Novel Synthesis of 2,4-Diarylquinolines by Photochemical followed by Thermal Transformations of 1,4,6-Triarylpyrimidin-2(1*H*)-ones

Takehiko Nishio * and Yoshimori Omote
Department of Chemistry, University of Tsukuba, Sakura-mura, Niihari-gun, Ibaraki 305, Japan

The 2,4-diarylquinolines (3) were obtained in a one-pot synthesis by photochemical and subsequent thermal reactions of 1,4,6-triarylpyrimidin-2(1*H*)-ones (1) in fair yield. The quinolines (3) were formed *via* thermal cycloreversion, followed by electrocyclic ring-closure, of the 1,3-diazabicyclo[2.2.0]hex-5-en-2-ones (2), which were produced by photochemical electrocyclization of the pyrimidin-2(1*H*)-ones (1).

The quinolines are an interesting and important group of chemicals since some alkaloids contain the quinoline nucleus and certain quinoline derivatives have valuable chemotherapeutic properties.[1] In our exploration of the photochemical reactivity of pyrimidin-2(1*H*)-ones,[2] we recently reported the novel synthesis of the di-imine derivatives which were produced by treatment of 1-aryl-4,6-disubstituted pyrimidin-2(1*H*)-ones with alkoxide ion, both photochemically and thermally.[3] We report herein a new method for the synthesis of the 2,4-diarylquinolines (3) by photochemical and subsequent thermal transformations of the 1,4,6-triarylpyrimidin-2(1*H*)-ones (1a—g).

Results and Discussion

Photochemical Reactions of the 1-Arylpyrimidin-2(1H)-ones (1).—Irradiation of 1,4,6-triphenylpyrimidin-2(1*H*)-one (1a) in benzene solution under nitrogen with a high-pressure mercury lamp through a Pyrex filter at room temperature for 15 h [4] gave 3,4,6-triphenyl-1,3-diazabicyclo[2.2.0]hex-5-en-2-one (2a) in 50% yield.† The structure of the photo-isomer (2a) was confirmed on the basis of physical properties and elemental analysis (see Experimental section). The photo-isomer (2a) thus obtained was heated in benzene or methanol at reflux temperature for 1—3 h to give 2,4-diphenylquinoline (3a) in quantitative yield. The structure of compound (3a) was identified by direct comparison of its i.r. and n.m.r. spectra with those of authentic material.[5] Similarly, irradiation of the pyrimidin-2(1*H*)-ones (1b, h, and i) in benzene or methanol–benzene under the same conditions as described above gave the corresponding 1,3-diazabicyclo[2.2.0]hex-5-en-2-ones (2b, h, and i) in 33—67% yield (Table 1). The structure of these photo-isomers was confirmed on the basis of spectral data and elemental analyses. The photo-isomer (2b) was unstable at room temperature and easily converted into 6-methyl-2,4-diphenylquinoline (3b) quantitatively; however, the photo-isomers (2h and i) were very stable at room temperature. The photoisomers (2h) and (2i) were heated at reflux temperature in dimethylformamide (DMF) and toluene, respectively, to be converted back into the starting pyrimidin-2(1*H*)-ones (1h and i) and the quinolines could not be obtained. The pyrimidin-2(1*H*)-ones (1j and k) were inert to photolysis (Table 1).

