Catalytic Action of Azolium Salts. II.[1] Aroylation of 4-Chloroquinazolines with Aromatic Aldehydes Catalyzed by 1,3-Dimethylbenzimidazolium Iodide

Akira MIYASHITA,*[,a] Hideaki MATSUDA,[b] Chihoko IIJIMA,[a] and Takeo HIGASHINO[a]

School of Pharmaceutical Sciences, University of Shizuoka,[a] 52-1 Yada, Shizuoka 422, Japan and Central Research Laboratories, S S Pharmaceutical Co., Ltd.,[b] 1143 Nanpeidai, Narita 286, Japan. *Received July 2, 1991*

When a mixture of 4-chloroquinazoline (7), an aromatic aldehyde 6, sodium hydride, and a catalytic amount of 1,3-dimethylbenzimidazolium iodide (1) in tetrahydrofuran (THF) was refluxed with stirring for an appropriate time, the chlorine atom of 7 was replaced with the aroyl group, and the 4-aroylquinazolines 10 were obtained in excellent yields. Similar treatments of 4-chloro-2-methylquinazoline (8) and 4-chloro-2-phenylquinazoline (9) led to the 4-aroyl-2-methylquinazolines 11 and the 4-aroyl-2-phenylquinazolines 12, respectively.

Use of *N,N*-dimethylformamide (DMF) instead of THF as the reaction solvent in the above reaction reduced the reaction time and increased the yields of the ketones 10 and 12 as compared with those in THF.

Keywords chloroquinazoline; catalytic aroylation; aromatic aldehyde; aroylquinazoline; benzimidazolium iodide

In the previous paper,[1] we reported that 1,3-dimethylbenzimidazolium iodide (**1**) is an effective catalyst for the preparation of the 4-aroyl-1*H*-pyrazolo[3,4-*d*]pyrimidines **4** and **5** by treatment of the 4-chloro-1*H*-pyrazolo[3,4-*d*]pyrimidines **2** and **3** with aromatic aldehydes **6** and sodium hydride (NaH) in refluxing tetrahydrofuran (THF) or in *N,N*-dimethylformamide (DMF), as shown in Chart 1. By analogy with the benzoin condensation process,[2] the aroylation using aromatic aldehydes **6**, which are the source of the aroyl group, is believed to proceed through the formation of the key intermediate B-2 *via* the ylide A generated by expulsion of the C^2 hydrogen of **1**. It is considered that the important intermediate B-2 is equivalent to the aroyl anion (Ar-$\bar{C}$=O). Utilization of the intermediate B-2 for preparation of aroyl compounds by nucleophilic reaction should be a useful method in organic synthesis. We therefore attempted to extend the new aroylation method to 4-chloroquinazolines, and found that the aroylation took place, resulting in the formation of the 4-aroylquinazolines. In the present paper, we describe the aroylations of 4-chloroquinazoline (**7**),[3,4] 4-chloro-2-methylquinazoline (**8**),[5] and 4-chloro-2-phenylquinazoline (**9**)[4] with aromatic aldehydes **6** catalyzed by **1**.

In the presence of **1**, 4-chloroquinazoline (**7**) with *p*-fluorobenzaldehyde (**6b**), *p*-chlorobenzaldehyde (**6d**), *p*-bromobenzaldehyde (**6f**), *p*-tolualdehyde (**6h**), *m*-anisaldehyde (**6j**), and 2-thiophenecarbaldehyde (**6s**) underwent nucleophilic aroylation in refluxing THF (method A) to give good yields of the expected 4-aroylquinazolines **10b**,**10d**,[6] **10f**, **10h**,[6] **10j**,[6] and **10s**. The 4-chloroquinazoline **7** reacted with benzaldehyde (**6g**) under the same conditions to give 4-benzoylquinazoline (**10g**)[6] as the main product in 96% yield together with 4-benzyloxyquinazoline (**13g**) in only 1% yield. A similar result was obtained in the reaction of **7** with 1-naphthaldehyde (**6q**). Namely, both the ketone **10q** and the 4-(1-naphthylmethyloxy)quinazoline (**13q**) were obtained in 28% and 12% yields, when a mixture of **7**, **6q**, NaH, and a catalytic amount of **1** in THF was refluxed for 4 h. On the other hand, the above reaction for 30 min gave the ketone **10q** in only 7% yield and the starting **7** was recovered in 53% yield. The reaction of **7** with *o*-chlorobenzaldehyde (**6c**) having a substituent at the *ortho* position of **6** in THF led to the ketone **10c**,[6] though the yield was low (21%) because of recovery of the starting **7** in 53% yield. Similarly, in the treatment with *o*-anisaldehyde (**6i**), starting **7** was recovered in 11% yield together with 35% yield of the ketone **10i**.[6] The low reactivity of *ortho*-substituted benzaldehydes might be caused by steric hindrance of the *ortho*-substituent to the aroylation. The 4-chloroquinazoline **7** was converted into the ketone **10r**[6] in the reaction with 2-furaldehyde (**6r**) in low yield (47%). On the other hand, an attempt at catalytic aroylation with *p*-nitrobenzaldehyde (**6m**) and *p*-cyanobenzaldehyde (**6n**), having a strong electron-withdrawing group at the *para*-position, resulted in recovery of the starting **7** in 67% and 46% yields, respectively. *p*-Nitrobenzoic acid (**16m**, 4%) and *p*-cyanobenzoic acid (**16n**, 9%) were formed together in the above reaction. But, the aroylation with *N,N*-dimethylaminobenzaldehyde (**6o**), having a strong electron-donating group, did proceed, leading to the ketone **10o** in 31% yield. In the previous paper,[1] we reported that use of DMF instead of THF as the reaction solvent for the catalytic aroylation was effective, and the reaction temperature and reaction time required to achieve the aroylation were reduced. Therefore, DMF was used as a solvent for the reaction of **7** with aromatic aldehydes **6**, and it was found to reduce the reaction time and increase the yields of the ketones. That is to say, the conversion of the 4-chloroquinazoline **7** into the 4-aroylquinazolines **10h**, **10i**, and **10r** could be accomplished by the reaction with **6h**, **6i**, and **6r** at 80 °C for 5 to

