The Reactions of *N*-Vinyliminophosphoranes. Part 14. A Short New Synthesis of [*n*](2,4)Pyridinophane Ring System (*n* = 9–6):[1,2] Static and Dynamic Structural Studies of [7]- and [6](2,4)Pyridinophanes

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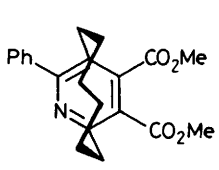
A short new synthesis of the [*n*](2,4)pyridinophane ring system (*n* = 9–6) consists of allowing *N*-vinyl- and *N*-(1-phenylvinyl)iminophosphoranes to react with cyclic α,β-unsaturated ketones. Structural studies of the compounds prepared were based on spectroscopic measurements and MNDO calculations. The ^{1}H and ^{13}C NMR spectra at various temperatures showed dynamic behaviour for the oligomethylene chains of [7]- and [6]-(2,4)pyridinophane derivatives (**8c,d**). The energy barriers $\Delta G_c^{\ddagger}$ of the bridge flipping are 12–13 kcal mol^{-1} (T_c, 20 °C) for (**8c**) and 21–22 kcal mol^{-1} kcal mol^{-1} (T_c, 150 °C) for (**8d**). The lower-energy process of the oligomethylene chain in (**8d**) is the pseudorotation with $E_a = 10.3 \pm 0.2$ kcal mol^{-1}, $\Delta H^{\ddagger} = 9.8 \pm 0.2$ kcal mol^{-1}, and $\Delta S^{\ddagger} = -4.8$ cal mol^{-1} deg^{-1}. Two stable conformations of the hexamethylene bridge of (**8d**) were unambiguously determined by low-temperature NMR. The strain of the [*n*](2,4)pyridinophane ring system was found to increase as the chain length becomes shorter. Remarkable deformation of the pyridine rings of (**8c,d**) was suggested by the geometrical optimization by MNDO calculation and the red shift of the UV spectrum.

The chemistry of strained and small-bridged aromatic compounds of cyclophane and heterophane has received much attention in recent years[3] as exemplifed by the synthesis of [5]paracyclophanes[4] and the spectroscopic characterization of [4]paracyclophane.[5] The most interesting aspects of these strained compounds are the static and dynamic behaviour of the oligomethylene chain and the correlation between aromatic character and distortion of the aromatic ring. Although there have been many studies of para-[4,5] and meta-cyclophanes,[6–8] little is known of small-bridged heterophanes. Our research group has previously reported the synthesis and spectroscopic properties of [6](2,5)pyridinophane (parapyridinophane) (**1**), which contains one of the most deformed pyridine rings so far reported.[9] The metapyridinophanes[10–12] containing the shortest methylene bridge are [6](2,4)pyridinophanes (**2**),[10a] the benzo derivative (**3**),[10c] and [6](2,6)pyridinophane (**4**).[12a] However, no information concerning the correlation between distortion of the pyridine rings and size of the oligomethylene chain has been obtained. Since the two compounds (**2**) and (**3**) have a bulky halogen substituent, they do not seem appropriate for a study of the dynamic behaviour of the hexamethylene bridge.



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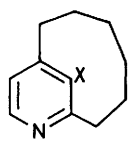
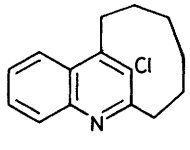
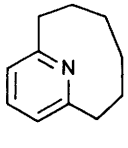


(**2**) X = Cl, Br



(**3**)

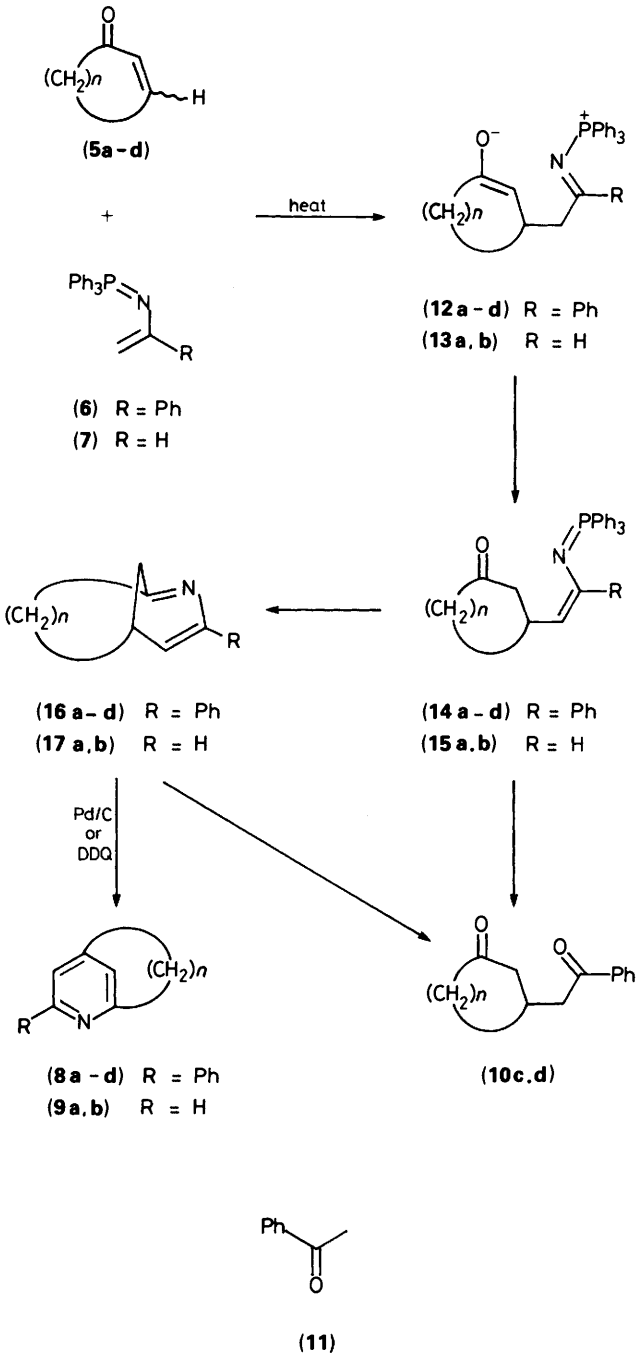


(**4**)

Recently, iminophosphoranes have attracted attention for the preparation of nitrogen heterocycles.[13] In this connection, we have demonstrated the simple preparation of *N*-vinyliminophosphoranes, which were found to react with α,β-unsaturated ketones, α-halogeno ketones, and tropone derivatives in an enamine alkylation process followed by an aza-Wittig reaction to provide convenient routes to pyridine,[14–16] pyrrole,[15,17,18] and 1-aza-azulene derivatives.[19,20] As an application of these studies, we describe here a short new synthesis of [*n*](2,4)-pyridinophanes (*n* = 9–6) and dynamic structural studies of phenyl-substituted [7]- and [6]-(2,4)pyridinophanes.

