Synthesis, Reactions and Spectroscopy of 3-Benzoyl-6-phenylpyridazines of Expected Biological Activity

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Pyridazine Derivatives, Biological Activity

Oxidative decyanation of phenyl(6-phenylpyridazin-3-yl)acetonitrile (**1**) in methanol yielded 3-benzoyl-6-phenylpyridazine (**2**). Phenyl(6-phenyl-pyridazin-3-yl)methanol (**3**) has been obtained *via* $NaBH_4$ reduction of ketone **2**. Reaction of **2** with hydroxylamine or its O-alkyl analogue has been found to yield 3-benzoyloxime-6-phenylpyridazine (**4**) and alkyloximes (**5**), respectively. Treatment of **4** with a mixture of acetic acid and sulfuric acid afforded ketone **2** again and not the rearranged products (**6** or **7**). Beckmann rearrangement has however been achieved for 3-benzoyl(O-ethyloxime)-6-phenylpyridazine (**5a**) and oxime **4** giving solely 3-carboxanilide-6-phenylpyridazine (**6**), 4-Benzoyloxime-3-phenyl-6-chloro-pyridazine (**17**) has been synthesized from the corresponding ketone **16**.

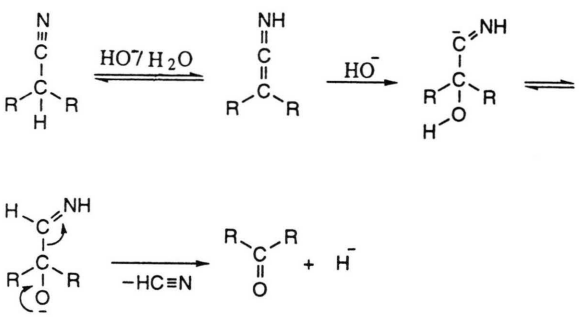
Introduction

Pyridazine derivatives appear to be of interest due to their pharmacological activities such as gastric antisecretory, antiulcer [1], hypolipidemic [2] and antihistaminic activities [3–5]. Because of this, much efforts have been devoted to synthesize various of pyridazines in order to enhance their pharmacological activity.

Here we wish to report the synthesis of 3-benzoyl-6-phenylpyridazine (**2**) together with its corresponding derivatives. Also, the preparations of the related chloropyridazinyl derivatives are presented. Similar pyridazinyl ketones of type 2 have been reported in a patent [6], and recent literature reports indicate that they could be obtained *via* oxidative decyanation [7–10] of their corresponding acetonitrile derivatives **1** in the presence of triethylbenzylammonium chloride (TEBA) as phase transfer catalyst. The latter method was adopted in our study for synthesis of our target compound **2**.

Results and Discussion

The required starting diarylacetonitrile **1** was prepared from 6-phenyl-3-chloropyridazine and phenylacetonitrile as previously described [1]. Treatment of the latter nitrile with TEBA in methanol and sodium hydroxide under air oxygen afforded the ketone **2** in good yield *via* the following mechanism. The structure of benzoyl phenylpyridazine **2** together with its chemical reactions outlined below (Scheme 1) was confirmed by IR, ^1H NMR, mass spectra and elemental analysis (Table I and Experimental).



Thus, treatment of **2** with sodium borohydride in methanol at room temperature yielded the corresponding alcohol **3** in almost quantitative yield. The ^1H NMR spectrum of the latter revealed two characteristic doublets with $J = 4$ Hz at δ 6.05 and 4.96 assignable to the OH and CH protons respectively.

Also, treatment of **2** with hydroxylamine hydrochloride in the presence of sodium hydroxide afforded the oxime **4** in an excellent yield (95%). The isolated oxime appears to exist as a mixture of two tautomeric forms. This conclusion comes from tlc analysis of this product which revealed the presence of two spots with close R_f values. The ^1H NMR spectrum showed two signals at $\delta = 12.14$ and 11.9. The integration of these two signals cor-

