On the Reactions of (Vinylimino)phosphoranes and Related Compounds. 27.[1] A Short New Synthesis of Azuleno[2,1-*b*]pyridines and Azuleno-Annulated [*n*](2,4)Pyridinophanes

Makoto Nitta,* Takuya Akie, and Yukio Iino

Department of Chemistry, School of Science and Engineering, Waseda University, Shinjuku-ku, Tokyo 169, Japan

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A short new synthesis of azuleno[2,1-*b*]pyridines **6a–g** consists of the reaction of 2-aminoazulene (**4**) with acyclic α,β-unsaturated ketones and aldehydes in an enamine-alkylation process, subsequent condensation of the amino group with a carbonyl function, and dehydrogenation in the presence of Pd/C. Similarly, the reaction of **4** with α,β-unsaturated cycloalkenones gives azuleno-annulated [*n*](2,4)pyridinophanes **12a–c** (*n* = 9–7) and dihydrogenated analogue **11d** (*n* = 6). Compound **11d** is converted to azuleno-annulated [6](2,5)pyridinophane **12d** by treatment with DDQ. ^{1}H NMR spectroscopy at various temperatures shows dynamic behavior for the oligomethylene chains of [7]- and [6](2,4)pyridinophanes **12c,d**. The energy barriers ($\Delta G_c^{\ddagger}$) for the bridge flipping are 10.8 kcal/mol (T_c, −30 °C) for **12c** and 18.1 kcal/mol (T_c, 90 °C) for **12d**. Although the strain of **12c,d** increases as the chainlength becomes shorter, the pyridine ring of **12c,d** can flex more easily than that of the corresponding unannulated [*n*](2,4)pyridinophanes. The deformation of the pyridine ring of **12a–d** is also suggested by red shifts of the UV and ^{1}H NMR spectra. The pK_a values of **12a–d** are independent of the size of the methylene bridge, suggesting that the energy differences between the protonated and nonprotonated forms are almost the same for **12a–d**.

The chemistry of small-bridged aromatic cyclophanes and heterophanes has been studied extensively.[2] Recent studies of these strained molecules have been focused on more sophisticated molecular orbital calculations,[3] the challenging synthesis of [5]paracyclophane,[4] and the spectroscopic characterization of [4]paracyclophane.[5] Although there have been many studies of paracyclophanes,[4,5] their areno-annulated derivatives,[6] and metacyclophanes,[7] little is known of small-bridged heterophanes. We have previously reported the convenient synthesis and spectroscopic properties of [*n*](2,5)pyridinophanes (parapyridinophane) **1** (*n* = 10, 8–6)[8] and [*n*](2,4)pyridinophanes (metapyridinophane) **2** (*n* = 9–6),[9] and the static and dynamic behaviors of the latter ring system have been studied. The metapyridinophanes with the smallest methylene bridge are 3-chloro[6](2,4)pyridinophane[10] and its benzo derivatives[11] and [6](2,6)pyridinophane.[11]

Recently, we have reported the reactions of novel 2-(phosphoranylideneamino)azulene **3a** and its aza analogue **3b** (Figure 1) with 2-halotropones to give 6-aza- and 6,7-diazaazuleno[1,2-*a*]azulenes in a single step.[13] Compounds **3a,b** as well as a 1,6-methano[10]annulene bearing a phosphoranylideneamino group,[14] are the first examples of (vinylimino)phosphoranes, in which the vinyl group is a part of the aromatic ring. When allowed to react with 2-halotropones, **3a,b** underwent an "enamine-type alkylation" and subsequent aza-Wittig reaction. When (phosphoranylideneamino)benzene was allowed to react with chalcone, however, an aza-Wittig reaction to give chalcone anil[14b] occurred, and no enamine-type alkylation was observed. The enhanced reactivities of **3a,b** and (phosphoranylideneamino)-1,6-methano[10]annulene were ascribed to the small resonance energies (resonance energy per electron REPE) of the azulene (12.8 kcal/mol; REPE = 1.28 kcal/mol) and 1,6-methano[10]annulene (17.5 kcal/mol; REPE = 1.75 kcal/mol) as compared to that of benzene (25.9 kcal/mol; REPE = 4.32 kcal/mol).[15] Although (vinylimino)phosphoranes are considered to be equivalents of primary enamines, which are generally unstable and undergo a rapid conversion to the imine tautomer, aromatic amines are widely available. The present study was focused on the enamine alkylation and subsequent con-

