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Studies on the Reaction of Quinazoline with Aromatic Aldehyde in the Presence of Cyanide Ion. I. The Extension of the Benzoin Condensation

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The possible reaction process for the formation of 4,4′-biquinazoline (II) obtained from the reaction of quinazoline (I) with cyanide ion were discussed and proposed by the scheme shown in Chart 1, which involved benzoin type condensation and oxidation, in successive step.

When the mixture of I and aromatic aldehyde treated with cyanide ion, aryl 4-quinazolinyl ketone (IX) was obtained together with II, even if both of the yields were poor. Typically, in the case of *o*-anisaldehyde and *m*-chlorobenzaldehyde, 2-methoxyphenyl 4-quinazolinyl ketone (IX-2), 3-chlorophenyl 4-quinazolinyl ketone (IX-6) and α-(2-methoxyphenyl)-4-quinazolinemethanol (VII-2), α-(3-chlorophenyl)-4-quinazolinemethanol (VII-6) were respectively obtained together with II. The reaction with benzaldehydes which was substituted with strongly electron donating (such as dimethylamino and hydroxyl group) or strongly electron attracting group (such as nitro and cyano group) did not give any of the corresponding IX. Especially, in the case of nitrobenzaldehyde, the corresponding dimethyl azodibenzoate (XV) and dimethyl azoxydibenzoate (XVI) were obtained.

Although there were the two possible reaction process for the formation of IX, path A and B, which were similar to that of cross benzoin condensation and oxidation in successive step, it might be considered that this cross benzoin type condensation might proceed by path A rather than path B.

It has been reported by Armarego and Willette that quinazoline (I) reacted with aqueous sodium cyanide to give 4,4′-biquinazoline (II).[2] But they did not explain the reaction process in detail except that the reaction might well be of benzoin condensation type followed by ready oxidation to fully aromatic system. It has been also reported by Hayashi and his co-workers that 4-isoquinolinecarbonitrile (III) reacted with potassium cyanide in dimethyl sulfoxide to give 1,1′-biisoquinoline-4,4′-dicarbonitrile (IV) and they discussed the reaction process involving a route concerning with benzoin condensation type and oxidation, in successive step.[3]

As it seems to be well similar to that of IV, we propose the reaction process for the formation of II as shown in Chart 2. Thus, addition of cyanide ion to I affords N-anion (**a**)

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[1] Location: *2-2-1, Oshika, Shizuoka-shi.*
[2] W.L.F. Armarego and R.E. Willette, *J. Chem. Soc.*, **1965**, 1258.
[3] E. Hayashi, H. Makino, and T. Higashino, *Yakugaku Zasshi*, **94**, 1041 (1974).

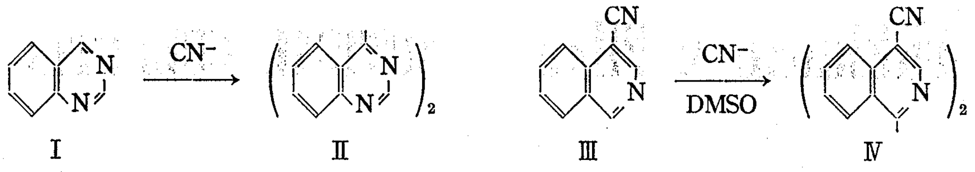


Chart 1

which rearranges to carbanion (**b**) by a prototropic shift. Nucleophilic addition of **b** to I provides an intermediate N-anion (**c**) which rearranges to N-anion (**d**). Loss of cyanide ion from **d** affords 3,4-dihydro-4,4′-biquinazoline (V) (a formal benzoin type condensation product from I) which undergoes oxidation to II. If I may act as hydride ion acceptor on V in this oxidation step, reduction product such as 3,4-dihydroquinazoline (VI) should be formed. But none of VI can be isolated, because VI is easily oxidized to form I. Consquently, it is not clear what substances act as hydride ion acceptor.

