

**PYRIDAZINES, 69.¹ 2-FLUOROPHENYL 3-PYRIDAZINYL KETONE
AS A VERSATILE PRECURSOR FOR BENZO-ANNELATED
HETEROCYCLIC SYSTEMS**

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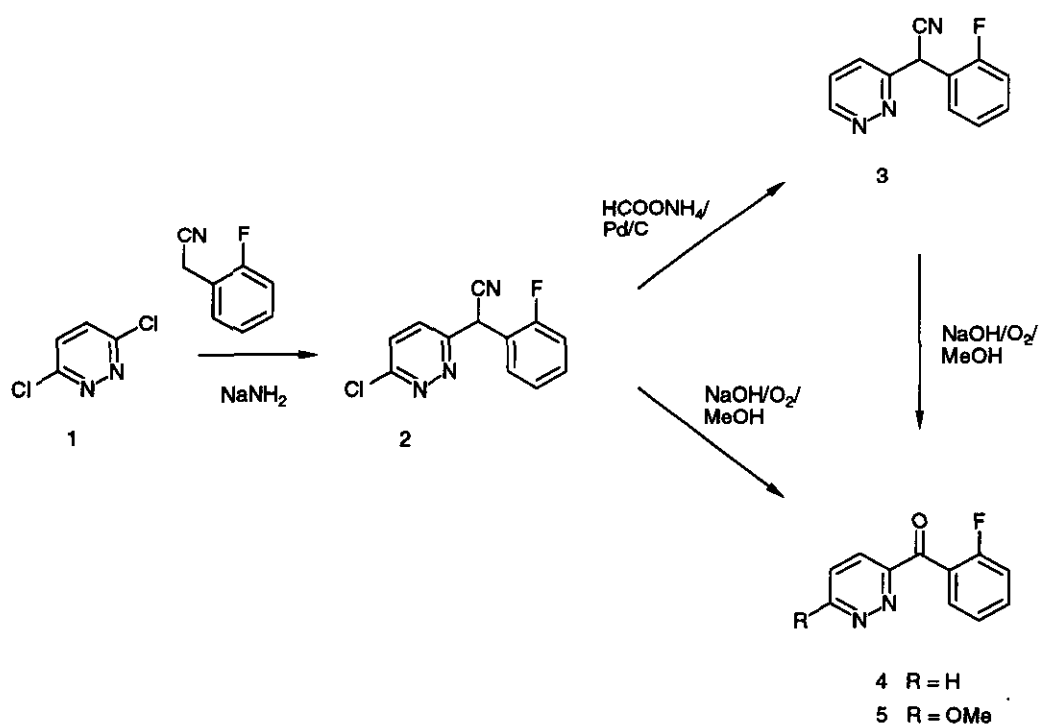
Abstract - The fluorophenyl pyridazinyl ketone (**4**), conveniently prepared from 3,6-dichloropyridazine, was shown to be a valuable precursor for so far not accessible pyridazinyl-substituted benzo-annelated five-, six-, or seven-membered heterocycles (**9**, **11**, **6a**, **b**) and for the two novel diazaacridones (**12**) and (**13**).

In continuation of an ongoing program aimed at the synthesis of bi- and tricyclic systems starting from functionalized aryl pyridazinyl ketones,² we here report on an efficient pathway to 2-fluorophenyl 3-pyridazinyl ketone (**4**) and on the exploitation of this novel bifunctional building block for the construction of a variety of pyridazinyl-substituted as well as pyridazine-fused heterocyclic ring systems.

Based on a previously published procedure³ permitting convenient access to phenyl 3-pyridazinyl ketone, the 2-fluorophenyl-3-pyridazinylmethane derivatives (**2-5**) were prepared starting from commercially available 3,6-dichloropyridazine (**1**). Thus, **1** was reacted with the sodium salt of 2-fluorophenylacetonitrile to give the nitrile (**2**). Catalytic transfer hydrogenation employing ammonium formate as the hydrogen source⁴ was found to permit reductive dechlorination without concomitant affection of the nitrile function.⁵ Compound (**3**), obtained in 55% overall yield, then smoothly underwent oxidative decyanation⁶ in methanolic sodium