One-pot Synthesis of the 2,4-Diarylquinolines (3) *by Photochemical followed by Thermal Transformations of the Pyrimidin-2(1H)-ones* (1).—As we found that the photo-isomer (2b) was not stable at room temperature and easily converted into the quinoline derivative (3b), we attempted the one-pot synthesis of the quinolines (3) by the transformation of the pyrimidin-2(1*H*)-ones (1). A solution of the pyrimidin-2(1*H*)-one (1a) in benzene was irradiated under the same conditions as described above and then the reaction mixture was refluxed under nitrogen for 1 h to give 2,4-diphenylquinoline (3a) in 50% yield. Similarly, the 2,4-diarylquinolines (3b—g) were obtained in 20—61% yield when the pyrimidin-2(1*H*)-ones (1b—g) were irradiated in benzene or methanol–benzene for 15—24 h and then the reaction mixture was refluxed for 1—3 h (Table 2). In the case of the pyrimidin-2(1*H*)-ones (1d and e), (1d) gave a 7 : 8 mixture of (3d) and (3d′), and (1e) gave a 1 : 5 mixture of (1e) and (1e′). These mixtures were not completely separated. The pyrimidin-2(1*H*)-ones (1h and i) could not give the 2,4-diarylquinolines since the 1,3-diazabicyclo[2.2.0]hex-5-en-2-ones (2h and i), which were formed by the photochemical electrocyclization of (1h and i), were stable even at 100 °C. Thermal reaction of (2h and i) at higher temperature [(2h) > 153 °C; (2i) > 110 °C] causes reversion to the starting pyrimidin-2(1*H*)-ones (1h and

Table 1. Preparation of the 1,3-diazabicyclo[2.2.0]hex-5-en-2-ones (2)

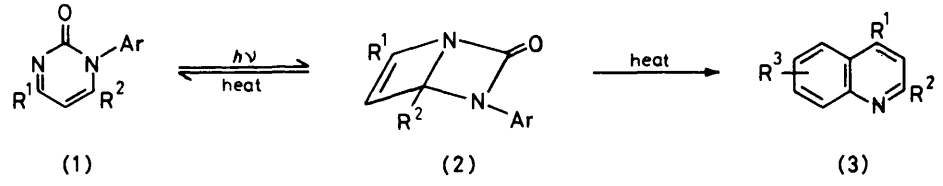
Starting compound	Yield (%) Diazabicyclohexenone (2)	Yield (%) Recovery (1)
(1a)	50	45
(1b)	50	47
(1h) [2a]	67	33
(1i)	33	66
(1j)	0	*ca.* 100
(1k)	0	*ca.* 100

Table 2. Quinolines (3) obtained by one-pot synthesis from the pyrimidin-2(1*H*)-ones (1)

Starting compound	Yield (%) Quinoline (3)	Yield (%) Recovery (1)
(1a)	50	45
(1b)	50	47
(1c)	20	60
(1d)	61 *	38
(1e)	53 *	55
(1f)	40	59
(1g)	29	60
(1h)	0	33
(1i)	0	66
(1j)	0	*ca.* 100
(1k)	0	*ca.* 100

* Combined yield of two isomers.

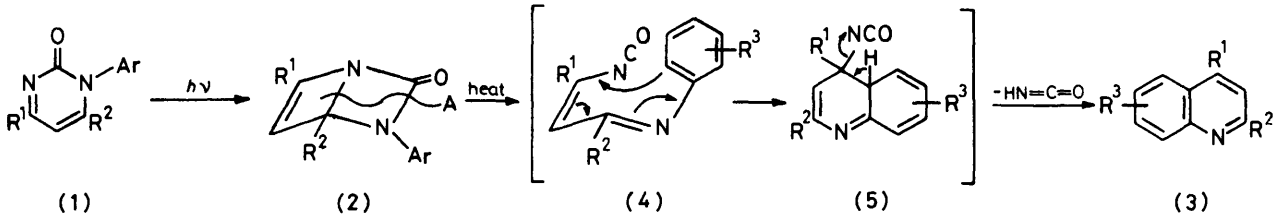
† We have already reported that several 1,4,6-trisubstituted pyrimidin-2(1*H*)-ones gave the corresponding 1,3-diazabicyclo-[2.2.0]hex-5-en-2-one by photochemical electrocyclization.[2a]



(1) (2) (3)

Ar	R^1	R^2
a; Ph	Ph	Ph
b; *p*-MeC_6H_4	Ph	Ph
c; *p*-$MeOC_6H_4$	Ph	Ph
d; *m*-MeC_6H_4	Ph	Ph
e; *m*-$MeOC_6H_4$	Ph	Ph
f; *p*-MeC_6H_4	*p*-MeC_6H_4	*p*-MeC_6H_4
g; Ph	Ph	*p*-MeC_6H_4
h; Ph	Me	Me
i; Ph	Me	Ph
j; Ph	Ph	Me
k; Ph	*p*-MeC_6H_4	Me

