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New Application of Heterocyclic Diazonium Salts: Synthesis of New Pyrazolo[3,4-*d*][1,2,3]triazin-4-ones

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7-Substituted 3,7-dihydro-4*H*-pyrazolo[3,4-*d*][1,2,3]triazin-4-ones **2a**–**d** were conveniently prepared by direct diazotization of 5-aminopyrazole-4-carbonitriles **1a**–**d** in HCl media. Different reaction conditions and the effects of substituents on N-1 of the pyrazole ring were studied. A possible mechanistic exlpanation of the observed process is proposed.

Introduction

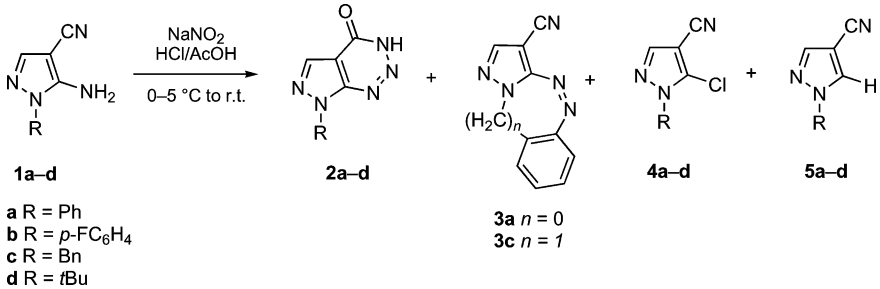
Polyfunctionally substituted heterocyclic compounds are present as important core structures in many biologically active compounds, both natural and synthetic. In this context, 5-aminopyrazoles are versatile reagents and have been extensively used as precursors in the preparation of several polysubstituted fused pyrazoles.[1] In addition, a large number of synthetic compounds containing the 1,2,3-triazine ring also present biological activity and nowadays are widely used as pharmaceuticals, herbicides, pesticides, dyes, etc.[2] As condensed heterocyclic systems are of considerable importance, not only for their potential biological activity but also because of their value as synthons in organic transformations, we were interested in the synthesis of new pyrazolo[3,4-*d*][1,2,3]triazin-4-ones, which are structurally related to the compounds described above. These systems are also structural analogues of the naturally occurring purine nucleosides adenosine and guanosine, so they could be useful chemotherapeutic agents.[3]

To the best of our knowledge, all of the methodologies previously used for the preparation of these compounds involve several steps with variable yields.[1b] We now report a one-step synthesis of pyrazolo[3,4-*d*][1,2,3]triazin-4-ones **2a**–**d** (Scheme 1) by diazotization of 5-amino-1*H*-pyrazole-4-carbonitriles **1a**–**d**. We also describe the effect of different reaction conditions for the diazotization process of compound **1a** that explain the formation of the side products.

Results and Discussion

3,7-Dihydro-4*H*-pyrazolo[3,4-*d*][1,2,3]triazin-4-ones **2a**–**d** were prepared by diazotization of the easily accessible 5-amino-1*H*-pyrazole-4-carbonitriles **1a**–**d**[1c] by treatment with aqueous $NaNO_2$ and a mixture of HCl/AcOH (3:1) as the acid reagents.

In all cases compounds **2a**–**d** were obtained in moderate to good yields, together with other products such as pyrazolecarbonitriles **4** and **5** and, in the cases of **1a** and **1c**,



Scheme 1. Diazotization reaction of pyrazoles **1a**–**d**.

the fused pyrazoles **3a** and **3c**, respectively. These results are shown in Scheme 1 and Table 1. The formation of compounds **2**–**5** can be explained by different mechanisms as discussed below.

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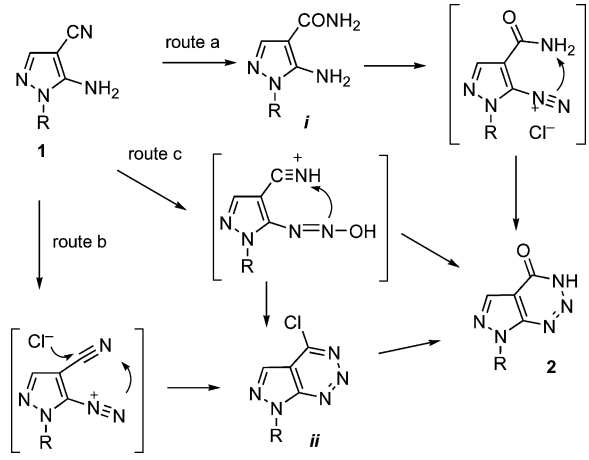
Table 1. Yields of products in the diazotization reaction of pyrazoles **1a**–**d**.