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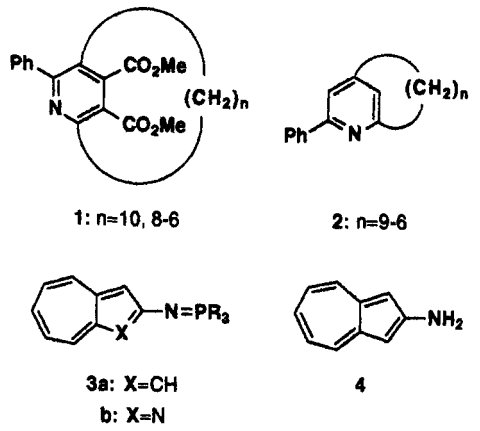
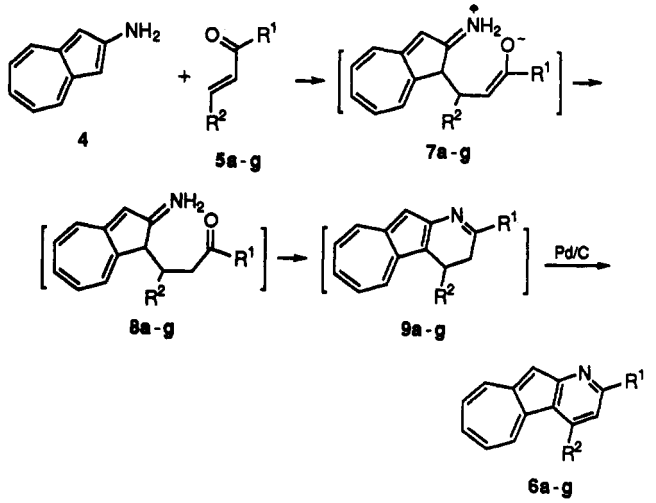


Figure 1.

Scheme 1



a: $R^1 = R^2 = Ph$; b: $R^1 = Me$, $R^2 = Ph$; c: $R^1 = R^2 = Me$; d: $R^1 = Ph$, $R^2 = H$; e: $R^1 = Me$, $R^2 = H$; f: $R^1 = H$, $R^2 = Ph$; g: $R^1 = H$, $R^2 = Me$

densation of 2-aminoazulene (4).[16] We describe here the novel reactions of 4 with acyclic α,β-unsaturated ketones and aldehydes and α,β-unsaturated cycloalkenones to give azuleno[2,1-*b*]pyridines and azuleno-annulated [*n*](2,4)-pyridinophanes (n = 9–6). The static and dynamic behaviors of the azuleno-annulated [7]- and [6](2,4)-pyridinophanes are also studied.

Results and Discussion

A. Preparation of Azuleno[2,1-*b*]pyridines and Azuleno-Annulated [*n*](2,4)-Pyridinophanes. Thermal reactions of 4[16] with α,β-unsaturated ketones **5a–e** and aldehydes **5f,g** in refluxing dry xylene in the presence of a catalytic amount of Pd/C gave azuleno[2,1-*b*]pyridines **6a–g** in a single step (Scheme 1). The reaction conditions and the yields of the products are listed in Table 1. Structures of compounds **6a–g** were deduced from their spectral data and elemental analyses (or high-resolution mass spectral data). All the ^{1}H NMR spectra of **6a–g** correlated well with each other and were in good accordance with the proposed structures. The postulated reaction pathway for the formation of **6a–g**, which is similar to that for (vinylimino)phosphoranes, is shown in Scheme 1.[13,14b] Enamine alkylation of 4 by the β-carbon atom of

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Table 1. Reactions of 4 with 5a–g[a]

enone				
compd	R^1	R^2	reactn time/h	product yield[b]/%
5a	Ph	Ph	17	**6a**, 56
5b	Me	Ph	23	**6b**, 37
5c	Me	Me	14	**6c**, 31
5d	Ph	H	2	**6d**, 37
5e	Me	H	2	**6e**, 58
5f	H	Ph	23	**6f**, 8
5g	H	Me	19	**6g**, 11

[a] All the reactions were carried out in refluxing xylene. [b] Yields of the products are based on the amount of 4 used.

Scheme 2

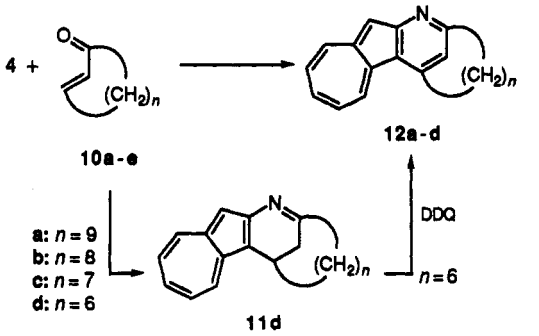

Table 2. Reactions of 4 with 10a–d

enone			
compd	[*n*]	reactn time/h	product yield/%
10a	9	16	**12a**, 43
10b	8	24	**12b**, 37
10c	7	24	**12c**, 37
10d	6	7	**12d**, 34[a] (86)[b]

[a] Overall yield obtained by dehydrogenation of isolated **11d** with DDQ. [b] Yield of isolated **11d**.

5a–g gave **7a–g**. The subsequent hydrogen migration in **7a–g** regenerated the 2-aminoazulene moiety in **8a–g**, which then underwent an intramolecular condensation to produce dihydropyridines **9a–g**. Dehydrogenation of **9a–g** with Pd/C under the reaction conditions resulted in the formation of **6a–g**.

