# Heterocyclic Analogues of Xanthone and Xanthione. 1H-Pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-ones and Thiones: Synthesis and NMR Data 

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#### Abstract

The synthesis of the title compounds is described. Reaction of 1-substituted 2-pyrazolin-5-ones with 5-chloro-1-phenyl-1H-pyrazole-4-carbonyl chloride or 5-chloro-3-methyl-1-phenyl-1H-pyrazole-4-carbonyl chloride, respectively, using calcium hydroxide in refluxing 1,4-dioxane gave the corresponding 4-heteroaroylpyrazol-5-ols, which were cyclized into $1 H$-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-ones by treatment with $\mathrm{K}_{2} \mathrm{CO}_{3} / \mathrm{DMF}$. The latter were converted into the corresponding thiones upon reaction with Lawesson's reagent. Detailed NMR spectroscopic investigations ( $\left.{ }^{1} \mathrm{H},{ }^{13} \mathrm{C},{ }^{15} \mathrm{~N}\right)$ of the ring systems and their precursors are presented.


Keywords: pyrazolones; 1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-ones; cyclization; Lawesson's reagent; NMR spectroscopy

## 1. Introduction

The xanthone system, shown in Figure 1, is the core of several biologically active compounds which play important roles in numerous biological processes [1,2]. Thus, for instance, xanthone derivatives with anti-cancer [3,4], cytotoxic [5,6], topoisomerase II inhibitory [5], monoamine oxidase inhibitory [6], antioxidant [6], and antimicrobial activity [7] have been described in the recent
literature. In view of this fact synthetic derivatives of xanthones are attractive compounds for medicinal chemists. As a result analogues in which one or both benzene rings of the parent xanthone system had been replaced by heteroaromatic moieties were also studied. As a representative example of these compounds the anti-ulcer agent amlexanox (Figure 1) may be cited [8].

In the course of a program devoted to the synthesis of new heterocyclic scaffolds for bioactive compounds we recently presented the synthesis of various [5,6]pyrano[2,3-c]pyrazol-4(1H)-ones of type 4, which can be considered as heterocyclic analogues of xanthone (Scheme 1) [9-16]. The synthesis of compounds $\mathbf{4}$ is based on the reaction of 2-pyrazolin-5-ones $\mathbf{1}$ with o-haloheteroarenecarbonyl chlorides 2 under the conditions described by Jensen for the C-4 acylation of pyrazolones (calcium hydroxide, dioxane, reflux) [17] and subsequent ring closure of the resulting 4-heteroaroyl-pyrazol-5-ols 3 (Scheme 1). Following this approach, we have obtained compounds of type $\mathbf{4}$ bearing amongst others - a pyridine (all positional isomers) [9], quinoline [9], pyridazine [11], pyrimidine [11], pyrazine [15], thiophene (all positional isomers) [10,11], benzo[b]thiophene [10] and thieno[2,3b]thiophene systems [11] as the variable heteroaromatic moiety ('Het') condensed to the central $\gamma$-pyranone ring.

Figure 1. Xanthone, xanthione and its heterocyclic analogue amlexanox.

xanthone (dibenzo- $\gamma$-pyrone)

xanthione

amlexanox
(Aphthasol ${ }^{\text {TM }}$ )

In continuation of these investigations we present here the synthesis and spectroscopic data of related congeners $\mathbf{4 a , b}$ and $\mathbf{4 d - g}$ containing a pyrazole system as the heteroaromatic moiety ('Het' $=$ pyrazole) (Scheme 1), i.e. substituted $1 H$-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-ones. Moreover, the corresponding thiones 5a,b and 5d-g are described. Considering that thio analogues of flavones, isoflavones, xanthones (= xanthione, Figure 1) and related systems have received considerable attention due to the importance of such molecules in biology and photochemistry [18], the latter systems 5 are interesting compounds in their own right as well [19,20].

Scheme 1. Synthesis of compounds 4 and 5.


## 2. Results and Discussion

### 2.1. Chemistry

Synthesis of the target compounds 4 was accomplished via the sequence shown in Scheme 2. 2-Pyrazolin-5-ones $\mathbf{1}$ are either commercially available or can be easily prepared according to known methods [21]. Acid chlorides 2, which can be considered as the key synthons in the approach presented, were prepared as follows: Vilsmaier-Haak formylation [22] of pyrazolones 1a and 1b, respectively, gave the 5 -chloropyrazole-4-carbaldehydes 6 , which were oxidized to the corresponding carboxylic acids 7 by treatment with potassium permanganate [23]. Transformation of acids 7 into the appropriate acid chlorides 2 was accomplished with thionyl chloride in refluxing toluene [9,11,12]. Compounds 2 were always freshly prepared before reacting them with pyrazolones $\mathbf{1}$; treatment of 7a,b with dry ethanol led to esters 9a,b [24] (Scheme 2).

Scheme 2. Synthesis of compounds 2-8.


Different pyrazolones 1a-e were reacted with acid chlorides 2a,b using calcium hydroxide in boiling dioxane [17] to afford the 4-pyrazoloylpyrazol-5-ols 3a-g (Scheme 2). However, in two cases (the reactions of $\mathbf{1 c}$ with $\mathbf{2 b}$, and $\mathbf{1 d}$ with $\mathbf{2 b}$, respectively) the corresponding compounds of type $\mathbf{3}$ were not obtained, and instead, the isomeric esters $\mathbf{8 a}$ and $\mathbf{8 b}$ resulting from O -aroylation of $\mathbf{1 c}$ and $\mathbf{1 d}$ were isolated as the major products from the reaction mixtures. Their structures could be easily
derived from the ${ }^{1} \mathrm{H}$-NMR spectra considering the characteristic singlet signal due to pyrazole $\mathrm{H}-4$ at $\delta$ 6.04 (8a) and $\delta 6.30 \mathrm{ppm}(\mathbf{8 b})$. Attempts to convert compounds $\mathbf{8}$ into their corresponding 4-aroyl congeners $\mathbf{3}$ failed. Finally, cyclization of intermediates $\mathbf{3}$ under standard conditions ( $\mathrm{K}_{2} \mathrm{CO}_{3}$ in DMF) [25] gave the target tricycles $\mathbf{4 a , b}$ and $\mathbf{4 d - g}$ in good yields. Treatment of the latter with Lawesson's reagent $[26-28]$ in refluxing toluene smoothly afforded the corresponding thiones $\mathbf{5 a}, \mathbf{b}$ and $\mathbf{5 d} \mathbf{- g}$. It should be mentioned that compounds $\mathbf{4 d}$ and $\mathbf{5 d}$ have already been described by Sarenko and coworkers [29]. Finally, the N-7 unsubstituted compounds $\mathbf{4 x}$ and $5 \mathbf{x}$ were prepared by treatment of the corresponding N7-PMB-protected congeners $\mathbf{4 f}$ and $\mathbf{5 f}$, respectively, with trifluoroacetic acid at $70^{\circ} \mathrm{C}$ [9,12] (Scheme 3).

Scheme 3. Synthesis of compounds $4 x$ and $5 x$ and their possible tautomeric forms.


### 2.2. NMR Spectroscopic Investigations

The NMR data of compounds 2, 3, 6-8 are given in the Experimental, whereas those of title compounds $\mathbf{4}$ and 5 are collected in Tables 2-5. Unequivocal assignment of signals was carried out by the combined application of standard NMR spectroscopic techniques such as ${ }^{1} \mathrm{H}$-coupled ${ }^{13} \mathrm{C}$-NMR spectra, APT, HMQC, gs-HSQC, gs-HMBC, COSY, TOCSY, NOESY and NOE-difference spectroscopy [30]. Moreover, in a few cases experiments with selective excitation (DANTE) of certain ${ }^{1} \mathrm{H}$-resonances were performed, such as long-range INEPT [31] and 2D $(\delta, J)$ long-range INEPT [32], the latter experiments were indispensable for the unambiguous mapping of long-range ${ }^{13} \mathrm{C},{ }^{1} \mathrm{H}$ coupling constants. Reliable and unambiguously assigned chemical shift data such as those presented here can be considered as important reference material for NMR prediction programs, such as CSEARCH [33]/NMRPREDICT [34] and ACD/C + H predictor [35] - programs which have become very popular in the last few years, particularly for predicting ${ }^{13} \mathrm{C}$-NMR chemical shifts.

4-Aroylpyrazol-5-ols 3 in each case contain two different pyrazole units which exhibit characteristic differences regarding their chemical shift data. The 5-OH group in the hydroxypyrazole moiety leads to a strong polarization of the $\mathrm{C} 4-\mathrm{C} 5$ bond resulting in small chemical shifts for pyrazole C-4 (103-106 ppm) and large ones for pyrazole C-5 (159-161 ppm). These differences are significantly smaller in the 5-chloropyrazole unit with $\delta$ pyrazole C-4 having 117-119 ppm and pyrazole C-5 127-131 ppm. In congeners carrying phenyl substituents at both pyrazole N-1's (compounds 3a-d) an explicit difference regarding the resonances due to $\mathrm{Ph} \mathrm{C}-2,6$ is quite obvious ( $\delta$ $\sim 121 \mathrm{ppm}$ in the $1-\mathrm{Ph}-\mathrm{pyrazol}-5$-ol unit, $\delta \sim 125.5 \mathrm{ppm}$ in the $1-\mathrm{Ph}-5-\mathrm{Cl}$-pyrazole unit). Moreover, also the ${ }^{15} \mathrm{~N}$-NMR chemical shifts in the mentioned pyrazole moieties differ markedly, both nitrogen atoms of the hydroxypyrazole system (for instance 3a: $\mathrm{N}-1-185.2 \mathrm{ppm}, \mathrm{N}-2-97.9 \mathrm{ppm}$ ) show distinctly smaller chemical shifts than the corresponding ones in the chloropyrazole system ( $\mathrm{N}-1-159.9 \mathrm{ppm}, \mathrm{N}-$
$2-72.4 \mathrm{ppm})$. The $\mathrm{C}=\mathrm{O}$ resonance in compounds $\mathbf{3}$ is located in the range from $181-184 \mathrm{ppm}$. In Figure $2,{ }^{1} \mathrm{H},{ }^{13} \mathrm{C}$ and ${ }^{15} \mathrm{~N}$-NMR chemical shift data are presented for $\mathbf{3 a}$ which can be considered as a typical example.

Figure 2. ${ }^{1} \mathrm{H}$ - (in italics), ${ }^{13} \mathrm{C}$ - and ${ }^{15} \mathrm{~N}-\mathrm{NMR}$ (in bold) chemical shifts in $\mathbf{3 a}, \mathbf{4 a}$ and $\mathbf{5 a}(\delta$, ppm , in $\mathrm{CDCl}_{3}$ ).




In Figure 2, the chemical shift data for the corresponding tricycles 4a and 5a are also depicted, which - exemplarily - permit one to follow the changes when switching from the central pyran-4-one (4a) to a pyran-4-thione (5a) system. The transformation $\mathbf{4 a} \rightarrow \mathbf{5 a}$ leaves the ${ }^{1} \mathrm{H}$ - and ${ }^{13} \mathrm{C}$-NMR chemical shifts due to the phenyl ring nearly unchanged; $\delta(\mathrm{N}-1), \delta(\mathrm{N}-2)$ and $\delta(\mathrm{C}-3)$ are also only slightly affected. However, in $\mathbf{4 a}$ a pronounced 'push-pull situation' is on hand which leads to a strong polarization of the pyrane $\mathrm{C}=\mathrm{C}$ bond resulting in a large chemical shift for $\mathrm{C} 7 \mathrm{a} / \mathrm{C} 8 \mathrm{a}(\delta 151.3 \mathrm{ppm})$ and a small for $\mathrm{C} 3 \mathrm{a} / \mathrm{C} 4 \mathrm{a}(\delta 108.8 \mathrm{ppm})$. In $\mathbf{5 a}$ this effect is much less pronounced leading to an upfield shift for $\mathrm{C} 7 \mathrm{a} / \mathrm{C} 8 \mathrm{a}$ ( $\delta 145.5 \mathrm{ppm}$ ) and a marked downfield shift for $\mathrm{C} 3 \mathrm{a} / \mathrm{C} 4 \mathrm{a}$ ( $\delta 117.8 \mathrm{ppm}$ ) compared to the appropriate shifts in 4a. Expectedly, C-4 suffers a distinct downfield shift (169.7 ppm $\rightarrow 192.1$ ppm ) when switching from $\mathbf{4 a}$ to $5 \mathbf{a}$, the difference of 22.4 ppm is comparable with corresponding values found in related systems [36].

Whereas assignment of signals in most cases is easy, the discrimination of signals due to N1-phenyl and N7-phenyl in 'asymmetric' compounds $\mathbf{4 b}$ and $\mathbf{5 b}$ is not trivial. Ultimately, this assignment is possible considering the correlations found in the ${ }^{15} \mathrm{~N},{ }^{1} \mathrm{H}-\mathrm{HMBC}$ spectra. Thus, for instance, in compound $\mathbf{5 b}$ the singlet signal due to $\mathrm{H}-5$ ( $\delta 8.32 \mathrm{ppm}$ ) exhibits a correlation to the ${ }^{15} \mathrm{~N}$ signal with $\delta-188.0 \mathrm{ppm}$, which consecutively must be that of $\mathrm{N}-7$. The latter is also connected to the $\mathrm{Ph} \mathrm{H}-2,6$ resonance at $\delta 7.82 \mathrm{ppm}$, which accordingly has to be part of the $\mathrm{N}-7$-phenyl system and thus can be unambiguously distinguished from $\mathrm{Ph} \mathrm{H}-2,6$ of the N1-phenyl moiety ( $\delta 7.81 \mathrm{ppm}$ ). On basis of COSY (TOCSY), HSQC and HMBC experiments then the unequivocal assignment of all proton and carbon signals due to $\mathrm{N} 1-\mathrm{Ph}$ and $\mathrm{N} 7-\mathrm{Ph}$ is possible.

