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PII: S0040-4039(18)31440-0
DOI: https://doi.org/10.1016/j.tetlet.2018.12.008
Reference: TETL 50471

To appear in: *Tetrahedron Letters*

Received Date: 5 November 2018
Revised Date: 28 November 2018
Accepted Date: 3 December 2018

Please cite this article as: Umeda, R., Shimizu, Y., Ida, Y., Ikeshita, M., Suzuki, S., Naota, T., Nishiyama, Y., Facile and practical synthesis of π-extended oxepins by benzannulation and intramolecular cyclization, *Tetrahedron Letters* (2018), doi: https://doi.org/10.1016/j.tetlet.2018.12.008

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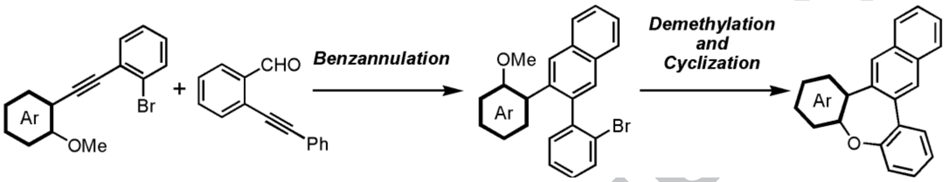

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Tetrahedron Letters
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Facile and practical synthesis of π-extended oxepins by benzannulation and intramolecular cyclization

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Oxepin
Benzannulation
Intramolecular cyclization
Copper catalyst

ABSTRACT

π-Extended oxepins **1** and dimer **8** were synthesized by the benzannulation of the corresponding asymmetric diarylacetylene derivatives and 2-(phenylethynyl)benzaldehyde followed by the Cu-catalyzed intramolecular cyclization. The optical properties of the π- extended oxepins **1** and **8** are also investigated.

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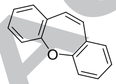
The dibenzo[*b,f*]oxepin derivative are known to display a wide range of biological activity and pharmaceutical properties and are expected to be used as broad pharmacological application such as antipsychotic, antidepressant, therapeutic agents, and so on.[1] Therefore, the synthesis of their derivatives has been intensively investigated.[2,3] On the other hand, it has been recently reported that a derivative having a tribenzo[*b,d,f*]oxepine skeleton can be used as an organic EL device, and further utilization of the π-extended oxepin derivatives would be expected.[4,5]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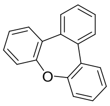
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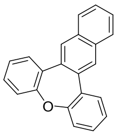
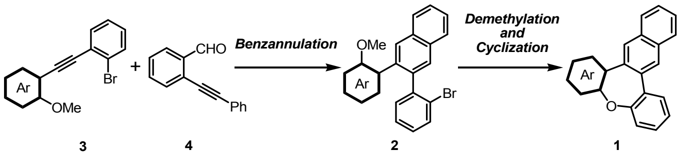

dibenzo[*b,f*]naphth[2,3-*d*]oxepin

Compared to derivatives of dibenzo[*b,f*]oxepin and tribenzo[*b,d,f*]oxepin, examples of the synthetic methods of dibenzo[*b,f*]naphth[*2,3-d*]oxepin and its derivatives are still rare. Ila and coworker have accomplished the first synthesis of dibenzo[*b,f*]naphth[*2,3-d*]oxepin from 10,11-dihydrodibenzoxepin-10-one as starting material, though this synthetic method required multiple steps.[6] Very recently, Korean[5b] and Japanese[7] groups reported independently the synthesis of dibenzo[*b,f*]naphth[*2,3-d*]oxepin derivative by the Pd-catalyzed annulative two-fold cross-coupling of dibromo diphenylether derivative and diborylnaphthalene derivative or dibromonaphthalene derivative and cyclic diarylborinic acid, respectively.[8]

We now plan to synthesize the dibenzo[*b,f*]naphth[*2,3-d*]oxepin derivatives **1** by the demethylation and intramolecular cyclization of **2**, which could be prepared by the Asao and Yamamoto benzannulation reaction[9,10] of asymmetric diarylacetylene **3** and 2-(phenylethynyl)benzaldehyde (**4**) (Scheme 1).



