

# Synthesis of 3-substituted 1-phenyl-1*H*-pyrazole-4-carbaldehydes and the corresponding ethanones by Pd-catalysed cross-coupling reactions

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## Abstract

An efficient synthetic route to construct *ortho*-substituted 1-phenyl-1*H*-pyrazole-4-carboxaldehydes and the corresponding ethanones starting from 1-phenyl-1*H*-pyrazol-3-ol is described. Carbon-carbon bond-forming Pd-catalysed cross-coupling reactions were applied for the functionalisation of the intermediate pyrazole triflates. Detailed NMR spectroscopic investigations were undertaken with all obtained products.

**Keywords:** Pyrazole, triflate, Pd-catalysed reactions, NMR (<sup>1</sup>H, <sup>13</sup>C, <sup>15</sup>N, <sup>19</sup>F)

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## Introduction

Palladium-catalysed cross-coupling reactions have proven to be one of the most powerful tools for the formation of the carbon-carbon bond in organic synthesis due to their excellent selectivity and broad tolerance for functional groups.<sup>1</sup> In recent years, this method has been increasingly employed for the functionalisation of nitrogen heterocycles.<sup>2</sup> A number of accordant studies on azoles with these reactions have been published.<sup>3</sup> These heteroarenes represent the prevalent substructures for a variety of target compounds, with applications ranging from pharmaceuticals to molecular organic materials. In particular, substituted pyrazoles (1,2-diazoles) are interesting building blocks and frequently encountered structural units in a variety of pharmaceuticals,<sup>4</sup> agrochemicals,<sup>5</sup> dyes<sup>6</sup> and complexing agents.<sup>7</sup> Appropriate pyrazole halides have mainly been

used as precursors for the functionalisation of pyrazoles *via* Heck,<sup>8</sup> Suzuki,<sup>8,9</sup> Sonogashira,<sup>8,9d-f,10</sup> and Stille couplings<sup>8,9e,11</sup>. Recently, pyrazole triflates have also been employed in Suzuki<sup>12</sup> and Negishi couplings.<sup>13</sup> These reactive species are readily available by triflation of the corresponding pyrazolones (hydroxypyrazoles), which are frequently available from commercial sources. The use of *O*-triflated pyrazoles as common intermediates for the preparation of *ortho*-substituted pyrazoles *via* palladium-mediated cross-coupling strategies remains largely unexplored but is anticipated as a powerful synthetic approach for the functionalisation of such compounds, especially to obtain fused systems containing pyrazole subunits.

In this respect, (hetero)aromatic systems bearing an alkyne moiety and a formyl (or acetyl) group in *ortho*-position represent suitable starting materials for various annulation reactions leading to the formation of condensed heterocyclic systems. Recent examples for such a synthetic approach include the transformations of 2-alkynylquinoline-3-carbaldehydes into benzo[*b*][1,6]naphthyridines,<sup>14</sup> 4-alkynylpyrimidine-5-carbaldehydes into quinoxalines or pyrido[4,3-*d*]pyrimidines,<sup>15</sup> and 5-acetyl-4-alkynylthiazoles into the corresponding pyrido[3,4-*c*]thiazoles.<sup>16</sup>

Moreover, an acetyl group and a phenyl ring attached at the *ortho*-position on a (hetero)aromatic system can be successfully employed for annulation reactions. For example, 2-acetylbiphenyl, obtained by the Suzuki reaction from *ortho*-bromoacetophenone, was easily transformed into phenanthridine *via* a dioxime oxalate intermediate.<sup>17</sup>

Given this proven utility, it seems reasonable that the development of efficient synthetic methods for the construction of new *ortho*-substituted heterocycles from easily available starting materials might provide additional lead molecules for use in drug discovery and for the development of advanced materials. Thus, we herein report on our corresponding adaption of the above approach to *ortho*-substituted pyrazoles including (1) the efficient synthesis of the starting 3-triflyloxy-1-phenyl-1*H*-pyrazole-4-carbaldehyde and the corresponding ethanone from the common synthetic precursor 1-phenyl-1*H*-pyrazol-3-ol, and (2) the preparation of the target 3-substituted products by the palladium mediated cross-coupling reactions of the intermediate triflates with (hetero)aryl boronic acids, phenylacetylene and various alkenes.

## Results and Discussion

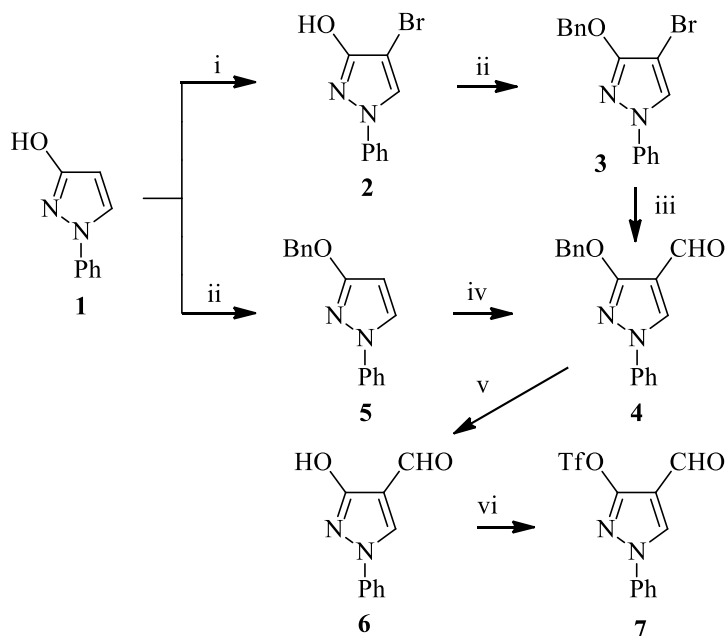
Triflates **7** and **9** represent the starting materials for our coupling reactions and hence are the key compounds of our investigations. Their synthesis was accomplished according to Scheme 1, originating from 3-hydroxy-1-phenyl-1*H*-pyrazole **1** as a common starting material. The latter was obtained from commercially available 1-phenylpyrazolidin-3-one following a known procedure.<sup>18</sup>

3-Hydroxy-1-phenyl-1*H*-pyrazole-4-carbaldehyde **6**, the precursor for the preparation of the triflate **7**, was obtained by a series of reactions including formylation at the 4-position. Although the preparation of **6** by oxidation of (3-benzyloxy-1-phenyl-1*H*-pyrazol-4-yl)methanol with

manganese dioxide and subsequent catalytic debenzoylation is reported in a patent application, neither a source of the starting material nor spectroscopic data of the products were provided.<sup>19</sup>

Several methods are known for the formylation of pyrazoles at the 4-position of the heteroaromatic ring, comprising synthesis *via* Grignard intermediates,<sup>20</sup> bromine-lithium exchange or direct *ortho*-lithiation followed by treatment with DMF,<sup>21</sup> and the Vilsmeier-Haack reaction.<sup>22</sup> However, the above mentioned metallation methods are not usually suitable in the case of unprotected hydroxyl derivatives, while formylation of hydroxypyrazoles by treatment with DMF/POCl<sub>3</sub> can lead to the replacement of the hydroxyl group by a chlorine atom.<sup>23</sup>

Facing these challenges, we explored two alternative synthetic strategies in order to obtain the desired aldehyde **6** (Scheme 1). The first approach is based on the transformation of compound **1** into a species suitable for selective lithiation. To this purpose, **1** was brominated according to a known procedure.<sup>18</sup> The obtained product **2** was further benzylated with benzyl chloride under standard conditions in alkaline medium to afford *O*-benzyl-4-bromo-1-phenyl-1*H*-pyrazole **3**. Treatment of **3** with *n*-BuLi at -78 °C gave rise to selective bromine-lithium exchange. Subsequent quenching of the intermediate 4-lithiopyrazole with 1.5 equiv of DMF afforded carbaldehyde **4** in 70% yield.



**Scheme 1.** Reagents and conditions: i: Br<sub>2</sub>, CHCl<sub>3</sub>, rt, 20 h, 75%; ii: BnCl, NaH, DMF, 0-60 °C, 1 h, 73% for **3**, 85% for **5**; iii: *n*-BuLi, THF, DMF, -78 °C, rt, 0.5 h, 70%; iv: POCl<sub>3</sub>, DMF, 70 °C, overnight, 60%; v: TFA, rt, 2 days, 85%; vi: Tf<sub>2</sub>O, TEA, DCM, rt, 1 h, 83%.

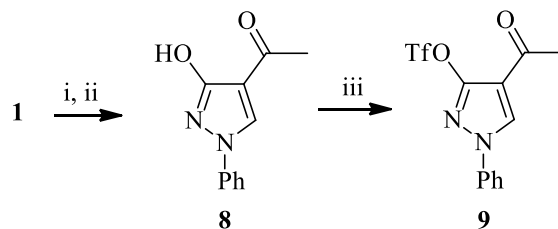
To find a more convenient method for the preparation of aldehyde **4**, we next explored the Vilsmeier-Haack reaction of 4-benzyloxy-1-phenyl-1*H*-pyrazole **5**, which was obtained by

benzylation of the starting compound **1**. After heating compound **5** with DMF/ $\text{POCl}_3$  at 70 °C for 12 h, the reaction gave the target carbaldehyde **4** in 60% yield.

Debenzylation of compound **4** was accomplished by treatment with TFA in toluene – conditions used for the selective deprotection of *O*-benzylsalicylaldehydes<sup>24</sup> – and furnished the target aldehyde **6** in 85% yield.

The most common method for the preparation of *O*-triflates consists of treatment of the hydroxylic substrates with  $\text{Tf}_2\text{O}$  in the presence of organic or inorganic base.<sup>12,13,16</sup> Hence, upon reaction of **6** with  $\text{Tf}_2\text{O}$  and TEA in  $\text{CH}_2\text{Cl}_2$  at room temperature and chromatography on silica gel, we obtained 3-triflyloxy-1*H*-pyrazole-4-carbaldehyde **7** in good yield and purity. No formation of unwanted mixture of *N*- and *O*-triflated products was detected (Scheme 1).