Results and Discussion

(*a*) *Synthesis of* [n](2,4)*Pyridinophanes.*—The thermal reactions of *N*-(1-phenylvinyl)iminotriphenylphosphorane (**6**)[15,19] or *N*-vinyliminotriphenylphosphorane (**7**)[16] with cyclic α,β-unsaturated ketones (**5a–d**) were examined in benzene both in the presence and in the absence of dehydrogenating reagent under reflux to give phenyl-substituted [*n*](2,4)pyridinophanes (**8a–d**) or unsubstituted [9]- and [8]-(2,4)pyridinophanes (**9a,b**) (see Scheme). The reaction conditions and the yields of the products are summarized in Table 1. The postulated reaction pathways[14–16] for the formation of (**8a–d**) or (**9a,b**) are also shown in the Scheme. The enamine-type alkylation of the iminophosphorane (**6**) or (**7**) to the β-carbon atom of (**5a–d**) gives (**12a–d**) or (**13a,b**), respectively. The following hydrogen transfer in (**12**) or (**13**) gives (**14a–d**) or (**15a,b**). These intermediates of iminophosphoranes then undergo an intramolecular aza-Wittig reaction to produce dihydropyridine derivatives (**16a–d**) or (**17a,b**), respectively. The dehydrogenation of (**9a–d**) with Pd/C or DDQ results in the formation of (**8a–d**) or (**9a,b**). Since the iminophosphoranes are labile to water,[20] the compounds (**10c,d**) could originate from the



Scheme. **a**, $n = 9$; **b**, $n = 8$; **c**, $n = 7$; **d**, $n = 6$.

hydrolysis of the intermediates (**14c,d**) and/or constrained imines (**16c,d**) upon work-up. Acetophenone (**11**) would derive from unchanged (**6**).

In the reactions of (**5a–c**) with 1.5 mol equiv. of (**6**) in the presence of Pd/C as dehydrogenating reagent, better yields of (**8a–c**) were obtained (Table 1, runs 1, 3, and 5). The reactions using 1.0 mol equiv. of (**6**) also afforded (**8a–c**) even in the absence of Pd/C (runs 2, 4, and 6). A reaction in the absence of Pd/C remarkably decreases the yield of (**8c**) (run 6) as compared with those of (**8a,b**) (runs 2 and 4), suggesting that the strain of (**8c**) disfavours the formation of the pyridine ring. In contrast, the reaction of (**5d**) with (**6**) in the presence of Pd/C did not afford (**8d**), giving only a small amount of diketone (**10d**) in addition to unchanged (**5d**) and acetophenone (**11**) (run 7). The

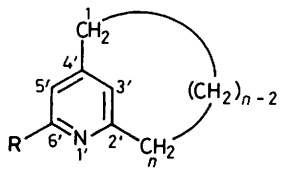


Figure 1. Numbering of (**8**) in a convenient manner.

intermediate (**16d**) having a hexamethylene bridge seems to require a strong dehydrogenating reagent because of the large strain in [6](2,4)pyridinophane. The preparation of [6](2,4)-pyridinophane (**8d**) was then achieved by dehydrogenation of a possible intermediate (**16d**) with 2,3-dichloro-5,6-dicyano-parabenzoquinone (DDQ) followed by treatment with aqueous NaOH (run 8). The preparation of parent [*n*](2,4)pyridinophanes was limited to the known [9](2,4)pyridinophane (**9a**)[10b] and novel [8](2,4)pyridinophane (**9b**) (runs 9 and 10), and the yields were lower than those of the corresponding phenyl-substituted pyridinophanes (runs 1 and 3). Isolation of the parent [7]- and [6]-(2,4)pyridinophanes was unsuccessful (runs 11 and 12). This fact is probably ascribed to the thermal lability and poor reactivity of (**7**),[16] and/or the instability of the strained intermediate of (**17**) ($n = 7$ and 6). The structures of the products were unequivocally characterized on the basis of their spectra properties and microanalyses. Although compound (**8d**) decomposed on distillation > 150 °C and compound (**9b**) is contaminated, its purification not being possible, satisfactory high resolution mass spectral data were obtained. The structures of (**10c,d**) were identified by comparison of the spectral data with those of the authenic specimens prepared independently by the reaction of α-morpholinostyrene[21] with (**5c,d**).

(*b*) *Conformational Studies of* [n](2,4)*Pyridinophanes.*—The ^{1}H NMR spectral results for (**8a–d**) are summarized in Table 2. A characteristic feature of (**8a–c**) is the equivalence of the geminal protons at the 'benzylic' positions, H-*n* and H-1 (Figure 1), the signals appearing as a couple of triplets. This is indicative of a rapid flipping of the oligomethylene chain of (**8a–c**) at room temperature; spectral properties similar to those of (**8a–c**) were

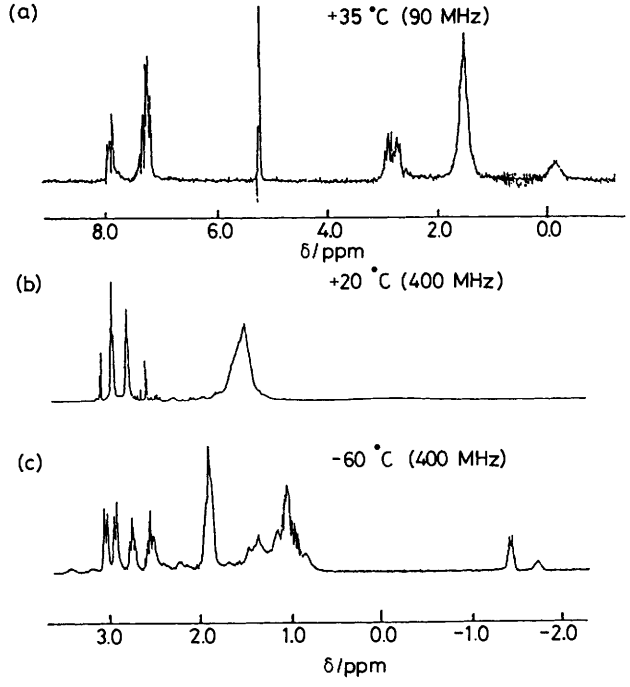


Figure 2. ^{1}H NMR spectra of (**8c**) in CD_2Cl_2 at various temperatures.