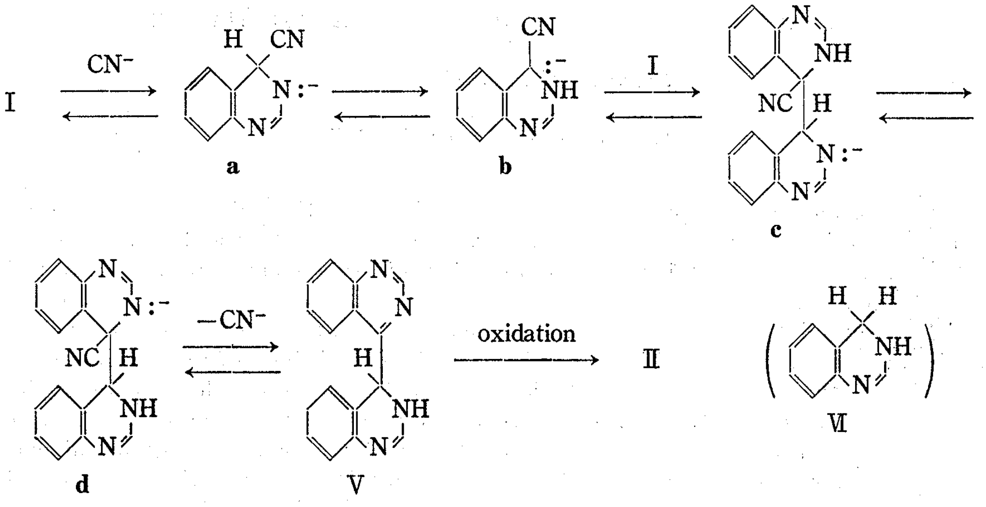


Chart 2

If the reaction process in Chart 2 is correct, it may be expected that the presence of aromatic aldehyde in the reaction system may undergo cross benzoin type condensation to give α-aryl-4-quinazolinemethanol (VII), aryl 3,4-dihydro-4-quinazolinyl ketone (VIII) or aryl 4-quinazolinyl ketone (IX) together with II, where VII and VIII are a formal cross benzoin type condensation product and IX is a product formed by followed oxidation of VII and VIII. Therefore, the reaction of I with aromatic aldehyde in the presence of cyanide ion is carried out.

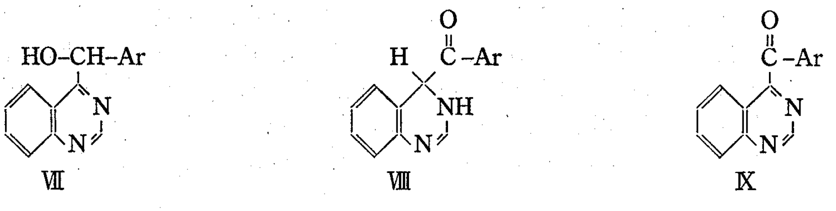


Chart 3

Aromatic aldehyde used in this reaction are as follows:

i) Benzaldehyde derivatives substituted by electron donating groups (X); benzaldehyde (X-1), *o*-anisaldehyde (X-2), *m*-anisaldehyde (X-3), *p*-anisaldehyde (X-4), *o*-chlorobenzaldehyde (X-5), *m*-chlorobenzaldehyde (X-6), *p*-chlorobenzaldehyde (X-7), *o*-tolualdehyde (X-8), *m*-tolualdehyde (X-9), *p*-tolualdehyde (X-10), *p*-acetamidobenzaldehyde (X-11), *p*-dimethylaminobenzaldehyde (X-12), *o*-hydroxybenzaldehyde (X-13), *m*-hydroxybenzaldehyde (X-14), *p*-hydroxybenzaldehyde (X-15) and vanillin (X-16).

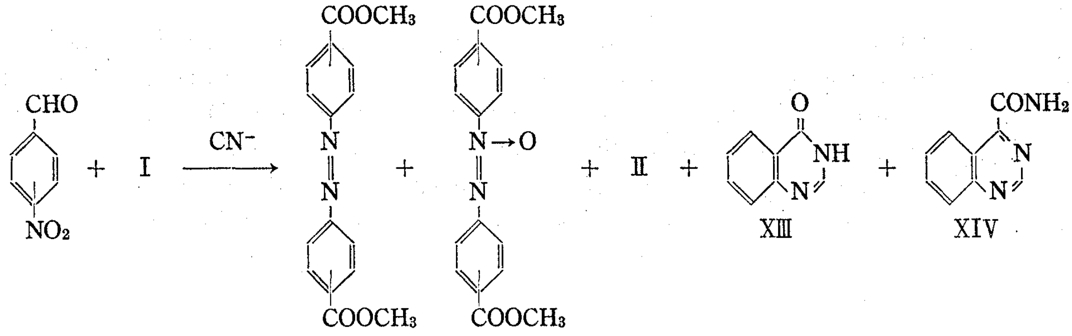
ii) Benzaldehyde derivatives substituted by electron attracting groups (XI); *o*-nitrobenzaldehyde (XI-1), *m*-nitrobenzaldehyde (XI-2), *p*-nitrobenzaldehyde (XI-3) and *o*-cyanobenzaldehyde (XI-4).

iii) Heterocyclic aromatic aldehyde (XII); furfural (XII-1) and isonicotinoaldehyde (XII-2).

In fact, when a solution of I, X (or XII) and potassium cyanide in methanol is allowed to stand overnight in a refrigerator, the formation of VII (only in the two cases of X-2 and X-6) and IX are recognized together with II, 4(3*H*)-quinazolinone (XIII)[4] and 4-quinazolinecarboxamide (XIV)[5] (only in the three cases of X-15, X-16 and XII-1), even if the yields of each products are poor. But in the case of benzaldehyde having strongly electron donating group such as hydroxyl or dimethylamino group (X-12 to X-16), the formation of the corresponding VII and IX is not recognized.