The triflate **9**, which contains a functional ethanone moiety, was obtained by triflation of 4-acetyl-1-phenyl-1*H*-pyrazol-3-ol **8**. The latter compound was synthesised using a known synthetic procedure involving the acetylation of 3-hydroxy-1-phenyl-1*H*-pyrazole following Fries rearrangement conditions ( $\text{AlCl}_3$ ,  $\text{CS}_2$ ) (Scheme 2).<sup>18</sup>

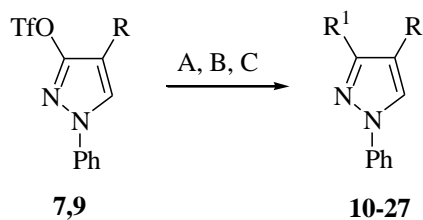


**Scheme 2.** Reagents and conditions: i:  $\text{Ac}_2\text{O}$ , 100 °C, 0.5 h, 75%; ii:  $\text{AlCl}_3$ ,  $\text{CS}_2$ , reflux, 3 h, 74%; iii  $\text{Tf}_2\text{O}$ , TEA, DCM, rt, 1 h, 85%.

Having successfully prepared pyrazole triflates **7** and **9**, we next examined their ability to participate in palladium-catalysed cross-coupling reactions. The triflates **7** and **9** smoothly underwent the Suzuki-type reaction with phenyl-, 3-chlorophenyl-, 4-(trifluoromethyl)phenyl-, 3-thiophene- and 2-naphthylboronic acids to give compounds **10-14** and **15-19**, respectively, in moderate to good yields (50-94%) (Table 1). In the course of these couplings,  $\text{Pd}(\text{PPh}_3)_4$  was used as a catalyst and anhydrous  $\text{K}_3\text{PO}_4$  as a base. The reaction was carried out in the presence of KBr, which is known to suppress triflate reduction by stabilizing the cationic ( $\sigma$ -aryl)-palladium transition state.<sup>25</sup> As outlined in Table 1, the final reaction times of triflates **7** and **9** were strongly dependent on the nature of the boronic acid, whereas prolonged reaction times had an opposite correlation with the yields of the target products. The synthesis of carbaldehyde **10** was reported earlier by a two-step pyrazole ring formation from acetophenone and phenylhydrazine to produce acetophenone phenylhydrazone, followed by Vilsmeier-Haack reaction to give the target carbaldehyde **10**,<sup>26</sup> which is widely used in the synthesis of biologically active molecules.<sup>27</sup> Carbaldehyde **14** was similarly obtained from acetophenone phenylhydrazone.<sup>28</sup>

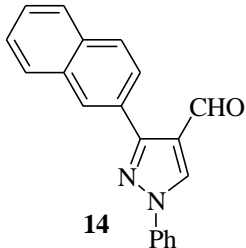
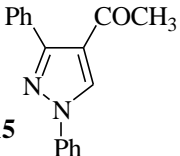
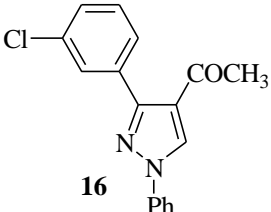
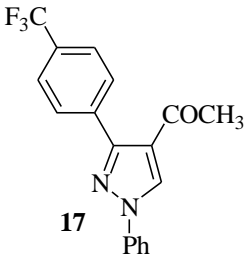
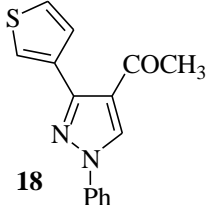
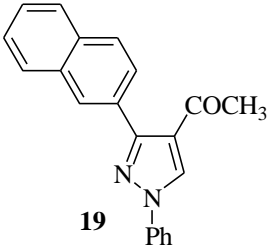
Standard Sonogashira reaction conditions [Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>, CuI, triethylamine] were applied to carry out cross-couplings of the triflates **7** and **9** with phenylacetylene. In both cases, the reaction proceeded smoothly to afford 3-(2-phenylethynyl)-1*H*-pyrazole-4-carbaldehyde **20** and [3-(2-phenylethynyl)-1*H*-pyrazol-4-yl]ethanone **21**, in 70 and 65% yield, respectively (entries 11, 12, Table 1).

**Table 1.** Preparation of 3-substituted 1-phenylpyrazole-4-carbaldehydes and the corresponding ethanones

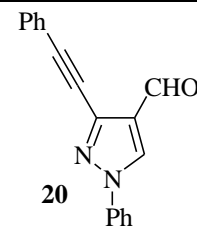
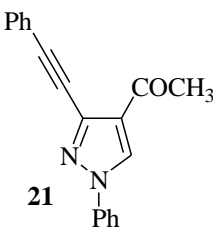
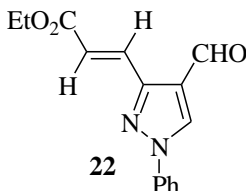
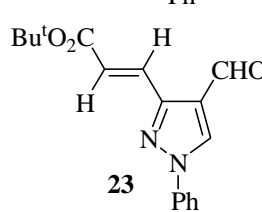
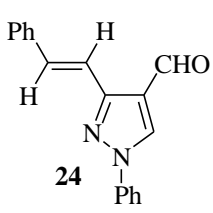
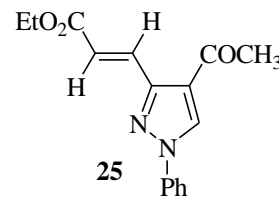
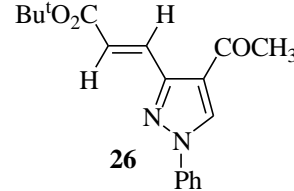


Entry	Substrate	Reagent	Conditions <sup>a</sup>	Time (h)	Product	Yield (%)
1	<b>7</b>	Phenylboronic acid	A	2		94
2	<b>7</b>	3-Chlorophenylboronic acid	A	1		82
3	<b>7</b>	4-(Trifluoromethyl)phenylboronic acid	A	8		60
4	<b>7</b>	3-Thienylboronic acid	A	1.5		80

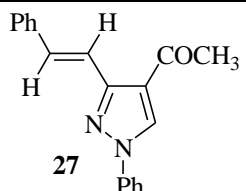
**Table 1.** Continued

Entry	Substrate	Reagent	Conditions <sup>a</sup>	Time (h)	Product	Yield (%)
5	<b>7</b>	2-Naphthylboronic acid	A	3		79
6	<b>9</b>	Phenylboronic acid	A	0.5		81
7	<b>9</b>	3-Chlorophenylboronic acid	A	24		50
8	<b>9</b>	4-(Trifluoromethyl)phenylboronic acid	A	3		82
9	<b>9</b>	3-Thienylboronic acid	A	24		60
10	<b>9</b>	2-Naphthylboronic acid	A	1		77

**Table 1.** Continued

Entry	Substrate	Reagent	Conditions <sup>a</sup>	Time (h)	Product	Yield (%)
11	<b>7</b>	Phenylacetylene	B	1	 <b>20</b>	81
12	<b>9</b>	Phenylacetylene	B	3	 <b>21</b>	65
13	<b>7</b>	Ethyl acrylate	C	9	 <b>22</b>	37
14	<b>7</b>	<i>tert</i> -Butyl acrylate	C	18	 <b>23</b>	13
15	<b>7</b>	Styrene	C	6	 <b>24</b>	15
16	<b>9</b>	Ethyl acrylate	C	12	 <b>25</b>	78
17	<b>9</b>	<i>tert</i> -Butyl acrylate	C	2	 <b>26</b>	58

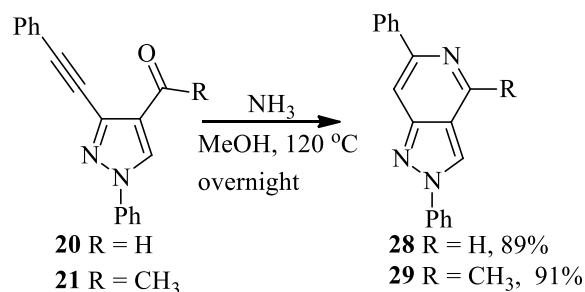
**Table 1.** Continued

Entry	Substrate	Reagent	Conditions <sup>a</sup>	Time (h)	Product	Yield (%)
18	<b>9</b>	Styrene	C	12	 <b>27</b>	55

<sup>a</sup>See Section 4.

To evaluate the effectiveness of Heck reactions with triflates **7** and **9**, styrene, ethyl and *tert*-butyl acrylates were representatively employed as coupling partners. The usual Heck reaction conditions [Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>, TEA] gave poor yields (13-37%) of 3-alkenylpyrazole-4-carbaldehydes **22-24** (entries 13-15, Table 1), though they were more successful (55-78%) for the 3-alkenylpyrazolyl ethanones **25-27** (entries 16-18, Table 1). The best yields were obtained by coupling the corresponding triflates with ethyl acrylate. Variations of the reaction parameters such as the catalyst [Pd(PPh<sub>3</sub>)<sub>4</sub>, Pd(PPh<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>, Pd(dba)<sub>3</sub>] and the base [TEA, NEt(*i*Pr)<sub>2</sub>], did not result in a marked improvement of yield. The cross-coupled products **22-27** were obtained in an isomerically pure *E*-form after isolation and purification by column chromatography.

The prepared 3,4-difunctionalized pyrazoles are potential synthons in the synthesis of annelated heterocyclic systems. This was briefly demonstrated by treatment of compounds **20** and **21** bearing the phenylethynyl moiety adjacent to the carbonyl group with dry ammonia under elevated temperature and pressure.<sup>16</sup> The direct formation of pyrazolo[4,3-*c*]pyridines **28** and **29** (Scheme 3) was observed in excellent yields.



### Scheme 3

Spectral and analytical data for all new compounds were consistent with the given structures. Most newly obtained compounds were subjected to detailed NMR spectroscopic investigations using standard techniques, leading to the unambiguous assignment of chemical shifts and relevant spin coupling constants (see Experimental).



## Conclusions

In conclusion, we developed a general approach for the preparation of 3-ethynyl-, 3-ethenyl- and 3-(het)aryl- substituted 1-phenyl-1*H*-pyrazole-4-carbaldehydes and the corresponding ethanones from 1-phenylpyrazol-3-ol *via* intermediate triflates by employing Suzuki, Sonogashira and Heck cross-coupling reactions.

## Experimental Section

**General.** Melting points were determined in capillary tubes on melting point apparatus Electrothermal MEL-TEMP®. Infrared spectra were recorded with Perkin Elmer Spectrum One spectrometer using potassium bromide pellets. <sup>1</sup>H NMR spectra were recorded at 300 MHz on a Varian UnityPlus spectrometer and at 500 MHz on a Bruker Avance 500 spectrometer, <sup>13</sup>C NMR spectra were registered at 75 and 125 MHz, respectively. Chemical shifts, expressed in ppm, were relative to tetramethylsilane (TMS). <sup>15</sup>N NMR spectra (50.68 MHz, referenced against external nitromethane) and <sup>19</sup>F NMR spectra (470.56 MHz, absolute referencing *via*  $\bar{\epsilon}$  ratio) were obtained on a Bruker Avance 500 instrument with a 'directly' detecting broadband observe probe (BBFO). Mass spectra were recorded using a Waters ZQ instrument (ion spray). Elemental analyses (C, H, N) were performed with an Exeter Analytical CE-440 Elemental Analyzer at the Microanalytical Laboratory, Kaunas University of Technology, and were in good agreement ( $\pm 0.4\%$ ) with the calculated values. For thin layer chromatographic (TLC) analyses, Merck precoated TLC plates (silica gel 60 F254) were used. Dry THF was distilled from sodium and benzophenone.