R^1	R^2	R^3
a; Ph	Ph	H
b; Ph	Ph	6-Me
c; Ph	Ph	6-MeO
d; Ph	Ph	5-Me
d'; Ph	Ph	7-Me
e; Ph	Ph	5-MeO
e'; Ph	Ph	7-MeO
f; *p*-MeC_6H_4	*p*-MeC_6H_4	6-Me
g; Ph	*p*-MeC_6H_4	H



(1) (2) (4) (5) (3)

Scheme.

i) quantitatively. A reasonable mechanism for the formation of the 2,4-diarylquinolines (3) by the transformation of the pyrimidin-2(1*H*)-ones (1) is proposed in the Scheme in which an unstable isocyanate intermediate (4), formed initially by thermal cleavage of the 1,3-diazabicyclo[2.2.0]hex-5-en-2-ones (2) [which were in turn produced by photochemical electrocyclization of the pyrimidin-2(1*H*)-ones (1) *] by the bond fission shown in path A, undergoes electrocyclic ring closure to give the intermediate (5), followed by subsequent loss of isocyanic acid, to give the 2,4-diarylquinolines (3). Support for this scheme comes from the fact that thermal reaction of the isolated compound (2a) gave the quinoline (3). Although the isocyanate intermediate (4) could not be trapped with alcohol when the 1,3-diazabicyclo[2.2.0]hex-5-en-2-one (2a) was refluxed in methanol, the formation of the isocyanate intermediate (4) was supported by the fact that the i.r. spectrum of the reaction mixture from (2a) in benzene showed an absorption at *ca.* 2 250 cm^{-1} due to the isocyanate group.

Experimental

M.p.s and b.p.s are uncorrected. M.p.s were measured with a Yanaco micro-melting-point apparatus (MP-J3). I.r. spectra were recorded on a Hitachi 260-30 spectrometer and u.v. spectra were determined with a JASCO UVIDEC-505 spectrometer. ^1H N.m.r. spectra were run on a JEOL FX 100 spectrometer using tetramethylsilane as internal standard. A HALōs (Eikosha EHP-300 W) high-pressure mercury lamp was used as an irradiation source.

Starting Materials.—The pyrimidin-2(1*H*)-ones (1a—d, f, h, and i) were prepared as described in reference 3 and (1e, g, j, and k) were prepared by a modification of this method.

1-(m-*Methoxyphenyl*)-4,6-*diphenylpyrimidin*-2(1H)-*one* (1e) had m.p. 158.5—160.0 °C (from chloroform–hexane); $\lambda_{max.}$ (MeOH) 211 (ε 2.64 × 10^4), 277 (1.82 × 10^4), and 337 nm (1.18 × 10^4); $\nu_{max.}$ (KBr) 1 660, 760, and 690 cm^{-1}; δ ($CDCl_3$) 3.69 (3 H, s), 6.69 (4 H, m), 6.87 (1 H, s), 7.10—7.33 (6 H, m), 7.42—7.57 (2 H, m), and 8.14—8.24 (2 H, m) (Found: C, 77.85; H, 5.1; N, 7.95. $C_{23}H_{18}N_2O_2$ requires C, 77.95; H, 5.1; N, 7.9%).

1,4-*Diphenyl*-6-(p-*tolyl*)*pyrimidin*-2(1H)-*one* (1g) had m.p. 173 °C (decomp.) (from chloroform–hexane); $\lambda_{max.}$ (MeOH) 212 (ε 2.16 × 10^4), 282 (1.60 × 10^4), and 339 nm (1.29 × 10^4); $\nu_{max.}$ (KBr) 1 665, 770, and 700 cm^{-1}; δ ($CDCl_3$–CD_3OD) 2.30 (3 H, s), 6.94 (1 H, s), 7.00—7.58 (12 H, m), and 8.10—8.20 (2 H, m) (Found: C, 81.55, H, 5.2; N, 8.25. $C_{23}H_{18}N_2O$ requires C, 81.65; H, 5.35; N, 8.3%).

