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Reaction of benzonitriles with acetylene in the KOBu^t/DMSO/THF system: self-organization of 2-aryl-3-ethynyl-4-aroyl-5-methylpyrroles and aminoacroleins

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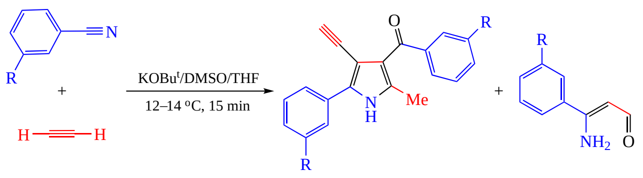
Benzonitriles react with acetylene gas (12–14 °C, 15 min) in the KOBu^t/DMSO/THF system to afford 2-aryl-3-ethynyl-4-aroyl-5-methylpyrroles and arylaminoacroleins that result from self-organization (in the presence of trace water) of two molecules of benzonitrile with three molecules of acetylene and one molecule of benzonitrile with one molecule of acetylene, respectively.



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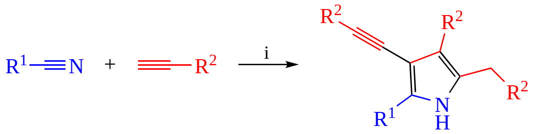
Organic nitriles are known to be a class of compounds with exceptionally rich chemistry that includes the reactions with various electrophiles, nucleophiles, free radicals and metal complexes providing carboxylic acids, amines, and diverse important heterocycles.[1–6] No wonder that nitriles are among the most studied objects of organic chemistry. Therefore it seemed hardly probable to encounter any new chemical transformation of organic nitriles. Meanwhile, we recently revealed that when nitriles contacted (15 min) with (het)arylacetylenes at room temperature in the KOBu^t/DMSO system, self-organization of 2-aryl-3-arylethynyl-4-aryl-5-benzyl-1*H*-pyrroles (up to 76% yield) took place (Scheme 1).[7]

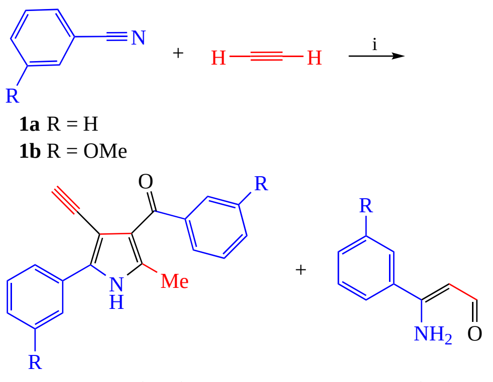
As follows from the pyrrole structure, the process involves one molecule of nitrile and three molecules of (het)arylacetylene. This finding is the logic of our previous systematic researches on acetylene reactivity in the superbase media, which while ago led us to the discovery of acetylenic carbanion addition to the C=N bond[8] and the self-organization phenomenon where several molecules of acetylene and simple nucleophiles deliver complex compounds under mild conditions.[9–11]

The next logical step in the development of this chemistry was our attempt to extend the reaction of aromatic nitriles with (het)arylacetylenes (Scheme 1) over acetylene gas, as industrially available and cheap acetylenic feedstock.[12–16] The preliminary results of this attempt are the subject of the present priority communication.

The reaction of benzonitriles **1a**,**b** with acetylene gas was carried out under the best conditions taken from the reaction of nitriles with arylacetylenes (room temperature, 15 min).[7] To our surprise, the self-organization process took absolutely another direction: instead of the pyrrole derivatives shown in Scheme 1, another type of tetrasubstituted pyrroles, 2-aryl-3-ethynyl-4-aroyl-5-methylpyrroles **2a**,**b** together with the corresponding aminoarylacroleins **3a**,**b** were formed (Scheme 2). The scrutinized optimization of the reaction conditions [variable parameters: temperature (12–30 °C), base nature (KOH, NaOBu^t, KOBu^t) and its content in the reaction mixture (0.5–2.0 equiv.), Bu^{t}OH or THF additives, and acetylene pressure (from atmospheric pressure to ~4–5 atm) did not increase yields of 21 and 10% for products **2** and **3**, respectively (Scheme 2). The conversion of starting nitriles **1a**,**b** was 68 and 71%, respectively. The best results were obtained, when nitrile **1** was added dropwise to the KOBu^t/DMSO/THF system at 12–14 °C for 15 min, while acetylene gas was passed through the reaction mixture. The presence of oxygen atoms in products **2** and **3** is due to the hydrolysis of highly reactive intermediates (see below) by trace of moisture in DMSO and isolation/purification procedure on silica gel.



Scheme 1 *Reagents and conditions*: i, KOBu^t (50 mol%), DMSO, room temperature, 15 min.

