

Article

Solvent Moisture-Controlled Self-Assembly of Fused Benzoimidazopyrrolopyrazines with Different Ring's Interposition

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Abstract: This article shows that two extremely important families of fused heterocyclic assemblies, namely 6-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine and 5a-methyl-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine, can be synthesized from only two available building blocks (*N*-allenylpyrrole-2-carbaldehyde and *o*-phenylenediamine) by controlling only one reaction parameter (water content of the medium). It should be emphasized that the latter class of compounds (with an *a/d* arrangement) is previously unknown. If the allene group is introduced not into the starting compound, but during the reaction (in superbases media), a heterocyclic ensemble, 5-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazines, with a different position of the methyl group is formed.

Keywords: aldehydes; allenes; cyclization; heterocycles



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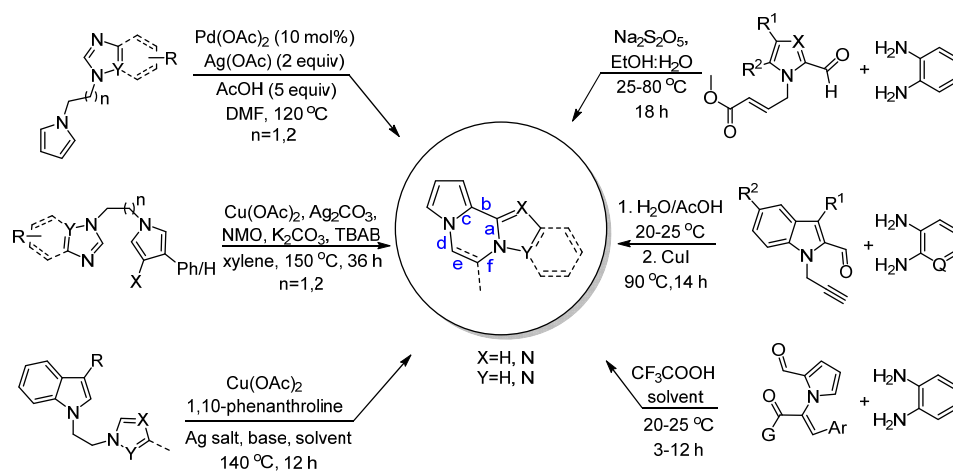


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1. Introduction

Fused heterocyclic compounds, namely, derivatives of imidazole, benzimidazole, and pyrazine, exhibit diverse biological activities. Imidazolopyrazines and imidazolopiperazines belong to the class of therapeutically efficient fused heterocycles. Imidazolopyrazine derivatives exert anti-inflammatory and antiviral actions, as well as inhibition MAPK-activated PK5 [1]. It was reported that imidazolopyrazines act as an effective CXCR3 antagonist (regulation of leukocyte transport) [2], and as a potent IGF-1R inhibitor [3]. The literature search reveals that the imidazolopiperazine motif is responsible for antimalarial action of known drugs [4], which can be enhanced via the introduction the pyrrole moiety in their structure.

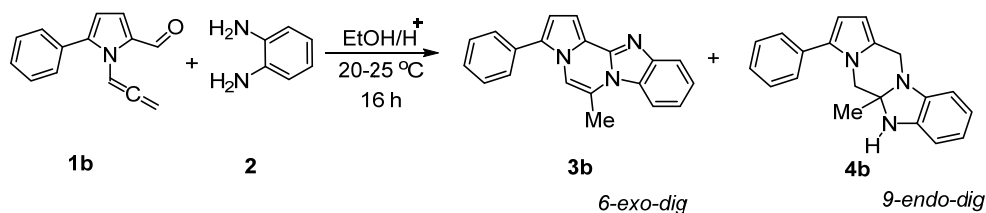
Despite a wide applicability of such compounds, facile and straightforward methods for the synthesis of these biologically active scaffolds still remain limited. Currently, only a few examples of assembling such systems are documented in the literature. They can be divided into two groups: intramolecular and intermolecular reactions (Scheme 1). Polyheterocyclic systems are obtained via intramolecular cyclization in the presence of palladium [5] or copper [6,7] salts as catalysts at high temperatures. Intermolecular cyclizations are also promoted by catalysts: transition metals [8], salts [9] or acids [10]. All the above reactions require expensive toxic catalysts, long reaction times or high temperatures, which are disadvantages from a synthetic point of view.



Scheme 1. Methods for the synthesis of polyheterocyclic systems: previous works.

2. Results

We have developed a strategy for the synthesis of benzimidazopyrrolopyrazines through the sequential addition of *o*-phenylenediamine (*o*-PDA) **2** to *N*-allenylpyrrole-2-carbaldehydes **1a–j** under mild conditions. Our investigation commenced with the reaction of 5-(2-phenyl)-*N*-allenylpyrrole-2-carbaldehyde **1b** and *o*-PDA **2**, which proceeded under conditions developed by us earlier for *N*-vinylpyrrole-2-carbaldehydes [11] in ethyl alcohol at room temperature for 16 h (Scheme 2).



Scheme 2. Synthesis of 6-methyl-3-phenylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine and 5a-methyl-3-phenyl-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine.

In contrast to the work with *N*-propargylindolecarbaldehyde [8], the allene fragment does not require activation with heavy metal salts (CuI), which opens up more possible directions for the reaction.

Experiments have shown that the reaction leads to a mixture of two products: the anticipated benzimidazopyrrolopyrazine **3b** and the unexpected dihydrobenzimidazopyrrolopyrazine **4b**. The process is influenced by the air humidity and hence by the presence of some amount of water in the reaction mixture. Thus, at a higher content of water in the air (wet season), the ratio of products **3b** and **4b** is 1:1 (NMR), while in a drier climate in the presence of commercial ethanol, this ratio is 64%:16% (19% of unreacted compound **1b**). Consequently, we have optimized this reaction by the addition of water and varying the solvents in order to direct it selectively to one of the two products (Table 1).

Optimization of the reaction conditions has revealed that in commercial DMSO, which usually contains some water, the process occurs with similar efficiency to that observed in aqueous ethanol (Entry 2). When the reaction was carried out in DMSO at a higher temperature (65 °C) for a shorter time (1 h), the products were obtained in the same ratio (Entry 3). However, in this case, the reaction was accompanied by the formation of hardly identifiable side products and afforded the target products in lower yield. Therefore, we further used the initial temperature conditions. Subsequently, we carried out experiments with dried ethanol in an inert atmosphere to avoid the effect of air humidity. In dry ethanol, a mixture of two products **3b** and **4b** was formed in a 9:1 ratio. Evidently, the

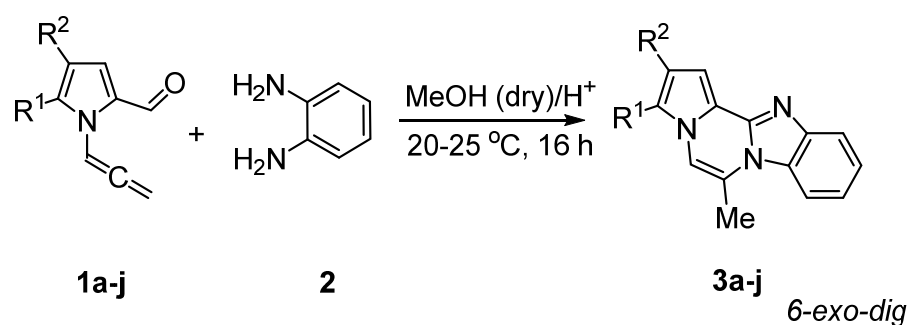
dried ethanol contained enough water to trigger a side reaction (Entry 5). In the presence of ethanol and 10% of water, a mixture of two compounds **3b** and **4b** was obtained in a 6:4 ratio (Entry 6). At a higher content of water (20%), the product ratio was again 1:1 (Entry 7), which evidenced the clear dependence of this ratio on the amount of water. However, when the process was implemented in a 1:1 mixture of ethanol-water (Entry 8), the starting compound **1b** was completely recovered due to poor solubility of such a mixture. Replacement of ethanol with methanol, which usually contains much less water, led to almost selective formation of product **3b** (Entry 9). The reaction in commercial (Entry 10) and dry benzene (Entry 11) also resulted in a higher selectivity with respect to compound **3b**, the conversion in the latter being decreased.

Table 1. Optimization of the reaction conditions ^a.

Entry	Solvent	H ₂ O (% from V Solvent)	T (°C)	t (h)	Ratio (¹ H NMR), %		
					1b	3b	4b
1 ^b	EtOH	–	20–25	12	–	50	50
2 ^c	DMSO	–	20–25	12	–	50	50
3 ^c	DMSO	–	65	1	–	50	50
4 ^d	EtOH	–	20–25	12	19	64	16
5	EtOH (dry)	–	20–25	12	–	90	10
6	EtOH (dry)	10	20–25	12	–	60	40
7	EtOH (dry)	20	20–25	12	–	50	50
8	EtOH (dry)	50	20–25	12	100	–	–
9	MeOH (dry)	–	20–25	12	–	96	traces
10	Benzene	–	20–25	12	–	85	15
11	Benzene (dry)	–	20–25	12	48	48	4

^a **1b** (0.0011 mol), **2** (0.00121 mol), solvent (2.2 mL), CF₃COOH (1%). ^b The reaction was carried out at high air humidity in unpressurized conditions (without drying agent). ^c Resinification. ^d Common ethanol.

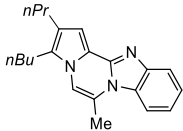
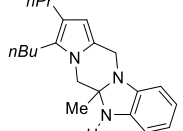
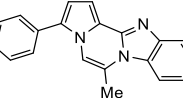
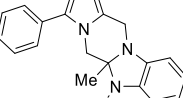
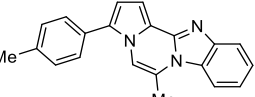
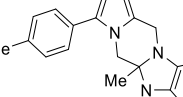
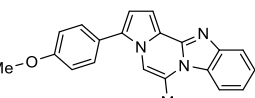
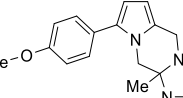
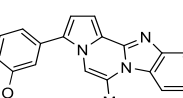
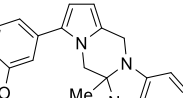
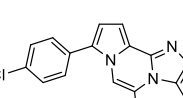
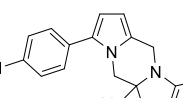
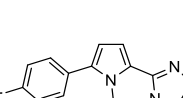
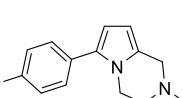
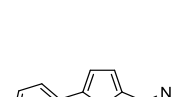
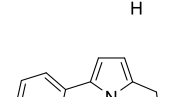
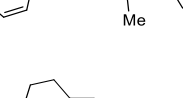
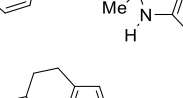
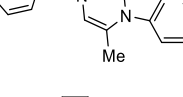
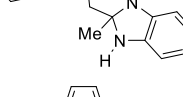
Thus, to selectively synthesize compounds **3**, it is most expedient to employ the reaction conditions shown in Entry 9. Under these conditions, a wide series of N-allenylpyrrole-2-carbaldehydes was involved in the process to selectively afford benzimidazopyrrolopyrazines **3a–j** (Scheme 3).



Scheme 3. Synthesis of 6-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazines.

