P_2O_5); *n*-hexane and diethyl ether (sodium benzophenone ketyl); ethyl acetate (K_2CO_3). All solvents used in reactions were freshly distilled from appropriate drying agents before use: $CHCl_3$ (P_2O_5); toluene (CaH_2); dioxane (Na, benzophenone). All other reagents were recrystallized or distilled as necessary. Column (flash) chromatography was carried out on silica gel (70–230 mesh). Mass spectra (EI) were obtained with an ionization voltage of 70 eV. Data are reported in the form *m*/*z* (intensity relative to base = 100). Infrared spectra were taken as neat oils in NaCl or as solids in KBr. Peaks are reported in cm^{-1}. ^1H NMR and ^{13}C NMR spectra were recorded at 300 and 75 MHz, respectively, using tetramethylsilane (0.00 ppm) or chloroform (7.26 ppm) as an internal reference in $CDCl_3$ or D_2O solutions for ^1H NMR, or chloroform (77.0 ppm) as an internal reference in $CDCl_3$ or D_2O solutions for ^{13}C NMR. ^{31}P NMR spectra were recorded at 120 MHz with 85% phosphoric acid as an external reference. Chemical shifts are given in ppm (δ); multiplicities are indicated by s (singlet), d (doublet), dd (double doublet), t (triplet), q (quadruplet), or m (multiplet). Coupling constants, *J*, are reported in hertz. All reactions were performed in oven-dried (125 °C) or flame-dried glassware under an inert atmosphere of dry N_2. Phosphazenes **1** were prepared as described in the literature.[3d,13b]

General Procedure for the Preparation of 2-Azadienes 3, 5, 15, 16, 18, and 24. Aldehyde (5 mmol) was added to a 0–10 °C solution of phosphazene **1** (5 mmol) in $CHCl_3$ or toluene (15 mL) under N_2, and the mixture was refluxed to adequate temperature (see Tables 1 and 2 in main text), until TLC indicated the disappearance of phosphazene. Evaporation of solvent under reduced pressure afforded an oil, which was chromatographed on neutral aluminum oxide to give the 2-azadienes **3**, **5**, **15**, **16**, **18**, and **24**.

(1*E*,3*Z*)-1-(2-Allyloxy-phenyl)-3-(2-furyl)-4-phenyl-2-azabuta-1,3-diene (3a). The general procedure was followed using 1,1,1,4-tetraphenyl-3-(2-furyl)-2-aza-1λ^5-phosphabuta-1,3-diene (2.225 g) and allyloxybenzaldehyde **2** (0.810 g) in $CHCl_3$. Chromatographic separation (5/1, hexane/ethyl acetate) gave 0.691 g (42%) of **3a** as a yellow oil: R_f = 0.36 (1/2, ethyl acetate/hexane); IR (KBr) ν 1623 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.56–4.59 (m, 2H), 5.21–5.37 (m, 2H), 5.92–6.05 (m, 1H), 6.30 (d, 1H, *J* = 3.3 Hz), 6.42 (dd, 1H, *J* = 3.3 Hz, *J* = 1.8 Hz), 6.60 (s, 1H), 6.93–7.60 (m, 9H), 8.28–8.31 (m, 1H), 8.97 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 69.2, 108.1, 111.5, 112.5, 112.6, 117.6–158.8 (m), 160.1; MS (EI) *m*/*z* 329 (M^+, 4). Anal. Calcd for $C_{22}H_{19}NO_2$ (329): C, 80.22; H, 5.81; N, 4.25. Found: C, 80.08; H, 5.89; N, 4.16.