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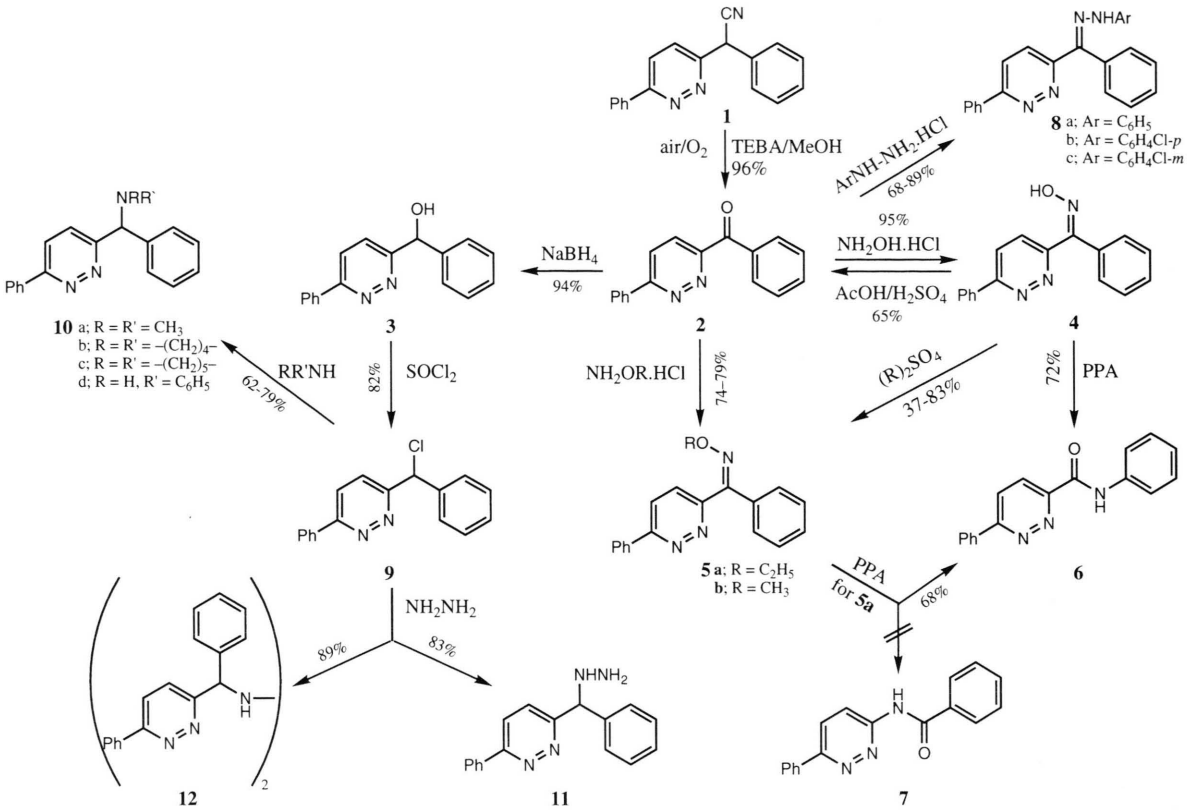
Table I. Analytical and spectral data of compounds **2–12**.