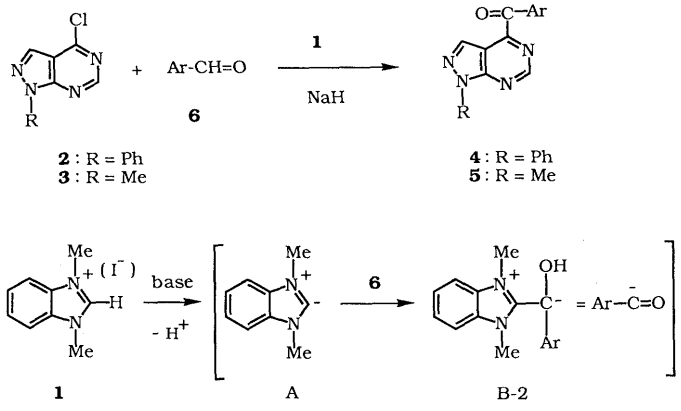


Chart 1

TABLE I. Aroylation of the 4-Chloroquinazolines **7**, **8**, and **9** with Aromatic Aldehydes **6** in the Presence of NaH Catalyzed by **1**

4-Chloroquinazoline	6	Reaction conditions			Products, yield (%)			
		Solvent[a]	Time (min)	Temperature[b] (°C)	Ketone		Others	Recovery
7	**6b**	THF	60	Refl.	**10b**	82		
7	**6c**	THF	60	Refl.	**10c**	21		53
7	**6c**	DMF	10	r.t.	**10c**	93		
7	**6d**	THF	60	Refl.	**10d**	85		
7	**6d**	DMF	15	r.t.	**10d**	77		
7	**6f**	THF	60	Refl.	**10f**	81		
7	**6g**	THF	60	Refl.	**10g**	96	**13g** 1	
7	**6h**	THF	60	Refl.	**10h**	79		
7	**6h**	DMF	10	80	**10h**	77		
7	**6i**	THF	60	Refl.	**10i**	35		11
7	**6i**	DMF	10	80	**10i**	65		
7	**6j**	THF	60	Refl.	**10j**	69		
7	**6k**	THF	30	Refl.	**10k**	35		38
7	**6k**	THF	150	Refl.	**10k**	79		
7	**6k**	DMF	15	r.t.	**10k**	—		87
7	**6k**	DMF	8	80	**10k**	90		
7	**6m**	THF	60	Refl.	**10m**	—		67[c]
7	**6m**	DMF	30	80	**10m**	—		21
7	**6n**	THF	60	Refl.	**10n**	—		46[d]
7	**6n**	DMF	5	r.t.	**10n**	59		
7	**6n**	DMF	5	80	**10n**	42		
7	**6o**	THF	60	Refl.	**10o**	31		
7	**6o**	DMF	60	80	**10o**	—		11
7	**6q**	THF	30	Refl.	**10q**	7		53
7	**6q**	THF	240	Refl.	**10q**	28	**13q** 12	
7	**6q**	DMF	10	r.t.	**10q**	23	**13q** 52	
7	**6q**	DMF	7	80	**10q**	58		
7	**6r**	THF	60	Refl.	**10r**	47		
7	**6r**	DMF	5	80	**10r**	93		
7	**6s**	THF	60	Refl.	**10s**	86		
8	**6d**	Dioxane	60	Refl.	**11d**	83		
8	**6g**	THF	20	Refl.	**11g**	85		
8	**6k**	Dioxane	60	Refl.	**11k**	51		
9	**6a**	THF	30	Refl.	**12a**	88	**14a** 2	
9	**6a**	DMF	20	r.t.	**12a**	79		
9	**6b**	THF	60	Refl.	**12b**	51	**14b** 3	
9	**6b**	DMF	7	80	**12b**	89		
9	**6d**	THF	60	Refl.	**12d**	65	**14d** 8	
9	**6d**	DMF	20	80	**12d**	76		
9	**6e**	DMF	20	r.t.	**12e**	81		
9	**6f**	DMF	20	r.t.	**12f**	85		
9	**6f**	DMF	10	80	**12f**	37		
9	**6g**	THF	60	Refl.	**12g**	35		42
9	**6g**	DMF	10	80	**12g**	95		
9	**6h**	THF	60	Refl.	**12g**	22		45
9	**6h**	Dioxane	60	Refl.	**12h**	64		
9	**6h**	DMF	30	r.t.	**12h**	—		90
9	**6h**	DMF	20	80	**12h**	92		
9	**6l**	THF	60	Refl.	**12l**	—		56
9	**6l**	DMF	40	r.t.	**12l**	—		86
9	**6l**	DMF	20	80	**12l**	81		
9	**6p**	THF	60	Refl.	**12p**	—		62
9	**6p**	DMF	20	r.t.	**12p**	—		85
9	**6p**	DMF	20	80	**12p**	72		
9	**6r**	THF	30	Refl.	**12r**	47	**14r** 28	
9	**6r**	DMF	10	80	**12r**	67		

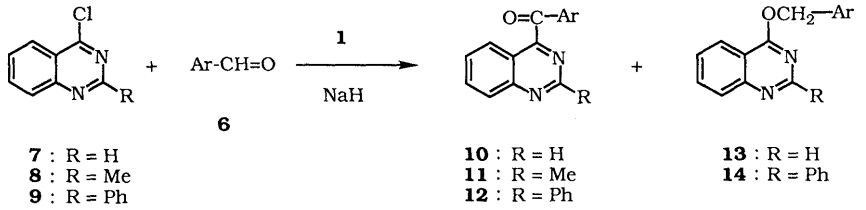
a) THF = tetrahydrofuran, DMF = *N*,*N*-dimethylformamide. *b*) Refl. = reflux, r.t. = room temperature. *c*) *p*-Nitrobenzoic acid (**16m**) was obtained in 4% yield. *d*) *p*-Cyanobenzoic acid (**16n**) was obtained in 9% yield.

