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Fused Pyrimidines. IV.¹⁾ The Reaction of 4-Alkylthio-2-chloroquinazolines with Alkylamines in Dimethylformamide²⁾

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The reaction of 4-alkylthio-2-chloroquinazolines with alkylamines in dimethylformamide afforded 2,4-bis(alkylthio)-, 2-alkylamino-4-alkylthio-, 4-alkylamino-2-chloro-, 4-alkylamino-2-alkylthio-, and 2,4-bis(alkylamino)quinazolines. The relative easiness of displacement of the chlorine and/or the alkylthio group in 4-alkylthio-2-chloroquinazolines depended on the bulkiness rather than the basicity of the alkylamine. A possible reaction mechanism is discussed.

Keywords—amination; isomer; substitution reaction; mechanism; 2-alkylamino-4-alkylthioquinazoline; 4-alkylamino-2-alkylthioquinazoline; 4-alkylthio-2-chloroquinazoline

In the course of research on quinazoline derivatives showing herbicidal activity, the displacement reaction of 4-alkylthio-2-chloroquinazolines (**1**) with alkylamines has been studied.

Curd *et al.* reported³⁾ that the reaction of 2-diethylaminoethylamine with 2-chloro-4-(4-chlorophenylthio)quinazoline gave 2,4-bis(4-chlorophenylthio)-, and 4-(2-diethylaminoethylamino)-2-(4-chlorophenylthio)quinazoline. On the other hand, they reported⁴⁾ that the reaction of 2-chloro-4-methylthioquinazoline with 4-chloroaniline gave 2-(4-chloroanilino)-4-methylthioquinazoline as a major product.

This paper deals with the migration of the chlorine *versus* the alkylthio group in derivatives of **1**. A possible reaction mechanism is discussed.

(i): The reaction of 2-chloro-4-methylthioquinazoline (**1a**) with methylamine in dimethylformamide at 20—25°C for 16 h gave **2a** as colorless needles (mp 78°C), **3a** as yellow needles (mp 131—132°C) and **4a** as colorless needles (mp 213°C).

Compound **2a** was confirmed to be 2,4-bis(methylthio)quinazoline⁵⁾ on the basis of its infrared (IR) and proton magnetic resonance (PMR) spectra. Similarly, **4a** was identified as 2-chloro-4-methylaminoquinazoline.⁶⁾

The elemental analysis of **3a** was in good agreement with the calculated values for C₁₀H₁₁N₃S. The IR spectrum of **3a** revealed an NH band at 3200 cm⁻¹. The PMR spectrum of **3a** indicated the presence of a methylthio group (δ : 2.48, 3H, s), an *N*-methyl group (δ : 2.99, 3H, s), an imino group (δ : 5.32, 1H, br s), and four aromatic protons (δ : 6.82—7.82, 4H, m). On the basis of these data, the structure of **3a** was established to be 2-methylamino-4-methylthioquinazoline.

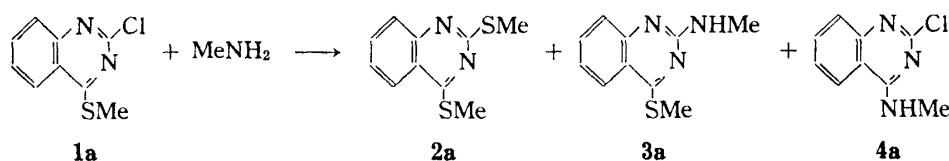


Chart 1

(ii): On the other hand, when the same reaction was carried out at 80—85°C for 20 min, compound **4a** was obtained exclusively. Then, the reaction of **1a** with ethylamine in dimethylformamide at 80—85°C for 20 min gave **2a**, **3b** as yellow needles (mp 79—80°C), **4b** as colorless

needles (mp 171°C), **5b** as colorless needles (149—150°C) and a trace amount of **6b** as colorless needles (mp 123—126°C).

