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One-Pot Synthesis of Aryl and Heteroaroyl-Substituted Hydroxypyrazolines from the Reactions of β-Alkoxyvinyl Trichloromethyl Ketones with Heteroarylhydrazides

Helio G. Bonacorso, Marli R. Oliveira, Michelle B. Costa, Roberta L. Drekener, Letícia B. da Silva, Nilo Zanatta, and Marcos A. P. Martins

Núcleo de Química de Heterociclos – NUQUIMHE, Departamento de Química, Universidade Federal de Santa Maria, 97.105-900 – Santa Maria, RS – Brazil

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ABSTRACT: *The one-step regiospecific synthesis of a novel series of 10 trichloromethyl-, aryl-, and heteroaroyl-substituted 5-hydroxy-2-pyrazolines affords 1-(2-thenoyl)-, 1-(2-furoyl)-, and 1-(isonicotinoyl)-3-aryl-5-hydroxy-5-trichloromethyl-4,5-dihydro-1H-pyrazoles in 63–92% yields from the cyclocondensation reactions of 1,1,1-trichloro-4-methoxy-4-aryl-3-buten-2-ones (where aryl substituents are –C_6H_5, 4-$CH_3C_6H_4$, 4-$OCH_3C_6H_4$, 4-FC_6H_4, 4-ClC_6H_4, 4-BrC_6H_4) with 2-thiophenecarboxylic hydrazide, furoic hydrazide, and isonicotinic acid hydrazide, respectively. Dehydration reaction of two 2-pyrazolines with P_2O_5 furnished the corresponding 1H-pyrazoles in low yields (21–29%).* © 2006 Wiley Periodicals, Inc. Heteroatom Chem 17:685–691, 2006; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20261

Correspondence to: Helio G. Bonacorso; e-mail: heliogb@base.ufsm.br.

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INTRODUCTION

Recently, β-alkoxyvinyl trichloromethyl ketones (**1**) proved to be useful building blocks for the synthesis of 5-, 6-, and 7-membered trichloromethylated heterocyclic compounds [1,2]. Trichloromethylated ketones (**1**) demonstrated to be one of the most useful synthons to introduce a trichloromethyl group into heterocycles. This approach relies on the trichloroacetylation of enol ethers or acetals [3–5] to give, in one-step and good yields, the ketones (**1**).

Lately, a great interest has been directed toward the synthesis of trifluoromethyl-substituted heteroaromatic compounds due to, in part, the unique biological properties exhibited by the fluorine [6]. On the other hand, trichloromethylated heterocycles are relatively rare but promising templates for biological activity. For example, trichloromethyl-substituted benzodiazepines, quinazolines, and pyrimidines have exhibited activity as acetyl cholinesterase and ATPDase inhibitors, anxiolytics, cyclin-dependent kinase (CDK) inhibitors in the cell cycle proteins, and ATP and ADP hydrolysis inhibitors in synaptosomes from rat cerebral cortex. Particularly, 3-aryl-5-trichloromethyl-5-hydroxy-4,

5-dihydro-1*H*-pyrazoles presented anti-inflammatory and analgesic activity [7].

Among several classes of N-heterocycles, the 2-pyrazolines have been used as antitumor [8], antibacterial, antifungal, antiviral, antiparasitic, antitubercular, and insecticidal agents [9–16]. Some of these compounds also showed anti-inflammatory, antidiabetic, anesthetic, and analgesic properties [17–19].

On the other hand, little is known about the metabolism of thiophene derivatives. Thiophene-containing drugs substituted with 2-arylketo moieties, such as suprofen or tienilic acid, are uricosuric diuretic agents [20]. During the 1980s, suprofen was also approved as a nonsteroidal anti-inflammatory drug (NSAID) having larger activity than that of indomethacin or ketoprofen, but was later removed from the market because of unexpected toxicity. In particular, aryl thienyl ketones have antiplatelet effects as a consequence of interfering with cyclooxygenase in the arachadonic acid cascade [21]. Furan and pyridine have played an important part in the development of theory in heterocyclic chemistry and also employed as useful synthons in organic synthesis. For example, the furan ring can undergo facile conversion to carboxylic acid by oxidation reactions [22].