Table 1. Reaction of the iminophosphoranes (**6**) and (**7**) with cyclic α,β-unsaturated ketones (**5a–d**)[a].

Run	(5)	[n]	Reaction conditions: Mol equiv. (6)	(7)	Time (h)	Product yield (%): (8)	(9)	(10)	(11)[d]	Recovery of (5) (%)
1	(5a)	9	1.5		48	68		0	24	21
2[b]	(5a)	9	1.0		48	47		0	20	18
3	(5b)	8	1.5		48	47		0	12	23
4[b]	(5b)	8	1.0		48	40		0	10	13
5	(5c)	7	1.5		48	69		3	26	7
6[b]	(5c)	7	1.0		48	12		4	25	24
7	(5d)	6	1.5		56	0		11	56	58
8[c]	(5d)	6	1.5		96	23		2	32	20
9	(5a)	9		3.0	24		22	—	—	0
10	(5b)	8		3.0	48		7	—	—	0
11	(5c)	7		3.0	48		0	—	—	12
12	(5d)	6		3.0	48		0	—	—	12

[a] All the reactions were carried out in the presence of catalytic amount of 4 mol% of Pd/C. [b] The reaction carried out in the absence of Pd/C. [c] DDQ was used for the dehydrogenation (see Experimental section). [d] Acetophenone derives from hydrolysis of (**6**).

Table 2. The chemical shifts (δ/ppm) of ^{1}H NMR spectra of (**8a–d**) in $CDCl_3$ at room temperature.

Compd.	Pyridine: $\delta_{3'\text{-H}}$	$\delta_{5'\text{-H}}$	Benzylic: $\delta_{n\text{-H}}$	$\delta_{1\text{-H}}$	Remaining methylene bridge	Phenyl group
(8a)[a]	7.11	7.30	2.94 (2 H, t, *J* 6.3 Hz)	2.69 (2 H, t, *J* 6.4 Hz)	0.90 (4 H m), 1.16 (6 H, m), 1.75 (4 H, m)	7.35–7.53 (3 H, m) 7.94–8.05 (2 H, m)
(8b)[a]	7.12	7.27	2.86 (2 H, t, *J* 6.1 Hz)	2.62 (2 H, t, *J* 5.9 Hz)	0.63 (4 H), 1.26 (4 H), 1.55 (4 H)	7.36–7.49 (3 H, m) 7.95–8.06 (2 H, m)
(8c)[a]	7.32	7.26	2.90 (2 H, t, *J* 5.7 Hz)	2.69 (2 H, t, *J* 5.4 Hz)	−0.16 (2 H, 4-H), 1.41 (8 H)	7.41–7.60 (3 H, m) 7.96–8.11 (2 H, m)
(8d)[b]	7.19	7.09	3.09 (1 H, ddd, *J* 13.2, 7.1, 6.4 Hz), 2.71 (1 H, ddd, *J* 13.2, 8.4, 7.3 Hz)	2.79 (1 H, ddd, *J* 13.0, 6.8, 6.1 Hz), 2.63 (1 H, ddd, *J* 13.0, 5.5, 5.1 Hz)	1.21 (2 H), 1.54 (1 H), 1.82 (3 H), 0.70 (1 H, 3x-H), 0.01 (1 H, 4x-H)	7.37 (1 H, t, *J* 7.3 Hz) 7.44 (2 H, dd, *J* 7.1, 7.3 Hz) 8.03 (2 H, d, *J* 7.1 Hz)

[a] Recorded on a Hitachi R-90H (90 MHz). [b] Recorded on a JEOL GSX400 (400 MHz).

also observed for (**9a,b**), which undergo rapid flipping. Dynamic NMR spectroscopy has been useful in investigating the conformation. The ^{1}H NMR spectra of (**8c**) at various temperatures are depicted in Figure 2.* The proton signal of 4x-H and 4y-H appears as a mean value at δ −0.16 because of a rapid flipping of the heptamethylene chain (Figure 3). The signal at δ −0.16 disappeared even at 20 °C, and the signal of 4x-H in conformer (**A**) [or 4y-H in conformer (**B**)] reappeared at δ −1.45 as of 1 H intensity with a clear coupling pattern at −60 °C. The counterpart is expected to appear at δ 1.13, but it was hidden behind the signals of other aliphatic protons. Furthermore, all the benzylic protons appear as four independent signals (δ 3.02 and 2.74 for 7-H, δ 2.92 and 2.54 for 1-H). These observations suggest that each geminal proton is located in a different environment and the flipping of the heptamethylene chain is frozen in the NMR time scale. Then, the coalescence temperature method[22] estimated that the energy barrier ($\Delta G_c^{\ddagger}$) of the conformational change between (**A**) and (**B**) is 12–13 kcal mol^{-1} (T_c, +20 °C). An observation of several minor and broad signals (δ −1.76, 3.13, and 3.39) at −60 °C (Figure 2) suggests a possibility of the existence of a further conformer of (**8c**).

In contrast, the four benzylic protons of (**8d**) exhibited different chemical shifts (Table 2), suggesting that the flipping of

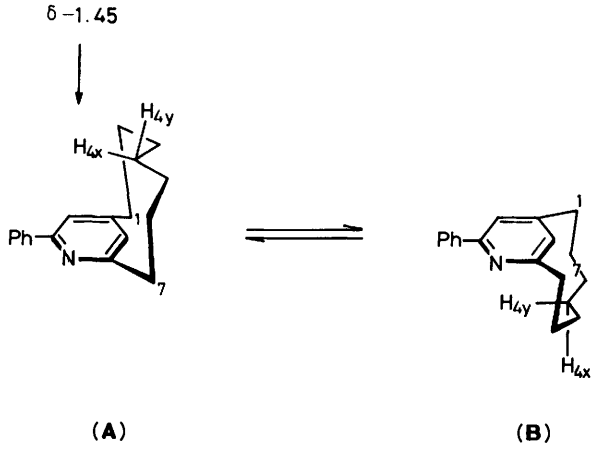


Figure 3. The flipping of the heptamethylene bridge of (**8c**).

the hexamethylene chain is frozen at room temperature. An increase in temperature > 150 °C (T_c, 90 MHz) provides a clear indication for coalescence of the benzylic protons (Figure 4). These characteristics indicate that (**8d**) also undergoes the bridge flipping of the hexamethylene chain [(C),(D) ⇌ (E),(F)] (Figure 5). Consequently, the $\Delta G_c^{\ddagger}$ value for the flipping was estimated to be 21–22 kcal mol^{-1}. The larger value of $\Delta G_c^{\ddagger}$ as compared to that of (**8c**) clearly indicates a high degree of strain in (**8d**).[23]

In the ^{1}H NMR spectra of 12-halogeno-8-aza[6]metacyclo-

* The authors are grateful to Prof. T. Miyashi, Prof. T. Kumagai, and Drs. S. Tanaka and T. Segawa of Tohoku University for obtaining the ^{1}H NMR spectra at various temperatures.

