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Mendeleev Commun., 2018, **28**, 20–21

Mendeleev Communications

Reaction of 1-(het)aryl-3-bromoprop-2-ynones with furans in solid metal oxides or salts: cross-coupling or cycloaddition?

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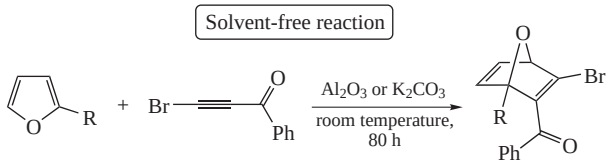
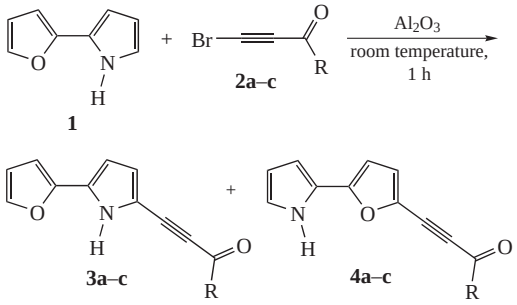
DOI: 10.1016/j.mencom.2018.01.004

1-(Het)aryl-3-bromoprop-2-ynones react with 2-(2-furyl)-pyrrole in the Al_2O_3 or K_2CO_3 dispersion (room temperature, 1 h) to afford the cross-coupling products either at the furan or pyrrole rings. Furan and 2-methylfuran with 3-bromo-1-phenylprop-2-ynone under the same conditions give the Diels–Alder cycloadducts, while furan-2-carbaldehyde and its acetals are inactive.

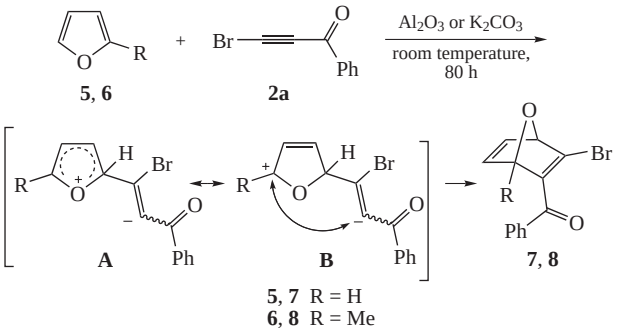


Recently,[1–7] simple and efficient transition metal-free cross-coupling between electron-deficient acylhaloacetylenes and pyrroles in the dispersion with solid metal oxides or salts was reported. Therefore, it seems resonable to extend this methodology over other electron-rich heterocycles. For this, furans, due to their importance as biologically active and synthetically valuable compounds,[8–22] can be obvious candidates. Previously,[23] it was noticed that, when 2-(2-furyl)pyrrole **1** was treated with acylhaloacetylenes **2a–c** in the solid Al_2O_3 dispersion (room temperature, 1 h), along with ethynylpyrroles **3a–c** as major products, ethynylfurans **4a–c** were also formed (Scheme 1). Interestingly, only the pyrrole or furan rings were separately ethynylated and no double ethynylation occurred.



Scheme 1

In this communication, we report on the reaction of 3-bromo-1-phenylprop-2-ynone **2a** with furan **5** and 2-methylfuran **6** in the solid Al_2O_3 or K_2CO_3 dispersion at room temperature. Surprisingly, it turned out that, instead of the expected cross-coupling, only Diels–Alder cycloaddition took place. The yield of cycloadduct **7** was ~44% in Al_2O_3 and 48% in K_2CO_3, and that of **8** was ~75% in Al_2O_3 and 70% in K_2CO_3 (Scheme 2).† Noteworthy, the reaction with 2-methylfuran is strictly regio- and stereoselective: despite obvious steric encumbrances in cycloadduct **8**, methyl and benzoyl substituents are located in the one side.



