adopted in each case, and refinement continued until no calculated shift in any parameter exceeded one-tenth of the corresponding esd.

Scattering functions for C, N, and O were taken from "International Tables for X-Ray Crystallography"[24] and for H from the compilation of Stewart, Davidson, and Simpson.[25] With the exception of MULTAN and ORTEP,[9] for which a CDC Cyber 172 computer was used, all calculations were carried out on an XDS Sigma 2 computer with programs written in this laboratory.

Acknowledgment. The 250 MHz spectra were obtained by Dr. Robert Rowan, III, and Dr. Robert P. Bittner at the NIH Facility for Biomedical Studies, Mellon Institute, Pittsburgh.

Registry No.—**3a,** 67921-99-7; **3b,** 67922-00-3; **3c,** 67922-01-4; **4a,** 67922-02-5; **4c,** 67922-03-6; **5a,** 67922-04-7; **5c,** 67922-05-8; **6b,** 67922-09-2; **7a,** 67922-06-9; **7b,** 67922-07-0; **7c,** 67922-08-1; **8a,** 67922-10-3; **8b,** 67951-69-3; **8c,** 67922-11-6; **10a,** 34964-86-8; **10b,** 67951-68-2; **10c,** 67922-12-7; **12c,** 67951-67-1; lithium diisopropylamide, 4111-54-0; 3-methylpyridine, 108-99-6; ethyl indole-2-carboxylate, 3770-50-1; ethyl methylindole-2-carboxylate, 18450-24-3; ethyl 5-methoxyindole-2-carboxylate, 4792-58-9; chloroacetyl chloride, 79-04-9; ethylene glycol, 107-21-1; (3-pyridyl)methyllithium, 26954-24-5; 5-methoxy-α,α-bis[(3-pyridinyl)methyl)]-1*H*-indole-2-methanol, 67922-13-8.

Supplementary Material Available: Fractional coordinates with estimated standard deviations for C, N, and O atoms for compounds **8b** and **12c,** ansisotropic thermal parameters for molecules A and B in **8b** and for **12c,** bond distances and estimated standard deviations for **8b** and **12c,** bond angles for **8b** and **12c,** selected torsional angles for the nonaromatic rings in **8b** and **12c,** and information on least-squares mean planes (13 pages). Ordering information is given on any current masthead page.

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(11) However, if the esd's derived from the least-squares matrices are accepted, apparently significant deviations from the mean values of the bond lengths ($\Delta > 2\sigma$) in A and B are found for C(7)–C(10), C(16)–C(17), and O(21)–C(22). At least in the case of the first two of these distances, there is no reason to expect these differences to have physical significance. It seems wiser to assume that the esd's are underestimated, and by assuming their true values to be 1.5 times those quoted, none of the differences found in chemically equivalent bond lengths and angles would be significant.
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Reaction of 2-(1-Alkoxyethylideneamino)benzophenones with Amines. A Novel Synthesis of 2-(*N*-Substituted-amino)-4-phenylquinolines

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When 2-(1-alkoxyethylideneamino)benzophenones (**1**) were allowed to react with aminoacetaldehyde dialkyl acetals (**2**) in alcohol using an acid catalyst, 3-(2,2-dialkoxyethyl)-3,4-dihydro-4-hydroxy-2-methyl-4-phenylquinazoline (**3**) was obtained in 51–70% yield after silica gel column chromatography together with the minor products 2-(2,2-dialkoxyethylamino)-4-phenylquinoline (**4**) and 2-aminobenzophenone (**5**). On the contrary, the reaction of **1** with **2** in toluene or xylene afforded a 56–76% yield of **4** as the major product. Heating of a xylene solution of **3** with an acid effected the conversion of **3** to **4**. Mechanistic pathways of the above reactions are presented.

2-(*N*-Substituted-amino)-4-phenylquinolines have typically been synthesized[1–4] from the corresponding 4-phenylcarbostyrils. In the course of synthetic studies on tricyclic diazepine compounds,[5] we have investigated the reaction of 2-(1-alkoxyethylideneamino)benzophenones (**1**) with amines, which led to a novel, convenient synthesis of 2-(*N*-substituted-amino)-4-phenylquinolines. The related reaction of **1** or 5-chloro-2-(acylamino)benzophenones with hydrazine hydrate has been reported to give 3,4-dihydro-4-hydroxy-4-phenylquinazolines.[6,7]

Results and Discussion

Compounds **1** were allowed to react with aminoacetaldehyde dialkyl acetals (**2**) using *p*-toluenesulfonic acid or sulfuric acid as the catalyst, and the results summarized in Table I were obtained. When the reactions were run in etha-