Pyrazole	R	Product yield[a]			
		2	**3**	**4**	**5**
1a	Ph	77.0	6.9	8.3	1.2
1b	*p*-FC_6H_4	69.8	–	2.7	1.0
1c	Bn	50.0	4.6	1.3	1.1
1d	*t*Bu	47.0	–	1.2	1.0

[a] Yields of isolated products.

The expected products from the diazotization reaction of **1a**–**d** would be the chlorinated products ***ii*** (Scheme 2);[4] instead of these, however, pyrazolotriazinones **2a**–**d** were obtained. These could possibly be formed in three ways as depicted in Scheme 2: (a) the hydrolysis of the cyano groups to give 5-amino-1*H*-pyrazole-4-carboxamides ***i***, diazotization of the amino group, and subsequent cyclization of the diazonium salt, (b) the initial formation of the chloropyrazolotriazine ***ii*** followed by hydrolysis to give the final product, and/or (c) the cyclization between the diazoic acid and the nitrilium ion, followed by addition of the nucleophilic species.



Scheme 2. Tentative mechanism for the formation of pyrazolotriazinones **2**.

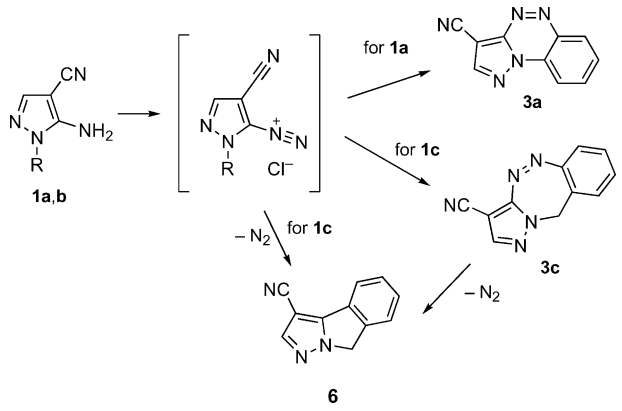
In order to provide some information to confirm or refute the proposed mechanisms, some experiments were carried out. Route (a) suggests that the hydrolysis of the cyano group is faster than the diazotization reaction, so amides ***i*** may be formed. To check whether the cyano group is stable under the acidic conditions of these reactions, pyrazole **1a** was subjected to an acid mixture and water in the absence of $NaNO_2$ for 24 h. After this time, carboxamide ***i*a** (57.8%) (Scheme 2) was obtained, which may be evidence of the formation of this intermediate under diazotization conditions. Anyway, no carboxamide ***i*a** was found in reactions of **1a** when $NaNO_2$ was used. This may be explained in at least two ways: diazotization and cyclization of the amide might be faster than hydrolysis [route (a)] or diazotization [route (b)] of **1**, or by other competitive processes.[5] Treatment of amides like ***i*** with sodium nitrite in hydrochloric acid has been reported to afford the corresponding fused triazines in moderate yields.[1b,6] Thus, when diazotization of compound ***i*a** was performed under the same conditions as used for pyrazole **1**, the pyrazolotriazinone **2a** was obtained as main product (85% yield). However, the stability of the diazonium salt is strongly dependant on the substitution of the pyrazole ring; it has been reported that in the case of 5-amino-1-[6-(*p*-tolyl)pyridazin-3-yl]-1*H*-pyrazole-4-carboxamide, the intramolecular cyclization to the corresponding triazinone did not take place, and it was possible to isolate the stable diazonium salt prior to the subsequent reactions.[7]

Route (b) in Scheme 2 is another possibility for the formation of **2**. In spite of the fact that no 4-chloro-7*H*-pyrazolo[3,4-*d*][1,2,3]triazines ***ii*** were found in the reaction mixture, we cannot discount the presence of these compounds. It is well established that chloro-substituted fused compounds such as ***ii*** are unstable and decompose or hydrolyze under acidic conditions:[1b] the hydrolysis of 4-chloro-2*H*-pyrazolo[3,4-*c*]pyridazines in cyclization reactions of 4-alkynylpyrazole-3-diazonium chloride has been described, for example.[8] In that case, the hydroxy derivatives were found at higher temperatures while the chloro derivatives were found at lower temperatures. For this reason we decided to perform the diazotization of compound **1a** at –15 and –20 °C. In this case, **2a** (72%), **3a** (9%), **4a** (9%), and **5a** (1%) were obtained as the main products, whereas no triazine ***ii*a** was detected.