10 min in DMF(method B). Moreover, the aroylation with **6c** and **6d** at room temperature resulted in the formation of the corresponding ketones **10c** and **10d** in excellent yields. The treatment of **7** with **6k** at room temperature resulted in recovery of the starting **7**, while at 80 °C the aroylation proceeded, giving the ketone **10k**[6] in 90% yield. The reaction of **7** with **6q** in DMF at room temperature gave the ketone **10q** together with the 4-(1-naphthylmethyloxy)quinazoline (**13q**) in 52% yield, and this is the same result as obtained in the reaction in THF. But, only the ketone **10q** was formed in the reaction at 80 °C for 7 min. The reaction with **6n** having a strong

electron-withdrawing group produced the ketone, 4-(4-cyanobenzoyl)quinazoline (**10n**), both at 80 °C and at room temperature, and there was no appreciable difference between the yields of the ketone obtained under the two conditions described above. With **6m**, the reaction at 80 °C for 30 min resulted in recovery of the starting **7**, and the result was similar to that obtained in the reaction using THF as the reaction solvent.

Next, the above aroylation was extended to **8** and **9**. When the 4-chloroquinazoline **8** was treated with **6d** and NaH in the presence of **1** in refluxing dioxane for 30 min, the aroylation took place, resulting in the formation of the ketone **11d** in 83% yield. Similar treatment with **6g** in refluxing THF for 20 min gave the expected ketone **11g** in 85% yield. A 51% yield of the ketone **11k** was obtained by the reaction of **8** with **6k** in dioxane.

The conversion of **9** into the corresponding ketones **12a**, **12b**, and **12d** was achieved by treatment with **6a**, **6b**, and **6d** in refluxing THF catalyzed by **1**, together with a small amount of the corresponding 4-(arylmethyloxy)quinazolines **14a**, **14b**, and **14d**. A similar result was obtained in the reaction of **9** with **6r** in refluxing THF for 30 min: the ketone was obtained in 47% yield together with 4-furfuryloxy-2-phenylquinazoline (**14r**) in 28% yield. In the reaction with **6g** for 60 min in refluxing THF, the ketone **12g** was obtained in low yield (35%) with recovery of a large amount of starting **9** (42%). Furthermore, when the aroylation was done with **6l** and **6p**, which have an electron-donating group at the *para*-position, in refluxing THF, the starting **9** was recovered in quantitative yield. These results prompted us to examine the new aroylation of **9**, whose 4-position may have weaker nucleophilic reactivity than that of **7**. The aroylation of **9** in DMF by the same method as described for the reaction of **7** with aromatic aldehydes **6** provided the ketone in excellent yield under mild conditions. Thus, the treatment of **9** with **6a**, **6d**, **6e**, and **6f**, bearing halogen substituent, in DMF at room temperature for 20 min gave the corresponding ketones **12a**, **12d**, **12e**, and **12f** in good yields. But, when the 4-chloroquinazoline **9** was treated with aromatic aldehydes **6h**, **6l**, and **6p**, which have an electron-donating group at the *para*-position, under similar conditions, none of the corresponding ketones was obtained and the starting **7** was recovered in quantitative yield. In contrast, when the same reactions were examined at 80 °C for 10 to 20 min, the expected ketones **12h**, **12l**, and **12p** were formed in



