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On the Chemistry of Pyridazines, XXXVI [1, 2]: Novel Diaza-Analogs of 10,11-Dihydro-5*H*-dibenzo[a,d]cyclohepten-5-one

Wolfgang Dostal, Gottfried Heinisch*, and Gerhard Lötsch

Institute of Pharmaceutical Chemistry, University of Vienna, A-1090 Wien, Österreich

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Procedures for the preparation of the novel tricyclic ketones 10,11-dihydro-5*H*-benzo[4,5]cyclohepta[1,2—*d*]pyridazin-5-one (**3**), 5,6-dihydro-11H-benzo-[4,5]cyclohepta[2,1—*c*]pyridazin-11-one (**4**), and 10,11-dihydro-5*H*-benzo[4,5]-cyclohepta[1,2—*c*]pyridazin-5-one (**5**) starting from a preformed 1,2-diazine system are proposed. The key intermediates **7**, **19**, and **11** are prepared from (2-phenylethyl)pyridazines **6** and **18** by introduction of a carboxylic functionality via homolytic alkoxycarbonylation or via a sulfonyl *Reissert*-type reaction.

[Keywords: Diaza-dihydrodibenzocycloheptenones; (2-Phenylethyl)pyridazines; Homolytic alkoxycarbonylation; Reissert-type reaction]

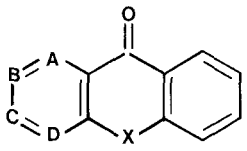
Zur Chemie von Pyridazinen, 36. Mitt. [1, 2]:
Neuartige Diazaanaloga des 10,11-Dihydro-5H-dibenzo[a,d]cyclohepten-5-ons

Methoden zur Darstellung der neuen trizyklischen Ketone 10,11-Dihydro-5*H*-benzo[4,5]cyclohepta[1,2—*d*]pyridazin-5-on (**3**), 5,6-Dihydro-11*H*-benzo-[4,5]cyclohepta[2,1—*c*]pyridazin-11-on (**4**) und 10,11-Dihydro-5*H*-benzo[4,5]-cyclohepta[1,2—*c*]pyridazin-5-on (**5**) ausgehend von einem präformierten 1,2-Diazinsystem werden vorgeschlagen. Die Schlüsselbausteine dieser Synthesen **7**, **19** und **11** werden durch Einführung einer Carboxylfunktion in die (2-Phenylethyl)pyridazine **6** und **18** über homolytische Alkoxycarbonylierung bzw. eine Sulfonyl-*Reissert*-Reaktion erhalten.

Introduction

Ketones derived from tricyclic systems like acridane, xanthene, thioxanthene and 10,11-dihydro-5*H*-dibenzo[a,d]cycloheptene represent important building blocks in syntheses of a variety of valuable drug substances. Accordingly, there is continuing interest in heteroaromatic and particularly in azaaromatic analogs of these compounds. Recently we succeeded in the preparation of novel diaza-analoguous systems of types **1**

and **2** [3, 4]. The present report deals with the synthesis of the three theoretically possible pyridazine-analogs **3–5**. Whereas the chemistry and pharmacology of linear pyridine-annelated benzocycloheptenes were subject of extensive studies [5], the 1,2-diazine isosteric systems so far remained unexplored.



1–5

	A	B	C	D	X
1	CH	N	N	CH	NH,NR,O,S
2	CH	CH	N	N	NH,NR,O,S
3	CH	N	N	CH	CH_2-CH_2
4	N	N	CH	CH	CH_2-CH_2
5	CH	CH	N	N	CH_2-CH_2

Results and Discussion

In order to gain access to tricyclic ketones **3–5** bearing no additional substituents in the 1,2-diazine moiety, approaches (as outlined in Schemes 1 and 2), employing vicinally disubstituted pyridazines as the key intermediates, were chosen.

