Preparation, Proton and Carbon-13 Structure Determination, and Fungicidal Activity of Chlorinated 1-Arylamino-1*H*-pyrrole-2,5-diones

Carmela Yaroslavsky* and Peretz Bracha

Makhteshim Chemical Works Ltd.,
P. O. Box 60, Beersheva 84100, Israel

Robert Glaser

Department of Chemistry, Ben Gurion University of the Negev,
Beersheva 84105, Israel

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1-(2',4'-dichloro)phenylamino-1*H*-pyrrole-2,5-dione and 1-(2',4',6'-trichloro)phenylamino-1*H*-pyrrole-2,5-dione were prepared *via* direct chlorination of 2-phenyl-3-oxo-6-hydroxy-2*H*-pyridazine. Both pmr and mass spectroscopy clearly showed that dichloro substitution occurred in the aromatic moiety and not in the vinylic region of the molecule. The former method showed that pyridiazine- to pyrrole-ring isomerization had occurred already at the level of dichlorination. The identical 2',4'-dichlorophenyl and 2',4',6'-trichlorophenylpyrrolediones were also prepared by reaction of maleic anhydride with the appropriate arylhydrazine. Similar 2',4-dichlorophenyl and 2',4',6'-trichlorophenyl analogues were prepared using dichloromaleic anhydride. Cmr spectroscopic techniques were used for pyridazine-/pyrrole-ring stereochemical assignment of products derived from dichloromaleic anhydride. 1-(2',4'-dichloro)phenylamino-1*H*-pyrrole-2,5-dione and the trichlorophenyl analogue were shown to exhibit fungicidal activity in both *in-vivo* and *in-vitro* assays.

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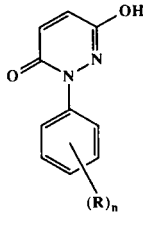
Introduction.



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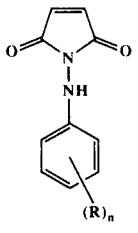

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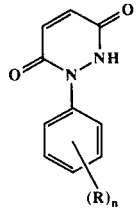

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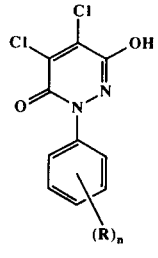
The reactions of maleic and dichloromaleic anhydride with arylhydrazines were studied in the quest for novel pesticides. Maleic anhydride reacts with arylhydrazines to yield the 2-aryl-3-oxo-6-hydroxy-2*H*-pyridazine (**1**) and the 1-arylamino-1*H*-pyrrole-2,5-dione (**2**) depending on the reaction media and the type of substitution on the phenyl ring [1,2]. For example, reaction of maleic anhydride with phenylhydrazine or 2-chlorophenylhydrazine in various media [*e.g.* refluxing hydrochloric acid] yields the corresponding pyridazine **1** (R = H or 2-Cl) [1,2]. Tautomeric diketo analogues **3** have also been reported [3]. Under milder conditions (*e.g.* ambient temperature, acetic acid) the intermediate hydrazido acid can be isolated and then later cyclized [acetic anhydride, 80°] to the relevant pyrrole-2,5-dione derivative, *e.g.* **2** (R = 2-Cl) [2]. Treatment of **2** with a variety of acids results in isomerization to the corresponding pyridazine **1** [2].

In contradistinction there is a greater tendency for 1-arylamino-3,4-dichloro-1*H*-pyrrole-2,5-dione (**5**) formation when dichloromaleic anhydride is used in place of maleic anhydride. Thus, phenylhydrazine, in this case, afforded the corresponding dichloropyrrole-2,5-dione **5** (R = H) [4]. This paper reports the preparation of pyrrole-2,5-dione derivatives **2** (R = 2',4'-dichloro and 2',4',6'-trichloro) *via* the direct chlorination of 2-phenyl-3-oxo-6-hydroxy-2*H*-pyridazine (**1**, R = H). The preparation and structure proof of the novel pyrrole-2,5-dione derivatives **2,5** (R = 2',4',6'-trichloro) when either maleic anhydride or dichloromaleic anhydride is reacted with 2,4,6-trichlorophenylhydrazine will also be discussed.



