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Studies on 4(1*H*)-Quinazolinones. I. A Convenient Synthesis and Some Reactions of 1-Phenyl-2-substituted-4(1*H*)-quinazolinones

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1-Phenyl-4(1*H*)-quinazolinones having various substituents at C-2 were synthesized and some of their reactions were examined. 1-Phenyl-2-substituted-4(1*H*))quinazolinones (**3**) were synthesized in good yield by the reaction of 2-phenylaminobenzamide (**1**) with excess acid chloride under mild reaction conditions. The 2-chloroalkyl derivatives (**3b—d**) react with nucleophiles in a characteristic manner depending on the length of the alkyl chain. Treatment of the 2-chloromethyl derivative (**3b**) with nucleophiles gave 2-(substituted-methyl)-4(1*H*)-quinazolinones (**4**). Reaction of 2-chloroethyl derivative (**3c**) with morpholine or alcohols gave 2-(β-substituted-ethyl) derivatives (**5—7**) through the intermediate (**8**), which was identified by isolation. Allowing a chloroform solution of the 2-(γ-chloropropyl) derivative (**3d**) to stand afforded the 4-oxoquinazolinium salt (**9a**) quantitatively.

Keywords——4(1*H*)-quinazolinone; acid-catalyzed cyclization; substitution reaction; elimination-addition mechanism; 4-oxoquinazolinium compound

As a part of our work on quinazolinone derivatives as potentially useful pharmacological agents, we have been interested in 1-phenyl-4(1*H*)-quinazolinones having various substituents at C-2. In this paper we report a convenient method for the synthesis of 1-phenyl-2-substituted-4(1*H*)-quinazolinones (**3**) and some reactions of 2-chloroalkyl-1-phenyl-4(1*H*)-quinazolinones (**3b—d**).

Several methods for the synthesis of 1-phenyl-4(1*H*)-quinazolinones have been reported: the thermal ring closure of 2-(N-acyl-N-phenylamino)benzamide,[2] the condensation of 2-phenylaminobenzamide with acid anhydrides[2] or acid orthoesters,[3] and the ring contraction of 1-phenyl-4,1-benzoxazepine-2,5(1*H*,3*H*)-dione with ammonia.[4] These methods, however, have drawbacks such as unsatisfactory yields, severe reaction conditions, and limitation of the substituents that can be placed at C-2 of 1-phenyl-4(1*H*)-quinazolinones.

In the course of our investigation of 4(3*H*)-quinazolinones, we found that the ring closure of 2-acetamidobenzanilide to 2-methyl-3-phenyl-4(3*H*)-quinazolinone is accelerated in the presence of hydrogen chloride.[5] By analogy with this reaction, we have found that 2-phenylaminobenzamide (**1**) readily reacts with acetyl chloride (2.5—3.0 molar eq.) in acetic acid without any base to give 2-methyl-1-phenyl-4(1*H*)-quinazolinone (**3a**) in good yield. No attempt was made to isolate the intermediate of this reaction. However, on TLC analysis of the reaction mixture, one intermediate which changed rapidly to **3a** could be detected. It seems likely that the intermediate is 2-(N-acetyl-N-phenylamino)benzamide. The reaction of **1** with acid chlorides is widely applicable for the synthesis of 1-phenyl-4(1*H*)-quinazolinones possessing various substituents at C-2. 1-Phenyl-4(1*H*)-quinazolinones (**3**) were synthesized in good yields by the reaction of **1** with the corresponding acid chlorides in chloroform at room or reflux

1) Location: *16-89 Kashima-3-chome, Yodogawa-ku, Osaka 532, Japan.*
2) H.M. Blatter, H. Lukaszewski, and G. deStevens, *J. Org. Chem.*, **30**, 1020 (1965).
3) A. Chatterjee and R. Raychaudhuri, *J. Org. Chem.*, **33**, 2546 (1968); J.P. Osselaere, *Arzneim.-Forsch.*, **25**, 712 (1975); K. Noda, A. Nakagawa, A. Yamazaki, K. Noguchi, T. Yatani, and H. Ide, Japan Patent Kokai, 77-78888 (1977).
4) J. Iacobelli, M. Uskokovic, and W. Wenner, *J. Heterocycl. Chem.*, **2**, 323 (1965).
5) J. Tani, Y. Yamada, T. Oine, T. Ochiai, R. Ishida, and I. Inoue, *J. Med. Chem.*, **22**, 95 (1979).

temperature, as summarized in Table I. It is remarkable that the reactive compounds, such as **3c** and **3d**, could be isolated in fairly good yields. The isolation of **3c** and **3d** may be a result of the low solubility of the hydrochloride of these compounds in the reaction medium.

