QUANTITATIVE DETERMINATION OF THE ELECTRONIC EFFECTS OF 3- AND 4-PYRIDAZINYL GROUPS FROM NMR SPECTRAL DATA FOR ISOMERIC AMINOPHENYL- AND PHENYLPYRIDAZINES

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The previously unknown aminophenylpyridazines were synthesized. The inductive and resonance constants of 3- and 4-pyridazinyl groups were calculated on the basis of ^1H and ^{13}C NMR spectral data for isomeric aminophenyl- and phenylpyridazines in dimethyl sulfoxide (DMSO).

Information regarding the electronic effects of 3- and 4-pyridazinyl groups is not available [1]; this is associated with the inaccessibility of the compounds and with the restrictions imposed by the methods for the determination of reactivity constants on the selection of model compounds. Nevertheless, a knowledge of such constants is useful not only in the prediction of the properties of compounds of the pyridazine series but is also of interest from a theoretical point of view.

Pyridazinyl groups occupy a special position in series of azinyl groups, since the nitrogen atoms in them are bonded directly to one another, which leads to appreciable alternation in the lengths [2] and orders [3, 4] of the π bonds and to a decrease in the degree of delocalization of the π electrons in the ring [5].

In analogy with other azinyl groups, one should expect the manifestation of electron-acceptor properties by pyridazinyl groups; this is confirmed qualitatively by some spectral data. Thus, increased (as compared with the benzene analogs) frequencies of the N–H and C=O stretching vibrations were recorded in the IR spectra of amino- [6] and formylpyridazines [7, 8]. An examination of the effect of various azinyl groups on the NH acidities of amino azines [9], as well as on the CH acidities of methyl azines [10] and acetyl azines [9], makes it possible to qualitatively determine the locations of pyridazinyl groups in series of such substituents. With respect to the ability to stabilize nitrogen and carbon anions, the 4-pyridazinyl group is close to the 4-pyrimidinyl group, whereas the 3-pyridazinyl group is close to the somewhat less electron-accepting 2- and 5-pyrimidinyl groups.

In the present research we determined the set of σ constants of 3- and 4-pyridazinyl groups on the basis of ^{13}C NMR spectral data for 3- (Ia) and 4-phenylpyridazine (IIa) and PMR spectral data for four isomeric m- and p-aminophenylpyridazines (Ib,c and IIb,c). Only the two phenylpyridazines [11, 12] and 3-(p-aminophenyl)pyridazine (Ic) [13] have been described.

We selected the scheme of synthesis that is usually employed in the preparation of 3-substituted pyridazines starting from aroylpropionic acids IIIa,d,e [14]. The chlorine atom was removed from 3-aryl-6-chloropyridazines VIa,d,e by catalytic hydrogenation in the presence of palladium on carbon. In the case of nitrophenyl derivative VId reductive dehalogenation was accompanied by reduction of the nitro group to give 3-(m-aminophenyl)pyridazine (Ib).

In the reduction of p-isomer VIe the resulting p-aminophenyl group appreciably retards the subsequent removal of a chlorine atom, and, despite an increase in the time and temperature, a small amount of chloro derivative VII was isolated from the products of reduction along with aminophenyl derivative Ic.* In addition to a broad signal of protons of an amino

*The melting point of Ic differs markedly from the data in [13].

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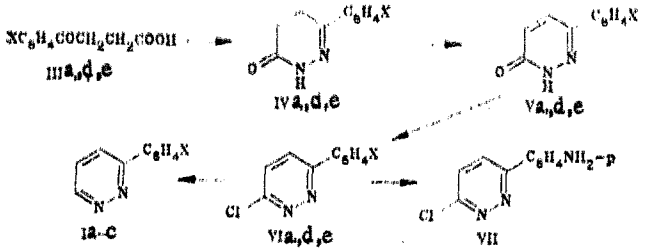
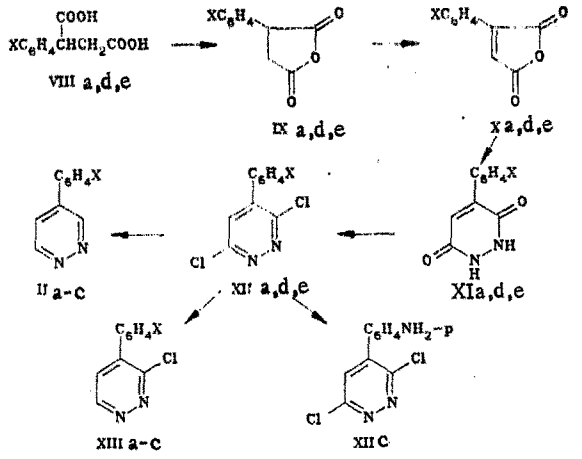
group and two doublet signals of aromatic protons of a p-substituted phenyl group (see Table 1), two doublets with J = 9.0 Hz, which is characteristic for spin–spin coupling coupling of 4-H and 5-H protons of the pyridazine ring [15], are present in the PMR spectrum of VII.