Compounds $\mathbf{4 x}$ and $5 \mathbf{x}$, bearing no substituent at $\mathrm{N}-7$, are interesting compounds capable of prototropic tautomerism with the $7 \mathrm{H}-, 6 \mathrm{H}$ - and XH -forms being possible (Scheme 3). The presence of XH-forms is improbable considering the chemical shifts for C-4 (4x: $170.5 \mathrm{ppm} ; 5 \mathrm{x}: 193.5 \mathrm{ppm}$ ) which perfectly match those for $\delta(\mathrm{C}-4)$ of all other $\mathrm{N}-7$ substituted congeners of type 4 and 5 , with the latter having no possibility for the formation XH-isomers. As irradiation of the resonance due to the pyrazole NH proton gives the $\mathrm{H}-5$ singlet a strong NOE (Scheme 3) a significant contribution of the 6 H -form to the overall tautomeric composition is evident. This assumption is supported by ${ }^{13} \mathrm{C}$
chemical shift data and by the size of certain ${ }^{13} \mathrm{C},{ }^{1} \mathrm{H}$ coupling constants. Hence, in $5 \mathbf{x}{ }^{2} J(\mathrm{C} 4 \mathrm{a}, \mathrm{H} 5)(7.8$ $\mathrm{Hz})$ is somewhat smaller than ${ }^{2} J(\mathrm{C} 3 \mathrm{a}, \mathrm{H} 3)(9.5 \mathrm{~Hz})$ on the opposite site of the molecule what can be explained by lone-pair effects according to lit. [38]. Also ${ }^{3} J(\mathrm{C} 8 \mathrm{a}, \mathrm{H} 3)=4.9 \mathrm{~Hz}$ markedly differs from the corresponding coupling constant ${ }^{3} J(\mathrm{C} 7 \mathrm{a}, \mathrm{H} 5)=8.5 \mathrm{~Hz}$. Moreover, $\delta \mathrm{C}-7 \mathrm{a}(155.0 \mathrm{ppm})$ is larger than $\delta \mathrm{C}-8 \mathrm{a}(147.6 \mathrm{ppm})$ and, conversely, $\delta \mathrm{C}-5(130.2 \mathrm{ppm})$ is significantly smaller than $\delta \mathrm{C}-3$ (137.7 ppm ). Both phenomena can smoothly be explained by a strong contribution of the 6 H -form in which C-5 is of 'pyrazole C-5 type' and C-7a of 'pyrazole C-3 type' - just opposite as for the 7 H -form and for 'fixed' forms with a substituent attached to N-7. For comparison, $\delta$ (C-3) in 3-methoxy-1phenylpyrazole ( 166.7 ppm ) is markedly larger than $\delta$ (C-5) in 5-methoxy-1-phenylpyrazole ( 155.5 ppm ), whereas - vice versa $-\delta$ (C-5) in 3-methoxy-1-phenylpyrazole ( 129.7 ppm ) is significantly smaller than $\delta$ (C-3) in 5-methoxy-1-phenylypyrazole (139.6 ppm) [37-39].

Lastly, the spectra of esters $\mathbf{8 a}$ and $\mathbf{8 b}$ are characterized by the occurence of a pyrazole C-H moiety with typically small chemical shifts for pyrazole H-4 (8a: $6.04 \mathrm{ppm}, \mathbf{8 b}: 6.30 \mathrm{ppm}$ ) and pyrazole C-4 ( $\mathbf{8 a}: 93.9 \mathrm{ppm}, \mathbf{8 b}: 94.9 \mathrm{ppm}$ ). Compared to the corresponding signals in 4 -aroylpyrazol-5-ols $\mathbf{3}$ ( $\sim 160 \mathrm{ppm}$ ) the resonance of pyrazole C-5 in the O-substituted pyrazole units of compounds $\mathbf{8}$ are significantly shifted upfield ( $\mathbf{8 a}$ : $144.6 \mathrm{ppm}, \mathbf{8 b}: 144.3 \mathrm{ppm}$ ). Furthermore, the $\mathrm{C}=\mathrm{O}$ resonances of compounds $\mathbf{8}$ exhibit remarkably small chemical shifts typical for ester carbonyl C-atoms of aryl esters (8a: $157.3 \mathrm{ppm}, \mathbf{8 b}: 157.2 \mathrm{ppm}$ ).

## 3. Experimental

### 3.1. General

Melting points were determined on a Reichert-Kofler hot-stage microscope and are uncorrected. Mass spectra were obtained on a Shimadzu QP 1000 instrument (EI, 70 eV), a Finnigan MAT 8230 instrument (EI, $70 \mathrm{eV}, \mathrm{HRMS}$ ), and a Finnigan MAT 900S instrument (ESI, 4 kV , MeOHacetonitrile). IR spectra ( KBr unless otherwise stated) were recorded on a Perkin-Elmer FT-IR 1605 spectrophotometer. Elemental analyses (C, H, N and S) were performed at the Microanalytical Laboratory, University of Vienna, and were in good agreement ( $\pm 0.4 \%$ ) with the calculated values. ${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}-\mathrm{NMR}$ spectra were recorded on a Varian UnityPlus 300 spectrometer at $28^{\circ} \mathrm{C}(299.95 \mathrm{MHz}$ for ${ }^{1} \mathrm{H}, 75.43 \mathrm{MHz}$ for ${ }^{13} \mathrm{C}$ ) or on a Bruker Avance 500 spectrometer at $293 \mathrm{~K}\left(500.13 \mathrm{MHz}\right.$ for ${ }^{1} \mathrm{H}$, 125.77 MHz for ${ }^{13} \mathrm{C}$ ). The center of the solvent signal was used as an internal standard, which was related to TMS with $\delta 7.26 \mathrm{ppm}\left({ }^{1} \mathrm{H}, \mathrm{CDCl}_{3}\right), \delta 2.49 \mathrm{ppm}\left({ }^{1} \mathrm{H}, \mathrm{DMSO}-d_{6}\right), \delta 77.0 \mathrm{ppm}\left({ }^{13} \mathrm{C}, \mathrm{CDCl}_{3}\right)$ and $\delta 39.5 \mathrm{ppm}\left({ }^{13} \mathrm{C}\right.$, DMSO- $\left.d_{6}\right) .{ }^{15} \mathrm{~N}$-NMR spectra $(50.68 \mathrm{MHz})$ were obtained on a Bruker Avance 500 spectrometer with a 'directly' detecting broadband observe probe (BBFO) and were referenced against external nitromethane. The digital resolution was $0.25 \mathrm{~Hz} /$ data point in the ${ }^{1} \mathrm{H}$ spectra and 0.4 $\mathrm{Hz} /$ data point in the ${ }^{13} \mathrm{C}$-NMR spectra. Systematic names were generated with ACD/Name [40] according to the IUPAC recommendations and were checked manually [41]. For chromatographic separations, Kieselgel 60 ( $70-230$ mesh, Merck) was used.

### 3.2. Synthetic procedures

### 3.2.1. General procedure for the synthesis of the carbaldehydes $\mathbf{6 a}$ and $\mathbf{6 b}$

Under anhydrous conditions, $\mathrm{POCl}_{3}(53.65 \mathrm{~g}, 32.5 \mathrm{~mL}, 350 \mathrm{mmol}$ ) was carefully added dropwise to dry DMF ( $11.70 \mathrm{~g}, 12.3 \mathrm{~mL}, 160 \mathrm{mmol}$ ) under cooling. Then pyrazolone $\mathbf{1}(50 \mathrm{mmol})$ was added and the mixture was heated to reflux for 2 hours. The reaction mixture was subsequently cooled to room temperature and the darkly coloured solution was poured onto ice water (approximately 300 mL ) while stirring. After 30 minutes the precipitate formed was filtered off, washed with $\mathrm{H}_{2} \mathrm{O}$ and dried.

5-Chloro-1-phenyl-1H-pyrazole-4-carbaldehyde (6a). Starting from 1-phenyl-2-pyrazolin-5-one ( $\mathbf{1 a}, 8.01 \mathrm{~g}, 50 \mathrm{mmol}) 8.69 \mathrm{~g}(84 \%)$ of compound $\mathbf{6 a}$ were obtained as brownish crystals; m.p. $68^{\circ} \mathrm{C}$ (lit. [42] m.p. $70{ }^{\circ} \mathrm{C}$ ); ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right.$ ): $\delta(\mathrm{ppm}) 9.92$ (s, $1 \mathrm{H}, \mathrm{CHO}$ ), 8.14 ( $\mathrm{s}, 1 \mathrm{H}, \mathrm{H}-3$ ), 7.46-7.57 (m, 5H, Ph-H); ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 182.9\left(\mathrm{CHO},{ }^{1} \mathrm{~J}=177.9 \mathrm{~Hz}\right.$, $\left.{ }^{3} J(\mathrm{CHO}, \mathrm{H}-3)=0.6 \mathrm{~Hz}\right), 140.9\left(\mathrm{C}-3,{ }^{1} J(\mathrm{C}-3, \mathrm{H}-3)=193.1 \mathrm{~Hz},{ }^{3} J(\mathrm{C}-3, \mathrm{CHO})=3.7 \mathrm{~Hz}\right), 136.8(\mathrm{Ph} \mathrm{C}-1)$, $132.4\left(\mathrm{C}-5,{ }^{3} J(\mathrm{C}-5, \mathrm{H}-3)=5.9 \mathrm{~Hz}\right), 129.4(\mathrm{Ph} \mathrm{C}-4), 129.3(\mathrm{Ph} \mathrm{C}-3,5), 125.1(\mathrm{Ph} \mathrm{C}-2,6), 120.1\left(\mathrm{C}-4,{ }^{2} J\right.$ $\left.(\mathrm{C}-4, \mathrm{H}-3)=9.5 \mathrm{~Hz},{ }^{2} J(\mathrm{C}-4, \mathrm{CHO})=25.2 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}\left(50 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm})-161.5(\mathrm{~N}-1)$, -70.3 (N-2); MS m/z (\%): 206/208 ( $\mathrm{M}^{+}, 89 / 30$ ), 205/207 (M+1, 93/38), 167 (33), 149 (100), 77 (75), 57 (46), 51 (58), 43 (36), 41 (42).

5-Chloro-3-methyl-1-phenyl-1H-pyrazole-4-carbaldehyde (6b). Starting from 3-methyl-1-phenyl-2-pyrazolin-5-one ( $\mathbf{1 b}, 8.71 \mathrm{~g}, 50 \mathrm{mmol}) 9.05 \mathrm{~g}(82 \%)$ of compound $\mathbf{6 b}$ were obtained as brownish crystals; m.p. $146{ }^{\circ} \mathrm{C}$ (lit. [43] m.p. $146-147{ }^{\circ} \mathrm{C}$ ); ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 9.96$ (s, 1 H , CHO), 7.53 (m, 2H, Ph H-2,6), 7.51 (m, 2H, Ph H-3,5), 7.46 (m, 1H, Ph H-4), 2.53 ( $\mathrm{s}, 3 \mathrm{H}, \mathrm{Me}$ ); ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 183.8\left(\mathrm{CHO},{ }^{1} J=176.2 \mathrm{~Hz}\right), 151.7\left(\mathrm{C}-3,{ }^{2} J(\mathrm{C}-3, \mathrm{Me})=7.0 \mathrm{~Hz}\right.$, $\left.{ }^{3} J(\mathrm{C}-3, \mathrm{CHO})=4.6 \mathrm{~Hz}\right), 136.9(\mathrm{Ph} \mathrm{C-1}), 133.4(\mathrm{C}-5), 129.2(\mathrm{Ph} \mathrm{C}-3,5), 129.1$ (Ph C-4), 125.1 (Ph C$2,6), 117.3\left(\mathrm{C}-4,{ }^{2} J(\mathrm{C}-4, \mathrm{CHO})=24.3 \mathrm{~Hz},{ }^{3} J(\mathrm{C}-4, \mathrm{Me})=2.5 \mathrm{~Hz}\right), 13.8\left(\mathrm{Me},{ }^{1} \mathrm{~J}=129.4 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}$ ( $50 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $-168.1(\mathrm{~N}-1),-76.1(\mathrm{~N}-2)$.
3.2.2. Preparation of 5-chloro-1-phenyl-1H-pyrazole-4-carboxylic acid (7a). To a solution of $\mathbf{6 a}$ $(1.03 \mathrm{~g}, 5 \mathrm{mmol})$ in a mixture of $\mathrm{H}_{2} \mathrm{O} / t$-butanol $1: 1(15 \mathrm{~mL}) 1.11 \mathrm{~g}(7 \mathrm{mmol}) \mathrm{KMnO}_{4}$ in $\mathrm{H}_{2} \mathrm{O}(20 \mathrm{~mL})$ was added dropwise over 3 h while stirring at $70-80^{\circ} \mathrm{C}$. Then an aqueous solution of $10 \% \mathrm{KOH}$ was added while stirring until the solution turned alkaline. The mixture was filtered, then the filtrate was acidified with concentrated hydrochloric acid to pH 2 . The precipitated solid was filtered off, washed with water and dried. Yield: 970 mg ( $88 \%$ ) of colorless crystals; m.p. $188^{\circ} \mathrm{C}$ (lit. [44] m.p. 187-188 ${ }^{\circ} \mathrm{C}$ ); ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, ~ D M S O-d_{6}\right): ~ \delta(\mathrm{ppm}) 12.97(\mathrm{~s}, 1 \mathrm{H}, \mathrm{OH}), 8.16(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}-3), 7.52-7.60(\mathrm{~m}, 5 \mathrm{H}$, $\mathrm{Ph}-\mathrm{H}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(75 \mathrm{MHz}\right.$, DMSO- $\left.d_{6}\right): \delta(\mathrm{ppm}) 162.3(\mathrm{C}=\mathrm{O}), 142.4\left(\mathrm{C}-3,{ }^{1} \mathrm{~J}(\mathrm{C}-3, \mathrm{H}-3)=193.5 \mathrm{~Hz}\right)$, $137.2(\mathrm{Ph}-\mathrm{C}-1), 130.2\left(\mathrm{C}-5,{ }^{3} J(\mathrm{C}-5, \mathrm{H}-3)=5.8 \mathrm{~Hz}\right), 129.3(\mathrm{Ph} \mathrm{C}-3,4,5), 125.7(\mathrm{Ph} \mathrm{C}-2,6), 112.3(\mathrm{C}-4$, $\left.{ }^{2} J(\mathrm{C}-4, \mathrm{H}-3)=8.9 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}\left(50 \mathrm{MHz}\right.$, DMSO- $\left.\mathrm{d}_{6}\right): \delta(\mathrm{ppm})-160.8(\mathrm{~N}-1),-70.2(\mathrm{~N}-2) . \mathrm{MS} \mathrm{m} / \mathrm{z}$ (\%): 222/224 ( $\mathrm{M}^{+}, 83 / 27$ ), 205 (32), 104 (19), 77 (100), 51 (92), 50 (28), 45 (26).