Scheme 2

† *Adducts* **7**, **8** (*general procedure*). 3-Bromo-1-phenylprop-2-ynone **2a** (0.5 g, 2.4 mmol) was carefully ground in a china mortar with Al_2O_3 or K_2CO_3 (5 g) at room temperature for 5 min. This mixture was placed into a tightly closing vessel, and furan **5**, **6** was added (3-fold excess, 7.2 mmol). The vessel was sealed and the mixture was shaken vigorously for 5 min and allowed to stay for 80 h at room temperature. Thereafter, the mixture was placed on the top of the column with silica gel and eluted with hexane and a mixture of hexane and diethyl ether (10 : 1) to afford pure product **7**, **8**.

(3-Bromo-7-oxabicyclo[2.2.1]hepta-2,5-dien-2-yl)(phenyl)methanone **7** was prepared from furan **5** and acetylene **2a** and isolated in 44% (Al_2O_3) or 48% (K_2CO_3) yield, colourless crystals, mp 93–95 °C. ^{1}H NMR ($CDCl_3$) δ: 7.86–7.84 (m, 2H, *o*-H_{Ph}), 7.63–7.59 (m, 1H, *p*-H_{Ph}), 7.51–7.47 (m, 2H, *m*-H_{Ph}), 7.40 (dd, 1H, H-6, *J* 1.8, 5.3 Hz), 7.15 (dd, 1H, H-5, *J* 1.8, 5.3 Hz), 5.69 (dd, 1H, H-1, *J* 1.5, 1.8 Hz), 5.46 (dd, 1H, H-4, *J* 1.5, 1.8 Hz). ^{13}C NMR ($CDCl_3$) δ: 190.8 (CO), 148.9 (C-2), 144.5 (C-3), 144.1 (C-6), 139.7 (C-5), 136.3 (*i*-Ph), 133.5 (*p*-Ph), 129.5 (*o*-Ph), 128.5 (*m*-Ph), 89.9 (C-4), 86.5 (C-1). IR (ν/cm^{-1}): 1639, 1585, 1550, 1444, 1321, 1283, 1265, 1226, 1182, 1137, 1093, 1076, 1022, 955, 908, 877, 811, 727, 703, 665, 634, 537, 494, 463. Found (%): C, 78.43; H, 4.77. Calc. for $C_{13}H_{10}O_2$ (%): C, 78.77; H, 5.09.

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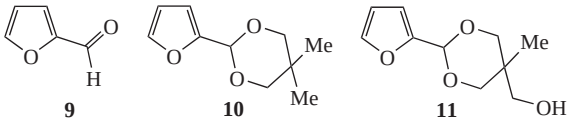
Furan derivatives with electron-acceptor substituents, such as furan-2-carbaldehyde **9** or its acetals **10**, **11**, were inactive and gave neither cross-coupling nor cycloaddition products.



9 **10** **11**

From the experimental results and according to the established mechanism for the same reaction with pyrroles,[24] it follows that the reactions starts with formation of zwitterionic intermediate **A** (see Scheme 2). Similar intermediate, formed from 2-(2-furyl)-pyrrole, distributes its positive charge over the pyrrole ring which promotes elimination of HBr to give cross-coupling products **3a**–**c**. In the zwitterionic intermediates generated from furans **5**, **6**, the positive charge is mostly concentrated at the oxygen atom and the 5-position (intermediate **B**) and, hence, the ring closure with carbanionic site is here preferred to afford cycloadducts **7**, **8**. Consequently, only one regioisomer is formed, when R = Me. Apparently, furans **9**–**11** with electron-acceptor substituents are not nucleophilic enough to form the zwitterionic intermediate of the type **B**.

In conclusion, reaction between acylhaloacetylenes and furans in the presence of solid metal oxides or salts may proceed as either the cross-coupling to afford acylethynyl derivatives or Diels–Alder type cycloaddition depending on nucleophilicity on the furan moiety. The results obtained predict that furans with substituents, capable of deep distribution of the positive charge in the intermediate zwitterion, will facilitate the cross-coupling that sounds promising for the furan synthetic chemistry.

This work was supported by the President of the Russian Federation (programs for the support of leading scientific schools, grant no. NSh-7145.2016.3). Authors acknowledge Baikal Analytical Center for collective use SB RAS for the equipment.

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Received: 16th March 2017; Com. 17/5203