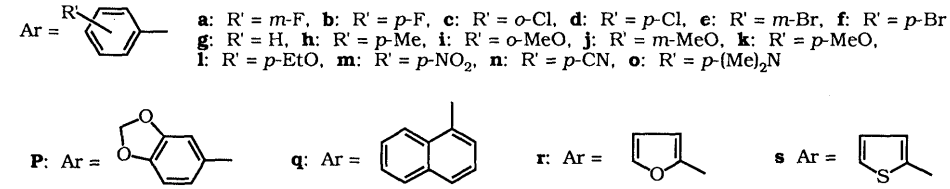


Chart 2

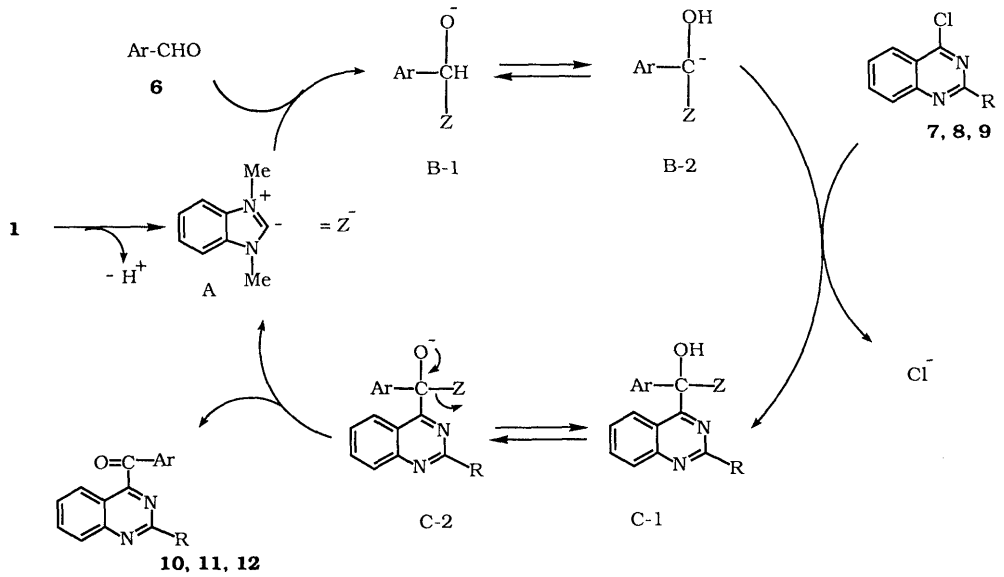


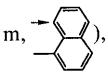
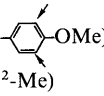
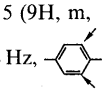
Chart 3

TABLE II. Melting Points, Mass Spectral Data, and Elemental Analyses for **10**, **11**, and **12**

Compd.	mp (°C)	Formula	Analysis (%) Calcd (Found) C	H	N	MS *m/z* M^+
10b	125.5—126[a,b]	$C_{15}H_9FN_2O$	71.42 (71.37)	3.60 3.52	11.11 11.07)	318
10c	74—76[c,b] (lit.[6] 80—81)	$C_{15}H_9ClN_2O$				
10d	130—131[a,b] (lit.[6] 128—129)	$C_{15}H_9ClN_2O$				
10f	126—127[a,b]	$C_{15}H_9BrN_2O$	57.53 (57.53	2.90 2.83	8.95 8.94)	378, 380
10g	98—99[d,e] (lit.[6] 97—98)	$C_{15}H_{10}N_2O$				
10h	130—131[e,f] (lit.[6] 129—130)	$C_{16}H_{12}N_2O$				
10i	98—100[b,g] (lit.[6] 100—101)	$C_{16}H_{12}N_2O_2$				
10j	122—123[b,g] (lit.[6] 122)	$C_{16}H_{12}N_2O_2$				
10k	120—121[a,b] (lit.[6] 119—120)	$C_{16}H_{12}N_2O_2$				
10n	162—163[d,b]	$C_{16}H_9N_3O$	74.12 (74.46	3.50 3.43	16.21 15.93)	258
10o	159[b,h]	$C_{17}H_{15}N_3O$	73.63 (73.72	5.45 5.47	15.15 15.21)	344
10q	151.5—152[b,h]	$C_{19}H_{12}N_2O$	80.27 (79.95	4.25 4.37	9.85 9.78)	368
10r	165.5—166[a,b] (lit.[6] 162)	$C_{13}H_8N_2O_2$				
10s	136—138[b,i]	$C_{13}H_8FN_2OS$	64.98 (64.89	3.36 3.31	11.66 11.65)	256
11d	141—142[b,i]	$C_{16}H_{11}ClN_2O$	67.97 (67.83	3.92 3.87	9.91 9.84)	256
11g	142—143[b,g]	$C_{16}H_{12}N_2O$	77.40 (77.36	4.87 4.88	11.28 11.14)	247
11k	142—144[b,g]	$C_{17}H_{14}N_2O_2$	73.37 (73.14	5.07 5.08	10.07 9.96)	266
12a	153—154[b,i]	$C_{21}H_{13}FN_2O$	76.82 (76.79	3.99 3.98	8.58 8.53)	329
12b	172—173[a,b]	$C_{21}H_{13}FN_2O$	76.82 (77.04	3.99 3.91	8.53 8.53)	328
12d	186—186.5[b,i]	$C_{21}H_{13}ClN_2O$	73.15 (73.05	3.80 3.71	8.12 8.07)	345
12e	181—184[e,i]	$C_{21}H_{13}BrN_2O$	64.80 (65.11	3.37 3.43	7.20 7.68)	388, 390
12f	181—183[b,i]	$C_{21}H_{13}BrN_2O$	64.80 (65.02	3.37 3.36	7.20 7.25)	388, 390
12g	151.5—152[e,i]	$C_{21}H_{14}N_2O$	81.27 (81.40	4.55 4.56	9.03 9.00)	256
12h	148—148.5[b,i]	$C_{22}H_{16}N_2O$	81.46 (81.29	4.97 4.95	8.64 8.46)	324
12l	147—148[b,i]	$C_{23}H_{18}N_2O_2$	77.95 (77.68	5.12 5.16	7.90 7.88)	354
12p	162.5—163[b,j]	$C_{22}H_{14}N_2O_3$	74.56 (74.68	3.98 3.93	7.98 7.90)	355
12r	151—152[b,j]	$C_{19}H_{12}N_2O_2$	75.99 (75.84	4.03 4.02	9.03 9.35)	301

a) Colorless needles. *b*) Recrystallized from MeOH. *c*) Slightly yellow granules. *d*) Pale yellow needles. *e*) Recrystallized from petroleum benzin. *f*) Slightly yellow scales. *g*) Slightly yellow prisms. *h*) Yellow prisms. *i*) Slightly yellow needles. *j*) Yellow needles.