Compound **4b** was confirmed to be 2-chloro-4-ethylaminoquinazoline by comparison of its spectral data with those of an authentic sample.⁶⁾

The elemental analysis of **6b** was in good agreement with the calculated values for $C_{12}H_{16}N_4$. The IR spectrum of compound **6b** showed an NH band at 3250 cm^{-1} , and the presence of two ethylamino groups was apparent in the PMR spectrum. On the basis of these data, the structure of **6b** was assigned as 2,4-bis(ethylamino)quinazoline.⁶⁾

Compounds **3b** and **5b** had the same molecular formula, $C_{11}H_{13}N_3S$, and their PMR spectra indicated the presence of an ethylamino group (δ : 1.12, 3.30—3.80 for **3b** and 1.22, 3.40—3.87 for **5b**) and a methylthio group (δ : 2.56 for **3b** and 2.57 for **5b**). However, the IR spectra and melting points of these compounds were different from each other. These results show that the structure of **3b** is isomeric with that of **5b**. In order to differentiate clearly the structures of **3b** and **5b**, these compounds were

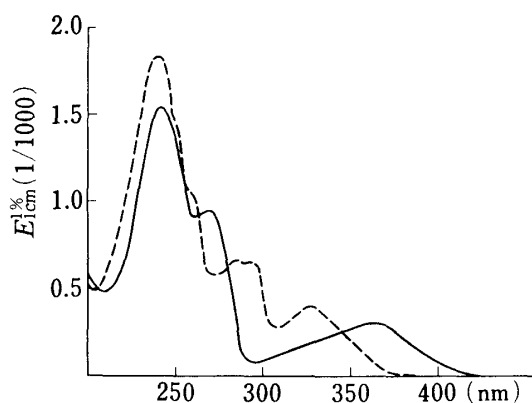
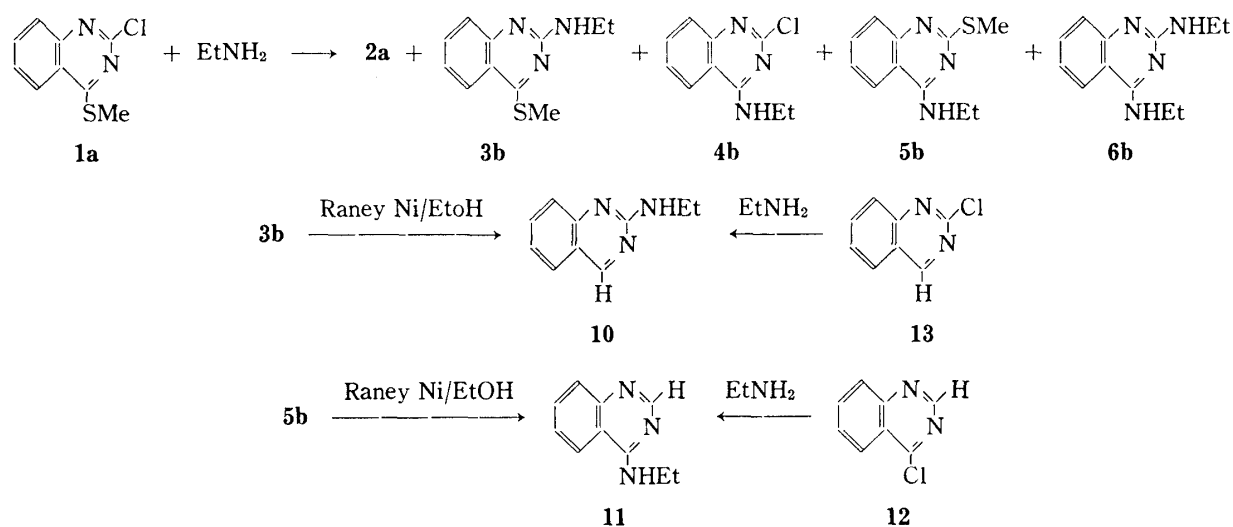
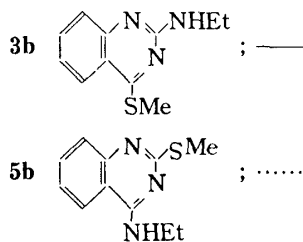


Fig. 1. UV Spectra of **3b** and **5b**



desulfurized with Raney nickel. Compound **3b** afforded **10** as colorless needles (mp 96—97°C), while **5b** gave **11** as colorless needles (mp 149—150°C). The elemental analyses of both **10** and **11** were in good agreement with the calculated values for $C_{10}H_{11}N_3$. Compound **11** was confirmed to be 4-ethylaminoquinazoline⁶⁾ by unequivocal synthesis, *via* the reaction of 4-chloroquinazoline⁷⁾ (**12**) with ethylamine.

