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Two-Step Synthesis of Blue Luminescent (Pyrrol-3-yl)-1*H*-(aza)indazoles Based on a Three-Component Coupling–Cyclocondensation Sequence

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(Pyrrol-3-yl)-1*H*-(aza)indazoles can be efficiently prepared by a two-step process that consists of a consecutive three-component coupling–cyclocondensation synthesis to give *ortho*-halo-3-acylpyrrol-3-yl-substituted (hetero)arenes followed by a cyclization–condensation–S_NAr sequence. Almost all derivatives display an intense blue emission upon excitation in the near UV with enormous Stokes shifts (6500–8300 cm^{-1}) and considerable high fluorescence quantum yields (Φ_f = 0.28–0.46). Electronic transitions can be plausibly rationalized by TD-DFT computations performed on DFT-optimized geometries. Reversible protonation leads to static fluorescence quenching in narrow pH-ranges, which qualifies the title compounds as favorable ON/OFF fluorescence switching systems.

Introduction

Indazoles[1] have received considerable attention for quite some time owing to their broad spectrum of biological activity.[2] Interestingly this heterocyclic core structure is only rarely found in nature, e.g. in the alkaloids nigellicine (isolated from *Nigella sativa L.*), nigeglanine (isolated from *Nigella glandulifera*), and nigellidine, which occur in the black cumin seed.[1a] Besides NO liberation of some derivatives[3,4] and concomitant anti-aggregation and vaso-relaxing activity in the human body,[5] and their high potency as male contraceptives, for treatment of osteoporosis, neurodegenerative diseases[6] and inflammation.[7,8] Furthermore, the indazole core has been recognized as a pharmacophore for the development of 5-HT (5-hydroxytryptamine, i.e. serotonin) receptor agonists and antagonists,[9–11] and some derivatives are useful as combination compounds for radiation oncology treatment of brain tumors.[12] In addition antimicrobial, antiparasitic, and antibacterial properties have been also reported.[13]

Remarkably, indazoles are known for their pronounced chemical stability and, among pyrazole derivatives indazoles are the most stable. Ring opening is only feasible under very harsh conditions and even NN-bond cleavage is rare and only under photochemical conditions.[1c] Therefore, the interest in new indazole syntheses has remained unabated.

Many syntheses of the indazole core are based upon cyclocondensation reaction of *ortho*-halo substituted aromatic aldehydes and ketones with corresponding hydrazine derivatives.[1b] As variations of this general approach, a Cu^{II} oxide catalyzed process was recently disclosed.[14] With hydrazones as presumed and actual intermediates a Pd-catalyzed version has been proposed, which only proceeds in modest yield.[15] Likewise after ligand adjustment *ortho*-halo-substituted aromatic *N*-tosylhydrazones have successfully been transformed into *N*-tosylindazoles, although these require relatively high catalyst loadings.[16]

For full color displays and illumination, blue is indispensable and, consequently, the development of blue emitters in organic light-emitting diodes (OLEDs) remain a challenging research goal.[17] Driven by our interest in the photophysical properties of heterocyclic blue emissive materials[18] and diversity-oriented chromophore syntheses in general,[19] we reasoned that indazoles might be equally well suited as heterocyclic chromophores with additional sites of protonation. Although structurally related pyrazolo[3,4-*b*]-quinolines,[20] pyrazolo[3,4-*b*]quinoxalines,[21] and dipyrazolo[3,4-*b*:4′,3′-*e*]pyridines[22] possess interesting photophysical properties that are well-suited for application in OLED technologies, the syntheses and properties of (3-pyrrol-3-yl)indazoles have largely remained unexplored.[23] Our retrosynthetic analysis suggests a disconnection of the pyrazole core to 3-acylpyrrole derivatives of *ortho*-halo substituted (hetero)arenes and hydrazines in a retro cyclizing condensation-S_NAr cut (Scheme 1). The former have become readily accessible by our recently published consecutive three-component coupling–cyclocondensation synthesis of 3-acylpyrrol-3-yl-substituted (hetero)arenes in a one-pot fashion.[24]

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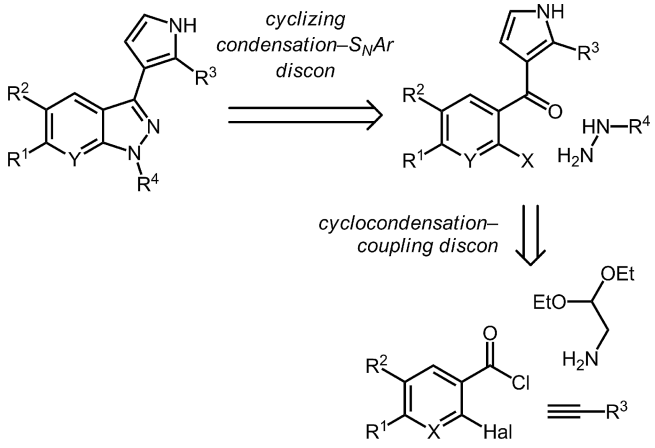


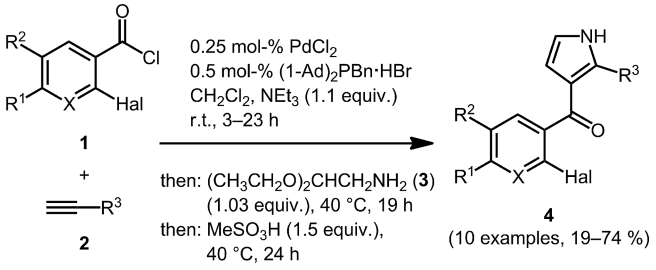
Scheme 1. Retrosynthetic analysis of 3-pyrrol-3-yl-substituted (aza)indazoles.

Here we report a diversity-oriented approach to 3-pyrrol-3-yl-substituted (aza)indazoles in a two-step fashion initiated by a three-component synthesis of the immediate precursor of a final cyclocondensation reaction. Furthermore, the electronic properties are studied by absorption and emission spectroscopy and the electronic structure is elucidated by DFT calculations of pronounced representatives.

Results and Discussion

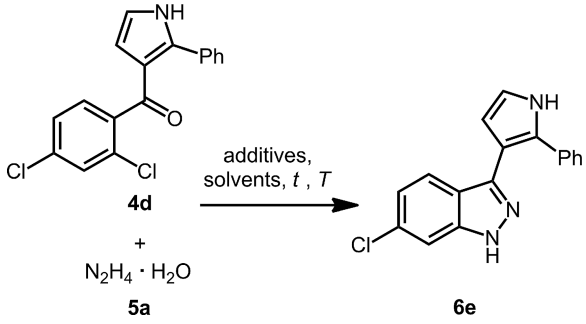
Synthesis

Alkynones are proven excellent intermediates in consecutive multi-component syntheses of numerous classes of heterocycles in a one-pot fashion.[25] Recently, we established a copper-free Pd-catalyst system[26] as an extension of the modified Sonogashira coupling reaction[27] for the efficient formation of alkynones from acid chlorides and terminal alkynes and applied it to a four-component synthesis of dihydropyrid-2-ones.[28] This catalyst system consists of $PdCl_2$ (1 mol-%) and di(1-adamantyl)-benzyl-phosphonium bromide (cataCXium® ABn·HBr; 2 mol-%)[29] and uses triethylamine as a base. By starting from (hetero)aroyl chlorides and alkynes, and based upon Langer's 3-acylpyrrole synthesis[30] 3-acylypyrrol-3-yl-substituted (hetero)arenes became accessible in moderate to good yields in the sense of a consecutive three-component synthesis.[24] We set out to scale up the synthesis of 10 *ortho*-halo-3-acylpyrrol-3-yl-substituted (hetero)arenes **4**, and also lower the catalyst loading to 0.25 mol-% of $PdCl_2$ and 0.5 mol-% of cataCXium® ABn·HBr, i.e. $(1\text{-Ad})_2$PBn·HBr. Upon coupling of *ortho*-halo-substituted (hetero)aroyl chlorides **1** and terminal alkynes **2**, followed by Michael addition of aminoacetaldehyde diethyl acetal (**3**) to the ynone intermediate to give the corresponding enaminone, the one-pot sequence was concluded by methanesulfonic acid mediated cyclocondensation reaction to furnish *ortho*-halo-3-acyl pyrrol-3-yl-substituted (hetero)arenes **4** after chromatography in multigram quantities with yields 19–74% (Scheme 2, Table 1).



Scheme 2. Three-component synthesis of 2-[2′-halo(hetero)aryl]-(1*H*-pyrrol-3-yl)methanones **4**.

With *ortho*-halo-3-acylpyrrol-3-yl-substituted (hetero)arenes **4** in hand we optimized the conditions of the cyclization–condensation–S_NAr indazole-forming step with respect to hydrazine concentration, additives, solvents, reaction time, and reaction temperature, which included conductive versus dielectric heating (Scheme 3, Table 2).



Scheme 3. Optimization of the cyclization–condensation–S_NAr reaction of **4d** with hydrazine hydrate (**5a**) to give 6-chloro-3-(2-phenyl-1*H*-pyrrol-3-yl)-1*H*-indazole (**6e**).

Table 1. Three-component synthesis of 2-(2′-halo(hetero)aryl)-(1*H*-pyrrol-3-yl)methanones **4**.[a]

Entry [a]	Acid chloride **1**	Alkyne **2**	t_1 [h]	Yield[b]
1	$R^1 = R^2 =$ H, Hal = F, X = CH (**1a**)	R^3 = Ph (**2a**)	3.5	**4a** (45%)
2	**1a**	R^3 = *n*Bu (**2b**)	23	**4b** (19%)
3	**1a**	R^3 = cyclopropyl (**2c**)	21	**4c** (23%)
4	R^1 = Cl, R^2 = H, Hal = Cl, X = CH (**1b**)	**2a**	3	**4d** (57%)
5	$R^1 = R^2$ = H, Hal = Cl, X = N (**1c**)	**2a**	4	**4e** (44%)
6	**1c**	R^3 = *p*-*t*BuC$_6$H$_4$ (**2d**)	2.75	**4f** (54%)
7	**1c**	**2c**	22	**4g** (39%)
8	R^1 = H, R^2 = O_2N, Hal = Cl, X = CH (**1d**)	**2a**	5.3	**4h** (74%)
9	**1d**	R^3 = *p*-MeC$_6$H$_4$ (**2e**)	3	**4i** (29%)
10	**1d**	**2c**	21	**4j** (22%)

[a] All reactions were carried out on a 8–20 mmol scale [c_0(**1**) = c_0(**2**) = 1.0]. [b] All yields refer to isolated and purified products.

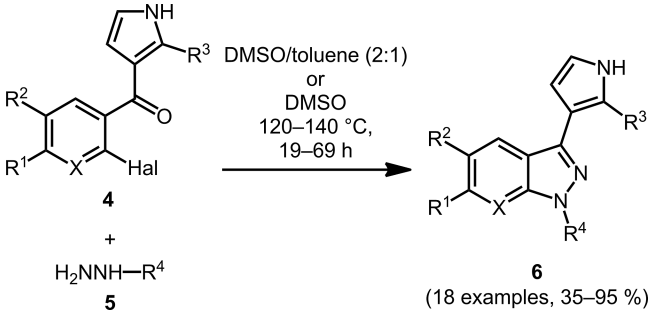
Table 2. Optimization of the synthesis of 6-chloro-3-(2-phenyl-1*H*-pyrrol-3-yl)-1*H*-indazole (**6e**).[a]

Entry	Solvent	*T*	*t*	Additives	Yield of **6e**[b]
1[c]	1,4-dioxane	120 °C (oil bath)	23 h	–	11%
2[c]	1,4-dioxane/DMF (2:1)	140 °C (oil bath)	23 h	–	–[d]
3[c]	toluene	140 °C (oil bath)	24 h	–	–[d]
4[c]	ethylene glycol	160 °C (oil bath)	19 h	–	–[e]
5[c]	ethylene glycol	200 °C (MW)	1 h	–	23%
6[c]	ethylene glycol	200 °C (MW)	4 h	–	23%
7[c]	DMSO	100 °C (oil bath)	26.5 h	–	16%
8[c]	DMSO	120 °C (oil bath)	21.5 h	–	20%
9[c]	DMSO	120 °C (oil bath)	26.5 h	K_2CO_3 (2 equiv.)	< 2%
10[c]	DMSO	120 °C (oil bath)	21 h	$MeSO_3H$ (0.5 equiv.)	19%
11[c]	DMSO	200 °C (MW)	0.5 h	–	–[f]
12[c]	DMSO	80 °C (oil bath)	16 h	CuI (5 mol-%), DMEDA (5 mol-%), K_2CO_3 (2 equiv.)	–[d]
13[c]	1,4-dioxane	110 °C (oil bath)	16 h	Cu_2O (5 mol-%), K_2CO_3 (2 equiv.)	10%
14[c]	1,4-dioxane	110 °C (oil bath)	16 h	CuI (5 mol-%), K_2CO_3 (2 equiv.)	–[d]
15[c]	1,4-dioxane	110 °C (oil bath)	20 h	$PdCl_2$ (2 mol-%), $(1\text{-Ad})_2P$*n*Bu·HI (4 mol-%), NaO*t*Bu (2 equiv.)	–[d]
16[c]	1,4-dioxane	110 °C (oil bath)	20 h	$PdCl_2$ (2 mol-%), $(1\text{-Ad})_2P$*n*Bn·HBr (4 mol-%), NaO*t*Bu (2 equiv.)	–[d]
17[g]	DMSO	120 °C (oil bath)	68 h	–	–[f]
18[g]	toluene/DMSO (2:1)	130 °C (oil bath)	65.5 h	–	54%
19[g]	**toluene/DMSO (1:2)**	**130 °C (oil bath)**	**69 h**	–	**72%**

[a] All reactions were carried out on a 0.5 mmol scale [c_0(**4d**) = 0.17]. [b] All yields refer to isolated and purified products. [c] 3 equiv. of hydrazine hydrate (**5a**). [d] No product **6e** formed as determined by TLC; DMEDA = *N,N′*-Dimethylethylenediamine. [e] No product **6e** formed as determined by TLC, but an unidentified byproduct was isolated. [f] DMSO decomposed. [g] 6 equiv. of hydrazine hydrate (**5a**).

The patent literature usually recommends the use of polar aprotic solvents with low permittivity for enabling nucleophilic aromatic substitution.[31] However in 1,4-dioxane at 110 °C for 23 h only 11% of compound **6e** was formed (Table 2, Entry 1). Whereas mixtures of 1,4-dioxane and dimethylformamide (DMF; 2:1), and toluene as sole solvent at 140 °C failed to furnish the product after 24 h (Table 2, Entries 2 and 3). Ethylene glycol was probed as a polar protic solvent, however only an unidentified byproduct was formed in small amounts under conductive heating (Table 2, Entry 4). Reactions in the microwave cavity furnished 23% of compound **6e** in ethylene glycol (Table 2, Entries 5 and 6), but failed in dimethyl sulfoxide (DMSO), which decomposed under dielectric heating at elevated temperatures (Table 2, Entry 11). Application of DMSO at 100 and 120 °C did not furnish the desired product, even though it is known that poor solvation of the nucleophile should enhance its reactivity (Table 2, Entries 7 and 8).[32] Base-mediated cyclization in DMSO at 120 °C only furnished 2% of product **6e** (Table 2, Entry 9), whereas acid catalysis did not exceed 19% (Table 2, Entry 10). Neither the addition of copper (Table 2, Entries 12–14) or of Pd catalysts (Table 2, Entries 15 and 16) led to any improvement. However, solvent mixtures of DMSO/toluene and extended heating did work (Table 2, Entries 18 and 19). With 72% isolated yield of compound **6e** (Table 2, Entry 19) in a 1:2 mixture of toluene and DMSO, optimal conditions for the cyclizing condensation-S_NAr synthesis of indazoles were identified.