We failed to selectively direct the reaction toward the formation of products **4**. Therefore, aqueous ethanol (Scheme 2) was used, followed by the isolation of individual compounds by column chromatography. The structures and yields of the products obtained by both methods are shown in Table 2.

Table 2. Structures of 6-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazines and 5a-methyl-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazines.

3	Product	Yield (Aqueous EtOH) ^a , %	Yield (MeOH Dry) ^b , %	4	Product	Yield (Aqueous EtOH) ^a , %
a		30 ^d	42	a ^c		4 ^d
b		34	87	b		31
c		32	85	c		30
d		40	90	d		35
e		38	89	e		33
f		34	82	f		32
g		37	84	g		33
h		28	79	h		19
i		34	76	i		28
j		41	88	j		37

^a **1** (0.0011 mol), **2** (0.00121 mol), EtOH (2.2 mL), H₂O (0.44 mL) CF₃COOH (1%); ^b **1** (0.0011 mol), **2** (0.00121 mol), MeOH dry (2.2 mL), CF₃COOH (1%); ^c Reaction time: 64 h; ^d Conversion of **1a** was 74%.

As can be seen from Table 2, aromatic and heteroaromatic substituents in the α -position of the pyrrole ring have the same effect on the yield of the reaction products. This is also the case for donating or accepting substituents in the para position of the phenyl substituent. A slight decrease in yields for bulky compounds **4h** and **4i** is due to the steric hindrance. The decreased yield and incomplete conversion in the case of starting pyrrole **1a** bearing donor alkyl substituents is expected for nucleophilic addition at the carbonyl group, since the donating substituents compensate the positive charge on the carbonyl carbon.

The structure of benzimidazopyrrolopyrazines **3** was unambiguously proven by X-ray diffraction analysis using compound **3e** as an example (Figure 1).

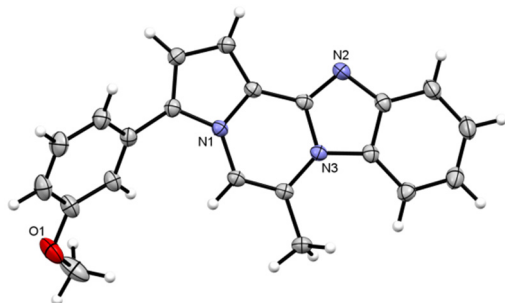


Figure 1. X-ray structure of 3-(3-methoxyphenyl)-6-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine **3e**.

The structure of **4** was established by NMR spectroscopy (^1H , ^{13}C , including 2D correlations, Figure 2a,b).

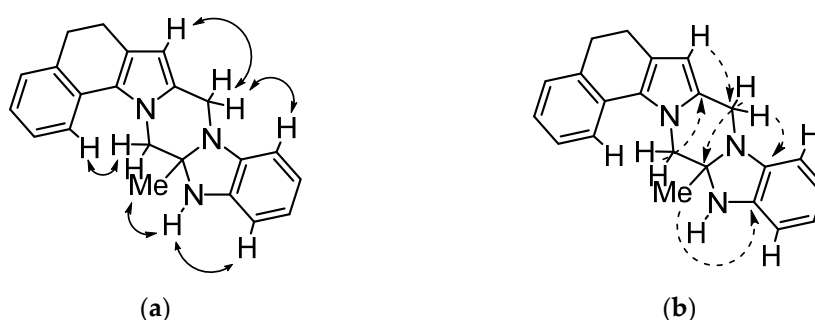
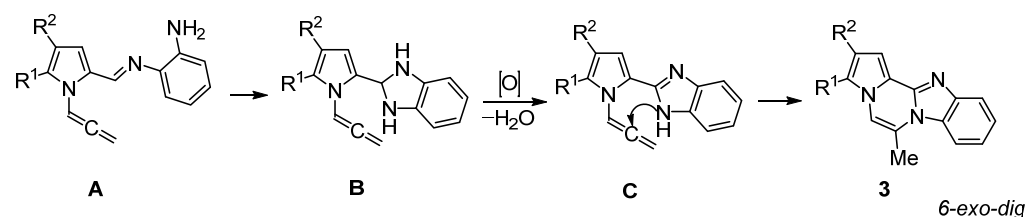


Figure 2. (a) NOESY and (b) HMBC for **4i**.

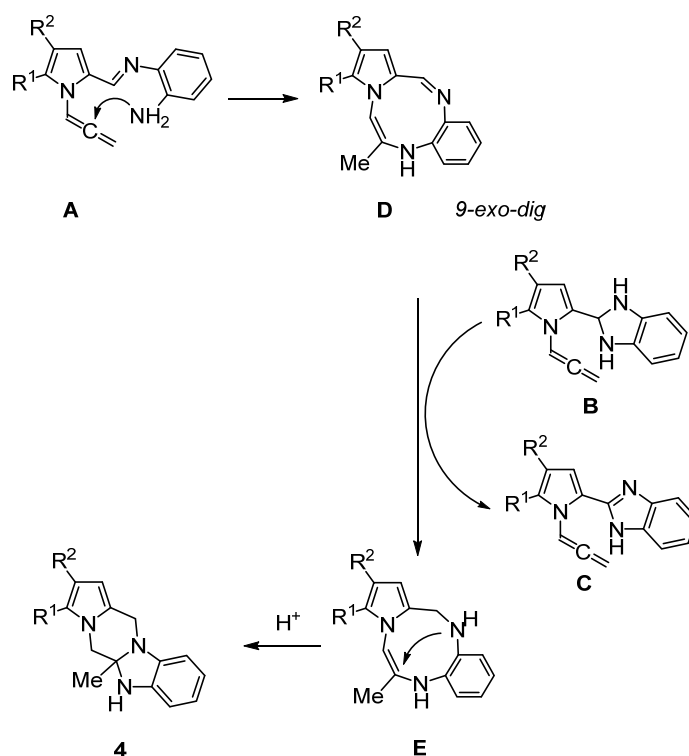
The formation of products **3** can be tentatively rationalized as follows [12,13]. The reaction starts with the addition of *o*-PDA to *N*-allenylpyrrole-2-carbaldehyde to furnish Schiff base **A**. The latter further undergoes intramolecular cyclization to give the benzimidazole skeleton **B** (*5-exo-trig*). This is a well-known reaction, in which ambient oxygen can act as an oxidizing agent for the intermediate imidazoline **B**. The *NH*-function of the benzimidazole attacks the central carbon atom (*sp*) of the allene moiety that leads to a *6-exo-dig* cyclization to finally deliver benzimidazopyrrolopyrazines **3** (Scheme 4).



Scheme 4. Possible mechanism of formation of 6-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazines.

It is more difficult to explain the formation of product **4**. We have proposed two possible reaction pathways.

Possible pathway 1: The formation of by-product **4** likely also commences with the addition of *o*-PDA to *N*-allenylpyrrole-2-carbaldehyde to produce the Schiff base **A**. Afterward, the second amino group is not added to the C=N bond (as in Scheme 4), but at the central allenic carbon to form a nine-membered ring **D** (Baldwin's rule [14–16]). Product **4** contains two more hydrogen atoms than compound **A**, i.e., some kind of reduction occurs. Apparently, the intermediate imidazoline **B** generated during the formation of compound **3** with the hydrogen transfer through the medium can act as a reducing agent. In the reduced intermediate **E**, the double bond is activated by the acid of the system to intramolecularly close the ring and to afford product **4** (Scheme 5).

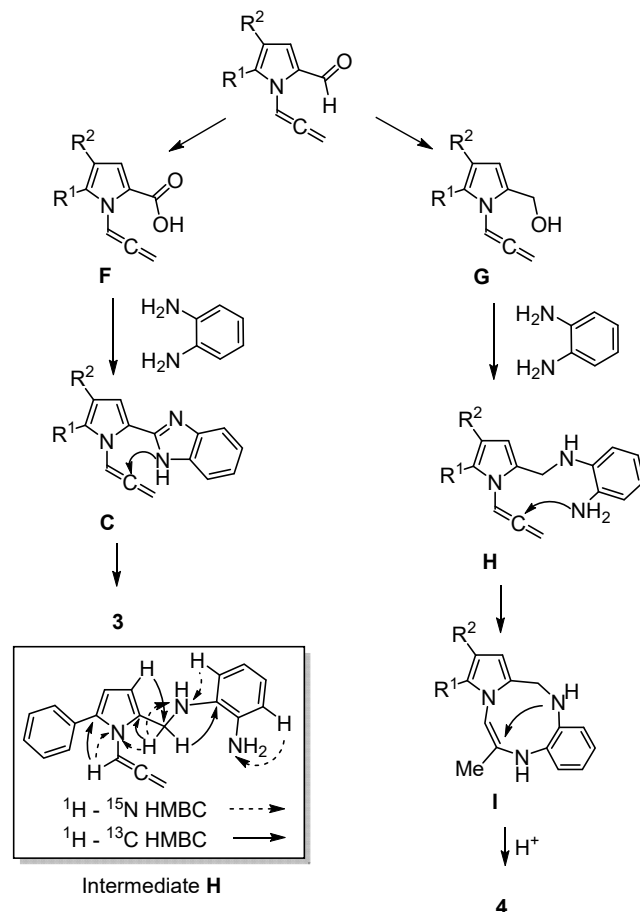


Scheme 5. Possible pathway 1 of formation of 5a-methyl-5a,6-dihydro-5H,12H-benzo[4,5]imidazo[1,2-a]pyrrolo[1,2-d]pyrazines.

As seen from the above mechanistic schemes, selectivity of the reaction depends on the behavior of the amino group in intermediate **A**, which attacks either the C=N or C=C bond. A possible reason for the effect of water on the reaction direction is assumed to be the presence of hydrogen bonding between water molecules and the amino group, which complicates the attack on the more sterically hindered C=N bond thus allowing an alternative addition at the C=C bond. This scheme is supported by the fact that the best ratio of products of **3**:**4** was 1:1 (Table 1, Entry 7); compound **4** cannot be formed without a reducing agent (intermediate **B**) delivering product **3**. Besides, a further increase in the water content to direct the reaction selectively to product **4** had no success due to the reduction of solubility of the starting compound in the water–alcohol mixture (Table 1, Entry 8).

Possible pathway 2: It can also be assumed that the reaction is triggered by disproportionation of the starting pyrrolicarbaldehyde **1** (the Cannizzaro type reaction [17]) to furnish carboxylic acid **F** and alcohol **G**, which further interact with *o*-PDA. In the case of carboxylic acid, the process involves the formation of product **3** similar to the reaction with aldehyde (such reactions are well known [18–20]). In alcohol **G**, the substitution at the hydroxyl group occurs with participation the *o*-PDA amino group to deliver the

intermediate **H**, followed by intramolecular addition of the second amino group at the allene producing a 9-membered ring **I**. The latter can undergo intramolecular cyclization due to the activation of the remaining double bond by the acid of the system to afford compound **4** (Scheme 6).



Scheme 6. Possible pathway 2 of formation of 5a-methyl-5a,6-dihydro-5H,12H-benzo[4,5]imidazo[1,2-a]pyrrolo[1,2-d]pyrazines.