TABLE III. IR and ^{1}H-NMR Spectral Data for **10**, **11**, and **12**

Compd.	IR ν_{KBr}^{max} cm^{-1}	^{1}H-NMR ($CDCl_3$) δ (ppm)
10b	1665 (CO)	9.28 (1H, s, C^2-H), 6.90—8.05 (8H, m, aromatic H)
10f	1660 (CO)	9.28 (1H, s, C^2-H), 7.40—8.10 (8H, m, aromatic H)
10n	1670 (CO) 2220 (CN)	9.25 (1H, s, C^2-H), 7.10—8.10 (8H, m, aromatic H)
10o	1640 (CO)	9.25 (1H, s, C^2-H), 7.50—8.10 (6H, m, aromatic H), 6.51 (2H, d, J=8 Hz, ), 3.05 (6H, s, $N(CH_3)_2$)
10q	1650 (CO)	9.25 (1H, s, C^2-H), 8.80—9.00 (1H, m, ), 7.30—8.15 (10H, m, aromatic H)
10s	1640 (CO)	9.30 (1H, s, C^2-H), 7.10 (1H, dd,  , J=6, 2 Hz), 7.50—8.30 (6H, m, aromatic H)
11d	1670 (CO)	7.20—8.00 (8H, m, aromatic H), 2.92 (3H, s, C^2-Me)
11g	1670 (CO)	7.38—8.04 (9H, m, aromatic H), 2.93 (3H, s, C^2-Me)
11k	1655 (CO)	7.39—7.95 (6H, m, aromatic H), 6.89 (2H, d, J=9 Hz, ), 3.85 (3H, s, OMe), 2.92 (3H, s, C^2-Me)
12a	1675 (CO)	8.58—8.60 (2H, m),[a] 7.35—8.20 (11H, m, aromatic H)
12b	1670 (CO)	8.58—8.60 (2H, m),[a] 7.20—8.20 (11H, m, aromatic H)
12d	1670 (CO)	8.35—8.55 (2H, m),[a] 7.20—8.05 (11H, m, aromatic H)
12e	1670 (CO)	8.45—8.62 (2H, m),[a] 7.35—8.30 (11H, m, aromatic H)
12f	1675 (CO)	8.40—8.65 (2H, m),[a] 7.30—8.10 (11H, m, aromatic H)
12g	1670 (CO)	8.35—8.55 (2H, m),[a] 7.20—8.05 (12H, m, aromatic H)
12h	1665 (CO)	8.60—8.62 (2H, m), 7.15—8.10 (11H, m, aromatic H), 2.40 (3H, s, Me)
12l	1660 (CO)	8.45—8.70 (2H, m),[a] 7.35—8.15 (9H, m, aromatic H), 6.90 (2H, d, J=8 Hz, ), 4.10 (2H, q, J=7 Hz, $OC\underline{H}_2CH_3$), 1.46 (3H, t, J=7 Hz, $OCH_2C\underline{H}_3$)
12p	1650 (CO)	8.60—8.62 (2H, m),[a] 7.50—8.15 (9H, m, aromatic H), 6.83 (1H, d, J=8 Hz, ), 6.01 (2H, s, $OC\underline{H}_2O$)
12r	1650 (CO)	7.40—8.70 (11H, m, aromatic H), 6.60 (1H, dd, J=6, 2 Hz,)

a) C^2- 

92%, 81%, and 72% yields. Similarly, the treatment of **9** with **6b**, **6d**, and **6r** in DMF at 80 °C for 7 to 10 min resulted in the formation of the ketones **12b**, **12d**, and **12r** in good yields. The reaction with **6f** at room temperature for 20 min gave the ketone **12f** in 85% yield, while the yield of the ketone decreased in the same reaction at 80 °C. This may be a result of further reaction, such as aryl migration,[7] proceeding through the ketone. The results obtained in this paper are summarized in Table I.

The structures of the newly obtained ketones were supported by the elemental analyses, infrared (IR) spectra, and proton (^{1}H-) and carbon (^{13}C-) nuclear magnetic resonance (NMR) spectra, as shown in Tables II, III, and IV. The structures of the 4-(arylmethyloxy)quinazolines **13** and **14** were determined by mixed melting point determination with authentic samples.

As illustrated in Chart 3, the formation of the ketones involving the catalytic action of **1** is considered to proceed through a similar process to that reported for the formation of 4-aroyl-1 *H*-pyrazolo[3,4-*d*]pyrimidines.[1] The for-