The third possibility [route (c)] was opportunely suggested by a referee, and we found it to be another possible explanation of the experimental results. In this case, the initially formed diazoic acid could undergo protonation at the nitrile group, followed by cyclization and addition of chlorine or water to give ***ii*** or product **2**, respectively. The formation of nitrilium ion intermediates is reasonable under the diazotization reaction conditions, and it is also known that this reactive species may cyclize with appropriate terminators.

At this point and with the experimental results shown above, we are not able to determine whether compounds **2a**–**d** are formed through a single mechanism – (a), (b), or (c) – or by some combination of the mechanisms depicted in Scheme 2.

Going back to Scheme 1, it can be seen that compounds **3a** and **3c** were formed in lower yields on treatment of **1a** and **1c**, respectively. The formation of these compounds could be explained in terms of an intramolecular coupling of the diazonium intermediates with the aromatic rings. This reaction has been used in the synthesis of imidazo[2,1-*c*][1,2,4]triazines from 2-amino-*N*-phenylimidazoles[9] and in the preparation of pyrazolo[3,4-*c*]cinnolines from 5-amino-4-arylpyrazoles. In reactions of the benzyl derivative **1c**, which afforded 10*H*-pyrazolo[5,1-*c*][1,2,4]benzotriazepine-3-carbonitrile (**3c**), 8*H*-pyrazolo[5,1-*a*]isoindole-3-carbonitrile (**6**) (Scheme 3) was also found. This compound may be formed by nitrogen elimination from benzotriazine **3c** or by nitrogen elimination from the diazonium ion followed by an internal electrophilic substitution, probably through a pyrazolyl cation intermediate.



Scheme 3. Mechanism for the formation of fused derivatives **3a** and **3c**.

Compounds **4** (Scheme 1) are the expected products when the diazotization solution is stirred in the presence of concentrated HCl or for long periods; under these conditions the diazonium ion can be substituted by chlorine.[10] It is known that this process takes place by different mechanisms – ionic or free radical – and that this is strongly dependant on the reaction conditions.[11] The intermediacy of aryl cations in the decomposition of aryldiazonium tetrafluoroborates has been proposed,[5,12] whereas a radical mechanism could be involved in reactions of diazonium halides (Cl^- and Br^-).[13]

The formation of pyrazoles **5** (Scheme 1) can easily be explained by a hydro-dediazoniation process. This behavior was also observed in reactions of imidazolediazonium fluoroborates, which undergo facile photoextrusion of nitrogen followed by fluorination or hydrogenation when reactions are carried out in ethanol.[5a] To investigate whether the same process was taking place in our experiments, a reaction of **1a** in the presence only of HCl in ethanol (no AcOH) was performed. Pyrazole **5a** was the main product (49.9%), and only a 18.4% yield of **2a** was obtained (Table 2). The mechanism of this process is unknown, but it may be that a heteroaryl cation intermediate is trapped by the solvent and that this reaction is improved when ethanol is employed.[12]

Table 2. Diazotization conditions for the reactions of pyrazole **1a**.

Method	Conditions[a]		Yield[b]			
	Acids	Other	**2a**	**3a**	**4a**	**5a**
A	HCl/AcOH (3:1)[c]	t = 20 h	76.7	8.3	1.2	6.9
B	HCl/AcOH (1:4)[c]	t = 20 h	0.0	0.0	78.0	8.4
C	HCl/AcOH (1:4)[c]	hν, t = 6 h	6.0	0.0	81.3	6.2
D	1 M HCl	EtOH, t = 20 h	18.4	0.0	0.0	49.9

[a] All reactions were performed at a concentration of $[NaNO_2]_{ac}$ = 1 M, and the temperature was from 0 °C to room temp. [b] Percentages of isolated products. [c] Ratio of volumes.

