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New 6-chloro- and 6,7-dichloro-4-(4-aminophenyl)-2-(*N*-alkylcarbamoyl)-1,2-dihydrophthalazines (**12**, **18**) were synthesized starting from 6-chloro- and 6,7-dichloro-4-(4-nitrophenyl)phthalazine (**8**). Routes to 1-unsubstituted (**12**) and 1-methyl (**18**) derivatives are different. Key intermediates **8** were prepared from 4-chloro- and 3,4-dichlorotoluene *via ortho*-formylbenzophenone derivatives **7**.

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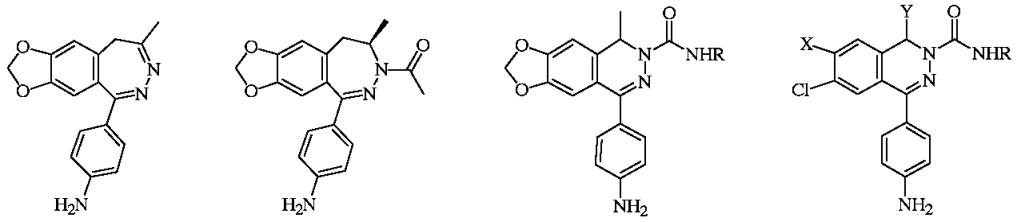
The amino acid L-glutamate plays a key role in the normal function of the central nervous system [1]. However, under pathological conditions (*e.g.* stroke, trauma) excessive extracellular concentrations of glutamate are associated with neuronal damage and cell death. AMPA receptor is a subtype of ionotropic glutamate receptors, which can be selectively activated by α-amino-3-hydroxy-4-methylisoxazolepropionic acid (AMPA). It is recognized that AMPA receptor antagonists reduce injury in animal models of stroke and epilepsy. Therefore the synthesis of new AMPA receptor modulators is an interesting target.The 2,3-benzodiazepine derivative GYKI 52466 (**1**) was the first of its class showing noncompetitive AMPA antagonist activity. One of the most potent derivatives of **1**, GYKI 53773 (**2**, LY 300164, talampanel) is in clinical evaluation [2,3] (Scheme 1).

Structurally related 1,2-dihydrophthalazines **3** and **4** were also shown to selectively and noncompetitively inhibit currents associated activation of AMPA recector [4].

It was found that AMPA antagonist activity was retained when the dioxolane ring of 2,3-benzodiazepine **2** was substituted with chlorine atoms [5] and the corresponding 7-fluoro analogue was approximately equipotent with 1,2-dihydrophthalazine **3** in the electrophysiological assay [6].

Scheme 1

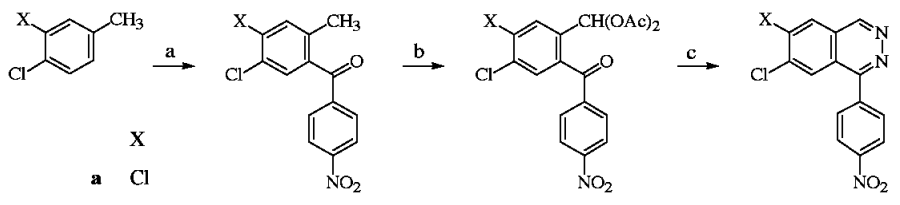


1 (GYKI-52466) **2** (GYKI-53773, LY 300164, talampanel) **3** R=Pr (SYM 2206) **4** R=Bu (SYM 2207) **5** (X: Cl, H; Y: H, Me)

We now report the synthesis of new chlorine substituted 1,2-dihydrophthalazines **5** [7] structurally related to methylenedioxy derivatives **3** and **4**.

Phthalazine intermediates **8** were synthesized starting from 3,4-dichloro-, or 4-chlorotoluene (Scheme 2). Friedel-Crafts nitrobenzoylation of 3,4-dichlorotoluene [8] followed by oxidation of the resulting benzophenone **6a** with chromium(VI) oxide [9] in a mixture of acetic anhydride and concentrated sulfuric acid gave

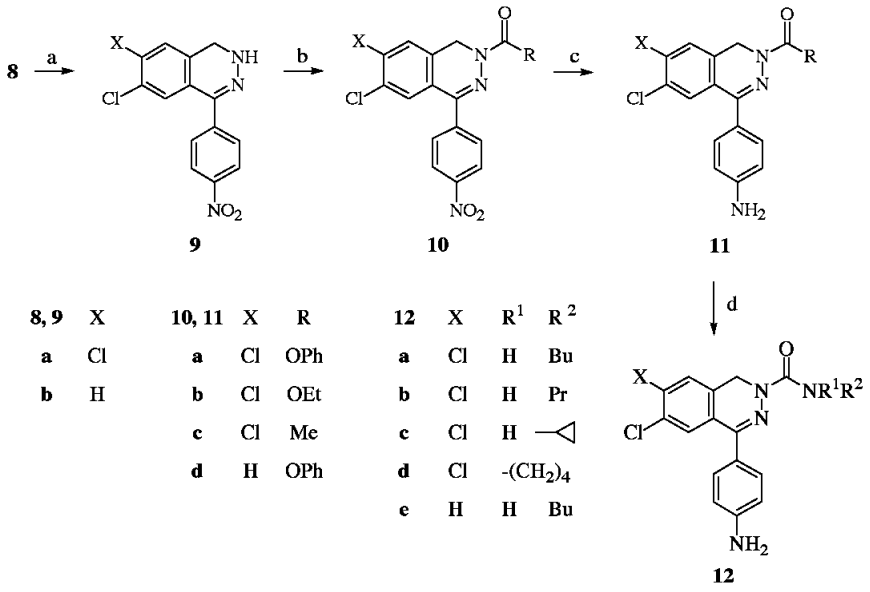
Scheme 2



X			
a	Cl	**6**	**7**	**8**
b	H			

(a) 4-nitrobenzoyl chloride, $AlCl_3$, CH_2Cl-CH_2Cl (b) CrO_3, cc. H_2SO_4, Ac_2O (c) NH_2-NH_2•H_2O, EtOH