### 3.2.3. Preparation of 5-chloro-3-methyl-1-phenyl-1H-pyrazole-4-carboxylic acid (7b)

The title compound was prepared according to a related procedure given in [23].
3.2.4. General procedure for the synthesis of the acid chlorides $\mathbf{2 a}$ and $\mathbf{2 b}$

A suspension of the accordant carboxylic acid $7(2 \mathrm{mmol})$ in toluene ( 10 mL ), excess $\mathrm{SOCl}_{2}$ ( 10 mL ) and 1 droplet of DMF was refluxed for 3 h . Then toluene and excess $\mathrm{SOCl}_{2}$ were distilled off. More toluene was added and the solvent was distilled off again. The remaining acid chloride was used immediately.

5-Chloro-1-phenyl-1H-pyrazole-4-carbonyl chloride (2a). Starting from 7 a ( $445 \mathrm{mg}, 2 \mathrm{mmol}$ ) 470 mg (98\%) of compound 2a were obtained as yellowish crystals; m.p. $134{ }^{\circ} \mathrm{C} ;{ }^{1} \mathrm{H}-\mathrm{NMR}(500 \mathrm{MHz}$, $\mathrm{CDCl}_{3}$ ): $\delta(\mathrm{ppm}) 8.25$ ( $\mathrm{s}, 1 \mathrm{H}, \mathrm{H}-3$ ), $7.54(\mathrm{~m}, 5 \mathrm{H}, \mathrm{Ph}-\mathrm{H}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 158.3$ $(\mathrm{C}=\mathrm{O}), 144.9\left(\mathrm{C}-3,{ }^{1} J(\mathrm{C}-3, \mathrm{H}-3)=196.2 \mathrm{~Hz}\right), 136.8(\mathrm{Ph} \mathrm{C}-1), 132.2\left(\mathrm{C}-5,{ }^{3} J(\mathrm{C}-5, \mathrm{H}-3)=4.5 \mathrm{~Hz}\right), 129.8$ (Ph C-4), 129.4 (Ph C-3,5), 125.3 (Ph C-2,6), $116.1\left(\mathrm{C}-4,{ }^{2} J(\mathrm{C}-4, \mathrm{H}-3)=8.8 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}(50 \mathrm{MHz}$, $\mathrm{CDCl}_{3}$ ): $\delta(\mathrm{ppm})-157.7(\mathrm{~N}-1),-71.0(\mathrm{~N}-2) ; \mathrm{MS} \mathrm{m} / \mathrm{z}(\%): 240 / 242 / 244\left(\mathrm{M}^{+}, 12 / 8 / 1\right), 205$ (100), 77 (51), 51 (36). HRMS Calcd. for $\mathrm{C}_{10} \mathrm{H}_{6} \mathrm{Cl}_{2} \mathrm{~N}_{2} \mathrm{O}: 239.9857$. Found: 239.9851.

5-Chloro-3-methyl-1-phenyl-1H-pyrazole-4-carbonyl chloride (2b). Starting from $7 \mathbf{7 b}(473 \mathrm{mg}$, $2 \mathrm{mmol}) 481 \mathrm{mg}(92 \%)$ of compound $\mathbf{2 b}$ were obtained as a colorless powder; m.p. $97^{\circ} \mathrm{C}$ (lit. [45] m.p. $87{ }^{\circ} \mathrm{C}$ ); ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 7.52(\mathrm{~m}, 5 \mathrm{H}, \mathrm{Ph}-\mathrm{H}), 2.57(\mathrm{~s}, 3 \mathrm{H}, 3-\mathrm{Me}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}(125$ $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 158.4(\mathrm{COCl}), 151.9\left(\mathrm{C}-3,{ }^{2} J(\mathrm{C}-3,3-\mathrm{Me})=7.1 \mathrm{~Hz}\right), 136.0(\mathrm{Ph} \mathrm{C-1}), 132.2$ (C-5), 128.6 (Ph C-4), 128.3 ( $\mathrm{Ph} \mathrm{C}-3,5$ ), $124.6\left(\mathrm{Ph} \mathrm{C-2,6)} ,113.2\left(\mathrm{C}-4,{ }^{3} J(\mathrm{C}-4,3-\mathrm{Me})=2.5 \mathrm{~Hz}\right), 14.5\right.$ (Me, $\left.{ }^{1} J=129.9 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}\left(50 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm})-164.9(\mathrm{~N}-1),-76.3(\mathrm{~N}-2)$; IR: 1740 $(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1} ; \mathrm{MS} \mathrm{m} / \mathrm{z}(\%): 254 / 256 / 258\left(\mathrm{M}^{+}, 8 / 5 / 1\right), 219$ (100), 155 (19), 91 (16), 77 (34), 51 (24).
3.2.5. Acylation of Pyrazolones: General procedure for the synthesis of 3a-g and 8a-b

A solution of the appropriate acid chloride $2(5 \mathrm{mmol})$ in dry 1,4-dioxane ( 5 mL ) was added dropwise to a suspension of pyrazolone ( $\mathbf{1 a - e}, 5 \mathrm{mmol})$ and $\mathrm{Ca}(\mathrm{OH})_{2}(10 \mathrm{mmol})$ in dry 1,4 -dioxane $(5 \mathrm{~mL})$. The reaction mixture was heated to reflux for 3 h under anhydrous conditions. After cooling to room temperature the mixture was treated with $2 \mathrm{~N} \mathrm{HCl}(20 \mathrm{~mL})$, stirred for 30 min and afterwards $\mathrm{H}_{2} \mathrm{O}(20 \mathrm{~mL})$ was added. Then the products were filtered off, washed with $\mathrm{H}_{2} \mathrm{O}$ and recrystallized. Spectroscopic and analytical data of 3a-g and 8a-b are summarized in Table 1.
(5-Chloro-1-phenyl-1H-pyrazol-4-yl)(5-hydroxy-1-phenyl-1H-pyrazol-4-yl)methanone (3a). Starting from pyrazolone 1a ( $801 \mathrm{mg}, 5 \mathrm{mmol}$ ) and acid chloride $2 \mathrm{a}(1.21 \mathrm{~g}, 5 \mathrm{mmol}) 1.58 \mathrm{~g}(86 \%)$ of compound 3a were obtained as yellowish crystals of m.p. $207^{\circ} \mathrm{C}(\mathrm{EtOH})$.
(5-Chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)(5-hydroxy-1-phenyl-1H-pyrazol-4-yl)methanone (3b). Starting from pyrazolone $\mathbf{1 a}(801 \mathrm{mg}, 5 \mathrm{mmol})$ and acid chloride $\mathbf{2 b}(1.28 \mathrm{~g}, 5 \mathrm{mmol}) 1.04 \mathrm{~g}(55 \%)$ of compound $\mathbf{3 b}$ were obtained as colorless crystals of m.p. $153{ }^{\circ} \mathrm{C}(\mathrm{EtOH})$.
(5-Chloro-1-phenyl-1H-pyrazol-4-yl)(5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl)methanone (3c). Starting from pyrazolone $\mathbf{1 b}(871 \mathrm{mg}, 5 \mathrm{mmol})$ and acid chloride $\mathbf{2 a}(1.21 \mathrm{~g}, 5 \mathrm{mmol}) 1.37 \mathrm{~g}(72 \%)$ of compound 3 c were obtained as brownish crystals of m.p. $168^{\circ} \mathrm{C}(\mathrm{EtOH})$.
(5-Chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)(5-hydroxy-3-methyl-1-phenyl-1H-pyrazol-4-yl) methan-one (3d). Starting from pyrazolone 1b ( $871 \mathrm{mg}, 5 \mathrm{mmol}$ ) and acid chloride $\mathbf{2 b}(1.28 \mathrm{~g}, 5$ $\mathrm{mmol}) 943 \mathrm{mg}(48 \%)$ of compound $3 \mathbf{d}$ were obtained as colorless crystals of m.p. 217-219 ${ }^{\circ} \mathrm{C}(\mathrm{EtOH})$ (lit. [29] m.p. 219-220 ${ }^{\circ} \mathrm{C}$ ).
(5-Chloro-1-phenyl-1H-pyrazol-4-yl)(5-hydroxy-1,3-dimethyl-1H-pyrazol-4-yl)methanone (3e). From pyrazolone 1c ( $561 \mathrm{mg}, 5 \mathrm{mmol}$ ) and acid chloride $2 \mathbf{a}(1.21 \mathrm{~g}, 5 \mathrm{mmol}) 1.03 \mathrm{~g}(65 \%)$ of compound $3 \mathbf{e}$ were obtained as colorless crystals of m.p. $184^{\circ} \mathrm{C}(\mathrm{EtOH})$.
(5-Chloro-1-phenyl-1H-pyrazol-4-yl)[5-hydroxy-1-(4-methoxybenzyl)-1H-pyrazol-4-yl]methanone (3f). Starting from pyrazolone $\mathbf{1 d}(1.02 \mathrm{~g}, 5 \mathrm{mmol})$ and acid chloride $\mathbf{2 a}(1.21 \mathrm{~g}, 5 \mathrm{mmol}) 1.40 \mathrm{~g}(68 \%)$ of compound $3 \mathbf{f}$ were obtained as colorless crystals of m.p. $166-167^{\circ} \mathrm{C}(\mathrm{EtOH})$.
(1-Benzyl-5-hydroxy-3-methyl-1H-pyrazol-4-yl)(5-chloro-1-phenyl-1H-pyrazol-4-yl)methanone (3g). Starting from pyrazolone $\mathbf{1 e}(941 \mathrm{mg}, 5 \mathrm{mmol})$ and acid chloride $\mathbf{2 a}(1.21 \mathrm{~g}, 5 \mathrm{mmol}) 1.92 \mathrm{~g}(98 \%)$ of compound 3 g were obtained as orange crystals of m.p. $119{ }^{\circ} \mathrm{C}(\mathrm{EtOH})$.

1,3-Dimethyl-1H-pyrazol-5-yl 5-chloro-3-methyl-1-phenyl-1H-pyrazole-4-carboxylate (8a). Starting from pyrazolone 1c ( $561 \mathrm{mg}, 5 \mathrm{mmol}$ ) and acid chloride $\mathbf{2 b}(1.28 \mathrm{~g}, 5 \mathrm{mmol}) 810 \mathrm{mg}(49 \%)$ of compound 8a were obtained as colorless crystals of m.p. $146^{\circ} \mathrm{C}(\mathrm{EtOH})$.

1-(4-Methoxybenzyl)-1H-pyrazol-5-yl 5-chloro-3-methyl-1-phenyl-1H-pyrazole-4-carboxylate (8b). Starting from pyrazolone $\mathbf{1 d}(1.021 \mathrm{~g}, 5 \mathrm{mmol})$ and acid chloride $\mathbf{2 b}(1.28 \mathrm{~g}, 5 \mathrm{mmol}) 1.08 \mathrm{~g}(51 \%)$ of compound $\mathbf{8 b}$ were obtained as colorless crystals of m.p. $116^{\circ} \mathrm{C}(\mathrm{EtOH})$.

Table 1. Spectroscopic and analytical data of compounds 3a-g and 8a-b.

| Entry | Structure | Spectroscopic and analytical data |
| :---: | :---: | :---: |
| 3 a |  | ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 8.26$ (s, 1H, H-3'), 8.02 (s, 1H, H-3), 7.89 (m, 2H, N1-Ph H-2,6), 7.54-7.58 (3H, N1'-Ph H-3,4,5), 7.57 (m, 2H, N1'-Ph $\mathrm{H}-2,6$ ), 7.50 (m, 2H, N1-Ph H-3,5), 7.35 (m, 1H, N1-Ph H-4), 6.0-8.5 (very broad s, $1 \mathrm{H}, \mathrm{OH}$ ); ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 181.5(\mathrm{C}=\mathrm{O}), 159.9(\mathrm{C}-$ $\left.5,{ }^{3} J(\mathrm{C}-5, \mathrm{H}-3)=4.9 \mathrm{~Hz}\right), 141.1\left(\mathrm{C}-3^{\prime},{ }^{1} J\left(\mathrm{C}-3^{\prime}, \mathrm{H}-3^{\prime}\right)=190.7 \mathrm{~Hz}\right), 138.5(\mathrm{C}-3$, $\left.{ }^{1} J(\mathrm{C}-3, \mathrm{H}-3)=189.3 \mathrm{~Hz}\right), 137.2(\mathrm{~N} 1-\mathrm{Ph} \mathrm{C}-1$ and $\mathrm{N}-1$ '-Ph C-1), 130.5 (C-5', ${ }^{3} J(\mathrm{C}-5 ', \mathrm{H}-3$ ') $=5.9 \mathrm{~Hz}$ ), 129.5 (N1'-Ph C-4), 129.3 (N1'-Ph C-3,5), 129.2 (N1Ph C-3,5), 127.2 (N1-Ph C-4), 125.5 (N1'-Ph C-2,6), 121.1 (N1-Ph C-2,6), $117.9\left(\mathrm{C}-4,{ }^{2}{ }^{2}\left(\mathrm{C}-4{ }^{\prime}, \mathrm{H}-3^{\prime}\right)=10.3 \mathrm{~Hz}\right), 103.7\left(\mathrm{C}-4,{ }^{2} \mathrm{~J}(\mathrm{C}-4, \mathrm{H}-3)=11.1 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-$ NMR ( $50 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta(\mathrm{ppm})-185.2(\mathrm{~N}-1),-159.9(\mathrm{~N}-1$ '), $-97.9(\mathrm{~N}-2)$, -72.4 (N-2'); IR: $1656(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1} ;$ MS m/z (\%): 364/266 ( $\left.\mathrm{M}^{+}, 23 / 8\right), 329$ (38), 186 (100), 91 (18), 77 (52), 51 (22). Calcd. for $\mathrm{C}_{19} \mathrm{H}_{13} \mathrm{ClN}_{4} \mathrm{O}_{2}$ (364.79): C, 62.56; H, 3.59; N, 15.36. Found: C, 62.39 ; H, 3.50; N, 15.16. |

Table 1. Cont.