No. (method)	Yield (%)	M.p. (°C) (recrystallization solvent)	Molecular formula (MWt)	Elemental analysis calcd/found C	H	N	Pyridazine H-4 (d, 1H)	H-5 (d, 1H)	$J_{4,5}$ (Hz)	^{1}H NMR ($CDCl_3$) δ (ppm) Other
2	96	125–126 (toluene)	$C_{17}H_{12}N_2O$ (260.30)	78.44 78.50	4.65 4.59	10.76 10.70	8.51	8.32	10	8.20–8.31 (m, 2H, Ph-2,6), 8.08–8.16 (m, 2H, Ph-3,5), 7.66–7.81 (m, 1H, Ph-4), 7.61–7.65 (m, 5H, Ph-pyridazine)[a]
3	94	157–159 (ethanol)	$C_{17}H_{14}N_2O$ (262.31)	77.84 77.50	5.38 5.27	10.68 10.47	8.06	7.80	8	7.22–8.04 (m, 10H, Ph), 6.05 (d, J = 4Hz, 1H, OH), 4.96 (d, J = 4Hz, 1H, CHOH)
4	95	187–188 (toluene)	$C_{17}H_{13}N_3O$ (275.31)	74.17 74.42	4.76 4.75	15.26 15.10	8.35	8.00	9	8.22–8.30 (m, 2H, Ph-2,6), 7.59–7.68 (m, 3H, Ph-3,4,5), 7.42–7.53 (m, 5H, Ph-pyridazine), 11.9 (s, 1H, OH)[b], 12.14 (s, 1H, NH)[c]
5a										
(A)	79	150–152	$C_{19}H_{17}N_3O$	75.23	5.65	13.85	8.16	7.93	9	8.16–8.28 (m, 2H, Ph-2,6), 7.22–7.71 (m, 8H, Ph), 4.12–4.28 (m, 2H, OCH_2), [1.36, 1.32 (t, J = 7Hz, 3H, CH_3)][a,d]
(B)	37	(ethanol)	(303.37)	75.58	5.69	13.87	7.96	7.80		
5b										
(A)	74	134–136	$C_{18}H_{15}N_3O$	74.72	5.23	14.52	8.22	7.91	9	8.10–8.22 (m, 2H, Ph-2,6), 7.38–7.62 (m, 8H, Ph), [4.09,4.01 (s, 3H, OCH_3)][e]
(B)	83	(cyclohexane)	(289.34)	74.93	5.29	14.26	7.85	7.76		
6	68	207–208 (acetonitrile)	$C_{17}H_{13}N_3O$ (275.31)	73.56 73.77	4.81 4.78	15.13 14.95[f]	8.46	8.52	9	(see Fig. 1)
8a	62	188–189 (methanol)	$C_{23}H_{18}N_4$ (350.42)	78.83 78.72	5.18 5.03	16.00 15.98				
8b	69	227–228 (methanol)	$C_{23}H_{17}N_4Cl$ (384.86)	71.78 71.62	4.45 4.41	14.56 14.36	8.76	8.18	10	7.43–7.97 (m, 14H, Ph), 7.95 (s, 1H, NH)[g]
8c	89	132–134 (methanol)	$C_{23}H_{17}N_4Cl$ (384.86)	71.78 71.57	4.45 4.21	14.56 14.16				
9	82	140–142 (cyclohexane)	$C_{17}H_{13}N_2Cl$ (280.76)	72.73 72.96	4.67 4.58	9.98 9.97	7.91	7.78	9	8.06–8.18 (m, 2H, Ph-2,6), 7.29–7.62 (m, 8H, Ph), 6.59 (s, 1H, CHCl).
10a	62	122–124 (cyclohexane)	$C_{19}H_{19}N_3$ (289.37)	78.86 78.70	6.62 6.43	14.52 14.51	8.27	8.03	8	7.72–8.01 (m, 2H, Ph-2,6), 7.41–7.76 (m, 5H, Ph-pyridazine), 7.12–7.34 (m, 3H, Ph-3,4,5), 4.73 (s, 1H, PhCH), 2.24 (s, 6H, CH_3).
10b	67	186–187 (cyclohexane)	$C_{21}H_{21}N_3$ (315.41)	79.97 80.31	6.71 6.32	13.32 13.13				
10c	79	212–213 (ethanol)	$C_{22}H_{23}N_3$ (329.44)	80.21 80.65	7.84 6.82	12.75 12.45	8.06	8.02	8	7.71–7.85 (m, 2H, Ph-2,6), 7.46–7.55 (m, 5H, Ph-pyridazine), 7.21–7.34 (m, 3H, Ph-3,4,5), 4.85 (s, 1H, PhCH), 2.21–2.51 (m, 4H, piperidine H-2,6) 1.41–1.62 (m, 6H, piperidine H-3,4,5)
10d	66	144–145 (ethanol)	$C_{23}H_{19}N_3$ (337.42)	81.87 81.73	5.68 5.33	12.45 12.15				
11	83	138–39 (ethanol)	$C_{17}H_{16}N_4$ (276.34)	73.89 73.70	5.84 5.58	20.27 19.95	8.31	7.82	9	8.14–8.23 (m, 1H, NH), 7.34–7.66 (m, 10H, Ph), 6.71 (d, J = 4Hz, 1H, PhCH), 4.62 (d, J =5, 2H, NH_2)
12	89	320–322 (DMF:H_2O) (8:1)	$C_{34}H_{28}N_6$ (520.63)	78.43 77.99	5.42 5.17	16.14 15.96	8.71–8.22 (4H,m)			8.26–8.31 (m, 2H, NH-NH), 7.45–8.00 (m, 20H, Ph), 6.7 (d, J = 4Hz, 2H, PhCH)[a]