With these optimized conditions in hand the cyclization–condensation–S_NAr synthesis of annelated pyrrole-substituted pyrazoles **6**, i.e. indazoles and azaindazoles, was performed by reacting *ortho*-halo-3-acylpyrrol-3-yl-substituted (hetero)arenes **4** with hydrazines **5** in DMSO/toluene (2:1) mixtures or in DMSO at 120–140 °C for 19–69 h to furnish title compounds **6** after workup and purification in moderate to excellent yields (Scheme 4, Table 3). The structures of all (1*H*-pyrrol-3-yl)-1*H*-indazoles **6** were unambiguously assigned by extensive ^1H and ^{13}C NMR spectroscopy and mass spectrometry. The molecular composition was derived either from combustion elemental analysis (C,H,N) or HRMS.

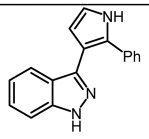
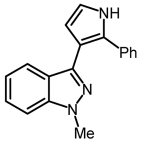
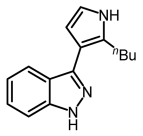
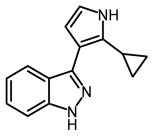
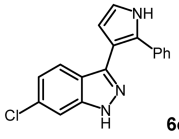
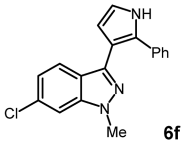
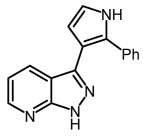
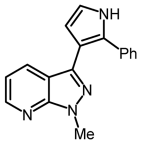
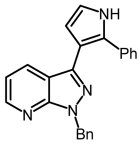
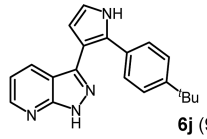
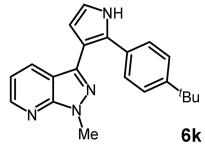
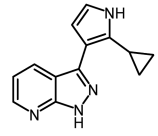
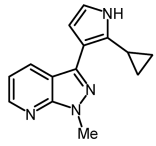
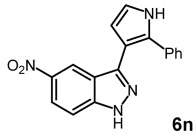
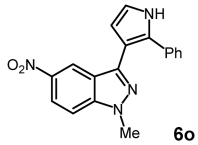
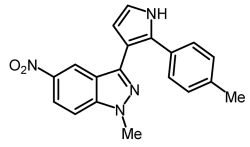
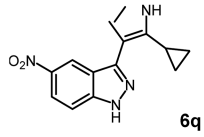
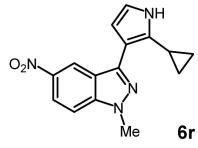


Scheme 4. Cyclization–condensation–S_NAr synthesis of 2′-substituted 3-(1*H*-pyrrol-3-yl)-1*H*-indazoles **6**.

Photophysical Properties (UV/Vis and Fluorescence Spectroscopy)

With exception of 5-nitro-3-(1*H*-pyrrol-3-yl)indazoles **6n**–**6r** all other indazoles **6a**–**6f** and azaindazoles **6g**–**6m** are intensely blue luminescent in solution upon excitation by UV light. Therefore, the photophysical properties of selected molecules **6b**, **6g**, **6h**, **6i**, **6j**, **6m**, and **6o** were examined in more detail by UV/Vis and fluorescence spectroscopy in dichloromethane as a solvent and at room temperature (Table 4). The fluorescence quantum yields Φ_f were determined with quinine sulfate in sulfuric acid (0.5 M) as a standard (Φ_f = 0.546).[33]

Table 3. Synthesis of 3-(1*H*-pyrrol-3-yl)-1*H*-indazoles **6**.[a]

Entry	3-Acyl-pyrrole **4**	*t* [h]	Hydrazine **5**	3-(1*H*-pyrrol-3-yl)indazoles **6** (yield)[b]
1	**4a**	24	R^4 = H (**5a**)[c]	 **6a** (81 %)
2	**4a**	24	R^4 = Me (**5b**)	 **6b** (82 %)
3	**4b**	22	**5a**[c]	 **6c** (49 %)
4	**4c**	4	**5a**[c]	 **6d** (63 %)
5	**4d**	65.5	**5a**[c]	 **6e** (72 %)
6	**4d**	69	**5b**	 **6f** (50 %)
7	**4e**	3	**5a**[c]	 **6g** (82 %)
8	**4e**	3	**5b**	 **6h** (85 %)
9	**4e**	3	R^4 = Bn (**5c**)[d]	 **6i** (50 %)
10	**4f**	3	**5a**[c]	 **6j** (90 %)
11	**4f**	3	**5b**	 **6k** (93 %)
12	**4g**	3	**5a**[c]	 **6l** (78 %)
13	**4g**	3	**5b**	 **6m** (58 %)
14	**4h**	5.3	**5a**[c]	 **6n** (83 %)
15	**4h**	3	**5b**	 **6o** (77 %)
16	**4i**	3	**5b**	 **6p** (75 %)
17	**4j**	3	**5a**[c]	 **6q** (65 %)
18	**4j**	3	**5b**	 **6r** (35 %)

[a] All reactions were carried out on a 0.5 mmol scale [c_0(**4**) = 0.17 ; c_0(**5**) = 0.2–1.0]. [b] All yields refer to isolated and purified products. [c] Employed as hydrazine hydrate. [d] Employed as hydrochloride and sodium acetate (62 mg, 0.75 mmol) was added.

For all the investigated compounds, indazoles **6b**, **6o** and azaindazoles **6g**, **6h**, **6i**, **6j**, and **6m**, two characteristic absorption maxima were seen. For compound **6b** these maxima appear at 293.5 and 311.5 nm with molar extinction coefficients ε of 14300 and 11000 $L\,mol^{-1}\,cm^{-1}$. The 5-nitro substitution in compound **6o** causes a considerable hypsochromic shift to 279.0 nm (ε = 21400 $L\,mol^{-1}\,cm^{-1}$) and a bathochromic shift of the longest wavelength absorption band to 376.5 nm (ε = 5200 $L\,mol^{-1}\,cm^{-1}$). The same behavior is observed for the investigated azaindazoles. The 7-azaindazole nitrogen atom exerts a strongly electron-withdrawing effect by blue-shifting the high-energy absorption

Table 4. Selected photophysical properties of selected 3-(1*H*-pyrrol-3-yl)substituted (aza)indazoles **6**.

	$\lambda_{max,abs}$ (ε)[a] [nm] ([L mol^{-1} cm^{-1}])	$\lambda_{max,em}$ (Φ_f)[b,c] [nm] (a.u.)	Stokes shift $\Delta\nu$[d] [cm^{-1}]
6b	293.5 (14300), 311.5 (11000)	390.5 (0.46)	6500
6g	283.5 (15100), 325.5 (5900)	438.0 (0.34)	7900
6h	285.5 (14200), 336.5 (6300)	440.5 (0.40)	7000
6i	284.0 (14000), 335.5 (6200)	440.5 (0.43)	7100
6j	282.0 (17800), 325.5 (6000)	446.0 (0.28)	8300
6m	231.0 (21400), 338.5 (5100)	454.0 (0.28)	7500
6o	279.0 (21400), 376.5 (5200)	–	–

[a] Recorded in CH_2Cl_2 UVASOL® at T = 293 K. [b] Recorded in CH_2Cl_2 UVASOL® at T = 293 K with λ_{exc} = 310.0 nm. [c] Quantum yields Φ_f were determined with quinine sulfate in sulfuric acid (0.5 M) as a standard, Φ_f = 0.546.[33] [d] $\Delta\nu = 1/\lambda_{max,abs} - 1/\lambda_{max,em}$ [cm^{-1}].

maxima in a range between 282.0 and 285.5 nm and by red-shifting the low energy bands in a range between 325.5 and 338.5 nm. The derivative with cyclopropyl substitution on the pyrrole core (compound **6m**) displays a strongly hypsochromically shifted first absorption maximum at 231.0 nm. As a consequence of the diminished π-system upon replacement of the aryl substituent by a cyclopropyl group on the pyrrole ring the observed hypsochromic shift can be rationalized as well as a significant overlap of the 2-aryl substituent in the electronic ground states of the 3-(1*H*-pyrrol-3-yl)-substituted (aza)indazoles.

Although for indazole **6b** an intense emission band at 390.5 nm with a fluorescence quantum yield Φ_f of 46% is determined, in dichloromethane emission of nitro derivative **6o** is completely quenched. For the azaindazole derivatives **6g**, **6h**, **6i**, **6j**, and **6m** the emission maxima is shifted bathochromically relative to indazole derivative **6b** and the maxima determined appear in a narrow range between 438.0 and 454.0 nm with fluorescence quantum yields Φ_f of between 28 and 43%.

The addition of acid clearly influences both the absorbance and the emission behavior of indazole **6b** and azaindazoles **6h**, **6j** as a consequence of protonation of the core nitrogen atoms. The addition of aliquots of trifluoroacetic acid (TFA) to a dichloromethane solution of compound **6b** was monitored photospectrometrically (Figure 1). Although the absorption maxima of the free base at 293.5 and 311.5 nm disappear upon exhaustive protonation, two new maxima at 259.0 and 357.5 nm can be detected, which indicates considerable change of the chromophore.

The occurrence of two isosbestic points in the titration experiments accounts for an equilibrium between indazole **6b** and its protonated conjugated acid **6b-H$^+$** without further intermediates. From the plot of the absorbance against the proton concentration, assuming $c(H^+) = c(TFA)$ for TFA as a strong, fully dissociated Brønsted acid the pK_a values of indazole derivative **6b** and azaindazoles **6h** and **6j** can be determined (Table 5, for plots see the Supporting Information).

N-Methylated (aza)indazoles **6b** and **6h** possess very similar pK_a values in dichloromethane. This supports the view

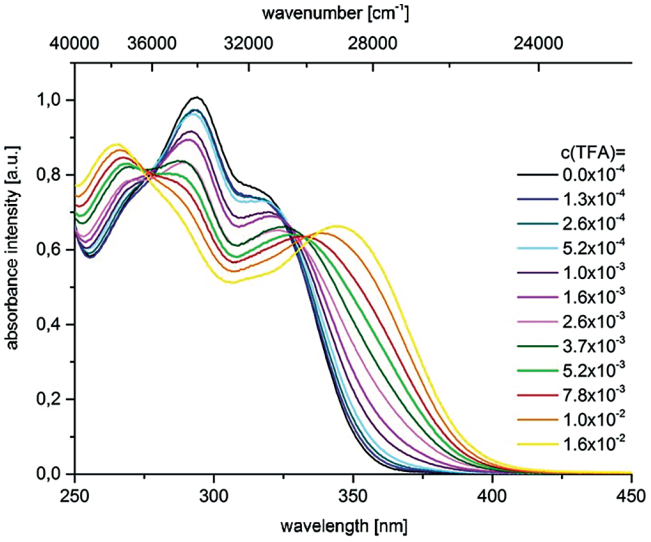


Figure 1. Absorption spectra of the titration of compound **6b** (c_0 = 3.3 × 10^{-5} mol L^{-1}) with TFA in dichloromethane UVASOL® (recorded at T = 293 K).

Table 5. Absorption maxima of **6** and **6-H$^+$** employed in the absorption-pH plots and pK_a values of selected (aza)indazoles **6** determined from the absorbance.

	λ_{max} (**6**) [nm]	λ_{max} (**6+H$^+$**) [nm]	pK_a (absorbance)
6b	293.5, 311.5	259.0, 357.5	2.62
6h	336.5	417.5	2.69
6j	325.0	398.5	4.09

that the more basic pyrazole nitrogen atom is the site of protonation. Conversely the pK_a value of azaindazole **6j** is one and a half orders of magnitude lower (pK_a 4.09), which indicates a facilitated and preferred protonation on the pyridyl nitrogen atom of this nonalkylated derivative.

Another characteristic feature of indazole **6b** and azaindazoles **6h** and **6j** is the quenching of fluorescence upon protonation with TFA. This property can be quantified by titration of the component with TFA. Especially for confirming the assumption of a single protonation of indazole **6b**, as observed by absorption spectroscopy, the protonation was also monitored and quantified by emission spectroscopy. If both isosbestic points (Figure 1) do not describe the equilibrium between a singly protonated and a non-protonated species rather a dynamic than a steady state quenching could be expected according to Stern–Volmer treatment.[34] Upon addition of aliquots of TFA as a quencher a Stern–Volmer plot was obtained that furnished a linear correlation between F/F_0 and the concentration of TFA, which assumes full dissociation of TFA in dichloromethane (Figure 2).

The Stern–Volmer constant K_{SV} of **6b** was found to be 1139 L/mol (Table 6). By definition of steady-state quenching the K_{SV} also correlates to the pK_a of **6b** (3.00) in the electronic ground state. This value nicely matches with the pK_a determined by absorption spectroscopy (2.62). For **6j** K_{SV} was determined as 66937 L/mol, which represents a

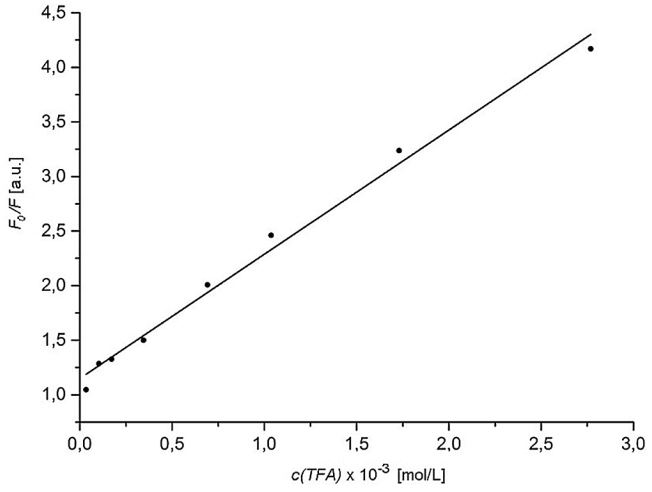


Figure 2. Stern–Volmer plot of compound **6b** [c_0(**6b**) = 1.25×10^{-7} mol/L in dichloromethane UVASOL®, T = 293 K, F_0/F = 1.148 + 1139 (H^+); (r^2 = 0.990)].

pK_a of 4.90. Again this value matches with the pK_a from absorption spectroscopy (4.09).

Table 6. Stern–Volmer constants K_{SV} and pK_a (from emission and absorption spectroscopy) of compounds **6b** and **6j**.