Scheme 3



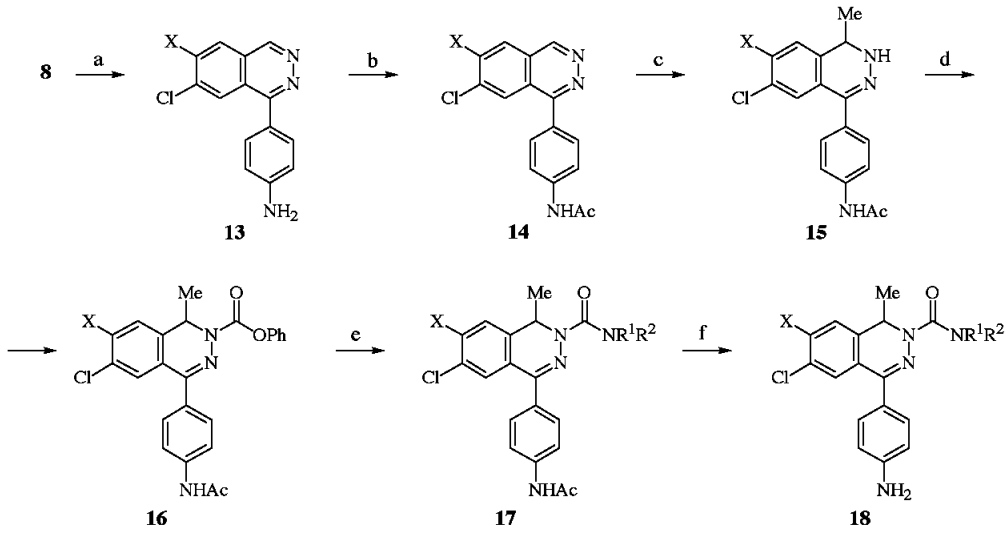
8, 9	X
a	Cl
b	H

10, 11	X	R
a	Cl	OPh
b	Cl	OEt
c	Cl	Me
d	H	OPh

12	X	R^1	R^2
a	Cl	H	Bu
b	Cl	H	Pr
c	Cl	H	
d	Cl		$-(CH_2)_4$
e	H	H	Bu

(a) $NaBH_4$, $CHCl_3$/MeOH (b) RCOCl or Ac_2O (c) Raney-Ni, THF or CH_2Cl_2/MeOH (d) HNR^1R^2, DMF

Scheme 4



8, 13-16	X
a	Cl
b	H

17,18	X	R^1	R^2
a	Cl	H	Bu
b	Cl	H	
c	Cl		$-(CH_2)_4-$
d	H	H	Bu

(a) Fe, cc. HCl, EtOH (b) Ac_2O, MeOH (c) MeLi, THF (d) PhOCOCl, TEA, THF (e) HNR^1R^2, DMF (f) NaOH, H_2O, MeOH

4,5-dichloro-2-(4-nitrophenyl)benzaldehyde acylal **7a**. Similar reaction sequence starting from Friedel-Crafts nitrobenzoylation of 4-chlorotoluene [10] gave a mixture of regioisomers containing 4-chloro-2-(4-nitrophenyl)-benzaldehyde acylal **7b**. Dichlorophthalazine **8a** was prepared by the reaction of *ortho*-aroylbenzaldehyde acylal **7a** with hydrazine in good yield. Since only *ortho*-dicarbonyl derivatives can undergo cyclisation with hydrazine to give phthalazine, chlorophthalazine **8b** was obtained easily by the reaction of hydrazine with the corresponding mixture of regioisomers containing **7b**.

The 2-carbamoyl moiety of compounds **3** and **4** was introduced by reacting the corresponding 1,2-dihydrophthalazine with isocyanates [4,6]. The use of isocyanates for the introduction of the *N*(2)-carbamoyl group has two major disadvantages: relatively few organic isocyanates are commercially available and *N*,*N*-disubstituted carbamoyl substituents can not be introduced by this method. Our strategy for the introduction of *N*(2)-carbamoyl moiety of 1,2-dihydrophthalazines was *N*(2)-alkoxy(aryloxy)carbonylation followed by treatment with various primary and secondary amines.

The synthesis of 2-carbamoyl-4-(4-aminophenyl)-1,2-dihydrophthalazines **12** is shown on Scheme 3. 1,2-Dihydrophthalazines **9** were obtained by sodium borohydride reduction [11] of phthalazines **8**. *N*(2)-Acylation of compounds **9** with chloroformic acid esters and acetic anhydride provided compounds **10** which were transformed to the corresponding **11** amines by catalytic reduction of the nitro group. Amidation of *N*(2)-phenoxycarbonyl derivatives **11a** and **11d** with various amines provided our target compounds **12**. Attempts to convert *N*(2)-ethoxycarbonyl derivative **11b** to compounds **12** failed.

The required 2-carbamoyl-1-methyl-1,2-dihydrophthalazines **18** were synthesized by a sequence starting with the reduction [12] of nitro compound **8** to the corresponding anilines **13** and subsequent acetylation to acetanilides **14** (Scheme 4). Addition of methyllithium [4,6,13] followed by 2-phenoxycarbonylation of the resulting 1-methyl-1,2-dihydrophthalazines **15** afforded phenylcarbamates **16**, which were treated with various amines to provide the corresponding 2-carbamoyl derivatives **17**. Final products **18** were obtained by deacetylation of compounds **17**.

EXPERIMENTAL

Melting points were determined on a Büchi 535 apparatus and were not corrected. The ^{1}H nmr spectra were recorded on a Varian Gemini-200, or a Varian Unity Inova 400 spectrometer, at 200 or 400 MHz and at 50.3 or 101 MHz, respectively. Chemical shifts were reported as δ values (ppm) down field from internal tetramethylsilane.

4,5-Dichloro-2-(4-nitrobenzoyl)toluene (**6a**).

A solution of 3,4-dichlorotoluene (64 ml, 80.5 g, 0.5 mole) in 1,2-dichloroethane (50 ml) was added to a solution of anhydrous aluminum chloride (76.0 g, 0.57 mole) and 4-nitrobenzoyl chloride (74.0 g, 0.4 mole) in 1,2-dichloroethane (80 ml) and the mixture was refluxed for 5 hours. The reaction mixture was poured into ice (1000 g) and extracted with chloroform (3 x 100 ml). The organic layer was washed with water (3 x 100 ml), dried ($MgSO_4$) and evaporated. The residual oil was triturated with hexane (200 ml), the crystalline product was collected by filtration and washed with hexane (50 ml). The crude product was recrystallized from acetic anhydride to give **6a** (65.8 g, 53 %) as colourless crystals: mp 121-122 °C. ^{1}H nmr (deuteriochloroform, 200 MHz): δ 8.33 (2H, d, *J* = 8.8 Hz), 7.94 (2H, d, *J* = 8.8 Hz), 7.45 (2H, s), 7.29 (2H, s), 2.33 (3H, s).

Anal. Calcd. for $C_{14}H_9Cl_2NO_3$ (310.14): C, 54.22, H, 2.92, Cl, 22.86, N, 4.52. Found C, 53.84, H, 2.87, Cl, 22.73, N, 4.51.

4,5-Dichloro-2-(4-nitrobenzoyl)benzaldehyde Acylal (**7a**).

Chromium(VI) oxide (20.0 g, 0.20 mole) was added to a solution of **6a** (20.0 g, 0.064 mole) in acetic anhydride (400 ml) at 5 °C. After addition of concentrated sulfuric acid (20 ml), the mixture was kept at 0-5 °C for 4 hours. It was poured into ice (1000 g), the resulting crystalline precipitate was collected by filtration, washed with ethanol and recrystallized from acetic anhydride to give **7a** (11.5 g, 42 %) as colourless crystals: mp 167-168 °C. ^{1}H nmr (deuteriochloroform, 200 MHz): δ 8.34 (2H, d, *J* = 8.9 Hz), 7.95 (2H, d, *J* = 8.9 Hz), 7.83 (1H, s), 7.68 (1H, s), 7.43 (1H, s), 2.02 (6 H, s).