### Synthetic procedures

**3-(Benzyloxy)-4-bromo-1-phenyl-1*H*-pyrazole (3).** A solution of 4-bromo-3-hydroxy-1-phenyl-1*H*-pyrazole **2**<sup>18</sup> (1.67 g, 7 mmol) in dry DMF (20 mL) was cooled to 0 °C under inert atmosphere and NaH (60% dispersion in mineral oil, 280 mg, 7 mmol) was added portion wise. After mixing for 15 min. benzyl chloride (0.8 mL, 7 mmol) was added drop wise. The mixture was stirred at 60 °C for 1 hour, then poured into water and extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtrated, the solvent was evaporated. The residue was purified by column chromatography (SiO<sub>2</sub>, eluent: ethyl acetate/*n*-hexane, 1:7, v/v) to give pure **3**. White solid, yield 73%, 1.68 g, mp 77-78 °C; IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 3135 (CH<sub>arom</sub>), 2925 (CH<sub>aliph</sub>), 1598, 1543, 1495, 1360 (C=C, C-N), 1218, 1097 (C-O), 754, 745, 687, 674 (CH=CH of monosubstituted benzenes). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  5.41 (s, 2H, CH<sub>2</sub>), 7.25 (m, 1H, NPh H-4), 7.37 (m, 1H, CPh H-4), 7.42 (m, 2H, CPh H-3,5), 7.44 (m, 2H, NPh H-3,5), 7.55 (m, 2H, CPh H-2,6), 7.58 (m, 2H, NPh H-2,6), 7.79 (s, 1H, H-5). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta_{\text{C}}$  71.1 (CH<sub>2</sub>, <sup>1</sup>J = 147.0 Hz, <sup>3</sup>J (OCH<sub>2</sub>,CPhH2,6)=4.6 Hz), 82.5 (C-4, <sup>2</sup>J(C4,H5)=5.2 Hz), 117.6 (NPh C-2,6), 125.7 (NPh C-4), 127.7 (C-5, <sup>1</sup>J = 192.0 Hz), 128.0

(CPh C-2,4,6), 128.4 (CPh C-3,5), 129.4 (NPh C-3,5), 136.7 (CPh C-1), 139.7 (NPh C-1), 160.6 (C-3,  $^3J(\text{C3,H5}) = 8.8$  Hz,  $^3J(\text{C3,OCH}_2) = 2.7$  Hz); MS  $m/z$  (%): 353/351 ( $[\text{M} + \text{Na}]^+$ , 100). Anal. Calcd for  $\text{C}_{16}\text{H}_{13}\text{BrN}_2\text{O}$ : C, 58.38; H, 3.98; N, 8.51. Found: C, 58.70; H, 4.07; N, 8.23.

**3-(Benzyloxy)-1-phenyl-1H-pyrazole-4-carbaldehyde (4). Method iii.** To a solution of **3** (656 mg, 2 mmol) in 16 mL of dry THF under inert atmosphere at  $-78$  °C *n*-BuLi (2.5 M in hexane, 0.8 mL, 2 mmol) was added drop wise and dry DMF (0.23 mL, 3 mmol) was added. The mixture was gradually warmed up to room temperature and stirred for 30 min. The reaction mixture was poured into water and extracted with ethyl acetate. The organic layers were combined, washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , filtrated, the solvent was evaporated. The residue was purified by column chromatography ( $\text{SiO}_2$ , eluent: ethyl acetate/*n*-hexane, 1:5, v/v) to give pure **4**. White solid, yield 70%, 389 mg.

**Method iv.** Phosphorus oxychloride (0.73 mL, 8 mmol) was added dropwise to dry DMF (0.61 mL, 8 mmol) at  $-10$  °C. Then **5** (500 mg, 2 mmol) was added to the Vilsmeier-Haack complex and the reaction mixture heated at  $70$  °C for 12 h. After neutralization with 10% aq  $\text{NaHCO}_3$ , the precipitate was filtered off and recrystallized from dichloromethane. Yield 60%, 334 mg, mp  $151$ - $153$  °C (lit. mp  $153$ - $154$  °C);<sup>19a</sup> IR ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3094 ( $\text{CH}_{\text{arom}}$ ), 2957 ( $\text{CH}_{\text{aliph}}$ ), 1667 (C=O), 1559, 1504, 1360 (C=C, C-N), 1222, 1203 (C-O), 753, 735, 687, 677 (CH=CH of monosubstituted benzenes),  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  5.46 (s, 2H,  $\text{CH}_2$ ), 7.34 (m, 1H, NPh H-4), 7.38 (m, 1H, CPh H-4), 7.42 (m, 2H, CPh H-3,5), 7.48 (m, 2H, NPh H-3,5), 7.53 (m, 2H, CPh H-2,6), 7.66 (m, 2H, NPh H-2,6), 8.27 (s, 1H, H-5), 9.89 (CHO).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{C}}$  71.1 ( $\text{CH}_2$ ,  $^1J = 147.4$  Hz,  $^3J(\text{OCH}_2, \text{CPhH-2,6}) = 4.3$  Hz), 111.5 (C-4,  $^2J(\text{C4,CHO}) = 25.0$  Hz,  $^2J(\text{C4,H5}) = 6.9$  Hz), 118.8 (NPh C-2,6), 127.2 (NPh C-4), 128.2 (CPh C-2,6), 128.3 (CPh C-4), 128.5 (CPh C-3,5), 129.3 (C-5,  $^1J = 190.1$  Hz,  $^3J(\text{C5,CHO}) = 5.1$  Hz), 129.6 (NPh C-3,5), 136.2 (CPh C-1), 139.0 (NPh C-1), 163.6 (C-3,  $^3J(\text{C3,H5}) = 8.8$  Hz,  $^3J(\text{C3,OCH}_2) = 2.7$  Hz), 183.3 (CHO,  $^1J = 176.5$  Hz); MS  $m/z$  (%): 301 ( $[\text{M} + \text{Na}]^+$ , 100); Anal. Calcd for  $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_2 \cdot 0.5 \text{H}_2\text{O}$ : C, 71.07; H, 5.26; N, 9.75. Found: C, 71.09; H, 5.14; N, 9.59.

**3-(Benzyloxy)-1-phenyl-1H-pyrazole (5).** This compound was synthesized in analogy to compound **3** from 3-hydroxy-1-phenyl-1H-pyrazole **1** (1.12 g, 7 mmol). White solid, yield 85%, 1.49 g, mp  $71$  °C; IR ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3035 ( $\text{CH}_{\text{arom}}$ ), 2954 ( $\text{CH}_{\text{aliph}}$ ), 1547, 1478, 1359 (C=C, C-N), 1048, 1019 (C-O), 758, 737, 699, 689 (CH=CH of monosubstituted benzenes).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  5.34 (s, 2H,  $\text{CH}_2$ ), 5.94 (d,  $J = 2.7$  Hz, 1H, H-4), 7.22 (m, 1H, CPh H-4), 7.36 (m, 1H, NPh H-4), 7.40 (m, 2H, CPh H-3,5), 7.43 (m, 2H, NPh H-3,5), 7.51 (m, 2H, CPh H-2,6), 7.63 (m, 2H, NPh H-2,6), 7.75 (d,  $J = 2.7$  Hz, 1H, H-5).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{C}}$  70.9 ( $\text{CH}_2$ ,  $^1J = 146.3$  Hz,  $^3J(\text{OCH}_2, \text{CPhH2,6}) = 4.6$  Hz), 94.1 (C-4,  $^1J = 179.8$  Hz,  $^2J(\text{C4,H5}) = 8.2$  Hz), 117.8 (NPh C-2,6), 125.3 (CPh C-4), 127.7 (C-5,  $^1J = 186.3$  Hz,  $^2J(\text{C5,H4}) = 8.6$  Hz), 128.0 (NPh C-4), 128.0 (CPh C-2,6,  $^3J(\text{C,OCH}_2) = 4.4$  Hz), 128.4 (CPh C-3,5), 129.3 (NPh C-3,5), 137.0 (CPh C-1,  $^2J(\text{C,OCH}_2) = 3.9$  Hz), 140.2 (NPh C-1), 164.3 (C-3,  $^2J(\text{C3,H4}) = 179.8$  Hz,  $^3J(\text{C3,H5}) = 10.4$  Hz,  $^3J(\text{C3,OCH}_2) = 2.5$  Hz); MS  $m/z$  (%): 274 ( $[\text{M} + \text{Na}]^+$ , 100). Anal. Calcd for  $\text{C}_{16}\text{H}_{14}\text{N}_2\text{O}$ : C, 76.78; H, 5.64; N, 11.19. Found: C, 76.89; H, 5.66; N, 11.23.

**3-Hydroxy-1-phenyl-1H-pyrazole-4-carbaldehyde (6).** To a solution of **4** (556 mg, 2 mmol) in toluene (10 mL) trifluoroacetic acid (10 mL) was added. The mixture was stirred for 2 days at rt. Toluene and trifluoroacetic acid were evaporated. The residue was purified by column chromatography (SiO<sub>2</sub>, eluent: ethyl acetate/*n*-hexane, 1:1, v/v) to give pure **6**. Pale solid, yield 85%, 320 mg, mp 195-197 °C (lit. mp 196-197 °C).<sup>19b</sup> IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 3292 (OH), 3122 (CH<sub>arom</sub>), 1671 (C=O), 1597, 1578, 1509, 1500, 1442 (C=C, C-N), 1284, 1214, 1186, 1170 (C-O), 760, 685 (CH=CH of monosubstituted benzene). <sup>1</sup>H NMR (300 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{H}}$  7.31 (m, 1H, Ph H-4), 7.48 (m, 2H, Ph H-3,5), 7.80 (m, 2H, Ph H-2,6), 8.91 (s, 1H, H-5), 9.75 (s, 1H, CHO), 11.51 (br s, 1H, OH). <sup>13</sup>C NMR (75 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\text{C}}$  111.0 (C-4, <sup>2</sup>*J*(C4,CHO)=25.0 Hz, <sup>2</sup>*J*(C4,H5)=7.0 Hz), 118.2 (Ph C-2,6), 126.7 (Ph C-4), 129.5 (Ph C-3,5), 131.0 (C-5, <sup>1</sup>*J* = 174.4 Hz), 138.7 (Ph C-1), 162.4 (C-3, <sup>3</sup>*J*(C3,H5)=8.9 Hz, <sup>3</sup>*J*(C3,CHO)=1.8 Hz), 183.2 (CHO); MS *m/z* (%): 211 ([M + Na]<sup>+</sup>, 100); Anal. Calcd for C<sub>10</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>: C, 63.82; H, 4.28; N, 14.89. Found: C, 64.01; H, 4.26; N, 14.52.

