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Condensation of Heteroaromatic Ketones with 2-Aminobenzophenones under MW Irradiation

KEYWORDS: Quinolines, MW irradiation, dibenzo[b,f][1,5]diazocines, self condensation

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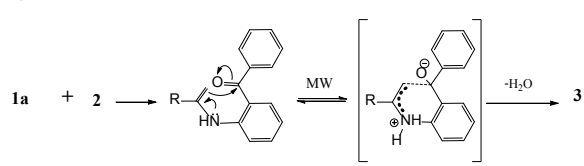
ABSTRACT *We first carried out Friedlander condensation of various heteroaromatic ketones 2a~f with 2-aminobenzophenones 1a~e under MW irradiation. To explore the scope and limitations of this condensation reaction under the above-mentioned reaction conditions, we generated a mini-library of quinolines. Acetylpyridines 2a~c 2-acetylfuran 2d, 2-acetylthiophene 2e, and 4-methylacetophenone 2f were condensed with 1a~e under the above-mentioned optimal reaction conditions. The results are summarized in Table 1. Condensation of 2a~f with 1a~e afforded quinolines in good yields (60.0~74.5%); in these reactions, dibenzo [b,f][1,5]diazocines 19a~d were isolated as the minor product. However, 6,12-diphenyldibenzo[b,f][1,5]diazocine 19a was the only product formed in low yield when 1a was reacted with 4-acetylmorpholine 2g, 3-acetyl-2-oxazolidinone 2h (an amide), and 4-acetylimidazole 2i (yield of the product obtained from 2g, 2h, and 2i was 34.0%, 42.0%, and 41.0%, respectively). The effect of MW irradiation on quinoline formation can be explained on the basis of MW activation effects caused by dipole-dipole interactions, mechanistic considerations, and the increase in the polarity of the system during the progress of the reaction.*

INTRODUCTION

Quinoline derivatives are prevalent in a variety of pharmacologically active synthetic and natural compounds. Quinolines have antiseptic, antipyretic, and antiperiodic properties and are used as antimalarials and for preparing other antimalarial drugs. The discovery of chloroquine, the most famous drug containing this scaffold, resulted in control and treatment of malaria for decades. Quinoline and its derivatives are widely used as fungicides, biocides, antibiotics, alkaloids, dyes, rubber chemicals, and flavoring, and flavoring agents. Additional industrial applications include their use as corrosion inhibitors, preservatives, and as solvents for resins and terpenes, and in transition-metal complex catalysis for uniform polymerization and luminescence chemistry. They are also used in manufacturing oil soluble dyes, food colorants, pharmaceuticals, pH indicators and other organic compounds. Quinoline is a catabolite of tryptophan, a fundamental structure in some antihypertensive agents such as the peripheral vasodilators prazosin and doxazosin.[1,2] Several synthetic routes have already been proposed for quinolines, and new methods are being extensively investgated.

Quinolines are usually synthesized under harsh heating conditions (heating for 24 h or longer) using large amounts of an acid catalyst and highly toxic solvents.[3,4] Recently, considerable attention has been paid to microwave (MW)-assisted organic reactions, which do not require any solvent.[5] Thermal reactions are often carried out in solution using large quantities of the reagents and may take several hours for completion. However, these reactions proceed to completion within minutes under MW irradiation. Herein, we report a new method involving MW irradiation for synthesizing quino lines and dibenzo [b,f][1,5] diazocines. Several benzo [b,f] [1,5] diazocines have shown pharmacologically useful properties such as antiviral, cholesterol-lowering and hormone-like activity.[6,7] Additionally, some members of the diazocine system have found applications as homologues of benzodiazepine drugs and as reversal agents in multidrug resistance.[8,9] In recent years, material chemists have explored the electrochemical properties of diaryldibenzo[b,f][1,5]diazocines (1), which were found to be useful as a basis for molecular machines and artificial muscles (Fig. 1).[10,11] These compounds are structurally similar to calcium channel antagonist such as diltiazem, which has been successfully tested as a chemosensitizer against multiple drug resistance (MDR).[12] We first carried out Friedlander[13,14] condensation of various heteroaromatic ketones 2a~f with 2-aminobenzophenones 1a~e under MW irradiation. To explore the scope and limitations of this condensation reaction under the above-mentioned reaction conditions, we generated a mini-library of quinolines. Acetylpyridines 2a~c 2-acetylfuran 2d, 2-acetylthiophene 2e, and 4-methylacetophenone 2f were condensed with 1a~e under the above-mentioned optimal reaction conditions. The results are summarized in Table 1. Condensation of 2a~f with 1a~e afforded quinolines in good yields (60.0~74.5%); in these reactions, dibenzo [b,f] [1,5]diazocines 19a~d were isolated as the minor product. However, 6,12-diphenyldibenzo[b,f][1,5]diazocine 19a was the only product formed in low yield when 1a was reacted with 4-acetylmorpholine 2g, 3-acetyl-2-oxazolidinone 2h (an amide), and 4-acetylimidazole 2i (yield of the product obtained from 2g, 2h, and 2i was 34.0%, 42.0%, and 41.0%, respectively). The effect of MW irradiation on quinoline formation can be explained on the basis of MW activation effects caused by dipole-dipole interactions, mechanistic considerations, and the increase in the polarity of the system during the progress of the reaction (Scheme 1).[15,16]



