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SYNTHESIS OF 2,4-DIPHENYL-1H-PYRROL-1-AMINE DERIVATIVES

L. M. Potikha[1]*, V. A. Kovtunenko[1], A. V. Turov[1], G. V. Palamarchuk[2], R. I. Zubatyuk[2], and O. V. Shishkin[2]

The direction of the reaction of 4-bromo-1,3-diphenyl-2-buten-1-one (γ-bromodypnone) with hydrazines depends on the nature of the substituent they contain. Reaction with 1-methylhydrazinium hydrosulfate gives 1-methyl-3,5-diphenylpyridazin-1-ium bromide but carboxylic acid hydrazides give N-(2,4-diphenyl-1H-pyrrol-1-yl)carboxylic acid amides. γ-Bromodypnone and phenylhydrazine give both 1,3,5-triphenyl-1,4-dihydropyridazine and N,2,4-triphenyl-1H-pyrrol-1-amine (15%). 1-(2,4-Dinitrophenyl)hydrazine gives the 2,4-dinitrophenylhydrazone of (Z)-4-bromo-1,3-diphenyl-2-buten-1-one. Condensation of 2,4-diphenyl-1H-pyrrol-1-amine with aromatic aldehydes readily leads to N-(arylmethylidene)-2,4-diphenyl-1H-pyrrol-1-amines and alkylation with methyl iodide gives N,N-dimethyl-2,4-diphenyl-1H-pyrrol-1-amine.

Keywords: 1-aminopyrrole, γ-bromodypnone, 2,4-diphenyl-1H-pyrrol-1-amine, 3,5-diphenylpyridazine.

Interest in arylpyrroles has steadily increased over the last 30 years. Among them are substances with a high level of biological activity which are used for treatment of cardiovascular, immunological, and CNS diseases [1, 2]. A number of arylpyrroles are used in agriculture, in the food industry, and in preparation of novel polymeric materials [2]. In this respect it is undoubtedly important to develop novel routes for the synthesis of 1-aminopyrroles as promising compounds for studying both their biological activity [3, 4] and their synthetic potential [5, 6].

Rather little attention has been paid to methods for obtaining 1-aminopyrroles *via* reaction of γ-halocarbonyl compounds with hydrazines [7]. It is known that these reactions can lead to pyridazine [8] or 1-aminopyrrole [7] derivatives depending on the structure of the reagents. Hence treatment of 4-bromo-1,3-diphenyl-2-buten-1-one (γ-bromodypnone) (**1**) with hydrazine hydrate gives 2,4-diphenyl-1H-pyrrol-1-amine (**2**) [9] and arylhydrazines give 1,3,5-triphenylpyridazines [9]. Our work relates to a wider investigation of the synthetic process for N-substituted 2,4-diphenyl-1H-pyrrol-1-amine derivatives **2**.

* To whom correspondence should be addressed, e-mail: potikha_l@mail.ru.

[1]Taras Shevchenko National University, Kiev 01033, Ukraine.
[2]Institute for Single Crystals, Ukraine National Academy of Sciences, Kharkiv 61001; e-mail: roman@xray.isc.kharkov.com.

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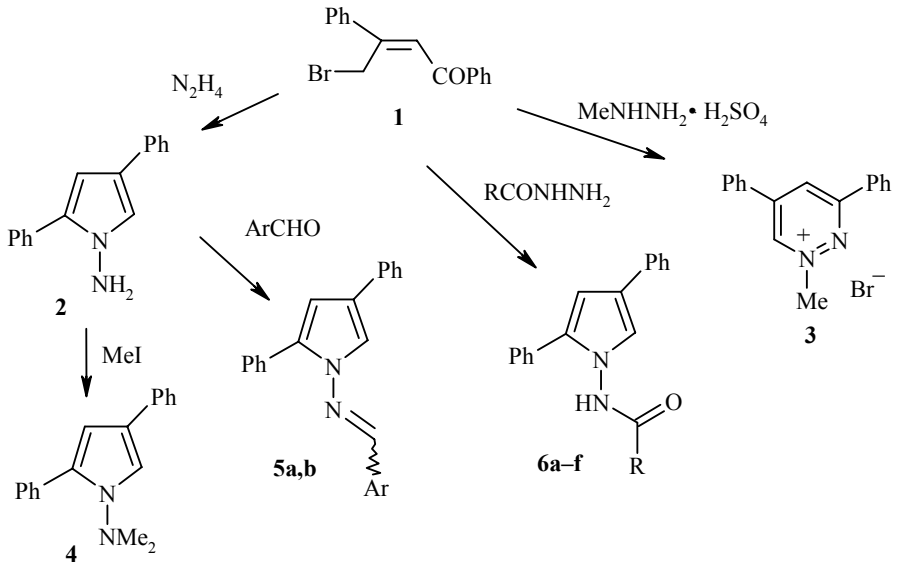
We have studied the reaction of γ-bromodypnone **1** with 1-methylhydrazinium hydrosulfate under varying conditions: melting, heating the starting materials with and without the presence of base, and heating in acetic acid. Investigations have shown that, when the reaction is carried out in the absence of base and independently of the conditions, it gives 2,4-diphenylfuran which is readily formed *via* intramolecular condensation of compound **1** induced by weak nucleophiles or in an acidic medium [10, 11]. In fact, in the presence of base (AcONa in the case of melting or $NaHCO_3$ when refluxing in alcohol) the ^{1}H NMR data shows a mixture of 2,4-diphenylfuran and the product of intermolecular condensation of γ-bromodypnone **1** and methylhydrazine is formed. The highest yield of the condensation product (53%) is achieved when the reaction is carried out in alcohol. According to elemental and mass-spectrometric analysis the reaction product is a bromide salt but attempts to liberate the free base from the salt using triethylamine led to its degradation.



