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Short Note

(2*E*)-3-(3-Methoxy-1-phenyl-1*H*-pyrazol-4-yl)-2-propenal

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Abstract: The palladium-catalyzed reaction of 4-bromo-3-methoxy-1-phenyl-1*H*-pyrazole with acrolein diethyl acetal 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; cross-coupling; Heck reaction; 2,3-unsaturated aldehyde

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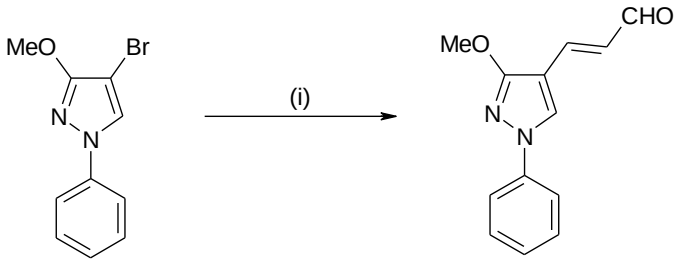
Aromatic 2,3-unsaturated aldehydes are useful precursors in synthetic organic chemistry. For example, cinnamaldehyde was used as a starting material for the synthesis of various heterocyclic compounds, including tetrahydrothiophene [1], dihydropyridine [2], hexahydro-1*H*-pyrrolizine [3], benzo[*a*]quinolizidine [4], and pyrido[1,2-a]indole [5] derivatives.

In recent years efficient protocols for the preparation of aromatic 2,3-unsaturated aldehydes by Heck type palladium catalyzed cross-coupling reactions of arylhalides with acrolein diethylacetal [6–8] or 3,3-diacetoxypropene [9] have been developed. These methods allowed also to prepare (hetero)aromatic 2,3-unsaturated aldehydes containing pyridine, chinoline, isoquinoline, thiophene and benzothiophene nuclei [6–9].

As a result of our interest in the synthesis of functionalized pyrazoles [10–13], we have developed a synthetic pathway to (2*E*)-3-(1-phenyl-3-methoxy-1*H*-pyrazol-4-yl)-2-propenal as a precursor to biologically active compounds and materials for non-linear optics.

As a starting material 4-bromo-3-methoxy-1-phenyl-1*H*-pyrazole (**1**) was used [14,15]. Palladium-catalyzed cross coupling of **1** with acrolein diethyl acetal afforded (2*E*)-3-(3-methoxy-1-phenyl-1*H*-pyrazol-4-yl)-2-propenal (**2**).The structure of **2** was confirmed by its spectroscopic data (^{1}H NMR, ^{13}C, NMR, ^{15}N NMR, IR, MS) as well as by elemental analysis. *E*-Configuration at the C=C double bond unequivocally follows from the magnitude of the vicinal coupling between the alkene protons H-2 and H-3 (^3J(H2,H3) = 15.8 Hz).

Scheme 1. Reagents and conditions: (i):H_2C=CHCH$(OEt)_2$, ^{n}Bu$_4$NOAc, K_2CO_3, KCl, $Pd(OAc)_2$, DMF, 90 ℃, 4 days.



1 **2**

Experimental

The melting point was determined on a Mel-Temp (Capillary Melting point Apparatus) and is uncorrected. Mass spectrum: Waters ZQ 2000 instrument (APCI+, 20 V). IR spectrum: Perkin Elmer Spectrum GX FT-IR System instrument (KBr-disc). The elemental analysis was performed with an Exeter Analytical CE-440 Elemental Analyzer. ^{1}H and ^{13}C NMR spectra were recorded on a Varian UnityPlus 300 spectrometer at 28 ℃ (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). A gradient selected ^{15}N,^{1}H-HMBC spectrum (50.68 MHz for ^{15}N) was obtained on a Bruker Avance 500 instrument with a 'directly' detecting broadband observe probe (BBFO) and was referenced against external nitromethane.

*(2E)-3-(3-Methoxy-1-phenyl-1*H*-pyrazol-4-yl)-2-propenal (**2**)*

To a stirred solution of 4-bromo-3-methoxy-1-phenyl-1*H*-pyrazole (**1**) (506 mg, 2.0 mmol) in DMF (8 mL) acrolein diethyl acetal (0.9 mL, 6 mmol), ^{n}Bu$_4$NOAc (1.206 g, 4.0 mmol), K_2CO_3 (414 mg, 3.0 mmol), KCl (149 mg, 2 mmol), and $Pd(OAc)_2$ (13 mg, 0.06 mmol) were added. The mixture was stirred for 4 days at 90 ℃. After cooling, 2N HCl was slowly added and the reaction mixture was stirred at room temperature for 10 min. Then, it was diluted with ethyl acetate and washed with water. The organic layer was dried over anhydrous Na_2SO_4, filtered and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, eluent: ethyl acetate–*n*-hexane, 1:4) to give 240 mg (53%) of **2** as colorless crystals, mp 131–133 ℃.

IR (KBr) ν (cm^{-1}): 3109, 2727, 1675, 1618, 1567, 1508, 1421, 1239, 1173, 747, 633.

MS (EI, 70 eV): (*m/z*, %) 229 ($[M+H]^+$, 100).

^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) 4.07 (s, 3H, OMe), 6.71 (dd, ^3J(H2,H3) = 15.8 Hz, ^3J(H2,CHO) = 8.0 Hz, 1H, H-2), 7.27 (m, 1H, Ph H-4), 7.32 (d, ^3J(H3,H2) = 15.8 Hz, 1H, H-3), 7.44 (m, 2H, Ph H-3,5), 7.62 (m, 2H, Ph H-2,6), 7.96 (s, 1H, pyrazole H-5), 9.56 (d, ^3J(CHO,H2) = 8.0 Hz, 1H, CHO).

^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) 56.5 (^1J = 146.5 Hz, OMe), 106.3 (^2J(pyrC4,pyrH5) = 7.4 Hz, ^2J(pyrC4,H3) = 1.6 Hz, ^3J(pyrC4,H2) = 5.3 Hz, pyrazole C-4), 118.1 (Ph C-2,6), 126.4 (Ph C-4), 127.3 (^1J = 162.8 Hz, ^2J(C2,CHO) = 25.0 Hz, ^2J(C2,H3) = 2.6 Hz, H-2), 128.1 (^1J = 186.9 Hz, ^3J(pyrC5,H3) = 4.9 Hz, pyrazole C-5), 129.5 (Ph C-3,5), 139.2 (Ph C-1), 141.4 (^1J = 152.5 Hz, ^3J(C3,CHO) = 1.5 Hz, ^3J(C3,pyrH5) = 1.5 Hz, C-3), 163.1 (^3J(pyrC3,pyrH5) = 9.1 Hz, ^3J(pyrC3,H3) = 6.8 Hz, ^3J(pyrC3,OMe) = 5.3 Hz, pyrazole C-3), 193.8 (^1J = 169.5 Hz, ^2J(CO,H2) = 1.7 Hz, ^3J(CO,H3) = 9.3 Hz, CHO).

^{15}N NMR ($CDCl_3$, 50.7 MHz): δ (ppm) –182.5 (pyrazole N-1), –118.5 (pyrazole C-2).

Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41%; H, 5.30%; N, 12.27%. Found: C, 68.30%; H, 5.49%; N, 12.24%.

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