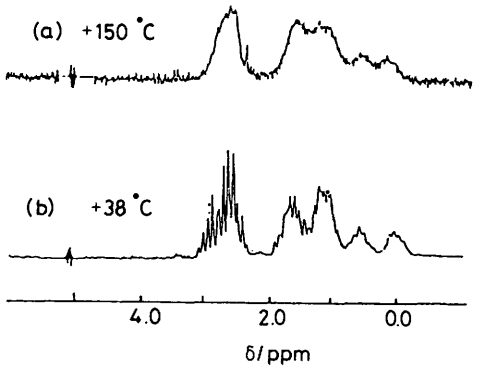


Figure 4. ^{1}H NMR spectra (90 MHz) of (**8d**) in C_2Cl_4 at different temperatures.

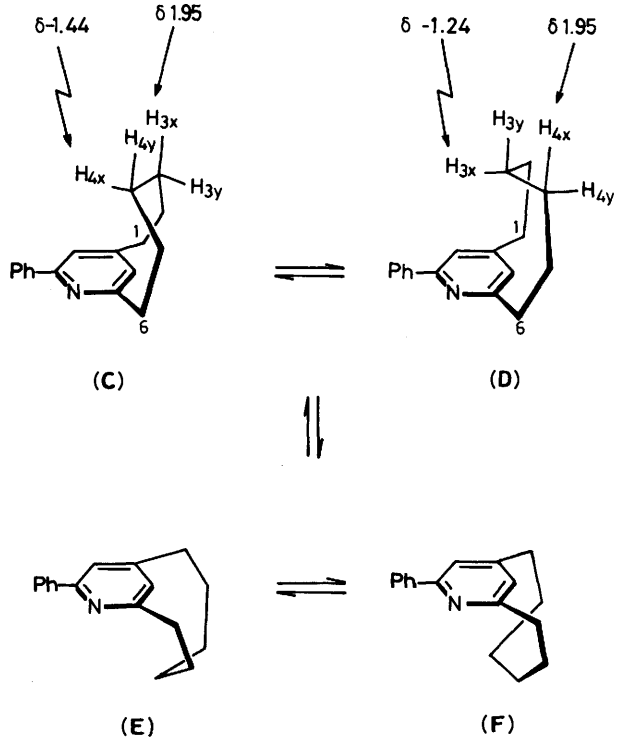


Figure 5. The flipping [(C),(D) ⇌ (E),(F)] and the pseudorotation [(C) ⇌ (D),(E) ⇌ (F)] of hexamethylene bridge of (**8d**).

phanes (**2**),[10a] there was no signal above *ca.* δ 0.8, an indication that the methylene protons were less shielded than the corresponding protons in 12-bromo- and other [6]metacyclophanes.[6] However, it was considered that the structure of (**8d**) is not fixed in either conformer (**C**) or (**D**) [(**E**) or (**F**)] at room temperature (Figure 6). Indeed, the ^{13}C NMR spectrum of (**8d**) at 20 °C exhibited six carbon signals in the aliphatic region. However, a decrease in temperature broadened the signals, and twelve signals for the hexamethylene carbons (six large and six small) were recorded at −90 °C (Figure 6). Temperature dependency was also observed in the aromatic carbons. These features clearly indicate that compound (**8d**) exists in two different conformers (**C**) and (**D**) [(**E**) and (**F**)] at low temperature and the equilibrium between them by pseudorotation was frozen. The energy barrier of the pseudorotation was obtained from their ^{13}C NMR spectra at various temperatures by using line-shape analysis, which furnished E_a = 10.3 ± 0.2 kcal mol^{-1}, $\Delta H^{\ddagger}$ = 9.8 ± 0.2 kcal mol^{-1}, and $\Delta S^{\ddagger}$ = −4.8 cal mol^{-1} deg^{-1}. Thus, $\Delta G^{\ddagger}$ for pseudorotation was calculated to be 9.8 kcal mol^{-1} (−30 °C).

The 400 MHz ^{1}H NMR spectra of (**8d**) at various temperatures were also shown in Figure 7.* The spectrum at −90 °C exhibited highly shielded signals at δ −1.44 and −1.24 in a ratio of 2:1, from which the free energy difference (ΔG_o at −90 °C) between (**C**) and (**D**) [(**E**) and (**F**)] is estimated to be 0.26 kcal mol^{-1}. Structural assignments for each conformer were made from the NMR spectra at −90 °C. The pseudo-contact ^{1}H NMR spectrum using Eu(fod)$_3$ at −90 °C induced a larger downfield shift of the methylene protons at C-6 as compared to those at C-1. Thus, the unambiguous assignment of all the bridge carbons and protons was successful for each of the two conformers from 2D ^{1}H NMR and 2D ^{13}C ^{1}H NMR spectral measurements (Table 3). The two highly shielded signals at δ −1.44 and −1.24 were assigned respectively to the protons bonded to C-4 of the major and C-3 of the minor conformers, the structures of which were unequivocally decided to be (**C**) [or (**E**)] and (**D**) [or (**F**)], respectively. Thus, highly shielded signals of the methylene protons of (**8d**) were observed as in the case of [6]metacyclophane[6] when the pseudorotation of the methylene bridge was frozen.

The kinetic parameters of the bridge flipping and pseudorotation for (**8c**), (**8d**), and the related compounds are summarized in Table 4. The energy barriers for the bridge flipping of (**8c,d**) are similar to those of the corresponding [*n*]metacyclophanes rather than those of the corresponding [*n*](2,6)pyridinophanes. Furthermore, there is no large difference between $\Delta G_c^{\ddagger}$ values for the pseudorotation of (**8d**) and [6]metacyclophane.

(*c*) *Deformation of the Pyridine Rings.*—The deformation of the aromatic rings in cyclophane molecules is generally evaluated from the red shifts in UV spectra of the latter.[24] The UV spectra of [*n*](2,4)pyridinophanes (**8a–d**) and a reference molecule of 2,4-dimethyl-6-phenylpyridine (**8s**) are summarized in Table 5. The ring strain of (**8a–d**) is reflected in the red-shift as the value of [*n*] decreases. The longest absorption maximum of (**8d**), which has a smallest value of [*n*] in the (**8**) series, is shifted exactly 20 nm to longer wavelength than that of (**8s**) which has a planar pyridine ring. Therefore, there can be no doubt that (**8d**) contains the most deformed pyridine ring in the (**8**) series.

