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SYNTHESIS, STRUCTURE, AND PROPERTIES OF 1,3,5-TRIARYLPYRIDAZINES

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Treatment of γ-bromodypnone with arylhydrazines gives differently structured products, i.e. γ-bromodypnone hydrazones, 1-aryl-3,5-diphenyl-1,4-dihydropyridazines, 1-aryl-3,5-diphenyl-1,6-dihydropyridazines, and aromatic 1,3,5-triarylpyridazinium salts. We have studied the pattern of formation of all of the products and their properties. Heating an alcohol solution of 1,3,5-triphenyl-1,4-dihydropyridazine gives N,2,4-triphenyl-1H-pyrrole-1-amine or to a 1,3,5-triphenylpyridazinium salt dependent upon the acidity of the medium. The product of addition of HBr to the 1,6-dihydropyridazine system is 5-bromo-1-(4-nitrophenyl)-3,5-diphenyl-1,4,5,6-tetrahydropyridazine.

Keywords: γ-bromodypnone, 1,3,5-triarylpyridazinium bromide, 1,3,5-triaryl-1,4-dihydropyridazine, 1,3,5-triaryl-1,6-dihydropyridazine, N,2,4-triphenyl-1H-pyrrole-1-amine.

Pyridazine derivatives are an important class of pharmacologically interesting structures [1, 2]. A significant stimulus for an intensive study of their properties and methods of preparation has come from the discovery in the 70's and 80's of natural, biologically active substances containing a pyridazine ring [3, 4]. The most popular methods for the synthesis of pyridazines are based on the use of γ-dicarbonyl compounds as starting materials [2, 3]. Examples are known of using γ-halocarbonyl compounds [3], including those that are unsaturated [5]. We have previously reported that 1,3,5-triarylpyridazines are readily formed by reaction of 4-bromo-1,3-diphenyl-2-buten-1-one (γ-bromodypnone) (**1**) with arylhydrazines [6].

The reaction of γ-bromodypnone **1** with arylhydrazines can lead to different products depending on the conditions and the structure of the starting hydrazine [6, 7]. The simplest variant of the reaction is formation of hydrazone **2a** with an open structure by treatment of the bromodypnone **1** with 1-(2,4-dinitrophenyl)hydrazine in alcohol [7]. Under the same conditions arylhydrazines gave the pyridazines **3a,b, 4a** [6] and 1H-pyrrole-1-amine **5** [7]. In our work we have clarified the mode of action of this reaction and broadened its scope both as regards the arylhydrazines used and the reaction conditions.

Independently of the conditions the γ-bromodypnone **1** and tolylhydrazines gave 1,3,5-triarylpyridazinium bromides **3a,b** [6]. At the same time, the result of the reaction with phenylhydrazine depends on the conditions used. The main product of the reaction of the γ-bromodypnone **1** with phenylhydrazine in alcohol is 1,3,5-triphenyl-1,4-dihydropyridazine **4a** [6, 7]. The ^{1}H NMR spectrum of the crude product also shows