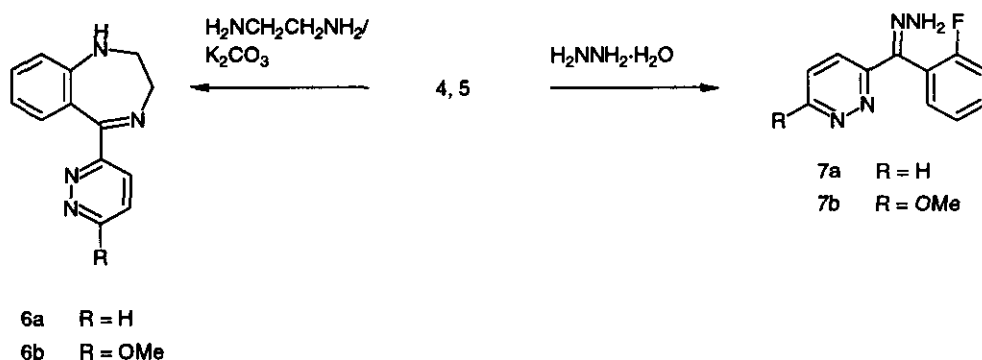
hydroxide to give the title ketone (4). Applying this oxidation procedure to the chloro-substituted nitrile (2) was found not only to generate the carbonyl function, but also to result in nucleophilic displacement of the chloro substituent by a methoxy group to afford compound (5).

Scheme 1



Preparation of compounds (6a, b), being of pharmaceutical interest as novel representatives of heteroaryl-substituted 1,4-benzodiazepines, could be achieved by reacting the fluoro ketones (4, 5) with ethylenediamine. Treatment of these ketones with hydrazine hydrate resulted in the formation of the hydrazones⁷ (7a, b) which, however, were found to withstand ring-closure to the corresponding indazoles (by intramolecular fluorine substitution) even under drastic conditions.⁸