6 a R = Ph, **b** R = 2-ClC_6H_4, **c** R = 4-ClC_6H_4, **d** R = 4-$O_2NC_6H_4$, **e** R = CH_2Ph, **f** R = CH_2CN; **5 a** Ar = Ph, **b** Ar = 4-$MeOC_6H_4$

In order to reveal the structure of the synthesized compound we have measured its ^{1}H and ^{13}C NMR spectra and also carried out 2D homonuclear (COSY, NOESY) and heteronuclear ^{13}C/^{1}H (HMQC, HMBC) correlation experiments. As in that of the starting compound **1** [12] the ^{1}H NMR spectrum of the condensation product shows the presence of aromatic protons signals as a narrow multiplet at 7.69 ppm (6H) and at lower field (around 8.30 ppm) two signals for the *o*-protons of the phenyl substituents. The spectrum also shows a methyl group singlet at 4.71 ppm and two one-proton singlets at lower field (10.49 and 9.31 ppm) which do not exchange with D_2O. According to the NOESY spectrum data the singlet at 10.49 ppm has a correlation with the methyl group proton signal and with the multiplet for the ortho protons of one of the benzene rings (8.28 ppm). This points to their steric proximity. On the basis of this analytical and spectroscopic data we have proposed that the condensation product of the γ-bromodypnone **1** with methylhydrazine hydrosulfate is the 1-methyl-3,5-diphenylpyridazin-1-ium bromide (**3**).

Further support for this conclusion was found by us in the heteronuclear correlation spectra (Fig. 1). Table 1 shows the position of the cross peaks found in the 2D HMQC, HMBC, and NOESY spectra for each of the ^{1}H NMR signals.

The presence of a correlation between the proton singlet at 10.49 ppm for H-6 and the methyl group carbon atom at 52.98 ppm (the protons of which also correlate with the tertiary C-6 atom at 147.5 ppm)

confirms the structure as the 1-methyl-3,5-diphenyl-substituted pyridazine. In an alternative variant as 1-methyl-4,6-diphenylpyridazin-1-ium bromide the lowest field singlet (H-3) is separated by more than 3 chemical bonds and cannot give a correlation in the HMBC spectrum.

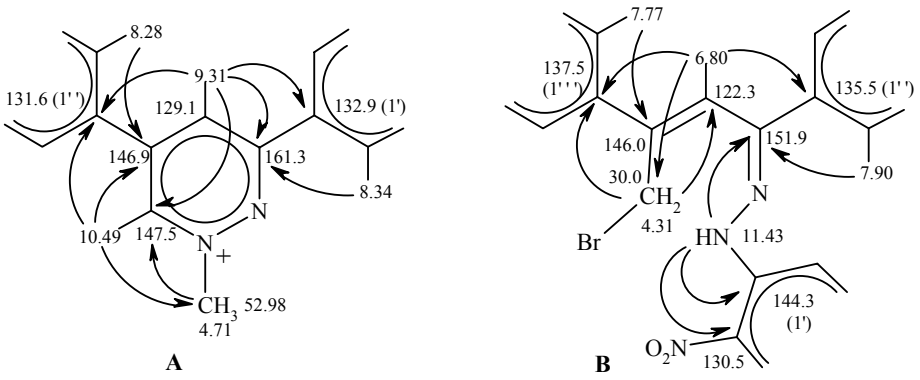


Fig. 1 Signal assignments. The arrows indicate HMBC structural correlations for compounds **3** (**A**) and **10** (**B**).

Since efforts to prepare an N-methyl-substituted 2,4-diphenyl-1H-pyrrol-1-amine in the absence of base in the reaction mixture gave only 2,4-diphenylfuran, we have attempted to carry out the synthesis via alkylation of the 2,4-diphenyl-1H-pyrrol-1-amine (**2**). However, heating a solution of compound **2** in acetonitrile with methyl iodide (independently of the ratio of reagents) did not stop at the monoalkylation stage but gave the N,N-dimethyl-2,4-diphenyl-1H-pyrrol-1-amine (**4**). This was supported by the absence of NH group signals in the IR or ^{1}H NMR spectra and the presence of methyl group signals at 2.19 and 1.87 ppm of overall intensity 6H in the proton spectrum (Tables 2, 3). The N-methyl groups in structure **4** are nonequivalent and this can point to hindered rotation of the dimethylamino groups relative to the pyrrole ring and to coplanarity. The reaction of compound **2** under the same conditions with other alkylating reagents (benzyl halides, γ-bromo-dypnone) gave a complex mixture of reaction products which we could not separate.