Anal. Calcd. for $C_{18}H_{13}Cl_2NO_7$ (426.22): C, 50.72, H, 3.07, Cl, 16.64, N, 3.29. Found: C, 50.42, H, 2.99, Cl, 16.35, N, 3.28.

6,7-Dichloro-1-(4-nitrophenyl)phthalazine (**8a**).

Hydrazine monohydrate (8 ml, 0.16 mole) was added to a solution of **7a** (6.8 g, 0.021 mole) in ethanol (120 ml) and the mixture was refluxed for 3 hours. The crystalline product was collected by filtration and washed with ethanol and recrystallized from methanol to give **8a** (6.1 g, 91 %) as yellow crystals: mp 288-289 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 400 MHz): δ 9.77 (1H, s), 8.72 (1H, s), 8.47 (2H, d, *J* = 8.7 Hz), 8.15 (1H, s), 8.06 (2H, d, *J* = 8.7 Hz).

Anal. Calcd. for $C_{14}H_7Cl_2N_3O_2$ (320.14): C, 52.53, H, 2.20, Cl, 22.15, N, 13.13. Found: C, 52.23, H, 2.16, Cl, 21.75, N, 12.95.

7-Chloro-1-(4-nitrophenyl)phthalazine (**8b**).

Step 1: A solution of 4-chlorotoluene (10.8 ml, 11.5 g, 0.09 mole) and 4-nitrobenzoyl chloride (27.1 g, 0.15 mole) in 1,2-dichloroethane (20 ml) was added to a mixture of anhydrous aluminium chloride (27.8 g, 0.21 mole) and 4-chlorotoluene (10.8 ml, 11.5 g, 0.09 mole) in 1,2-dichloroethane (30 ml) and the mixture was refluxed for 5 hours. It was poured into ice (200 g) and extracted with chloroform (3 x 20 ml). The organic layer was washed with water (3 x 50 ml), dried ($MgSO_4$) and evaporated. The oily residue was recrystallized from ethanol (100 ml) to give a mixture of regioisomers (30.0 g) containing 4-chloro-2-(4-nitrobenzoyl)toluene (**6b**) as colourless solid.

Step 2: The mixture obtained in *Step 1* (30.0 g, 0.11 mole) was dissolved in acetic anhydride (600 ml) and chromium(VI) oxide (30.0 g, 0.30 mole) and concentrated sulfuric acid (30 ml) was

added at 5 °C and the mixture was kept at 0-5 °C for 4 hours. It was poured into ice (1000 g) and extracted with ethyl acetate (3 x 300 ml). The organic layer was washed with brine (3 x 300 ml), dried ($MgSO_4$) and evaporated. The oily residue was crystallized from ethanol (300 ml) to give a mixture of regioisomers (19.1 g) containing 4-chloro-2-(4-nitrobenzoyl)benzaldehyde acylal (**7b**) as colourless solid.

Step 3: Hydrazine monohydrate (34.0 ml, 0.68 mole) was added to a solution of the mixture of isomers obtained in Step 2 (19.1 g, 0.049 mole) in ethanol (100 ml) and it was refluxed for 3 hours. The crystalline product was collected by filtration and washed with ethanol and recrystallized from methanol to give **8b** (4.6 g, 11 %, based on 4-nitrobenzoyl chloride used in step 1) as colourless crystals: mp 225-226 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 400 MHz): δ 9.82 (1H, d, *J* = 0.9 Hz), 8.47 (2H, d, *J* = 8.9 Hz), 8.38 (1H, d, *J* = 8.6 Hz), 8.16 (1H, dd, *J* = 8.6, 2.0 Hz), 8.06 (2H, d, *J* = 8.9 Hz), 7.94 (1H, m).

Anal. Calcd. for $C_{14}H_8ClN_3O_2$ (285.68): C, 58.86, H, 2.82, Cl, 12.41, N, 14.71. Found: C, 58.73, H, 2.75, Cl, 12.20, N, 14.46.

6,7-Dichloro-4-(4-nitrophenyl)-1,2-dihydrophthalazine (**9a**).

Sodium borohydride (1.5 g, 40 mmoles) was added to a solution of **8a** (4.0 g, 12.5 mmoles) in a mixture of methanol (30 ml) and chloroform (100 ml). After stirring at 25 °C for 3 hours aqueous acetic acid (50 %, 20 ml) was added and the reaction mixture was extracted with chloroform (3 x 100 ml). The combined organic layer was washed with water (3 x 50 ml), dried ($MgSO_4$) and evaporated and recrystallized from methanol to give **9a** (3.5 g, 87 %) as yellow crystals: mp 253-254 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 400 MHz): δ 8.56 (1H, s), 8.33 (2H, d, *J* = 9.2 Hz), 7.84 (2H, d, *J* = 9.2 Hz), 7.63 (1 H, s), 7.27 (1 H, s), 4.20 (2 H, s).

Anal. Calcd. for $C_{14}H_9Cl_2N_3O_2$ (322.15): C, 52.20, H, 2.82, Cl, 22.01, N, 13.04. Found: C, 51.89, H, 2.83, Cl, 21.82, N, 12.87.

6-Chloro-4-(4-nitrophenyl)-1,2-dihydrophthalazine (**9b**).

This compound was prepared analogously to **9a** starting from **8b** (8.6 g, 30 mmoles) and recrystallized from methanol to give **9b** (5.5 g, 64%) as yellow crystals: mp 220-222 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 400 MHz): δ 8.51 (1H, s), 8.30 (2H, d, *J* = 8.9 Hz), 7.84 (2H, d, *J* = 8.9 Hz), 7.51 (1H, dd, *J* = 8.1, 2.1 Hz), 7.35 (1H, d, *J* = 8.1 Hz),7.10 (1H, d, *J* = 2.1 Hz), 4.19 (2H, s).

Anal. Calcd. for $C_{14}H_{10}ClN_3O_2$ (287.70): C, 58.44, H, 3.50, Cl, 12.32, N, 14.60. Found: C, 58.19, H, 3.57, Cl, 12.65, N, 14.36.

6,7-Dichloro-4-(4-nitrophenyl)-2-phenoxycarbonyl-1,2-dihydrophthalazine (**10a**).

Phenyl chloroformate (10 ml, 12.5 g, 80 mmoles) was added to **9a** (1.0 g, 2.3 mmoles) and the mixture was stirred at 140 °C for 2 hours. After cooling to ambient temperature, the crystalline product was collected by filtration and recrystallized from ethanol (20 ml) to give **10a** (0.9 g, 89 %) as yellow crystals: mp 206-207 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 200 MHz): δ 8.38 (2 H, d, *J* = 8.8 Hz), 7.90 (2H, d, *J* = 8.8 Hz), 7.47-7.19 (7H, m), 5.07 (2H, s).