**4-Formyl-1-phenyl-1H-pyrazol-3-yl trifluoromethanesulfonate (7).** Pyrazole **6** (1.13 g, 6.0 mmol), trifluoromethanesulfonic anhydride (1 mL, 6 mmol) and triethylamine (1 mL, 7.2 mmol) were dissolved in dichloromethane (20 mL) and the mixture was stirred at rt for 1 hour. The reaction mixture was poured into water and extracted with ethyl acetate. Combined organic layers were washed with brine and dried over Na<sub>2</sub>SO<sub>4</sub>, the solvent was evaporated. The residue was purified by flash chromatography (SiO<sub>2</sub>, eluent: ethyl acetate/*n*-hexane, 1:4, v/v). Pale solid, yield 83%, 1.59 g, mp 73-74 °C; IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 3130 (CH<sub>arom</sub>), 1681 (C=O), 1557, 1458, 1429, 1393 (C=C, C-N), 1247, 1228, 1204, 1136 (C-O, C-F, S=O), 763, 687 (CH=CH of monosubstituted benzene). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  7.44 (m, 1H, Ph H-4), 7.53 (m, 2H, Ph H-3,5), 7.67 (m, 2H, Ph H-2,6), 8.41 (s, 1H, H-5), 9.92 (s, 1H, CHO). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta_{\text{C}}$  114.7 (C-4, <sup>2</sup>*J*(C4,H5)=7.0 Hz, <sup>2</sup>*J*(C4,CHO)=27.1 Hz), 118.6 (CF<sub>3</sub>, <sup>1</sup>*J* = 321.2 Hz), 119.5 (Ph C-2,6), 128.8 (Ph C-4), 129.9 (Ph C-3,5), 130.9 (C-5, <sup>1</sup>*J* = 193.3 Hz, <sup>2</sup>*J*(C5,CHO)=3.3 Hz), 138.2 (Ph C-1), 152.3 (C-3, <sup>3</sup>*J*(C3,H5)=10.3 Hz, <sup>3</sup>*J*(C3,CHO)=2.2 Hz), 181.0 (CHO), <sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>):  $\delta_{\text{F}}$  -72.0 (CF<sub>3</sub>); MS *m/z* (%): 321 ([M + H]<sup>+</sup>, 100). Anal. Calcd for C<sub>11</sub>H<sub>7</sub>F<sub>3</sub>N<sub>2</sub>O<sub>4</sub>S: C, 41.26; H, 2.20; N, 8.75. Found: C, 41.04; H, 2.16; N, 8.56.

**4-Acetyl-1-phenyl-1H-pyrazol-3-yl trifluoromethanesulfonate (9).** This compound was synthesized in analogy to compound **7** synthesis using pyrazole **8** (1.21 g, 6 mmol). White crystals, yield 85%, 1.70 g, mp 89 °C; IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 3137 (CH<sub>arom</sub>), 1678 (C=O), 1556, 1427 (C=C, C-N), 1275, 1240, 1211, 1135 (C-O, C-F, S=O), 745, 712 (CH=CH of monosubstituted benzene). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  2.53 (s, 3H, CH<sub>3</sub>), 7.41 (m, 1H, Ph H-4), 7.51 (m, 2H, Ph H-3,5), 7.66 (m, 2H, Ph H-2,6), 8.35 (s, 1H, H-5). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta_{\text{C}}$  28.7 (CH<sub>3</sub>, <sup>1</sup>*J* = 128.1 Hz), 115.0 (C-4, <sup>2</sup>*J*(C4,H5)=6.9 Hz, <sup>3</sup>*J*(C4,CH<sub>3</sub>)=1.5 Hz), 118.6 (CF<sub>3</sub>, <sup>1</sup>*J* = 321.2 Hz), 119.4 (Ph C-2,6), 128.5 (Ph C-4), 129.8 (Ph C-3,5), 131.0 (C-5, <sup>1</sup>*J* = 192.6 Hz), 138.3 (Ph C-1), 151.3 (C-3, <sup>3</sup>*J*(C3,H5)=10.7 Hz), 189.3 (CO, <sup>2</sup>*J*(CO,CH<sub>3</sub>)=6.2 Hz). <sup>15</sup>N NMR (50 MHz, CDCl<sub>3</sub>):  $\delta_{\text{N}}$  -173.8 (N-1), N-2 was not found. <sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>):  $\delta_{\text{F}}$  -72.3 (CF<sub>3</sub>); MS *m/z* (%): 335 ([M + H]<sup>+</sup>, 100). Anal. Calcd for C<sub>12</sub>H<sub>9</sub>F<sub>3</sub>N<sub>2</sub>O<sub>4</sub>S: C, 43.12; H, 2.71; N, 8.38. Found: C, 43.51; H, 2.78; N, 8.53.

**General procedure for the preparation of 4-substituted 1-phenyl-1H-pyrazol-4-carbaldehydes and ketones by Suzuki-Miyaura cross-coupling reaction: method A**

To a solution of appropriate pyrazole **7** or **9** (0.5 mmol) in 1,4-dioxane (5 mL) under argon atmosphere anhydrous  $K_3PO_4$  (318 mg, 1.5 mmol), an appropriate boronic acid (1.5 mmol),  $Pd(PPh_3)_4$  (46 mg, 0.04 mmol) and KBr (66 mg, 0.55 mmol) were added. After refluxing for the given time under argon atmosphere the mixture was diluted with water and the extraction was done with ethyl acetate. The combined organic layers were washed with brine, dried over  $Na_2SO_4$ , filtrated, the solvent was evaporated. The residue was purified by flash chromatography ( $SiO_2$ , eluent: ethyl acetate/*n*-hexane, 1:4, v/v) to yield compounds **10-19**.

**1,3-Diphenyl-1H-pyrazole-4-carbaldehyde (10)**. White solid, Yield 94%, 117 mg, mp 142-144 °C (lit. mp 137-145 °C).<sup>27</sup> IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 3126 ( $CH_{arom}$ ), 2839 ( $CH_{aliph}$ ), 1674 (C=O), 1525, 1510 (C=C, C-N), 772, 753, 699, 688 (CH=CH of monosubstituted benzenes).  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta_H$  7.40 (m, 1H, NPh H-4), 7.47-7.55 (m, 5H, CPh H-3,4,5 and NPh H-3,5), 7.80 (m, 2H, NPh H-2,6), 7.83 (m, 2H, CPh H-2,6), 8.55 (s, 1H, H-5), 10.06 (s, 1H, CHO).  $^{13}C$  NMR (75 MHz,  $CDCl_3$ ):  $\delta_C$  119.8 (NPh C-2,6), 122.6 (C-4,  $^2J(C4,C5)=7.0$  Hz,  $^2J(C4,CHO)=25.7$  Hz), 128.0 (NPh C-4), 128.7 (CPh C-3,5), 129.0 (CPh C-2,6), 129.3 (CPh C-4), 129.7 (NPh C-3,5), 130.9 (C-5,  $^1J = 190.1$  Hz,  $^3J(C5,CHO)=4.6$  Hz), 131.4 (CPh C-1), 139.0 (NPh C-1), 154.8 (C-3,  $^3J(C3,H5)=7.2$  Hz), 185.1 (CHO,  $^1J = 176.1$  Hz,  $^3J(CHO,H5)=1.0$  Hz); MS  $m/z$  (%): 249 ( $[M + H]^+$ , 100). Anal. Calcd for  $C_{16}H_{12}N_2O \cdot 0.2 H_2O$ : C, 76.29; H, 4.96; N, 11.12. Found: C, 76.67; H, 5.01; N, 10.85.

**3-(3-Chlorophenyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (11)**. White solid, yield 82%, 116 mg, mp 99-101 °C; IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 3113 ( $CH_{arom}$ ), 1683 (C=O), 759, 747, 687 (CH=CH of mono- and disubstituted benzene).  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta_H$  7.40 (m, 1H, NPh H-4), 7.42 (m, 1H, 3CIPh H-4), 7.43 (m, 1H, 3CIPh H-5), 7.51 (m, 2H, NPh H-3,5), 7.75 (m, 1H, 3CIPh H-6), 7.78 (m, 2H, NPh H-2,6), 7.88 (s, 1H, 3CIPh H-2), 8.53 (s, 1H, H-5), 10.03 (s, 1H, CHO);  $^{13}C$  NMR (75 MHz,  $CDCl_3$ ):  $\delta_C$  119.7 (NPh C-2,6), 122.5 (C-4,  $^2J(C4,CHO)=25.8$  Hz,  $^3J(C4,H5)=7.0$  Hz), 127.1 (3CIPh C-6), 128.1 (NPh C-4), 128.8 (3CIPh C-2), 129.3 (3CIPh C-4), 129.7 (NPh C-3,5), 129.9 (3CIPh C-5), 131.8 (C-5,  $^1J = 190.3$ ,  $^3J(C5,CHO)=4.1$ ), 133.0 (3CIPh C-1), 134.6 (3CIPh C-3), 138.8 (NPh C-1), 152.9 (C-3,  $^3J(C3,H5)=7.3$  Hz,  $^3J(C3,CHO)=1.7$  Hz), 184.5 (CHO,  $^1J = 175.9$  Hz,  $^3J(CHO,H5)=1.0$  Hz);  $^{15}N$  NMR (50 MHz,  $CDCl_3$ ):  $\delta_N$  -159.9 (N-1), N-2 was not found; MS  $m/z$  (%): 285/283 ( $[M + H]^+$ , 37/100). Anal. Calcd for  $C_{16}H_{11}ClN_2O$ : C, 67.97; H, 3.92; N, 9.91. Found: C, 68.09; H, 4.12; N, 9.56.

