

Article

# Heterocyclic Analogues of Xanthone and Xanthione. 1*H*-Pyrano[2,3-*c*:6,5-*c*]dipyrazol-4(7*H*)-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-1*H*-pyrazole-4-carbonyl chloride or 5-chloro-3-methyl-1-phenyl-1*H*-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(7*H*)-ones by treatment with K<sub>2</sub>CO<sub>3</sub>/DMF. The latter were converted into the corresponding thiones upon reaction with Lawesson's reagent. Detailed NMR spectroscopic investigations (<sup>1</sup>H, <sup>13</sup>C, <sup>15</sup>N) of the ring systems and their precursors are presented.

**Keywords:** pyrazolones; 1*H*-pyrano[2,3-*c*:6,5-*c*]dipyrazol-4(7*H*)-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 As a result analogues in which one or both benzene rings of the parent xanthone system had been replaced by heteroaromatic moieties were also studied.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(1*H*)-ones of type **4**, which can be considered as heterocyclic analogues of xanthone (Scheme 1) [9-16]. The synthesis of compounds **4** is based on the reaction of 2-pyrazolin-5-ones **1** with *o*-haloheteroarene-carbonyl 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 **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[2,3-*b*]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.



In continuation of these investigations we present here the synthesis and spectroscopic data of related congeners 4a,b and 4d-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(7*H*)-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].





#### 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 **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 **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 **1c** with **2b**, and **1d** with **2b**, respectively) the corresponding compounds of type **3** were not obtained, and instead, the isomeric esters **8a** and **8b** resulting from O-aroylation of **1c** and **1d** were isolated as the major products from the reaction mixtures. Their structures could be easily

derived from the <sup>1</sup>H-NMR spectra considering the characteristic singlet signal due to pyrazole H-4 at  $\delta$  6.04 (**8a**) and  $\delta$  6.30 ppm (**8b**). Attempts to convert compounds **8** into their corresponding 4-aroyl congeners **3** failed. Finally, cyclization of intermediates **3** under standard conditions (K<sub>2</sub>CO<sub>3</sub> in DMF) [25] gave the target tricycles **4a**,**b** and **4d-g** in good yields. Treatment of the latter with Lawesson's reagent [26-28] in refluxing toluene smoothly afforded the corresponding thiones **5a**,**b** and **5d-g**. It should be mentioned that compounds **4d** and **5d** have already been described by Sarenko and coworkers [29]. Finally, the N-7 unsubstituted compounds **4x** and **5x** were prepared by treatment of the corresponding N7-PMB-protected congeners **4f** and **5f**, respectively, with trifluoroacetic acid at 70 °C [9,12] (Scheme 3).

Scheme 3. Synthesis of compounds 4x and 5x 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 **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 <sup>1</sup>H-coupled <sup>13</sup>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 <sup>1</sup>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 <sup>13</sup>C, <sup>1</sup>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 <sup>13</sup>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 C4–C5 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 Ph C-2,6 is quite obvious ( $\delta$  ~121 ppm in the 1-<u>Ph</u>-pyrazol-5-ol unit,  $\delta$  ~125.5 ppm in the 1-<u>Ph</u>-5-Cl-pyrazole unit). Moreover, also the <sup>15</sup>N-NMR chemical shifts in the mentioned pyrazole moieties differ markedly, both nitrogen atoms of the hydroxypyrazole system (for instance **3a**: N-1 –185.2 ppm, N-2 –97.9 ppm) show distinctly smaller chemical shifts than the corresponding ones in the chloropyrazole system (N-1 –159.9 ppm, N-

2 –72.4 ppm). The C=O resonance in compounds **3** is located in the range from 181–184 ppm. In Figure 2, <sup>1</sup>H, <sup>13</sup>C and <sup>15</sup>N-NMR chemical shift data are presented for **3a** which can be considered as a typical example.

**Figure 2.** <sup>1</sup>H- (*in italics*), <sup>13</sup>C- and <sup>15</sup>N-NMR (in **bold**) chemical shifts in **3a**, **4a** and **5a** ( $\delta$ , ppm, in CDCl<sub>3</sub>).



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 **4a**  $\rightarrow$  **5a** leaves the <sup>1</sup>H- and <sup>13</sup> C-NMR chemical shifts due to the phenyl ring nearly unchanged;  $\delta$  (N-1),  $\delta$  (N-2) and  $\delta$  (C-3) are also only slightly affected. However, in **4a** a pronounced 'push-pull situation' is on hand which leads to a strong polarization of the pyrane C=C bond resulting in a large chemical shift for C7a/C8a ( $\delta$  151.3 ppm) and a small for C3a/C4a ( $\delta$  108.8 ppm). In **5a** this effect is much less pronounced leading to an upfield shift for C7a/C8a ( $\delta$  145.5 ppm) and a marked downfield shift for C3a/C4a ( $\delta$  117.8 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 **4a** to **5a**, 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 **4b** and **5b** is not trivial. Ultimately, this assignment is possible considering the correlations found in the <sup>15</sup>N,<sup>1</sup>H-HMBC spectra. Thus, for instance, in compound **5b** the singlet signal due to H-5 ( $\delta$  8.32 ppm) exhibits a correlation to the <sup>15</sup>N signal with  $\delta$  -188.0 ppm, which consecutively must be that of N-7. The latter is also connected to the Ph H-2,6 resonance at  $\delta$  7.82 ppm, which accordingly has to be part of the N-7-phenyl system and thus can be unambiguously distinguished from Ph H-2,6 of the N1-phenyl moiety ( $\delta$  7.81 ppm). On basis of COSY (TOCSY), HSQC and HMBC experiments then the unequivocal assignment of all proton and carbon signals due to N1-Ph and N7-Ph is possible.

Compounds **4x** and **5x**, bearing no substituent at N-7, are interesting compounds capable of prototropic tautomerism with the 7*H*-, 6*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 ppm; **5x**: 193.5 ppm) which perfectly match those for  $\delta$  (C-4) of all other 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 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 <sup>13</sup>C

chemical shift data and by the size of certain <sup>13</sup>C, <sup>1</sup>H coupling constants. Hence, in **5x** <sup>2</sup>*J*(C4a,H5) (7.8 Hz) is somewhat smaller than <sup>2</sup>*J*(C3a,H3) (9.5 Hz) on the opposite site of the molecule what can be explained by lone-pair effects according to lit. [38]. Also <sup>3</sup>*J*(C8a,H3) = 4.9 Hz markedly differs from the corresponding coupling constant <sup>3</sup>*J*(C7a,H5) = 8.5 Hz. Moreover,  $\delta$  C-7a (155.0 ppm) is larger than  $\delta$  C-8a (147.6 ppm) and, conversely,  $\delta$  C-5 (130.2 ppm) is significantly smaller than  $\delta$  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-1-phenylpyrazole (166.7 ppm) is markedly larger than  $\delta$  (C-5) in 5-methoxy-1-phenylpyrazole (129.7 ppm) is significantly smaller than  $\delta$  (C-3) in 5-methoxy-1-phenylpyrazole (139.6 ppm) [37-39].

Lastly, the spectra of esters **8a** and **8b** are characterized by the occurence of a pyrazole C–H moiety with typically small chemical shifts for pyrazole H-4 (**8a**: 6.04 ppm, **8b**: 6.30 ppm) and pyrazole C-4 (**8a**: 93.9 ppm, **8b**: 94.9 ppm). Compared to the corresponding signals in 4-aroylpyrazol-5-ols **3** (~160 ppm) the resonance of pyrazole C-5 in the O-substituted pyrazole units of compounds **8** are significantly shifted upfield (**8a**: 144.6 ppm, **8b**: 144.3 ppm). Furthermore, the C=O resonances of compounds **8** exhibit remarkably small chemical shifts typical for ester carbonyl C-atoms of aryl esters (**8a**: 157.3 ppm, **8b**: 157.2 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 eV, 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. <sup>1</sup>Hand <sup>13</sup>C-NMR spectra were recorded on a Varian UnitvPlus 300 spectrometer at 28 °C (299.95 MHz for <sup>1</sup>H, 75.43 MHz for <sup>13</sup>C) or on a Bruker Avance 500 spectrometer at 293 K (500.13 MHz for <sup>1</sup>H, 125.77 MHz for <sup>13</sup>C). The center of the solvent signal was used as an internal standard, which was related to TMS with  $\delta$  7.26 ppm (<sup>1</sup>H, CDCl<sub>3</sub>),  $\delta$  2.49 ppm (<sup>1</sup>H, DMSO-d<sub>6</sub>),  $\delta$  77.0 ppm (<sup>13</sup>C, CDCl<sub>3</sub>) and  $\delta$  39.5 ppm (<sup>13</sup>C, DMSO-*d*<sub>6</sub>). <sup>15</sup>N-NMR spectra (50.68 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 Hz/data point in the <sup>1</sup>H spectra and 0.4 Hz/data point in the <sup>13</sup>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

Under anhydrous conditions,  $POCl_3$  (53.65 g, 32.5 mL, 350 mmol) was carefully added dropwise to dry DMF (11.70 g, 12.3 mL, 160 mmol) under cooling. Then pyrazolone **1** (50 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 H<sub>2</sub>O and dried.