TABLE IV. ^{13}C-NMR Spectral Data for **10**, **11**, and **12**

Compd.	^{13}C-NMR ($CDCl_3$) δ ppm
10b[a]	115.5 (d), 116.5 (d), 122.0 (s), 125.8 (d), 128.8 (d), 129.1 (d), 130.6 (s), 133.2 (d), 133.7 (d), 134.6 (d), 151.3 (s), 153.7 (d), 160.8 (s), 163.5 (s),172.2 (s), 191.2 (s, CO)
10f	122.0 (s), 125.6 (d), 128.8 (d), 129.1 (d), 129.9 (s), 132.0 (d), 134.0 (s), 134.6 (d), 151.4 (s), 153.7 (d), 163.8 (s), 191.7 (s, CO)
10n	117.2 (s, CN), 121.9 (s), 125.5 (d), 129.2 (d), 131.0 (d), 132.3 (d), 134.9 (d), 138.4 (s), 151.6 (s), 153.5 (d), 161.7 (s), 191.4 (s, CO)
10o	40.0 (q, –NMe), 110.8 (d), 122.3 (s), 123.0 (s), 126.3 (d), 128.3 (d), 128.8 (d), 133.0 (d), 134.4 (d), 150.9 (s), 154.1 (d), 154.3 (s), 166.1 (s), 190.5 (s, CO)
10q	122.2 (s), 124.1 (d), 125.9 (d), 126.8 (d), 128.7 (d), 128.9 (d), 129.0 (d),131.3 (s), 132.3 (s), 133.9 (d), 134.4 (d), 134.9 (d), 151.3 (s), 154.8 (d), 165.2 (s), 195.3 (s, CO)
10s	121.7 (s), 126.1 (d), 128.4 (d), 129.0 (d), 134.4 (d), 136.8 (d), 137.1 (d), 141.5 (s), 151.7 (s), 153.6 (d), 161.7 (s), 184.4 (s, CO)
11d	26.4 (q, Me), 119.7 (s), 125.5 (d), 127.8 (d), 128.4 (d), 129.1 (d), 132.0 (d), 133.6 (s), 134.6 (d), 141.1 (s), 151.6 (s), 163.3 (s), 163.7 (s), 191.8 (s, CO)
11g	26.4 (q, Me), 119.8 (s), 125.6 (d), 127.7 (d), 128.3 (d), 128.8 (d), 130.6 (d), 134.49 (d), 134.54 (d), 135.2 (s), 151.4 (s), 163.4 (s), 164.6 (s), 193.2 (s, CO)
11k	26.4 (q, Me), 55.6 (q, OMe), 114.1 (d), 119.8 (s), 125.8 (d), 127.5 (d), 128.2 (d), 133.1 (d), 134.5 (d), 151.3 (s), 163.4 (s), 164.7 (s), 165.2 (s), 191.6 (s, CO)
12a[a]	116.9 (d), 117.3 (d), 120.5 (s), 121.1 (d), 121.5 (d), 125.6 (d), 126.8 (d), 126.9 (d), 128.2 (d), 128.7 (d), 129.4 (d), 130.3 (d), 130.4 (d), 131.0 (d), 134.6 (d), 137.3 (s), 152.2 (s), 159.5 (s), 160.9 (s), 163.1 (s), 164.5 (s), 191.7 (s, CO)
12b[a]	115.8 (d), 116.1 (d), 120.5 (s), 125.7 (d), 128.1 (d), 128.7 (d), 129.2 (s), 129.3 (d), 131.0 (d), 131.9 (s), 133.5 (d), 133.7 (d), 134.6 (d), 137.3 (s), 152.2 (s), 159.5 (s), 163.5 (s), 164.6 (s), 168.4 (s), 191.4 (s, CO)
12d	120.5 (s), 125.7 (d), 128.1 (d), 128.6 (d), 128.7 (d), 129.0 (d), 129.3 (d), 131.0 (d), 132.2 (d), 133.8 (s), 134.6 (d), 137.3 (s), 140.9 (s), 152.2 (s), 159.5 (s), 163.1 (s), 191.8 (s, CO)
12e	120.5 (s), 123.0 (s), 125.6 (d), 125.8 (s), 128.2 (d), 128.65 (d), 128.70 (d), 128.9 (s), 129.4 (d), 129.6 (d), 130.2 (d), 131.0 (d), 131.1 (s), 133.4 (d), 134.6 (d), 137.0 (d), 137.2 (s), 152.3 (s), 193.6 (s, CO)
12f	120.6 (s), 125.7 (d), 128.0 (d), 128.6 (d), 128.7 (d), 129.3 (d), 130.8 (d), 130.9 (d), 131.8 (s), 134.3 (d), 134.5 (d), 135.4 (s), 137.5 (s), 152.1 (s), 159.6 (s), 164.1 (s), 193.1 (s, CO)
12g	120.5 (s), 125.7 (d), 127.9 (d), 128.6 (d), 128.7 (d), 129.3 (d), 130.8 (d), 130.9 (d), 134.3 (d), 134.4 (d), 135.4 (s), 137.4 (s), 152.0 (s), 159.6 (s), 164.1 (s), 193.1 (s, CO)
12h	21.9 (t, Me), 120.6 (s), 125.8 (d), 127.9 (d), 128.4 (s), 128.6 (d), 128.7 (d), 129.2 (d), 129.4 (d), 130.85 (d), 130.90 (d), 134.4 (d), 137.5 (s), 145.5 (s), 152.0 (s), 159.6 (s), 164.5 (s), 192.7 (s, CO)
12l	14.6 (q, $-OCH_2\underline{C}H_3$), 63.9 (t, $-O\underline{C}H_2CH_3$), 114.4 (d), 120.6 (s), 125.9 (d), 127.8 (d), 128.2 (s), 128.6 (d), 128.7 (d), 129.2 (d), 130.8 (d), 133.2 (d), 134.4 (d), 137.5 (s), 151.9 (s), 159.6 (s), 164.0 (s), 164.8 (s), 191.6 (s, CO)
12p	102.1 (t, $-OCH_2O-$), 108.1 (d), 109.4 (d), 120.6 (s), 125.8 (d), 127.9 (d), 128.6 (d), 128.7 (d), 129.2 (d), 130.2 (s), 130.9 (d), 134.4 (d), 137.5 (s), 148.4 (s), 151.9 (s), 153.1 (s), 159.6 (s), 164.7 (s), 191.2 (s, CO)
12r	112.9 (d), 120.4 (s), 124.4 (d), 125.9 (d), 128.3 (d), 128.6 (d), 128.8 (d), 129.2 (d), 131.0 (d), 134.5 (d), 137.4 (s), 148.8 (d), 151.5 (s), 152.5 (s), 159.5 (s), 161.3 (s), 179.9 (s, CO)

a) The spectrum was observed with ^{13}C–^{19}F coupling.

mation of the ketones showed that the 4-chloroquinazoline react preferentially with the carbanion B-2 rather than the *O*-anion B-1, as an intermediate in the aroylation. In this recycling process, 1,3-dimethylbenzimidazolium iodide (**1**) acts as a catalyst.

