On the Reaction of (Vinylimino)phosphoranes. Part 17.[1] Preparation of *N*-Vinylcarbodiimides and Their [4+2] Cycloaddition with Several Dienophiles to Give Pyridine Ring System[2]

Makoto NITTA,* Hironobu SOEDA, Shinya KOYAMA, and Yukio IINO
Department of Chemistry, School of Science and Engineering, Waseda University, Shinjuku-ku, Tokyo 169
(Received November 14, 1990)

The aza-Wittig reaction of (vinylimino)triphenylphosphorane and its several derivatives was examined to give *N*-phenyl-*N'*-vinylcarbodiimide and its derivatives, all of which underwent a [4+2] cycloaddition reaction with electron-rich dienophiles (enamines) and/or electron-deficient dienophiles (activated acetylenes), resulting in the formation of a pyridine ring system. The regioselectivity of the cycloaddition reaction could be rationalized on the basis of a frontier orbital consideration.

The [4+2] cycloaddition reaction of azadiene has proved to be one of the most powerful methods for the synthesis of six-membered nitrogen heterocycles.[3] Thus, the development of a new azadiene should provide a convenient way to produce heterocycles containing a pyridine ring. During the last decade, the synthesis and reaction of acyclic 2-aza-1,3-butadiene **1** have been studied extensively. For example, the [4+2] cycloaddition reaction of a 2-aza-1,3-butadiene (**1A**) having an electron-donating substituent, such as an amino[4-6] or silyloxy[7] group, with electron deficient dienophiles has been successfully examined; the reactivity and regioselectivity of the reaction have been rationalized on the basis of the frontier orbital treatment.[6] A compound of type (**1B**), which has an alkyl or aryl substituent, has been demonstrated to undergo [4+2] cycloaddition with both hetero-dienophiles[8,9] and electron-deficient dienophiles.[9,10] Furthermore, a 2-aza-1,3-butadiene (**1C**) having an electron-withdrawing substituent[11] has also been clarified to undergo a [4+2] cycloaddition reaction with enamines.[12] A few examples of C=C-conjugated carbodiimide, which also has a 2-aza-1,3-butadiene unit, has been known[13-15] and intermolecular cycloaddition with tetracyanoethylene[13] and intramolecular cyclization[14] has been reported.

We have recently demonstrated a simple preparation method of various (vinylimino)phosphoranes, which were found to react with α-bromo ketones, α,β-unsaturated ketones, and tropone derivatives in an enamine alkylation process followed by aza-Wittig reaction to provide convenient routes to pyrroles,[16,17] pyridines,[18] [*n*](2,4)pyridinophanes (*n*=6—9),[19] and 1-azaazulenes.[20] As part of a series of studies on (vinylimino)phosphoranes and related compounds, we examined the aza-Wittig reaction of (vinylimino)-phosphoranes with phenyl isocyanate to give C=C-conjugated carbodiimide derivatives, which undergo a [4+2] cycloaddition reaction with several dienophiles to give a pyridine ring system.

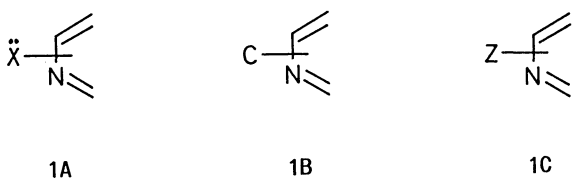
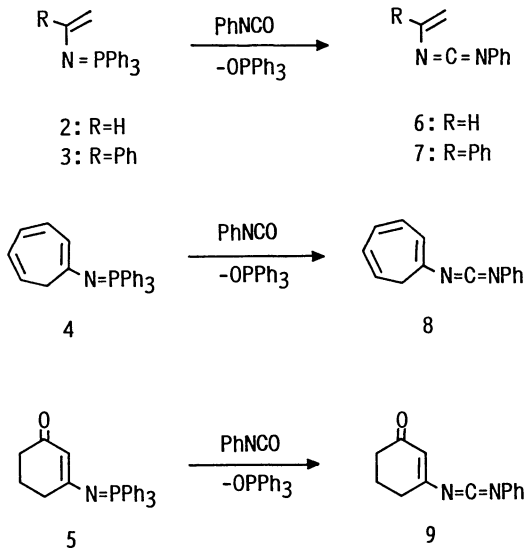


Fig. 1.

Results and Discussion

Preparation and [4+2] Cycloaddition Reaction of *N*-Phenyl-*N'*-vinylcarbodiimide and Its Derivatives. *N*-Vinyl-, *N*-(1-phenylvinyl)-, *N*-(1,3,5-cycloheptatrienyl)-, and *N*-(3-oxo-1-cyclohexenyl)-substituted carbodiimides (**6**), (**7**), (**8**), and (**9**), were prepared by the aza-Wittig reaction of phenyl isocyanate with the corresponding (vinylimino)triphenylphosphorane (**2**) and its derivatives **3**—**5** (Scheme 1). Compounds **6**—**8** could be purified by column chromatography on silica gel, and the structural assignment was based on high-resolution mass, IR, and ^{1}H NMR spectral data.

