Peculiarities of the reactions of α,β-unsaturated γ-bromoketones with hydrazine derivatives

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The reaction result of α,β-unsaturated γ-bromoketones with hydrazines depends on the structure of the reagents. Reaction with hydrazine hydrate leads to the mixture of 3,5- di(R)pyridazine, 3,6-di(R)pyridazine and 2,4-di(R)-1*H*-pyrrol-1-amine derivatives. The formation of three types of products is due to the structure of the unsaturated aliphatic ketone. Two competing reaction schemes of ketones with hydrazines are considered, which include condensation or Michael-type addition in the first stage. The main products of the reactions of halogen-substituted derivatives of γ-bromodipnone with arylhydrazines are 1,3,5-triaryl-1,6-dihydropyridazines, which easily form aromatic salts under reaction conditions (when heated in EtOH).

Introduction

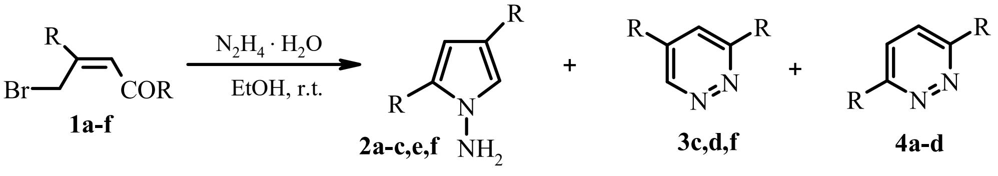
Hydrazine and its derivatives are popular reagents in the synthesis of various nitrogen-containing heterocycles. In particular, hydrazines are the basic reagents in a number of schemes for construction of 1-aminopyrrole skeleton. 1-Aminopyrroles represent pharmacologically important heterocycles. Recently, 1-aminopyrroles have been employed as intermediates during the synthesis of polypyrrole-silica nanocomposites [1], conductive polymers [2], catalyst [3], as intermediates during the synthesis of pyrrolo[1,2-*b*][1,2,4]triazines [4], phytochromes [5], analgesics [6], as well as *N*-methyl-D-aspartate receptor and angiotensin II antagonists [7]. Despite these applications, the limited presence of 1-aminopyrroles in the literature can be ascribed to the few procedures which exist for their preparation [8]. Therefore, the development of new methods for the synthesis of these compounds is of considerable interest.

Synthetic routes to 1-aminopyrroles are relatively few [4,8-13], and these derivatives seem to be difficult to prepare by Knorr and its modified procedures, since the condensation of hydrazine with 1,4-dicarbonyl compounds provides only low yields of 1-aminopyrroles, and dihydropyrazines [14-16] or bispyrroles [13] are formed as byproducts. It has been depicted in recent work of our research group [17] that the reactions of 1,3-diphenyl-4-bromo-2-buten-1-one (γ-bromodipnone) with hydrazine hydrate and carboxylic acid hydrazides produce aryl derivatives of 1-aminopyrrole with high yield. A similar result was also obtained by

Gadzhily RA, at al. [18] from γ-halogen-α,β-unsaturated aliphatic ketones. In this paper we present the results of studying the peculiarities of the reaction of hydrazines with γ-bromo-α,β-unsaturated aliphatic ketones (**1**), depending on the structure of reagents.

Results and discussion

We have found that the interaction of γ-bromodipnone derivatives with hydrazine hydrate in alcohol leads to a mixture of products (**2-4**, **Scheme 1**), in contrast to γ-chloroalkyl ketones, for which 1-aminopyrrols of type **2** have been described as single products of the reaction [18]. The composition of the mixture depends on the nature of the substituents in the arene groups. In the case of γ-bromodipnones **1a,b**, the main products of the conversion are 2,4-diaryl-1*H*-pyrrole-1-amines **2a,b**, which are obtained with high yields (50-61%). Also, 3,6-diarylpyridazines **4a,b** were isolated from the reaction mixture with low yields (10-20%). In reaction with *bis*(4-chlorophenyl)ketone **1c**, the formation of three products **2c**, **3c**, **4c** (in accordance with mass spectrometry data) in a ratio of 3:1:2. The reported ratios have been obtained by ^{1}H NMR. In the case of *bis*(4-bromophenyl)ketone **1d** the transformation gives exclusively pyridazine derivatives **3d** and **4d** in the ratio of 1.3:1. Chloro- (**2c-4c**) and bromosubstituted products (**3d**, **4d**) could not be separated by chromatographic methods (HPLC (silica gel 4060) and TLC (silica gel G/UV_{254}), the solvent system: $CHCl_3$, $CHCl_3$-EtOAc 70:30, $CHCl_3$-EtOAc 90:10). Only 3,6-diarylpyridazine derivatives **4c,d** could isolated in pure form by multiple recrystallization, albeit in low yields (15% and 13%, respectively).