Consequently, the structure of **5b** was confirmed to be 4-ethylamino-2-methylthioquinazoline, and compounds **10** and **3b** were assigned as 2-ethylaminoquinazoline and 2-ethylamino-4-methylthioquinazoline, isomers of **11** and **5b**, respectively. The structure of **10** was also confirmed by synthesis from 2-chloroquinazoline⁸⁾ (**13**) and ethylamine.

Compound **3b** showed a characteristic ultraviolet (UV) absorption maximum at 362 nm, while **5b** had an absorption at 328 nm. By

comparing their UV spectra in the region of about 300–400 nm, 2-alkylamino-4-alkylthioquinazoline (3) and 4-alkylamino-2-alkylthioquinazolines (5) can be easily and unequivocally differentiated.

To investigate the scope and limitations of this type of reaction, the study was extended to include the use of other alkylamines (*e.g.*, butyl-, *sec*-butyl-, *tert*-butyl-, dimethyl-, dipropyl-, and diisopropylamine). The results are summarized in Table I and II.

TABLE I. The Reaction of 4-Alkylthio-2-chloroquinazoline with Alkylamine

Starting materials R ¹	R ² R ³ NH	Reaction time (h)	Reaction conditions Temp (°C)	Products and yields (%)					
Me	MeNH ₂	16	20–25	2a (5)	3a (21)	4a (65)	—	—	
Me	MeNH ₂	1/3	80–85	—	—	4a (92)	—	—	
Me	EtNH ₂	1/3	80–85	2a (2)	3b (38)	4b (54)	5b (3)	6b (1)	
Me	BuNH ₂	1/3	80–85	2a (6)	3c (34)	4c (33)	5c (9)	6c (3)	
Me	<i>tert</i> -BuNH ₂	3	Reflux	—	3d (25)	4d (1)	—	—	
<i>tert</i> -Bu	<i>sec</i> -BuNH ₂	1/3	80–85	—	3e (19)	—	—	—	
Me	Me ₂ NH	1/3	80–85	2a (5)	3f (26)	4f (35)	5f (13)	6f (1)	
Me	Pr ₂ NH	3	Reflux	—	3g (92)	—	—	—	
Me	iso-Pr ₂ NH	3	Reflux	—	—	—	—	—	

TABLE II. UV Absorption Maxima of 3 and 5 in EtOH

3	nm ($\epsilon_{\max}$)	5	nm ($\epsilon_{\max}$)
3a	365(2135)	—	
3b	362(6570)	5b	328(8320)
3c	365(5340)	5c	330(6870)
3d	366(4997)	—	
3e	366(5647)	—	
3f	370(4420)	5f	337(7400)
3g	377(4639)	—	

An alkylamine which is not bulky, such as methyl-, ethyl-, butyl- or dimethylamine, reacts with the chlorine at the 2-position and/or the methylthio group at the 4-position in the quinazoline ring to afford 2- and/or 4-alkylaminoquinazolines.

A bulky amine, such as *sec*-butyl-, *tert*-butyl- or dipropylamine, reacts with the chlorine at the 2-position to give 2-alkylamino-4-alkylthioquinazolines as a major product. Even bulkier amines, such as diisopropylamine, do not react with 1.

The results of these studies show that the reaction of 1 with alkylamines is substantially affected by the bulkiness rather than the basicity of the alkylamines.

Some reactions were attempted in order to clarify the mechanism of formation of compounds 2–6. The reaction of 2a with butylamine in dimethylformamide at 80–85°C for 20 min gave mainly 5c instead of 3c. The reaction of 3c with butylamine gave chiefly 6c, but 4c and 5c did not react with butylamine.

On the basis of these results, a possible mechanism for the reaction of 1 with alkylamines is shown in Chart 3.

The herbicidal activities of the quinazoline derivatives are now under investigation and will be reported shortly.

