

The novel transition metal free synthesis of 1,1'-biazulene

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Abstract—Reaction of 1-azulenyl methyl sulfoxide (**1**) under acidic conditions gave the 1,1'-biazulene derivative **3**. Methylmercapt groups of **3** were readily converted to formyl groups by Vilsmeier reaction to afford 3,3'-diformyl-1,1'-biazulene (**4**), which reacted with pyrrole in the presence of acetic acid to give the parent 1,1'-biazulene (**5**). Reaction of **5** with pyridine in the presence of Tf₂O gave 3,3'-dihydropyridyl-1,1'-biazulene derivative **6**. 3,3'-(4-Pyridyl)-1,1'-biazulene (**7**) was obtained by the reaction of **3** with KOH in EtOH at room temperature in good yield.

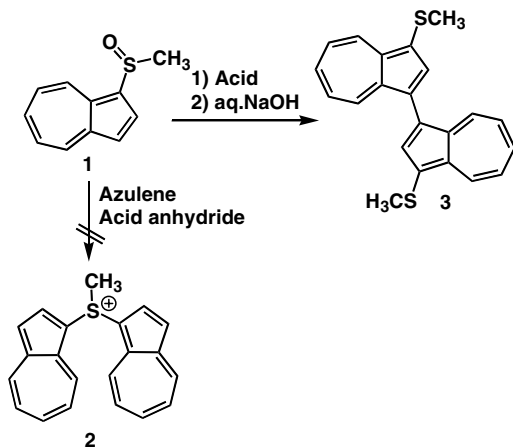
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Recently, a number of transition metal-mediated aryl–aryl coupling reactions such as Stille-,¹ Suzuki-,² and Ullmann-type reactions³ have been developed for the facile synthetic methodologies to construct the biaryl compounds. In case of azulene derivatives, Morita and Takase reported the synthesis of biazulenes using Ullmann reaction. However, the reaction required very high temperature.⁴ In 1985, Iyoda and co-workers also reported nickel-mediated synthesis of the parent 1,1'-biazulene (**5**), but the procedure afforded 1,1',3',1''-ter- and 1,1':3',1'':3'''-quaterazulenes as by-products.⁵ Razus and co-workers reported the reaction of *N*-(azulenyl-1-yl-methylene)arylamines with FeCl₃ afforded the 1,1'-biazulene derivatives in mild condition and reaction mechanism was supposed as a radical reaction.⁶ Recently, we have reported the transition metal-catalyzed synthesis of arylazulenes.⁷ However, transition metal-catalyzed synthesis of 1,1'-biazulenes might be difficult because of instability of 1-haroazulenes required. Moreover, preparation of metal reagents for the coupling reaction is not easy and the most promising borane reagent is unstable to exhibit easy hydrolysis to afford hydrocarbon derivative.⁸ Herein, we report the transition metal and coupling metal reagent free synthesis and pyridinylation of 1,1'-biazulene (**5**).

Recently, we have reported the synthesis and properties of tri(1-azulenyl)methyl cations⁹ and di(1-azulenyl)-*p*-tolylamines.¹⁰ As the part of these studies, we have attempted the preparation of (1-azulenyl)sulfonium ion. Previously, the preparation of triphenylsulfonium ion has been reported by reaction of diphenylsulfoxide and benzene derivatives in the presence of trifluoromethanesulfonic anhydride (Tf₂O).¹¹ We examined the synthesis of di(1-azulenyl)methyl sulfonium ion (**2**) using the similar reaction conditions as described in the literature. At first, the reaction of 1-azulenyl methyl sulfoxide (**1**)¹² with acid anhydride such as Tf₂O, trifluoroacetic anhydride, and acetic anhydride was investigated. In these cases, we expected the formation of di(1-azulenyl)methyl sulfonium ion (**2**). However, the reaction of **1** with azulene in the presence of trifluoromethanesulfonic anhydride or trifluoroacetic anhydride did not afford the desired product **2**, but decomposition of **1** was observed. Furthermore, the sulfoxide **1** did not react with azulene in the presence of acetic anhydride and starting materials were recovered. However, we found that the unexpected compound, 1,1'-biazulene derivative **3**, was obtained by changing the acid anhydrides to the corresponding acids. Reaction of **1** with trifluoroacetic acid at 0 °C afforded 3,3'-methylmercapt-1,1'-biazulene (**3**)¹³ as a sole product in 89% yield. Similarly, sulfoxide **1** reacted with 60% HPF₆ and HCl to give **3** in 87% and 75% yield, respectively. However, trifluoromethanesulfonic acid and sulfuric acid were revealed not to be efficient for this coupling reaction because of the decomposition of the azulene under these reaction conditions.

Keywords: Azulene; Biazulene; Aryl–aryl coupling; Pyridinylation.

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Scheme 1.