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Table I. Reaction of 2-(1-Alkoxyethylideneamino)benzophenones (1) with Aminoacetaldehyde Dialkyl Acetals (2)

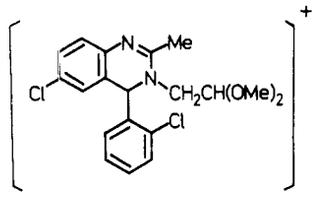
starting material[a]			reaction conditions			product (% yield[b])		
rxn	imino ether	amine	solvent[c]	refluxing period, h	catalyst[d]	dihydrohydroxy quinazoline	quinoline	aminobenzophenone
1	**1a**	**2a**	methanol	7	PTS	**3a** (70)		
2	**1b**	**2a**	ethanol	12.5	H_2SO_4	**3b** (52)	**4b** (11)	**5b** (16)
3[e]	**1c**	**2a**	ethanol	38	PTS	**3c** (51)	**4c** (4)	**5c** (13)
4	**1c**	**2b**	ethanol	46	PTS	**3d** (60)	**4d** (10)	**5c** (13)
5	**1a**	**2a**	xylene	24	PTS	**3a** (2)	**4a** (76[f])	**5a** (16)
6	**1b**	**2a**	toluene	36	PTS		**4b** (76[f])	**5b** (21)
7	**1c**	**2a**	xylene	38.5	PTS		**4c** (56)	**5c** (13)

[a] The molar ratios of **1** and **2** employed were 1:1.24–1.21. [b] Unless otherwise noted, yields are those of compounds isolated by silica gel column chromatography. The eluents were selected from benzene, benzene–ethyl acetate, ethyl acetate, and ethyl acetate–methanol. [c] Dried solvents were employed. [d] PTS = *p*-toluenesulfonic acid monohydrate. [e] 2-Acetamido-2,5-dichlorobenzophenone, which was apparently generated by hydrolysis of remaining **1c**, was also isolated in 31% yield by chromatography. [f] Yield of combined **4** obtained by crystallization of an oily product with ether and subsequent filtration and by chromatography of the mother liquor.

nol, the major reaction product was 3-(2,2-dialkoxyethyl)-3,4-dihydro-4-hydroxy-2-methyl-4-phenylquinazoline (**3**), obtained in a yield of 51–70%, which was accompanied by the minor products 2-(2,2-dialkoxyethylamino)-4-phenylquinoline (**4**) and 2-aminobenzophenone (**5**) (Scheme I). When the above reactions were carried out in refluxing toluene or xylene, markedly different product ratios resulted, and **4** became the major product (in 56–76% yield).

The IR and NMR spectra of **4** showed the absence of the carbonyl and the methyl group, respectively. The NMR spectra (in $CDCl_3$) exhibited a singlet of 1 H in the range δ 6.42–6.60 and a broad peak of 1 H centered at δ 4.94–5.05, each assignable to H-3 of the quinoline ring and the NH proton, respectively. The disappearance of the NH proton signal of 6-chloro-2-(2,2-dimethoxyethylamino)-4-phenylquinoline (**4b**) with added deuterium oxide with concomitant degeneration of a triplet due to $NHCH_2CH$ to a doublet supported the assignment of the NH signal. In the case of **3**, the observations that neither carbonyl stretching vibration nor NH proton signal was present in the IR and NMR spectra, respectively, and that a singlet due to the C-2 methyl group was exhibited in the NMR spectra are in agreement with the structure.

The dihydrohydroxyquinazolines **3c** and **3d** were converted to the 4-ethoxy derivatives **6c** and **6d**, respectively, in high yields by refluxing in ethanol with *p*-toluenesulfonic acid. In the mass spectrum of **6c** at 70 eV, a peak of 74% relative intensity was observed at *m/e* 377 ($M^+ - OC_2H_5$) together with appropriate isotope peaks at *m/e* 379 and 381 due to two chlorine atoms. These peaks are ascribable to the species **7**, and this mass spectral observation is evidence for the 3,4-dihydroquinazoline structure of **6c**. The UV spectrum[9] of **3c**



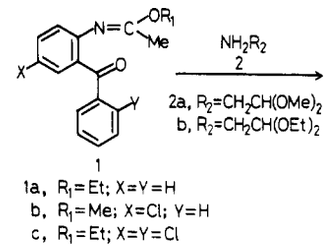
7

[λ_{max} (2-propanol) 224 nm (ϵ 18 600), 233 (12 300), 281 (10 400), 291 (12 600), 321 (3640)], which compared favorably with the reported UV spectra[8] of 3-amino-3,4-dihydro-4-hydroxy-4-phenylquinazolines, was very similar to that of **6c**, supporting in turn the 3,4-dihydroquinazoline structure for **3c**. The NMR C-2 methyl signal of **3a–c** appeared at a considerably higher magnetic field (δ 1.41–1.57) than the corresponding signal of **6c,d** (δ 2.44–2.49).