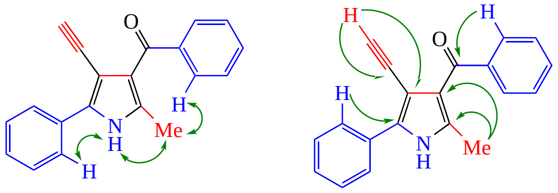


1a R = H
1b R = OMe

2a R = H (21%)
2b R = OMe (10%)

3a R = H (6%)
3b R = OMe (3%)

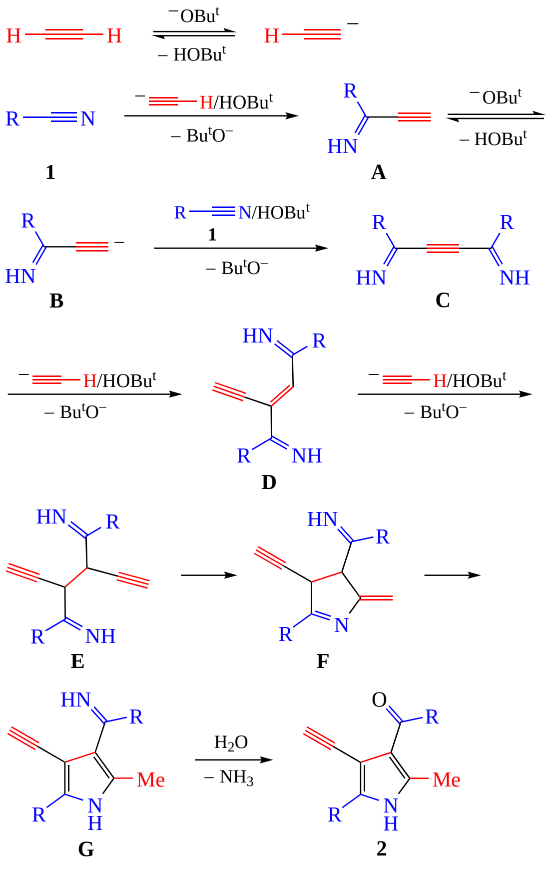
Scheme 2 *Reagents and conditions*: i, **1** (2 mmol), KOBu^t (1.5 mmol), DMSO (6 ml), THF (0.6 ml), 12–14 °C, 15 min.



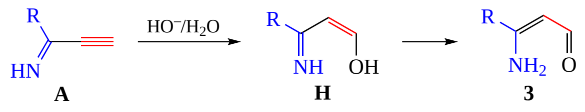
2a **2a**

Scheme 3 Main NOESY (↔) and ^{1}H–^{13}C (→) HMBC correlations for pyrrole **2a**.

A large part of the starting materials were consumed to form insoluble oligomers having averaged –C(Ar)=N–[CH=CH–]$_{(3–4)}$ blocks (according to elemental analysis). Notably, under the acetylene pressure, the oligomers are formed exclusively. Polyazapolyene structure of the oligomers was supported by the ESR spectrum, which contains a narrow (ΔH = 7.1 G) symmetric (asymmetry parameter A/B = 1.08) strong signal (g = 2.0060, N = 2.7 × 10^{18} spin g^{-1}) typical for semi-conducting polyacetylenes.[17,18] In the backbone of these polyconjugated oligomers, pyrrole-, fused pyrrole- and microcyclic structures may be produced (depending on the reaction conditions) and hence such materials deserve a special attention as objects for photoelectronics. However, this is beyond the scope of the present work. Besides, aminoarylacroleins **3**, the second isolable products of this self-organization process, can undergo head-to-tail auto-condensation to deliver alternating polyazapolyenes, which should also be among the formed oligomers. Other type of auto-condensation might be expected for pyrroles **2** having ethynyl and keto substituents which should barely coexist in a molecule especially in strongly basic media (possibility of the head-to-tail Favorsky reaction). Still another auto-condensation (addition of NH function to the triple bond) may occur with imino precursors of pyrroles **2** (see below mechanistic rationale). Importantly, no transformations of acetylene occurred without nitrile, likewise the nitrile remained almost completely intact, if acetylene was not added to the reaction mixture. It follows that acetylenic carbanions are triggers and drivers of the whole self-organization process including the oligomerization.



Scheme 4



Scheme 5

The structure of pyrrole **2a** was unambiguously proved by NMR analysis (COSY, NOESY, ^{1}H–^{13}C HSQC and ^{1}H–^{13}C HMBC experiments) (Scheme 3).

The reaction sequence involving the self-organization of pyrroles **2** assumingly starts with the addition of an acetylenic carbanions to the C≡N bond of nitriles **1** (Scheme 4). The intermediate carbanions **B** attack the next molecule of nitriles **1** to give symmetrical acetylenic diimines **C**, to which a second acetylenic carbanion is added. To the intermediate adducts **D** a third acetylenic carbanion is added to form intermediates **E**, which undergo intramolecular vinylation (the addition of N-centered anion of the imine moiety to the triple bonds) to deliver methylenedihydropyrroles **F** that aromatize to pyrroles **G**. The imine group of these pyrroles is then hydrolyzed (with trace moisture in DMSO and also during chromatography on silica gel) to finally afford pyrroles **2**.

The formation of aminoacroleins **3** likely includes the attack of acetylenic imines **A** by hydroxide anion (resulted from partial hydrolysis of KOBu^t by trace moisture) and expected prototropic rearrangement of adducts **H** to aminoacroleins **3** (Scheme 5).

Thus, the self-organization processes disclosed here open (when further properly optimized) a new window of possibilities for organic synthesis. At this stage, the one-pot preparation of pyrroles **2**, even in low yields, serves to demonstrate the high chemical compatibility (particularly in strongly basic media) of substituents such as ethynyl, carbonyl, and NH groups. The work will be of interest to the organic chemist due to the simplicity and industrial availability of the starting materials (nitriles and acetylene gas), the inexpensive superbase system (KOBu^t/DMSO/THF), the very mild reaction conditions (12–14 °C, 15 min), and the simplicity of the synthetic operation. From the theoretical point of view, the results obtained help generating fresh ideas concerning reactivity of nitriles and acetylenes in strongly basic media.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2024.10.031.

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