R = Ph (**a**), 4-F-C_6H_4 (**b**), 4-Cl-C_6H_4 (**c**), 4-Br-C_6H_4 (**d**), 2-Thienyl (**e**), t-Bu (**f**)

Scheme 1. The reaction between γ-brom-α,β-unsaturated ketones and hydrazine hydrate.

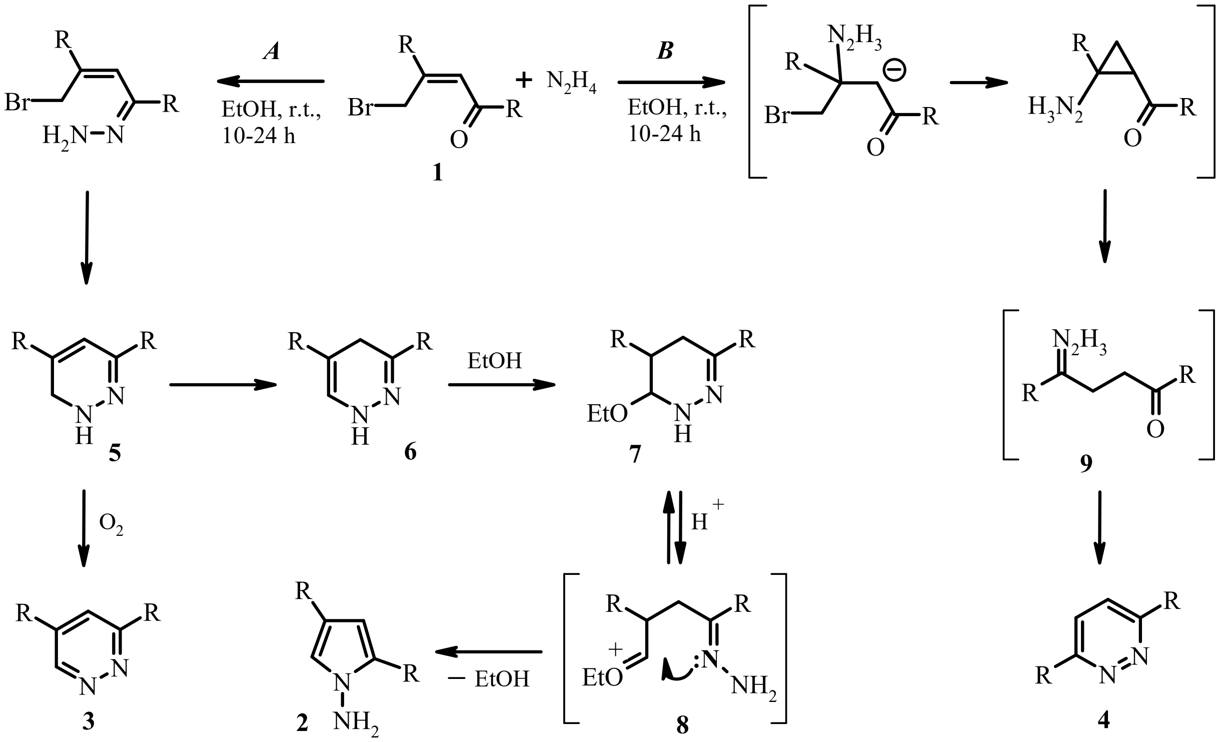
The reaction of hydrazine hydrate with 4-bromo-1,3-di-2-thienylbut-2-ene-1-one **1e** produced the expected 2,4-di-2-thienyl-1*H*-pyrrole-1-amine **2e** with a satisfactory yield (45%). The reaction proceeds with the formation of a significant number of by-products, among which pyridazine derivatives could not be reliably identified by spectral methods. The reaction of 5-(bromomethyl)-2,2,6,6-tetramethylhept-4-en-3-one **1f** with hydrazine hydrate results in a mixture of two products in almost equal quantities, which was separated by HPLC and previously unknown 2,4-di-*tert*-butyl-1*H*-pyrrol-1-amine (**2f**) and 3,5-di-*tert*-butylpyridazine (**3f**) were obtained.