Scheme 1

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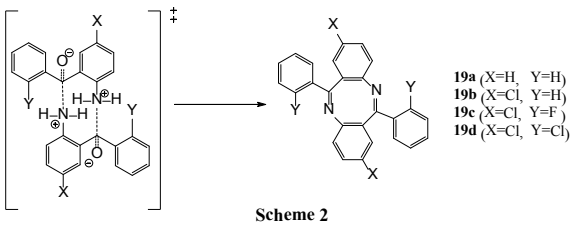
6,12-Diphenyl-dibenzo[b,f][1,5]diazocines 19a~d are minor products formed by the self-condensation of 1a, b and 1d,e (Scheme 2).



Scheme 2

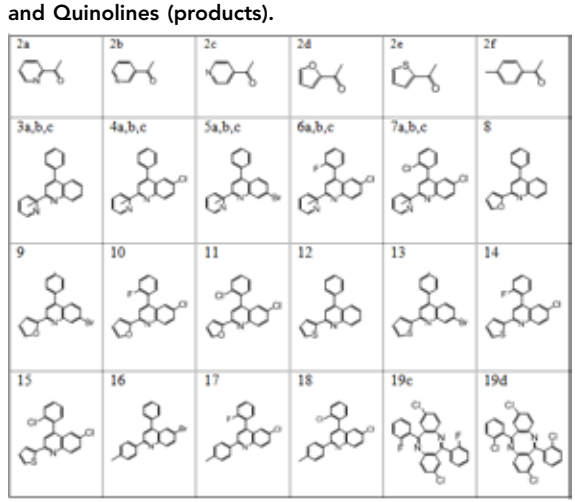
EXPERIMENT AND RESULTS

In order to broaden the scope of the proposed reaction, we carried out reactions of 2-amino-4-bromobenzophenone 1c with acetyl pyridines 2a~c, 7--bromo-4-phenyl-2-(pyridin-2-yl) quinoline 5a, 7-bromo-4-phenyl-2-(pyridin-3-yl) quino line 5b, and 7-bromo-4-phenyl-2-(pyridin-4-yl) quino line 5c, were isolated as the major products in the good yields from 2a, 2b, and 2c respectively. In the case, (5z, 11z)-3,9-dibromo-6,12-diphenyl dibenzo[b,f][1,5] diazocine was obtained as the minor product in low yield (2a:13.2%; 2b:15.1%; 2c:9.4%). Therefore, it is important to ensure that the bromo functionality is unaffected under the present reaction conditions. The self-condensation of 1a afforded 19a as the only product. In order to investigate the effect of DPP (diphenyl phosphate) on product formation, the synthesis of 19a was carried out under MW irradiation using different amounts (in equivalents) of DPP (Table 2). The obtained yield of 19 was higher when using anhydrous DPP than when using HCl, H_3PO_4, CH_3COOH, and $(CH_3CO)_2O$. The cyclization reaction proceeded very effectively in the presence of DPP, as shown in the two reaction mechanisms for the formation of quinolines and dibenzo [b,f][1,5] quinoline.[17] In summary, we have employed a MW-assisted solvent-free method ('green chemistry' conditions) to synthesize quino line and dibenzo [b,f][1,5] diazocine derivatives. The yields obtained with the proposed synthesis method are markedly higher than those obtained in conventional thermal reactions; further, this method does not require hazardous solvents and excess amounts expensive acidic catalysts. In addition, This method is economical, environmentally benign, and affords the desired product within a short time.

Table 1. Condensation of 1a~e with various ketones 2a~f under MW irraddiation.

Entry	2-Aminobenzo-Phenones 1a~e	Various ketones 2a~f	product	
			Quinolines	Yields(%)[a]
1	1a	2a	3a	71.0
2		2b	3b	74.5
3		2c	3c	71.0
4	1b	2a	4a	70.0
5		2b	4b	72.0
6		2c	4c	66.5
7	1c	2a	5a	71.0
8		2b	5b	74.3
9		2c	5c	66.5
10	1d	2a	6a	64.1
11		2b	6b	57.9
12		2c	6c	40.3
13	1e	2a	7a	71.4
14		2b	7b	37.1
15		2c	7c	62.9
16	1a	2d	8	68.0
17	1c		9	78.5
18	1d		10	74.3
19	1e		11	67.8
20	1a	2e	12	60.0
21	1c		13	72.5
22	1d		14	66.1
23	1e		15	70.4
24	1c	2f	16	77.7
25	1d		17	56.1
26	1e		18	60.1

Table 2. Structures of ketones (starting materials 2a~f) and Quinolines (products).



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a. Isolated yields.

Table 3. Synthesis of 19 using various catalysts under MW irradiation.