The 2-chloroalkyl derivatives (**3b—d**) readily react with a variety of nucleophiles. Treatment of **3b** with sodium methoxide in methanol gave 2-methoxymethyl-1-phenyl-4(1*H*)quinazolinone (**4a**) in 75% yield. Reaction of **3b** with sodium acetate provided the 2-acetoxymethyl derivative **4b**. Similarly, secondary amines (diethylamine, morpholine, and piperidine) react with **3b** to give the 2-aminomethyl derivatives (**4c—e**, respectively).

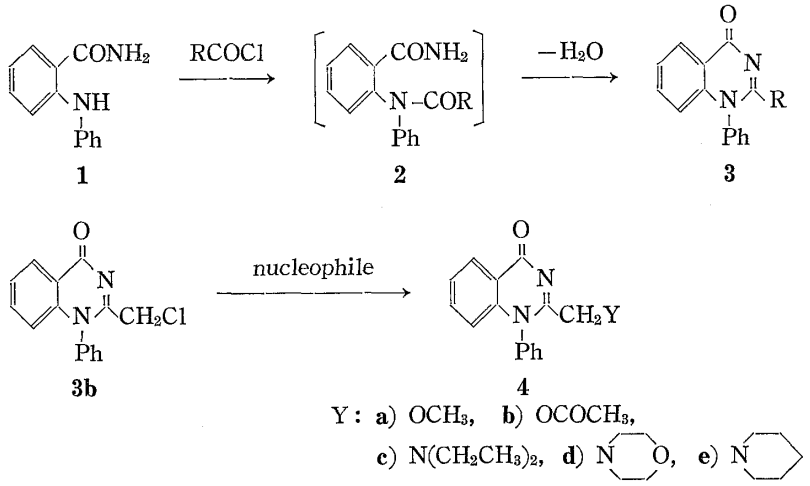
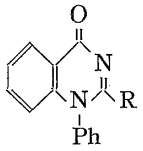


Chart 1

TABLE I. 1-Phenyl-2-substituted-4(1*H*)-quinazolinones (3)



Compd.	R	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd (Found) C	H	N	Cl
3a	CH_3	79	226—228[a]					
3b	CH_2Cl	88	212—213	$C_{15}H_{11}ClN_2O$	66.51 (66.16	4.09 4.40	10.35 10.25	13.10 12.88)
3c	CH_2CH_2Cl	91	205—210[b]	$C_{16}H_{13}ClN_2O$	67.48 (67.24	4.60 4.80	9.84 9.89	12.45 12.40
3d	$CH_2CH_2CH_2Cl$	78	140[c]	$C_{17}H_{15}ClN_2O$	68.34 (67.94	5.06 5.11	9.37 9.38	11.86 11.86)
3e		61	241—242	$C_{17}H_{14}N_2O$	77.84 (77.69	5.37 5.48	10.68 10.41)	
3f	$CO_2C_2H_5$	84	193—195	$C_{17}H_{14}N_2O_3$	69.38 (69.19	4.79 4.72	9.52 9.64)	
3g	t-C_4H_9	66	221—223	$C_{18}H_{18}N_2O$	77.67 (77.42	6.52 6.44	10.07 10.01)	
3h		92	233—235	$C_{20}H_{20}N_2O$	78.92 (78.98	6.62 6.75	9.20 9.15)	

a) Lit. mp 231—233°; H.M. Blatter, H. Lukaszewski, and G. deStevens, *J. Org. Chem.*, **30**, 1020 (1965).
b) Gradual decomposition.
c) Change of the crystal form began at this temperature owing to the formation of compound **9a**.