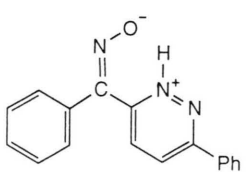
[a] Recorded from deuteriodimethylsulfoxide; [b] 4B; [c] 4A; [d] (0.5 : 9.5); [e] (2 : 8); [f] calculated $C_{17}H_{13}N_3O$ + 1/8 H_2; [g] exchangeable with D_2O.



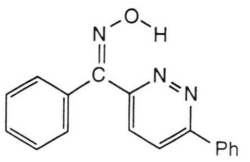
Scheme 1

responds to one proton and their ratio is 1 : 9 respectively. Furthermore, the structure of product **4** is evidenced by its IR spectrum which reveals a broad absorption band near $\nu = 2840\ cm^{-1}$, assignable to strongly intramolecular hydrogen bonded OH or HN^+ group. Attempts to separate the two isomers were met with failure. Accordingly, the isolated oxime **4** was considered to exist as a mixture of the two forms the zwitterionic **4A** and the *Z* isomer **4B** which is predominant as indicated by the foregoing ^1H NMR data.

The assignment of the Z isomer of the product **4** was further confirmed by its alkylation and rearrangement of O-alkyl derivatives obtained. Thus, treatment of **4** with diethyl or dimethyl sulfates in aqueous sodium hydroxide afforded the O-alkyloximes **5a,b** respectively. The latter could be also obtained *via* an alternative route involving treatment of ketone **2** with the corresponding alkoxylamine hydrochloride in ethanol and in the presence of 10% sodium hydroxide. As expected, both compounds, **5a,b**, showed a mixture from two isomers (Table I). The structure of the latter products was consistent with their IR, ^1H NMR and the elemental analysis in addition to the mass spectrum of **5a** which revealed $m/z = 303$ (84%), corresponding to the molecular ion peak (see Experimental).



4A (10%)



4B (90%)

Treatment of **5a** with polyphosphoric acid afforded the dealkylated [11] and the rearranged product *N*,6-diphenylpyridazine-3-carboxyamide **6** which was identified by comparison with an authentic sample of **7** prepared from benzoyl chloride and 3-phenyl-6-aminopyridazine. The com-

parison included tlc, m.p., IR, in addition to the 2D-NMR analysis. The results obtained, clearly demonstrate that compound **6** was the product of a Beckmann rearrangement of **5a** and not compound **7**. The structure of **6** was established by the following facts; *a)* its m.p. (207–208 °C) was different from that of compound **7** (m.p. 231–232 °C), *b)* IR spectra of both compounds showed different NH and CO stretching frequencies, thus, compound **6** showed bands at ν = 3343 (NH) and 1682 cm^{-1} (CO), while compound **7** showed stretching frequencies at ν = 3478 (NH) cm^{-1}, 1722 (CO) cm^{-1}, *c)* both compounds showed different signals in ^1H NMR and ^{13}C NMR, *e.g.*, compound **6** showed (CO) at δ = 161.3, while compound **7** at δ 166.6 ppm, *d)* from 2D-HC correlation, using the HMBC pulse sequence [12]. Compound **6** showed a correlation between H-4 of pyridazine (d, 8.4) and CO (δ = 161.3) while compound **7** showed a correlation between CO (δ = 166.6) and the benzoyl *ortho* protons at (δ = 8.14). Total assignments of proton and carbon signals for both compounds are illustrated in Fig. 1 and 2. The structure of **6** was also confirmed by its mass spectrum which showed a molecular ion peak at *m/z* = 275 (99%).

The foregoing results, when taken collectively, substantiate the *Z* configuration assigned for, both, the O-alkyloximes **5a,b** and their precursors **4**.