Entry	2-Amino benzophenones (1.0mmol)	Product	catalyst	Yields of 19[a] %
1	1a	19a	DPP	a: 89.4
2	1d	19d		d: 76.2
3	1e	19e		e: 77.5
4	1a	19a	HCl	a: 61.6
5	1d	19d		d: 56.3
6	1e	19e		e: 51.7
7	1a	19a	H_3PO_4	a: 45.7
8	1d	19d		b: 40.2
9	1e	19e		c: 41,8
10	1a	19a	CH_3COOH	a: 18.9
11	1d	19d		b: 16.7
12	1e	19e		c: 14.4
13	1a	19a	$(CH_3CO)_2O$	a: 23.7
14	1d	19d		b: 15.7
15	1e	19e		c: 16.5

a. Isolated yields.

2-Amino -4-bromobenzophenone 1c (0.2g, 1mmol) and 2-acetylpyridine 2a (0.12g, 1mmol), diphenyl phosphate (0.13g, 0.5mmol, purchased from Aldrich) were mixed in the absence of any organic solvent and submitted for 5 min to microwave irradiation inside a domestic microwave oven. After the reaction was completed, the reaction mixture was diluted with ethylacetate 50mL and neutralized with aqueous 10% NaOH. It was extracted with ethylacetate (two times), washed with water, and dried using MgSO4 and vacuum filtered.. The excess solvent was removed via rotary evaporate. This products were purified by column chromatography (eluent ; n-Hexane : CHCl3 : MeOH = 20 : 1 : 1 v/v/v) to give of the corresponding 7-bromo-4-phenyl-2-(pyridin-2-yl)quinoline 5a (0.20g, yield ; 71.0%). (pale yellow solid). 7-bromo-4-phenyl-2-(pyridin-2-yl)quinoline 5a: isolated yield: 71.0%; mp: 140~ 142^{0}C) Rf: 0.51 (TLC eluent; n-Hexane : $CHCl_3$: MeOH = 20 : 1 : 1 v/v/v), ^{1}H NMR ($CDCl_3$, 200MHz): δ 7.9(d, 2H), 7.9(s, 1H), 7.8~7.9(d, 1H), 7.6~7.7(t, 2H), 7.1~7.5(m, 6H), 6.9~7.0(t, 1H); ^{13}C NMR ($CDCl_3$, 50MHz) : δ 155.3, 151.1, 150.3, 149.2, 145.3, 139.8, 137.2, 131.0, 130.6, 129.8, 129.2, 127.4, 124.0, 123.6, 121.4, 118.6, 102.6. Anal. Calcd. for $C_{20}H_{13}BrN_2$: C, 66.50; H, 3.63; Br, 22.12; N, 7.75. Found : C, 66.53; H, 3.64; Br, 22.11; N, 7.72. 7-bromo-4-phenyl-2-(pyridin-3-yl)quinoline 5b: isolated yield: 74.3%; mp: 151~ 152^{0}C) Rf: 0.50 (TLC eluent; n-Hexane : $CHCl_3$: MeOH = 20 : 1 : 1 v/v/v), ^{1}H NMR ($CDCl_3$, 200MHz): δ 7.9(s, 1H), 7.8~7.9(d, 1H), 7.6~7.7(d, 1H), 7.5~7.6(d, 1H), 7.4~7.5(d, 1H), 7.3(s, 1H), 7.0(t, 1H), 6.9~7.0(m, 6H); ^{13}C NMR ($CDCl_3$, 50MHz) : δ 154.5, 150.7, 149.5, 148.9, 144.4, 139.8, 134.6, 134.5, 131.0, 130.6, 129.2, 127.4, 121.2, 101.0. Anal. Calcd. for $C_{20}H_{13}BrN_2$: C, 66.50; H, 3.36; Br, 22.12; N, 7.75. Found : C, 66.51; H, 3.62; Br, 30.10; N, 5.77. 7-bromo-4-phenyl-2-(pyridin-4-yl)quinoline 5c: isolated yield: 66.5%; mp: 139~140^{0}C) Rf: 0.51 (TLC eluent; n-Hexane : $CHCl_3$: MeOH = 20 : 1 : 1 v/v/v), ^{1}H NMR ($CDCl_3$, 200MHz): δ 8.3(d, 2H), 7.7(d, 2H), 7.6~7.7(d, 1H), 7.5(d, 1H), 7.4(s, 1H), 7.3~7.4(t, 1H), 6.9~7.0(m, 5H); ^{13}C NMR ($CDCl_3$, 50MHz) : δ 157.4, 150.3, 149.8, 145.7, 145.3, 139.8, 131.0, 130.6, 129.8, 129.2, 127.4, 124.0, 121.4, 118.6, 102.6. Anal. Calcd. for $C_{20}H_{13}BrN_2$: C, 66.50; H, 3.63; Br, 22.12; N, 7.75. Found : C, 66.46; H, 3.65; Br, 22.11; N, 7.78. 7-bromo-2-(furan-2-yl)-4-phenylquinoline 9: isolated yield: 77.0%; mp: 122~125^{0}C) Rf: 0.51 (TLC eluent; n-Hexane : $CHCl_3$: MeOH = 20 : 1 : 1 v/v/v), ^{1}H NMR ($CDCl_3$, 200MHz): δ 8.3(s, 1H), 7.7(d, 1H), 7.6~7.7(m, 5H), 7.2~7.5(m, 5H), 6.6(t, 1H); ^{13}C NMR ($CDCl_3$, 50MHz) : δ 158.8, 157.7, 150.3, 145.3, 142.9, 139.8, 131.0, 130.6, 129.8, 129.2, 127.4, 124.0, 118.6, 112.0, 107.1, 102.6. Anal. Calcd. for $C_{19}H_{12}BrNO$: C, 66.16; H, 3.45; Br, 22.82; N, 4.00; O, 4.57. Found : C, 65.11; H, 3.47; Br, 22.83; N, 4.02; O, 4.57. 