Alkynylic $S_{RN}1$ Reaction: Feasible or Not?

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A comparison of the relative propensity of aryl-, vinyl-, and ethynyl-halides towards a $S_{RN}1$ reaction is made possible by an investigation of some nucleophilic reactions with bromophenylethyne.

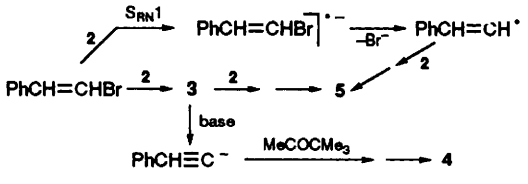
Our recent quest for a $S_{RN}1$-like nucleophilic reaction of vinyl halides[1] has prompted an extension of the study to the less investigated ethynyl halides. The reduction potentials of the ethynyl halides favour the $S_{RN}1$ pathway, as can be seen from the series PhBr, −2.9; PhCH=CHBr, −2.27; PhC≡CBr, −2.11 V (*vs.* SCE);[2] this suggests a relatively easy reduction of bromophenylethyne **1** in the $S_{RN}1$ initiation step.

To check this expection, **1** was synthesised[3] and treated with a threefold excess of the enolate ion of pinacolone **2** in Me_2SO under either photostimulation or iron(II) ion catalysis.[4] In both cases, and after a short reaction time (10 min) at room temp., **1** disappeared to yield PhC≡CH (**3**, 60–80%), along with smaller amounts of **4** (10–20%) and **5** (6–10%) [eqn. (1)].

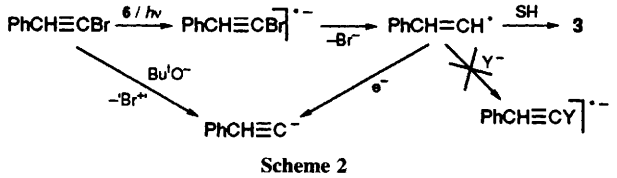
$$\underset{\mathbf{1}}{PhC{\equiv}CBr} + \underset{\mathbf{2}}{{}^-CH_2COCMe_3} \rightarrow \underset{\mathbf{3}}{PhC{\equiv}CH} + \underset{\mathbf{4}}{PhC{\equiv}C{-}C(OH)(Me)CMe_3} + \underset{\mathbf{5}}{PhCH{=}CHCH_2COCMe_3} \quad (1)$$

In the analogous reaction with **2**, β-bromostyrene has already been reported to give **3** by a α,β-elimination (Scheme 1);[1] subsequent addition of the conjugate base of phenylacetylene to the ketone and protonation gives **4**, while addition of **2** to **3** and protonation affords **5**. However, the latter compound is also formed by the competing $S_{RN}1$ reaction.[1]

It is therefore conceivable that, following formation of **3** from **1** [eqn. (1)], partial conversion of it into **4** and **5** can occur, according to Scheme 1. Analogous reactions [see eqn. (1)] of **1** with either $(EtO)_2PO^-$ or $PhCOCH_2^-$ **6** as nucleophiles under iron(II) catalysis or photostimulation gave instead only **3**, in quantitative yield.



Scheme 1



Scheme 2

A better appreciation of the origin of **3** comes from other reactions carried out on **1** with **6**, instead of **2**. Partial incorporation (15%) of deuterium in **3** occurred when the reaction was conducted in $(CD_3)_2SO$ while a moderate increase (30%) of incorporation was obtained in the presence of small amounts of a radical scavenger. It appears therefore that photostimulated or iron(II) induced ET from the nucleophile Y^- to **1** (a step inhibited by the scavenger) does occur to produce $\mathbf{1}^{\cdot-}$, which fragments to PhC≡C·; abstraction of hydrogen (or deuterium) from the solvent leads to **3** in a ECC process. However, interception and reduction of PhC≡C· by further ET may afford $PhC{\equiv}C^-$, which protonates to **3** in a ECEC process. In addition, a blank reaction with Bu^tO^- *alone*, which is the base used in slight excess to generate the anions (Y^-), shows that **1** can suffer efficient Br^+-abstraction to produce $PhC{\equiv}C^-$, which protonates to give **3** (*ca.* 75% in 10 min); this ionic pathway, which is unaffected by the electron-scavenger, is not available to the enolate ion, or at least not with comparable efficiency (Scheme 2).

In no cases was the $S_{RN}1$ substitution product (*i.e.* PhC≡CY) observed from **1**. This finding is in sharp contrast to the fact that an aryl halide such as PhBr gives only $S_{RN}1$ substitution and no reduction of the halogen.[5] Consistently, also vinyl halides other than β-bromostyrene, *i.e.* structurally unable to any competing α,β-elimination and ensuing pathways thereafter (Scheme 1), did give unambiguous $S_{RN}1$ substitution as the major pathway, accompanied by minor amounts of hydrodehalogenation.[1b] In comparison to this behaviour of the aryl and vinyl halides, the X^+-abstraction step by the base, as also the 'two-electron' reduction occurring with the ethynyl halide, both processes affording the carbanion $PhC{\equiv}C^-$, can reflect the relative stability (pK_a) of the conjugate base of the parent hydrocarbons Ph^- and $PhCH{=}CH^-$ (*ca.* 42–44),[6] $PhC{\equiv}C^-$ (28.7).[7]

In conclusion, the initial ET-induced dehalogenation of **1** is followed by further reduction of the alkynylic radical intermediate to $PhC{\equiv}C^-$, the latter deriving also from a competing X^+-removal step due to the slight excess of the base (Bu^tO^-).

Received, 23rd May 1994; Com. 4/03062A

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