Table 1. Synthesis of 3,3'-methylmercapt-1,1'-biazulene (3)

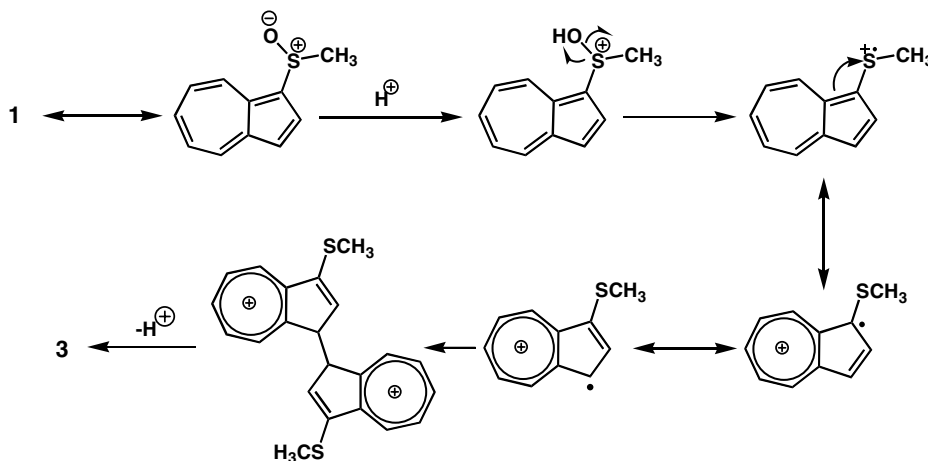
Entry	Acid	Reaction time	Yield (%)
1	CF ₃ CO ₂ H	5 min	89
2	60% HPF ₆	5 min	87
3	37% HCl	5 min	75
4	CF ₃ SO ₃ H	5 min	39
5	H ₂ SO ₄	5 min	Decomp.
6	CCl ₃ CO ₂ H	24 h	No reaction
7	CH ₃ CO ₂ H	24 h	No reaction

No reaction was observed when trichloroacetic acid and acetic acid were used as an acid (Scheme 1 and Table 1). Although the detail reaction mechanism of this reaction

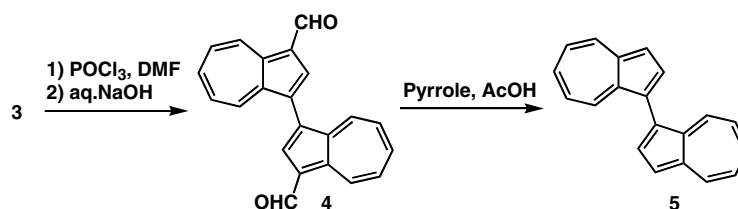
is unclear, reaction was might be radical mechanism such as Razus et al. previously reported (Scheme 2).

There are several reports for the preparation of 1,1'-biazulenes, but those methodologies require high temperature or transition-metal reagents.^{4,5} In this method, the reaction proceeds under much milder conditions and very short reaction time within 5 min. Furthermore, this method does not require prior modification of azulene such as halogenation, borylation, or stannylation. Therefore, this synthetic strategy may have great advantage comparing with the transition metal-mediated synthesis of 1,1'-biazulenes.

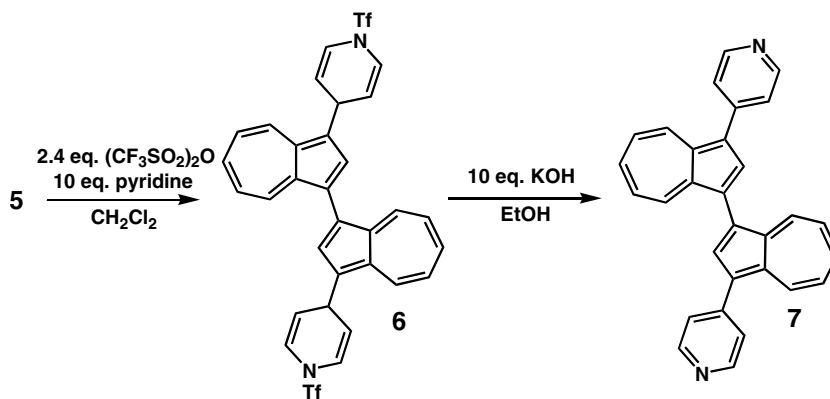
To evaluate this methodology, we attempted the conversion of product 3 to the parent 1,1'-biazulene (5). In 1962, Hafner et al. have reported that 1,3-dialkyl-substituted azulene derivatives undergo the electrophilic *ipso*-substitution such as Friedel–Crafts acylation and Vilsmeier formylation at the 1 and/or 1,3-positions.¹⁴ We found that as similar to the reaction of 1,3-dialkyl-substituted azulenes, 3,3'-formyl-1,1'-biazulene (4)⁶ was obtained by Vilsmeier formylation of 3 in 90% yield. This is the first example that the methylmercapt group behaved as a leaving group in electrophilic *ipso*-substitution in the azulene chemistry. Thus, the methylmercapt group can be regarded as a synthon of the formyl group, which is useful functional group in organic synthesis. Conversion to the parent 1,1'-biazulene (5) from the formyl compound 4 was established by the reaction with pyrrole in acetic acid.¹⁵ The reaction of 4 with pyrrole in acetic acid gave the corresponding 1,1'-biazulene (5) in 71% yield (Scheme 3).¹⁶



Scheme 2.