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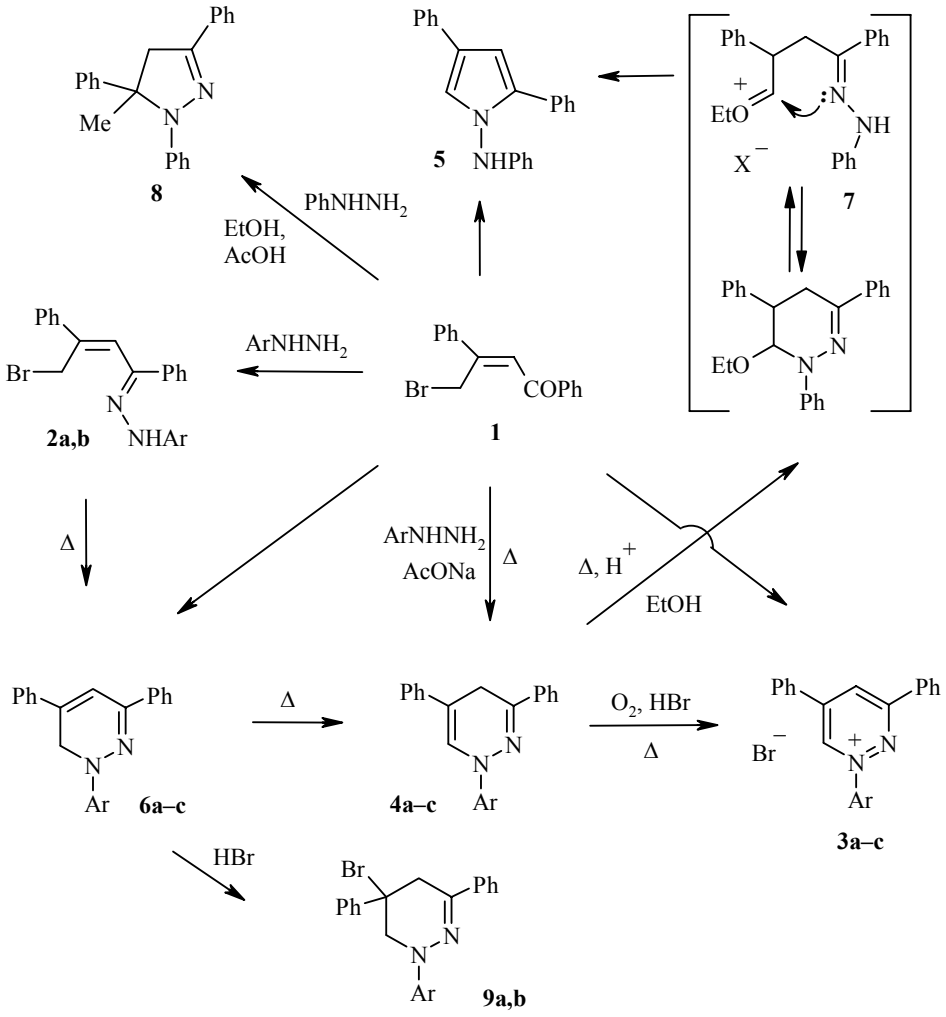
signals at 4.72 ppm (2H, s) and 7.29 ppm (1H, s) which differ from those in compound **4a**. It was found that the content of this product increases at lower temperature and with shortening of the heating time of the reaction mixture both when carrying out the reaction in alcohol and when fusing in the presence of sodium acetate. The greatest effect (according to the content of the unknown product in the mixture) is seen when carrying the reaction out in the presence of acetic acid (AcOH–EtOH, 2:3, 25-40ºC).



2 a Ar = 2,4-$(O_2N)_2C_6H_3$, **b** Ar = Ph; **3 a** Ar = 2-MeC_6H_4, **b** Ar = 3-MeC_6H_4, **c** Ar = Ph;

4a, 6a Ar = Ph, **4b, 6b, 9a** Ar = 4-$O_2NC_6H_4$, 4**c, 6c, 9b** Ar = 4-$HO_2CC_6H_4$

Elemental analytical data and mass spectrometric, infrared, and ^{1}H NMR spectroscopic data for the unknown material separated in a pure state showed that it is a tautomer of compound **4a** and has the structure 1,3,5-triphenyl-1,6-dihydropyridazine (**6a**). With the aim of confirming this hypothesis we have measured the HMQC, HMBC, and NOESY spectra of compounds **4a** and **6a**. Analysis of the heteronuclear correlations in the HMBC spectra (see Table 1 and Figure 1) unambiguously prove the cyclic structure of the 1,3,5-triphenyl-pyridazine in the molecules studied. The main differences in the spectra permit a safe assignment of the tautomers **4a** and **6a** through the presence (or absence) of a correlation between the C-3 atom signal in the region 142.2-141.1 ppm and the –CH_2– and =CH– groups protons. For compound **4a** a correlation is seen with

the signal for the methylene group protons at 3.64 ppm and for compound **6a** with the methine proton signal at 7.29 ppm. Differences were also seen in the UV spectra of the tautomers **4a** and **6a**. In the case of compound **4a** two bands were seen above 300 nm with maxima at 318 ($\varepsilon = 27\times10^3$) and 392 nm ($\varepsilon = 10^4$). In the spectrum of compound **6a** both bands (with comparable intensities) were shifted by 35-36 nm to shorter wavelength (282 nm) or to longer wavelength (427 nm) respectively. The latter points to an increase in the conjugated chain in the molecule and this is in agreement with the structure of the 1,6-dihydro derivative.

