

Short Note

3-Methyl-1-phenyl-1*H*-pyrazol-5-yl 2-Bromo-3-furan-carboxylate

Wolfgang Holzer ^{1,*}, Changbin Guo ^{1,2} and Karin Schalle ¹

¹ Department of Drug and Natural Product Synthesis, University of Vienna, Althanstrasse 14, A-1090 Vienna, Austria

² Department of Chemistry, Capital Normal University, Xisanhuanbei Road 105, Beijing 100048, China

* Author to whom correspondence should be addressed; E-mail: wolfgang.holzer@univie.ac.at

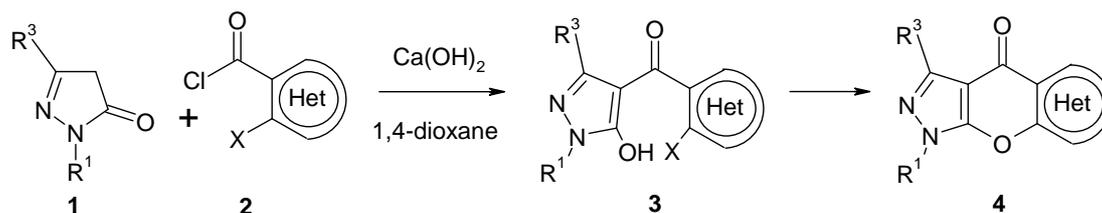
Received: 29 May 2009 / Accepted: 1 July 2009 / Published: 3 July 2009

Abstract: The reaction of 3-methyl-1-phenyl-2-pyrazolin-5-one and 2-bromo-3-furoyl chloride in the presence of Ca(OH)₂ in 1,4-dioxane gave the title compound. The latter was also obtained in much higher yield upon reaction of the starting materials in the system dichloromethane / triethylamine. Detailed spectroscopic data (¹H NMR, ¹³C NMR, ¹⁵N NMR, IR, MS) are presented.

Keywords: pyrazolones; arylation; NMR spectroscopy

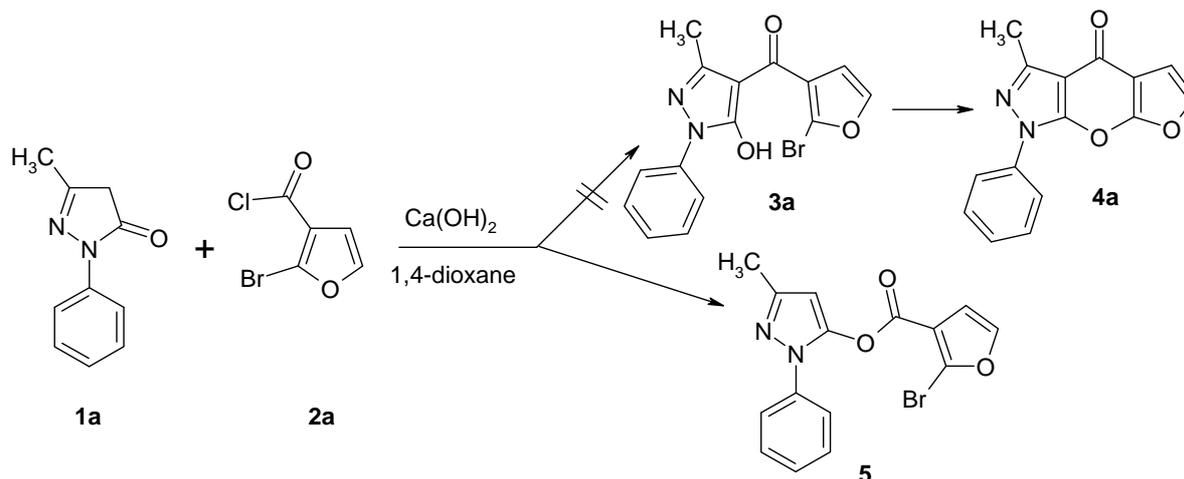
In a series of papers we recently described a short and efficient approach to novel heterocyclic systems containing a pyrano[2,3-*c*]pyrazol-4(1*H*)-one substructure *via* reaction of 2-pyrazolin-5-ones **1** with *o*-haloheteroarene-carbonyl chlorides **2** under the conditions of the ‘Jensen’-reaction (calcium hydroxide, refluxing 1,4-dioxane) and subsequent cyclization of the thus obtained 4-aryopyrazol-5-ols **3** into the target compounds **4** (Scheme 1) [1-6].

