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Synthesis of poly-functionalized pyrazoles under Vilsmeier-Haack reaction conditions

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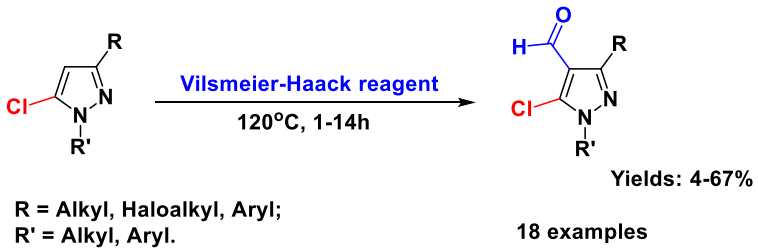
Abstract

Synthesis of 1,3-disubstituted 5-chloro-1*H*-pyrazole-4-carbaldehydes was achieved by formylation of the corresponding 5-chloro-1*H*-pyrazoles under Vilsmeier-Haack conditions.



Keywords: Pyrazoles, 5-chloropyrazoles, pyrazole-4-carbaldehydes, Vilsmeier-Haack reaction, formylation

Introduction

The pyrazole core is a privileged structural motif of the modern drugs and bioactive natural compounds. This heterocycle and its derivatives are important building blocks for organic, bioorganic, pharmaceutical and supramolecular chemistry as well as materials science.[1-9] In fact, the pyrazole ring ranks 44th in a frequency among 351 ring systems found in currently marketed drugs.[10] The incorporation of functional groups into the pyrazolic architecture attracts considerable interest because this modification opens the possibility for further transformations. These poly-functionalized heterocyclic systems have shown promising applications in the search of new biologically active candidates for drug discovery as well as polydental ligand systems. Among them the pyrazoles bearing a halogen atom and formyl group are of particular interest.[11]

Thus, halopyrazoles show a diverse range of biological activity.[12] Moreover, the introduction of a halogen atom into the pyrazole ring represents often a first step in the synthesis of hard-to-reach derivatives. Many of the metal-catalyzed carbon-carbon coupling reactions, such as Sonogashira, Heck–Mizoroki, Stille, Negishi, and Suzuki–Miyaura are based on halopyrazoles.[13-16] On the other hand, 4-formylpyrazoles are currently used for the preparation of nitronylnitroxyl pyrazole-containing ligands, which are promising building blocks in design of new heterospin magnetics,[17] as well as diverse heteropolycyclic derivatives.[18] It is worth mentioning that the poly-condensed heterocyclic ring system, which was synthesized from 5-chloro-1*H*-pyrazole-4-carbaldehyde, exhibited potent anti-inflammatory and analgesic activities. In this case, the incorporation of pyrazole nucleus to quinoxaline moiety caused significant biologically activities.[19]

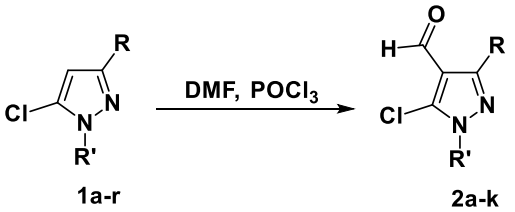
Generally, the methods for synthesis of formyl(halo)pyrazoles can be divided into two groups. The first approach presupposes the use of polyfunctional starting materials in cascade assembly of the heterocyclic core. The second one is based on the incorporation of the functional group into previously prepared pyrazoles. The modification of the existing heterocyclic system seems to be a more convenient approach to target compounds.

The methods for preparation of halo-substituted formyl pyrazoles, to the best of our knowledge, have rarely been reported. One of the approaches to 3/5-chloro (or 5-bromo)-4-formyl pyrazole derivatives is based on pyrazolones which undergo haloformylation under Vilsmeier-Haack reaction. [13,20,21] Taking into account that pyrazolones are produced by refluxing of hydrazines with 1,3-dicarbonyl compounds,[22] this method was extended only for derivatives obtained from the most available representatives of 1,3-diketones or β-ketoesters.[13] In addition, the pyrazolones were often obtained in low yields.[23,24]

Other pathways to target compounds are based on the reaction of 3-halo-*1H*-pyrazoles with organometallics[25] or diazonium derivatives.[26] However, low availability of the starting materials as well as high laboriousness are disadvantages of these approaches. Thus, a straightforward approach to functionalized pyrazoles from available initial reagents is of interest. Herein, we report a general and efficient method for the synthesis of halo-substituted formylpyrazoles by simple formylation of corresponding halopyrazoles.

Results and Discussion

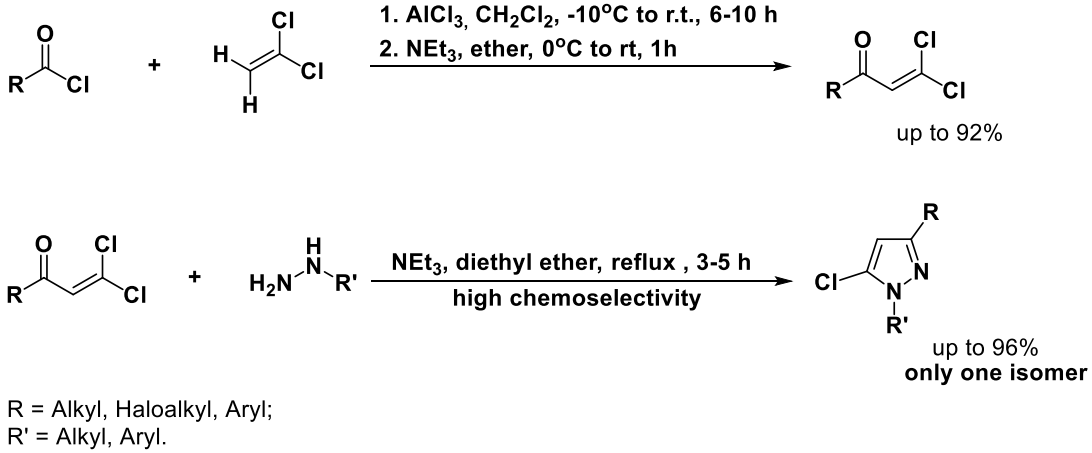
Our aim was to formylate 1,3-disubstituted 5-chloro-1*H*-pyrazoles **1** under Vilsmeier-Haack conditions to yield the corresponding 5-chloro-1*H*-pyrazole-4-carbaldehydes **2** (Scheme 1). Most of the starting materials were readily prepared by base-catalyzed condensation of dichlorovinyl ketones with hydrazines (Scheme 2).[27-30] An important advantage of this method is highly selective formation of 5-chloropyrazoles.