Anal. Calcd. for $C_{21}H_{13}Cl_2N_3O_4$ (442.26): C, 57.03, H, 2.96, Cl, 16.03, N, 9.50. Found: C, 56.97, H, 2.93, Cl, 15.93, N, 9.47.

6,7-Dichloro-2-ethoxycarbonyl-4-(4-nitrophenyl)-1,2-dihydrophthalazine (**10b**).

This compound was prepared analogously to **10a** starting from **9a** (1.0 g, 3.1 mmoles) and ethyl chloroformate (10 ml, 11.4 g, 104.6 mmoles) and recrystallized from ethanol to give **10b** (1.04 g, 85 %) as yellow crystals: mp 238-240 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 200 MHz): δ 8.37 (2H, d, *J* = 8.8 Hz), 7.87 (2H, d, *J* = 8.8 Hz), 7.43 (1H, s), 7.30 (1H, s), 4.91 (2H, d), 4.40 (2H, q, *J* = 7.0 Hz), 1.42 (3H, t, *J* = 7.0 Hz).

Anal. Calcd. for $C_{17}H_{13}Cl_2N_3O_4$ (394.22): C, 51.79, H, 3.32, Cl, 17.99, N, 10.66. Found: C, 51.50, H, 3.34, Cl, 18.03, N, 10.49.

2-Acetyl-6,7-dichloro-4-(4-nitrophenyl)-1,2-dihydrophthalazine (**10c**).

This compound was prepared analogously to **10a** starting from **9a** (0.53 g, 1.6 mmoles) and acetic anhydride (5 ml, 5.4 g, 53.0 mmoles) and recrystallized from methanol to give **10c** (0.46 g, 79 %) as yellow crystals: mp 274-275 °C. ^{1}H nmr (deuteriochloroform, 400 MHz): δ 8.38 (2H, d, *J* = 8.9 Hz), 7.82 (2H, d, *J* = 8.9 Hz), 7.41 (1H, s), 7.31 (1H, s), 4.97 (2H, s), 2.43 (3H, s).

Anal. Calcd. for $C_{16}H_{11}Cl_2N_3O_3$ (364.20): C, 52.76, H, 3.04, Cl, 19.47, N, 11.54. Found: C, 52.72, H, 3.07, Cl, 19.16, N, 11.52.

6-Chloro-4-(4-nitrophenyl)-2-phenyloxycarbonyl-1,2-dihydrophthalazine (**10d**).

This compound was prepared analogously to **10a** starting from **9b** (3.5 g, 12 mmoles) and phenyl chloroformate (30 ml, 37.4 g, 239.1 mmole) and recrystallized from ethanol to give **10d** (4.0 g, 82 %) as yellow crystals: mp 208-210 °C. ^{1}H nmr (deuteriochloroform, 200 MHz): δ 8.37 (2H, d, *J* = 9.0 Hz), 7.92 (2H, d, *J* = 9.0 Hz), 7.52 (1H, dd, *J* = 8.1, 2.2 Hz), 7.43-7.20 (7H, m), 5.03 (2H, s).

Anal. Calcd. for $C_{21}H_{14}ClN_3O_4$ (407.81): C, 61.85, H, 3.46, Cl, 8.70, N, 10.30. Found: C, 61.64, H, 3.57, Cl, 8.49, N, 10.22.

4-(4-Aminophenyl)-6,7-dichloro-2-phenyloxycarbonyl-1,2-dihydrophthalazine (**11a**).

A solution of **10a** (0.8 g, 1.8 mmoles) in tetrahydrofuran (30 ml) was hydrogenated in the presence of Raney-Ni (0.4 g) at room temperature under 10 bar hydrogen pressure. The catalyst was removed, and the solvent was evaporated. The residue was recrystallized from methanol (10 ml) to give **11a** (0.6 g, 81 %) as yellow crystals: mp 245-247 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 200 MHz): δ 7.92 (1H, s), 7.49-7.21 (8H, m), 6.70 (2H, d, *J* = 8.5 Hz), 5.60 (2H, s), 4.95 (2H, s).

Anal. Calcd. for $C_{21}H_{15}Cl_2N_3O_2$ (412.28): C, 61.17, H, 3.64, Cl, 17.23, N, 10.19. Found: C, 60.89, H, 3.67, Cl, 17.01, N, 9.98.

4-(4-Aminophenyl)-6,7-dichloro-2-ethoxycarbonyl-1,2-dihydrophthalazine (**11b**).

This compound was prepared analogously to **11a** starting from **10b** (1.0 g, 2.5 mmoles) and Raney-Ni (0.2 g) in dichloromethane (60 ml) and methanol (30 ml) and recrystallized from methanol to give **11b** (0.90 g, 98 %) as yellow crystals: mp 182-184 °C. ^{1}H nmr (deuteriochloroform, 200 MHz): δ 7.46 (2H, d, *J* = 8.4 Hz), 7.45 (1H, s), 7.37 (1H, s), 6.74 (2H, d, *J* = 8.4 Hz), 4.81 (2H, s), 4.35 (2H, q, *J* = 7.3 Hz), 1.38 (3 H, t, *J* = 7.3 Hz).

Anal. Calcd. for $C_{17}H_{15}Cl_2N_3O_2$ (364.24): C, 56.06, H, 4.15, Cl, 19.47, N, 11.54. Found: C, 55.80, H, 4.21, Cl, 19.29, N, 11.50.

2-Acetyl-4-(4-aminophenyl)-6,7-dichloro-1,2-dihydrophthalazine (**11c**).

This compound was prepared analogously to **10a** starting from **10c** (0.86 g, 2.4 mmole) and Raney-Ni (0.2 g) in dichloromethane (60 ml) and methanol (30 ml) and recrystallized from methanol to give **11c** (0.78 g, 97 %) as yellow crystals: mp 218-220 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 200 MHz): δ 7.86 (1H, s), 7.40 (1H, s), 7.36 (2H, d, *J* = 8.5 Hz), 6.67 (2H, d, *J* = 8.5 Hz), 5.59 (2H, s), 4.87 (2H, s), 2.29 (3H, s).

Anal. Calcd. for $C_{16}H_{13}Cl_2N_3O$ (334.21): C, 57.50, H, 3.92, Cl, 21.22, N, 12.57. Found: C, 57.44, H, 4.02, Cl, 21.62, N, 12.31.

4-(4-Aminophenyl)-6-chloro-2-phenyloxycarbonyl-1,2-dihydrophthalazine (**11d**).

This compound was prepared analogously to **11a** starting from **10d** (2.0 g, 4.9 mmole) and Raney-Ni (0.4 g) in dichloromethane (120 ml) and methanol (60 ml) and recrystallized from methanol to give **11d** (1.6 g, 86 %) as yellow crystals: mp 224-226 °C. ^{1}H nmr (deuteriochloroform, 200 MHz): δ 7.54 (2H, d, *J* = 8.4 Hz), 7.49-7.23 (8H, m), 6.78 (2H, d, *J* = 8.4 Hz), 4.95 (2H, s), 3.95 (2H, bs).