3,6-Diarylpyridazines **4a-d** are described in the literature [19-22], and the physicochemical properties of the products obtained in this work coincided with those indicated. The conclusion about their structure confirmed by comparing the properties of compound **4a**, obtained by a known procedure [19], with the product formed in reaction **1a** with hydrazine. The structure of the 1-aminopyrrole derivatives **2** and the presence of 3,5-diarylpyridazine derivatives **3c,d** in the reaction mixtures were determined on the basis of mass spectrometry data and on the correspondence of their spectral data to the known [17, 18, 23-25]. In particular, all proton signals of asymmetric pyridazines **3c,d** in NMR spectra are observed separately: $\delta_H \sim 9.54$ ppm (d, $J = 2.0$ Hz, H-4) and $\delta_H \sim 8.46$ ppm (d, $J = 2.0$ Hz, H-6), protons of *para*-substituted arenes are observed in the form of four double-proton doublets. In the case of symmetric 3,6-disubstituted pyridazines **4c,d**, only three signals are present in the spectra: two doublets of 4-halophenyl substituents and one singlet of H-4, H-5 ($\delta_H \sim 7.8$ ppm).

Analyzing the results obtained, it can be noted that the degree of conversion to pyridazines increases with an increase of the –*I*-effect of substituents R. This is also facilitated by the presence of a bulk substituent for imino group (*t*-Bu).

To explain the results obtained, we analyzed the known data (including our work [25]) on the properties of γ-bromodipnone **1a** and dihydropyridazines. Based on this analysis, the following scheme (**Scheme 2**) is proposed for the formation of three types of products in reactions of unsaturated γ-bromoketones with hydrazine hydrate. The possibility of the reaction proceeding in three alternative directions is due to the nature of the substituents at the atoms C(1) and C(3) in the system of unsaturated ketone. A well-known scheme for the reaction of ketones with hydrazines is the formation of hydrazones (*path A*), which ends with an intramolecular cyclization in 1,6-dihydropyridazine (**5**) in the case of γ-halogen derivatives. Compounds of type **5** can be transformed in two ways: oxidation in derivatives **3** [25, 26] and by tautomeric conversion into 1,4-dihydropyridazines (**6**) [15, 25, 27], followed by rearrangement into 1-aminopyrroles **2** [25, 27, 28]. The mechanism of rearrangement involves the stage of the reversible splitting of the C(6)-N(1) bond in the intermediate **7**, which is the result of the EtOH molecule addition to the olefinic bond C(5)=C(6) in **6**. Recycling of the intermediate **8** leads to 1*H*-pyrrole-1-amine **2**. Obviously, the efficiency of the conversion of compounds **6** to the pyrroles increases with a relative increase of the –*I*-effect of the substituent at N(1), as indicated by the previously known data [14, 17, 25, 27, 28], and the results obtained in this paper. An increase in the substituent volume at C(5) may interfere with the addition of EtOH by this scheme, and this is reflected in the decrease of the relative yield of the product **2f** (R = *t*-Bu). In general, the relatively low total yield of reaction products in the case of di(*t*-