	K_{SV} [L mol^{-1}]	pK_a (emission)	pK_a (absorption)
6b	1139	3.00	2.62
6j	66937	4.90	4.09

Electronic Transitions (DFT and TD-DFT Calculations)

For selected 3-(1*H*-pyrrol-3-yl)-substituted (aza)indazoles **6b**, **6h**, and **6i** quantum chemical calculations were performed to elucidate the electronic structure and to rationalize the observed optical absorptions. Geometries of theses selected compounds were optimized on the DFT-level of theory[35] (B3LYP functional[36] and 6-311G* basis set[37]) and the local minima were verified by frequency analysis. Solvent effects on molecular properties were modeled by applying the Polarizable Continuum Model (PCM) for dichloromethane as a solvent.[38] The optimized geometries of indazole **6b** and azaindazole **6h** clearly show that the pyrrole ring is twisted out of coplanarity with the bicyclic substituent by 41–43° (Figure 3). For the torsion angle of the 2-phenyl ring on the pyrrole moiety 33–38° are found.

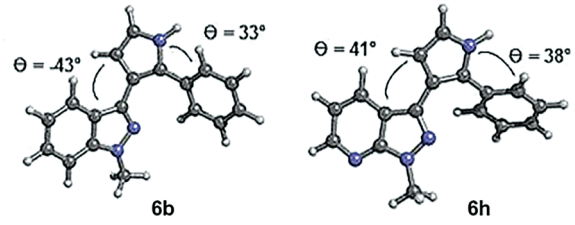


Figure 3. DFT-Optimized (B3LYP, 6-311G**) geometries and selected torsional angles of structures **6b** and **6h**.

With geometry-optimized structures **6b**, **6h**, and **6i**, TD-DFT calculations of vertical excitation with linear response solvation were performed by applying the hybrid exchange correlation functional CAM-B3LYP[39] for accounting charge-transfer (CT) bands (Table 7). In addition a non-equilibrium state of solvation was assumed for state specific solvation upon vertical excitation.[40]

Table 7. Experimental ($\lambda_{abs,exp}$) and TD-DFT-calculated (CAM-B3LYP/6-311G**) vertical excitation with linear response solvation ($\lambda_{abs,calcd}$) absorption maxima of structures **6b**, **6h**, and **6i**.

	$\lambda_{abs,exp}$ (ε)[a] [nm] ([L mol^{-1} cm^{-1}])	$\lambda_{abs,calcd.}$ [nm]
6b	294 (14300)	261 (67% HOMO→LUMO+1)
	312 (11000)	286 (289[b]) (83% HOMO→LUMO)
6h	286 (14200)	266 (69% HOMO→LUMO+1)
	337 (6300)	306 (325[b]) (81% HOMO→LUMO)
6i	284 (14000)	266 (69% HOMO→LUMO+1)
	336 (6200)	305 (324[b]) (80% HOMO→LUMO)

[a] Recorded in CH_2Cl_2 UVASOL® at T = 293 K. [b] State specific solvation.

The comparison of experimental and calculated absorption bands reveals a self-consistent trend of the two major bands. Although the longest wavelength maxima are consequently calculated with a blue shift of 3000 cm^{-1}, the calculated highest intensity band of indazole **6b** deviates to higher energy by 4300 cm^{-1}, whereas the corresponding transitions of azaindazoles **6h** and **6i** are only blue-shifted by 2500 cm^{-1}. The longest wavelength maxima can be clearly assigned to dominant HOMO–LUMO transitions (83%), whereas the next bands are 69% from HOMO to LUMO+1 transitions. According to configuration interaction minor contributions stem from HOMO–2 to LUMO and HOMO–1 to LUMO+1 transitions. As already determined from the UV/Vis spectra for azaindazoles **6h** and **6i**, substituent effects on the azaindazole core and on the pyrrole moiety according to TD-DFT calculations are only minimal.

Closer inspection of the Kohn–Sham frontier molecular orbitals of azaindazole **6h** reveals considerable coefficient density on the 2-phenylpyrrole substituent for the HOMO, whereas the LUMO clearly accounts for localization of the coefficient density in the azaindazole moiety (Figure 4). The HOMO–LUMO transition may be interpreted as a Franck–Condon state with significant CT contribution. Due to considerable coefficient density overlap in the central pyrazole moiety in the HOMO and LUMO this longest wavelength transition is accompanied with significant oscillator strength.

Furthermore the inspection of the Kohn–Sham HOMO and LUMO of azaindazole **6i** additionally supports that an influence of the *N*-substituent on the longest wavelength absorption band can be ruled out because this substituent does not bare coefficient density in either the HOMO or LUMO (Figure 5).

Finally, protonation of azaindazole **6h** was modeled to rationalize the effect on the absorption spectrum (vide supra). The geometry optimization of protonated species **6h-H$^+$** reveals that protonation on the pyridyl nitrogen atom (as deduced from the measured pK_a values) only affect the

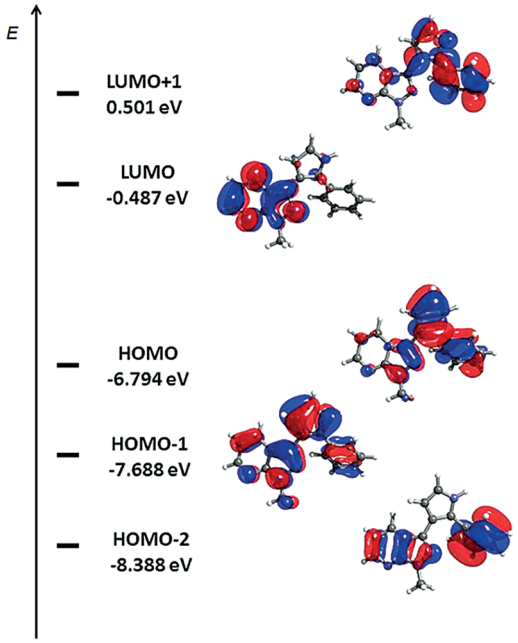


Figure 4. DFT-Calculated (B3LYP, 6-311G**) Kohn–Sham frontier molecular orbitals of structure **6h**.

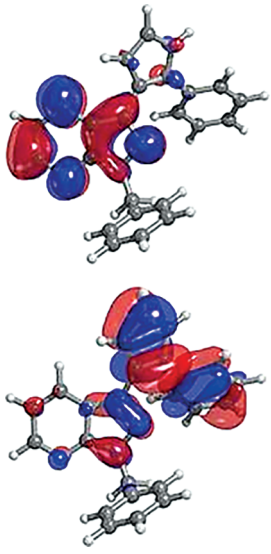


Figure 5. DFT-Calculated (B3LYP, 6-311G**) Kohn–Sham HOMO (bottom) and LUMO (top) of structure **6i**.

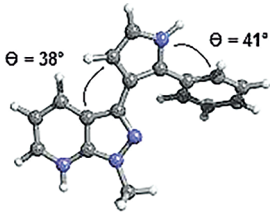


Figure 6. DFT-Optimized (B3LYP, 6-311G**) geometry and selected torsional angles of structure **6h-H$^+$**.

torsional angles between the azaindazole core and pyrrole and between the pyrrole and phenyl substituent to a minor extend (Figure 6).

Based on this optimized geometry a TD-DFT calculations (CAM-B3LYP[39]/6-311G**) were performed for free base **6h** and protonated species **6h-H$^+$** (Table 8). The trend of the blue shift of the calculated highest intensity band and the longest wavelength absorption band relative to the experimental spectra is also self-consistent for protonated species **6h-H$^+$**. Although the former absorptions arise from HOMO to LUMO+1 (for **6h**) and HOMO to LUMO+2 (for **6h-H$^+$**) transitions, the latter lowest energy absorption bands can be predominantly assigned to HOMO to LUMO transitions. This bathochromic shift of the CT band upon protonation on the pyridyl nitrogen moiety is nicely rationalized by lowering the LUMO energy, whereas the HOMO only possesses minor coefficient density at this nitrogen atom. As shown before, protonation causes static fluorescence quenching in a range typical for pyridyl derivatives. The reversibility of this feature might be particularly interesting for protonation-induced ON/OFF switches, i.e. ON as a free base and OFF in its protonated form.[41]

Table 8. Experimental ($\lambda_{abs,exp}$) and TD-DFT-calculated (CAM-B3LYP/6-311G**) ($\lambda_{abs,calcd}$) absorption maxima of structures **6h** and **6h-H$^+$**.

	$\lambda_{abs,exp}$ (ε)[a] [nm]	$\lambda_{abs,calcd.}$ [nm]
6h	286	266 (69% HOMO→LUMO+1)
	337	306 (325[b]) (81% HOMO→LUMO)
6h-H$^+$	286	266 (90% HOMO→LUMO+2)
	417	386 (376[b]) (86% HOMO→LUMO)

[a] Recorded in CH_2Cl_2 UVASOL® at T = 293 K. [b] PCM-corrected values.

Conclusions

In conclusion we have disclosed an efficient diversity-oriented two-step synthesis of pyrrol-3-yl-1*H*-substituted (aza)indazoles. Based upon a previously reported consecutive three-component coupling-cyclocondensation synthesis, *ortho*-halo-3-acylpyrrol-3-yl-substituted (hetero)arenes were transformed in a cyclization–condensation–S_NAr sequence to give the title compounds in moderate to excellent yield. Almost all derivatives display intense blue emission upon excitation in the near UV with enormous Stokes shifts and considerable high fluorescence quantum yields. Upon protonation, the fluorescence can be reversibly quenched by a static quenching mechanism that correlates nicely with protonation of the pyrazole nitrogen atom for indazoles and the pyridyl nitrogen atom for azaindazoles. This reversible ON/OFF fluorescence-switching system is ideally suited as biooptical tool for acidity sensing in cells in a narrow pH-range. Further studies are currently underway.

Experimental Section

General Considerations: All reactions were carried out in flame-dried glassware under a nitrogen atmosphere. Reagents and catalysts were purchased reagent-grade and used as received, except triethylamine, which was dried with calcium hydride and stored

over potassium hydroxide under a nitrogen atmosphere. Solvents were dried by a solvent purification system. Dielectric heating was performed in a single mode microwave cavity that produced continuous irradiation at 2450 MHz. Further purification of the compounds was performed with flash column chromatography (silica gel 60, mesh 230–400). TLC: silica-coated aluminum plates (Kieselgel 60, F_{254}). ^{1}H, ^{13}C, DEPT and NOESY NMR spectra were recorded in $CDCl_3$, $CDCl_2$, or [D_6]acetone with a 300 MHz (Bruker AVIII) or 600 MHz (Bruker Avance III-600) NMR spectrometer. The assignments of C_{quat}, CH, CH_2 and CH_3 nuclei were based on DEPT spectral analysis. Elemental analyses were carried out in the microanalytical laboratory with a Perkin–Elmer Series ii Analyser 2400 of the Pharmazeutisches Institut of the Heinrich-Heine-Universität Düsseldorf. Mass spectra were recorded with a GC/MS-spectrometer Finnigan Trace DSQ with Finnigan Trace GC Ultra (Thermo Electron Corp.) or with an ESI spectrometer Ion-Trap-API-mass spectrometer Finnigan LCQDeca (Thermo Quest). High-resolution mass spectra were measured on a UHR-QTOF maxis 4G (BrukerDaltonics). Infrared spectra were recorded with a Shimadzu IR Affinity-1 with ATR technique. The intensities of signals are abbreviated as s (strong), m (medium), and w (weak). Absorption spectra were recorded in CH_2Cl_2 or cyclohexane UVASOL® at 298 K with a Perkin–Elmer UV/Vis/NIR Lambda 19 Spectrometer. Emission spectra were recorded in CH_2Cl_2 or cyclohexane UVASOL® at 298 K with a Perkin–Elmer LS55 spectrometer.

General Procedure for the Three-Component Synthesis of 2-[2′-Halo(hetero)aryl]-(1*H*-pyrrol-3-yl)methanones 4: Palladium(II) chloride (0.25 mol-%) and di(1-adamantyl)benzylphosphonium hydrobromide (0.50 mol-%) were placed in a dry Schlenk tube under an argon atmosphere and dry dichloromethane (8–20 mL) was added. (Hetero)aroyl chloride **1** (8–20.0 mmol), alkyne **2** (8–20.0 mmol), and reagent grade triethylamine (1.2–3.0 mL, 110 mol-%) were added, and the mixture was stirred at room temperature for 3–23 h (t_1) until complete conversion (monitored by TLC; for experimental details see Table 9). Aminoacetaldehyde diethyl acetal (**3**; 1.03 equiv.) was added and the reaction mixture was stirred for 19 h at 40 °C (oil bath). Then, the reaction mixture was cooled to room temperature and methanesulfonic acid (1.50 equiv.) was successively added. After stirring for 24 h at 40 °C (oil bath) the reaction mixture was cooled to room temperature. The solvents were removed in vacuo and the residue was purified by flash chromatography on silica gel (hexane/ethyl acetate, 4:1) to give compounds **4** as pale yellow to red solids or brownish resins and oils.

(2-Fluorophenyl)(2-phenyl-1*H*-pyrrol-3-yl)methanone (4a): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 5:2) 2.39 g (45%) of compound **4a** was obtained as a red solid, m.p. 118 °C. R_f (*n*-hexane/acetone, 4:1) = 0.10. ^{1}H NMR (600 MHz, [D_6]DMSO): δ = 6.33 (t, J = 2.6 Hz, 1 H), 6.90 (t, J = 2.7 Hz, 1 H), 7.08–7.12 (m, 1 H), 7.15 (t, J = 7.4 Hz, 1 H), 7.25–7.31 (m, 3 H), 7.37–7.43 (m, 2 H), 7.44–7.47 (m, 2 H), 11.87 (s, 1 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 112.4 (CH), 115.6 (d, J = 21.6 Hz, CH), 119.0 (CH), 120.6 (C_{quat}), 124.0 (d, J = 3.1 Hz, CH), 127.7 (2 CH), 127.8 (CH), 128.9 (2 CH), 129.6 (d, J = 15.5 Hz, C_{quat}), 129.8 (d, J = 3.2 Hz, CH), 131.7 (C_{quat}), 131.9 (d, J = 8.3 Hz, CH), 137.4 (C_{quat}), 158.8 (d, J = 247.8 Hz, C_{quat}), 187.3 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 265.1 (67) [M^+], 170.1 (100) [$M^+ - C_6H_4F$], 142.1 (8) [$M^+ - C_7H_4FO$], 123.0 (9) [$M^+ - C_{10}H_8N$], 115.1 (59) [$M^+ - C_8H_6FNO$], 95.0 (23) [$M^+ - C_{11}H_8NO$]. IR: $\tilde{\nu}$ = 3233 [ν (N–H), m], 3109 (w), 2988 (m), 2972 (m), 2901 (m), 2795 (w), 1620 (s), 1609 [ν (C=O), s], 1578 (w), 1558 (w), 1474 (s), 1452 (s), 1431 (s), 1396 (s), 1362 (w), 1306 (m), 1290 (w), 1267 (w), 1225 (m), 1211 (w), 1177 (w), 1152 (w), 1101 (m), 1076 (m), 1057 (m), 999 (w), 901 (m), 885 (s), 812 (m), 787 (w), 756 (s), 739 (w), 721 (m), 689 (s), 677 (m), 654 (m), 613 (w) cm^{-1}. $C_{17}H_{12}FNO$ [265.3]: calcd. C 76.97, H 4.56, N 5.28; found C 76.77, H 4.75, N 5.03.

