DOMINO REACTION CASCADES TO HETEROARENE FUSED BENZOFLUORENES FROM ENEDIYNE ALCOHOLS: [2,3]-SIGMATROPIC REARRANGEMENT OR S_N2' REACTION FOLLOWED BY A THERMAL C^2-C^6-BIRADICAL CYCLIZATION. (1)

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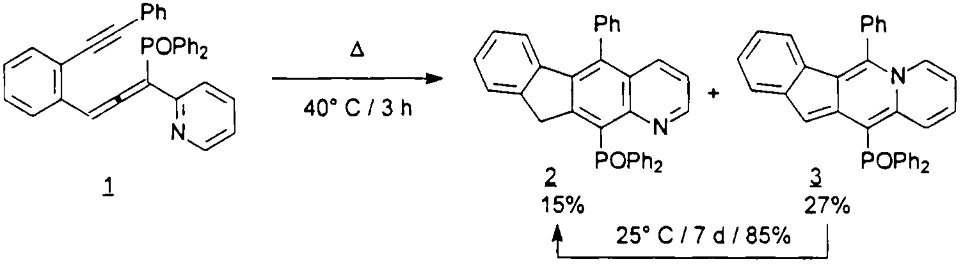
ABSTRACT: Starting from readily accessible enediyne alcohols two different domino reactions were developed that furnish tetracyclic 6-5-6-5 membered heteroarenes by generating the two central rings. The reaction cascade involves the intermediate formation of enyne-allenes and their subsequent thermal cyclization via biradical intermediates to the heteroarene fused benzofluorenes.

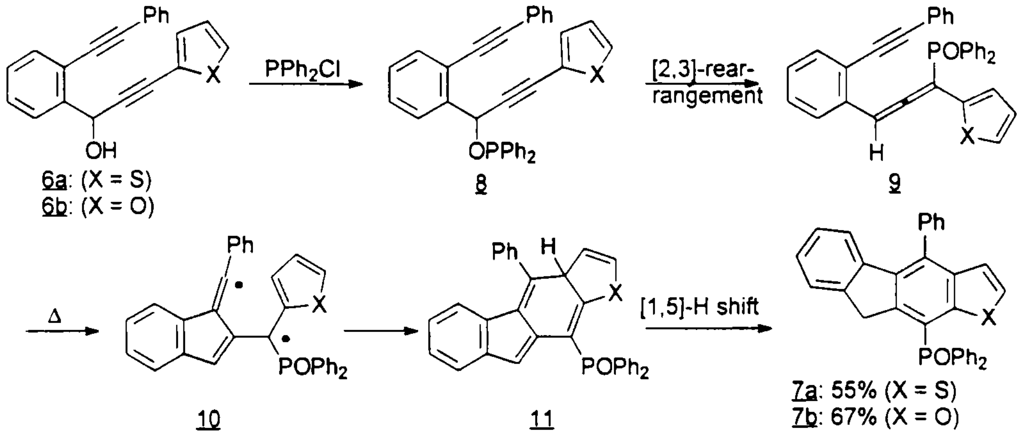
INTRODUCTION

In the context of the thermal reactions of enyne-allenes we have recently disclosed a remarkable switch from the well-known Myers-Saito cycloaromatization (2) to an unprecedented C^2-C^6-cyclization affording benzofulvenes in high yield (3), the mechanistic details of which have been identified (4). It seems, that the C^2-C^6-cyclization is a mild and fairly general thermal transformation for enyne-allenes as shortly after our first report related C^2-C^6-cyclizations have been observed by two other groups as well (5).



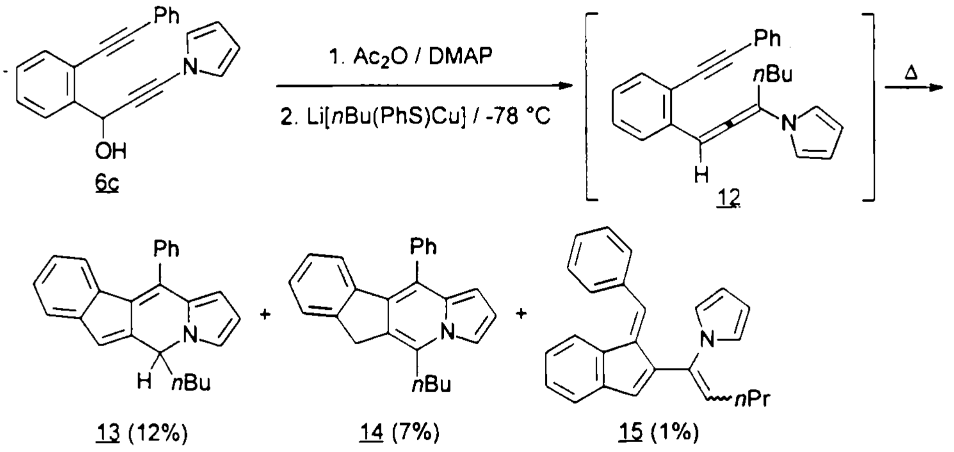
Scheme 1. Synthesis of the indeno[1,2-*g*]quinoline 2 via C^2-C^6-cyclization.