Treatment of the 2-(β-chloroethyl)-derivative **3c** with morpholine in THF gave 2-(β-morpholinoethyl)-1-phenyl-4(1*H*)-quinazolinone (**5**). We unexpectedly found that allowing a methanolic solution of **3c** to stand at room temperature afforded 2-(β-methoxyethyl)-1-phenyl-4(1*H*)-quinazolinone hydrochloride (**6**·HCl) in good yield. Neutralization of the hydrochloride (**6**·HCl) with aqueous $NaHCO_3$ gave 2-(β-methoxyethyl)-1-phenyl-4(1*H*)-quinazolinone (**6**). The structure of **6** was confirmed by its spectral data and elemental analysis. Similarly, 2-(β-ethoxyethyl)-1-phenyl-4(1*H*)-quinazolinone (**7**) was obtained from an ethanolic solution of **3c**. Compounds **6** and **7** were converted into each other in methanol or ethanol containing a catalytic amount of hydrogen chloride.

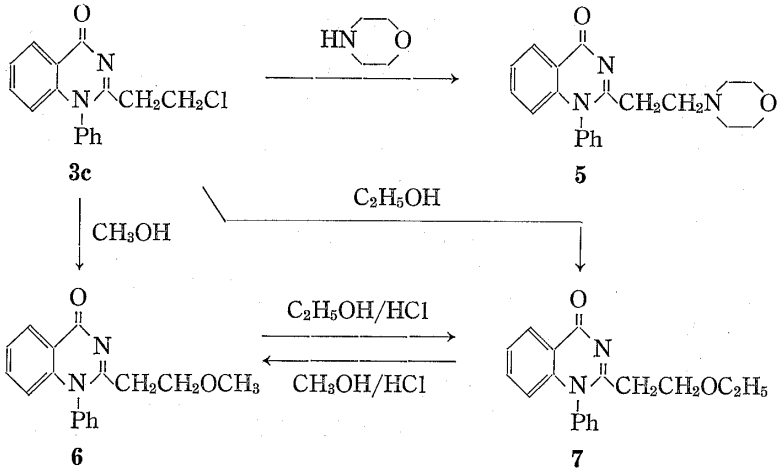


Chart 2

These unexpected results with **3c**, **6** and **7** suggest that the reactions may not be simple nucleophilic substitutions. Treatment of **3c** with monodeutero methanol (MeOD) at room temperature gave the monodeutero compound (**6**-d_1) containing deuterium at the β-position relative to the methoxy group of **6**. The structure of **6**-d_1 was established on the basis of its NMR and mass spectra. The NMR spectrum of **6**-d_1 showed six protons of the CH_3OCH_2CHD group at δ 2.69 (t, 1H, J=7 Hz), 3.29 (s, 3H), and 3.84 (d, 2H, J=7 Hz). The mass spectrum showed a molecular ion peak at *m/e* 281. Thus, 1-phenyl-2-vinyl-4(1*H*)-quinazolinone (**8**) may be an intermediate in the reaction. In order to confirm this, we attempted to isolate the intermediate. Treatment of **3c** with an excess of triethylamine in THF gave **8** in 92% yield. Compound **8** was moderately stable in neutral methanol but reacted smoothly with methanol in the presence of a catalytic amount of hydrogen chloride to afford **6** quantitatively. Morpholine also reacted with **8** in THF to give **5**. It became clear that the elimination-addition reaction proceeded *via* the same intermediate **8** in the reactions of **3c** with alcohols and amines, and also in the interconversion between **6** and **7**.