R = Pr, R' = Me (**a**); R' = Pr (**b**); R' = CH_2CH_2OH (**c**); R' = Bn (**d**); R' = Ph (**f**); R' = 2,4-$(NO_2)_2$-C_6H_3 (**p**); R' = *t*-Bu (**r**);
R = Me, R' = Bn (**e**); R' = Ph (**g**); R' = Me (**m**); R = Ph, R' = Me (**h**); R = 4-Me-C_6H_4, R' = Me (**i**); R = 4-Br-C_6H_4, R' = Me (**j**);
R = 4-F-C_6H_4, R' = Me (**k**); R = 4-NO_2-C_6H_4, R' = Me (**l**); R = CH_2Cl, R' = Me (**n**); R = CH_3CHCl, R' = Me (**o**);
R = CF_3, R' = Me (**q**);

Scheme 1. The general approach for preparation of 5-chloro-1*H*-pyrazole-4-carbaldehydes.

Moreover, since dichlorovinyl ketones can be obtained from readily available reagents (vinylidene chloride and acyl chlorides[31-34]), synthesis of a series of 3-substituted pyrazoles **1** *a priori* could be easily accessible.



R = Alkyl, Haloalkyl, Aryl;
R' = Alkyl, Aryl.

Scheme 2. Simple and efficient method for preparation of 5-chloro-1*H*-pyrazoles.

First, we sought the optimal reaction conditions using 1-methyl-3-propyl-5-chloro-1*H*-pyrazole (**1a**; R = Pr, R' = Me) (Sheme 1) as a model compound and the results are shown (Table 1). When reaction was carried out at 70°C, no products were observed at all (Entry 1). The best results were obtained when the pyrazole **1a** was treated with excess of DMF and $POCl_3$ at 120°C. For instance, using a 5-fold excess of DMF and 2-fold excess of $POCl_3$ at 120°C for 2 h gives carbaldehyde **2a** in 55% yield instead of 32% only for 2-fold excess of the same reagents (Entries 2, 3).

The use of excess of $POCl_3$ leads to increasing amounts of chloroiminium ions, the key intermediates of the Vilsmeier-Haack reaction, and therefore favors the formation of target pyrazole. The excess of DMF ensures homogeneity of the process and solvates the released hydrogen chloride. The yield of **2a** is not increased when more than 6 and 4 equivalents of DMF and $POCl_3$ are used. At this ratio of reagents, a further increase in the reaction time does not affect the yield of the target product (Entries 7, 8). The use of microwave assistance did not favor the formation of target pyrazole **2a** (Entries 4, 5). Thus, the optimum conditions of the process are heating the mixture of 5-chloropyrazole **1a** with 6 equivalents of DMF and 4 equivalents of $POCl_3$ at 120°C for 1 h. Under such conditions, yield of the target 1*H*-pyrazole-4-carbaldehyde **2a** reached 67% (Entry 7).

Table 1. Optimization of the reaction conditions (ratio of the 3 reactants, temperature, duration of reaction) for the conversion of 1-methyl-3-propyl-5-chloro-1*H*-pyrazole (**1a**; R = Pr, R' = Me) into 1-methyl-3-propyl-5-chloro-1*H*-pyrazole-4-carbaldehyde (**2a**; R = Pr, R' = Me) (Scheme 1)

Entry	Molar ratio[a] **1a** : DMF : $POCl_3$	T, °C	Time, h	Conversion of **1a**, %	Yield[b] of **2a**, %
1	1 : 2 : 2	70	7	4	trace
2	1 : 2 : 2	120	7	51	32
3	1 : 5 : 2	120	2	74	55
4[c]	1 : 5 : 2	120	1	62	45
5[c]	1 : 5 : 2	140	2	9	trace
6	1 : 5 : 3	120	2	82	61
7	1 : 6 : 4	120	1	92	67
8	1 : 6 : 4	120	2	95	65
9	1 : 6 : 4	140	1	89	66
10	1 : 6 : 5	120	2	87	64

[a] 2 mmol of **1a** were used in screening of the reaction conditions.

[b] Yield of the isolated product.

[c] Under microwave activation

Under the selected optimized conditions, the various 5-chloropyrazoles **1b-r** were examined (Table 2). The experiments suggested that the reaction result is dependent on the substrate structure. To our delight, like model compound **1a**, a total conversion of starting 5-chloro-1,3-dialkyl-substituted pyrazoles **1b,d,e,m,n** (Entries 2,4,5,13,14) was achieved after refluxing at 120°C for 1-2.5 h. In contrast, 1-aryl and 3-aryl substituted pyrazoles **1f-1l** needed much more time to complete the reaction (Entries 6-12).

Table 2. Preparation of 1,3-disubstituted 5-chloro-1*H*-pyrazole-4-carbaldehydes **2** by formylation of the corresponding 5-chloro-1*H*-pyrazoles **1** under Vilsmeier-Haack conditions (Scheme 1)[a]

Entry	Compound number	R	R'	Time (h) [b]	Yield, %
1	**2a**	Pr	Me	1	67
2	**2b**	Pr	Pr	1	65
3	**2c**	Pr	$-CH_2CH_2Cl$	8	58
4	**2d**	Pr	Bn	2.5	55
5	**2e**	Me	Bn	2.5	61
6	**2f**	Pr	Ph	14	54
7	**2g**	Me	Ph	14	52
8	**2h**	Ph	Me	10	50
9	**2i**	4-Me-C_6H_4	Me	10	56
10	**2j**	4-Br-C_6H_4	Me	10	55
11	**2k**	4-F-C_6H_4	Me	10	53
12	**2l**	4-NO_2-C_6H_4	Me	14	46
13	**2m**	Me	Me	1	66
14	**2n**	CH_2Cl	Me	1	59
15	**2o**	$-CHClCH_3$	Me	2	4
16	**2p**	Pr	2,4-$(NO_2)_2$-C_6H_3	14	no reaction [d]
17	**2q**	CF_3	Me	14	no reaction [d]
18	**2r**	Pr	*t*-Bu	2	no target product [e]

[a] All reactions were carried out on a 2.00 mmol scale.

[b] The time for full conversion of 5-chloro-1*H*-pyrazole was monitored by TLC.

[c] All yields refer to isolated and purified products.