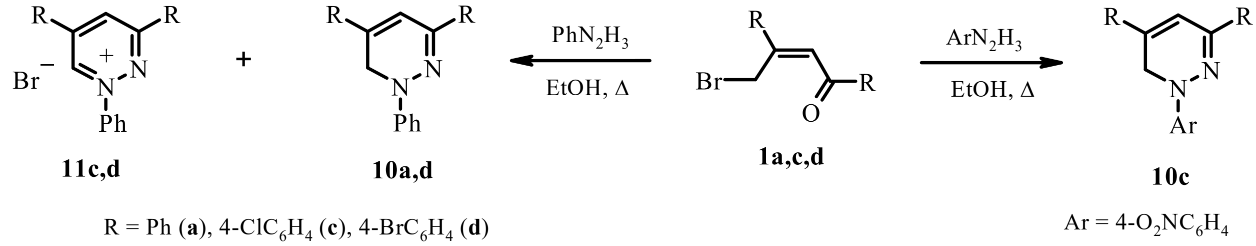
butyl)ketone **1f** (49%) is evidently due to steric barriers at the stage of condensation in hydrazone. On the contrary, the aromatization of 1,6-dihydropyridazines **6** contributes to the relative increase of –*I*-effect of the substituents at C(3)...C(6) [26, 29].



Scheme 2. The scheme of the formation of three types of products.

When the unsaturated γ-bromoketones react with the bases, may be a Michelle-type addition of nucleophiles at position 3 (*path **B***), which is accompanied by intramolecular cyclization and rearrangement into the 1,4-dicarbonyl derivatives of type **9** [30, 31]. Obviously, the probability of the realization of such a mechanism increases with the presence of an acceptor substituent at the atom C(3). This explains the increase in the content of 3,6-diarylpyridazines **4** of a symmetrical structure in product mixtures in the case of ketone **1c,d** reactions. At the same time, an increase in the donor effect and the steric hindrance of the substituent at C(3) (compound **1f** and γ-chloroalkyl ketones [18]) prevent the reaction by the indicated mechanism.

The above explanations are consistent with the results of the reactions of halogen substituted derivatives of γ-bromodipnone **1c,d** with arylhydrazines (**Scheme 3**). Previously [25], we have shown that the reaction of the unsubstituted derivative **1a** with phenylhydrazine leads to 1,6-dihydropyridazine **10a** with a high yield already at room temperature. In contrast to **1a**, the reaction of ketones **1c,d** occurs more slowly and only when heated. In this case, the formation of two types of derivatives of pyridazine – 1,3,5-triaryl-1,6-dihydropyridazines **10** and aromatic salts **11**,



Scheme 3. The reaction between γ-bromodiponones and arylhydrazines.

was observed. When bromo ketone **1c** is reacted with phenylhydrazine in EtOH, the 3,5-*bis*(4-chlorophenyl)-1-phenylpyridazin-1-ium bromide (**11c**) is isolated from the reaction mixture, and 1,6-dihydropyridazine **10c** when 4-nitrophenylhydrazine is used. The heating of *p*-bromosubstituted γ-bromodipnone **1d** with phenylhydrazine leads to a mixture of 1,6-dihydropyridazine (**10d**, isolated in individual condition) and 3,5-*bis*(4-bromophenyl)-1-phenylpyridazine-1-one (**11d**). The low solubility of the reaction product **10d** in alcohol can lead to a large portion of it from the reaction medium and prevent further oxidation. The formation of salt **11d** is proved by the data of the ^1H NMR spectrum of the crude product on the characteristic signals of H-6 (10.65 ppm, 1H, s) and H-4 (9.58 ppm, 1H, s).

Conclusions on the structure of products **10**, **11** are made according to the criteria for determining the structure of isomeric dihydropyridazines and their aromatic salts identified by us earlier [25].

Conclusions

γ-Bromo-α,β-unsaturated aliphatic ketones are polyfunctional electrophilic reagents and convenient precursors for the synthesis of heterocycles. In reactions with hydrazines, three types of products can be obtained whose structure depends on the nature of the substituents in the ketone. The main conversion pathway involves the formation of 1,6-dihydropyridazines which can be transformed by oxidation into aromatic 3,5-disubstituted pyridazines and by tautomeric conversion into 1,4-dihydropyridazines, followed by rearrangement into 1-aminopyrroles. An alternative path involves a Michelle-type addition of hydrazine, which is accompanied by a rearrangement into 1,4-dicarbonyl derivatives and subsequent cyclization to 3,6-disubstituted pyridazines. In conjunction with arylhydrazines, one scheme is implemented which leads to pyridazines.