Similarly, the reaction of 4 with 2-cycloalkenones **10a–d** (n = 9–6) in xylene afforded 2,4-polymethylene-substituted azuleno[2,1-*b*]pyridines (azuleno-annulated [*n*](2,4)-pyridinophanes) **12a–c** and dihydrogenated analogue **11d** (Scheme 2). The reaction conditions and the yields of the products are also summarized in Table 2. The reaction pathway for the formation of **12a–c** is considered to be similar to that shown in Scheme 1; however, intermediate **11d**, which has a hexamethylene bridge, was resistant to dehydrogenation in the presence of Pd/C under the reaction conditions. This fact indicates a high degree of ring strain in the hexamethylene bridge. Compound **11d** was dehydrogenated by treatment with DDQ followed by DBU to give **12d** in 40% yield. Although [5]paracyclophanes have been successfully prepared,[4] there are no known pyridinophanes or annulated pyridinophanes with five-methylene bridges. Thus, our attempted synthesis of azuleno-annulated [5](2,4)pyridinophane was unsuccessful at this stage. Compounds **12a–d** and **11d** were characterized on the basis of their spectral properties and microanalyses (or high-resolution mass spectral data).

B. Deformation of the Pyridine Ring. The ^{1}H NMR spectral data of **12a–d** and **6c** are listed in Table 3 (see the convenient numbering of the methylene illustrated in

Table 3. ^{1}H NMR (400 MHz, $CDCl_3$) Spectral Data (δ/ppm) for 6c and 12a–c[a,b]

compd	δ_{av}	pyridine δ H-3	benzylic δ H-1′	benzylic δ H-n′	remaining methylene bridge
6c	7.58[c]	7.05	2.78 (3H, s)	2.93 (3H, s)	none
12a	7.60[c]	7.27	3.11 (2H, dd, J = 6.8, 6.4 Hz)	3.43 (2H, dd, J = 6.4, 6.3 Hz)	0.87–0.93 (4H, m), 1.04–1.19 (6H, m), 1.86–1.95 (2H, m), 1.95–2.11 (2H, m)
12b	7.60[c]	7.32	3.06 (2H, dd, J = 6.4, 5.9 Hz)	3.40 (2H, dd, J = 6.4, 5.9 Hz)	0.66–0.75 (2H, m), 0.81–0.91 (2H, m), 1.02–1.12 (2H, m), 1.12–1.22 (2H, m), 1.71–1.81 (2H, m), 1.81–1.89, (2H, m)
12c	7.62[c]	7.49	3.07 (2H, t, J = 5.9 Hz)	3.38–3.52 (2H, m)	−0.23 to −0.66 (2H, broad s, H-4′), 1.41–1.54 (4H, m), 1.58–1.68 (2H, m), 1.68–1.78 (2H, m)
12d	7.62[c]	7.32	2.93 (1H, ddd, J = 12.7, 5.4, 4.4 Hz), 3.15 (1H, ddd, J = 12.7, 8.8, 6.3 Hz)	3.27 (1H, ddd, J = 14.2, 6.8, 6.4 Hz), 3.65 (1H, ddd, J = 14.2, 6.8, 6.4 Hz)	−0.03 to −0.21 (1H, br s), 0.60–0.87 (1H, br s), 1.18–1.32 (1H, m), 1.32–1.44 (1H, m), 1.59–1.73 (1H, m), 1.85–2.03 (3H, m)

[a] The ^{1}H NMR spectral data (δ/ppm) for the protons on the azulene nuclei of 6c and 12a–d are summarized in the Experimental Section. [b] Numbering of the methylene bridge for 12a–d is depicted in Figure 2. [c] Average chemical shift of protons on the azulene moiety.

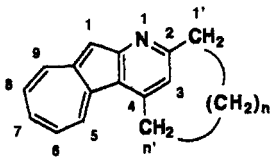

Figure 2. Numbering of the methylene bridge of 12.

Figure 2). Although the spectral data of **6a–f** are similar, the average chemical shift (δ_{av} = 7.58) of the azulene moiety of **6c** is downfield compared to those of azulene (δ_{av} = 7.42)[16,17] and benz[*a*]azulene (δ_{av} = 7.36).[18] This fact is indicative of the electron-withdrawing property of the pyridine ring. The average chemical shifts of the azulene moieties of **12a–d** (δ_{av}) (Table 3) are similar to that of **6c**, but a subtle downfield shift is observed as the methylene bridge becomes short. The distortion of the pyridine ring is reflected remarkably in the chemical shifts of the protons on the ring.[8,19] The H-3 signals in **12a–c** shift downfield as the methylene bridge becomes short. This behavior is attributable to steric compression between H-3 and the methylene chain of **12a–c**.[7a] In contrast, the corresponding signal in **12d** appears at a higher field than that of **12c**. This fact is mainly ascribed to reduced ring current in the strained pyridine ring of **12d** rather than steric compression.

The deformation of the aromatic rings in cyclophanes is evaluated by the red shift of the UV spectra.[20] The UV spectra of **12a–d** and **6c** summarized in Table 4 indicate that the absorption maximum of the pyridinophanes gradually shift to a longer wavelength as the methylene chain becomes short. The longest absorption maximum of **12d**, which has the smallest [*n*] value, has a wavelength 18 nm longer than that of **6c**. Consequently, **12d** has the most deformed pyridine ring in the series **12a–d**.