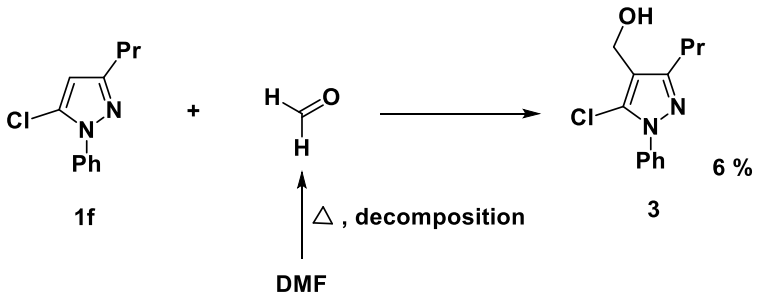
[d] The starting pyrazoles were isolated in quantitative yield.

[e] Conversion of the starting pyrazole was 100% and 1*H*-pyrazole-4-carbaldehyde was not formed.

We concluded that the aromatic substituents, being more electron-withdrawing than the alkyl groups, prevent the formylation of 5-chloropyrazoles. This is especially evident for the nitrophenyl-substituted derivative **1l** (Entry 12).

It should be noted that only a single example of formylation of 5-chloropyrazole **1g** with the $POCl_3$/DMF system was reported.[35] Our attempts to reproduce this experiment under the conditions described failed. In contrast, the application of optimal conditions found in our study allowed us to prepare the target formylated pyrazole in moderate yield (Entry 7).

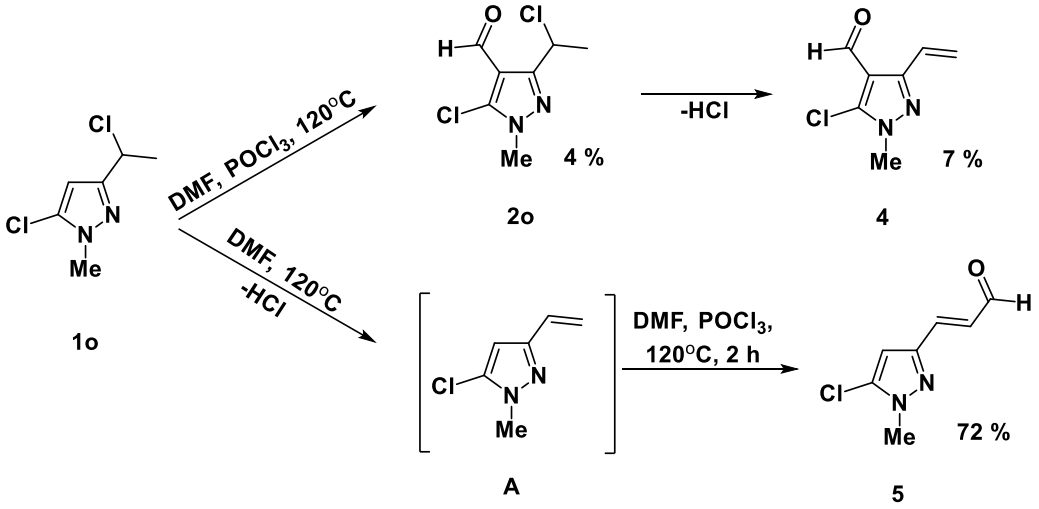
We hypothesized that such yields of pyrazoles **2f,g** can be explained by formation of by-products. In fact, when the reaction of substrate **1f** with DMF and $POCl_3$ was conducted under optimal conditions, the target pyrazole **2f** (52%) was isolated together with a minor amount of heterocycle **3** (6%). Its formation seems to be the result of the reaction of initial substrate **1f** with formaldehyde which was generated *in situ* in small quantity under long heating of DMF (Scheme 3).



Scheme 3. Hydroxymethylation of 5-chloro-1-phenyl-3-propyl-1*H*-pyrazole **1f.**

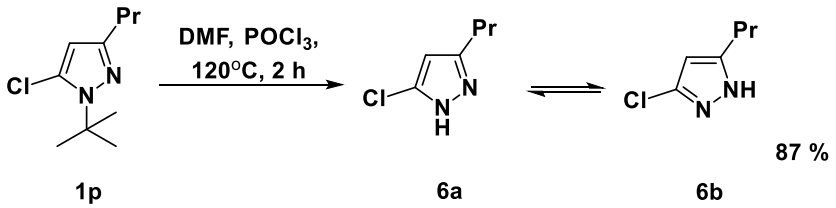
Formylation of 5-chloro-1-(2-hydroxyethyl)-3-propylpyrazole **1c** is accompanied by substitution of the hydroxyl group by chlorine atom to afford 5-chloro-1-(2-chloroethyl)-3-propyl-1*H*-pyrazole-4-carbaldehyde **2c** in 58% yield (Entry 3).

An unexpected result was obtained when 5-chloro-3-(1-chloroethyl)-1-methyl-1*H*-pyrazole **1o** was treated with DMF and $POCl_3$ under optimal conditions. In this case the formylated pyrazole **2o** is a minor product while the pyrazole **5** was isolated in 72% yield. We assumed that the latter compound was formed in one-pot tandem reaction sequence *via* elimination of the hydrogen chloride[30] and following formylation of vinyl moiety of intermediate **A**, as we have described in our previous work[36]. The target pyrazole **2o** undergoes also dehydrochlorination under reaction conditions to afford 5-chloro-1-methyl-3-vinyl-1*H*-pyrazole-4-carbaldehyde **4** in 7% yield (Scheme 4).



Scheme 4. Reactions of 5-chloro-3-(1-chloroethyl)-1-methyl-1*H*-pyrazole **1o** under Vilsmeier-Haack conditions.

The reaction's scope is quite broad but pyrazoles **1p-r** bearing strong electron-withdrawing groups on benzene ring or bulky moiety showed a low reactivity. Thus, the conversion of **1p,q** achieved only 5% after refluxing of the mixture for a long time (entries 16,17). Finally, with pyrazole **1r** the dealkylation reaction was observed: only a mixture of tautomers **6** was isolated (Scheme 5). This heterocycle does not afford formylated pyrazole under selected conditions.[37]



Scheme 5. Dealkylation of 1-(*tert*-butyl)-5-chloro-3-propyl-1*H*-pyrazole **1p.**

Conclusions

An efficient method for the synthesis of previously unknown or hardly accessible 4-formylpyrazoles containing also a chlorine atom in position 5 has been developed. A number of different 5-chloro-4-formylpyrazoles bearing diverse substitution patterns can be synthesized by this method. The simplicity of execution, ready availability of starting materials and importance of the prepared pyrazoles make this procedure attractive for synthetic chemists. The method supplements the known approaches to halo-substituted formylpyrazoles and opens further routes to a variety of pyrazole derivatives, promising for the study of reactivity and possessing numerous valuable properties.