7-bromo-4-phenyl-2-(thiophen-2-yl)quinoline 13: isolated yield: 72.5%; mp: 143~144^{0}C) Rf: 0.49 (TLC eluent; n-Hexane : $CHCl_3$: MeOH = 20 : 1 : 1 v/v/v), ^{1}H NMR ($CDCl_3$, 200MHz): δ 8.6(d, 1H), 7.7(d, 1H), 7.6~7.7(m, 6H), 7.6(m, 3H), 7.3(t, 1H); ^{13}C NMR ($CDCl_3$, 50MHz) : δ 158.8, 150.3, 145.3, 142.4, 139.8, 131.0, 130.6, 129.8, 129.2, 128.6, 128.0, 127.6, 127.4, 124.0, 118.6, 102.6. Anal. Calcd. for $C_{19}H_{12}BrNS$: C, 62.30; H, 3.30; Br, 21.82; N, 3.82; S, 8.75. Found : C, 62.30; H, 3.33; Br, 21.79; N, 3.81; S, 8.76. 7-bromo-4-phenyl-2-p-tolylquinoline 16: isolated yield: 77.7%; mp: 144~145^{0}C) Rf: 0.48 (TLC eluent; n-Hexane : $CHCl_3$: MeOH = 20 : 1 : 1 v/v/v), ^{1}H NMR ($CDCl_3$, 200MHz): δ 8.1(m, 3H), 7.6(t, 1H), 7.5(m, 3H), 7.4(s, 1H), 7.3~7.4(m, 2H), 7.3(s, 1H), 6.6(d, 2H), 2.4(s, 3H); ^{13}C NMR ($CDCl_3$, 50MHz) : δ 157.4, 150.3, 145.3, 139.8, 136.0, 131.0, 130.6, 130.3, 129.8, 129.5, 129.2, 127.4, 124.0, 123.3, 118.6, 102.6. 21.3. Anal. Calcd. for $C_{22}H_{16}BrN$: C, 70.60; H, 4.31; Br, 21.35; N, 3.74. Found : C, 70.65; H, 4.29; Br, 21.34; N, 3.72. 6-chloro-4-(2-fluorophenyl)-2-(pyridin-2-yl)quinoline 6a: isolated yield: 64.05%; mp: 179~ 181) Rf: 0.6 (TLC eluent; E.A : n-Hexane = 3 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 8.66(m, 2H), 8.56(s, 1H), 8.19(d, 1H), 7.90(td, J=7.8, 1.5, 1H), 7.69(m, 2H), 7.49(m, 2H), 7.35(m, 3H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 111.72, 115.42, 120.72, 121.14, 122.69, 124.51, 126.23, 127.23, 129.53, 130.31, 131.03, 131.32, 132.14, 136.33, 145.84, 146.21, 148.80, 154.62, 159.12, 161.22. Anal. Calcd. for $C_{20}H_{12}ClFN_2$: C, 71.75; H, 3.61; Cl, 10.59; F, 5.67; N, 8.37. Found : C, 71.74; H, 3.62; Cl, 10.59; F, 5.66; N, 8.38. (5E, 11E)-2,8-dichloro-6,12-bis(2-fluorophenyl)dibenzo[b,f][1,5] diazocine 19c: isolated yield: 19.48%; mp: 212~ 214^{0}C) Rf: 0.56 (TLC eluent; n-Hexane : E.A = 3 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 7.67(m, 1H), 7.35(m, 8H), 7.02(d, 1H), 6.87(d, 1H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 117.58, 122.06, 122.50, 125.32, 127.21, 129.25, 130.13, 131.02, 131.05, 132.16, 149.22, 164.21, 167.58. Anal. Calcd. for $C_{26}H_{14}Cl_2F_2N_2$: C, 67.40; H, 3.05; Cl, 15.30; F, 8.20; N, 6.05. Found : C, 67.39; H, 3.06; Cl, 15.29; F, 8.21; N, 6.05. 6-chloro-4-(2-chlorophenyl)-2-(pyridin-3-yl)quinoline 6b: isolated yield: 57.90%; mp: 203~206^{0}C) Rf: 0.46 (TLC eluent; E.A : n-Hexane = 3 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 9.38(d, 1H), 8.72(dd, J=4.5, 1.5Hz, 1H), 8.52(dt, J=8.1, 1.8Hz, 1H), 8.19(d, 1H), 7.87(s, 1H), 7.70(m, 2H), 7.45(m, 5H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 111.72, 115.42, 121.14, 123.44, 124.51, 126.23, 127.23, 129.53, 130.31, 131.03, 131.32, 132.14, 134.42, 136.42, 145.84, 146.21, 146.50, 150.30, 154.62, 161.22. Anal. Calcd. for $C_{20}H_{12}ClFN_2$: C, 71.75; H, 3.61; Cl, 10.59; F, 5.67; N, 8.37. Found : C, 71.76; H, 3.62; Cl, 10.59; F, 5.66; N, 8.36. 6-chloro-4-(2-fluorophenyl)-2-(pyridin-4-yl)quinoline 6c: isolated yield: 39.94%; mp: 175~177^{0}C) Rf: 0.46 (TLC eluent; E.A : n-Hexane = 3 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 8.66(d, 2H), 8.37(d, 2H), 8.23(d, 1H), 7.95(s, 1H), 7.78(dd, J=9.3, 2.4Hz, 1H), 7.70(m, 1H), 7.59(m, 1H), 7.44(m, 3H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 111.72, 115.42, 121.14, 124.51, 125.00, 126.23, 127.23, 129.53, 130.31, 131.03, 131.32, 132.14, 145.84, 146.21, 146.89, 148.78, 154.62, 161.22. Anal. Calcd. for $C_{20}H_{12}ClFN_2$: C, 71.75; H, 3.61; Cl, 10.59; F, 5.67; N, 8.37. Found : C, 71.74; H, 3.60; Cl, 10.58; F, 5.68; N, 8.39. 6-chloro-4-(2-fluorophenyl)-2-