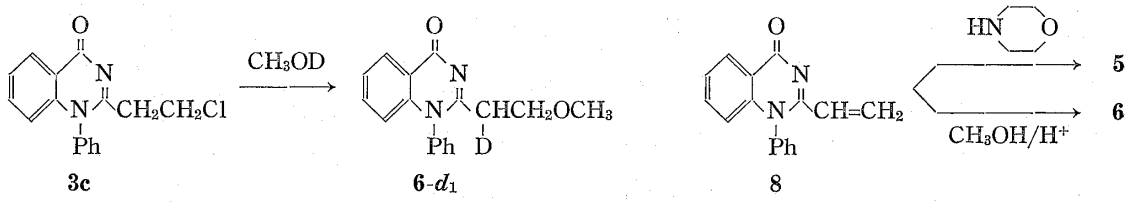


Chart 3

Simply allowing a chloroform solution of the 2-(γ-chloropropyl) derivative **3d** to stand at room temperature produced colorless needles quantitatively. The product was determined to be the 4-oxoquinazolinium salt **9a** on the basis of elemental analysis, spectral data, and its

chemical reactions. The IR spectrum showed typical bands of 4-oxoquinazolinium salts at 1710, 1630, and 1560 cm^{-1}.[6] The NMR spectrum exhibited the signals of a trimethylene group at δ 2.1—2.5 (m, 2H), 3.21 (t, 2H, J=7 Hz), and 4.40 (t, 2H, J=7 Hz) and aromatic hydrogens at δ 6.85—7.05 (m, 1H), 7.65—8.05 (m, 6H), and 8.38—8.50 (m, 1H). The signals of the aromatic hydrogens were shifted downfield compared with those of compounds **3** by the presence of a positive charge on the quinazolinone ring. Reduction of **9a** with sodium borohydride gave 4-phenyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]-quinazolin-9-one (**10**) in 75% yield.

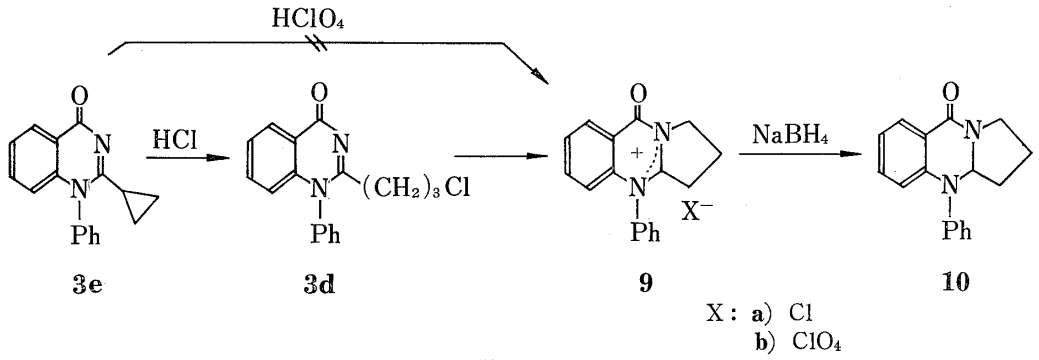


Chart 4

Treatment of **3e** with hydrogen chloride saturated in methylene chloride also gave **9a** in good yield. However, conversion of **3e** to **9b** did not proceed in the presence of hydrogen perchloride instead of hydrogen chloride. Based on these results, it can be considered that the rearrangement of **3e** to **9a** proceeds *via* **3d** as an intermediate. The behavior of **3e** in the reactions with hydrogen chloride and hydrogen perchloride is consistent with the results on the rearrangement of cyclopropylimines to 2-pyrrolines reported by Stevens and co-workers.[7]

Thus, we have developed a convenient and useful method for the synthesis of 1-phenyl-4(1*H*)-quinazolinone derivatives with various substituents at C-2. We have also shown that the 2-chloroalkyl derivatives (**3c—e**) react with nucleophiles in a characteristic manner, depending on the length of the alkyl chains.

Experimental

All melting points were determined on a Yamato MP-21 apparatus and are uncorrected. IR spectra were determined using a Shimadzu IR-27G spectrometer. NMR spectra were recorded on a Hitachi Perkin-Elmer R-20A instrument using TMS as an internal standard. The mass spectra were measured with a Hitachi M-60 mass spectrometer.