Experimental part

^1H NMR were recorded on the Varian VXR-400, internal standard was TMS. IR spectra were recorded on the PerkinElmer Spectrum BX. Elemental analyses were made on the universal analyzer vario MikroCube, for the determination of halogens the Sheninger method is used. Melting points were determined on a Tile heating instrument. A check on the purity of the obtained compounds was effected by the GLC mass spectrometric method on an Agilent 1100 Series instrument, with an Agilent LC/MSD SL selective detector (samples were introduced in a matrix of CF_3CO_2H, ionization by EI) (2*Z*)-4-Bromo-1,3-di-Rbut-2-en-1-ones were prepared as reported [32] (**1a-d**), [33] (**1e**), [34] (**1f**). All other chemicals and solvents are commercially available and were used without further purification.

General procedures of synthesis of 2,4-di(R)-1H-pyrrole-1amines **2**.

A mixture of 3.32 mmol of γ-bromo-α,β-unsaturated aliphatic ketone (**1a,b,e,f**) and 2.6 ml of hydrazine hydrate (80%) in 50 ml of EtOH was heated to completely dissolve the bromo ketone and kept at room temperature (10-24 h). The formed precipitate was filtered off, washed with EtOH, dried, and recrystallized from propan-2-ol to afford light yellow solid of **2a,b,e**. In the case of ketone **1c**, 0.71 g (total yield: 71%) of a mixture of products (**2c+3c+4c**; 3:1:2) was obtained in which the content of **2c** was 50%. In the case of ketone **1f** no precipitate is formed. The solvent was removed under reduced pressure to give 0.32 g (total yield: 50%) of a mixture of **2f** and **3f** (1:1.3), which then was separated by column chromatography (silica gel 4060, $CHCl_3$-EtOAc, 70:30).

2,4-Diphenyl-1H-pyrrol-1-amine **2a**. Yield: 0.47 g, 60%; mp 143–145 °C (*i*-PrOH), lit. mp: 144 °C [17].

2,4-Bis(4-fluorophenyl)-1H-pyrrol-1-amine **2b**. Yield: 0.45 g, 50%; mp 118–120 °C (*i*-PrOH); IR (KBr): ν 3367 (NH), 3339 (NH), 1561, 1499, 1239, 842, 814, 607 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, *J* Hz): δ 7.72 (2H, d, ^3J = 8.0, H-2’, H-6’), 7.47 (2H, d, ^3J = 8.0, H-2”, H-6”), 7.11 (1H, broad. d, H-5), 7.10 (2H, m, H-3’, H-5’), 7.02 (2H, m, H-3”, H-5”), 6.38 (1H, broad. d, H-3), 5.77 (2H, broad. s, NH_2) ppm; ^{13}C NMR (100.7 MHz, DMSO-d_6): δ 161.6 (1C, d, J_{CF} = 245.0, C-4’), 160.9 (1C, d, J_{CF} = 245.0, C-4’’), 133.2 (C-2), 132.6 (C-1’), 130.3 (2C, d, J_{CF} = 8.0, C-2’, C-6’), 129.5 (C-1’’), 126.5 (2C, d, J_{CF} = 8.0, C-2’’, C-6’’), 122.0 (C-5), 119.9 (C-4), 115.6 (2C, d, J_{CF} = 42.5, C-3’, C-5’), 115.7 (2C, d, J_{CF} = 42.5, C-3’’, C-5’’), 103.8 (C-3) ppm; ^{19}F NMR (100.7 MHz, DMSO-d_6): δ -116.6, -118.5 ppm; MS (CI): *m/z* = 271.3 ($[M+H]^+$); Analysis (calcd, found)%: C (71.10, 71.19); H (4.48, 4.53); N (10.36, 10.30).