(2-*n*Butyl-1*H*-pyrrol-3-yl)(2-fluorophenyl)methanone (4b): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 5:1) 0.92 g (19%) of compound **4b** was obtained as a brown oil. R_f (*n*-hexane/acetone, 4:1) = 0.15. ^{1}H NMR (600 MHz, [D_6]DMSO): δ = 0.86 (t, J = 7.4 Hz, 3 H), 1.26 (h, J = 7.4 Hz, 2 H), 1.55 (tt, J = 7.7, 6.7 Hz, 2 H), 2.79–2.84 (m, 2 H), 6.01–6.04 (m, 1 H), 6.63 (dd, J = 3.0, 2.3 Hz, 1 H), 7.25–7.30 (m, 2 H), 7.41 (td, J = 7.3, 1.8 Hz, 1 H), 7.49–7.54 (m, 1 H), 11.47 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D_6]DMSO): δ = 13.7 (CH_3), 21.9 (CH_2), 26.5 (CH_2), 31.1 (CH_2), 111.2 (CH), 115.9 (d, J = 21.9 Hz, CH), 116.8 (CH), 119.4 (C_{quat}), 124.3 (d, J = 3.2 Hz, CH), 129.2 (d, J = 3.8 Hz, CH), 130.0 (d, J = 16.9 Hz, C_{quat}), 131.5 (d, J = 7.9 Hz, CH), 140.8 (C_{quat}), 158.4 (d, J = 246.9 Hz, C_{quat}), 187.2 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 245.2 (38) [M^+], 216.0 (27) [$M^+ - C_2H_5$], 202.1 (29) [$M^+ - C_3H_7$], 123.1 (100) [$M^+ - C_8H_{12}N$], 95.1 (19) [$M^+ - C_9H_{12}NO$]. IR: $\tilde{\nu}$ = 3350–3200 [ν (N–H), w], 2957 (w), 2930 (w), 2872 (w), 2860 (w), 1715 (w), 1611 [ν (C=O), s], 1557 (m), 1483 (m), 1456 (s), 1381 (m), 1350 (m), 1331 (m), 1269 (m), 1246 (m), 1223 (m), 1150 (w), 1101 (m), 1076 (w), 1032 (w), 999 (w), 947 (w), 916 (w), 885 (s), 862 (w), 843 (w), 812 (m), 754 (s), 719 (m), 691 (w), 650 (m), 615 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{16}FNO+H^+$ 246.12887; found 246.12834.

(2-Cyclopropyl-1*H*-pyrrol-3-yl)(2-fluorophenyl)methanone (4c): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 5:1 to 4:1) 1.05 g (23%) of compound **4c** was obtained as a reddish brown resin. R_f (*n*-hexane/acetone, 4:1) = 0.19. ^{1}H NMR (300 MHz, [D_6]DMSO): δ = 0.79–0.86 (m, 2 H), 0.86–0.95 (m, 2 H), 2.59 (tt, J = 8.5, 5.5 Hz, 1 H),

Table 9. Experimental details for the three-component synthesis of 2-[2′-halo(hetero)aryl]-substituted (1*H*-pyrrol-3-yl)methanones **4**.

Entry	Acid chloride **1**	Alkyne **2**	t_1 [h]	Aminoacetaldehyde diethyl acetal **3**	Methanesulfonic acid	Methanones **4**
1	3.24 g (20.0 mmol), **1a**	2.09 g (20.0 mmol), **2a**	3.5	2.79 g (20.6 mmol)	2.88 g (30.0 mmol)	2.39 g (45%), **4a**
2	3.24 g (20.0 mmol), **1a**	1.67 g (20.0 mmol), **2b**	23	2.79 g (20.6 mmol)	2.88 g (30.0 mmol)	0.92 g (19%), **4b**
3	3.24 g (20.0 mmol), **1a**	1.37 g (20.0 mmol), **2c**	21	2.79 g (20.6 mmol)	2.88 g (30.0 mmol)	1.05 g (23%), **4c**
4	4.28 g (20.0 mmol), **1b**	2.09 g (20.0 mmol), **2a**	3	2.79 g (20.6 mmol)	2.88 g (30.0 mmol)	3.60 g (57%), **4d**
5	3.56 g (20.0 mmol), **1c**	2.09 g (20.0 mmol), **2a**	4	2.79 g (20.6 mmol)	2.88 g (30.0 mmol)	2.50 g (44%), **4e**
6	1.42 g (8.00 mmol), **1c**	1.32 g (8.00 mmol), **2d**	2.75	1.11 g (8.20 mmol)	1.165 g (12.00 mmol)	1.466 g (54%), **4f**
7	3.56 g (20.0 mmol), **1c**	1.37 g (20.0 mmol), **2c**	22	2.79 g (20.6 mmol)	2.88 g (30.0 mmol)	1.92 g (39%), **4g**
8	4.58 g (20.0 mmol), **1d**	2.09 g (20.0 mmol), **2a**	5.3	2.79 g (20.6 mmol)	2.88 g (30.0 mmol)	4.83 g (74%), **4h**
9	1.83 g (8.00 mmol), **1d**	0.948 g (8.000 mmol), **2e**	3	1.11 g (8.20 mmol)	1.165 g (12.00 mmol)	0.785 g (29%), **4i**
10	2.75 g (12.0 mmol), **1d**	0.82 g (12.0 mmol), **2c**	21	1.69 g (12.4 mmol)	1.75 g (18.0 mmol)	0.763 g (22%), **4j**

6.00 (ddd, *J* = 3.1, 2.3, 1.4 Hz, 1 H), 6.56 (d, *J* = 3.1, 2.4 Hz, 1 H), 7.24–7.32 (m, 2 H), 7.40–7.49 (m, 1 H), 7.49–7.56 (m, 1 H), 11.05 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 8.7 (2 CH_2), 8.7 (CH), 111.3 (d, *J* = 1.5 Hz, CH), 115.9 (d, *J* = 21.7 Hz, CH), 116.6 (CH), 120.8 (C_{quat}), 124.3 (d, *J* = 3.4 Hz, CH), 129.2 (d, *J* = 3.9 Hz, CH), 130.2 (d, *J* = 16.9 Hz, C_{quat}), 131.5 (d, *J* = 8.1 Hz, CH), 142.2 (C_{quat}), 158.4 (d, *J* = 246.7 Hz, C_{quat}), 187.3 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 229.1 (9) [M$^+$], 228.1 (10) [M$^+$ – H], 215.1 (14) [M$^+$ – CH_2], 214.1 (100) [M$^+$ – CH_3], 201.1 (7) [M$^+$ – C_2H_4], 134.1 (15) [M$^+$ – C_6H_4F], 123.1 (22) [M$^+$ – C_7H_8N], 106.1 (30) [M$^+$ – C_7H_4FO], 95.1 (26) [M$^+$ – C_8H_8NO]. IR: $\tilde{\nu}$ = 3267 [ν (N–H), w], 1709 (w), 1607 [ν (C=O), m], 1562 (m), 1484 (m), 1456 (m), 1393 (m), 1350 (m), 1317 (w), 1273 (m), 1248 (w), 1221 (m), 1202 (m), 1188 (w), 1177 (w), 1157 (w), 1148 (w), 1126 (w), 1096 (w), 1072 (w), 1057 (w), 1022 (w), 953 (w), 920 (w), 883 (w), 872 (w), 841 (w), 808 (m), 841 (m), 808 (m), 783 (w), 754 (s), 719 (m), 683 (m), 665 (m), 631 (m), 615 (m) cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{12}FNO+H^+$ 230.09757; found 230.09722.

(2,4-Dichlorophenyl)(2-phenyl-1*H*-pyrrol-3-yl)methanone (4d): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 5:2) 3.60 g (57%) of compound **4d** was obtained as a pale orange solid, m.p. 167 °C. R_f (*n*-hexane/acetone, 4:1) = 0.19. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 6.28 (t, *J* = 2.8 Hz, 1 H), 6.90 (t, *J* = 2.7 Hz, 1 H), 7.30 (dt, *J* = 4.5, 2.8 Hz, 3 H), 7.31–7.33 (m, 2 H), 7.41–7.45 (m, 2 H), 7.51 (d, *J* = 1.7 Hz, 1 H), 11.91 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]-DMSO): δ = 112.3 (CH), 119.3 (CH), 119.9 (C_{quat}), 126.9 (CH), 127.7 (2 CH), 127.9 (CH), 128.9 (CH), 129.0 (2 CH), 130.1 (CH), 130.8 (C_{quat}), 131.5 (C_{quat}), 134.2 (C_{quat}), 138.0 (C_{quat}), 139.5 (C_{quat}), 188.0 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 317.1 (18) [M$^+$($Cl^{37}Cl^{35}$)], 315.1 (26) [M$^+$(Cl_2^{35})], 280.1 (6) [M$^+$(Cl_2^{35}) – Cl^{35}], 170.1 (100) [M$^+$ – $C_6H_3Cl_2$], 147.0 (8) [M$^+$($Cl^{37}Cl^{35}$) – $C_{11}H_8NO$], 145.0 (12) [M$^+$(Cl_2^{35}) – $C_{11}H_8NO$], 141.1 (8) [M$^+$ – $C_7H_3Cl_2O$], 115.1 (65) [M$^+$ – $C_8H_5Cl_2NO$], 111.0 (7) [M$^+$(Cl^{37}) – $C_{11}H_8ClNO$], 109.0 (19) [M$^+$(Cl^{35}) – $C_{11}H_8ClNO$]. IR: $\tilde{\nu}$ = 3237 [ν (N–H), m], 1599 [ν (C=O), s], 1587 (s), 1576 (m), 1556 (m), 1526 (w), 1464 (w), 1445 (s), 1435 (s), 1377 (m), 1341 (m), 1294 (m), 1182 (w), 1101 (m), 1074 (m), 912 (m), 881 (s), 827 (m), 791 (m), 779 (m), 762 (s), 743 (m), 718 (m), 696 (s), 683 (w), 669 (w) cm^{-1}. $C_{17}H_{11}Cl_2NO$ [316.2]: calcd. C 64.58, H 3.51, N 4.43; found C 64.40, H 3.63, N 4.28.

(2-Chloropyridin-3-yl)(2-phenyl-1*H*-pyrrol-3-yl)methanone (4e): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 2:1) 2.50 g (44%) of compound **4e** was obtained as a pale yellow solid, m.p. 195 °C. R_f (*n*-hexane/acetone, 4:1) = 0.05. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 6.32 (dd, *J* = 3.0, 2.4 Hz, 1 H), 6.91 (t, *J* = 2.8 Hz, 1 H), 7.24–7.33 (m, 4 H), 7.38–7.45 (m, 2 H), 7.75 (dd, *J* = 7.5, 1.9 Hz, 1 H), 8.32 (dd, *J* = 4.9, 1.9 Hz, 1 H), 11.95 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]-DMSO): δ = 112.1 (CH), 119.5 (CH), 119.9 (C_{quat}), 122.6 (CH), 127.8 (2 CH), 128.1 (CH), 129.0 (2 CH), 131.4 (C_{quat}), 136.7 (C_{quat}), 137.8 (CH), 138.3 (C_{quat}), 145.9 (C_{quat}), 149.8 (CH), 187.3 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 284.1 (13) [M$^+$(Cl^{37})], 282.1 (34) [M$^+$(Cl^{35})], 247.1 (2) [M$^+$ – Cl], 170.1 (100) [M$^+$ – C_5H_3ClN], 142.1 (9) [M$^+$ – C_7H_3ClNO], 141.1 (9) [M$^+$ – C_6H_4ClNO], 115.1 (68) [M$^+$ – $C_7H_5ClN_2O$], 114.1 (14) [M$^+$(Cl^{37}) – $C_{11}H_8NO$] 112.0 (13) [M$^+$(Cl^{35}) – $C_{11}H_8NO$]. IR: $\tilde{\nu}$ = 3202 [ν (N–H), m], 3144 (w), 3088 (w), 1649 [ν (C=O), s], 1601 (w), 1576 (m), 1557 (m), 1470 (m), 1450 (m), 1433 (m), 1393 (s), 1321 (w), 1298 (s), 1277 (w), 1258 (w), 1244 (w), 1207 (w), 1128 (w), 1098 (m), 1070 (m), 1057 (m), 1032 (m), 901 (m), 880 (s), 862 (w), 820 (s), 779 (s), 754 (s), 727 (s), 692 (s), 679 (s), 652 (m), 613 (w) cm^{-1}. $C_{16}H_{11}ClN_2O$ [282.7]: calcd. C 67.97, H 3.92, N 9.91; found C 68.03, H 4.14, N 9.63.

{2-[4-(*tert*-Butyl)phenyl]-1*H*-pyrrol-3-yl}(2-chloropyridin-3-yl)-methanone (4f): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 2:1) 1.466 g (54%) of compound **4f** was obtained as a pale yellow solid, m.p. 183 °C. R_f (*n*-hexane/acetone, 3:1) = 0.14. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 1.27 (s, 9 H), 6.33 (t, *J* = 2.8 Hz, 1 H), 6.91 (t, *J* = 2.8 Hz, 1 H), 7.25–7.27 (m, 1 H), 7.27–7.30 (m, 2 H), 7.32–7.35 (m, 2 H), 7.70 (dd, *J* = 7.5, 1.9 Hz, 1 H), 8.30 (dd, *J* = 4.8, 1.9 Hz, 1 H), 11.89 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 30.9 (3 CH_3), 34.3 (C_{quat}), 111.9 (CH), 119.3 (CH), 119.9 (C_{quat}), 122.5 (CH), 124.5 (2 CH), 128.5 (C_{quat}), 128.8 (2 CH), 136.7 (C_{quat}), 137.6 (CH), 138.6 (C_{quat}), 145.9 (C_{quat}), 149.7 (CH), 150.6 (C_{quat}), 187.2 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 340.3 (32) [M$^+$(Cl^{37})], 338.3 (100) [M$^+$(Cl^{35})], 325.2 (34) [M$^+$(Cl^{37}) – CH_3], 323.2 (85) [M$^+$(Cl^{35}) – CH_3], 287.3 (32) [M$^+$ – CH_3Cl], 283.2 (3) [M$^+$(Cl^{37}) – C_4H_9], 281.2 (9) [M$^+$(Cl^{35}) – C_4H_9], 272.2 (19) [M$^+$ – C_2H_6Cl], 226.1 (13) [M$^+$ – C_5H_3ClN], 210.2 (19) [M$^+$ – C_6H_6ClN], 168.2 (15) [M$^+$ – $C_9H_{12}ClN$], 142.1 (20) [M$^+$(Cl^{37}) – $C_{14}H_{16}N$], 140.1 (47) [M$^+$(Cl^{35}) – $C_{14}H_{16}N$], 114.1 (35.8) [M$^+$(Cl^{37}) – $C_{15}H_{16}NO$] 112.1 (34) [M$^+$(Cl^{35}) – $C_{15}H_{16}NO$]. IR: $\tilde{\nu}$ = 3211 [ν (N–H), w], 3076 (w), 2970 (w), 2951 (w), 2905 (w), 2884 (w), 2866 (w), 1649 [ν (C=O), s], 1612 (w), 1576 (w), 1557 (w), 1518 (w), 1508 (w), 1474 (w), 1445 (m), 1393 (m), 1366 (w), 1306 (w), 1296 (w), 1269 (w), 1207 (w), 1126 (w), 1105 (w), 1074 (w), 1057 (w), 1026 (w), 905 (w), 881 (s), 839 (s), 822 (m), 779 (w), 735 (s), 689 (w), 654 (w), 606 (w) cm^{-1}. $C_{20}H_{19}ClN_2O$ [338.8]: calcd. C 70.90, H 5.65, N 8.27; found C 71.16, H 5.56, N 8.10.