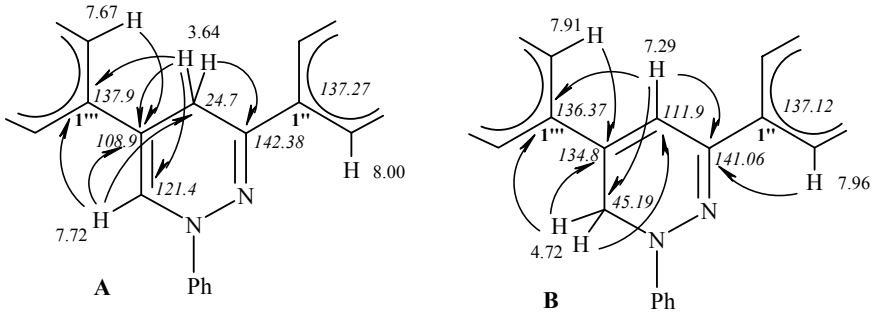


Fig. 1. Structurally significant HMBC correlations for compounds **4a** (**A**) and **6a** (**B**).

The dihydropyridazines **4a, 6a** do not change upon prolonged storage or in solutions of different polarity solvents in neutral medium at room temperature. In the presence of acid (EtOH–HBr, 25ºC) a solution of the 1,6-dihydropyridazine **6a** does not undergo a marked change (according to TLC). Under the same conditions compound **4a** is gradually converted to 1,3,5-triphenylpyridazinium bromide (**3c**). The structure of the oxidation product **3c** was proved from its spectroscopic properties which agreed with data obtained previously for the pyridazinium bromides **3a,b** [6]. Analysis of the heteromuclear correlations in the HMQC and HMBC spectra of salts **3a, 3c** (see Table 1) and 1-methyl-3,5-diphenylpyridazinium bromide [7] fully confirmed the conclusions concerning the structure of salts **3a-c**.

Heating solutions of 1,6-dihydropyridazine **6a** in protonic solvents gave tautomer **4a** (according to TLC and ^{1}H NMR data). However this method cannot be used preparatively since the 1,4-dihydropyridazine **4a** is readily aromatized or undergoes more profound changes. Hence by heating **4a** in alcohol in the presence of acid (HBr, $HClO_4$) we separated a low yield (17-20%) of N,2,4-triphenyl-1H-pyrrole-1-amine (**5**), previously obtained from the reaction mixture of γ-bromodypnone **1** with phenylhydrazine in alcohol [7]. The mechanism of formation of pyrrole **5** includes a stage of reversible cleavage of the C(6)–N(1) bond [8, 9] which is due to addition of EtOH to the C(5)=C(6) olefinic bond through acid catalysis [8]. Recyclization of product **7** give the 1H-pyrrole-1-amine **5**.

With the aim of finding optimum conditions for the method of synthesizing compound **6a** we attempted to minimise the unwanted process of conversion of **6a** to **4a**. However, it was found that carrying out the reaction of the γ-bromodypnone **1** with phenylhydrazine at room temperature (EtOH–AcOH, 2:3) gave the (*Z*)-4-bromo-1,3-diphenyl-2-buten-1-one N-phenylhydrazone (**2b**). The spectroscopic parameters of the product obtained were fully in agreement with those observed previously for N-(2,4-dinitrophenyl)hydrazone **2a** [7]. In contrast to the derivative **2a** compound **2b** proved less stable. Even with attempts to recrystallize it from alcohol or AcOH or upon storage (over 3 weeks) it was readily converted to the 1,6-dihydropyridazine **6a**.

Lowering the yield of product **6a** upon heating the reaction mixture (EtOH–AcOH, 2: 3) was due both to the indicated conversion of **6a** to **4a** and also to the occurrence of a side reaction involving reduction of the bromomethyl group by the hydrazine. The material isolated from the reaction mixture in less than 15% yield was the product of an intramolecular cyclization of the 1,3-diphenyl-2-buten-1-one N-phenylhydrazone (which was formed by reduction of the hydrazone **2b**), i.e. 5-methyl-1,3,5-triphenyl-4,5-dihydro-1H-pyrazole (**8**). The ^{1}H and ^{13}C NMR spectra and melting point of the substance obtained fully agreed with that of a sample synthesized by a previously reported method [10] from dypnone and phenylhydrazine.