Scheme 2

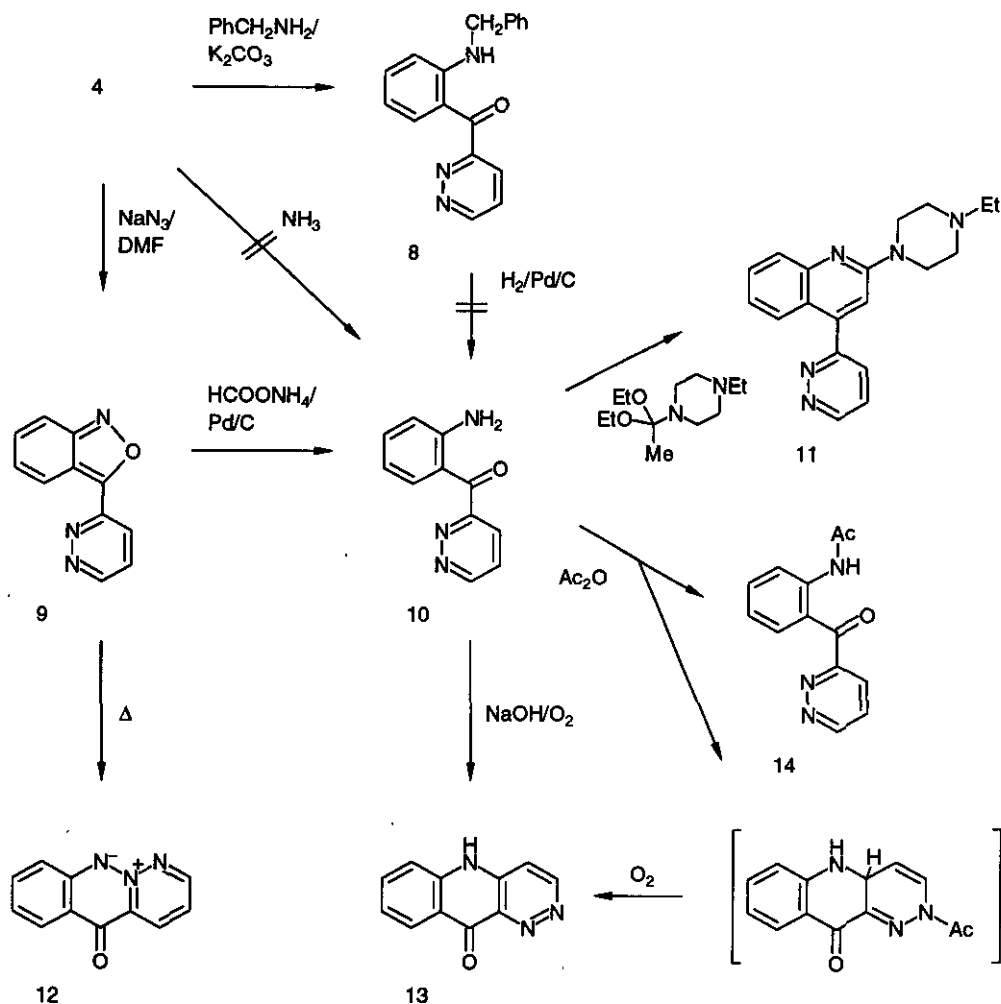


Similar to previous observations with 2-fluorophenyl 4-pyridazinyl ketone,⁹ treatment of the *o*-fluoro ketone (4) with sodium azide in refluxing dimethylformamide permits preparation of the pyridazinyl-substituted 2,1-benzisoxazole (9) via an intermediate azido compound, probably by an intramolecular 1,3-dipolar cycloaddition mechanism.¹⁰ The anthranil (9) thus obtained in high yield proved to be a valuable precursor for 2-aminophenyl 3-pyridazinyl ketone (compound 10) which represents a pyridazine analogue of 2-amino-benzophenone. It should be noted that this bifunctional building block¹¹ is neither accessible directly from the fluoro ketone (4) (by reaction with ammonia) nor by hydrogenolytic debenzoylation (Pd/C) of the easily available benzylamino ketone (8). The synthesis of compound (10) now was accomplished by reductive opening (catalytic transfer hydrogenation,⁴ ammonium formate, Pd/C) of the isoxazole ring in 9.

The synthetic utility of the amino ketone (10) could be demonstrated by its convenient conversion into the quinoline derivative (11) which was considered an interesting target compound in view of the recently reported anti-ulcer activity of 4-aryl-substituted 2-piperazinylquinolines.¹² Moreover, intramolecular $\text{S}_{\text{N}}^{\text{H}}$ reaction of 10 was found to represent an efficient route to the novel diazaacridone (13):¹³ refluxing of 10 in aqueous sodium hydroxide (air oxygen as the oxidant) gives 13 in almost quantitative yield.

A first hint for the susceptibility of pyridazine C-4 in compound (10) towards attack of the amino function was given on attempted preparation of the amide (14). Along with a 58% yield of 14, the tricyclic compound (13) was isolated as a side product (25% yield). Formation of the latter under these conditions has to be interpreted in terms of nucleophilic attack of the amino function to an initially formed *N*-1-acetylated pyridazinium species, oxidation by air oxygen and subsequent loss of the acetyl moiety. It is of interest to note that in the case of the isomeric 2-aminophenyl 4-pyridazinyl ketone, an intermediate *N*-acetyldihydrodiazaacridone had been isolated.^{9,14}

Scheme 3



Prompted by previous observations of intramolecular N-N bond formation on pyrolysis of 2-pyridyl-substituted 2,1-benzisoxazoles,¹⁵ we finally could elaborate an effective synthesis of the mesoionic tricyclic compound (12) (an isomer of the diazaacridone 13), which represents a hitherto unknown ring system: refluxing of the anthranil (9) in 1,2,4-trichlorobenzene gave a 75% yield of the inner salt (12) which was fully characterized by elemental analysis, ms, ir, ^1H -nmr and ^{13}C -nmr data (see Experimental).

In summary, the fluorophenyl pyridazinyl ketone (4) proved to be a precursor for so far not accessible pyridazinyl-substituted derivatives of 2,1-benzisoxazole, quinoline, and 1,4-benzodiazepine. Moreover, compound (4) provides convenient access to the two diazaacridones (12) and (13).

EXPERIMENTAL

All melting points were determined on a Kofler hot-stage microscope and are uncorrected. Ir spectra were recorded for KBr pellets on a Jasco IRA-1 and on a Perkin Elmer 1605 FT-IR spectrophotometer; ^1H -nmr spectra were recorded on a Varian EM 390 (90 MHz), a Bruker AC 80 (80 MHz), or a Bruker AM 400 (400 MHz) spectrometer with TMS as internal reference (chemical shifts in δ ppm), the ^{13}C -nmr spectrum was recorded on the Bruker AM 400 instrument. Mass spectra were obtained on a Hewlett-Packard 5890A/5970B GC/MSD or on a Shimadzu GC/MS-QP 1000 instrument. Column chromatography was carried out on Merck Kieselgel 60, 0.063-0.200 mm. Microanalyses were performed by Mag. J. Theiner, Institute of Physical Chemistry, University of Vienna.