C. Conformational Studies of Azuleno-Annulated [*n*](2,4)Pyridinophanes. The dynamic behavior of **12a–d** is also interesting because no annulated [*n*](2,4)-pyridinophanes have been previously synthesized. A characteristic feature of **12a–c** is the equivalence of the geminal protons at the "benzylic" positions, H-1′ and H-*n*′ (Figure 2). These protons appear as two doublets of doublets or as a triplet and a multiplet. This splitting pattern is indicative of a rapid flipping of the methylene bridge of **12a-c** at room temperature. The ^{1}H NMR spectra of **12c** at variable temperatures are depicted in Figure 3. At 40 °C, the proton signal of H-4′x and H-4′y appears as a singlet at δ −0.49 because of a rapid flipping of the heptamethylene chain (Figure 4). The signal disappears at −30 °C, and the signals of H-4′x in conformer **A** [or H-4′y in **B**] and H-4′y in conformer **A** [or H-4′x in **B**] reappear at δ −1.12 and δ 0.83, respectively. Furthermore, the benzylic protons H-7′ appear as two distinct signals. These observations suggest that each of the geminal protons is located in a different environment and that the bridge flipping is frozen on the NMR time scale. By the coalescence temperature method[21] the energy barrier $\Delta G_c^{\ddagger}$) of the conformational change between **A** and **B** of **12c** was estimated to be 10.8 kcal/mol (T_c = −30 °C). In contrast, the four benzylic protons of **12d** exhibited different chemical shifts (Table 3), suggesting that the flipping of the hexamethylene chain is slow at room temperature. An increase in temperature provides a clear indication for the coalescence of H-6′ as well as H-3′ at 90 °C (Figure 5). Each signal becomes a singlet at 140 °C, indicating the bridge flipping of **12d** (Figure 4). The $\Delta G_c^{\ddagger}$ value for **12d** was also estimated to be 18.1 kcal/mol (T_c = 90 °C). The lower values of $\Delta G_c^{\ddagger}$ for **12c** and **12d** as compared to those of **2** (*n* = 7 and 6) (Table 5) suggest that the pyridine rings of **12c,d** can flex more easily than that of **2**.

D. Basicity of Azuleno-Annulated [*n*](2,5)-Pyridinophanes. The basicity of amine is determined by the availability of the lone pair electron on the nitrogen (Scheme 3). When **6c** and **12a–d** were protonated, their electronic spectra changed; each absorption maximum was shifted to a shorter wavelength (Table 4). This shift implies protonation of the nitrogen atom of **12a–d** and suggests the enhanced electron-withdrawing properties of the resulting pyridinium ion in **13a–d**.[22] Only a few studies of correlation between the base strength and deformation of the pyridine ring[11] have appeared. The basicities of **6c** and **12a–d** (that is, the acidities (pK_a) of their conjugate acids) were determined, and the results, along with the data reported[11] for **14** (*n* = 9 and 6) and 3-chloro-2,4-dimethylquinoline (**15**) (Figure 6), are summarized in Table 6. The results suggest that the defor-

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Table 4. UV–vis Spectral Data of 6c and 12a–d

compd	[n]	solvent	λ_{max}/nm (log ε)
6c		EtOH	312 (4.72), 343 (3.53), 361 (3.70), 380 (3.79), 402 (3.65), 526 (2.37), 568 (2.42), 620 (2.27), 682 (1.75)
		EtOH–CF_3CO_2H	303 (4.61), 318 (4.59), 332 (4.54), 399 (3.96), 423 (4.12), 494 (2.66), 532 (2.67), 574 (2.53)
12a	9	EtOH	316 (4.72), 345 (3.58), 363 (3.70), 383 (3.76), 405 (3.57), 530 (2.35), 572 (2.39), 624 (2.25), 685 (1.73)
		EtOH–CF_3CO_2H	308 (4.59), 321 (4.60), 336 (4.57), 401 (3.95), 426 (4.12), 493 (2.65), 535 (2.64), 579 (2.51)
12b	8	EtOH	316 (4.70), 346 (3.53), 364 (3.66), 384 (3.71), 406 (3.51), 531 (2.35), 573 (2.39), 626 (2.25), 695 (1.73)
		EtOH–CF_3CO_2H	308 (4.57), 321 (4.58), 334 (4.56), 400 (3.92), 425 (4.10), 493 (2.65), 536 (2.65), 579 (2.52)
12c	7	EtOH	317 (4.72), 349 (3.58), 367 (3.70), 387 (3.73), 408 (3.48), 534 (2.35), 574 (2.39), 627 (2.25), 697 (1.72)
		EtOH–CF_3CO_2H	309 (4.57), 322 (4.61), 336 (4.61), 401 (3.97), 427 (4.14), 495 (2.65), 535 (2.65), 579 (2.52)
12d	6	EtOH	320 (4.71), 355 (3.51), 373 (3.61), 393 (3.61), 415 (3.24), 540 (2.30), 578 (2.37), 632 (2.24), 700 (1.71)
		EtOH–CF_3CO_2H	311 (4.51), 326 (4.57), 339 (4.60), 405 (3.94), 430 (4.09), 502 (2.63), 540 (2.65), 583 (2.53)