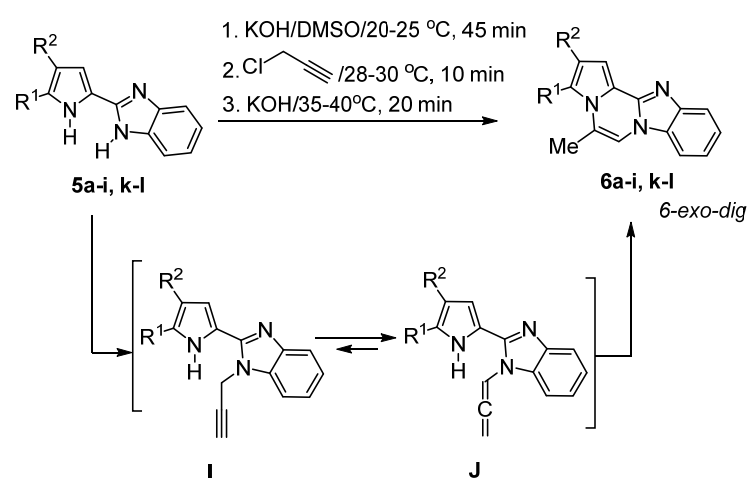
We indirectly proved such direction of the process by involving the separately obtained alcohol in the reaction. Among the reaction products, an intermediate compound was identified and characterized by NMR spectroscopy (see Supplementary Information). The obvious disadvantage of such an explanation of the possible mechanism is that upon disproportionation, the ratio of products should be close to 1:1, but in our case, compound **3** most often predominates. This can be rationalized by the fact that the starting pyrrolecarbaldehyde **1** is not only disproportionated, but also directly reacts with *o*-PDA (Scheme 2), thereby increasing the content of product **3** in the mixture. Probably, water here directly affects the direction of Cannizzaro reaction and somehow promotes the hydrogen transfer from the oxidizing site to the reducing one thus enhancing the contribution of Cannizzaro-type reaction to the overall process. This also explains the impossibility to shift the ratio of products **3** and **4** by more than 1:1. Similar to the case of pathway 1, a further increase in the concentration of water decreases solubility of the reactants and worsens the outcome of the reaction.

Non-conjugated dihydrobenzimidazopyrrolopyrazines **4** represent a rather rare class of compounds. To the best of our knowledge, chemical databases contain no such structures. We managed to find a structure with a similar 5/6/5 arrangement at the *a/d* position, containing only one nitrogen atom and synthesized by the Pauson–Khand reaction [21–23], all the obtained compounds being considered as promising alkaloids. Meanwhile, these com-

pounds are expected to exhibit valuable biological properties and can be widely employed as synthons in organic synthesis.

Often, the relative position of substituents in a molecular backbone and the presence of free positions suitable for further functionalization are essential for biological applications. In all disclosed protocols for the assembly of benzimidazopyrrolopyrazines **3**, the spacer between the pyrrole/indole nitrogen and the imidazole ring nitrogen either does not bear a methyl substituent at all, or contains a methyl moiety in the α -position relative to the imidazole ring. Synthesis of benzimidazopyrrolopyrazines with the methyl group located closer to the pyrrole/indole fragment will expand the synthetic potential, which possibly complements the existing backbones to afford new biological targets.

To address this challenge, we have employed the following synthetic approach based on our previous research (Scheme 7). At the first stage, a series of *NH*-pyrrolylbenzimidazoles **5** were prepared via the published procedure [11]. Further, the obtained compounds were involved in the reaction with propargyl chloride under the conditions reported earlier [24]. The superbase in this reaction has an advantage over the common bases: it catalyzes not only substitution of the *NH*-function with propargyl chloride, but also the complete (quantitative) acetylene-allene isomerization to furnish allene, which is almost always selectively attacked at the *sp* atom. Since in compound **5**, the *NH*-function of imidazole ($pK_a = 14.4$) is more mobile than that of pyrrole ($pK_a = 23.0$), substitution occurs on the former. Product **I** undergoes isomerization into intermediate **J**, the *sp* atom of which is subjected to an intramolecular attack by the pyrrole *NH*-moiety and *6-exo-dig* cyclization to deliver a new series of benzimidazopyrrolopyrazines **6**, isomeric to compounds **3**, but with a different disposition of the methyl group. We checked the generality of this strategy on a series of substrates, and the product yields are shown in Table 3.



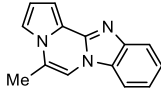
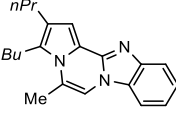
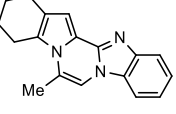
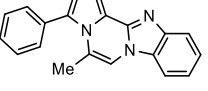
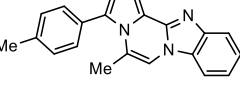
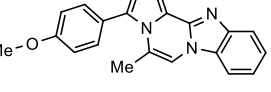
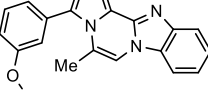
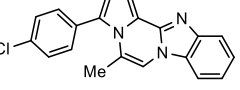
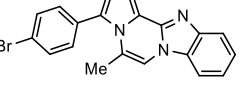
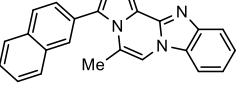
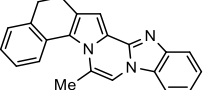
Scheme 7. Synthesis of 5-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazines.

We checked the generality of this strategy on a series of substrates, and the product yields are shown in Table 3.

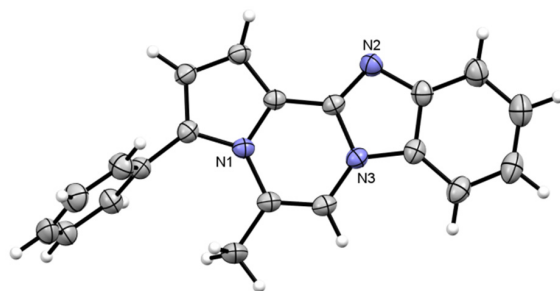
The reaction was found to be of general character. It was shown that aromatic and heteroaromatic substituents did not affect yields of the products (**6a-i, k-l**). If the *p*-position of the phenyl ring contained donating (**6d**, 90%) or accepting substituents (**6g**, 96%), the yields were approximately the same. In the case of a donating substituent in the pyrrole ring (**6l**), the yield decreased to moderate.

The structure of the obtained compounds was unambiguously proven by X-ray single-crystal analysis using **6b** as an example (Figure 3). For all the processes described above (Schemes 2 and 3; Table 3), at each stage of several possible (allowed) directions, according to Baldwin's rule, only one is always realized, i.e., all reactions are regioselective.

Table 3. Structures of 5-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazines ^a.

6	Product	Yield, %
k		82
a		61
l		51
b		81
c		85
d		90
e		88
f		83
g		96
h		79
i		84

^a **5** (0.0011 mol), KOH (0.0044 mol), DMSO (2.2 mL), C₃H₃Cl (0.0022 mol), KOH (0.0132 mol).

**Figure 3.** X-ray structure of 3-(3-methoxyphenyl)-6-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine **6b**.

3. Materials and Methods

3.1. General Information

All reagents were purchased from a commercial supplier, such as Sigma-Aldrich Co. LLC (St. Louis, MO, USA). *N*-Allenylpyrrole-2-carbaldehydes were obtained according to the procedure [25]. DMSO was used with a water content of 0.1–0.3%, ethyl alcohol with a water content of 5%. Methyl alcohol used 99.5%. Ethanol and benzene were dried according to the literature data [26]. Propargyl chloride was purified by simple distillation (58 °C). NMR spectra were recorded from solutions in CDCl₃ and DMSO-*d*₆ on Bruker DPX-400 and AV-400 spectrometers (400.1 MHz for ¹H and 100.6 MHz for ¹³C). Chemical shifts (δ) are quoted in parts per million (ppm). The residual solvent peak, $\delta_{\text{H}} = 7.27$ and $\delta_{\text{C}} = 77.16$ for CDCl₃, $\delta_{\text{H}} = 2.50$ and $\delta_{\text{C}} = 39.52$ for DMSO-*d*₆, was used as a reference. Coupling constants (*J*) are reported in Hertz (Hz). The multiplicity abbreviations used are: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad signal.

3.2. General Procedures

General procedure for the synthesis products **3** and **4**. A mixture of the *N*-allenylpyrrole-2-carbaldehyde **1** (0.0011 mol), *o*-PDA **2** (0.131 g, 0.00121 mol), EtOH (2.2 mL), H₂O (0.44 mL) and CF₃COOH (1%) was stirred at r.t. for 16 h. Solvent was evaporated. The resulting products were separated on a column with Al₂O₃ using flash chromatography (eluent hexane then hexane/diethyl ether 1:1).

General procedure for the synthesis products **3**. A mixture of the *N*-allenylpyrrole-2-carbaldehyde **1** (0.0011 mol), *o*-PDA **2** (0.131 g, 0.00121 mol), MeOH (dry, 2.2 mL) and CF₃COOH (1%) was stirred at r.t. for 16 h in an inert atmosphere. The resulting precipitate was collected.

General procedure for synthesis of **5**. Compounds **5** were prepared according to procedure [11]. Compounds **5a**, **5c–i**, **5l** were synthesized for the first time. Product yields depend on the complexity of the purification of the raw product. A mixture of *NH*-pyrrole-2-carbaldehyde (0.002 mol), *o*-PDA **2** (0.216 g, 0.002 mol) and CF₃COOH (1% with respect to the combined mass of both reagents) in DMSO (2 mL) was stirred at 70–80 °C for 1 h with continuous air bubbling. The reaction mixture was diluted with aq 1% NaHCO₃ soln (8 mL), extracted with Et₂O (5 × 5 mL) and the extracts were dried (K₂CO₃). The solvent was evaporated, and the crude product was passed through a neutral alumina column (eluent hexane, then hexane/diethyl ether (1:1)) to give **5**.

General procedure for synthesis of **6**. A mixture of **5** (0.0011 mol), KOH pellets (0.286 g, 0.0044 mol) and DMSO (water content < 0.2%) (2.2 mL) was stirred at r.t. for 45 min. Subsequently, freshly distilled propargyl chloride (0.164 g, 0.0022 mol) was added over 10 min, while keeping the internal temperature between 28 and 30 °C (exothermic reaction). A further amount of KOH pellets (0.858 g, 0.0132 mol) was added, while heating between 35 and 40 °C for 20 min, and then the reaction mixture was poured into H₂O under efficient stirring. The formed precipitate was filtered off.

3.3. Characterization Data of Products **3**, **4**, **5** and **6**

3-Butyl-6-methyl-2-propylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**3a**). White powder (0.078 g, 30% yield; 0.147 g, 42% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.86–7.83 (m, 2H, Ph), 7.36 (t, *J* = 7.6 Hz, 1H, Ph), 7.21 (t, *J* = 7.7 Hz, 1H, Ph), 7.13 (s, 1H, CH), 6.92 (s, 1H, pyrrole), 2.83 (s, 3H, CH₃), 2.79 (t, *J* = 7.6 Hz, 2H, CH₂), 2.57 (t, *J* = 7.5 Hz, 2H, CH₂), 1.71–1.66 (m, 2H, CH₂), 1.61–1.56 (m, 2H, CH₂), 1.44–1.39 (m, 2H, CH₂), 1.01–0.95 (m, 6H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.8, 143.5, 131.2, 126.9, 125.6, 123.6, 121.3, 119.7, 119.3, 118.7, 112.5, 107.1, 105.6, 31.3, 28.3, 24.1, 23.8, 22.7, 18.1, 14.1, 14.0. Elemental analysis calcd (%) for C₂₁H₂₅N₃: C 78.96, H 7.89, N 13.15; found: C 79.12; H 7.93; N 13.28.