2-(2-Fluorophenyl)-2-(6-chloro-3-pyridazinyl)acetonitrile (2)

To a solution of 2-fluorophenylacetonitrile (20.27 g, 150 mmol) in 500 ml of toluene (dried over molecular sieve, $4\text{\AA}$), sodium amide (11.7 g, 300 mmol) was added at 0°C . After stirring for 10 min, 3,6-dichloropyridazine (22.35 g, 150 mmol) was added in small portions, the ice bath was removed, and stirring was continued for 3 h. After cooling, the mixture was neutralized with 2 *N* H_2SO_4 and extracted exhaustively with toluene. The organic layer was dried (Na_2SO_4), concentrated *in vacuo* and the residue was subjected to flash chromatography (dichloromethane) to give 26.0 g (70%) of a yellow oil, which was used without purification for further reactions. A sample of the product was recrystallized from ethanol to afford colorless needles, mp $67\text{--}69^\circ\text{C}$. *Anal.* Calcd for $\text{C}_{12}\text{H}_7\text{N}_3\text{ClF}$: C, 58.20; H, 2.85; N, 16.97. Found: C, 58.05; H, 2.82; N, 16.85. *Ms*: m/z (rel. int.) 247/249 (54/17%, M^+), 228/230 (100/35), 211 (10), 158 (12), 134 (10), 107 (13). Ir (cm^{-1}): 2240 (CN). ^1H -Nmr (CDCl_3) δ : 5.80 (s, 1 H, PhCH), 6.9-7.8 (m, 6 H, H-4, H-5, C_6H_4).

2-(2-Fluorophenyl)-2-(3-pyridazinyl)acetonitrile (3)

A mixture of **2** (9.90 g, 40 mmol), ammonium formate (7.56 g, 120 mmol) and Pd/C (10%; 1.25 g) in methanol (250 ml) was stirred under an atmosphere of argon at 40°C . Additional portions of ammonium formate were added until the starting material was completely consumed (tlc monitoring; ethyl acetate). After removal of the catalyst and evaporation of the solvent, the residue thus obtained was partitioned between dichloromethane and water. The organic layer was dried (Na_2SO_4) and evaporated. Recrystallisation from ethanol gave 6.84 g (77%) of **3** as colorless crystals, mp $91\text{--}92^\circ\text{C}$. *Anal.* Calcd for $\text{C}_{12}\text{H}_8\text{N}_3\text{F}$: C, 67.60; H, 3.78; N, 19.71. Found: C, 67.53; H, 3.65; N, 19.78. *Ms*: m/z (rel. int.) 213 (45%, M^+), 212 (36), 194 (100), 158 (10), 107 (11). Ir (cm^{-1}): 2240 (CN). ^1H -Nmr (CDCl_3) δ : 5.85 (s, 1 H, PhCH), 7.0-7.9 (m, 6 H, H-4, H-5, C_6H_4), 9.20 (dd, $J_{4-6} = 2\text{ Hz}$, $J_{5-6} = 5\text{ Hz}$, 1 H, H-6).

General Procedure for the Preparation of the Ketones (4) and (5)

To a solution of **3** (5.3 g, 25 mmol) or **2** (6.2 g, 25 mmol), respectively, and benzyltriethylammonium chloride (450 mg, 2 mmol) in 150 ml of methanol, 5 ml of 30% aqueous NaOH were added dropwise. The solution was stirred vigorously at room temperature, while a stream of air was bubbled through, until the starting material was completely consumed (tlc monitoring; light petroleum/ethyl acetate, 1:1). Water (150 ml) was added, and the mixture was extracted exhaustively with dichloromethane. The extract was dried (Na_2SO_4) and evaporated to give a dark residue.

2-Fluorophenyl 3-Pyridazinyl Ketone (4)

The oily residue obtained as described above was purified by flash chromatography (light petroleum/ethyl acetate, 1:1) to give 3.8 g (75%) of **4** as colorless crystals, mp 79-80°C (ethanol/water). *Anal.* Calcd for $\text{C}_{11}\text{H}_7\text{N}_2\text{OF}$: C, 65.35; H, 3.49; N, 13.86. Found: C, 65.37; H, 3.52; N, 13.94. Ms: m/z (rel. int.) 202 (46%, M^+), 174 (66), 123 (100), 95 (51), 75 (30). Ir (cm^{-1}): 1660 (CO). $^1\text{H-Nmr}$ (CDCl_3) δ : 7.1-8.0 (m, 5 H, H-5, C_6H_4), 8.20 (dd, $J_{4,5} = 8$ Hz, $J_{4,6} = 2$ Hz, 1 H, H-4), 9.40 (dd, $J_{4,6} = 2$ Hz, $J_{5,6} = 5$ Hz, 1 H, H-6).