TLC (silica gel) of the reaction mixture of the above reaction of **1** with **2** in alcohol indicated the presence of a substance whose R_f value was between those of **3** and **4** (the most polar among the three) and equal to that of **6**,[10] but the substance could not be isolated by silica gel column chromatography. From the ease of the conversion of **3** to **6** in ethanol as demonstrated by the experiments mentioned above, it was assumed that the initially formed **3** was transformed by ethanol to **6**, which was then hydrolyzed back to **3** during the column chromatography. To substantiate this assumption further, the crystalline 4-ethoxy derivative **6c** (separately prepared from **3c**) was chromatographed on silica gel to give the 4-hydroxy compound **3c** in 98% yield. Finally, in a 38-h reaction of the imino ether **1c** with aminoacetaldehyde dimethyl acetal (**2a**) in refluxing ethanol, the NMR spectrum showed that **3c** was essentially all in its ethoxy form **6c**, and actually crystalline pure **6c** was obtained from the product mixture by crystallization with the aid of seeding crystalline **6c** followed by trituration with ether–*n*-hexane. The pure **6c** thus obtained afforded **3c** upon silica gel chromatography.

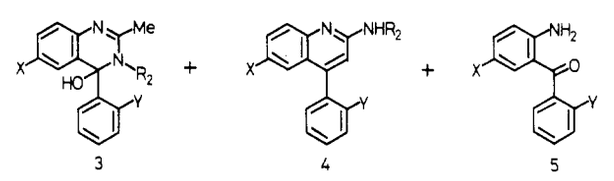
The pathway of the reaction of **1** and **2** is envisaged as depicted in Scheme II. The attack of **2** with the imino ether

Scheme I



1

1a, R_1=Et; X=Y=H
b, R_1=Me; X=Cl; Y=H
c, R_1=Et; X=Y=Cl

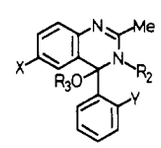


3 4 5

3,4a, R_2=$CH_2CH(OMe)_2$; X=Y=H
b, R_2=$CH_2CH(OMe)_2$; X=Cl; Y=H
c, R_2=$CH_2CH(OMe)_2$; X=Y=Cl
d, R_2=$CH_2CH(OEt)_2$; X=Y=Cl

5a, X=Y=H
b, X=Cl; Y=H
c, X=Y=Cl

R_3OH



6

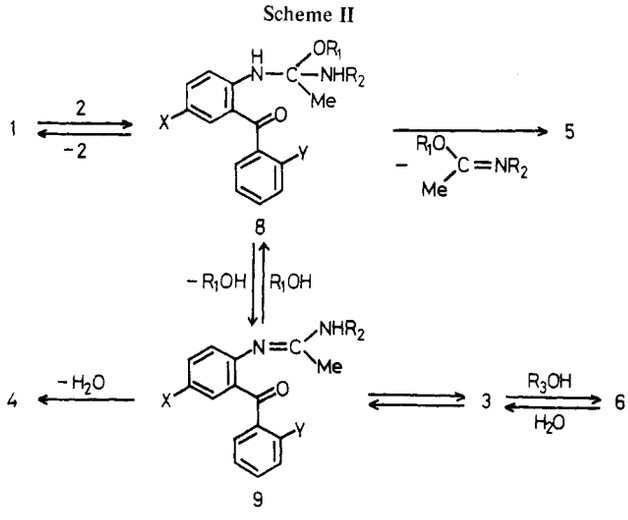
6c, R_2=$CH_2CH(OMe)_2$; R_3=Et; X=Y=Cl
d, R_2=$CH_2CH(OEt)_2$; R_3=Et; X=Y=Cl

Table II. Physical and Spectral Data for Dihydrohydroxyquinazolines (3), Quinolines (4), and Alkoxydihydroquinazolines (6)