6-Methyl-3-phenylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**3b**). White powder (0.111 g, 34% yield; 0.284 g, 87% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, *J* = 7.8 Hz, 1H, Ph), 7.82 (d, *J* = 8.3 Hz, 1H, Ph), 7.54–7.47 (m, 4H, Ph), 7.42–7.38 (m, 1H, Ph), 7.37–7.35 (m, 1H, Ph), 7.33 (d, *J* = 4.0 Hz, 1H, pyrrole), 7.24 (s, 1H, CH), 7.22–7.18 (m, 1H, Ph), 6.72

(d, $J = 4.0$ Hz, 1H, pyrrole), 2.73 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.8, 143.5, 131.5, 131.2, 130.8, 129.1 (2C), 128.7 (2C), 128.1, 123.9, 121.9, 121.4, 120.9, 119.6, 112.9, 112.6, 107.5, 106.3, 18.0. Elemental analysis calcd (%) for C₂₀H₁₅N₃: C 80.78, H 5.08, N 14.13; found: C 80.81, H 5.12, N 14.17.

6-Methyl-3-(p-tolyl)benzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**3c**). White powder (0.109 g, 32% yield; 0.29 g, 85% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, $J = 8.1$ Hz, 1H, Ph), 7.86 (d, $J = 8.4$ Hz, 1H, Ph), 7.46 (d, $J = 8.0$ Hz, 2H, Ph), 7.40–7.38 (m, 1H, Ph), 7.36–7.35 (m, 1H, Ph), 7.34–7.31 (m, 2H, Ph, pyrrole), 7.26–7.22 (m, 2H, Ph, CH), 6.71 (d, $J = 3.9$ Hz, 1H, pyrrole), 2.77 (s, 3H, CH₃), 2.44 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.7, 143.5, 138.1, 131.2, 130.9, 129.8 (2C), 128.6 (2C), 128.5, 123.8, 121.8, 121.1, 120.7, 119.6, 112.6, 107.6, 106.3, 21.4, 18.0. Elemental analysis calcd (%) for C₂₁H₁₇N₃: C 81.00, H 5.50, N 13.49; found: C 81.09, H 5.56, N 13.54.

3-(4-Methoxyphenyl)-6-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**3d**). Pink powder (0.144 g, 40% yield; 0.324 g, 90% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.90–7.87 (m, 2H, Ph), 7.49 (d, $J = 8.7$ Hz, 2H, Ph), 7.39 (t, $J = 7.8$ Hz, 1H, Ph), 7.35 (d, $J = 3.9$ Hz, 1H, pyrrole), 7.28–7.24 (m, 2H, CH, Ph), 7.06 (d, $J = 8.7$ Hz, 2H, Ph), 6.69 (d, $J = 3.9$ Hz, 1H, pyrrole), 3.89 (s, 3H, CH₃), 2.81 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 159.4, 144.5, 143.3, 130.9, 130.4, 129.8 (2C), 123.6, 121.6, 120.6, 120.5, 119.2, 114.4 (2C), 112.4, 112.2, 107.3, 105.9, 55.3, 17.8. Elemental analysis calcd (%) for C₂₁H₁₇N₃O: C 77.04, H 5.23, N 12.84; found: C 77.08, H 5.27, N 12.87.

3-(3-Methoxyphenyl)-6-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**3e**). White powder (0.137 g, 38% yield; 0.32 g, 89% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.90 (m, 2H, Ph), 7.45–7.40 (m, 2H, Ph), 7.38–7.33 (m, 2H, pyrrole, Ph), 7.28–7.25 (m, 1H, CH), 7.16–7.14 (m, 1H, Ph), 7.10 (s, 1H, Ph), 6.99–6.96 (m, 1H, Ph), 6.76 (d, $J = 3.9$ Hz, 1H, pyrrole), 3.88 (s, 3H, CH₃), 2.81 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 160.1, 144.8, 143.4, 132.7, 131.2, 130.6, 130.1, 123.9, 121.9, 121.4, 120.99, 120.90, 119.6, 114.5, 113.4, 112.9, 112.6, 107.6, 106.3, 55.5, 18.0. Elemental analysis calcd (%) for C₂₁H₁₇N₃O: C 77.04, H 5.23, N 12.84; found: C 77.06, H 5.25, N 12.86.

3-(4-Chlorophenyl)-6-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**3f**). White powder (0.124 g, 34% yield; 0.299 g, 82% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, $J = 8.1$ Hz, 1H, Ph), 7.86 (d, $J = 8.4$ Hz, 1H, Ph), 7.49 (s, 4H, Ph), 7.39 (t, $J = 7.6$ Hz, 1H, Ph), 7.35 (d, $J = 4.0$ Hz, 1H, pyrrole), 7.27–7.25 (m, 1H, Ph), 7.20 (s, 1H, CH), 6.72 (d, $J = 4.0$ Hz, 1H, pyrrole), 2.79 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.8, 143.3, 134.1, 131.2, 129.98, 129.94 (2C), 129.5, 129.4 (2C), 124.0, 122.0, 121.7, 121.2, 119.7, 113.2, 112.6, 107.3, 106.4, 18.1. Elemental analysis calcd (%) for C₂₀H₁₄ClN₃: C 72.40, H 4.25, N 12.66; found: C 72.47, H 4.29, N 12.67.

3-(4-Bromophenyl)-6-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**3g**). White powder (0.153 g, 37% yield; 0.347 g; 84% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.90 (d, $J = 8.1$ Hz, 1H, Ph), 7.87 (d, $J = 8.3$ Hz, 1H, Ph) 7.65 (d, $J = 8.3$ Hz, 2H, Ph), 7.43 (d, $J = 8.4$ Hz, 2H, Ph), 7.39–7.34 (m, 2H, pyrrole, Ph), 7.27–7.26 (m, 1H, Ph), 7.20 (s, 1H, CH), 6.73 (d, $J = 3.9$ Hz, 1H, pyrrole), 2.79 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.7, 143.3, 132.3 (2C), 131.2, 130.4, 130.1 (2C), 129.5, 124.0, 122.2, 122.0, 121.7, 121.2, 119.7, 113.1, 112.6, 107.2, 106.5, 18.0. Elemental analysis calcd (%) for C₂₀H₁₄BrN₃: C 63.84, H 3.75, N 11.17; found, %: C 63.91, H 3.82, N 11.20.

6-Methyl-3-(naphthalen-2-yl)benzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**3h**). White powder (0.107 g, 28% yield; 0.302 g, 79% yield). ¹H NMR (400 MHz, CDCl₃) δ 8.02–7.97 (m, 2H, Ph), 7.92–7.88 (m, 4H, Ph), 7.68–7.66 (m, 1H, Ph), 7.57–7.54 (m, 2H, Ph), 7.43–7.39 (m, 2H, pyrrole, Ph), 7.37 (s, 1H, CH), 7.29–7.25 (m, 1H, Ph), 6.85 (d, $J = 4.0$ Hz, 1H, pyrrole), 2.80 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.9, 143.5, 133.6, 132.9, 131.3, 130.8, 128.95, 128.91, 128.2, 127.9, 127.5, 126.8, 126.68, 126.61, 124.0, 122.0, 121.6, 121.0, 119.8, 113.4, 112.7, 107.7, 106.6, 18.1. Elemental analysis calcd (%) for C₂₄H₁₇N₃: C 82.97, H 4.93, N 12.10; found: C 83.02, H 4.98, N 12.17.

6-Methyl-13,14-dihydrobenzo[*g*]benzo[4',5']imidazo[2',1':3,4]pyrazino[1,2-*a*]indole (**3i**). White powder (0.121 g, 34% yield; 0.270 g, 76% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.90–

7.88 (m, 2H, Ph), 7.70–7.65 (m, 2H, Ph), 7.42–7.33 (m, 3H, Ph), 7.28–7.24 (m, 1H, pyrrole), 7.22–7.19 (m, 2H, CH, Ph), 2.97–2.93 (m, 2H, indole), 2.90–2.88 (m, 5H, indole, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.8, 143.3, 137.2, 131.2, 129.0, 128.7, 126.8, 126.7, 126.2, 125.9, 123.9, 121.7, 121.3, 120.7, 120.2, 119.5, 112.6, 108.2, 104.6, 30.7, 22.6, 18.1. Elemental analysis calcd (%) for C₂₂H₁₇N₃: C 81.71, H 5.30, N 12.99; found: C 81.75, H 5.37; N 13.34.

6-Methyl-3-(thiophen-2-yl)benzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**3j**). White powder (0.137 g, 41% yield; 0.294 g, 88% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, *J* = 8.1 Hz, 1H, Ph), 7.75 (d, *J* = 8.1 Hz, 1H, Ph), 7.32–7.31 (m, 1H, thienyl), 7.30–7.28 (m, 2H, thienyl), 7.22 (d, *J* = 4.0 Hz, 1H, pyrrole), 7.16–7.12 (m, 2H, CH, Ph), 7.09–7.07 (m, 1H, Ph), 6.70 (d, *J* = 4.0 Hz, 1H, pyrrole), 2.69 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.8, 143.1, 132.6, 131.1, 127.8, 126.3, 126.1, 124.0, 123.5, 122.0, 121.7, 121.2, 119.7, 114.1, 112.6, 107.6, 106.3, 18.1. Elemental analysis calcd (%) for C₁₈H₁₃N₃S: C 71.26, H 4.32, N 13.85; found: C 71.29, H 4.37, N 13.90.

3-Butyl-5a-methyl-2-propyl-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine (**4a**). Orange oil (0.01 g, 4% yield). ¹H NMR (400 MHz, CDCl₃) δ 6.79 (m, 1H, Ph), 6.75–6.60 (m, 2H, Ph), 6.39 (d, *J* = 7.6 Hz, 1H, Ph), 5.81 (s, 1H, pyrrole), 4.47 (d, *J* = 14.8 Hz, 1H, CH₂), 4.44 (d, *J* = 14.8 Hz, 1H, CH₂), 3.92 (d, *J* = 12.0 Hz, 1H, CH₂), 3.85 (s, 1H, NH), 3.70 (d, *J* = 12.0 Hz, 1H, CH₂), 2.50–2.45 (m, 2H, CH₂), 2.34 (t, *J* = 15.2 Hz, 2H, CH₂), 1.56–1.50 (m, 2H, CH₂), 1.43–1.39 (m, 2H, CH₂), 1.37–1.31 (m, 2H, CH₂), 1.26 (s, 3H, CH₃), 0.95–0.90 (m, 6H, CH₃).

5a-Methyl-3-phenyl-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine (**4b**). Red oil (0.102 g, 31% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.42–7.35 (m, 4H, Ph), 7.31–7.27 (m, 1H, Ph), 6.80 (t, *J* = 7.5 Hz, 1H, Ph), 6.64 (t, *J* = 7.5 Hz, 1H, Ph), 6.59–6.57 (m, 1H, Ph), 6.46 (d, *J* = 7.5 Hz, 1H, Ph), 6.27 (d, *J* = 3.5 Hz, 1H, pyrrole), 6.12 (d, *J* = 3.5 Hz, 1H, pyrrole), 4.65 (d, *J* = 14.6 Hz, 1H, CH₂), 4.52 (d, *J* = 14.6 Hz, 1H, CH₂), 4.16 (d, *J* = 12.1 Hz, 1H, CH₂), 3.88 (d, *J* = 12.1 Hz, 1H, CH₂), 3.68 (s, 1H, NH), 1.22 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 142.5, 138.8, 134.6, 132.5, 128.7 (2C), 128.2 (2C), 126.8, 126.1, 121.6, 119.3, 110.4, 108.2, 107.4, 105.2, 79.9, 52.1, 43.2, 24.7. Elemental analysis calcd (%) for C₂₀H₁₉N₃: C 79.70, H 6.35, N 13.94; found: C 79.78, H 6.41, N 13.99.