| 3b |  | ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right.$ ): $\delta(\mathrm{ppm}) 10.18$ (broad s, $1 \mathrm{H}, \mathrm{OH}$ ), 7.92 ( $\mathrm{s}, 1 \mathrm{H}, \mathrm{H}-$ 3), 7.89 (m, 2H, N1-Ph H-2,6), 7.58 (m, 2H, N1'-Ph H-2,6), 7.53 (m, 2H, N1'Ph H-3,5), 7.49 (m, 2H, N1-Ph H-3,5), 7.48 ( $1 \mathrm{H}, \mathrm{Nl}$ '-Ph H-4), 7.34 (m, 1H, $\mathrm{N} 1-\mathrm{Ph} \mathrm{H}-4), 2.50\left(\mathrm{~s}, 3 \mathrm{H}, 3^{\prime}-\mathrm{Me}\right)$; ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 183.0$ $(\mathrm{C}=\mathrm{O}), 160.0\left(\mathrm{C}-5,{ }^{3} \mathrm{~J}(\mathrm{C}-5, \mathrm{H}-3)=4.7 \mathrm{~Hz}\right), 150.5\left(\mathrm{C}-3^{\prime},{ }^{2} \mathrm{~J}\left(\mathrm{C}-3^{\prime}, 3^{\prime} \cdot \mathrm{Me}\right)=6.9\right.$ $\mathrm{Hz}), 140.1\left(\mathrm{C}-3,{ }^{1} J(\mathrm{C}-3, \mathrm{H}-3)=191.1 \mathrm{~Hz}\right), 137.3(\mathrm{~N} 1$ '-Ph C-1), $137.2(\mathrm{~N} 1-\mathrm{Ph}$ $\mathrm{C}-1$ ), 129.2 ( N 1 '-Ph C-3,5), 129.15 ( $\mathrm{N} 1-\mathrm{Ph} \mathrm{C-3,5)}$,129.05 ( N 1 '-Ph C-4), 127.6 (C-5'), 127.0 (N1-Ph C-4), 125.4 ( $\mathrm{N}^{\prime}$ '-Ph C-2,6), 120.9 (N1-Ph C-2,6), $117.4\left(\mathrm{C}-4^{\prime},{ }^{3} \mathrm{~J}\left(\mathrm{C}-4^{\prime}, 3^{\prime}-\mathrm{Me}\right)=2.8 \mathrm{~Hz}\right), 104.2\left(\mathrm{C}-4,{ }^{2} \mathrm{~J}(\mathrm{C}-4, \mathrm{H}-3)=10.6 \mathrm{~Hz}\right)$, $13.8\left(3^{\prime}-\mathrm{Me},{ }^{1} J=129.1 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}\left(50 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm})-186.0(\mathrm{~N}-$ 1), -167.8 ( $\mathrm{N}-1^{\prime}$ ), -97.3 (N-2), -75.8 (N-2'); IR: 1559 (C=O) $\mathrm{cm}^{-1}$; MS m/z (\%): 378/380 (M $\left.{ }^{+}, 12 / 4\right), 343(45), 219$ (11), 186 (100), 118 (12), 91 (15), 77 (43), 51 (16). Calcd. for $\mathrm{C}_{20} \mathrm{H}_{15} \mathrm{ClN}_{4} \mathrm{O}_{2}$ (378.81): C, $63.41 ; \mathrm{H}, 3.99 ; \mathrm{N}, 14.79$. Found: C, 63.24; H, 3.81; N, 14.74. |
| :---: | :---: | :---: |
| 3c |  | ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 8.01\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}-3{ }^{\prime}\right), 7.87(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N} 1-\mathrm{Ph}$ H-2,6), 7.60 (m, 2H, N1'-Ph H-2,6), 7.55 (m, 2H, N1'-Ph H-3,5), 7.52 (m, 1H, N1'-Ph H-4), 7.48 (m, 2H, N1-Ph H-3,5), 7.32 (m, N1-Ph H-4), 2.39 (s, 3H, 3Me ), OH not found; ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 182.9$ (C=O), $161.0(\mathrm{C}-5), 147.3\left(\mathrm{C}-3,{ }^{2} J(\mathrm{C}-3,3-\mathrm{Me})=6.8 \mathrm{~Hz}\right), 140.8\left(\mathrm{C}-3^{\prime},{ }^{1} J\left(\mathrm{C}-3^{\prime}, \mathrm{H}-3^{\prime}\right)=\right.$ 192.0 Hz), 137.3 (N1'-Ph C-1), 137.1 (N1-Ph C-1), 129.3 (N1'-Ph C-3,4,5), 129.1 (N1-Ph C-3,5), $129.0\left(\mathrm{C}-5^{\prime},{ }^{3} J\left(\mathrm{C}-5^{\prime}, \mathrm{H}-3^{\prime}\right)=5.6 \mathrm{~Hz}\right), 126.9$ (N1-Ph C-4), 125.4 ( $\mathrm{N} 1^{\prime}-\mathrm{Ph} \mathrm{C}-2,6$ ), 120.9 ( $\mathrm{N} 1-\mathrm{Ph} \mathrm{C}-2,6$ ), 118.4 (C-4', ${ }^{2} J\left(\mathrm{C}-4^{\prime}, \mathrm{H}-3^{\prime}\right)=10.1$ $\mathrm{Hz}), 104.4\left(\mathrm{C}-4,{ }^{3} J(\mathrm{C}-4,3-\mathrm{Me})=2.7 \mathrm{~Hz}\right), 15.6\left(3-\mathrm{Me},{ }^{1} \mathrm{~J}=128.8 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-$ NMR ( $50 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta(\mathrm{ppm})-190.3(\mathrm{~N}-1),-161.7\left(\mathrm{~N}-1{ }^{\prime}\right),-100.8(\mathrm{~N}-2)$, -74.2 (N-2'); IR: 1619 (C=O) cm ${ }^{-1}$; MS m/z (\%): 378/380 ( $\mathrm{M}^{+}, 8 / 3$ ), 342 (48), 200 (100), 91 (37), 77 (58), 51 (25). Calcd. for $\mathrm{C}_{20} \mathrm{H}_{15} \mathrm{ClN}_{4} \mathrm{O}_{2}$ (378.81): C, 63.41; H, 3.99; N, 14.79. Found: C, 63.71; H, 3.91; N, 14.69. |
| 3d |  | ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 9.20$ (broad s, $1 \mathrm{H}, \mathrm{OH}$ ), $7.87(\mathrm{~m}, 2 \mathrm{H}$, N1-Ph H-2,6), 7.56 (m, 2H, N1'-Ph H-2,6), 7.52 (m, 2H, N1'-Ph H-3,5), 7.47 (m, 2H, N1-Ph H-3,5), 7.47 (m, 1H, N1'-Ph H-4), 7.31 (m, 1H, N1-Ph H-4), 2.41 (s, $\left.3 \mathrm{H}, 3^{3}-\mathrm{Me}\right), 2.23(\mathrm{~s}, 3 \mathrm{H}, 3-\mathrm{Me}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm})$ 183.8 (C=O), 160.8 (C-5), 148.8 (C-3', $\left.{ }^{2} J\left(\mathrm{C}-3^{\prime}, 3^{\prime}-\mathrm{Me}\right)=6.8 \mathrm{~Hz}\right), 148.1(\mathrm{C}-3$, $\left.{ }^{2} J(\mathrm{C}-3,3-\mathrm{Me})=6.7 \mathrm{~Hz}\right), 137.4(\mathrm{~N} 1$ '-Ph C-1), $137.1(\mathrm{~N} 1-\mathrm{Ph} \mathrm{C-1}), 129.2(\mathrm{~N} 1$ '$\mathrm{Ph} \mathrm{C}-3,5), 129.1$ ( $\mathrm{N} 1-\mathrm{Ph} \mathrm{C}-3,5$ ), 128.9 (N1'-Ph C-4), 126.8 (N1-Ph C-4), 126.7 (C-5'), 125.2 (N1'-Ph C-2,6), 120.7 (N1-Ph C-2,6), 117.8 (C-4, ${ }^{3}$ J(C$\left.\left.4^{\prime}, 3^{\prime}-\mathrm{Me}\right)=3.0 \mathrm{~Hz}\right), 105.5\left(\mathrm{C}-4,{ }^{3} J(\mathrm{C}-4,3-\mathrm{Me})=2.8 \mathrm{~Hz}\right), 13.9\left(3-\mathrm{Me},{ }^{1} J=\right.$ $129.0 \mathrm{~Hz}), 13.0\left(3^{3}-\mathrm{Me},{ }^{1} J=128.9 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}\left(50 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm})$ -190.3 ( $\mathrm{N}-1$ ), -168.8 ( $\mathrm{N}-1$ '), -100.0 ( $\mathrm{N}-2$ ), -76.6 ( $\mathrm{N}-\mathrm{2}^{\prime}$ ); MS m/z (\%): 392/394 (M+, 5/2), 356 (39), 219 (10), 200 (100), 132 (13), 91 (31), 77 (40), 67 (12), 51 (15). Calcd. for $\mathrm{C}_{21} \mathrm{H}_{17} \mathrm{ClN}_{4} \mathrm{O}_{2}$ (392.84): C, $64.21 ; \mathrm{H}, 4.36$; N, 14.26. Found: C, 64.04; H, 4.18; N, 14.21. |
| 3e |  | ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right.$ ): $\delta(\mathrm{ppm}) 10.35$ (broad s, $1 \mathrm{H}, \mathrm{OH}$ ), 7.94 (s, $1 \mathrm{H}, \mathrm{H}-$ $3^{\prime}$ ), $7.44-7.59\left(\mathrm{~m}, 5 \mathrm{H}, \mathrm{N1}{ }^{\prime}-\mathrm{Ph}\right), 3.62(\mathrm{~s}, 3 \mathrm{H}, \mathrm{N} 1-\mathrm{Me}), 2.27(\mathrm{~s}, 3 \mathrm{H}, 3-\mathrm{Me}) ;{ }^{13} \mathrm{C}-$ NMR ( $75 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta(\mathrm{ppm}) 183.4(\mathrm{C}=\mathrm{O}), 160.2\left(\mathrm{C}-5,{ }^{3} \mathrm{~J}(\mathrm{C}-5, \mathrm{~N} 1-\mathrm{Me})=\right.$ $2.3 \mathrm{~Hz}), 146.2\left(\mathrm{C}-3,{ }^{2} J(\mathrm{C}-3,3-\mathrm{Me})=6.9 \mathrm{~Hz}\right), 140.6\left(\mathrm{C}-3{ }^{\prime},{ }^{1} \mathrm{~J}\left(\mathrm{C}-3^{\prime}, \mathrm{H}-3^{\prime}\right)=\right.$ $191.7 \mathrm{~Hz}), 137.4$ ( N 1 '-Ph C-1), 129.2 ( N 1 '-Ph C-3,4,5), 128.6 (C-5', ${ }^{3}$ J(C$\left.\left.5^{\prime}, \mathrm{H}-3^{\prime}\right)=5.7 \mathrm{~Hz}\right), 125.3\left(\mathrm{~N} 1^{\prime}-\mathrm{Ph} \mathrm{C}-2,6\right), 119.0\left(\mathrm{C}-4^{\prime},{ }^{2} J\left(\mathrm{C}-4^{\prime}, \mathrm{H}^{\prime} 3^{\prime}\right)=10.1\right.$ $\mathrm{Hz}), 103.2\left(\mathrm{C}-4,{ }^{3} \mathrm{~J}(\mathrm{C}-4,3-\mathrm{Me})=2.7 \mathrm{~Hz}\right), 32.5\left(\mathrm{~N} 1-\mathrm{Me},{ }^{1} \mathrm{~J}=140.9 \mathrm{~Hz}\right), 15.2$ ( $3-\mathrm{Me},{ }^{1} J=128.6 \mathrm{~Hz}$ ); ${ }^{15} \mathrm{~N}-\mathrm{NMR}\left(50 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm})-207.9(\mathrm{~N}-1)$, -162.2 ( $\mathrm{N}-1^{\prime}$ ), -100.5 ( $\mathrm{N}-2$ ), -74.7 ( $\mathrm{N}-2^{\prime}$ ); IR: 1636 ( $\mathrm{C}=\mathrm{O}$ ) $\mathrm{cm}^{-1} ; \mathrm{MS} \mathrm{m} / \mathrm{z}(\%)$ : $316 / 318\left(\mathrm{M}^{+}, 11 / 4\right), 281(26), 138$ (100), 77 (21), 51 (17). Calcd. for $\mathrm{C}_{15} \mathrm{H}_{13} \mathrm{ClN}_{4} \mathrm{O}_{2}$ (316.74): C, 56.88; H, 4.14; N, 17.69. Found: C, 57.12; H, 3.97; N, 17.61. |

Table 1. Cont.