**3-[4-(Trifluoromethyl)phenyl]-1-phenyl-1H-pyrazole-4-carbaldehyde (12)**. White solid, yield 60%, 95 mg, mp 144 °C; IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 3130 ( $CH_{arom}$ ), 1678 (C=O), 1523 (C=C, C-N), 856, 760, 686 (CH=CH of mono- and disubstituted benzenes).  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta_H$  7.42 (m, 2H, NPh H-4), 7.54 (m, 2H, NPh H-3,5), 7.76 (m, 2H,  $4CF_3Ph$  H-3,5), 7.80 (m, 2H, NPh H-2,6), 8.03 (m, 2H,  $4CF_3Ph$  H-2,6), 8.57 (s, 1H, H-5), 10.07 (s, 1H, CHO).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta_C$  119.8 (NPh C-2,6), 122.7 (C-4,  $^2J(C4,CHO)=26.0$  Hz,  $^2J(C4,H5)=7.0$  Hz), 124.0 ( $CF_3$ ,  $^1J = 272.3$  Hz), 125.6 ( $4CF_3Ph$  C-3,5), 128.2 (NPh C-4), 129.2 ( $4CF_3Ph$  C-2,6), 129.8 (NPh C-3,5), 131.1 ( $4CF_3Ph$  C-4), 132.4 (C-5,  $^1J = 190.1$ ,  $^3J(C5,CHO)=3.8$  Hz), 134.9 ( $4CF_3Ph$

C-1), 138.1 (NPh C-1), 152.7 (C-3,  $^3J(\text{C3},\text{H5})=7.4$  Hz,  $^3J(\text{C3},\text{CHO})=2.0$  Hz), 184.1 (CHO,  $^1J = 175.8.0$  Hz,  $^3J(\text{CHO},\text{H5})=1.2$  Hz).  $^{15}\text{N}$  NMR (50 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{N}} -159.5$  (N-1), N-2 was not found;  $^{19}\text{F}$  NMR (470 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{F}} -62.7$  ( $\text{CF}_3$ ); MS  $m/z$  (%): 317 ( $[\text{M} + \text{H}]^+$ , 100). Anal. Calcd for  $\text{C}_{17}\text{H}_{11}\text{F}_3\text{N}_2\text{O}\cdot 0.3 \text{H}_2\text{O}$ : C, 63.47; H, 3.63; N, 8.71. Found: C, 63.59; H, 3.55; N, 8.82.

**1-Phenyl-3-(3-thienyl)-1H-pyrazole-4-carbaldehyde (13).** Brown solid, yield 80%, 102 mg, mp 120 °C; IR ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3126 ( $\text{CH}_{\text{arom}}$ ), 1671 (C=O), 756, 688 (CH=CH of monosubstituted benzene).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  7.40 (m, 1H, Ph H-4), 7.43 (dd,  $^3J(\text{H5},\text{H4})=5.0$  Hz,  $^4J(\text{H5},\text{H2})=3.0$ , Th H-5), 7.52 (m, 2H, Ph H-3,5), 7.71 (dd,  $^3J(\text{H4},\text{H5})=5.0$  Hz,  $^4J(\text{H4},\text{H2})=1.2$  Hz, 1H, Th H-4), 7.79 (m, 2H, Ph 2,6-H), 8.19 (dd,  $^4J(\text{H2},\text{H5})=3.0$  Hz,  $^4J(\text{H2},\text{H4})=1.2$ , 1H, Th H-2), 8.50 (s, 1H, H-5), 10.10 (s, 1H, CHO).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{C}}$  119.7 (Ph C-2,6), 122.6 (C-4,  $^2J(\text{C4},\text{CHO})=25.7$  Hz,  $^3J(\text{C4},\text{H5})=7.0$  Hz), 125.9 (Th C-5,  $^1J = 187.7$  Hz,  $^2J(\text{C5},\text{H4})=6.0$  Hz,  $^3J(\text{C5},\text{H2})=6.0$  Hz), 126.1 (Th C-2,  $^1J = 187.1$  Hz,  $^3J(\text{C2},\text{H4})=8.7$  Hz,  $^3J(\text{C2},\text{H5})=4.6$  Hz), 127.6 (Th C-4,  $^1J = 167.8$  Hz), 127.9 (Ph C-4), 129.7 (Ph C-3,5), 132.4 (Th C-3,  $^2J(\text{C3},\text{H2})=3.4$  Hz,  $^2J(\text{C3},\text{H4})=4.6$  Hz,  $^3J(\text{C3},\text{H5})=10.4$  Hz), 132.7 (C-5,  $^1J = 189.3$ ,  $^3J(\text{C5},\text{CHO})=3.2$ ), 138.9 (Ph C-1), 149.3 (C-3,  $^3J(\text{C3},\text{H5})=7.4$  Hz,  $^3J(\text{C3},\text{ThH2})=3.1$  Hz,  $^3J(\text{C3},\text{CHO})=3.2$  Hz), 184.0 (CHO,  $^1J = 174.7$  Hz,  $^3J(\text{CHO},\text{H5})=1.4$  Hz); MS  $m/z$  (%): 255 ( $[\text{M} + \text{H}]^+$ , 100). Anal. Calcd for  $\text{C}_{14}\text{H}_{10}\text{N}_2\text{OS}$ : C, 66.12; H, 3.96; N, 11.02. Found: C, 66.43; H, 3.97; N, 11.34.

**3-(2-Naphthyl)-1-phenyl-1H-pyrazole-4-carbaldehyde (14).** White solid, yield 79%, 118 mg, mp 139-140 °C (lit. mp 140-141 °C).<sup>26</sup> IR ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3125 ( $\text{CH}_{\text{arom}}$ ), 1697, 1668 (C=O), 1531, 1512 (C=C, C-N), 752, 692 (CH=CH of benzenes).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  7.41 (m, 1H, Ph H-4), 7.53 (m, 2H, Ph H-3,5), 7.55 (m, 1H, Nph H-7), 7.55 (m, 1H, Nph H-6), 7.83 (m, 2H, Ph H-2,6), 7.91 (m, 1H, Nph H-5), 7.95 (m, 1H, Nph H-8), 7.98 (s, 1H, Nph H-3), 7.98 (m, 1H, Nph H-4), 8.34 (s, 1H, Nph H-1), 8.58 (s, 1H, H-5), 10.15 (s, 1H, CHO).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{C}}$  119.8 (Ph C-2,6), 122.7 (C-4,  $^2J(\text{C4},\text{H5})=6.9$  Hz,  $^2J(\text{C4},\text{CHO})=25.5$  Hz), 126.2 (Nph C-3), 126.5 (Nph C-7), 126.8 (Nph C-6), 127.7 (Nph C-5), 128.0 (Ph C-4), 128.5 (Nph C-4), 128.5 (Nph C-8), 128.6 (Nph C-1), 128.7 (Nph C-2), 129.7 (Ph C-3,5), 131.2 (C-5,  $^1J = 190.1$ ,  $^3J(\text{C5}, \text{CHO})=4.5$ ), 133.2 (Nph C-8a), 133.6 (Nph C-4a), 139.0 (Ph C-1), 154.7 (C-3), 185.2 (CHO,  $^1J = 175.8$ ,  $^3J(\text{CHO},\text{C5})=1.1$  Hz).  $^{15}\text{N}$  NMR (50 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{N}} -160.2$  (N-1), N-2 was not found; MS  $m/z$  (%): 299 ( $[\text{M} + \text{H}]^+$ , 100). Anal. Calcd for  $\text{C}_{20}\text{H}_{14}\text{N}_2\text{O}$ : C, 80.52; H, 4.73; N, 9.39. Found: C, 80.38; H, 4.76; N, 8.99.

**1-(1,3-Diphenyl-1H-pyrazol-4-yl)ethanone (15).** White solid, yield 81%, 106 mg, 81%, mp 103-104 °C (lit. mp 99-104 °C);<sup>29</sup> IR ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3119 ( $\text{CH}_{\text{arom}}$ ), 1665 (C=O), 1525, 1448 (C=C, C-N), 754, 732, 696, 688 (CH=CH of monosubstituted benzenes).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  2.39 (s, 3H,  $\text{CH}_3$ ), 7.39 (m, 1H, NPh H-4), 7.45 (m, 1H, CPh H-4), 7.46 (m, 2H, CPh H-3,5), 7.50 (m, 2H, NPh H-3,5), 7.75 (m, 2H, CPh H-2,6), 7.78 (m, 2H, NPh H-2,6), 8.46 (s, 1H, H-5).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{C}}$  29.3 ( $\text{CH}_3$ ,  $^1J = 127.6$  Hz), 119.6 (NPh C-2,6), 122.9 (C-4,  $^2J(\text{C4},\text{C5})=7.3$  Hz,  $^3J(\text{C4},\text{CH}_3)=1.1$  Hz), 127.6 (NPh C-4), 128.1 (CPh C-3,5), 128.9 (CPh C-4), 129.4 (CPh C-2,6), 129.6 (NPh C-3,5), 131.5 (C-5,  $^1J = 188.0$ ), 132.1 (CPh C-1), 139.2 (NPh C-1), 153.5 (C-3,  $^3J(\text{C3},\text{H5})=7.5$  Hz,  $^3J(\text{C3},\text{CPhH-2,6})=3.9$  Hz), 192.4 (CO,  $^2J(\text{CO},\text{CH}_3)=7.3$  Hz);

MS  $m/z$  (%): 263 ( $[M + H]^+$ , 100). Anal. Calcd for  $C_{17}H_{14}N_2O \cdot 0.3 H_2O$ : C, 76.27; H, 5.50; N, 10.46. Found: C, 76.03; H, 5.32; N, 10.10.

**1-[3-(3-Chlorophenyl)-1-phenyl-1H-pyrazol-4-yl]ethanone (16).** Yellow solid, yield 50%, 74 mg, mp 76-77 °C; IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 3130 ( $CH_{arom}$ ), 1674 (C=O), 1527, 1504, 1450 (C=C, C-N), 797, 760, 688 (CH=CH of mono- and disubstituted benzenes).  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta_H$  2.45 (s, 3H,  $CH_3$ ), 7.37 (m, 1H, 3ClPh H-5), 7.38 (m, 1H, NPh H-4), 7.40 (m, 1H, 3ClPh H-4), 7.51 (m, 2H, NPh H-3,5), 7.70 (m, 1H, 3ClPh H-6), 7.77 (m, 2H, NPh H-2,6), 7.82 (m, 1H, 3ClPh H-2), 8.45 (s, 1H, H-5).  $^{13}C$  NMR (75 MHz,  $CDCl_3$ ):  $\delta_C$  29.3 ( $CH_3$ ,  $^1J = 127.6$  Hz), 119.6 (NPh C-2,6), 122.6 (C-4,  $^2J(C4,C5)=7.3$  Hz,  $^3J(C4,CH_3)=1.1$  Hz), 127.7 (3ClPh C-6), 127.8 (NPh C-4), 128.9 (3ClPh C-4), 129.2 (3ClPh C-5), 129.4 (3ClPh C-2), 129.6 (NPh C-3,5), 131.8 (C-5,  $^1J = 188.0$ ), 134.0 (3ClPh C-3), 134.2 (3ClPh C-1), 139.0 (NPh C-1), 152.0 (C-3,  $^3J(C3,H5)=7.6$  Hz), 191.8 (CO,  $^2J(CO,CH_3)=6.0$  Hz).  $^{15}N$  NMR (50 MHz,  $CDCl_3$ ):  $\delta_N$  -163.3 (N-1), N-2 was not found; MS  $m/z$  (%): 321/319 ( $[M + Na]^+$ , 30/100). Anal. Calcd for  $C_{17}H_{13}ClN_2O$ : C, 68.81; H, 4.42; N, 9.44. Found: C, 68.99; H, 4.46; N, 9.80.