The ^{1}H NMR chemical shifts of aromatic protons are also helpful in examining the distortion of the pyridine ring of [*n*](2,4)pyridinophanes (Table 2).[25] The 3′-H signals (Figure 1) in (**8a–c**) shift downfield as the methylene chain becomes shorter, behaviour attributable to steric compression between 3′-H and the methylene bridge.[6] In contrast, the 3′-H signal in (**8d**) appears at higher field than that of (**8c**), a result mainly of reduced ring current for the strained pyridine ring rather than steric compression. Furthermore, the 5′-H signals in (**8a–d**) shift to higher fields as the methylene chain is shortened. A similar tendency appears in ^{13}C NMR spectra of (**8a–d**). The chemical shifts of C-3′ exhibited a downfield shift from δ 122.5 for (**8a**) to δ 127.13 for (**8d**) as a result of steric compression.[26] The chemical shift of C-5′ showed, in contrast, an upfield shift from δ 118.5 for (**8a**) to δ 114.7 for (**8d**).

(*d*) *Structural Study by the MNDO Method.*—Geometrical optimization of (**8c**), (**8d**), and a reference molecule (**8s**) was carried out by a MNDO calculation (Figure 8). The optimized structures of (**8c,d**) revealed that each of them has a methylene proton closely located over the pyridine ring as is expected from ^{1}H NMR spectroscopic studies. Structural parameters and heat of formation are listed in Table 6. The calculated ΔH_c for the conformer (**C**) [or (**E**)] of (**8d**) is lower than that for the

* See footnote on page 1121.

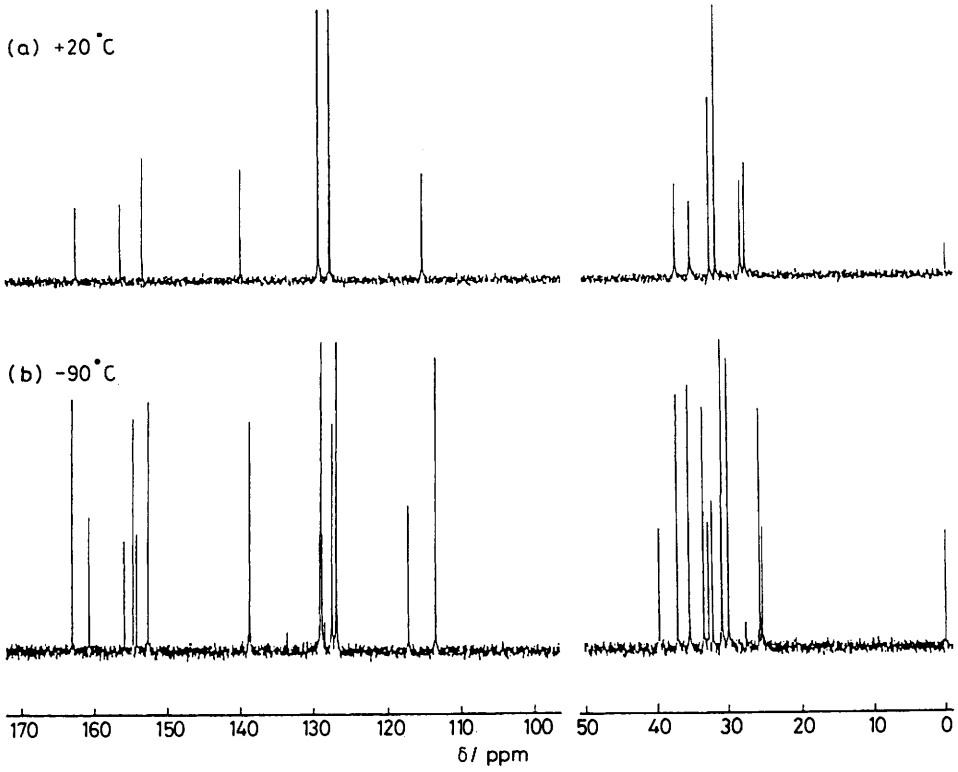


Figure 6. ^{13}C NMR spectra of (**8d**) in CD_2Cl_2 at different temperatures.

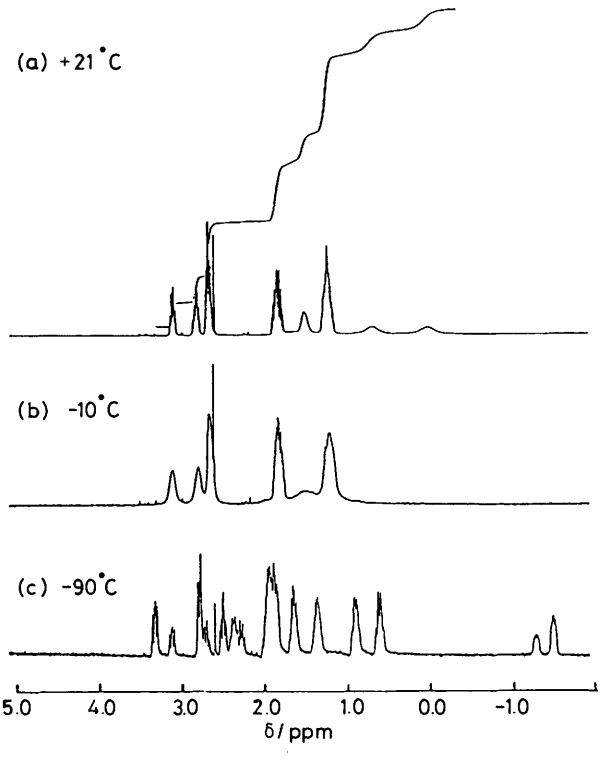


Figure 7. ^1H NMR spectra (400 MHz) of (**8d**) in CD_2Cl_2 at various temperatures.

conformer (**D**) [or (**F**)] of (**8d**) by 0.7 kcal mol^{-1}. This is compatible with the experimental result which implies that conformer (**C**) [or (**E**)] is thermodynamically more stable (0.26 kcal mol^{-1}) than (**D**) [or (**F**)]. A large strain energy is stored in