We further studied the reaction of γ-bromodypnone **1** with 4-nitrophenylhydrazine and with 4-hydrazinobenzoic acid. The reactions occur with more prolonged heating (30 min compared with 15 min in the case of phenylhydrazine [6]) of the solution of starting materials in alcohol to give the 1-aryl-3,5-diphenyl-1,6-dihydropyridazines **6b,c**. Formation of substantial amounts of 1,4-dihydropyridazines **4b,c** was observed only when carrying out the reaction by fusion in the presence of NaOAc. The content of compounds **4b,c** in the mixtures obtained reached 20% in the case of the reaction with 4-nitrophenylhydrazine and 55% for that of 4-hydrazinobenoic acid. The overall yields of the fusion reaction products proved almost twice less than when carryied out in alcohol. In contrast to compound **6a** the 1,6-dihydropyridazines **6b,c** proved more stable upon heating in solvents, the ^{1}H NMR spectra in DMSO-d_6 showing only trace amounts of the tautomers of structure **4** (H-4 signal at 3.71 ppm for **4b** and 3.69 ppm for **4c**). Only prolonged heating (~ 1 h) of their solutions in AcOH in the presence of HBr led to partial oxidation but principally to opening of the pyridazine ring and to formation of hydrolysis products (arylhydrazines according to ^{1}H NMR spectroscopic data).

The 1,6-dihydropyridazine structure contains a fragment of the original dypnone compound and it was found that, just as the latter [14], can add polar molecules of the type H–X to the olefinic C(4)=C(5) bond. Hence prolonged holding of acetic solutions of compounds **6b,c** in the presence of HBr gives the 1-(4-aryl)-5-bromo-3,5-diphenyl-1,4,5,6-tetrahydropyridazines **9a,b**. The yield of the compounds is low (18% for **9a** and < 8% for **9b**). We were unable to prepare an analytically pure sample of the tetrahydropyridazine **9b** because the material was severely contaminated by admixtures and, evidently, has a low resistance to heating in solvents [3]. Characteristic features of the ^{1}H NMR spectra of compounds **9a,b** are the presence of signals for two methylene groups in the region 4.8-3.5 ppm as AB type spin systems with geminal spin-spin couplings of 18.0 and 12.0 Hz.

TABLE 1. Proton-Carbon Correlations for Compounds **3a**, **4a**, **6a**, and **9a**

^{1}H NMR, δ, ppm	HMBC, δ, ppm	^{1}H NMR, δ, ppm	HMBC, δ, ppm
	3a		**4a**
2.41	127.95, 133.3, 144.2	3.64	108.87, 121.42, 137.89, 142.38
7.59	19.0, 127.05, 127.95, 132.55, 144.2	7.04	116.03, 129.9
7.68	129.0, 130.2, 131.55, 132.9, 133.1, 133.53	7.24	124.74
7.97	132.3, 133.3, 144.2	7.38	116.03, 124.74, 129.1, 129.9, 137.89, 144.82
8.42	129.0, 133.1, 133.53, 147.8, 161.4	7.45	126.38
9.56	131.55, 132.9, 149.0	7.48	129.1, 137.27
10.59	130.05, 131.55, 144.2, 147.8	7.65	116.03, 122.85, 142.38
		7.67	108.87, 126.38, 127.11
		7.72	24.72, 108.87, 137.89
		8.00	126.38, 129.9
	6a		**9a**
4.72	111.94, 134.76, 136.37	3.55	38.58, 72.56, 141.99, 151.24
7.00	115.33	3.99	38.58, 72.56, 141.99, 151.24
7.29	45.19, 136.37, 141.06	4.61	51.83, 72.56
7.35	125.47	4.75	51.83
7.38	129.63, 147.9	7.08	—
7.43	129.22, 137.12	7.34	126.07
7.49	129.38, 136.37	7.40	72.56, 126.07, 128.85, 130.12, 141.99
7.53	115.33, 121.65, 147.09	7.46	127.02, 129.52, 131.5
7.91	126.11, 129.93, 134.76	7.79	127.02, 130.65, 151.24
7.96	125.47, 128.67, 141.06	7.99	126.12, 139.01, 148.18

2D HMQC, HMBC, and NOESY spectra of compound **9a** were studied in order to confirm the structure of the 5-bromo-1,4,5,6-tetrahydropyridazines **9a,b** (see Table 1). Analysis of the molecular model and the proton-proton correlations in the NOESY spectrum also allows us to deduce the steric structure of compounds **9a,b**. These compounds have a *distorted boat* structure with an equatorial orientation of all of the benzene rings. The equatorial position of the benzene ring at C-5 points to the presence of the steric proximity of its *o*-protons and the protons of the CH_2 group at position 6.