**1-[3-[4-(Trifluoromethyl)phenyl-1-phenyl-]1H-pyrazol-4-yl]ethanone (17).** White solid, yield 82%, 136 mg, mp 73-75 °C; IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 3136 ( $CH_{arom}$ ), 1668 (C=O), 1524 (C=C, C-N), 1327, 1126, 1068 (C-F), 758, 686 (CH=CH of mono- and disubstituted benzenes).  $^1H$  NMR (500 MHz,  $CDCl_3$ ):  $\delta_H$  2.49 (s, 3H,  $CH_3$ ), 7.40 (m, 2H, NPh H-4), 7.52 (m, 2H, NPh H-3,5), 7.70 (m, 2H, 4CF<sub>3</sub>Ph H-3,5), 7.78 (m, 2H, NPh H-2,6), 7.94 (m, 2H, 4CF<sub>3</sub>Ph H-2,6), 8.47 (s, 1H, H-5).  $^{13}C$  NMR (125 MHz,  $CDCl_3$ ):  $\delta_C$  29.2 ( $CH_3$ ,  $^1J = 127.6$  Hz), 119.6 (NPh C-2,6), 122.5 (C-4,  $^2J(C4,C5)=7.4$  Hz,  $^3J(C4,CH_3)=1.0$  Hz), 124.2 (CF<sub>3</sub>,  $^1J = 272.3$  Hz), 124.9 (4CF<sub>3</sub>Ph C-3,5), 127.9 (NPh C-4), 129.67 (NPh C-3,5), 129.73 (4CF<sub>3</sub>Ph C-2,6), 130.6 (4CF<sub>3</sub>Ph C-4), 132.0 (C-5,  $^1J = 187.9$ ), 135.9 (4CF<sub>3</sub>Ph C-1), 139.0 (NPh C-1), 152.0 (C-3,  $^3J(C3,H5)=7.6$  Hz,  $^3J(C3,4CF_3Ph\ C-2,6)=3.8$  Hz), 191.7 (CO,  $^2J(CO,CH_3)=6.0$  Hz).  $^{19}F$  NMR (470 MHz,  $CDCl_3$ ):  $\delta_F$  -62.6 (CF<sub>3</sub>); MS  $m/z$  (%): 331 ( $[M + H]^+$ , 100). Anal. Calcd for  $C_{18}H_{13}F_3N_2O$ : C, 65.45; H, 3.97; N, 8.48. Found: C, 65.24; H, 4.06; N, 8.32.

**1-[1-Phenyl-3-(3-thienyl)-1H-pyrazol-4-yl]ethanone (18).** White solid, yield 60%, 80 mg, mp 80-81 °C; IR ( $\nu_{max}$ ,  $cm^{-1}$ ): 3117 ( $CH_{arom}$ ), 1675 (C=O), 1519, 1499 (C=C, C-N), 771, 691 (CH=CH of monosubstituted benzene).  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta_H$  2.51 (s, 3H,  $CH_3$ ), 7.35 (dd,  $^3J(H5,H4)=5.0$  Hz,  $^4J(H5,H2)=3.1$ , Th H-5), 7.37 (m, 1H, Ph H-4), 7.51 (m, 2H, Ph H-3,5), 7.72 (dd,  $^4J(H4,H2)=1.2$  Hz, 1H, Th H-4), 7.78 (m, 2H, Ph 2,6-H), 8.34 (dd, 1H, Th H-2), 8.42 (s, 1H, H-5).  $^{13}C$  NMR (75 MHz,  $CDCl_3$ ):  $\delta_C$  29.3 ( $CH_3$ ,  $^1J = 127.6$  Hz), 119.6 (Ph C-2,6), 122.2 (C-4,  $^2J(C4,C5)=7.2$  Hz), 124.7 (Th C-5,  $^1J = 185.8$  Hz,  $^2J(C5,H4)=7.8$  Hz,  $^3J(C5,H2)=6.0$  Hz), 126.6 (Th C-2,  $^1J = 188.5$  Hz,  $^3J(C2,H4)=8.4$  Hz,  $^3J(C2,H5)=4.5$  Hz), 128.4 (Th C-4,  $^1J = 169.9$  Hz,  $^2J(C4,H5)=5.1$  Hz,  $^3J(C4,H2)=8.7$  Hz), 127.6 (Ph C-4), 129.6 (Ph C-3,5), 132.8 (Th C-3,  $^2J(C3,H2)=3.1$  Hz,  $^2J(C3,H4)=4.1$  Hz,  $^3J(C3,H5)=10.0$  Hz), 132.0 (C-5,  $^1J = 187.1$ ), 139.1 (Ph C-1), 148.6 (C-3,  $^3J(C3,H5)=7.6$  Hz,  $^3J(C3,ThH2)=3.0$  Hz,  $^3J(C3,ThH4)=1.3$  Hz), 191.8 (CO,  $^1J(CO,CH_3)=5.8$  Hz).  $^{15}N$  NMR (50 MHz,  $CDCl_3$ ):  $\delta_N$  -165.2 (N-1), N-2 was not found; MS  $m/z$  (%): 269 ( $[M + H]^+$ , 100). Anal. Calcd for  $C_{15}H_{12}N_2OS \cdot 0.5 H_2O$ : C, 64.96; H, 4.72; N, 10.10. Found: C, 64.97; H, 4.57; N, 9.92.

**1-[3-(2-Naphtyl)-1-phenyl-1H-pyrazol-4-yl]ethanone (19).** White solid, yield 77%, 120 mg, mp 114-116 °C; IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3130 ( $\text{CH}_{\text{arom}}$ ), 1670 (C=O), 1527, 1502 (C=C, C-N), 758, 688 ( $\text{CH}=\text{CH}$  of benzenes).  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  2.43 (s, 3H,  $\text{CH}_3$ ), 7.38 (m, 1H, Ph H-4), 7.51 (m, 2H, Ph H-3,5), 7.51 (m, 1H, Nph H-7), 7.52 (m, 1H, Nph H-6), 7.81 (m, 2H, Ph H-2,6), 7.87 (d,  $^3J(\text{H}_3,\text{H}_4)=8.6$  Hz, 1H, Nph H-3), 7.89 (m, 1H, Nph H-5), 7.92 (m, 1H, Nph H-4), 7.93 (m, 1H, Nph H-8), 8.31 (s, 1H, Nph H-1), 8.49 (s, 1H, H-5).  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{C}}$  29.4 ( $\text{CH}_3$ ,  $^1J(\text{CH}_3)=127.6$  Hz), 119.6 (Ph C-2,6), 123.0 (C-4,  $^2J(\text{C}_4,\text{H}_5)=7.3$  Hz,  $^3J(\text{C}_4,\text{CH}_3)=1.2$  Hz), 126.1 (Nph C-7), 126.5 (Nph C-6), 127.0 (Nph C-3), 127.6 (Nph C-4), 127.64 (Ph C-4), 127.67 (Nph C-5), 128.5 (Nph C-8), 128.8 (Nph C-1), 129.6 (Ph C-3,5), 129.9 (Nph C-2), 131.7 (C-5,  $^1J = 188.1$  Hz), 133.1 (Nph C-8a), 133.4 (Nph C-4a), 139.1 (Ph C-1), 153.5 (C-3,  $^3J(\text{C}_3,\text{H}_5)=7.5$  Hz), 192.4 (CO,  $^2J(\text{CO},\text{CH}_3)=6.0$  Hz).  $^{15}\text{N}$  NMR (50 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{N}}$  -163.5 (N-1), N-2 was not found; MS  $m/z$  (%): 335 ( $[\text{M} + \text{Na}]^+$ , 100). Anal. Calcd for  $\text{C}_{21}\text{H}_{16}\text{N}_2\text{O}\cdot 0.2 \text{H}_2\text{O}$ : C, 79.83; H, 5.23; N, 8.87. Found: C, 79.88; H, 5.21; N, 8.90.

**General procedure for the preparation of 4-substituted 1-phenyl-1H-pyrazol-4-carbaldehydes and ketones by Sonogashira cross-coupling reaction: method B**

To a solution of appropriate pyrazole **7** or **9** (0.5 mmol) in dry DMF (5 mL) under argon atmosphere triethylamine (0.11 mL, 0.75 mmol), phenylacetylene (0.08 mL, 0.75 mmol),  $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$  (35 mg, 0.05 mmol) and CuI (9 mg, 0.05 mmol) were added. The mixture was stirred for the given time under argon atmosphere at 65 °C, diluted with water and the extraction was done with ethyl acetate. The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$ , the solvent was evaporated. The residue was purified by flash chromatography ( $\text{SiO}_2$ , eluent: ethyl acetate/*n*-hexane, 1:5, v/v) to yield compounds **20**, **21**.