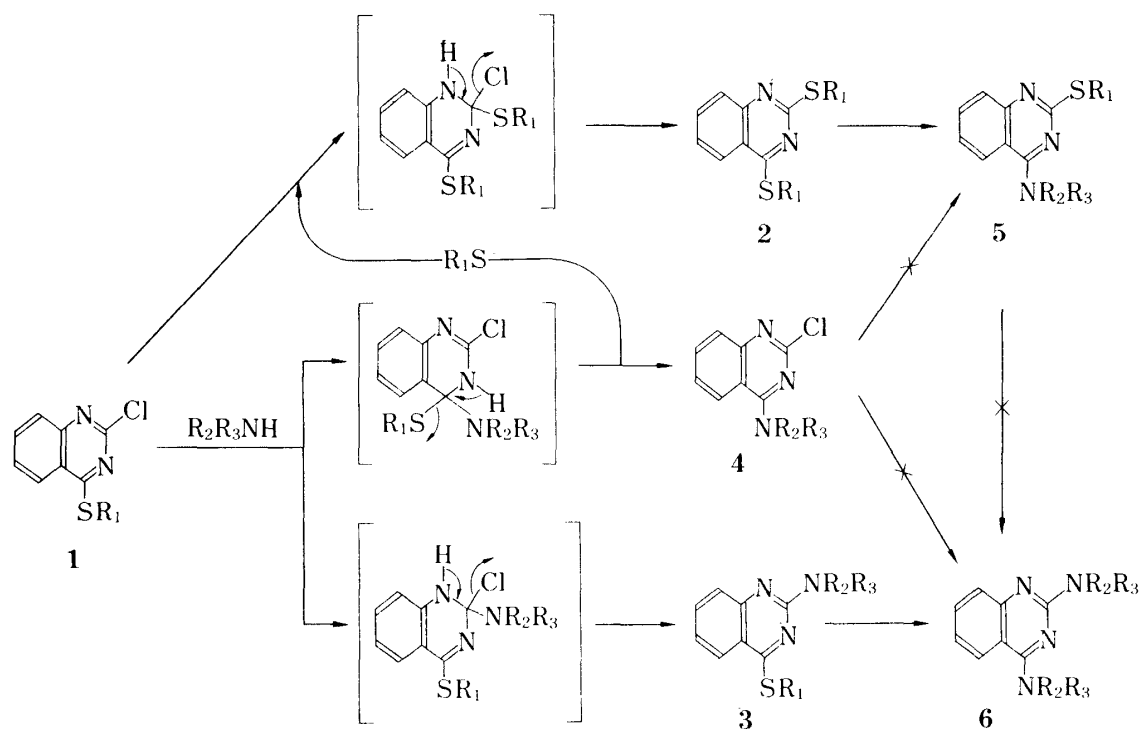


Chart 3

Experimental

Melting points were determined with a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were recorded by using a Hitachi EPI-3 spectrophotometer, and PMR spectra were taken with a Hitachi R-24 spectrometer; chemical shifts are expressed in ppm (δ) from tetramethylsilane as an internal standard. The following abbreviations are used: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad. UV spectra were recorded with a Shimadzu UV-210 spectrophotometer. Silica gel (Kiesel gel, Merck) was used for column chromatography.

2-Chloro-4-methylthioquinazoline (1a)—A mixture of 2,4-dichloroquinazoline⁹⁾ (2.0 g, 10.0 mmol) and methylmercaptan sodium salt (*ca.* 15% in water, 4.7 g, 10.0 mmol) in acetone (30 ml) was stirred at 10–15°C for 1 h. The resulting mixture was poured into ice-water, and extracted with dichloromethane (50 ml $\times$ 3). The extract was dried over magnesium sulfate, and concentrated. The residue was recrystallized from acetonitrile to give 1.7 g of **1a** as colorless needles, mp 119–120°C, (lit.,⁴⁾ mp 122°C).

2-Chloro-4-*tert*-butylthioquinazoline (1e)—A mixture of 2,4-dichloroquinazoline (2.0 g, 10.0 mmol) and *tert*-butylmercaptan potassium salt (1.3 g, 10.2 mmol) in acetone (30 ml) was worked up as described for **1a** to give 1.6 g of **1e** as pale yellow needles, mp 114–115°C. *Anal.* Calcd for $C_{12}H_{14}ClN_3$: C, 61.14; H, 5.99; N, 17.83. Found: C, 61.01; H, 5.49; N, 17.56.