Hence the reaction of γ-bromodypnone **1** with arylhydrazines is a multistage process, the result of which is determined by two factors, i.e. the reaction conditions and the structure of the arylhydrazine. The arylhydrazones of structure **2** formed in the first step is converted to the 1,3,5-triarylpyridazine cyclic derivatives **3, 4** and **6**. The rate of cyclization and the structure of the pyridazine depend on the nature of the substituent in the benzene ring of the N-aryl molecular fragment. Increased acceptor properties lead to a hindrance to the cyclization process on the one hand and to stabilization of the tautomeric form of the 1,6-dihydropyridazine **6** on the other. Increasing the donor properties of the substituent increases the rate of cyclization and tendency to form the 1,4-dihydropyridazine **4** tautomer form which can then rearrange with the participation of alcohol as nucleophile to the N,2,4-triaryl-1H-pyrrole-1-amine **5** or oxidize by the oxygen in the air to give the aromatic pyridazinium salt **3**. The tendency to form salt **3** strengthens with increase in the donor properties of the substituent in the N-aryl fragment. The correctness of our conclusions relating to the observed dependence is supported by data for the properties of the 1-substituted dihydropyridazines [3]. In particular, we have previously [9, 11-13] noted their tendency towards oxidation by atmospheric oxygen upon heating and the dependence of the stability towards oxidation on the nature on the substituent on the N(1) atom, in fact to the increase in the stability of the 1,6-dihydropyridazines with increase in the electronegativity of the particular substituent [11, 13].

Speeding up of the succession of reactions **2** → **6** → **4** is enabled by increasing temperature and the basicity of the reaction medium. Heating in the presence of acid stimulates the rearrangement process of the pyridazine **4** formed to the N-aminopyrrole **5** and also its conversion to salt **3**.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury instrument (400 and 100 MHz respectively) using DMSO-d_6 with TMS as internal standard. UV spectra were obtained on a Lambda 20 UV/VIS spectrometer using MeOH. IR spectra were taken on a Pye Unicam SP3-300 instrument for KBr tablets. Mass spectra were obtained using HPLC on an AGILENT 1200 SL instrument (CI, acetonitrile, 0.05% formic acid). Melting points for the synthesized compounds were measured on a Boetius type heating apparatus and were not corrected. Monitoring of the course of the reaction and the purity of the products were carried out by TLC on Silufol UV-254 plates. Elemental analytical data and ^{1}H NMR spectra (DMSO-d_6) for 1-(2-methyl-phenyl)-3,5-diphenylpyridazinium bromide (**3a**) and 1,3,5-triphenyl-1,4-dihydropyridazine (**4a**) have been given in the study [6] and for N,2,4-triphenyl-1H-pyrrole-1-amine (**5**) in [7]. Assignment of the signals in the ^{1}H and ^{13}C NMR spectra of 5-methyl-1,3,5-triphenyl-4,5-dihydro-1H-pyrazole **8** were made from the experimental HMBC, HMQC, and NOESY data.

(*Z*)-4-Bromo-1,3-diphenyl-2-buten-1-one N-Phenylhydrazone (2b). γ-Bromodypnone **1** (1 g, 3.32 mmol) was dissolved with heating in a mixture of alcohol (20 ml) and acetic acid (30 ml). Phenylhydrazine (0.33 ml, 3.32 mmol) was added to the cooled solution and held at room temperature for 36 h. The precipitate formed was filtered off and washed with alcohol. Yield 0.52 g (40%). ^{1}H NMR spectrum, δ, ppm (J, Hz): 10.32 (1H, s, NH); 8.10 (2H, d, ^3J = 9.0, H-2',6'); 7.78 (4H, d, ^3J = 7.5, H-2",6", H-2'",6'"); 7.49 (2H, t, ^3J = 8.0, H-3',5'); 7.45-7.38 (7H, m, H-4', H-3"–H-5", H-3'"–H-5'"); 6.80 (1H, s, H-2); 4.28 (2H, s, H-4).