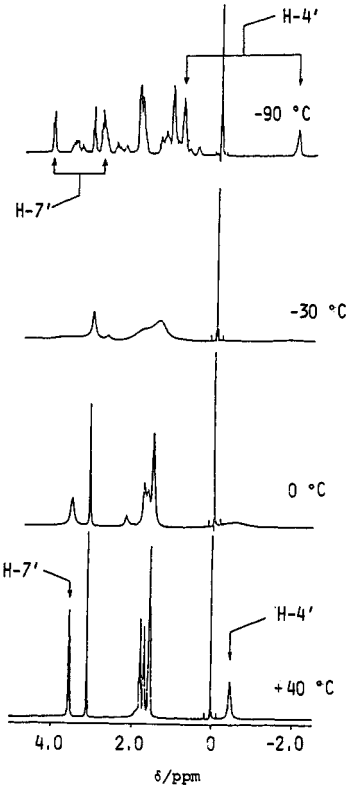


Figure 3. ^1H NMR (400 MHz) spectra of 12c in CD_2Cl_2 at various temperatures.

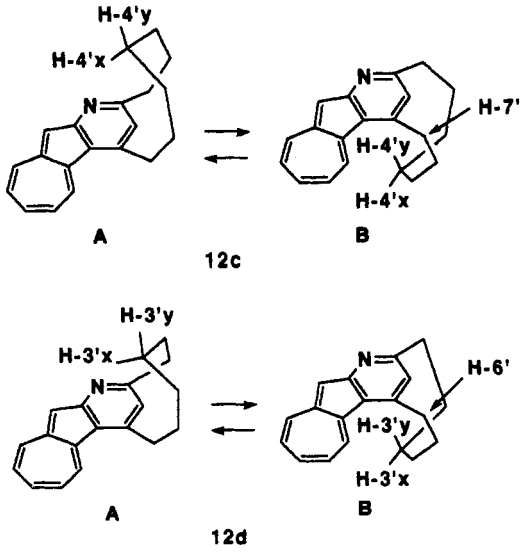


Figure 4. Flipping of the methylene bridge of 12c,d.

mation of the pyridine ring does not affect the basicity. The pK_a values in 6c and 12a–d seem to be similar to that of 2,4-dimethylpyridine,[23] and the energy differences between the protonated and nonprotonated forms seem to be independent of the size of the methylene bridge.

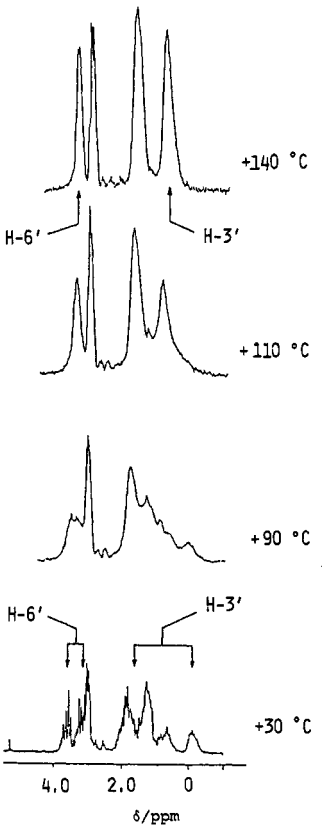


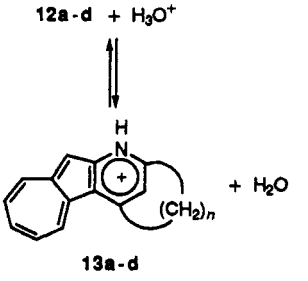
Figure 5. ^1H NMR (90 MHz) spectra of 12d in tetrachloroethylene at various temperatures.

Table 5. Energy Barrier ($\Delta G_c^{\ddagger}$) of the Bridge Flipping of 12c,d and 2

[n]	12[a]	2[b]
7	10.8 kcal/mol (−30 °C)	12–13 kcal/mol (20 °C)
6	18.1 kcal/mol (90 °C)	21–22 kcal/mol (150 °C)

[a] This work. [b] Reference 9.

Scheme 3



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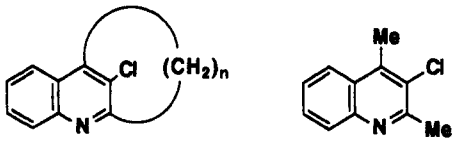

14a: n=10; b: n=6 15

Figure 6. Known quinolinophanes and reference compound.

Table 6. pK_a Values of 12c,d 14a,b, and Reference Compounds 6c and 15

[n]	12[a]	6c[a]	14[b]	15[b]
		6.63		3.04 ± 0.03
10			2.88 ● 0.03	
9	6.46			
8	6.50			
7	6.47			
6	6.64		3.03 ± 0.03	

[a] This work. [b] Reference 11.