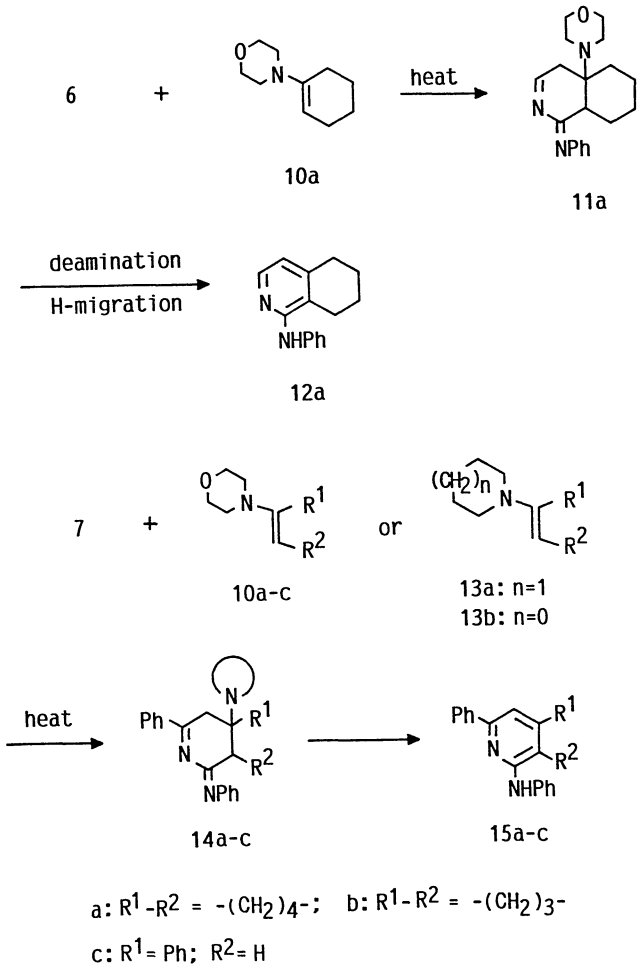


Scheme 1.

Table 1. Results for the Reaction of **6** or **7** with Enamines **10a—c** or **13a,b**[a]

Entry	Compound	Enamine	Solvent	Product	Yield/%
1	**6**	**10a**	PhMe	**12a**	9
2	**7**	**10a**	PhBr	**15a**	41
3	**7**	**10a**	DMF[b]	**15a**	33
4	**7**	**10b**	PhBr	**15b**	34
5	**7**	**10c**	PhBr	**15c**	30
6	**7**	**13a**	PhBr	**15a**	38
7	**7**	**13b**	PhBr	**15b**	39

a) Reactions were carried out under refluxing for 0.5 h. b) Denote *N*,*N*-dimethylformamide.



Scheme 2.

Compound **9** was unstable and decomposed through chromatography on silica gel, and the structural proof for **9** was not obtained from the ^{1}H NMR spectrum of crude **9**. Thus, the reaction was conveniently carried out using a one-pot procedure without isolating **9**.

A thermal reaction of **6** with enamine **10a** was carried out in toluene to give an isoquinoline derivative **12a** in low yield (Scheme 2, Table 1, Enty 1). Similarly, reactions of **7** with enamines **10a—c** and **13a,b** were carried out in bromobenzene under refluxing to give isoquinoline derivatives **15a,b** and pyridine derivative **15c** in modest yields (Scheme 2). The results are also summarized in Table 1 (Entries 2—7). Neither the yields of the products nor the reaction time was dependent on the amine moiety of the enamines (Entries 7 and 8). Furthermore, no drastic change in the reaction time and yield of the product was observed, even in a polar solvent (DMF) (Entry 3). Thus, the reaction seemed to proceed via a concerted [4+2] cycloaddition rather than an ionic process. Furthermore, enamines from cycloalkanones, **10a,b**, resulted in higher yields of the products, as compared to that of **10c**.

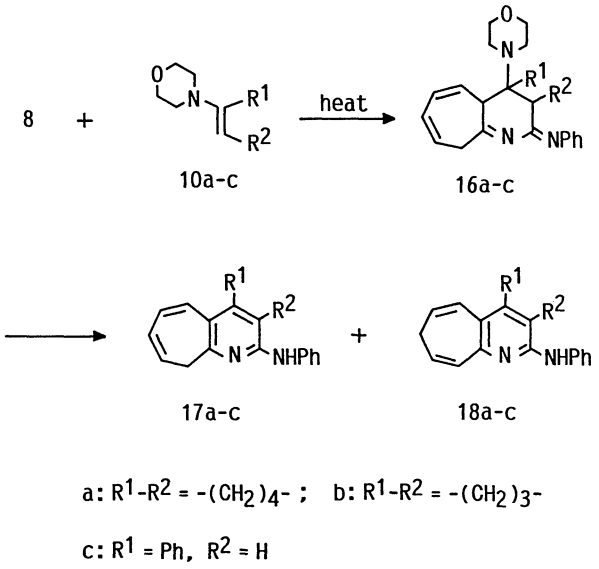
Each of the ^{1}H NMR spectra of the new compounds **12a** and **15a,b** showed, besides signals for the aromatic ring, characteristic signals for the alicyclic methylene chain. The assignment of the signals are summarized in the Experimental section. Furthermore, the structure of **15c** was deduced on the basis of the spectral data, the ^{1}H NMR spectrum of which showed a pair of doublets at δ=7.02 and δ=7.42 (J=1.1 Hz, meta-coupled), thus, **15c** could be differentiated from the other regioisomer, 2-phenylamino-3,6-diphenylpyridine (**23**), which exhibited a signal at δ=7.34 (J=7.7 Hz, ortho-coupled) (vide infra). Thus, in the formation of compounds **12a**, **15a—c** is postulated to proceed through intermediates **11a** and **14a—c**, all of which undergo hydrogen migration and subsequent deamination. The regioselectivity of the enamine addition process giving **11a** or **14a—c** is suggested by the formation of **15c**, as well as with frontier molecular orbital consideration (vide infra).