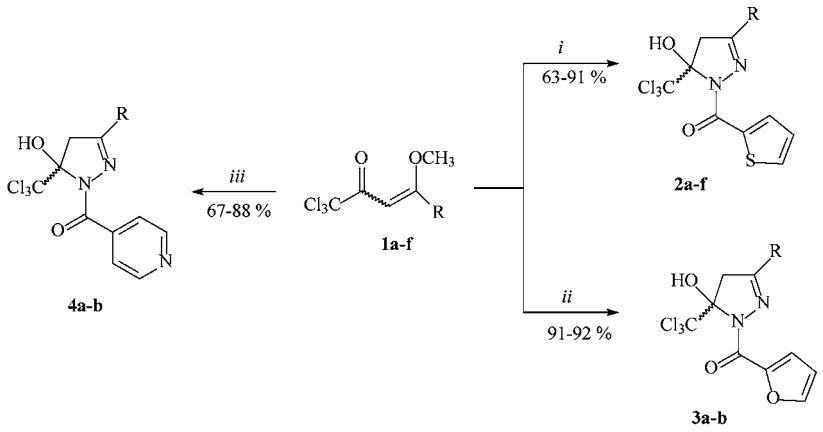
Although many methods have been published for the synthesis of 1*H*-pyrazoles and functionalized derivatives, the attempts to perform the synthesis of a very simple 4,5-dihydro-1*H*-pyrazoles (2-pyrazolines) are not yet successful [23–26]. By conventional procedure, pyrazoles have been obtained by direct reactions of β-diketones and derivatives with hydrazines [23]. However, in most cases, 5-hydroxy-4,5-dihydro-1*H*-pyrazoles have been obtained when the N-1 atom is substituted by a strong electron-withdrawing group that hinders the elimination of water and the subsequent aromatization of the pyrazoline ring [23]. In a few cases, some structures of 5-trifluoromethylated- or 5-trichloromethylated-5-hydroxy-1*H*-pyrazolines and pyrazolidines intermediates can be isolated, however, the N-alkylated parent compounds were not easily isolated [27]. In particular, the reactions between aryl or heteroarylhydrazides and fluorinated β-diketones ($CF_3COCH_2COCF_3$ or CF_3COCH_2COR) are rare in the literature [28–33], and the trichloromethylated analogs, such as noncondensed carbonyl 5,5- and 5,6-bisheterocycle systems **2–4**, are not known so far.

Considering the importance of 2-pyrazolines, the carbonyl derivatives of these four classes of heterocycles and the possibility to obtain new trichloromethylated structures with promising biological properties, prompted us to devote special attention to the chemistry of the trichloromethyl contained building blocks and their application in the heterocyclic chemistry. Thus, the aim of this work is to report the results of the cyclocondensation reactions of 1,1,1-trichloro-4-methoxy-4-aryl-3-buten-2-ones (**1**) with 2-thiophenecarboxylic hydrazide, furoic hydrazide, and isonicotinic acid hydrazide to obtain new trichloromethylated 2-pyrazolines and the subsequently dehydration reactions of two 2-pyrazolines to obtain the respective aromatic heteroaroylpyrazoles.

RESULTS AND DISCUSSION

The reactions of **1a–f** with 2-thiophenecarboxylic hydrazide were carried out in methanol at reflux for 16 h to give the corresponding **2a–f** in 63–91% yields. The same reaction conditions were employed for reactions of **1a** and **1b** with furoic hydrazide. In this case, **3a** and **3b** were isolated in 91% and 92% yields, respectively. The reactions of **1a** and **1b** with isonicotinic acid hydrazide were carried out in methanol at room temperature for 24 h to give the corresponding **4a** and **4b** in 67% and 88% yield, respectively. Normally, the heteroaroylpyrazolines crystallized in the course of the reaction. For the synthesis of **2a-f**, **4a**, and **4b,** the course of the reactions was monitored by the formation of a white precipitate, which appears soon after the addition of the reagents. The compounds **3a** and **3b** were isolated by simple filtration, but only after the reaction time (16 h) and by refrigeration at low temperature (0–10°C). The crystalline solids were isolated by filtration, washed with cold methanol, and recrystallized from methanol or acetone (Scheme 1). Yields and purity by elemental analyses are listed in Table 1.