6-*Methyl*-1,4-*diphenylpyrimidin*-2(1H)-*one* (1j) had m.p. 172—173 °C (from chloroform–hexane); $\lambda_{max.}$ (MeOH) 209 (ε 2.26 × 10^4), 234 (1.91 × 10^4), and 315 nm (8.14 × 10^3); $\nu_{max.}$ (KBr) 1 650, 770, and 700 cm^{-1}; δ ($CDCl_3$) 2.40 (3 H, s), 6.20 (1 H, s), and 6.90—7.11 (10 H, m) (Found: C, 78.05; H, 5.4; N, 10.9. $C_{17}H_{14}N_2$ requires C, 77.85; H, 5.35; N, 10.65%).

6-*Methyl*-1-*phenyl*-4-(p-*tolyl*)*pyrimidin*-2(1H)-*one* (1k) had m.p. 268—270 °C (from chloroform–hexane); $\lambda_{max.}$ (MeOH) 211 (ε 2.07 × 10^4), 221 (1.96 × 10^4), 285 (2.20 × 10^4), and 325 nm (1.37 × 10^4); $\nu_{max.}$ (KBr) 1 645, 830, 790, 770, and 700 cm^{-1}; δ ($CDCl_3$) 2.05 (3 H, d, *J* 0.7 Hz), 2.41 (3 H, s), 6.75 (1 H, d, *J* 0.7 Hz), 7.18—7.54 (7 H, m), and 8.05 (2 H, d, *J* 8.3 Hz) (Found: C, 78.15; H, 5.8; N, 10.15. $C_{18}H_{16}N_2O$ requires C, 78.25; H, 5.85; N, 10.15%).

General Procedure for the Photochemical Reactions of the Pyrimidin-2(1H)-*ones* (1a, b, and h—k).—A solution of the

* We did not succeed in isolating the 1,3-diazabicyclo[2.2.0]hex-5-en-2-ones (2c—g) due to their instability; however, their formation was suggested by the fact that the photolysate from (1c—g) showed an absorption band at *ca.* 1 780 cm^{-1} in the i.r. spectrum due to four-membered ring amide carbonyl.

pyrimidin-2(1*H*)-one (1) (200 mg) in benzene (50 ml) or methanol–benzene (50 ml; 1 : 49—1 : 4) was irradiated under nitrogen with a high-pressure mercury lamp through a Pyrex filter for 15—24 h at room temperature. After removal of the solvent the residue was chromatographed on a silica-gel column with benzene–ethyl acetate (4 : 1 or 2 : 1) as eluant to give the corresponding 1,3-diazabicyclo[2.2.0]hex-5-en-2-one (2).

(i) 3,4,6-*Triphenyl*-1,3-*diazabicyclo*[2.2.0]*hex*-5-*en*-2-*one* (2a) (yield 50%), m.p. 95.5—97 °C (from benzene–hexane); $\nu_{max.}$ (KBr) 1 780, 1 620, 1 590, 1 500, 770, and 695 cm^{-1}; δ ($CDCl_3$) 6.85 (1 H, s), 7.14—7.82 (13 H, m), and 7.92—8.29 (2 H, m) (Found: C, 81.4H, 5.05; N, 8.5. $C_{22}H_{16}N_2O$; requires C, 81.45; H, 4.95; N, 8.65%).

(ii) 4,6-Diphenyl-3-(*p*-tolyl)-1,3-diazabicyclo[2.2.0]hex-5-en-2-one (2b) (yield 50%), $\nu_{max.}$ (KBr) 1 780, 1 620, 1 595, 1 490, 830, 790, 760, and 705 cm^{-1}; δ ($CDCl_3$) 2.40 (3 H, s), 6.83 (1 H, s), 7.10—7.80 (12 H, m), and 8.10—8.35 (2 H, m). The elemental analysis of the photo-isomer (2b) was not in accord with the calculated values since (2b) was unstable and easily converted into 6-methyl-2,4-diphenylquinoline (3b) in quantitative yield even at room temperature.

