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Heck reactions of *ortho*-substituted arenediazonium salts: critical observations on electronic effects

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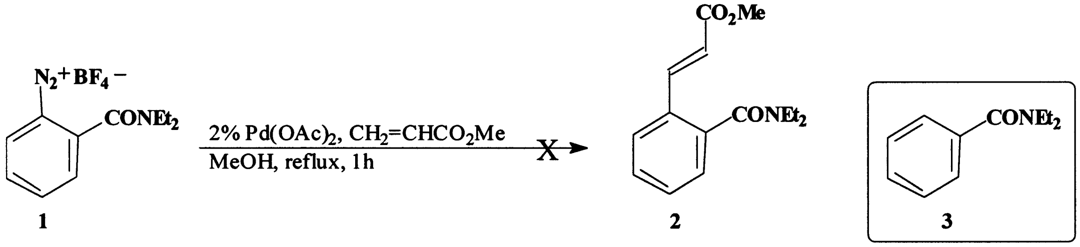
Abstract—An attempted Heck reaction of *o*-diethylamido phenyldiazonium tetrafluoroborate follows a unique radical-chain protodediazoniation pathway that is triggered by a facile 1,5-[*H*] shift of the derived aryl radical. Other *ortho*-substituted salts, irrespective of their redox potentials and structure, behave in the normal way. © 2001 Published by Elsevier Science Ltd.

Recently, much attention has been paid to arenediazonium salts as alternative substrates to aryl halides and triflates for palladium catalyzed reactions. We and others have shown that these salts are much superior to aryl bromides, triflates and even, iodides in Heck[1] and boronic acid cross-coupling reactions.[2] Heck reactions of arenediazonium salts are a facile process, e.g. producing high yields of products under mild conditions ($Pd(OAc)_2$, EtOH or MeOH, with or without $CaCO_3$, 60–80°C) and within short reaction times (30 min to 1 h). With a view to expanding the scope of these reactions, we became interested in Heck reactions of the *ortho*-diethylamido phenyldiazonium salt **1** so that the immensely useful *ortho*-metallation chemistry of aryl diethylamides[3] could be synthetically linked to the Pd-catalyzed reactions of arenediazonium salts.

Much to our surprise, the Heck reaction of **1** with methyl acrylate in MeOH gave *N*,*N*-diethyl benzamide (**3**) in 78% yield (Scheme 1). None of the expected cinnamate product **2** could be isolated from this reaction. We initially rationalized this to be a case of radical-chain protodediazoniation caused by the high redox potential of the electron deficient diazonium salt **1**.[4] Such an argument drew support from our previous observations that highly electron-poor nitro-substituted diazonium salts also failed in their Heck and cross-coupling reactions.[5] However, later on we were confronted with results that are contrary to this argument. Thus, the ester-substituted diazonium salts **4a** and **b** also having high redox potentials, successfully underwent Heck reactions with methyl acrylate to give **5a** and **b** in good yields (Scheme 2). Moreover, the *p*-diethylamido salt **4c** also reacted smoothly to produce the cinnamate product **5c** in 67% yield. Since aryl radical formation is equally favored from **1** and **4a**–**c**, the fact that protodediazoniation occurs only for **1** could no longer be explained through simple trapping of the derived aryl radical with the solvent methanol. This led us to propose an alternative mechanism for the protodediazoniation of **1** taking into account the unique structural features of this salt and the derived aryl radical. Thus,



Scheme 1.

Keywords: Heck reaction; arenediazonium salts; aryl radicals; radical translocation.

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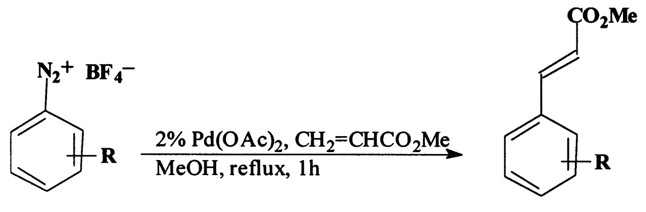
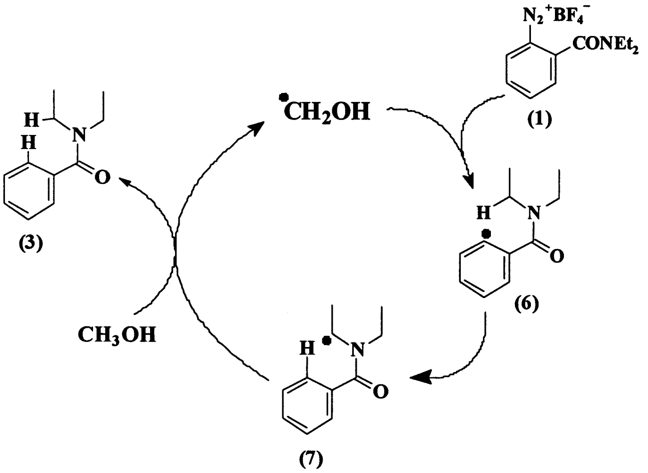