5-*Chloro-1-phenyl-1H-pyrazole-4-carbaldehyde* (**6a**). Starting from 1-phenyl-2-pyrazolin-5-one (**1a**, 8.01 g, 50 mmol) 8.69 g (84%) of compound **6a** were obtained as brownish crystals; m.p. 68 °C (lit. [42] m.p. 70 °C); <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 9.92 (s, 1H, CHO), 8.14 (s, 1H, H-3), 7.46–7.57 (m, 5H, Ph-H); <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 182.9 (CHO, <sup>1</sup>*J* = 177.9 Hz, <sup>3</sup>*J* (CHO,H-3) = 0.6 Hz), 140.9 (C-3, <sup>1</sup>*J* (C-3,H-3) = 193.1 Hz, <sup>3</sup>*J*(C-3,CHO) = 3.7 Hz), 136.8 (Ph C-1), 132.4 (C-5, <sup>3</sup>*J*(C-5,H-3) = 5.9 Hz), 129.4 (Ph C-4), 129.3 (Ph C-3,5), 125.1 (Ph C-2,6), 120.1 (C-4, <sup>2</sup>*J* (C-4,H-3) = 9.5 Hz, <sup>2</sup>*J*(C-4,CHO) = 25.2 Hz); <sup>15</sup>N-NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) –161.5 (N-1), -70.3 (N-2); MS *m*/*z* (%): 206/208 (M<sup>+</sup>, 89/30), 205/207 (M<sup>+</sup>-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-2pyrazolin-5-one (**1b**, 8.71 g, 50 mmol) 9.05 g (82%) of compound **6b** were obtained as brownish crystals; m.p. 146 °C (lit. [43] m.p. 146–147 °C); <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ (ppm) 9.96 (s, 1H, 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 (s, 3H, Me); <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>): δ (ppm) 183.8 (CHO, <sup>1</sup>*J* = 176.2 Hz), 151.7 (C-3, <sup>2</sup>*J*(C-3,Me) = 7.0 Hz, <sup>3</sup>*J*(C-3,CHO) = 4.6 Hz), 136.9 (Ph C-1), 133.4 (C-5), 129.2 (Ph C-3,5), 129.1 (Ph C-4), 125.1 (Ph C-2,6), 117.3 (C-4, <sup>2</sup>*J*(C-4,CHO) = 24.3 Hz, <sup>3</sup>*J*(C-4,Me) = 2.5 Hz), 13.8 (Me, <sup>1</sup>*J* = 129.4 Hz); <sup>15</sup>N-NMR (50 MHz, CDCl<sub>3</sub>): –168.1 (N-1), –76.1 (N-2).

3.2.2. Preparation of 5-chloro-1-phenyl-1H-pyrazole-4-carboxylic acid (**7a**). To a solution of **6a** (1.03 g, 5 mmol) in a mixture of H<sub>2</sub>O/t-butanol 1:1 (15 mL) 1.11 g (7 mmol) KMnO<sub>4</sub> in H<sub>2</sub>O (20 mL) was added dropwise over 3 h while stirring at 70–80 °C. Then an aqueous solution of 10% 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 °C (lit. [44] m.p. 187–188 °C); <sup>1</sup>H-NMR (300 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  (ppm) 12.97 (s, 1H, OH), 8.16 (s, 1H, H-3), 7.52–7.60 (m, 5H, Ph-H); <sup>13</sup>C-NMR (75 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  (ppm) 162.3 (C=O), 142.4 (C-3, <sup>1</sup>*J*(C-3,H-3) = 193.5 Hz), 137.2 (Ph-C-1), 130.2 (C-5, <sup>3</sup>*J*(C-5,H-3) = 5.8 Hz), 129.3 (Ph C-3,4,5), 125.7 (Ph C-2,6), 112.3 (C-4, <sup>2</sup>*J*(C-4,H-3) = 8.9 Hz); <sup>15</sup>N-NMR (50 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  (ppm) –160.8 (N-1), –70.2 (N-2). MS *m*/*z* (%): 222/224 (M<sup>+</sup>, 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 2a and 2b

A suspension of the accordant carboxylic acid 7 (2 mmol) in toluene (10 mL), excess  $SOCl_2$  (10 mL) and 1 droplet of DMF was refluxed for 3 h. Then toluene and excess  $SOCl_2$  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 **7a** (445 mg, 2 mmol) 470 mg (98%) of compound **2a** were obtained as yellowish crystals; m.p. 134 °C; <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>): δ (ppm) 8.25 (s, 1H, H-3), 7.54 (m, 5H, Ph-H); <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>): δ (ppm) 158.3 (C=O), 144.9 (C-3, <sup>1</sup>*J*(C-3,H-3) = 196.2 Hz), 136.8 (Ph C-1), 132.2 (C-5, <sup>3</sup>*J*(C-5,H-3) = 4.5 Hz), 129.8 (Ph C-4), 129.4 (Ph C-3,5), 125.3 (Ph C-2,6), 116.1 (C-4, <sup>2</sup>*J*(C-4,H-3) = 8.8 Hz); <sup>15</sup>N-NMR (50 MHz, CDCl<sub>3</sub>): δ (ppm) –157.7 (N-1), –71.0 (N-2); MS *m*/*z* (%): 240/242/244 (M<sup>+</sup>, 12/8/1), 205 (100), 77 (51), 51 (36). HRMS Calcd. for C<sub>10</sub>H<sub>6</sub>Cl<sub>2</sub>N<sub>2</sub>O: 239.9857. Found: 239.9851.

5-*Chloro-3-methyl-1-phenyl-1H-pyrazole-4-carbonyl chloride* (**2b**). Starting from **7b** (473 mg, 2 mmol) 481 mg (92%) of compound **2b** were obtained as a colorless powder; m.p. 97 °C (lit. [45] m.p. 87 °C); <sup>1</sup>H-NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 7.52 (m, 5H, Ph-H), 2.57 (s, 3H, 3-Me); <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 158.4 (COCl), 151.9 (C-3, <sup>2</sup>*J*(C-3,3-Me) = 7.1 Hz), 136.0 (Ph C-1), 132.2 (C-5), 128.6 (Ph C-4), 128.3 (Ph C-3,5), 124.6 (Ph C-2,6), 113.2 (C-4, <sup>3</sup>*J*(C-4,3-Me) = 2.5 Hz), 14.5 (Me, <sup>1</sup>*J* = 129.9 Hz); <sup>15</sup>N-NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) -164.9 (N-1), -76.3 (N-2); IR: 1740 (C=O) cm<sup>-1</sup>; MS *m/z* (%): 254/256/258 (M<sup>+</sup>, 8/5/1), 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 mmol) in dry 1,4-dioxane (5 mL) was added dropwise to a suspension of pyrazolone (**1a-e**, 5 mmol) and Ca(OH)<sub>2</sub> (10 mmol) in dry 1,4-dioxane (5 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 N HCl (20 mL), stirred for 30 min and afterwards H<sub>2</sub>O (20 mL) was added. Then the products were filtered off, washed with H<sub>2</sub>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 mg, 5 mmol) and acid chloride 2a (1.21 g, 5 mmol) 1.58 g (86%) of compound 3a were obtained as yellowish crystals of m.p. 207 °C (EtOH).

(5-*Chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl*)(5-*hydroxy-1-phenyl-1*H-*pyrazol-4-yl*)*methanone* (**3b**). Starting from pyrazolone **1a** (801 mg, 5 mmol) and acid chloride **2b** (1.28 g, 5 mmol) 1.04 g (55%) of compound **3b** were obtained as colorless crystals of m.p. 153 °C (EtOH).

(5-*Chloro-1-phenyl-1H-pyrazol-4-yl*)(5-*hydroxy-3-methyl-1-phenyl-1*H-*pyrazol-4-yl*)*methanone* (3c). Starting from pyrazolone 1b (871 mg, 5 mmol) and acid chloride 2a (1.21 g, 5 mmol) 1.37 g (72%) of compound 3c were obtained as brownish crystals of m.p. 168 °C (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 mg, 5 mmol) and acid chloride **2b** (1.28 g, 5 mmol) 943 mg (48%) of compound **3d** were obtained as colorless crystals of m.p. 217–219 °C (EtOH) (lit. [29] m.p. 219–220 °C).

(5-*Chloro-1-phenyl-1H-pyrazol-4-yl*)(5-*hydroxy-1,3-dimethyl-1*H-*pyrazol-4-yl*)*methanone* (**3e**). From pyrazolone **1c** (561 mg, 5 mmol) and acid chloride **2a** (1.21 g, 5 mmol) 1.03 g (65%) of compound **3e** were obtained as colorless crystals of m.p. 184 °C (EtOH).