Moreover, the reaction with XI gives II (only in the two cases of XI-2 and XI-4), XIII and XIV in poor yield but does not give any VII and IX; especially, the reaction of nitrobenzaldehyde (XI-1 to XI-3) is different from that of X and gives dimethyl azodibenzoate (XV) and dimethyl azoxydibenzoate (XVI) in poor yield. Thus, XI-1 gives dimethyl 2,2′-azoxydibenzoate (XVI-1),[6] XI-2 does dimethyl 3,3′-azodibenzoate (XV-2)[7] and dimethyl 3,3′-azoxydibenzoate (XVI-2),[8] XI-3 does dimethyl 4,4′-azodibenzoate (XV-3)[6a] and dimethyl 4,4′-azoxydibenzoate (XVI-3).[6a]

Experimental results are summarized in Table I.



o-NO$_2$ (XI-1)	—	XVI-1 (0.5%)	—	(31.0%)	(6.5%)
m-NO$_2$ (XI-2)	XV-2 (0.7%)	XVI-2 (1.4%)	(1.8%)	(1.1%)	(3.3%)
p-NO$_2$ (XI-3)	XV-3 (0.4%)	XVI-3 (14.4%)	—	(5.4%)	(4.6%)

Chart 4

Both structures of VII and IX are established by elemental analyses, mass, infrared (IR) and nuclear magnetic resonance (NMR) spectra. Taking up α-(2-methoxyphenyl)-4-quinazolinemethanol (VII-2) and 2-methoxyphenyl 4-quinazolinyl ketone (IX-2) as a sample, establishment of their structures are as follows. Elemental analytical values of VII-2 correspond with $C_{16}H_{14}O_2N_2$ and its molecular ion (M^+) shows *m/e* 266 in its mass spectrum. There is no carbonyl absorption peak but a broad peak due to hydroxyl group at 3160 cm^{-1} is recognized in its IR spectrum. In its NMR spectrum singlet peaks at 0.80 τ, 3.18 τ and

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[4] M.M. Endicott, E. Wick, M.L. Mercury, and M.L. Sherrill, *J. Am. Chem. Soc.*, **68**, 1300 (1946).

[5] T. Higashino, *Yakugaku Zasshi*, **80**, 247 (1960).

[6] *a*) R. Meier and F. Böhler, *Chem. Ber.*, **89**, 2301 (1956); *b*) E. Hayashi and T. Nagao, *Yakugaku Zasshi*, **85**, 475 (1965).

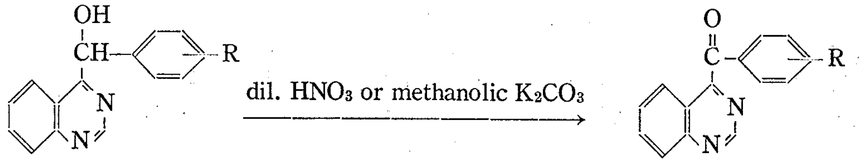
[7] B.M. Bogoslovskii, *J. Gen. Chem.* (U.S.S.R.), **16**, 193 (1946).

[8] M.L. Black and H.A. Smith, *J. Org. Chem.*, **17**, 1315 (1952).

Table I. Reaction of I with Aromatic Aldehyde in the Presence of Cyanide Ion

Aldehyde	Product				
	IX(%)	II(%)	XIII(%)	XIV(%)	VII(%)
X- 1	11.0 IX- 1	1.4	0.7	—	—
X- 2	7.0 IX- 2	13.9	1.2	—	6.7 VII-2
X- 3	18.3 IX- 3	5.7	—	—	—
X- 4	17.0 IX- 4	23.0	0.5	—	—
X- 5	6.3 IX- 5	29.6	3.6	—	—
X- 6	17.5 IX- 6	11.8	—	—	8.8 VII-6
X- 7	24.5 IX- 7	8.8	—	—	—
X- 8	7.1 IX- 8	19.8	—	—	—
X- 9	13.1 IX- 9	9.8	—	—	—
X-10	26.5 IX-10	12.0	0.8	—	—
X-11	19.4 IX-11	10.2	0.8	—	—
X-12	—	86.0	9.8	—	—
X-13	—	12.4	0.1	—	—
X-14	—	17.6	—	—	—
X-15	—	0.3	—	2.0	—
X-16	—	4.2	—	4.7	—
XI- 1	—	—	31.0	6.5	—
XI- 2	—	1.8	1.1	3.3	—
XI- 3	—	—	5.4	4.6	—
XI- 4	—	12.8	1.4	1.0	—
XII- 1	23.9 IX-21	0.9	4.5	8.5	—
XII- 2	1.1 IX-22	11.3	—	—	—