4a-d

5a (70%)
5b (77%)
5c (67%)
5d (81%)

a: R = *o*-CO_2Me; **b**: R = *p*-CO_2Me;
c: R = *p*-$CONEt_2$; **d**: R = *o*-OC_3H_7-*n*

Scheme 2.



Scheme 3.

the aryl radical **6**, generated from **1**, is ideally poised for a facile 1,5-[*H*] shift to give the more stable α-amido radical **7** and it is this translocated radical (and not **6**) which abstracts a hydrogen from methanol to produce **3** and $^{\bullet}CH_2OH$ (Scheme 3). Although we have no conclusive proof for this mechanism at this moment (labeling studies are in progress), it may be noted that 1,5-[*H*] shifts in *ortho*-substituted aryl radicals have wide precedence in the literature[6–9] and are especially common for *ortho*-dialkylamido aryl radicals.[6,9b] Trapping of the translocated radical **7** with MeOH must be an extremely fast process since products arising out of reaction of this radical with methyl acrylate[9b] were not observed in our case.

The lack of protodediazoniation in **4a**–**c** can also be explained in light of the above mechanism. Thus, a 1,5-[*H*] shift is geometrically precluded for aryl radicals from **4b** and **c** and hence the latter prefer the Pd-mediated pathway. On the other hand, a 1,5-[*H*] shift although feasible for the *ortho*-ester radical **8** derived from **4a** is unlikely since this latter radical should exist almost entirely in the more stable *anti*-conformations **8a** and **b**[10] where, again, a 1,5-[*H*] shift is geometrically precluded (Scheme 4).

However, it could still be argued that Heck reactions of arenediazonium salts have an inherent radical component and in those cases (viz. **1**) where the aryl radical can find a thermodynamic sink, e.g. via a 1,5-[*H*] shift, the radical pathway should take preference over the Pd-mediated process. Hence, the protodediazoniation reaction observed for **1** may not be a unique case and should occur for other diazonium salts also where, irrespective of their redox potentials, geometric requirements for a 1,5-[*H*] shift are properly met. In fact, Beckwith et al. have shown that, if geometry permits, even electron rich diazonium salts, e.g. the *ortho*-ethoxyphenyl diazonium salt, lead to rapid 1,5-[*H*] shifts under radical generating conditions.[7] To answer this, we carried out the Heck reaction of the *ortho*-*n*-propyloxyphenyl diazonium salt **4d** with methyl acrylate which produced the normal Heck-product **5d** in 81% yield (Scheme 2). Hence, in Heck reactions of arenediazonium salts, meeting the geometric requirements for a 1,5-[*H*] shift cannot be the sole reason for a switch over to radical pathways. The protodediazoniation of **1** must be a unique case where the high redox potential of the salt and a 1,5-[*H*] shift of the aryl radical worked in unison.

While our investigations continue, we believe that the above results provide important structural and electronic guidelines for the choice of *ortho*-substituted arenediazonium salts in Pd-catalyzed reactions.

Acknowledgements

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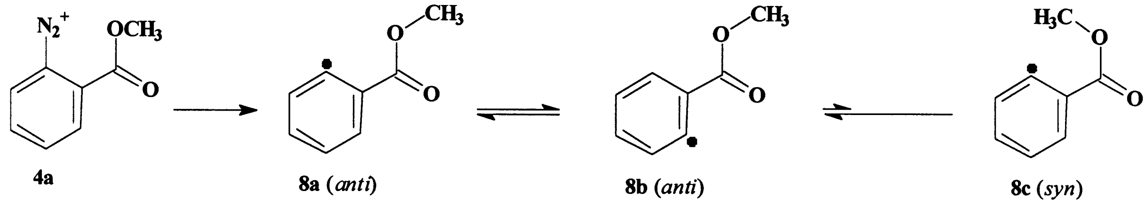

4a

8a (*anti*)

8b (*anti*)

8c (*syn*)

Scheme 4.

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