2-Fluorophenyl 6-Methoxy-3-pyridazinyl Ketone (5)

Water (100 ml) was added to the solid residue obtained as described above, the precipitate was collected and washed with water. Yield: 4.4 g (76%) of colorless needles, mp 106-107°C (ethanol/water). *Anal.* Calcd for $\text{C}_{12}\text{H}_9\text{N}_2\text{O}_2\text{F}$: C, 62.07; H, 3.91; N, 12.06. Found: C, 62.27; H, 4.00; N, 11.99. Ms: m/z (rel. int.) 232 (52%, M^+), 204 (31), 189 (61), 123 (100), 95 (54), 75 (25). Ir (cm^{-1}): 1660 (CO). $^1\text{H-Nmr}$ (CDCl_3) δ : 4.25 (s, 3 H, CH_3), 7.0-7.9 (m, 5 H, H-5, C_6H_4), 8.15 (d, $J = 9$ Hz, 1 H, H-4).

General Procedure for the Preparation of the 1,4-Benzodiazepines (6a) and (6b)

A mixture of the appropriate 2-fluorophenyl 3-pyridazinyl ketone (**4** or **5**, respectively, 1 mmol), ethylenediamine (600 mg, 10 mmol), and K_2CO_3 (138 mg, 1 mmol) in toluene (15 ml) was refluxed for 24 h. After cooling, the mixture was extracted with 2 *N* HCl; the aqueous layer was made alkaline (pH = 8) with 2 *N* NaOH and was extracted exhaustively with dichloromethane. The extract was washed with water, dried (Na_2SO_4) and evaporated.

2,3-Dihydro-5-(3-pyridazinyl)-1*H*-1,4-benzodiazepine (6a)

Purification by column chromatography (ethyl acetate/methanol, 4:1) afforded 170 mg (75%) of **6a** as yellow crystals, mp 125-126°C (ethyl acetate/charcoal). *Anal.* Calcd for $\text{C}_{13}\text{H}_{12}\text{N}_4$: C, 69.62; H, 5.39; N, 24.98. Found: C, 69.79; H, 5.33; N, 24.94. Ms: m/z (rel. int.) 224 (100%, M^+), 223 (82), 196 (49), 169 (21), 168 (23), 140 (10), 117 (13), 115 (11), 77 (10). Ir (cm^{-1}): 3600-3000 (br, NH). $^1\text{H-Nmr}$ (CDCl_3) δ : 3.7-3.9 (m, 2

H, CH₂), 4.1-4.2 (m, 2 H, CH₂), 4.2-4.5 (br m, 1 H, NH), 6.5-7.4 (m, 4 H, C₆H₄), 7.55 (dd, J₄₋₅ = 9 Hz, J₅₋₆ = 5 Hz, 1 H, H-5), 7.95 (dd, J₄₋₅ = 9 Hz, J₄₋₆ = 2 Hz, 1 H, H-4), 9.20 (dd, J₄₋₆ = 2 Hz, J₅₋₆ = 5 Hz, 1 H, H-6).

2,3-Dihydro-5-(6-methoxy-3-pyridazinyl)-1H-1,4-benzodiazepine (6b)

Recrystallisation from ethanol/charcoal afforded 178 mg (70%) of **6b** as yellow crystals, mp 175-176°C. *Anal.* Calcd for C₁₄H₁₄N₄O: C, 66.13; H, 5.55; N, 22.03. Found: C, 55.92; H, 5.80; N, 21.74. Ms: *m/z* (rel. int.) 254 (100%, M⁺), 226 (34), 154 (9), 77 (10). Ir (cm⁻¹): 3300 (NH). ¹H-Nmr (CDCl₃) δ: 3.5-3.9 (m, overlapped by br m, together 3 H, CH₂, NH), 4.0-4.2 (m, 2 H, CH₂), 4.20 (s, 3 H, OCH₃), 6.6-7.4 (m, overlapped by d, J = 9 Hz, together 5 H, H-5, C₆H₄), 8.00 (d, J = 9 Hz, 1 H, H-4).

General Procedure for the Preparation of the Hydrazones (7a) and (7b)

A mixture of the appropriate 2-fluorophenyl 3-pyridazinyl ketone (**4** or **5**, respectively, 1 mmol) and hydrazine hydrate (3 ml; 80% aqueous solution) was heated to 120°C for 30 min. After addition of 20 ml of water, the suspension was extracted exhaustively with dichloromethane. The extract was washed with water, dried (Na₂SO₄) and evaporated.