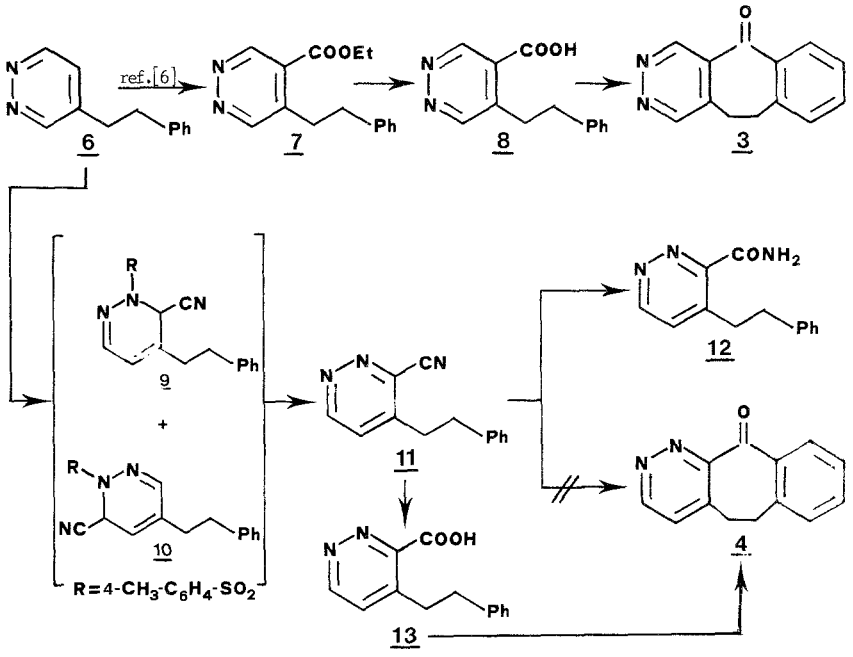
According to Ref. [6] an alkoxycarbonyl group can be introduced with a high degree of regioselectivity into C-5 of 4-(2-phenylethyl)pyridazine (**6**) by means of radicalic substitution in a two-phase system. The free carboxylic acid **8** obtained upon alkaline hydrolysis of **7** turned out to cyclize smoothly when heated in polyphosphoric acid (*PPA*) affording 10,11-dihydro-5*H*-benzo[4,5]-cyclohepta[1,2—*d*]pyridazin-5-one (**3**) in 65% yield.

Introduction of a carboxylic functionality into C-3 of **6** was achieved by applying a reaction sequence recently employed in high yield syntheses of 3-pyridazinecarbonitriles [7]. In contrast to the findings with 4-methylpyridazine [7], the reaction of **6** with 4-toluenesulfonyl chloride/trimethylsilyl cyanide in the presence of catalytic amounts of aluminium trichloride, however, afforded a mixture of two isomers (**9**, **10**) as indicated by the ^{1}H-nmr spectra of the products resulting upon detosylation mediated by 1,8-diazabicyclo[5.4.0]undec-7-ene (*DBU*)*. Accordingly, the required phenylethylpyridazinecarbonitrile **11** is obtained in only moderate yield (17% based on starting **6**). Heating of the

* The formation of compound **10** is evidenced by a one-proton doublet at 9.2 ppm (J = 2 Hz) in the spectrum of the second reaction product separable by mplc after treatment of the **9** + **10** mixture with *DBU*. In the ^{1}H-nmr spectrum of compound **11** the signal of H-6 is characterized by a coupling constant of 6 Hz.

nitrile **11** in a large excess of *PPA* (150 °C, 6 hours) only resulted in the formation of the carboxamide **12**. The desired ring closure reaction to give the tricyclic ketone **4**, however, can be accomplished smoothly if the carboxylic acid **13**, conveniently accessible from **11**, is subjected to these conditions.