Also, oxime **4** was subjected to a mixture of acetic and sulfuric acid in order to achieve a Beckmann rearrangement. Under these very mild conditions, deoximation was achieved, and ketone **2** was obtained instead of any expected rearranged product **6** or **7**. It is worth to note that deoximation usually takes place under drastic conditions with very strong reducing, oxidizing or expensive reagents [13]. However we achieved this rearrangement upon treatment of **4** with polyphosphoric acid to give **6** (Scheme 1).

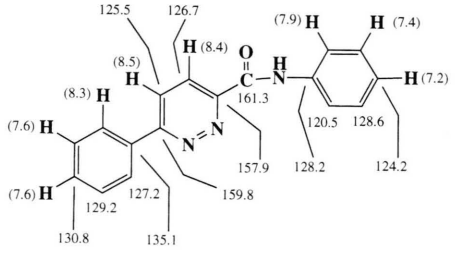


Fig. 1. Proton and carbon assignments of compounds **6** based on HMBC experiments.

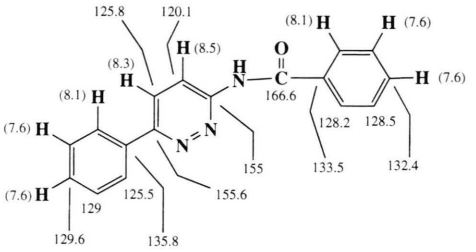


Fig. 2. Proton and carbon assignments of compound **7** based on HMBC experiments.

An even more convenient access to 3-benzoyl-*N*-arylhydrazone-6-phenylpyridazine **8a-c** was established by treatment of our target ketone **2** with substituted phenylhydrazine hydrochloride in presence of sodium acetate and methanol giving high yields of hydrazones **8**.

Transformation of alcohol **3** into the corresponding chloride **9** was achieved in a satisfactory yield employing thionyl chloride in dry toluene at room temperature.

According to the literature [14], the action of secondary aliphatic amines to 4-α-chlorobenzylpyridazine was found to result in an attack at the heteroaromatic system. On the other hand, attack of said aliphatic amines gives 4-a-aminobenzylpyridazine in addition to 20% of isomeric *tele*-substitution products (4-benzyl-5-aminopyridazines [14]. In contrast, 3-α-chlorobenzylpyridazine derivative **9** has shown to be attacked exclusively at the benzylic carbon atom (^1H NMR signals for pyridazinyl H-4,5 in addition to analysis of the reaction mixture by tlc), so, treatment of the chloro derivative **9** with secondary aliphatic, aromatic or cyclic amines showed a pronounced regioselectivity in the smooth replacement of chlorine by *N*-nucleophiles leading quantitatively to the corresponding amino derivatives **10a-d**. The structure of the products is consistent with their IR and ^1H NMR in addition to mass spectrum of **10b** which revealed *m/z* = 315 (0.6%).

Much efforts have been devoted to synthesis of the hydrazine **11**. Unfortunately 90% yield of the disubstituted derivative **12** always was obtained in addition to a poor yield of compound **11** despite of the use of different reaction conditions. Finally, we have succeeded to obtain compound **11** in good

yield (83%) by adding a solution of compound **9** in methanol dropwise to a stirred hydrazine hydrate solution at room temperature. The elemental analysis and spectroscopic data of compounds **11** and **12** are compatible with the assigned structures (Table I).

In continuation of our work, and due to the pharmacological potential of pyridazines [15,16], we extended our efforts towards the synthesis of ketone **16** with a 6-chloro substituent at the pyridazine ring, (Scheme 2). Therefore, we prepared α-(3-phenyl-6-chloropyridazin-4-yl)phenylacetonitrile (**15**) in good yield by reaction of 3-phenyl-4,6-dichloropyridazine (**13**) *via* adaption of a published procedure [8] to give either compound **14** or **15**. To deduce which compound had actually been obtained, the product was subjected to reductive dehalogenation (ammonium formate/Pd/C), and the product was compared with nitrile **1** (Scheme 1). A remarkable difference between the two nitriles was observed (using tlc, m.p., spectroscopic analysis) which indicated that our product is **15** and not **14**, so the chlorine at C-4 was replaced during the reaction and not at C-6. The IR spectrum of compound **15** revealed an absorption band at ν = 2221 (CN) cm^{-1}, while its ^1H NMR showed a singlet at δ = 8.11 (pyridazine H-5), a multiplet at 6.92–7.07 (Ph H-2,6), a multiplet at 7.21–7.61 (Ph H-3,4,5 and C_6H_5 at pyridazine) and a singlet at 5.93 (benzyl proton) [*cf.* Experimental].