The reaction of the carbodiimide **8** with enamines **10a—c** were examined in bromobenzene under refluxing to give a mixture of 9*H*-cyclohepta[*b*]pyridine (**17a—c**) and 7*H*-cyclohepta[*b*]pyridine (**18a—c**) derivatives (Scheme 3). Compounds **18a—c** are possibly derived from base catalyzed isomerization of **17a—c**,

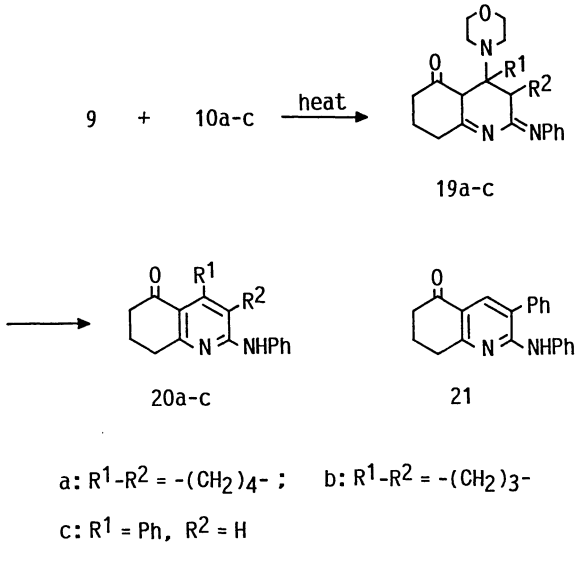
Table 2. Results for the Reaction of **8** with Enamines **10a—c** to Give **17a—c** and **18a—c**[a]

Enamine	Product yield/%	Molar ratio of **17**/**18**
10a	47	1.85
10b	61	0.33
10c	48	1.50

a) Reactions were carried out in bromobenzene under refluxing for 0.5 h.



Scheme 3.



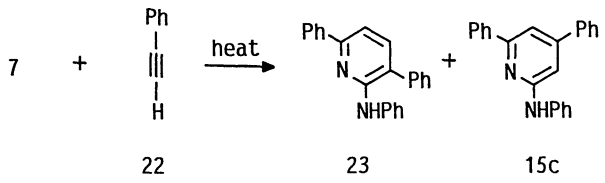
Scheme 4.

respectively. The results are summarized in Table 2. The spectral data of the new compounds were consistent with the proposed structures (Experimental). Each of the ^{1}H NMR spectra of the mixtures showed, in addition to signals for the substituted pyridine ring and phenyl group, characteristic signals for the cycloheptatriene ring and annulated methylene chain.[18]

The methylene signal of the cycloheptatriene moiety of **17a—c** appears around δ=2.4 as a triplet, and that of **18a—c** appears around δ=3.2, which is typical for 9*H*-cyclohepta[*b*]pyridines.[18] Thus, the ratio (**17**/**18**) was estimated by using these signals (Experimental). The regiochemistry of the enamine addition process giving intermediate **16a—c** was postulated as depicted in Scheme 3 by assuming a similarity to the reaction of **7**. Although the position of a phenyl group on the pyridine ring of **17c** and **18c** is unclear from the ^{1}H NMR spectrum, the structures of **17c** and **18c** have been tentatively assigned by assuming a mechanistic similarity (vide infra) to the reaction of **7** with enamine **10c**.

The reaction of the carbodiimide **9**, which could not be isolated in its pure form, with enamines **10a—c** were also examined in a one-pot procedure to give ring-annulated pyridine derivatives (Scheme 4). After a solution of iminotriphenylphosphorane **5** was reacted with phenyl isocyanate in bromobenzene at room temperature, the enamines **10a—c** were added to the solution. The mixtures were then heated under reflux to give **20a—c**. The results are summarized in Table 3. The structures of the new compounds **20a,b** were easily assigned on the basis of the spectral data. However, compound **20c** could not be differentiated from the other regioisomer **21** by spectral data. Therefore, **20c** was tentatively assigned by assuming a mechanistic similarity (vide infra) to the reaction of **7** with enamine **10c**.

On the other hand, the cycloaddition reaction of **7** with phenylacetylene in bromobenzene under refluxing for 3 h resulted in the formation of a pair of regioisomers, **23** and **15c**, in 5 and 2% yields, respectively (Scheme 5). This reaction was not regioselec-



Scheme 5.

Table 3. Results for the Reaction of **9** with Enamines **10a—c** to Give **20a—c**[a]

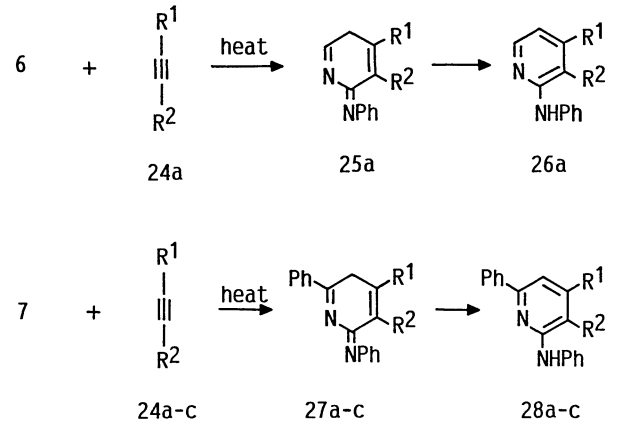
Enamine	Product yield/%
10a	49
10b	50
10c	42

a) Reactions were carried out in bromobenzene under refluxing for 3 h.

Table 4. Results for the Reaction of **6** or **7** with Activated Acetylenes **24a—c** to Give **26a** or **28a—c**[a]

Compound	Acetylene **24**	Reaction time/h	Product yield/%
6	**24a**	72	20
7	**24a**	8	24
7	**24b**	20	22
7	**24c**	9	28

a) Reactions were carried out in bromobenzene under refluxing.



Scheme 6.

tive, and the new compound **23** was easily assigned on the basis of a comparison of the spectral data with those of **15c**.

The cycloaddition reaction of **6** or **7** with activated acetylenes, **24a** or **24a—c**, respectively, in bromobenzene under refluxing also resulted in the formation of a pyridine derivative **26a** or **28a—c** in modest yield (Scheme 6). The results are summarized in Table 4. The spectral data of the new compounds, **26a** and **28a—c**, were consistent with the proposed structures. In the reaction of **7** with **24b,c**, regioselectivity was observed and only one regioisomer was obtained in each case. The regioselectivity was rationalized with the frontier molecular orbital consideration (vide infra).