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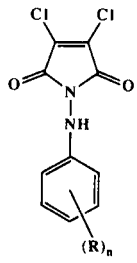

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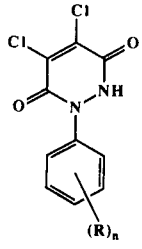

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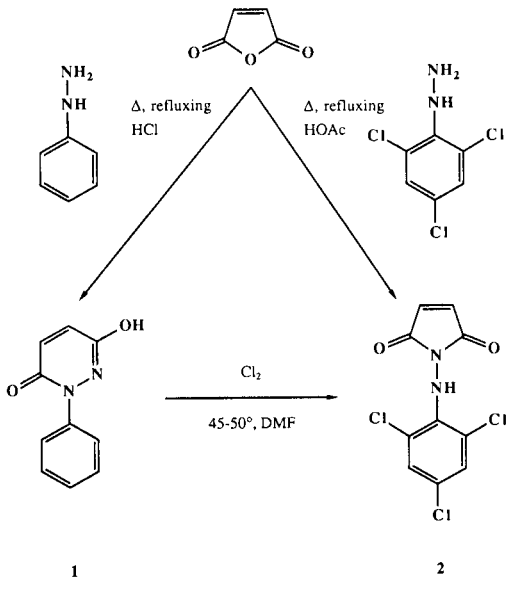
Results and Discussion.

The direct chlorination of 2-phenyl-3-oxo-6-hydroxy-2*H*-pyridazine (**1**, R = H) in polar solvents such as dimethylformamide or glacial acetic acid afforded the 1-(2',4'-dichloro and 2',4',6'-trichlorophenylamino)-1*H*-pyrrole-2,5-diones (**2**, R = 2',4'-dichloro and 2',4',6'-trichloro), see scheme. Gas chromatographic monitoring of the chlorination reaction, and subsequent quenching upon the initial appearence of the trichloro-analogue, enabled the isolation of the 2',4'-dichlorophenylpyrrole product (**2**, R =

2',4'-dichloro). More extensive chlorination afforded the corresponding 2',4',6'-trichlorophenylpyrrole product (**2**, R = 2',4',6'-trichloro). Pmr and mass spectroscopy clearly showed that dichloro substitution occurred in the aromatic moiety and not in the vinylic region of the molecule. The former method showed that pyridazine-to pyrrole-ring isomerization had occurred already at the level of dichlorination. The spectroscopic evidence will be presented later on in this paper.

Scheme



1 2

These same 2',4'-dichlorophenyl- and 2',4',6'-trichlorophenyl-substituted compounds could also be produced *via* reaction of the appropriate 2,4-dichloro or 2,4,6-trichlorophenylhydrazine and maleic anhydride in acetic acid (90°). In a similar manner, 1-(2',4',6'-trichlorophenylamino)-3,4-dichloro-1*H*-pyrrole-2,5-dione (**5**, R = 2',4',6'-trichloro) was prepared starting from dichloromaleic anhydride. We have observed that the type and number of aryl ring-substituents and the reaction media greatly effects the distribution of products **1**,**2** and also **4**,**5** [5]. The more acidic the reaction medium, the greater the quantity of **1** *vs.* **2** and also **4** *vs.* **5** [5]. Thus, refluxing aqueous hydrochloric acid transforms **2** into **1** and **5** into **4** [5]. For example, the ease of the transformation of **5** into **4** is in the order of R = CH_3 > H > *Cl* > 2*Cl* [5]. The pyrrole-2,5-dione derivatives mentioned above are typically yellow-orange in color, while the pyridazino analogues are colorless. In general, the pyrrolediones appear to be kinetically controlled products which then may isomerized into the usually more thermodynamically stable pyridazine constitutionally heteromeric isomers. This is seen in the reaction with *ortho*- or *para*-tolylhydrazines and dichloromaleic anhydride [in hydrochloric acid] where the yellow color of the pyrrole-dione is initially observed and then gradually disappears as the colorless pyridazine product is formed [5]. On the other hand, in spite of the fact that it appears that electron withdrawing groups retard the pyrrole to pyridazine isomerization it is noted that 1-aryl-3,6-dioxo-2*H*-pyridazines (**3**, R = 2'-NO_2 or 2'-$NO_2$4'-Br or 2',4'-dinitro) are known to be formed from the reaction of the appropriately substituted phenylhydrazines and maleic anhydride [2]. Therefore, in our case, a combination of steric factors as well as electronic factors appear to stabilize the 2',4',6'-trichlorophenyl substituted pyrrole-dione form *vis-a-vis* the pyridazine isomer. More work is needed to elucidate the factors influencing the relative stabilities of the two isomers.

