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REACTIONS OF 8-(TRIPHENYLPHOSPHOIMINO)QUINOLINE WITH ARYL ALDEHYDES AND ARYL ISOCYANATES: FORMATION OF 2-ARYL-4*H*-IMIDAZO[4,5,1-*ij*]QUINOLINES AND RELATED SYSTEMS†

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Abstract – The reaction of 8-(triphenylphosphoimino)quinoline with aryl aldehydes gave 2-aryl-4*H*-imidazo[4,5,1-*ij*]quinolines. In the reaction, tandem aza-Wittig reaction and cyclization attended with hydride shift occurred. The reaction of 8-(triphenylphosphoimino)quinoline with aryl isocyanates gave 1,3-diaryl-1,2,3,9a-tetrahydro[1,3,5]triazolo[2',3':2,1;3',4'-*a*]imidazo[4,5,1-*ij*]quinolin-2-ones (**11**) and 2-(arylamino)imidazo[4,5,1-*ij*]quinolin-4(4*H*)-ones (**12**). The structures of **11a** (Ar = Ph) and **12a** (Ar = Ph) were confirmed by X-Ray structure analyses.

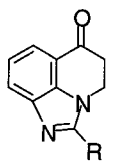
INTRODUCTION

4,5-Dihydro-6*H*-imidazo[4,5,1-*ij*]quinolin-6-one system, such as **1** and **2**, is known to have physiological activities such as inhibition of poly(ADP-ribosyl)transferase, inhibition of IgE antibody production, and amelioration of the effects of stroke, head trauma, and neurodegenerative disease.[1-4] It is thought that 4*H*-imidazo[4,5,1-*ij*]quinoline system (**3**) would have potentially physiological activities and be a good precursor of 4,5-dihydro-6*H*-imidazo[4,5,1-*ij*]quinolin-6-one system. We previously reported the synthesis of 2-phenyl-2a,3-dihydro-1,2a-diazacyclopent[*cd*]azulene (2-phenyl-4*H*-cyclohepta[1'2':3,2;2',3'-*d*]pyrrolo[1,2-*c*]imidazole) system (**4**), which is a isomeric system of **3**, by the

† Dedicated to Dr. Satoshi Ōmura occasion of his 70th birthday.

reaction of 8-(triphenylphosphoimino)-1-azaazulene (8-(triphenylphosphoimino)cyclohepta[*b*]pyrrole) derivative (**5**) with aryl aldehyde.[5] Therefore, it is considered that the reaction of 8-(triphenylphosphoimino)quinoline (**6**), being an isomer of 8-(triphenylphosphoimino)-1-azaazulene system, with aryl aldehyde would produce 2-aryl-4*H*-imidazo[4,5,1-*ij*]quinoline.

It is known that the iminophosphoranes reveal synthetic versatility for the construction of fused heterocycles.[6-9] We also reported the synthesis and some reactions of the 8-phosphoimino-1-azaazulene derivative (**5**).[5,10,11] In the structure of **5**, the interaction between N-1 and the P atoms was observed, and **5** had a ticyclic charactor.[10] Although a few researches about 2-phosphoiminoquinoline are known,[12-14] the reaction of 8-phosphoiminoquinoline was not reported so far. Therefore, for the comparison of the cases of 8-phosphoimino-1-azaazulene and 2-phosphoiminoquinoline, the studies about the synthesis and reactions of 8-phosphoiminoquinoline, being an isomer of 8-phosphoimino-1-azaazulene, would be meaningful.



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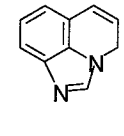

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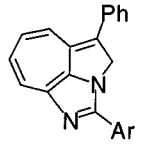

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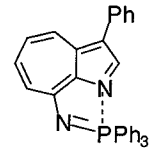

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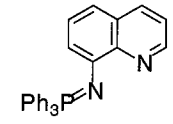


6

RESULTS AND DISCUSSION

8-(Triphenylphosphoimino)quinoline (**6**) was prepared in good yields in two ways as follows; Method A) a reaction of 8-aminoquinoline with dibromotriphenylphosphorane, and Method B) a reaction of 8-aminoquinoline with triphenylphosphine and hexachloroethane in the presence of triethylamine. Thus **6** was obtained in 82% (Method A) and 94% yields (Method B), respectively, and the structure of **6** was deduced by spectroscopic data as well as elemental analyses. Its ^{31}P NMR spectrum showed a signal at δ_P 15.955, and this chemical shift is adequate as a phosphoimine derivative.[14] In the ^{1}H NMR spectrum of **6**, the quinoline ring protons appeared at δ_H 7.05 (dd, *J* 7.6 and 1.3, H-5), 7.07 (dd, *J* 8.2 and 4.1, H-3), 7.29 (dd, *J* 7.6 and 6.7, H-6), 7.30 (dd, *J* 6.7 and 1.3, H-7), 7.93 (dd, *J* 8.2 and 1.7, H-4), and 8.18 (dd, *J*