TABLE 1. Proton-Carbon and Proton-Proton Correlations for the 1-Methyl-pyridazinium Salt **3** and Hydrazone **10**

Com-pound	δ, ppm			
	^{1}H NMR	HMQC	HMBC	NOESY
3	4.71	52.98	147.5	10.49
	7.69	133.05, 130.31, 130.13	128.8, 129.01, 130.1, 130.3, 131.6, 132.9, 133.0	8.28, 8.34
	8.28	129.01	128.8, 133.0, 146.9	7.69, 9.31, 10.49
	8.34	128.80	129.0, 133.0, 161.3	7.69, 9.31
	9.31	129.1	131.6, 132.9, 147.5, 161.3	8.28, 8.34
	10.49	147.5	52.98, 128.8, 131.6, 146.9	4.71, 8.28
10	11.43	—	151.95, 144.3, 130.53, 117.33	—
	8.93	123.4	144.3, 138.4, 130.94, 130.53	—
	8.42	130.94	144.3	8.21
	8.21	117.33	138.4, 130.94, 130.53	8.42
	7.90	127.68	151.95, 131.3	7.50
	7.77	127.5	146.0, 129.95, 127.5	4.31, 6.80, 7.50
	7.50	131.3, 129.95, 129.6, 129.4	137.5, 135.5, 129.6, 129.4, 127.68, 127.5	7.90, 7.77
	6.80	122.3	146.0, 137.5, 135.5, 30.03	7.77
	4.31	30.03	146.0, 137.5, 123.3	7.77

TABLE 2. IR Spectra of the 1-Aminopyrroles **4-6, 8**

Compound	ν, cm^{-1}
4	3050, 1600, 1570, 745, 723, 680
5a	3010, 1610 (C=N), 1495, 1475, 1460, 1405, 1333, 1232, 1195, 755, 695
5b	3000, 2940, 1602 (C=N), 1510, 1460, 1405, 1330, 1302, 1250 (C–O), 1163, 1035, 752
6a	3210 (NH), 1660 (C=O), 1605, 1480, 1280, 750, 685
6b	3220 (NH), 3020, 1660 (C=O), 1295, 910, 750, 690
6c	3200 (NH), 3020, 1660 (C=O), 1590, 1295, 910, 750, 690
6d	3230 (NH), 1650 (C=O), 1590, 1470, 1315 (NO_2), 1260, 750, 685
6e	3220 (NH), 3030, 1660 (C=O), 1610, 1335, 1035, 730
6f	3220 (NH), 3050, 2260 (CN), 1660 (C=O), 1205, 740, 680
8	3310 (NH), 3040, 1590, 1480, 745, 685