(5-*Chloro-1-phenyl-1H-pyrazol-4-yl*)[5-*hydroxy-1-(4-methoxybenzyl*)-1H-*pyrazol-4-yl*]*methanone* (**3f**). Starting from pyrazolone **1d** (1.02 g, 5 mmol) and acid chloride **2a** (1.21 g, 5 mmol) 1.40 g (68%) of compound **3f** were obtained as colorless crystals of m.p. 166–167 °C (EtOH).

(1-Benzyl-5-hydroxy-3-methyl-1H-pyrazol-4-yl)(5-chloro-1-phenyl-1H-pyrazol-4-yl)methanone (3g). Starting from pyrazolone 1e (941 mg, 5 mmol) and acid chloride 2a (1.21 g, 5 mmol) 1.92 g (98%) of compound 3g were obtained as orange crystals of m.p. 119 °C (EtOH).

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

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

Entry	Structure	Spectroscopic and analytical data
<b>3</b> a	H O H 3 2 N 4 4 5 5' N 1 OH Cl 1'	<sup>1</sup> H-NMR (300 MHz, CDCl <sub>3</sub> ): $\delta$ (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 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, 1H, OH); <sup>13</sup> C-NMR (75 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) 181.5 (C=O), 159.9 (C-5, <sup>3</sup> <i>J</i> (C-5,H-3) = 4.9 Hz), 141.1 (C-3', <sup>1</sup> <i>J</i> (C-3',H-3') = 190.7 Hz), 138.5 (C-3, <sup>1</sup> <i>J</i> (C-3,H-3) = 189.3 Hz), 137.2 (N1-Ph C-1 and N-1'-Ph C-1), 130.5 (C-5', <sup>3</sup> <i>J</i> (C-5',H-3') = 5.9 Hz), 129.5 (N1'-Ph C-4), 129.3 (N1'-Ph C-3,5), 129.2 (N1-Ph 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 (C-4', <sup>2</sup> <i>J</i> (C-4',H-3') = 10.3 Hz), 103.7 (C-4, <sup>2</sup> <i>J</i> (C-4,H-3) = 11.1 Hz); <sup>15</sup> N-NMR (50 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) -185.2 (N-1), -159.9 (N-1'), -97.9 (N-2), -72.4 (N-2'); IR: 1656 (C=O) cm <sup>-1</sup> ; MS <i>m</i> / <i>z</i> (%): 364/266 (M <sup>+</sup> , 23/8), 329 (38), 186 (100), 91 (18), 77 (52), 51 (22). Calcd. for C <sub>19</sub> H <sub>13</sub> CIN <sub>4</sub> O <sub>2</sub> (364.79): C, 62.56; H, 3.59; N, 15.36. Found: C, 62.39; H, 3.50; N, 15.16.

Table 1.	Spectroscop	ic and anal	vtical data o	f compounds 3	<b>Ba-g</b> and <b>8a-b</b> .
	r r r r r r r r		J		

 Table 1. Cont.