Concluding Remarks

Of the four types of pyridines annulated at the five-membered ring of azulene, azuleno[2,1-*b*]-[24] and azuleno-[1,2-*b*]pyridines[25] are known as their derivatives, and azuleno[2,1-*c*]- and azuleno[1,2-*c*]pyridines are known in their unsubstituted forms.[26] This work shows for the first time that easily accessible 2-aminoazulene, an aromatic amine, reacts with α,β-unsaturated carbonyl compounds in an enamine-alkylation process followed by condensation and dehydrogenation to give azuleno[2,1-*b*]pyridine ring systems, including azuleno-annulated [*n*](2,5)pyridinophanes. The facile enamine-type alkylation process is ascribed to the small resonance energy of the azulene.[15] The barriers for the bridge flipping of azuleno-annulated [7]- and [6](2,4)pyridinophanes suggest that they are constrained, but their bridges can flex more easily than those of the corresponding phenyl-substituted but unannulated pyridinophanes.[9] Further studies are underway to explore the scope and limitations of this enamine-type alkylation process, which is also involved in (vinylimino)-phosphoranes,[9,13,14] and to find further useful applications of this method for the preparation of nitrogen heterocycles of theoretical interest and demonstrated utility.

Experimental Section

General Methods. General experimental conditions and spectroscopic instrumentation used have been described.[9,14]

Materials. 2-Aminoazulene (**4**),[16] *trans*-2-cyclododecenone (**10a**), *cis*-2-cyclononenone (**10d**), and cis–trans mixtures of 2-cycloundecenone (**10b**) and 2-cyclodecenone (**10c**) were prepared as described previously.[10]

General Procedure for the Reactions of 4 with 5a–g. A solution of **4** (72 mg, 0.5 mmol), **5a–g** (1 mmol), and 10% Pd/C (25 mg) in dry xylene (5 mL) was refluxed for the period indicated in Table 1. After the reaction was complete, the reaction mixture was chromatographed on silica gel. The fractions eluted with benzene were concentrated and separated by preparative TLC on silica gel (3:1 benzene–ethyl acetate) to give azuleno[2,1-*b*]-pyridines **6a–g**. The results are summarized in Table 1.

6a: mp 195–196 °C (from benzene–hexane); ^{1}H NMR (90 MHz, $CDCl_3$) δ 6.63–7.31 (3H, m), 7.37–7.68 (4H, m), 7.58 (5H, s), 7.65 (1H, s), 7.80 (1H, d, J = 8.6 Hz), 8.10 (1H, d, J = 10.8 Hz), 8.07–8.28 (2H, m); IR ($CHCl_3$) 1589, 1545 cm^{-1}; UV (EtOH) λ_{max} (log ϵ) 328 (4.78), 372 (3.82), 394 (3.76), 534 (2.42), 585 (2.42), 633 (2.35), 707 (1.89) nm; UV (EtOH–CF_3CO_2H) λ_{max} (log ϵ) 356 (4.65), 412 (3.99), 437 (4.02), 506 (2.82), 547 (2.88), 594 (2.91), 647 (2.48) nm; MS *m/z* (rel intensity) 331 (M$^+$, 40), 164 (100). Anal. Calcd for $C_{25}H_{17}N$: C, 90.60; H, 5.17; N, 4.23. Found: C, 90.57; H, 5.20; N, 4.10.

6b: oil; ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.80 (3H, s), 6.58–725 (3H, m), 7.03 (1H, s), 7.49 (6H, s), 7.76 (1H, d, J = 8.6 Hz), 8.05 (1H, d, J = 10.1 Hz); IR ($CHCl_3$) 1588, 1543 cm^{-1}; MS *m/z* (rel intensity) 269 (M$^+$, 100). Picrate of **6b**: mp 207–208 °C (from EtOH). Anal. Calcd for $C_{26}H_{18}N_2O_4$: C, 62.65; H, 3.64; N, 11.24. Found: C, 62.54; H, 3.59; N, 11.18.

6c: mp 125–126 °C (from benzene–hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.78 (3H, s), 2.93 (3H, s), 6.99 (1H, dd, J = 10.7, 8.8 Hz), 7.05 (1H, s), 7.14 (1H, dd, J = 8.8, 11.2 Hz), 7.28 (1H, dd, J = 11.2, 8.8 Hz), 7.47 (1H, s), 8.10 (1H, s, J = 10.7 Hz), 8.41 (1H, d, J = 8.8 Hz); ^{13}C NMR (100.60 MHz, $CDCl_3$) δ 21.9, 25.0, 116.4, 116.5, 120.2, 120.2, 120.6, 125.1, 126.1, 132.6, 134.9, 136.4, 139.3, 142.2, 143.4, 159.1, 159.3; IR ($CHCl_3$) 1587, 1561 cm^{-1}; MS *m/z* (rel intensity) 207 (M$^+$ 100). Anal. Calcd for $C_{15}H_{13}N$: C, 86.92; H, 6.32; N, 6.76. Found: C, 86.92; H, 6.40; N, 6.69.

6d: dark green needles; mp 215–216 °C (from $CHCl_3$); ^{1}H NMR (90 MHz, $CDCl_m$) δ 6.85–7.35 (3H, m), 7.35–7.60 (4H, m), 7.83 (1H, d, J = 8.4 Hz), 8.00–8.35 (4H, m), 8.63 (1H, d, J = 8.1 Hz); IR ($CHCl_3$) 1590, 1579, 1558 cm^{-1}; UV (EtOH) λ_{max} (log ϵ) 327 (4.81), 372 (3.84), 392 (3.77), 543 (2.21), 585 (2.20), 637 (2.09), 710 (1.63) nm; UV (EtOH–CF_3CO_2H) λ_{max} (log ϵ) 352 (4.50), 410 (3.86), 436 (3.91), 507 (2.63), 549 (2.68), 594 (2.68), 650 (2.25) nm; MS *m/z* (rel intensity) 255 (M$^+$, 100); HRMS *m/z* 255.1063, calcd for $C_{19}H_{13}N$ 255.1049.