Nmr Spectroscopy.

Pmr spectroscopy is very diagnostic for differentiation between the pair of pyridazine- **1** and pyrrole-ring **2** isomers formed by reaction of an arylhydrazine with maleic anhydride. Heterotopic vinylic protons in the former give rise to the expected *AB*-quartet [J(AB) 9.8(2) Hz for **1** (R = H)]. On the other hand, vinylic protons in the latter are chemical shift equivalent by symmetry since they are either homotopic or enantiotopic [depending on the aryl-ring substitution pattern]. While the lactam **3** also contains heterotopic vinylic protons, the presence of the characteristic lactim hydroxyl-proton absorbance at *ca.* 11.5 ppm enables one to discriminate between tautomeric forms **1**,**3**. In addition, it is also noted that lactim hydroxyl-proton acidity imparts solubility for 3-oxo-6-hydroxypyridazines **1** in 10% sodium carbonate solution.

Only one isomer was obtained in the case of the 2',4'-dichloro and 2',4',6'-trichlorophenyl substituted products of the chlorination reaction on 2-phenyl-3-oxo-6-hydroxy-2*H*-pyridazine (**1**, R = H) [6]. Similarly, only one isomer was isolated in the reactions between 2,4,6-trichlorophenylhydrazine and maleic anhydride or dichloromaleic anhydride) [6]. Therefore, the single product from maleic anhydride could be either structure **1** or **2** or **3**. While that from dichloromaleic anhydride is either of type **4** or **5** or **6**. In the case of structures **1**-**3**, infrared and pmr spectroscopy plus solubility in aqueous basic solutions could readily distinguish between diketo analogues **2** or **3** or the lactim **1**. The inital chlorination product was readily shown to contain a 2',4'-dichlorophenyl moiety by the three aromatic proton resonances exhibiting characteristic meta J(3'-5') = 2.7 Hz and ortho J(5'-6') = 8.6 Hz coupling patterns. Thus, chlorination did not occur in the heterocyclic ring. This was confirmed by the appearance in the mass spectrum of a dichloro substituted azacyclic-"tropylium-type" ion, m/e = 160 $[C_6H_3Cl_2NH]^+$. The observance of a single isochronous resonance (δ 7.13) for the two enantiotopic vinylic protons showed that pyridazine-ring to pyrrole-ring isomerization had occurred already at the dichlorination stage of the reaction.

Further chlorination was also in the aromatic ring since the trisubstituted product had a single aromatic two proton singlet [H(3',5')], and the characteristic single isochronous resonance (δ 7.12) for the two enantiotopic vinylic protons. Thus, the pyrrole-2,5-dione moiety now remained intact in the additional chlorination step. Again, the mass spectrum showed a trichloro substituted azacyclic-"tropylium-type" ion, m/e = 194 [$C_6H_2Cl_3NH$]$^+$. The reaction products of 2,4-dichloro or 2,4,6-trichlorophenylhydrazine and maleic anhydride afforded identical mp, infrared, pmr and mass spectra to the corresponding chlorination products noted above.

Mroczkiewicz [7] has also reported that the pyrrole-2,5-dione moiety remained intact in the bromina-

Table I

Carbon-13 NMR Spectral Paramaters for 2-Phenyl-3-oxo-6-hydroxy-2*H*-pyridazine (**1**, R = H); 1-(2',4',6'-Trichloro)phenylamino-1*H*-pyrrole-2,5-dione (**2**, R = 2',4',6'-trichloro); 2-Phenyl-3-oxo-4,5-dichloro-6-hydroxy-2*H*-pyridazine (**4**, R = H); 1-Phenylamino-3,4-dichloro-1*H*-pyrrole-2,5-dione (**5**, R = H); and 1-(2',4',6'-Trichloro)phenylamino-3,4-dichloro-1*H*-pyrrole-2,5-dione (**5**, R = 2',4',6'-trichloro) [a]