(1*E*,3*Z*)-3-(2-Furyl)-4-phenyl-1-(2-propargyloxy-phenyl)-2-azabuta-1,3-diene (5a). The general procedure was followed using 1,1,1,4-tetraphenyl-3-(2-furyl)-2-aza-1λ^5-phosphabuta-1,3-diene (2.225 g) and propargyloxybenzaldehyde **4** (0.800 g) in $CHCl_3$. Chromatographic separation (5/1, hexane/ethyl acetate) gave 1.186 g (73%) of **5a** as a yellow oil: R_f = 0.61 (1/1, ethyl acetate/hexane); IR (KBr) ν 3304, 1606 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.04 (s, 1H), 4.72 (d, 2H, *J* = 2.4 Hz), 6.28 (d, 1H, *J* = 3.3 Hz), 6.42 (dd, 1H, *J* = 3.3 Hz, *J* = 1.8 Hz), 6.59 (s, 1H), 7.01–8.33 (m, 10H), 8.92 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 56.4, 76.1, 78.0, 108.1–157.6 (m), 159.9; MS (EI) *m*/*z* 327 (M^+, 4). Anal. Calcd for $C_{22}H_{17}NO_2$ (327): C, 80.71; H, 5.20; N, 4.28. Found: C, 80.77; H, 5.16; N, 4.32.

(1*E*,3*Z*)-3-(2-Furyl)-4-phenyl-1-(*N*-allyl-2-pyrrolyl)-2-azabuta-1,3-diene (15). The general procedure was followed using 1,1,1,4-tetraphenyl-3-(2-furyl)-2-aza-1λ^5-phosphabuta-1,3-diene (2.225 g) and 1-(*N*-allyl)pyrrolecarboxaldehyde **12** (0.675 g) in toluene. Chromatographic separation (8/1, hexane/ethyl acetate) gave 0.724 g (48%) of **15** as a yellow oil: R_f = 0.73 (1/1, ethyl acetate/hexane); IR (KBr) ν 1620 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.87–5.22 (m, 4H), 6.02–6.23 (m, 1H), 6.24 (dd, 1H, *J* = 3.3 Hz, *J* = 2.7 Hz), 6.39 (dd, 1H, *J* = 3.3 Hz, *J* = 1.8 Hz), 6.51 (s, 1H), 6.64 (dd, 1H, *J* = 3.9 Hz, *J* = 1.8 Hz), 6.90 (t, 1H, *J* = 1.8 Hz), 7.09–7.56 (m, 7H), 8.22 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 50.8, 108.1, 109.3, 111.4, 111.8, 116.1, 119.8–152.5 (m), 154.9; MS (EI) *m*/*z* 302 (M^+, 40). Anal. Calcd for $C_{20}H_{18}N_2O$ (302): C, 79.44; H, 6.00; N, 9.26. Found: C, 79.53; H, 5.92; N, 9.28.

(1*E*,3*Z*)-3-(2-Furyl)-4-phenyl-1-(*N*-propargyl-2-pyrrolyl)-2-azabuta-1,3-diene (16a) The general procedure was followed using 1,1,1,4-tetraphenyl-3-(2-furyl)-2-aza-1λ^5-phosphabuta-1,3-diene (2.225 g) and 1-(*N*-propargyl)pyrrolecarboxaldehyde **13** (0.660 g) in toluene. Chromatographic separation (5/1, hexane/ethyl acetate) gave 0.780 g (52%) of **16a** as a yellow oil: R_f = 0.51 (1/5, ethyl acetate/hexane); IR (KBr) ν 3292, 1619 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.45 (d, 2H, *J* = 2.6 Hz), 6.21 (dd, 1H, *J* = 3.8 Hz, *J* = 2.7 Hz), 5.25 (d, 1H, *J* = 3.2 Hz), 6.35 (dd, 1H, *J* = 3.3 Hz, *J* = 1.8 Hz), 6.48 (s, 1H), 6.55 (dd, 1H, *J* = 4.0 Hz, *J* = 1.8 Hz), 7.07–7.54 (m, 8H), 8.20 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 38.2, 73.6, 78.8, 108.1–154.9 (m); MS (EI) *m*/*z* 300 (M^+, 80). Anal. Calcd for $C_{20}H_{16}N_2O$ (300): C, 79.98; H, 5.37; N, 9.33. Found: C, 79.89; H, 5.36; N, 9.34.