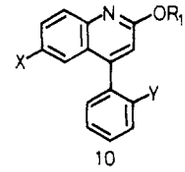
compd[a]	mp, °C[b]	^{1}H NMR spectral data[c]	IR spectral data[d]
3a	166.0–167.0	1.41 (s, 3, CCH_3), 2.94–3.23 (m, 2, NCH_2), 2.98 (s, 3, OCH_3), 3.05 (s, 3, OCH_3), 3.62–3.80 (m, 1, O-CH-O), 6.78–7.84 (m, aromatic H)	1590, 1559, 1484, 1451, 1429, 1404
3b	160.0–161.0	1.52 (s, 3, CCH_3), 2.97 (s, 3, OCH_3), 3.07 (s, 3, OCH_3), 2.81–3.77 (m, 3, NCH_2 and O-CH-O), 6.76 (d, J = 2.0 Hz, 1, H-5), 7.00 (d, J = 8.0 Hz, 1, H-8), 7.17 (dd, 1, J = 8.0 and 2.0 Hz, H-7), 7.52–7.64 (m, 5, aromatic H)	1600,[e] 1586, 1552, 1477, 1449, 1407
3c	183.5–185.0	1.57 (s, 3, CCH_3), 2.94 (s, 3, OCH_3), 3.17 (s, 3, OCH_3), 3.09–3.67 (m, 3, NCH_2 and O-CH-O), 6.66 (d, J = 2.0 Hz, 1, H-5), 6.96 (d, J = 8.0 Hz, 1, H-8), 7.16 (dd, J = 8.0 and 2.0 Hz, 1, H-7), 7.22–7.53 (m, 4, aromatic H), 8.34–8.50 (m, 1, aromatic H)	1602,[e] 1587, 1550, 1481, 1439, 1407
3d	171.0–172.0	0.98 (t, J = 7.0 Hz, 3, CH_2CH_3), 1.08 (t, J = 7.0 Hz, 3, CH_2CH_3), 1.55 (s, 3, CH_3), 3.00 (g, J = 7.0 Hz, 4, $2CH_2CH_3$), 2.90–3.79 (m, 3, NCH_2 and O-CH-O), 6.69 (d, J = 2.0 Hz, 1, H-5), 6.95–7.55 (m, 5, aromatic H), 8.37–8.48 (m, 1, aromatic H)	1601,[e] 1586, 1558, 1479, 1435, 1402
4a	123.0–123.5	3.45 (s, 6, $2OCH_3$), 3.77 (t, J = 5.5 Hz, 2, NCH_2), 4.65 (t, J = 5.5 Hz, 1, O-CH-O), 4.94 (broad s, 1, NH), 6.42 (s, 1, H-3), 7.37–7.80 (m, aromatic H)	3360, 1610, 1598,[e] 1520, 1500, 1394
4b	132.0–133.0	3.42 (s, 6, $2OCH_3$), 3.72 (t, J = 5.5 Hz, 2, NCH_2), 4.60 (t, J = 5.5 Hz, 1, O-CH-O), 5.05 (broad t, 1, NH), 6.55 (s, 1, H-3), 7.32–7.72 (m, 8, aromatic H)	3350, 1614, 1601, 1527, 1407
4c[f]	101.5–102.5	3.45 (s, 6, $2OCH_3$), 3.73 (t, J = 5.7 Hz, 2, NCH_2), 4.63 (t, J = 5.4 Hz, 1, O-CH-O), 5.05 (broad t, 1, NH), 6.60 (s, 1, H-3), 7.20–7.84 (m, 7, aromatic H)	3395, 1618, 1523, 1408
4d	127.0–128.0	1.24 (t, J = 7.1 Hz, 6, $2CH_2CH_3$), 3.45–3.88 (m, 6, $2OCH_2$ and NCH_2), 4.73 (t, J = 5.0 Hz, 1, O-CH-O), 5.00 (broad, 1, NH), 6.57 (s, 1, H-3), 7.16–7.72 (m, 7, aromatic H)	3320, 1618, 1593, 1525, 1407
6c[g]	123.5–124.5	1.17 (t, J = 5.0 Hz, 3, CH_2CH_3), 2.44 (s, 3, C-2 CH_3), 3.11 (s, 3, OCH_3), 3.18 (s, 3, OCH_3), 2.8–3.6 (m, 4, CH_2CH_3 and NCH_2), 3.85 (t, J = 5.8 Hz, 1, O-CH-O), 6.58 (d, J = 2.0 Hz, 1, H-5), 7.02–7.52 (m, 5, aromatic H), 8.19–8.32 (m, 1, aromatic H)	1603, 1581, 1554, 1481, 1437, 1400
6d	135.5–136.5	1.07 (t, J = 6.5 Hz, 3, CH_2CH_3), 1.11 (t, J = 6.5 Hz, 3, CH_2CH_3), 1.19 (t, J = 5.5 Hz, 3, C-4 (OCH_2CH_3), 2.49 (s, 3, C-2 CH_3), 2.83–3.66 (m, 8, $3OCH_3$ and NCH_2), 3.90 (t, J = 5.5 Hz, 1, O-CH-O), 6.59 (d, J = 2.5 Hz, 1, H-5), 7.03–7.47 (m, 5, aromatic H), 8.19–8.32 (m, 1, aromatic H)	1604, 1585, 1560, 1478, 1428, 1402