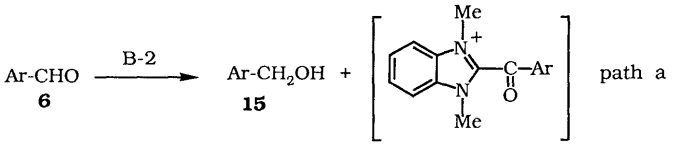


Chart 4

The formation of the 4-(arylmethyloxy)quinazolines **13** and **14** may be considered to involve nucleophilic substitution between the arylmethoxide ion and the 4-chloroquinazolines **7** and **9**. The arylmethanol **15**, the source of the arylmethoxide ion, may be formed in the following two ways, involving oxidation–reduction reaction of the aldehydes: a) redox reaction between the intermediate B-2 and aromatic aldehyde, as reported in the previous paper,[1] and b) Cannizzaro reaction[8] between two molecules of the aromatic aldehyde with hydroxide ion derived from contaminating water in the reaction solvent and NaH. Our results support path b because the acids **16**, which might not be formed *via* path a, were obtained from the reaction of **7** with **6m** and **6n**, but it is not yet clear whether the arylmethanols **15** were formed through path a or path b. In fact, neither the arylmethanols **15** nor the 4-(arylmethyloxy)quinazolines **13** were formed together with the acids **16** in the above reaction.

In conclusion, the nucleophilic aroylation of the 4-chloroquinazolines **10**, **11**, and **12** with aromatic aldehydes **6** under the catalytic action of 1,3-dimethylbenzimidazolium iodide (**1**) provides a useful method for the preparation of the 4-aroylquinazolines **10**, **11**, and **12**, being superior to the other methods reported.[6,7,9]

Experimental

All melting points are uncorrected. Infrared (IR) absorption spectra were recorded on a Jasco A-102 diffraction grating IR spectrometer. ^{1}H-NMR spectra were measured at 60 MHz on a Hitachi R-24B high-resolution NMR spectrometer, and ^{13}C-NMR spectra were obtained with a JEOL JNM-FX90Q FT-NMR spectrometer operating at 22.5 MHz. Chemical shifts are quoted in parts per million (ppm) with tetramethylsilane as an internal standard, and coupling constants (J) are given in hertz (Hz). The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, and m=multiplet. Mass spectra (MS) were recorded on a JEOL JMS D-100 mass spectrometer. Samples were vaporized in a direct inlet system. Column chromatography was carried out on SiO_2, Wakogel C-200. The 4-chloroquinazolines **7**,[3,4] **8**,[5] and **9**[4] and 1,3-dimethylbenzimidazolium iodide (**1**)[1] were prepared by the reported procedures.

Reaction of the 4-Chloroquinazolines (7, 8, and 9) with Aromatic Aldehydes 6 in the Presence of NaH Catalyzed by 1,3-Dimethylbenzimidazolium Iodide (1) General Procedure for Method A: A stirred solution of a 4-chloroquinazoline (**7**, **8**, or **9**, 4 mmol), an aromatic aldehyde (**6**, 4.8 mmol), and 1,3-dimethylbenzimidazolium iodide (**1**, 274 mg, 1.0 mmol) in THF (20 ml) or in dioxane (20 ml) was treated with NaH (50% in oil, 230 mg, 4.8 mmol) under an N_2 atmosphere, and then the mixture was refluxed with stirring in an oil bath for an appropriate time (the progress of the reaction was checked by TLC, and the reaction conditions are shown in Table I). After cooling, the resultant mixture was poured into an ice-water mixture, and extracted with $CHCl_3$ (100 ml×2). The organic layer was dried over Na_2SO_4 and concentrated to dryness. The residue was dissolved in a small portion of benzene, and chromatographed on a column of SiO_2 with benzene, and then $CHCl_3$. The fraction eluted with benzene provided the starting 4-chloroquinazoline and the fraction eluted with $CHCl_3$ gave the ketone (yield, recrystallized solvent, and

spectral data are shown in Tables I—IV).

In the reaction of **7** with **6g**, the fraction eluted with benzene gave 4-benzyloxyquinazoline (**13g**, 10 mg 1%) and the fraction eluted with $CHCl_3$ gave 4-benzoylquinazoline (**10g**, 900 mg, 96%).

In the reaction of **7** with **6q**, the fraction eluted with benzene gave 4-(1-naphthylmethyloxy)quinazoline (**13q**, 137 mg, 12%), and the fraction eluted with $CHCl_3$ gave 4-(1-naphthoyl)quinazoline (**10q**, 322 mg, 28%).

In the reaction of **7** with **6m**, after extraction with $CHCl_3$ the H_2O layer was acidified with AcOH, and extracted with $CHCl_3$, then the extract was dried over Na_2SO_4. After removal of the $CHCl_3$ by evaporation, the residue was recrystallized from MeOH to give 4-nitrobenzoic acid (**16m**, 32 mg, 4%).

In the reaction of **7** with **6n**, work-up as described for the reaction with **6m** gave 4-cyanobenzoic acid (**16n**, 64 mg, 9%).

In the reaction of **9** with **6a**, the fraction eluted with benzene gave 4-(3-fluorobenzyloxy)-2-phenylquinazoline (**14a**, 20 mg, 2%), and the fraction eluted with $CHCl_3$ gave 4-(3-fluorobenzoyl)-2-phenylquinazoline (**12a**, 1160 mg, 88%).

In the reaction of **9** with **6b**, the first fraction eluted with benzene gave 4-(4-fluorobenzyloxy)-2-phenylquinazoline (**14b**, 33 mg, 3%), and the second fraction eluted with benzene gave 4-(4-fluorobenzoyl)-2-phenylquinazoline (**12b**, 892 mg, 68%).