2-Fluorophenyl 3-Pyridazinyl Ketone Hydrazone (7a)

Recrystallisation from ethyl acetate gave 195 mg (90%) of **7a** as colorless needles, mp 152-153°C. *Anal.* Calcd for C₁₁H₉N₄F: C, 61.11; H, 4.20; N, 25.91. Found: C, 61.34; H, 4.23; N, 26.04. Ms: *m/z* (rel. int.) 216 (25%, M⁺), 215 (100), 197 (14), 187 (10), 168 (10), 133 (27). Ir (cm⁻¹): 3440, 3320, 3230 (NH₂). ¹H-Nmr (CDCl₃) δ: 5.99 (br s, 2 H, NH₂), 7.2-7.5 (m, 5 H, H-5, C₆H₄), 8.17 (dd, J₄₋₅ = 9 Hz, J₄₋₆ = 2 Hz, 1 H, H-4), 9.01 (dd, J₄₋₆ = 2 Hz, J₅₋₆ = 5 Hz, 1 H, H-6).

2-Fluorophenyl 6-Methoxy-3-pyridazinyl Ketone Hydrazone (7b)

Column chromatography (ethyl acetate) gave 104 mg (42%) of **7b** as colorless crystals, mp 139-140°C (ethyl acetate). *Anal.* Calcd for C₁₂H₁₁N₄OF: C, 58.53; H, 4.50; N, 22.75. Found: C, 58.62; H, 4.62; N, 22.98. Ms: *m/z* (rel. int.) 245 (100%, M⁺), 227 (11). Ir (cm⁻¹): 3430, 3320, 3250 (NH). ¹H-Nmr (CDCl₃) δ: 4.10 (s, 3 H, OCH₃), 5.85 (br s, 2 H, NH₂), 6.95 (d, J = 9 Hz, 1 H, H-5), 7.1-7.6 (m, 4 H, C₆H₄), 8.15 (d, J = 9 Hz, 1 H, H-4).

2-Benzylaminophenyl 3-Pyridazinyl Ketone (8)

A mixture containing **4** (202 mg, 1 mmol), benzylamine (1070 mg, 10 mmol), and K₂CO₃ (138 mg, 1 mmol) in 20 ml of toluene was refluxed for 36 h. After filtration, the solution was evaporated and the residue was partitioned between dichloromethane and 0.1 N HCl. The organic layer was dried (Na₂SO₄) and evaporated. Recrystallisation from diisopropyl ether/ethanol afforded 238 mg (82%) of **8** as yellow crystals, mp 97°C.

Anal. Calcd for $C_{18}H_{15}N_3O$: C, 74.72; H, 5.23; N, 14.52. Found: C, 74.80; H, 5.05; N, 14.63. Ms: m/z (rel. int.) 289 (39%, M^+), 270 (100), 260 (90), 184 (21), 182 (17), 180 (24), 91 (55), 77 (16), 65 (17). Ir (cm^{-1}): 3380 (NH), 1630 (CO). 1H -Nmr ($CDCl_3$) δ : 4.55 (d, $J = 6$ Hz, s after addition of D_2O , 2 H, $PhCH_2$), 6.5-8.0 (m, 11 H, H-4, H-5, C_6H_4 , C_6H_5), 9.25-9.5 (br t, overlapped by dd, $J_{4-6} = 2$ Hz, $J_{5-6} = 5$ Hz, together 2 H, NH, H-6).

3-(3-Pyridazinyl)-2,1-benzisoxazole (9)

A suspension of **4** (202 mg, 1 mmol) and NaN_3 (78 mg, 1.2 mmol) in 10 ml of DMF was stirred at $120^\circ C$ for 15 h. After evaporation of the solvent, water (10 ml) was added, the precipitate was filtered off and washed thoroughly with water. The filtrate was extracted exhaustively with dichloromethane; the organic layer was dried (Na_2SO_4) and evaporated. Recrystallisation of the combined materials from ethanol afforded 150 mg (76%) of **9** as colorless needles, mp $165-166^\circ C$. *Anal.* Calcd for $C_{11}H_7N_3O$: C, 67.00; H, 3.58; N, 21.31. Found: C, 66.95; H, 3.60; N, 21.33. Ms: m/z (rel. int.) 198 (79%), 197 (100, M^+), 196 (76), 168 (30), 142 (34), 140 (36), 114 (63), 90 (48), 63 (85). 1H -Nmr ($CDCl_3$) δ : 7.20 (dd, $J_{4-5} = 9$ Hz, $J_{5-6} = 6$ Hz, 1 H, H-5), 7.41 (ddd, $J_{4-6} = 1$ Hz, $J_{5-6} = 6$ Hz, $J_{6-7} = 9$ Hz, 1 H, H-6), 7.66 (d, $J_{6-7} = 9$ Hz, 1 H, H-7) overlapped by 7.68 (dd, $J_{4-5} = 8$ Hz, $J_{5-6} = 5$ Hz, 1 H, pyridazine H-5), 8.27 (dd, $J_{4-5} = 8$ Hz, $J_{4-6} = 1.5$ Hz, 1 H, pyridazine H-4), 8.50 (d, $J_{4-5} = 9$ Hz, 1 H, H-4), 9.23 (dd, $J_{4-6} = 1.5$ Hz, $J_{5-6} = 5$ Hz, 1 H, pyridazine H-6).