[a] Satisfactory analytical data (±0.4% for C, H, and N) were obtained for all compounds listed in the table. [b] Melting points are for crystals obtained by recrystallization from methylene chloride–*n*-hexane. [c] Values are given in δ units relative to tetramethylsilane as an internal standard. All spectra were recorded in $CDCl_3$. [d] Values are given in cm^{-1} units. All spectra were recorded in KBr. [e] Shoulder. [f] NMR spectral data were obtained on a Varian EM 360 nuclear magnetic resonance spectrometer. [g] The mass spectral data of this compound: *m/e* (relative intensity) [426 (1), 424 (3), and 422 (5)] (M) [381 (10), 379 (49), and 377 (74)] (M – OC_2H_5), 380 (13), 378 (21), 267 (26), 89 (28), 88 (26), 75 (100). The UV spectral data of this compound: λ_{max} (2-propanol) 224 nm (ϵ 19 900), 232 (12 400), 280 (11 700), 290 (13 500), 319 (3510).

Scheme II



moiety of 1 gives the intermediate 8,[7] which, depending on which of the two C–N bonds or the C–O bond is cleaved, collapses to **1**, **5**, or the amidine **9**. The acyclic amidine **9** takes the cyclic form **3**. The conversion of **9** to **3** is reversible, and under forced reaction conditions (i.e., continued heating in toluene or xylene) the quinoline **4** is obtained from **9** (regenerated from **3**) by acid-catalyzed, dehydrative cyclization. Another possible mechanistic pathway from **1** and **2** to **4**, ring closure of **1** between the methyl and carbonyl groups to form 2-alkoxy-4-phenylquinoline (**10**) followed by the nucleophilic attack on



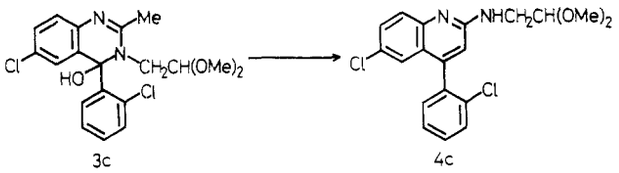
10

10a, R_1=Et; X=Y=Cl

Table III. Analytical Data for 3, 4, and 6

compd no.	formula	C, % calcd	C, % found	H, % calcd	H, % found	N, % calcd	N, % found
3a	$C_{19}H_{22}N_2O_3$	69.91	69.82	6.80	6.67	8.58	8.45
3b	$C_{19}H_{21}ClN_2O_3$	63.24	62.98	5.87	5.69	7.76	7.87
3c	$C_{19}H_{20}Cl_2N_2O_3$	57.73	57.53	5.10	5.03	7.09	6.79
3d	$C_{21}H_{24}Cl_2N_2O_3$	59.58	59.56	5.71	5.68	6.62	6.72
4a	$C_{19}H_{20}N_2O_2$	73.99	73.79	6.54	6.43	9.09	9.03
4b	$C_{19}H_{19}ClN_2O_2$	66.57	66.47	5.59	5.53	8.17	8.05
4c	$C_{19}H_{18}Cl_2N_2O_2$	60.49	60.55	4.81	4.61	7.43	7.40
4d	$C_{21}H_{22}Cl_2N_2O_2$	62.23	62.41	5.47	5.45	6.91	6.83
6c	$C_{21}H_{24}Cl_2N_2O_3$	59.58	59.68	5.71	5.75	6.62	6.43
6d	$C_{23}H_{28}Cl_2N_2O_3$	61.20	61.13	6.25	6.21	6.21	5.99

10 by **2** to afford **4**, was excluded by an experiment of refluxing a solution of **1c** and a catalytic amount of *p*-toluenesulfonic acid in xylene; in the worked up reaction mixture neither 6-chloro-4-(2-chlorophenyl)-2-ethoxyquinoline (**10a**) nor 6-chloro-4-(2-chlorophenyl)carbostyril, which may arise from **10a** during the workup process, was detected by NMR spectroscopy. According to the reaction pathway shown in Scheme II, the dihydroquinazolines **3** are converted to the quinolines **4** under the reaction conditions employed in the reaction of **1** with **2**. Actually, the isolated **3c** was heated at reflux in xylene with *p*-toluenesulfonic acid for 24.5 h with the result that **4c** was obtained in a yield of 74% after column chromatography.