(1*E*,3*Z*)-1-(*N*-But-3-enyl-2-pyrrolyl)-4-phenyl-3-(2-thienyl)-2-azabuta-1,3-diene (18b). The general procedure was followed using 1,1,1,4-tetraphenyl-3-(2-thienyl)-2-aza-1λ^5-phosphabuta-1,3-diene (2.305 g) and 1-(*N*-but-3-enyl)-pyrrolecarboxaldehyde **14** (0.740 g) in toluene. Chromatographic sepa-

ration (5/1, hexane/ethyl acetate) gave 0.690 g (42%) of **18b** as a yellow oil: $R_f = 0.57$ (1/2, ethyl acetate/hexane); IR (KBr) ν 1618 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.57−2.64 (m, 2H), 4.48−4.60 (m, 2H), 4.99−5.13 (m, 2H), 5.69−5.88 (m, 1H), 6.16−6.21 (m, 1H), 6.43 (s, 1H), 6.48−7.57 (m, 8H), 8.22 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 36.0, 48.4, 108.9, 113.7, 117.3, 119.4−148.5 (m), 154.6; MS (EI) *m*/*z* 332 (M$^+$, 12). Anal. Calcd for $C_{21}H_{20}N_2S$ (332): C, 75.87; H, 6.06; N, 8.43; S, 9.64. Found: C, 76.09; H, 5.96; N, 8.34; S, 9.57.

(1*E*,3*Z*)-4-Phenyl-1-(*N*-propargyl-2-indolyl)-3-(2-thienyl)-2-azabuta-1,3-diene (24). The general procedure was followed using 1,1,1,4-tetraphenyl-3-(2-thienyl)-2-aza-1λ^5-phosphabuta-1,3-diene (2.305 g) and 1-(*N*-propargyl)-2-indolecarboxaldehyde **23** (0.910 g) in toluene. Chromatographic separation (5/1, hexane/ethyl acetate) gave 0.960 g (51%) of **24** as a yellow oil: $R_f = 0.57$ (1/2, ethyl acetate/hexane); IR (KBr) ν 3397, 1626 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.34 (s, 1H), 5.81−5.86 (m, 3H), 6.52 (s, 1H), 6.90−7.66 (m, 12H), 8.48 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.4, 72.2, 79.2, 110.3−143.9 (m), 155.9; MS (EI) *m*/*z* 366 (M$^+$, 10). Anal. Calcd for $C_{24}H_{18}N_2S$ (366): C, 78.65; H, 4.95; N, 7.64; S, 8.75. Found: C, 78.89; H, 5.06; N, 7.73; S, 8.63.

General Procedure for Intramolecular [4 + 2] Cycloaddition Reaction of 2-Azadienes. A 2-azadiene (**3**, **5**, **15**, **16**, **18**, **24**) (5 mmol) solution in xylenes (20 mL) was stirred at reflux (see Tables 1 and 2 in main text) until TLC indicated the total disappearance of 2-azadiene. The crude of the reaction was chromatographed on silica gel to give compounds **6**, **17**, **19**, **21**, and **25**.

2-(2-Furyl)-3-phenyl-5*H*-benzopyrano[4,3-*b*]pyridine (6a). The general procedure was followed using (1*E*,3*Z*)-1-(2-allyloxy-phenyl)-3-(2-furyl)-4-phenyl-2-azabuta-1,3-diene (**3a**) (1.640 g), and isolation of the reaction compound by chromatographic separation (5/1, hexane/ethyl acetate) gave 0.650 g (40%) of **6a** as a yellow solid, mp 92−93 °C. The same compound **6a** was obtained using (1*E*,3*Z*)-3-(2-furyl)-1-(2-propargyloxy-phenyl)-4-phenyl-2-azabuta-1,3-diene (**5a**) (1.62 g) in 60% yield (0.98 g): IR (KBr) ν 1490 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.26 (s, 2H), 6.28 (d, $J = 3.0$ Hz, 1H), 6.33 (s, 1H), 6.97−7.42 (m, 10H), 8.88 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 67.6, 111.2−156.4 (m); MS (EI) *m*/*z* 325 (M$^+$, 100). Anal. Calcd for $C_{22}H_{15}NO_2$ (325): C, 81.21; H, 4.65; N, 4.30. Found: C, 81.19; H, 4.66; N, 4.34.