6.13 τ due to a proton at 2-position of quinazoline ring, to a proton at α-position and to protons of methoxyl group at 2-position of phenyl group are respectively recognized. A broad singlet at 4.68 τ due to a proton of hydroxyl group is easily removed by D_2O exchange. Moreover, VII-2 and α-(3-chlorophenyl)-4-quinazolinemethanol (VII-6) are easily oxidized to IX-2 and 3-chlorophenyl 4-quinazolinyl ketone (IX-6), respectively, by allowing to stand overnight in diluted nitric acid solution or to stand several hours in methanolic potassium carbonate solution.



-R: -2-OCH3 (VII-2)
-R: -3-Cl (VII-6)

IX-2
IX-6

Chart 5

The structure of IX-2 is also established by the same method with that of VII-2. Thus, its elemental analytical values correspond with $C_{16}H_{12}O_2N_2$. Its IR spectrum shows a peak at 1680 cm^{-1} due to carbonyl group. Singlet peaks at 0.80 τ and 6.70 τ due to a proton at 2-position of quinazoline ring and to protons of methoxyl group at 2-position of phenyl group are respectively recognized in its NMR spectrum. The fragmentation of IX under electron impact proceeds by two main dissociation path. One is loss of quinazolinyl radical from M^+ to form a fragment ion **e**. Another is elimination of carbon monoxide to give a radical ion of 4-arylquinazoline (**f**). Sequent fragmentation of **f** may proceed by two dissociation path in which one is loss of aryl radical to form evenelectron quinazolinium cation (**g**)[9] and

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[9] T.J. Batterham, A.C.K. Triffett, and J.A. Wunderlich, *J. Chem. Soc.* (*B*), **1967**, 892.

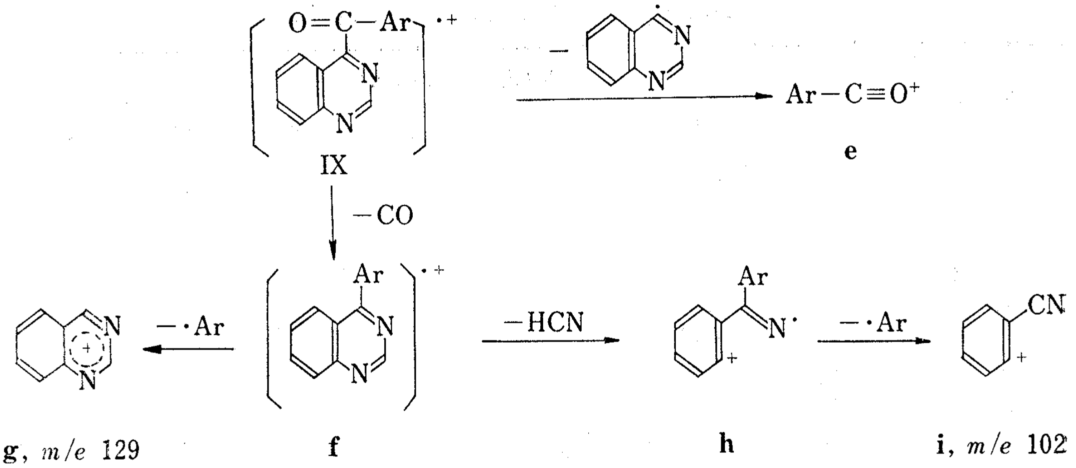

Chart 6

Table II. α-Aryl-4-quinazolinemethanol (VII) and Aryl 4-Quinazolinyl Ketone (IX)