I, III—VI a X=H, b X=*m*-NH_2, c X=*p*-NH_2, d X=*m*-NO_2, e X=*p*-NO_2

Isomeric 4-aminophenylpyridazines IIb,c were obtained from nitrophenylsuccinic acids VIIId,e as in the scheme in [11] for the synthesis of 4-phenylpyridazine (IIa). In its last step we noted stepwise reductive dehalogenation of 4-nitrophenyl-3,6-dichloropyridazines XIId,e. The chlorine atom adjacent to the aryl group was removed with difficulty; this led to the production of, in addition to aminophenylpyridazines IIb,c, certain amounts of 4-aminophenyl-3-chloropyridazines XIIIb,c. In addition to broad signals of the protons of the amino group, two doublets, one of them at weak field with characteristic constant $^3J_{5,6}$ = 5.0 Hz [15], were recorded in their PMR spectra (see Table 1). The presence of a chlorine atom in the 3 position of the pyridazine ring is confirmed by the correspondence of the 5-H and 6-H chemical shifts in the PMR spectra of XIIIb,c with the values calculated via an additive scheme from the spectra of 3-chloropyridazine and 4-aminophenyl derivatives IIb,c.

In the reductive dehalogenation of XIIa we also recorded the formation of 4-phenyl-3-chloropyridazine (XIIIa) as an intermediate. Under conditions of incomplete dehalogenation of XIIa with the absorption of an equimolar amount of hydrogen we isolated IIa and XIIIa in a ratio of 1.2:1. As in the spectra of XIIIb,c discussed above, two doublets with $^3J_{5,6}$ = 5.0 Hz are observed in the PMR spectrum of XIIIa.



II, VIII—XIII a X=H, b X=*m*-NH_2, c X=*p*-NH_2, d X=*m*-NO_2 e X=*p*-NO_2

The chemical shifts (CS) and spin–spin coupling constants (SSCC) of Ib,c and IIb,c (Table 1) correspond to the data in [16, 17]. The ^{13}C NMR spectra were recorded for phenylpyridazines Ia and IIa (Table 2). The assignment of the signals to the carbon atoms of the phenyl groups was made in analogy with the assignment in the spectra of phenylpyridines [18] and phenylpyrimidines [19] with allowance for the relative intensities of the signals. The remaining signals were assigned to the carbon atoms of the pyridazine ring on the basis of quantitative data on the effect of a phenyl group as a substituent on the ^{13}C CS in the benzene and pyridine rings in the case of phenylpyridines [18]. For comparison, the ^{13}C CS of unsubstituted pyridazine, which we determined for a dilute solution in DMSO, are presented in Table 2.

The σ_I and σ_R^0 constants for the pyridazinyl groups as substituents were calculated in accordance with [19] starting from the CS of the m- and p-carbon atoms ($\Delta\delta'_{C_m}$ and $\Delta\delta'_{C_p}$) of