**1-Phenyl-3-(phenylethynyl)-1H-pyrazole-4-carbaldehyde (20).** Pale solid, yield 81%, 110 mg, 81%, mp 134-136 °C; IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3119 ( $\text{CH}_{\text{arom}}$ ), 1675 (C=O), 1527, 1504 (C=C, C-N), 753, 685 ( $\text{CH}=\text{CH}$  of monosubstituted benzenes).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  7.40 (m, 1H, NPh H-4), 7.40 (m, 3H, CPh H-3,4,5), 7.50 (m, 2H, NPh H-3,5), 7.62 (m, 2H, CPh H-2,6), 7.74 (m, 2H, NPh H-2,6), 8.44 (s, 1H, H-5), 10.10 (s, 1H, CHO).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{C}}$  78.8 ( $\text{PhC} \equiv \text{C}$ ), 94.9 ( $\text{PhC} \equiv \text{C}$ ,  $^3J(\text{C},\text{CPh}_{2,6}\text{-H})=5.4$  Hz), 119.8 (NPh C-2,6), 121.7 (CPh C-1), 125.8 (C-4,  $^2J(\text{C}_4,\text{CHO})=25.7$  Hz,  $^2J(\text{C}_4,\text{C}_5)=7.0$  Hz), 128.3 (NPh C-4), 128.5 (CPh C-3,5), 129.3 (CPh C-4), 129.7 (NPh C-3,5), 128.6 (C-5,  $^1J = 192.4$ ,  $^3J(\text{C}_5,\text{CHO})=4.9$  Hz), 132.0 (CPh C-2,6), 138.5 (C-3,  $^3J(\text{C}_3,\text{H}_5)=8.4$  Hz), 138.7 (NPh C-1), 184.3 (CHO,  $^1J = 177.9$  Hz); MS  $m/z$  (%): 295 ( $[\text{M} + \text{Na}]^+$ , 100). Anal. Calcd for  $\text{C}_{18}\text{H}_{12}\text{N}_2\text{O}\cdot 0.6 \text{H}_2\text{O}$ : C, 76.36; H, 4.70; N, 9.89. Found: C, 76.43; H, 4.52; N, 9.49.

**1-[1-Phenyl-3-(2-phenylethynyl)-1H-pyrazol-4-yl]ethanone (21).** Pale solid, yield 65%, 93 mg, mp 112-113 °C; IR ( $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3129 ( $\text{CH}_{\text{arom}}$ ), 1668 (C=O), 1523, 1498 (C=C, C-N), 767, 751, 706, 691 ( $\text{CH}=\text{CH}$  of monosubstituted benzenes).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  2.73 (s, 3H,  $\text{CH}_3$ ), 7.38 (m, 1H, NPh H-4), 7.39 (m, 3H, CPh H-3,4,5), 7.49 (m, 2H, NPh H-3,5), 7.62 (m, 2H, CPh H-2,6), 7.74 (m, 2H, NPh H-2,6), 8.45 (s, 1H, H-5).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{C}}$  29.0 ( $\text{CH}_3$ ,  $^1J = 127.8$  Hz), 81.2 ( $\text{PhC} \equiv \text{C}$ ,  $^3J(\text{C},\text{CPh}_{2,6}\text{-H})=5.3$  Hz), 94.7 ( $\text{PhC} \equiv \text{C}$ ,

$^3J(\text{C}, \text{CPh}_{2,6}\text{-H})=5.4$  Hz), 119.7 (NPh C-2,6), 122.0 (CPh C-1), 127.0 (C-4,  $^2J(\text{C4}, \text{C5})=6.7$  Hz,  $^3J(\text{C4}, \text{CH}_3)=1.4$  Hz), 128.0 (NPh C-4), 128.4 (CPh C-3,5), 129.2 (CPh C-4), 129.6 (NPh C-3,5), 129.9 (C-5,  $^1J = 191.5$ ), 131.7 (CPh C-2,6), 138.8 (NPh C-1), 136.0 (C-3,  $^3J(\text{C3}, \text{H5})=8.1$  Hz), 192.1 (CO,  $^2J(\text{CO}, \text{CH}_3)=6.2$  Hz); MS  $m/z$  (%): 287 ( $[\text{M} + \text{H}]^+$ , 100). Anal. Calcd for  $\text{C}_{19}\text{H}_{14}\text{N}_2\text{O} \cdot 0.4 \text{H}_2\text{O}$ : C, 77.74; H, 5.08; N, 9.54. Found: C, 77.82; H, 4.91; N, 9.26.

### General procedure for the preparation of 4-substituted 1-phenyl-1H-pyrazol-4-carbaldehydes and ketones by Heck cross-coupling reaction: method C

To a solution of appropriate pyrazole **7** or **9** (0.5 mmol) in dry DMF (5 mL) under argon atmosphere triethylamine (0.11 mL, 0.75 mmol), appropriate alkene (1 mmol) and  $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$  (35 mg, 0.05 mmol) were added. The reaction mixture was stirred for the given time at 100 °C under argon atmosphere, then diluted with water and exhaustively extracted with ethyl acetate. The combined organic layers were washed with brine, dried over  $\text{Na}_2\text{SO}_4$  and evaporated under reduced pressure. The residue was purified by flash chromatography ( $\text{SiO}_2$ , eluent: ethyl acetate/*n*-hexane, 1:4, v/v) to yield compounds **22-27**.

**Ethyl (2E)-3-(4-formyl-1-phenyl-1H-pyrazol-3-yl)acrylate (22)**. Yellow liquid, yield 37%, 50 mg; IR ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3113 ( $\text{CH}_{\text{arom}}$ ), 1700, 1682 (C=O), 1196 (C–O), 751, 688 (CH=CH of monosubstituted benzene).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  1.33 (t, 3H,  $^3J = 7.3$  Hz,  $\text{CH}_3$ ), 4.28 (q, 2H,  $^3J = 7.3$  Hz,  $\text{CH}_2$ ), 6.57 (d, 1H,  $^3J_{\text{trans}} = 16.1$  Hz, CHCHCO), 7.42 (m, 1H, Ph H-4), 7.51 (m, 2H, Ph H-3,5), 7.74 (m, 2H Ph H-2,6), 7.98 (d, 1H,  $^3J_{\text{trans}} = 16.1$  Hz, CHCHCO), 8.44 (s, 1H, H-5), 10.08 (CHO).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{C}}$  14.3 ( $\text{CH}_3$ ), 60.7 ( $\text{CH}_2$ ), 119.7 (Ph C-2,6), 123.8 (COCH), 127.0, 128.3, 129.7 (Ph C-3,5), 130.1, 132.80 (COCHCH), 138.7 (Ph C-1), 148.5 (C-3), 166.5 (CHCHCO), 183.4 (CHO); MS  $m/z$  (%): 271 ( $[\text{M} + \text{H}]^+$ , 100). Anal. Calcd for  $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_3$ : C, 66.66; H, 5.22; N, 10.36. Found: C, 66.37; H, 5.53; N, 10.58.

**tert-Butyl (2E)-3-(4-formyl-1-phenyl-1H-pyrazol-3-yl)acrylate (23)**. Beige liquid, yield 13%, 20 mg. IR ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3122 ( $\text{CH}_{\text{arom}}$ ), 2978 ( $\text{CH}_{\text{aliph}}$ ), 1710, 1687 (C=O), 757, 689 (CH=CH of monosubstituted benzenes).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  1.54 (s, 9H,  $\text{CH}_3$ ), 6.96 (d, 1H,  $^3J_{\text{trans}} = 15.75$  Hz, COCHCH), 7.40 (m, 1H, Ph H-4), 7.52 (m, 2H, Ph H-3,5), 7.75 (m, 2H, Ph H-2,6), 7.90 (d, 1H,  $^3J_{\text{trans}} = 15.75$  Hz, COCHCH), 8.43 (s, 1H, H-5), 10.09 (CHO); MS  $m/z$  (%): 339 ( $[\text{M} + \text{K} + \text{H}]^+$ , 100). Anal. Calcd for  $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_3$ : C, 68.44; H, 6.08; N, 9.39. Found: C, 68.80; H, 6.17; N, 9.64.

**1-Phenyl-3-[(E)-2-phenylethenyl]-1H-pyrazole-4-carbaldehyde (24)**. Yellow liquid, yield 15%, 21 mg. IR ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3160 ( $\text{CH}_{\text{arom}}$ ), 1682 (C=O), 753, 687 (CH=CH of monosubstituted benzenes).  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta_{\text{H}}$  7.31-7.42 (m, 4H, Ar), 7.48-7.63 (m, 4H, Ar), 7.60 (d, 1H,  $^3J_{\text{trans}} = 16.5$  Hz, CHCHPh), 7.78 (m, 2H, NPh H-2,6), 7.75 (d, 1H,  $^3J_{\text{trans}} = 16.5$  Hz, CHCHPh), 8.41 (s, 1H, H-5), 10.12 (CHO); MS  $m/z$  (%): 275 ( $[\text{M} + \text{H}]^+$ , 100). Anal. Calcd for:  $\text{C}_{18}\text{H}_{14}\text{N}_2\text{O}$ : C, 78.81; H, 5.14; N, 10.21. Found: C, 79.10; H, 5.16; N, 9.97.

**Ethyl (2E)-3-(4-acetyl-1-phenyl-1H-pyrazol-3-yl)acrylate (25)**. Yellow solid, yield 78%, 111 mg, mp 105-107 °C; IR ( $\nu_{\text{max}}$ ,  $\text{cm}^{-1}$ ): 3133 ( $\text{CH}_{\text{arom}}$ ), 1702, 1692, 1673 (C=O), 1596, 1530 (C=C, C–N), 1280, 1252, 1204 (C–O), 767, 688 (CH=CH of monosubstituted benzene).  $^1\text{H}$  NMR (300



MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  1.33 (t, 3H,  $^3J = 7.1$  Hz, CH<sub>2</sub>CH<sub>3</sub>), 2.52 (s, 3H, COCH<sub>3</sub>), 4.26 (q, 2H,  $^3J = 7.1$  Hz, CH<sub>2</sub>), 6.96 (d, 1H,  $^3J_{\text{trans}} = 16.0$  Hz, COCHCH), 7.38 (m, 1H, Ph H-4), 7.50 (m, 2H, Ph H-3,5), 7.74 (m, 2H, Ph H-2,6), 8.19 (d,  $^3J_{\text{trans}} = 16.0$  Hz, 1H, COCHCH), 8.36 (s, 1H, H-5). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta_{\text{C}}$  14.1 (CH<sub>2</sub>CH<sub>3</sub>,  $^1J = 127.0$  Hz,  $^2J(\text{CH}_2\text{CH}_3, \text{CH}_2) = 26.0$  Hz), 28.9 (COCH<sub>3</sub>,  $^1J = 127.6$  Hz), 60.5 (CH<sub>2</sub>CH<sub>3</sub>,  $^1J = 147.4$  Hz,  $^2J(\text{CH}_2, \text{CH}_2\text{CH}_3) = 4.4$  Hz), 119.7 (Ph C-2,6), 122.9 (COCHCH,  $^1J = 165.9$  Hz,  $^2J(\text{C}, \text{COCHCH}) = 3.6$  Hz), 123.1 (C-4,  $^2J(\text{C}_4, \text{H}_5) = 7.3$  Hz), 128.0 (Ph C-4), 129.7 (Ph C-3,5), 131.3 (C-5,  $^1J = 188.1$  Hz), 133.9 (COCHCH,  $^1J = 164.7$  Hz,  $^2J(\text{C}, \text{COCHCH}) = 2.4$  Hz), 138.9 (Ph C-1), 148.3 (C-3,  $^2J(\text{C}_3, \text{COCHCH}) = 3.2$  Hz,  $^3J(\text{C}_3, \text{COCHCH}) = 6.0$  Hz,  $^3J(\text{C}_3, \text{H}_5) = 7.4$  Hz), 166.6 (COCHCH), 191.9 (COCH<sub>3</sub>,  $^2J(\text{COCH}_3, \text{CH}_3) = 6.0$  Hz); MS  $m/z$  (%): 307 ([M + Na]<sup>+</sup>, 100). Anal. Calcd for C<sub>16</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub>•0.3 H<sub>2</sub>O: C, 66.33; H, 5.78; N, 9.67. Found: C, 66.37; H, 5.53; N, 9.28.