2,4-Bis(4-chlorophenyl)-1H-pyrrol-1-amine **2c** (50% purity). ^1H NMR (400 MHz, DMSO-d_6, *J* Hz): δ 7.74 (2H, d, ^3J = 8.0, H-2’, H-6’), 7.49 (2H, d, ^3J = 8.0, H-2”, H-6”), 7.35 (2H, d, ^3J = 8.0, H-3’, H-5’), 7.27 (2H, d, ^3J = 8.0, H-3”, H-5”), 7.21 (1H, d, ^4J = 2.0, H-5), 6.52 (1H, d, ^4J = 2.0, H-3), 5.90 (2H, broad. s, NH_2) ppm.

2,4-Di-2-thienyl-1H-pyrrole-1-amine **2e**. Yield: 0.37 g, 45%; mp 125–126 °C (*i*-PrOH); IR (KBr): ν 3328 (NH), 3266 (NH), 1161, 839, 783, 697 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, *J* Hz): δ 7.42 (1H, d, ^3J = 3.0, H-5’), 7.27 (1H, d, ^3J = 6.2, H-3’), 7.13 (1H, d, ^3J = 6.2, H-3”), 7.04–7.01 (3H, m, H-5, H-4’, H-5’’), 6.96 (1H, m, H-4”), 6.41 (1H, d, ^4J = 2.0, H-3), 5.93 (2H, broad. s, NH_2) ppm; ^{13}C NMR (100.7 MHz, DMSO-d_6): δ 139.4 (C-2’), 133.9 (C-2’’), 128.9

(C-2), 128.4 (C-5’), 127.6 (2C), 125.2 (C-5’’), 124.2 (C-5), 122.6 (2C), 121.5 (2C), 121.2 (2C), 115.9 (C-4), 102.7 (C-3) ppm; MS (CI): *m/z* = 247.4 ($[M+H]^+$); Analysis (calcd, found)%: C (58.50, 58.58); H (4.09, 4.11); N (11.37, 11.35).

2,4-Di-tert-butyl-1H-pyrrol-1-amine **2f**. Yield: 0.14 g, 22%; mp 136–137 °C (*i*-PrOH); IR (KBr): ν 3322 (NH), 3210 (NH), 2955, 2900, 2867, 1464, 1360, 1251,1237, 1205, 932,796, 689 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, *J* Hz): δ 6.29 (1H, d, ^4J = 1.2, H-5), 5.50 (3H, ушир. m, H-3, NH_2), 1.37 (9H, s, 2-$C(CH_3)_3$), 1.13 (9H, s, 4-$C(CH_3)_3$) ppm; ^{13}C NMR (100.7 MHz, DMSO-d_6): δ 160.6 (C-2), 154.4 (C-5), 149.9 (C-4), 125.0 (C-3), 45.3 (2-$\underline{C}(CH_3)_3$), 35.5 (4-$\underline{C}(CH_3)_3$), 29.7 (2-$C(\underline{C}H_3)_3$), 28.3 (4-$C(\underline{C}H_3)_3$) ppm; MS (CI): *m/z* = 195.3 ($[M+H]^+$); Analysis (calcd, found)%: C (74.17, 74.25); H (11.41, 11.35); N (14.42, 14.45).

3,5-Di-tert-butylpyridazine **3f**.

Synthesis was performed according to the procedure for the preparation of compounds **2**. The product **3f** was separated by column chromatography (silica gel 4060, $CHCl_3$-EtOAc, 70:30) from a mixture of **2f** and **3f** (1:1.3).

Yield: 0.17 g, 27%; mp 90–92 °C (*i*-PrOH); IR (KBr): ν 2965, 2904, 2872, 1584, 1478, 1383, 1367, 1260, 902 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, *J* Hz): δ 9.18 (1H, s, H-6), 7.57 (1H, s, H-4), 1.39 (9H, s, 3-$C(CH_3)_3$), 1.32 (9H, s, 5-$C(CH_3)_3$) ppm; ^{13}C NMR (100.7 MHz, DMSO-d_6): δ 169.4 (C-3), 149.8 (C-6), 148.7 (C-6), 119.7 (C-4), 37.4 (3-$\underline{C}(CH_3)_3$), 34.1 (5-$\underline{C}(CH_3)_3$), 30.5 (3-$C(\underline{C}H_3)_3$), 30.4 (5-$C(\underline{C}H_3)_3$) ppm; MS (CI): *m/z* = 193.2 ($[M+H]^+$); Analysis (calcd, found)%: C (74.95, 75.01); H (10.48, 10.46); N (14.57, 14.60).