| 3f |  | ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right.$ ): $\delta(\mathrm{ppm}) 8.18$ (s, 1H, H-3'), 7.30-8.00 (very broad s, 1H, OH), 7.82 (broad, s, 1H, H-3), 7.55 (m, 2H, N1'-Ph H-2,6), 7.52 ( $\mathrm{m}, 3 \mathrm{H}, \mathrm{N} 1$ '- $\mathrm{Ph} \mathrm{H}-3,4,5$ ), 7.31 (m, 2H, CH 2 - $\mathrm{Ph} \mathrm{H}-2,6$ ), $6.88\left(\mathrm{CH}_{2}-\mathrm{Ph} \mathrm{H}-3,-5\right)$, 5.13 (broad s, $2 \mathrm{H}, \mathrm{CH}_{2}$ ), $3.79(\mathrm{~s}, 3 \mathrm{H}, \mathrm{OMe}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta$ (ppm) 181.7 (C=O), $159.5\left(\mathrm{CH}_{2}-\mathrm{Ph} \mathrm{C}-4\right), 159.0(\mathrm{C}-5), 141.1$ (C-3', ${ }^{1} J(\mathrm{C}-3$ ', $\mathrm{H}-$ $\left.\left.3^{\prime}\right)=190.7 \mathrm{~Hz}\right), 137.9\left(\mathrm{C}-3,{ }^{1} \mathrm{~J}(\mathrm{C}-3, \mathrm{H}-3)=188.8 \mathrm{~Hz}\right), 137.3\left(\mathrm{~N} 1^{\prime}-\mathrm{Ph} \mathrm{C}-1\right)$, 130.3 (C-5'), $129.6\left(\mathrm{CH}_{2}-\mathrm{Ph} \mathrm{C}-2,6\right), 129.4$ (N1'-Ph C-4), 129.2 (N1'-Ph C3,5), $127.5\left(\mathrm{CH}_{2}-\mathrm{Ph} \mathrm{C}-1\right), 125.5\left(\mathrm{~N} 1^{\prime}-\mathrm{Ph} \mathrm{C}-2,-6\right), 118.2\left(\mathrm{C}-4{ }^{\prime},{ }^{2} J\left(\mathrm{C}-4{ }^{\prime}, \mathrm{H}-3^{\prime}\right)=\right.$ $10.0 \mathrm{~Hz}), 114.2\left(\mathrm{CH}_{2}-\mathrm{Ph} \mathrm{C} 3,5\right), 103.1(\mathrm{C}-4), 55.3\left(\mathrm{OMe},{ }^{1} \mathrm{~J}=143.9 \mathrm{~Hz}\right), 49.8$ $\left(\mathrm{CH}_{2},{ }^{1} J=140.6 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}\left(50 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm})-189.2(\mathrm{~N}-1)$, $-160.3\left(\mathrm{~N}-1^{\prime}\right),-98.3(\mathrm{~N}-2),-73.1\left(\mathrm{~N}-2\right.$ '); IR: $1621(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1} ; \mathrm{MS} \mathrm{m} / \mathrm{z}(\%)$ : 408/410 ( $\mathrm{M}^{+}, 7 / 2$ ), 373 (25), 121 (100), 77 (23). Calcd. for $\mathrm{C}_{21} \mathrm{H}_{17} \mathrm{ClN}_{4} \mathrm{O}_{3}$ (408.84): C, $61.69 ;$ H, $4.19 ;$ N, 13.70. Found: C, 61.47 ; H, 4.13, N, 13.55. |
| :---: | :---: | :---: |
| 3g |  | ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 7.70-8.20($ broad s, 1H, OH), $7.96(\mathrm{~s}$, 1H, H-3'), 7.58 (m, 2H, N1'-Ph H-2,6), 7.53 (m, 2H, N1'-Ph H-3,5), 7.48 (m, $1 \mathrm{H}, \mathrm{N} 1$ '- $\mathrm{Ph} \mathrm{H}-4$ ), $7.28-7.38\left(\mathrm{~m}, 5 \mathrm{H}, \mathrm{CH}_{2}-\mathrm{Ph}\right), 5.12\left(\mathrm{~s}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.28(\mathrm{~s}, 3 \mathrm{H}$, $3-\mathrm{Me})$; ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 183.3(\mathrm{C}=\mathrm{O}), 160.3\left(\mathrm{C}-5,{ }^{3} \mathrm{~J}(\mathrm{C}-\right.$ $\left.\left.5, \mathrm{CH}_{2}\right)=2.4 \mathrm{~Hz}\right), 146.6\left(\mathrm{C}-3,{ }^{2} J(\mathrm{C}-3,3-\mathrm{Me})=7.0 \mathrm{~Hz}\right), 140.7\left(\mathrm{C}-3{ }^{\prime},{ }^{1} J\left(\mathrm{C}-3^{\prime}, \mathrm{H}-\right.\right.$ $\left.\left.3^{\prime}\right)=192.0 \mathrm{~Hz}\right), 137.4\left(\mathrm{~N} 1\right.$ '-Ph C-1), $135.5\left(\mathrm{CH}_{2}-\mathrm{Ph} \mathrm{C}-1\right), 129.2\left(\mathrm{~N} 1^{\prime}-\mathrm{Ph} \mathrm{C}-\right.$ $3,4,5), 128.7\left(\mathrm{CH}_{2}-\mathrm{Ph} \mathrm{C}-3,5\right.$ and $\left.\mathrm{C}-5^{\prime},{ }^{3} J\left(\mathrm{C}-5^{\prime}, \mathrm{H}-3^{\prime}\right)=5.7 \mathrm{~Hz}\right), 128.0\left(\mathrm{CH}_{2}-\mathrm{Ph}\right.$ C-2,4,6), 125.3 (N1'-Ph C-2,6), 118.9 (C-4', $\left.{ }^{2} J\left(\mathrm{C}^{\prime} \mathbf{4}^{\prime}, \mathrm{H}-3^{\prime}\right)=10.1 \mathrm{~Hz}\right), 103.4$ $\left(\mathrm{C}-4,{ }^{3} J(\mathrm{C}-4,3-\mathrm{Me})=2.6 \mathrm{~Hz}\right), 49.8\left(\mathrm{CH}_{2},{ }^{1} J=140.2 \mathrm{~Hz}\right), 15.4\left(3-\mathrm{Me},{ }^{1} J=\right.$ 128.6 Hz ); ${ }^{15} \mathrm{~N}-\mathrm{NMR}\left(50 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm})-196.4(\mathrm{~N}-1),-162.1(\mathrm{~N}-1 ')$, $-101.1(\mathrm{~N}-2),-74.7\left(\mathrm{~N}-2^{\prime}\right)$; IR: $1633(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1}$; MS m/z (\%): 392/394 ( $\mathrm{M}^{+}$, 8/3), 356 (91), 91 (100), 77 (25), 51 (18). Calcd. for $\mathrm{C}_{21} \mathrm{H}_{17} \mathrm{ClN}_{4} \mathrm{O}_{2}$ (392.84): C, 64.21; H, 4.36; N, 14.26. Found: C, 64.13; H, 4.27; N, 14.11. |
| 8a |  | ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 7.52(\mathrm{~m}, 5 \mathrm{H}, \mathrm{Ph}-\mathrm{H}), 6.04$ (s, 1H, H-4), 3.74 ( $\mathrm{s}, 3 \mathrm{H}, \mathrm{N}-\mathrm{Me}$ ), 2.59 (s, 3H, $3^{\text {'-Me }}$ ), 2.25 (s, 3H, 3-Me); ${ }^{13} \mathrm{C}-\mathrm{NMR}$ ( 75 Hz , $\left.\mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 157.3(\mathrm{C}=\mathrm{O}), 153.1\left(\mathrm{C}-3^{\prime},{ }^{2} J\left(\mathrm{C}-3^{\prime}, 3^{\prime}-\mathrm{Me}\right)=6.9 \mathrm{~Hz}\right), 147.2$ $\left(\mathrm{C}-3,{ }^{2} J(\mathrm{C}-3,3-\mathrm{Me})=6.7 \mathrm{~Hz},{ }^{2} J(\mathrm{C}-3, \mathrm{H}-4)=4.3 \mathrm{~Hz}\right), 144.6\left(\mathrm{C}-5,{ }^{3} J(\mathrm{C}-5, \mathrm{~N}-\right.$ $\left.\left.\mathrm{CH}_{3}\right)=2.2 \mathrm{~Hz},{ }^{2} \mathrm{~J}(\mathrm{C} 5, \mathrm{H}-4)=4.4 \mathrm{~Hz}\right), 137.2(\mathrm{Ph}-\mathrm{C}-1), 132.2\left(\mathrm{C}-5{ }^{\prime}\right), 129.3$ (Ph-C-4), 129.2 (Ph-C-3,5), 125.5 (Ph-C-2,-6), 108.3 (C-4', ${ }^{3} J\left(\mathrm{C}-4^{\prime}, 3^{\prime}-\mathrm{Me}\right)=$ $2.7 \mathrm{~Hz}), 93.9\left(\mathrm{C}-4,{ }^{1} J(\mathrm{C}-4, \mathrm{H}-4)=181.2 \mathrm{~Hz},{ }^{3} J(\mathrm{C}-4,3-\mathrm{Me})=3.5 \mathrm{~Hz}\right), 14.8\left(3^{\prime}-\right.$ $\left.\mathrm{Me},{ }^{1} J=129.5 \mathrm{~Hz}\right), 14.2\left(3-\mathrm{Me},{ }^{1} \mathrm{~J}=127.5 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}\left(50 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta$ (ppm) -202.2 (N-1), -165.8 (N-1'), -98.9 (N-2), -75.7 (N-2'); IR: 1745 $(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1}$; MS m$/ \mathrm{z}(\%): 330\left(\mathrm{M}^{+}, 0.1\right), 219$ (100), 77 (42), 51 (19). Calcd. for $\mathrm{C}_{16} \mathrm{H}_{15} \mathrm{ClN}_{4} \mathrm{O}_{2}$ (330.77): C, 58.10; H, 4.57; N, 16.94. Found: C, 58.14; H, 4.37; N, 16.90 . |
| 8b |  | ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(300 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 7.53\left(\mathrm{~d}, 1 \mathrm{H}, \mathrm{H}-3,{ }^{3} \mathrm{~J}(\mathrm{H} 3, \mathrm{H} 4)=2.1 \mathrm{~Hz}\right)$, $7.52(\mathrm{~m}, 5 \mathrm{H}, \mathrm{N} 1 '-\mathrm{Ph}), 7.12\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}-\mathrm{Ph} \mathrm{H}-2,6\right), 6.82\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}-\mathrm{Ph} \mathrm{H}-\right.$ $3,5), 6.30\left(\mathrm{~d}, 1 \mathrm{H}, \mathrm{H}-4,{ }^{3} \mathrm{~J}(\mathrm{H} 4, \mathrm{H} 3)=2.1 \mathrm{~Hz}\right), 5.28\left(\mathrm{~s}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 3.75(\mathrm{~s}, 3 \mathrm{H}, \mathrm{O}-$ Me ), $2.52\left(\mathrm{~s}, 3 \mathrm{H}, 3\right.$ '-Me); ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(75 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 159.2\left(\mathrm{CH}_{2}-\mathrm{Ph}\right.$ C4), $157.2(\mathrm{C}=\mathrm{O}), 153.2\left(\mathrm{C}-3^{\prime},{ }^{2} J\left(\mathrm{C}-3^{\prime}, 3^{\prime}-\mathrm{Me}\right)=7.0 \mathrm{~Hz}\right), 144.3(\mathrm{C}-5), 138.7$ $\left(\mathrm{C}-3,{ }^{1} J(\mathrm{C}-3, \mathrm{H}-3)=187.6 \mathrm{~Hz},{ }^{2} J(\mathrm{C}-3, \mathrm{H}-4)=4.8 \mathrm{~Hz}\right), 137.2(\mathrm{~N} 1$ '-Ph C-1), 132.2 (C-5'), 129.4 (N1'-Ph C-4), 129.2 (N1'-Ph C-3,5), 128.4 ( $\mathrm{CH}_{2}-\mathrm{Ph} \mathrm{C}-$ 2,6), $128.3\left(\mathrm{CH}_{2}-\mathrm{Ph} \mathrm{C}-1\right), 125.5(\mathrm{~N} 1 '-\mathrm{Ph} \mathrm{C}-2,6), 114.1\left(\mathrm{CH}_{2}-\mathrm{Ph} \mathrm{C}-3,5\right), 108.2$ $\left(\mathrm{C}-4{ }^{\prime},{ }^{3} J\left(\mathrm{C}-4^{\prime}, 3^{\prime}-\mathrm{Me}\right)=2.7 \mathrm{~Hz}\right), 94.9\left(\mathrm{C}-4,{ }^{1} J(\mathrm{C}-4, \mathrm{H}-4)=183.4 \mathrm{~Hz},{ }^{2} J(\mathrm{C}-4, \mathrm{H}-\right.$ 5) $=10.5 \mathrm{~Hz}), 55.2\left(\mathrm{O}-\mathrm{Me},{ }^{1} J=143.8 \mathrm{~Hz}\right), 51.3\left(\mathrm{CH}_{2},{ }^{1} J=140.0 \mathrm{~Hz}\right.$, $\left.{ }^{3} J\left(\mathrm{CH}_{2}, \mathrm{Ph}-\mathrm{H}-2,6\right)=4.3 \mathrm{~Hz}\right), 14.8\left(3^{\prime}-\mathrm{Me},{ }^{1} J=129.6 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}(50 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm})-185.1(\mathrm{~N}-1),-165.7(\mathrm{~N}-1 '),-95.3(\mathrm{~N}-2),-75.7(\mathrm{~N}-2$ '); IR: $1745(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1} ; \mathrm{MS} \mathrm{m} / \mathrm{z}(\%): 422\left(\mathrm{M}^{+}, 0.1\right), 219$ (100), 121 (25), 77 (20). Calcd. for $\mathrm{C}_{22} \mathrm{H}_{19} \mathrm{ClN}_{4} \mathrm{O}_{3}$ (422.86): C, 62.49; H, 4.53; N, 13.25. Found: C, 62.45; H, 4.40; N, 13.15 . |

### 3.2.6. Cyclization of 4-Aroylpyrazolones 3a-g: General procedure for the synthesis of 4a-b, 4d-g

Under anhydrous conditions, $\mathrm{K}_{2} \mathrm{CO}_{3}(138 \mathrm{mg}, 1 \mathrm{mmol})$ was added to a solution of the appropriate type 3 compound ( 1 mmol ) in dry DMF ( 10 mL ), then the mixture was heated to reflux for 2 h . After evaporation of the solvent, 20 mL of $\mathrm{H}_{2} \mathrm{O}$ were added to the residue. The precipitate was filtered off, washed with water and recrystallized from EtOH . NMR data of the products are given in Tables 2-5.

1,7-Diphenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-one (4a). Starting from 3a ( $365 \mathrm{mg}, 1 \mathrm{mmol}$ ) $304 \mathrm{mg}(93 \%)$ of compound $\mathbf{4 a}$ were obtained as colorless crystals; m.p. $256{ }^{\circ} \mathrm{C}(\mathrm{EtOH})$; IR: 1673 $(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1}$; MS m/z (\%): $328\left(\mathrm{M}^{+}, 77\right), 187$ (30), 77 (100), 51 (40). Calcd. for $\mathrm{C}_{19} \mathrm{H}_{12} \mathrm{~N}_{4} \mathrm{O}_{2}$ (328.32): C, 69.51; H, 3.68; N, 17.06. Found: C, 69.36; H, 3.53; N, 16.84.

3-Methyl-1,7-diphenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-one (4b). Starting from 3b (379 mg, $1 \mathrm{mmol}) 288 \mathrm{mg}(84 \%)$ of compound $\mathbf{4 b}$ were obtained as colorless crystals. Alternatively, starting from 3c ( $379 \mathrm{mg}, 1 \mathrm{mmol}$ ) $219 \mathrm{mg}(64 \%)$ of compound $\mathbf{4 b}$ were obtained as colorless crystals; m.p. $220{ }^{\circ} \mathrm{C}$ (EtOH); IR: $1664(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1} ; \mathrm{MS} \mathrm{m} / \mathrm{z}(\%): 342\left(\mathrm{M}^{+}, 66\right), 156$ (14), 91 (24), 77 (100), $67(20)$, 51 (45). Calcd. for $\mathrm{C}_{20} \mathrm{H}_{14} \mathrm{~N}_{4} \mathrm{O}_{2}$ (342.35): C, 70.14; H, 4.12; N, 16.37. Found: C, 69.93; H, 3.96; N, 16.34.