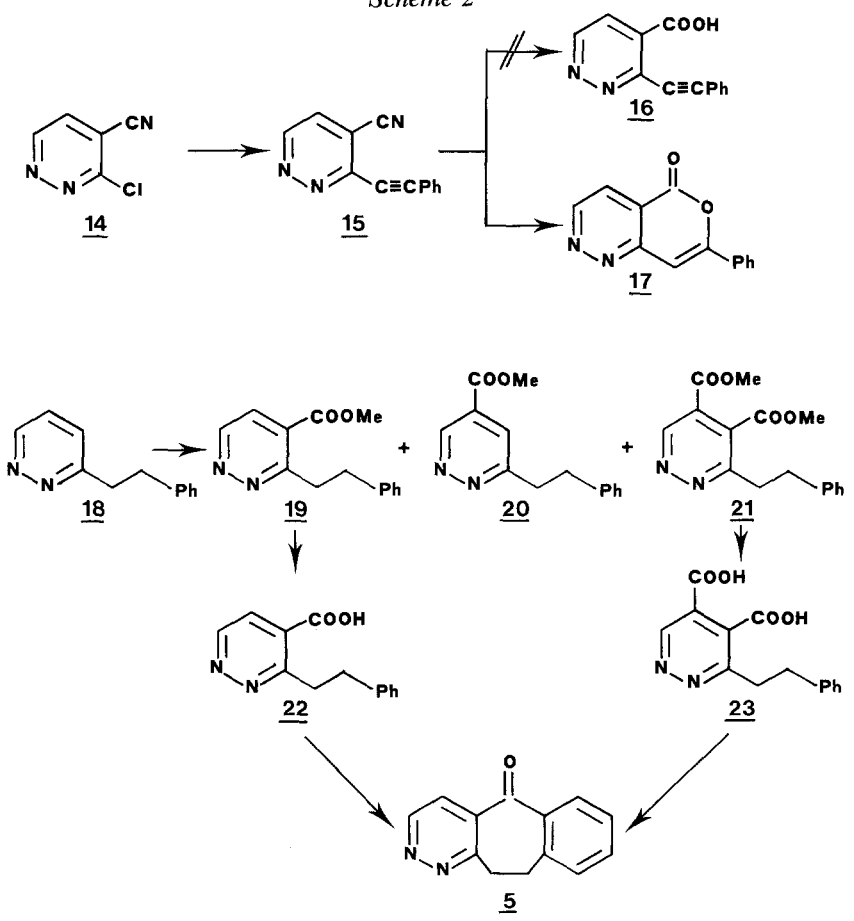
Scheme 1



Initial attempts to employ 3-phenylethinyl-4-pyridazinecarbonitrile (**15**), obtained in high yield by a Pd-assisted cross coupling reaction of readily available [8] 3-chloro-4-pyridazinecarbonitrile (**14**) [9], as an educt for compound **5** met with a failure. Hydrogenation of the triple bond in compound **15** could not be achieved without concomitant reduction of the nitrile function. The corresponding carboxylic acid **16**, on the other hand, turned out to form the lactone **17** spontaneously. Hence, also for the preparation of 10,11-dihydro-5*H*-benzo[4,5]cyclohepta[1,2—*c*]pyridazin-5-one (**5**) a procedure involving a radicalic alkoxycarbonylation as the key reaction step is proposed. It is well documented [6] that with pyridazine and derivatives thereof having both β-positions free, *Minisci*-type reactions with alkoxycarbonyl radicals, even when performed in the presence of dichloromethane, in general result in attack both at C-4 and C-5. The two-phase-system procedure [10] in this case only permits to

avoid further radicalic attack at the α-positions. Expectedly, treatment of 3-(2-phenylethyl)pyridazine (**18**) with methyl pyruvate/hydrogen peroxide/ferrous sulfate in dilute sulfuric acid/dichloromethane afforded the dimethyl dicarboxylate **21** along with a mixture of two phenylethylpyridazine monocarboxylic acid esters (**19** and **20**). The ratio of products **19**:**20**:**21** = 43:23:34 was determined by glc-analysis and ^{1}H-nmr spectroscopy. Separation of **21** from **19** and **20** could be achieved by preparative thin-layer chromatography; however, it appears to be more convenient to employ the mixture of carboxylic acids, obtained by alkaline hydrolysis, in the *PPA*-promoted ring closure reaction (150 °C, 6 hours) despite the fact that only two of its components are capable of intramolecular cyclisation. Thus, a 10% overall yield of **5** based on starting **18** is obtained.