Experimental Section

General. The ^{1}H, ^{13}C and ^{15}N NMR spectra were recorded in $CDCl_3$ solutions at room temperature on Bruker DPX-400 and AV-400 spectrometers (400.13, 100.61 and 40.56 MHz, respectively). ^{1}H, ^{13}C and ^{15}N Chemical shifts (δ in ppm) were measured with accuracy of 0.01, 0.02 and 0.1 ppm, respectively, and referred to TMS (^{1}H, ^{13}C) and nitromethane (^{15}N). The assignment of ^{1}H and ^{13}C signals in spectra was performed using 2D heteronuclear correlation HMBC-gp and HSQC-gp ^{13}C-^{1}H methods. The values of the δ ^{15}N were obtained through the 2D ^{1}H-^{15}N HMBC-gp experiment. Coupling constants (*J* in Hz) values approaches to 0.1 Hz.
IR spectra were recorded on a Bruker Vertex-70 instrument. MS analyses were recorded on a Shimadzu GCMS-QP5050A instrument (ionization potential 70 eV). Column and thin-layer chromatography were carried out on commercial available SiO_2 (Sigma-Aldrich).
Commercially available acyl chlorides, vinylidene chloride and hydrazines of the company Sigma-Aldrich were used. Alkyl hydrazines were distilled before reactions. Synthesis of 2,2-dichlorovinylketones and pyrazoles **1a, g-j, l-r** was presented in previous work.[27-34] Pyrazoles **1b-f,k** are described here for the first time.

3,3-Dichloro-1-(4-fluorophenyl)prop-2-en-1-one. A solution of a 4-fluorobenzoyl chloride (4.758 g, 30 mmol) in CH_2Cl_2 (50 mL) and $AlCl_3$ 4 (4.0 g, 30 mmol) was shaken for 20 min at -5°C. Then vinylidene chloride (3.490 g, 36 mmol) was added dropwise over a period of 20 min to avoid the temperature exceeding of 0°C. After that, the reaction mass was stirred for 4 h at rt, poured upon ice. An organic layer was separated and a water layer was extracted with CH_2Cl_2 (3×50 mL). The collected organic layer were dried over $MgSO_4$ and evaporated under reduced pressure. The residual mass was dissolved in diethyl ether (30 mL), treated with triethylamine (3.036 g, 30 mmol) at -5°C for 10 min and kept to rt, filtered and evaporated. The crude product was purified by silica gel column chromatography to give 3,3-dichloro-1-(4-fluorophenyl)prop-2-en-3-one, 4.995 g (76%), R_f=0.70 (trichloromethane), colorless needles, m.p. 29°C.[Lit.[38] 29-29.9°C] ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.96-

7.93 (m, 2H), 7.22 (s, 1H), 7.17-7.13 (m, 2H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 185.0, 166.0 (d, $^{1}J_{C,F}$ 256.0 Hz), 135.6, 133.2 (d, $^{4}J_{C,F}$ 2.4 Hz), 131.1 (d, $^{3}J_{C,F}$ 9.6 Hz), 123.8, 116.0 (d, $^{2}J_{C,F}$ 22.0 Hz) ppm. Anal. calcd. for $C_9H_5Cl_2FO$: C, 49.35; H, 2.30; Cl, 32.37. Found %: C, 49.24; H, 2.32; Cl, 32.45.

General procedure for the synthesis of 1*H*-pyrazoles (1). A triethylamine (2 mmol) was added to a solution of dichlorovinylketone (2 mmol) in diethyl ether (10 mL) under cooling with ice-water bath. After that a hydrazine (2 mmol) was added dropwise for 20 min. In the synthesis of *N*-methylpyrazole 1k 2 equiv (4 mmol) of dimethylhydrazine was used without using of triethylamine. The reaction mixture was stirred for 1.5 h at room temperature. The reaction mixture was filtered off and diethyl ether was evaporated. Individual pyrazoles usable for further purposes without additional purification were obtained.

5-Chloro-1,3-dipropyl-1*H*-pyrazole (1b). The general procedure was followed using triethylamine (2 mmol), 1,1-dichlorohex-1-en-3-one (2 mmol) and propylhydrazine (2 mmol), reaction time: 1.5 h, 344 mg (92%), yellow oil. IR (film): 3186, 3123, 2963, 2875, 1724, 1516, 1461, 773 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 5.95 (s, 1H), 4.01 (t, 2H, *J* 7.2 Hz), 2.52 (t, 2H, *J* 7.6 Hz), 1.81 (m, 2H), 1.61 (m, 2H), 0.93 (t, 3H, *J* 7.3 Hz), 0.89 (t, 3H, *J* 7.4 Hz) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 152.8, 126.4, 102.8, 50.2, 30.6, 23.2, 22.7, 13.7, 10.9 ppm. Anal. calcd. for $C_9H_{15}ClN_2$: C, 57.91; H, 8.10; Cl, 18.99; N, 15.01. Found %: C, 57.81; H, 8.06; Cl, 19.06; N, 15.07.

2-(5-chloro-3-propyl-1*H*-pyrazol-1-yl)ethan-1-ol (1c). The general procedure was followed using triethylamine (2 mmol), 1,1-dichlorohex-1-en-3-one (2 mmol) and 2-hydrazineylethan-1-ol (2 mmol), reaction time: 1.5 h, 328 mg (87%) orange oil. IR (film): 3326, 3131, 2958, 2873, 1516, 1463, 775 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 6.03 (s, 1H), 4.17 (t, 2H), 3.98 (t, 2H), 2.54 (t, 2H, *J* 7.5 Hz), 1.64 (m, 2H), 0.95 (t, 3H, *J* 7.4 Hz) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 153.6, 127.3, 103.2, 61.4, 49.9, 30.6, 22.5, 13.8 ppm. Anal. calcd. for $C_8H_{13}ClN_2O$: C, 50.93; H, 6.95; Cl, 18.79; N, 14.85. Found %: C, 51.01; H, 6.93; Cl, 18.70; N, 14.90.

1-Benzyl-5-chloro-3-propyl-1*H*-pyrazole (1d). The general procedure was followed using triethylamine (2 mmol), 1,1-dichlorohex-1-en-3-one (2 mmol) and benzylhydrazine (2 mmol), reaction time: 1.5 h, 418 mg (89%), orange oil. IR (film): 3127, 3063, 2959, 2873, 1708, 1574, 1457, 724 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.25-7.39 (m, 5H), 6.12 (s, 1H), 5.36 (s, 2H), 1.64 (t, 2H, *J* 7.6 Hz), 1.72 (m, 2H), 1.02 (t, 3H, *J* 7.3 Hz) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 153.3, 136.2, 128.6, 127.7, 127.1, 126.3, 103.6, 52.3, 30.5, 22.6, 13.7 ppm. Anal. calcd. for $C_{13}H_{15}ClN_2$: C, 66.52; H, 6.44; Cl, 15.10; N, 11.93. Found %: C, 66.62; H, 6.42; Cl, 15.06; N, 11.90.