Anal. Calcd. for $C_{21}H_{16}ClN_3O_2$ (377.83): C, 66.75, H, 4.27, Cl, 9.39, N, 11.12. Found: C, 66.49, H, 4.18, Cl, 9.52, N, 11.33.

4-(4-Aminophenyl)-2-(*N*-butylcarbamoyl)-6,7-dichloro-1,2-dihydrophthalazine (**12a**).

Butylamine (0.7 ml, 0.51 g, 7.0 mmoles) was added to a solution **11a** (2.5 g, 6.0 mmoles) in dimethylformamide (20 ml). After stirring at 60 °C for 3 hours the mixture was poured into ice (50 g). The crystalline product was filtered and recrystallized from 2-propanol (5 ml) to give **12a** (1.8 g, 77 %) as yellow crystals: mp 169-172 °C. ^{1}H nmr (deuteriochloroform, 400 MHz): δ 7.40-7.35 (4H, m), 6.78 (2H, d, *J* = 8.4 Hz), 6.55 (1H, t, *J* = 6.8 Hz), 4.83 (2H, s), 3.28 (2H, q, *J* = 6.8 Hz), 1.57-1.51 (2H, m), 1.41-1.35 (2H, m), 0.94 (3H, t, *J* = 7.6 Hz).

Anal. Calcd. for $C_{19}H_{20}Cl_2N_4O$ (391.31): C, 58.32, H, 5.15, Cl, 18.12, N, 14.32. Found: C, 58.09, H, 5.15, Cl, 17.86, N, 14.04.

4-(4-Aminophenyl)-6,7-dichloro-2-(*N*-propylcarbamoyl)-1,2-dihydrophthalazine (**12b**).

This compound was prepared analogously to **12a** starting from **11a** (0.75 g, 1.8 mmoles) and propylamine (0.5 ml, 0.36 g, 6.1 mmoles) in dimethylformamide (5 ml) and recrystallized from isopropanol to give **12b** (0.62 g, 91 %) as yellow crystals: mp 218-219 °C. ^{1}H nmr (deuteriochloroform, 400 MHz): δ 7.39 (2H, s), 7.36 (2H, d, *J* = 8.4 Hz), 6.77 (2H, d, *J* = 8.4 Hz), 6.58 (1H, t, *J* = 6.3), 4.84 (2H, s), 3.93 (2H, bs), 3.30 (2H, q, *J* = 6.3), 1.59 (2H, m), 0.95 (3H, t, *J* = 7.4).

Anal. Calcd. for $C_{18}H_{18}Cl_2N_4O$ (377.28): C, 57.30, H, 4.81, Cl, 18.79, N, 14.85. Found: C, 57.02, H, 4.84, Cl, 18.77, N, 14.63.

4-(4-Aminophenyl)-2-(*N*-cyclopropylcarbamoyl)-6,7-dichloro-1,2-dihydrophthalazine (**12c**).

This compound was prepared analogously to **12a** starting from **11a** (0.8 g, 1.9 mmoles) and cyclopropylamine (2.0 ml, 1.63 g, 28.5 mmoles) in dimethylformamide (5 ml) and recrystallized from isopropanol to give **12c** (0.63 g, 91 %) as yellow crystals: mp 233-234 °C. ^{1}H nmr (deuteriochloroform, 200 MHz): δ 7.38 (1H, s), 7.36 (2H, d, *J* = 8.4 Hz), 7.36 (1H, s), 6.77 (2H, d, *J* = 8.4 Hz), 6.65 (1H, s), 4.84 (2H, s), 3.93 (2H, bs), 2.73-2.67 (1H, m), 0.78 (2H, m), 0.58 (2 H, m).

Anal. Calcd. for $C_{18}H_{16}Cl_2N_4O$ (375.27): C, 57.61, H, 4.30, Cl, 18.90, N, 14.93. Found: C, 57.37, H, 4.47, Cl, 19.23, N, 14.97.

4-(4-Aminophenyl)-6,7-dichloro-2-(pyrrolidine-1-carbonyl)-1,2-dihydrophthalazine (**12d**).

This compound was prepared analogously to **12a** starting from **11a** (1.0 g, 2.4 mmoles) and pyrrolidine (0.6 ml, 0.52 g, 7.3 mmoles) in dimethylformamide (8 ml) and recrystallized from isopropanol to give **12d** (0.9 g, 96 %) as yellow crystals: mp 124-126 °C. ^{1}H nmr (deuteriochloroform, 200 MHz): δ 7.41 (2H, d, *J* = 8.4 Hz), 7.39 (1H, s), 7.36 (1H, s), 6.84 (2H, d, *J* = 8.4 Hz), 4.61 (2H, s), 4.3 (2H, bs), 3.63 (4H, m), 1.88 (4H, m).

Anal. Calcd. for $C_{19}H_{18}Cl_2N_4O$ (389.29): C, 58.62, H, 4.66, Cl, 18.22, N, 14.39. Found: C, 58.34, H, 4.77, Cl, 17.82, N, 14.05.

4-(4-Aminophenyl)-2-(*N*-butylcarbamoyl)-6-chloro-1,2-dihydrophthalazine (**12e**).

This compound was prepared analogously to **12a** starting from **11a** (2.0 g, 5.3 mmoles) and butylamine (0.7 ml, 0.51 g, 7.0 mmoles) in dimethylformamide (20 ml). The product was dissolved in ethyl acetate (10 ml) and hydrochloric acid solution in ethyl acetate was added to give the hydrochloride salt of **12e** (1.70g, 61 %) as yellow crystals: mp 123-124 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 400 MHz): δ 7.81 (2H, d, *J* = 8.2), 7.59 (1H, dd, *J* = 8.0, 2.0), 7.51 (1H, d, *J* = 8.0), 7.38 (2H, d, *J* = 8.2), 7.32 (2H, s), 7.14 (1H, d, *J* = 2.0), 4.76 (2H, s), 3.17 (2H, q, *J* =3.6), 1.46 (2H, m), 1.28 (2H, m), 0.88 (3H, t, *J* = 7.2).

Anal. Calcd. for $C_{19}H_{22}Cl_2N_4O$ (393.32): C, 58.02, H, 5.60, Cl, 18.07, N, 14.25. Found: C, 57.71, H, 5.73, Cl, 17.82, N, 13.89.

1-(4-Aminophenyl)-6,7-dichlorophthalazine (**13a**).

A mixture **8a** (14.6 g, 46 mmoles), iron powder (15.0 g), concentrated hydrochloric acid (25 ml) and ethanol (150 ml) was refluxed for 1 hour. It was filtered, the ethanol was evaporated and the residue was extracted with chloroform (3 x 100 ml). The organic layer was washed with water (3 x 50 ml), dried ($MgSO_4$) and evaporated and recrystallized from ethanol to give **13a** (11.3 g, 85 %) as yellow crystals: mp 198-200 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 400 MHz): δ 9.38 (1H, s), 8.28 (1H, s), 8.10 (1H, s), 7.58 (2H, d, *J* = 8.8 Hz), 6.87 (2H, d, *J* = 8.8 Hz), 3.62 (2H, bs).