5a-Methyl-3-(*p*-tolyl)-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine (**4c**). Red oil (0.104 g, 30% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.31 (d, *J* = 8.0 Hz, 2H, Ph), 7.26 (d, *J* = 8.0 Hz, 2H, Ph), 6.84 (t, *J* = 7.5 Hz, 1H, Ph), 6.68 (t, *J* = 7.5 Hz, 1H, Ph), 6.61 (d, *J* = 7.4 Hz, 1H, Ph), 6.49 (d, *J* = 7.5 Hz, 1H, Ph), 6.28 (d, *J* = 3.5 Hz, 1H, pyrrole), 6.15 (d, *J* = 3.5 Hz, 1H, pyrrole), 4.68 (d, *J* = 14.6 Hz, 1H, CH₂), 4.55 (d, *J* = 14.6 Hz, 1H, CH₂), 4.17 (d, *J* = 12.1 Hz, 1H, CH₂), 3.90 (d, *J* = 12.1 Hz, 1H, CH₂), 3.70 (s, 1H, NH), 2.43 (s, 3H, CH₃), 1.24 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 142.4, 138.8, 136.5, 134.6, 129.6, 129.3 (2C), 128.2 (2C), 125.7, 121.6, 119.2, 110.3, 107.8, 107.3, 105.0, 79.9, 52.0, 43.2, 24.7, 21.2. Anal. Calcd for C₂₁H₂₁N₃, %: C, 79.97; H, 6.71; N, 13.32. Found, %: C, 80.02; H, 6.74; N, 13.35.

3-(4-Methoxyphenyl)-5a-methyl-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine (**4d**). Red oil (0.127 g, 35% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.29 (d, *J* = 8.7 Hz, 2H, Ph), 6.95 (d, *J* = 8.6 Hz, 2H, Ph), 6.82–6.78 (m, 1H, Ph), 6.65–6.62 (m, 1H, Ph), 6.59 (d, *J* = 8.8 Hz, 1H, Ph), 6.45 (d, *J* = 7.4 Hz, 1H, Ph), 6.18 (d, *J* = 3.4 Hz, 1H, pyrrole), 6.10 (d, *J* = 3.4 Hz, 1H, pyrrole), 4.64 (d, *J* = 14.7 Hz, 1H, CH₂), 4.51 (d, *J* = 14.7 Hz, 1H, CH₂), 4.11 (d, *J* = 12.1 Hz, 1H, CH₂), 3.84 (s, 3H, CH₃), 3.80 (d, *J* = 12.1 Hz, 1H, CH₂), 3.67 (s, 1H, NH), 1.22 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 158.7, 142.6, 138.8, 134.4, 129.6 (2C), 125.4, 125.1, 121.7, 119.2, 114.1 (2C), 110.4, 107.4, 104.9, 79.9, 77.3, 55.4, 52.0, 43.2, 24.8. Elemental analysis calcd (%) for C₂₁H₂₁N₃O: C 76.11, H 6.39, N 12.68; found: C 76.18, H 6.47, N 12.74.

3-(3-Methoxyphenyl)-5a-methyl-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine (**4e**). Red oil (0.120 g, 33% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.33–7.29 (m, 1H, Ph), 7.26–7.23 (m, 1H, Ph), 6.95–6.93 (m, 1H, Ph), 6.86–6.83 (m, 1H, Ph), 6.82–6.78 (m, 1H, Ph), 6.64 (t, *J* = 7.5 Hz, 1H, Ph), 6.59–6.57 (m, 1H, Ph), 6.46 (d, *J* = 7.5 Hz, 1H, Ph), 6.28 (d, *J* = 3.5 Hz, 1H, pyrrole), 6.12 (d, *J* = 3.5 Hz, 1H, pyrrole), 4.65 (d, *J* = 14.6 Hz, 1H, CH₂), 4.51 (d, *J* = 14.6 Hz, 1H, CH₂), 4.15 (d, *J* = 12.1 Hz, 1H, CH₂), 3.91 (d, *J* = 12.1 Hz, 1H, CH₂), 3.84 (s, 3H, CH₃), 3.69 (s, 1H, NH), 1.22 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃):

δ 159.8, 142.3, 138.9, 134.5, 133.8, 129.6, 126.2, 121.4, 120.6, 119.3, 113.8, 112.2, 110.1, 108.4, 107.3, 105.2, 79.9, 55.3, 52.1, 43.2, 24.7. Elemental analysis calcd (%) for $C_{21}H_{21}N_3O$: C 76.11, H 6.39, N 12.68. found: C 76.20, H 6.45, N 12.78.

3-(4-Chlorophenyl)-5a-methyl-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine (**4f**). Red oil (0.118 g, 32% yield). 1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, $J = 8.6$ Hz, 2H, Ph), 7.30 (d, $J = 8.6$ Hz, 2H, Ph), 6.82 (t, $J = 7.6$ Hz, 1H, Ph), 6.66 (t, $J = 7.5$ Hz, 1H, Ph), 6.61 (d, $J = 7.4$ Hz, 1H, Ph), 6.47 (d, $J = 7.5$ Hz, 1H, Ph), 6.27 (d, $J = 3.5$ Hz, 1H, pyrrole), 6.13 (d, $J = 3.5$ Hz, 1H, pyrrole), 4.65 (d, $J = 14.7$ Hz, 1H, CH_2), 4.52 (d, $J = 14.7$ Hz, 1H, CH_2), 4.14 (d, $J = 12.1$ Hz, 1H, CH_2), 3.82 (d, $J = 12.1$ Hz, 1H, CH_2), 3.71 (s, 1H, NH), 1.23 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.5, 138.8, 133.4, 132.6, 130.9, 129.3 (2C), 128.9 (2C), 126.5, 121.7, 119.4, 110.5, 108.6, 107.4, 105.4, 79.8, 52.1, 43.1, 24.7. Elemental analysis calcd (%) for $C_{20}H_{18}ClN_3$: C 71.53, H 5.40, N 12.51; found: C 71.59, H 5.48, N 12.55.

3-(4-Bromophenyl)-5a-methyl-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine (**4g**). Red oil (0.138 g, 33% yield). 1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, $J = 8.4$ Hz, 2H, Ph), 7.23 (d, $J = 8.4$ Hz, 2H, Ph), 6.83 (t, $J = 7.4$ Hz, 1H, Ph), 6.65 (t, $J = 7.0$ Hz, 1H, Ph), 6.60 (d, $J = 7.5$ Hz, 1H, Ph), 6.46 (d, $J = 7.3$ Hz, 1H, Ph), 6.27 (d, $J = 3.5$ Hz, 1H, pyrrole), 6.13 (d, $J = 3.5$ Hz, 1H, pyrrole), 4.64 (d, $J = 14.7$ Hz, 1H, CH_2), 4.51 (d, $J = 14.7$ Hz, 1H, CH_2), 4.13 (d, $J = 12.1$ Hz, 1H, CH_2), 3.82 (d, $J = 12.1$ Hz, 1H, CH_2), 3.69 (s, 1H, NH), 1.22 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.4, 138.7, 133.4, 131.8 (2C), 131.4, 129.6 (2C), 126.6, 121.7, 120.7, 119.4, 110.5, 108.7, 107.4, 105.4, 79.8, 52.1, 43.1, 24.7. Elemental analysis calcd (%) for $C_{20}H_{18}BrN_3$: C 63.17, H 4.77, N 11.05; found: C 63.23, H 4.85, N 11.13.

5a-Methyl-3-(naphthalen-2-yl)-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine (**4h**). Red oil (0.073 g, 19% yield). 1H NMR (400 MHz, $CDCl_3$) δ 7.89–7.83 (m, 3H, Ph), 7.79 (s, 1H, Ph), 7.55–7.46 (m, 3H, Ph), 6.83 (t, $J = 7.5$ Hz, 1H, Ph), 6.69 (t, $J = 7.5$ Hz, 1H, Ph), 6.60 (d, $J = 7.4$ Hz, 1H, Ph), 6.49 (d, $J = 7.5$ Hz, 1H, Ph), 6.41 (d, $J = 3.5$ Hz, 1H, pyrrole), 6.19 (d, $J = 3.5$ Hz, 1H, pyrrole), 4.69 (d, $J = 14.6$ Hz, 1H, CH_2), 4.56 (d, $J = 14.6$ Hz, 1H, CH_2), 4.26 (d, $J = 12.2$ Hz, 1H, CH_2), 3.97 (d, $J = 12.2$ Hz, 1H, CH_2), 3.67 (s, 1H, NH), 1.22 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.5, 138.8, 134.7, 133.6, 132.2, 129.9, 128.3, 127.9, 127.8, 126.7, 126.5, 126.4, 126.2, 125.9, 121.7, 119.3, 110.4, 108.8, 107.4, 105.5, 79.9, 52.4, 43.3, 24.8. Elemental analysis calcd (%) for $C_{24}H_{21}N_3$: C 82.02, H 6.02, N 11.96; found: C 82.14, H 6.16, N 12.12.

14a-Methyl-5,8,14a,15-tetrahydro-6*H*,14*H*-benzo[*g*]benzo[4',5']imidazo[1',2':4,5]pyrazino[1,2-*a*]indole (**4i**). Red oil (0.1 g, 28% yield). 1H NMR (400 MHz, $CDCl_3$) δ 7.29–7.24 (m, 2H, Ph), 7.21–7.18 (m, 1H, Ph), 7.06 (t, $J = 7.4$ Hz, 1H, Ph), 6.82 (t, $J = 7.5$ Hz, 1H, Ph), 6.68–6.62 (m, 1H, Ph), 6.44 (d, $J = 7.7$ Hz, 1H, Ph), 5.97 (s, 1H, pyrrole), 4.62 (d, $J = 14.7$ Hz, 1H, CH_2), 4.55 (d, $J = 14.7$ Hz, 1H, CH_2), 4.35 (d, $J = 11.9$ Hz, 1H, CH_2), 4.20 (d, $J = 11.9$ Hz, 1H, CH_2), 3.75 (s, 1H, NH), 2.95–2.82 (m, 2H, indole), 2.72–2.58 (m, 2H, indole), 1.29 (s, 1H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.5, 138.7, 136.1, 129.5, 129.0, 128.6, 126.6, 126.1, 124.6, 122.7, 121.9, 120.3, 119.1, 110.8, 107.0, 103.8, 79.5, 77.3, 55.3, 42.8, 31.1, 24.4, 22.5. Elemental analysis calcd (%) for $C_{22}H_{21}N_3$: C 80.70, H 6.46, N 12.83; found: C 80.78, H 6.51, N 12.90.