Molecular Orbital Consideration. A frontier molecular orbital treatment has been successfully applied in order to rationalize both the reactivity and regioselectivity of cycloaddition reactions.[21] We found that this treatment predicts the high regioselectivity for cycloaddition reactions of the vinylcarbodiimide **7**. The frontier orbital energies and coefficients of butadiene (**29**), 2-aza-1,3-butadiene (**30**), vinylcarbodiimide (**31**) (model for **6**, **7**, **8**, and **9**), aminoethylene (**32**) (model for enamines **10a—c**), acetylene (**33**) (model for phenylacetylene), and propynal (**34**) (model for activated acetylenes **24a—c**) were estimated using the MNDO method (Fig. 2). In the [4+2] cycloaddition reaction, both the HOMO(diene)-LUMO(dienophile) and LUMO(diene)-HOMO(dienophile) interactions are important.[21] Since the HOMO of propynal (**34**) is located in a plane including the molecular framework (H-C≡CCH=O), the NHOMO is considered to be the frontier orbital. As shown in Fig. 2, the energy levels of HOMO and LUMO of vinylcarbodiimide **31** are lower than those of butadiene (**29**) and 2-aza-1,3-butadiene (**30**). The lower energy of LUMO (**31**) would increase the interaction with HOMO of dienophiles, such as aminoethylene (**32**). The magnitudes of coefficients of the LUMO (**31**)-HOMO (**32**) interactions were in accord with the observed regioselectivity in the reaction of **7** with unsymmetrical enamine **10c**. Carbodiimide **6**, **7**, **8**, and **9**, all of which have a phenyl group on the nitrogen atom, and **7**, **8**, and **9** are further conjugated with phenyl, C=C and C=O double bond, respectively. Consequently, the energy level of the

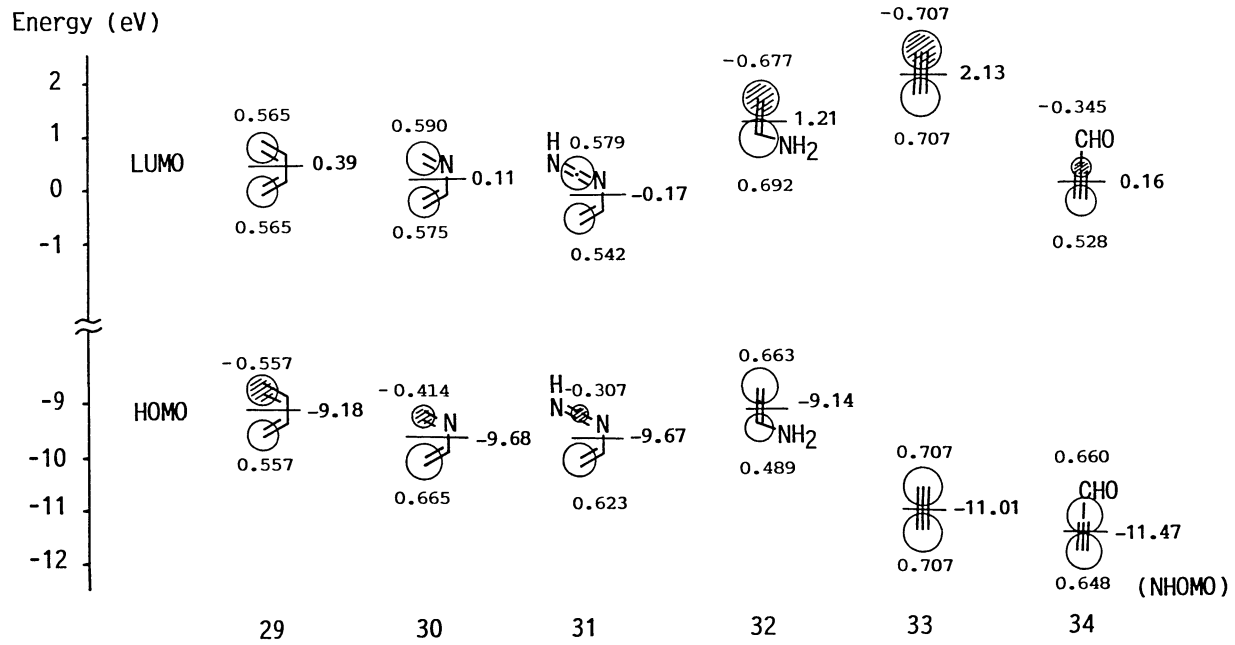


Fig. 2. Energies and coefficients of HOMO and LUMO estimated with MNDO method.

HOMO's of these compounds are expected to be raised and those of the LUMO's are lowered, and the LUMO(**6**—**9**)-HOMO(**10a**—**c**) interaction seems to be operative in the reaction of *N*-vinylcarbodiimides with enamines. Thus, the assignments of the structures of **17c**, **18c**, and **20c** also seems to be reasonable.

On the contrary, the lower energy of the LUMO (**34**) would increase the interaction with HOMO (**31**). The magnitude of the coefficient of the HOMO of **31** was also in accord with the observed regioselectivity in the reaction of **7** with unsymmetrical activated acetylenes, **24b,c**. In the reaction of **7** with phenylacetylene (**22**), the regioselectivity was not observed, and a pair of regioisomers was obtained.

In conclusion, the *N*-phenyl-*N'*-vinylcarbodiimides, which are easily prepared by the reaction of (vinylimino)triphenylphosphoranes with phenyl isocyanate, underwent a regioselective [4+2] cycloaddition reaction with electron-rich enamines as well as activated acetylenes. This type of cycloaddition reaction could also serve as a convenient route for the preparation of pyridines and an annulated pyridine ring system.

Experimental

The IR spectra were recorded on a Shimadzu IR-400 spectrometer. The ^{1}H NMR spectra were recorded on a Hitachi R-24, R-90H, JEOL JNM-PMX60SI, and JNM-GSX400 spectrometers, and the chemical shifts are given in ppm (δ) relative to the internal $SiMe_4$ standard. Mass spectral and high-resolution mass spectral studies were run on a Shimadzu GCMS-QP1000 or a JEOL DX-300 spectrometer. All of the melting points are uncorrected.