1-(2-Methylphenyl)-3,5-diphenylpyridazinium Bromide (3a). IR spectrum, ν, cm^{-1}: 3050, 1597 (C=N), 1390, 1260, 1155, 755, 665. ^{13}C NMR spectrum, δ, ppm: 161.4 (C-3); 149.0 (C-6); 147.8 (C-5); 144.2 (C-1'); 133.5 (C-4"); 133.3 (C-2'); 133.1 (C-4'"); 132.9 (C-1"); 132.6 (C-6'); 132.3 (C-4'); 131.6 (C-1'"); 130.22 (C-3",5"); 130.18 (C-3'",C-5'"); 130.05 (C-4); 129.5 (C-2",6"); 129.0 (C-2'",C-6'"); 127.9 (C-3'); 127.0 (C-5'); 19.0 (CH_3). Mass spectrum, *m/z* (I_{rel}, %): 323 $[M-Br]^+$ (100), 325 (40).

1,3,5-Triphenylpyridazinium Bromide (3c). A solution of concentrated hydrobromic acid (3 ml) was added to a solution of compound **4a** (0.3 g, 1 mmol) in ethanol (20 ml) and held at room temperature for 48 h. Solvent was evaporated *in vacuo* without heating. The residue was recrystallized from acetic acid. Yield 0.25 g (65%); mp 165-168ºC (AcOH). IR spectrum, ν, cm^{-1}: 3050, 1595 (C=N), 1390, 1255, 1155, 760, 670. ^1H NMR spectrum, δ, ppm (*J*, Hz): 10.59 (1H, d, ^4J = 1.2, H-6); 9.47 (1H, d, ^4J = 1.2, H-4); 8.45 (2H, d, ^3J = 8.0, H-2',6'); 8.38 (2H, m, H-2",6"); 8.28 (2H, m, H-2'",6'"); 7.79 (3H, m, H-3'–H-5'); 7.70-7.65 (6H, m, H-3"–H-5", H-3'"–H-5'"). Found, %: C 67.97; H 4.51; Br 20.52; N 7.22. $C_{22}H_{17}BrN_2$. Calculated, %: C 67.88; H 4.40; Br 20.53; N 7.20.

1,3,5-Triphenyl-1,4-dihydropyridazine (4a). A mixture of γ-bromodypnone **1** (1 g, 3.32 mmol), AcONa (0.33 g, 4.0 mmol), and phenylhydrazine (0.33 ml, 3.32 mmol) was fused on an oil bath at 140ºC for 1 h. After cooling, water (10 ml) was added to the melt and thoroughly triturated. The solid was filtered off, thoroughly washed with water and then 2-propanol, and recrystallized. Yield 0.67 g (65%); mp 131-133ºC (EtOH) (mp 133ºC [6]); R_f 0.59 (Silufol UV-254, hexane–benzene, 2:1). IR spectrum, ν, cm^{-1}: 3040, 1590 (C=N), 1490, 1335, 1247, 1200, 745, 680. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-3}$): 202 (50.49), 240 (23.62), 318 (27.23), 392 (10.08). ^{13}C NMR spectrum, δ, ppm: 144.82 (C-1'); 142.38 (C-3); 137.89 (C-1'"); 137.27 (C-1"); 129.88 (C-3',5',4"); 129.11 (C-3",5"); 129.08 (C-3'",5'"); 127.11 (C-4'"); 126.38 (C-2",6"); 124.74 (C-2'",6'"); 122.85 (C-4'); 121.42 (C-6); 116.03 (C-2',6'); 108.87 (C-5); 24.72 (C-4). Mass spectrum, *m/z* (I_{rel}, %): 311 $[M+1]^+$ (20), 310 $[M]^+$ (40), 309 $[M-1]^+$ (100).

N,2,4-Triphenyl-1H-pyrrole-1-amine (5). 1,4-Dihydropyridazine **4a** (0.3 g, 1 mmol) was dissolved in ethanol (5 ml). A solution of $HClO_4$ (60%, 1 ml) was added and heated to reflux. Solvent was evaporated to half volume and left at room temperature for 3 h. The precipitate was filtered off and recrystallized. Yield 0.06 g (20%); mp 164-165ºC (2-PrOH) (mp 165ºC [7]).