Scheme 1

The synthesis of π-extended oxepins **1** is shown in Scheme 2. First, 1-iodo-2-methoxybenzene derivatives **5a-c** and 1-iodo-2-methoxynathpthlene (**5d**) as starting materials can be easily prepared by direct iodination of the corresponding aromatic compounds with iodine and periodic acid.[11] The Sonogashira coupling of 1-iodo-2-methoxybenzene derivatives **5a-c** or 1-iodo-2-methoxynathpthlene (**5d**) and 1-bromo-2-ethynylbenzene (**6**) gave the corresponding asymmetric diarylacetylene derivatives **3a-d** in excellent yields. The Cu-catalyzed benzannulation of 2-(phenylethynyl)benzaldehyde (**4**) and **3a-c** in the presence of the trichloroacetic acid afforded **2a-c** in good yields. In the case of sterically bulky **2d**, the yield of **2d** was slightly lower than those of **2a-c** and **2d** was obtained as an inseparable mixture of rotamers (3:2). Finally, the demethylation of **2a-d** by the treatment with BBr_3 under -78 ˚C occurred to form **7a-d** followed by the Cu-catalyzed intramolecular cyclization to give the π-

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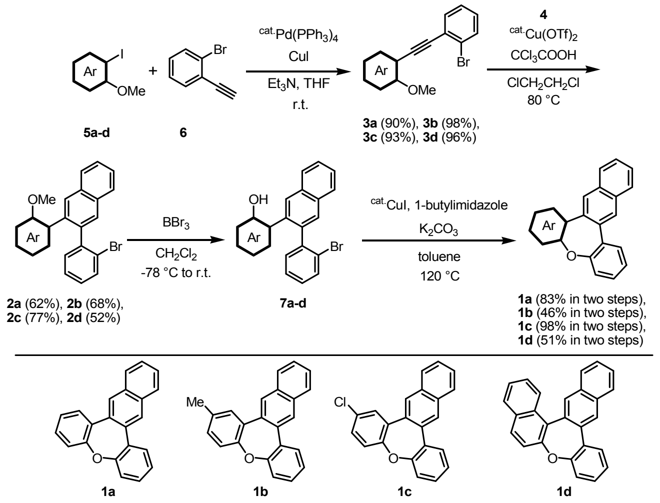
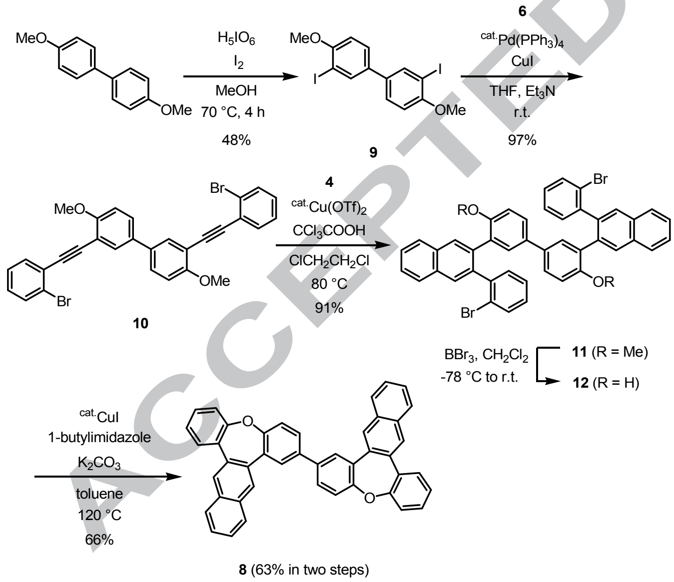
extended oxepins **1a-d** in moderate to excellent yields. The yield of **1b** having methoxy group, electron donor group, is lower than those of **1a** and **1c**. These results are probably due to the acidity of hydroxy groups of **7**.



Scheme 2

Next, the dibenzo[*b,f*]naphth[*2,3-d*]oxepin dimer **8** was also prepared in same manner as described for **1** (Scheme 3). First, the double iodination of 4,4'-dimethoxybiphenyl gave 3,3'-diiodo-4,4'-dimethoxybiphenyl (**9**). Sonogashira coupling of **9** and 1-bromo-2-ethynylbenzene (**6**) afforded **10** and then Cu-catalyzed benzannulation with 2-(phenylethynyl)benzaldehyde (**4**) gave **11** in 91% yield. The dibenzonaphthoxepin dimer **8** was obtained by demethylation and intramolecular cyclization.