TABLE 1. PMR Spectra of Arylpyridazines I, II, VII, XIIc, and XIII in DMSO

Compound	Substituents in the pyridazine ring	Chemical shift,* ppm						$\Delta\delta_{NH_2}$†	$\Delta\delta'_{NH_2}$‡
		3-H (dd)	4-H	5-H	6-H	Ar	NH_2		
Ia	3-C_6H_5	—	8,20 dd	7,79 dd	9,26 dd	7,50—7,67m; 8,10—8,32 m	—	—	—
Ib	3-(*m*-$H_2NC_6H_4$)	—	7,98 dd	7,72 dd	9,16 dd	6,63—7,50 m	5,25	−0,35	−0,32
Ic	3-(*p*-$H_2NC_6H_4$)	—	7,98 dd	7,62 dd	9,05 dd	6,74 d; 7,92 d	5,53	−0,63	−0,61
IIa	4-C_6H_5	9,68	—	8,00 dd	9,33 dd	7,44—7,69m; 7,77—8,07 m	—	—	—
IIb	4-(*m*-$H_2NC_6H_4$)	9,56	—	7,85 dd	9,30 dd	6,67—7,38 m	5,31	−0,41	−0,38
IIc	4-(*p*-$H_2NC_6H_4$)	9,52	—	7,78 dd	9,09 dd	6,73 d; 7,67 d	5,64	−0,74	−0,72
VII	6-Cl-3-(*p*-$H_2NC_6H_4$)	—	8,09 d	7,80 d	—	6,72 d; 7,88 d	5,66	—	—
XIIc	3,6-Di-Cl-4-(*p*-$H_2NC_6H_4$)	—	—	7,89 s	—	6,71 d; 7,40 d	5,75	—	—
XIIIa	3-Cl-4-C_6H_5	—	—	7,83d	9,34 d	7,57 s	—	—	—
XIIIb	3-Cl-4-(*m*-$H_2NC_6H_4$)	—	—	7,71d	9,26 d	6,56—7,32m	5,30	—	—
XIIIc	3-Cl-4-(*p*-$H_2NC_6H_4$)	—	—	7,69 d	9,19 d	6,72 d; 7,36 d	5,63	—	—

*In the pyridazine ring $^3J_{4,5}$ = 8.3-9.0, $^3J_{5,6}$ = 4.5-5.5, $^4J_{3,5}$ = 2.4-2.7, $^4J_{4,6}$ = 1.5, and $^3J_{3,6}$ = 1.2-1.5 Hz. In the p-disubstituted benzene ring ^3J = 8.5-9.0Hz.

†Relative to the signal of aniline in DMSO (4.90 ppm), the negative values correspond to a shift to weak field.

‡With allowance for the magnetic anisotropy of the pyridazine ring.

TABLE 2. ^{13}C NMR Spectra of Pyridazine and Phenylpyridazines Ia and IIa in DMSO

Compound	Chemical shift, δ, ppm								$\Delta\delta^*$, ppm		$\Delta\delta^{*\dagger}$, ppm	
	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	$C_{(6)}$	C_i	C_o	C_m	C_p	C_m	C_p	C_m	C_p
Pyridazine	151,89	126,86	126,86	151,89	—	—	—	—	—	—	—	—
Ia	158,56	124,18	127,54	150,51	136,22	126,89	129,02	130,03	0,61	1,62	0,46	1,52
IIa	149,34	137,05	123,10	151,56	133,87	127,10	129,33	130,03	0,92	1,62	0,77	1,52

*Relative to the signal of benzene in DMSO (128.41 ppm).
†With allowance for the magnetic anisotropy of the pyridizaine ring.

TABLE 3. σ Constants of Pyridazinyl Groups

Group	σ_I			σ_R^0	σ_R	σ_m	σ_p
	PMR	^{13}C NMR	Av.				
3-Pyridazinyl	0,18	0,17	0,18	0,04	0,30	0,28	0,48
4-Pyridazinyl	0,21	0,27	0,24	0,02	0,35	0,36	0,59

the phenyl groups in the ^{13}C NMR spectra of phenylpyridazines Ia and IIa (Table 2) determined relative to the signal of benzene (128.41 ppm) with allowance for corrections for the diamagnetic anisotropy of the pyridazine ring.

The σ_I and σ_R constants were calculated in accordance with [20] on the basis of the CS of the protons of the amino group in the PMR spectra of aminophenylpyridazines Ib and Ic, as well as IIb and IIc, reckoned relative to the signal of the protons of the amino group of aniline (4.90 ppm) with allowance for corrections for the diamagnetic anisotropy of the pyridazine ring.