4.1 and 1.7, H-2). The conformation of phosphoimine moiety was deduced by its ^{13}C NMR spectrum. The signal of C(7) was appeared at δ_C 128.90 (J 14.5) as doublet, being long-range coupling with P. On the other hand, the signal of C(2) was appeared at δ_C 145.51 as singlet. In the case of 8-phosphoimino-1-azaazulene (**5**), where the coupling of P-C(2) was clearly observed in NMR spectra, and **5** was exist in as cyclic structure. The results suggest that interaction between P and N(1) did not exist. For determination of the conformation and the nature of **6**, we performed the molecular orbital calculation by Gaussian 98 using RHF / 6-31G*.[15] The optimized structure of **6** is shown in Figure 1. The atomic charge of C(2) position is rather positive, and this suggests the possibility that the further cyclization could be occurred at C(2).

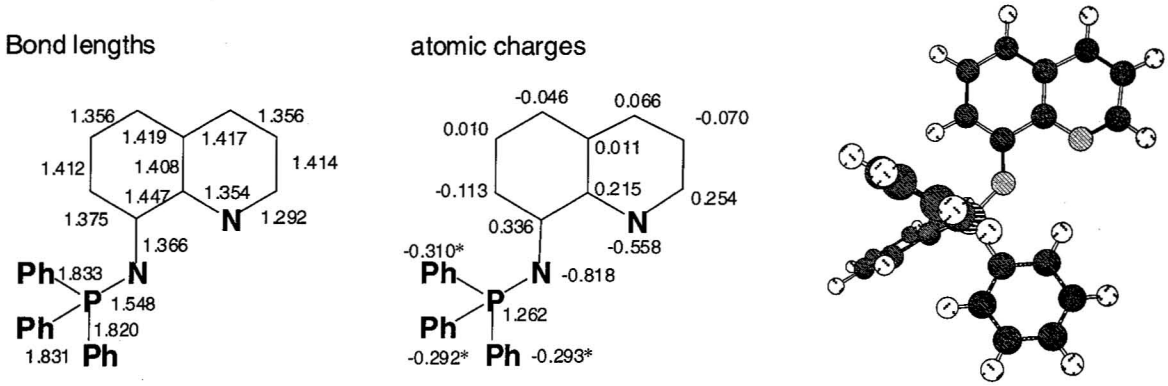


Figure 1. Calculated bond lengths (Å), atomic charges, and the optimized structure of **6**.
*Atomic charges of phenyl carbon atom connected with phosphorus atom

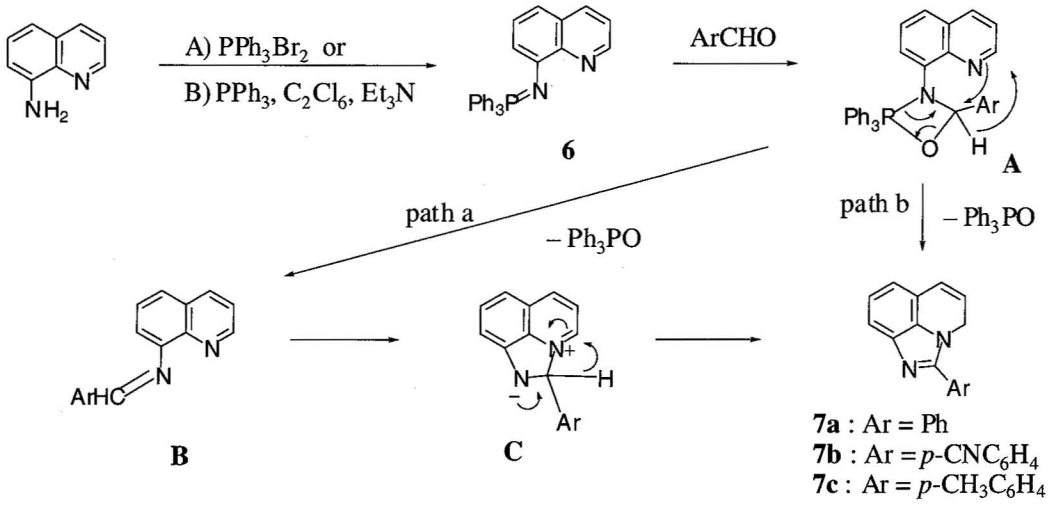
When **6** was treated with benzaldehyde in xylene under heating at 125 ℃ for 200 h, the cycloadduct (**7a**) was obtained in 73% yield as pale yellow needles. In the MS spectrum of **7a**, the molecular peak appeared at *m/z* 232 as a parent peak. Thus **7a** was analyzed as $C_{16}H_{12}N_2$ from its MS and elemental analyses. In its ^{13}C NMR spectrum, a methylene carbon appeared at δ47.76. In the ^1H NMR spectrum of **7a**, methylene protons were appeared at δ_H 5.30 (dd, J 3.5 and 2.3), and two vinylic protons on dihydropyridine ring were seen at δ_H 5.82 (dt, J 10.0 and 3.5, H-5) and 6.61 (dt, J 10.0 and 2.3, H-6). Three protons of benzene moiety were seen at δ_H 6.86 (d, J 7.1, H-7), 7.08 (dd, J 8.2 and 7.1, H-8), and 7.54 (d, J 8.2, H-9). From the results, we assigned the structure of **7a** as 2-phenyl-4*H*-imidazo[4,5,1-*ij*]quinoline.