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(furan-2-yl)quinoline 10: isolated yield: 74.30%; mp: 137~139^{0}C) Rf: 0.63 (TLC eluent; n-Hexane : E.A = 3 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 8.13(d, 1H), 7.81(s, 1H), 7.60(m, 4H), 7.39(m, 3H), 7.23(m, 1H), 6.60(m, 1H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 106.38, 110.20, 111.72, 115.42, 121.14, 124.51, 126.23, 127.23, 129.53, 130.31, 131.03, 131.32, 132.14, 140.79, 145.84, 146.21, 152.33, 154.62, 161.22. Anal. Calcd. for $C_{19}H_{11}ClFNO$: C, 70.49; H, 4.35; Cl, 10.95; F, 5.87; N, 4.03. Found : C, 70.50; H, 4.34; Cl, 10.96; F, 5.88; N, 4.03. 6-chloro-4-(2-chlorophenyl)-2-(thiophen-2-yl)quinoline 14: isolated yield: 66.04%; mp: 165~167^{0}C) Rf: 0.43 (TLC eluent; n-Hexane : E.A = 3 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 8.10(d, 1H), 7.78(s, 1H), 7.74(dd, J=3.9, 1.2Hz, 1H), 7.65(dd, J=9.2, 2.4Hz, 1H), 7.53(m, 3H), 7.43(m, 1H), 7.33(m, 2H), 7.15(dd, 1H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 111.72, 115.42, 121.14, 123.78, 124.51, 125.40, 126.23, 127.20, 127.23, 129.53, 130.31, 131.03, 131.32, 138.88, 145.84, 146.21, 154.62, 161.22. Anal. Calcd. for $C_{19}H_{11}ClFNS$: C, 67.16; H, 3.26; Cl, 10.43; F, 5.59; N, 4.12; S, 9.44. Found : C, 67.15; H, 3.25; Cl, 10.44; F, 5.60; N, 4.11; S, 9.45. 6-chloro-4-(2-fluorophenyl)-2-(p-tolyl)quinoline 17: isolated yield: 56.10%; mp: 165~167^{0}C) Rf: 0.60 (TLC eluent; n-Hexane : E.A = 5 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 8.18(d, 1H), 8.09(d, 2H), 7.85(s, 1H), 7.65(m, 2H), 7.49(m, 3H), 7.43(m, 3H), 2.42(s, 3H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 111.72, 115.42, 121.14, 124.51, 125.21, 126.23, 127.23, 128.97, 129.53, 130.31, 130.59, 131.03, 131.32, 132.14, 138.22, 145.84, 146.21, 154.62, 161.22. Anal. Calcd. for $C_{22}H_{15}ClFN$: C, 75.97; H, 4.35; Cl, 10.19; F, 5.46; N, 4.03. Found : C, 75.98; H, 4.34; Cl, 10.20; F, 5.46; N, 4.04. 6-chloro-4-(2-chlorophenyl)-2-(pyridin-2-yl)quinoline 7a: isolated yield: 71.42%; mp: 175~177^{0}C) Rf: 0.18 (TLC eluent; n-Hexane : E.A = 10 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 8.70(dd, J=8.7, 1.2Hz 2H), 8.53(s, 1H), 8.19(d, 1H), 7.90(td, J=9.00, 3.00Hz, 1H), 7.68(m, 1H), 7.59(m, 1H), 7.43(m, 5H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 110.80, 120.72, 122.01, 123.60, 124.11, 128.32, 128.41, 129.63, 129.84, 130.11, 130.22, 131.13, 131.99, 136.90, 145.82, 147.21, 148.84, 153.40, 158.12, 162.98. Anal. Calcd. for $C_{20}H_{12}Cl_2N_2$: C, 68.39; H, 3.44; Cl, 20.19; N, 7.98. Found : C, 68.37; H, 3.45; Cl, 20.20; N, 7.97. (5E, 11E)-2,8-dichloro-6,12-bis(2-chlorophenyl) dibenzo[b,f][1,5]diazocine 19d: isolated yield: 10.20%; mp: 202~ 204^{0}C) Rf: 0.55 (TLC eluent; n-Hexane : E.A = 10 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 7.67(m, 2H), 7.35(m, 8H), 7.03(d, 2H), 6.87(d, 2H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 125.22, 127.21, 129.13, 129.80, 129.85, 130.05, 130.30, 131.11, 131.20, 132.15, 138.71, 149.21, 168.56. Anal. Calcd. for $C_{26}H_{14}Cl_4N_2$: C, 62.93; H, 2.84; Cl, 28.58; N, 5.65. Found : C, 62.91; H, 2.85; Cl, 28.55; N, 5.66. 