The contribution of the "ring current" induced in the benzene ring by the magnetic field to the CS of the resonating ring as a function of the coordinates of the latter relative to the center of the benzene ring was previously calculated in [21]. These data can also be used in the case of six-membered nitrogen heterocycles under the condition that, if the geometrical parameters of the heteroring differ little from the benzene parameters, the π-electron structure undergoes little perturbation when a nitrogen heteroatom is introduced into it. Such assumptions were previously made with respect to pyridine [18] and pyrimidine [20]. On the basis of calculations of the anisotropy of the diamagnetic susceptibilities of six-membered nitrogen heterocycles [22], it might be assumed that the corrections for the magnetic anisotropy of pyridazinyl groups would differ by no more than 10% of the values previously estimated for the phenyl group. However, with allowance for the certain certain degree of decrease in the bond lengths in substituted pyridazines as compared with the benzene analogs this difference will be even less appreciable, and this makes it possible to use in this case corrections of 0.15 ppm for the m-carbon atoms (C_m), 0.10 ppm for the p-carbon atoms (C_p), 0.03 ppm for the m-amino groups, and 0.02 ppm for the p-amino groups.

The σ constants of the pyridazinyl groups calculated from the corresponding equations are presented in Table 3. Whereas for the 3-pyridazinyl group the induction constants determined by the two methods coincide completely, they differ for the 4-pyridazinyl group. The reason for this difference may consist in conferring the same status to the σ_R and σ_R^- constants, which is valid only to a rough approximation. Nevertheless, the average σ_I value for the 4-pyridazinyl group (0.24) is comparable to the corresponding constant of the 4-pyridyl group (0.21 [18]).

As expected, the 4-pyridazinyl group displays a stronger resonance effect than the 3-pyridazinyl group; the σ_R constants for the two groups are approximately averages between the constants of 2- and 4-pyridyl and pyrimidinyl groups. This can be stated to an equal degree with respect to the generalized σ_p Hammett constants.

TABLE 4. Characteristics of Arylpyridazines I, II, Ve, VIe, VII, XId, XIId, and XIII

Compound	mp,* °C	UV spectrum, λ_{max} (log ε)	Found, %			Empirical formula	Calc., %			Yield, %
			C	H	N (Cl)		C	H	N (Cl)	
Ia	102—104 102—103 [11]	249 (4,28), 276, sh (3,81)								38
Ib	139—140	238 (4,34), 263, sh (4,02), 323 (3,11)	70,5	5,17	24,9	$C_{10}H_9N_3$	70,2	5,30	24,5	50
Ic	173—174 146—147 [13]	238, sh (3,97), 310 (4,30)	70,0	5,34	24,2	$C_{10}H_9N_3$	70,2	5,30	24,5	65
IIa	85,5—87 86—86,5 [24]	224, sh (4,02), 266 (4,26)								91
IIb	138,5—140,5	226, sh (4,18), 243 (4,25), 267, sh (4,16), 333 (3,40)	69,9	5,30	24,6	$C_{10}H_9N_3$	70,2	5,30	24,5	18
IIc	213—214	240 (4,05), 350 (4,30)	70,2	5,20	24,4	$C_{10}H_9N_3$	70,2	5,30	24,5	21
Ve	284—286		55,4	3,62	19,6	$C_{10}H_7N_3O_3$	55,3	3,25	19,4	80
VIe	289—291		51,0	2,40	17,9 (15,1)	$C_{10}H_6ClN_3O_2$	51,0	2,57	17,8 (15,1)	95
VIId	166—168		58,6	4,09	20,5	$C_{10}H_8ClN_3$	58,4	3,92	20,4	10
XId	320—321		51,3	3,12	18,1	$C_{10}H_7N_3O_4$	51,5	3,03	18,0	60
XIId	182,5—183,5		44,2	1,94	15,4 (26,4)	$C_{10}H_5Cl_2N_3O_2$	44,5	1,87	15,6 (26,3)	90
XIIIa	110—111		63,1	3,54	14,7	$C_{10}H_7ClN_2$	63,0	3,70	14,7	16
XIIIb	149—150		58,4	3,82	20,6	$C_{10}H_8ClN_3$	58,4	3,92	20,4	4
XIIIc	189—190		58,5	3,93	20,7	$C_{10}H_8ClN_3$	58,4	3,92	20,4	22

*The compounds were crystallized: Ib and Ve from ethanol, and XIIIb from acetone (with decomposition); Ve, VIe, and XId in capillaries.

