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# An Approach to the Synthesis of the Benzo[*b*]fluorene Core of the Kinamycins by an Arylalkyne-Allene Cycloaddition

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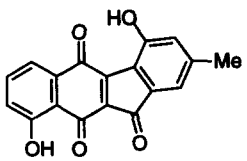
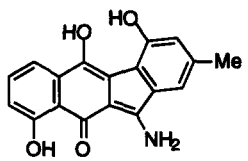
***Abstract:*** The cyclization of an arylalkyne to an allene followed by ring closure was applied for the ready construction of the tetracyclic core of the kinamycin family of antibiotics.


Benzo[*b*]fluorene natural products such as kinoscurinone (**1**), stealthin C (**2**), and cysfluoretin (**3**)[1] comprise a group of metabolites structurally related to the kinamycins[2] which display a variety of interesting biological activities.



**1**



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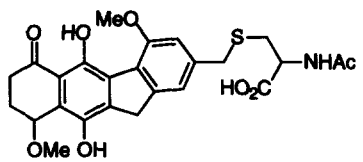
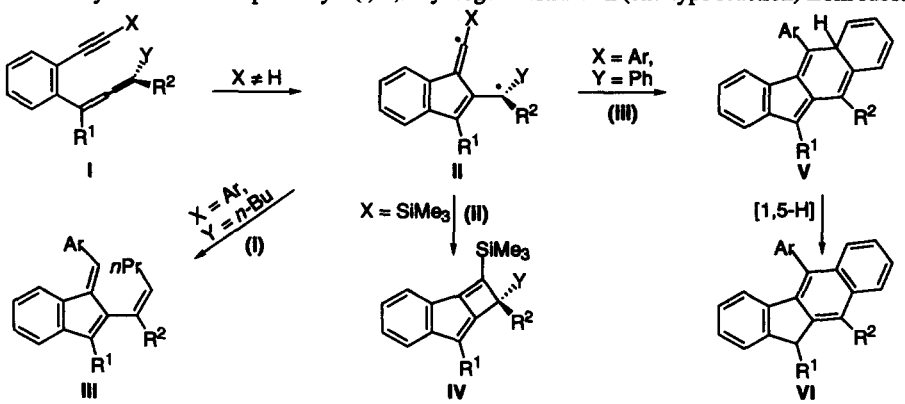


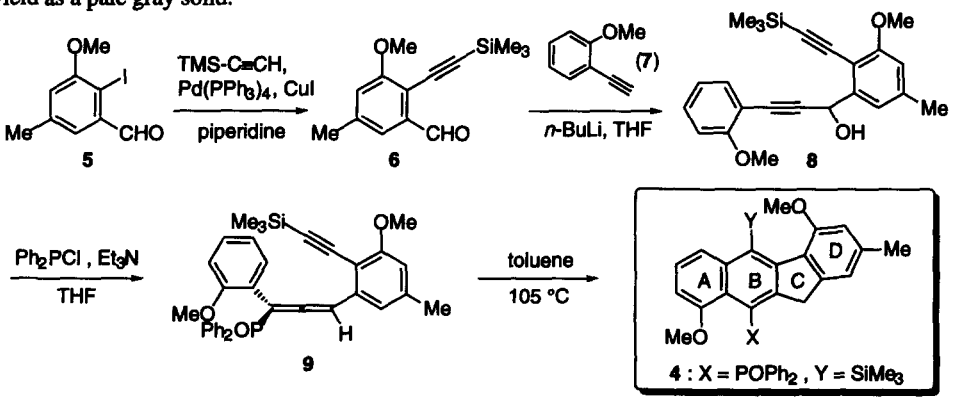
**3**

As part of a program on the synthesis of this type of naturally occurring quinones,[3,4] we decided to study the prospect of applying the novel [4+2] cycloaddition recently uncovered by Schmittel[5] for the construction of the tetracyclic nucleus of the benzo[*b*]fluorene antibiotics. Although arylalkyne-allenes ("masked enyne-allenes") **I** usually undergo a Myers-Saito[6] cyclization under thermal conditions to furnish naphthalene derivatives, terminally substituted alkynes (X ≠ H) have recently shown to suffer an alternative C-C bond formation between C-2 and C-6 (enyne-allene numbering) to form benzofulvene biradical **II**.[5,7] Intermediate **II** may then evolve by three different pathways: (i) 1,5-hydrogen abstraction (ene-type reaction) from substituent Y



to give benzofulvene **III**,[5] (ii) ring closure of the biradical to afford the formal [2+2] cycloadduct **IV** (X = $SiMe_3$),[7] or (iii) formation of a six-membered ring by collapse of the benzyl radical (Y = Ph or Ar) with the vinyl radical to form **V**, which can finally lead to benzo[*b*]fluorene **VI**.[5] Herein we report that a substrate **I** bearing both trimethylsilyl and aryl substituents on the alkyne and allene (X = $SiMe_3$, Y = Ar) preferentially undergoes a formal [4+2] cycloaddition (pathway iii) to give benzo[*b*]fluorene **4** bearing a substituent at C-11 different from aryl which could allow for the late transformation of ring B into a quinone.

Sonogashira coupling[8] of the aryl iodide **5**[9] with trimethylsilylacetylene gave **6** (23 °C; 54%), which was treated with the lithium acetylide of **7** (THF, 23 °C) to furnish **8** (80% yield) as a pale yellow solid. Phosphorylation of **8** with $Ph_2PCl$ and $Et_3N$ followed by [2,3] sigmatropic rearrangement (THF, -70 to -40 °C) gave stable allene **9**, which could be purified by flash column chromatography (93% yield).[5,6b] Finally, heating of **9** and excess 1,4-cyclohexadiene in toluene under reflux[5] gave **4** as the major compound, which was isolated in 38% yield as a pale gray solid.[10]




Therefore, this work demonstrates that the cyclization of trimethylsilyl aryls with allenes proceeds through pathway iii by preferential [4+2] cycloaddition to form a tetracyclic derivative. This cycloaddition can be applied for the ready construction of benzo[*b*]fluorenes with the substitution pattern shown by the kinamycins. Application of this strategy for the synthesis of members of this family of antibiotics is in progress.

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## References and Notes

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9. Iodoaryl **5** was prepared by iodolysis (*ca.* 80 % yield) of the corresponding known tributylstannane.[3]
10. The NMR spectra of **4** showed line broadening ($CH_2$ in $^1H$ NMR and some aromatic signals in $^{13}C$ NMR) characteristic of hindered rotation of the phosphine oxide. For a similar results, see: Schmittel, M.; Kiau, S. *Liebigs Ann./ Recueil* **1997**, 733.

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