(iii) 4,6-Dimethyl-3-phenyl-1,3-diazabicyclo[2.2.0]hex-5-en-2-one (2h) has already been described in ref. 2*a*.

(iv) 6-*Methyl*-3,4-*diphenyl*-1,3-*diazabicyclo*[2.2.0]*hex*-5-*en*-2-*one* (2i) (yield 33%), b.p. 170 °C (Kugelrohr temperature) at 2 mmHg (decomp.); $\nu_{max.}$ (film) 1 780, 1 645, 1 600, 1 505, 750, and 690 cm^{-1}; δ ($CDCl_3$) 2.17 (3 H, d, *J* 1.7 Hz), 6.50 (1 H, q, *J* 1.7 Hz), and 6.96—7.61 (10 H, m) (Found: C, 77.55; H, 5.55; N, 10.55. $C_{17}H_{14}N_2O$ requires C, 77.85; H, 5.35; N, 10.65%).

Irradiation of the pyrimidin-2(1*H*)-one (1j or k) in benzene–methanol (50 ml; 4 : 1) under the same conditions as described above for 15—24 h and usual work-up gave no photoproducts and the pyrimidin-2(1*H*)-one (1j or k) was recovered quantitatively.

Thermal Reaction of 3,4,6-*Triphenyl*-1,3-*diazabicyclo*[2.2.0]-*hex*-5-*en*-2-*one* (2a).—A solution of the 1,3-diazabicyclo-[2.2.0]hex-5-en-2-one (2a) (100 mg) in benzene (15 ml) or methanol (15 ml) was refluxed for 1—3 h. After removal of the solvent the residue was recrystallized from chloroform–hexane to give 2,4-diphenylquinoline (3a) quantitatively.

Thermal Reaction of the 1,3-*Diazabicyclo*[2.2.0]*hex*-5-*en*-2-*one* (2h).—A solution of compound (2h) (100 mg) in DMF (10 ml) was refluxed for 1 h and then the reaction mixture was poured into water and extracted with methylene dichloride. The extract was washed with water and dried over anhydrous magnesium sulphate. After removal of the solvent the residue was recrystallized from chloroform–hexane to give 4,6-dimethyl-1-phenylpyrimidin-2(1*H*)-one (1h) in quantitative yield. The same result was obtained by the thermolysis of molten (2h) in a sealed tube at 200 °C.

Thermal Reaction of the 1,3-*Diazabicyclo*[2.2.0]*hex*-5-*en*-2-*one* (2i).—A solution of compound (2i) (100 mg) in toluene (10 ml) was refluxed for 3 h. Then the solution was concentrated under reduced pressure and the residue was recrystallized from chloroform–hexane to give the pyrimidin-2(1*H*)-one (1i) quantitatively.

General Procedure for One-pot Synthesis of the 2,4-*Diarylquinolines* (3a—g).—A solution of a pyrimidin-2(1*H*)-one (1a—g) (200 mg) in benzene (50 ml) or methanol–benzene (50 ml; 1 : 4) was irradiated under the same conditions as described above for 15—24 h and then the reaction mixture was refluxed for 1—3 h. After removal of the solvent the residue was chromatographed on a silica-gel column with benzene–ethyl acetate (4 : 1) as eluant to give the corresponding 2,4-diarylquinoline (3).

(i) 2,4-Diphenylquinoline (3a) had m.p. 109—111 °C (from benzene–hexane) (lit.,[6] 114;[7] 111.3—111.8 °C); $\nu_{max.}$ (KBr) 3 050, 3 030, 1 590, 1 545, 1 490, 1 445, 1 405, 1 360, 800, 770, and 705 cm^{-1}; δ ($CDCl_3$) 7.34—7.95 (13 H, m) and 8.14—8.30 (2 H, m).