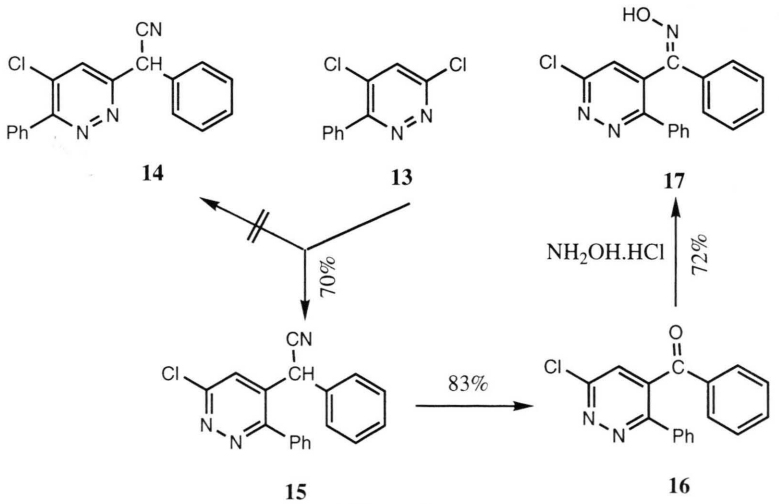
Thus, the diarylacetonitrile **15** was conveniently accessible to synthesize ketone **16**. We have so far failed in the preparation of an analytically pure sample owing to its poor stability, so the crude chloropyridazinyl ketone **16** was reacted with hydroxylamine hydrochloride in the presence of sodium hydroxide to afford oxime **17**.

Experimental

Melting points are uncorrected. Elemental analyses were performed on a Carlo Erba 1106 analyzer. IR spectra were measured using Perkin Elmer 298 spectrophotometer. The ^1H NMR spectra were recorded on an Varian Gemini 200 MHz instrument, ^{13}C NMR spectra were recorded at 50 MHz on XL 200; 2D-HC correlation was obtained on Bruker 360 MHz using a HMBC pulse sequence, according to [12]. Mass spectra were recorded on Shimadzu, GC MS-QP 1000 EX instrument. All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel $60F_{254}$ (Merck) plates.

The analytical and spectral data of compounds **2–12** are compiled in Table I and the experimental, compounds **15–17** at the experimental part.

3-Benzoyl-6-phenylpyridazine (**2**): A solution of 10.84 g (40 mmol) of **1** [1], 15 ml of 30% NaOH and 0.80 g (3.5 mmol) triethylbenzylammonium chloride in 200 ml of methanol was stirred at 45 °C for 12 h and air was pumped through it. Then, 200 ml water was added, and the precipitate was crystallized from toluene. Yield: 10.1 g (96%); – IR: ν = 1673 (CO).



Scheme 2

Phenyl(6-phenylpyridazin-3-yl)methanol (**3**): To a solution of 2.60 g (10 mmol) of **2** in 50 ml of methanol 0.10 g (2.5 mmol) of sodium borohydride was added within 15 min and the reaction mixture was stirred at room temperature for 2 h. The mixture was acidified with 2 *N* sulfuric acid, then methanol was removed *in vacuo*. The ice-cooled solution was made alkaline with 50% aqueous sodium hydroxide. The precipitate was recrystallized from ethanol. Yield: 2.48 g (94%); – IR: ν = 3159 (OH).

3-Benzoyloxime-6-phenylpyridazine (**4**): A solution of 2.60 g (10 mmol) of **2** in 20 ml of methanol was added to a solution of 2.08 g (30 mmol) of hydroxylamine hydrochloride in 10 ml of water, and 10 ml of 10% sodium hydroxide. The mixture was refluxed for 45 min. After cooling 100 ml water was added and the precipitate was crystallized from toluene. Yield: 2.61 g (95%).