EXPERIMENTAL

The UV spectra of solutions of the compounds in ethanol were recorded with a Specord UV-vis spectrophotometer. The PMR spectra of 0.5 M solutions of the compounds in DMSO were recorded with a Varian A-56/60-A spectrometer (60 MHz) with the ^{13}C—H satellite of DMSO [221 Hz from the signal of tetramethylsilane (TMS)] as the internal standard. The ^{13}C NMR spectra were recorded with a Bruker WP-200-SY spectrometer (50.33 MHz) under pulse conditions; the pulse width was 20 μsec, the lag between pulses was 10 sec, the scanning width was 10 kHz, and the digital resolution was 0.6 Hz.

The characteristics and the results of elementary analysis of the synthesized compounds are presented in Table 4.

3-(p-Nitrophenyl)-6-oxo-1,6-dihydropyridazine (Ve). A solution of 5.8 g (55 mmole) of hydrazine hydrochloride in 55 ml of 1 N KOH was added to a heated (to 90°C) solution of 11.2 g (50 mmole) of p-nitrobenzoylpropionic acid (IIIe) in 50 ml of 1 N KOH, and the mixture was refluxed for 2 h. It was then cooled, and the resulting red-brown precipitate of 3-(p-nitrophenyl)-6-oxo-1,4,5,6-tetrahydropyridazine (IVe) was separated, washed with water, and dried. An additional amount of IVe was obtained from the filtrate after treatment with acetic acid and trituration of the liberated oily product with acetic acid. The overall yield of IVe, with mp 228-231°C, was 4.7 g (45%).

A solution of 3.5 g (22 mmole) of bromine in 5 ml of acetic acid was added dropwise with stirring at 70°C to a saturated solution of 4.4 g (20 mmole) of IVe in acetic acid, and the mixture was heated with stirring for another hour. It was then cooled, and the precipitate was separated and washed with acetic acid and ether to give 4.85 g (80%) of the hydrobromide of Ve. This product was recrystallized successively from acetic acid and ethanol to give greenish-yellow crystals of Ve.

3-(p-Nitrophenyl)-6-chloropyridazine (VIe). A mixture of 5.8 g (27 mmole) of Ve, 20 ml of $POCl_3$, and 2 ml of N,N-dimethylaniline was heated at 130°C for 7 h, after which the ex-

cess $POCl_3$ was removed by vacuum distillation, and the residue was decomposed with ice. The aqueous mixture was neutralized with $NaHCO_3$, and the precipitate was separated and washed with water and $CHCl_3$. For analysis, the product was crystallized successively from monoglyme and DMSO and sublimed *in vacuo*.

3-Phenyl-6-chloropyridazine (VIa) and 3-(m-Nitrophenyl)-6-chloropyridazine (VId). These compounds were obtained by a method similar to that used to prepare VIe. Their constants corresponded to those presented in [11, 14].

3-Phenylpyridazine (Ia). A mixture of 3.81 g (20 mmole) of VIa, 1.65 g (20 mmole) of sodium acetate, and 0.1 g of 10% palladium on carbon in 15 ml of ethanol was hydrogenated with hydrogen at atmospheric pressure. After hydrogen absorption had ceased, the mixture was filtered, the filtrate was evaporated, and the residue was crystallized from petroleum ether and sublimed *in vacuo*.

3-(m-Aminophenyl)pyridazine (Ib). A mixture of 0.59 g (2.5 mmole) of VId, 0.25 g (3 mmole) of sodium acetate, 0.2 g of 10% palladium on carbon, 20 ml of ethanol, and 10 ml of acetic acid was hydrogenated with hydrogen at 40°C. Upon completion of hydrogen absorption the mixture was filtered, the filtrate was evaporated, and the residue was treated with Na_2CO_3 solution. The mixture was then extracted with $CHCl_3$, and the extract was dried and evaporated. The residue was crystallized from benzene and sublimed *in vacuo*.