Reaction of 1a with Methylamine—A mixture of **1a** (4.2 g, 20.0 mmol), methylamine (40% in water, 1.7 g, 21.9 mmol) and triethylamine (2.1 g, 21.0 mmol) in dimethylformamide (30 ml) was stirred at 20–25°C for 16 h. The resulting mixture was poured into ice-water, and extracted with dichloromethane (50 ml $\times$ 3). The extract was washed with water, dried over magnesium sulfate and concentrated. The residue was subjected to column chromatography on silica gel. Elution with acetone–hexane (1:2) gave 0.11 g of 2,4-bis(methylthio)quinazoline (**2a**) as colorless needles (mp 78°C), 0.86 g of 2-methylamino-4-methylthioquinazoline (**3a**) as yellow needles (mp 131–132°C), and 2.5 g of 2-chloro-4-methylaminoquinazoline (**4a**) as colorless needles (mp 213°C). **3a**: *Anal.* Calcd for $C_{10}H_{11}N_3S$: C, 58.31; H, 5.25; N, 20.46. Found: C, 58.39; H, 5.20; N, 20.52. PMR ($CDCl_3$): 2.48 (3H, s, SCH_3), 2.99 (3H, d, NCH_3), 5.32 (1H, br s, NH), 6.82–7.82 (4H, m, Ar-H). IR (Nujol): 3200 cm^{-1} (NH).

Reaction of 1a with Ethylamine—A mixture of **1a** (4.2 g, 20.0 mmol), ethylamine (70% in water, 1.6 g, 24.9 mmol) and triethylamine (2.1 g, 21.0 mmol) in dimethylformamide (30 ml) was stirred at 80–85°C for 20 min. The resulting mixture was worked up as described for the reaction of **1a** with methylamine to give 0.05 g of **2a**, 1.7 g of 2-ethylamino-4-methylthioquinazoline (**3b**) as yellow needles (mp 79–80°C), 2.24 g of 2-chloro-4-ethylaminoquinazoline (**4b**) as colorless needles (mp 171°C), 0.13 g of 4-ethylamino-2-methylthioquinazoline (**5b**) as colorless needles (mp 149–151°C), and 0.04 g of 2,4-bis(ethylamino)quinazoline (**6b**) as colorless needles (mp 123–126°C). **3b**: *Anal.* Calcd for $C_{11}H_{13}N_3S$: C, 60.24; H, 5.97; N, 19.16. Found: C, 60.35; H, 5.83; N, 19.09. PMR ($CDCl_3$): 1.21 (3H, t, CH_3), 2.56 (3H, s, SCH_3), 3.30–3.80 (2H, m, CH_2),

5.24 (1H, br s, NH), 6.95—8.01 (4H, m, Ar-H). IR (Nujol): 3230 cm^{-1} (NH). **5b**: *Anal.* Calcd for $\text{C}_{11}\text{H}_{13}\text{N}_3\text{S}$: C, 60.24; H, 5.97; N, 19.16. Found: C, 60.40; H, 5.91; N, 19.37. PMR (CDCl_3): 1.22 (3H, t, CH_3), 2.57 (3H, s, SCH_3), 3.40—3.87 (2H, m, CH_2), 6.19 (1H, br s, NH), 7.10—7.82 (4H, m, Ar-H). IR (Nujol): 3220 cm^{-1} (NH).

Desulfurization of 3b with Raney Nickel—A mixture of **3b** (0.5 g, 2.3 mmol) and Raney nickel (2.0 g) in ethanol (30 ml) was refluxed for 3 h. The reaction mixture was filtered, and the residue was washed with ethanol. The filtrate and washings were combined, and concentrated. The residue was recrystallized from acetonitrile to give 0.15 g (37.7%) of 2-ethylaminoquinazoline (**10**), mp 96—97°C. *Anal.* Calcd for $\text{C}_{10}\text{H}_{11}\text{N}_3$: C, 69.34; H, 6.40. Found: C, 69.21; H, 6.56. PMR (CDCl_3): 2.30 (3H, t, CH_3), 3.56, 3.68 (2H, qq, CH_2), 5.72 (1H, br s, NH), 7.50—7.90 (4H, m, Ar-H), 9.00 (1H, s, Ar-H).

Desulfurization of 5b with Raney Nickel—Compound **5b** was worked up as described for the desulfurization of **3b** to give 0.22 g (55.3%) of 4-ethylaminoquinazoline (**11**) as colorless needles, mp 149—150°C. PMR (CDCl_3): 1.32 (3H, t, CH_3), 3.68, 3.76 (2H, qq, CH_2), 6.38 (1H, br s, NH), 7.25—8.04 (4H, m, Ar-H), 8.72 (1H, s, Ar-H).