δ (C)		**1** (R = H) [b]	**2** (R = 2',4',6'-trichloro) [b]	**4** (R = H) [b]	5(R = H) [b]	5 (R = 2',4',6'-trichloro) [b]
C(2)		-	168.44	-	162.78	161.17
C(3)		157.93	133.35	153.91	132.29	131.62
C(4)		134.10 [c]	133.35	136.05 [c]	132.29	131.62
C(5)		127.48 [c]	168.44	130.72 [c]	162.78	161.17
C(6)		152.91	-	148.58	-	-
C(1')		141.71	137.97	140.93	146.88	137.09
C(2',6')		125.39	123.03	125.57	113.19	124.38
C(3',5')		128.53	129.00	128.51	129.65	128.91
C(4')		127.73	125.58	128.00	120.97	126.96
^nJ(C-H)	n					
C(2)-H(3)	2	-	9.0(1)	-	[d]	[d]
C(2)-H(4)	3	-	9.0(1)	-	[d]	[d]
C(3)-H(3)	1	-	186.5(1)	-	[d]	[d]
C(3)-H(4)	2	-	1.7(1)	-	[d]	[d]
C(1')-H(3')	3	-	6.8	-	9.1(1)	
C(2')-H(2')	1	-	[d]	-	160.5(2)	[d]
C(2')-H(3')	2	-	2.3	-		
C(2')-H(4')	3	-	[d]	-	6.0(7)	[d]
C(2')-H(6')	3	-	[d]	-	6.0(7)	[d]
C(3')-H(3')	1	-	172.5(7)	-	174.4(1)	161.4(2)
C(3')-H(5')	3	-	6.2(7)	-	5.8(1)	7.7(2)
C(4')-H(2')	3	-	[d]	-	7.1(2)	[d]
C(4')-H(3')	2	-	5.1(8)	-		
C(4')-H(4')	1	-	[d]	-	162.9(1)	[d]

[a] 50.3 MHz, dimethyl sulfoxide-d_6, 298° K, broad-band proton decoupled and undecoupled modes. [b] Chemical shifts are PPM downfield from tetrramethylsilane, coupling constants are in Hz, and their standard deviation is given in parenthesis. [c] Chemical shifts for both carbons may be reversed. [d] Not applicable.

tion reaction [$CHCl_3$ solvent] of 1-(2'-bromophenylamino)-1*H*-pyrrole-2,5-dione (**2**, R = 2') to yield the corresponding dibromominated analogue (**2**, R = 2',4'-dibromo). However, he noted that pyrrole-ring to pyridazine-ring isomerization occurred in bromine-acetic acid solution to yield 2-(2'-bromo)phenyl-3-oxo-6-hydroxy-2*H*-pyridazine (**1**, R = 2'-bromo) without formation of the corresponding dibromination product [7].

The methodology utilized to characterize the chlorination products (and reaction products from arylhydrazines with maleic anhydride) did not permit structural differentiation between the two potential diketo isomers **5,6** derived from dichloromaleic anhydride. This had to be based primarily on cmr spectroscopy due to the absence of vinylic protons on the respective pyridazine or pyrrole rings. The lower symmetry of the pyridazine moiety in **6** *versus* the higher symmetry in the pyrrole moiety in **5** again provided the basis for the cmr characterization of both constitutionally heteromeric diketo isomers. The observation of *two sets* of isochronous enantiotopic vinylic and carbonyl carbon atoms for the 2',4',6'-trichlorophenyl substituted product ruled out the possibility of pyridazine-ring stereochemistry (either **4** or the corresponding diketo tautomer **6**). Thus, its structure was able to be assigned as pyrrole-2,5-dione **5** (R = 2',4',6'-trichloro). Similar findings were noted for the reaction product **2** between 2,4,6-trichlorophenylhydrazine and maleic anhydride. The cmr spectral parameters of the **4,5** (R = H) isomeric pair are presented in Table I for comparison with those of **1** (R = H) and **2,5** (R = 2',4',6'-trichloro).