2-Aminophenyl 3-Pyridazinyl Ketone (10)

A mixture of **9** (197 mg, 1 mmol), ammonium formate (68 mg, 1.1 mmol) and Pd/C (10%; 60 mg) in 25 ml of methanol was stirred under an atmosphere of N_2 at $60^\circ C$. Additional portions of ammonium formate were added until the starting material was completely consumed (tlc monitoring; dichloromethane/methanol, 9:1). After removal of the catalyst and evaporation of the solvent, the residue was partitioned between dichloromethane and water. The organic layer was dried (Na_2SO_4), evaporated and recrystallized from ethyl acetate to give 131 mg (66%) of **10** as yellow crystals, mp $195^\circ C$. *Anal.* Calcd for $C_{11}H_9N_3O$: C, 66.31; H, 4.55; N, 21.09. Found: C, 66.04; H, 4.41; N, 20.86. Ms: m/z (rel. int.) 199 (35%, M^+), 170 (100), 117 (11), 92 (19), 65 (22). Ir (cm^{-1}): 3430, 3300, 3170 (NH_2), 1625 (CO). 1H -Nmr ($CDCl_3$) δ : 6.48 (ddd, $J_{3-5} = 1$ Hz, $J_{4-5} = 7$ Hz, $J_{5-6} = 8$ Hz, 1 H, aniline H-5), 6.88 (dd, $J_{3-4} = 9$ Hz, $J_{3-5} = 1$ Hz, 1 H, aniline H-3), 7.3-7.4 (m, 2 H, aniline H-4, aniline H-6), 7.46 (br s, 2 H, NH_2), 7.89 (dd, $J_{4-5} = 8$ Hz, $J_{5-6} = 5$ Hz, 1 H, H-5), 7.97 (dd, $J_{4-5} = 8$ Hz, $J_{4-6} = 2$ Hz, 1 H, H-4), 9.37 (dd, $J_{4-6} = 2$ Hz, $J_{5-6} = 5$ Hz, 1 H, H-6).

2-(4-Ethyl-1-piperazinyl)-4-(3-pyridazinyl)quinoline (11)

A mixture of dimethylacetamide dimethyl acetal (1.33 g, 10 mmol) and dry 1-ethylpiperazine (2.28 g, 20 mmol) was heated to $190^\circ C$ for a period of 5 h during which a slow stream of dry N_2 was bubbled through the solution. After cooling, compound (**10**) (199 mg, 1 mmol) was added and the mixture was heated to $130^\circ C$ for

2 h. The excess reagent was removed *in vacuo* and the residue was subjected to column chromatography (dichloromethane/methanol, 9:1) and subsequent recrystallisation from ethyl acetate to yield 170 mg (53%) of **11** as colorless crystals, mp 120-124°C. *Anal.* Calcd for $C_{19}H_{21}N_5 \cdot \frac{1}{2}H_2O$: C, 69.49; H, 6.75; N, 21.32. Found: C, 69.77; H, 6.45; N, 21.05. *Ms:* m/z (rel. int.) 319 (12%, M^+), 235 (100), 97 (27), 84 (25), 57 (14). 1H -Nmr ($CDCl_3$) δ : 1.20 (t, $J = 7$ Hz, 3 H, CH_2CH_3), 2.3-2.6 (m, 6 H, NCH_2), 3.8-4.0 (m, 4 H, $ArNCH_2$), 6.90 (s, 1 H, quinoline H-3), 7.1-7.9 (m, 6 H, quinoline-H, pyridazine H-4, pyridazine H-5), 9.35 (dd, $J_{4,6} = 2$ Hz, $J_{5,6} = 5$ Hz, 1 H, pyridazine H-6).