Subsequently, 1-(2-thenoyl)- (**2a**) and 1-(2-furoyl)-3-phenyl-5-hydroxy-5-trichloromethyl-4,5-dihydro-1*H*-pyrazoles (**3a**) were dehydrated by stirring with a mixture of chloroform and P_2O_5 at reflux for 24 h (Scheme 2). The corresponding aromatic pyrazoles **5a** and **5b** were obtained by similar procedure described in the literature [34] in 29% and 21% yields, respectively. After the reaction time (24 h), the resulting compounds were filtered and compounds **5a** and **5b** isolated by extraction with a mixture of chloroform/water. Thus, pyrazoles **5a** and **5b** were obtained in good purity (GC-MS) by evaporation of the residual solvent under reduced pressure. Compound **5a** presented as an oily substance and **5b** as a solid, which was recrystallized from a mixture of ethyl acetate and hexane. The 1-(isonicotinoyl)-3-phenyl-5-hydroxy-5-trichloromethyl-4,5-dihydro-1*H*-pyrazole (**4a**) was extremely resistant to dehydration reactions with



(*i*) 2-Thiophenecarboxylic hydrazide, Methanol, 60–65 °C, 16 h; (*ii*) Furoic hydrazide, Methanol, 60–65 °C, 16 h; (*iii*) Isonicotinic acid hydrazide, Methanol, 20 – 25 °C, 24 h.

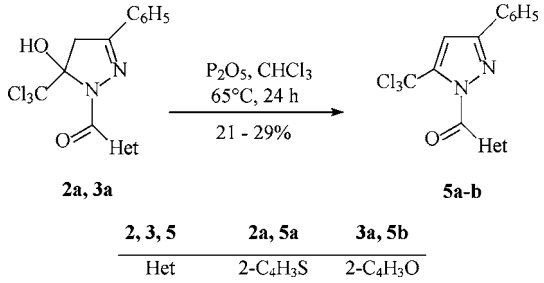
SCHEME 1 Synthesis of 2-pyrazolines **2–4**.

chloroform/P_2O_5 at reflux for 48 h or with acetic acid at reflux for 4 h. In both cases, the 2-pyrazoline (**4a**) was recovered without any structural modification. When stronger dehydration conditions were tried, that is, chloroform/sulfuric acid at reflux, in order to increase the yields for **5a** and **5b** or to dehydrate, aromatic pyrazoles missing the 2-thenoyl, 2-furoyl, and isonicotinoyl groups were isolated. It is interesting to note that the CCl_3 substituent was not converted into carboxyl group in contrast to the dehydration reaction described by Spiegler and Götz [1], which resulted into isoxazole-5-carboxylic

TABLE 1 Selected Physical Data of 1-(Heteroaroyl)-3-aryl-5-hydroxy-5-trichloromethyl-4,5-dihydro-1*H*-pyrazoles (**2–4)**

				Analysis (%)[c] *(Calcd/Found)*		
Compd.	*Yield (%)*[a]	*MP (°C)*[b]	*Molecular Formula (g/mol)*	C	H	N
2a	88	166–167	$C_{15}H_{11}Cl_3N_2O_2S$	46.23	2.85	7.19
			(389.5)	45.96	2.55	7.09
2b	81	142–143	$C_{16}H_{13}Cl_3N_2O_2S$	47.60	3.25	6.94
			(403.5)	47.80	3.06	6.88
2c	84	176–178	$C_{16}H_{13}Cl_3N_2O_3S$	45.79	3.12	6.67
			(419.5)	45.31	2.99	6.54
2d	91	153–155	$C_{15}H_{10}Cl_3FN_2O_2S$	44.19	2.47	6.87
			(407.5)	43.69	2.32	6.63
2e	63	170–172	$C_{15}H_{10}Cl_4N_2O_2S$	42.48	2.38	6.60
			(424.0)	42.68	2.36	6.66
2f	87	192–194	$C_{15}H_{10}BrCl_3N_2O_2S$	38.45	2.15	5.98
			(468.5)	37.96	2.05	5.73
3a	92	148–150	$C_{15}H_{11}Cl_3N_2O_3$	48.22	2.97	7.50
			(373.5)	48.14	2.79	7.56
3b	91	184–186	$C_{16}H_{13}Cl_3N_2O_3$	49.57	3.38	7.23
			(387.5)	49.57	3.43	7.10
4a	88	145–147	$C_{16}H_{12}Cl_3N_3O_2$	49.96	3.14	10.92
			(384.5)	49.77	3.23	10.79
4b	67	142–144	$C_{17}H_{14}Cl_3N_3O_2$	51.22	3.54	10.54
			(398.5)	50.93	3.39	10.16

[a]Yield of isolated compounds.
[b]The melting points are uncorrected.
[c]Elemental analyses were performed on a Perkin Elmer 2400 CHN elemental analyzer.