6-chloro-4-(2-chlorophenyl)-2-(pyridin-3-yl)quinoline 7b: isolated yield: 37.14%; mp: 163~165^{0}C) Rf: 0.14 (TLC eluent; n-Hexane : E.A = 2 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 9.38(d, 1H), 8.72(dd, J=5.10, 2.10Hz, 1H), 8.53(dt, J=8.40, 2.10Hz, 1H), 8.19(d, 1H), 7.83(s, 1H), 7.7(dd, J=9.00, 2.10Hz, 1H), 7.63(m, 1H), 7.49(m, 4H), 7.39(m, 1H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 110.82, 122.02, 123.04, 124.09, 128.32, 128.42, 129.62, 129.78, 130.11, 130.23, 131.11, 132.08, 133.41, 136.43, 136.92, 145.79, 146.99, 147.18, 150.21, 153.37. Anal. Calcd. for $C_{20}H_{12}Cl_2N_2$: C, 68.39; H, 3.44; Cl, 20.19; N, 7.98. Found : C, 68.38; H, 3.43; Cl, 20.18; N, 7.99. 6-chloro-4-(2-chlorophenyl)-2-(pyridin-4-yl)quinoline 7c: isolated yield: 62.85%; mp: 161~163^{0}C) Rf: 0.10 (TLC eluent; n-Hexane : E.A = 2 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 8.76(d, 2H), 8.46(d, 2H), 8.22(d, 1H), 7.90(s, 1H), 7.77(dd, J=9, 2.4Hz, 1H), 7.64(m, 1H), 7.52(m, 3H), 7.37(m, 1H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 110.81, 122.01, 124.12, 124.40, 128.31, 128.44, 129.62, 129.79, 130.11, 130.22, 131.09, 132.13, 136.91, 145.80, 147.02, 147.21, 149.63, 153.41. Anal. Calcd. for $C_{20}H_{12}Cl_2N_2$: C, 68.39; H, 3.44; Cl, 20.19; N, 7.98. Found : C, 68.36; H, 3.45; Cl, 20.21; N, 7.97. 6-chloro-4-(2-chlorophenyl)-2-(furan-2-yl)quinoline 11: isolated yield: 67.84%; mp: 166~168^{0}C) Rf: 0.46 (TLC eluent; n-Hexane : E.A = 10 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 8.13(d, 1H), 7.76(s, 1H), 7.63(m, 3H), 7.48(m, 2H), 7.25(dd, J=3.60, 0.60Hz, 1H), 6.6(dd, J=3.60, 1.80Hz, 1H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 106.09, 110.83, 111.31, 122.04, 124.13, 128.30, 128.42, 129.64, 129.79, 130.14, 130.21, 131.11, 132.09, 136.90, 143.24, 145.77, 147.18, 153.40, 155.72. Anal. Calcd. for $C_{19}H_{11}Cl_2NO$: C, 67.08; H, 3.26; Cl, 20.84; N, 4.12; O, 4.70. Found : C, 64.06; H, 3.28; Cl, 20.83; N, 4.13; O, 4.68. 6-chloro-4-(2-chlorophenyl)-2-(thiophen-2-yl)quinoline 15: isolated yield: 70.42%; mp: 164~166^{0}C) Rf: 0.43 (TLC eluent; n-Hexane : E.A = 10 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 8.09(d, 1H), 7.72(s, 2H), 8.19(d, 1H), 7.63(m, 2H), 7.48(m, 3H), 7.38(m, 2H), 7.26(dd, J=5.10, 3.60Hz, 1H); ^{13}C NMR ($CDCl_3$, 300MHz) : δ 110.80, 122.04, 124.05, 126.60, 127.01, 127.61, 128.33, 128.41, 129.62, 129.80, 130.11, 130.22, 131.13, 132.13, 136.90, 140.10, 145.82, 147.21, 153.39. Anal. Calcd. for $C_{19}H_{11}Cl_2NS$: C, 64.05; H, 3.11; Cl, 19.90; N, 3.93. S, 9.00. Found : C, 64.04; H, 3.09; Cl, 19.92; N, 3.94; S, 9.01. 6-chloro-4-(2-chlorophenyl)-2-(p-tolyl) quinoline 18: isolated yield: 60.60%; mp: 129~131^{0}C) Rf: 0.44 (TLC eluent; n-Hexane : E.A = 10 : 1 v/v), ^{1}H NMR ($CDCl_3$, 300MHz): δ 8.16(d, 1H), 8.09(d, 2H), 7.80(s, 1H), 7.63(m, 2H), 7.44(m, 4H), 7.33(d, 2H), 2.44(s, 3H). ^{13}C NMR ($CDCl_3$, 300MHz) : δ 21.21, 110.80, 122.21, 124.12, 124.22, 128.32, 128.44, 128.91, 129.59, 129.82, 130.11, 130.19, 131.13, 132.14, 136.89, 137.15, 145.80, 147.22, 153.42. Anal. Calcd. for $C_{22}H_{15}Cl_2N$: C, 72.54; H, 4.15; Cl, 19.47; N, 3.85. Found : C, 72.52; H, 4.16; Cl, 19.49; N, 3.84.