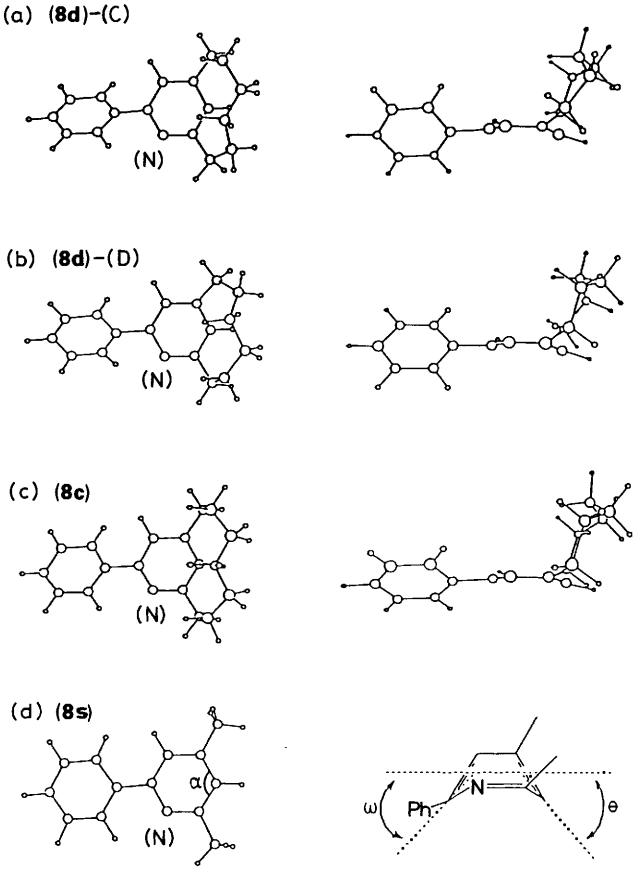


Figure 8. Optimized structure from vertical and horizontal viewpoints calculated by MNDO method.

Table 3. Chemical shifts (δ/ppm) of ^1H and ^{13}C NMR spectra of (**8d**) in CD_2Cl_2.[a]

		Conformer (C) (−90 °C)		Conformer (D) (−90 °C)		Equilibrium mixture (+20 °C)	
		δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
Bridge	C-1	36.94	2.51, 2.79	32.12	3.12, 2.30	35.17	2.79, 2.63
	C-2	33.34	0.66, 1.87	30.96	1.95, 1.69	32.47	1.82, 1.21
	C-3	29.94	1.95 (3x-H), 0.93 (3y-H)	25.29	−1.24 (3x-H), 1.41 (3y-H)	28.19	0.70 (3x-H), 1.21 (3y-H)
	C-4	25.64	−1.44 (4x-H), 1.41 (4y-H)	29.94	1.95 (4x-H), 0.93 (4y-H)	27.58	0.01 (4x-H), 1.21 (4y-H)
	C-5	30.80	1.69, 2.01	32.68	1.90, 0.66	31.60	1.54, 1.82
	C-6	35.34	2.43, 3.35	39.49	2.82, 2.73	37.20	2.71, 3.09
Pyridine	C-2′	163.34		161.01		162.45	
	C-3′	127.56	7.21	127.64	7.19	127.45	7.21
	C-4′	152.79		154.39		153.10	
	C-5′	113.52	7.15	117.20	7.14	114.73	7.15
	C-6′	154.90		156.10		156.17	

[a] Recorded on a JEOL GSX400.

Table 4. Energy barrier ($\Delta G_c^{\ddagger}$/kcal mol^{-1}) of the flipping and pseudo-rotation of (**8c,d**), [*n*]metacyclophanes, and [*n*](2,6)pyridinophanes.

[*n*]		(**8**)[a]	[*n*]Meta-cyclophane[b]	[*n*](2,6)-Pyridinophane
6	Flipping	21–22 (+150 °C)	17.4 (+76.5 °C)	11.0[c] (−40 °C)
	Pseudo-rotation	9.8 (−30 °C)	11.1 (−31.5 °C)	
7	Flipping	12–13 (+20 °C)	11.5 (−28 °C)	9.0[d] (−75.5 °C)

[a] This work. [b] Ref. 6. [c] Ref. 12*a*. [d] Ref. 12*b*.

Table 5. UV spectra of 2,4-dimethyl-6-phenylpyridine (**8s**) and (**8a–d**) in EtOH.

Compound	[*n*]	λ_{max}/nm (log ε)		
(**8s**)		207.8 (4.37)	245.6 (4.13)	278.8 (4.09)
(**8a**)	9	210.2 (4.33)	248.0 (4.05)	280.6 (4.00)
(**8b**)	8	210.6 (4.37)	248.4 (4.10)	281.6 (4.04)
(**8c**)	7	211.4 (4.39)	249.0 (4.08)	284.6 (3.98)
(**8d**)	6	208.2 (4.44)	254.8 (4.04)	299.0 (3.89)

Table 6. Structural parameters of (**8c**), (**8d**), and (**8s**) calculated by MNDO method.

Compound	Bond angle α/°	Deviation angle θ/°	Deviation angle ω/°	Heat of formation ΔH_c/kcal mol^{-1}
(**8d**) (C)	116.52	24	10	56.76
(**8d**) (D)	116.46	23	8–9	57.46
(**8c**)	118.50	17	7	42.52
(**8s**)	119.59	0	0	40.39

(**8d**), the $\Delta H_c^{\ddagger}$ value of which is higher than that of (**8s**) by 16–17 kcal mol^{-1}. The dihedral angles θ and ω give a measure of deformation of the pyridine ring. The optimized structure of (**8d**) demonstrates the considerable deformation with θ and ω taking the values of 23–24° and 8–10°, respectively. Although a little information concerning deformation of aromatic rings is available from [*n*]metapyridinophanes and [*n*]metacyclophanes, the MNDO calculation for [5]metacyclophane was studied and the angle of deformation corresponding to θ and ω of the benzene ring was found to be 32 and 9°, respectively.[7d] Thus, the results obtained for (**8d**) are reasonably in agreement with those expected from the MNDO method. The large strain in (**8d**) is also reflected in the bond angle α, which is in accord with strong compression between C-3′ and C-5′ as a result of bridging. The less strained nature of (**8c**) as compared to (**8d**) is also observed in $\Delta H_c^{\ddagger}$, and other structural parameters.