5a-Methyl-3-(thiophen-2-yl)-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*]pyrazine (**4j**). Red oil (0.125 g, 37% yield). 1H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, $J = 3.6$ Hz, 1H, thienyl), 7.10–7.08 (m, 1H, thienyl), 6.98 (d, $J = 3.5$ Hz, 1H, thienyl), 6.82 (t, $J = 7.4$ Hz, 1H, Ph), 6.67 (m, 1H, Ph), 6.62 (d, $J = 7.2$ Hz, 1H, Ph), 6.47 (d, $J = 7.5$ Hz, 1H, Ph), 6.35 (d, $J = 3.5$ Hz, 1H, pyrrole), 6.11 (d, $J = 3.5$ Hz, 1H, pyrrole), 4.63 (d, $J = 15.1$ Hz, 1H, CH_2), 4.55 (d, $J = 15.1$ Hz, 1H, CH_2), 4.11 (d, $J = 12.2$ Hz, 1H, CH_2), 4.02 (d, $J = 12.2$ Hz, 1H, CH_2), 3.74 (s, 1H, NH), 1.33 (s, 1H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ 142.1, 138.7, 134.3, 127.5, 126.6, 126.2, 124.9, 124.7, 121.6, 119.2, 110.5, 109.6, 107.1, 105.0, 79.6, 51.5, 42.5, 24.3. Elemental analysis calcd (%) for $C_{18}H_{17}N_3S$: C 70.33, H 5.57, N 13.67; found: C 70.45, H 5.67, N 13.76.

2-(5-Butyl-4-propyl-1*H*-pyrrol-2-yl)-1*H*-benzo[*d*]imidazole (**5a**). Yellow powder (0.157 g, 28% yield). 1H NMR (400 MHz, $DMSO-d_6$) δ 12.25 (s, 1H, NH), 11.18 (s, 1H, NH), 7.43 (s, 2H, Ph), 7.08–7.05 (m, 2H, Ph), 6.60 (s, 1H, pyrrole), 2.51–2.47 (m, 2H, CH_2), 2.31 (t,

$J = 7.4$ Hz, 2H, CH₂), 1.54–1.45 (m, 4H, CH₂), 1.26–1.19 (m, 2H, CH₂), 0.89 (t, $J = 7.4$ Hz, 3H, CH₃), 0.84 (t, $J = 7.3$ Hz, 3H, CH₃). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 147.2, 132.7, 121.24, 121.4, 120.3, 119.9, 106.6, 32.2, 27.5, 24.8, 24.1, 21.9, 13.9, 13.8. Elemental analysis calcd (%) for C₁₈H₂₃N₃: C 76.83, H 8.24, N 14.93; found: C 76.96, H 8.31, N 15.03.

2-(4,5,6,7-Tetrahydro-1*H*-indol-2-yl)-1*H*-benzo[*d*]imidazole (**5l**). Yellow powder (0.175 g, 37% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.27 (s, 1H, NH), 11.20 (s, 1H, NH), 7.85–7.38 (m, 2H, Ph), 7.10–7.08 (m, 2H, Ph), 6.55 (s, 1H, pyrrole), 2.57–2.55 (m, 2H, indole), 2.47–2.42 (m, 2H, indole), 1.74–1.67 (m, 2H, indole). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 177.6, 147.3, 130.8, 121.4, 121.3, 121.1, 120.5, 117.6, 110.4, 108.1, 30.75, 23.5, 22.9, 22.63, 22.62. Elemental analysis calcd (%) for C₁₅H₁₅N₃: C 75.92, H 6.37, N 17.71; found: C 76.03, H 6.48, N 17.82.

2-(5-(*p*-Tolyl)-1*H*-pyrrol-2-yl)-1*H*-benzo[*d*]imidazole (**5c**). Beige powder (0.41 g, 75% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.48 (s, 1H, NH), 11.96 (s, 1H, NH), 7.76 (d, $J = 8.0$ Hz, 2H, Ph), 7.59–7.49 (m, 2H, Ph), 7.20–7.16 (m, 4H, Ph), 6.95 (d, $J = 3.2$ Hz, 1H, pyrrole), 6.65 (d, $J = 3.2$ Hz, 1H, pyrrole), 2.30 (s, 3H, CH₃). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 146.4, 143.9, 135.6, 134.8, 134.5, 129.2 (2C), 124.4 (2C), 123.8, 121.7, 121.3, 117.8, 111.1, 110.6, 107.1, 20.7. Elemental analysis calcd (%) for C₁₈H₁₅N₃: C 79.10, H 5.53, N 15.37; found: C 79.15, H 5.58, N 15.41.

2-(5-(4-Methoxyphenyl)-1*H*-pyrrol-2-yl)-1*H*-benzo[*d*]imidazole (**5d**). Pink powder (0.121 g, 21% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.48 (s, 1H, NH), 11.90 (s, 1H, NH), 7.79 (d, $J = 8.7$ Hz, 2H, Ph), 7.57–7.47 (m, 2H, Ph), 7.16–7.14 (m, 2H, Ph), 6.97 (d, $J = 8.7$ Hz, 2H, Ph), 6.92 (d, $J = 3.6$ Hz, 1H, pyrrole), 6.57 (d, $J = 3.6$ Hz, 1H, pyrrole), 3.77 (s, 3H, CH₃). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 146.7, 144.2, 135.9, 135.2, 134.8, 129.6 (2C), 124.7 (2C), 124.2, 122.1, 121.6, 118.1, 111.4, 107.5, 21.1. Elemental analysis calcd (%) for C₁₈H₁₅N₃O: C 74.72, H 5.23, N 14.52; found: C 74.77, H 5.29, N 14.58.

2-(5-(3-Methoxyphenyl)-1*H*-pyrrol-2-yl)-1*H*-benzo[*d*]imidazole (**5e**). Red powder (0.231 g, 40% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.53 (s, 1H, NH), 12.09 (s, 1H, NH), 7.59 (m, 1H, Ph), 7.51 (m, 1H, Ph), 7.48–7.47 (m, 1H, Ph), 6.40–7.38 (m, 1H, Ph), 7.28 (t, $J = 7.9$ Hz, 1H, Ph), 7.17–7.16 (m, 2H, Ph), 6.94 (d, $J = 3.0$ Hz, 1H, pyrrole), 6.79–6.77 (m, 1H, Ph), 6.72 (d, $J = 3.0$ Hz, 1H, pyrrole), 3.83 (s, 3H, CH₃). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 146.0, 133.4, 131.4, 131.2, 126.3 (2C), 124.6, 121.6 (2C), 119.1, 114.2, 111.2, 108.3. Elemental analysis calcd (%) for C₁₈H₁₅N₃O: C 74.72, H 5.23, N 14.52; found: C 74.87, H 5.36, N 14.65.

2-(5-(4-Chlorophenyl)-1*H*-pyrrol-2-yl)-1*H*-benzo[*d*]imidazole (**5f**). Brown powder (0.487 g, 83% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.57 (s, 1H, NH), 12.10 (s, 1H, NH), 7.87 (d, $J = 8.5$ Hz, 2H, Ph), 7.59 (s, 1H, Ph), 7.47 (s, 1H, Ph), 7.44 (d, $J = 8.5$ Hz, 2H, Ph), 7.17–7.16 (m, 2H, Ph), 6.96 (d, $J = 3.7$ Hz, 1H, pyrrole), 6.73 (d, $J = 3.7$ Hz, 1H, pyrrole). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 146.2, 133.5, 130.9, 130.8, 128.8 (2C), 126.1 (2C), 124.6, 122.1, 121.6, 118.0, 111.3, 110.8, 108.4. Elemental analysis calcd (%) for C₁₇H₁₂ClN₃: C 69.51, H 4.12, N 14.30; found: C 69.64, H 4.21, N 14.42.

2-(5-(4-Bromophenyl)-1*H*-pyrrol-2-yl)-1*H*-benzo[*d*]imidazole (**5g**). Light yellow powder (0.277 g, 41% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.66 (s, 1H, NH), 12.13 (s, 1H, NH), 7.84 (d, $J = 8.4$ Hz, 2H, Ph), 7.57–7.53 (m, 4H, Ph), 7.18–7.16 (m, 2H, Ph), 6.96 (d, $J = 3.2$ Hz, 1H, pyrrole), 6.74 (d, $J = 3.2$ Hz, 1H, pyrrole). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 146.0, 133.4, 131.4, 131.2, 126.3 (2C), 124.6, 121.6 (2C), 119.1, 114.2, 111.2, 108.3. Elemental analysis calcd (%) for C₁₇H₁₂BrN₃: C 60.37, H 3.58, N 12.42; found: C 60.42, H 4.05, N 12.47.

2-(5-(Naphthalen-2-yl)-1*H*-pyrrol-2-yl)-1*H*-benzo[*d*]imidazole (**5h**). Beige powder (0.185 g, 30% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.54 (s, 1H, NH), 12.18 (s, 1H, NH), 8.48 (s, 1H, Ph), 8.02–7.99 (m, 1H, Ph), 7.92–7.87 (m, 3H, Ph), 7.63–7.61 (m, 1H, Ph), 7.53–7.44 (m, 3H, Ph), 7.19–7.17 (m, 2H, Ph), 7.00 (d, $J = 3.2$ Hz, 1H, pyrrole), 6.87 (d, $J = 3.2$ Hz, 1H, pyrrole). ¹³C NMR (100 MHz, DMSO-*d*₆): δ 146.2, 143.9, 134.59, 134.52, 133.4, 131.7, 129.4, 128.0, 127.7, 127.5, 126.4, 125.5, 124.6, 123.5, 121.9, 121.8, 121.3, 117.8, 111.1, 110.7, 108.4. Elemental analysis calcd (%) for C₂₁H₁₅N₃: C 81.53, H 4.89, N 13.58; found: C 81.58, H 4.95, N 13.64.

2-(1*H*-Benzo[*d*]imidazol-2-yl)-4,5-dihydro-1*H*-benzo[*g*]indole (**5i**). Beige powder (0.313 g, 55% yield). ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.43 (s, 1H, NH), 12.05 (s, 1H, NH), 7.85 (d, J

= 8.5 Hz, 1H, Ph), 7.49 (s, 2H, Ph), 7.16–7.11 (m, 4H, Ph), 7.04–7.00 (m, 1H, Ph), 6.75 (s, 1H, pyrrole), 2.84 (t, $J = 7.3$ Hz, 2H, indole), 2.67 (t, $J = 7.3$ Hz, 2H, indole). ^{13}C NMR (100 MHz, DMSO- d_6): δ 146.5, 134.7, 130.4, 128.9, 127.9, 126.6, 125.4, 123.2, 121.4, 120.8, 120.7, 108.6, 29.4, 21.3. Elemental analysis calcd (%) for $\text{C}_{19}\text{H}_{15}\text{N}_3$: C 79.98, H 5.30, N 14.73; found: C 80.02, H 5.36, N 14.77.

5-Methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**6k**). Beige powder (0.199 g, 82% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.89 (d, $J = 8.4$ Hz, 1H, Ph), 7.61 (d, $J = 7.9$ Hz, 1H, Ph), 7.43–7.39 (m, 2H, Ph, pyrrole), 7.34–7.30 (m, 1H, pyrrole), 7.28–7.27 (m, 2H, CH, pyrrole), 6.79–6.78 (m, 1H, pyrrole), 2.53 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 143.8, 142.0, 129.6, 123.8, 121.6, 121.4, 120.1, 119.2, 115.7, 112.8, 109.1, 106.8, 105.4, 15.6. Elemental analysis calcd (%) for $\text{C}_{14}\text{H}_{11}\text{N}_3$: C 76.00, H 5.01, N 18.99; found: C 76.12, H 5.17, N 19.13.