2-(2-Furyl)-3-phenyl-5*H*-pyrido[2,3-*a*]pyrrolizine (17a). The general procedure was followed using (1*E*,3*Z*)-1-(2-allylpyrrolyl)-3-(2-furyl)-4-phenyl-2-azabuta-1,3-diene (**15**) (1.510 g), and isolation of the reaction compound by chromatographic separation (5/1, hexane/ethyl acetate) gave 0.74 g (50%) of **17a** as a white solid, mp 105−106 °C. The same compound **17a** was obtained using (1*E*,3*Z*)-3-(2-furyl)-4-phenyl-1-(*N*-propargyl-2-pyrrolyl)-2-azabuta-1,3-diene (**16a**) (1.500 g) in 70% yield (1.04 g): IR (KBr) ν 1432 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.87 (s, 2H), 5.93−7.39 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 48.4, 101.6−152.5 (m); MS (EI) *m*/*z* 298 (M$^+$, 100). Anal. Calcd for $C_{20}H_{14}N_2O$ (298): C, 80.52; H, 4.73; N, 9.38. Found: C, 80.39; H, 5.06; N, 9.44.

3-Phenyl-2-(2-thienyl)-5*H*,6*H*-pyrido[3,2-*g*]indolizine (19b). The general procedure was followed using (1*E*,3*Z*)-4-phenyl-1-(*N*-but-3-enyl-2-pyrrolyl)-3-(2-thienyl)-2-azabuta-1,3-diene (**18b**) (1.660 g), and isolation of the reaction compound by chromatographic separation (5/1, hexane/ethyl acetate) gave 1.110 g (68%) of **19b** as a yellow solid: mp 123−124 °C; IR (KBr) ν 1575 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.10 (t, $J = 6.6$ Hz, 2H), 4.14 (t, $J = 6.6$ Hz, 2H), 6.29 (dd, $J = 3.9$ Hz, $J = 2.7$ Hz, 1H), 6.55 (d, $J = 3.9$ Hz, 1H), 6.74−7.76 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.1, 43.8, 107.5, 109.5, 117.6−140.3 (m); MS (EI) *m*/*z* 328 (M$^+$, 100). Anal. Calcd for $C_{21}H_{16}N_2S$ (328): C, 76.80; H, 4.91; N, 8.53. Found: C, 77.39; H, 4.86; N, 8.50.

2-(1-But-3-enyl-1*H*-pyrrol-2-yl)-3,5-diphenylpyridine (21e). The general procedure was followed using 4-phenyl-1-(*N*-but-3-enyl-2-pyrrolyl)-2-azabuta-1,3-diene (**18e**) (1.250 g), and isolation of the reaction compound by chromatographic separation (5/1, hexane/ethyl acetate) gave 1.050 g (60%) of **21e** as a yellow oil: $R_f = 0.39$ (1/5, ethyl acetate/hexane); IR (KBr) ν 1434, 1248 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.25−2.32 (m, 2H), 4.03 (t, $J = 6.7$ Hz, 2H), 4.91−4.98 (m, 2H), 5.54−5.69 (m, 1H), 5.80 (dd, $J = 3.7$ Hz, $J = 1.1$ Hz, 1H), 5.95 (dd, $J = 3.7$ Hz, $J = 2.6$ Hz, 1H), 6.61 (d, $J = 1.7$ Hz, 1H), 7.20−7.70 (m, 9H), 7.83 (d, $J = 2.3$ Hz, 1H), 8.81 (d, $J = 2.0$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 35.6, 47.3, 107.5, 113.2, 116.7, 122.8, 126.9−137.4 (m), 140.1, 146.1, 149.1; MS (EI) *m*/*z* 350 (M$^+$, 50). Anal. Calcd for $C_{25}H_{22}N_2$ (350): C, 85.68; H, 6.33; N, 7.99. Found: C, 85.39; H, 6.30; N, 7.87.