Experimental

IR spectra were recorded on a Shimadzu IR-400 spectrometer. ^1H NMR spectra were recorded on a Hitachi R-24, a Hitachi R-90H, and a JEOL GSX400 spectrometers. The chemical shifts are given in ppm (δ) relative to the internal $SiMe_4$ standard. The mass spectral or high resolution mass spectral studies were run on a Shimadzu GCMS QP-1000 or a JEOL JMS-DX300 spectrometer. All the reactions were carried out under a dry nitrogen atmosphere. Microanalyses were performed at the Science and Engineering Research Laboratory of Waseda University. M.p.s were recorded on a Büchi apparatus and are uncorrected. *trans*-Cyclododec-2-enone (**5a**),[27] a mixture of *cis*- and *trans*-cycloundec-2-enone (**5b**), a mixture of *cis*- and *trans*-cyclodec-2-enone (**5c**),[28] and *cis*-cyclonon-2-enone (**5d**) were prepared from the corresponding cyclic ketones *via* acetalization, bromination, dehydrobromination, and hydrolysis. The desired cyclic ketones were prepared by repeated ring contraction reactions starting from the commercially available cyclododecanone.[29]

General Procedure for the Reaction of α,β-Unsaturated Ketones (**5a–d**) *with* N-(1-*Phenylvinyl*)*iminotrophenylphosphorane* (**6**).—A solution of (**5**) (0.50 mmol) and (**6**) (0.50 mmol or 0.75 mmol) in anhydrous benzene (5 ml) was heated under reflux either in the presence or in the absence of 10% Pd/C (20 mg, 4 mol%). After this, the reaction mixture was filtered through Celite and the filtrate was concentrated, the residue was separated by TLC on silica gel using ether–hexane (1:4) as a developer. The first band from the TLC plates gave the [*n*](2,4)pyridinophane derivative (**8**). The second band from the TLC plates gave the starting material (**5**). The third band contained acetophenone (**11**). In the reactions of (**5c,d**), 3-(2-oxo-2-phenylethyl)cyclodecanone (**10c**) and 3-(2-oxo-2-phenylethyl)cyclononanone (**10d**) were obtained from the fourth band of the TLC plates. The detailed reaction conditions and the yields of the products are summarized in Table 1.

For compound (**8a**): m.p. 50–52 °C; b.p. 185 °C (0.06 mmHg); $\delta_C(CDCl_3)$ 24.9 (t), 25.2 (t), 25.3 (t), 25.7 (2 C, t), 25.8 (t), 25.9 (t), 34.7 (t, C-1), 37.5 (t, C-9), 118.5 (d, C-5′), 122.5 (d, C-3′), 126.9

(2 C, d, Ph), 128.3 (3 C, d, Ph), 139.8 (s, Ph), 151.0 (s, C-4'), 156.9 (s, C-6'), and 161.2 (s, C-2'); $\nu_{max}(CCl_4)$ 3 058, 3 040, 2 924, 2 857, 1 603, 1 558, 1 464, 1 445, 1 427, and 689 cm^{-1}; *m/z* 279 (M^+, 100%) (Found: M^+, 279.1988; C, 85.74; H, 9.23; N, 4.71. $C_{20}H_{25}N$ requires *M*, 279.1987; C, 85.97; H, 9.02; N, 5.01%).

For compound (**8b**): m.p. 53–54 °C; b.p. 180 °C (0.07 mmHg); $\delta_C(CDCl_3)$ 23.4 (t), 24.0 (t), 26.5 (t), 27.0 (t), 28.2 (t), 29.5 (t), 35.7 (t, C-1), 38.5 (t, C-9), 117.6 (d, C-5'), 123.3 (d, C-3'), 126.9 (2 C, d, Ph), 128.3 (3 C, d, Ph), 139.7 (s, Ph), 151.7 (s, C-4'), 157.6 (s, C-6'), and 161.0 (s, C-2'); $\nu_{max}(CCl_4)$ 3 067, 3 049, 2 933, 2 865, 1 605, 1 563, 1 464, 1 452, 1 445, 1 427, 1 366, 1 225, 1 037, 861, and 693 cm^{-1}; *m/z* 265 (M^+, 70%) and 222 (100) (Found: M^+, 165.1834; C, 85.75; H, 9.00; N, 5.10. $C_{19}H_{23}N$ requires *M*, 265.1830; C, 85.98; H, 8.74; N, 5.28%).

For compound (**8c**): yellow oil, b.p. 175 °C (0.07 mmHg); $\delta_C(CDCl_3)$ 27.3 (t), 28.6 (t), 28.8 (t), 29.5 (t), 30.1 (t), 36.9 (t, C-1), 39.6 (t, C-7), 116.6 (d, C-5'), 124.1 (d, C-3'), 126.9 (2 C, d, Ph), 128.3 (2 C, d, Ph), 128.4 (d, Ph), 139.4 (s, Ph), 152.1 (s, C-4'), 157.3 (s, C-6'), and 161.1 (s, C-2'); $\nu_{max}(CCl_4)$ 3 058, 3 044, 2 924, 2 857, 1 595, 1 558, 1 462, 1 441, 1 429, 1 366, 1 326, 1 215, 1 032, and 693 cm^{-1}; *m/z* 251 (M^+, 100%) (Found: M^+, 251.1712; C, 85.15; H, 8.54; N, 5.74. $C_{18}H_{21}N$ requires *M*, 251.1674; C, 86.01; H, 8.42; N, 5.57%).

For compound (**10c**): yellow oil; $\delta_H(CCl_4)$ 1.39 (12 H, m), 2.45 (4 H, m), 2.91 (3 H, m), 7.39 (3 H, m), and 7.81 (2 H, m); $\nu_{max}(CCl_4)$ 3 068, 2 934, 1 687, 1 601, 1 586, 1 473, 1 454, 1 417, 1 358, 1 261, 1 208, 1 183, and 983 cm^{-1}; *m/z* 272 (M^+, 1.4%) and 105 (100) (Found: M^+, 272.1801. $C_{18}H_{24}O_2$ requires *M*, 272.1776).

For compound (**10d**): yellow oil; $\delta_H(CCl_4)$ 1.43 (10 H, m), 2.34 (4 H, m), 2.86 (3 H, m), 7.34 (3 H, m), and 7.76 (2 H, m); $\nu_{max}(CCl_4)$ 3 059, 2 934, 1 693, 1 601, 1 586, 1 466, 1 452, 1 411, 1 358, 1 264, 1 207, 1 184, and 988 cm^{-1}; *m/z* 258 (M^+, 1.3%) and 120 (100) (Found: M^+, 258.1625. $C_{18}H_{24}O_2$ requires *M*, 258.1620).

Synthesis of [6](2,4)*Pyridinophane* (**8d**).—A solution of (**5d**) (414 mg, 3.0 mmol) and (**6**) (1.71 g, 4.5 mmol) in anhydrous benzene (15 ml) was heated under reflux for 96 h. The solvent was then removed under reduced pressure and the residue was chromatographed on silica gel, which was pre-treated with aqueous NH_4OH, to remove triphenylphosphine oxide. The fractions eluted with benzene were concentrated and the residue was treated with DDQ (680 mg, 3.0 mmol) in benzene (20 ml) at room temperature for 1.5 h to give black precipitates. The precipitates were collected by filtration and the precipitates were treated with 30 ml of 1% aqueous NaOH and 20 ml of benzene for 0.5 h with vigorous stirring. The reaction mixture was extracted with benzene and the extract dried (Na_2SO_4). After the benzene had been removed, the resulting mixture was purified by TLC on silica gel using ether–hexane (1:4) as a developer to give (**8d**) (164 mg, 23%). The former filtrate, from which the precipitates were removed, was concentrated and separated by TLC on silica gel using ether–hexane (1:5) as a developer to give (**11**) (172 mg, 32%), (**5d**) (82 mg, 20%), and (**10d**) (17 mg, 2%).