General Procedure for the Preparation of 1-Phenyl-2-substituted-4(1*H*)-quinazolinones (3). Typical Procedure——(a) 2-Methyl-1-phenyl-4(1*H*)-quinazolinone ((**3a**): A stirred solution of 2-phenylaminobenzamide (**1**, 2.5 g, 0.0118 mol) in acetic acid (25 ml) was treated with 2.5 g (0.032 mol) of acetyl chloride at room temperature. The mixture was stirred for 3 hr and the solvent was evaporated off *in vacuo*. The residue was dissolved in H_2O and neutralized with aqueous K_2CO_3 to give a crude product (2.5 g, 89.8%). Recrystallization from EtOH gave a pure sample as colorless needles (2.2 g, 79.1%): mp 226—228°; NMR ($CDCl_3$) δ: 2.27 (s, 3H), 6.5—6.7 (m, 1H), 7.2—7.8 (m, 7H), 8.18—8.3 (m, 1H). Analytical data are listed in Table I.

(b) 2-Cyclopropyl-1-phenyl-4(1*H*)-quinazolinone (**3h**): A stirred solution of **1** (4.6 g, 0.0217 mol) in chloroform (30 ml) was treated with cyclopropane carbonylchloride (6.8 g, 0.065 mol) under ice-cooling. The mixture was stirred at room temperature for 28 hr. The precipitates that had formed were collected by filtration and neutralized with aqueous $NaHCO_3$ to give a crude product (3.7 g, mp 225—230°). Recrystallization from 2-PrOH gave a pure sample as colorless pillars (3.47 g, 61%): mp 239—241°; NMR ($CDCl_3$)

6) K. Okumura, T. Oine, Y. Yamada, G. Hayashi, M. Nakama, and T. Nose, *J. Med. Chem.*, **11**, 788 (1968).
7) R.V. Stevens, *Accounts Chem. Res.*, **10**, 193 (1977); R.V. Stevens, M.C. Ellis, and M.P. Wentland, *J. Am. Chem. Soc.*, **90**, 5576 (1968).

δ: 0.75—1.70 (m, 5H), 6.5—6.75 (m, 1H), 7.3—7.9 (m, 7H), 8.25—8.45 (m, 1H). Analytical data are listed in Table I.

2-Methoxymethyl-1-phenyl-4(1*H*)-quinazolinone (4a)——A stirred suspension of **3b** (2.7 g, 0.01 mol) in MeOH (20 ml) was treated with a solution of MeONa (0.6 g, 0.011 mol) in MeOH (10 ml) at room temperature. After stirring for 10 hr, the solvent was removed *in vacuo*. The crystalline residue was triturated with H_2O and collected by filtration. Recrystallization from 2-PrOH–diisopropyl ether (1: 4) gave pure **4a** (2.0 g, 75%) as colorless prisms: mp 172—174°; NMR ($CDCl_3$) δ: 3.31 (s, 3H), 4.18 (s, 2H), 6.65 (m, 1H), 7.2—7.8 (m, 7H), 8.35 (m, 1H). *Anal.* Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.23; H, 5.17; N, 10.40.

2-Acetoxymethyl-1-phenyl-4(1*H*)-quinazolinone (4b)——A solution of **3b** (3.5 g, 0.013 mol) in acetic acid (20 ml) was treated with potassium acetate (3.9 g, 0.04 mol). The mixture was stirred under reflux for 1.5 hr. After removal of the solvent, the residue was dissolved in $CHCl_3$. The chloroform solution was washed with H_2O, dried on $MgSO_4$, and evaporated to dryness. The crystalline residue was recrystallized from C_6H_6–diisopropyl ether (1: 1) to give **4b** as colorless needles (2.1 g, 58.5%): mp 150—153°; NMR ($CDCl_3$) δ: 2.10 (s, 3H), 4.72 (s, 2H), 6.52 (m, 1H), 7.2—7.85 (m, 7H), 8.1—8.37 (m, 1H). *Anal.* Calcd for $C_{17}H_{14}N_2O_3$: C, 69.37; H, 4.80; N, 9.52. Found: C, 69.46; H, 4.80; N, 9.56.