Similar reaction of **6** with *p*-cyanobenzaldehyde and *p*–tolualdehyde gave **7b** and **7c** in 52% and 68% yields, respectively.

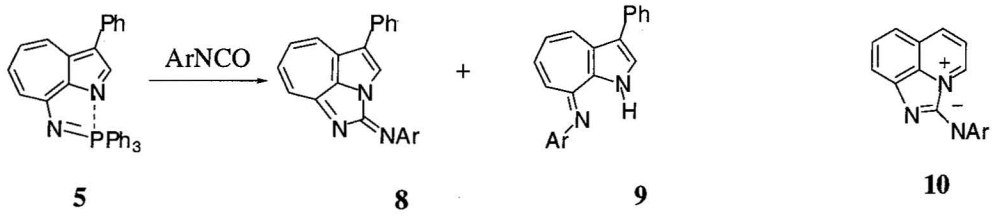
The reaction resembled to the case of 8-phosphoimino-1-azaazulene (**5**).[5] Plausible reaction mechanism

is shown in Scheme 1. Two reaction pathways are considered as follows. Cycloaddition of aryl aldehyde with the iminophosphorane (**6**) would produce the intermediate (**A**). Eilimination of triphenylphosphine oxide from **A** gives the Shiff base (**B**) (Aza-Wittig reaction) and successive cyclization gives **C**. Hydride shift to the iminium carbon furnishes **7** (Path a). When cyclization and elimination of triphenylphosphine oxide occurred attended with hydride shift concertedly, **7** would be produced (Path b).

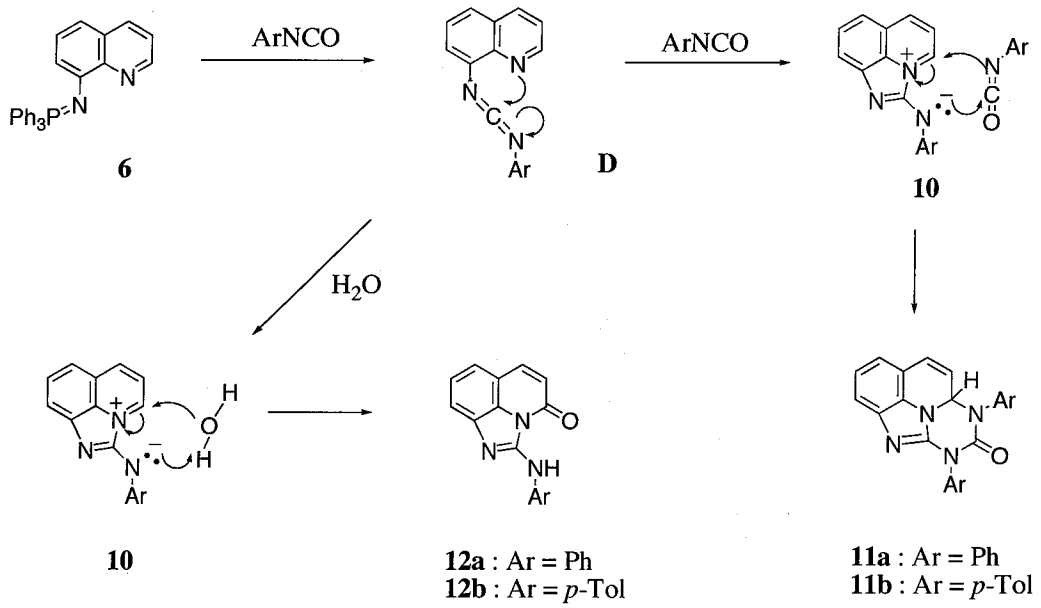
Some Shiff bases (**B**) are known as stable crystals and some properties were reported,[16] but about the cyclization of **B** was not mentioned. Therefore, we examined the synthesis and cyclization of **B** (Ar = Ph, *p*-CNC_6H_4, *p*-$CH_3C_6H_4$). Treatment of 8-aminoquinoline with benzaldehyde in the presence of *p*-toluenesulfonic acid and molecular sieves 4A (MS4A) under reflux in toluene gave 8-benzylideneiminoquinoline (**B** : Ar = Ph) as colorless crystals. Heating the crystals in xylene at 125 ℃ for 200 h gave **7a** in an extremely low yield (0.2%). The result suggested that the cyclization of 8-benzylideneiminoquinoline would not be preferential. Therefore, we preferred the path b as a main route.