Reaction of 1a with Butylamine—A mixture of **1a** (4.2 g, 20.0 mmol), butylamine (1.5 g, 20.5 mmol) and triethylamine (2.1 g, 21.0 mmol) in dimethylformamide (30 ml) was stirred at 80—85°C for 20 min. The resulting mixture was worked up as described for the reaction of **1a** with ethylamine to give 0.13 g of **2a**, 1.7 g of 2-butylamino-4-methylthioquinazoline (**3c**) as yellow needles (mp 59°C), 1.56 g of 4-butylamino-2-chloroquinazoline⁶⁾ (**4c**) as colorless needles (mp 115—116°C), 0.45 g of 4-butylamino-2-methylthioquinazoline (**5c**) as colorless needles (mp 99—100°C) and 0.16 g of 2,4-bis(butylamino)quinazoline⁶⁾ (**6c**) as a yellow oil (n_D^{20} 1.5631). **3c**: *Anal.* Calcd for $\text{C}_{13}\text{H}_{17}\text{N}_3\text{S}$: C, 63.12; H, 6.93; N, 16.99. Found: C, 63.08; H, 6.95; N, 16.92. PMR (CDCl_3): 0.55—1.95 (7H, m, $\text{CH}_2\text{CH}_2\text{CH}_3$), 2.53 (3H, s, SCH_3), 3.49 (2H, q, CH_2), 5.40 (1H, br s, NH), 6.85—7.28 (1H, m, Ar-H), 7.35—7.65 (2H, m, Ar-H), 7.65—8.00 (1H, d, Ar-H). IR (Nujol): 3250 cm^{-1} (NH). **4c**: *Anal.* Calcd for $\text{C}_{12}\text{H}_{14}\text{N}_3\text{Cl}$: C, 61.15; H, 5.99; N, 17.83. Found: C, 60.96; H, 5.93; N, 17.54. PMR (CDCl_3): 0.65—1.12 (3H, m, CH_3), 1.12—2.04 (4H, m, CH_2CH_2), 3.47—4.00 (2H, m, CH_2), 6.75 (1H, br s, NH), 7.21—8.18 (4H, m, Ar-H). IR (Nujol): 3250 cm^{-1} (NH). **5c**: *Anal.* Calcd for $\text{C}_{13}\text{H}_{17}\text{N}_3\text{S}$: C, 63.12; H, 6.93; N, 16.99. Found: C, 63.23; H, 7.01; N, 16.81. PMR (CDCl_3): 0.68—1.12 (3H, br s, CH_3), 0.68—1.90 (4H, m, CH_2CH_2), 2.58 (2H, s, SCH_3), 3.37—3.82 (2H, br q, CH_2), 5.98 (1H, br s, NH), 7.05—7.49 (1H, m, Ar-H), 7.49—7.80 (3H, m, Ar-H). IR (Nujol): 3250 cm^{-1} (NH). **6c**: PMR (CDCl_3): 0.59—2.25 (14H, m, $\text{CH}_2\text{CH}_2\text{CH}_3 \times 2$), 3.13—3.89 (4H, m, $\text{CH}_2 \times 2$), 5.50 (1H, br s, NH), 6.65—7.26 (2H, m, Ar-H, NH), 7.30—7.60 (2H, br d, Ar-H), 7.72—8.10 (1H, br d, Ar-H). IR (Nujol): 3300 cm^{-1} (NH).