5,10-Dihydro-5-oxopyridazino[2,3-*b*]cinnolin-11-ium Hydroxide Inner Salt (**12**)

A solution of the 2,1-benzisoxazole (**9**) (197 mg, 1 mmol) in 20 ml of 1,2,4-trichlorobenzene was heated to 220°C for 20 h. After removal of the solvent *in vacuo*, the solid residue was purified by column chromatography (ethyl acetate/methanol, 3:2) to yield 147 mg (75%) of **12** as yellow crystals, mp 249-250°C (ethanol). *Anal.* Calcd for $C_{11}H_7N_3O$: C, 67.00; H, 3.58; N, 21.31. Found: C, 66.83; H, 3.66; N, 21.24. *Ms:* m/z (rel. int.) 197 (100%, M^+). *Ir* (cm^{-1}): 1630 (CO), 1585. 1H -Nmr ($DMSO-d_6$) δ : 7.52 (ddd, $J = 8$ Hz, 5 Hz, 3 Hz, 1 H, cinnoline-H), 7.57 (dd, $J_{2,3} = 5$ Hz, $J_{3,4} = 9$ Hz, 1 H, H-3), 7.85-7.9 (m, 2 H, cinnoline-H), 8.21 (d, $J = 9$ Hz, 1 H, cinnoline-H), 8.84 (dd, $J_{2,4} = 2$ Hz, $J_{3,4} = 9$ Hz, 1 H, H-4), 9.15 (dd, $J_{2,3} = 5$ Hz, $J_{2,4} = 2$ Hz, 1 H, H-2). ^{13}C -Nmr ($DMSO-d_6$) δ : 169.5, 152.9, 147.4, 134.2, 133.6, 132.7, 125.8, 125.5, 123.9, 120.9, 118.1.

Pyridazino[4,3-*b*]quinolin-10(5*H*)-one (**13**)

A suspension of **10** (199 mg, 1 mmol) in 20 ml of 2 *N* aqueous NaOH was refluxed for 36 h. After cooling, the solution was made weakly acidic (ph = 4-5) with 2 *N* aqueous HCl. The precipitate was collected and washed with water and methanol to give 180 mg (91%) of **13** as pale yellow crystals, mp >300°C. *Anal.* Calcd for $C_{11}H_7N_3O$: C, 67.00; H, 3.58; N, 21.31. Found: C, 66.75; H, 3.82; N, 21.03. *Ms:* m/z (rel. int.) 197 (100%, M^+), 168 (20), 141 (30), 140 (31), 114 (34), 51 (32). *Ir* (cm^{-1}): 3300-2600 (br, NH), 1650 (CO). 1H -Nmr ($CDCl_3$) δ : 7.37 (dd, $J_{7,8} = 8$ Hz, $J_{8,9} = 9$ Hz, H-8), 7.55 (d, $J_{6,7} = 9$ Hz, 1 H, H-6), 7.67 (d, $J_{3,4} = 6$ Hz, 1 H, H-4), 7.83 (ddd, $J_{6,7} = 9$ Hz, $J_{7,8} = 8$ Hz, $J_{7,9} = 1.5$ Hz, 1 H, H-7), 8.30 (dd, $J_{8,9} = 9$ Hz, $J_{7,9} = 1.5$ Hz, 1 H, H-9), 9.91 (d, $J_{3,4} = 6$ Hz, 1 H, H-3).

N-[2-(3-Pyridazinylcarbonyl)phenyl]acetamide (**14**)

A solution of **10** (199 mg, 1 mmol) in 20 ml (212 mmol) of acetic anhydride was heated to 100°C for 20 min. After removal of the reagent *in vacuo*, the residue was taken up in dichloromethane. Insoluble material (compound **13**) was filtered off, and the filtrate was evaporated. The crude product was purified by column chromatography (dichloromethane/methanol, 94:6) to give 140 mg (58%) of **14** as colorless crystals, mp 112-113°C. *Anal.* Calcd for $C_{13}H_{11}N_3O_2$: C, 64.72; H, 4.60; N, 17.42. Found: C, 64.70; H, 4.52; N, 17.39. *Ms:*

m/z (rel. int.) 241 (19%, M^+), 213 (14), 212 (16), 199 (31), 198 (36), 171 (48), 170 (100), 122 (27), 120 (15), 92 (21), 65 (16). Ir (cm^{-1}): 3300 (NH), 1700 (CO), 1650 (CO). $^1\text{H-Nmr}$ (CDCl_3) δ : 2.25 (s, 3 H, CH_3), 7.0-8.2 (m, overlapped by dd, $J_{4-5} = 8 \text{ Hz}$, $J_{5-6} = 5 \text{ Hz}$ and dd, $J_{4-5} = 8 \text{ Hz}$, $J_{4-6} = 2 \text{ Hz}$, together 5 H, aniline H-4, H-5, H-6, pyridazine H-5, H-4), 8.80 (d, $J = 9 \text{ Hz}$, 1 H, aniline H-3), 9.40 (dd, $J_{4-6} = 2 \text{ Hz}$, $J_{5-6} = 5 \text{ Hz}$, 1 H, pyridazine H-6), 11.0-11.3 (br s, 1 H, NH).

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