TABLE 3. ^{1}H NMR Spectra of Compounds **4-6** and **8**

Compound	Chemical shifts, δ, ppm (*J*, Hz)		
	NH, 1H, s	ArH *	Other signals
4	—	7.55 (2H, d, *J* = 8.0, H-2',6'); 7.49 (2H, d, *J* = 8.0, H-2",6"); 7.36-7.30 (4H, m, H-3',5',3",5"); 7.22 (1H, t, *J* = 8.0, H-4'); 7.13 (1H, t, *J* = 8.0, H-4"); 7.11 (1H, d, *J* = 1.6, H-5); 6.68 (1H, d, *J* = 1.6, H-3)	2.19 (3H, s, CH_3); 1.87 (3H, s, CH_3)
5a	—	8.18 (1H, d, *J* = 1.2, H-5); 7.80 (2H, m, H-2'",6'"); 7.70 (2H, d, *J* = 8.0, H-2',6'); 7.65 (2H, d, *J* = 8.0, H-2",6"); 7.45 (3H, m, H-3'"-H-5'"); 7.42 (2H, t, *J* = 8.0, H-3',5'); 7.36 (2H, t, *J* = 8.0, H-3",5"); 7.29 (1H, t, *J* = 8.0, H-4'); 7.18 (1H, t, *J* = 8.0, H-4"); 6.75 (1H, d, *J* = 1.2, H-3)	8.90 (1H, s, –N=CH–)
5b	—	8.09 (1H, d, *J* = 1.2, H-5); 7.74 (2H, d, *J* = 8.5, H-2'",6'"); 7.70 (2H, d, *J* = 8.0, H-2',6'); 7.63 (2H, d, *J* = 7.5, H-2",6"); 7.40 (2H, t, *J* = 8.0, H-3',5'); 7.35 (2H, t, *J* = 7.5, H-3",5"); 7.28 (1H, t, *J* = 8.0, H-4'); 7.17 (1H, t, *J* = 7.5, H-4"); 6.99 (2H, d, *J* = 8.5, H-3'",5'"); 6.71 (1H, d, *J* = 1.2, H-3)	8.82 (1H, s, –N=CH–); 3.85 (3H, s, CH_3)
6a	11.74	7.89 (2H, d, *J* = 8.0, H-2'",6'"); 7.59-7.47 (7H, m, ArH); 7.36-7.30 (5H, m, H-3',5',3",5", H-5); 7.23 (1H, t, *J* = 7.5, H-4'); 7.15 (1H, t, *J* = 8.0, H-4"); 6.70 (1H, d, *J* = 1.2, H-3)	—
6b	11.67	7.57 (4H, m, ArH); 7.49-7.27 (10H, m, ArH, H-5); 7.15 (1H, t, *J* = 8.0, H-4"); 6.67 (1H, d, *J* = 2.0, H-3)	—
6c	11.81	7.90 (2H, d, *J* = 8.0, H-2'",6'"); 7.58 (2H, d, *J* = 8.0, H-2',6'); 7.52 (4H, m, H-3'",5'", H-2",6"); 7.32 (5H, m, H-3',5', H-3",5", H-5); 7.22 (1H, t, *J* = 7.5, H-4'); 7.14 (1H, t, *J* = 7.5, H-4"); 6.69 (1H, s, H-3)	—
6d	12.09	8.33 (2H, d, *J* = 8.2, H-3'",5'"); 8.12 (2H, d, *J* = 8.2, H-2'", H-6'"); 7.57 (2H, d, *J* = 8.0, H-2',6'); 7.52 (2H, d, *J* = 8.0, H-2",6"); 7.37-7.31 (5H, m, H-3',5', H-3",5", H-5); 7.24 (1H, t, *J* = 8.0, H-4'); 7.15 (1H, t, *J* = 7.5, H-4"); 6.71 (1H, d, *J* = 2.0, H-3)	—
6e	11.36	7.53 (2H, d, *J* = 8.0, H-2',6'); 7.37 (2H, d, *J* = 8.0, H-2",6"); 7.32-7.21 (10H, m, ArH); 7.17 (1H, d, *J* = 2.0, H-5); 7.12 (1H, t, *J* = 7.5, H-4"); 6.61 (1H, d, *J* = 2.0, H-3)	3.52 (2H, s, CH_2)
6f	11.58	7.54 (2H, d, *J* = 8.0, H-2',6'); 7.46 (2H, d, *J* = 8.0, H-2",6"); 7.40 (2H, t, *J* = 8.0, H-3',5'); 7.33 (3H, m, H-3",5",4'); 7.24 (1H, s, H-5); 7.15 (1H, t, *J* = 7.5, H-4"); 6.65 (1H, s, H-3)	3.75 (2H, s, CH_2)
8	9.20	7.60 (2H, d, ^3J = 8.0, H-2',6'); 7.55 (2H, d, ^3J = 8.0, H-2",6"); 7.29 (4H, m, H-3',5',3",5"); 7.22 (1H, d, ^4J = 1.6, H-5); 7.18 (1H, t, ^3J = 7.5, H-4'); 7.11 (3H, m, H-3'",5'",4"); 6.72 (2H, m, H-3, H-4'"); 6.46 (2H, d, ^3J = 8.0, H-2'",6'")	—

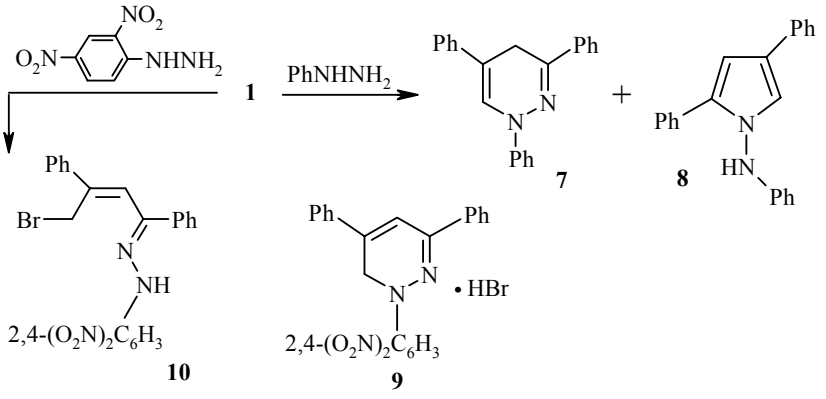
* Numbering of the benzene ring aromatic protons: 2-Ph – 2' to 6', 4-Ph – 2" to 6", 1-N-Ar – 2'" to 6'"

The 2,4-diphenyl-1H-pyrrol-1-amines **2** and **4** do not form stable protonated salts. It should be noted that such salts have only been described for the more basic trialkyl-substituted 1H-pyrrol-1-amines [13]. Attempts to prepare a quaternary methylammonium salt of compound **4** were also unsuccessful. Prolonged heating of the N,N-dimethyl derivative **4** with methyl tosylate or dimethyl sulfate led only to its partial degradation.

Condensation of the pyrrol-1-amine **2** with aromatic aldehydes occurred comparatively readily in alcohol. In this way the 2,4-diphenyl-N-(arylmethylidene)-1H-pyrrol-1-amines **5a,b** were prepared in 75-76% yield.