Reaction of oxime **4** with acetic and sulfuric acids*:* A mixture of 1.4 g (5 mmol) of **4**, 100 ml of acetic acid and 50 ml of sulfuric acid was refluxed for 4 h, the mixture was cooled, then 100 g of ice was aded, then neutralized with ammonium hydroxide. The precipitate was crystallized from toluene. Yield: 0.85 g (65%) of ketone **2**.

3-Benzoyl-(O-alkyloxime)-6-phenylpyridazines (**5a,b**) *(Method A):* A solution of 2.60 g (10 mmol) of **2** in 20 ml of ethanol containing 30 mmol of appropriate alkoxylamine hydrochloride, 10 ml of water, and 10 ml of 10% sodium hydroxide was refluxed for 1.5 h, work up according to **4**. Yield: 2.41 g (79%) of **5a** and 2.13 g (74%) of **5b**, respectively. – MS (70 ev): for **5a,** *m/z* (%), 303 (84), 302 (100), 274 (65), 258 (31), 244 (94), 104 (381), 77 (98), 51 (67).

Method B: The appropriate dialkylsulfate (30 mml) was added in portions to a stirred solution of 2.75 g (10 mmol) of **4** in 20 ml of ethanol and 10 ml of 10% sodium hydroxide. Stirring was continued for 1 h at room temperature, the excess dialkylsulfate was evaporated *in vacuo*, then 100 ml of water was added. The separated precipitate was crystallized from the appropriate solvent. Yield: 1.14 g (37%) of **5a** and 2.41 g (83%) of **5b**.

3-Carboxanilide-6-phenylpyridazine (**6**): A mixture of (10 mmol) of **4** or **5a** and 30 g of polyphosphoric acid was kept at 110 °C with stirring for 1 h, the mixture was cooled, 100 g of ice was added and the isolated product was crystallized from acetonitrile. Yield: 1.98 g (72%) and 1.87 g (68%) respectively. – 2-D^{1}H NMR, ^{13}C NMR: (Fig. 1). – MS (70 ev): *m/z* (%), 275 (99), 274 (81), 182 (2), 156 (25), 120 (2), 104 (100), 92 (6), 78 (6), 77 (59), 53 (99).

N-(6-Phenylpyridazin-3-yl)benzamide (**7**)*:* This compound was obtained as colourless crystals from ethanol. m.p. 231–232 °C. – 2-D^{1}H NMR, ^{13}C NMR (Fig. 2).

$C_{17}H_{13}N_3O$ (275.31)

Calcd	C 74.17	H 4.76	N 15.26%,
Found	C 73.91	H 4.54	N 15.08%.

3-Benzoyl-N-arylhydrazone-6-phenylpyridazines (**8a-c**) *(General procedure):* A solution of phenylhydrazine hydrochloride or its *m*-, *p*-chloro analogue (10 mmol) and 2 g of sodium acetate in 10 ml of water was added to 2.60 g (10 mmol) of **2** in 30 ml of methanol, then the mixture was refluxed for 1 h. The precipitate was crystallized from the appropriate solvent to yield 2.52 g (62%), 3.11 g (69%), 3.41 g (89%) of **8a,8b** or **8c** respectively. – IR: ν = 3078 (NH).

α-(6-Phenylpyridazin-3-yl)benzylchloride (**9**): Thionyl chloride (2 ml) was added to a stirred suspension of 2.62 g (10 mmol) of **3** in 100 ml of dry toluene at 0 °C within 15 min. The mixture was allowed to warm up to room temperature and then stirred for 3 h. A saturated solution of aqueous sodium hydrogen carbonate was added at 0 °C. The aqueous layer was extracted with dichloromethane, the combined organic extracts were dried over anhydrous sodium sulfate, and then concentrated *in vacuo*. The residue was crystallized from cyclohexane to yield 1.72 g (82%).