3-Butyl-5-methyl-2-propylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**6a**). Yellow powder (0.214 g, 61% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.71 (d, $J = 8.0$ Hz, 1H, Ph), 7.43 (d, $J = 8.0$ Hz, 1H, Ph), 7.24 (t, $J = 7.6$ Hz, 1H, Ph), 7.15–7.13 (m, 2H, Ph, CH), 6.92 (s, 1H, pyrrole), 2.89–2.85 (m, 2H, CH_2), 2.59 (s, 3H, CH_3), 2.44 (t, $J = 7.5$ Hz, 2H, CH_2), 1.62–1.56 (m, 2H, CH_2), 1.49–1.45 (m, 2H, CH_2), 1.36–1.30 (m, 2H, CH_2), 0.92–0.84 (m, 6H, CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 144.4, 142.7, 130.7, 129.7, 127.3, 123.8, 121.3, 121.1 (2C), 119.0, 108.9, 107.2, 106.2, 34.5, 28.4, 25.9, 23.8, 22.6, 18.6, 14.2, 13.9. Elemental analysis calcd (%) for $\text{C}_{21}\text{H}_{25}\text{N}_3$: C 78.96, H 7.89, N 13.15; found: C 79.05, H 7.97, N 13.21.

6-Methyl-1,2,3,4-tetrahydrobenzo[4',5']imidazo[2',1':3,4]pyrazino[1,2-*a*]indole (**6l**). Beige powder (0.154 g, 51% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.80 (d, $J = 8.1$ Hz, 1H, Ph), 7.44 (d, $J = 8.0$ Hz, 1H, Ph), 7.44 (t, $J = 7.6$ Hz, 1H, Ph), 7.33 (t, $J = 7.6$ Hz, 1H, Ph), 7.21 (t, $J = 7.6$ Hz, 1H, Ph), 7.06 (s, 1H, CH), 6.82 (s, 1H, pyrrole), 3.11 (t, $J = 6.0$ Hz, 2H, indole), 2.69 (t, $J = 5.5$ Hz, 2H, indole), 2.54 (s, 3H, CH_3), 1.88–1.84 (m, 2H, indole), 1.77–1.74 (m, 2H, indole). ^{13}C NMR (100 MHz, CDCl_3): δ 144.3, 142.5, 129.7, 128.2, 124.1, 123.6, 121.7, 121.1, 119.0, 108.9, 106.0, 105.2, 77.36, 25.9, 24.0, 23.8, 22.7, 18.6. Elemental analysis calcd (%) for $\text{C}_{18}\text{H}_{17}\text{N}_3$: C 78.52, H 6.22, N 15.26; found: C 78.65, H 6.35, N 15.36.

5-Methyl-3-phenylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**6b**). Brown powder (0.264 g, 81% yield). ^1H NMR (400 MHz, CDCl_3) δ 8.8 (d, $J = 8.1$ Hz, 1H, Ph), 7.59 (d, $J = 7.9$ Hz, 1H, Ph), 7.48–7.46 (m, 2H, Ph), 7.45–7.38 (m, 5H, Ph, pyrrole), 7.30 (t, $J = 7.5$ Hz, 1H, Ph), 7.10 (s, 1H, CH), 6.65 (d, $J = 3.9$ Hz, 1H, pyrrole), 2.03 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 144.1, 142.7, 134.3, 133.1, 131.1 (2C), 129.6, 128.6, 127.7 (2C), 124.0, 122.8, 122.0, 121.6, 119.2, 115.9, 109.1, 106.8, 106.7, 19.6. Elemental analysis calcd (%) for $\text{C}_{20}\text{H}_{15}\text{N}_3$: C 80.78, H 5.08, N 14.13; found: C 80.83, H 5.14, N 14.19.

5-Methyl-3-(*p*-tolyl)benzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**6c**). Yellow powder (0.291 g, 85% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.91 (d, $J = 8.1$ Hz, 1H, Ph), 7.51 (d, $J = 7.9$ Hz, 1H, Ph), 7.44 (d, $J = 3.9$ Hz, 1H, pyrrole), 7.40–7.36 (m, 3H, Ph), 7.28–7.24 (m, 3H, Ph), 6.95 (s, 1H, CH), 6.63 (d, $J = 3.9$ Hz, 1H, pyrrole), 2.48 (s, 3H, CH_3), 2.00 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 144.1, 142.6, 138.4, 133.0, 131.1, 130.8 (2C), 129.5, 128.2 (2C), 123.7, 122.5, 121.8, 121.3, 119.0, 115.5, 109.0, 106.5, 106.3, 21.3, 19.4. Elemental analysis calcd (%) for $\text{C}_{21}\text{H}_{17}\text{N}_3$: C 81.00, H 5.50, N 13.49; found: C 81.13, H 5.58, N 13.60.

3-(4-Methoxyphenyl)-5-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**6d**). Brown powder (0.323 g, 90% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, $J = 8.0$ Hz, 1H, Ph), 7.55 (d, $J = 8.1$ Hz, 1H, Ph), 7.40 (d, $J = 3.9$ Hz, 1H, pyrrole), 7.38 (d, $J = 8.5$ Hz, 2H, Ph), 7.29–7.25 (m, 2H, Ph), 7.03 (s, 1H, CH), 6.94 (d, $J = 8.7$ Hz, 2H, Ph), 6.59 (d, $J = 3.9$ Hz, 1H, pyrrole), 3.87 (s, 3H, CH_3), 2.00 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 159.9, 144.1, 142.7, 132.8, 132.2 (2C), 129.6, 126.3, 123.8, 122.5, 121.9, 121.4, 119.1, 115.6, 113.0 (2C), 109.0, 106.6, 106.4, 55.4, 19.4. Elemental analysis calcd (%) for $\text{C}_{21}\text{H}_{17}\text{N}_3\text{O}$: C 77.04, H 5.23, N 12.84; found: C 77.10, H 5.28, N 12.91.

3-(3-Methoxyphenyl)-5-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**6e**). Brown powder (0.317 g, 88% yield). ^1H NMR (400 MHz, CDCl_3) δ 7.76 (d, $J = 8.1$ Hz, 1H, Ph), 7.44 (d, $J = 8.1$ Hz, 1H, Ph), 7.30 (d, $J = 3.9$ Hz, 1H, pyrrole), 7.27–7.25 (m, 1H, Ph), 7.22–7.14 (m, 2H, Ph), 6.93–6.86 (m, 4H, CH, Ph), 6.52 (d, $J = 3.9$ Hz, 1H, pyrrole), 3.73 (s, 3H, CH_3), 2.95 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3): δ 158.9, 144.2, 142.7, 135.5, 132.8,

129.7, 128.6, 123.9, 123.7, 122.9, 121.9, 121.6, 119.3, 116.8, 115.7, 114.2, 109.1, 106.8, 106.5, 55.4, 19.3. Elemental analysis calcd (%) for C₂₁H₁₇N₃O: C 77.04, H 5.23, N 12.84; found: C 77.10; H 5.28, N 12.91.

3-(4-Chlorophenyl)-5-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**6f**). Brown powder (0.303 g, 83% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 8.1 Hz, 1H, Ph), 7.61 (d, *J* = 8.0 Hz, 1H, Ph), 7.43–7.39 (m, 6H, Ph, pyrrole), 7.32 (t, *J* = 7.6 Hz, 1H, Ph), 7.13 (s, 1H, CH), 6.63 (d, *J* = 3.9 Hz, 1H, pyrrole), 2.05 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.2, 142.5, 134.7, 132.7, 132.2 (2C), 131.5, 129.6 (2C), 127.9, 124.1, 123.1, 121.7, 121.6, 119.4, 116.1, 109.1, 107.0, 106.7, 19.8. Elemental analysis calcd (%) for C₂₀H₁₄ClN₃: C 72.40, H 4.25, N 12.66; found: C 72.49, H 4.31, N 12.74.

3-(4-Bromophenyl)-5-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**6g**). Yellow powder (0.397 g, 96% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 8.1 Hz, 1H, Ph), 7.59–7.56 (m, 3H, Ph), 7.42–7.39 (m, 1H, pyrrole), 7.36 (d, *J* = 8.0 Hz, 2H, Ph), 7.33–7.27 (m, 2H, Ph), 7.10 (s, 1H, CH), 6.63 (d, *J* = 3.9 Hz, 1H, pyrrole), 2.04 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.1, 142.4, 133.1, 132.4 (2C), 131.4, 130.8 (2C), 129.5, 124.0, 123.1, 122.8, 121.6, 121.5, 119.2, 116.0, 109.1, 106.9, 106.6, 19.7. Elemental analysis calcd (%) for C₂₀H₁₄BrN₃: C 63.84, H 3.75, N 11.17; found, %: C 63.95, H 3.81, N 11.28.

5-Methyl-3-(naphthalen-2-yl)benzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine (**6h**). Light brown powder (0.302 g, 79% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.97 (s, 1H, Ph), 7.93–7.87 (m, 4H, Ph), 7.61–7.56 (m, 4H, Ph), 7.48 (d, *J* = 3.9 Hz, 1H, pyrrole), 7.41 (t, *J* = 7.3 Hz, 1H, Ph), 7.32 (t, *J* = 7.4 Hz, 1H, Ph), 7.13 (s, 1H, CH), 6.73 (d, *J* = 3.9 Hz, 1H, pyrrole), 2.06 (s, 3H, CH₃). Elemental analysis calcd (%) for C₂₄H₁₇N₃: C 82.97, H 4.93, N 12.10; found: C 83.11, H 5.07, N 12.19.

7-Methyl-13,14-dihydrobenzo[*g*]benzo[4',5']imidazo[2',1':3,4]pyrazino[1,2-*a*]indole (**6i**). Brown powder (0.299 g, 84% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.89 (d, *J* = 7.9 Hz, 1H, Ph), 7.65 (d, *J* = 7.9 Hz, 1H, Ph), 7.42 (t, *J* = 7.4 Hz, 1H, Ph), 7.35–7.26 (m, 5H, Ph, pyrrole), 7.19–7.16 (m, 2H, Ph, CH), 2.95 (t, *J* = 6.7 Hz, 2H, indole), 2.79 (t, *J* = 6.7 Hz, 2H, indole), 2.58 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 144.4, 142.7, 136.8, 130.6, 129.9, 129.6, 129.3, 128.0, 125.9, 125.8, 125.1, 124.5, 124.1, 121.9, 121.7, 119.4, 109.3, 108.1, 105.9, 30.8, 23.4, 19.8. Elemental analysis calcd (%) for C₂₂H₁₇N₃: C 81.71, H 5.30, N 12.99; found: C 81.78, H 5.39, N 13.07.

3.4. X-ray Crystallography

Crystal Data for 3e: Formula: C₂₁H₁₇N₃O·CHCl₃ (M = 327.38 g/mol): monoclinic, space group P21/c (No. 14), a = 10.3012(10) Å, b = 22.0073(19) Å, c = 7.2627(7) Å, β = 90.469(3)°, V = 1566.72(9) Å³, Z = 4, T = 296(2) K, μ(CuKα) = 1.076 mm⁻¹, D_{calc} = 1.261 g/cm³, 43,389 reflections measured (2.30° ≤ θ ≤ 30.06°), 4583 unique (R_{int} = 0.1327; R_{sigma} = 0.0865), which were used in all calculations. The final R₁ was 0.0699 (I > 2σ(I)) and wR₂ was 0.1920 (all data). CCDC 2102328 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via <http://www.ccdc.cam.ac.uk> (accessed on 10 August 2021).