3c 4c

On substituting benzylamine for aminoacetaldehyde dialkyl acetals (**2**), 2-benzylamino-6-chloro-4-phenylquinoline[3] (**11**) was obtained by heating a solution of **1** and benzylamine in xylene with *p*-toluenesulfonic acid as catalyst.

Experimental Section

Melting points were taken with a Yanagimoto hot-stage apparatus and are uncorrected. Combustion analyses were carried out by the Analytical Chemistry Laboratory of Central Research Institute, Teijin Ltd. IR spectra were recorded on a Hitachi EPI-S2 spectrophotometer. UV spectra were measured on a Hitachi 323 spectrophotometer. NMR spectra were obtained on a JEOL JNM-MH-100 spectrometer unless otherwise noted, and chemical shifts are expressed in parts per million (δ) relative to tetramethylsilane as an internal standard. Mass spectra were run on a LKB 9000 spectrometer at an ionizing voltage of 70 eV. In the workup described below, the reaction mixture, after changing the solvent system when necessary. was washed with saturated aqueous sodium bicarbonate solution and aqueous sodium chloride solution and dried over anhydrous sodium sulfate.

Reaction of 2-(1-Alkoxyethylideneamino)benzophenones (1) with Aminoacetaldehyde Dialkyl Acetals (2) in an Alcohol (Tables I–III). Typical Procedure and Result. A stirred solution of 2′,5-dichloro-2-(1-ethoxyethylideneamino)benzophenone (**1c**; 9.15 g, 27.2 mmol), aminoacetaldehyde diethyl acetal (**2b**; 5.00 g, 37.5 mmol), and *p*-toluenesulfonic acid monohydrate (40 mg) in absolute ethanol (25 mL) was heated at reflux for 46 h. The solvent was evaporated, and the residue was taken up in benzene (50 mL), washed, dried, and evaporated. The residue was chromatographed on silica gel. The column was eluted first with benzene to give 0.97 g (13%) of 2-amino-2′,5-dichlorobenzophenone (**5c**), then with benzene–ethyl acetate (19:1) to give 1.04 g (9%) of 6-chloro-4-(2-chlorophenyl)-2-(2,2-diethoxyethylamino)quinoline (**4d**), and finally with benzene–ethyl acetate (2:1) to give 6.93 g (60%) of 6-chloro-4-(2-chlorophenyl)-3-(2,2-diethoxyethyl)-3,4-dihydro-4-hydroxy-2-methylquinazoline (**3d**). The physical and spectral data are shown in Table II, and the analytical data are given in Table III.

Reaction of 1 with 3 in Toluene or Xylene (Tables I–III). Typical Procedure and Result. A stirred solution of 5-chloro-2-(1-methoxyethylideneamino)benzophenone (**1b**; 4.01 g, 13.9 mmol), aminoacetaldehyde dimethyl acetal (**2a**; 2.00 g, 19.0 mmol), and *p*-toluenesulfonic acid monohydrate (20 mg) in dry toluene (20 mL) was heated at reflux for 36 h. The cooled reaction mixture was diluted with benzene (20 mL), washed, dried, and evaporated. The residual oil was crystallized with ether, and 2.50 g of colorless crystalline 6-chloro-2-(2,2-dimethoxyethylamino)-4-phenylquinoline (**4b**) was collected by filtration. The filtrate was evaporated, and the residue was chromatographed on silica gel. The column was first eluted with benzene to give 0.666 g (21%) of 2-amino-5-chlorobenzophenone (**5b**) and then with benzene–ethyl acetate (9:1) to give 1.14 g of **4b** [3.64 g (76%) in total]. The physical and spectral data are shown in Table II, and the analytical data are given in Table III.

6-Chloro-4-(2-chlorophenyl)-3-(2,2-dimethoxyethyl)-4-ethoxy-3,4-dihydro-2-methylquinazoline (6c). (a) A stirred solution of 6-chloro-4-(2-chlorophenyl)-3-(2,2-dimethoxyethyl)-3,4-dihydro-4-hydroxy-2-methylquinazoline (**3c**; 253 mg, 63.9 mmol) and *p*-toluenesulfonic acid monohydrate (30 mg) in absolute ethanol (12.5 mL) was heated at reflux for 3 h. The solvent was evaporated. The residue was taken up in benzene (15 mL), washed, dried, and evaporated. The residual material was recrystallized from methylene chloride–*n*-hexane to give 185 mg (68%) of **6c**. The physical and spectral data are shown in Table II, and the analytical data are given in Table III.