Prolonged heating (10 h) of compound **2** in acetic anhydride in the presence of sodium acetate did not give the N-(2,4-diphenyl-1H-pyrrol-1-yl)acetamide acylation product. However, the corresponding N-(2,4-diphenyl-1H-pyrrol-1-yl)carboxylic acid amides **6a-f** were readily prepared by refluxing the γ-bromodypnone **1** with carboxylic acid hydrazides in alcohol. Fusing the components in the presence of sodium acetate gave the same result but in lower yield. In the case of the arylcarboxylic acid hydrazides having electron acceptor substituents in the benzene ring fusing in the presence of sodium acetate also gave a significant amount (~ 50% according to ^{1}H NMR spectroscopic data) of 2,4-diphenylfuran and the yield of the target reaction products was less than 20%.

The structure of compounds **6** was determined on basis of its spectroscopic data (Tables 2 and 3). Hence there are signals for the NH group in the IR spectra at 3200-3250 cm^{-1} and in the ^{1}H NMR spectra at 12.09-11.36 ppm. Characteristic signals for the pyrrole ring [11] protons in the 2,4-diphenylpyrroles are seen as singlets or doublets with $J_{3,5}$ = 1.2-2.0 Hz at 7.30-7.17 (H-5) and 6.71-6.61 ppm (H-3).



The results of the experiments with acid hydrazides show that the direction of the reaction of the γ-bromodypnone **1** with hydrazines is determined by the nature of the substituent in the latter. The presence of donor substituents (alkyl) leads to pyridazine derivatives whereas acceptor substituents (acyl) principally give 1-aminopyrroles. Such a dependence is also seen in the reaction of γ-bromodypnone **1** with arylhydrazines. Hence treatment of γ-bromodypnone **1** with phenylhydrazine gave 1,3,5-triphenyl-1,4-dihydropyridazine (**7**) [9]. However, according to TLC data, compound **7** is not the sole reaction product. We were able to separate a low yield (15%) of N,2,4-tri-phenyl-1H-pyrrol-1-amine (**8**) from the reaction mixture. This structure for **8** is supported by the IR and ^{1}H NMR data, primarily the presence of signals for the NH group and pyrrole ring protons (doublet with ^4J = 1.6 at 7.22 (H-3) and signal at 6.72 ppm (H-5)). Treatment of the γ-bromodypnone **1** with alkylphenyl-hydrazines [9] led exclusively to a pyridazine derivatives.

It would be logical to expect that the use of arylhydrazines with acceptor substituents in the ring in the reaction would lead to an increased content of the N-arylpyrrole in the reaction mixture. With this aim we have used 1-(2,4-dinitrophenyl)hydrazine. Heating a mixture of the reagents in alcohol gave a single product according to TLC data and this was separated in high yield (84%). The ^{1}H NMR spectrum of the product obtained showed methylene group protons signals (s, 2H at 4.31 ppm), a methine proton (s, 1H at 6.80 ppm) and a proton which exchanged with D_2O (s, 1H at 11.43 ppm). According to elemental analytical data the molecule of this compound contains a bromine atom. This suggests that the reaction product is not a pyrrole

derivative (the probability of forming an unstable 5H-form is very low) but it might be the pyridazine hydrobromide **9** or have the noncyclic hydrazone **10** structure. To clarify the structure of the reaction product the 2D (HMQC, HMBC, NOESY) spectra were studied. Analysis of the heteronuclear correlations in the HMBC spectrum (Table 1 and Fig. 1) showed unambiguously the presence of the dypnone structural fragment in the molecule and excludes the possibility of a 1,4-dihydropyridazine type structure **7**. This is supported by the correlation between the singlet at 6.80 ppm (1H) and both of the quaternary carbon atoms of the benzene rings C-1" (135.3) and C-1"' (137.5 ppm). A correlation for the methylene group protons (4.31 ppm) is also observed but only with carbon atom (C-1"').

The final conclusion for the structure of the reaction product as the N-(2,4-dinitrophenyl)hydrazone of (*Z*)-4-bromo-1,3-diphenyl-2-buten-1-one (**10**) was confirmed by X-ray structural analysis (Fig. 2 and Tables 4 and 5).

The hydrazone fragment lies virtually in the plane of the dinitrophenyl ring (torsional angles C(2)–C(1)–N(3)–N(4) 0.3(5)º and C(1)–N(3)–C(4)–C(7) -174.3(3)º) leading to the formation of an intramolecular hydrogen bond N(3)–H···O(4) (H···O 2.00 Å, N–H···O 127º). The phenyl substituent C(8)···C(13) is somewhat

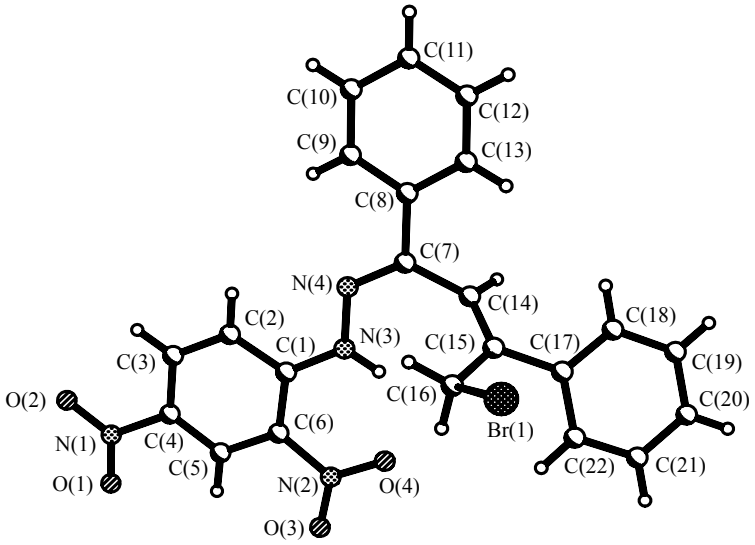


Fig. 2. Structure of the compound **10** molecule.