Scheme 2



The proposed synthetic approaches to compounds **3–5** are anticipated to guarantee a high degree of variability with respect to the substituent pattern in the benzene moiety of these novel diazatricyclic systems, since a wide variety of (2-arylethenyl)pyridazines can be prepared conveniently [11, 12] from readily available methylpyridazines.

Experimental

Melting points (uncorrected) were determined with a *Kofler* apparatus. ^{1}H-nmr spectra were recorded on a Varian EM 390 (90 MHz, *TMS* as internal standard, δ-values in ppm), mass spectra on a Varian MAT CH-7 and on a Hewlett Packard HP 5970 MSD, ir spectra on a Jasco IRA-1 (KBr disks; $\bar{\nu}$ in cm^{-1}). Medium pressure liquid chromatography (mplc) was carried out on Lobar glass columns (Merck), filled with 250 g LiChroprep Si 60 (40–63 μm, Merck). Preparative thin layer chromatography (prep. tlc) was carried out on silica gel plates F-254 (Merck). Petroleum benzine refers to the fraction of b.p. 50 to 70 °C. Microanalyses were performed by Dr. *Zak*, "Institut für Physikalische Chemie" (University of Vienna).

5-(2-Phenylethyl)-4-pyridazinecarboxylic acid (**8**)

A solution of **7** [6] (2.5 g, 10 mmol) and NaOH (1.2 g) in 50% aqu. ethanol (80 ml) is heated to reflux for 2 h. After removal of ethanol *in vacuo*, the mixture is brought to *pH* = 2 by addition of 2*N* HCl and allowed to stand for 24 h. The precipitate is filtered with suction and dried over P_2O_5 for several days.

Yield: 1.94 g (85%); m.p. = 194–200 °C (decomp.); $C_{13}H_{12}N_2O_2$ (228.25).

Ir: 1 720 (C=O), 3 400 (O—H).

^{1}H-nmr (*DMSO-d_6*: δ = 9.42 (s, 1 H, H-3), 9.29 (s, 1 H, H-6), 7.5–7.2 (m, 5 H, phenyl-H), 3.5–2.7 (m, 4 H, —CH_2CH_2—).

Ms: *m/z* (%) = 228 (M^+, 11), 184 (6), 91 (100), 65 (26).

10,11-Dihydro-5H-benzo[4,5]cyclohepta[1,2—d]pyridazin-5-one (**3**)

A mixture of **8** (0.5 g, 2.2 mmol) and 25 ml of *PPA* is heated at 150 °C for 3 h. After cooling, the mixture is diluted with 100 ml of water and brought to *pH* = 10 with 30% aqu. NaOH. The solution is then extracted exhaustively with dichloromethane and the combined extracts are dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue is recrystallized from diethyl ether to give yellow crystals. Yield: 305 mg (66%); m.p. = 99–102 °C.

$C_{13}H_{10}N_2O$ (210.23). Calcd. C 74.27 H 4.79 N 13.32.
Found C 74.20 H 4.91 N 13.07.

Ir: 1 643 (C=O).

^{1}H-nmr ($CDCl_3$): δ = 9.54 (d, *J* = 1.5 Hz, 1 H, H-4), 9.2–9.1 (m, 1 H, H-1), 8.1–7.1 (m, 4 H, H-6, 7, 8, 9), 3.4–3.2 (m, 4 H, —CH_2CH_2—).

Ms: *m/z* (%) = 210 (M^+, 72), 182 (26), 128 (27), 93 (59), 89 (33), 77 (47), 76 (44), 69 (35), 65 (36), 63 (53), 51 (55), 50 (32), 45 (100).