In the series of five compounds listed in Table I, all the aryl C(3',5') *meta*-carbons were protonated and thus their signal intensities were, as expected, all higher than those from the unprotonated nuclei. Their chemical shift values were also all very similar [*ca.* 128.9(5) ppm, standard deviation in parenthesis]. Inspection of the aryl chemical shifts in Table I shows the effect of dichloro substitution at the 4,5-positions on the pyridazine ring in **4** or at the 3,4-positions on the pyrrole ring in **5**. Comparison of pyridazine **1** *versus* **4** (R = H) and pyrrole **2** *versus* **5** (R = 2',4',6'-trichloro) shows that dichloro substitution in the heterocycle resulted in an upfield shift of *ca.* 0.83(7) ppm for aryl *ipso*-carbons in both cases, a downfield shift of *ca.* 0.3(1) ppm for the aryl *ortho*-carbons in both cases, almost no change for the aryl *meta*-carbons in both cases, and a downfield shift of 0.27 ppm (**1** *vs.* **4**) and 1.38 ppm (**2** *vs.* **5**) for the aryl *para*-carbons. Of the four carbons in the pyridazine ring of **1**, the protonated vinylic carbons C(4,5) were assigned on the basis of their relatively higher signal intensities. Dichloro substitution at these 4,5-positions on the pyridazine ring of **4** resulted in upfield shifts of *ca.* 4.2(2) ppm for both the carbonyl C(3) and the COH C(6) atoms. Assuming that the lower field vinylic carbons in **1** and **4** both occupy the same respective pyridazine-ring position, then dichloro substitution at the 4,5-positions on the pyridazine ring of **4** resulted in a downfield shift of *ca.* 2.6(9) ppm of both C(4,5). Dichloro-substitution at the 3,4-positions of the pyrrole ring resulted in an upfield shift of 7.07 ppm for the carbonyl carbons in **5** *versus* **2** (R = 2',4',6'-trichloro), while now the C(3,4) carbons themselves also suffer an upfield shift (although smaller in magnitude, 1.73 ppm).

In the pair of 3,4-dichloropyrroles **5** (R = H and 2',4',6'-trichloro) the trichloro-substitution in the aryl moiety resulted in an upfield shift of 1.61 ppm for the carbonyl carbons C(2,5) and a smaller upfield shift of 0.67 ppm for the vinylic carbons C(3,4). The two enantiotopic vinylic protons are clearly magnetically non-equivalent for each carbonyl carbon. However, in the undecoupled spectrum of **2** (R = 2',4',6'-trichloro) the carbonyl carbons are split into an apparent triplet [J 9.0(1) Hz] by virtual coupling to the geminal and vicinal H(3,4) proton pair.

Table II

Fungicidal Activities of 1-(2',4'-Dichloro)phenylamino-1*H*-pyrrole-2,5-dione (**2**, R= 2',4'-Dichloro) and 1-(2',4',6'-Trichloro)phenylamino-1*H*-pyrrole-2,5-dione (**2**, R= 2',4',6'-trichloro) as Measured by *in-vivo* and *in-vitro* assays

in-vivo assays:

R-group in **2**	*peronospora* on lettuce sprouts (% contamination/untreated)	estimation of *stemphylium* (scale 0-5 [5 untreated])
2',4'-dichloro	47/90.5	2.25
2',4'6'-trichloro	1.75/86.4	0.75

in-vitro assays of percent growth on substrates: [a]

R-group in **2**	*botrytis cinerea*	*pyricularia oryzae*	*venturia inequalis*	*pythium aphanidermatus*	*sclerotium rolfsii*
2',4'-dichloro	6	13	10	25	60
2',4'6'-trichloro	33	62	75	75	0

[a] 100 percent growth in the control assay.

Fungicidal Acitivity.

The di- and trichlorophenyl compounds **2** (R = 2',4'-dichloro and 2',4',6'-trichloro) were tested for fungicidal activity both *in-vivo* and *in-vitro*, and the results are listed in Table II. Both compounds showed substantial fungicidal activity. The trichlorophenyl derivative showed more potent *in-vivo* activity in the two assays, while the dichlorophenyl analogue showed greater activity in four out of the five *in-vitro* assays. In the corresponding family of 2',4'-dichloro [4] and 2',4',6'-trichloro compounds **5**, only the former has fungicidal activity.