Compd.	mp (°C)	Formula	Analysis (%) Calcd. (Found) C	H	N	IR ν_{max}^{KBr} cm⁻¹ >C=O
IX- 1[a]	97— 98	$C_{15}H_{10}ON_2$	76.91 (76.87)	4.30 (4.37)	11.96 (12.40)	1680
IX- 2[b]	100—101	$C_{16}H_{12}O_2N_2$	72.71 (72.41)	4.58 (4.45)	10.60 (10.59)	1680
IX- 3[b]	122	$C_{16}H_{12}O_2N_2$	72.71 (72.56)	4.58 (4.58)	10.60 (10.72)	1680
IX- 4[a]	119—120	$C_{16}H_{12}O_2N_2$	72.71 (72.38)	4.58 (4.80)	10.60 (10.33)	1670
IX- 5[c]	80— 81	$C_{15}H_9ON_2Cl$	67.05 (67.10)	3.38 (3.48)	10.43 (10.44)	1700
IX- 6[a]	116—117	$C_{15}H_9ON_2Cl$	67.05 (66.98)	3.38 (3.43)	10.43 (10.30)	1680
IX- 7[a]	128—129	$C_{15}H_9ON_2Cl$	67.05 (66.81)	3.38 (3.45)	10.43 (10.37)	1690
IX- 8[d]	86	$C_{16}H_{12}ON_2$	77.40 (77.32)	4.87 (5.02)	11.28 (11.57)	1680
IX- 9[b]	83	$C_{16}H_{12}ON_2$	77.40 (77.39)	4.87 (4.98)	11.28 (11.20)	1680
IX-10[b]	129—130	$C_{16}H_{12}ON_2$	77.40 (77.66)	4.87 (4.98)	11.28 (11.46)	1680
IX-11[e]	195—197	$C_{17}H_{13}O_2N_3$	70.09	4.50	14.43 (14.21)	1670 3100 (NH)
IX-21[a]	162	$C_{13}H_8O_2N_2$	69.64 (69.68)	3.60 (3.71)	12.50 (12.40)	1675
IX-22[f]	110—112	$C_{14}H_9ON_3$	71.48	3.86	17.86 (17.82)	1695
VII- 2[b]	151—153	$C_{16}H_{14}O_2N_2$	72.16 (72.07)	5.30 (5.21)	10.52 (10.60)	3160 (OH)
VII- 6[b]	160—161	$C_{15}H_{11}ON_2Cl$	66.55 (66.15)	4.10 (4.15)	10.35 (10.42)	3100 (OH)

a) white needles; *b*) white prisms; *c*) white particles; *d*) white scales; *e*) pale yellow needles; *f*) crystals

another is loss of hydrogen cyanide and aryl radical, in successive step, to form a fragment ion (**i**) *via* a radical ion (**h**) as shown in Chart 6.

Table III. NMR Spectra of VII and IX

Compd.	NMR (τ) in $CDCl_3$						
	2-H^s	-$OCH_3{}^s$	-$CH_3{}^s$	-CO-$CH_3{}^s$	>NH^{bs}	>CH-O^s	-OH^{bs}
VII- 2	0.80	6.13				3.18	4.68
VII- 6	0.78					3.73	4.85
IX- 1	0.63						
IX- 2	0.80	6.70					
IX- 3	0.68	6.20					
IX- 4	0.68	6.20					
IX- 5	0.77						
IX- 6	0.70						
IX- 7	0.65						
IX- 8	0.75		7.38				
IX- 9	0.70		7.64				
IX-10	0.70		7.61				
IX-11	0.70			7.86	1.75		
IX-21	0.70						
IX-22	0.66						

s: singlet; bs: broad singlet and exchangeable with D_2O

The formation of XIII and XIV may be originated from N-anion (**a**) which leads to 4-quinazolinecarbonitrile (XVII) with loss of hydride ion. Successive hydrolysis[10] may give XIII and XIV as shown in Chart 7. This shows that cyanide ion attacks 4-position of I in the first step of the reaction process.

It may be considered that there is two possible reaction process, path A and B, for the formation of IX. Both A and B are similar to that of cross benzoin condensation.