3b	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	<sup>1</sup> H-NMR (500 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) 10.18 (broad s, 1H, OH), 7.92 (s, 1H, 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 (1H, N1'-Ph H-4), 7.34 (m, 1H, N1-Ph H-4), 2.50 (s, 3H, 3'-Me); <sup>13</sup> C-NMR (125 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) 183.0 (C=O), 160.0 (C-5, <sup>3</sup> <i>J</i> (C-5,H-3) = 4.7 Hz), 150.5 (C-3', <sup>2</sup> <i>J</i> (C-3',3'-Me) = 6.9 Hz), 140.1 (C-3, <sup>1</sup> <i>J</i> (C-3,H-3) = 191.1 Hz), 137.3 (N1'-Ph C-1), 137.2 (N1-Ph C-1), 129.2 (N1'-Ph C-3,5), 129.15 (N1-Ph C-3,5), 129.05 (N1'-Ph C-4), 127.6 (C-5'), 127.0 (N1-Ph C-4), 125.4 (N1'-Ph C-2,6), 120.9 (N1-Ph C-2,6), 117.4 (C-4', <sup>3</sup> <i>J</i> (C-4',3'-Me) = 2.8 Hz), 104.2 (C-4, <sup>2</sup> <i>J</i> (C-4,H-3) = 10.6 Hz), 13.8 (3'-Me, <sup>1</sup> <i>J</i> = 129.1 Hz); <sup>15</sup> N-NMR (50 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) -186.0 (N- 1), -167.8 (N-1'), -97.3 (N-2), -75.8 (N-2'); IR: 1559 (C=O) cm <sup>-1</sup> ; MS <i>m</i> / <i>z</i> (%): 378/380 (M <sup>+</sup> , 12/4), 343 (45), 219 (11), 186 (100), 118 (12), 91 (15), 77 (43), 51 (16). Calcd. for C <sub>20</sub> H <sub>15</sub> ClN <sub>4</sub> O <sub>2</sub> (378.81): C, 63.41; H, 3.99; N, 14.79. Found: C, 63.24; H, 3.81; N, 14.74.
Зс	CH <sub>3</sub> O H 3 2 N 4 4' N 2' N 5 5' N 1 OH CI 1'	<sup>1</sup> H-NMR (500 MHz, CDCl <sub>3</sub> ): δ (ppm) 8.01 (s, 1H, H-3'), 7.87 (m, 2H, N1-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, 3-Me), OH not found; <sup>13</sup> C-NMR (125 MHz, CDCl <sub>3</sub> ): δ (ppm) 182.9 (C=O), 161.0 (C-5), 147.3 (C-3, <sup>2</sup> <i>J</i> (C-3, 3-Me) = 6.8 Hz), 140.8 (C-3', <sup>1</sup> <i>J</i> (C-3', H-3') = 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 (C-5', <sup>3</sup> <i>J</i> (C-5',H-3') = 5.6 Hz), 126.9 (N1-Ph C-4), 125.4 (N1'-Ph C-2,6), 120.9 (N1-Ph C-2,6), 118.4 (C-4', <sup>2</sup> <i>J</i> (C-4',H-3') = 10.1 Hz), 104.4 (C-4, <sup>3</sup> <i>J</i> (C-4,3-Me) = 2.7 Hz), 15.6 (3-Me, <sup>1</sup> <i>J</i> = 128.8 Hz); <sup>15</sup> N-NMR (50 MHz, CDCl <sub>3</sub> ): δ (ppm) -190.3 (N-1), -161.7 (N-1'), -100.8 (N-2), -74.2 (N-2'); IR: 1619 (C=O) cm <sup>-1</sup> ; MS <i>m</i> /z (%): 378/380 (M <sup>+</sup> , 8/3), 342 (48), 200 (100), 91 (37), 77 (58), 51 (25). Calcd. for C <sub>20</sub> H <sub>15</sub> CIN <sub>4</sub> O <sub>2</sub> (378.81): C, 63.41; H, 3.99; N, 14.79. Found: C, 63.71; H, 3.91; N, 14.69.
3d	$\begin{array}{c} CH_3 & O & CH_3 \\ 3 & I & I \\ 2 N & I & I \\ N & I \\ S & S \\ I & OH CI & I \\ \end{array}$	<sup>1</sup> H-NMR (500 MHz, CDCl <sub>3</sub> ): δ (ppm) 9.20 (broad s, 1H, OH), 7.87 (m, 2H, 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, 3H, 3'-Me), 2.23 (s, 3H, 3-Me); <sup>13</sup> C-NMR (125 MHz, CDCl <sub>3</sub> ): δ (ppm) 183.8 (C=O), 160.8 (C-5), 148.8 (C-3', <sup>2</sup> <i>J</i> (C-3', 3'-Me) = 6.8 Hz), 148.1 (C-3, <sup>2</sup> <i>J</i> (C-3,3-Me) = 6.7 Hz), 137.4 (N1'-Ph C-1), 137.1 (N1-Ph C-1), 129.2 (N1'-Ph C-3,5), 129.1 (N1-Ph 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', <sup>3</sup> <i>J</i> (C-4',3'-Me) = 3.0 Hz), 105.5 (C-4, <sup>3</sup> <i>J</i> (C-4,3-Me) = 2.8 Hz), 13.9 (3-Me, <sup>1</sup> <i>J</i> = 129.0 Hz), 13.0 (3'-Me, <sup>1</sup> <i>J</i> = 128.9 Hz); <sup>15</sup> N-NMR (50 MHz, CDCl <sub>3</sub> ): δ (ppm) -190.3 (N-1), -168.8 (N-1'), -100.0 (N-2), -76.6 (N-2'); MS <i>m/z</i> (%): 392/394 (M <sup>+</sup> , 5/2), 356 (39), 219 (10), 200 (100), 132 (13), 91 (31), 77 (40), 67 (12), 51 (15). Calcd. for C <sub>21</sub> H <sub>17</sub> ClN <sub>4</sub> O <sub>2</sub> (392.84): C, 64.21; H, 4.36; N, 14.26. Found: C, 64.04; H, 4.18; N, 14.21.
Зе	$\begin{array}{c} CH_{3} & O & H \\ CH_{3} & O & H \\ C & N & C \\ N & C & S^{C} \\ H_{3} C & O H C I \\ \end{array} \\ \begin{array}{c} N & C \\ N \\ N & C \\ N & C \\ N & C \\ N & C \\ N \\ N & C \\ N \\ C \\ N & C \\ N & C \\ N \\ C \\ N \\ \mathsf$	<sup>1</sup> H-NMR (300 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) 10.35 (broad s, 1H, OH), 7.94 (s, 1H, H- 3'), 7.44–7.59 (m, 5H, N1'-Ph), 3.62 (s, 3H, N1-Me), 2.27 (s, 3H, 3-Me); <sup>13</sup> C- NMR (75 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) 183.4 (C=O), 160.2 (C-5, <sup>3</sup> <i>J</i> (C-5,N1-Me) = 2.3 Hz), 146.2 (C-3, <sup>2</sup> <i>J</i> (C-3,3-Me) = 6.9 Hz), 140.6 (C-3', <sup>1</sup> <i>J</i> (C-3',H-3') = 191.7 Hz), 137.4 (N1'-Ph C-1), 129.2 (N1'-Ph C-3,4,5), 128.6 (C-5', <sup>3</sup> <i>J</i> (C- 5',H-3') = 5.7 Hz), 125.3 (N1'-Ph C-2,6), 119.0 (C-4', <sup>2</sup> <i>J</i> (C-4',H-3') = 10.1 Hz), 103.2 (C-4, <sup>3</sup> <i>J</i> (C-4,3-Me) = 2.7 Hz), 32.5 (N1-Me, <sup>1</sup> <i>J</i> = 140.9 Hz), 15.2 (3-Me, <sup>1</sup> <i>J</i> = 128.6 Hz); <sup>15</sup> N-NMR (50 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) –207.9 (N-1), –162.2 (N-1'), –100.5 (N-2), –74.7 (N-2'); IR: 1636 (C=O) cm <sup>-1</sup> ;MS <i>m</i> /z (%): 316/318 (M <sup>+</sup> , 11/4), 281 (26), 138 (100), 77 (21), 51 (17). Calcd. for C <sub>15</sub> H <sub>13</sub> ClN <sub>4</sub> O <sub>2</sub> (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	H O H 3 2 N 4 4' N 2' N 5 5' N 1 OH Cl 1' OMe	<sup>1</sup> H-NMR (300 MHz, CDCl <sub>3</sub> ): $\delta$ (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 (m, 3H, N1'-Ph H-3,4,5), 7.31 (m, 2H, CH <sub>2</sub> -Ph H-2,6), 6.88 (CH <sub>2</sub> -Ph H-3,-5), 5.13 (broad s, 2H, CH <sub>2</sub> ), 3.79 (s, 3H, OMe); <sup>13</sup> C-NMR (75 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) 181.7 (C=O), 159.5 (CH <sub>2</sub> -Ph C-4), 159.0 (C-5), 141.1 (C-3', <sup>1</sup> <i>J</i> (C-3', H-3') = 190.7 Hz), 137.9 (C-3, <sup>1</sup> <i>J</i> (C-3,H-3) = 188.8 Hz), 137.3 (N1'-Ph C-1), 130.3 (C-5'), 129.6 (CH <sub>2</sub> -Ph C-2,6), 129.4 (N1'-Ph C-4), 129.2 (N1'-Ph C-3,5), 127.5 (CH <sub>2</sub> -Ph C-1), 125.5 (N1'-Ph C-2,-6), 118.2 (C-4', <sup>2</sup> <i>J</i> (C-4',H-3') = 10.0 Hz), 114.2 (CH <sub>2</sub> -Ph C3,5), 103.1 (C-4), 55.3 (OMe, <sup>1</sup> <i>J</i> = 143.9 Hz), 49.8 (CH <sub>2</sub> , <sup>1</sup> <i>J</i> = 140.6 Hz); <sup>15</sup> N-NMR (50 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) -189.2 (N-1), -160.3 (N-1'), -98.3 (N-2), -73.1 (N-2'); IR: 1621 (C=O) cm <sup>-1</sup> ;MS <i>m</i> / <i>z</i> (%): 408/410 (M <sup>+</sup> , 7/2), 373 (25), 121 (100), 77 (23). Calcd. for C <sub>21H17</sub> ClN <sub>4</sub> O <sub>3</sub> (408.84): C, 61.69; H, 4.19; N, 13.70. Found: C, 61.47; H, 4.13, N, 13.55.
3g	$\begin{array}{c} CH_3 & O & H \\ 3 & & & 3' \\ 2 & N & & 4 & 4' \\ N & & 5 & 5' \\ 1 & OH  CI & 1' \\ \end{array}$	<sup>1</sup> H-NMR (300 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) 7.70–8.20 (broad s, 1H, OH), 7.96 (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, 1H, N1'-Ph H-4), 7.28–7.38 (m, 5H, CH <sub>2</sub> - <u>Ph</u> ), 5.12 (s, 2H, CH <sub>2</sub> ), 2.28 (s, 3H, 3-Me); <sup>13</sup> C-NMR (75 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) 183.3 (C=O), 160.3 (C-5, <sup>3</sup> <i>J</i> (C-5,CH <sub>2</sub> ) = 2.4 Hz), 146.6 (C-3, <sup>2</sup> <i>J</i> (C-3,3-Me) = 7.0 Hz), 140.7 (C-3', <sup>1</sup> <i>J</i> (C-3', H-3') = 192.0 Hz), 137.4 (N1'-Ph C-1), 135.5 (CH <sub>2</sub> - <u>Ph</u> C-1), 129.2 (N1'-Ph C-3,4,5), 128.7 (CH <sub>2</sub> - <u>Ph</u> C-3,5 and C-5', <sup>3</sup> <i>J</i> (C-5',H-3') = 5.7 Hz), 128.0 (CH <sub>2</sub> - <u>Ph</u> C-2,4,6), 125.3 (N1'-Ph C-2,6), 118.9 (C-4', <sup>2</sup> <i>J</i> (C-4',H-3') = 10.1 Hz), 103.4 (C-4, <sup>3</sup> <i>J</i> (C-4,3-Me) = 2.6 Hz), 49.8 (CH <sub>2</sub> , <sup>1</sup> <i>J</i> = 140.2 Hz), 15.4 (3-Me, <sup>1</sup> <i>J</i> = 128.6 Hz); <sup>15</sup> N-NMR (50 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) –196.4 (N-1), –162.1 (N-1'), –101.1 (N-2), –74.7 (N-2'); IR: 1633 (C=O) cm <sup>-1</sup> ; MS <i>m</i> / <i>z</i> (%): 392/394 (M <sup>+</sup> , 8/3), 356 (91), 91 (100), 77 (25), 51 (18). Calcd. for C <sub>21</sub> H <sub>17</sub> ClN <sub>4</sub> O <sub>2</sub> (392.84): C, 64.21; H, 4.36; N, 14.26. Found: C, 64.13; H, 4.27; N, 14.11.