3,5-Dimethyl-1,7-diphenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-one (4d). Starting from 3d ( $393 \mathrm{mg}, 1 \mathrm{mmol}$ ) 264 mg ( $74 \%$ ) of compound $\mathbf{4 d}$ were obtained as colorless crystals; m.p. $243{ }^{\circ} \mathrm{C}$ (EtOH) (lit. [29] m.p. $240-241{ }^{\circ} \mathrm{C}$ ). IR: $1521(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1}$; MS m/z (\%): $356\left(\mathrm{M}^{+}, 100\right), 178$ (10), 156 (18), 91 (31), 77 (99), 67 (30), 51 (41). Calcd. for $\mathrm{C}_{21} \mathrm{H}_{16} \mathrm{~N}_{4} \mathrm{O}_{2}(356.37) \cdot 0.2 \mathrm{H}_{2} \mathrm{O}: \mathrm{C}, 70.07$; H, 4.59; N, 15.72. Found: C, 69.96; H, 4.38; N, 15.56.

1,3-Dimethyl-7-phenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-one (4e). Starting from 3e (317 mg, $1 \mathrm{mmol}) 185 \mathrm{mg}(66 \%)$ of compound $\mathbf{4 e}$ were obtained as colorless crystals; m.p. $204{ }^{\circ} \mathrm{C}(\mathrm{EtOH}) ;$ IR: $1654(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1}$; MS m/z (\%): $280\left(\mathrm{M}^{+}, 100\right)$, 139 (25), 77 (74), 51 (43). Calcd. for $\mathrm{C}_{15} \mathrm{H}_{12} \mathrm{~N}_{4} \mathrm{O}_{2}$ (280.28): C, 64.28; H, 4.32; N, 19.99. Found: C, 64.17; H, 4.23; N, 19.82.

1-(4-Methoxybenzyl)-7-phenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-one (4f). Starting from $\mathbf{3 f}$ ( $409 \mathrm{mg}, 1 \mathrm{mmol}$ ) 276 mg ( $74 \%$ ) of compound $\mathbf{4 f}$ were obtained as colorless crystals; m.p. $245{ }^{\circ} \mathrm{C}$ (EtOH); IR: $1667(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1}$; MS m/z (\%): $372\left(\mathrm{M}^{+}, 20\right)$, 121 (100), 77 (15). Calcd. for $\mathrm{C}_{21} \mathrm{H}_{16} \mathrm{~N}_{4} \mathrm{O}_{3}$ (372.38): C, 67.73; H, 4.33; N, 15.05. Found: C, 67.78; H, 4.18; N, 14.97.

1-Benzyl-3-methyl-7-phenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4-(7H)-one (4g). Starting from $\mathbf{3 g}$ ( $393 \mathrm{mg}, 1 \mathrm{mmol}$ ) 258 mg ( $73 \%$ ) of compound 4 g were obtained as colorless crystals; m.p. $210{ }^{\circ} \mathrm{C}$ (EtOH); IR: $1659(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-1}$; MS m/z (\%): 356 ( $\mathrm{M}^{+}, 39$ ), 265 (33), 91 (100), 77 (28), 51 (14). Calcd. for $\mathrm{C}_{21} \mathrm{H}_{16} \mathrm{~N}_{4} \mathrm{O}_{2}$ (356.38): C, 70.77; H, 4.53; N, 15.72. Found: C, 70.89; H, 4.34; N, 15.64.

### 3.2.7. General procedure for the synthesis of 5a-b and 5d-g

Lawesson's Reagent ( $202 \mathrm{mg}, 0.5 \mathrm{mmol}$ ) was added to a solution of the appropriate oxo compound 4 in 15 mL of toluene and the mixture was heated to reflux for approx. 14 h . After cooling, the precipitate was filtered off and recrystallized from EtOH. In case of $5 \mathbf{b}$ no precipitate was formed, here the solvent was evaporated and the residue was subjected to column chromatography (silica gel, mobile phase $\mathrm{CH}_{2} \mathrm{Cl}_{2}: \mathrm{MeOH} / 9: 1$ ) in order to obtain the colored thione which was crystallized from EtOH for analytical purposes. NMR data of the products are given in Tables 2-5.

1,7-Diphenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-thione (5a). Starting from 4 a ( $328 \mathrm{mg}, 1 \mathrm{mmol}$ ) $204 \mathrm{mg}(60 \%)$ of compound 5 a were obtained as reddish crystals; m.p. $254-256{ }^{\circ} \mathrm{C}(\mathrm{EtOH}) ; \mathrm{MS} \mathrm{m} / \mathrm{z}$ (\%): 344 ( $\mathrm{M}^{+}, 100$ ), 201 (30), 77 (84), 51 (57). Calcd. for $\mathrm{C}_{19} \mathrm{H}_{12} \mathrm{~N}_{4} \mathrm{OS}$ (344.39)•0.2 $\mathrm{H}_{2} \mathrm{O}: \mathrm{C}, 65.58 ; \mathrm{H}$, 3.59; N, 16.10. Found: C, 65.57 ; H, 3.37; N, 15.73.

3-Methyl-1,7-diphenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-thione (5b). Starting from 4b resp. 4c ( $342 \mathrm{mg}, 1 \mathrm{mmol}$ ) $356 \mathrm{mg}(99 \%)$ of compound $5 \mathbf{b}$ were obtained as orange crystals; m.p. 195-197 ${ }^{\circ} \mathrm{C}$ (EtOH); MS m/z (\%): $358\left(\mathrm{M}^{+}, 22\right), 356$ (100), 77 (50), 51 (25). Calcd. for $\mathrm{C}_{20} \mathrm{H}_{14} \mathrm{~N}_{4} \mathrm{OS}$ (358.42): C, 67.02; H, 3.94; N, 15.63. Found: C, 67.03; H, 3.82; N, 15.57.

3,5-Dimethyl-1,7-diphenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-thione (5d). Starting from 4d $356 \mathrm{mg}, 1 \mathrm{mmol}) 268 \mathrm{mg}(72 \%)$ of compound $5 \mathbf{d}$ were obtained as deep yellow crystals; m.p. $286{ }^{\circ} \mathrm{C}$ (EtOH) (lit. [29] m.p. 285-286 ${ }^{\circ} \mathrm{C}$ ); MS m/z (\%): $373\left(\mathrm{M}^{+}+1,23\right), 372\left(\mathrm{M}^{+}, 100\right), 186$ (11), 77 (46), 51 (27).

1,3-Dimethyl-7-phenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-thione (5e). Starting from $\mathbf{4 e}$ ( 280 mg , $1 \mathrm{mmol}) 138 \mathrm{mg}(47 \%)$ of compound 5 e were obtained as yellowish crystals; m.p. $212{ }^{\circ} \mathrm{C}(\mathrm{EtOH})$; MS $\mathrm{m} / \mathrm{z}(\%): 296\left(\mathrm{M}^{+}, 18\right), 275$ (42), 73 (100). Calcd. for $\mathrm{C}_{15} \mathrm{H}_{12} \mathrm{~N}_{4} \mathrm{OS}$ (296.35): C, 60.79; H, 4.08; N, 18.91. Found: C, 60.77 ; H, 3.94; N, 18.58 .

1-(4-Methoxybenzyl)-7-phenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-thione (5f). Starting from $\mathbf{4 f}$ ( $372 \mathrm{mg}, 1 \mathrm{mmol}$ ) 314 mg ( $81 \%$ ) of compound 5 f were obtained as yellowish crystals; m.p. $222{ }^{\circ} \mathrm{C}$ ( EtOH ); MS m/z (\%): $388\left(\mathrm{M}^{+}, 13\right), 121$ (100), 91 (10), 77 (31), 51 (14). Calcd. for $\mathrm{C}_{21} \mathrm{H}_{16} \mathrm{~N}_{4} \mathrm{O}_{2} \mathrm{~S}$ (388.44)•0.2 H2O: C, 64.34; H, 4.22; N, 14.29. Found: C, 64.40; H, 3.96; N, 14.12.

1-Benzyl-3-methyl-7-phenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4-(7H)-thione (5g). Starting from $\mathbf{4 g}$ ( $356 \mathrm{mg}, 1 \mathrm{mmol}$ ) $268 \mathrm{mg}(72 \%)$ of compound 5 g were obtained as yellowish crystals; m.p. $224^{\circ} \mathrm{C}$ (EtOH); MS m/z (\%): $373\left(\mathrm{M}^{+}+1,21\right), 372\left(\mathrm{M}^{+}, 100\right), 281$ (75), 91 (97), 77 (37), 51 (33). Calcd. for $\mathrm{C}_{21} \mathrm{H}_{16} \mathrm{~N}_{4} \mathrm{OS}$ (372.44): C, 67.72; H, 4.33; N, 15.04. Found: C, 67.37; H, 4.15; N, 14.85.
3.2.8. General procedure for the synthesis of $\mathbf{4 x}$ and $5 \mathbf{x}$

Under anhydrous conditions, a solution of the PMB-substituted congener $\mathbf{4 f}$ or $5 \mathbf{f}(0.5 \mathrm{mmol})$ and trifluoroacetic acid (TFA, $1.43 \mathrm{~g}, 12.5 \mathrm{mmol}$ ) was heated to reflux overnight. After removal of excess

TFA under reduced pressure the residue was stored over solid KOH . Then ice-cold diethyl etheracetone (3:1) was added. The precipitate was filtered off and washed with cold diethyl ether-acetone. NMR data of the products are given in Tables 2-5

1-Phenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-one (4x). Starting from 4 f ( $186 \mathrm{mg}, 0.5 \mathrm{mmol}$ ) $61 \mathrm{mg}(48 \%)$ of compound $4 x$ were obtained as brown powder; m.p. 327-329 ${ }^{\circ} \mathrm{C}$; IR: $1681(\mathrm{C}=\mathrm{O}) \mathrm{cm}^{-}$ ${ }^{1}$; MS m/z (\%): $253\left(\mathrm{M}^{+}+1,16\right), 252(\mathrm{M}+$, 100), 111 (87), 77 (46), 51 (38). HRMS Calcd. for $\mathrm{C}_{13} \mathrm{H}_{8} \mathrm{~N}_{4} \mathrm{O}_{2}: 252.0647$. Found: 252.0644.

1-Phenyl-1H-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-thione (5x). Starting from $5 \mathbf{f}$ (194 mg, 0.5 mmol ) $69 \mathrm{mg}(51 \%)$ of compound 5 x were obtained as a greenish powder; m.p. $271-273{ }^{\circ} \mathrm{C}$; MS m/z (\%): 269 $\left(\mathrm{M}^{+}+1,18\right), 268\left(\mathrm{M}^{+}, 100\right), 267\left(\mathrm{M}^{+}-1,45\right) 127(43), 77(54), 51$ (45). HRMS Calcd. for $\mathrm{C}_{13} \mathrm{H}_{7} \mathrm{~N}_{4} \mathrm{OS}$ $\left(\mathrm{M}^{+}-1\right): 267.0341$. Found: 267.0335.

Table 2. ${ }^{1} \mathrm{H}-\mathrm{NMR}$ chemical shifts of $\mathbf{4 a - b}, \mathbf{4 d - g}, \mathbf{5 a - b}, 5 \mathrm{~d}-\mathrm{g}, \mathbf{4 x}$ and $\mathbf{5 x}$ ( $\delta$ in ppm).

| Comp | Solvent | $\mathbf{H}$ of $\mathbf{R}^{1}$ | $\mathbf{H}$ of $\mathbf{R}^{3}$ | $\mathbf{H}$ of $\mathbf{R}^{5}$ | $\mathbf{H}$ of $\mathbf{R}^{7}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 4a | $\mathrm{CDCl}_{3}$ | $\begin{gathered} \hline \text { Ph: } 7.82(2,6), 7.55(3,5), \\ 7.44(4) \\ \hline \end{gathered}$ | 8.22 (H-3) | 8.22 (H-5) | Ph: 7.82 (2,6), 7.55 (3,5), 7.44 (4) |
| 4b | $\mathrm{CDCl}_{3}$ | $\begin{gathered} \text { Ph: } 7.78(2,6), 7.52(3,5), \\ 7.40(4) \\ \hline \end{gathered}$ | 2.66 (Me) | 8.17 (H-5) | Ph: 7.80 (2,6), 7.53 (3,5), 7.43 (4) |
| 4d | $\mathrm{CDCl}_{3}$ | $\begin{gathered} \text { Ph: } 7.78(2,6), 7.51(3,5), \\ 7.39(4) \\ \hline \end{gathered}$ | 2.65 (Me) | 2.65 (Me) | Ph: 7.78 (2,6), 7.51 (3,5), 7.39 (4) |
| 4e | $\mathrm{CDCl}_{3}$ | 3.87 (Me) | 2.55 (Me) | 8.13 (H-5) | Ph: 7.79 (2,6), 7.56 (3,5), 7.43 (4) |
| 4f | $\mathrm{CDCl}_{3}$ | $\begin{gathered} \text { Ph: } 7.28(2,6), 6.89 \\ (3,5) ; 5.37\left(\mathrm{CH}_{2}\right), 3.79 \\ (\mathrm{OMe}) \\ \hline \end{gathered}$ | 8.05 (H-3) | 8.17 (H-5) | Ph: 7.66 (2,6), 7.56 (3,5), 7.46 (4) |
| 4g | $\mathrm{CDCl}_{3}$ | $\begin{gathered} \text { Ph: } 7.37(4), 7.36(3,5), \\ 7.31(2,6) ; 5.35\left(\mathrm{CH}_{2}\right) \\ \hline \end{gathered}$ | 2.60 (Me) | 8.12 (H-5) | Ph: 7.60 (2,6), 7.52 (3,5), 7.42 (4) |
| 5 a | $\mathrm{CDCl}_{3}$ | $\begin{gathered} \text { Ph: } 7.84(2,6), 7.57(3,5), \\ 7.46(4) \end{gathered}$ | 8.39 (H-3) | 8.39 (H-5) | Ph: 7.84 (2,6), 7.57 (3,5), 7.46 (4) |
| 5b | $\mathrm{CDCl}_{3}$ | $\begin{gathered} \hline \text { Ph: } 7.81(2,6), 7.54(3,5), \\ 7.42(4) \\ \hline \end{gathered}$ | 2.78 (Me) | 8.32 (H-5) | Ph: 7.82 (2,6), 7.55 (3,5), 7.44 (4) |
| 5d | $\mathrm{CDCl}_{3}$ | $\begin{gathered} \hline \text { Ph: } 7.80(2,6), 7.53(3,5), \\ 7.41(4) \end{gathered}$ | 2.80 (Me) | 2.80 (Me) | Ph: 7.80 (2,6), 7.53 (3,5), 7.41 (4) |
| 5e | $\mathrm{CDCl}_{3}$ | 3.89 (Me) | 2.65 (Me) | 8.27 (H-5) | Ph: 7.81 (2,6), 7.57 (3,5), 7.45 (4) |
| 5 f | $\mathrm{CDCl}_{3}$ | $\begin{gathered} \mathrm{Ph}: 7.28(2,6), 6.90 \\ (3,5) ; 5.38\left(\mathrm{CH}_{2}\right), 3.79 \\ (\mathrm{OMe}) \\ \hline \end{gathered}$ | 8.20 (H-3) | 8.32 (H-5) | Ph: 7.66 (2,6), 7.56 (3,5), 7.47 (4) |
| 5 g | $\mathrm{CDCl}_{3}$ | $\begin{gathered} \text { Ph: } 7.38(3,4,5), 7.33 \\ (2,6) ; 5.37\left(\mathrm{CH}_{2}\right) \\ \hline \end{gathered}$ | 2.73 (Me) | 8.29 (H-5) | Ph: 7.61 (2,6), 7.53 (3,5), 7.43 (4) |
| 4x | DMSO-d ${ }_{6}$ | $\begin{gathered} \text { Ph: } 7.85(2,6), 7.62(3,5), \\ 7.48(4) \end{gathered}$ | 8.24 (H-3) | 8.56 (H-5) | 13.78 (NH) |
| 5x | DMSO-d ${ }_{6}$ | $\begin{gathered} \text { Ph: } 7.87(2,6), 7.64(3,5), \\ 7.50(4) \end{gathered}$ | 8.34 (H-3) | 8.66 (H-5) | 14.00 (NH) |