Crystal Data for 6b: Formula: C₂₀H₁₅N₃·CHCl₃ (M = 297.35 g/mol): monoclinic, space group P21/c (No. 14), a = 10.4033(3) Å, b = 20.1257(7) Å, c = 7.8873(3) Å, β = 108.427(2)°, V = 1646.4(3) Å³, Z = 4, T = 296(2) K, μ(CuKα) = 0.083 mm⁻¹, D_{calc} = 1.321 g/cm³, 42,575 reflections measured (3.36° ≤ θ ≤ 30.05°), 4804 unique (R_{int} = 0.0288; R_{sigma} = 0.0186), which were used in all calculations. The final R₁ was 0.0555 (I > 2σ(I)) and wR₂ was 0.0774 (all data). CCDC 2102327 contains the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via <http://www.ccdc.cam.ac.uk> (accessed on 10 August 2021).

4. Conclusions

In conclusion, three different series of valuable and highly promising annulated heterocyclic assemblies have been synthesized from available building blocks, pyrrole/indolecarb-aldehyde, *o*-phenylenediamine and propargyl chloride, by simply controlling the water

content of the reaction. Moreover, 5a-methyl-5a,6-dihydro-5*H*,12*H*-benzo[4,5]imidazo[1,2-*a*]pyrrolo[1,2-*d*] **4** and 5-methylbenzo[4,5]imidazo[1,2-*a*]pyrrolo[2,1-*c*]pyrazine **6** with the methyl group in α -position to pyrrole were obtained for the first time. These compounds represent important scaffolds for pharmaceutical chemistry, given the wide biological activity of nitrogen-containing heterocycles and manifold possibilities of their further functionalization.

Supplementary Materials: The following supporting information can be downloaded at <https://www.mdpi.com/article/10.3390/molecules27082460/s1>. Synthesis S1: procedure for the synthesis intermediate **H** and ^1H NMR spectra; Figures S1 and S2: 2D NOESY and HMBC of **H**; Figures S3–S80: ^1H and ^{13}C NMR spectra for **3**, **4**, **5** and **6**; Figures S81–S88: selected 2D NMR spectra for **4i**, **6e**; Tables S1–S3: crystallographic data of **3e** and **6d**. References [27,28] are cited in the supplementary materials.

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Sample Availability: Samples of the compounds **1,3,4,5** and **6** are available from the authors.

References

1. Andrews, M.J.I.; Edwards, P.; Brys, R.C.X.; Huxley, P.; Schmidt, W.; Birault, V.; Chambers, M.S.; Harris, C.J.; Macleod, A.; Hirst, K.L.; et al. Imidazolopyrazine compounds useful for the treatment of degenerative and inflammatory diseases. US Patent 817,365,6B2, 15 May 2012.
2. Du, X.; Gustin, D.J.; Chen, X.; Duquette, J.; Mcgee, L.R.; Wang, Z.; Ebsworth, K.; Henne, K.; Lemon, B.; Ma, J.; et al. Imidazopyrazine derivatives as potent CXCR3 antagonists. *Med. Chem. Lett.* **2009**, *19*, 5200–8204. [[CrossRef](#)] [[PubMed](#)]
3. Jin, M.A.; Kleinberg, A.; Cooke, A.; Gokhale, P.C.; Foreman, K.; Dong, H.; Siu, K.W.; Bittner, M.A.; Mulvihill, K.M.; Yao, Y.; et al. Potent and Selective Cyclohexyl-Derived Imidazopyrazine Insulin-Like Growth Factor 1 Receptor Inhibitors with in vivo Efficacy. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 1176–1180. [[CrossRef](#)] [[PubMed](#)]
4. Wu, T.; Nagle, A.; Kuhen, K.; Gagaring, K.; Borboa, R.; Franneck, C.; Chen, Z.; Plouffe, D.; Goh, A.; Lakshminarayana, S.B.; et al. Imidazolopiperazines: Hit to Lead Optimization of New Antimalarial Agents. *Med. Chem.* **2011**, *54*, 5116–5130. [[CrossRef](#)] [[PubMed](#)]
5. Tripathia, K.N.; Bansode, A.H.; Singh, R.P. Palladium-Catalyzed Oxidative Annulation of Pyrrolylalkyl-1*H*-azoles: Towards the Synthesis of Polyheterocyclic Arenes. *Synthesis* **2020**, *52*, 719–726. [[CrossRef](#)]
6. Tripathi, K.N.; Ray, D.; Singh, R.P. Synthesis of Pyrrole-Annulated Heterocycles through Copper-Catalyzed Site-Selective Dehydrogenative Cross-Coupling. *Eur. J. Org. Chem.* **2017**, *2017*, 5809–5813. [[CrossRef](#)]
7. Ray, D.; Manikandan, T.; Roy, A.; Tripathia, K.N.; Singh, R.P. Ligand-Promoted Intramolecular Dehydrogenative Cross-Coupling with Cu Catalyst: A Direct Access to Polycyclic Heteroarenes. *Chem. Commun.* **2015**, *51*, 7065–7068. [[CrossRef](#)]
8. Ramesh, S.; Kr Ghosh, S.; Nagarajan, R. Copper Catalyzed Synthesis of Fused Benzimidazolopyrazine Derivatives via Tandem Benzimidazole Formation/Annulation of δ -Alkynyl Aldehyde. *Org. Biomol. Chem.* **2013**, *11*, 7712–7720. [[CrossRef](#)]
9. Srinivasulu, V.; Shehadeh, I.; Khanfar, M.A.; Malik, O.G.; Tarazi, H.; Abu-Yousef, I.A.; Sebastian, A.; Baniowda, N.; O'Connor, M.J.; Al-Tel, T.H. One-Pot Synthesis of Diverse Collections of Benzoxazepine and Indolopyrazine Fused to Heterocyclic Systems. *J. Org. Chem.* **2019**, *84*, 934–948. [[CrossRef](#)]
10. Dagar, A.; Joshi, D.R.; Kim, I. Solvent-Controlled Divergent Syntheses of Polycyclic *N*-Fused Heteroaromatics. *Synthesis* **2020**, *52*, 2841–2856. [[CrossRef](#)]

11. Trofimov, B.A.; Ivanov, A.V.; Skital'tseva, E.V.; Vasil'tsov, A.M.; Ushakov, I.A.; Petrushenko, K.B.; Mikhaleva, A.I. A Straightforward Synthesis of 2-(1-Vinyl-1H-pyrrol-2-yl)-1H-benzimidazoles from 1-Vinyl-1H-pyrrole-2-carbaldehydes and o-Phenylenediamine. *Synthesis* **2009**, *21*, 3603–3610. [[CrossRef](#)]
12. Eynde, J.J.V.; Delfosse, F.; Lor, P.; Haverbeke, Y.V. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone, a mild catalyst for the formation of carbon-nitrogen bonds. *Tetrahedron* **1995**, *51*, 5813–5818. [[CrossRef](#)]
13. Lin, S.; Yang, L. A simple and efficient procedure for the synthesis of benzimidazoles using air as the oxidant. *Tetrahedron Lett.* **2005**, *46*, 4315–4319. [[CrossRef](#)]
14. Gharpure, S.J.; Nanda, S.K.; Fartade, D.J. Expedient diastereoselective synthesis of medium ring heterocycle-fused chromenes via tandem 8/9-endo-dig and 8-exo-dig hydroalkoxylation-formal-[4 + 2] cycloaddition. *Org. Biomol. Chem.* **2019**, *17*, 8806–8810. [[CrossRef](#)] [[PubMed](#)]
15. Wright, N.E.; Snyder, S.A. 9-Membered Carbocycle Formation: Development of Distinct Friedel–Crafts Cyclizations and Application to a Scalable Total Synthesis of (±)-Caraphenol A. *Angew. Chem. Int. Ed.* **2014**, *53*, 3409–3413. [[CrossRef](#)]
16. Gilmore, K.; Mohamed, R.K.; Alabugin, I.V. The Baldwin rules: Revised and extended. *WIREs Comput. Mol. Sci.* **2016**, *6*, 487–514. [[CrossRef](#)]
17. Smith, M.B.; March, J. *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 6th ed.; Wiley-Interscience: New York, NY, USA, 2007.
18. Huynh, T.-K.-C.; Nguyen, T.-H.-A.; Tran, N.-H.-S.; Nguyen, T.-D.; Hoang, T.-K.-D. A facile and efficient synthesis of benzimidazole as potential anticancer agents. *J. Chem. Sci.* **2020**, *132*, 84–92. [[CrossRef](#)]
19. EL-Sayed, T.H.; Aboelnaga, A.; Hagar, M. Ball Milling Assisted Solvent and Catalyst Free Synthesis of Benzimidazoles and Their Derivatives. *Molecules* **2016**, *21*, 1111. [[CrossRef](#)]
20. Malakooti, R.; Rostami-Nasab, M.; Mahmoudi, H.; Oskooie, H.A.; Heravi, M.; Karimi, N.; Amouchi, A.; Kohansal, G. Synthesis of 2-substituted benzimidazoles and 2-aryl-1H-benzimidazoles using $[Zn(bpdo)_2 \cdot 2H_2O]^{2+}$ /MCM-41 catalyst under solvent-free conditions. *Reac. Kinet. Mech. Cat.* **2014**, *111*, 663–677. [[CrossRef](#)]
21. Perez-Serrano, L.; Gonzalez-Perez, P.; Casarrubios, L.; Dominguez, G.; Perez-Castells, J. Synthesis of Polycycloindoles by Stereoselective Pauson-Khand Reactions. *Synlett* **2000**, *9*, 1303–1305. [[CrossRef](#)]
22. Perez-Serrano, L.; Dominguez, G.; Perez-Castells, J. New Approach to Indole Alkaloids Based on the Intramolecular Pauson-Khand Reaction. *J. Org. Chem.* **2004**, *69*, 5413–5418. [[CrossRef](#)]
23. Tucker, J.W.; Narayanam, J.M.R.; Krabbe, S.W.; Stephenson, C.R.J. Electron Transfer Photoredox Catalysis: Intramolecular Radical Addition to Indoles and Pyrroles. *Org. Lett.* **2010**, *2*, 368–371. [[CrossRef](#)] [[PubMed](#)]
24. Tarasova, O.A.; Brandsma, L.; Trofimov, B.A. Facile One-Pot Syntheses of 1-Allenylpyrroles. *Synthesis* **1993**, *6*, 571–572. [[CrossRef](#)]
25. Martynovskaya, S.V.; Shcherbakova, V.S.; Ushakov, I.A.; Borodina, T.N.; Ivanov, A.V. Expedient synthesis of a new class of organic building blocks: N-allenylpyrrole-2-carbaldehydes. *Tetrahedron. Lett.* **2020**, *61*, 152666. [[CrossRef](#)]
26. Ford, R.A.; Gordon, A.J. *The Chemist's Companion*, 1st ed.; Wiley: Hoboken, NJ, USA, 1972; 560p.
27. Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H. OLEX2: A complete structure solution, refinement and analysis program. *J. Appl. Cryst.* **2009**, *42*, 339–341. [[CrossRef](#)]
28. Sheldrick, G.M. A short history of SHELX. *Acta Cryst.* **2008**, *64*, 112–122. [[CrossRef](#)] [[PubMed](#)]