General procedures of synthesis of 3,6-diaryl-pyridazines **4**.

Synthesis was performed according to the procedure for the preparation of compounds **2**. The remaining filtrate after the separation of pyrrolamines **2a,b** was evaporated under reduced pressure and the residue was recrystallized from EtOH to afford light yellow solid of **4a,b**. In the case of ketones **1c,d**, formed precipitate was filtered off, washed with EtOH, dried, and recrystallized from EtOH four times to afford light yellow solid of **4c,d**.

3,6-Diphenylpyridazine **4a**. Yield: 0.08 g, 10%; mp 220–221 °C (EtOH), lit. mp: 220 °C [19]. ^1H NMR (400 MHz, DMSO-d_6, *J* Hz): δ 8.21 (2H, s, H-4, H-5), 8.19 (4H, d, ^3J = 8.0, H-2’, H-6’, H-2’’, H-6’’), 7.57–7.50 (6H, m, H-3’–H-5’, H-3’’–H-5’’) ppm.

3,6-Bis(4-fluorophenyl)pyridazine **4b**. Yield: 0.18 g, 20%; mp 249–250 °C (EtOH), lit. mp: 259 °C [22]. IR (KBr): ν 1605, 1510, 1225, 1158, 839, 822 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, *J* Hz): δ 7.79 (4H, m, H-2’, H-6’, H-2’’, H-6’’), 7.74 (2H, s, H-4, H-5), 7.22 (4H, m, H-3’, H-5’, H-3’’, H-5’’) ppm.

3,6-Bis(4-chlorophenyl)pyridazine **4c**. Yield: 0.15 g, 15%; mp 262–263 °C (EtOH), lit. mp: 264 °C [20]. IR (KBr): ν 1597, 1490, 1421, 1097, 822 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6, *J* Hz): δ 8.38 (2H, s, H-4, H-5), 8.34 (4H, d, ^3J

= 8.0, H-2’, H-6’, H-2’’, H-6’’), 7.67 (4H, d, ^3J = 8.0, H-3’, H-5’, H-3’’, H-5’’) ppm.

3,6-Bis(4-bromophenyl)pyridazine **4d**. Yield: 0.17 g, 13%; mp 285–287 °C (EtOH), lit. mp: 286 °C [21]. ^{1}H NMR (400 MHz, DMSO-d_6, *J* Hz): δ 8.38 (2H, s, H-4, H-5), 8.27 (4H, d, ^3J = 8.0, H-2’, H-6’, H-2’’, H-6’’), 7.81 (4H, d, ^3J = 8.0, H-3’, H-5’, H-3’’, H-5’’) ppm.

3,5-Bis(4-chlorophenyl)-1-(4-nitrophenyl)-1,6-dihydropyridazine **10c**.

To a stirred solution of **1c** (0.4 g, 1.08 mmol) in EtOH (20 ml) was added (4-nitrophenyl)hydrazine (0.17 g, 1.08 mmol). The reaction mixture was then boiled for 3h. The solution was cooled and the formed precipitate was filtered off, washed with EtOH, dried, and recrystallized from $MeNO_2$ to afford yellow solid of **10c**.

Yield: 0.27 g, 60%; mp 250–253 °C (decomp., $MeNO_2$); IR (KBr): ν 1580, 1495 (NO_2^{as}), 1320 (NO_2^{s}), 1280, 1165, 1085, 810 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6, *J* Hz): δ 8.20 (2H, d, ^3J = 9.0, H-3’, H-5’), 8.01 (2H, d, ^3J = 8.0, H-2’’, H-6’’), 7.96 (2H, d, ^3J = 8.0, H-2’’’, H-6’’’), 7.66 (2H, d, ^3J = 9.0, H-2’, H-6’), 7.48 (2H, d, ^3J = 8.0, H-3’’, H-5’’), 7.44 (2H, d, ^3J = 8.0, H-3’’’, H-5’’’), 7.33 (1H, s, H-4), 4.85 (2H, s, C(6)H_2) ppm; MS (CI): *m/z* = 380.0 ([M+H]$^+$, 100%), 382.0 ([M+2+H]$^+$), 384.0 ([M+4+H]$^+$); Analysis (calcd, found)%: C (62.28, 62.21); H (3.56, 3.49); Cl (16.71, 16.75); N (9.90, 9.91).