Reaction of 1a with *tert*-Butylamine—A mixture of **1a** (4.2 g, 20.0 mmol), *tert*-butylamine (2.0 g, 27.4 mmol) and triethylamine (2.1 g, 21.0 mmol) in dimethylformamide (30 ml) was refluxed for 3 h. The resulting mixture was worked up as described for the reaction of **1a** with ethylamine to give 1.2 g of 2-*tert*-butylamino-4-methylthioquinazoline (**3d**) as yellow needles (mp 87—89°C), followed by 0.43 g of 2-chloro-4-*tert*-butylaminoquinazoline (**4d**) as colorless needles (mp 139—141°C), and 2.8 g of **1a** was recovered. **3d**: *Anal.* Calcd for $\text{C}_{13}\text{H}_{17}\text{N}_3\text{S}$: C, 63.12; H, 6.93; N, 16.99. Found: C, 62.57; H, 6.66; N, 16.85. PMR (CDCl_3): 1.32 (9H, s, $\text{CH}_3 \times 3$), 2.38 (3H, s, SCH_3), 5.45 (1H, s, NH), 6.69—7.00 (1H, m, Ar-H), 7.26—7.47 (2H, m, Ar-H), 7.50—7.76 (1H, s, Ar-H). **4d**: *Anal.* Calcd for $\text{C}_{12}\text{H}_{14}\text{N}_3\text{Cl}$: C, 61.15; H, 5.99; N, 17.83. Found: C, 60.83; H, 5.86; N, 17.90. PMR (CDCl_3): 1.61 (9H, br s, $\text{CH}_3 \times 3$), 6.15 (1H, br s, NH), 7.32—8.00 (4H, m, Ar-H). IR (Nujol): 3290 cm^{-1} (NH).

Reaction of 1e with *sec*-Butylamine—A mixture of **1e** (4.8 g, 20.1 mmol), *sec*-butylamine (2.0 g, 27.4 mmol) and triethylamine (2.1 g, 21.0 mmol) in dimethylformamide (30 ml) was stirred at 80—85°C for 20 min. The resulting mixture was worked up as described for the reaction of **1a** with ethylamine to give 1.0 g of 2-*sec*-butylamino-4-*tert*-butylthioquinazoline (**3e**) as yellow needles (mp 85—86°C), and 3.4 g of **1e** was recovered. **3e**: *Anal.* Calcd for $\text{C}_{16}\text{H}_{23}\text{N}_3\text{S}$: C, 66.39; H, 8.01; N, 14.52. Found: C, 66.39; H, 8.15; N, 14.63. PMR (CDCl_3): 0.96 (3H, t, CH_3), 1.25 (3H, d, CH_3), 1.56 (2H, m, CH_2), 1.69 (9H, s, $\text{CH}_3 \times 3$), 4.23 (1H, m, CH), 5.15 (1H, br d, NH), 7.03—7.49 (1H, m, Ar-H), 7.55—7.70 (1H, m, Ar-H), 7.96—8.19 (1H, br d, Ar-H). IR (Nujol): 3260 cm^{-1} (NH).

Reaction of 1a with Dimethylamine—A mixture of **1a** (4.2 g, 20.0 mmol), dimethylamine (50% in water, 2.5 g, 27.8 mmol) and triethylamine (2.1 g, 21.0 mmol) in dimethylformamide (30 ml) was stirred at 80—85°C for 20 min. The resulting mixture was worked up as described for the reaction of **1a** with ethylamine to give 0.11 g of **2a**, 1.2 g of 2-dimethylamino-4-methylthioquinazoline (**3f**) as yellow needles (mp 65—66°C), 1.45 g of 2-chloro-4-dimethylaminoquinazoline (**4f**) as colorless needles mp 67°C (lit.⁶⁾ mp 67.5°C), 0.6 g of 4-dimethylamino-2-methylthioquinazoline (**5f**) as colorless needles (mp 100—101°C) and 0.04 g of 2,4-bis(dimethylamino)quinazoline (**6f**) as a yellow oil.⁶⁾ **3f**: *Anal.* Calcd for $\text{C}_{11}\text{H}_{13}\text{N}_3\text{S}$: C, 60.24; H, 5.97; N, 19.16. Found: C, 59.92; H, 5.57; N, 18.83. PMR (CDCl_3): 2.58 (3H, s, SCH_3), 3.24 (6H, s, $\text{NCH}_3 \times 2$), 6.88—7.29 (1H, m, Ar-H), 7.45—7.65 (2H, m, Ar-H), 7.69—7.93 (1H, br d, Ar-H). **5f**: *Anal.* Calcd for $\text{C}_{11}\text{H}_{13}\text{N}_3\text{S}$: C, 60.24; H, 5.97; N, 19.16. Found: C, 60.01; H, 6.06; N, 18.91. PMR (CDCl_3): 2.58 (3H, s, SCH_3), 3.29 (6H, s, $\text{NCH}_3 \times 2$), 7.03—7.48 (1H, m, Ar-H), 7.53—7.73 (2H, m, Ar-H), 7.80—8.03 (1H, br d, Ar-H). **6f**: *Anal.* Calcd for $\text{C}_{12}\text{H}_{16}\text{N}_4$: C, 66.64; H, 7.46. Found: C, 66.26; H, 7.78.