TABLE 4. Some Valence (ω) and Torsional (φ) Angles for Compound **10** Molecule

Angle	ω, deg	Angle	φ, deg
C(1)–N(3)–N(4)	118.6(3)	C(1)–N(3)–N(4)–C(7)	-174.3(3)
C(7)–N(4)–N(3)	118.1(3)	N(4)–N(3)–C(1)–C(2)	0.3(5)
N(4)–C(7)–C(8)	116.5(3)	N(3)–N(4)–C(7)–C(8)	177.4(3)
N(4)–C(7)–C(14)	126.5(3)	N(3)–N(4)–C(7)–C(14)	-0.3(5)
C(8)–C(7)–C(14)	117.0(3)	C(14)–C(7)–C(8)–C(13)	-15.4(5)
C(13)–C(8)–C(7)	122.1(4)	N(4)–C(7)–C(8)–C(9)	-14.5(5)
C(9)–C(8)–C(7)	120.1(3)	N(4)–C(7)–C(14)–C(15)	-60.0(6)
C(15)–C(14)–C(7)	129.0(3)	C(8)–C(7)–C(14)–C(15)	122.3(4)
C(14)–C(15)–C(17)	120.5(3)	C(7)–C(14)–C(15)–C(16)	2.7(6)
C(14)–C(15)–C(16)	121.4(3)	C(17)–C(15)–C(16)–Br(1)	54.5(4)
C(17)–C(15)–C(16)	118.1(3)	C(14)–C(15)–C(17)–C(18)	38.6(5)
C(15)–C(16)–Br(1)	113.0(3)	C(16)–C(15)–C(17)–C(22)	40.2(5)
C(18)–C(17)–C(15)	120.7(4)		
C(22)–C(17)–C(15)	120.5(4)		

TABLE 5. Some Bond Lengths (*l*) in the Compound **10** Molecule

Bond	*l*, nm	Bond	*l*, nm
Br(1)–C(16)	1.930(4)	C(7)–C(14)	1.494(5)
N(3)–C(1)	1.354(5)	C(14)–C(15)	1.320(5)
N(3)–N(4)	1.368(4)	C(15)–C(17)	1.487(5)
N(4)–C(7)	1.285(5)	C(15)–C(16)	1.502(5)
C(7)–C(8)	1.482(5)		

twisted relative to this fragment (torsional angle N(4)–C(7)–C(8)–C(9) -14.5(5)º) as a result of repulsion between the C(14) and H(13A) atoms (distance 2.59 Å, sum of van der Waal radii [14] 2.87 Å). The steric effects (shortening of the intramolecular contacts C(16)···N(5) 3.059 (sum of van der Waal radii 3.21), N(3)···H(16B) 2.55 (2.66), C(16)···H(3A) 2.56, C(16)···H(22A) 2.77 Å, and C(14)···H(18A) 2.73 Å) are also specified by rotation of the plane of the double bond C(14)–C(15) both relative to the phenyl substituent C(17)···C(22) and to the plane of the hydrazone fragment (torsional angles C(14)–C(15)–C(17)–C(18) 38.6(5)º and C(15)–C(14)–C(7)–N(4) -60.0(6)º). This accompanies a disturbance of the conjugation between the π-systems of the double bond and the fragments mentioned above as indicated by lengthening of the C(14)–C(7) and C(15)–C(17) bonds to 1.494(5) and 1.487(5) Å respectively (mean value for a conjugated C(sp^2)–C(sp^2) bonds = 1.43 Å [15]).

It was interesting to note the formation in the crystal of a shortened Br(1)···C(19)$'$ intramolecular contact (x, y, 1+z) of 3.51 Å (sum of van der Waal radii 3.68 Å [15]) inferring the presence of an attractive Br···π interaction (C–Br···C angle 164.1º) which can be considered as a halogen bond [16].