3,5-Bis(4-bromophenyl)-1-phenyl-1,6-dihydropyridazine **10d**.

Synthesis was performed according to the procedure for the preparation of compound **10c**, using 0.5 g (1.08 mmol) of ketone 1d and 0.11 ml (1.08 mmol) of phenylhydrazine. The remaining filtrate after the separation of 1,6-dihydropyridazine **10d** was evaporated under reduced pressure and the residue was recrystallized from AcOH to give 0.12 g of a mixture (**10d+11d**) in which the content of **11d** was < 40%.

Yield: 0.29 g, 57%; mp 143–145 °C ($MeNO_2$); IR (KBr): ν 1600, 1595, 1210, 1080, 1010, 805 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6, *J* Hz): δ 7.88 (2H, d, ^3J = 8.0, H-2’’, H-6’’), 7.79 (2H, d, ^3J = 8.0, H-2’’’, H-6’’’), 7.62–7.47 (6H, m, H-2’, H-6’, H-3’’, H-5’’, H-3’’’, H-5’’’), 7.34 (2H, t, ^3J = 8.0, H-3’, H-5’), 7.24 (1H, s, H-4), 6.98 (1H, t, ^3J = 8.0, H-4’), 4.70 (2H, s, C(6)H_2) ppm; ^{13}C NMR (100.7 MHz, DMSO-d_6): δ 146.8, 139.6, 136.2, 135.4, 133.4, 132.4, 132.2 (2C), 132.1 (2C), 130.0, 129.6 (2C), 128.2 (2C), 127.4 (2C), 122.0, 115.4 (2C), 112.0, 45.0 (CH_2) ppm; MS (CI): *m/z* = 469.1 ([M+H]$^+$), 471.0 ([M+2+H]$^+$, 100%), 473.1 ([M+4+H]$^+$); Analysis (calcd, found)%: C (56.44, 56.37); H (3.44, 3.39); Br (34.13, 34.18); N (5.98, 6.00).

3*,5-Bis(4-chlorophenyl)-1-phenylpyridazin-1-ium bromide* **11c**.

Synthesis was performed according to the procedure for the preparation of compound **10c**, using 0.11 ml (1.08 mmol) of phenylhydrazine. The solvent was removed under reduced pressure and then to the residue was added 10 ml of methyltrebutyl ether. The formed precipitate was filtered off, washed with ether, dried, and recrystallized from propan-2-ol to afford light yellow solid of **11c**.

Yield: 0.24 g, 48%; mp 321–323 °C (decomp., *i*-PrOH); IR (KBr): ν 1595, 1390, 1090, 820, 752 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d$_6$, J Hz): δ 10.64 (1H, s, H-6), 9.53 (1H, s, H-4), 8.50 (4H, m, H-2', H-6', H-2'', H-6''), 8.29 (2H, m, H-2''', H-6'''), 7.79 (3H, m, H-3'–H-5'), 7.71 (4H, m, H-3'', H-5'', H-3''', H-5''') ppm; ^{13}C NMR (100.7 MHz, DMSO-d$_6$): δ 160.5, 146.7, 146.6 (2C), 144.7, 138.5, 138.2, 132.9, 131.4 (2C), 130.9 (2C), 130.7 (2C), 130.6, 130.3 (2C), 130.2 (2C), 130.1, 125.2 (2C) ppm; MS (CI): *m/z* = 378.3 ([M-Br]$^+$, 100%), 380.0 ([M+2-Br]$^+$), 382.1 ([M+4-Br]$^+$); Analysis (calcd, found)%: C (57.67, 57.62); H (3.30, 3.28); Br (17.44, 17.45); Cl (15.48, 15.46); N (6.11, 6.14).

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