6e: oil; ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.81 (3H, s), 6.93–7.02 (1H, m), 7.02–7.12 (1H, m), 7.12–7.31 (1H, m), 7.23 (1H, d, J = 7.9 Hz), 7.43 (1H, s), 8.10 (1H, d, J = 10.1 Hz), 8.29 (1H, d, J = 7.5 Hz), 8.46 (1H, d, J = 8.1 Hz); IR ($CHCl_3$) 1580 1400 cm^{-1}; MS *m/z* (rel intensity) 193 (M$^+$, 100); HRMS *m/z* 193.0924, calcd for $C_{14}H_{11}N$ 193.0891.

6f: oil; ^{1}H NMR (90 MHz, $CDCl_3$) δ 6.62–7.50 (3H, m), 7.18 (1H, d, J = 5.1 Hz), 7.35 (1H, s), 7.54 (5H, s), 7.84 (1H, d, J = 8.6 Hz), 8.10 (1H, d, J = 10.6 Hz), 8.89 (1H, d, H = 5.1 Hz); IR ($CHCl_3$) 1585, 1567 1397 cm^{-1}; MS *m/e* (rel intensity) 255 (M$^+$, 100). Picrate of **6f**: mp 231–232 °C (from EtOH). Anal. Calcd for $C_{25}H_{16}N_4O_7$: C, 61.99; H, 3.33; N, 11.57. Found: C, 62.09; H, 3.27; N, 11.43.

6g: oil; ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.97 (3H, s), 6.55–7.31 (4H, m), 7.50 (1H, s), 8.08 (1H, d, J = 10.5 Hz), 8.44 (1H, d, J = 7.9 Hz), 8.78 (1H, d, J = 5.1 Hz); IR ($CHCl_3$) 1590, 1557, 1450 cm^{-1}; MS *m/z* (rel intensity) 193 (M$^+$, 100); MS *m/z* 193.0889, calcd for $C_{14}H_{11}N$ 193.0891.

General Procedure for the Reactions of 4 with 10a–d. A solution of **4** (72 mg, 0.5 mmol), **10a–d** (1 mmol), and 10% Pd/C (25 mg) in dry xylene (5 mL) was refluxed for the period indicated in Table 2. Workup similar to that described above afforded **12a–c** and **11d**. The results are summarized in Table 2. Only the protons on the azulene rings of **12a–c** are listed in the ^{1}H NMR data below; the remaining signals are listed in Table 3.

12a: mp 153–154 °C (from EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (1H, dd, J = 10.7, 8.8 Hz), 7.14 (1H, dd, J = 10.7, 8.8 Hz), 7.27 (1H, dd, J = 8.8, 10.7 Hz), 7.27 (1H, s), 7.51 (1H, s), 8.10 (1H, d, J = 11.2 Hz), 8.43 (1H, d, J = 8.8 Hz); ^{13}C NMR (100.60 MHz, $CDCl_3$) δ 24.1, 24.6, 25.2, 25.8, 26.5, 26.6, 26.8, 33.9, 37.8, 117.1, 120.4, 121.1, 124.9, 126.0, 132.2, 134.8, 136.4, 138.9, 142.2, 146.4, 160.0, 162.4; IR ($CHCl_3$) 1590, 1552, 1463 cm^{-1}; MS *m/z* (rel intensity) 303 (M$^+$, 19), 207 (100). Picrate of **12a**: mp 199–200 °C (from EtOH). Anal. Calcd for $C_{28}H_{28}N_4O_7$: C, 63.15; H, 5.30; N, 10.5. Found: C, 63.02; H, 5.37; N, 10.32.

12b: mp 168–169 °C (from EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.00 (1H, dd, J = 10.7, 8.8 Hz), 7.14 (1H, dd, H = 10.7, 8.8 Hz), 7.29 (1H, dd, J = 8.8, 10.7 Hz), 7.51 (1H, s), 8.11 (1H, d, J = 10.7 Hz), 8.45 (1H, d, J = 8.8 Hz); ^{13}C NMR (100.60 MHz, $CDCl_3$) δ 22.8, 24.1, 25.1, 26.1, 26.9, 27.9, 34.0, 38.5, 117.0, 120.0, 120.6, 124.9, 126.0, 131.9, 134.8, 136.4, 138.9, 142.2, 146.9, 160.2, 162.9; IR ($CHCl_3$) 1589, 1552, 1468 cm^{-1}; MS *m/z* (rel intensity) 289 (M$^+$, 20), 207 (100). Picrate of **12b**: mp 204–205 °C (from EtOH).

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Anal. Calcd for $C_{27}H_{26}N_4O_7$: C, 62.54; H, 5.05; N, 10.81. Found: C, 62.27; H, 4.84; N, 10.78.