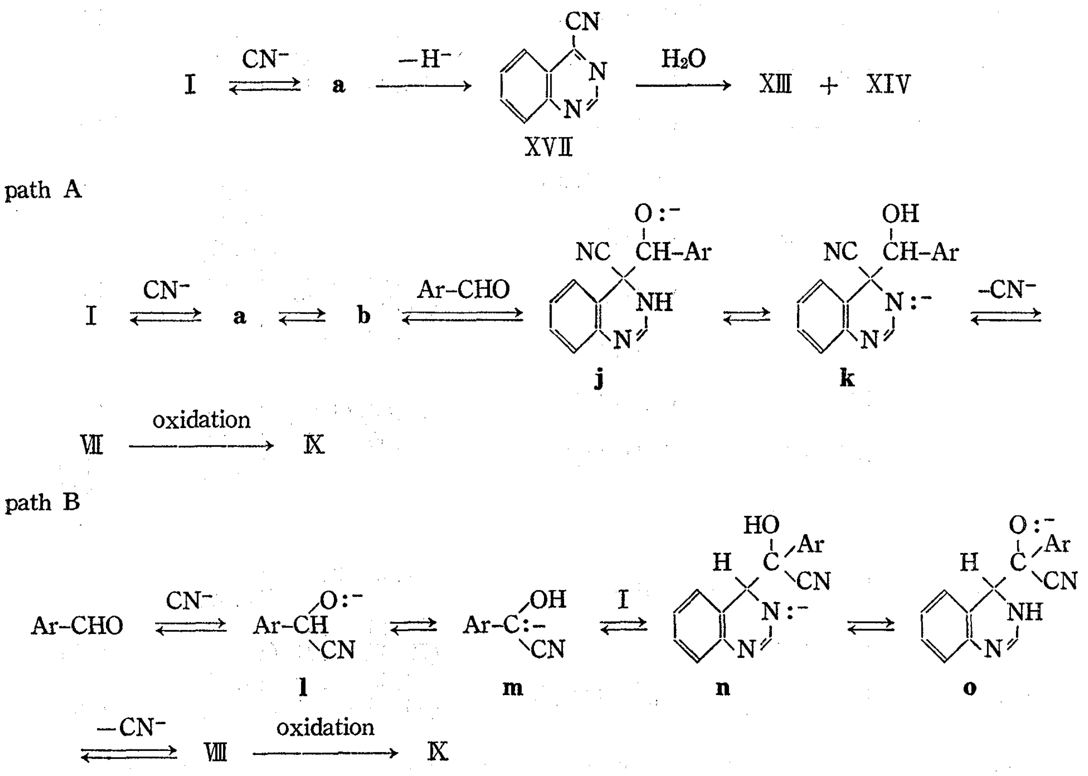

Chart 7

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[10] *a*) T. Higashino, *Yakugaku Zasshi*, **80**, 842 (1960); *b*) *Idem*, *ibid.*, **80**, 1404 (1960).

TABLE IV. Mass Spectra of VII and IX

Compd.																		
VII-2	*m/e*	267	266	237	236	235	234	233	218	205	159	150	149	144	138	137	136	135
	I (%)	5	18	5	21	100	6	21	5	6	9	5	26	11	5	29	6	23
	m/e	131	130	129	124	122	121	109	108	107	105	104	103	102	94	93	92	91
	I (%)	18	34	29	7	8	21	8	9	26	11	12	24	18	8	5	11	6
	m/e	90	89	79	78	77	76	75	74									
	I (%)	5	5	8	11	38	23	15	5									
VII-6	*m/e*	273	272	271	270	269	255	254	253	252	251	241	235	218	217	190	160	159
	I (%)	7	27	20	70	16	6	5	16	5	5	5	7	11	7	5	6	43
	m/e	141	139	131	130	129	127	126	115	113	111	104	103	102	78	77	76	75
	I (%)	11	9	26	100	30	5	9	5	16	11	11	70	34	8	57	27	25
	m/e	74																
	I (%)	7																
IX-1	*m/e*	235	234	233	206	205	179	129	106	105	103	102	78	77	76	75	74	
	I (%)	9	39	25	23	18	11	16	11	100	9	39	10	95	25	27	11	
IX-2	*m/e*	264	249	235	234	233	205	179	144	137	136	135	129	120	105	102	92	79
	I (%)	3	3	4	11	50	3	3	6	3	10	100	4	4	3	10	16	4
	m/e	78	77	76	75													
	I (%)	4	20	6	6													
IX-3	*m/e*	265	264	263	249	237	236	235	234	233	232	222	221	220	209	207	206	205
	I (%)	9	38	18	8	7	36	25	5	15	4	3	8	4	5	4	6	9
	m/e	193	192	136	135	129	108	107	103	102	93	92	79	78	77	76	75	74
	I (%)	3	4	11	100	20	5	49	6	40	5	46	5	6	51	22	24	8
IX-4	*m/e*	265	264	263	249	236	235	233	205	136	135	129	107	102	92	79	78	77
	I (%)	7	24	8	4	8	5	4	4	11	100	8	12	20	28	4	4	32
	m/e	76	75	74														
	I (%)	12	14	4														
IX-5	*m/e*	270	268	240	239	235	234	233	213	205	149	141	140	139	129	113	111	103
	I (%)	3	4	3	4	3	20	100	6	6	5	15	5	44	9	7	20	4
	m/e	102	77	76	75	74												
	I (%)	18	4	9	16	4												
IX-6	*m/e*	271	270	269	268	267	242	241	240	239	233	213	205	141	140	139	129	113
	I (%)	5	11	13	29	20	6	6	11	7	17	6	9	33	11	100	26	18
	m/e	112	111	103	102	77	76	75	74									
	I (%)	6	46	6	37	5	16	33	9									
IX-7	*m/e*	271	270	269	268	267	242	241	240	239	234	233	213	205	177	142	141	140
	I (%)	6	22	23	55	36	9	9	18	12	6	23	8	12	5	6	35	8
	m/e	139	129	113	112	111	103	102	85	77	76	75	74					
	I (%)	100	68	16	6	42	6	29	5	5	13	29	9					
IX-8	*m/e*	249	248	247	234	233	221	220	219	218	205	193	129	120	119	102	92	91
	I (%)	7	30	13	7	31	9	52	78	9	6	5	6	11	100	6	7	48
IX-9	*m/e*	249	248	247	233	221	220	219	205	193	149	129	120	119	102	92	91	78
	I (%)	7	37	15	16	5	17	12	5	4	6	3	7	54	3	3	100	3
IX-10	*m/e*	250	249	248	247	235	234	233	221	220	219	218	205	193	149	129	120	119
	I (%)	4	13	57	23	4	5	20	7	28	11	4	10	7	8	5	11	100
	m/e	102	92	91	78													
	I (%)	3	4	29	14													
IX-11	*m/e*	292	291	290	263	250	249	248	233	221	220	205	203	202	186	185	184	183
	I (%)	15	64	15	9	6	23	17	5	9	6	4	11	70	5	9	9	6
	m/e	170	163	162	159	158	157	149	144	131	129	121	120	119	105	104	103	102
	I (%)	8	13	98	13	9	6	11	5	10	12	17	100	13	6	9	9	16
	m/e	93	92	91	90	78	77	76	75									
	I (%)	11	36	20	6	6	38	10	9									
IX-21	*m/e*	225	224	197	196	195	171	170	169	168	142	141	140	130	129	128	115	114
	I (%)	6	14	17	81	14	8	22	78	8	8	14	11	8	44	6	8	14
	m/e	113	103	102	101	100	99	98	96	95	88	87	86	77	76	75	74	
	I (%)	6	14	83	8	8	8	11	11	100	11	6	6	6	28	35	11	
IX-22	*m/e*	236	235	234	209	208	207	181	180	179	153	150	149	146	130	129	106	104
	I (%)	13	87	65	9	26	43	9	26	11	7	7	52	7	11	57	52	9
	m/e	103	102	101	79	78	77	76	75	74	51							
	I (%)	17	96	5	26	74	9	44	48	13	100							