TABLE 6. Physicochemical Characteristics of the Compounds Synthesized

Compound	Empirical formula	Found, % / Calculated, %				mp, °C*	Yield, %*[2]
		C	H	Hal	N		
3	$C_{17}H_{15}BrN_2$	62.21 / 62.40	4.32 / 4.62	24.48 / 24.42	8.60 / 8.56	227-230 (dec.)	53
4	$C_{18}H_{18}N_2$	82.56 / 82.41	7.03 / 6.92	—	10.54 / 10.68	88-91	41
5a	$C_{23}H_{18}N_2$	85.73 / 85.68	5.71 / 5.63	—	8.53 / 8.69	131-133	75
5b	$C_{24}H_{20}N_2O$	81.83 / 81.79	5.79 / 5.72	—	7.92 / 7.95	182-183	76
6a	$C_{23}H_{18}N_2O$	81.50 / 81.63	5.16 / 5.36	—	8.30 / 8.28	208-209	55
6b	$C_{23}H_{17}ClN_2O$	73.91 / 74.09	4.52 / 4.60	9.56 / 9.51	7.55 / 7.51	210-212	50
6c	$C_{23}H_{17}ClN_2O$	73.99 / 74.09	4.64 / 4.60	9.49 / 9.51	7.48 / 7.51	224-226	51
6d	$C_{23}H_{17}N_3O_3$	72.25 / 72.05	4.53 / 4.47	—	10.86 / 10.96	253-255	52
6e	$C_{24}H_{20}N_2O$	81.86 / 81.79	5.79 / 5.72	—	8.00 / 7.95	228-229	68
6f	$C_{19}H_{15}N_3O$	75.85 / 75.73	5.19 / 5.02	—	19.88 / 19.94	235-237 (dec.)	62
8	$C_{22}H_{18}N_2$	85.20 / 85.13	5.89 / 5.85	—	9.01 / 9.03	162-165	15
10	$C_{22}H_{17}BrN_4O_4$	55.00 / 54.90	3.61 / 3.56	16.63 / 16.60	11.62 / 11.64	182-185	84

* Solvent for recrystallization: AcOH (compounds **3, 10**), 2-PrOH (compounds **4, 8**), EtOH (compounds **5a,b, 6e**), MeCN (compounds **6a-d,f**).
*[2] Yields of compounds **6a-f** obtained using method B.

An attempt to carry out cyclization of hydrazone **10** by heating a suspension in ethanol in the presence of base (Et_3N, morpholine) gave a complex mixture of products which could not be separated.

EXPERIMENTAL

IR spectra (KBr tablets) were recorded on a Pye Unicam SP3-300 instrument. ^1H and ^{13}C NMR spectra were taken on a Varian Mercury 400 instrument (400 and 100 MHz respectively) using DMSO-d_6 solvent and with TMS as internal standard. UV spectra for compound **10** were obtained on a Lambda 20 UV-vis spectrometer using methanol. Mass spectra were taken for compounds **3, 8** using HPLC with an AGILENT/100 apparatus (CI, acetonitrile, 0.05% formic acid). Monitoring of the course of the reaction and the purity of the product obtained was carried out using TLC on Silufol UV-254 plates. The physicochemical characteristics of the compounds synthesized are given in Table 6.

2,4-Diphenyl-1H-pyrrol-1-amine (2) was prepared by the method reported in [9]. IR spectrum, δ, cm^{-1}: 3370 (NH), 3350 (NH), 3045, 1595, 1470, 880, 745, 690.

1-Methyl-3,5-diphenylpyridazin-1-ium Bromide (3). A mixture of 1-methylhydrazinium hydrosulfate (0.48 g, 3.32 mmol) and $NaHCO_3$ (0.28 g, 3.32 mmol) in ethanol (50 ml) was heated for 10 min and the solid residue was filtered off. γ-Bromodypnone **1** (1 g, 3.32 mmol) was added and the mixture was refluxed for 30 min. The solvent was evaporated and the residue was recrystallized from AcOH. IR spectrum, δ, cm^{-1}: 3020, 1600 (C=N), 1385, 1250, 755, 667. ^1H NMR spectrum, δ, ppm (*J*, Hz): 10.49 (1H, s, H-6); 9.31 (1H, s, H-4); 8.34 (2H, dd, ^3J = 8.0, ^4J = 4.0, H-2',6'); 8.28 (2H, m, H-2",6"); 7.69 (6H, m, H-3'–H-5', H3"–H-5"); 4.71 (3H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 161.29 (C-3); 147.48 (C-6); 146.86 (C-5); 133.09 (C-4'); 133.01 (C-4"); 132.88 (C-1'); 131.57 (C-1"); 130.31 (C-3',5'); 130.13 (C-3",5"); 129.03 (C-4); 129.01 (C-2',6'); 128.80 (C-2", 6"); 52.98 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 249 (70), 247 $[M-Br]^+$ (100).

N,N-Dimethyl-2,4-diphenyl-1H-pyrrol-1-amine (4). Methyl iodide (0.13 ml, 2.13 mmol) was added to a solution of 1-aminopyrrole **2** (0.5 g, 2.13 mmol) in acetonitrile (45 ml) and refluxed for 1 h. A further 0.13 ml of methyl iodide was added and refluxing continued for 2 h. The solvent was evaporated. 2-Propanol was added to the oily residue and heated to full solution. The precipitate formed on cooling was filtered off and washed with 2-propanol.

N-(Arylmethylidene)-2,4-diphenyl-1H-pyrrol-1-amines 5a,b. Benzaldehyde (0.22 ml, 2.13 mmol) or anisaldehyde was added to a solution of 1-aminopyrrole **2** (0.5 g, 2.13 mmol) in ethanol (60 ml) and refluxed for 30 min. The precipitate formed on cooling was filtered off and washed with alcohol.