Scheme 1



We previously reported that **5** reacted with aryl isocyanate to give **8** and **9**. It is thought that if similar cyclization reaction occurred between **6** and aryl isocyanate, the twitter ion (**10**) would be produced. Therefore, we next examined the reaction of **6** with some aryl isocyanates. Treatment of **6** with phenyl isocyanate in benzene at 80 ℃ for 24 h gave **11a** and **12a** in 33% and 6% yields, respectively. In the ^{1}H NMR spectrum of **11a**, a methine proton was appeared δ_H 7.02 (t, *J* 2.1), and two vinylic protons on the dihydropyridine ring were seen at δ_H 5.47 (dt, *J* 10.1 and 2.1, H-8) and 6.78 (dt, *J* 10.1 and 2.1, H-9). In its ^{13}C NMR spectrum, a methine carbon was observed at δ_C 65.28. In the ir spectrum of **11a**, a carbonyl signal was seen at 1690 cm^{-1}. From the results, we assigned the structure of **11a** as 1,3-diphenyl-1,2,3,9a-tetrahydro[1,3,5]triazolo[2',3':2,1;3',4'-*a*]imidazo[4,5,1-*ij*]quinolin-2-one. Finally, the structure of **11a** was confirmed by X-Ray structure analysis. Ortep drawing[16] of **11a** is shown in Figure 2.



Scheme 2

In the ^{1}H NMR spectrum of **12a**, a couple of A,B-doublets signals were seen at δ_H 6.74 (d, *J* 9.4, H-5) and 7.97 (d, *J* 9.4, H-6) and NH proton was observed at δ_H 9.82. Three protons of benzene moiety were seen at δ_H 7.43-7.47 (m, H-7 and 8) and 7.70 (d, *J* 5.9 and 2.4, H-9), along with phenyl protons at δ_H 7.15 (dt, *J* 7.4 and 1.0, H-*p*-phenyl), 7.42 (dd, *J* 8.7 and 7.4, H-*m*-phenyl), and 7.89 (dd, *J* 8.7 and 1.0, H-*o*-phenyl). In the ir spectrum of **12a**, an amino peak and a carbonyl peak were seen at 3268 and 1679 cm^{-1}, respectively. From the results, we assigned the structure of **12a** as 2-(*N*-anilino)imidazo[4,5,1-*ij*]quinolin-4(4*H*)-one. The structure of **12a** was confirmed by X-Ray structure analysis. Ortep

drawing[17] of **12a** is shown in Figure 3.

In the similar manner, reaction of **6** with *p*-tolyl isocyanate gave **11b** (8%) and **12b** (2%).

Plausible mechanism is shown in Scheme 2. Aza-Wittig reaction of **6** with aryl isocyanate gives the carbodiimide (**D**). Intramolecular cyclization of **D** would afford twitter ion (**10**). Cycloaddition of **10**

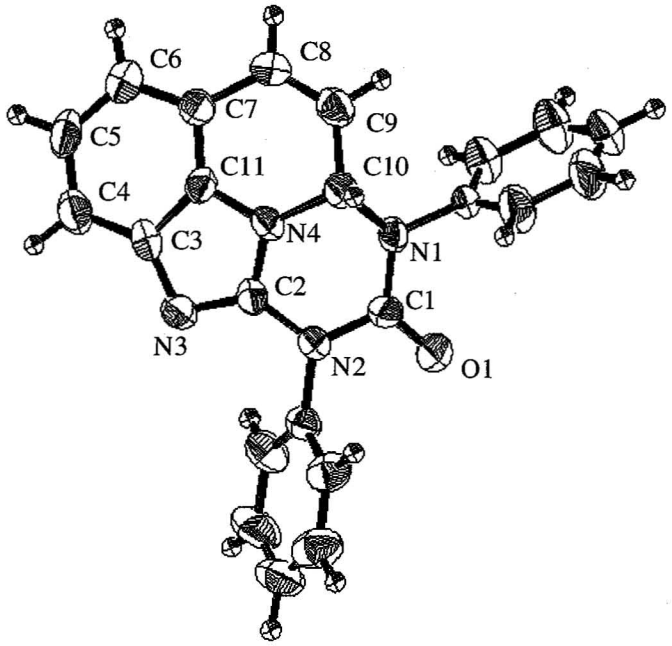


Figure 2. ORTEP drawing of **11a** with thermal ellipsoids (50% probability)

Selective bond length (Å): O(1)−C(1) 1.220(8), N(1)−C(10) 1.495(7), N(1)−C(1) 1.375(8), N(2)−C(1) 1.409(7), N(2)−C(2) 1.391(8), N(3)−C(2) 1.326(8), N(3)−C(3) 1.421(9), N(3)−C(11) 1.414(9), N(2)−C(2) 1.394(9), N(3)−C(2) 1.390(9), N(3)−C(3) 1.421(9), N(3)−C(3) 1.404(9), N(4)−C(10) 1.395(9), N(4)−C(2) 1.350(8), N(4)−C(11) 1.368(8), C(3)−C(4) 1.395(9), C(3)−C(11) 1.389(9), C(4)−C(5) 1.391(10), C(5)−C(6) 1.393(9), C(6)−C(7) 1.392(9), C(7)−C(8) 1.462(9), C(7)−C(11) 1.370(9), C(8)−C(9) 1.339(9), C(9)−C(10) 1.495(9).