1,3,5-Triphenyl-1,6-dihydropyridazine (6a). γ-Bromodypnone **1** (1 g, 3.32 mmol) was dissolved with heating in a mixture of alcohol (30 ml) and acetic acid (20 ml). Phenylhydrazine (0.33 ml, 3.32 mmol) was added to the warm solution and the product was held at room temperature for 10 h. The precipitate formed was filtered, washed with an alcoholic solution of sodium carbonate (15%), and recrystallized. Yield 0.52 g (51%); mp 143-145ºC (EtOH–AcOH, 1:1); R_f 0.47 (Silufol UV-254, hexane–benzene, 2:1). IR spectrum, ν, cm^{-1}: 3040, 1590 (C=N), 1485, 1335, 1273, 1190, 915, 735, 670. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-3}$): 204 (45.83), 228 (17.58), 256 (27.54), 282 (33.06), 427 (10.37). ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.96 (2H, d, ^3J = 8.0, H-2",6"); 7.91 (2H, d, ^3J = 8.0, H-2'",6'"); 7.53 (2H, d, ^3J = 8.0, H-2',6'); 7.49 (2H, t, ^3J = 8.0, H-3'",5'"); 7.43 (3H, m, H-3",5", H-4'"); 7.38 (2H, t, ^3J = 8.0, H-3',5'); 7.35 (1H, t, ^3J = 8.0, H-4"); 7.29 (1H, s, H-4); 7.00 (1H, t, ^3J = 8.0, H-4'); 4.72 (2H, s, H-6). ^{13}C NMR spectrum, δ, ppm: 147.08 (C-1'); 141.06 (C-3); 137.12 (C-1"); 136.36 (C-1'"); 134.76 (C-5); 129.93 (C-4'"); 129.63 (C-3',5'); 129.38 (C-3'",5'"); 129.22 (C-3",5"); 128.67 (C-4"); 126.11 (C-2'",6'"); 125.47 (C-2",6"); 122.65 (C-4'); 115.33 (C-2',6'); 111.94 (C-4); 45.19 (C-6). Mass spectrum, *m/z* (I_{rel}, %): 311 $[M+1]^+$ (100), 309 $[M-1]^+$ (40). Found, %: C 85.40; H 5.90; N 9.09. $C_{22}H_{18}N_2$. Calculated, %: C 85.13; H 5.85; N 9.03.

1-(Aryl)-3,5-diphenyl-1,6-dihydropyridazines 6b,c (**General Method**). A mixture of γ-bromodypnone **1** (1 g, 3.32 mmol) and 4-nitrophenylhydrazine or 4-hydrazinobenzoic acid (3.32 mmol) was refluxed in nitromethane (50 ml) for 30 min. The solution was cooled and the precipitate was filtered off, washed with alcohol, and recrystallized from acetic acid.

Compound 6b. Yield 0.79 g (67%); mp 190-192ºC ($MeNO_2$). IR spectrum, ν, cm^{-1}: 3070; 1590 (C=N); 1495 (NO_2^{as}); 1317 (NO_2^{s}); 1285, 1185, 1110, 915, 830, 745, 685. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-3}$): 202 (37.93), 274 (27.13), 450 (24.28). ^1H NMR spectrum, δ, ppm (*J*, Hz): 8.18 (2H, d, ^3J = 9.0, H-3',5'); 7.96

(2H, d, ^3J = 7.5, H-2",6"); 7.88 (2H, d, ^3J = 7.5, H-2"',6"'); 7.63 (2H, d, ^3J = 9.0, H-2',6'); 7.50-7.37 (6H, m, H-3"–H-5", H-3"'–H-5"'); 7.24 (1H, s, H-4); 4.86 (2H, s, H-6). Mass spectrum, *m/z* (I_{rel}, %): 355 $[M-Br]^+$ (30), 354 $[M-Br-1]^+$ (100). Found, %: C 74.48; H 4.93; N 11.81. $C_{22}H_{17}N_3O_2$. Calculated, %: C 74.35; H 4.82; N 11.82.

