

Short Note

5-Chloro-4-iodo-1,3-dimethyl-1*H*-pyrazole

Gytė Vilkauskaitė^{1,2}, Gernot A. Eller¹, Algirdas Šačkus² and Wolfgang Holzer^{1,*}

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

² Institute of Synthetic Chemistry, Kaunas University of Technology, Radvilenu pl. 19, LT-50254 Kaunas, Lithuania

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

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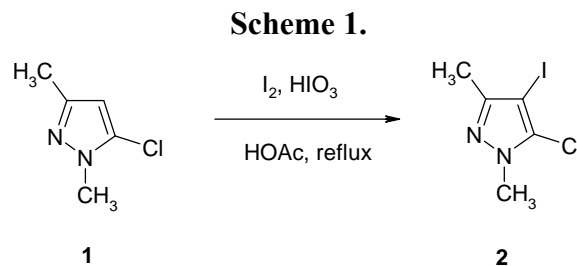
Abstract: Reaction of 5-chloro-1,3-dimethyl-1*H*-pyrazole with I₂/HIO₃ in refluxing acetic acid gives the title compound in good yield. Detailed spectroscopic data (¹H NMR, ¹³C NMR, ¹⁵N NMR, IR, MS) are presented.

Keywords: pyrazole; iodination; NMR spectroscopy

(Hetero)aryl halides are valuable starting materials for different transition-metal-catalyzed cross coupling reactions. In the recent past, these reactions have emerged as extraordinarily important methods for C–C and also C–X (X = O, N, S) bond formation in organic chemistry [1,2].

In the Sonogashira coupling, terminal acetylenes react with, for instance, (hetero)aryl halides or triflates to afford the corresponding (hetero)aryl alkynes [3,4]. Comparing the reactivity of the possible aryl reactants, the general order of reactivity is aryl iodides > aryl triflates ≥ aryl bromides >> aryl chlorides [4]. Accordingly, the best results in many reactions can be obtained with aryl iodides. This is also confirmed for pyrazolyl halides, in which a clear preference for iodides over bromides and chlorides is evident [5].

In the course of a synthetic program dedicated to the functionalization of halogenopyrazoles [6-9], we were interested in 4-iodopyrazole **2**, which was – amongst others – considered as a possible precursor in Sonogashira-type couplings. The synthesis of compound **2** was achieved by reaction of commercially available 5-chloro-1,3-dimethyl-1*H*-pyrazole (**1**) with I₂/HIO₃ in refluxing acetic acid (Scheme 1). Thus, the desired iodopyrazole **2** was obtained in 75% yield after flash chromatography.



Experimental

The melting point was determined on a Reichert–Kofler hot-stage microscope and is uncorrected. 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). The ^{15}N NMR spectrum (50.68 MHz, refocused and decoupled INEPT) was obtained on a Bruker Avance 500 instrument with a ‘directly’ detecting broadband observe probe (BBFO) and was referenced against external nitromethane.

5-Chloro-4-iodo-1,3-dimethyl-1H-pyrazole (2)

To a solution of 5-chloro-1,3-dimethyl-1H-pyrazole (**1**) (2.500 g, 19.15 mmol) in glacial acetic acid (10 mL) was added HIO_3 (674 mg, 3.8 mmol) and the mixture was stirred for 10 minutes. Then I_2 (3.884 g, 15.3 mmol) was added and the mixture was heated to reflux for 4 h. After cooling, the mixture was treated with 2N NaOH until the dark color disappeared, then some drops of $\text{Na}_2\text{S}_2\text{O}_3$ solution were added to obtain a colorless solution. The mixture was exhaustively extracted with dichloromethane, the combined organic layers were washed with water, dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, eluent: light petroleum–ethyl acetate, 10:1) to afford 3.683 g (75%) of **2** as colorless crystals, mp 64–65 °C.

IR (KBr) ν (cm^{-1}): 2923, 1497, 1350, 1271, 1107, 1053, 1022, 638.

MS (EI, 70 eV): (m/z , %) 256/258 (M^+ , 19/7), 160 (14), 128 (24), 96 (18), 64 (100).

^1H NMR (CDCl_3): δ (ppm) 2.22 (s, 3H, 3-Me), 3.84 (s, 3H, 1-Me).

^{13}C NMR (CDCl_3): δ (ppm) 14.4 (3-Me, $^1J = 128.3$ Hz), 37.1 (1-Me, $^1J = 141.1$ Hz), 60.8 (C-4, $^3J(\text{C}4,3\text{-Me}) = 4.3$ Hz), 131.3 (C-5, $^3J(\text{C}5,1\text{-Me}) = 2.4$ Hz), 150.4 (C-3, $^2J(\text{C}3,3\text{-Me}) = 6.9$ Hz).

^{15}N NMR (CDCl_3): δ (ppm) –186.1 (N-1), –77.5 (N-2).

Anal. Calcd for C₅H₆ClIN₂: C, 23.42%; H, 2.36%; N, 10.92%. Found: C, 23.76%; H, 2.34%; N, 10.81%.

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