SCHEME 2 Dehydration reactions of 2-pyrazolines **2a** and **3a**.

acid from the reaction of 5-trichloromethylisoxazole with 96% sulfuric acid at 110°C for 4–12 h. The physical data of compounds **5a** and **5b** are presented in Table 2.

The unambiguous ^{1}H and ^{13}C NMR chemical shifts assignments of 3-aryl-5-hydroxy-5-trichloromethyl-1-(heteroaryl-carbonyl)-4,5-dihydro-1*H*-pyrazoles (**2a–f, 3a, 3b, 4a, 4b,** and **5a, 5b**), were obtained with the help of homo- and heteronuclear COSY, HMQC, and HMBC 2D-NMR experiments and by comparison with NMR data of other 2-pyrazolines formerly synthesized in our laboratory.

Compounds **2–4** show the chemical shifts of the diastereotopic methylene protons (H4a and H4b) as a characteristic of AB system and as a doublet in average at δ 4.09 and another doublet at δ ca 3.87, respectively, with a *geminal* coupling constant in a range of ^{2}J = 18.8–19.6 Hz.

Compounds **2a–f** present the typical ^{13}C chemical shifts of pyrazoline ring carbons at δ ca 153.8 (C3), 46.6 (C4), 102.8 (C5), and 103.2 (CCl_3). The thiophen ring carbons show chemical shifts in average at δ 134.3 (C2′), 135.6 (C3′), 127.0 (C4′), and 135.7 (C5′). The carbonyl carbon for this series shows signals at δ ca 160.5 (Table 3).

Compounds **3a** and **3b** present the typical ^{13}C chemical shifts of pyrazoline ring carbons in average at δ 154.6 (C3), 46.4 (C4), 103.0 (C5), and 103.3 (CCl_3). The furan ring carbons show chemical shifts at δ ca 146.8, 145.5, 120.6, and 112.2. The carbonyl carbon for this series shows signals at δ ca 157.4 (Table 3).

Compounds **4a** and **4b** present the typical ^{13}C chemical shifts of pyrazoline ring carbons in average at δ 153.9 (C3), 46.9 (C4), 102.3 (C5), and 103.1 (CCl_3). The pyridine ring carbons show chemical shifts at δ ca 149.5, 143.0, and 122.4. The carbonyl carbon for this series shows signals in average at δ 166.8 (Table 3).

The structures of the heteroaryl carbonyl pyrazoles (**5a** and **5b)** were deduced from their NMR spectra and were characterized by ^{1}H chemical shift signal as a singlet in average at δ 7.18 for the aromatic proton attached to the pyrazole-C4. Compounds **5a** and **5b** present the typical ^{13}C chemical shifts of pyrazole ring carbons in average at δ 155.1 (C3), 108.5 (C4), 148.5 (C5), and 89.6 (CCl_3). The carbonyl carbon for this series shows signals in average at δ 158.8 and the chemical shifts for the heteroaryl carbons of 2-thienyl and 2-furyl presented similar data as shown for the respective heteroaryl carbonyl pyrazolines **2** and **3** (Table 4).

In conclusion, one can consider the cyclocondensation reaction reported here as a useful, simple, and convenient procedure to obtain new regiospecific 3-aryl-5-trichloromethyl-substituted 2-pyrazolines derived from phenones, thiophene, furan, and pyridine. In addition, this work used for the first time β-alkoxyvinyl trichloromethyl ketones (**1**) in cyclocondensation reactions with heteroarylhydrazides. Unfortunately, the subsequent dehydration reaction of 2-pyrazolines under various reaction conditions furnished low yields.

