

# Intramolecular formal [4+2] cycloaddition reactions of secondary and tertiary aryldiacetylene alcohols

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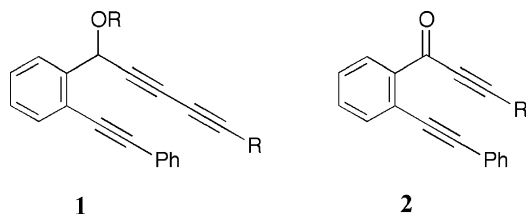
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**Abstract**—Thermal and thionyl chloride induced cycloaromatizations of secondary and tertiary aryldiacetylene alcohols were studied. The secondary alcohol did not respond to thionyl chloride, but in all the other cases presumptive biradical intermediates evolved either by intramolecular radical coupling or, when derived from a xanthene scaffold, by intramolecular radical acylation to a diketone that finally afforded a *p*-methylene-quinone.

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Current research on the thermal biradical cyclizations of polyenyne systems such as enediynes (Bergman cyclization) or enyne-allenes (the Myers-Saito and Schmittel cyclizations) focuses on the synthesis of models of the natural enediyne antibiotics<sup>1</sup> and on their utilization in the construction of polycyclic ring systems.<sup>2</sup> For example, our group has reported an approach to the benzo[*b*]fluorene and benzo[*c*]fluorene skeletons involving the thermal cycloaromatization of aryldiacetylenes such as nonconjugated benzotriynes **1**<sup>3</sup> and benzodiyenes **2**.<sup>4</sup>



Wang and co-workers<sup>5</sup> have reported that thionyl chloride promotes room-temperature cycloaromatiza-

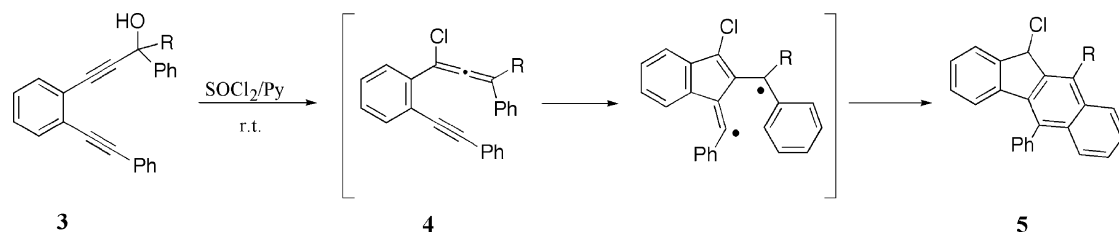
tion of the conjugated aryldiacetylene tertiary alcohols **3** into benzo[*b*]fluorenyl chlorides **5** via the reactive chlorinated benzoenyne-allenes **4** (Scheme 1), Schmittel cyclization of **4** providing a biradical that evolves to the formal Diels–Alder polycyclic adduct **5** through an intramolecular radical coupling involving the vinyl  $\sigma$ -radical, which is more reactive than the conjugated  $\pi$ -radical.

In this Letter we report the results of thermal and thionyl chloride induced cycloaromatization of the nonconjugated aryldiacetylene alcohols **6a–c**. We found that only the tertiary alcohols cyclized under Wang's conditions, and that the rigidity of **6c** hindered its thermal cyclization unless AcOH was present, in which case the acetylated biradical intermediate underwent intramolecular transacylation prior to the final cyclization.