According to the literature,[7,10,14] the course of the cyclization reaction of the pyrazolediazonium ion markedly depends on the electrophilicity of the diazo group and the stability of the salt under the reaction conditions. It is also remarkable that the nature of the substituent on N-1 of the pyrazole ring influences the course of the cyclization reaction of the diazonium salt. Thus, in our case the salt was more stable with aryl substituents than with alkyl substituents, probably due to π-electronic effects. The presence of the fluorine atom in the *para* position of the phenyl ring also affected the formation of pyrazolotriazines: in this case the yield of **2b** was lower than that of **2a**, and no 1,2,4-triazine **3b** was observed. It is clear that electrophilic substitution was not promoted by the inductive withdrawing effect of fluorine. In a continuation of the study of these reactions, we decided to change the nature of the acid medium to see if this change has any influence on the product composition (Table 2). Thus, when diazotization of **1a** was carried out in HCl/AcOH (1:4) (Entry B), pyrazole **4a** was the main product, and no pyrazolotriazinone was obtained. This result shows that at higher concentrations of AcOH, displacement of the diazonium group by a nucleophilic chloride ion is favored over the reaction of the diazo group with the CN group. The elimination of nitrogen from the diazonium salt was also accelerated when the reaction mixture was irradiated at 350 nm for only 6 h. In this case, complete conversion of the starting material to give an 81% yield of the chloro derivative **4** was observed, with compounds **2a** and **5** as minor products.

Conclusions

Pyrazolotriazines **2a**–**d** were obtained from aminopyrazoles **1a**–**d** in a one-step process. In the cases of pyrazoles **1a** and **1c**, electrophilic substitution of the phenyl ring by the diazonium ion or by the heterocyclic cation was observed as a competitive process. According to the results obtained for compound **1a**, a change of diazotization reaction conditions affects the different product compositions. The stability of the diazonium ion has an important effect on the course of the reaction.

Experimental Section

General: NMR spectra were recorded with Bruker AC 200 and 400 spectrometers. Chemical shifts are reported in ppm relative to internal TMS. All chemicals were of reagent grade and were used without purification. High-resolution mass spectra were recorded with an Agilent LCTOF instrument. Column chromatography was carried out on grade 60 silica gel (70–230). Compounds **1a**–**d** were prepared from the monosubstituted hydrazine (**1a**), the monosubstituted hydrazine hydrochlorides (**1b**, **1d**), or the monosubstituted hydrazine dihydrochloride (**1c**) and ethoxymethylenemalononitrile by the methodology described in the literature.[1c] Pyrazolotriazinones **2a**–**d** were prepared in 47–77% yields and minor products **3a**,**c**, **4a**–**d**, **5a**–**d** and **6** were isolated in very low yields (1–8%).

General Procedure for Diazotization of Aminopyrazoles 1a–d: Aqueous $NaNO_2$ (1.0 mmol, 1 mL) was added to a well-stirred and cooled solution (0–5 °C) of the pyrazole (1 mmol) in a mixture of HCl/AcOH (3:1, 20 mL) over a period of 10 min. The reaction mixture was allowed to warm to room temperature and stirred for 20 h. After this time, the precipitate of pyrazolotriazinone was filtered

off, and the residue was diluted with water (10 mL), extracted with dichloromethane (3 × 30 mL), and dried with anhydrous $MgSO_4$. The resulting solution was concentrated to dryness, and the solid was then subjected to chromatographic column separation with dichloromethane and dichloromethane/ethyl acetate (4:1).

5-Amino-1-phenyl-1*H*-pyrazole-4-carbonitrile (1a): This compound was obtained as white crystals, m.p. 140.0–140.5 °C (EtOH). Yield 63% (3.1314 g). ^{1}H NMR ($CDCl_3$, 200MHz): δ = 4.64 (s, 2 H), 7.40–7.59 (m, 5 H), 7.63 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50.33 MHz): δ = 75.95, 114.22, 124.33, 128.96, 130.01, 137.05, 141.39, 150.09 ppm.[15]