4-(2-Phenylethyl)-3-pyridazinecarbonitrile (**11**)

To a stirred solution of **6** (4.60 g, 25 mmol), trimethylsilyl cyanide (3.47 g, 35 mmol) and $AlCl_3$ (10 mg) in dry CH_2Cl_2 (30 ml) under dry nitrogen, a solution of 4-toluenesulfonyl chloride (6.69 g, 35 mmol) in CH_2Cl_2 (60 ml) is added during

3 h. After additional stirring for 5 h, volatile components are removed *in vacuo* to yield 4.40 g of an oily residue. 1.55 g of this material and 1,8-diazabicyclo[5.4.0]undec-7-ene (612 mg, 4 mmol) are dissolved in dry *THF* (20 ml) and stirred under dry nitrogen for 1 h. Then, a saturated aqueous NH_4Cl-solution (20 ml) is added and the mixture is poured into water (20 ml). The suspension is extracted exhaustively with ethyl acetate and the combined organic layers are dried over anhydrous Na_2SO_4. After evaporation of the solvent and separation of the residue by mplc (ethyl acetate/petroleum benzine = 2/3) yellow crystals are obtained. Yield: 310 mg (17%, related to **6**); m.p. = 64–67 °C.

$C_{13}H_{11}N_3$ (209.25). Calcd. C 74.62 H 5.30 N 20.08.
Found C 74.45 H 5.48 N 19.84.

Ir: 2250 (C≡N).

^{1}H-nmr ($CDCl_3$): δ = 9.20 (d, J = 6 Hz, H-6), 7.4–7.1 (m, 6 H, H-5, phenyl-H), 3.4–2.9 (m, 4 H, —CH_2CH_2—).

Ms: m/z (%) = 209 (M^+, 15), 92 (100), 42 (69).

4-(2-Phenylethyl)-3-pyridazinecarboxamide (**12**)

A mixture of **11** (263 mg, 1.3 mmol) and *PPA* (10 ml) was heated at 150 °C for 6 h. After cooling, the mixture was diluted with water (30 ml), adjusted to pH = 8 with 30% NaOH, and was then extracted exhaustively with CH_2Cl_2. The combined organic layers were dried over anhydrous Na_2SO_4. After removal of the solvent *in vacuo* the residue was recrystallized from ethyl acetate/petroleum benzine to give colourless crystals. Yield: 200 mg (63%); m.p. = 119–122 °C.

$C_{13}H_{13}N_3O$ (227.27). Calcd. C 68.70 H 5.77 N 18.49.
Found C 69.18 H 5.89 N 18.21.

Ir: 3300, 3150 (N—H), 1675 (C=O), 1590 (N—H).

^{1}H-nmr ($CDCl_3$): δ = 9.12 (d, J = 6 Hz, 1 H, H-6), 8.3–8.0 (br s, 1 H, NH), 7.5–7.1 (m, 6 H, H-5, phenyl-H), 6.5–6.1 (br s, 1 H, NH), 3.7–2.8 (m, 4 H, —CH_2CH_2—).

Ms: m/z (%) = 227 (M^+, 100), 92 (100).

4-(2-Phenylethyl)-3-pyridazinecarboxylic acid (**13**)

A mixture of **11** (660 mg, 3.2 mmol) and 0.5 *N* NaOH (40 ml) is heated to 80 °C for 3 h. After cooling, the solution is brought to pH = 2 with conc. hydrochloric acid and concentrated to 10 ml *in vacuo*. The precipitated solid is washed with water and dried *in vacuo* to yield colourless crystals. Yield: 525 mg (72%); m.p. = 116–119 °C; $C_{14}H_{12}N_2O_4$ (228.25).

Ir: 3200 (O—H), 1740 (C=O).

^{1}H-nmr (*DMSO-d*$_6$): δ = 9.18 (d, J = 6 Hz, 1 H, H-6), 7.65 (d, J = 6 Hz, 1 H, H-5), 7.4–7.1 (m, 5 H, phenyl-H), 5.4 (br s, 1 H, OH), 3.3–2.7 (m, 4 H, —CH_2CH_2—).