Scheme 1. Synthesis of annelated pyrano[2,3-*c*]pyrazol-4(1*H*)-ones **4**.



In the course of these investigations we were also interested in furo[3',2':5,6]pyrano[2,3-*c*]pyrazol-4(1*H*)-ones (**4**, Het = furane). The synthesis of a corresponding representative **4a** ($R^1 = \text{Ph}$, $R^3 = \text{Me}$) should be carried out similarly as outlined in Scheme 1, i.e. by reaction of 3-methyl-1-phenyl-2-pyrazolin-5-one (**1a**) and 2-bromo-3-furoyl chloride (**2a**) under 'Jensen'-conditions [7] followed by cyclization of the key intermediate **3a** (Scheme 2).

Scheme 2. Reaction of **1a** and **2a** under 'Jensen'-conditions.



However, the reaction of **1a** and **2a** in the presence of $\text{Ca}(\text{OH})_2$ in refluxing 1,4-dioxane did not afford the expected C-acyl product **3a** but resulted in a complex reaction mixture, from which the ester **5** was isolated as the main component. Compound **5** could be easily identified considering its characteristic spectral data. Thus, the $^1\text{H-NMR}$ spectrum of **5** exhibits a singlet signal of pyrazole H-4 at δ 6.25 ppm, the corresponding pyrazole C-4 resonance (δ 95.8 ppm) shows a doublet structure in the ^1H -coupled ^{13}C NMR spectrum ($^1J = 181.7$ Hz). Moreover, the carbonyl absorption at 1752 cm^{-1} in the IR spectrum is typical for an ester-carbonyl moiety and definitely rules out a diaryl ketone substructure with intramolecular hydrogen bond as present in **3a**. For the $\text{C}=\text{O}$ absorption in the latter a much smaller value ($\sim 1620\text{ cm}^{-1}$) for $\nu_{\text{C}=\text{O}}$ has to be expected [3].

Expectedly, reaction of **1a** and **2a** in dichloromethane in the presence of triethylamine according to ref. [8] afforded the title compound **5** as the sole product in high yields (82% after purification by column chromatography).

Experimental

Mass spectrum: Shimadzu QP 1000 instrument (EI, 70 eV). IR spectrum: Perkin-Elmer FTIR Spectrum 1000 instrument (KBr-disc). The elemental analysis was performed at the Microanalytical Laboratory, University of Vienna. ^1H and ^{13}C NMR spectra were recorded on a Varian UnityPlus 300 spectrometer at 28 °C (299.95 MHz for ^1H , 75.43 MHz for ^{13}C). The centre of the solvent signal was used as an internal standard which was related to TMS with $\delta = 7.26$ ppm (^1H in CDCl_3), and $\delta = 77.0$ ppm (^{13}C in CDCl_3). The digital resolutions were 0.2 Hz/data point in the ^1H and 0.4 Hz/data point in the ^1H -coupled ^{13}C -NMR spectra (gated decoupling). ^{15}N NMR spectra were obtained on a Bruker Avance 500 instrument (50.69 MHz for ^{15}N) with a 'directly' detecting broadband observe probe and were referenced against external nitromethane. The reactants **1a** and **2a** are commercially available.