EXPERIMENTAL

Pmr and cmr spectra (4.7 T) were recorded at 200.1 and 50.3 MHz, respectively, on a Bruker WP-200-SY Fourier transform spectrometer. Cmr spectra were acquired in the broad-band proton decoupling and undecoupled mode. The dimethyl sulfoxide-d_6 solvent was used as an internal lock, and tetramethylsilane was used as an internal reference. Mass spectra were performed on VG-Instruments model VG-7035 mass spectrometer operating in the electron ionization mode, 70 eV. 2-phenyl-3-oxo-6-hydroxy-2*H*-pyridazine (**1**, R = H) was prepared according to literature methods [8].

1-(2',4'-Dichloro)phenylamino-1*H*-pyrrole-2,5-dione (**2**, R = 2',4'-dichloro).

Method (a).

Chlorine was bubbled into a solution of 2-phenyl-3-oxo-6-hydroxy-2*H*-pyridazine (28 g, 150 mmoles) in dimethylformamide (200 ml) heated to 80°. The reaction was monitored by gas chromatography (5% SE-30, 220°) until the trichloro-analogue began to appear (30 minutes, 7 g chlorine). The mixture was then poured into cold water. The starting material was precipitated and filtered off. After the filtrate was extracted with ether (3 x 25 ml), the organic layers were combined, dried over magnesium sulfate, and evaporated *in vacuo*. A yellow paste was obtained which after two recrystallizations from ethanol afforded 2 g of the title compound (**2**, R = 2',4'-dichloro) as a yellow solid, mp 151-153°; ir (Nujol): ν 3338 (N-H), 1725 (C=O) cm^{-1}; pmr (dimethyl sulfoxide-d_6): δ 8.07 (s, 1H, N*H*), 7.47 (d, 1H, H(3'), J(3'-5') = 2.7 Hz), 7.18 (dd, 1H, H(5'), J(3'-5') = 2.7 Hz, J(5'-6') = 8.6 Hz), 7.13 (s, 2H, H(3,4)), 6.73 (d, 1H, H(6'), J(5'-6') = 8.6 Hz); ms: m/e 260 (2%, $[M+4]^+$), 258 (16%, $[M+2]^+$), 256 (25%, $[M = C_{10}H_6N_2O_2Cl_2]^+$), 223 (45%, $[(M+2)\text{-}Cl]^+$), 221 (100%, $[M\text{-}Cl]^+$), 164 (1%, $[(C_6H_3Cl_2NH)+4]^+$), 162 (7%, $[(C_6H_3Cl_2NH)+2]^+$), 160 (7%, $[C_6H_3Cl_2NH]^+$), 159 (1%, $[C_6H_3Cl_2N]^+$), 124 (23%).

Anal. Calcd. for $C_{10}H_6N_2O_2Cl_2$ (257.08): C, 46.72; H, 2.35; N, 10.90; Cl, 27.58. Found: C, 46.66; H, 2.19; N, 10.36; Cl, 27.66.

Method (b).

To a solution of maleic anhydride (1.74 g, 17.7 mmoles) dissolved in acetic acid (50 ml) was added, portion-wise, 2,4-dichlorophenylhydrazine (3.14 g, 17.7 mmoles). A yellow material precipitated, and the resulting mixture was stirred 4 hours at 90°. After cooling, water was added to the solution, the precipitate was filtered, and then washed with 10% aqueous sodium carbonate followed by water. After drying and recyrstallization from ethanol, 2.5 g [55%] of the title compound (**2**, R = 2',4'-dichloro) was obtained as a yellow solid, mp 151-153°. The ir, ms, and pmr spectra were identical to those obtained for the product from method (a).

1-(2',4',6'-Trichloro)phenylamino-1*H*-pyrrole-2,5-dione (**2**, R = 2',4',6'-trichloro).

Method (a).

