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Short Note

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

Gytė Vilkauskaitė [1,2], Gernot A. Eller [1], Algirdas Šačkus [2] 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 I_2/HIO_3 in refluxing acetic acid gives the title compound in good yield. Detailed spectroscopic data (^{1}H NMR, ^{13}C NMR, ^{15}N NMR, IR, MS) are presented.

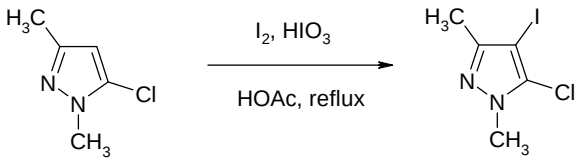
Keywords: pyrazole; iodination; NMR spectroscopy

(Hetero)aryl halides are valuable starting materials for different transition-metal-catalyzed cross coupling reactions. In the recent past, these reactions have emerged as extraordinaryly 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 I_2/HIO_3 in refluxing acetic acid (Scheme 1). Thus, the desired iodopyrazole **2** was obtained in 75% yield after flash chromatography.

Scheme 1.



1 **2**

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. ^{1}H and ^{13}C NMR spectra were recorded on a Varian UnityPlus 300 spectrometer at 28 °C (299.95 MHz for ^{1}H, 75.43 MHz for ^{13}C). The centre of the solvent signal was used as an internal standard which was related to TMS with δ = 7.26 ppm (^{1}H in $CDCl_3$) and δ = 77.0 ppm (^{13}C in $CDCl_3$). The digital resolutions were 0.2 Hz/data point in the ^{1}H and 0.4 Hz/data point in the ^{1}H-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-1*H*-pyrazole* (**2**)

To a solution of 5-chloro-1,3-dimethyl-1*H*-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 $Na_2S_2O_3$ 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).

^{1}H 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, ^{1}J = 128.3 Hz), 37.1 (1-Me, ^{1}J = 141.1 Hz), 60.8 (C-4, ^{3}J(C4,3-Me) = 4.3 Hz), 131.3 (C-5, ^{3}J(C5,1-Me) = 2.4 Hz), 150.4 (C-3, ^{2}J(C3,3-Me) = 6.9 Hz).

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

Anal. Calcd for $C_5H_6ClIN_2$: C, 23.42%; H, 2.36%; N, 10.92%. Found: C, 23.76%; H, 2.34%; N, 10.81%.

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