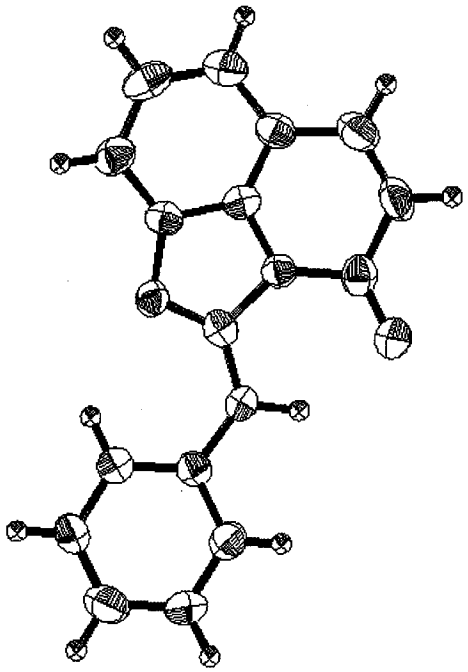


Figure 3. ORTEP drawing of **12a** with thermal ellipsoids (50% probability)

with another molar aryl isocyanate furnishes to **11**. When **10** reacts with water, **12** is produced. Although it is thought that hydrolysis of the carbodiimide (**D**) could afford urea derivative, cyclization adducts (**12a,b**) were obtained. Therefore, it is thought that cyclization of **D** would easily occur. It is known that silica gel causes hydrolysis. Therefore we next treated **6** with *p*-tolyl isocyanate in the presence of silica gel, and **12b** obtained in improved yield (14%). Silica gel would facilitate the addition of water to the twitter ion (**10**). In the reaction of **6** with aryl isocyanate, blue color appeared. We assumed the color substance would be the twitter ion (**10**), and tried to isolate **10** under the reaction at room temperature, but the attempt failed.

CONCLUSION

2-Aryl-4*H*-imidazo[4,5,1-*ij*]quinoline system was easily constructed in good yield by the reaction of 8-(triphenylphosphoimino)quinoline with aryl aldehydes through tandem aza-Wittig reaction and cyclization. The reaction of 8-(triphenylphosphoimino)quinoline with aryl isocyanates afforded 1,3-

diaryl-1,2,3,9a-tetrahydro[1,3,5]triazolo[2',3':2,1;3',4'-*a*]imidazo[4,5,1-*ij*]quinolin-2-ones (**11**) and 2-(arylamino)imidazo[4,5,1-*ij*]quinolin-4(4*H*)-ones (**12**) via the carbodiimide and twitter ionic mediacy.

EXPERIMENTAL

Mps are measured using a Yanagimoto micro-melting apparatus and uncorrected. ^{1}H NMR spectra (including HH-COSY and CH-COSY NMR) were recorded on a Bruker AVANCE 400S (400 MHz) and ^{13}C NMR spectra were recorded on a Bruker AVANCE 400S (100.6 MHz) using deuteriochloroform as a solvent with tetramethylsilane as an internal standard; *J* values are recorded in Hz. ^{31}P NMR spectra were recorded on a Bruker AVANCE 400S using deuteriochloroform as a solvent with triphenylphosphine as an internal standard. IR spectra were recorded for KBr pellets on a Nicolet FT-IR Impact 410. MS spectra were taken with on an LC-MS Waters Integrity System. Elemental analyses were taken with a Perkin Elmer 2400II. Kieselgel 60 was used for column chromatography and Kieselgel 60G was used for thin-layer chromatography.

Synthesis of 8-(triphenylphosphoimino)qunoline (6)

Method A - Under argon atmosphere, a mixture of 8-aminoquinoline (**7**) (0.086 g, 0.59 mmol), dibromotriphenylphosphorane (0.345 g, 0.82 mmol), triethylamine (0.34 mL, 2.46 mmol) in dry benzene (3.0 mL) was stirred for 24 h at rt. The solvent was evaporated, and the residue was recrystallized from hexane-chloroform to give **6** as yellow powder (0.196 g, 82%).

Method B - Under argon atmosphere, to a solution of **7** (0.440 g, 3.05 mmol) in dry benzene (30.0 mL) were added consecutively triethylamine (1.0 mL, 9.9 mmol), triphenylphosphine (0.950 g, 3.62 mmol) and hexachloroethane (0.722 g, 3.05 mmol). After refluxed for 10.5 h, the precipitate was filtered off. The filtrate was evaporated, and the residue was chromatographed with hexane-ethyl acetate to give **6** (1.159 g, 94%).