Anal. Calcd. for $C_{14}H_9Cl_2N_3$ (290.15): C, 57.95, H, 3.12, Cl, 24.44, N, 14.48. Found: C, 57.63, H, 3.09, Cl, 24.20, N, 14.36.

1-(4-Aminophenyl)-7-chlorophthalazine (**13b**).

This compound was prepared analogously to **13a** starting from 6-chloro-4-(4-nitrophenyl)phthalazine **8b** (10.86 g, 38 mmoles) and iron powder (10.0 g, 179 mmoles) in ethanol (100 ml) and recrystallized from ethanol to give **13b** (8.9 g, 92 %) as yellow

crystals: mp 224-226 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 200 MHz): δ 9.62 (1 H, s), 8.25 (1 H, d, *J* = 9.5 Hz), 8.07-8.01 (2 H, m), 7.50 (2 H, d, *J* = 8.4 Hz), 6.83 (2 H, d, *J* = 8.4 Hz), 5.68 (2 H, s).

Anal. Calcd. for $C_{14}H_{10}ClN_3$ (255.70): C, 65.76, H, 3.94, Cl, 13.87, N, 16.43. Found: C, 65.39, H, 3.99, Cl, 13.97, N, 16.21.

1-(4-Acetaminophenyl)-6,7-dichlorophthalazine (**14a**).

A solution of **13a** (14.8 g, 51 mmoles) and acetic anhydride (20 ml, 21.6 g, 212.0 mmoles) in methanol (400 ml) was stirred at reflux for 4 hours. The crystalline product was collected by filtration and washed with methanol to give **14a** (14.2 g, 84 %) as yellow crystals: mp 270-272 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 400 MHz): δ 10.22 (1H, s), 9.66 (1H, s), 8.64 (1H, s), 8.15 (1H, s), 7.84 (2H, d, *J* = 8.6 Hz), 7.72 (2H, d, *J* = 8.6 Hz), 2.12 (3H, s).

Anal. Calcd. for $C_{16}H_{11}Cl_2N_3O$ (332.20): C, 57.85, H, 3.34, Cl, 21.35, N, 12.65. Found: C, 57.49, H, 3.31, Cl, 20.91, N, 12.65.

1-(4-Acetaminophenyl)-7-chlorophthalazine (**14b**).

This compound was prepared analogously to **14a** starting from **13b** (5.32 g, 21 mmoles) and acetic anhydride (10 ml, 10.8 g, 106.0 mmoles) in methanol (100 ml) to give **14b** (4.6 g, 74 %) as yellow crystals: mp 224-225 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 200 MHz): δ 10.24(1H, s), 9.72 (1H, s), 8.33(1H, d, *J* = 8.5 Hz), 8.11 (1H, dd, *J* = 8.5, 1.8 Hz), 7.97 (1H, d, *J* = 1.8 Hz), 7.85 (2H, d, *J* = 8.6 Hz), 7.71 (2H, d, *J* = 8.6 Hz), 2.13 (3H, s).

Anal. Calcd. for $C_{16}H_{12}ClN_3O$ (297.74): C, 64.54, H, 4.06, Cl, 11.91, N, 14.11. Found: C, 64.29, H, 4.03, Cl, 11.73, N, 13.77.

4-(4-Acetaminophenyl)-6,7-dichloro-1-methyl-1,2-dihydrophthalazine (**15a**).

Methyllithium (1 *M* solution in tetrahydrofuran, 50 ml, 50 mmoles) was added to a solution of **14a** (5.2 g, 16 mmoles) in tetrahydrofuran (30 ml) at 0 °C and the mixture was stirred at 0 °C for 1 hour. It was poured into water (150 ml), acidified with aqueous hydrochloric acid solution (10 %) and extracted with tetrahydrofuran (3 x 50 ml). The organic layer was washed with brine (3 x 50 ml), dried ($MgSO_4$) and evaporated. The residue was separeted by column chromatography (eluent: dichloromethane:methanol, 100:1) and recrystallized from ethanol to give **15a** (3.2 g, 58 %) as yellow crystals: mp 222-224 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 200 MHz): δ 10.05 (1H, s), 8.04 (1H, s), 7.66 (2H, d, *J* = 8.8 Hz), 7.57 (1H, s), 7.46 (2H, d, *J* = 8.8 Hz), 7.21 (1H, s), 4.27 (1H, q, *J* = 6.6 Hz), 2.07 (3H, s), 1.37 (3H, d, *J* = 6.6 Hz).

Anal. Calcd. for $C_{17}H_{15}Cl_2N_3O$ (348.24): C, 58.62, H, 4.31, Cl, 20.40, N, 12.07. Found: C, 58.54, H, 4.25, Cl, 20.33, N, 12.04.

4-(4-Acetaminophenyl)-6-chloro-1-methyl-1,2-dihydrophthalazine (**15b**).

This compound was prepared analogously to **15a** starting from **14b** (4.3 g, 14.4 mmoles) in tetrahydrofuran (100 ml) and methyllithium (1 *M* solution in tetrahydrofuran, 40 ml, 40 mmoles) and recrystallized from ethanol to give **15b** (2.3 g, 51 %) as yellow crystals: mp 236-238 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 200 MHz): δ 10.06 (1H, s), 8.31 (1H, s), 7.66 (2H, d, *J* = 8.8 Hz), 7.46 (2H, d, *J* = 8.8 Hz), 7.48 (1H, dd, *J* = 8.1, 1.8 Hz), 7.30 (1H, d, *J* = 8.1 Hz), 7.05 (1H, d, *J* = 1.8 Hz), 4.25 (1H, q, *J* = 6.4 Hz), 2.08 (3H, s), 1.37 (3H, d, *J* = 6.4 Hz).

Anal. Calcd. for $C_{17}H_{16}ClN_3O$ (313.79): C, 65.07, H, 5.14, Cl, 11.30, N, 13.39. Found: C, 65.31, H, 4.94, Cl, 11.24, N, 13.59.

4-(4-Acetaminophenyl)-6,7-dichloro-1-methyl-2-phenyloxycarbonyl-1,2-dihydrophthalazine (**16a**).