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Tetrahedron Letters. 2009, 50, 5805. | General procedure for the synthesis of 3~18: 2-aminobenzophenon 1 (1.0 mmol), heteroaromatic ketone 2 (1.0 mmol), and equiv of DPP (0.5 mmol, purchased form Aldrich) were mixed in the absence of any organic solvent and then submitted for 3 min to microwave irradiation inside a domestic microwave oven (Samsung, RE-555 TCW), After the reaction was completed, the reaction mixture was diluted with ethyl acetate and neutralized with aqueous 10%NaOH. It was extracted with ethyl acetate (three times), washed with water, and dried (MgSO4), After the reaction, products were purified by colume chromatography (EtOAc/n-hexane = 1 : 20 ~ 1 : 40, v/v) to give the corresponding quinolines. 4-phenyl-2-pyridine-2-yl-quinoline 3a: yield: 71.0%; pale yellow solid; mp: 138.3~140.2^{0}C; 1H NMR (CDCl3, 200MHz): δ 8.70(d, j=7.4Hz, 2H), 8.53(s, 1H), 8.26(d, J=8.3Hz, 1H), 7.96(d, J=8.4Hz, 2H), 7.75(d, J=1.5Hz, 1H), 7.55(m, 6H), 7.46(t, J=1.1Hz, 1H); 13C NMR (CDCl3, 50MHz) : δ 156.3, 155.6, 149.2, 149.1, 148.5, 136.9, 130.2, 129.6, 129.4, 128.4, 128.3, 126.8, 125.8, 124.0, 121.8, 119.2; FT-IR(KBr) cm-1: 1357, 1489, 1590, 2986, 3053; GC/MS m/z 282 (M+). 4-phenyl-2-pyridine-3-yl-quinoline 3b: yield: 74.5%; pale yellow solid; mp: 152.0~154.0^{0}C; 1H NMR (CDCl3, 200MHz): δ 9.38(s, 1H), 8.70(d, J=3.7Hz, 1H), 8.53(d, J=7.9Hz, 1H), 8.24(d, J=8.7Hz, 1H), 7.93(d, J=8.4Hz, 1H), 7.82(s, 1H), 7.78(t, J=6.9Hz, 1H), 7.53(m, 7H); 13C NMR (CDCl3, 50MHz) : δ 154.2, 150.2, 149.6, 148.8, 140.0, 135.0, 130.1, 129.8, 129.5, 128.7, 128.6, 126.8, 125.9, 125.8, 123.7, 118.9; FT-IR(KBr) cm-1: 1355, 1475, 1590, 2986, 3054; GC/MS m/z 282 (M+). 4-phenyl-2-pyridine-4-yl-quinoline 3c: yield: 71.0%; pale yellow solid; mp: 138.0~138.5^{0}C; 1H NMR (CDCl3, 200MHz): δ 8.78(s, 2H), 8.26(d, J=8.9Hz, 1H), 8.10(d, J=6.2Hz, 2H), 7.93(d, J=8.4Hz, 1H), 7.84(s, 1H), 7.78(t, J=6.9Hz, 1H), 7.54(m, 6H); 13C NMR (CDCl3, 50MHz) : δ 154.0, 150.4, 149.8, 148.8, 146.6, 137.9, 130.3, 129.9, 129.5, 128.7, 127.2, 125.7, 121.7, 118.8; FT-IR(KBr) cm-1: 1357, 1485, 1593, 2985, 3050; GC/MS m/z 282 (M+). 2-furan-2-yl-4-phenylquinoline 8: yield: 68.0%; brown solid; mp: 90.0~92.0^{0}C; 1H NMR (CDCl3, 200MHz): δ 8.21(d, J=8.3Hz, 1H), 7.83(d, J=8.1Hz, 1H), 7.76(s, 1H), 7.69(t, J=6.9Hz, 1H), 7.61(s, 1H), 7.45(m, 6H), 7.23(d, J=3.4Hz, 1H), 6.57(t, J=1.5Hz, 1H); 13C NMR (CDCl3, 50MHz) : δ 153.6, 148.9, 148.5, 148.4, 143.9, 137.9, 129.6, 129.4, 128.9, 128.5, 128.3, 125.6, 125.5, 117.6, 112.1, 110.1; FT-IR(KBr) cm-1: 1353, 1480, 1595, 2989, 3048; GC/MS m/z 271 (M+). 4-phenyl-2-pyridine-2-yl-quinoline 12: yield: 60.0%; pale yellow solid; mp: 80.4~83.8^{0}C; 1H NMR (CDCl3, 200MHz): δ 8.26(d, J=8.3Hz, 1H), 7.89(d, J=8.2Hz, 1H), 7.77(s, 1H), 7.72(m, 2H), 7.56(m, 7H), 7.15(dd, J=3.8,4.9Hz, 1H); 13C NMR (CDCl3, 50MHz) : δ 157.6, 148.7, 148.4, 148.1, 137.9, 129.4, 129.3, 129.2, 128.6, 128,4, 128.2, 127.8, 127.7, 125.7, 125.6, 125.4, 117.6; FT-IR(KBr) cm-1: 1359, 1486, 1590, 2988, 3057; GC/MS m/z 287 (M+). 