6: Yellow powder (from hexane-dichloromethane), mp 180-182 ℃; δ_H 7.05 (1H, dd, *J* 7.6 and 1.3, H-5), 7.07 (1H, dd, *J* 8.2 and 4.1, H-3), 7.29 (1H, dd, *J* 7.6 and 6.7, H-6), 7.30 (1H, dd, *J* 6.7 and 1.3, H-7), 7.32-7.50 (9H, m, H-*m*,*p*-phenyl), 7.77-7.85 (6H, dddd, *J* 11.8 (J_{P-H}), 8.2, 2.1, and 1.3, H-*o*-phenyl), 7.93 (1H, dd, *J* 8.2 and 1.7, H-4), and 8.18 (1H, dd, *J* 4.1 and 1.7, H-2); δ_C 116.61, 120.20 (d, *J* 20.3), 121.08, 128.24, 128.90 (d, *J* 14.5), 129.74, 131.70, 132.73 (d, *J* 9.7), 136.20, 142.20 (d, *J* 9.4), and 145.51; δ_P 15.955; ν_{max} / cm^{-1} 1460 (P–phenyl), 750, 720, and 691 (phenyl); *m/z* (rel intensity) 405 (M^+ + 1, 92), 404 (M^+, 68), 328 (53), 262 (19), 249 (35), 183 (83), 173 (100), 144 (27). *Anal.* Calcd for $C_{27}H_{21}N_2P$: C, 80.18 H, 5.23; N, 6.93. Found: C, 80.05; H, 5.33; N, 6.78.

Reaction of 6 with aryl aldehyde

Typical procedure - Under argon atmosphere, a mixture of **6** (0.276 g, 0.68 mmol), benzaldehyde (0.071 mL, 0.68 mmol) in dry xylene (6.0 mL) was heated at 125 ℃ for 200 h in a sealed tube, then the mixture was evaporated. Chromatography of the residue gave **7a** (0.115 g, 73%).

In the similar manner, reaction of **6** with *p*-cyanobenzaldehyde and *p*-tolyl isocyanate gave **7b** (52%) and **7c** (68%).

7a: Pale yellow needles (from hexane-chloroform), mp 113-114 ℃; δ_H 5.30 (2H, dd, *J* 3.5 and 2.3, H-methylene), 5.82 (1H, dt, *J* 10.0 and 3.5, H-5), 6.61 (1H, dt, *J* 10.0 and 2.3, H-6), 6.86 (1H, d, *J* 7.1, H-7), 7.08 (1H, dd, *J* 8.2 and 7.1, H-8), 7.47 (1H, dd, *J* 7.4 and 1.4, H-*p*-phenyl), 7.48 (2H, dd, *J* 7.9 and 7.4, H-*m*-phenyl), 7.54 (1H, d, *J* 8.2, H-9), and 7.87 (2H, dd, *J* 7.9 and 1.4, H-*o*-phenyl); δ_C 47.76, 118.23, 119.72, 119.83, 122.65, 123.46, 123.86, 128.41, 129.22, 130.09, 130.70, 133.53, 140.81, and 151.81; ν_{max} / cm^{-1} 750, 721, and 691 (phenyl); *m/z* (rel intensity) 232 (M^+, 100), 231 (60), 157 (12), 128 (26), 115 (22), 108 (90), and 77 (11). *Anal.* Calcd for $C_{16}H_{12}N_2$: C, 82.73; H, 5.21; N, 12.06. Found: C, 82.64; H, 5.28; N, 12.21

7b: Pale yellow needles (from hexane-chloroform), mp 173-174 ℃; δ_H 5.41 (2H, dd, *J* 3.5 and 2.3, H-methylene), 5.89 (1H, dt, *J* 10.0 and 3.5, H-5), 6.69 (1H, dt, *J* 10.0 and 2.3, H-6), 6.93 (1H, d, *J* 7.1, H-7), 7.15 (1H, dd, *J* 8.3 and 7.1, H-8), 7.57 (1H, d, *J* 8.3, H-9), 7.81, (2H, dd, *J* 8.6 and 1.8, H-*m*-phenyl), and 8.07 (2H, dd, *J* 8.6 and 1.8, H-*o*-phenyl); δ_C 48.07, 113.46, 118.72, 119.08, 119.91, 120.20, 122.42, 124.02, 128.73, 132.99, 133.74, 135.04, 140.92, and 149.41; ν_{max} / cm^{-1} 2224 (CN); *m/z* (rel intensity) 257 (M^+, 64), 256 (100), 128 (14), and 101(24). *Anal.* Calcd for $C_{17}H_{11}N_3$: C, 79.36; H, 4.31; N, 16.33. Found: C, 79.26; H, 4.33; N, 16.47.