Ms: m/z (%) = 228 (M^+, 34), 183 (33), 91 (100).

5,6-Dihydro-11H-benzo[4,5]cyclohepta[2,1—c]pyridazin-11-one (**4**)

A mixture of **13** (430 mg, 1.9 mmol) and *PPA* (10 ml) is heated at 150 °C for 3 h. After cooling, the mixture is diluted with 100 ml of water and brought to pH = 10 with 30% aqu. NaOH. The solution is then extracted exhaustively with dichloromethane and the combined extracts are dried over anhydrous Na_2SO_4.

After evaporation of the solvent, the residue is recrystallized from toluene/petroleum benzine to yield pale yellow crystals. Yield: 245 mg **4** (62%, related to **13**); m.p. = 108–110 °C.

$C_{13}H_{10}N_2O$ (210.24). Calcd. C 74.27 H 4.79 N 13.32.
Found C 74.49 H 4.95 N 13.18.

Ir: 1 670 (C=O).

^{1}H-nmr ($CDCl_3$): δ = 9.25 (d, J = 6 Hz, 1 H, H-3), 8.3–8.1 (m, 1 H, H-10), 7.7–7.1 (m, 4 H, H-4, 7, 8, 9), 3.5–3.0 (m, 4 H, —CH_2CH_2—).

Ms: m/z (%) = 210 (M^+, 100), 209 (58), 182 (31), 91 (36).

3-(2-Phenylethinyl)-4-pyridazinecarbonitrile (**15**)

A mixture of **14** [8] (278 mg, 2 mmol), phenylacetylene (510 mg, 5 mmol), bis(triphenylphosphin)-palladium(II)-chloride (28 mg, 0.04 mmol), copper(I)-iodide (20 mg, 0.1 mmol) and triethylamine (3 ml) was stirred under argon at room temperature for 7 h. After addition of water the mixture was extracted exhaustively with CH_2Cl_2. The combined organic layers were washed with water and then dried over anhydrous Na_2SO_4. After removal of the solvent *in vacuo* the residue was separated by column chromatography (gradient elution using ethyl acetate/petroleum benzine 2/3 to 2/1). Recrystallisation from ethanol gave colourless crystals. Yield: 320 mg (78%); m.p. = 162–165 °C.

$C_{13}H_7N_3$ (205.22). Calcd. C 76.07 H 3.44 N 20.48.
Found C 75.74 H 3.60 N 20.38.

Ir: 2 220 (C≡N, C≡C).

^{1}H-nmr ($CDCl_3$): δ = 9.45 (d, J = 6 Hz, 1 H, H-6), 7.9–7.4 (m, 6 H, H-5, phenyl-H).

Ms: m/z (%) = 205 (M^+, 89), 177 (40), 152 (100), 126 (64).

Reaction of **15** *with Polyphosphoric Acid (PPA)*

A mixture of **15** (300 mg, 1.5 mmol) and polyphosphoric acid (2 g) was heated at 120 °C for 9 h. After addition of ice water the mixture was extracted exhaustively with CH_2Cl_2. The combined organic layers were washed with water and then dried over anhydrous Na_2SO_4. Removal of the solvent *in vacuo* and crystallisation from methanol yielded 5*H*-7-phenylpyrano[4,3—*c*]pyridazin-5-one (**17**) as yellow crystals. Yield: 50 mg (15%); m.p. = 191–194 °C; $C_{13}H_8N_2O_2$ (224.22).

Ir: 1 740 (C=O), 1 620 (C=C).

^{1}H-nmr (*DMSO-d_6*): δ = 9.60 (d, J = 6 Hz, 1 H, H-3), 8.35 (d, J = 6 Hz, 1 H, H-4), 8.2–8.0 (m, 2 H, phenyl-H), 7.90 (s, 1 H, H-8), 7.7–7.4 (m, 3 H, phenyl-H).

Ms: m/z (%) = 224 (M^+, 100), 196 (35), 105 (99), 77 (74).