8-Phenyl-9-(2-thienyl)-10-aza-5*H*,6*H*-indeno[2,1-*a*]indole (25). The general procedure was followed using (1*E*,3*Z*)-4-phenyl-1-(*N*-propargyl-2-indolyl)-3-(2-thienyl)-2-azabuta-1,3-diene (**24**) (1.830 g), and isolation of the reaction compound by chromatographic separation (5/1, hexane/ethyl acetate) gave 1.240 g (68%) of **25** as a yellow solid: mp 151−152 °C; IR (KBr) ν 1422 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.02 (s, 2H), 6.65−7.75 (m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 46.7, 109.2−151.6 (m); MS (EI) *m*/*z* 364 (M$^+$, 100). Anal. Calcd for $C_{24}H_{16}N_2S$ (364): C, 79.09; H, 4.42; N, 7.69; S, 8.80. Found: C, 79.19; H, 4.36; N, 7.64; S, 8.81.

General Procedure for RuO_4 Oxidations. To a solution of 5*H*-benzopyrano[4,3-*b*]pyridine (**6**) (1 mmol) in CH_3CN (2 mL) were added 2 mL of CCl_4, 3 mL of H_2O, and 877 mg (4.1 mmol) of $NaIO_4$. The biphasic mixture was vigorously stirred, and 5 mg of $RuCl_3 \cdot H_2O$ (2.2%) was added in one portion. After 60 min the mixture was diluted with 25 mL of CH_2Cl_2, and the supernatant organic layer was decanted carefully; this operation was repeated three times. The combined organic layers were treated with Na_2SO_4 and concentrated under reduced pressure. The residue was disolved in 15 mL of ether and treated with a solution of freshly prepared diazomethane in ether. The reaction mixture was stirred until the yellow color of diazomethane disappeared. The mixture was washed with brine, the aqueous layer was extracted with ether (2 × 20 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The solid was purified by flash chromatography (SiO_2, hexane/EtOAc).

3,4-Diphenyl-5-oxo-benzopyrano[4,3-*b*]pyridine (9). The general procedure was followed using 2,3-diphenyl-5*H*-benzopyrano[4,3-*b*]pyridine (**6b**) (0.340 g), and isolation of the reaction compound by chromatographic separation (5/1, hexane/ethyl acetate) gave 0.290 g (83%) of **9** as a white solid: mp 160−162 °C; IR (KBr) ν 1725, 1420 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15−8.71 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 115.6, 117.1, 119.3, 124.7−163.0 (m); MS (EI) *m*/*z* 349 (M$^+$, 60). Anal. Calcd for $C_{24}H_{15}NO_2$ (349): C, 82.50; H, 4.33; N, 4.01. Found: C, 82.19; H, 4.36; N, 4.04.

Methyl-3-phenyl-5-oxo-benzopyrano[4,3-*b*]pyridine-2-carboxylate (10). The general procedure was followed using 2-(2-furyl)-3-phenyl-5*H*-benzopyrano[4,3-*b*]pyridine (**6a**) (0.320 g), and isolation of the reaction compound by chromatographic separation (5/1, hexane/ethyl acetate) gave 0.260 g (80%) of **10** as a yellow solid: mp 160−161 °C; IR (KBr) ν 1739, 1421 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.7 (s, 3H), 7.19−8.65 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 52.8, 117.2−166.9 (m); MS (EI) *m*/*z* 331 (M$^+$, 80). Anal. Calcd for $C_{20}H_{13}NO_4$ (331): C, 72.50; H, 3.95; N, 4.23. Found: C, 72.19; H, 4.06; N, 4.34.

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Supporting Information Available: Preparation, elemental analysis, and spectral data (^{1}H NMR, ^{13}C NMR, IR, and MS) for 2-azadienes **3c**,**d**, **5b**−**f**, **16c**,**e**,**f**, and **18a**,**e**,**f** and compounds **6b**−**f**, **17c**, **19a**, and **21f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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