General Procedure for the Preparation of 2-(Aminomethyl)-1-phenyl-4(1*H*)-quinazolinones (4c—4e). Typical Procedure——(a) 2-Morpholinomethyl-1-phenyl-4(1*H*)-quinazolinone (**4d**): A mixture of **3b** (2.7 g, 0.01 mol) and morpholine (2.7 g, 0.031 mol) in THF (50 ml) was stirred at room temperature for 15 hr. Removal of the solvent *in vacuo* gave a crystalline solid. The solid was collected by filtration and washed with H_2O to give almost pure **4d** (2.8 g, 87.4%): mp 177—182. Recrystallization from 2-PrOH gave a pure sample of **4d** as colorless prisms (2.6 g, 84.5%): mp 184—186°; NMR ($CDCl_3$) δ: 2.2—2.5 (m, 4H), 3.28 (s, 2H), 3.4—3.8 (m, 4H), 6.5—6.8 (m, 1H), 7.3—7.8 (m, 7H), 8.2—8.5 (m, 1H). *Anal.* Calcd for $C_{19}H_{19}N_3O_2$: C, 71.01; H, 5.96; N, 13.08. Found: C, 70.78; H, 5.91; N, 13.08.

(b) 2-(Diethylaminomethyl)-1-phenyl-4(1*H*)-quinazolinone (**4c**): was prepared by the reaction of **3b** with diethylamine as described above and recrystallized from diisopropyl ether to give colorless needles: mp 101—103°; 50% yield; NMR ($CDCl_3$) δ: 0.75 (t, 6H, J=7 Hz), 2.41 (q, 4H, J=7 Hz), 3.40 (s, 2H), 6.5—6.75 (m, 1H), 7.35—7.85 (m, 7H), 8.27—8.55 (m, 1H). *Anal.* Calcd for $C_{19}H_{21}N_3O$: C, 74.24; H, 6.89; N, 13.67. Found: C, 74.02; H, 6.75; N, 13.49.

(c) 1-Phenyl-2-piperidinomethyl-4(1*H*)-quinazolinone (**4e**): was prepared as above using piperidine as a secondary amine. mp 152—153°; 94% yield; NMR ($CDCl_3$) δ: 1.40 (br.s, 6H), 2.25 (br.s, 4H), 3.21 (s, 2H), 6.5—6.8 (m, 1H), 7.2—7.8 (m, 7H), 8.2—8.5 (m, 1H). *Anal.* Calcd for $C_{20}H_{21}N_3O$: C, 75.21; H, 6.63; N, 13.16. Found: C, 75.19; H, 6.73; N, 12.93.

2-(β-Morpholinoethyl)-1-phenyl-4(1*H*)-quinazolinone (5)——Method A: A mixture of **3c** (2.0 g, 0.007 mol) and morpholine (1.3 g, 0.015 mol) in THF (30 ml) was stirred at room temperature for 2.5 hr. The solvent was evaporated off *in vacuo* and the residue was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with H_2O, dried ($MgSO_4$), and concentrated to give **5** (2.0 g, 83.7%); 156—160°. Recrystallization from 2-PrOH–diisopropyl ether gave pure **5** (1.61 g, 68.6%): mp 162—164°; NMR ($CDCl_3$) δ: 2.2—2.5 (m, 4H), 2.5—3.2 (m, 4H), 3.4—3.8 (m, 4H), 6.48—6.8 (m, 1H), 7.2—7.9 (m, 7H), 8.2—8.5 (m, 1H). *Anal.* Calcd for $C_{20}H_{21}N_3O_2 \cdot 1/2H_2O$: C, 69.74; H, 6.44; N, 12.20. Found: C, 69.63; H, 6.57; N, 12.07.

Method B: Finely powdered **8** (300 mg, 1.2 mmol) was added in one portion to a stirred solution of morpholine (200 mg, 2.3 mmol) in THF (3 ml). Stirring was continued at room temperature for 20 min; during this period crystals formed. The crystals were collected by filtration to give 390 mg (96.2%) of **5**: mp 161—163°. This product was identical with **5** obtained by method A.