Preparation of *N*-Phenyl-*N'*-vinylcarbodiimide (6). A solution of (vinylimino)triphenylphosphorane (**2**)[18] (303 mg, 1 mmol) and phenyl isocyanate (143 mg, 1.2 mmol) in anhydrous benzene (5 ml) was refluxed for 4 h under a nitrogen atmosphere. After the reaction mixture was concentrated in vacuo, the residue was dissolved in hexane and the mixture was filtered to remove insoluble materials. The filtrate was concentrated and chromatographed on silica gel using hexane as an eluent to give **6** (74 mg, 51%): ^{1}H NMR (60 MHz, CCl_4) δ=4.73 (1H, d, J=7.6 Hz, H-*trans*), 5.06 (1H, d, J=15.0 Hz, H-*gem*), 6.43 (1H, dd, J=15.0, 7.6 Hz, H-*cis*), 7.01—7.36 (5H, m, Ph); IR (film) 3056, 2914, 2139, 1623, 1594, 1449, 1487, 1202, 1161, 1070, 755 cm^{-1}. Found: m/z 144.0651. Calcd for $C_9H_8N_2$: 144.0688.

Preparation of *N*-Phenyl-*N'*-(1-phenylvinyl)carbodiimide (7). A solution of [(1-phenylvinyl)imino]triphenylphosphorane (**3**) (3.78 g, 10 mmol) and phenyl isocyanate (1.19 g, 10 mmol) in anhydrous benzene (20 ml) was stirred for 30 min at room temperature under a nitrogen atmosphere. After the reaction mixture was concentrated in vacuo, hexane was added to the residue. The mixture was filtered to remove any insoluble materials, and the filtrate was concentrated. The resulting residue was chromatographed on silica gel using ether-hexane (1/49) as an eluent to give **7** (1.65 g, 75%): ^{1}H NMR (60 MHz, CCl_4) δ=5.08 (1H, s, H-*cis*), 5.25 (1H, s, H-*trans*), 7.00—7.69 (10H, m, Ph); IR (film) 3040, 2258, 2132, 1586, 1480, 1253, 1195, 749 cm^{-1}. Found: m/z 220.0995. Calcd for $C_{15}H_{12}N_2$: M, 220.1002.

Preparation of *N*-(1,3,5-Cycloheptatrienyl)-*N'*-phenylcarbodiimide (8). A solution of [(1,3,5-cycloheptatrienyl)-imino]triphenylphosphorane (**4**) (3.67 g, 10 mmol) and phenyl isocyanate (1.19 g, 10 mmol) in anhydrous benzene was stirred for 20 min at room temperature under a nitrogen atmosphere. The reaction mixture was concentrated in vacuo and hexane was added to the residue. After the mixture was filtered to remove any insoluble materials, the filtrate was concentrated and the residue was chromatographed on silica gel using ether-hexane (1/19) as an eluent to give **8** (1.70 g, 82%): ^{1}H NMR (90 MHz, $CDCl_3$) δ=2.61 (2H, d, J=6.9 Hz, H-7), 5.45 (1H, td, J=7.1, 9.0 Hz, H-6), 6.00—6.10 (1H, m, H-2), 6.22 (1H, dm, J=9.0 Hz, H-5), 6.40—6.50 (2H, m, H-3,4), 7.00—7.40 (5H, m, Ph); IR (film) 3016, 2881, 2123, 1611, 1593, 1501, 1239, 1161, 1072, 756, 708, 690 cm^{-1} Found: m/z 208.1001. Calcd for $C_{14}H_{12}N_2$: M, 208.1002.

Reaction of 6 with Enamine 10a. A solution of **6** (74 mg, 0.5 mmol) and enamine **10a** (167 mg, 1 mmol) in anhydrous toluene (3 ml) was refluxed for 15 min under a nitrogen atmosphere. The reaction mixture was separated by TLC on silica gel using AcOEt-hexane (1/2) as a developer to give 5,6,7,8-tetrahydro-1-(phenylamino)isoquinoline **12** (10 mg, 6%): Mp 181—182.5 °C (picrate); ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.65—2.00 (4H, m, H-6, 7), 2.33—2.71 (4H, m, H-5, 8), 6.15 (1H, broad s, NH), 6.40 (1H, d, J=5.0 Hz, H-4), 6.90—7.00 (1H, m, Ph), 7.14—7.51 (4H, m, Ph), 7.85 (1H, d, J=5.0 Hz, H-3); IR ($CHCl_3$) 3422, 2925, 1606, 1578, 1518, 1502, 1443, 1388, 1358 cm^{-1}. Found: m/z 224.1303. Calcd for $C_{15}H_{16}N_2$: M, 224.1315.

General Procedure for the Reaction of 7 with Enamines 10a—c and 13a,b. A solution of **7** (110 mg, 0.5 mmol) and enamines **10a—c** and **13a,b** (3 molar equiv) in anhydrous bromobenzene (3 ml) was refluxed for 30 min under a nitrogen atmosphere. The reaction mixture was chromatographed on silica gel using AcOEt-hexane (1/19) as an eluent to give pyridine derivatives **15a—c**. The results are summarized in Table 1. The structural proof for the pyridine derivatives **15a—c** were based on the following physical data.

5,6,7,8-Tetrahydro-1-phenylamino-3-phenylisoquinoline (**15a**): Mp 159—160 °C (from ethanol); ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.60—2.00 (4H, m, H-6, 7), 2.30—2.90 (4H, m, H-5, 8), 6.19 (1H, broad s, NH), 6.90—7.50 (7H, m, H-4 and Ph), 7.68 (2H, dm, J=7.8 Hz, Ph), 7.90—8.10 (2H, m, Ph); IR ($CHCl_3$) 3456, 3014, 2936, 1603, 1571, 1517, 1495, 1425, 1409, 1389 cm^{-1}. Found: m/z 300.1639. Calcd for $C_{21}H_{20}N_2$: M, 300.1628.