3-Methyl-1-phenyl-1H-pyrazol-5-yl 2-bromo-3-furancarboxylate (5)

(a) To a mixture of 3-methyl-1-phenyl-2-pyrazolin-5-one (**1a**) (87 mg, 0.5 mmol) and $\text{Ca}(\text{OH})_2$ (74 mg, 1 mmol) in 4 mL of dry 1,4-dioxane was slowly added a solution of 2-bromo-3-furoyl chloride (**2a**) (105 mg, 0.5 mmol) in 1,4-dioxane (1 mL) and the whole was heated to reflux for 3 h. After cooling to rt, 2N HCl (2 mL) was added and the mixture was stirred for 15 min before it was poured onto H_2O (30 mL). The aqueous phase was extracted with EtOAc (4×20 mL), the combined organic phases were washed with H_2O , dried (Na_2SO_4) and evaporated under reduced pressure. The residue was subjected to column chromatography (silica gel, eluent: petroleum ether – EtOAc, 5:1). The main component (least retarded fraction) turned out to be compound **5**. Yield: 35 mg (20%) of a yellowish oil which slowly solidified on standing.

(b) A mixture of **1a** (174 mg, 1 mmol), **2a** (230 mg, 1 mmol) and triethylamine (1 mL) in CH_2Cl_2 (20 mL) was refluxed for 3 h. Then solid products were filtered off, the filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (silica gel, eluent: petroleum ether – EtOAc, 5:1) to afford 283 mg (82%) of **5**.

^1H NMR (300 MHz, CDCl_3): δ (ppm) 7.57 (m, 2H, Ph H-2/6), 7.48 (d, $^3J = 2.2$ Hz, 1H, furane H-5), 7.43 (m, 2H, Ph H-3/5), 7.32 (m, 1H, Ph H-4), 6.76 (d, $^3J = 2.2$ Hz, 1H, furane H-4), 6.25 (s, 1H, pyrazole H-4), 2.35 (s, 3H, Me).

^{13}C NMR (75 MHz, CDCl_3): δ (ppm) 156.9 (C=O), 149.1 (pyrazole C-3, $^2J(\text{C}3,3\text{-Me}) = 6.7$ Hz, $^2J(\text{C}3, \text{H}4) = 4.1$ Hz), 144.9 (furane C-5, $^1J = 210.3$ Hz, $^2J(\text{C}5, \text{H}4) = 9.7$ Hz), 143.8 (pyrazole C-5, $^2J(\text{C}5, \text{H}4) = 4.7$ Hz), 138.0 (Ph C-1), 131.6 (furane C-2, $^3J(\text{C}2, \text{H}4) = 8.4$ Hz, $^3J(\text{C}2, \text{H}5) = 8.4$ Hz), 129.0 (Ph C-3/5), 127.3 (Ph C-4), 123.5 (Ph C-2/6), 115.7 (furane C-3, $^2J(\text{C}3, \text{H}4) = 3.0$ Hz, $^3J(\text{C}3, \text{H}5) = 5.8$ Hz), 112.6 (furane C-4, $^1J = 182.7$ Hz, $^2J(\text{C}4, \text{H}5) = 12.9$ Hz), 95.8 (pyrazole C-4, $^1J = 181.7$ Hz, $^3J(\text{C}4, 3\text{-Me}) = 3.5$ Hz), 14.5 (Me, $^1J = 127.7$ Hz).

^{15}N NMR (50 MHz, CDCl_3): δ (ppm) -183.6 (pyrazole N-1), -96.7 (pyrazole N-2).

IR (KBr) ν (cm^{-1}): 1752 (C=O).

MS (m/z, %): 348 (M^+ , 4), 346 (M^+ , 4), 173 (100).

Elemental Analysis: Calculated for $\text{C}_{15}\text{H}_{11}\text{BrN}_2\text{O}_3$ (347.16): C, 51.90%; H, 3.19%; N, 8.07%. Found: C, 51.90%; H, 3.26%; N, 7.77%.

Acknowledgements

Changbin Guo gratefully acknowledges a scholarship provided by the Eurasia-Pacific Uninet program.

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