Scheme 3

In order to investigate the photophysical properties of π-extended oxepin derivatives **1a-d** and **8**, we measured the UV-vis spectra in dichloromethane solvent and their results are shown in Figure 1 and Table 1. When UV-vis absorption spectra of **1a** was measured, a strong broad and shoulder peaks were observed 265 nm and around 290 nm, respectively, and the absorption of **1a** was observed up to 330 nm. In the case of **1b** substituted with a methyl group, the absorption wavelength did not change greatly, though the molar extinction coefficient of **1b** observed significantly larger than that of **1a**. UV-vis absorption spectra of **1c** substituted with a chlorine group exhibited almost the same as that of **1a**. In the absorption spectra of **1d** having two naphthalene rings, a new broad absorption was observed at 277 nm and at 331 nm. On the other hand, in the UV-vis absorption spectra of the dimer **8**, the absorption wavelength was not shifted as compared with that of the monomer **1a**, and the molar absorption coefficient at 265 nm was only increased. This result suggests that no effective conjugation is working between the two oxepin units. Although the fluorescence spectra of π-extended oxepin derivatives **1a-d** and **8** were measured, no fluorescence emission was observed.

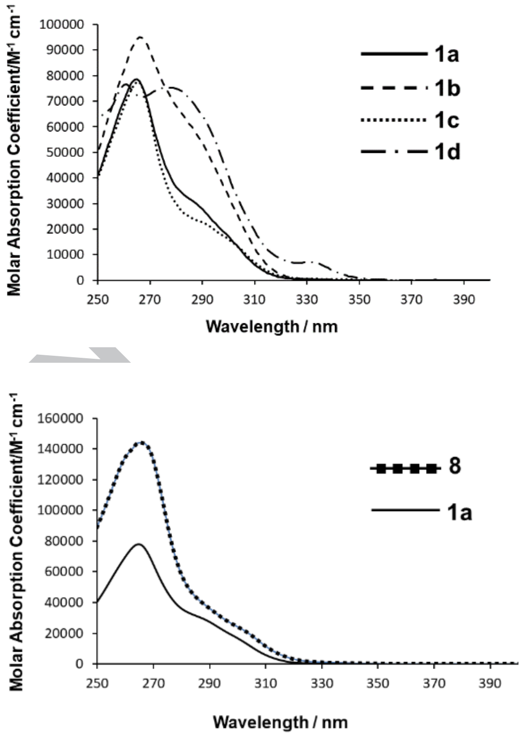


Figure 1. UV-vis absorption spectra of π-extended oxepin derivatives **1a-d** and **8** in CH_2Cl_2.

Table 1. Optical properties of π-extended oxepin derivatives **1** and **8** in CH_2Cl_2

	Absorption[a] λ_{abs} / nm (ε / $M^{-1}cm^{-1}$)
1a	265 (77500), 290 (*sh*, 22600)
1b	266 (95000), 290 (*sh*, 53600)
1c	265 (78600), 290 (*sh*, 27800)
1d	261 (76700), 277 (75300), 331 (7100)
8	265 (144100), 290 (*sh*, 36000)

[a] [c] = ~10^{-5} M.

In conclusion, we succeeded in the synthesis of π-extended oxepin derivatives **1a-d** and **8** by the Cu-catalyzed benzannulation and intramolecular cyclization. The preparation of various substituted π-extended oxepin derivatives using this methodology is being undertaken in our laboratories. Also, further study will be focused on the computational analysis of them and progress will be reported in due course.

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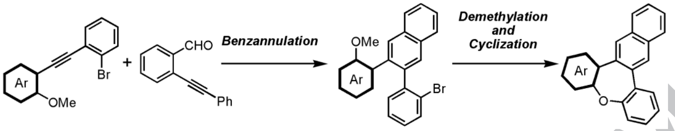

Highlights

A copper catalyzed seven-membered ring system is described.
A new synthetic method of the π-extended oxepins is developed.
Photophysical properties of π-extended oxepins are disclosed.

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