5-Amino-1-(4-fluorophenyl)-1*H*-pyrazole-4-carbonitrile (1b): This compound was obtained as a white powder, m.p. 177.0–178.0 °C (MeOH). Yield 97% (1.6436 g). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 4.62 (s, 2 H), 7.16–7.28 (m, 2 H), 7.44–7.54 (m, 2 H), 7.62 (s, 1 H) ppm. ^{13}C NMR [$(CD_3)_2CO$, 50.33 MHz]: δ = 75.69, 114.59, 117.20 (J = 23.8 Hz), 127.82 (J = 8.9 Hz), 135.03, 142.13, 152.16, 162.91 (J = 245.6 Hz) ppm. MS: m/z (%) = 203 (97) $[M + 1]^+$, 202 (100) $[M]^+$, 123 (16), 122 (18), 121 (19), 96 (33), 95 (57), 75 (39). HRMS: calcd. for $C_{10}H_7FN_4$ 203.0733; found 203.0734.

5-Amino-1-benzyl-1*H*-pyrazole-4-carbonitrile (1c): This compound was obtained as white crystals, m.p. 141.2–142.7 °C. Yield 70% (0.7136 g). ^{1}H NMR (CD_3CN, 200 MHz): δ = 4.49 (s, 2 H), 5.07 (s, 2 H), 7.22–7.42 (m, 5 H), 7.80 (s, 1 H) ppm. ^{13}C NMR (CD_3CN, 50.33 MHz): δ = 56.55, 79.21, 114.74, 128.88, 129.14, 129.76, 136.42, 137.34, 158.49 ppm. MS (EI): m/z (%) = 199 (94) $[M + 1]^+$, 198 (96) $[M]^+$, 93 (96), 92 (100), 91 (100).

5-Amino-1-*tert*-butyl-1*H*-pyrazole-4-carbonitrile (1d): This compound was obtained as yellow crystals, m.p. 92.9–94.5 °C. Yield 65% (0.6600g). ^{1}H NMR [$(CD_3)_2CO$, 200 MHz]: δ = 1.55 (s, 9 H), 4.43 (s, broad, 2 H), 7.21 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 29.07, 60.10, 78.23, 114.58, 138.38, 150.00 ppm. MS: m/z (%) = 164 (12) $[M]^+$, 108 (100), 57 (25).

7-Phenyl-3,7-dihydro-4*H*-pyrazolo[3,4-*d*][1,2,3]triazin-4-one (2a): This compound was obtained as white crystals after column chromatography, m.p. 137.1 °C (dec.). Yield 77% (0.1781 g). ^{1}H NMR (CD_3CN, 400 MHz): δ = 7.51 (t, J = 7.0 Hz, 1 H), 7.62 (t, J = 7.4 Hz, 2 H), 8.06 (d, J = 7.8 Hz, 1 H), 8.36 (s, 1 H), 12.85 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 108.13, 122.82, 128.76, 129.67, 135.39, 137.87, 147.93, 154.04. HRMS (ESI+): calcd. for $C_{10}H_8N_5O^+$ 214.0729; found 214.0724.

7-(4-Fluorophenyl)-3,7-dihydro-4*H*-pyrazolo[3,4-*d*][1,2,3]triazin-4-one (2b): This derivative was obtained as a white power after column chromatography, m.p. 153.7 °C (dec.). Yield 70% (0.1678 g). ^{1}H NMR [$(CD_3)_2CO$, 400 MHz]: δ = 7.43 (m, 2 H), 8.20 (m, 2 H), 8.43 (s, 1 H), 14.02 (br. signal, 1 H) ppm. ^{13}C NMR [$(CD_3)_2CO$, 100 MHz]: δ = 108.14, 116.26, 116.49, 125.01, 125.10, 134.68, 134.70, 135.19, 148.60, 154.20, 161.11, 163.56 ppm. HRMS (ESI+): calcd. for $C_{10}H_7FN_5O^+$ 232.0635; found 232.0633.