(2-Chloropyridin-3-yl)(2-cyclopropyl-1*H*-pyrrol-3-yl)methanone (4 g): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 5:2 to 3:2) 1.92 g (39%) of compound **4g** was obtained as a yellow solid, m.p. 162 °C. R_f (*n*-hexane/acetone, 4:1) = 0.08. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 0.80–0.84 (m, 2 H), 0.84–0.89 (m, 2 H), 2.43 (td, *J* = 8.4, 4.6 Hz, 1 H), 5.97 (t, *J* = 2.7 Hz, 1 H), 6.59 (t, *J* = 2.7 Hz, 1 H), 7.51 (dd, *J* = 7.5, 4.8 Hz, 1 H), 7.88 (dd, *J* = 7.5, 2.0 Hz, 1 H), 8.49 (dd, *J* = 4.8, 1.9 Hz, 1 H), 11.16 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 8.6 (2 CH_2), 8.8 (CH), 111.0 (CH), 117.2 (CH), 120.1 (C_{quat}), 123.1 (CH), 137.3 (C_{quat}), 137.3 (CH), 142.7 (C_{quat}), 145.7 (C_{quat}), 149.9 (CH), 187.2 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 247.1 (9) [M$^+$(Cl^{37})], 245.1 (7) [M$^+$(Cl^{35})], 233.1 (33) [M$^+$(Cl^{37}) – CH_3], 231.1 (100) [M$^+$(Cl^{35}) – CH_3], 211.1 (27) [M$^+$ – Cl], 106.1 (56) [M$^+$ – C_6H_3ClNO]. IR: <= Gn=> = 3196 [ν (N–H), w], 3100 (w), 3042 (w), 2976 (w), 2938 (w), 2901 (w), 1722 (w), 1636 (m), 1618 (m), 1595 [ν (C=O), s], 1574 (s), 1501 (w), 1460 (s), 1422 (w), 1393 (s), 1358 (s), 1319 (w), 1300 (w), 1281 (w), 1260 (w), 1248 (w), 1231 (w), 1207 (w), 1198 (w), 1123 (m), 1094 (w), 1057 (s), 995 (w), 962 (w), 916 (m), 880 (s), 814 (s), 775 (s), 758 (m), 725 (s), 687 (m), 662 (m), 635 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{13}H_{11}ClN_2O+H^+$ 247.06327; found 247.06350.

(2-Chloro-5-nitrophenyl)(2-phenyl-1*H*-pyrrol-3-yl)methanone (4h): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 5:2) 4.83 g (74%) of compound **4h** was obtained as a pale beige solid, m.p. 195 °C. R_f (*n*-hexane/acetone, 3:1) = 0.23. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 6.42 (t, *J* = 2.7 Hz, 1 H), 6.95 (t, *J* = 2.8 Hz, 1 H), 7.22–7.27 (m, 3 H), 7.36–7.41 (m, 2 H), 7.66 (d, *J* = 8.8 Hz, 1 H), 8.06 (d, *J* = 2.8 Hz, 1 H), 8.11 (dd, *J* = 8.8, 2.8 Hz, 1 H), 12.00 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 112.0 (CH), 119.6 (CH), 119.7 (C_{quat}), 123.8 (CH), 125.0 (CH), 127.7 (2 CH), 128.1 (CH), 129.1 (2 CH), 131.1 (CH), 131.4 (C_{quat}), 136.6 (C_{quat}), 138.7 (C_{quat}),

141.2 (C_{quat}), 145.7 (C_{quat}), 186.4 (C_{quat}) ppm. MS (EI) [70 eV]: *m/z* (%) = 328.1 (11.6) [$M^+(Cl^{37})$], 326.1 (34.6) [$M^+(Cl^{35})$], 281.1 (1) [$M^+(Cl^{37}) - NO_2$], 279.1 (3) [$M^+(Cl^{35}) - NO_2$], 244.1 (3) [$M^+ - ClNO_2$], 170.1 (100) [$M^+ - C_6H_3ClNO_2$], 142.1 (7) [$M^+ - C_7H_3ClNO_3$], 115.1 (42) [$M^+ - C_9H_5ClNO_3$]. IR: ṽ = 3296 [ν (N–H), w], 2980 (w), 2970 (w), 2361 (w), 2342 (w), 1609 [ν (C=O), s], 1572 (w), 1555 (w), 1524 (s), 1468 (m), 1435 (s), 1344 [ν (Ar-NO_2), s], 1294 (w), 1287 (m), 1273 (w), 1252 (w), 1173 (w), 1069 (w), 1051 (w), 937 (w), 907 (w), 893 (w), 853 (s), 770 (s), 758 (m), 739 (s), 718 (m), 700 (s), 654 (m), 613 (w) cm^{-1}. $C_{17}H_{11}ClN_2O_3$ [326.7]: calcd. C 62.49, H 3.39, N 8.57; found C 62.40, H 3.32, N 8.31.

(2-Chloro-5-nitrophenyl)[2-(*p*-tolyl)-1*H*-pyrrol-3-yl]methanone (4i): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 3:1) 0.785 g (29%) of compound **4i** was obtained as an orange solid, m.p. 219 °C. R_f (*n*-hexane/acetone, 3:1) = 0.23. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 2.25 (s, 3 H), 6.37 (t, *J* = 2.7 Hz, 1 H), 6.92 (t, *J* = 2.8 Hz, 1 H), 7.06 (d, *J* = 7.8 Hz, 2 H), 7.28–7.32 (m, 2 H), 7.67 (d, *J* = 8.8 Hz, 1 H), 8.04 (d, *J* = 2.7 Hz, 1 H), 8.13 (dd, *J* = 8.8, 2.8 Hz, 1 H), 11.95 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 20.7 (CH_3), 112.0 (CH), 119.4 (CH), 119.5 (C_{quat}), 123.7 (CH), 124.9 (CH), 128.2 (2 CH), 128.5 (C_{quat}), 129.0 (2 CH), 131.1 (CH), 136.6 (C_{quat}), 137.6 (C_{quat}), 138.8 (C_{quat}), 141.3 (C_{quat}), 145.7 (C_{quat}), 186.3 (C_{quat}) ppm. MS (EI) [70 eV]: *m/z* (%) = 342.2 (16.6) [$M^+(Cl^{37})$], 340.2 (39.0) [$M^+(ClP^{35})$], 327.2 (1) [$M^+(Cl^{37}) - CH_3$], 235.2 (3) [$M^+(Cl^{35}) - CH_3$], 294.2 (2) [$M^+(Cl^{35}) - NO_2$], 259.2 (3) [$M^+ - ClNO_2$], 184.2 (100) [$M^+ - C_6H_3ClNO_2$], 156.2 (6) [$M^+ - C_7H_3ClNO_3$], 129.2 (34) [$M^+ - C_9H_5ClNO_3$]. IR: ṽ = 3186 [ν (N–H), w], 3134 (w), 3117 (w), 3073 (w), 3003 (w), 2949 (w), 2916 (w), 2859 (w), 1605 [ν (C=O), s], 1570 (w), 1518 (s), 1472 (w), 1441 (s), 1395 (w), 1375 (w), 1344 [ν (Ar-NO_2), s], 1302 (w), 1271 (w), 1248 (w), 1179 (w), 1103 (w), 1080 (w), 1057 (w), 1007 (w), 941 (w), 897 (w), 881 (w), 854 (s), 843 (w), 820 (s), 787 (w), 741 (m), 725 (m), 716 (w), 702 (w), 660 (w), 625 (w) cm^{-1}. $C_{18}H_{13}ClN_2O_3$ [340.8]: calcd. C 63.44, H 3.85, N 8.22; found C 63.19, H 3.93, N 7.94.

(2-Chloro-5-nitrophenyl)(2-cyclopropyl-1*H*-pyrrol-3-yl)methanone (4j): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 3:1 to 5:2) 0.763 g (22%) of compound **4j** was obtained as a pale beige solid, m.p. 121 °C. R_f (*n*-hexane/acetone, 4:1) = 0.23. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 0.80–0.94 (m, 4 H), 1.08–1.20 (m, 1 H), 6.01 (dd, *J* = 3.1, 2.3 Hz, 1 H), 6.58–6.62 (m, 1 H), 7.84 (d, *J* = 8.8 Hz, 1 H), 8.18 (d, *J* = 2.7 Hz, 1 H), 8.29 (dd, *J* = 8.8, 2.8 Hz, 1 H), 11.21 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 8.7 (2 CH_2), 8.8 (CH), 111.2 (CH), 117.3 (CH), 119.7 (C_{quat}), 123.0 (CH), 125.0 (CH), 131.3 (CH), 136.2 (C_{quat}), 142.0 (C_{quat}), 143.1 (C_{quat}), 146.2 (C_{quat}), 186.5 (C_{quat}) ppm. MS (EI) [70 eV]: *m/z* (%) = 292.1 (23) [$M^+(Cl^{37})$], 290.2 (50) [$M^+(Cl^{35})$], 277.1 (33) [$M^+(Cl^{37}) - CH_3$], 275.1 (100) [$M^+(Cl^{35}) - CH_3$], 264.1 (4) [$M^+(Cl^{37}) - CH_2N$], 262.1 (8) [$M^+(Cl^{35}) - CH_2N$], 255.1 (8) [$M^+ - Cl$], 231.1 (9), 229.2 (34), 208.1 (16) [$M^+ - ClNO_2$], 154.1 (10) [$M^+(Cl^{37}) - C_8H_6NO$], 152.2 (19) [$M^+(Cl^{35}) - C_8H_6NO$], 134.1 (43) [$M^+ - C_6H_3ClNO_2$], 106.1 (73) [$M^+ - C_7H_5ClN_2O_2$], 79.1 (79) [$M^+ - C_8H_5ClN_2O_3$]. IR: ṽ = 3265 [ν (N–H), w], 3152 (w), 3105 (w), 3086 (w), 3067 (w), 2361 (w), 1607 [ν (C=O), s], 1560 (w), 1524 (s), 1501 (w), 1449 (m), 1387 (w), 1346 [ν (Ar-NO_2), s], 1310 (w), 1292 (w), 1271 (w), 1256 (w), 1200 (w), 1184 (w), 1173 (w), 1132 (w), 1107 (w), 1090 (w), 1045 (m), 1024 (w), 943 (w), 912 (w), 895 (w), 872 (m), 851 (m), 827 (w), 806 (w), 781 (w), 760 (w), 733 (s), 719 (m), 691 (m), 667 (w), 642 (w), 656 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{14}H_{11}ClN_2O_3$+H^+ 291.05310; found 291.05334.

Typical Procedure for the Synthesis of (Aza)indazoles 6: 2-[2′-Halo(hetero)aryl]-(1*H*-pyrrol-3-yl)methanones **4** (1.0 equiv.) were placed in a dry Schlenk tube under an argon atmosphere and DMSO (3 mL) or DMSO (2 mL) and toluene (1 mL) were added. Then hydrazines **5** (1–3 equiv.) [for the hydrochloride of **5c** sodium acetate (62 mg, 0.75 mmol) was additionally added] were added and the reaction mixture was stirred at 130–140 °C (oil bath) for the time indicated (for experimental details see Table 10). After cooling to room temperature dichloromethane (50 mL) was added and the organic layer was extracted with saturated aqueous sodium hydrogen carbonate solution (15 mL). The aqueous layer was extracted with dichloromethane (2× 10 mL) and the combined organic layers were dried with anhydrous magnesium sulfate. The solvents were removed in vacuo and the residue, adsorbed on Celite®, was purified by flash chromatography on silica gel (hexane/ethyl acetate) to give compounds **6** as pale yellow to red solids or brownish resins and oils.

3-(2-Phenyl-1*H*-pyrrol-3-yl)-1*H*-indazole (6a): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 2:1 to 1:1) 104 mg (81%) of compound **6a** was obtained as a yellow solid, m.p. 90 °C. R_f (*n*-hexane/acetone, 1:1)

Table 10. Experimental details for the synthesis of 3-(1*H*-pyrrol-3-yl)indazoles **6**.

Entry	3-Acylpyrrole **4**	*t* [h]	Hydrazine **5**	Indazoles **6**
1	132 mg (0.50 mmol), **4a**	24	77 mg (1.50 mmol), hydrazine hydrate (**5a**)	104 mg (81%), **6a**
2	132 mg (0.50 mmol), **4a**	24	71 mg (1.50 mmol), methylhydrazine (**5b**)	112 mg (82%), **6b**
3	123 mg (0.50 mmol), **4b**	22	154 mg (3.00 mmol), hydrazine hydrate (**5a**)	59 mg (49%), **6c**
4	115 mg (0.50 mmol), **4c**	4	77 mg (1.50 mmol), hydrazine hydrate (**5a**)	70 mg (63%), **6d**
5	158 mg (0.50 mmol), **4d**	65.5	154 mg (3.00 mmol), hydrazine hydrate (**5a**)	105 mg (72%), **6e**
6	158 mg (0.50 mmol), **4d**	69	142 mg (3.00 mmol), methylhydrazine (**5b**)	77 mg (50%), **6f**
7	141 mg (0.50 mmol), **4e**	3	77 mg (1.50 mmol), hydrazine hydrate (**5a**)	107 mg (82%), **6g**
8	141 mg (0.50 mmol), **4e**	3	71 mg (1.50 mmol), methylhydrazine (**5b**)	117 mg (85%), **6h**
9	141 mg (0.50 mmol), **4e**	3	100 mg (0.61 mmol), benzylhydrazine hydrochloride (**5c**)[a]	87 mg (50%), **6i**
10	170 mg (0.50 mmol), **4f**	3	77 mg (1.50 mmol), hydrazine hydrate (**5a**)	142 mg (90%), **6j**
11	170 mg (0.50 mmol), **4f**	3	71 mg (1.50 mmol), methylhydrazine (**5b**)	154 mg (93%), **6k**
12	123 mg (0.50 mmol), **4g**	3	77 mg (1.50 mmol), hydrazine hydrate (**5a**)	87 mg (78%), **6l**
13	123 mg (0.50 mmol), **4g**	3	71 mg (1.50 mmol), methylhydrazine (**5b**)	69 mg (58%), **6m**
14	164 mg (0.50 mmol), **4h**	5.3	77 mg (1.50 mmol), hydrazine hydrate (**5a**)	126 mg (83%), **6n**
15	327 mg (1.00 mmol), **4h**	3	142 mg (3.00 mmol), methylhydrazine (**5b**)	245 mg (77%), **6o**
16	171 mg (0.50 mmol), **4i**	3	71 mg (1.50 mmol), methylhydrazine (**5b**)	124 mg (75%), **6p**
17	146 mg (0.50 mmol), **4j**	3	77 mg (1.50 mmol), hydrazine hydrate (**5a**)	87 mg (65%), **6q**
18	146 mg (0.50 mmol), **4j**	3	71 mg (1.50 mmol), methylhydrazine (**5b**)	50 mg (35%), **6r**

[a] Sodium acetate (62 mg, 0.75 mmol) was added.