Keeping the temperature at 45-50°, chlorine was bubbled into a solution of 2-phenyl-3-oxo-6-hydroxy-2*H*-pyridazine (120 g, 0.64 mole) in dimethylformamide (400 ml) over a period of 105 minutes (149 g of chlorine). After pouring the reaction mixture into water, the precipitate was filtered off, and then washed with 10% aqueous sodium carbonate, water, and then ethanol. After drying, 98 g [53% yield] of the title compound (**2**, R = 2',4',6'-trichloro) was obtained as a yellow crystalline solid, mp 156-158°; ir (Nujol): ν 3280 (N-H), 1725 (C=O) cm^{-1}; pmr (dimethyl sulfoxide-d_6): δ 7.94 (s, 1H, N*H*), 7.57 (s, 2H, H(3',5')), 7.12 (s, 2H, H(3,4)); cmr data are presented in Table I; ms: m/e 296 (1%, $[M+6]^+$), 294 (8%, $[M+4]^+$), 292 (24%, $[M+2]^+$), 290 (25%, $[M = C_{10}H_5N_2O_2Cl_3]^+$), 259 (11%, $[(M+4)\text{-}Cl]^+$), 257 (59%, $[(M+2)\text{-}Cl]^+$), 255 (100%, $[M\text{-}Cl]^+$), 198 (3%, $[(C_6H_2Cl_3NH)+4]^+$), 196 (9%, $[(C_6H_2Cl_3NH)+2]^+$, 194 (10%, $[C_6H_2Cl_3NH]^+$), 193 (4%, $[C_6H_2Cl_3N]^+$), 158 (15%), 144 (17%), 82 (24%).

Anal. Calcd. for $C_{10}H_5N_2O_2Cl_3$ (291.52): C, 41.20; H, 1.73; N, 9.61; Cl, 36.49. Found: C, 41.08; H, 1.57; N, 9.44; Cl, 36.44.

Method (b).

A mixture of 2,4,6-trichlorophenylhydrazine (11.6 g, 55 mmoles) and maleic anhydride (5.4 g, 55 mmoles) in acetic acid (100 ml) was brought to reflux and stirred 3 hours at that temperature. Upon cooling, cold water (125 ml) was added. The resulting yellow precipitate was filtered, washed twice with ethanol, and dried to afford 7.3 g [46%] of the title compound (**2**, R = 2',4',6'-trichloro), mp 158-159°. The ir, ms, pmr, and cmr spectra were identical to those obtained for the product from method (a).

1-(2',4',6'-trichloro)phenylamino-3,4-dichloro-1*H*-pyrrole-2,5-dione (**5**, R = 2',4',6'-trichloro).

A solution of 2,4,6-trichlorophenylhydrazine (10.57 g, 50 mmoles), dichloromaleic anhydride (8.4 g, 50 mmoles) and acetic acid (100 ml) were stirred 2.5 hours at 108°. After cooling, water and chloroform were added, the chloroform phase was separated, washed with water, 10% aqueous sodium carbonate (100 ml) and then again with water. The residue which was obtained upon evaporation of the chloroform solution *in vacuo* was recrystallized from cyclohexane to give 8.5 g [47% yield] of the title compound (**5**, R = 2',4',6'-trichloro), mp 127-130°; pmr (dimethyl sulfoxide-d_6): δ 7.97 (s, 1H, N*H*), 7.62 (s, 2H, H(3',5')); cmr data are presented in Table I; ms: m/e 366 (1%, $[M+8]^+$), 364 (14%, $[M+6]^+$), 362 (61%, $[M+4]^+$), 360 (100%, $[M+2]^+$), 358 (60%, $[M = C_{10}H_3N_2O_2Cl_5]^+$), 329 (3%, $[(M+6)\text{-}Cl]^+$), 327 (27%, $[(M+4)\text{-}Cl]^+$), 325 (65%, $[(M+2)\text{-}Cl]^+$), 323 (48%, $[M\text{-}Cl]^+$), 198 (18%, $[(C_6H_2Cl_3NH)+4]^+$), 196 (72%, $[(C_6H_2Cl_3NH)+2]^+$), 194 (76%, $[C_6H_2Cl_3NH]^+$), 193 (24%, $[C_6H_2Cl_3N]^+$), 183 (5%), 181 (25%), 179 (25%), 171 (8%), 169 (38%), 169 (41%), 158 (52%), 144 (24%), 87 (50%).

Anal. Calcd. for $C_{10}H_3N_2O_2Cl_5$ (360.42): C, 33.32; H, 0.84; N, 7.77. Found: C, 33.25; H, 0.88; N, 7.51.

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* To whom correspondence should be addressed.

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