12c: mp 151–152 °C (from MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 (1H, dd, J = 10.7, 8.3 Hz), 7.14 (1H, dd, J = 10.7, 8.3 Hz), 7.29 (1H, dd, H = 8.3, 10.7 Hz), 7.51 (1H, s), 8.11 (1H, d, J = 10.8 Hz), 8.53 (1H, d, J = 8.8 Hz); ^{13}C NMR (100.60 MHz, $CDCl_3$) δ 26.8, 28.0, 28.9, 29.2, 29.6, 35.6, 40.2, 116.7, 119.9, 121.1, 125.0, 126.1, 131.6, 134.8, 136.2, 139.0, 142.4, 148.3, 160.4, 163.0; IR ($CHCl_3$) 1590, 1551, 1483 cm^{-1}; MS m/z (rel intensity) 275 (M^+, 25), 207 (100). Picrate of **12c**: mp 217–218 °C (from EtOH). Anal. Calcd for $C_{26}H_{24}N_4O_7$: C, 61.90; H, 4.79; N, 11.11. Found: C, 61.64; H, 4.72; N, 11.00.

11d: oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.22–1.37 (2H, m), 1.37–1.53 (2H, m) 1.54–1.64 (1H, m), 1.66–1.74 (2H, m), 1.78–1.91 (2H, m), 2.07–2.18 (1H, m), 2.54–2.63 (1H, m), 2.60 (1H, dd, J = 7.3, 15.6 Hz), 2.72–2.82 (1H, m), 3.01 (1H, d, J = 15.6 Hz), 3.45–3.52 (1H, m), 7.07 (1H, dd, J = 9.3, 9.8 Hz), 7.08 (1H, dd, J = 9.8, 9.3 Hz), 7.33 (1H, s), 7.43 (1H, dd, J = 9.8, 9.8 Hz), 8.10 (1H, d, J = 9.8 Hz), 8.21 (1H, d, J = 9.3 Hz); ^{13}C NMR (22.6 MHz, $CDCl_3$) δ 19.3, 23.3, 26.8, 29.1, 30.1, 33.1, 34.1, 41.2, 96.0, 111.4, 120.1, 122.1, 123.0, 132.1, 132.5, 135.1, 140.7, 153.8, 180.4; IR ($CHCl_3$) 1593, 1460 cm^{-1}; MS m/z (rel intensity) 263 (M^+, 26), 193 (100); HRMS m/z 263.1674, calcd for $C_{19}H_{21}N$ 263.1675.

Dehydrogenation of 11d with DDQ. A solution of **11d** (0.2 mmol) and DDQ (0.21 mmol) in dry benzene was stirred at rt for 15 min. Precipitates were collected by filtration and dissolved in CH_2Cl_2, and DBU (0.4 mmol) was added. This mixture was stirred at rt for 1 h, extracted with CH_2Cl_2, and dried over Na_2SO_4. After solvent removal in vacuo, the residue was purified by TLC (silica gel, 3:1 hexane–ethyl acetate) to give a 40% yield of **12d**: mp 116–1176 °C (from EtOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03 (1H, dd, J = 10.7, 8.8 Hz), 7.14 (1H, dd, J = 10.8, 8.8 Hz), 7.31 (1H, dd, J = 8.8, 10.8 Hz), 7.32 (1H, s), 7.48 (1H, s), 8.13 (1H, d, J = 10.7 Hz), 8.52 (1H, d, J = 8.3 Hz); ^{13}C NMR (100.60 MHz, $CDCl_3$) δ 27.7, 28.4, 31.5, 32.0, 32.6, 38.6, 115.9, 121.1, 123.8, 124.9, 125.9, 131.1, 134.7, 136.1, 138.5, 142.0, 148.4, 160.2, 163.7; IR ($CHCl_3$) 1588, 1551, 1482 cm^{-1}; MS (rel intensity) 261 (M^+, 16), 207 (100). Anal. Calcd for $C_{19}H_{19}N$: C, 87.31; H, 7.33; N, 5.36. Found: C, 87.23; H, 7.39; N, 5.29. Only the protons on the azulene ring are listed in the ^{1}H NMR data above; the remaining signals are listed in Table 3.

Determination of pK_a Values of 6c and 12a–d. Buffer solutions of slightly different acidities (pH 4–8) were prepared by mixing a citric acid solution (0.1 M) in 20% aqueous MeCN (1:4 by volume) and a solution of $NaHPO_4$ (0.2 M) in 20% aqueous MeCN, in various proportions. For the preparation of sample solutions, 1-mL portions of the stock solution, prepared by dissolving 1 mg of the pyridine derivatives in MeCN (10 mL), were diluted to 10 mL with the buffer solution. The UV–vis spectrum was recorded for each pyridine derivative in 10 different solutions of buffers. Immediately after recording the spectrum, the pH of each sample solution was determined on a pH meter calibrated with standard buffers. The observed absorbance at the specific absorption wavelength (around 560–580-nm band for **6c** and **12a–d**) of each pyridine derivative was plotted against the pH to give a classical titration curve, whose midpoint was taken as the pK_a.

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Supplementary Material Available: ^{1}H and ^{13}C NMR spectra of **6c**, **11d**, and **12a–d** and UV–vis spectra of **6c** and **12a–d** (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.