Table 3. ${ }^{13} \mathrm{C}-\mathrm{NMR}$ chemical shifts of $\mathbf{4 a - b}, \mathbf{4 d - g}, \mathbf{5 a - b}, 5 \mathbf{d}-\mathbf{g}, \mathbf{4 x}$ and $\mathbf{5 x}$ ( $\delta$ in ppm, solvents as listed in Table 2).

| Comp | C-3 | C-3a | C-4 | C-4a | C-5 | C-7a | C-8a | C of $\mathrm{R}^{1}$ | $\mathbf{C o f ~} \mathrm{R}^{3}$ | C of $\mathrm{R}^{5}$ | C of $\mathbf{R}^{7}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 4a | 136.7 | 108.8 | 169.7 | 108.8 | 136.7 | 151.3 | 151.3 | $\begin{gathered} \text { Ph: } 136.6(1), 129.6(3,5), \\ 128.3(4), 121.3(2,6) \\ \hline \end{gathered}$ | - | - | Ph: 136.6 (1), $129.6(3,5), 128.3$ <br> (4), $121.3(2,6)$ |
| 4b | 148.1 | 106.5 | 170.6 | 108.9 | 136.6 | 151.3 | 151.4 | $\begin{gathered} \text { Ph: } 136.6(1), 129.48(3,5), \\ 127.8(4), 121.1(2,6) \end{gathered}$ | $\begin{gathered} 14.0 \\ (\mathrm{Me}) \end{gathered}$ | - | Ph: 136.7 (1), 129.53 (3,5), 128.1 <br> (4), $121.2(2,6)$ |
| 4d | 148.0 | 106.6 | 171.8 | 106.6 | 148.0 | 151.5 | 151.5 | $\begin{gathered} \text { Ph: } 136.7(1), 129.5(3,5), \\ 127.7(4), 121.0(2,6) \end{gathered}$ | $\begin{aligned} & 14.0 \\ & (\mathrm{Me}) \end{aligned}$ | $\begin{aligned} & 14.0 \\ & (\mathrm{Me}) \end{aligned}$ | Ph: 136.7 (1), $129.5(3,5), 127.7$ <br> (4), $121.0(2,6)$ |
| 4e | 146.8 | 105.0 | 170.7 | 108.7 | 136.6 | 151.3 | 152.6 | 34.1 (Me) | $\begin{array}{r} 13.9 \\ (\mathrm{Me}) \\ \hline \end{array}$ | - | $\begin{gathered} \text { Ph: } 136.7(1), 129.6(3,5), 128.1 \\ (4), 121.5(2,6) \\ \hline \end{gathered}$ |
| 4f | 135.5 | 107.8 | 169.8 | 108.6 | 136.7 | 151.4 | 152.0 | $\begin{gathered} \text { Ph: } 159.9(4), 129.4(2,6), \\ 126.2(1), 114.4(3,5) ; 55.3 \\ (\mathrm{OMe}), 52.4\left(\mathrm{CH}_{2}\right) \\ \hline \end{gathered}$ | - | - | Ph: 136.6 (1), $129.6(3,5), 128.2$ <br> (4), $121.6(2,6)$ |
| 4g | 146.9 | 105.5 | 170.7 | 108.8 | 136.6 | 151.3 | 152.4 | $\begin{gathered} \text { Ph: } 134.6(1), 129.0(3,5), \\ 128.6(4), 127.7(2,6) ; 52.3 \\ \left(\mathrm{CH}_{2}\right) \end{gathered}$ | $\begin{gathered} \hline 14.0 \\ (\mathrm{Me}) \end{gathered}$ | - | Ph: 136.7 (1), $129.5(3,5), 128.0$ <br> (4), $121.4(2,6)$ |
| 5 a | 138.1 | 117.8 | 192.1 | 117.8 | 138.1 | 145.5 | 145.5 | $\begin{gathered} \text { Ph: } 136.6(1), 129.7(3,5), \\ 128.3(4), 121.3(2,6) \end{gathered}$ | - | - | Ph: 136.6 (1), $129.7(3,5), 128.3$ <br> (4), $121.3(2,6)$ |
| 5b | 150.1 | 114.8 | 193.5 | 118.1 | 138.2 | 145.1 | 146.0 | $\begin{gathered} \text { Ph: } 136.4(1), 129.56(3,5), \\ 128.0(4), 121.2(2,6) \\ \hline \end{gathered}$ | $\begin{array}{r} 15.6 \\ (\mathrm{Me}) \\ \hline \end{array}$ | - | $\begin{gathered} \text { Ph: } 136.6(1), 129.6(3,5), 128.2 \\ (4), 121.1(2,6) \\ \hline \end{gathered}$ |
| 5d | 150.2 | 115.1 | 195.5 | 115.1 | 150.2 | 145.8 | 145.8 | $\begin{gathered} \hline \text { Ph: } 136.5(1), 129.6(3,5), \\ 127.9(4), 121.2(2,6) \\ \hline \end{gathered}$ | $\begin{aligned} & 15.9 \\ & (\mathrm{Me}) \\ & \hline \end{aligned}$ | $\begin{array}{r} 15.9 \\ (\mathrm{Me}) \\ \hline \end{array}$ | Ph: 136.5 (1), $129.6(3,5), 127.9$ <br> (4), $121.2(2,6)$ |
| 5 e | 148.8 | 113.5 | 193.5 | 117.7 | 138.1 | 145.3 | 147.3 | 34.2 (Me) | $\begin{aligned} & 15.2 \\ & (\mathrm{Me}) \\ & \hline \end{aligned}$ | - | Ph: 136.7 (1), $129.6(3,5), 128.2$ <br> (4), $121.4(2,6)$ |
| 5 f | 136.9 | 117.0 | 192.2 | 117.5 | 138.1 | 145.5 | 146.2 | $\begin{gathered} \hline \text { Ph: } 159.9(4), 129.4(2,6), \\ 126.0(1), 114.4(3,5) ; 55.3 \\ (\mathrm{OMe}), 52.5\left(\mathrm{CH}_{2}\right) \end{gathered}$ | ${ }^{-}$ | - | Ph: 136.5 (1), $129.6(3,5), 128.3$ <br> (4), $121.5(2,6)$ |
| 5 g | 148.9 | 114.1 | 193.6 | 117.9 | 138.2 | 145.2 | 147.0 | $\begin{gathered} \text { Ph: } 134.4(1), 129.1(3,5), \\ 128.7(4), 127.8(2,6) ; 52.4 \\ \left(\mathrm{CH}_{2}\right) \end{gathered}$ | $\begin{gathered} 15.4 \\ (\mathrm{Me}) \end{gathered}$ | - | Ph: 136.6 (1), $129.6(3,5), 128.1$ <br> (4), $121.3(2,6)$ |
| 4x | 136.3 | 107.4 | 170.5 | 106.7 | 128.6 | 160.6 | 153.0 | $\begin{gathered} \text { Ph: } 136.5(1), 129.6(3,5), \\ 128.0(4), 121.8(2,6) \\ \hline \end{gathered}$ | - | - | - |
| 5x | 137.7 | 116.9 | 193.5 | 115.8 | 130.2 | 155.0 | 147.6 | $\begin{gathered} \hline \text { Ph: } 136.3(1), 129.6(3,5), \\ 128.2(4), 121.8(2,6) \end{gathered}$ | - | - | - |

Table 4. Selected ${ }^{13} \mathrm{C},{ }^{1} \mathrm{H}$ spin coupling constants of $\mathbf{4 a - b}, \mathbf{4 d} \mathbf{- g}, \mathbf{5 a - b}, \mathbf{5 d} \mathbf{- g}, \mathbf{4 x}$ and $\mathbf{5 x}(\mathrm{Hz}$, solvents as listed in Table 2).