N-(2,4-diphenyl-1H-pyrrol-1-yl)carboxylic acid amides 6a-f. A. A mixture of γ-bromodypnone **1** (1 g, 3.32 mmol), sodium acetate (0.27 g), and benzoic acid hydrazide (0.45 g, 3.32 mmol) was fused on an oil bath at 120-130ºC for 15 min. After cooling, water (10 ml) was added to the melt and triturated thoroughly. The filtered solid residue was thoroughly washed with water and 2-propanol and recrystallized. Yield 0.4 g (36%).

B. A mixture of the γ-bromodypnone **1** (1 g, 3.32 mmol) and the carboxylic acid hydrazide (3.32 mmol) in ethanol (50 ml) was heated to full solution of the γ-bromodypnone and refluxed for a further 3 h. The precipitate formed on cooling was filtered off and washed with alcohol.

N,2,4-Triphenyl-1H-pyrrol-1-amine (8). The method used was as reported in [9]. A mixture of the γ-bromodypnone **1** (1 g, 3.32 mmol) and phenylhydrazine (0.33 ml, 3.32 mmol) in alcohol (50 ml) was refluxed for 15 min. Solvent was evaporated and the residue was dissolved with heating in alcohol. The solution was cooled for 1 h to form a precipitate of the 1,3,5-triphenyl-1,4-dihydropyridazine **7**. After 3 days a precipitate of compound **8** was formed in the filtrate and this was filtered off and washed with a small amount of 2-propanol. Mass spectrum, *m/z* (I_{rel}, %): 311 $[M+1]^+$ (100), 309 $[M-1]^+$ (20).

2,4-Dinitrophenylhydrazone of (*Z*)-4-bromo-1,3-diphenyl-2-buten-1-one (10). A mixture of the γ-bromodypnone **1** (1 g, 3.32 mmol) and 2,4-dinitrophenylhydrazine (0.66 g, 3.32 mmol) in alcohol (50 ml) was

refluxed for 3 h. The solution was cooled and the precipitate formed was filtered off, washed with alcohol and recrystallized from acetic acid. IR Spectrum, δ, cm^{-1}: 3300 (NH), 1610 (C=N), 1569 ($^{as}NO_2$), 1500, 1420, 1335 ($^{s}NO_2$), 1313, 1112, 760. UV spectrum, λ_{max}, nm (ε x 10^{-3}): 202 (45.13), 247 (23.34, sh), 382 (26.12). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11.43 (1H, s, NH); 8.93 (1H, d, ^4J = 1.2, H-3'); 8.42 (1H, dd, ^3J = 8.0, ^4J = 1.2, H-5'); 8.21 (1H, d, ^3J = 8.0, H-6'); 7.90 (2H, m, H-2",6"); 7.77 (2H, d, ^3J = 7.5, H-2"',6"'); 7.57-7.42 (6H, m, H-3"-H-5", H-3"'–H-5"'); 6.80 (1H, s, H-2); 4.31 (2H, s, 4-CH_2). ^{13}C NMR spectrum, δ, ppm: 151.95 (C-1); 146.0 (C-3); 144.3 (C-1'); 138.4 (C-4'); 137.5 (C-1"'); 135.5 (C-1"); 131.3 (C-4"); 130.94 (C-5'); 130.53 (C-2'); 129.95 (C-4"'); 129.6 (C-3",5"); 129.4 (C-3"',5"'); 127.68 (C-2",6"); 127.5 (C-2"',6"'); 123.6 (C-3'); 122.3 (C-2); 117.33 (C-6'); 30.03 (C-4).

Crystallographic data. Crystals of **10** are monoclinic and grown from acetic acid, $C_{22}H_{17}BrN_4O_4$, at 293ºK: *a* = 11.5767(5) Å, *b* = 25.5245(9) Å, *c* = 7.3670(3) Å, β = 106.589(4)º, *V* = 2086.3(1) $Å^3$, M_r = 481.31, *Z* = 4, space group $P2_1/c$, d_{calc} = 1.532 g/cm^3, μ(MoKα) = 2.008 mm^{-1}, *F*(000) = 976. The unit cell parameters and intensities of 16,116 reflections (4719 independent, R_{int} = 0.037) were measured on an Xcalibur diffractometer (MoKα radiation, CCD detector, graphite monochromator, ω-scanning to $2\theta_{max}$ = 55º). The structure was solved by a direct method using the SHELXTL program package [17]. The positions of the hydrogen atoms were revealed using electron density difference synthesis and refined with the "riding" model with U_{iso} = 1.2 U_{eq} for the non-hydrogen atom bound to the given hydrogen. The structure was refined using F^2 full matrix least squares analysis in the anisotropic approximation for non-hydrogen atoms to wR_2 = 0.149 for 4705 reflections (R_1 = 0.059 for 2803 reflections with $F > 4\sigma(F)$, *S* = 1.00). The full X-ray structural analytical data can be obtained from the Cambridge Crystallographic Data Centre (CCDC 670372).

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