1-Benzyl-5-chloro-3-methyl-1*H*-pyrazole (1e). The general procedure was followed using triethylamine (2 mmol), 4,4-dichlorobut-3-en-2-one (2 mmol) and benzylhydrazine (2 mmol), reaction time: 1.5 h, 343 mg (83%), orange oil. IR (film): 3128, 3033, 2932, 1605, 1518, 1451, 776 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.25-7.38 (m, 5H), 6.08 (s, 1H), 5.32 (s, 2H), 2.30 (s, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 148.6, 136.2, 128.5, 127.7, 127.1, 127.0, 104.4, 52.3, 13.9 ppm. Anal. calcd. for $C_{11}H_{11}ClN_2$: C, 63.93; H, 5.36; Cl, 17.15; N, 13.55. Found %: C, 63.80; H, 5.34; Cl, 17.22; N, 13.64.

5-chloro-1-phenyl-3-propyl-1*H*-pyrazole (1f). The general procedure was followed using triethylamine (2 mmol), 1,1-dichlorohex-1-en-3-one (2 mmol) and phenylhydrazine (2 mmol), reaction time: 1.5 h, 353 mg (80%), yellow oil. IR (film): 3121, 2058, 2959, 2870, 1597, 1523, 1453, 763 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.58-7.35 (m, 5H), 6.21 (s, 1H), 2.64 (t, 2H, *J* 7.6 Hz), 1.72 (m, 2H), 1.01 (t, 3H, *J* 7.3 Hz) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 154.3, 138.3, 128.8, 127.8, 126.7, 124.8, 105.3, 30.6, 22.5, 13.8 ppm. Anal. calcd. for $C_{12}H_{13}ClN_2$: C, 65.31; H, 5.94; Cl, 16.06; N, 12.69. Found %: C, 65.40; H, 5.96; Cl, 16.00; N, 12.64.

5-Chloro-3-(4-fluorophenyl)-1-methyl-1*H*-pyrazole (1k). The general procedure was followed using 3,3-dichloro-1-(4-fluorophenyl)prop-2-en-1-one (2 mmol) and 1,1-dimethylhydrazine (4 mmol), reaction time: 1.5 h, 345 mg (82%), beige solid, m.p. 50-52 °C. IR (film): υ 3125, 3058, 2944, 2877, 1658, 1603, 1497, 779 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 7.72-7.69 (m, 2H), 7.11-7.07 (m, 2H), 6.45 (s, 1H), 3.89 (s, 3H) ppm. ^{13}C NMR

(100.61 MHz, $CDCl_3$): δ 162.7 (d, $^1J_{C,F}$ 247.3 Hz), 149.9, 129.0 (d, $^4J_{C,F}$ 2.8 Hz), 128.2, 127.0 (d, $^3J_{C,F}$ 8.4 Hz), 115.5 (d, $^2J_{C,F}$ 21.6 Hz), 101.5, 36.2 ppm. Anal. calcd. for $C_{10}H_8ClFN_2$: C, 57.02; H, 3.83; Cl, 16.83; N, 13.30. Found %: C, 56.85; H, 3.84; Cl, 16.87; N, 13.34.

General procedure for the synthesis of 1*H*-pyrazole-4-carbaldehydes (2). $POCl_3$ (4 equiv.) was added to DMF (6 equiv.) at 0 °C. After 10–15 min, pyrazole (1.0 equiv.) was added to the reaction mixture, which was then stirred at 120°C until the pyrazole was completely consumed (based on TLC analysis). The reaction was quenched with water and was neutralized with a saturated solution of Na_2CO_3 to pH~7. The mixture was extracted with chloroform (3 times). The combined organic layers were dried with Mg_2SO_4, and filtered. The solvent was removed under vacuum and the residue was purified by silica gel column chromatography (diethyl ether/hexane) to afford the 1*H*-pyrazole-4-carbaldehyde.

5-Chloro-1-methyl-3-propyl-1*H*-pyrazole-4-carbaldehyde (2a). The general procedure was followed using 5-chloro-1,3-dimethyl-1*H*-pyrazole 1a (2 mmol), reaction time: 1 h, 250 mg (67%) orange oil, R_f 0.33 (diethyl ether/hexane, 1:1 v/v). IR (film): 2961, 2931, 2873, 1682, 1510, 1470, 772 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.85 (s, 1H), 3.83 (s, 3H), 2.81 (t, 2H, *J* 7.3 Hz), 1.67 (m, 2H), 0.97 (t, 3H, *J* 7.0 Hz) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.2, 154.9, 133.6, 115.8, 35.9, 29.8, 21.8, 13.8 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -75.8, -180.7 ppm. MS (EI, 70 eV): *m*/z (%) 186 (98, [M+]), 171 (85), 157 (81), 130 (100), 76 (45). Anal. calcd. for $C_8H_{11}ClN_2O$: C, 51.48; H, 5.94; Cl, 19.00; N, 15.01. Found %: C, 51.62; H, 5.95; Cl, 18.95; N, 14.98.

5-Chloro-1,3-dipropyl-1*H*-pyrazole-4-carbaldehyde (2b). The general procedure was followed using 5-chloro-1,3-dipropyl-1*H*-pyrazole (1b, 2 mmol), reaction time: 1 h, 279 mg (65%), orange oil, R_f 0.30 (diethyl ether/hexane, 1:1 v/v). IR (film): 2964, 2934, 2875, 1683, 1521, 1469, 776 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.86 (s, 1H), 4.08 (t, 2H, *J* 7.2 Hz), 2.82 (t, 2H, *J* 7.7 Hz), 1.83-1.93 (m, 2H), 1.64-1.73 (m, 2H), 0.92-0.98 (m, 6H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.3, 154.9, 133.1, 115.6, 50.5, 29.9, 22.8, 21.9, 13.8, 10.9 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -77.4, -169.2 ppm. MS (EI, 70 eV): *m*/z (%) 214 (76, [M+]), 199 (50), 186 (45), 179 (60), 158 (100), 143 (55). Anal. calcd. for $C_{10}H_{15}ClN_2O$: C, 55.94; H, 7.04; Cl, 16.51; N, 13.05. Found %: C, 51.82; H, 7.06; Cl, 16.56; N, 13.03.