| Comp | $J$ of C-3 | $J$ of C-3a | $J$ of C-4a | $J$ of C-5 | $J$ of C-7a | $J$ of C-8a | other couplings |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 4a | ${ }^{1} \mathrm{~J}=194.7$ | $\begin{gathered} { }^{2} J(\mathrm{H}-3)= \\ 9.9 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5)= \\ 9.9 \end{gathered}$ | ${ }^{1} J=194.7$ | $\begin{gathered} { }^{3} J(\mathrm{H}-5)= \\ 5.2 \end{gathered}$ | $\begin{gathered} { }^{3} J(\mathrm{H}-3)= \\ 5.2 \end{gathered}$ |  |
| 4b | $\begin{gathered} { }^{2} J(3-\mathrm{Me})= \\ 7.2 \end{gathered}$ | $\begin{gathered} { }^{3} J(3-\mathrm{Me})= \\ 2.9 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5)= \\ 10.0 \end{gathered}$ | ${ }^{1} J=194.4$ | $\begin{gathered} { }^{3} J(\mathrm{H}-5)= \\ 5.1 \end{gathered}$ |  | ${ }^{1} J(3-\mathrm{Me})=129.4$ |
| 4d | $\begin{gathered} { }^{2} J(3-\mathrm{Me})= \\ 7.1 \end{gathered}$ | $\begin{gathered} { }^{3} J(3-\mathrm{Me})= \\ 2.7 \end{gathered}$ | $\begin{gathered} { }^{3} J(5-\mathrm{Me})= \\ 2.7 \end{gathered}$ | $\begin{gathered} { }^{2} J(5-\mathrm{Me})= \\ 7.1 \end{gathered}$ |  |  | $\begin{gathered} { }^{1} J(3-\mathrm{Me})= \\ \\ 129.3 .{ }^{1} J(5-\mathrm{Me})= \\ \\ 129.3 \end{gathered}$ |
| 4 e | $\begin{gathered} { }^{2} J(3-\mathrm{Me})= \\ 7.1 \end{gathered}$ | $\begin{gathered} { }^{3} J(3-\mathrm{Me})= \\ 2.6 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5)= \\ 9.9 \end{gathered}$ | ${ }^{1} J=194.1$ | $\begin{gathered} { }^{3} J(\mathrm{H}-5)= \\ 5.2 \end{gathered}$ | $\begin{gathered} { }^{3} J(\mathrm{~N}-\mathrm{Me}) \\ =2.1 \end{gathered}$ | $\begin{gathered} { }^{1} J(\mathrm{~N}-\mathrm{Me})= \\ 141.7 .{ }^{1}{ }^{\mathrm{I}} J(3-\mathrm{Me})= \\ 129.1 \end{gathered}$ |
| 4f | ${ }^{1} J=194.1$ | $\begin{gathered} { }^{2} J(\mathrm{H}-3)= \\ 10.0 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5)= \\ 9.9 \end{gathered}$ | ${ }^{1} J=194.6$ | $\begin{gathered} { }^{3} J(\mathrm{H}-5)= \\ 5.2 \end{gathered}$ | $\begin{gathered} { }^{3} J(\mathrm{H}-3) \sim \\ 5.2,{ }^{3} J(\mathrm{~N}- \\ \left.\mathrm{CH}_{2}\right)=2.8 \end{gathered}$ | ${ }^{1} J(\mathrm{OMe})=144.1,{ }^{1} \mathrm{~J}\left(\mathrm{~N}-\mathrm{CH}_{2}\right)$ $=141.5,{ }^{3} J\left(\mathrm{NCH}_{2}, \mathrm{Ph} \underline{\mathrm{H}}-2,6\right)=$ $4.9,{ }^{2} J\left(\mathrm{Ph} \underline{\mathrm{C}}-1, \mathrm{NCH}_{2}\right)=4.7$, $J\left(\mathrm{Ph} \underline{\mathrm{C}}-2 / 6, \mathrm{NCH}_{2}\right)=4.4$ |
| 4g | $\begin{gathered} { }^{2} J(3-M e)= \\ 7.1 \end{gathered}$ | $\begin{gathered} { }^{3} J(3-\mathrm{Me})= \\ 2.8 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5)= \\ 10.0 \end{gathered}$ | ${ }^{1} J=194.2$ | $\begin{gathered} { }^{3} J(\mathrm{H}-5)= \\ 5.2 \end{gathered}$ | $\begin{gathered} { }^{3} J\left(\mathrm{~N}^{2} \mathrm{CH}_{2}\right) \\ =2.7 \end{gathered}$ | $\begin{aligned} & { }^{1} J\left({\left.\mathrm{~N}-\mathrm{CH}_{2}\right)=141.0,{ }^{1} J(3-\mathrm{Me})}^{3}=\right. \\ & =129.2,{ }^{3} J\left(\mathrm{NCH}_{2}, \operatorname{Ph} \underline{\mathrm{H}-2,6)}{ }_{4}^{4.7}\right. \end{aligned}$ |
| 5 a | ${ }^{1} J=195.8$ | $\begin{gathered} { }^{2} J(\mathrm{H}-3)= \\ 9.3 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5)= \\ 9.3 \end{gathered}$ | ${ }^{1} J=195.8$ | $\begin{gathered} { }^{3} J(\mathrm{H}-5)= \\ 5.1 \end{gathered}$ | $\begin{gathered} { }^{3} J(\mathrm{H}-3)= \\ 5.1 \end{gathered}$ |  |
| 5b | $\begin{gathered} { }^{2} J(3-\mathrm{Me})= \\ 7.1 \end{gathered}$ | $\begin{gathered} { }^{3} J(3-\mathrm{Me})= \\ 2.6 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5)= \\ 9.1 \end{gathered}$ | ${ }^{1} J=195.5$ | $\begin{gathered} { }^{3} J(\mathrm{H}-5)= \\ 5.0 \end{gathered}$ |  | ${ }^{1} \mathrm{~J}(3-\mathrm{Me})=129.7$ |
| 5d | $\begin{gathered} { }^{2} J(3-\mathrm{Me})= \\ 7.2 \end{gathered}$ | $\begin{gathered} { }^{3} J(3-\mathrm{Me})= \\ 2.5 \end{gathered}$ | $\begin{gathered} { }^{3} J(5-\mathrm{Me})= \\ 2.5 \end{gathered}$ | $\begin{gathered} { }^{2} J(5-\mathrm{Me})= \\ 7.2 \end{gathered}$ |  |  | $\begin{gathered} { }^{1} J(3-\mathrm{Me})=129.6,{ }^{1} J(5-\mathrm{Me})= \\ 129.6 \end{gathered}$ |
| 5 e | $\begin{gathered} { }^{2} J(3-M e)= \\ 7.1 \end{gathered}$ | $\begin{gathered} { }^{3} J(3-\mathrm{Me})= \\ 2.7 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5)= \\ 9.1 \end{gathered}$ | ${ }^{1} J=195.3$ | $\begin{gathered} { }^{3} J(\mathrm{H}-5)= \\ 5.1 \end{gathered}$ | $\begin{gathered} { }^{3} J(\mathrm{~N}-\mathrm{Me}) \\ =2.4 \end{gathered}$ | $\begin{gathered} { }^{1} J(\mathrm{~N}-\mathrm{Me})= \\ 141.9,{ }^{1}{ }^{\mathrm{I}} J(3-\mathrm{Me})= \\ 129.4 \end{gathered}$ |
| 5 f | ${ }^{1} \mathrm{~J}=195.0$ | $\begin{gathered} { }^{2} J(\mathrm{H}-3)= \\ 9.4 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5)= \\ 9.3 \end{gathered}$ | ${ }^{1} J=195.5$ | $\begin{gathered} { }^{3} J(\mathrm{H}-5)= \\ 5.1 \end{gathered}$ | $\begin{gathered} { }^{3} J(\mathrm{H}-3)= \\ 5.1,{ }^{3} J(\mathrm{~N}- \\ \left.\mathrm{CH}_{2}\right)=2.6 \end{gathered}$ | $\begin{aligned} & { }^{1} J(\mathrm{OMe})=144.1,{ }^{1} J\left({\left.\mathrm{~N}-\mathrm{CH}_{2}\right)}^{\prime}\right. \\ & =141.4,{ }^{3}\left(\mathrm{NCH}_{2}, \operatorname{Ph}\right. \\ & 4.6-2,6 \end{aligned}$ |
| 5 g | $\begin{gathered} { }^{2} J(3-\mathrm{Me})= \\ 7.1 \end{gathered}$ | $\begin{gathered} { }^{3} J(3-\mathrm{Me})= \\ 2.7 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5)= \\ 9.2 \end{gathered}$ | ${ }^{1} J=195.3$ | $\begin{gathered} { }^{3} J(\mathrm{H}-5)= \\ 5.1 \end{gathered}$ | $\begin{gathered} { }^{3} J\left(\mathrm{~N}^{2} \mathrm{CH}_{2}\right) \\ =2.8 \end{gathered}$ | $\begin{gathered} { }^{1} J\left(\mathrm{~N}-\mathrm{CH}_{2}\right)=141.2,{ }^{1}{ }^{J} J(3-\mathrm{Me}) \\ =129.5,{ }^{3} J\left(\mathrm{NCH}_{2}, \mathrm{Ph} \underline{\mathrm{H}-2,6)}\right. \\ = \\ =4.4 \end{gathered}$ |
| 4 x | ${ }^{1} \mathrm{~J}=193.8$ | $\begin{gathered} { }^{2} J(\mathrm{H}-3)= \\ 10.2 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5) \sim \\ 8.5 \end{gathered}$ | ${ }^{1} \mathrm{~J} \sim 195.0$ | $\begin{aligned} & { }^{3} J(\mathrm{H}-5)= \\ & \text { not } \\ & \text { resolved } \end{aligned}$ | $\begin{gathered} { }^{3} J(\mathrm{H}-3)= \\ 5.2 \end{gathered}$ |  |
| 5 x | ${ }^{1} \mathrm{~J}=194.7$ | $\begin{gathered} { }^{2} J(\mathrm{H}-3)= \\ 9.5 \end{gathered}$ | $\begin{gathered} { }^{2} J(\mathrm{H}-5)= \\ 7.8 \end{gathered}$ | ${ }^{1} J=195.9$ | $\begin{gathered} { }^{3} J(\mathrm{H}-5)= \\ 8.5 \end{gathered}$ | $\begin{gathered} { }^{3} J(\mathrm{H}-3)= \\ 4.9 \end{gathered}$ |  |

Table 5. ${ }^{15} \mathrm{~N}$-NMR chemical shifts of investigated compounds ( $\delta$ in ppm , solvents as listed in Table 2).

| $\mathbf{C o m p}$ | $\mathbf{N}-\mathbf{1}$ | $\mathbf{N}-\mathbf{2}$ | $\mathbf{N}-\mathbf{6}$ | $\mathbf{N}-\mathbf{7}$ |
| :---: | :---: | :---: | :---: | :---: |
| $\mathbf{4 a}$ | -186.8 | -86.8 | -86.8 | -186.8 |
| $\mathbf{4 b}$ | -193.1 | -93.6 | -87.7 | -187.1 |
| $\mathbf{4 d}$ | -193.4 | -94.2 | -94.2 | -193.4 |
| $\mathbf{4} \mathbf{e}$ | -211.8 | -91.7 | -88.0 | -187.5 |
| $\mathbf{4} \mathbf{f}$ | -191.8 | -85.2 | -87.5 | -187.3 |
| $\mathbf{4 g}$ | -200.0 | -91.3 | -88.2 | -187.4 |
| $\mathbf{5 a}$ | -187.6 | -84.5 | -84.5 | -187.6 |
| $\mathbf{5 b}$ | -195.3 | -92.1 | -85.5 | -188.0 |
| $\mathbf{5 d}$ | -196.2 | -92.9 | -92.9 | -196.2 |
| $\mathbf{5 e}$ | -213.7 | -89.7 | -85.6 | -188.2 |
| $\mathbf{5}$ | -192.4 | -82.2 | -84.9 | -187.9 |
| $\mathbf{5 g}$ | -201.9 | -89.5 | -85.8 | -188.2 |
| $\mathbf{4 x}$ | -186.4 | -87.7 | $-179.2^{*}$ | $-179.2^{*}$ |
| $\mathbf{5 x}$ | -186.7 | -84.3 | $-175.5^{*}$ | $-175.5^{*}$ |

* Not unambiguously classifiable.


### 3.2.9. General procedure for the synthesis of 9a and $\mathbf{9 b}$

According to a known procedure [24], to a solution of the corresponding carboxylic acid 7 (5 $\mathrm{mmol})$ in absolute ethanol $(30 \mathrm{~mL}), \mathrm{H}_{2} \mathrm{SO}_{4}(2 \mathrm{~mL})$ was added and the mixture was refluxed for 8 h . After the reaction mixture was concentrated in vacuo, the residue was neutralized with a saturated solution of $\mathrm{NaHCO}_{3}$ and then extracted with dichloromethane $(3 \times 15 \mathrm{~mL})$. Organic layers were combined and dried over sodium sulfate. The solvent was evaporated and the residue was purified by column chromatography (silica gel, mobile phase $\mathrm{CH}_{2} \mathrm{Cl}_{2}: \mathrm{MeOH} / 9: 1$ ).

Ethyl 5-chloro-1-phenyl-1H-pyrazole-4-carboxylate (9a). Starting from 7a ( $1.11 \mathrm{~g}, 5 \mathrm{mmol}) 1.02 \mathrm{~g}$ ( $81 \%$ ) of compound $\mathbf{9 b}$ were obtained as colorless crystals; m.p. $57^{\circ} \mathrm{C}$ (lit. [46] m.p. $59-60^{\circ} \mathrm{C}$ ); ${ }^{1} \mathrm{H}-$ NMR ( $500 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ): $\delta(\mathrm{ppm}) 8.12(\mathrm{~s}, 1 \mathrm{H}, \mathrm{H}-3), 7.44-7.56(\mathrm{~m}, 5 \mathrm{H}, \mathrm{Ph}-\mathrm{H}), 4.36(\mathrm{q}, 7.1 \mathrm{~Hz}, 2 \mathrm{H}$, $\left.\mathrm{OCH}_{2}\right), 1.38(\mathrm{t}, 7.1 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{Me}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(125 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 161.5(\mathrm{C}=\mathrm{O}$, $\left.{ }^{3} J\left(\mathrm{CO}, \mathrm{OCH}_{2}\right)=3.3 \mathrm{~Hz}\right), 142.3\left(\mathrm{C}-3,{ }^{1} J(\mathrm{C}-3, \mathrm{H}-3)=193.6 \mathrm{~Hz}\right), 137.4(\mathrm{Ph} \mathrm{C}-1), 131.1\left(\mathrm{C}-5,{ }^{3} J(\mathrm{C}-5, \mathrm{H}-3)\right.$ $=5.4 \mathrm{~Hz}), 129.2(\mathrm{Ph} \mathrm{C}-4), 129.1(\mathrm{Ph} \mathrm{C}-3,5), 125.5(\mathrm{Ph} \mathrm{C-2,6}), 112.3\left(\mathrm{C}-4,{ }^{2} J(\mathrm{C}-4, \mathrm{H}-3)=8.7 \mathrm{~Hz}\right), 60.6$ $\left(\mathrm{OCH}_{2},{ }^{1} J=147.7 \mathrm{~Hz} ;{ }^{2} J\left(\mathrm{OCH}_{2}, \mathrm{Me}\right)=4.4 \mathrm{~Hz}\right), 14.3\left(\mathrm{Me},{ }^{1} J=127.1 \mathrm{~Hz} ;\right.$ $\left.{ }^{2} J\left(\mathrm{Me}, \mathrm{OCH}_{2}\right)=2.7 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}\left(50 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm})-162.0(\mathrm{~N}-1),-75.8(\mathrm{~N}-2) ; \mathrm{MS} \mathrm{m} / \mathrm{z}$ (\%): 250/252 ( $\mathrm{M}^{+}, 34 / 11$ ), 222 (37), 205 (100), 77 (89), 51 (61).

Ethyl 5-chloro-3-methyl-1-phenyl-1H-pyrazole-4-carboxylate (9b). Starting from 7b (1.18 g, 5 mmol$)$ $688 \mathrm{mg}(52 \%)$ of compound $\mathbf{9 b}$ were obtained as colorless crystals; m.p. $72-73{ }^{\circ} \mathrm{C}$ (lit. [47] m.p. $74{ }^{\circ} \mathrm{C}$ ); ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(500 \mathrm{MHz}, \mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 7.41(\mathrm{~m}, 2 \mathrm{H}, \mathrm{Ph} \mathrm{H}-2,6), 7.36(\mathrm{~m}, 2 \mathrm{H}, \mathrm{Ph} \mathrm{H}-3,5)$, $7.30(\mathrm{~m}, 1 \mathrm{H}, \mathrm{Ph} \mathrm{H}-4), 4.24\left(\mathrm{q}, 7.1 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{OCH}_{2}\right), 2.43(\mathrm{~s}, 3 \mathrm{H}, 3-\mathrm{Me}), 1.27(\mathrm{t}, 7.1 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{Me}) ;{ }^{13} \mathrm{C}-$ NMR (125 MHz, $\left.\mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm}) 161.9\left(\mathrm{CO},{ }^{3} J\left(\mathrm{CO}, \mathrm{CH}_{2}\right)=3.1 \mathrm{~Hz}\right), 151.7(\mathrm{C}-3$, $\left.{ }^{2} J(\mathrm{C}-3,3-\mathrm{Me})=7.0 \mathrm{~Hz}\right), 137.2(\mathrm{Ph}-\mathrm{C}-1), 130.8(\mathrm{C}-5), 128.7(\mathrm{Ph} \mathrm{C}-3,5), 128.5(\mathrm{Ph} \mathrm{C}-4), 125.1(\mathrm{Ph} \mathrm{C}-$ $2,6), 109.8\left(\mathrm{C}-4,{ }^{3} J(\mathrm{C}-4,3-\mathrm{Me})=2.7 \mathrm{~Hz}\right), 59.9\left(\mathrm{OCH}_{2},{ }^{1} J=147.6 \mathrm{~Hz},{ }^{2} J\left(\mathrm{OCH}_{2}, \mathrm{CH}_{2}\right)=4.4 \mathrm{~Hz}\right), 14.4$ $\left(3-\mathrm{Me},{ }^{1} J=129.2 \mathrm{~Hz}\right), 13.9$ (ester-Me, $\left.{ }^{1} J=127.0 \mathrm{~Hz},{ }^{2} J\left(\underline{C H}_{3}, \mathrm{CH}_{2}\right)=2.6 \mathrm{~Hz}\right) ;{ }^{15} \mathrm{~N}-\mathrm{NMR}(50 \mathrm{MHz}$,
$\left.\mathrm{CDCl}_{3}\right): \delta(\mathrm{ppm})-168.2(\mathrm{~N}-1),-77.6(\mathrm{~N}-2) ; \mathrm{MS} \mathrm{m} / \mathrm{z}(\%): 264 / 266\left(\mathrm{M}^{+}, 53 / 18\right), 219$ (100), 155 (12), 77 (56), 51 (26).

## 4. Conclusions

Starting from appropriately substituted 2-pyrazolin-5-ones we have presented a widely applicable method for the preparation of substituted $1 H$-pyrano[2,3-c:6,5-c]dipyrazol-4(7H)-ones. Moreover, conversion of the latter into the corresponding thiones has been performed. Detailed NMR spectroscopic studies of the title compounds and their precursors were provided.

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