I: relative intensities

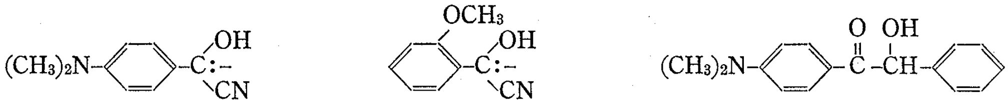
Table V. UV Spectra of VII and IX

Compd.	UV $\lambda_{\max}^{\mathrm{EtOH}}$ mμ (log ε)			
Ⅶ- 2	274(3.67)	281(3.65)	306(3.60)	312(3.60)
Ⅶ- 6	270(3.52)	283(3.47)	307(3.55)	314(3.52)
Ⅸ- 1	259(4.13)	315(3.62)		
Ⅸ- 2	256(4.06)	315(3.84)		
Ⅸ- 3	261(3.64)	315(3.33)		
Ⅸ- 4	220(4.48)	295(4.13)		
Ⅸ- 5	240(4.28)	313(3.69)		
Ⅸ- 6	250(4.27)	310(3.81)		
Ⅸ- 7	269(4.20)	314(3.66)		
Ⅸ- 8	260(4.03)	305(3.69)		
Ⅸ- 9	260(4.10)	305(3.67)		
Ⅸ-10	271(4.22)	313(3.76)		
Ⅸ-11	270(3.98)	313(4.50)		
Ⅸ-22	246(4.18)	292(4.22)		

Path A: Addition of cyanide ion across 3 and 4-position of I affords N-anion (**a**) which rearranges to carbanion (**b**) by a prototropic shift. Nucleophilic attack of **b** to carbonyl carbon atom of aromatic aldehyde gives an intermediate (**j**). Loss of cyanide ion from N-anion (**k**), which is tautomeric isomer of **j**, affords VII. Successive oxidation of VII gives IX. The intermediate VII in this process is a formal cross benzoin type condensation product.

Path B: Cyanide ion attacks carbonyl carbon atom of aromatic aldehyde to yield O-anion (**l**) which rearranges to cyanohydrin carbanion (**m**) by a prototropic shift. Nucleophilic addition of **m** across 3 and 4-position of I forms N-anion (**n**). Loss of cyanide ion from O-anion (**o**), which is tautomeric isomer of **n** gives VIII. Successive oxidation of VIII gives IX. The intermediate VIII in this process is a formal cross benzoin type condensation product.

Now, we take up the reaction with X-2 and X-12 as a sample and discuss which path the reaction will take, A or B.



l-12 **l**-2 XVIII

Chart 8

It is well known that X-12 does not undergo self benzoin condensation but does cross benzoin condensation with X-1 to give 4-dimethylaminobenzoin (XVIII). This fact means that anion **l**-12 is formed from X-12.[11] If it is supposed that the reaction takes path B, anion **l**-12, which is greater nucleophile than anion **l**-2 due to strongly electron donating effect of dimethylamino group, will add across 3 and 4-position of I to give 4-dimethylaminophenyl 3,4-dihydroquinazolinyl ketone (VIII-12) or 4-dimethylaminophenyl 4-quinazolinyl ketone (IX-12). However X-12 gives VII-2 and IX-2 but X-12 does not give any of VIII-12 and IX-12. These facts are shown that the reaction may not take path B. Considering that carbanion **b** is able to react with aromatic aldehyde, which can undergo self benzoin condensation, and is unable to react with aromatic aldehyde, which can not undergo self benzoin condensation, together with the fact that VII-2 and VII-6, which are a formal cross benzoin type condensation product in path A, are easily oxidized to IX-2 and IX-6 in methanolic potassium carbonate solution, the formation of IX can be well explained by path A rather than path B. But it is not clear as yet what substances act as hydride ion acceptor in oxidation steps of both path A and B.