3-(p-Aminophenyl)pyridazine (Ic) and 3-(p-Aminophenyl)-6-chloropyridazine (VII). A mixture of 1.18 g (5 mmole) of VIe, 0.5 g (6 mmole) of sodium acetate, 0.3 g of 10% palladium on carbon, 30 ml of ethanol, and 10 ml of acetic acid was hydrogenated with hydrogen at 50°C. After hydrogen absorption had ceased, the mixture was filtered, and the filtrate was evaporated *in vacuo*. The residue was treated with K_2CO_3 solution, and the mixture was extracted with $CHCl_3$. The extract was evaporated to give a mixture of products, which were separated by thin-layer chromatography (TLC) on silica gel with the addition of a luminophore and ethyl acetate–$CHCl_3$ (1:1) as the mobile phase. The zones were detected in UV light. The lower zone was collected and eluted with ethanol, and the eluate was evaporated. The residue was crystallized from benzene with activated charcoal and sublimed at 160°C (0.2 mm) to give Ic.

Compound VII was obtained from the upper zone after elution with ethanol, evaporation of the eluate, crystallization of the residue from benzene, and sublimation at 160°C (0.2 mm).

m-Nitrophenylsuccinic Anhydride (IXd). A mixture of 4.3 g (18 mmole) of m-nitrophenylsuccinic acid (VIIId), 20 ml of acetyl chloride, and 2 ml of thionyl chloride was refluxed until HCl evolution ceased, after which it was evaporated *in vacuo*, and the residue was sublimed at 180–185°C (4 mm) and crystallized from benzene–CCl_4 (1:3) to give 3.8 g (95%) of IXd with mp 109–111°C. Found: C 54.6; H 3.18; N 6.21%. $C_{10}H_7NO_5$. Calculated: C 54.3; H 3.19; N 6.33%.

m-Nitrophenylmaleic Anhydride (Xd). A mixture of 4.8 g (22 mmole) of IXd, 7.7 g (43 mmole) of N-bromosuccinimide, 0.1 g of benzoyl peroxide, and 100 ml of dry CCl_4 was refluxed for 26 h with periodic removal by distillation of the bromine accumulated in the reaction mixture. The mixture was then evaporated, and the residue was extracted several times with boiling benzene. The extract was cooled, the succinimide was separated, and the filtrate was evaporated. The residue was triturated with dry acetone and squeezed dry on the filter to give 1.8 g (38) of Xd with mp 158–159°C (from acetone). Found: C 55.1; H 2.53; N 6.37%. $C_{10}H_5NO_5$. Calculated: C 54.8; H 2.30; N 6.39%.

4-(m-Nitrophenyl)-3,6-dioxo-1,2,3,6-tetrahydropyridazine (XId). A solution of 1.75 g (8 mmole) of Xd in 15 ml of dry monoglyme was added in small portions to a refluxing solution of 1.26 g (12 mmole) of hydrazine hydrate in 40 ml of water, and the resulting suspension was refluxed for 3 h. It was then cooled, and the precipitate was separated, washed with water, and dried. For analysis, the product was crystallized from ethanol and sublimed *in vacuo*.

4-(m-Nitrophenyl)-3,6-dichloropyridazine (XIId). A mixture of 1.12 g (5 mmole) of XId and 5 ml of $POCl_3$ was refluxed for 1 h, after which the excess $POCl_3$ was removed by vacuum distillation, and the residue was treated with ice. The precipitate was separated, washed with water, dried, crystallized from benzene–isooctane (1:1), and sublimed at 150–160°C (4 mm).

4-Phenyl-3,6-dichloropyridazine (XIIa) and 4-(p-Nitrophenyl)-3,6-dichloropyridazine (XIIe). These compounds were obtained by a method similar to that used to prepare XIId. Their constants corresponded to the data in [12, 23].

4-Phenylpyridazine (IIa). A mixture of 3.9 g (17 mmole) of XIIa, 2.7 g (34 mmole) of sodium acetate, 0.5 g of 10% palladium on carbon, and 50 ml of ethanol was hydrogenated with hydrogen at 40°C. At the end of the hydrogenation, the temperature was raised to 60°C, and the mixture was filtered. The filtrate was evaporated, and the residue was extracted with $CHCl_3$. The extract was passed through a layer of Al_2O_3 and evaporated to dryness, and the residue was sublimed *in vacuo*.