6,7-Dihydro-1-phenylamino-3-phenyl-5*H*-cyclopenta-[*c*]pyridine (**15b**): Mp 128.5—129.5 °C (from ethanol); ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.85—2.35 (2H, m, H-6), 2.66 (2H, t, J=7.0 Hz, H-7), 2.85 (2H, t, J=6.2 Hz, H-5), 6.00 (1H, broad s, NH), 6.90—7.50 (7H, m, H-4 and Ph), 7.60 (2H, dm, J=8.0 Hz, Ph), 7.90—8.10 (2H, m, Ph); IR ($CHCl_3$) 3441, 3011, 2961, 1605, 1573, 1521, 1497, 1447, 1413, 1401 cm^{-1}. Found: m/z 286.1480. Calcd for $C_{20}H_{18}N_2$: M, 286.1471.

2-Phenylamino-4,6-diphenylpyridine (**15c**): Mp 220.5—222.0 °C (picrate): ^{1}H NMR (400 MHz, $CDCl_3$) δ=6.79 (1H, broad s, NH), 7.02 (1H, d, J=1.1 Hz, H-3), 7.07 (1H, tt, J=7.3, 1.1 Hz, Ph), 7.36 (2H, t, J=8.1 Hz, Ph), 7.42 (1H, d, J=1.1 Hz, H-5), 7.42—7.50 (8H, m, Ph), 7.62—7.65 (2H, m, Ph), 8.04—8.06 (2H, m, Ph); IR ($CHCl_3$) 3416, 3002, 1594,

1550, 1498, 1450, 1419, 1077, 1010 cm^{-1}. Found: *m/z* 322.1469. Calcd for $C_{23}H_{18}N_2$: M, 322.1471.

General Procedure for the Reaction of 8 with 10a—c. A solution of **8** (104 mg, 0.5 mmol) and enamines **10a—c** (3 molar equiv) in anhydrous bromobenzene (2 ml) was refluxed for 30 min under nitrogen atmosphere. The reaction mixture was chromatographed on silica gel using AcOEt-hexane (1/19) as an eluent to give a mixture of pyridine derivatives **17a—c** and **18a—c**. The results are summarized in Table 2.

2,3,4,7-Tetrahydro-5-phenylamino-1*H*-cyclohepta[*c*]-isoquinoline (**17a**) and 2,3,4,9-tetrahydro-5-phenylamino-1*H*-cyclohepta[*c*]isoquinoline (**18a**): ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.70—2.00 (4H, m, H-2, 3), 2.30—2.90 (4H, m, H-1, 4), 2.39 (0.7 H, t, *J*=6.3 Hz, **18a**-H-9), 3.13 (1.3 H, d, *J*=6.3 Hz, **17a**-H-7), 5.60—7.70 (10H, m, olefin, Ph, and NH); IR ($CHCl_3$) 3456, 3011, 2941, 2876, 1598, 1581, 1555, 1499, 1441, 1381 cm^{-1}. Found: *m/z* 288.1619. Calcd for $C_{20}H_{20}N_2$: M, 288.1628.

1,2,3,6-Tetrahydro-4-(phenylamino)cyclohepta[*b*]cyclopenta[*d*]pyridine (**17b**) and 1,2,3,8-tetrahydro-4-(phenylamino)cyclohepta[*b*]cyclopenta[*d*]pyridine (**18b**): ^{1}H NMR (90 MHz, $CDCl_3$) δ=1.95—2.25 (2H, m, H-2), 2.44 (1.5H, t, *J*=6.7 Hz, **18b**-H-8), 2.50—3.00 (4H, m, H-1, 3), 3.18 (0.5H, d, *J*=6.8 Hz, **17b**-H-6), 5.50—7.70 (10H, m, olefin, Ph, and NH); IR ($CHCl_3$) 3440, 2965, 2855, 1587, 1567, 1499, 1437, 1395, 1369, 1303, 910 cm^{-1}. Found: *m/z* 274.1481. Calcd for $C_{19}H_{18}N_2$: M, 274.1471.

4-Phenyl-2-phenylamino-9*H*-cyclohepta[*b*]pyridine (**17c**) and 4-phenyl-2-phenylamino-7*H*-cyclohepta[*b*]pyridine (**18c**): ^{1}H NMR (60 MHz, CCl_4) δ=2.45 (0.8H, t, *J*=6.6 Hz, **18c**-H-7), 3.09 (1.2H, d, *J*=6.0 Hz, **17c**-H-9), 5.50—7.32 (16H, m, olefin, H-4, Ph, and NH); IR ($CHCl_3$) 3416, 3011, 1593, 1561, 1497, 1417, 1401 cm^{-1}. Found: *m/z* 310.1482. Calcd for $C_{22}H_{18}N_2$: M, 310.1471.

General Procedure for the Reaction of *N*-(3-Oxo-1-cyclohexenyl)-*N'*-phenylcarbodiimide (9) with Enamines 10a—c. A solution of [(3-oxo-1-cyclohexenyl)imino]-triphenylphosphorane (**10**) (186 mg, 0.5 mmol) and phenyl isocyanate (71 mg, 0.6 mmol) in anhydrous bromobenzene (3 ml) was stirred for 1 h under a nitrogen atmosphere. To the solution was added enamines **10a—c** (3 molar equiv) and the mixture was refluxed another 3 h. The reaction mixture was concentrated and the residue was chromatographed on silica gel using AcOEt-hexane (1/4) as an eluent to give quinoline derivatives **20a—c**. The results are summarized in Table 3.