A solution of phenyl chloroformate (6 ml, 7.5 g, 47.8 mmoles), **15a** (3.2 g, 9 mmoles) and triethylamine (3 ml, 2.18 g, 22 mmoles) in tetrahydrofuran (50 ml) was stirred at 0 °C for 1 hour. The reaction mixture was washed with water (3 x 50 ml), dried ($MgSO_4$) and evaporated. The residue was separated by column chromatography (eluent: dichloromethane:methanol, 100:1) and recrystallized from ethanol to give **16a** (2.6 g, 62 %) as yellow crystals: mp 300-302 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 200 MHz): δ 10.20 (1H, s), 7.97 (1H, s), 7.77 (2 H, d, *J* = 8.9 Hz), 7.62 (2 H, d, *J* = 8.9 Hz), 7.50-7.25 (6 H, m), 5.76 (1 H, q, *J* = 6.4 Hz), 2.09 (3 H, s), 1.36 (3 H, d, *J* = 6.4 Hz).

Anal. Calcd. for $C_{24}H_{19}Cl_2N_3O_3$ (468.34): C, 61.55, H, 4.09, Cl, 15.14, N, 8.97. Found: C, 61.41, H, 4.13, Cl, 14.98, N, 8.90.

4-(4-Acetaminophenyl)-6-chloro-1-methyl-2-phenyloxycarbonyl-1,2-dihydrophthalazine (**16b**).

This compound was prepared analogously to **16a** starting from **15b** (1.7 g, 5.4 mmoles), triethylamine (1.2 ml, 0.87 g, 8.6 mmoles) and phenyl chloroformate (1.0 ml, 1.25 g, 8.0 mmoles) in tetrahydrofuran (10 ml) and recrystallized from isopropanol to give **16b** (1.75 g, 75 %) as yellow crystals: mp 130-131 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 200 MHz): δ 10.20 (1H, s), 7.77 (2 H, d, *J* = 8,4 Hz), 7.69 (1 H, d, *J* = 8.1, 1.8 Hz), 7.64 (1 H, s), 7.62 (2 H, d, *J* = 8.4 Hz), 7.49-7.41 (2 H, m), 7.33-7.23 (4 H, m), 5.74 (1 H, q, *J* = 6.6 Hz), 2.10 (3 H, s), 1.35 (3 H, d, *J* = 6.6 Hz).

Anal. Calcd. for $C_{24}H_{20}ClN_3O_3$ (433.89): C, 66.43, H, 4.65, Cl, 8.17, N, 9.68. Found: C, 66.05, H, 4.73, Cl, 7.98, N, 9.54.

4-(4-Acetaminophenyl)-2-(*N*-butylcarbamoyl)-6,7-dichloro-1-methyl-1,2-dihydrophthalazine (**17a**).

A solution of **16a** (2.5 g, 5.3 mmoles) and butylamine (0.7 ml, 0.51 g, 7 mmoles) in dimethylformamide (20 ml) was stirred at 60 °C for 3 hours. The reaction mixture was poured into ice (50 g). After filtration the product was recrystallized from isopropanol to give **17a** (1.8 g, 76 %) as yellow crystals: mp 127-128 °C. ^{1}H nmr (deuteriochloroform, 200 MHz): δ 7.67 (2H, d, *J* = 8.4 Hz), 7.56 (2H, d, *J* = 8.4 Hz), 7.45 (1H, s), 7.37 (1H, s), 7.33 (1H, s), 6.55 (1H, t, J = 5.9 Hz), 5.75 (1H, q, *J* = 6.6 Hz), 3.37-3.32 (2H, m), 2.24 (3H, s), 1.62-1.52 (2H, m), 1.43-1.32 (2H, m), 1.27 (3H, d, *J* = 6.6 Hz), 0.94 (3H, t, *J* = 7.0 Hz).

Anal. Calcd. for $C_{22}H_{24}Cl_2N_4O_2$ (447.37): C, 59.03, H, 5.40, Cl, 15.84, N, 12.52. Found: C, 58.89, H, 5.47, Cl, 15.63, N, 12.14.

4-(4-Acetaminophenyl)-2-(*N*-cyclopropylcarbamoyl)-6,7-dichloro-1-methyl-1,2-dihydrophthalazine (**17b**).

This compound was prepared analogously to **17a** starting from **16a** (1.0 g, 2.1 mmoles) in tetrahydrofuran (8 ml) and cyclopropylamine (2.0 ml, 0.12 g, 29 mmoles) and recrystallized from ethanol to give **17b** (0.67 g, 74 %) as yellow crystals: mp 157-158 °C. ^{1}H nmr (deuteriochloroform, 400 MHz): δ 7.75 (1H, s), 7.69 (2H, d, *J* = 8.5 Hz), 7.53 (2H, d, *J* = 8.5 Hz), 7.36 (1H, s), 7.33 (1H, s), 6.65 (1H, d, *J* = 1.8 Hz), 5.75 (1H, q, J = 6.7 Hz), 2.75-2.69 (1H, m), 2.25 (3H, s), 1.28 (3H, d, *J* = 6.7 Hz) 0.80-0.77 (2H, m), 0.59-0.58 (2H, m).

Anal. Calcd. for $C_{21}H_{20}Cl_2N_4O_2$ (431.33): C, 58.48, H, 4.67, Cl, 16.44, N, 12.99. Found: C, 58.18, H, 4.74, Cl, 16.37, N, 12.62.

4-(4-Acetaminophenyl)-6,7-dichloro-1-methyl-2-(pyrrolidine-1-carbonyl)-1,2-dihydrophthalazine (**17c**).

This compound was prepared analogously to **17a** starting from **16a** (0.8 g, 1.7 mmoles) in tetrahydrofuran (8 ml) and pyrrolidine (2.0 ml, 1.72 g, 24.2 mmoles) and recrystallized from isopropanol to give **17c** (0.6 g, 79 %) as yellow crystals: mp 119-120 °C. ^{1}H nmr (deuteriochloroform, 200 MHz): δ 7.67 (2H, d, *J* = 8.4 Hz), 7.56 (2H, d, *J* = 8.4 Hz), 7.38 (1H, s), 7.32 (1H, s), 5.45 (1H, q, *J* = 6.4 Hz), 3.82-3.66 (2H, m), 3.60-3.44 (2H, m), 2.24 (3H, s), 2.05-1.85 (2H, m), 1.85-1.60 (3H, m), 1.34 (3H, d, *J* = 6.4 Hz).

Anal. Calcd. for $C_{22}H_{22}Cl_2N_4O_2$ (445.35): C, 59.33, H, 4.98, Cl, 15.92, N, 12.58. Found: C, 58.99, H, 5.02, Cl, 16.22, N, 12.27.

4-(4-Acetaminophenyl)-2-(*N*-butylcarbamoyl)-6-chloro-1-methyl-1,2-dihydrophthalazine (**17d**).

This compound was prepared analogously to **17a** a starting from **16b** (1.5 g, 3.5 mmoles) in tetrahydrofuran (10 ml) and butylamine (3.0 ml, 2.2 g, 30 mmoles) and recrystallized from ethanol to give **17d** (1.4 g, 97 %) as yellow crystals: mp 125-127°C. ^{1}H nmr (deuteriochloroform, 200 MHz): δ 7.93 (1H, s), 7.71 (2H, d, *J* = 8.6 Hz), 7.58 (2H, d, *J* = 8.6 Hz), 7.41 (1H, dd, *J* = 8.1, 2.2 Hz), 7.27 (1H, d, *J* = 2.2 Hz), 7.16 (1H, d, *J* = 8.1 Hz), 6.60 (1H, t), 5.77 (1H, q, *J* = 7.0 Hz), 3.41-3.29 (2H, m), 2.25 (3H, s), 1.63-1.49 (2H, m), 1.47-1.32 (2H, m), 1.27 (3H, d, *J* = 6.6 Hz), 0.94 (3H, t, *J* = 7.0 Hz).