2-(β-Methoxyethyl)-1-phenyl-4(1*H*)-quinazolinone (6)——Method A: A solution of **3c** (4.0 g, 0.014 mol) in MeOH (50 ml) was allowed to stand for 1 hr at room temperature. Removal of the solvent under reduced pressure gave 4.25 g (95.5%) of crystalline hydrochloride (**6**·HCl): mp 210—225° (dec.). The hydrochloride (4 g) was neutralized with aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The CH_2Cl_2 layer was dried ($MgSO_4$) and concentrated to give a colorless crystalline product (3.4 g, 85%). Recrystallization from MeOH–diisopropyl ether (1: 1) gave pure **6** (2.8 g, 70%) as colorless needles: mp 161—163° (dec.); NMR ($CDCl_3$) δ: 2.67 (t, 2H, J=7 Hz), 3.37 (s, 3H), 3.84 (t, 2H, J=7 Hz), 6.48—6.75 (m, 1H), 7.2—7.8 (m, 7H), 8.2—8.5 (m, 1H). *Anal.* Calcd for $C_{17}H_{16}N_2O$: C, 72.84; H, 5.75; N, 9.99. Found: C, 72.66; H, 5.89; N, 10.10.

Method B: A solution of **7** (50 mg) in 1%HCl–MeOH (2 ml) was allowed to stand at room temperature for 2 hr. The mixture was then concentrated to dryness *in vacuo*. The residue was neutralized with aqueous $NaHCO_3$ and extracted with $CHCl_3$. The $CHCl_3$ layer was dried ($MgSO_4$) and concentrated to give a crystalline product (40 mg): mp 153—155°. Recrystallization from MeOH–diisopropyl ether gave a pure sample as colorless needles (25 mg): mp 160—163° (dec.). The compound was identical with a sample of **6** obtained by method A in terms of IR and NMR spectra.

Method C: One drop of methanolic HCl (10%) was added to a solution of **8** (100 mg) in MeOH (4 ml). The mixture was stirred at room temperature for 2 hr. After removing MeOH *in vacuo*, the residue was neutralized with aqueous $NaHCO_3$ and extracted with $CHCl_3$. The $CHCl_3$ layer was dried and concentrated to dryness to give crude **6**. Recrystallization from MeOH–diisopropyl ether (1: 2) gave colorless needles (60 mg): mp 160—163° (dec.). This product was identical with a sample of **6** obtained by method A.

2-(α-Deutero-β-methoxyethyl)-1-phenyl-4(1*H*)-quinazolinone (6-d_1)——A solution of **3c** (500 mg) in MeOD (5 ml) was stirred at room temperature for 3 hr. The solution was concentrated *in vacuo*, neutralized with aqueous, $NaHCO_3$, and extracted with CH_2Cl_2. The CH_2Cl_2 layer was dried ($MgSO_4$) and concentrated *in vacuo* to yield a crystalline product (400 mg): mp 145—147° (dec.). Recrystallization from MeOH–diisopropyl ether gave colorless needles: mp 157—159° (dec.); NMR ($CDCl_3$) δ: 2.69 (t, 1H, J=7 Hz), 3.29 (s, 3H), 3.84 (d, 2H, J=7 Hz), 6.47—6.75 (m, 1H), 7.2—7.8 (m, 7H), 8.25—8.5 (m, 1H); MS *m/e*: 281 (M^+), 266, 249, 248, 195.

2-(β-Ethoxyethyl)-1-phenyl-4(1*H*)-quinazolinone (7)——A solution of **3c** (500 mg, 1.76 mmol) in EtOH (10 ml) was allowed to stand at room temperature for 1 hr. The solvent was evaporated off to give the colorless crystalline hydrochloride (510 mg, 88%); mp 230—240° (dec.). The hydrochloride (400 mg) was neutralized with aqueous $NaHCO_3$ and dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with H_2O, dried ($MgSO_4$), and concentrated to give **7** (250 mg, 49%, mp 108—110°), and recrystallization from C_6H_6–*n*-hexane afforded 200 mg of pure **7** as colorless prisms; mp 108—110°; NMR ($CDCl_3$) δ: 1.23 (t, 3H, J=7 Hz), 2.70 (t, 2H, J=7 Hz), 3.45 (q, 2H, J=7 Hz), 3.90 (t, 2H, J=7 Hz), 6.48—6.8 (m, 1H), 7.2—7.9 (m, 7H), 8.20—8.50 (m, 1H). *Anal.* Calcd for $C_{18}H_{18}N_2O$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.40; H, 6.31; N, 9.76.