7c: Pale yellow needles (from hexane-chloroform), mp 153 - 155 ℃; δ_H 2.43 (3H, s, Me), 5.34 (2H, dd, *J* 3.4 and 2.3, H-methylene), 5.84 (1H, dt, *J* 9.9 and 3.4, H-5), 6.64 (1H, dt, *J* 9.9 and 2.3, H-6), 6.86 (1H, d, *J* 7.1, H-7), 7.09 (1H, dd, *J* 8.2 and 7.1, H-8), 7.31 (2H, d, *J* 8.1, H-*m*-phenyl), 7.54 (1H, d, *J* 8.2, H-9), and 7.80 (2H, d, *J* 8.1, H-*o*-phenyl); δ_C 21.82, 47.82, 118.06, 119.62, 119.78, 122.65, 123.31, 123.94, 127.93, 128.30, 133.56, 140.26, 140.88, and 152.01; *m/z* (rel intensity) 246 (M^+, 100). *Anal.* Calcd for $C_{17}H_{14}N_2$: C, 82.90; H, 5.73; N, 11.37. Found: C, 82.78; H, 5.64; N, 11,54

Synthesis and reaction of 8-benzilideneiminoquinoline

Under argon atmosphere, a mixture of 8-aminoquinoline (0.4475 g, 3.1 mmol), benzaldehyde (0.31 mL, 2.97 mmol), and *p*-toluenesulfonic acid (0.10 g) in dry benzene (100 mL) was heated under reflux for 27 h and the water was removed azeotropically. Then the solvent was evaporated. The residue was dried in vacuo, then dissolved in xylene (20 mL). The mixture was heated at 125 ℃ for 200 h in a sealed tube, then the mixture was evaporated. Chromatography of the residue gave **7a** (0.0016 g, 0.2%).

Reaction of 6 with aryl isocyanate

Typical procedure - Under argon atmosphere, a mixture of **6** (0.202 g, 0.50 mmol), phenyl isocyanate (0.17 mL, 1.5 mmol) in dry benzene (5.0 mL) was heated at 80 ℃ for 24 h in a sealed tube, then the mixture was evaporated. Chromatography of the residue with hexane-ethyl acetate (5 : 1) and fractional precipitation gave **11a** (0.0593 g, 33%) and **12a** (0.0079 g, 6%).

In the similar manner, reaction of **6** with *p*-tolyl isocyanate gave **11b** (8%) and **12b** (2%).

11a: Colorless prisms (from acetonitrile), mp 201 ℃; δ_H 5.47 (1H, dd, *J* 10.1 and 2.1, H-8), 6.78 (1H, dd, *J* 10.1 and 2.1, H-9), 7.01 (1H, d, *J* 6.9, H-7), 7.02 (1H, t, *J* 2.1, H-9a), 7.13 (1H, dd, *J* 8.0 and 7.9, H-6), 7.35 (2H, br d, *J* 7.3, H-*o*-phenyl), 7.42 (1H, tm, *J* 7.4, H-*p*-phenyl), 7.44 (1H, tm, *J* 7.2, H-*p*-phenyl), 7.48-7.51, (4H, m, H-*m*-phenyl), and 7.51-7.57 (3H, m, H-5 and H-*o*-phenyl); δ_C 65.28, 116.32, 117.78, 118.71, 120.50, 123.86, 127.20, 128.46, 129.00, 129.03, 129.19, 129.81, 130.08, 135.32, 136.87, 140.36, 148.20, and 152.97; ν_{max} / cm^{-1} 1690 (C=O). *Anal.* Calcd for $C_{23}H_{16}N_4O$: C, 75.81; H, 4.43; N, 15.38. Found: C, 76.02; H, 4.39; N, 15.13.

12a: Pale yellow prisms (from acetonitrile), mp 168-170 ℃; δ_H 6.74 (1H, d, *J* 9.4, H-5), 7.15 (1H, dt, *J* 7.4 and 1.0, H-*p*-phenyl), 7.42 (1H, dd, *J* 8.7 and 7.4, H-*m*-phenyl), 7.43-7.47 (2H, m, H-7 and 8), 7.70 (1H, dd, *J* 5.9 and 2.4, H-9), 7.89 (2H, dd, *J* 8.7 and 1.0, H-*o*-phenyl), 7.97 (1H, d, *J* 9.4, H-6), and 9.82 (1H, s, NH); δ_C 116.25, 119.48, 120.07, 120.13, 122.98, 124.08, 126.19, 129.71, 129.84, 138.23, 141.19, 141.33, 150.78, and 161.70; ν_{max} / cm^{-1} 3268 (NH), 1679 (C=O) and 1641 (C=N). *Anal.* Calcd for $C_{16}H_{11}N_3O$: C, 73.55; H, 4.24; N, 16.08. Found: C, 73.43; H, 4.18; N, 16.02.