(**b**) A stirred solution of **1c** (1.13 g, 3.36 mmol), **2a** (0.428 g, 4.07 mmol), and *p*-toluenesulfonic acid monohydrate (20 mg) in absolute ethanol (50 mL) was heated at reflux for 38.5 h. The mixture was evaporated, and the residue was taken up in benzene (40 mL), washed, dried, and evaporated. The residue was crystallized by seeding with **6c**, prepared as described in (a) above and triturated with ether–*n*-hexane. Crystalline **6c** (0.447 g, 31% yield) was collected by filtration. Recrystallization from methylene chloride–*n*-hexane gave colorless prisms of mp 123.5–124.5 °C, showing identical IR and NMR spectra with those of **6c** prepared from **3c**.

6-Chloro-4-(2-chlorophenyl)-3-(2,2-diethoxyethyl)-4-ethoxy-3,4-dihydro-2-methylquinazoline (6d). A stirred solution of **3d** (510 mg, 1.20 mmol) and *p*-toluenesulfonic acid monohydrate (20 mg) in absolute ethanol (15 mL) was heated at reflux for 1 h. The solvent was evaporated. The residue was taken up in benzene (25 mL), washed, dried, and evaporated. The residue was crystallized by treating with ether to give 497 mg (92%) of 6-chloro-4-(2-chlorophenyl)-3-(2,2-diethoxyethyl)-4-ethoxy-3,4-dihydro-2-methylquinazoline (**6d**). The physical and spectral data are shown in Table II, and the analytical data are given in Table III.

Conversion of 6c to 3c. Compound **6c** (158 mg, 0.373 mmol) was chromatographed on silica gel (8 g). The column was eluted successively with benzene (100 mL), benzene–ethyl acetate (9:1, 100 mL), ethyl acetate (100 mL), ethyl acetate–methanol (9:1, 100 mL), and ethyl acetate–methanol (7:3, 200 mL). Fractions eluted with ethyl acetate and thereafter were combined and evaporated to give 144 mg (98%) of **3c** as colorless crystals. The IR and NMR spectra were identical with those of **3c** obtained by the reaction of **1c** with **2a**.

Conversion of 3d to 4d. A stirred solution of **3d** (500 mg, 1.18 mmol) and *p*-toluenesulfonic acid monohydrate (30 mg) in dry xylene (5 mL) was heated at reflux for 24.5 h. The cooled reaction mixture was diluted with benzene (15 mL), washed, dried, and evaporated. The residue was chromatographed on silica gel with methylene chloride and then benzene–ethyl acetate (9:1) as eluent to give 355 mg (74%) of **4d** as colorless crystals, mp 123–125 °C. The IR and NMR spectra were identical with those of **4d** obtained by the reaction of **1c** with **2b**.

2-Benzylamino-6-chloro-4-phenylquinoline[3] (11). A stirred solution of 5-chloro-2-(1-ethoxyethylideneamino)benzophenone (**1c**; 500 mg, 1.66 mmol), benzylamine (267 mg, 2.49 mmol), and *p*-toluenesulfonic acid monohydrate (5 mg) in dry xylene (4 mL) was heated

at reflux for 2.25 h. The cooled reaction mixture was diluted with benzene (5 mL), washed, dried, and evaporated. The residue was chromatographed on silica gel with *n*-hexane–benzene (1:4) and then with benzene as eluent to afford 271 mg (47%) of **11**, which was recrystallized from benzene–*n*-hexane to give colorless needles: mp 127–128.5 °C (lit.[3] mp 124–125 °C); NMR ($CDCl_3$) δ 4.71 (d, J = 5.6 Hz, 2, CH_2), 4.92–5.20 (broad, 1, NH), 6.36 (s, 1, H-3), 7.08–7.84 (m, 13, aromatic H); mass spectrum, *m/e* (relative intensity) 346 (M^+, 23), 345 (23), 344 (M^+, 69), 343 (21), 239 (31), 106 (100), 91 (35), 28 (49).

Anal. Calcd for $C_{22}H_{17}ClN_2$: C, 76.62; H, 4.97; N, 8.13. Found: C, 76.51; H, 4.98; N, 7.95.

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Registry No.—**1a**, 67873-09-0; **1b**, 67873-10-3; **1c**, 54567-69-0; **2a**, 22483-09-6; **2b**, 645-36-3; **3a**, 67873-12-5; **3b**, 67873-13-6; **3c**, 67873-14-7; **3d**, 67873-11-4; **4a**, 67873-18-1; **4b**, 67873-15-8; **4c**, 67873-16-9; **4d**, 67873-17-0; **5a**, 2835-77-0; **5b**, 719-59-5; **5c**, 2958-36-3; **6c**, 67873-19-2; **6d**, 67873-20-5; **11**, 51478-50-3; benzylamine, 100-46-9.