Anal. Calcd. for $C_{22}H_{25}ClN_4O_2$ (412.92): C, 63.99, H, 6.10, Cl, 8.59, N, 13.57. Found: C, 63.69, H, 6.12, Cl, 8.50, N, 13.28.

4-(4-Aminophenyl)-2-(*N*-butylcarbamoyl)-6,7-dichloro-1-methyl-1,2-dihydrophthalazine (**18a**).

A solution of **17a** (2.5 g, 5.6 mmoles) and aqueous sodium hydroxide solution (40 %, 8 ml) in methanol (20 ml) was refluxed for 3 hours. The reaction mixture was extracted with ethylacetate (3 x 20 ml), the organic layer was washed with brine (3 x 20 ml), dried ($MgSO_4$) and evaporated. Chromatography over silicagel (eluent: dichloromethane:methanol, 100:1) and recrystallization from isopropanol gave **18a** (2.1 g, 93 %) as yellow crystals: mp 101-102 °C. ^{1}H nmr (deuteriochloroform, 200 MHz): δ 7.43 (2H, d, *J* = 8.6 Hz), 7.41 (1H, s), 7.32 (1H, s), 6.88 (2H, d, *J* = 8.6 Hz), 6.55 (1H, t, *J* = 5.9 Hz), 5.74 (1H, q, *J* = 6.6 Hz), 3.36-3.32 (2H, m), 1.57-1.53 (2H, m), 1.41-1.35 (2 H, m), 1.26 (3H, d, *J* = 6.6 Hz), 0.94 (3H, t, *J* = 7.3 Hz).

Anal. Calcd. for $C_{20}H_{22}Cl_2N_4O$ (405.33): C, 59.26, H, 5.47, Cl, 17.49, N, 18.82. Found: C, 59.58, H, 5.49, Cl, 17.17, N, 13.61.

4-(4-Aminophenyl)-2-(*N*-cyclopropylcarbamoyl)-6,7-dichloro-1-methyl-1,2-dihydrophthalazine (**18b**).

This compound was prepared analogously to **18a** starting from **17b** (1.0 g, 2.3 mmoles), aqueous sodium hydroxide solution (40 %, 8 ml) in methanol (20 ml) and recrystallized from methanol to give **18b** (0.6 g, 67 %) as yellow crystals: mp 240-242 °C. ^{1}Hnmr (deuteriochloroform, 400 MHz): δ 7.44 (2H, d, *J* = 8.4 Hz), 7.39 (1H, s), 7.33 (1H, s), 6.96 (2H, d, *J* = 8.4 Hz), 6.63 (1H, d, *J* = 1.6 Hz), 5.74 (1H, q, *J* = 6.7 Hz), 2.74-2.70 (1H, m), 1.27 (3H, d, *J* = 6.7 Hz), 0.81-0.76 (2H, m), 0.60-0.56 (2H, m).

Anal. Calcd. for $C_{19}H_{18}Cl_2N_4O$ (389.29): C, 58.61, H, 4.63, Cl, 18.25, N, 14.40. Found: C, 58.35, H, 4.53, Cl, 18.05, N, 14.15.

4-(4-Aminophenyl)-2-(pyrrolidine-1-carbonyl)-6,7-dichloro-1-methyl-1,2-dihydrophthalazine (**18c**).

This compound was prepared analogously to **18a** starting from **17c** (1.1 g, 2.5 mmoles), aqueous sodium hydroxide solution (40 %, 8 ml) in methanol (20 ml) and recrystallized from ethanol to give **18c** (0.8 g, 79 %) as yellow crystals: mp 134-135 °C. ^{1}H nmr (deuteriochloroform, 400 MHz): δ 7.43 (1H, s), 7.40 (2H, d, *J* = 8.5 Hz), 7.30 (1H, s), 6.77 (2H, d, *J* = 8.5 Hz), 5.43 (1H, q, *J* = 6.6 Hz), 3.89 (2H, s), 3.80-3.65 (2H, m), 3.54-3.49 (2H, m), 2.00-1.90 (2H, m), 1.85-1.70 (2H, m), 1.33 (3H, d, *J* = 6.6).

Anal. Calcd. for $C_{20}H_{20}Cl_2N_4O$ (403.32): C, 59.56, H, 5.00, Cl, 17.58, N, 13.89. Found: C, 59.23, H, 5.09, Cl, 17.33, N, 13.58.

4-(4-Aminophenyl)-2-(*N*-butylcarbamoyl)-6-chloro-1-methyl-1,2-dihydrophthalazine (**18d**).

This compound was prepared analogously to **18a** starting from **17d** (1.1 g, 2.7 mmoles), aqueous sodium hydroxide solution (40 %, 8 ml) in methanol (20 ml). The product was recrystallized from ethanol, dissolved in ethyl acetate (10 ml) and hydrochloric acid solution in ethyl acetate was added to give the hydrochloride salt of **18d** (0.35 g, 32 %) as yellow crystals: mp 178-180 °C. ^{1}H nmr (dimethyl sulfoxide-d_6, 400 MHz): δ 7.73 (2H, d, *J* = 8.3 Hz), 7.61 (1H, dd, *J* = 8.2, 2.0 Hz), 7.52 (1H, d, *J* = 8.2 Hz), 7.29 (1H, t, *J* = 5.8 Hz), 7.19 (1H, d, *J* = 2.0 Hz), 7.17 (2H, d, *J* = 8.3 Hz), 5.68 (1H, q, *J* = 6.6 Hz), 4.65 (2H, bs), 3.19 (2H, q, *J* = 6.6 Hz), 1.50-1.43 (2 H, m), 1.33-1.24 (2H, m), 1.12 (3H, d, *J* = 6.6 Hz), 0.89 (3H, t, *J* = 7.3 Hz).

Anal. Calcd. for $C_{20}H_{24}Cl_2N_4O$ (406.34): C, 58.97, H, 5.94, Cl, 17.41, N, 13.75. Found: C, 58.78, H, 6.15, Cl, 17.22, N, 13.94.

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[12] For analogy see: S. A. Mahood and P. V. L. Schaffner, in Organic Syntheses, Coll. Vol. **II**., Wiley, New York, 1943, p 160 and B. A. Fox and T. L. Threlfall, in Organic Syntheses,Coll. Vol. **V**., Wiley, New York, 1973, p 346.

[13] A. Hirsch and D. G. Orphanos, *J. Heterocyclic Chem.* **3**, 38 (1966).