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Reactive Intermediates

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A “Hot, Energized” Benzyne**

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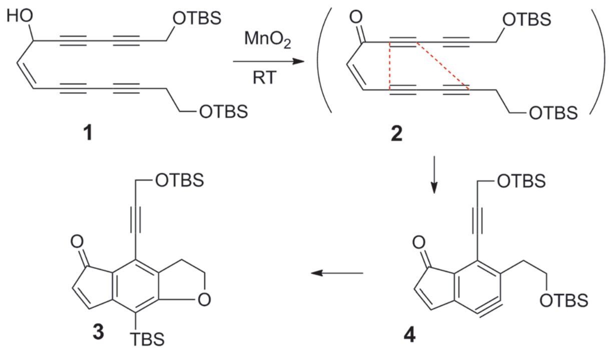
[4+2] cycloaddition · arynes · chemical activation

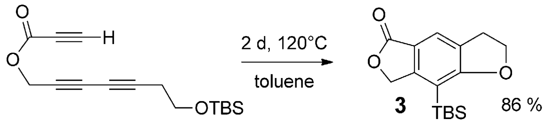
Once in a while Nature tries to tell us something. Chemists therefore should be prepared and willing to listen! T. Hoye et al. were understandably surprised when a seemingly trivial oxidation of **1** took an unexpected course (Scheme 1).[1]



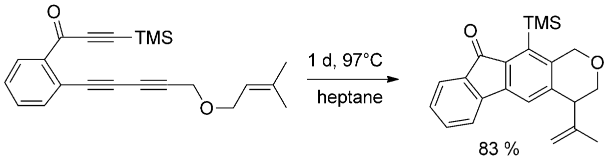
Scheme 1. Unexpected formation of an aryne by [4+2] cycloaddition.

Instead of ketone **2** the tricyclic product **3** was obtained in 53% yield. The course of the events could be rationalized readily and pointed to the unprecedented cyclization of ketone **2** to give the benzyne derivative **4** in a [4+2] cycloaddition between a diyne and an yne moiety. In fact, this intramolecular cycloaddition turned out to be a viable route to generate arynes bearing electron-withdrawing substituents,[1] a substitution pattern that is not always amenable to the standard methods for generating arynes. Thus, this surprising reaction broadens the scope of benzyne chemistry, as illustrated by the prototypical transformation in Scheme 2.

In both reactions, the reaction cascade is terminated by an insertion of the aryne into the silicon–oxygen bond. This is another unusual feature, because arynes are not known to cleave TBS ethers;[2] benzyne, though, reluctantly attacks ethers such as THF.[3] The ready intramolecular insertion into the TBS ether in **4** can perhaps be ascribed to a proximity effect, but could also indicate the particularly high reactivity of the aryne **4** generated by the intramolecular cycloaddition from **2**. Likewise, benzyne undergoes Alder–ene reactions with low yields only.[4] However, when the aryne is generated by the above cycloaddition an intramolecular ene reaction proceeds readily (Scheme 3).[1]

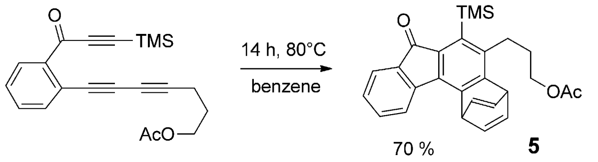


Scheme 2. Intentional formation of an aryne by [4+2] cycloaddition.



Scheme 3. Intramolecular trapping of an aryne by an Alder–ene reaction.

Such heightened reactivity appears also when arynes generated in this manner are trapped intermolecularly by reaction with the solvent.[1] The transformation shown in Scheme 4 is significant. Hitherto, the trapping of benzyne by benzene gave only low yields of benzobarrelene.[5] Hence the formation of **5** in 70% yield is spectacular and points again to a high reactivity of the aryne involved.



Scheme 4. Intermolecular trapping of an aryne by addition to benzene solvent.

Hoye et al. report[1] that this [4+2] cycloaddition to give an aryne is exothermic by about 50 kcal mol^{-1}. Thus, the aryne generated in this manner would initially carry a substantial amount of excess energy. Could it be that the aryne could use this excess energy to undergo intramolecular trapping reactions? Normally, excess energy of a chemically activated species is rapidly dissipated as intramolecular vibrations and

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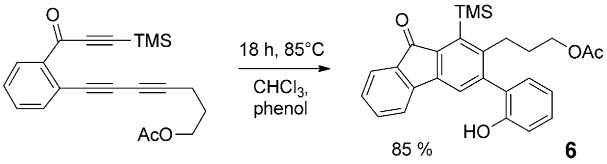
rotations. If during dissipation the excess energy enters vibrational and rotational modes relevant for a follow-up reaction, this reaction can indeed be chemically triggered and could be selectively favored over other competing reactions.[6] Whether this applies to the intramolecular trapping of the arynes generated by [4+2] cycloaddition remains a topic of speculation at the moment. In turn, however, arynes generated by this [4+2] cycloaddition could be a rewarding subject to study the possibility and scope of chemical activation[7] in solution. Likewise, the specific formation of **5** by the reaction of the aryne with the solvent benzene might be a consequence of an "energized" aryne and its attendant increased reactivity.

Hoye et al. noted[1] another feature of the aryne they generated, a behavior that is not necessarily connected to its excess energy: In the trapping reaction with phenol the aryne C arylates it in the *ortho* position to give **6** (Scheme 5), whereas normally phenols are consistently O arylated by arynes.[8] This observation may have to do with the fact that the aryne generated by [4+2] cycloaddition arises in the absence of innocent and not-so-innocent coproducts.[1]



Scheme 5. Intermolecular trapping of an aryne by addition to phenol.

All in all, the novel generation of arynes by intramolecular [4+2] cycloaddition between a diyne and an (electronically activated) alkyne not only provides a new route to generate arynes, but possibly provides a training ground on which to discover fundamental aspects of chemically activated reactive intermediates.

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