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[11] E.S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt Co., 1959, p. 396.

Experimental[12]

Ultraviolet (UV) spectra were measured in 99.5% EtOH on a Hitachi Spectrophotometer Model ESP-2U.

IR spectra were recorded with a JASCO Grating Infrared Spectrophotometer Model IRA-1.

NMR spectra were measured at 60 Mc and 23° on a Japan Electron Optics Lab. Spectrophotometer Model JNM-C-60H. Tetramethylsilane was used as internal standard.

Mass spectra were recorded on a Hitachi RMS-4 single focusing mass spectrometer. The ionisation energy normally used was 80 eV. Samples were vaporised in all glass inlet system for compounds having melting point below 150° and direct inlet system for those above 150°.

Reaction of Quinazoline (I) with Aromatic Aldehyde in the Presence of KCN——To a solution of 0.010 mole of I and 0.011 mole of aromatic aldehyde dissolved in 20 ml of MeOH, a solution of 1.3 g of KCN in 2 ml of H_2O was added slowly under ice-cooling and the mixture was allowed to stand overnight in a refrigerator. Then MeOH was removed under reduced pressure, the residue was acidified by 1N HCl and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over anhyd. Na_2SO_4 and $CHCl_3$ was evaporated to dryness. The residue was passed through a column of Al_2O_3. The first fraction from elution with benzene gave 4,4′-biquinazoline (II),[2] mp 245°, recrystallized from MeOH, and the second fraction gave aryl 4-quinazolinyl ketone (IX) recrystallized from MeOH. In the case of nitrobenzaldehyde, the first fraction from elution with $CHCl_3$ gave dimethyl azodibenzoate (XV)[6–8] and the second fraction gave dimethyl azoxydibenzoate (XVI).[6–8]

The HCl solution was neutralized with anhyd. K_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ solution was dried over anhyd. Na_2SO_4 and $CHCl_3$ was evaporated to dryness. The residue was passed through a column of Al_2O_3 by changing eluate as follows; benzene, $CHCl_3$ and MeOH. The elution with benzene gave α-aryl-4-quinazolinemethanol (VII) recrystallized from MeOH, the elution with $CHCl_3$ gave 4-quinazolinecarboxamide (XIV),[5] mp 169°, recrystallized from MeOH, and the elution with MeOH gave 4(3*H*)-quinazolinone (XIII),[4] mp 212—213°, recrystallized from MeOH.

The yields of the products described above were summarized in Table I and melting point and elemental analytical data were also done in Table II.

Aryl 4-Quinazolinyl Ketone (IX)——i) A solution of 25 mg of α-(2-methoxyphenyl)-4-quinazolinemethanol (VII-2) dissolved in 2 ml of 28% HNO_3 was allowed to stand overnight at room temperature. The reaction mixture was neutralized with anhyd. K_2CO_3 and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over anhyd. Na_2SO_4 and $CHCl_3$ was removed. The residue was recrystallized from MeOH to give 2-methoxyphenyl 4-quinazolinyl ketone (IX-2), mp 100—101°, in 20% yield (5 mg).

A solution of 25 mg of α-(3-chlorophenyl)-4-quinazolinemethanol (VII-6) dissolved in 2 ml of 28% HNO_3 was allowed to stand overnight at room temperature. When the reaction mixture was treated as same manner as that described above, 3-chlorophenyl 4-quinazolinyl ketone (IX-6), mp 116—117° was obtained in 56% yield (14 mg).

ii) To a solution of 184 mg of VII-2 dissolved in 20 ml of MeOH, a solution of 200 mg of K_2CO_3 dissolved in 5 ml of H_2O was added and the reaction mixture was allowed to stand for 2 days at room temperature. MeOH was removed under reduced pressure, separated crystals were collected by suction and recrystallized from MeOH to give IX-2 in 68% yield (124 mg).

To a solution of 150 mg of VII-6 dissolved in 20 ml of MeOH, a solution of 200 mg of K_2CO_3 dissolved in 5 ml of H_2O was added and the reaction mixture was allowed to stand for 10 hr at room temperature. The treatment of the reaction mixture as same manner as that described above gave IX-6 in 43% yield (64 mg).

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[12] All melting points were not corrected.