6-Phenylamino-3,4,7,8,9,10-hexahydro-1(2*H*)-phenanthridinone (**20a**): Mp 164—165 °C (from ethanol); ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.60—2.20 (6H, m, H-3, 8, 9), 2.20—2.75 (4H, m, H-2, 7), 2.85—3.30 (4H, m, H-4, 10), 6.49 (1H, broad s, NH), 6.80—7.40 (3H, m, Ph), 7.62 (2H, dm, *J*=8.0 Hz, Ph); IR ($CHCl_3$) 3451, 3006, 2946, 2876, 1657, 1598, 1563, 1497, 1438, 1375, 1271, 1179 cm^{-1}. Found: *m/z* 292.1573. Calcd for $C_{19}H_{20}N_2O$: M, 292.1577.

4-Phenylamino-1,2,3,6,7,8-hexahydro-9*H*-cyclopenta-[*c*]quinolin-9-one (**20b**): Mp 182.5—183.5 °C (from ethanol); ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.90—2.40 (4H, m, H-2, 7), 2.40—2.70 (4H, m, H-3, 8), 3.02 (2H, t, *J*=6.0 Hz, H-6), 3.34 (2H, t, *J*=8.0 Hz, H-1), 6.30 (1H, broad s, NH), 6.90—7.40 (3H, m, Ph), 7.62 (2H, dm, *J*=8.0 Hz, Ph); IR ($CHCl_3$) 3436, 2956, 1661, 1605, 1573, 1497, 1443, 1369, 1271 cm^{-1}. Found: *m/z* 278.1405. Calcd for $C_{18}H_{18}N_2O$: M, 278.1420.

4-Phenyl-2-phenylamino-7,8-dihydro-5(6*H*)-quinolinone (**20c**): Mp 182.5—183.5 °C (from ethanol); ^{1}H NMR (60 MHz, $CDCl_3$) δ=1.90—2.35 (2H, m, H-7), 2.54 (2H, t, *J*=6.0 Hz, H-6), 2.99 (2H, t, *J*=5.9 Hz, H-8), 6.40 (1H, s, NH), 6.90—8.00 (11H, m, H-3 and Ph); IR ($CHCl_3$) 3406, 3011, 2956, 1663, 1581, 1543, 1493, 1411, 1289 cm^{-1}. Found: *m/z* 314.1427. Calcd for $C_{21}H_{18}N_2O$: M, 314.1420.

Reaction of 7 with Phenylacetylene (22). A solution of **7** (1.01 g, 4.59 mmol) and phenylacetylene (1.40 g, 13.7 mmol) in anhydrous bromobenzene (3 ml) was refluxed for 3 h. The reaction mixture was separated by column chromatography on silica gel. The fractions eluted with ether-hexane (1/49) contained 2-phenylamino-3,6-diphenylpyridine (**23**) (81 mg, 5%): Mp 115.5—116 °C (from ethanol); ^{1}H NMR (400 MHz, $CDCl_3$) δ=6.66 (1H, broad s, NH), 6.99 (1H, tt, *J*=7.3, 1.1 Hz, Ph), 7.30 (2H, tm, *J*=7.3 Hz, Ph), 7.34 (1H, d, *J*=7.7 Hz, H-5), 7.41 (1H, tt, *J*=7.3, 1.1 Hz, Ph), 7.43—7.53 (8H, m, H-4 and Ph), 7.67 (2H, broad d, *J*=7.7 Hz, Ph), 8.08—8.10 (2H, m, Ph); IR (KBr) 3406, 3051, 1603, 1587, 1563, 1519, 1493, 1429, 1409, 1331, 1184, 750, 694 cm^{-1}. Found: *m/z* 322.1447. Calcd for $C_{23}H_{18}N_2$: M, 322.1471.

The fractions eluted with AcOEt-hexane (5/95) contained **15c** (26 mg, 2%).

Reaction of 6 with Dimethyl Acetylenedicarboxylate (24a). A solution of **6** (30 mg, 0.21 mmol) and **24a** (118 mg, 0.84 mmol) in anhydrous toluene (2 ml) was refluxed for 72 h under nitrogen atmosphere. The reaction mixture was concentrated and separated by TLC on silica gel using AcOEt-hexane (5/1) as a developer to give 2-phenylamino-3,4-bis(methoxycarbonyl)pyridine (**26a**) (12 mg, 20%): Mp 145.5—147 °C (picrate); ^{1}H NMR (90 MHz, $CDCl_3$) δ=3.91 (6H, s, Me), 6.74 (1H, d, *J*=3.2 Hz, H-5), 7.07 (1H, t, *J*=8.1 Hz, Ph), 7.33 (2H, t, *J*=8.1 Hz, Ph), 7.58 (2H, d, *J*=8.1 Hz, Ph), 8.39 (1H, d, *J*=3.2 Hz, H-6), 9.64 (1H, broad s, NH); IR ($CHCl_3$) 3337, 3008, 2960, 1731, 1697, 1600, 1580, 1562, 1525, 1434, 1286, 1158, 1122, 1014 cm^{-1}. Found: *m/z* 286.0941. Calcd for $C_{15}H_{14}N_2O_4$: M, 286.0954.

General Procedure for the Reaction of 7 with 24a—c. A solution of **7** (110 mg, 0.5 mmol) and **24a—c** in anhydrous bromobenzene (3 ml) was refluxed for the period indicated in Table 4 under a nitrogen atmosphere. The reaction mixture was concentrated and the residue was chromatographed on silica gel using CH_2Cl_2. The fractions eluted with CH_2Cl_2 were concentrated and further separated by TLC on silica gel using AcOEt-hexane (3/1) as a developer to give pyridine derivatives **28a—c**. The results are summarized in Table 4.