α-(6-Phenylpyridazin-3-yl)benzylamines (**10a-d**): *(General procedure):* A mixture of 1.40 g (5 mmol) of **9** and 20 mmol of the appropriate amine in 15 ml of ethanol was refluxed for 5–7 h. After cooling, the precipitate was crystallized from appropriate solvent to yield 0.89 g (62%), 1.52 g (67%), 1.29 g (79%), or 1.19 g (66%) of **10a**, **10b**, **10c** or **10d** respectively. – MS (70 ev): of **10b,** *m/z* (%) 315 (0.6), 271 (16), 246 (100), 245 (35), 115 (12), 77(8), 70(2).

α-(6-Phenylpyridazin-3-yl)benzylhydrazine (**11**)*:* To a stirred sample of 30 ml of hydrazine hydrate a solution of 1.40 g (5 mmol) of **9** in 10 ml of methanol was added dropwise at room temperature within 30 min. The stirring was continued for 3 h. The excess hydrazine and ethanol were evaporated *in vacuo*. The residue was crystallized from ethanol. Yield: 1.14 g (83%). – IR: ν = 3192 (NH), ν = 3057 (NH_2). – MS (70 ev): *m/z*(%) 276 (20), 275 (2), 199 (12), 121 (100), 119 (10), 77 (35).

N,N'-Bis[α-(6-phenylpyridazin-3-yl)benzyl]-hydrazine (**12**): A mixture of 2.8 g (10 mmol) of **9** and 10 ml of hydrazine hydrate in 20 ml of ethanol was refluxed for 2 h. The excess hydrazine hydrate

and solvent were removed *in vacuo*. The residue was crystallized from DMF and water (8:1). Yield: 2.31 g (89%). – IR: ν = 3300–3050 (NH-NH).

α-(3-Phenyl-6-chloropyridazin-4-yl)phenylacetonitrile (**15**): To a stirred solution of 2.9 g (18.33 mmol) of phenylacetonitrile in 40 ml of dry toluene 1.9 g (47.5 mmol) of sodium amide was added in portions at 0 °C. Then 5.63 g (25 mmol) of 3-phenyl-4,6-dichloropyridazine was added. The mixture was worked up according to ref. [8]. Yield: 5.6 g (70%) m.p. 138–139 °C (ethanol), – IR: ν = 2221 (CN). – ^{1}H NMR (DMSO-d_6): δ = 8.11 (s, 1H, pyridazine H-5), 6.92–7.07 (m, 2H, Ph-2,6), 7.21–7.61 (m, 8H, Ph-3,4,5, C_6H_5-pyridazine), 5.93 (s, 1H, PhCH).

$C_{18}H_{12}ClN_3$ (305.77)

Calcd	C 70.71	H 3.96	N 13.74%,
Found	C 71.00	H 3.89	N 13.75%.

4-Benzoyl-3-phenyl-6-chloropyridazine (**16**): A solution of 3.06 g (10 mmol) of **15**, 15 ml of 30% NaOH and 0.23 g (1 mmol) of triethylbenzylammonium chloride in 50 ml of methanol then the mixture was worked up analogous to the preparatione of **2.** Yield: 2.8 g (83%) m.p 70- 71 °C. – IR: ν = 1669 (C=O). – ^{1}H NMR (DMSO-d_6): δ = 8.21(s, 1H, pyridazine H-5), 7.67–7.39 (m, 10H, Ph).

4-Benzoyloxime-3-phenyl-6-chloropyridazine (**17**): A solution of 1.47 g (5 mmol) of **16** in 20 ml of methanol was added to a solution of 1.04 g (15 mmol) of hydroxylamine hydrochloride in 5 ml of water and 5 ml of 10% sodium hydroxide then the mixture was worked up analogous to the preparation of **4**. Yield: 1.12 g (72%) m.p. > 300 °C (DMF). – IR: ν = 3220 (OH). - ^{1}H NMR (DMSO-d_6): δ = 8.33 (s, 1H, pyridazine H-5), 7.79–7.42 (m, 10H, Ph), 12.11 (s, 1H, OH).

$C_{17}H_{12}ClN_3O$ (309.75)

Calcd	C 65.91	H 3.90	N 13.57%,
Found	C 65.72	H 3.50	N 13.50%.

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