**tert-Butyl (2E)-3-(4-acetyl-1-phenyl-1H-pyrazol-3-yl)acrylate (26).** Brown liquid, yield 58%, 91 mg; IR ( $\nu_{\text{max}}$ , cm<sup>-1</sup>): 3124 (CH<sub>arom</sub>), 2978 (CH<sub>aliph</sub>), 1700, 1651 (C=O), 754, 690 (CH=CH of monosubstituted benzene). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  1.53 (s, 9H, COO(CH<sub>3</sub>)<sub>3</sub>), 2.51 (s, 3H, COCH<sub>3</sub>), 6.88 (d, 1H,  $^3J_{\text{trans}} = 16.11$  Hz, COCH), 7.37 (m, 1H, Ph H-4), 7.49 (m, 2H, Ph H-3,5), 7.73 (m, 2H, Ph H-2,6), 8.09 (d, 1H,  $^3J_{\text{trans}} = 16.11$  Hz, COCHCH), 8.35 (s, 1H, H-5). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>):  $\delta_{\text{C}}$  29.26 (COCH<sub>3</sub>), 29.43 (COO(CH<sub>3</sub>)<sub>3</sub>), 80.80 (C(CH<sub>3</sub>)<sub>3</sub>), 119.91 (Ph C-2,6), 123.32 (C-4), 125.11 (Ph C-4), 128.32 (CHCO), 129.93 (Ph C-3,5), 131.60 (C-5), 133.24 (CHCHCO), 139.23 (Ph C-1), 148.74 (C-3), 166.22 (CHCHCO), 192.21 (COCH<sub>3</sub>); MS  $m/z$  (%): 313 ([M + H]<sup>+</sup>, 100). Anal. Calcd for C<sub>18</sub>H<sub>20</sub>N<sub>2</sub>O<sub>3</sub>: C, 69.21; H, 6.45; N, 8.97. Found: C, 69.61; H, 6.49; N, 8.94.

**1-{1-Phenyl-3-[(E)-2-phenylethenyl]-1H-pyrazol-4-yl}ethanone (27).** White solid, yield 55%, 79 mg, mp 95 °C; IR ( $\nu_{\text{max}}$ , cm<sup>-1</sup>): 3127 (CH<sub>arom</sub>), 1659 (C=O), 756, 687 (CH=CH of monosubstituted benzenes). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  2.53 (s, 3H, CH<sub>3</sub>), 7.29 (m, 1H, CPh H-4), 7.37 (m, 2H, CPh H-3,5), 7.38 (m, 1H, NPh H-4), 7.51 (m, 2H, NPh H-3,5), 7.61 (m, 2H, CPh H-2,6), 7.69 (d, 1H,  $^3J_{\text{trans}} = 16.4$  Hz, CHCHPh), 7.77 (d,  $^3J_{\text{trans}} = 16.4$  Hz, 1H, CHCHPh), 7.78 (m, 2H, NPh H-2,6), 8.33 (s, 1H, H-5). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta_{\text{C}}$  29.0 (CH<sub>3</sub>,  $^1J = 127.3$  Hz), 118.4 (PhCHCH), 119.7 (NPh C-2,6), 121.9 (C-4,  $^2J(\text{C}_4, \text{H}_5) = 7.5$  Hz,  $^3J(\text{C}_4, \text{CHCHPh}) = 1.2$  Hz), 127.1 (CPh C-2,6), 127.6 (NPh C-4), 128.1 (CPh C-4), 128.6 (CPh C-3,5), 129.6 (NPh C-3,5), 131.3 (C-5,  $^1J = 186.6$  Hz), 133.1 (Ph-CH), 136.9 (CPh C-1), 139.2 (NPh C-1), 151.0 (C-3,  $^2J(\text{C}_3, \text{CHCHPh}) = 3.2$  Hz,  $^3J(\text{C}_3, \text{CHCHPh}) = 6.4$  Hz,  $^3J(\text{C}_3, \text{H}_5) = 7.3$  Hz), 192.4 (CO,  $^2J(\text{CO}, \text{CH}_3) = 6.0$  Hz). <sup>15</sup>N NMR (50 MHz, CDCl<sub>3</sub>):  $\delta_{\text{N}}$  -164.5 (N-1), -85.6 (N-2); MS  $m/z$  (%): 311 ([M + Na]<sup>+</sup>, 100). Anal. Calcd for C<sub>19</sub>H<sub>16</sub>N<sub>2</sub>O: C, 79.14; H, 5.59; N, 9.72. Found: C, 79.02; H, 5.63; N, 10.07.

### General procedure for the cyclization of 1-Phenyl-3-(phenylethynyl)-1H-pyrazole-4-carbaldehyde (20) and corresponding ethanone (21)

A solution of **20** or **21** (0.5 mmol) in dry ammonia and methanol (NH<sub>3</sub>/MeOH 2 M, 8 ml) was heated at 120 °C overnight in a steel reactor. The solvent was evaporated and the crude was

purified by flash chromatography (SiO<sub>2</sub>, eluent: ethyl acetate/*n*-hexane, 1:4, v/v) to yield compounds **28**, **29**.

**2,6-Diphenyl-2*H*-pyrazolo[4,3-*c*]pyridine (28)**. White solid, yield 89%, 121 mg, mp 160 °C; IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 3047 (CH<sub>arom</sub>), 1622, 1596, 1506 (C=C, C-N), 759, 745, 691 (CH=CH of monosubstituted benzenes). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  7.41 (m, 1H, CPh 4-H), 7.47 (m, 1H, NPh 4-H), 7.50 (m, 2H, CPh 3,5-H), 7.57 (m, 2H, NPh 3,5-H), 7.93 (m, 2H, NPh 2,6-H), 8.03 (s, 1H, 7-H), 8.09 (m, 2H, CPh 2,6-H), 8.58 (s, 1H, 3-H), 9.33 (s, 1H, 4-H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta_{\text{C}}$  107.0 (C-7, <sup>1</sup>J = 164.0 Hz, <sup>4</sup>J(C7,H4)=1.6 Hz), 119.7 (C-3, <sup>2</sup>J(C3a,H3)=8.1 Hz, <sup>2</sup>J(C3a,H4)=9.8 Hz, <sup>3</sup>J(C3,H7)=4.2 Hz), 121.3 (NPh C-2,6), 121.8 (C-3, <sup>1</sup>J = 192.1 Hz), 127.0 (CPh C-2,6), 128.4 (CPh C-4), 128.7 (CPh C-3,5), 128.8 (NPh C-4), 129.8 (NPh C-3,5), 139.9 (CPh C-1), 140.0 (NPh C-1), 147.1 (C-4, <sup>1</sup>J = 181.7 Hz), 151.3 (C-6, <sup>3</sup>J(C6,H4)=12.4 Hz), 151.7 (C-7a, <sup>3</sup>J(C7a,H3)=7.2 Hz, <sup>3</sup>J(C7a,H4)=5.0 Hz); <sup>15</sup>N NMR (50 MHz, CDCl<sub>3</sub>):  $\delta_{\text{N}}$  -145.9 (N-2), -85.6 (N-5), N-1 was not found; MS *m/z* (%): 272 ([M + H]<sup>+</sup>, 100). Anal. Calcd for C<sub>18</sub>H<sub>13</sub>N<sub>3</sub>•0.4 H<sub>2</sub>O: C, 77.62; H, 4.99; N, 15.09. Found: C, 77.48; H, 4.81; N, 15.46.

**4-Methyl-2,6-diphenyl-2*H*-pyrazolo[4,3-*c*]pyridine (29)**. White solid, yield 91%, 130 mg, mp 161 °C; IR ( $\nu_{\max}$ , cm<sup>-1</sup>): 3048 (CH<sub>arom</sub>), 1611, 1594 (C=C, C-N), 772, 745, 696 (CH=CH of monosubstituted benzenes). <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta_{\text{H}}$  2.89 (s, 3H, CH<sub>3</sub>), 7.39 (m, 1H, CPh 4-H), 7.45 (m, 1H, NPh 4-H), 7.49 (m, 2H, CPh 3,5-H), 7.56 (m, 2H, NPh 3,5-H), 7.85 (s, 1H, 7-H), 7.92 (m, 2H, NPh 2,6-H), 8.08 (m, 2H, CPh 2,6-H), 8.53 (s, 1H, 3-H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta_{\text{C}}$  23.3 (CH<sub>3</sub>, <sup>1</sup>J = 127.3 Hz, <sup>4</sup>J(CH<sub>3</sub>,H3)=1.0 Hz), 104.9 (C-7, <sup>1</sup>J = 164.7 Hz), 119.8 (C-3a), 121.1 (NPh C-2,6), 121.6 (C-3, <sup>1</sup>J = 190.9 Hz), 127.1 (CPh C-2,6), 128.6 (NPh C-4), 128.2 (CPh C-4), 128.6 (CPh C-3,5), 129.7 (NPh C-3,5), 140.0 (NPh C-1), 140.1 (CPh C-1), 151.2 (C-6), 152.0 (C-7a, <sup>3</sup>J(C7a,H3)=7.0 Hz), 155.8 (C-4). <sup>15</sup>N NMR (50 MHz, CDCl<sub>3</sub>):  $\delta_{\text{N}}$  -148.2 (N-2), -88.9 (N-5), -75.8 (N-1); MS *m/z* (%): 286 ([M + H]<sup>+</sup>, 100). Anal. Calcd for C<sub>19</sub>H<sub>15</sub>N<sub>3</sub>•0.6 H<sub>2</sub>O: C, 77.06; H, 5.51; N, 14.19. Found: C, 76.77; H, 5.39; N, 14.39.

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