8a	$H_{3}C$ $(3)$ $(4)$ $(3)$ $(4)$ $(3)$ $($	<sup>1</sup> H-NMR (300 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) 7.52 (m, 5H, Ph-H), 6.04 (s, 1H, H-4), 3.74 (s, 3H, N-Me), 2.59 (s, 3H, 3'-Me), 2.25 (s, 3H, 3-Me); <sup>13</sup> C-NMR (75Hz, CDCl <sub>3</sub> ): $\delta$ (ppm) 157.3 (C=O), 153.1 (C-3', <sup>2</sup> <i>J</i> (C-3',3'-Me) = 6.9 Hz), 147.2 (C-3, <sup>2</sup> <i>J</i> (C-3,3-Me) = 6.7 Hz, <sup>2</sup> <i>J</i> (C-3,H-4) = 4.3 Hz), 144.6 (C-5, <sup>3</sup> <i>J</i> (C-5,N- CH <sub>3</sub> ) = 2.2 Hz, <sup>2</sup> <i>J</i> (C 5,H-4) = 4.4 Hz), 137.2 (Ph-C-1), 132.2 (C-5'), 129.3 (Ph-C-4), 129.2 (Ph-C-3,5), 125.5 (Ph-C-2,-6), 108.3 (C-4', <sup>3</sup> <i>J</i> (C-4',3'-Me) = 2.7 Hz), 93.9 (C-4, <sup>1</sup> <i>J</i> (C-4,H-4) = 181.2 Hz, <sup>3</sup> <i>J</i> (C-4,3-Me) = 3.5 Hz), 14.8 (3'- Me, <sup>1</sup> <i>J</i> = 129.5Hz), 14.2 (3-Me, <sup>1</sup> <i>J</i> = 127.5 Hz); <sup>15</sup> N-NMR (50 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) -202.2 (N-1), -165.8 (N-1'), -98.9 (N-2), -75.7 (N-2'); IR: 1745 (C=O) cm <sup>-1</sup> ; MS <i>m</i> / <i>z</i> (%): 330 (M <sup>+</sup> , 0.1), 219 (100), 77 (42), 51 (19). Calcd. for C <sub>16</sub> H <sub>15</sub> ClN <sub>4</sub> O <sub>2</sub> (330.77): C, 58.10; H, 4.57; N, 16.94. Found: C, 58.14; H, 4.37; N, 16.90.
8b	H 3 2 N 1 5 0 4 0 CH <sub>3</sub> 3' N <sup>2'</sup> 0 CH <sub>3</sub> 3' N <sup>2'</sup> 0 O CH <sub>3</sub> 1 N <sup>2'</sup> O O CH <sub>3</sub> 1 O CH <sub>3</sub> CH <sub>1</sub> CH <sub>1</sub>	<sup>1</sup> H-NMR (300 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) 7.53 (d, 1H, H-3, <sup>3</sup> <i>J</i> (H3,H4) = 2.1 Hz), 7.52 (m, 5H, N1'-Ph), 7.12 (m, 2H, CH <sub>2</sub> - <u>Ph</u> H-2,6), 6.82 (m, 2H, CH <sub>2</sub> - <u>Ph</u> H- 3,5), 6.30 (d, 1H, H-4, <sup>3</sup> <i>J</i> (H4,H3) = 2.1 Hz), 5.28 (s, 2H, CH <sub>2</sub> ), 3.75 (s, 3H, O- Me), 2.52 (s, 3H, 3'-Me); <sup>13</sup> C-NMR (75 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) 159.2 (CH <sub>2</sub> - <u>Ph</u> C4), 157.2 (C=O), 153.2 (C-3', <sup>2</sup> <i>J</i> (C-3',3'-Me) = 7.0 Hz), 144.3 (C-5), 138.7 (C-3, <sup>1</sup> <i>J</i> (C-3,H-3) = 187.6 Hz, <sup>2</sup> <i>J</i> (C-3,H-4) = 4.8 Hz), 137.2 (N1'-Ph C-1), 132.2 (C-5'), 129.4 (N1'-Ph C-4), 129.2 (N1'-Ph C-3,5), 128.4 (CH <sub>2</sub> - <u>Ph</u> C- 2,6), 128.3 (CH <sub>2</sub> - <u>Ph</u> C-1), 125.5 (N1'-Ph C-2,6), 114.1 (CH <sub>2</sub> - <u>Ph</u> C-3,5), 108.2 (C-4', <sup>3</sup> <i>J</i> (C-4',3'-Me) = 2.7 Hz), 94.9 (C-4, <sup>1</sup> <i>J</i> (C-4,H-4) = 183.4 Hz, <sup>2</sup> <i>J</i> (C-4,H- 5) = 10.5 Hz), 55.2 (O-Me, <sup>1</sup> <i>J</i> = 143.8 Hz), 51.3 (CH <sub>2</sub> , <sup>1</sup> <i>J</i> = 140.0 Hz, <sup>3</sup> <i>J</i> ( <u>C</u> H <sub>2</sub> ,Ph-H-2,6) = 4.3 Hz), 14.8 (3'-Me, <sup>1</sup> <i>J</i> = 129.6 Hz); <sup>15</sup> N-NMR (50 MHz, CDCl <sub>3</sub> ): $\delta$ (ppm) -185.1 (N-1), -165.7 (N-1'), -95.3 (N-2), -75.7 (N-2'); IR: 1745 (C=O) cm <sup>-1</sup> ; MS <i>m</i> /z (%): 422 (M <sup>+</sup> , 0.1), 219 (100), 121 (25), 77 (20). Calcd. for C <sub>22</sub> H <sub>19</sub> ClN <sub>4</sub> O <sub>3</sub> (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,  $K_2CO_3$  (138 mg, 1 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 H<sub>2</sub>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-1*H-*pyrano*[*2,3*-c:*6,5*-c]*dipyrazol-4*(*7H*)-*one* (**4a**). Starting from **3a** (365 mg, 1 mmol) 304 mg (93%) of compound **4a** were obtained as colorless crystals; m.p. 256 °C (EtOH); IR: 1673 (C=O) cm<sup>-1</sup>; MS m/z (%): 328 (M<sup>+</sup>, 77), 187 (30), 77 (100), 51 (40). Calcd. for C<sub>19</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub> (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*(7*H*)-*one* (**4b**). Starting from **3b** (379 mg, 1 mmol) 288 mg (84%) of compound **4b** were obtained as colorless crystals. Alternatively, starting from **3c** (379 mg, 1 mmol) 219 mg (64%) of compound **4b** were obtained as colorless crystals; m.p. 220 °C (EtOH); IR: 1664 (C=O) cm<sup>-1</sup>; MS m/z (%): 342 (M<sup>+</sup>, 66), 156 (14), 91 (24), 77 (100), 67 (20), 51 (45). Calcd. for C<sub>20</sub>H<sub>14</sub>N<sub>4</sub>O<sub>2</sub> (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 mg, 1 mmol) 264 mg (74%) of compound 4d were obtained as colorless crystals; m.p. 243 °C (EtOH) (lit. [29] m.p. 240–241 °C). IR: 1521 (C=O) cm<sup>-1</sup>; MS m/z (%): 356 (M<sup>+</sup>, 100), 178 (10), 156 (18), 91 (31), 77 (99), 67 (30), 51 (41). Calcd. for C<sub>21</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub> (356.37)•0.2 H<sub>2</sub>O: 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 mmol) 185 mg (66%) of compound **4e** were obtained as colorless crystals; m.p. 204 °C (EtOH); IR: 1654 (C=O) cm<sup>-1</sup>; MS *m/z* (%): 280 (M<sup>+</sup>, 100), 139 (25), 77 (74), 51 (43). Calcd. for C<sub>15</sub>H<sub>12</sub>N<sub>4</sub>O<sub>2</sub> (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 **3f** (409 mg, 1 mmol) 276 mg (74%) of compound **4f** were obtained as colorless crystals; m.p. 245 °C (EtOH); IR: 1667 (C=O) cm<sup>-1</sup>; MS m/z (%): 372 (M<sup>+</sup>, 20), 121 (100), 77 (15). Calcd. for C<sub>21</sub>H<sub>16</sub>N<sub>4</sub>O<sub>3</sub> (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-1*H-*pyrano*[2,3-c:6,5-c]*dipyrazol-4-(7H)-one* (**4g**). Starting from **3g** (393 mg, 1 mmol) 258 mg (73%) of compound **4g** were obtained as colorless crystals; m.p. 210 °C (EtOH); IR: 1659 (C=O) cm<sup>-1</sup>; MS *m/z* (%): 356 (M<sup>+</sup>, 39), 265 (33), 91 (100), 77 (28), 51 (14). Calcd. for C<sub>21</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub> (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 mg, 0.5 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 **5b** no precipitate was formed, here the solvent was evaporated and the residue was subjected to column chromatography (silica gel, mobile phase  $CH_2Cl_2:MeOH/9:1$ ) 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 **4a** (328 mg, 1 mmol) 204 mg (60%) of compound **5a** were obtained as reddish crystals; m.p. 254–256 °C (EtOH); MS *m/z* (%): 344 (M<sup>+</sup>, 100), 201 (30), 77 (84), 51 (57). Calcd. for C<sub>19</sub>H<sub>12</sub>N<sub>4</sub>OS (344.39)•0.2 H<sub>2</sub>O: C, 65.58; 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*(7*H*)-*thione* (**5b**). Starting from **4b** resp. **4c** (342 mg, 1 mmol) 356 mg (99%) of compound **5b** were obtained as orange crystals; m.p. 195–197 °C (EtOH); MS m/z (%): 358 (M<sup>+</sup>, 22), 356 (100), 77 (50), 51 (25). Calcd. for C<sub>20</sub>H<sub>14</sub>N<sub>4</sub>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 mg, 1 mmol) 268 mg (72%) of compound **5d** were obtained as deep yellow crystals; m.p. 286 °C (EtOH) (lit. [29] m.p. 285–286 °C); MS *m/z* (%): 373 (M<sup>+</sup>+1, 23), 372 (M<sup>+</sup>, 100), 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 **4e** (280 mg, 1 mmol) 138 mg (47%) of compound **5e** were obtained as yellowish crystals; m.p. 212 °C (EtOH); MS m/z (%): 296 (M<sup>+</sup>, 18), 275 (42), 73 (100). Calcd. for C<sub>15</sub>H<sub>12</sub>N<sub>4</sub>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*(7*H*)-*thione* (**5f**). Starting from **4f** (372 mg, 1 mmol) 314 mg (81%) of compound **5f** were obtained as yellowish crystals; m.p. 222 °C (EtOH); MS m/z (%): 388 (M<sup>+</sup>, 13), 121 (100), 91 (10), 77 (31), 51 (14). Calcd. for C<sub>21</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>S (388.44)•0.2 H<sub>2</sub>O: 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 **4g** (356 mg, 1 mmol) 268 mg (72%) of compound **5g** were obtained as yellowish crystals; m.p. 224 °C (EtOH); MS m/z (%): 373 (M<sup>+</sup>+1, 21), 372 (M<sup>+</sup>, 100), 281 (75), 91 (97), 77 (37), 51 (33). Calcd. for C<sub>21</sub>H<sub>16</sub>N<sub>4</sub>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 4x and 5x