EXPERIMENTAL

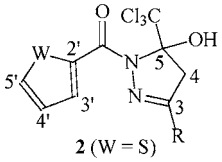
Unless otherwise indicated, all common reagents and solvents were used as obtained from commercial suppliers without further purification. All melting points were determined on a Reichert Thermovar apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were acquired on a Bruker DPX 400 spectrometer (^{1}H at 400.13 MHz and ^{13}C at 100.62 MHz),

TABLE 2 Selected Physical Data of 1-(Heteroaroyl)-3-aryl-5-trichloromethyl-1*H*-pyrazoles (**5a**, **5b**)

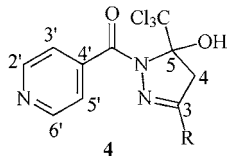
Compd.	*Yield (%)*[a]	*MP (°C)*[b]	*Molecular Formula (g/mol)*	*GC-MS m/z (%)*
5a	29	Oil	$C_{15}H_9Cl_3N_2OS$ (371.67)	372 (M^+, 15), 335 (11), 126 (25), 111 (100), 83 (16)
5b	21	111–113	$C_{15}H_9Cl_3N_2O_2$ (355.61)	354 (M^+,7), 319 (16), 291 (15), 126 (22), 95 (100)

[a]Yield of isolated compounds.
[b]The melting points are uncorrected.

TABLE 3 Selected ^{1}H and ^{13}C MNR Spectral Data[a] of 1-(Heteroaroyl)-3-aryl-5-hydroxy-5-trichloromethyl-4,5-dihydro-1*H*-pyrazoles (**2–4**)



2 (W = S)
3 (W =O)