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(9) It was confirmed that **3c** was not transformed into the corresponding 4-(2-propoxy) derivative in the UV sample solution by the measurement of the NMR spectrum of the recovered material.
(10) When pure **6** was applied to TLC (silica gel), two spots were observed: one for **6** and the other at the R_f value of the corresponding **3**.

Reactions of Ketene Acetals, Ketene Thioacetals, and Ketene Aminals with Ethyl Benzoylazocarboxylate

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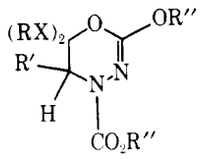
Ethyl benzoylazocarboxylate reacts regiospecifically at room temperature with ketene acetals to give 2-phenyl-4-carboethoxy-6,6-dialkoxy-5,6-dihydrooxadiazines together with varying amounts of 1,1-dialkoxy-2-(*N*-carboethoxy-*N'*-benzoylhydrazinyl)ethylenes. Reaction of ketene thioacetals with ethyl benzoylazocarboxylate gives only the hydrazinylketene dialkyl thioacetals. 1,1-Di(*N*-morpholinyl)ethylene reduces ethyl benzoylazocarboxylate to the dianion and a paramagnetic species, believed to be the cation radical of the aminal.

Diethyl and dimethyl azodicarboxylate esters have been shown to react with ketene acetals, ketene thioacetals, and ketene aminals to give 5,6-dihydrooxadiazines (**1**) and/or hydrazinylketene acetals, hydrazinylketene thioacetals, or hydrazinylketene aminals (**2**).[1] It was shown that in the case



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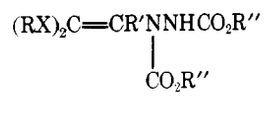
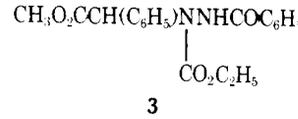


2

of the reactions of phenylketene dimethyl acetal with dimethyl and diethyl azodicarboxylate that the 5,6-dihydrooxadiazine **1** (X = O, R = CH_3, R' = C_6H_5, R'' = CH_3 or C_2H_5) is formed initially but undergoes ring opening and irreversible proton transfer to give the corresponding hydrazinylketene acetal **2**. No 1,2-diazetidines were detected in these reactions. This was surprising, because 1,2-diazetidines have been reported as products in the reactions of azocarboxylate esters with vinyl ethers,[2,4,5,15] vinyl thioethers,[2,6,7] enamines,[2,3,13] vinyl acetates,[2] perfluoroethylenes,[8–10] tetramethoxyethylene,[11] and tetramethoxyallene.[12] The report that 1,2-diazetidines are formed with indene[14] is incorrect.[15,16]

Reaction of ethyl benzoylazocarboxylate with phenylketene dimethyl acetal in benzene at room temperature, followed by chromatography of the reaction mixture on alumina, gave two solids, A and B, mp 88–90 and 116.5–117.5 °C, respectively. Elemental analyses indicated that A was a 1:1 adduct and that B was a hydrolysis product of a 1:1 adduct. Compound A on standing in air or on heating with 5% hydrochloric acid is hydrolyzed to B. Compound B was identified as *N*-(carbomethoxybenzyl)-*N*-carboethoxy-*N'*-benzoylhydrazine (**3**).



3

It was synthesized by reaction of methyl 2-chlorophenylacetate with benzoylhydrazine, followed by acylation of the product with ethyl chloroformate. The samples were shown to be identical (IR, NMR, mixed melting point).

Compounds **4–6** could be reasonably expected to give **3** on hydrolysis and were considered as candidates for compound A. However structure **4** was eliminated by the absence of N–H peaks in the IR and NMR. The NMR spectrum of A contained peaks at 1.30 (t, 3 H), 3.35 (s, 6 H), 4.23 (q, 2 H), 5.72 (s, 1 H), and 7.3–8.1 ppm (m, 10 H). The ultraviolet spectrum of A contained a maximum at 278 nm (ϵ 1.47 × 10^4).

Firl and Sommer studied the reaction of dibenzoyldiimide with styrene, vinyl thioethers, vinyl ethers, and enamines[7] and concluded that the products had the 5,6-dihydrooxadiazine structure, analogous to **6**. Their structural assignments were

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