2-Phenylamino-6-phenyl-3,4-bis(methoxycarbonyl)pyridine (**28a**): Mp 107.0—107.5 °C (from ethanol); ^{1}H NMR (90 MHz, $CDCl_3$) δ=3.82 (3H, s, Me), 3.87 (3H, s, Me), 7.00—7.50 (7H, m, H-5 and Ph), 7.70 (2H, dm, *J*=8.0 Hz, Ph), 7.90—8.10 (2H, m, Ph), 9.85 (1H, broad s, NH); IR ($CHCl_3$) 3325, 3000, 2945, 1733, 1688, 1599, 1578, 1549, 1241, 1160, 1126 cm^{-1}. Found: *m/z* 362.1247. Calcd for $C_{21}H_{18}N_2O_4$: M, 362.1267.

2-Phenylamino-6-phenyl-3-(methoxycarbonyl)pyridine (**28b**): Mp 66.5—67.0 °C (from ethanol); ^{1}H NMR (90 MHz, $CDCl_3$) δ=3.88 (3H, s, Me), 6.90—7.50 (6H, m, Ph), 7.14 (1H, d, *J*=8.1 Hz, H-5), 7.73—8.00 (4H, m, Ph), 8.22 (1H, d, *J*=8.1 Hz, H-4), 10.23 (1H, broad s, NH); IR ($CHCl_3$) 3325, 3004, 2857, 1586, 1603, 1590, 1571, 1293, 1251, 1146 cm^{-1}. Found: *m/z* 304.1231. Calcd for $C_{19}H_{16}N_2O_2$: M, 304.1213.

3-Benzoyl-2-phenylamino-6-phenylpyridine (**28c**): Mp 118.0—118.5 °C (from ethanol); ^{1}H NMR (90 MHz, $CDCl_3$) δ=6.90—7.60 (11H, m, Ar), 7.12 (1H, d, J=8.4 Hz, H-3), 7.75—8.10 (4H, m, Ph), 7.88 (1H, d, J=8.4 Hz, H-4), 11.10 (1H, broad s, NH); IR ($CHCl_3$) 3280, 3008, 1601, 1590, 1563, 1519, 1500, 1298, 1245, 909 cm^{-1}. Found: m/z 350.1409. Calcd for $C_{24}H_{18}N_2O$: M, 350.1420.

Financial support by the Science and Engineering Research Laboratory of Waseda University is greatly acknowledged.

References

1) Part 16: M. Nitta, M. Ohnuma, and Y. Iino, *J. Chem. Soc., Perkin Trans. 1,* in press.

2) A part of this paper was presented at the National Meeting of the Chemical Society of Japan, Sendai, October 1988, Abstr., No. 1A302.

3) D. L. Boger, *Chem. Rev.*, **86**, 781 (1986); T. Kametani and S. Hibino, *Adv. Heterocycl. Chem.*, **42**, 246 (1987).

4) A. Demoulin, H. Gorissen, A.-M. H.-Frisque, and L. Ghosez, *J. Am. Chem. Soc.*, **97**, 4409 (1975).

5) R. Gompper and U. Heinemann, *Angew. Chem., Int. Ed. Engl.*, **20**, 296 (1981).

6) Y. Nomura, Y. Takeuchi, S. Tomoda, and M. M. Itoh, *Bull. Chem. Soc. Jpn.*, **54**, 2779 (1981).

7) F. Sainte, B. Serckx-Poncin, A.-M. Hasbain-Frisque, and L. Ghosez, *J. Am. Chem. Soc.*, **104**, 1428 (1982); P. Bayard and L. Ghoses, *Tetrahedron Lett.*, **29**, 6115 (1988); and references cited therein.

8) J. Barluenga, F. J. Gonzalez, V. Gotov, and S. Fustero, *J. Chem. Soc., Perkin Trans. 1,* **1988**, 1739; J. Barluenga, J. Joglar, S. Fustero, V. Gotov, C. Kruger, and M. J. Romao, *Chem. Ber.*, **118**, 3652 (1985).

9) J. Barluenga, F. J. Gonzalez, S. Fustero, and V. Gotov, *J. Chem. Soc., Chem. Commun.*, **1986**, 1179.

10) J. Barluenga, F. J. Gonzalez, S. Fustero, M. de la C. F. Foces, F. H. Cano, and A. S. Faliciano, *J. Chem. Res., Synop.*, **1898**, 66.

11) G. Wulff and H. Bohnke, *Angew. Chem., Int. Ed. Engl.*, **25**, 90 (1986); J. Barluenga, M. Ferrero, and F. Palacios, *Tetrahedron Lett.*, **29**, 4863 (1988).

12) J. Barluenga, M. Tomas, A. Ballesteros, and V. Gotov, *J. Chem. Soc., Chem. Commun.*, **1987**, 1195.

13) T. Saito, M. Nakane, M. Endo, M. Yamashita, Y. Oyamada, and S. Motoki, *Chem. Lett.*, **1986**, 135.

14) P. Molina, P. M. Fresneda, and F. de Ciencias, *Tetrahedron Lett.*, **29**, 379 (1988).

15) J. Barluenga, M. Ferrero, and F. Palacios, *Tetrahedron Lett.*, **29**, 4863 (1988).

16) Y. Iino, T. Kobayashi, and M. Nitta, *Heterocycles,* **24**, 2437 (1986).

17) M. Nitta, H. Soeda, and Y. Iino, *Bull. Chem. Soc. Jpn.*, **63**, 932 (1990); Y. Iino, E. Hara, and M. Nitta, *Bull. Chem. Soc. Jpn.*, **62**, 1913 (1989).

18) Y. Iino and M. Nitta, *Bull. Chem. Soc. Jpn.*, **61**, 2235 (1988); M. Nitta and Y. Iino, *J. Chem. Soc., Perkin Trans. 1,* **1990**, 435.

19) N. Kanomata and M. Nitta, *J. Chem. Soc., Perkin Trans. 1,* **1990**, 1119.

20) M. Nitta, Y. Iino, E. Hara, and T. Kobayashi, *J. Chem. Soc., Perkin Trans. 1,* **1989**, 51; and references cited therein.

21) I. Fleming, "Frontier Orbitals and Organic Reactions," John Wiley and Sons, London (1976).