= 0.58. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 6.41 (t, J = 2.6 Hz, 1 H), 6.92 (dd, J = 8.2, 6.7 Hz, 1 H), 6.98 (t, J = 2.7 Hz, 1 H), 7.13–7.18 (m, 1 H), 7.22–7.25 (m, 2 H), 7.26–7.29 (m, 2 H), 7.45 (d, J = 7.6 Hz, 2 H), 7.48 (d, J = 8.5 Hz, 1 H), 11.37 (s, 1 H), 12.85 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 110.0 (CH), 111.1 (CH), 113.1 (C$_{quat}$), 118.7 (CH), 119.6 (CH), 120.9 (CH), 121.5 (C$_{quat}$), 125.6 (CH), 126.0 (CH), 126.9 (2 CH), 128.1 (2 CH), 128.9 (C$_{quat}$), 133.4 (C$_{quat}$), 140.8 (C$_{quat}$), 141.3 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 260.0 (13) [M$^+$], 259.0 (76) [M$^+$], 258.0 (100) [M$^+$], 257.0 (14) [M$^+$], 231.0 (6) [M$^+$ – CH$_2$N], 129.4 (9) [M$^+$ – C$_8$H$_8$N], 128.4 (9) [M$^+$ – C$_8$H$_8$N]. IR: $\tilde{\nu}$ = 3406 [ν (N–H), w], 3206–2870 (w), 1680 (w), 1589 (w), 1520 (w), 1495 (w), 1447 (w), 1398 (w), 1337 (w), 1292 (w), 1250 (w), 1219 (w), 1177 (w), 1148 (w), 1099 (w), 1067 (w), 1040 (w), 1003 (w), 935 (w), 905 (w), 893 (w), 847 (w), 745 (m), 692 (s), 638 (w), 623 (w), 614 (w) cm^{-1}. HRMS (ESI): calcd. for C$_{17}$H$_{13}$N$_3$ + H$^+$ 260.11822; found 260.11784.

1-Methyl-3-(2-phenyl-1*H*-pyrrol-3-yl)-1*H*-indazole (6b): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 3:1) 112 mg (81%) of compound **6b** was obtained as a yellow solid, m.p. 147 °C. R_f (*n*-hexane/acetone, 2:1) = 0.36. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 4.03 (s, 3 H), 6.38 (t, J = 2.6 Hz, 1 H), 6.90 (dd, J = 8.0, 6.9 Hz, 1 H), 6.97 (t, J = 2.7 Hz, 1 H), 7.13–7.17 (m, 2 H), 7.23 (t, J = 7.7 Hz, 2 H), 7.29–7.32 (m, 1 H), 7.40–7.44 (m, 2 H), 7.56 (d, J = 8.4 Hz, 1 H), 11.37 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 35.2 (CH$_3$), 109.5 (CH), 111.1 (CH), 112.7 (C$_{quat}$), 118.8 (CH), 119.6 (CH), 121.1 (CH), 121.8 (C$_{quat}$), 125.7 (CH), 126.1 (CH), 126.9 (2 CH), 128.2 (2 CH), 128.9 (C$_{quat}$), 133.3 (C$_{quat}$), 140.3 (C$_{quat}$), 140.5 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 274.2 (20) [M$^+$], 273.2 (100) [M$^+$], 272.2 (64) [M$^+$], 258.2 (13) [M$^+$ – CH$_3$], 257.2 (53) [M$^+$ – CH$_3$], 245.1 (2) [M$^+$ – CH$_2$N], 229.1 (4) [M$^+$ – C$_2$H$_5$N], 169.1 (5) [M$^+$ – C$_7$H$_7$N], 115.1 (13) [M$^+$ – C$_{11}$H$_{11}$N], 77.1 (8.4) [M$^+$ – C$_{12}$H$_{10}$N$_3$]. IR: $\tilde{\nu}$ = 3144–3015 [ν (N–H), w], 2967 (w), 2932 (w), 2855 (w), 2822 (w), 1616 (w), 1585 (w), 1524 (w), 1497 (w), 1433 (w), 1398 (w), 1342 (w), 1298 (w), 1254 (w), 1211 (w), 1188 (w), 1111 (w), 1040 (w), 916 (w), 893 (w), 773 (m), 764 (w), 741 (s), 696 (s), 687 (m), 627 (w) cm^{-1}. C$_{18}$H$_{15}$N$_3$ [273.3]: calcd. C 79.10, H 5.53, N 15.37; found C 78.83, H 5.57, N 15.09. HRMS (ESI): calcd. for C$_{18}$H$_{15}$N$_3$ + H$^+$ 274.13387; found 274.13397.

3-(2-Butyl-1*H*-pyrrol-3-yl)-1*H*-indazole (6c): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 3:1) 59 mg (49%) of compound **6c** was obtained as an orange red resin. R_f (*n*-hexane/acetone, 2:1) = 0.24. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 0.85 (t, J = 7.4 Hz, 3 H), 1.26–1.30 (m, 2 H), 1.56–1.62 (m, 2 H), 2.84–2.92 (m, 2 H), 6.44–6.48 (m, 1 H), 6.71 (t, J = 2.7 Hz, 1 H), 7.07 (t, J = 7.5 Hz, 1 H), 7.29–7.33 (m, 1 H), 7.47 (d, J = 8.3 Hz, 1 H), 7.84 (d, J = 8.1 Hz, 1 H), 10.78 (s, 1 H), 12.69 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 13.8 (CH$_3$), 22.0 (CH$_2$), 26.1 (CH$_2$), 31.8 (CH$_2$), 107.4 (CH), 109.9 (CH), 111.6 (C$_{quat}$), 115.9 (CH), 119.6 (CH), 121.0 (CH), 121.4 (C$_{quat}$), 125.6 (CH), 130.3 (C$_{quat}$), 140.7 (C$_{quat}$), 141.7 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 240.2 (11) [M$^+$], 239.2 (65) [M$^+$], 238.2 (3) [M$^+$], 210.1 (38) [M$^+$ – CH$_3$], 197.1 (40) [M$^+$ – C$_3$H$_7$], 196.1 (100) [M$^+$ – C$_3$H$_7$], 195.1 (18) [M$^+$ – C$_3$H$_7$], 169.1 (11) [M$^+$ – C$_4$H$_9$N], 167.1 (20) [M$^+$ – C$_4$H$_9$N], 115.1 (7) [M$^+$ – C$_8$H$_{12}$N], 77.1 (6) [M$^+$ – C$_9$H$_{13}$N$_3$]. IR: $\tilde{\nu}$ = 3400–3049 [ν (N–H), w], 2957 (w), 2928 (w), 2870 (w), 2860 (w), 2361 (s), 2342 (s), 1684 (w), 1620 (w), 1558 (w), 1520 (w), 1489 (w), 1456 (w), 1437 (w), 1418 (w), 1377 (w), 1337 (m), 1306 (w), 1290 (w), 1263 (m), 1248 (w), 1221 (w), 1180 (w), 1148 (w), 1126 (w), 1098 (w), 1072 (w), 1049 (w), 1005 (w), 959 (w), 905 (w), 893 (m), 841 (w), 772 (m), 735 (s), 700 (s), 640 (m), 611 (w) cm^{-1}. HRMS (ESI): calcd. for C$_{15}$H$_{17}$N$_3$ + H$^+$ 240.14952; found 240.14973.

3-(2-Cyclopropyl-1*H*-pyrrol-3-yl)-1*H*-indazole (6d): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 2:1 to 1:1) 70 mg (63%) of compound **6d** was obtained as a reddish solid. R_f (*n*-hexane/acetone, 2:1) = 0.54. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 0.71–0.75 (m, 2 H), 0.81–0.85 (m, 2 H), 1.03–1.20 (m, 1 H), 6.42 (t, J = 2.6 Hz, 1 H), 6.65 (t, J = 2.7 Hz, 1 H), 7.08 (dd, J = 8.1, 6.8 Hz, 1 H), 7.30–7.34 (m, 1 H), 7.49 (d, J = 8.3 Hz, 1 H), 7.86 (d, J = 8.1 Hz, 1 H), 10.43 (s, 1 H), 12.71 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 7.5 (2 CH$_2$), 8.5 (CH), 107.8 (CH), 110.0 (CH), 112.8 (C$_{quat}$), 115.7 (CH), 119.6 (CH), 121.0 (CH), 121.5 (C$_{quat}$), 125.6 (CH), 131.0 (C$_{quat}$), 140.8 (C$_{quat}$), 141.6 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 224.1 (9) [M$^+$], 223.1 (54) [M$^+$], 222.1 (13) [M$^+$], 209.1 (14) [M$^+$ – CH$_3$], 208.1 (100) [M$^+$ – CH$_3$], 195.1 (5) [M$^+$ – CH$_2$N], 194.1 (6) [M$^+$ – CH$_2$N], 181.1 (11) [M$^+$ – C$_2$H$_3$N], 77.1 (11) [M$^+$ – C$_8$H$_9$ClN$_3$]. IR: $\tilde{\nu}$ = 3400–3050 [ν (N–H), w], 2995 (w), 2968 (w), 2932 (w), 2907 (w), 2870 (w), 1682 (w), 1620 (w), 1591 (w), 1522 (w), 1495 (w), 1460 (w), 1342 (m), 1279 (w), 1248 (w), 1148 (w), 1126 (w), 1096 (w), 1072 (w), 1047 (w), 1072 (w), 1047 (m), 1022 (w), 1005 (w), 961 (m), 941 (w), 907 (w), 891 (m), 876 (w), 843 (w), 812 (w), 772 (m), 743 (s), 696 (s), 648 (w), 611 (w) cm^{-1}. HRMS (ESI): calcd. for C$_{14}$H$_{13}$N$_3$ + H$^+$ 224.11822; found 224.11841.

6-Chloro-3-(2-phenyl-1*H*-pyrrol-3-yl)-1*H*-indazole (6e): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 4:1) 105 mg (72%) of compound **6e** was obtained as an orange yellow solid. R_f (*n*-hexane/acetone, 1:1) = 0.64. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 6.40 (t, J = 2.5 Hz, 1 H), 6.92 (dd, J = 8.6, 1.8 Hz, 1 H), 6.98 (t, J = 2.7 Hz, 1 H), 7.15–7.18 (m, 1 H), 7.20 (d, J = 8.6 Hz, 1 H), 7.25 (t, J = 7.7 Hz, 2 H), 7.40–7.43 (m, 2 H), 7.54 (d, J = 1.8 Hz, 1 H), 11.40 (s, 1 H), 12.98 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 109.5 (CH), 111.0 (CH), 112.4 (C$_{quat}$), 118.9 (CH), 120.2 (C$_{quat}$), 120.3 (CH), 122.4 (CH), 126.2 (CH), 126.9 (2 CH), 128.2 (2 CH), 129.1 (C$_{quat}$), 130.7 (C$_{quat}$), 133.2 (C$_{quat}$), 141.2 (C$_{quat}$), 141.7 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 294.2 (42) [M$^+$(Cl^{37})], 293.2 (78) [M$^+$], 292.2 (100) [M$^+$(Cl^{35})], 265.1 (4) [M$^+$(Cl^{35}) – CH$_2$N], 257.2 (40) [M$^+$ – Cl], 229.2 (8) [M$^+$ – CH$_2$ClN], 115.1 (20) [M$^+$ – C$_{10}$H$_8$ClN], 77.1 (6) [M$^+$ – C$_{11}$H$_7$ClN$_3$]. IR: $\tilde{\nu}$ = 3400–3040 [ν (N–H), w], 1682 (w), 1614 (w), 1574 (w), 1516 (w), 1495 (w), 1447 (w), 1435 (w), 1398 (w), 1321 (w), 1298 (w), 1263 (w), 1229 (w), 1186 (w), 1134 (w), 1098 (w), 1061 (m), 1040 (w), 1022 (w), 997 (w), 922 (m), 895 (w), 845 (w), 799 (m), 768 (m), 758 (m), 739 (w), 694 (s), 658 (s), 638 (w), 617 (w) cm^{-1}.

6-Chloro-1-methyl-3-(2-phenyl-1*H*-pyrrol-3-yl)-1*H*-indazole (6f): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 3:1) 77 mg (50%) of compound **6f** was obtained as a yellow solid, m.p. 211 °C. R_f (*n*-hexane/acetone, 3:1) = 0.23. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 4.02 (s, 3 H), 6.38 (t, J = 2.6 Hz, 1 H), 6.90 (dd, J = 8.6, 1.7 Hz, 1 H), 6.98 (t, J = 2.7 Hz, 1 H), 7.08 (d, J = 8.5 Hz, 1 H), 7.15–7.19 (m, 1 H), 7.23–7.27 (m, 2 H), 7.38–7.41 (m, 2 H), 7.76 (d, J = 1.7 Hz, 1 H), 11.42 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 35.4 (CH$_3$), 109.3 (CH), 111.0 (CH), 112.0 (C$_{quat}$), 119.0 (CH), 120.2 (CH), 120.4 (C$_{quat}$), 122.6 (CH), 126.3 (CH), 127.0 (2 CH), 128.2 (2 CH), 129.1 (C$_{quat}$), 130.9 (C$_{quat}$), 133.1 (C$_{quat}$), 140.7 (C$_{quat}$), 141.0 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 309.2 (32) [M$^+$(Cl^{37})], 308.2 (44), 307.2 (100) [M$^+$(Cl^{35})], 306.2 (60), 293.2 (16) [M$^+$(Cl^{37}) – CH$_3$], 291.2 (42) [M$^+$(Cl^{35}) – CH$_3$], 271.2 (10) [M$^+$ – Cl], 257.2 (10) [M$^+$ – CH$_3$Cl], 228.9 (2) [M$^+$ – C$_2$H$_5$ClN], 167.9 (3) [M$^+$ – C$_7$H$_6$ClN], 140.1 (9) [M$^+$ – C$_8$H$_8$ClN$_2$], 115.1 (17) [M$^+$ – C$_9$H$_8$ClN$_3$], 104.1 (4) [M$^+$ – C$_{11}$H$_8$ClN$_2$], 77.0 (11) [M$^+$ – C$_{12}$H$_9$ClN$_3$], 75.1 (13) [M$^+$ – C$_{12}$H$_9$ClN$_3$]. IR: $\tilde{\nu}$ = 3159 [ν (N–H), w], 2980–2816 (w), 1609 (w), 1587 (w), 1524 (w), 1497 (w), 1458

(w), 1375 (w), 1343 (w), 1248 (w), 1207 (w), 1115 (w), 1067 (w), 947 (w), 928 (m), 916 (w), 893 (m), 851 (w), 806 (m), 768 (m), 756 (m), 737 (m), 696 (s), 687 (m), 665 (w), 654 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{15}N_3 + H^+$ 308.09490; found 308.09498.