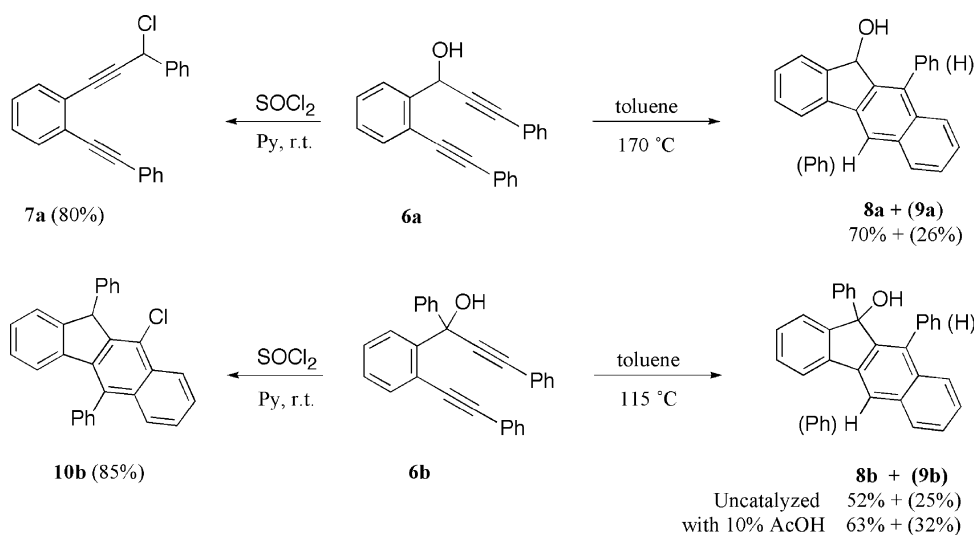
When Wang's conditions were applied to the secondary propargyl alcohol **6a** no cycloaromatization was observed and the only product isolated was the transposed propargyl chloride **7a** (Scheme 2).<sup>6</sup> Heating **6a** at 150 °C in toluene induced no reaction at all even when a 10% volume of AcOH was present,<sup>7</sup> and in the presence of TFA led to a complex mixture. However, heating at 170 °C in toluene gave an almost quantitative combined yield of the two regioisomeric benzo[*b*]fluorenols **8a** and **9a**,<sup>3</sup> no doubt as a result of intramolecular coupling of a

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Scheme 1.



Scheme 2.

1,4-divinyl biradical intermediate producing strained cyclic allenes that evolved to the final aromatic products.<sup>4a</sup>

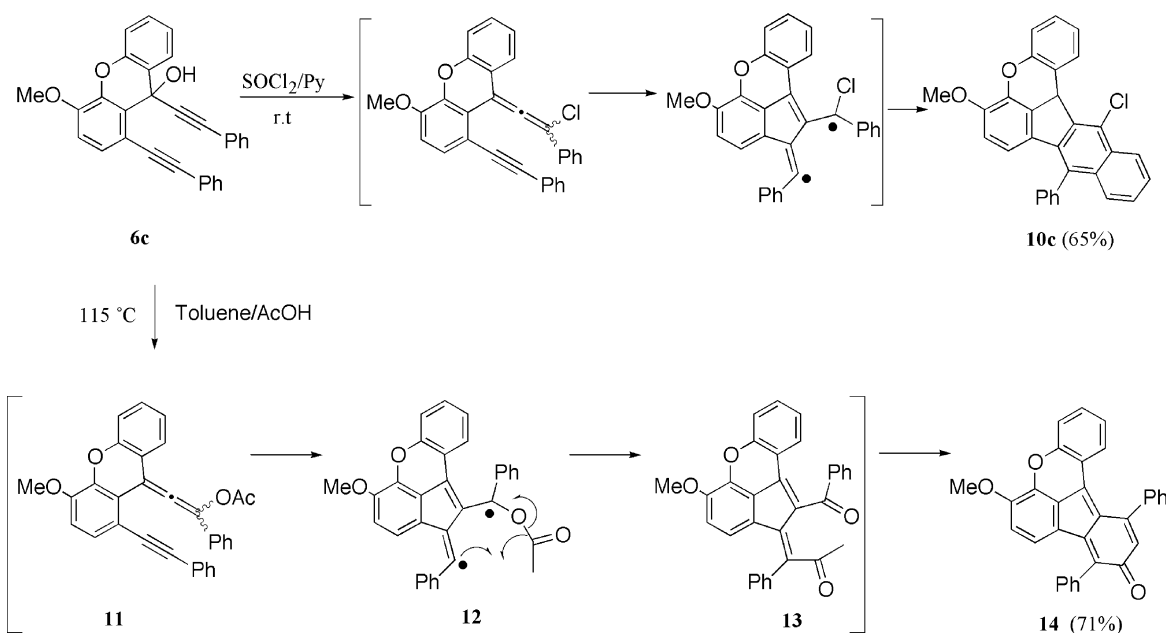
The tertiary propargyl alcohol **6b**<sup>8</sup> was much more reactive than the secondary alcohol **6a**, both under Wang's conditions and when heated. When **6b** was treated with thionyl chloride the chlorinated benzo[*b*]fluorene **10b** was obtained in an excellent 85% yield, presumably by Schmitt cyclization of benzo[*b*]fluorene generated in situ<sup>9</sup> and subsequent radical coupling; while thermolysis of **6b** took place at 115 °C in toluene giving the regioisomers **8b** and **9b**<sup>10</sup> in 52% and 25% yield, respectively. In the presence of a 10% volume of AcOH the reaction gave higher yields and the same regioisomer ratio (63% of **8b** and 32% of **9b**). It thus appeared that both secondary and tertiary propargylic alcohols were amenable to nonregioselective thermal cycloaromatization, but that only tertiary alcohols undergo the regioselective thionyl chloride induced process.