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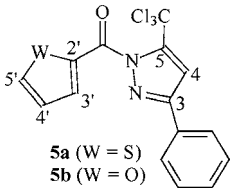
Compd.	*^{1}H NMR (DMSO-d_6/TMS, δ, J (Hz)/ ^{13}C NMR (DMSO-d_6/TMS, δ)*
2a	8.21 (bs, OH), 8.11 (dd, $J = 3.6$, $J = 1.2$, H3′), 8.01 (dd, $J = 4.8$, $J = 1.2$, H5′), 7.94–7.92 (m, 2H, Ph), 7.56–7.54 (m, 3H, Ph), 7.24 (dd, $J = 4.8$, $J = 4.0$, H4′), 4.10 (d, $J = 19.2$, H4a), 3.88 (d, $J = 19.2$, H4b) 160.5 (C=O), 154.2 (C3), 135.7 (C5′), 135.5 (C3′), 134.3 (C2′), 131.0; 129.7; 128.9; 126.9 (6C, Ph), 127.0 (C4′), 103.2 (CCl_3), 102.8 (C5), 46.6 (C4)
2b	8.19 (s, OH), 8.10 (dd, $J = 4.0$, $J = 1.2$, H3′), 8.00 (dd, $J = 5.2$, $J = 1.2$, H5′), 7.81 (d, 2H, Ph), 7.35 (d, 2H, Ph), 7.24 (dd, $J = 4.8$, $J = 4.0$, H4′), 4.06 (d, $J = 18.8$, H4a), 3.84 (d, $J = 19.2$, H4b), 2.38 (s, CH_3) 160.5 (C=O), 154.3 (C3), 135.8 (C5′), 135.6 (C3′), 134.3 (C2′), 141.1; 129.5; 127.0; 126.9 (6C, Ph), 127.0 (C4′), 103.3 (CCl_3), 102.7 (C5), 46.6 (C4), 21.1 (CH_3)
2c	8.17 (s, OH), 8.10 (dd, $J = 3.8$, $J = 1.4$, H3′), 8.00 (dd, $J = 5.2$, $J = 1.2$, H5′), 7.87 (d, 2H, Ph), 7.23 (dd, $J = 5.2$, $J = 4.0$, H4′), 7.09 (d, 2H, Ph), 4.06 (d, $J = 19.2$, H4a), 3.84 (s, OCH_3), 3.83 (d, $J = 19.2$, H4b) 160.5 (C=O), 154.2 (C3), 135.6 (C5′), 135.4 (C3′), 134.3 (C2′), 161.5; 128.7; 122.1; 114.4 (6C, Ph), 126.9 (C4′), 103.3 (CCl_3), 102.6 (C5), 55.3 (OCH_3), 46.6 (C4)
2d	8.21 (s, OH), 8.09 (dd, $J = 3.8$, $J = 1.4$, H3′), 7.98 (dd, $J = 5.2$, $J = 1.4$, H5′), 7.97–7.95 (m, 2H, Ph), 7.39–7.35 (m, 2H, Ph), 7.23 (dd, $J = 5.2$, $J = 4.0$, H4′), 4.09 (d, 1H, $J = 19.2$, H4a), 3.85 (d, 1H, $J = 19.2$, H4b) 160.6 (C=O), 153.4 (C3), 135.7 (C5′), 135.6 (C3′), 134.3 (C2′), 163.7 (d, Ph, $^1J_{CF} = 247.6$), 129.5 (d, Ph, $^3J_{CF} = 8.9$), 126.4 (d, Ph, $^4J_{CF} = 3.3$), 116.1 (d, Ph, $^2J_{CF} = 21.6$), 127.1 (C4′), 103.2 (CCl_3), 102.9 (C5), 46.7 (C4)
2e	8.22 (s, OH), 8.09 (dd, $J = 3.6$, $J = 1.6$, H3′), 8.01 (dd, $J = 4.8$, $J = 1.2$, H5′), 7.86 (d, 2H, Ph), 7.75 (d, 2H, Ph), 7.24 (dd, $J = 5.2$, $J = 3.6$, H4′), 4.10 (d, $J = 19.2$, H4a), 3.86 (d, $J = 19.2$, H4b) 160.4 (C=O), 153.4 (C3), 135.7 (C5′), 135.6 (C3′), 134.3 (C2′), 132.0; 129.0; 128.8; 124.6 (6C, Ph), 127.1 (C4′), 103.1 (CCl_3), 103.0 (C5), 46.5 (C4)
2f	8.23 (s, OH), 8.10 (dd, $J = 3.6$, $J = 1.2$, H3′), 8.02 (dd, $J = 5.2$, $J = 1.2$, H5′), 7.87 (d, 2H, Ph), 7.75 (d, 2H, Ph), 7.25 (dd, $J = 4.8$, $J = 4.0$, H4′), 4.10 (d, $J = 19.2$, H4a), 3.87 (d, $J = 19.6$, H4b) 160.4 (C=O), 153.4 (C3), 135.7 (C5′), 135.6 (C3′), 134.3 (C2′), 132.0; 129.0; 128.8; 124.6 (6C, Ph), 127.0 (C4′), 103.1 (CCl_3), 103.0 (C5), 46.5 (C4)
3a	8.20 (bs, OH), 8.03 (d, 1H, Fu), 7.91–7.86 (m, 2H, Ph), 7.63 (d, 1H, Fu), 7.54–7.52 (m, 3H, Ph), 6.76 (dd, 1H, Fu), 4.05 (d, $J = 19.4$, H4a), 3.83 (d, $J = 19.2$, H4b) 157.5 (C=O), 154.7 (C3), 146.9 (1C, Fu), 145.5 (1C, Fu), 131.0; 129.8; 128.9; 126.8 (6C, Ph), 120.7 (1C, Fu), 112.3 (1C, Fu), 103.4 (CCl_3), 103.1 (C5), 46.5 (C4)
3b	8.18 (bs, OH), 8.02 (d, 1H, Fu), 7.77 (d, 2H, Ph), 7.63 (d, 1H, Fu), 7.33 (d, 2H, Ph), 6.75 (dd, 1H, Fu), 4.02 (d, $J = 19.4$, H4a), 3.80 (d, $J = 19.4$, H4b), 2.37 (s, CH_3) 157.4 (C=O), 154.6 (C3), 146.8 (1C, Fu), 145.5 (1C, Fu), 141.0; 129.4; 127.0; 126.7 (6C, Ph), 120.6 (1C, Fu), 112.2 (1C, Fu), 103.3 (CCl_3), 102.9 (C5), 46.4 (C4), 21.0 (CH_3)
4a	8.76 (d, 2H, $J = 4.6$, Py), 8.38 (s, OH), 7.67–7.61 (m, 2H, Ph; 2H, Py), 7.47–7.44 (m, 3H, Ph), 4.09 (d, $J = 19.6$, H4a), 3.84 (d, $J = 19.4$, H4b) 166.8 (C=O), 153.9 (C3), 149.6 (2C, Py), 143.0 (1C, Py), 130.8; 129.6; 128.7; 126.5 (6C, Ph), 122.4 (2C, Py), 103.1 (CCl_3), 102.4 (C5), 46.9 (C4)
4b	8.76 (d, 2H, $J = 4.6$, Py), 8.34 (s, OH), 7.62 (d, 2H, $J = 5.8$, Py), 7.55 (d, 2H, Ph), 7.25 (d, 2H, Ph), 4.06 (d, $J = 19.6$, H4a), 3.81 (d, $J = 19.4$, H4b), 2.32 (s, CH_3) 166.8 (C=O), 153.9 (C3), 149.5 (2C, Py), 143.0 (1C, Py), 140.9; 129.3; 126.8; 126.5 (6C, Ph), 122.4 (2C, Py), 103.1 (CCl_3), 102.3 (C5), 46.9 (C4), 20.9 (CH_3)

[a]The NMR spectra were recorded on a Bruker DPX 400 spectrometer (^{1}H at 400.13 MHz and ^{13}C at 100.62 MHz).