1-Phenyl-2-vinyl-4(1*H*)-quinazolinone (8)——A stirred suspension of **3c** (1.26 g, 4.7 mmol) in THF (30 ml) was treated with triethylamine (1.5 g, 0.015 mol) at room temperature. Stirring was continued at the same temperature for 5 hr. Triethylamine hydrochloride that had precipitated during the reaction was filtered off and the filtrate was concentrated to dryness *in vacuo*. The residual crystals were triturated with 2-PrOH and collected by filtration to give almost pure **8** (1.0 g, 92%). Recrystallization from MeOH–diisopropyl ether yielded an analytically pure sample as colorless prisms; mp 226—230° (dec.); NMR ($CDCl_3$) δ: 5.66 (d.d, 1H, J=10 Hz, J=2.5 Hz), 6.11 (d.d, 1H, J=16 Hz, J=10 Hz), 6.50—6.70 (m, 1H), 6.90 (d.d, 1H, J=16 Hz, J=2.5 Hz), 7.25—7.90 (7H, m), 8.25—8.50 (m, 1H). *Anal.* Calcd for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.28. Found: C, 76.99; H, 5.11; N, 11.54.

4-Oxoquinazolinium Compound (9a)——Method A: A solution of **3d** (6.96 g) in $CHCl_3$ (100 ml) was stirred at room temperature for 52 hr. The colorless crystals which had precipitated were collected by filtration to give almost pure **9a** (6.7 g, 96.2%). Recrystallization from 2-PrOH–diisopropyl ether (2: 1) gave an analytically pure sample as colorless prisms; mp>280°; IR ν_{max}^{Nujol} cm^{-1}: 1710, 1630, 1560. NMR (DMSO-d_6) δ: 2.1—2.5 (m, 2H), 3.21 (t, 2H, J=7 Hz), 4.40 (t, 2H, J=7 Hz), 6.85—7.05 (1H, m), 7.65—8.05 (m, 6H), 8.38—8.50 (m, 1H); *Anal.* Calcd for $C_{17}H_{15}ClN_2O$: C, 68.34; H, 5.06; N, 9.37; Cl, 11.86. Found: C, 67.94; H, 5.24; N, 9.12; Cl, 12.13.

Method B: A stirred solution of **3e** (1.5 g) in CH_2Cl_2 (50 ml) was saturated with dry hydrogen chloride under ice-cooling. The mixture was refluxed for 50 hr. After cooling, the solvent was evaporated off and the residue was triturated with diisopropyl ether to afford crude **9a** (1.8 g, 88%). Recrystallization from 2-PrOH–diisopropyl ether gave colorless needles (1.7 g); mp>280°. The IR spectrum of this product was identical with that of a sample obtained by method A.

4-Phenyl-1,2,3,3a,4,9-hexahydropyrrolo[2,1-*b*]quinazolin-9-one (10)——$NaBH_4$ (0.26 g, 6.7 mmol) was added to a stirred solution of **9a** (2.0 g, 6.7 mmol) in EtOH (50 ml) in small portions under ice-cooling. The mixture was stirred at room temperature for 1 hr. The solvent was removed *in vacuo* and the residue was dissolved in $CHCl_3$. The $CHCl_3$ solution was washed with H_2O, dried ($MgSO_4$), and concentrated to dryness. The residual crystals (1.4 g) were recrystallized from 2-PrOH to give **10** (1.0 g, 56%) as pale yellow prisms: mp 188—190°; NMR ($CDCl_3$) δ: 1.70—2.25 (m, 4H), 3.63—3.97 (m, 2H), 5.21—5.60 (m, 1H), 6.25 (d.d, 1H, J=8 Hz, J=2 Hz), 6.7—7.7 (m, 7H), 8.02 (d.d, 1H, J=8 Hz, J=2 Hz); MS *m/e*: 264 (M^+), 236, 208, 195; *Anal.* Calcd for $C_{17}H_{16}N_2O$: C, 77.25; H, 6.10; N, 10.60. Found: C, 77.24; H, 6.28; N, 10.55.

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