Under anhydrous conditions, a solution of the PMB-substituted congener **4f** or **5f** (0.5 mmol) and trifluoroacetic acid (TFA, 1.43 g, 12.5 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-1*H-*pyrano*[2,3-c:6,5-c]*dipyrazol-4*(7H)-*one* (**4x**). Starting from **4f** (186 mg, 0.5 mmol) 61 mg (48%) of compound **4x** were obtained as brown powder; m.p. 327–329 °C; IR: 1681 (C=O) cm<sup>-1</sup>; MS m/z (%): 253 (M<sup>+</sup>+1, 16), 252 (M+, 100), 111 (87), 77 (46), 51 (38). HRMS Calcd. for C<sub>13</sub>H<sub>8</sub>N<sub>4</sub>O<sub>2</sub>: 252.0647. Found: 252.0644.

*1-Phenyl-1*H-*pyrano*[2,3-c:6,5-c]*dipyrazol-4*(7H)-*thione* (**5**x). Starting from **5f** (194 mg, 0.5 mmol) 69 mg (51%) of compound **5x** were obtained as a greenish powder; m.p. 271–273 °C; MS m/z (%): 269 (M<sup>+</sup>+1, 18), 268 (M<sup>+</sup>, 100), 267 (M<sup>+</sup>-1, 45)127 (43), 77 (54), 51 (45). HRMS Calcd. for C<sub>13</sub>H<sub>7</sub>N<sub>4</sub>OS (M<sup>+</sup>-1): 267.0341. Found: 267.0335.

Comp	Solvent	H of R <sup>1</sup>	H of R <sup>3</sup>	H of R <sup>5</sup>	H of R <sup>7</sup>
4a	CDCl <sub>3</sub>	Ph: 7.82 (2,6), 7.55 (3,5),	8.22 (H-3)	8.22 (H-5)	Ph: 7.82 (2,6), 7.55 (3,5), 7.44 (4)
		7.44 (4)			
<b>4</b> b	CDCl <sub>3</sub>	Ph: 7.78 (2,6), 7.52 (3,5),	2.66 (Me)	8.17 (H-5)	Ph: 7.80 (2,6), 7.53 (3,5), 7.43 (4)
		7.40 (4)			
4d	CDCl <sub>3</sub>	Ph: 7.78 (2,6), 7.51 (3,5),	2.65 (Me)	2.65 (Me)	Ph: 7.78 (2,6), 7.51 (3,5), 7.39 (4)
		7.39 (4)			
<b>4</b> e	CDCl <sub>3</sub>	3.87 (Me)	2.55 (Me)	8.13 (H-5)	Ph: 7.79 (2,6), 7.56 (3,5), 7.43 (4)
<b>4f</b>	CDCl <sub>3</sub>	Ph: 7.28 (2,6), 6.89	8.05 (H-3)	8.17 (H-5)	Ph: 7.66 (2,6), 7.56 (3,5), 7.46 (4)
		(3,5); 5.37 (CH <sub>2</sub> ), 3.79			
		(OMe)			
4g	CDCl <sub>3</sub>	Ph: 7.37 (4), 7.36 (3,5),	2.60 (Me)	8.12 (H-5)	Ph: 7.60 (2,6), 7.52 (3,5), 7.42 (4)
		7.31 (2,6); 5.35 (CH <sub>2</sub> )			
5a	CDCl <sub>3</sub>	Ph: 7.84 (2,6), 7.57 (3,5),	8.39 (H-3)	8.39 (H-5)	Ph: 7.84 (2,6), 7.57 (3,5), 7.46 (4)
		7.46 (4)			
5b	CDCl <sub>3</sub>	Ph: 7.81 (2,6), 7.54 (3,5),	2.78 (Me)	8.32 (H-5)	Ph: 7.82 (2,6), 7.55 (3,5), 7.44 (4)
		7.42 (4)			
5d	CDCl <sub>3</sub>	Ph: 7.80 (2,6), 7.53 (3,5),	2.80 (Me)	2.80 (Me)	Ph: 7.80 (2,6), 7.53 (3,5), 7.41 (4)
		7.41 (4)			
<b>5</b> e	CDCl <sub>3</sub>	3.89 (Me)	2.65 (Me)	8.27 (H-5)	Ph: 7.81 (2,6), 7.57 (3,5), 7.45 (4)
5f	CDCl <sub>3</sub>	Ph: 7.28 (2,6), 6.90	8.20 (H-3)	8.32 (H-5)	Ph: 7.66 (2,6), 7.56 (3,5), 7.47 (4)
		(3,5); 5.38 (CH <sub>2</sub> ), 3.79			
		(OMe)			
5g	CDCl <sub>3</sub>	Ph: 7.38 (3,4,5), 7.33	2.73 (Me)	8.29 (H-5)	Ph: 7.61 (2,6), 7.53 (3,5), 7.43 (4)
		$(2,6); 5.37 (CH_2)$			
4x	DMSO- $d_6$	Ph: 7.85 (2,6), 7.62 (3,5),	8.24 (H-3)	8.56 (H-5)	13.78 (NH)
		7.48 (4)			
5x	DMSO- $d_6$	Ph: 7.87 (2,6), 7.64 (3,5),	8.34 (H-3)	8.66 (H-5)	14.00 (NH)
		7.50 (4)			

**Table 2.** <sup>1</sup>H-NMR chemical shifts of **4a-b**, **4d-g**, **5a-b**, **5d-g**, **4x** and **5x** ( $\delta$  in ppm).