Compound 6c. Yield 0.58 g (68%); mp 193-195ºC (AcOH). IR spectrum, ν, cm^{-1}: 3000 (br. CH, OH), 1593 (C=N), 1420, 1270 (br. δ OH), 1170, 910, 745, 675. UV spectrum, λ_{max}, nm ($\varepsilon\times10^{-3}$): 202 (53.14), 2388 (31.52), 430 (15.64). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 12.23 (1H, br. s, OH); 7.93 (4H, m, H-3',5',2",6"); 7.85 (2H, d, ^3J = 8.0, H-2"',6"'); 7.54 (2H, d, ^3J = 8.8, H-2',6'); 7.49-7.41 (5H, m, H-3"–H-5", H-3"',5"'); 7.35 (1H, t, ^3J = 8.0, H-4"'); 7.21 (1H, s, H-4); 4.80 (2H, s, H-6). Found, %: C 78.00; H 5.23; N 7.92. $C_{23}H_{18}N_2O_2$. Calculated, %: C 77.95; H 5.12; N 7.90.

5-Methyl-1,3,5-triphenyl-4,5-dihydro-1H-pyrazole (8). The reaction of bromodypnone **1** with phenylhydrazine was carried out as reported in the method above for the preparation of the dihydropyridazine **6a**. The filtrate formed after separation of the solid product **6a** was evaporated at room temperature. The residue was washed with a small amount of 2-propanol and recrystallized several times from 2-propanol. Yield 0.1 g (9.5%); mp 177-179ºC (2-PrOH) (mp 180ºC [10]). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.69 (2H, d, ^3J = 8.0, H-2",6"); 7.48 (2H, d, ^3J = 8.0, H-2"',6"'); 7.38 (4H, t, ^3J = 8.0, H-3",5",3"',5"'); 7.30 (1H, t, ^3J = 8.0, H-4"'); 7.28 (1H, t, ^3J = 8.0, H-4"); 7.03 (2H, t, ^3J = 8.0, H-3',5'); 6.91 (2H, d, H-2',6'); 6.69 (1H, t, ^3J = 8.0, H-4'); 3.54 (1H, d, ^2J = 17.2, H_A-4); 3.33 (1H, d, ^2J = 17.2 H_B-4); 1.79 (3H, s, CH_3). ^{13}C NMR spectrum, δ, ppm: 146.5 (C-3); 146.2 (C-1"'); 143.9 (C-1'); 133.2 (C-1"); 129.6 (C-4"); 129.3 (C-3',5',3",5",3"',5"'); 127.9 (C-4"'); 126.3 (C-2",6"); 126.1 (C-2"',6"'); 119.7 (C-4'); 115.2 (C-2',6'); 70.53 (C-5); 53.5 (C-4); 22.36 (CH_3).

5-Bromo-1-(4-nitrophenyl)-3,5-diphenyl-1,4,5,6-tetrahydropyridazine (9a). Using the method above for the synthesis of compounds **6b,c** from the γ-bromodypnone **1** (1 g, 3.32 mmol) and 4-nitrophenyl-hydrazine (1.18 g, 3.32 mmol) to give the product **6b**. The acetic filtrate obtained after recrystallization of compound **6b** was held for 5 days and filtered to give a precipitate of compound **9a**. Yield 0.26 g (18%); mp 192-194ºC (AcOH). IR spectrum, ν, cm^{-1}: 1580 (C=N); 1480, 1295, 1100, 835, 752, 675. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.99 (2H, d, ^3J = 8.0, H-3',5'); 7.79 (2H, m, H-2",6"); 7.46 (3H, m, H-3"–H-5"); 7.40 (4H, m, H-2"',3"',5"',6"'); 7.34 (1H, t, ^3J = 7.5, H-4"'); 7.09 (2H, br. m, H-2',6'); 4.75 (1H, d, ^2J = 12.0, H_A-6); 4.61 (1H, d, ^2J = 12.0, H_B-6); 3.99 (1H, d, ^2J = 18.0, H_A-4); 3.55 (1H, d, ^2J = 18.0, H_B-4). ^{13}C NMR spectrum, δ, ppm: 151.24 (C-3); 148.18 (C-4'); 141.99 (C-1"'); 139.01 (C-1'); 131.50 (C-1"); 130.65 (C-4"); 130.12 (C-3"',5"'); 129.52 (C-3",5"); 128.85 (C-4"'); 127.02 (C-2",6"); 126.12 (C-3',5'); 126.07 (C-2"',6"'); 113.51 (C-2',6'); 72.56 (C-5); 51.83 (C-4); 38.58 (C-6). Found, %: C 60.62; H 4.20; Br 18.30; N 9.65. $C_{22}H_{18}BrN_3O_2$. Calculated, %: C 60.56; H 4.16; Br 18.31; N 9.63.

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