7-Benzyl-3,7-dihydro-4*H*-pyrazolo[3,4-*d*][1,2,3]triazin-4-one (2c): In this case the reaction was carried out with **1c** (0.5715 g, 2.883 mmol). The compound was obtained as colorless crystals after column chromatography, m.p. at 176.7 °C (dec.). Yield 50% (0.1188 g). ^{1}H NMR [$(CD_3)_2CO$, 400 MHz]: δ = 5.71 (s, 2 H), 7.33–7.48 (m, 5 H), 8.69 (s, 1 H), 13.46 (s, 1 H) ppm. ^{13}C NMR [$(CD_3)_2CO$, 100 MHz]: δ = 58.29, 107.73, 128.98, 129.29, 129.37, 129.72, 136.47, 154.89, 158.17 ppm. MS: m/z (%) = 228 (15) $[M + 1]^+$, 227 (15) $[M]^+$, 185 (20), 184 (19), 92 (42), 91 (100), 65 (30). HRMS (ESI+): calcd. for $C_{11}H_{10}N_5O^+$ 228.0885; found 228.0881.

7-*tert*-Butyl-3,7-dihydro-4*H*-pyrazolo[3,4-*d*][1,2,3]triazin-4-one (2d): In this case the reaction was carried out with **1d** (0.1074 g, 0.654 mmol). The compound was obtained as white solid after column chromatography, m.p. 143.0 °C (dec.). Yield 47% (0.1188 g). ^{1}H NMR (CD_3CN, 200 MHz): δ = 1.88 (s, 9 H), 8.19 (s, 1 H), 12.85 (br., 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 29.87, 63.13, 132.58, 138.46, 148.27, 155.00 ppm.

Pyrazolo[5,1-*c*][1,2,4]benzotriazine-3-carbonitrile (3a): This compound was isolated as a yellow solid after column chromatography. Yield 7% (0.0146 g). ^{1}H NMR (CD_3CN, 400MHz): δ = 7.97 (t, J = 7 Hz, 1 H), 8.18 (t, J = 7 Hz, 1 H), 8.51 (d, J = 8 Hz, 1 H), 8.65 (s, 1 H), 8.75 (d, J = 8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 88.79, 111.51, 114.79, 125.29, 128.94, 131.68, 136.72, 139.93, 146.09, 146.38 ppm. MS: m/z (%) = 195 (100) $[M]^+$, 140 (57), 113 (31), 102 (25). HRMS (ESI+): calcd. for $C_{10}H_{11}N_5^+$ 196.0623; found 196.0621.

10*H*-Pyrazolo[5,1-*c*][1,2,4]benzotriazepine-3-carbonitrile (3c): In this case the reaction was carried out with **1c** (0.5715 g, 2.883 mmol). The compound was isolated from the crude reaction product together with compound **6**. Yield 5% (0.0275 g). ^{1}H NMR [$(CD_3)_2CO$, 400 MHz]: δ = 5.20 (s, 2 H), 7.65 (d, J = 8 Hz, 1 H), 7.50–7.57 (m, 2 H), 7.81–7.83 (m, 1 H), 7.94 (s, 1 H) ppm.

5-Chloro-1-phenyl-1*H*-pyrazole-4-carbonitrile (4a): This compound was obtained as colorless crystals after column chromatography, m.p. 79.2–80.4 °C. Yield 8% (0.0183 g). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.54 (m, 5 H), 7.96 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 94.49, 111.50, 125.14, 129.56, 129.83, 133.38, 137.10, 142.63 ppm. MS (EI): m/z (%) = 205 (33) $[M + 2]^+$, 204 (96), 203 (100) $[M]^+$, 168 (27), 141 (48), 77 (77), 51 (39). HRMS (ESI+): calcd. for $C_{10}H_7ClN_3^+$ 204.0329; found 204.0326.

5-Chloro-1-(4-fluorophenyl)-1*H*-pyrazole-4-carbonitrile (4b): This compound was obtained as a yellow solid after column chromatography, m.p. 121.0–122.0 °C. Yield 3% (0.0063 g). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.35–7.47 (m, 2 H), 7.69–7.78 (m, 2 H), 8.24 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ = 94.63, 111.39, 116.69 (J = 23.1 Hz), 127.25 (J = 9.5 Hz), 133.11, 133.52, 142.71, 163.07 (J = 250.9 Hz) ppm. MS (EI): m/z (%) = 224 (26) $[M + 3]^+$, 223 (32) $[M + 2]^+$, 222 (92) $[M + 1]^+$, 221 (100) $[M]^+$, 187 (30), 186 (35), 160 (52), 159 (72), 132 (22), 96 (54), 95 (90), 75 (73).