4-Phenyl-3-chloropyridazine (XIIIa). A mixture of 0.3 g (1.3 mmole) of XIIa, 0.11 g (1.3 mmole) of sodium acetate, 0.05 g of 10% palladium on carbon, and 10 ml of ethanol was hydrogenated with hydrogen at room temperature. After an equimolar amount of hydrogen had been absorbed, the mixture was filtered, and the filtrate was evaporated. The resulting mixture of products (IIa, XIIIa, and traces of XIIa) was separated by TLC on silica gel with the addition of a luminophore and $CHCl_3$—ethanol (100:1.5) as the mobile phase; the zones were detected in UV light. The product was eluted from the middle zone with ethanol, and the eluate was evaporated. The residue was crystallized from hexane and sublimed *in vacuo* to give XIIIa.

The product was eluted from the lower zone on the TLC plate with ethanol, the eluate was evaporated, and the residue was crystallized from hexane and sublimed *in vacuo* to give 0.03 g (19%) of IIa with mp 86-87°C.

4-(m-Aminophenyl)pyridazine (IIb) and 4-(m-Aminophenyl)-3-chloropyridazine (XIIIb). A mixture of 1.2 g (4.4 mmole) of XIId, 0.75 g (9 mmole) of sodium acetate, 0.3 g of 10% palladium on carbon, 40 ml of ethanol, and 40 ml of acetic acid was hydrogenated with hydrogen at 40°C with periodic heating of the mixture to 60°C. After hydrogen absorption had ceased, the suspension was filtered, and the filtrate was evaporated. The residue was treated with K_2CO_3 solution and extracted with $CHCl_3$. The extract was evaporated, and the mixture of products was separated on silica gel as described above with diethyl ether as the mobile phase. The product was eluted from the lower zone with ethanol, the eluate was evaporated to dryness, and the residue was dissolved in the minimum amount of acetone and precipitated with ether. The precipitate was separated, crystallized from acetonitrile, and sublimed at 130-140°C (0.2 mm) to give IIb.

The product was eluted from the middle zone with ethanol, the eluate was evaporated, and the residue was crystallized from $CHCl_3$. For analysis, the product was sublimed at 150-160°C (0.05 mm) and crystallized from acetone to give XIIIb.

4-(p-Aminophenyl)pyridazine (IIc). A mixture of 1.35 g (5 mmole) of XIIe, 0.5 g (6 mmole) of sodium acetate, 0.3 g of 10% palladium on carbon, 40 ml of ethanol, and 40 ml of acetic acid was hydrogenated with hydrogen at 40°C with periodic heating of the mixture to 60°C. The mixture was then filtered, the filtrate was evaporated, and the residue was treated with K_2CO_3 solution. The mixture was extracted with $CHCl_3$, the extract was evaporated, and the residue was washed with the minimum amount of acetonitrile. It was then crystallized from acetonitrile and sublimed at 160-170°C (4 mm).

4-(p-Aminophenyl)-3-chloropyridazine (XIIIc) and 4-(p-Aminophenyl)-3,6-dichloropyridazine (XIIc). A 0.3 g (1.1 mmole) sample of XIIe was hydrogenated with hydrogen at 40°C under the conditions of the preceding experiment. After 4.5 mmole of hydrogen had been absorbed, the mixture was filtered, and the filtrate was worked up as in the preceding experiment. The resulting mixture of products was separated by TLC on silica gel with the addition of a luminophore and diethyl ether as the mobile phase; the zones were detected in UV light. Elution of the upper zone with ethanol, evaporation of the eluate, and crystallization of the residue from benzene gave 0.05 g (19%) of XIIc; the p-nitrobenzoyl derivative had mp 268-272°C (in a capillary) (mp 259-264°C [23]).

Elution of the middle zone on the TLC plate with ethanol, evaporation of the eluate, and crystallization of the residue from acetonitrile and sublimation *in vacuo* gave XIIIc.

Workup of the lower zone on the TLC plate by the same method gave 0.03 g (16%) of IIc with mp 208-210°C.

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