As was expected in view of the foregoing, the tertiary propargyl alcohol **6c**<sup>11</sup> reacted smoothly under Wang's conditions, giving the chlorinated benzo[*b*]fluorene **10c**<sup>10</sup> in 65% yield (Scheme 3). However, because of the rigidity of its skeleton, which prevents its  $\pi$ -electron moieties from becoming coplanar, **6c** is substantially less susceptible to thermal cycloaromatization than **6b** (no reaction was observed at 150 °C in toluene). It was

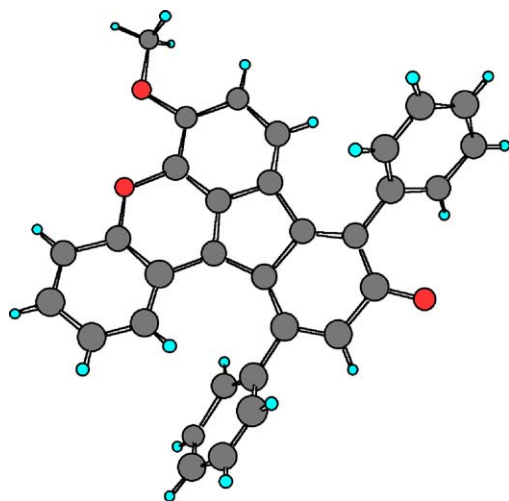
therefore to our surprise that when a 10% volume of acetic acid was used as cosolvent at 115 °C there occurred a smooth reaction giving the methylene-quinone **14**<sup>12</sup> in 71% yield (Scheme 3 and Fig. 1).

A plausible mechanism for the formation of **14** is that formation of the benzo[*b*]fluorene acetate **11** (presumably through rearrangement of the corresponding propargyl acetate)<sup>13</sup> is followed by Schmitt cyclization to the biradical **12** and intramolecular radical acylation, affording a dicarbonyl intermediate **13** that in the acidic working conditions would evolve to the final methylene-quinone **14** through an aldol-type condensation (Scheme 3). As far as we know, this would be the first example of intramolecular acylation of a biradical.<sup>14</sup> Some support for the hypothesized mechanism is provided by the finding that replacement of the acetic acid cosolvent with organic acids lacking  $\alpha$ -protons, such as TFA, benzoic acid, *p*-TsOH or formic acid, results in complex reaction mixtures with no methylene-quinone, a result that can be interpreted as due to the corresponding benzofulvenes **13**, which are unable to undergo aldol condensation, evolving by other pathways.

In conclusion, we have found that intramolecular formal [4+2] cycloaddition reactions of tertiary aryldiacetylene alcohols **6b,c** regioselectively afforded chlorinated benzo[*b*]fluorenes by mild treatment with thionyl chloride. In contrast, neutral or acidic thermolysis of secondary and tertiary substrates **6a,b** afforded



Scheme 3.

Figure 1. Chem3D representation of the solid-state structure of the *p*-methylene-quinone **14**.

benzo[*b*]fluorenols by nonregioselective cycloaromatization processes, and an unexpected *p*-methylene-quinone when starting from xanthenyl alcohol **6c**.

### Acknowledgements

Support of this work by the Spanish Ministry of Science and Technology in collaboration with ERDF (Projects BQU2002-01176 and BQ2002-02135), and by Johnson & Johnson Pharmaceutical Research and Development, is gratefully acknowledged. D. Rodríguez also thanks the University of Santiago de Compostela for a post-doctoral grant.

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  - Crystallographic data for the structure **14** in this paper, have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-211466. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44(0)-1223-336033 or e-mail: [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk)).
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