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Novel [3 + 2] Radical Annulations of Cyano-Substituted Aryl Radicals with Alkynes

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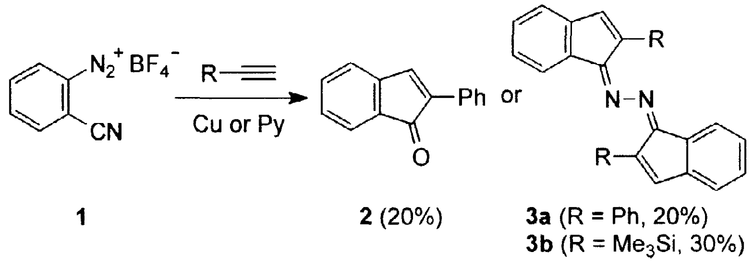
Abstract: New radical annulation reactions are described involving addition of *ortho*-cyano-substituted aryl radicals to alkynes. Addition of the aryl radical to the C-C triple bond gives rise to a vinyl radical, whose cyclisation onto the carbon atom of the nitrile moiety produces an iminyl radical. The final reaction products derive from the iminyl by hydrogen abstraction — followed by hydrolysis —, dimerisation, or cyclisation onto another aromatic ring. In the last case, new nitrogen heterocycles are formed through a novel application of the radical addition, tandem cyclisation strategy.

The past twenty years have witnessed an explosive growth in the use of free-radical methodologies and now the literature displays an extraordinary number of multistep syntheses involving radicals as key intermediates.[1] Our group has been drawing special attention for more than a decade to radical annulation reactions, which allow the construction of polycyclic — often heterocyclic — molecules starting from simple, readily accessible materials. In this regard we have reported the syntheses of benzothiophene,[2] quinoline,[3] benzotriazine,[4] phenanthrene,[5] and quinoxaline[6] derivatives through [4 + 2] or [3 + 2] radical annulations involving alkyl, vinyl, or imidoyl radicals. Our recent results on the addition of imidoyl radicals to cyano groups[6] prompted us to further investigate the possibility of radical annulations involving vinyl radicals and nitrile moieties. Examples of addition of vinyl radicals to nitriles are indeed extremely rare and, to our knowledge, the only reported results concern migration of the cyano group to the vinyl radical centre.[7] No examples have appeared dealing with radical annulation reactions involving, as key steps, intermolecular addition of a carbon radical to an alkyne and cyclisation of the resulting vinyl radical onto a C-N triple bond. Here we report the preliminary results obtained by reacting *ortho*-cyano aryl radicals with some alkynes.

The aryl radicals were generated from the corresponding diazonium tetrafluoroborate **1** (1 equiv) by copper-[2b] or pyridine-mediated[5,6b,8] decomposition. With phenyl- or trimethylsilylacetylene (5 equiv), the reaction afforded either ketone **2**[9] or azines **3a,b**,[10] depending on the experimental conditions (Scheme 1).



Scheme 1

The fate of the final iminyl radical involved in the annulation process depends on the reaction medium. In acetone, it can readily abstract a hydrogen atom to give an imine (not isolated) and, after column chromatography, the ketone **2**. In the absence of hydrogen donors, *i. e.* in pyridine, the iminyl dimerises to afford the azines **3**.[11] Potentially interesting results might be obtained if the iminyl radical is given the chance to further cyclise onto an additional unsaturated group of the starting aryl radical or alkyne, for instance a C-C double bond[12] or another aromatic ring.[13] In this case, we could design novel one-step syntheses of heterocyclic compounds through cascade radical reactions.

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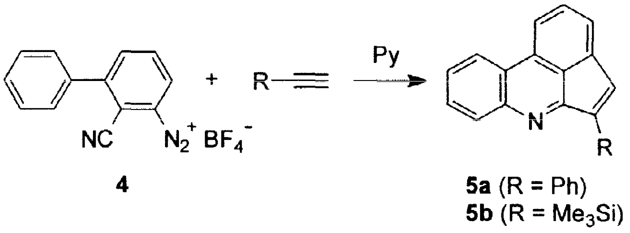
Indeed, when the aryldiazonium salt **4** was allowed to react in pyridine with phenylacetylene or trimethylsilylacetylene, we obtained the novel cyclopentaphenanthridines **5a,b**[10] in *ca.* 20% yield (Scheme 2). These new heterocyclic compounds arise from addition of the aryl radical to the C-C triple bond of the alkyne, cyclisation of the derived vinyl radical onto the cyano group, and final homolytic aromatic substitution of the resulting iminyl radical on the phenyl ring of **4**.



Scheme 2

This result seems to open — notwithstanding the low yield — novel, exciting routes to nitrogen heterocycles with elaborate frameworks. Studies are underway to improve the reaction outcome and to extend the procedure to a very wide set of nitriles and unsaturated radical acceptor/radical donor systems.

The preliminary results reported here are, to our knowledge, the first example of [3 + 2] radical annulation involving cyano-substituted radicals and alkynes. A similar outcome could in principle be obtained from other radicals substituted with heteronuclear unsaturated bonds and, indeed, we are currently achieving some results showing that an analogous annulation can be performed on azo- or imino-substituted aryl radicals. Studies are in progress to investigate this prospect thoroughly.

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