In the reaction of **9** with **6d**, the fraction eluted with benzene gave 4-(4-chlorobenzyloxy)-2-phenylquinazoline (**14d**, 111 mg, 8%), and the fraction eluted with $CHCl_3$ gave 4-(4-chlorobenzoyl)-2-phenylquinazoline (**12d**, 896 mg, 65%).

In the reaction of **9** with **6r**, the first fraction eluted with benzene gave 4-furfuryloxy-2-phenylquinazoline (**14r**, 338 mg, 28%), and the second fraction eluted with benzene gave 4-(2-furoyl)-2-phenylquinazoline (**12r**, 564 mg, 47%).

General Procedure for Method B: A stirred solution of a 4-chloroquinazoline (**7** or **9**, 4 mmol), an aromatic aldehyde (**6**, 4.8 mmol), and 1,3-dimethylbenzimidazolium iodide (**1**, 274 mg, 1.0 mmol) in DMF (20 ml) was treated with NaH (50% in oil, 230 mg, 4.8 mmol) under an N_2 atmosphere and then the mixture was stirred in an oil bath under heating or at room temperature. The resultant mixture was poured into an ice-water mixture, extracted with AcOEt (100 ml × 2), dried over Na_2SO_4, and concentrated to dryness. The residue was chromatographed on a column of SiO_2 with benzene and then $CHCl_3$. The fraction eluted with benzene gave 4-chloroquinazoline and the fraction eluted with $CHCl_3$ gave the ketone.

In the reaction of **7** with **6q** at room temperature for 10 min, the fraction eluted with benzene gave **13q** (260 mg, 23%), and the fraction eluted with $CHCl_3$ gave the ketone (**10q**, 593 mg, 52%).

General Procedure for the Preparation of 4-(Arylmethyloxy)quinazolines (13 and 14) A stirred solution of a 4-chloroquinazoline (**7** or **9**, 3.0 mmol) and an arylmethanol (**15**, 3.6 mmol) was treated with NaH (50% in oil, 173 mg, 3.6 mmol), and the mixture was refluxed in an oil bath with stirring. After cooling, the resultant mixture was poured into an ice-water mixture, and extracted with $CHCl_3$. The extract was dried over Na_2SO_4, and concentrated to dryness. In order to purify it, the residue was passed through a short column of SiO_2 with benzene to give the 4-(arylmethyloxy)quinazoline (**13** or **14**).

4-Benzyloxyquinazoline (**13g**): Yield 92% (650 mg). A colorless oil (picrate, yellow needles from MeOH, mp 164—165°C. *Anal.* Calcd for $C_{21}H_{15}N_5O_8$: C, 54.20; H, 3.25; N, 15.05. Found: C, 54.28; H, 3.24; N, 15.04). ^{1}H-NMR ($CDCl_3$): 8.72 (1H, s, C^2-H), 7.15—8.05 (9H, m, aromatic H), 5.45 (2H, s, $C\underline{H}_2$).

4-(1-Naphthylmethyloxy)quinazoline (**13q**): Yield 94% (810 mg). Colorless prisms (recrystallized from MeOH), mp 104—104.5°C. *Anal.* Calcd for $C_{19}H_{14}N_2O$: C, 79.70; H, 4.93; N, 9.78. Found: C, 79.59; H, 4.99; N, 9.71. ^{1}H-NMR ($CDCl_3$): 8.78 (1H, s, C^2-H), 7.20—8.10 (11H, m, aromatic H), 6.01 (2H, s, $C\underline{H}_2$).

4-(3-Fluorobenzyloxy)-2-phenylquinazoline (**14a**): Yield 96% (949 mg). Colorless needles (recrystallized from petroleum benzin), mp 123—123.5°C. *Anal.* Calcd for $C_{21}H_{15}FN_2O$: C, 76.35; H, 4.58; N, 8.48. Found: C, 76.12; H, 4.46; N, 8.51. ^{1}H-NMR ($CDCl_3$): 6.90—8.60 (13H, m, aromatic H), 5.65 (2H, s, $C\underline{H}_2$).

4-(4-Fluorobenzyloxy)-2-phenylquinazoline (**14b**): Yield 93% (917 mg). Colorless needles (recrystallized from petroleum benzin), mp 92—93°C. *Anal.* Calcd for $C_{21}H_{15}FN_2O$: C, 76.35; H, 4.58; N, 8.48. Found: C, 76.12; H, 4.46; N, 8.51.

4-(4-Chlorobenzyloxy)-2-phenylquinazoline (**14d**): Yield 88% (910 mg). Colorless prisms (recrystallized from MeOH), mp 132—133°C. *Anal.* Calcd for $C_{21}H_{15}ClN_2O$: C, 72.73; H, 4.36; N, 8.08. Found: C, 72.66; H, 4.37; 4.36; N, 8.03. ^{1}H-NMR ($CDCl_3$): 8.40—8.58 (2H, m), 7.20—8.05 (11H, m, aromatic H), 5.50 (2H, s, $C\underline{H}_2$).

4-Furfuryloxy-2-phenylquinazoline (**14r**): Yield 86% (780 mg). Colorless prisms (recrystallized from MeOH), mp 90—91°C. *Anal.* Calcd for $C_{19}H_{14}N_2O_2$: C, 75.48; H, 4.67; N, 9.27. Found: C, 75.43; H, 4.63; N, 9.21. ^{1}H-NMR ($CDCl_3$): 7.27—8.70 (10H, m, aromatic H), 6.42 (1H, d, J=4 Hz), 6.31 (1H, dd, J=4, 2 Hz).

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