1-Benzyl-5-chloro-1*H*-pyrazole-4-carbonitrile (4c): In this case the reaction was carried out with **1c** (0.5715 g, 2.883 mmol). The compound was obtained as a yellow solid after column chromatography. Yield 1% (0.0082 g). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.35 (s, 2 H), 7.29 (d, J = 9 Hz, 2 H), 7.33–7.39 (m, 3 H), 7.81 (s, 1 H) ppm. MS (EI): m/z (%) = 217 (16) $[M]^+$, 182 (14), 91 (100), 65 (18).

1-*tert*-Butyl-5-chloro-1*H*-pyrazole-4-carbonitrile (4d): In this case the reaction was carried out with **1d** (0.1074 g, 0.654 mmol). The compound was obtained as colorless crystals after column chromatography, m.p. 114.0–115.0 °C. Yield 1% (0.0014 g). ^{1}H NMR [$(CD_3)_2CO$, 200 MHz]: δ = 1.65 (s, 9 H), 7.56 (s, 1 H) ppm. ^{13}C NMR [$(CD_3)_2CO$, 50.3 MHz]: δ = 29.37, 63.30, 95.60, 96.34, 110.57, 130.83, 139.32 ppm. MS (EI): m/z (%) = 185 (3) $[M + 2]^+$, 183 (9) $[M]^+$, 168 (5), 130 (7), 128 (21), 91 (2), 64 (2), 57 (100), 56 (95).

1-Phenyl-1*H*-pyrazole-4-carbonitrile (5a): This pyrazole was obtained as white crystals after column chromatography, m.p. 91.9–92.6 °C. Yield 1% (0.0022 g). ^{1}H NMR ($CDCl_3$, 200 MHz): δ = 7.37–7.55 (m, 4 H), 7.67 (d, J = 8 Hz, 1 H), 7.99 (s, 1 H), 8.30 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100MHz): δ = 94.52, 113.17, 128.32, 120.08, 128.46, 129.94, 131.95, 138.92, 143.19 ppm. HRMS (ESI+): calcd. for $C_{10}H_8N_3^+$ 170.0718; found 170.0713.

1-(4-Fluorophenyl)-1*H*-pyrazole-4-carbonitrile (5b): This compound was obtained as a yellow solid after column chromatography. m.p.

168.0–169.0 °C. Yield 1% (0.0019 g). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.31–7.40 (m, 2 H), 7.90–7.97 (m, 2 H), 8.18 (s, 1 H), 8.99 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100MHz): δ = 94.7, 112.98, 116.67, 117.13, 122.00, 122.17, 132.00, 142.47, 143.44, 159.82, 164.78 ppm.

1-Benzyl-1*H*-pyrazole-4-carbonitrile (5c): In this case the reaction was carried out with **1c** (0.5715 g, 2.883 mmol). The compound was obtained as a yellow solid after column chromatography. Yield 1% (0.0060 g). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.32 (s, 2 H), 7.24–7.26 (m, 2 H), 7.38–7.39 (m, 3 H), 7.75 (s, 1 H), 7.82 (s, 1 H) ppm. MS (EI): *m*/*z* (%) = 183 (36) $[M]^+$, 182 (62), 91 (100), 65 (22).

1-*tert*-Butyl-1*H*-pyrazole-4-carbonitrile (5d): In this case the reaction was carried out with **1d** (0.1074 g, 0.654 mmol). The compound was identified in the reaction mixture. Yield 1% (0.0010 g). MS (EI): *m*/*z* (%) = 149 (19) $[M]^+$, 134 (37), 94 (82), 57 (86), 56 (100), 41 (67).

8*H*-Pyrazolo[5,1-*a*]isoindole-3-carbonitrile (6): In this case the reaction was carried out with **1c** (0.5715 g, 2.883 mmol). The compound was isolated from the crude reaction product together with compound **3c**. Yield 1% (0.0060 g). ^{1}H NMR [$(CD_3)_2CO$, 400 MHz]: δ = 5.34 (s, 2 H), 7.28 (d, *J* = 7 Hz, 2 H), 7.32–7.40 (m, 1 H), 7.50–7.57 (m, 1 H), 7.83–7.86 (m, 1 H), 8.15 (s, 1 H) ppm. MS (EI): *m*/*z* (%) = 181 (100) $[M]^+$, 154 (91), 127 (39).

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