3-(2-Phenylethyl)pyridazine (**18**) [13]

A mixture of 3-styrylpyridazine [14] (5.46 g, 30 mmol) and 10% Pd/C catalyst (750 mg) in ethanol (500 ml) is stirred under H_2 atmosphere until no more hydrogen is taken up (675 ml). After filtration of the mixture the solvent is removed *in vacuo*. The residue is recrystallized from *THF*/cyclohexane to yield **18** as pale yellow crystals. Yield: 5.05 g (91%); m.p. = 31–33 °C (Ref. [13]: 32–33 °C).

Radicalic Methoxycarbonylation of **18**

30% H_2O_2 (11.3 g, 100 mmol) is added with stirring and cooling to methyl pyruvate (15.3 g, 150 mmol) at − 10–0 °C. This solution is then added with stirring

and cooling (− 5–0 °C) to a mixture of **18** (1.84 g, 10 mmol), conc. H_2SO_4 (3 g), H_2O (8 g), $FeSO_4 \cdot 7H_2O$ (28.0 g, 100 mmol) and CH_2Cl_2 (30 ml). After further stirring for 15 min, the resulting mixture is poured into ice water, the organic layer is separated and the aqueous phase is extracted exhaustively with CH_2Cl_2. After drying the combined organic layers over anhydrous Na_2SO_4, the solvent and excess methyl pyruvate is removed *in vacuo*. The residue is separated by prep. tlc (dichloromethane/ethyl acetate 5/1).

Fraction I:

Dimethyl 3-(2-phenylethyl)-4,5-pyridazinedicarboxylate (**21**).
Yellow crystals; yield: 931 mg (31%); m.p. = 35–39 °C.
$C_{16}H_{16}N_2O_4$ (300.31). Hrms calcd.: 300.111 (0); found: 300.111 (9) ± 0.003.
Ir: 1 750 (C=O).
^{1}H-nmr ($CDCl_3$): δ = 9.60 (s, 1 H, H-6), 7.4–7.2 (m, 5 H, phenyl-H), 4.01 (s, 6 H, 2 × CH_3), 3.6–3.1 (m, 4 H, —CH_2CH_2—).
Ms: *m/z* (%) = 300 (30, M^+), 268 (49), 239 (42), 225 (30), 210 (33), 182 (60), 181 (90), 91 (100), 65 (40).

Fraction II:

510 mg of a yellow oil; crystallisation from diisopropyl ether gives pale yellow crystals of methyl 3-(2-phenylethyl)-5-pyridazinecarboxylate (**20**). Yield: 339 mg (14%); m.p. = 102–112 °C.

$C_{14}H_{14}N_2O_2$ (242.29). Calcd. C 69.41 H 5.82 N 11.56.
Found C 69.42 H 5.93 N 11.59.

Ir: 1 740 (C=O).
^{1}H-nmr ($CDCl_3$): δ = 9.58 (d, 1 H, J = 2 Hz, H-6), 7.75 (d, 1 H, J = 2 Hz, H-4), 7.4–7.1 (m, 5 H, phenyl-H), 3.99 (s, 3 H, CH_3), 3.5–3.1 (m, 4 H, —CH_2CH_2—).
Ms: *m/z* (%) = 242 (76, M^+), 241 (100), 227 (45), 183 (37), 165 (53), 91 (73), 69 (78).

Evaporation of the mother liquor *in vacuo* gives a yellow oil, consisting of methyl 3-(2-phenylethyl)-4-pyridazinecarboxylate (**19**) together with **20** and minor amounts of unidentified byproducts.
^{1}H-nmr ($CDCl_3$) (besides signals of **20**): δ = 9.30 (d, 1 H, J = 6 Hz, H-6), 7.71 (d, 1 H, J = 6 Hz, H-5), 7.4–7.1 (m, 5 H, phenyl-H, overlapping with phenyl-H of **20**), 3.95 (s, 3 H, CH_3), 3.8–3.0 (m, 4 H, —CH_2CH_2—, overlapping with —CH_2CH_2— of **20**).
19: glc/ms: *m/z* (%) = 242 (49, M^+), 227 (100), 183 (36), 91 (61), 65 (30).