3-(2-Phenyl-1*H*-pyrrol-3-yl)-1*H*-pyrazolo[3,4-*b*]pyridine (6g): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 1:1) 107 mg (82%) of compound **6g** was obtained as a pale yellow solid, m.p. 246 °C. R_f (*n*-hexane/acetone, 1:1) = 0.42. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 6.45 (d, J = 2.6 Hz, 1 H), 6.97 (dd, J = 8.0, 4.4 Hz, 1 H), 6.99 (d, J = 2.7 Hz, 1 H), 7.16–7.22 (m, 1 H), 7.26 (t, J = 7.7 Hz, 2 H), 7.41–7.46 (m, 2 H), 7.56 (dd, J = 8.0, 1.5 Hz, 1 H), 8.42 (dd, J = 4.5, 1.6 Hz, 1 H), 11.44 (s, 1 H), 13.39 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 110.7 (CH), 112.7 (C_{quat}), 113.0 (C_{quat}), 116.0 (CH), 119.0 (CH), 126.4 (CH), 127.2 (2 CH), 128.2 (2 CH), 129.2 (C_{quat}), 130.1 (CH), 133.2 (C_{quat}), 140.7 (C_{quat}), 148.3 (CH), 152.6 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 261.2 (11) [M$^+$], 260.2 (67) [M$^+$], 259.2 (100) [M$^+$], 258.2 (8) [M$^+$], 232.2 (7) [M$^+$ – CH_2N], 231.1 (6) [M$^+$ – CH_2N], 168.1 (2) [M$^+$ – $C_5H_4N_2$], 167.1 (3) [M$^+$ $C_5H_4N_2$], 140.2 (5) [M$^+$ – $C_6H_6N_3$], 77.1 (8) [M$^+$ – $C_{11}H_9N_3$]. IR: $\tilde{\nu}$ = 3215 [ν (N–H), w], 3144 (w), 3096 (w), 3034 (w), 3022 (w), 3009 (w), 2955 (w), 2897 (w), 2830 (w), 2785 (w), 2720 (w), 1611 (m), 1587 (m), 1558 (w), 1541 (w), 1522 (w), 1493 (w), 1447 (w), 1425 (m), 1408 (w), 1385 (w), 1362 (w), 1337 (w), 1287 (s), 1269 (w), 1238 (w), 1217 (w), 1184 (w), 1128 (w), 1101 (w), 1067 (w), 1022 (w), 920 (s), 910 (m), 893 (m), 851 (w), 839 (w), 802 (w), 775 (s), 762 (s), 741 (s), 694 (s), 665 (m), 625 (m), 610 (m) cm^{-1}. $C_{16}H_{12}N_4$ [260.3]: calcd. C 73.83, H 4.65, N 21.52; found C 73.64, H 4.74, N 21.25.

1-Methyl-3-(2-phenyl-1*H*-pyrrol-3-yl)-1*H*-pyrazolo[3,4-*b*]pyridine (6h): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 3:2) 117 mg (85%) of compound **6h** was obtained as a pale yellow solid, m.p. 162 °C. R_f (*n*-hexane/acetone, 1:1) = 0.62. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 4.05 (s, 3 H), 6.43 (t, J = 2.6 Hz, 1 H), 6.96 (dd, J = 8.1, 4.5 Hz, 1 H), 6.98 (t, J = 2.7 Hz, 1 H), 7.18–7.22 (m, 1 H), 7.25–7.29 (m, 2 H), 7.39–7.42 (m, 2 H), 7.43 (dd, J = 8.1, 1.5 Hz, 1 H), 8.46 (dd, J = 4.4, 1.6 Hz, 1 H), 11.43 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 33.4 (CH_3), 110.6 (CH), 112.4 (C_{quat}), 113.3 (C_{quat}), 116.0 (CH), 119.1 (CH), 126.5 (CH), 127.3 (2 CH), 128.3 (2 CH), 129.3 (C_{quat}), 130.5 (CH), 133.1 (C_{quat}), 139.6 (C_{quat}), 148.4 (CH), 150.6 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 276.2 (2) [M$^+$], 275.2 (18) [M$^+$], 274.2 (100) [M$^+$], 273.2 (76) [M$^+$], 258.3 (29) [M$^+$ – CH_3], 246.2 (3) [M$^+$ – CH_2N], 231.1 (4) [M$^+$ – C_2H_5N], 168.1 (2) [M$^+$ – $C_6H_6N_2$], 167.2 (2) [M$^+$ – $C_6H_6N_2$], 140.2 (4) [M$^+$ – $C_7H_8N_3$], 77.1 (6) [M$^+$ – $C_{11}H_9N_3$]. IR: $\tilde{\nu}$ = 3188 [ν (N–H), w], 3171 (w), 3107 (w), 3065 (w), 3044 (w), 3015 (w), 2978 (w), 2932 (w), 1591 (m), 1570 (w), 1524 (w), 1497 (w), 1472 (w), 1445 (w), 1418 (w), 1375 (w), 1300 (w), 1269 (m), 1234 (w), 1179 (w), 1119 (w), 1103 (w), 1070 (w), 1022 (w), 922 (w), 912 (w), 895 (m), 849 (w), 760 (s), 737 (m), 696 (s), 669 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{17}H_{14}N_4 + H^+$ 275.12912; found 275.12922.

1-Benzyl-3-(2-phenyl-1*H*-pyrrol-3-yl)-1*H*-pyrazolo[3,4-*b*]pyridine (6i): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 2:1) 87 mg (50%) of compound **6i** was obtained as a yellow solid, m.p. 187 °C. R_f (*n*-hexane/acetone, 2:1) = 0.27. ^{1}H NMR (600 MHz, [D$_6$]-DMSO): δ = 5.67 (s, 2 H), 6.47 (t, J = 2.6 Hz, 1 H), 7.00 (t, J = 2.7 Hz, 1 H), 7.06 (dd, J = 8.0, 4.5 Hz, 1 H), 7.18–7.21 (m, 1 H), 7.24 (dd, J = 8.4, 6.8 Hz, 2 H), 7.26–7.30 (m, 3 H), 7.31–7.34 (m, 2 H), 7.44–7.47 (m, 2 H), 7.67 (dd, J = 8.1, 1.5 Hz, 1 H), 8.50 (dd, J = 4.5, 1.5 Hz, 1 H), 11.47 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 49.7 (CH_2), 110.7 (CH), 112.1 (C_{quat}), 113.9 (C_{quat}), 116.5 (CH), 119.1 (CH), 126.4 (CH), 127.2 (2 CH), 127.4 (CH), 127.5 (2 CH), 128.2 (2 CH), 128.5 (2 CH), 129.4 (C_{quat}), 130.7 (CH), 133.0 (C_{quat}), 137.7 (C_{quat}), 140.2 (C_{quat}), 148.6 (CH), 150.5 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 351.2 (19) [M$^+$], 350.2 (75) [M$^+$], 349.2 (27) [M$^+$], 259.1 (26) [M$^+$ – C_7H_7], 258.2 (24) [M$^+$ – C_7H_7], 91.1 (100) [M$^+$ – $C_{16}H_{11}N_4$]. 77.1 (11) [M$^+$ – $C_{17}H_{13}N_4$]. IR: $\tilde{\nu}$ = 3256–3240 [ν (N–H), w], 3053 (w), 2980 (w), 2970 (w), 2947 (w), 2889 (w), 2361 (w), 2344 (w), 2324 (w), 1595 (w), 1570 (w), 1558 (w), 1524 (w), 1495 (w), 1456 (w), 1447 (w), 1425 (w), 1412 (w), 1375 (w), 1354 (w), 1294 (w), 1269 (w), 1258 (w), 1240 (w), 1225 (w), 1182 (w), 1111 (w), 1092 (w), 1070 (w), 1030 (w), 1013 (w), 970 (w), 941 (w), 920 (w), 910 (w), 889 (w), 845 (w), 822 (w), 806 (w), 773 (m), 766 (m), 741 (m), 696 (s), 673 (w), 642 (m) cm^{-1}. $C_{23}H_{18}N_4$ [350.4]: calcd. C 78.83, H 5.18, N 15.99; found C 78.55, H 5.16, N 15.70.

3-{2-[4-(*tert*-Butyl)phenyl]-1*H*-pyrrol-3-yl}-1*H*-pyrazolo[3,4-*b*]pyridine (6j): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 1:1) 142 mg (90%) of compound **6j** was obtained as a colorless solid, m.p. 247 °C. R_f (*n*-hexane/acetone, 2:1) = 0.25. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 1.25 (s, 9 H), 6.45 (t, J = 2.6 Hz, 1 H), 6.96 (t, J = 2.7 Hz, 1 H), 6.97–6.99 (m, 1 H), 7.28–7.31 (m, 2 H), 7.38–7.41 (m, 2 H), 7.61 (dd, J = 8.1, 1.5 Hz, 1 H), 8.43 (dd, J = 4.5, 1.6 Hz, 1 H), 11.33 (s, 1 H), 13.38 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 31.1 (CH_3), 34.2 (C_{quat}), 110.5 (CH), 112.4 (C_{quat}), 113.2 (C_{quat}), 116.0 (CH), 118.6 (CH), 124.8 (2 CH), 127.1 (2 CH), 129.3 (C_{quat}), 130.2 (CH), 130.4 (C_{quat}), 140.9 (C_{quat}), 148.3 (CH), 148.8 (C_{quat}), 152.4 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 317.1 (19) [M$^+$], 316.2 (100) [M$^+$], 315.2 (61) [M$^+$], 301.2 (85) [M$^+$ – CH_3], 285.1 (11) [M$^+$ – C_2H_6], 259.1 (22) [M$^+$ – C_4H_9], 143.1 (17) [M$^+$ – $C_{12}H_{16}N_2$]. IR: $\tilde{\nu}$ = 3215 (w), 3202 (w), 3148 (w), 3090 (w), 2980 (w), 2963 (m), 2899 (w), 2830 (w), 2783 (w), 2720 (w), 1611 (w), 1587 (w), 1528 (w), 1506 (w), 1458 (w), 1433 (w), 1383 (w), 1360 (w), 1287 (m), 1271 (w), 1117 (w), 1098 (w), 1067 (w), 939 (w), 920 (m), 835 (m), 800 (w), 773 (s), 750 (w), 733 (m), 702 (m), 673 (w), 658 (w), 611 (w) cm^{-1}. $C_{20}H_{20}N_4$ [316.4]: calcd. C 75.92, H 6.37, N 17.71; found C 75.95, H 6.52, N 17.54.

3-{2-[4-(*tert*-Butyl)phenyl]-1*H*-pyrrol-3-yl}-1-methyl-1*H*-pyrazolo[3,4-*b*]pyridine (6k): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 4:1) 154 mg (93%) of compound **6k** was obtained as a beige solid, m.p. 105 °C. R_f (*n*-hexane/acetone, 2:1) = 0.38. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 1.25 (s, 9 H), 4.06 (s, 3 H), 6.42 (t, J = 2.6 Hz, 1 H), 6.94 (dd, J = 8.0, 4.4 Hz, 1 H), 6.96 (t, J = 2.7 Hz, 1 H), 7.28–7.31 (m, 2 H), 7.36–7.39 (m, 2 H), 7.42 (dd, J = 8.0, 1.5 Hz, 1 H), 8.45 (dd, J = 4.5, 1.5 Hz, 1 H), 11.36 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 31.1 (CH_3), 33.4 (CH_3), 34.2 (C_{quat}), 110.5 (CH), 112.1 (C_{quat}), 113.4 (C_{quat}), 115.9 (CH), 118.7 (CH), 125.0 (2 CH), 127.1 (2 CH), 129.4 (C_{quat}), 130.3 (C_{quat}), 130.6 (CH), 139.7 (C_{quat}), 148.3 (CH), 149.0 (C_{quat}), 150.6 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 331.3 (22) [M$^+$], 330.3 (91) [M$^+$], 329.3 (14), 315.3 (100) [M$^+$ – CH_3], 299.2 (12), 273.2 (7) [M$^+$ – C_4H_9], 143.2 (14) [M$^+$ – $C_{13}H_{19}N_2$]. IR: $\tilde{\nu}$ = 3215 [ν (N–H), w], 2959 (w), 2903 (w), 2886 (w), 2357 (w), 2324 (w), 1697 (w), 1595 (w), 1570 (w), 1506 (m), 1458 (w), 1406 (w), 1395 (w), 1364 (w), 1310 (w), 1273 (s), 1242 (w), 1215 (w), 1202 (w), 1184 (w), 1121 (w), 1099 (w), 1061 (w), 1024 (w), 1001 (w), 968 (w), 949 (w), 922 (m), 893 (m), 837 (s), 802 (w), 772 (s), 750 (w), 733 (w), 702 (s), 683 (w), 662 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{22}N_4 + H^+$ 331.19172; found 331.19209.

3-(2-Cyclopropyl-1*H*-pyrrol-3-yl)-1*H*-pyrazolo[3,4-*b*]pyridine (6l): In accordance with the general procedure and after chromatography

on silica gel (*n*-hexane/ethyl acetate, 3:2) 87 mg (78%) of compound **6l** was obtained as a colorless solid, m.p. 199 °C. R_f (*n*-hexane/acetone, 1:1) = 0.64. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 0.69–0.79 (m, 2 H), 0.82–0.89 (m, 2 H), 2.57 (tt, J = 8.5, 5.4 Hz, 1 H), 6.47 (t, J = 2.6 Hz, 1 H), 6.66 (t, J = 2.7 Hz, 1 H), 7.15 (dd, J = 8.0, 4.5 Hz, 1 H), 8.33 (dd, J = 8.0, 1.6 Hz, 1 H), 8.48 (dd, J = 4.5, 1.6 Hz, 1 H), 10.51 (s, 1 H), 13.27 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 7.6 (CH$_2$), 8.5 (CH), 107.7 (CH), 112.5 (C$_{quat}$), 113.2 (C$_{quat}$), 115.9 (CH), 116.0 (CH), 130.4 (CH), 131.3 (C$_{quat}$), 141.3 (C$_{quat}$), 148.3 (CH), 152.3 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 225.2 (9) [M$^+$], 224.2 (48) [M$^+$], 223.1 (11) [M$^+$], 222.2 (3) [M$^+$], 209.1 (100) [M$^+$ – CH$_3$], 196.1 (5) [M$^+$ – CH$_2$N], 155.1 (4) [M$^+$ – C$_4$H$_7$N], 142.2 (4) [M$^+$ – C$_5$H$_8$N], 77.1 (10) [M$^+$ – C$_8$H$_9$N$_3$]. IR: $\tilde{\nu}$ = 3210 [ν (N–H), w], 3154 (w), 3094 (w), 3034 (w), 3001 (w), 2980 (w), 2951 (w), 2893 (w), 2824 (w), 2771 (w), 2720 (w), 1609 (m), 1589 (w), 1526 (w), 1506 (w), 1456 (w), 1433 (w), 1406 (w), 1389 (w), 1283 (s), 1254 (w), 1130 (w), 959 (w), 922 (m), 897 (m), 878 (w), 849 (w), 802 (w), 770 (s), 729 (m), 700 (s), 665 (w), 617 (w) cm^{-1}. HRMS (ESI): calcd. for C$_{13}$H$_{13}$N$_4$ + H$^+$ 225.11347; found 225.11349.