Reaction of 1a with Dipropylamine—A mixture of **1a** (4.2 g, 20.0 mmol), dipropylamine (2.3 g, 22.8 mmol) and triethylamine (2.1 g, 21.0 mmol) in dimethylformamide (30 ml) was refluxed for 3 h. The resulting

mixture was poured into ice-water and extracted with chloroform (50 ml $\times$ 3). The extract was washed with satd. sodium chloride aq., dried over magnesium sulfate and concentrated. The residue was recrystallized from *n*-hexane to give 5.0 g (90%) of 2-dipropylamino-4-methylthioquinazoline (**3g**) as yellow needles (mp 52–54°C). *Anal.* Calcd for $C_{15}H_{21}N_3S$: C, 65.41; H, 7.69; N, 15.26. Found: C, 65.44; H, 7.61; N, 15.16. PMR ($CDCl_3$): 0.98 (6H, t, CH_3), 1.79 (4H, m, $CH_2 \times 2$), 2.66 (3H, s, SCH_3), 3.76 (4H, m, $CH_2 \times 2$), 7.09–7.39 (1H, m, Ar-H), 7.62–7.82 (2H, m, Ar-H), 7.90–8.15 (1H, br d, Ar-H).

Reaction of 1a with Diisopropylamine—A mixture of **1a** (4.2 g, 20.0 mmol), diisopropylamine (2.3 g, 22.8 mmol) and triethylamine (2.1 g, 21.0 mmol) in dimethylformamide (30 ml) was worked up as described for the reaction of **1a** with ethylamine, but **1a** was recovered quantitatively.

Reaction of 2a with Butylamine—A mixture of **2a** (2.2 g, 10.0 mmol) and butylamine (2.0 g, 27.4 mmol) in dimethylformamide (30 ml) was stirred at 80–85°C for 3 h. The reaction mixture was poured into ice-water and extracted with chloroform (30 ml $\times$ 3). The extract was washed with water, dried over magnesium sulfate and concentrated. The residue was recrystallized from acetonitrile to give 1.9 g (76.9%) of **5c** as colorless needles, mp 100°C.

Reaction of 3c with Butylamine—Compound **3c** (2.5 g) was worked up as described for the reaction of **2a** with butylamine to give 2.6 g (92.9%) of **6c** as a yellow oil.

Reaction of 5c with Butylamine—Compound **5c** (2.5 g) was worked up as described for the reaction of **3c** with butylamine, but **5c** was recovered.

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References and Notes

- 1) H. Miki, Fused Pyrimidines. III. accepted.
- 2) A part of this work was reported as a communication. H. Miki and J. Yamada, *Heterocycles*, **19**, 10 (1982).
- 3) F.H.S. Curd, J.K. Landquist, and F.L. Rose, *J. Chem. Soc.*, **1947**, 775.
- 4) F.H.S. Curd, H. Hoggarth, J.K. Landquist, and F.L. Rose, *J. Chem. Soc.*, **1948**, 1776.
- 5) H. Meerwein, P. Laasch, R. Mersch, and J. Nentwig, *Chem. Ber.*, **89**, 224 (1956).
- 6) J.R. Geigy, Akt.-Ges., Brit. Patent 822069 (1959). [*Chem. Abstr.*, **55**, 2005d (1961)].
- 7) W.L.F. Armarego, *J. Appl. Chem.*, **11**, 70 (1961).
- 8) Gj. Stefanović, Lj. Lorenc, and M. Lj. Mihailović, *Recl. Trav. Chim. Pays-Bas*, **80**, 149 (1961).
- 9) D. Libermann and A. Rouaix, *Bull. Soc. Chim. Fr.*, **1959**, 1793.
- 10) T. Stephen and H. Stephen, *J. Chem. Soc.*, **1956**, 4173.
- 11) H.C. Scarborough, B.C. Lawes, J.L. Minielli, and J.L. Compton, *J. Org. Chem.*, **27**, 957 (1962).