(ii) 6-Methyl-2,4-diphenylquinoline (3b) had m.p. 130—131 °C (from benzene–hexane) lit.,[7] 129—129.5 °C); $\nu_{max.}$ (KBr) 3 050, 1 590, 1 570, 1 545, 1 490, 1 450, 1 360, 875, 820, 780, 755, and 700 cm^{-1}; δ ($CDCl_3$) 2.45 (3 H, s), 7.44—7.76 (12 H, m), and 8.10—8.20 (2 H, m).

(iii) 6-Methoxy-2,4-diphenylquinoline (3c) had m.p. 121—122 °C (from chloroform–hexane) (lit.,[7] 121.5—122 °C;[8] 119—120 °C); $\nu_{max.}$ (KBr) 3 055, 3 025, 1 615, 1 585, 1 545, 1 400, 1 360, 1 265, 1 235, 1 225, 1 025, 835, 780, 760, and 695 cm^{-1}; δ ($CDCl_3$) 3.78 (3 H, s), 7.15—7.28 (1 H, m), 7.31—7.60 (9 H, m), 7.76 (1 H, s), and 8.10—8.20 (3 H, m).

(iv) 5- and 7-*Methyl*-2,4-*diphenylquinoline* (3d and d'); $\nu_{max.}$ (KBr) 3 055, 3 030, 1 620, 1 590, 1 545, 1 485, 1 450, 1 360, 825, 775, 765, and 700 cm^{-1}; δ ($CDCl_3$) 2.03 (1.4 H, s, 5-Me), 2.57 (1.6 H, s, 7-Me), 7.21—7.84 (12 H, m), and 8.03—8.23 (2 H, m) {Found [for a mixture of (3d) and (3d')]: C, 89.4; H, 5.75; N, 4.5. $C_{22}H_{17}N$ requires C, 89.45; H, 5.8; N, 4.75%}.

(v) 5- and 7-*Methoxy*-2,4-*diphenylquinoline* (3e and e'); $\nu_{max.}$ (KBr) 3 050, 3 025, 1 620, 1 585, 1 545, 1 510, 1 490, 1 455, 1 415, 1 360, 1 215, 1 035, 825, 765, 735, and 705 cm^{-1}; δ ($CDCl_3$) 3.50 (0.5 H, s, 5-MeO), 3.97 (2.5 H, s, 7-MeO), 7.05—7.82 (12 H, m), and 8.11—8,20 (2 H, m) {Found [for a mixture of (3e) and (3e')]: C, 85.5; H, 5.5; N, 4.5. $C_{22}H_{17}NO$ requires C, 84.85; H, 5.5; N, 4.5%}.

(vi) 6-*Methyl*-2,4-*di*-(p-*tolyl*)*quinoline* (3f) had m.p. 105—106 °C (from chloroform–hexane); $\nu_{max.}$ (KBr) 3 050, 3 025, 1 610, 1 585, 1 545, 1 510, 1 495, 1 355, and 825 cm^{-1}; δ ($CDCl_3$) 2.41 (3 H, s), 2.46 (3 H, s), 2.47 (3 H, s), 7.23—7.73 (9 H, m), and 8.03—8.15 (3 H, m) (Found: 3, 88.85; H, 6.6; N, 4.35. $C_{25}H_{21}N$ requires C, 89.1; H, 6.55; N, 4.35%).

(vii) 4-Phenyl-2(*p*-tolyl)quinoline (3g) had m.p. 104.5—106 °C (from chloroform–hexane) (lit.,[7] 105.7—106.5 °C; lit.[9] 106 °C); $\nu_{max.}$ (KBr) 3 050, 3 025, 1 595, 1 545, 1 485, 1 355, 825, 775, 765, and 705 cm^{-1}; δ ($CDCl_3$) 2.40 (3 H, s), 7.20—7.70 (8 H, m), 7.75—7.91 (3 H, m), and 8.04—8.27 (3 H, m).

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