Noticeably, the mild reaction conditions could be exploited recently (Scheme 1) for the synthesis of indeno[1,2-*g*]quinoline 2 (3b) thus promising that such a strategy could equally be utilized for the preparation of tetracyclic fulvenes 11 in a stepwise Diels-Alder cycloaddition. A succeeding [1,5]-H shift then completes the multistep transformation to the annulated heterocycles 7a,b (Scheme 3). Again, ample evidence for a biradical route has been established in earlier work, *e.g.* in the formation of 2 and 3 and related carbocycles (3b,4).



Scheme 3. Mechanism of the multistep transformation of endiyne alcohols 6a,b to 7a,b.

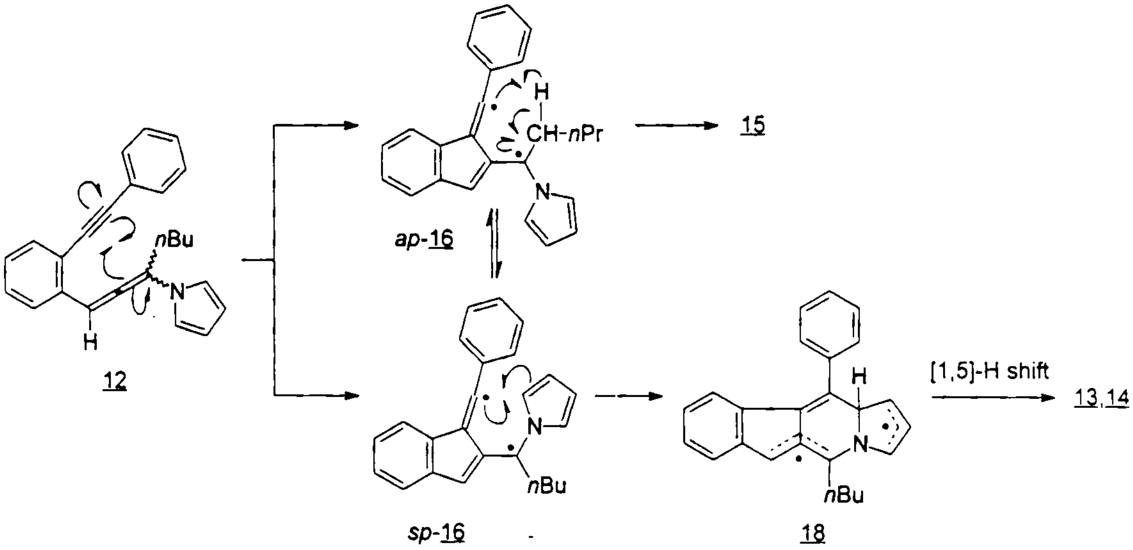
As the phosphine oxide functionality in 7 is not a versatile synthon for subsequent group transformations we have sought for alternatives to generate the intermediate enyne-allene. Fortunately, the rate determining step of the formal Diels-Alder cycloaddition in the enyne-allene thermolysis is a thermal C^2-C^6-biradical cyclization which should not depend decisively on the nature of the heteroarene substituent at the allene terminus (4). Hence, to illustrate the wide scope of our domino reaction strategy we have synthesized the thermally labile enyne-allene 12 by an S_N2' reaction. Therefore, enediyne alcohol 6c was prepared from 4 and *N*-ethynylpyrrole (12) and treated after acylation with readily available lithium butyl(phenylthio)cuprate at -78 °C following a preparation elaborated by Nantz (13) that was recently utilized by us to synthesize enyne-allenes (14).



Scheme 4. A domino reaction consisting of S_N2' substitution and thermal C^2-C^6 cyclization.

Again, as before, we were not able to isolate the intermediate enyne-allene 12 since it was thermally cyclized under the reaction conditions to products 13 - 15 (Scheme 4). In this context, the formation of vinylbenzofulvene 15 is mechanistically important as it is cleary derived from the intermediate enyne-allene 12 through a formal ene-reaction. As can be deduced from earlier investigations (3a,4), however, the formal ene-reaction 12 ⟶ 15 most likely is not a concerted but stepwise process via the intermediate biradical *ap*-16.

At present we can only speculate about the mechanism leading from 12 to 13,14. Since 15, however, is a typical product of an enyne-allene C^2-C^6-cyclization via biradical *ap*-16, it seems plausible to invoke the same reactive intermediate, but now in the synperiplanar conformation, in the formation of 13 and 14 as well. In contrast to the situation with biradicals 10, however, there is no straightforward biradical pathway to formal Diels-Alder products starting from *sp*-16. As a consequence, biradical *sp*-16 undergoes a 6-*exo-trig* cyclization to biradical 18 which after a [1,5]-H shift gives rise to the isolated indolizine derivatives (Scheme 5).



Scheme 5. Postulated mechanism leading to products 13-15. (*ap*- antiperiplanar; *sp*- synperiplanar)

CONCLUSION

From the above results it seems promising to further elaborate domino reactions of enediyne alcohols as one-pot reactions to interesting heterocyclic ring systems. While the thermal C^2-C^6-cyclization of intermediate enyne-allenes constitutes the second step in the reaction cascade, the first step used to build up the thermally labile enyne-allene can be widely altered.

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