For compound (**8d**): yellow oil; $\delta_C(CDCl_3)$ 27.2 (t), 27.9 (t), 31.2 (t), 32.1 (t), 34.8 (t, C-1), 36.9 (t, C-6), 114.5 (d, C-5'), 127.08 (2C, d, Ph), 127.13 (d, C-3'), 128.5 (2C, d, Ph), 128.7 (d, Ph), 139.3 (s, Ph), 152.6 (s, C-4'), 156.4 (s, C-6'), and 162.1 (s, C-2'); $\nu_{max}(CCl_4)$ 3 063, 2 929, 2 863, 1 597, 1 562, 1 438, 1 425, 1 362, 1 034, 917, and 697 cm^{-1}; *m/z* 237 (M^+, 100%) (Found: M^+, 237.1516. $C_{17}H_{19}N$ requires *M*, 237.1518).

Independent Preparation of (**10c**).—A solution of (**5c**) (152 mg, 1.0 mmol) and α-morpholinostyrene (**18**)[21] (227 mg, 1.2 mmol) in anhydrous benzene (5 ml) was heated under reflux for 24 h. After the reaction was completed, the solvent was removed under reduced pressure and the residue was separated by TLC on silica gel using ether–hexane (1:4) as a developer. The first band from the TLC plates contained (**11**) (48 mg, 40%) and (**5c**) (58 mg, 38%). The second band from the TLC plates afforded (**10c**) (28 mg, 10%), the spectral data of which were identical with those obtained by the above reactions.

Independent Preparation of (**10d**).—A solution of (**5d**) (69 mg, 0.5 mmol) and (**18**) (113 mg, 0.6 mmol) in anhydrous benzene (5 ml) was heated under reflux for 24 h in the presence of a catalytic amount of trifluoroborane–diethyl ether. To the reaction mixture was added 3 ml of 1M hydrochloric acid and the whole stirred for 10 min at room temperature. The reaction mixture was extracted with benzene and dried (Na_2SO_4). After removal of the solvent under reduced pressure, the residue was separated by TLC on silica gel using ether–hexane (1:4) as a developer. The first band from the TLC plates gave (**12**) (12 mg, 17%). The second band gave (**11d**) (16 mg, 20%), the spectral data of which were identical with those obtained by the above reactions.

General Procedure for the Reaction of (**5a–c**) *with* N-*Vinyliminotriphenylphosphorane* (**7**).—A mixture of (**5**) (1.00 mmol), (**7**) (909 mg, 3.0 mmol), and 10% Pd/C (40 mg, 4 mol%) in benzene was heated under reflux. The reaction mixture was then filtered through Celite, and the resulting triphenylphosphine oxide was removed by column chromatography on silica gel using hexane–ethyl acetate (1:1) as an eluant. The fractions were then concentrated, and the residue was purified by TLC on silica gel using ether–hexane (1:4) as a developer to give [*n*](2,4)pyridinophanes (**9**). The detailed reactions conditions and the yields of the products are summarized in Table 1.

For compound (**9a**):[10b] $\delta_H(CDCl_3)$ 0.89 (4 H, m), 1.16 (6 H, m), 1.74 (4 H, m), 2.47 (2 H, t, *J* 6.4 Hz, 1-H), 2.88 (2 H, t, *J* 6.4 Hz, 9-H), 6.90 (1 H, d, *J* 4.7 Hz, 5'-H), 7.19 (1 H, s, 3'-H), and 8.40 (1 H, d, *J* 4.7 Hz, 6'-H); $\delta_C(CDCl_3)$ 24.8 (t), 25.0 (t), 25.2 (t), 25.6 (t), 25.7 (2 C, t), 25.9 (t), 34.5 (t, C-1), 37.2 (t, C-9), 121.7 (d, C-5'), 124.2 (d, C-3'), 148.9 (d, C-6'), 150.6 (s, C-4'), and 161.1 (s, C-2'); $\nu_{max}(CCl_4)$ 3 049, 3 012, 2 924, 2 857, 1 603, 1 558, 1 462, 1 447, and 1 412 cm^{-1}; λ_{max}(EtOH) 206, 262, and 267sh nm (log ε 3.86, 3.47, and 3.43).

For compound (**9b**): oil; $\delta_H(CDCl_3)$ 0.63 (4 H, m), 1.26 (4 H, m), 1.53 (4 H, m), 2.60 (2 H, t, *J* 5.9 Hz, 1-H), 2.80 (2 H, t, *J* 6.0 Hz, 8-H), 6.89 (2 H, d, *J* 4.9 Hz, 5'-H), 7.22 (1 H, s, 3'-H), and 8.41 (1 H, d, *J* 4.9 Hz, 6'-H); $\delta_C(CDCl_3)$ 23.4 (t), 23.9 (t), 26.4 (t), 27.0 (t), 28.1 (t), 29.5 (t), 35.6 (t, C-1), 38.2 (t, C-8), 120.9 (d, C-5'), 124.8 (d, C-3'), 149.6 (d, C-6'), 151.4 (s, C-4'), and 161.0 (s, C-2'); $\nu_{max}(CCl_4)$ 3 032, 3 005, 2 917, 2 851, 1 602, 1 556, 1 461, 1 438, and 1 414 cm^{-1}; λ_{max}(EtOH) 208, 264, and 268sh nm (log ε 3.91, 3.46, and 3.43); *m/z* 189 (M^+, 24) and 146 (100) (Found: M^+, 189.1516. $C_{13}H_{19}N$ requires *M*, 189.1518).

Preparation of 2,4-*Dimethyl*-6-*phenylpyridine* (**8s**).—A solution of pent-3-en-2-one (168 mg, 2.0 mmol) and (**6**) (758 mg, 2.0 mmol) in benzene (10 ml) was heated under reflux for 48 h in the presence of 10% Pd/C (80 mg, 4 mol%). The reaction mixture was then filtered through Celite, and the filtrate was concentrated under reduced pressure. The residue was separated by MPLC on silica gel using ether–hexane (1:4) as an eluant to give (**8s**) (89 mg, 24%), the spectral data of which were identical with those of an authentic specimen.[30]

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