4-phenyl-2-pyridine-2-yl-quinoline 4a: yield: 70.0%; pale yellow solid; mp: 171.5~173.0^{0}C; 1H NMR (CDCl3, 200MHz): δ 8.73(s, 1H), 8.67(d, J=10.7Hz, 1H), 8.54(s, 1H), 8.18(d, J=8.9Hz, 1H), 7.88(m, 2H), 7.65(d, J=8.9Hz, 1H), 7.55(m, 5H), 7.37(t, J=5.9Hz, 1H); 13C NMR (CDCl3, 50MHz) : δ 155.8, 149.3, 149.1, 148.5, 146.8, 137.7, 137.0, 132.7, 131.8, 130.3, 129.5, 128.7, 124.7, 124.2, 121.9, 120.0, 119.9; FT-IR(KBr) cm-1: 1356, 1487, 1588, 2980, 3051; GC/MS m/z 314 (M+). 4-phenyl-2-pyridine-2-yl-quinoline 4b: yield: 72.0%; pale yellow solid; mp: 191.5~192.5^{0}C; 1H NMR (CDCl3, 200MHz): δ 9.37(d, J=1.9Hz, 1H), 8.71(dd, J=1.6,4.8Hz, 1H), 8.51(d, J=6.0Hz, 1H), 8.17(d, J=8.9Hz, 1H), 7.88(d, J=2.3Hz, 1H), 7.83(s, 1H), 7.68(dd, J=2.4,8.9Hz, 1H), 7.50(m, 6H); 13C NMR (CDCl3, 50MHz) : δ 154.4, 150.4, 148.7, 147.2, 137.3, 135.0, 134.7, 132.8, 131.8, 130.3, 129.4, 128.9, 126.7, 124.6, 123.7, 119.6; FT-IR(KBr) cm-1: 1359, 1483, 1585, 2991, 3055; GC/MS m/z 314 (M+). 4-phenyl-2-pyridine-2-yl-quinoline 4c: yield: 66.5%; pale yellow solid; mp: 188.0~192.0^{0}C; 1H NMR (CDCl3, 200MHz): δ 8.79(d, J=6.0Hz, 2H), 8.18(d, J=8.9Hz, 1H), 8.07(dd, J=1.4,4.5Hz, 2H), 7.87(m, 2H), 7.69(dd, J=2.4,8.9Hz, 1H), 7.53(m, 5H); 13C NMR (CDCl3, 50MHz) : δ 154.4, 150.6, 150.5, 149.1, 147.5, 146.1, 137.3, 133.2, 131.9, 131.8, 130.9, 130.8, 129.4, 128.9, 127.1, 124.6, 124.5, 121.6, 121.4, 119.5; FT-IR(KBr) cm-1: 1357, 1485, 1593, 2988, 3052; GC/MS m/z 314 (M+). General procedure for the preparation of dibenzo[b,f][1,5] diazocines 19: aminobenzophenon (1.0 mmol), and equiv of DPP (0.5 mmol, purchased form Aldrich) were mixed in the absence of any organic solvent and then submitted for 3 min to microwave irradiation inside a domestic microwave oven (Samsung, RE-555 TCW), The work-up procedure is same as that given in Ref. 12. After concentration under reduced pressure, the residue was purified by colume chromatography on silica gel (EtOAc/n-hexane = 1 : 20, v/v) to give the corresponding dibenzo[b,f][1,5]diazocines. 6,12-diphenyl-dibenzo[b,f][1,5]diazocine 19a: yield: 89.4%; yellow solid; mp: 190.5~192.0^{0}C; 1H NMR (CDCl3, 200MHz): δ 7.78(m, 4H), 7.36(m, 8H), 7.03(m, 6H); 13C NMR (CDCl3, 50MHz) : δ 169.5, 151.8, 138.8, 131.0, 129.6, 129.4, 128.2, 127.5, 126.9, 123.3, 120.9; FT FT-IR(KBr) cm-1: 1355, 1492, 1585, 2983, 3056; GC/MS m/z 358 (M+). 2,8-dichloro-6,12-diphenyl-dibenzo[b,f][1,5]diazocine 19b: yield: 79.8%; yellow solid; mp: 210.0~212.5^{0}C; 1H NMR (CDCl3, 200MHz): δ 7.74(m, 4H), 7.37(m, 8H), 6.99(m, 4H); 13C NMR (CDCl3, 50MHz) : δ 168.7, 150.1, 137.1, 131.2, 130.0, 129.3, 128.4, 128.0, 127.1, 122.4; FT-IR(KBr) cm-1: 1357, 1490, 1583, 2989, 3051; GC/MS m/z 428 (M+).