5-Chloro-1-(2-chloroethyl)-3-propyl-1*H*-pyrazole-4-carbaldehyde (2c). The general procedure was followed using 2-(5-chloro-3-propyl-1*H*-pyrazol-1-yl)ethanol (1c, 2 mmol), reaction time: 8 h, 273 mg (58%), colorless needles, m.p. 77-79 °C, R_f 0.16 (diethyl ether/hexane, 1:2 v/v). IR (film): 2962, 2933, 2872, 1682, 1522, 1464, 778 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.88 (s, 1H), 4.43 (t, 2H, *J* 6.4 Hz), 3.91 (t, 2H, *J* 6.1 Hz), 2.83 (t, 2H, *J* 7.8 Hz), 1.64-1.73 (m, 2H), 0.96 (t, 3H, *J* 7.3 Hz) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.2, 155.7, 134.4, 115.9, 49.7, 41.4, 29.9, 21.6, 13.7 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$) δ -78.5, -176.8 ppm. MS (EI, 70 eV): *m*/z (%) 234 (60, [M+]), 219 (62), 206 (60), 178 (100), 157 (56), 143 (52), 63 (88). Anal. calcd. for $C_9H_{12}Cl_2N_2O$: C, 45.98; H, 5.14; Cl, 30.16; N, 11.91. Found %: C, 46.10; H, 5.14; Cl, 30.08; N, 11.90.

1-Benzyl-5-chloro-3-propyl-1*H*-pyrazole-4-carbaldehyde (2d). The general procedure was followed using 1-benzyl-5-chloro-3-propyl-1*H*-pyrazole (1d, 2 mmol), reaction time: 2.5 h, 289 mg (55%), orange powder, mp 35 °C, R_f 0.47 (diethyl ether/hexane, 1:1 v/v). IR (film): υ 3066, 2962, 2932, 2873, 1683, 1521, 1463, 775 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.88 (s, 1H), 7.25-7.37 (m, 5H), 5.33 (s, 2H), 2.85 (t, 2H, *J* 7.7 Hz), 1.67-1.76 (m, 2H), 0.98 (t, 3H, *J* 7.4 Hz) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.2, 155.2, 134.8, 133.4, 128.9, 128.3, 127.5, 116.1, 52.7, 29.8, 21.8, 13.8 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -75.6, -170.4 ppm. MS (EI, 70 eV): *m*/z (%) 262 (23, [M+]), 91 (100), 65 (34), 130 (100), 76 (45). Anal. calcd. for $C_{14}H_{15}ClN_2O$: C, 64.00; H, 5.75; Cl, 13.49; N, 10.66. Found %: C, 64.18; H, 5.77; Cl, 13.53; N, 10.62.

1-Benzyl-5-chloro-3-methyl-1*H*-pyrazole-4-carbaldehyde (2e). The general procedure was followed using 1-benzyl-5-chloro-3-methyl-1*H*-pyrazole (1e, 2 mmol), reaction time: 2.5 h, 286 mg (61%), orange powder, m.p.

101-102 °C, R_f 0.30 (diethyl ether/hexane, 1:2 v/v). IR (film): 3062, 2961, 2849, 1681, 1526, 1460, 765 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.87 (s, 1H), 7.25-7.37 (m, 5H), 5.30 (s, 2H), 2.47 (s, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.2, 151.0, 134.8, 133.5, 128.7, 128.2, 127.4, 116.3, 52.5 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -75.5, -170.4 ppm. MS (EI, 70 eV): *m*/z (%) 234 (15, [M+]), 199 (11), 91 (100), 65 (17). Anal. calcd. for $C_{12}H_{11}ClN_2O$: C, 61.42; H, 4.72; Cl, 15.11; N, 11.94. Found %: C, 61.35; H, 4.75; Cl, 15.07; N, 11.98.

5-Chloro-1-phenyl-3-propyl-1*H*-pyrazole-4-carbaldehyde (2f). The general procedure was followed using 5-chloro-1-phenyl-3-propyl-1*H*-pyrazole (1f, 2 mmol), reaction time: 14 h, 269 mg (54%), light brown needles, m.p. 151-152 °C, R_f 0.23 (diethyl ether/hexane, 1:8 v/v). IR (film): υ 3064, 2951, 2923, 2854, 1675, 1525, 1462, 766 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.97 (s, 1H), 7.45-7.56 (m, 5H), 2.90 (t, 2H, *J* 7.6 Hz), 1.70-1.79 (m, 2H), 1.00 (t, 3H, *J* 7.3 Hz) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.6, 155.7, 136.9, 133.4, 129.2, 129.0, 125.1, 116.9, 29.8, 21.6, 13.8 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -73.0, -165.3 ppm. MS (EI, 70 eV): *m*/z (%) 248 (45, [M+]), 220 (41), 192 (82), 133 (35), 77 (100). Anal. calcd. for $C_{13}H_{13}ClN_2O$: C, 62.78; H, 5.27; Cl, 14.25; N, 11.26. Found %: C, 62.60; H, 5.25; Cl, 14.20; N, 13.30.

5-Chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde (2g). The general procedure was followed using 5-chloro-3-methyl-1-phenyl-1*H*-pyrazole (1g, 2 mmol), reaction time: 14 h, 230 mg (52%), dark red needle, m.p. 142-143 °C, R_f 0.17 (diethyl ether/hexane, 1:5 v/v). IR (film): 3065, 2927, 1676, 1527, 1469, 764 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.97 (s, 1H), 7.46-7.55 (m, 5H), 2.54 (s, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.8, 151.7, 136.8, 133.4, 129.2, 129.1, 125.1, 117.3, 13.8 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -72.9, -165.1 ppm. MS (EI, 70 eV): *m*/z (%) 220 (93, [M+]), 219 (100), 155 (22), 77 (63), 51 (50). Anal. calcd. for $C_{11}H_9ClN_2O$: C, 59.88; H, 4.11; Cl, 16.07; N, 12.70. Found %: C, 59.73; H, 4.09; Cl, 16.10; N, 12.73.