3-(2-Cyclopropyl-1*H*-pyrrol-3-yl)-1-methyl-1*H*-pyrazolo[3,4-*b*]pyridine (6m): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 3:2) 69 mg (58%) of compound **6m** was obtained as a yellow solid, m.p. 159 °C. R_f (*n*-hexane/acetone, 1:1) = 0.39. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 0.71–0.77 (m, 2 H), 0.83–0.90 (m, 2 H), 2.58 (tt, J = 8.6, 5.3 Hz, 1 H), 4.05 (s, 3 H), 6.46 (t, J = 2.6 Hz, 1 H), 6.66 (t, J = 2.8 Hz, 1 H), 7.17 (dd, J = 8.0, 4.5 Hz, 1 H), 8.34 (dd, J = 8.1, 1.5 Hz, 1 H), 8.52 (dd, J = 4.5, 1.5 Hz, 1 H), 10.53 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 7.7 (CH$_2$), 8.5 (CH), 33.4 (CH$_3$), 107.7 (CH), 112.2 (C$_{quat}$), 113.7 (C$_{quat}$), 116.0 (CH), 116.1 (CH), 130.8 (CH), 131.5 (C$_{quat}$), 140.1 (C$_{quat}$), 148.3 (CH), 150.4 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 239.2 (9) [M$^+$], 238.2 (57) [M$^+$], 237.2 (9) [M$^+$], 223.2 (100) [M$^+$ – CH$_3$], 210.2 (4) [M$^+$ – CH$_2$N], 208.2 (23) [M$^+$ – C$_2$H$_4$N], 195.1 (5) [M$^+$ – C$_2$H$_5$N], 182.1 (3) [M$^+$ – C$_3$H$_6$N], 77.1 (11) [M$^+$ – C$_9$H$_{11}$N$_3$]. IR: $\tilde{\nu}$ = 3208 [ν (N–H), w], 3179 (w), 3109 (w), 3083 (w), 3055 (w), 3044 (w), 3007 (w), 2932 (w), 2895 (w), 2849 (w), 1595 (m), 1568 (w), 1522 (w), 1501 (w), 1464 (w), 1437 (w), 1414 (w), 1373 (w), 1341 (w), 1308 (w), 1271 (s), 1236 (w), 1211 (w), 1165 (w), 1121 (w), 1103 (w), 1020 (w), 939 (m), 893 (m), 876 (w), 849 (w), 806 (w), 766 (s), 729 (m), 702 (m), 692 (m), 673 (w) cm^{-1}. C$_{14}$H$_{14}$N$_4$ [238.3]: calcd. C 70.57, H 5.92, N 23.51; found C 70.29, H 5.94, N 23.23.

5-Nitro-3-(2-phenyl-1*H*-pyrrol-3-yl)-1*H*-indazole (6n): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 2:1 to 1:1) 126 mg (83%) of compound **6n** was obtained as an orange solid, m.p. 268 °C. R_f (*n*-hexane/acetone, 1:1) = 0.56. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 6.50 (t, J = 2.6 Hz, 1 H), 7.04 (t, J = 2.7 Hz, 1 H), 7.16–7.23 (m, 1 H), 7.24–7.31 (m, 2 H), 7.41–7.46 (m, 2 H), 7.66 (d, J = 9.2 Hz, 1 H), 8.06 (d, J = 2.1 Hz, 1 H), 8.12 (dd, J = 9.1, 2.1 Hz, 1 H), 11.54 (s, 1 H), 13.55 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 110.8 (CH), 111.0 (CH), 111.6 (C$_{quat}$), 119.0 (CH), 119.3 (CH), 120.5 (C$_{quat}$), 120.7 (CH), 126.6 (CH), 127.4 (2 CH), 128.3 (2 CH), 129.7 (C$_{quat}$), 132.9 (C$_{quat}$), 140.9 (C$_{quat}$), 142.8 (C$_{quat}$), 144.6 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 305.0 (19) [M$^+$], 304.0 (100) [M$^+$], 303.0 (98) [M$^+$], 258.0 (16) [M$^+$ – NO$_2$], 257.0 (74) [M$^+$ – NO$_2$], 229.0 (14), 167.0 (5) [M$^+$ – C$_6$H$_5$N$_2$O$_2$], 128.9 (15) [M$^+$ – C$_8$H$_7$N$_3$O$_2$], 115.0 (22) [M$^+$ – C$_8$H$_6$N$_4$O$_2$]. IR: $\tilde{\nu}$ = 3360 [ν (N–H), w], 3163 (w), 3129 (w), 3092 (w), 3036 (w), 2982 (w), 2936 (w), 2905 (w), 2818 (w), 1620 (w), 1585 (w), 1518 (w), 1481 (m), 1445 (w), 1341 (s), 1319 [ν (Ar-NO$_2$), s], 1288 (m), 1180 (w), 1092 (s), 1061 (w), 1020 (w), 941 (w), 912 (w), 895 (w), 845 (w), 818 (w), 791 (w), 760 (m), 746 (s), 694 (s), 654 (w), 608 (w) cm^{-1}. C$_{17}$H$_{12}$N$_4$O$_2$ [304.3]: calcd. C 67.10, H 3.97, N 18.41; found C 66.99, H 4.05, N 18.31.

1-Methyl-5-nitro-3-(2-phenyl-1*H*-pyrrol-3-yl)-1*H*-indazole (6o): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 3:1) 245 mg (77%) of compound **6o** was obtained as an orange solid, m.p. 204 °C. R_f (*n*-hexane/acetone, 2:1) = 0.29. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 4.11 (s, 3 H), 6.47 (t, J = 2.6 Hz, 1 H), 7.03 (t, J = 2.7 Hz, 1 H), 7.17–7.24 (m, 1 H), 7.28 (ddt, J = 8.1, 6.3, 1.2 Hz, 2 H), 7.39–7.44 (m, 2 H), 7.77 (dd, J = 9.2, 0.6 Hz, 1 H), 7.91–7.93 (m, 1 H), 8.13 (dd, J = 9.2, 2.1 Hz, 1 H), 11.55 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 35.8 (CH$_3$), 110.6 (CH), 110.7 (CH), 111.2 (C$_{quat}$), 119.2 (CH), 119.4 (CH), 120.6 (CH), 126.8 (CH), 127.4 (2 CH), 128.4 (2 CH), 129.8 (C$_{quat}$), 132.8 (C$_{quat}$), 140.8 (2 C$_{quat}$), 142.3 (C$_{quat}$), 143.7 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 319.3 (20) [M$^+$], 318.2 (100) [M$^+$], 317.2 (20) [M$^+$], 223.2 (6) [M$^+$ – CH$_3$], 288.2 (1) [M$^+$ – CH$_2$N], 272.2 (12) [M$^+$ – NO$_2$], 271.2 (37) [M$^+$ – NO$_2$], 257.2 (19), 256.2 (12), 243.2 (9), 242.2 (5), 229.2 (11), 228.2 (12), 136.1 (8) [M$^+$ – C$_{12}$H$_{11}$N$_2$], 77.0 (10) [C$_6$H$_5^+$]. IR: $\tilde{\nu}$ = 3186 [ν (N–H), w], 3102 (w), 2980 (w), 1614 (w), 1518 (w), 1487 (w), 1325 [ν (Ar-NO$_2$), s], 1271 (w), 1238 (w), 1153 (w), 1113 (w), 1088 (w), 862 (w), 812 (w), 793 (w), 773 (m), 743 (m), 700 (s), 689 (w) cm^{-1}. C$_{18}$H$_{14}$N$_4$O$_2$ [318.3]: calcd. C 67.91, H 4.43, N 17.60; found C 67.81, H 4.52, N 17.32.

1-Methyl-5-nitro-3-[2-(*p*-tolyl)-1*H*-pyrrol-3-yl]-1*H*-indazole (6p): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 2:1) 124 mg (75%) of compound **6p** was obtained as an yellow solid. R_f (*n*-hexane/acetone, 2:1) = 0.30. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 2.25 (s, 3 H), 4.11 (s, 3 H), 6.46 (t, J = 2.6 Hz, 1 H), 7.00 (t, J = 2.7 Hz, 1 H), 7.06–7.12 (m, 2 H), 7.28–7.34 (m, 2 H), 7.76 (d, J = 9.2 Hz, 1 H), 7.94 (d, J = 2.1 Hz, 1 H), 8.13 (dd, J = 9.2, 2.1 Hz, 1 H), 11.48 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 20.7 (CH$_3$), 35.8 (CH$_2$), 110.5 (CH), 110.6 (CH), 110.9 (C$_{quat}$), 119.0 (CH), 119.3 (CH), 120.6 (CH), 120.7 (C$_{quat}$), 127.4 (2 CH), 128.9 (2 CH), 129.9 (C$_{quat}$), 130.0 (C$_{quat}$), 136.1 (C$_{quat}$), 140.8 (C$_{quat}$), 142.3 (C$_{quat}$), 143.8 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 333.3 (26) [M$^+$], 332.2 (100) [M$^+$], 331.2 (13) [M$^+$], 315.2 (7) [M$^+$ – CH$_3$], 304.2 (1) [M$^+$ – CH$_2$N], 286.2 (9) [M$^+$ – NO$_2$], 285.2 (28) [M$^+$ – NO$_2$], 271.1 (10), 270.1 (25), 257.0 (4), 243.0 (7), 181.0 (6), 156.0 (3), 140.0 (5), 77.0 (10) [C$_6$H$_5^+$]. IR: $\tilde{\nu}$ = 3271 [ν (N–H), w], 2982 (w) 2970 (w), 2940 (w), 2893 (w), 1614 (w), 1530 (w), 1508 (w), 1489 (m), 1456 (w), 1431 (w), 1410 (w), 1398 (w), 1323 [ν (Ar-NO$_2$), s], 1294 (w), 1269 (w), 1202 (w), 1192 (w), 1171 (w), 1107 (w), 1084 (m), 1051 (w), 1016 (w), 939 (w), 895 (w), 862 (w), 824 (m), 814 (m), 791 (m), 754 (m), 741 (s), 719 (s), 704 (w), 679 (w), 619 (w) cm^{-1}. C$_{18}$H$_{14}$N$_4$O$_2$ [318.3]: calcd. C 68.66, H 4.85, N 16.86; found C 68.52, H 4.89, N 16.62.

3-(2-Cyclopropyl-1*H*-pyrrol-3-yl)-5-nitro-1*H*-indazole (6q): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 3:2) 87 mg (65%) of compound **6q** was obtained as an orange solid. R_f (*n*-hexane/acetone, 2:1) = 0.25. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 0.74–0.80 (m, 2 H), 0.84–0.91 (m, 2 H), 2.47 (td, J = 8.5, 4.3 Hz, 1 H), 6.47 (t, J = 2.6 Hz, 1 H), 6.72 (t, J = 2.7 Hz, 1 H), 7.67 (d, J = 9.1 Hz, 1 H), 8.18 (dd, J = 9.1, 2.2 Hz, 1 H), 8.79 (d, J = 2.1 Hz, 1 H), 10.63 (s, 1 H), 13.44 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 7.7 (CH$_2$), 8.5 (CH), 107.8 (CH), 110.8 (CH), 111.4 (C$_{quat}$), 116.4 (CH), 119.1 (CH), 120.7 (C$_{quat}$), 120.8 (CH), 132.0 (C$_{quat}$), 141.0 (C$_{quat}$), 142.7 (C$_{quat}$), 144.9 (C$_{quat}$) ppm. MS (EI) [70 eV]: *m*/*z* (%)

= 269.2 (14) [M^+], 268.2 (74) [M^+], 267.1 (8) [M^+], 253.1 (100) [$M^+ - CH_3$], 221.1 (15) [$M^+ - NO_2$], 207.2 (92), 206.2 (17), 195.0 (8), 194.0 (9), 182.0 (4), 77.0 (15) [$C_6H_5^+$]. IR: $\tilde{\nu}$ = 3379 [ν (N–H), w], 3229 [ν (N–H), w], 3181 (w), 3105 (w), 3076 (w), 2995 (w), 1618 (w), 1593 (w), 1508 (m), 1477 (w), 1431 (w), 1393 (w), 1333 (s), 1312 [ν (Ar-NO_2), s], 1269 (m), 1194 (w), 1163 (w), 1132 (w), 1090 (m), 1065 (w), 1045 (w), 1034 (w), 1016 (w), 968 (w), 935 (w), 916 (w), 897 (w), 878 (w), 843 (m), 826 (w), 808 (w), 791 (m), 762 (w), 741 (s), 700 (s), 683 (m), 642 (w), 613 (w) cm^{-1}. $C_{14}H_{12}N_4O_2$ [268.3]: calcd. C 62.68, H 4.51, N 20.88; found C 62.42, H 4.71, N 20.62.

3-(2-Cyclopropyl-1*H*-pyrrol-3-yl)-1-methyl-5-nitro-1*H*-indazole (6r): In accordance with the general procedure and after chromatography on silica gel (*n*-hexane/ethyl acetate, 5:1) 50 mg (35%) of compound **6r** was obtained as an red brown solid. R_f (*n*-hexane/acetone, 2:1) = 0.33. ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 0.76–0.79 (m, 2 H), 0.87–0.91 (m, 2 H), 2.44–2.48 (m, 1 H), 4.11 (s, 3 H), 6.45 (t, J = 2.6 Hz, 1 H), 6.71 (t, J = 2.7 Hz, 1 H), 7.79 (t, J = 9.2 Hz, 1 H), 8.22 (dd, J = 9.2, 2.1 Hz, 1 H), 8.77 (d, J = 2.4 Hz, 1 H), 10.64 (s, 1 H) ppm. ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 7.8 (CH_2), 8.5 (CH), 35.7 (CH_3), 107.8 (CH), 110.4 (CH), 111.0 (C_{quat}), 116.6 (CH), 119.2 (CH), 120.7 (CH), 121.0 (C_{quat}), 132.1 (C_{quat}), 141.0 (C_{quat}), 142.1 (C_{quat}), 144.1 (C_{quat}) ppm. MS (EI) [70 eV]: *m*/*z* (%) = 283.2 (12) [M^+], 282.2 (68) [M^+], 281.2 (5) [M^+], 267.2 (100) [$M^+ - CH_3$], 235.2 (9) [$M^+ - NO_2$], 222.1 (13), 221.1 (67), 220.2 (15), 208.1 (11), 207.1 (12), 206.1 (18), 193.1 (11), 77.1 (14) [$C_6H_5^+$]. IR: $\tilde{\nu}$ = 3218 [ν (N–H), w], 3103 (w), 3078 (w), 3003 (w), 2990 (w), 2974 (w), 2936 (w), 2901 (w), 2870 (w), 1695 (w), 1612 (m), 1589 (w), 1520 (s), 1485 (m), 1456 (w), 1404 (w), 1323 [ν (Ar-NO_2), s], 1269 (m), 1236 (w), 1190 (w), 1177 (w), 1150 (w), 1086 (s), 1036 (m), 1018 (m), 953 (w), 905 (w), 880 (w), 862 (w), 837 (w), 806 (m), 789 (s), 762 (m), 741 (s), 729 (m), 694 (s), 667 (w), 648 (w), 627 (w) cm^{-1}. HRMS (ESI): calcd. for $C_{15}H_{14}N_4O_2$ + H^+: 283.11895, found 283.11890.

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