C-3	C-3a	C-4	C-4a	C-5	C-7a	C-8a	C of R <sup>1</sup>	C of R <sup>3</sup>	C of R <sup>5</sup>	C of R <sup>7</sup>
136.7	108.8	169.7	108.8	136.7	151.3	151.3	Ph: 136.6 (1), 129.6 (3,5),	-	-	Ph: 136.6 (1), 129.6 (3,5), 128.3
							128.3 (4), 121.3 (2,6)			(4), 121.3 (2,6)
148.1	106.5	170.6	108.9	136.6	151.3	151.4	Ph: 136.6 (1), 129.48 (3,5),	14.0	-	Ph: 136.7 (1), 129.53 (3,5), 128.1
							127.8 (4), 121.1 (2,6)	(Me)		(4), 121.2 (2,6)
148.0	106.6	171.8	106.6	148.0	151.5	151.5	Ph: 136.7 (1), 129.5 (3,5),	14.0	14.0	Ph: 136.7 (1), 129.5 (3,5), 127.7
							127.7 (4), 121.0 (2,6)	(Me)	(Me)	(4), 121.0 (2,6)
146.8	105.0	170.7	108.7	136.6	151.3	152.6	34.1 (Me)	13.9	-	Ph: 136.7 (1), 129.6 (3,5), 128.1
								(Me)		(4), 121.5 (2,6)
135.5	107.8	169.8	108.6	136.7	151.4	152.0	Ph: 159.9 (4), 129.4 (2,6),	-	-	Ph: 136.6 (1), 129.6 (3,5), 128.2
							126.2 (1), 114.4 (3,5); 55.3			(4), 121.6 (2,6)
							(OMe), 52.4 (CH <sub>2</sub> )			
146.9	105.5	170.7	108.8	136.6	151.3	152.4	Ph: 134.6 (1), 129.0 (3,5),	14.0	-	Ph: 136.7 (1), 129.5 (3,5), 128.0
							128.6 (4), 127.7 (2,6); 52.3	(Me)		(4), 121.4 (2,6)
							(CH <sub>2</sub> )			
138.1	117.8	192.1	117.8	138.1	145.5	145.5	Ph: 136.6 (1), 129.7 (3,5),	-	-	Ph: 136.6 (1), 129.7 (3,5), 128.3
							128.3 (4), 121.3 (2,6)			(4), 121.3 (2,6)
150.1	114.0	102.5	110.1	120.2	145 1	146.0	$\mathbf{D}_{1}$ 12( 4 (1) 120 5( (2.5)	15 (		DL: 12( ( (1) 120 ( (2.5) 129 2
150.1	114.8	193.5	118.1	138.2	145.1	146.0	Pn: 136.4 (1), 129.56 (3,5), $128.0 (4)$ , $121.2 (2,6)$	15.0 (Ma)	-	Ph: 136.6 (1), 129.6 (3,5), 128.2
150.2	115 1	105.5	115 1	150.2	145.0	145.0	$\frac{126.0(4), 121.2(2,0)}{126.5(1), 120.6(2,5)}$	(IVIE)	15.0	(4), 121.1 (2,0) $(4), 1265 (1), 1206 (2,5), 127.0$
130.2	113.1	195.5	113.1	130.2	143.8	143.8	$\begin{array}{c} \text{PII. 150.5 (1), 129.0 (5,5),} \\ 127.0 (4) 121.2 (2.6) \end{array}$	13.9 (Ma)	15.9 (Ma)	$\begin{array}{c} \text{PII. 150.5 (1), 129.0 (5,5), 127.9} \\ \text{(4) 121.2 (2.6)} \end{array}$
140.0	112.5	102.5	1177	129.1	145.2	147.2	$\frac{127.9}{4}$ , 121.2 (2,0)	(1010)	(Me)	(4), 121.2 (2,0) $Dh: 126.7 (1), 120.6 (2.5), 128.2$
140.0	115.5	195.5	11/./	130.1	145.5	147.5	34.2 (Me)	13.2 (Ma)	-	FII. 150.7 (1), 129.0 (5,5), 128.2 $(4)$ 121 4 (2.6)
126.0	117.0	102.2	117.5	128 1	145.5	146.2	$Dh \cdot 150.0(A) \cdot 120.4(2.6)$	(IVIC)		$\begin{array}{c} (4), 121.4 (2,0) \\ \hline \\ \text{Pb} \cdot 126.5 (1), 120.6 (2.5), 128.2 \\ \hline \end{array}$
130.9	117.0	192.2	117.5	130.1	145.5	140.2	111. 139.9 (4), 129.4 (2,0), 126 0 (1) 114 4 (3.5) 55.3	-	-	$\begin{array}{c} 111. \ 150.5 \ (1), \ 129.0 \ (5,5), \ 128.5 \\ (4) \ 121 \ 5 \ (2 \ 6) \end{array}$
							$(OMe) 52.5 (CH_{e})$			(4), 121.3 (2,0)
1/8 0	11/1	103.6	117.0	138.2	145.2	147.0	$\frac{(0100)}{2}, 52.5(0112)}$	15.4		Ph: 136.6 (1) 129.6 (3.5) 128.1
140.9	114.1	195.0	117.9	130.2	143.2	147.0	111. 134.4 (1), 129.1 (3,3), 128.7 (4), 127.8 (2,6), 52.4	13.4 (Me)	-	(4) 1213(26)
							$(CH_2)$	(IVIC)		(+), 121.3 (2,0)
136.3	107.4	170.5	106.7	128.6	160.6	153.0	$\frac{(C11_2)}{Ph^{-}1365(1), 1296(35)}$	_	_	
150.5	107.7	170.5	100.7	120.0	100.0	155.0	128 0 (4) 121 8 (2 6)			
137.7	116.9	193 5	115.8	130.2	155.0	147.6	Ph: 136 3 (1) 129 6 (3 5)	_	-	
197.7	110.7	175.5	110.0	150.2	100.0	11/.0	128 2 (4) 121 8 (2 6)			
	C-3 136.7 148.1 148.0 146.8 135.5 146.9 138.1 150.1 150.1 150.2 148.8 136.9 148.9 136.3 137.7	C-3C-3a $136.7$ $108.8$ $148.1$ $106.5$ $148.0$ $106.6$ $146.8$ $105.0$ $135.5$ $107.8$ $146.9$ $105.5$ $138.1$ $117.8$ $150.1$ $114.8$ $150.2$ $115.1$ $148.8$ $113.5$ $136.9$ $117.0$ $148.9$ $114.1$ $136.3$ $107.4$ $137.7$ $116.9$	C-3C-3aC-4 $136.7$ $108.8$ $169.7$ $148.1$ $106.5$ $170.6$ $148.0$ $106.6$ $171.8$ $146.8$ $105.0$ $170.7$ $135.5$ $107.8$ $169.8$ $146.9$ $105.5$ $170.7$ $138.1$ $117.8$ $192.1$ $150.1$ $114.8$ $193.5$ $150.2$ $115.1$ $195.5$ $148.8$ $113.5$ $193.5$ $136.9$ $117.0$ $192.2$ $148.9$ $114.1$ $193.6$ $136.3$ $107.4$ $170.5$ $137.7$ $116.9$ $193.5$	C-3C-3aC-4C-4a $136.7$ $108.8$ $169.7$ $108.8$ $148.1$ $106.5$ $170.6$ $108.9$ $148.0$ $106.6$ $171.8$ $106.6$ $146.8$ $105.0$ $170.7$ $108.7$ $135.5$ $107.8$ $169.8$ $108.6$ $146.9$ $105.5$ $170.7$ $108.8$ $138.1$ $117.8$ $192.1$ $117.8$ $150.1$ $114.8$ $193.5$ $118.1$ $150.2$ $115.1$ $195.5$ $115.1$ $148.8$ $113.5$ $193.5$ $117.7$ $136.9$ $117.0$ $192.2$ $117.5$ $148.9$ $114.1$ $193.6$ $117.9$ $136.3$ $107.4$ $170.5$ $106.7$ $137.7$ $116.9$ $193.5$ $115.8$	C-3C-3aC-4C-4aC-5 $136.7$ $108.8$ $169.7$ $108.8$ $136.7$ $148.1$ $106.5$ $170.6$ $108.9$ $136.6$ $148.0$ $106.6$ $171.8$ $106.6$ $148.0$ $146.8$ $105.0$ $170.7$ $108.7$ $136.6$ $135.5$ $107.8$ $169.8$ $108.6$ $136.7$ $146.9$ $105.5$ $170.7$ $108.8$ $136.6$ $138.1$ $117.8$ $192.1$ $117.8$ $138.1$ $150.1$ $114.8$ $193.5$ $118.1$ $138.2$ $150.2$ $115.1$ $195.5$ $115.1$ $150.2$ $148.8$ $113.5$ $193.5$ $117.7$ $138.1$ $136.9$ $117.0$ $192.2$ $117.5$ $138.1$ $148.9$ $114.1$ $193.6$ $117.9$ $138.2$ $136.3$ $107.4$ $170.5$ $106.7$ $128.6$ $137.7$ $116.9$ $193.5$ $115.8$ $130.2$	C-3C-3aC-4C-4aC-5C-7a $136.7$ $108.8$ $169.7$ $108.8$ $136.7$ $151.3$ $148.1$ $106.5$ $170.6$ $108.9$ $136.6$ $151.3$ $148.0$ $106.6$ $171.8$ $106.6$ $148.0$ $151.5$ $146.8$ $105.0$ $170.7$ $108.7$ $136.6$ $151.3$ $135.5$ $107.8$ $169.8$ $108.6$ $136.7$ $151.4$ $146.9$ $105.5$ $170.7$ $108.8$ $136.6$ $151.3$ $138.1$ $117.8$ $192.1$ $117.8$ $138.1$ $145.5$ $150.1$ $114.8$ $193.5$ $118.1$ $138.2$ $145.1$ $150.2$ $115.1$ $195.5$ $115.1$ $150.2$ $145.8$ $148.8$ $113.5$ $193.5$ $117.7$ $138.1$ $145.3$ $136.9$ $117.0$ $192.2$ $117.5$ $138.1$ $145.2$ $148.9$ $114.1$ $193.6$ $117.9$ $138.2$ $145.2$ $136.3$ $107.4$ $170.5$ $106.7$ $128.6$ $160.6$ $137.7$ $116.9$ $193.5$ $115.8$ $130.2$ $155.0$	C-3C-3aC-4C-4aC-5C-7aC-8a136.7108.8169.7108.8136.7151.3151.3148.1106.5170.6108.9136.6151.3151.4148.0106.6171.8106.6148.0151.5151.5146.8105.0170.7108.7136.6151.3152.6135.5107.8169.8108.6136.7151.4152.0146.9105.5170.7108.8136.6151.3152.4138.1117.8192.1117.8138.1145.5145.5150.2115.1193.5115.1150.2145.8145.8148.8113.5193.5117.7138.1145.3147.3136.9117.0192.2117.5138.1145.2145.2136.3107.4170.5106.7128.6160.6153.0137.7116.9193.5115.8130.2155.0147.6	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$

Table 3. <sup>13</sup>C-NMR chemical shifts of 4a-b, 4d-g, 5a-b, 5d-g, 4x and 5x (δ in ppm, solvents as listed in Table 2).

Table 4. Selected <sup>13</sup> C, <sup>1</sup> H spin coupling constants of 4a-b, 4d-g, 5a-b, 5d-g, 4x and 5x (Hz,
solvents as listed in Table 2).