Scheme 3.



Scheme 4.

For the further expansion of the never reported π -electron system and heteroarylation of 1,1'-biazulene (5), pyridinylation of 1,1'-biazulene (5) at the 3- and 3'-positions was also investigated. Recently, we have demonstrated that the reaction of azulene with the triflate of N-containing heterocycles, which are readily available from the reaction of N-containing heterocycles with Tf_2O , gives 1-(dihydroheteroaryl)- and 1,3-bis(dihydroheteroaryl)azulene derivatives.¹⁷ The transformation from the dihydroarylazulene derivatives to 1-heteroaryl- and 1,3-bis(heteroaryl)azulene derivatives opened a new two-step strategy for the heteroarylation of azulene.¹⁸ The pyridinylation of 1,1'-biazulene (5) was established by the procedure similar to the other azulene derivatives reported. The reaction of 5 with pyridine in the presence of Tf_2O gave 3,3'-dihydropyridyl-1,1'-biazulene derivative 6 in 85% yield. The desired 3,3'-(4-pyridyl)-1,1'-biazulene (7)¹⁹ was obtained by the reaction of product 6 with KOH in EtOH at room temperature in 95% yield (Scheme 4).

In conclusion, we have established the novel synthesis of the parent 1,1-biazulene (5). Reaction of 1-azulenyl methyl sulfoxide (1) with an acid gave 1,1'-biazulene derivative 3. Methylmercapt groups of 3 were readily converted to formyl groups by Vilsmeier reaction. 3,3'-Formyl-1,1'-biazulene (4) reacted with pyrrole in acetic acid to afford the parent 1,1-biazulene (5). We also established the further transformation of the pyridinylation of 1,1-biazulene (5) to expand the π -electron conjugation system of 5. Reaction of 5 with pyridine in the presence of Tf_2O gave 3,3'-dihydropyridyl-1,1'-biazulene derivative 6, which reacted with KOH in EtOH at room temperature to afford the presumed 3,3'-(4-pyridyl)-1,1'-biazulene (7). Further expansion of π -electron systems using the 1,1'-biazulene core and physical properties of these new compounds are now investigated in our laboratory.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.tetlet.2007.05.109](https://doi.org/10.1016/j.tetlet.2007.05.109).

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- Synthesis of 3,3'-methylmercapt-1,1'-biazulene (3)*: to a solution of 1-azulenyl methyl sulfoxide (1) (190 mg,

- 1.00 mmol) in CH_2Cl_2 (10 mL) was added CF_3COOH (10 mL) and stirred for 5 min. The reaction mixture was poured into 1 M NaOH, extracted with toluene, and purified by column chromatography on silicagel with hexane/AcOEt = 4:1 to give 1,1'-methylsulfanyl-3,3'-biazulene (**3**) (154 mg, 89%) as brown crystals; ^1H NMR (400 MHz, CDCl_3) δ = 8.62 (d, 2H, J = 10.4 Hz, H-8), 8.24 (d, 2H, J = 10.4 Hz, H-4), 8.11 (s, 2H, H-2), 7.59 (t, 2H, J = 10.4 Hz, H-6), 7.20 (t, 2H, J = 10.4 Hz, H-7), 7.06 (t, 2H, J = 10.4 Hz, H-5), and 2.56 (s, 6H, 3,3'-SCH₃); ^{13}C NMR (100 MHz, CDCl_3) δ = 140.45, 139.55, 139.17, 138.23, 136.45, 135.65, 125.13, 123.68, 123.14, 121.63, and 20.29 (3,3'-SCH₃); HRMS (ESI) calcd for $\text{C}_{22}\text{H}_{18}\text{S}_2$ [M]⁺: 346.0850. Found: 346.0844; Anal. Calcd for $\text{C}_{22}\text{H}_{18}\text{S}_2$: C, 76.26; H, 5.24. Found: C, 75.98; H, 5.46.
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19. *Compound 7*: green crystals; ^1H NMR (400 MHz, CDCl_3) δ = 8.72 (d, 4H, J = 4.8 Hz, H-2,6 of pyridine), 8.66 (d, 2H, J = 9.6 Hz, H-4), 8.42 (d, 2H, J = 9.6 Hz, H-8), 8.25 (s, 2H, H-2), 7.68 (t, 2H, J = 9.6 Hz, H-6), 8.66 (d, 2H, J = 9.6 Hz, H-4), 7.62 (d, 4H, J = 4.8 Hz, H-3,5 of pyridine), 7.27 (t, 2H, J = 9.6 Hz, H-5), and 7.17 (t, 2H, J = 9.6 Hz, H-7); ^{13}C NMR (100 MHz) δ = 150.04, 144.69, 139.67, 139.34, 138.25, 137.19, 136.76, 135.71, 127.28, 125.53, 124.76, 124.46, and 124.24; HRMS (ESI) calcd for $\text{C}_{30}\text{H}_{20}\text{N}_2+\text{H}$ [$\text{M}+\text{H}$]⁺: 409.1705. Found: 409.1699.