5-Chloro-1-methyl-3-phenyl-1*H*-pyrazole-4-carbaldehyde (2h). The general procedure was followed using 5-chloro-1-methyl-3-phenyl-1*H*-pyrazole (1h, 2 mmol), reaction time: 14 h, 221 mg, (50%) beige oil, R_f 0.50 (diethyl ether/hexane, 1:1 v/v). IR (film): 3062, 2946, 1683, 1502, 1448, 779 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.92 (s, 1H), 7.72-7.73 (m, 2H), 7.43-7.45 (m, 3H), 3.90 (s, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.3, 153.3, 133.1, 130.9, 129.2, 128.6, 128.4, 115.3, 36.2 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$) δ -75.0, -176.7 ppm. MS (EI, 70 eV): *m*/z (%) 220 (100, [M+]). Anal. calcd. for $C_{11}H_9ClN_2O$: C, 59.88; H, 4.11; Cl, 16.07; N, 12.70. Found %: C, 59.71; H, 4.10; Cl, 16.08; N, 12.75.

5-Chloro-1-methyl-3-(4-methylphenyl)-1*H*-pyrazole-4-carbaldehyde (2i). The general procedure was followed using 5-chloro-1-methyl-3-(4-methylphenyl)-1*H*-pyrazole (1i, 2 mmol), reaction time: 14 h, 263 mg (56%), beige powder, mp 105-107 °C, R_f 0.33 (diethyl ether/hexane, 1:1 v/v). IR (film): 3058, 2920, 1673, 1492, 1451, 830 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$) δ 9.95 (s, 1H), 7.62-7.64 (m, 2H), 7.27-7.29 (m, 2H), 3.94 (s, 3H), 2.42 (s, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.6, 153.6, 139.4, 133.0, 129.2, 128.6, 128.4, 115.3, 36.2 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -75.8, -177.8 ppm. MS (EI, 70 eV): *m*/z (%) 234 (100, [M+]), 219 (66), 116 (28), 91 (23), 76 (19). Anal. calcd. for $C_{12}H_{11}ClN_2O$: C, 61.41; H, 4.72; Cl, 15.11; N, 11.94. Found %: C, 61.52; H, 4.71; Cl, 15.08; N, 11.93.

3-(4-Bromophenyl)-5-chloro-1-methyl-1*H*-pyrazole-4-carbaldehyde (2j). The general procedure was followed using 3-(4-bromophenyl)-5-chloro-1-methyl-1*H*-pyrazole (1g, 2 mmol), reaction time: 10 h, 330 mg (55%), light yellow needles, mp 74-76 °C, R_f 0.23 (diethyl ether/hexane, 1:2 v/v). IR (film): 3076, 2945, 1684, 1499, 1446, 834, 778 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.94 (s, 1H), 7.69-7.71 (m, 2H), 7.59-7.61 (m, 2H), 3.95 (s, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.0, 151.8, 134.3, 131.6, 130.2, 130.0, 123.7, 115.4, 36.4 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -74.6, -177.1 ppm. MS (EI, 70 eV): *m*/z (%) 298 (70, [M+]), 219 (53), 109 (29), 76 (42), 50 (18). Anal. calcd. for $C_{11}H_8BrClN_2O$: C, 44.11; H, 2.69; Br, 26.67; Cl, 11.84; N, 9.35. Found %: C, 44.07; H, 2.68; Cl, 11.88; N, 9.32.

5-Chloro-3-(4-fluorophenyl)-1-methyl-1*H*-pyrazole-4-carbaldehyde (2k). The general procedure was followed using 5-chloro-3-(4-fluorophenyl)-1-methyl-1*H*-pyrazole (1k, 2 mmol), reaction time: 10 h, 253 mg (53%), peach powder, m.p. 226-227 °C; R_f 0.37 (diethyl ether/hexane, 1:1 v/v). IR (film): 3076, 2945, 1684, 1499, 1446, 778 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.93 (s, 1H), 7.78-7.81 (m, 2H), 7.13-7.17 (m, 2H), 3.95 (s, 3H, CH_3) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.0, 163.4 (d, $^1J_{C,F}$ 249.3 Hz), 151.9, 134.1, 130.5 (d, $^3J_{C,F}$ 8.4 Hz), 127.1 (d, $^4J_{C,F}$ 3.2 Hz), 115.4 (d, $^2J_{C,F}$ 21.6 Hz), 115.2, 36.2 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -75.4, -177.4 ppm. MS (EI, 70 eV): *m*/z (%) 238 (100, [M+]), 203 (27), 175 (20), 156 (41), 131 (18), 107 (40), 95 (32), 76 (54). Anal. calcd. for $C_{11}H_8ClFN_2O$: C, 55.36; H, 3.38; Cl, 14.86; F, 7.96, N, 11.74. Found %: C, 55.45; H, 3.39; Cl, 14.80; N, 11.75.

5-Chloro-1-methyl-3-(4-nitrophenyl)-1*H*-pyrazole-4-carbaldehyde (2l). The general procedure was followed using 5-chloro-1-methyl-3-(4-nitrophenyl)-1*H*-pyrazole (1m, 2 mmol), reaction time: 14 h, 244 mg (46%), beige powder, mp 171-172 °C; R_f 0.23 (diethyl ether/hexane, 1:1 v/v). IR (film): 3106, 3080, 2922, 2850, 1688, 1519, 1345, 778 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.97 (s, 1H), 8.29-8.31 (m, 2H), 8.08-8.10 (m, 2H), 3.99 (s, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 182.6, 149.9, 148.2, 137.4, 135.7, 129.5, 123.6, 115.8, 36.6 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -8.1, -69.9, -176.3 ppm. MS (EI, 70 eV): *m*/z (%) 265 (100, [M+]), 248 (16), 218 (33), 107 (29), 76 (27), 50 (15). Anal. calcd. for $C_{11}H_8ClN_3O_3$: C, 49.73; H, 3.04; Cl, 13.35; N, 15.82. Found %: C, 49.81; H, 3.03; Cl, 13.30; N, 15.77.

5-Chloro-1,3-dimethyl-1*H*-pyrazole-4-carbaldehyde (2m). The general procedure was followed using 5-chloro-1,3-dimethyl-1*H*-pyrazole (1l, 2 mmol), reaction time: 1 h, 209 mg (66%), orange needles, mp 67-68 °C, R_f 0.38 (diethyl ether/hexane, 2:1 v/v). IR (film): 2937, 1682, 1528, 1476, 771 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.95 (s, 1H), 3.81 (s, 3H), 2.44 (s, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.3, 150.8, 133.6, 116.2, 35.8, 13.6 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -77.0, -180.5 ppm. MS (EI, 70 eV): *m*/z (%) 158 (54, [M+]), 157 (100). Anal. calcd. for $C_6H_7ClN_2O$: C, 45.44; H, 4.45; Cl, 22.36; N, 17.66. Found %: C, 45.29; H, 4.44; Cl, 22.41; N, 17.61.