10,11-Dihydro-5H-benzo[4,5]cyclohepta[1,2—c]pyridazin-5-one (**5**)

The mixture of the carboxylic acid esters **19–21** (5.4 g), obtained as described above, and NaOH (2.4 g), dissolved in 50% aqu. methanol is heated to reflux for 2 h. After removal of methanol, the reaction mixture is brought to pH = 2 with 2 N HCl and is allowed to stand for 24 h. The precipitate obtained is dried over P_2O_5 for several days. 430 mg of this material and 10 ml of *PPA* are heated at 150 °C for 4 h. After cooling, the mixture is diluted with 100 ml of water and brought to pH = 10 with 30% aqu. NaOH. The solution is then extracted exhaustively with dichloromethane and the combined extracts are dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue is recrystallized from toluene/petroleum benzine to give yellow crystals.

Yield: 35 mg (10%, related to **18**); m.p. = 94–96 °C.

$C_{13}H_{10}N_2O$ (210.23). Calcd. C 74.27 H 4.79 N 13.32.
Found C 74.40 H 4.95 N 13.29.

Ir: 1630 (C=O).

^{1}H-nmr ($CDCl_3$): δ = 9.40 (d, J = 6 Hz, 1 H, H-3), 8.2–7.2 (m, 5 H, H-4, 6, 7, 8, 9), 3.9–3.2 (m, 4 H, —CH_2CH_2—).

Ms: m/z (%) = 210 (M^+, 100), 181 (37), 153 (54), 152 (40).

Acknowledgements

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References

[1] Pyridazines XXXV: *Haider N, Heinisch G, Laßnigg D* J Heterocycl Chem, in the press
[2] Presented as part of a lecture at the 11th International Congress of Heterocyclic Chemistry, Heidelberg, 1987
[3] *Haider N, Heinisch G* (1988) J Chem Soc Perkin Trans I: 401
[4] *Heinisch G, Laßnigg D* (1987) Arch Pharm (Weinheim) 320: 1222
[5] For some representative examples see, *Van der Stelt C, Hofman PS, Funcke ABH, Nauta WT* (1968) Arzneim Forsch 18: 756; *Villani FJ, Daniels PJL, Claire AE, Mann TA, Wang K* (1971) J Heterocycl Chem 8: 73; *Villani FJ, Wefer EA, Mann TA, Mayer J, Peer L, Levy AS* (1972) J Heterocycl Chem 9: 1203; *Brenner DG, Halczenko W, Shepard KL* (1982) J Heterocycl Chem 19: 897; *Halczenko W, Shepard KL* (1982) J Heterocycl Chem 19: 967; *Brenner DG, Halczenko W, Shepard KL* (1985) J Heterocycl Chem 22: 555; *Villani FJ, Magatti CV, Vashi DB, Wong J, Popper TL* (1986) Arzneim Forsch 36: 1311
[6] *Heinisch G, Lötsch G* (1985) Tetrahedron 41: 1199
[7] *Dostal W, Heinisch G* (1986) Heterocycles 24: 793
[8] *Dornow A, Abele W* (1964) Chem Ber 97: 3349
[9] *Laßnigg D* (1987) PhD Thesis University of Vienna
[10] *Heinisch G, Lötsch G* (1985) Angew Chem 97: 694, (1985) Angew Chem Int Ed Engl 24: 692
[11] *Heinisch G, Mayrhofer A* (1980) Arch Pharm (Weinheim) 313: 53
[12] *Heinisch G, Mayrhofer A* (1982) Sci Pharm (Wien) 50: 120
[13] *Ohsawa A, Uezu T, Igeta H* (1978) Chem Pharm Bull 26: 2428
[14] *Heinisch G, Mayrhofer A* (1977) Monatsh Chem 108: 213