5-mm sample tubes, 298 K, digital resolution ±0.01 ppm, in DMSO-d_6, and using TMS as the internal reference. Mass spectra were registered in an HP 6890 GC connected to an HP 5973 MSD and interfaced by a Pentium PC. The GC was equipped with a split–splitless injector, autosampler, cross-linked HP-5 capillary column (30 m, 0.32 mm of internal diameter), and helium was used as the carrier gas. The CHN elemental analyses were performed on a Perkin Elmer 2400 CHN elemental analyzer. Compounds

TABLE 4 Selected ^{1}H and ^{13}C NMR Spectral Data[a] of 1-(Heteroaroyl)-3-aryl-5-trichloromethyl-1*H*-pyrazoles (**5a**, **5b**)



5a (W = S)
5b (W = O)

Compd.	*^{1}H NMR (DMSO-d_6/TMS, δ, J(Hz)/ ^{13}C NMR (DMSO-d_6/TMS, δ)*
5a	8.28 (d, $J = 4.0$, H3′), 8.20 (d, $J = 5.2$, H5′), 7.58–7.46 (m, 5H, Ph), 7.31 (dd, $J = 4.8$, $J = 4.0$, H4′), 7.14 (s, H4) 158.7 (C=O), 155.6 (C3), 148.5 (C5), 139.2 (C5′), 138.9 (C3′), 132.1 (C2′), 129.0; 128.7; 127.9; 127.9 (6C, Ph), 127.8 (C4′), 108.7 (C4), 89.6 (CCl_3)
5b	8.24 (s, H5′), 7.88 (d, $J = 3.6$, H3′), 7.58–7.47 (m, 5H, Ph), 7.23 (s, H4), 6.89 (dd, $J = 3.6$, $J = 1.4$, H4′) 155.9 (C=O), 154.7 (C3), 150.2 (1C, Fu), 148.5 (C5), 144.0 (1C, Fu), 129.2; 128.8; 128.6; 128.1 (6C, Ph), 125.5 (1C, Fu), 113.3 (1C, Fu), 108.3 (C4), 89.6 (CCl_3)

[a]The NMR spectra were recorded on a Bruker DPX 400 spectrometer (^{1}H at 400.13 MHz and ^{13}C at 110.62 MHz).

1a–f were prepared according to the literature procedures [17].

*Preparation of 1-(Heteroaroyl)-3-aryl-5-hydroxy-5-trichloromethyl-4,5-dihydro-1H-pyrazoles (**2a–f**, **3a**, **3b**, and **4a**, **4b**)*

General Procedure. To a stirred solution of 4-alkoxy-4-aryl-1,1,1-trichloro-3-buten-2-one (**1a–f)** (5 mmol) in 6 mL of methanol, anhydrous 2-thiophenecarboxylic hydrazide, furoic hydrazide, or isonicotinic acid hydrazide (5 mmol) was added at 20–25°C. The mixture was stirred for 16 h at 60–65°C (2-thenoyl and 2-furoyl derivatives) or for 24 h at 20–25°C (isonicotinoyl derivatives). After cooling (<10°C), the crystalline solids were isolated by filtration, washed with cold methanol, and recrystallized from methanol or acetone. Yields and purity by elemental analyses are listed in Table 1.

*Preparation of 1-(Heteroaroyl)-3-phenyl-5-trichloromethyl-1H-pyrazoles (**5a**, **5b**)*

General Procedure. At room temperature, **2a** (**3a**) (2 mmol) was added in a 25-mL flask containing a mixture of P_2O_5 (2.5 g) and chloroform (10 mL). After 24 h under reflux, the residue was removed by filtration. The organic layer (chloroform) was washed with water (3 × 15 mL), dried with anhydrous calcium chloride, and evaporated. Compound **5a** was isolated as an oily and **5b** as a solid, which was recrystallized from hexane with few drops of ethyl acetate. Yields and mass spectrometric data are listed in Table 2.

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