5-Chloro-3-(chloromethyl)-1-methyl-1*H*-pyrazole-4-carbaldehyde (2n). The general procedure was followed using 5-chloro-3-(chloromethyl)-1-methyl-1*H*-pyrazole (1n, 2 mmol), reaction time: 1 h, 228 mg (59%), white powder, mp 105-106 °C, R_f 0.20 (diethyl ether/hexane, 1:1 v/v). IR (film): 2927, 2858, 1671, 1517, 1482, 769 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.90 (s, 1H), 4.78 (s, 2H), 3.89 (s, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 182.5, 149.4, 134.1, 115.7, 36.9, 36.3 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -70.1, -178.4 ppm. MS (EI, 70 eV): *m*/z (%) 193 (43, [M+]), 192 (80), 191 (59), 157 (100), 156 (50), 76 (41). Anal. calcd. for $C_6H_6Cl_2N_2O$: C, 37.33; H, 3.13; Cl, 36.73; N, 14.51. Found %: C, 37.20; H, 3.14; Cl, 36.75; N, 14.49.

5-Chloro-3-(1-chloroethyl)-1-methyl-1*H*-pyrazole-4-carbaldehyde (2o). The general procedure was followed using 5-chloro-3-(1-chloroethyl)-1-methyl-1*H*-pyrazole (1o, 2 mmol), reaction time: 2 h, 17 mg (4%); R_f 0.27 (diethyl ether/hexane, 1:2 v/v). ^1H NMR (400.13 MHz, $CDCl_3$): δ 9.92 (s, 1H), 5.58 (q, *J* 6.9 Hz, 1H), 3.88 (s, 3H), 1.88 (d, *J* 6.9 Hz, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 182.6, 150.0, 134.2, 114.8, 49.4, 36.3, 23.1 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -72.3, -179.4 ppm.

(5-chloro-1-phenyl-3-propyl-1*H*-pyrazol-4-yl)methanol (3). The general procedure was followed using 5-chloro-1-phenyl-3-propyl-1*H*-pyrazole (1f, 2 mmol), reaction time: 14 h, 30 mg, (6%), yellow oil, R_f 0.40 (diethyl ether/hexane, 1:8 v/v). IR (film): 3062, 2960, 2929, 2869, 1551, 1502, 1464, 1423, 761, 693 cm^{-1}. ^1H NMR (400.13 MHz, $CDCl_3$): δ 7.54-7.56 (m, 1H), 7.46-7.50 (m, 2H), 7.39-7.42 (m, 2H), 4.57 (s, 2H), 2.71 (t, *J* 7.8 Hz, 2H), 1.75-1.81 (m, 2H), 1.04 (t, *J* 7.3 Hz, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 153.1, 138.2, 129.0, 128.2, 127.0, 124.9, 114.2, 29.1, 22.3, 16.1, 13.8 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -76.0, -169.1 ppm. MS (EI, 70 eV): *m*/z (%) 233 [100], 205 [64], 77 [84], 51 [66]. Anal. calcd. for $C_{13}H_{15}ClN_2O$: C, 62.28; H, 6.03; Cl, 14.14; N, 11.17. Found %: C, 62.18; H, 6.02; Cl, 14.18; N, 11.21.

5-chloro-3-ethenyl-1-methyl-1*H*-pyrazole-4-carbaldehyde (4). The general procedure was followed using 5-chloro-3-(1-chloroethyl)-1-methyl-1*H*-pyrazole (1o, 2 mmol), reaction time: 2 h, 24 mg (7%), R_f 0.27 (diethyl ether/hexane, 1:2 v/v). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 9.90 (s, 1H), 7.04 (dd, *J* 11.3, 17.7 Hz, 1H), 6.22 (dd, *J* 17.7, 1.0 Hz, 1H), 5.50 (dd, *J* 11.3, 1.0 Hz, 1H), 3.88 (s, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 183.0, 150.0, 133.9, 126.3, 119.8, 115.4, 36.2 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -78.8 , -179.4 ppm.

(2E)-3-(5-chloro-1-methyl-1*H*-pyrazol-3-yl)prop-2-enal (5). The general procedure was followed using 5-chloro-3-(1-chloroethyl)-1-methyl-1*H*-pyrazole (1o, 2 mmol), reaction time: 2 h, 246 mg (72%), white powder, mp 68-70°C, R_f 0.15 (diethyl ether/hexane, 1:2 v/v). IR (film): 3134, 2851, 2827, 1672, 1633, 1504, 974, 786 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 9.87 (d, *J* 7.8 Hz, 1H), 7.37 (d, *J* 15.9 Hz, 1H), 6.59 (dd, *J* 7.8, 15.9 Hz, 1H), 6.52(s, 1H), 3.90 (s, 3H) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 193.4, 146.9, 143.4, 129.5, 129.2, 104.0, 36.6 ppm. ^{15}N NMR (40.56 MHz, $CDCl_3$): δ -66.1, -175.6 ppm. MS (EI, 70 eV) *m/z* %: 170 (20, [M+]), 142 (100), 141 (53), 107 (22), 81 (32). Anal. calcd. for $C_7H_7ClN_2O$: C, 49.28; H, 4.14; Cl, 20.78; N, 16.42. Found %: C, 49.16; H, 4.16; Cl, 20.73; N, 16.47.

5(3)-Chloro-3(5)-propyl-1*H*-pyrazole (6). The general procedure was followed using 1-*tert*-butyl-5-chloro-3-propyl-1*H*-pyrazole (1p, 2 mmol), reaction time: 2 h, 252 mg (87%), yellow oil, R_f 0.20 (diethyl ether/hexane, 1:1 v/v). IR (film): 3186, 3141, 2965, 2871, 1576, 1462, 1368, 798 cm^{-1}. ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 6.00 (s, 1H), 2.69 (t, 2H, *J* 7.6 Hz), 1.67 (m, 2H), 0.98 (t, 3H, *J* 7.3 Hz) ppm. ^{13}C NMR (100.61 MHz, $CDCl_3$): δ 146.6, 139.7, 102.7, 27.8, 22.4, 13.6 ppm. ^{15}N NMR (40.56 MHz): δ -101.3, -178.3 ppm. MS (EI, 70 eV): *m*/z (%) 144 (47, [M+]), 116 (100), 115 (92). Anal. calcd. for $C_6H_9ClN_2$: C, 49.84; H, 6.27; Cl, 24.52; N, 19.37. Found %: C, 50.00; H, 6.28; Cl, 24.46; N, 19.30.

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Supplementary Material

Copies of spectra of compounds are provided in the supplementary material file available on the Publisher's web site.

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