11b: Colorless prisms (from acetonitrile), mp 206 ℃; δ_H 2.39 (3H, s, Me), 2.40 (3H, s, Me), 5.46 (1H, dd, *J* 10.1 and 2.0, H-8), 6.75 (1H, dd, *J* 10.1 and 2.1, H-9), 6.95 (1H, dd, *J* 2.1 and 2.0, H-9a), 6.99 (1H, d, *J* 7.3, H-7), 7.11 (1H, dd, *J* 8.0 and 7.3, H-6), 7.21 (2H, br d, *J* 7.9, H-*o*-phenyl), 7.28 (2H, d, *J* 7.9, H-*m*-phenyl), 7.30 (2H, d, *J* 8.3, H-*m*-phenyl), 7.42, (2H, dd, *J* 8.3 and 1.9, H-*o*-phenyl), and 7.48 (1H, d, *J* 8.0, H-5); δ_C 21.59, 21.66, 65.25, 116.31, 117.97, 118.56, 120.41, 123.74, 127.03, 128.48, 128.70, 130.48, 130.69, 132.72, 134.21, 138.97, 139.09, 140.40, 148.48, and 153.09; ν_{max} / cm^{-1} 1683 (C=O) and 1657 (C=N). *Anal.* Calcd for $C_{25}H_{20}N_4O$: C, 76.51; H, 5.14; N, 14.28. Found: C, 76.73; H, 5.11; N, 14.02.

12b: Yellow needles (from hexane-chloroform), mp 173.5-174 ℃; δ_H 2.36 (3H, s, H-Me), 6.72 (1H, d, *J* 9.4, H-5), 7.24 (2H, d, *J* 8.4, H-*m*-phenyl), 7.38-7.46 (2H, m, H-7 and 8), 7.67 (1H, dd, *J* 6.5 and 1.7, H-9), 7.75 (2H, d, *J* 8.4, H-*o*-phenyl), 7.96 (1H, d, *J* 9.4, H-6), and 9.74 (1H, s, NH); δ_C 21.30, 116.22, 119.57, 119.85, 119.84, 122.96, 126.15, 129.93, 130.21, 133.76, 135.69, 141.28, 141.34, 150.99, and 161.69; ν_{max} / cm^{-1} 3264 (NH), 1675 (C=O) and 1639 (C=N). *Anal.* Calcd for $C_{17}H_{13}N_3O$: C, 74.17; H, 4.76; N, 15.26. Found: C, 74.44; H, 4.68; N, 14.98.

Reaction of 6 with tolyl isocyanate in the presence of silica gel

Under argon atmosphere, a mixture of **6** (0.101 g, 0.25 mmol), tolyl isocyanate (0.040 mg, 0.3 mmol), and silica gel (0.500 g) in dry benzene (5.0 mL) was heated at 80 ℃ for 24 h in a sealed tube, then the mixture was evaporated. The residue was chromatographed with hexane-ethyl acetate (5 : 1) repeatedly to give **12b** (0.098 g, 14%).

X-Ray structure determination

Crystal data of 11a: colorless prism, $C_{23}H_{16}N_4O$, M = 364.41, monoclinic, space group $P2_1/a$, a = 8.954(5) Å, b = 18.485(7) Å, c = 10.968(4) Å, β= 93.91(3)°, V = 1811.1(12) Å^3, Z = 4, D_{calc} = 1.336 g/cm^3, crystal dimension 0.64 x 0.42 x 0.16 mm. Data were measured on a Rigaku AFC 5S radiation diffractometer with graphite-monochromated Mo-Kα radiation. Total 4459 reflections (4363 unique) were collected using ω-2θ scan technique with in a 2θ range of 55.0°. The structure was solved by direct methods (SIR92),[18] and refined a full-matrix least squares methods with 269 variables and 1447 observed reflections [$I > 2\sigma(I)$]. The final refinement converged to R = 0.067 and Rw = 0.051. All calculations were performed using the CrystalStructure[19,20] crystallographic software package.

Crystal data of 12a: colorless prism, $C_{16}H_{11}N_3O$, M = 261.28, monoclinic, space group C2/c, a = 17.9360(19) Å, b = 7.0519(19) Å, c = 19.555(2) Å, β= 92.716(9)°, V = 2470.6(8) Å^3, Z = 8, D_{calc} = 1.405 g/cm^3, crystal dimension 0.58 x 0.42 x 0.08 mm. Data were measured on a Rigaku AFC 5S radiation diffractometer with graphite-monochromated Mo-Kα radiation. Total 3001 reflections (2929 unique) were collected using ω-2θ scan technique with in a 2θ range of 55.0°. The structure was solved by direct methods (SIR92),[18] and refined a full-matrix least squares methods with 192 variables and 1252 observed reflections [$I > 2\sigma(I)$]. The final refinement converged to R = 0.0614 and Rw = 0.0441. All calculations were performed using the CrystalStructure[19,20] crystallographic software package.

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