Comp	J of C-3	J of C-3a	J of C-4a	<i>J</i> of C-5	J of C-7a	J of C-8a	other couplings
4a	${}^{1}J = 194.7$	$^{2}J(\text{H-3}) = 9.9$	$^{2}J(\text{H-5}) = 9.9$	${}^{1}J = 194.7$	${}^{3}J(\text{H-5}) = 5.2$	${}^{3}J(\text{H-3}) = 5.2$	
4b	$^{2}J(3-Me) = 7.2$	${}^{3}J(3-\text{Me}) = 2.9$	${}^{2}J(\text{H-5}) =$ 10.0	${}^{1}J = 194.4$	${}^{3}J(\text{H-5}) = 5.1$		$^{1}J(3-\text{Me}) = 129.4$
4d	${}^{2}J(3-\text{Me}) = 7.1$	${}^{3}J(3-\text{Me}) = 2.7$	${}^{3}J(5-Me) = 2.7$	${}^{2}J(5-Me) = 7.1$			${}^{1}J(3-Me) = 129.3, {}^{1}J(5-Me) = 129.3$
<b>4</b> e	$^{2}J(3-Me) = 7.1$	${}^{3}J(3-\text{Me}) = 2.6$	$^{2}J(\text{H-5}) =$ 9.9	${}^{1}J = 194.1$	${}^{3}J(\text{H-5}) = 5.2$	${}^{3}J(\text{N-Me}) = 2.1$	${}^{1}J(\text{N-Me}) = 141.7, {}^{1}J(3-\text{Me}) = 129.1$
4f	${}^{1}J = 194.1$	${}^{2}J(\text{H-3}) =$ 10.0	$^{2}J(\text{H-5}) = 9.9$	$^{1}J = 194.6$	${}^{3}J(\text{H-5}) = 5.2$	${}^{3}J(H-3) \sim$ 5.2, ${}^{3}J(N-CH_{2}) = 2.8$	${}^{1}J(OMe) = 144.1, {}^{1}J(N-CH_{2})$ = 141.5, ${}^{3}J(N\underline{CH}_{2}, Ph \underline{H}_{2}, 26) =$ 4.9, ${}^{2}J(Ph \underline{C}_{-1}, NC\underline{H}_{2}) = 4.7,$ ${}^{3}J(Ph \underline{C}_{-2}/6, NC\underline{H}_{2}) = 4.4$
4g	$^{2}J(3-Me) = 7.1$	${}^{3}J(3-\text{Me}) =$ 2.8	${}^{2}J(\text{H-5}) =$ 10.0	$^{1}J = 194.2$	${}^{3}J(\text{H-5}) = 5.2$	${}^{3}J(\text{N-CH}_{2}) = 2.7$	${}^{1}J(\text{N-CH}_{2}) = 141.0, {}^{1}J(3-\text{Me})$ = 129.2, ${}^{3}J(\text{NCH}_{2},\text{Ph} \underline{\text{H}}\text{-}2,6) = 4.7$
5a	$^{1}J = 195.8$	$^{2}J(\text{H-3}) = 9.3$	$^{2}J(\text{H-5}) = 9.3$	$^{1}J = 195.8$	${}^{3}J(\text{H-5}) = 5.1$	${}^{3}J(\text{H-3}) = 5.1$	
5b	$^{2}J(3-Me) = 7.1$	${}^{3}J(3-\text{Me}) = 2.6$	${}^{2}J(\text{H-5}) =$ 9.1	$^{1}J = 195.5$	${}^{3}J(\text{H-5}) = 5.0$		$^{1}J(3-\text{Me}) = 129.7$
5d	$^{2}J(3-Me) = 7.2$	${}^{3}J(3-Me) = 2.5$	${}^{3}J(5-Me) = 2.5$	${}^{2}J(5-Me) =$ 7.2			${}^{1}J(3-\text{Me}) = 129.6, {}^{1}J(5-\text{Me}) = 129.6$
5e	$^{2}J(3-Me) = 7.1$	${}^{3}J(3-\text{Me}) = 2.7$	${}^{2}J(\text{H-5}) =$ 9.1	$^{1}J = 195.3$	${}^{3}J(\text{H-5}) = 5.1$	${}^{3}J(\text{N-Me}) = 2.4$	${}^{1}J(\text{N-Me}) = 141.9, {}^{1}J(3-\text{Me}) = 129.4$
5f	$^{1}J = 195.0$	$^{2}J(\text{H-3}) = 9.4$	${}^{2}J(\text{H-5}) =$ 9.3	$^{1}J = 195.5$	${}^{3}J(\text{H-5}) = 5.1$	${}^{3}J(H-3) =$ 5.1, ${}^{3}J(N-CH_{2}) = 2.6$	${}^{1}J(OMe) = 144.1, {}^{1}J(N-CH_{2})$ = 141.4, ${}^{3}J(N\underline{C}H_{2},Ph \underline{H}-2,6) =$ 4.6
5g	$^{2}J(3-Me) = 7.1$	${}^{3}J(3-Me) = 2.7$	$^{2}J(\text{H-5}) =$ 9.2	$^{1}J = 195.3$	${}^{3}J(\text{H-5}) = 5.1$	${}^{3}J(\text{N-CH}_{2}) = 2.8$	${}^{1}J(\text{N-CH}_{2}) = 141.2, {}^{1}J(3-\text{Me})$ = 129.5, ${}^{3}J(\text{NCH}_{2}, \text{Ph} \underline{\text{H}}\text{-}2,6)$ = 4.4
4x	$^{1}J = 193.8$	${}^{2}J(\text{H-3}) =$ 10.2	$^{2}J(\text{H-5}) \sim 8.5$	$^{1}J \sim 195.0$	${}^{3}J(\text{H-5}) =$ not resolved	${}^{3}J(\text{H-3}) = 5.2$	
5x	$^{1}J = 194.7$	$^{2}J(\text{H-3}) = 9.5$	$^{2}J(\text{H-5}) = 7.8$	$^{1}J = 195.9$	${}^{3}J(\text{H-5}) = 8.5$	${}^{3}J(\text{H-3}) = 4.9$	

Comp	N-1	N-2	N-6	N-7
4a	-186.8	-86.8	-86.8	-186.8
4b	-193.1	-93.6	-87.7	-187.1
4d	-193.4	-94.2	-94.2	-193.4
4e	-211.8	-91.7	-88.0	-187.5
<b>4</b> f	-191.8	-85.2	-87.5	-187.3
4g	-200.0	-91.3	-88.2	-187.4
5a	-187.6	-84.5	-84.5	-187.6
5b	-195.3	-92.1	-85.5	-188.0
5d	-196.2	-92.9	-92.9	-196.2
5e	-213.7	-89.7	-85.6	-188.2
5f	-192.4	-82.2	-84.9	-187.9
5g	-201.9	-89.5	-85.8	-188.2
4x	-186.4	-87.7	-179.2*	-179.2*
5x	-186.7	-84.3	-175.5*	-175.5*

**Table 5.** <sup>15</sup>N-NMR chemical shifts of investigated compounds ( $\delta$  in ppm, solvents as listed in Table 2).

\* Not unambiguously classifiable.

#### 3.2.9. General procedure for the synthesis of 9a and 9b

According to a known procedure [24], to a solution of the corresponding carboxylic acid 7 (5 mmol) in absolute ethanol (30 mL), H<sub>2</sub>SO<sub>4</sub> (2 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 NaHCO<sub>3</sub> and then extracted with dichloromethane (3 × 15 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 CH<sub>2</sub>Cl<sub>2</sub>:MeOH/9:1).

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

*Ethyl 5-chloro-3-methyl-1-phenyl-1*H-*pyrazole-4-carboxylate* (**9b**). Starting from **7b** (1.18 g, 5 mmol) 688 mg (52%) of compound **9b** were obtained as colorless crystals; m.p. 72–73 °C (lit. [47] m.p. 74 °C); <sup>1</sup>H-NMR (500 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 7.41 (m, 2H, Ph H-2,6), 7.36 (m, 2H, Ph H-3,5), 7.30 (m, 1H, Ph H-4), 4.24 (q, 7.1 Hz, 2H, OCH<sub>2</sub>), 2.43 (s, 3H, 3-Me), 1.27 (t, 7.1 Hz, 3H, Me); <sup>13</sup>C-NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  (ppm) 161.9 (CO, <sup>3</sup>*J*(CO,CH<sub>2</sub>) = 3.1 Hz), 151.7 (C-3, <sup>2</sup>*J*(C-3,3-Me) = 7.0 Hz), 137.2 (Ph-C-1), 130.8 (C-5), 128.7 (Ph C-3,5), 128.5 (Ph C-4), 125.1 (Ph C-2,6), 109.8 (C-4, <sup>3</sup>*J*(C-4,3-Me) = 2.7 Hz), 59.9 (OCH<sub>2</sub>, <sup>1</sup>*J* = 147.6 Hz, <sup>2</sup>*J*(OCH<sub>2</sub>,CH<sub>2</sub>) = 4.4 Hz), 14.4 (3-Me, <sup>1</sup>*J* = 129.2 Hz), 13.9 (ester-Me, <sup>1</sup>*J* = 127.0 Hz, <sup>2</sup>*J*(CH<sub>3</sub>,CH<sub>2</sub>) = 2.6 Hz); <sup>15</sup>N-NMR (50 MHz,

CDCl<sub>3</sub>): δ (ppm) –168.2 (N-1), –77.6 (N-2); MS *m*/*z* (%): 264/266 (M<sup>+</sup>, 53/18), 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 1H-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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Sample Availability: Samples of the compounds are available from the authors.

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