

# Synthesis and Structure of Macrocyclic Diaza-bis-enediynes

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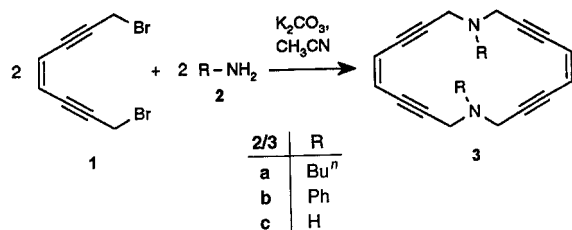
The reaction of 1,8-dibromooct-4-ene-2,6-diyne (**1**) with secondary amines, such as *n*-butylamine (**2a**), yields macrocyclic 2:2 substitution products **3**; the structure of **3a** was investigated by X-ray crystallography.

We recently reported the synthesis of **1** and its facile reaction with malonates to yield macrocyclic bis-enediynes.<sup>1</sup> Heteroatom nucleophiles of weak basicity, such as phenolates or carboxylates, are also suitable reactants for replacing the two prop-2-ynyl bromine substituents of **1**.<sup>2</sup> In this paper we report our attempts at using nitrogen nucleophiles in the ring-closing reaction with **1**.

Equimolar amounts of **1** and *n*-butylamine (**2a**) were allowed to react in CH<sub>3</sub>CN in the presence of K<sub>2</sub>CO<sub>3</sub> as base at room temperature. Compound **3a** was isolated as the only product by column chromatography. The isolated yields are low because of the competing decomposition of the starting material **1** and the product **3a** under the reaction conditions and during isolation. However, neither smaller (1:1) nor larger alkylation products could be detected in the reaction mixture. The absence of nine-membered 1:1 alkylation products is to be attributed to the insufficient driving force of the nucleophilic displacement reaction for the synthesis of a highly strained compound.

The reaction of **1** with aniline (**2b**) yielded small amounts of the labile compound **3b**. The compound is not stable and decomposes rapidly. The rapid decomposition of all the synthesized diaza-bisenediynes may be rationalized by a base-induced prop-2-ynyl-allene isomerisation. The resulting ene-yne-allene is not stable at room temperature because of the facile Myers–Saito<sup>3</sup> cyclisation.

The reaction of **1** with NH<sub>3</sub> gave **3c** in 25% yield. The possible reaction of **3c** with a third molar equivalent of **1** was not observed.



Scheme 1

Single crystals of **3a** were obtained by slow evaporation of a chloroform solution. The X-ray structure shows a twisted conformation for the macrocyclic bis-enediyne. The distances between the acetylenic enediyne carbons C(10)—C(15) and C(2)—C(7) are 420.8 and 421.5 pm, respectively.

**Crystal data for 3a.**† C<sub>24</sub>H<sub>30</sub>N<sub>2</sub>, *M<sub>r</sub>* = 346, *F*(000) = 1504, orthorhombic, *a* = 1023.8(3), *b* = 1716.4(7), *c* = 2455.4(4) pm, *V* = 4.315(2) nm<sup>3</sup>, space group *Pbca*, *Z* = 8, *D<sub>x</sub>* = 1.067 Mg m<sup>-3</sup>, *T* = 143 K. A pale yellow prism, ca. 0.8 × 0.7 × 0.5 mm, was mounted on a glass fibre in an inert oil and transferred to the cold gas stream of a Stoe STADI-4 diffractometer with a Siemens LT-2 low-temperature attachment. A

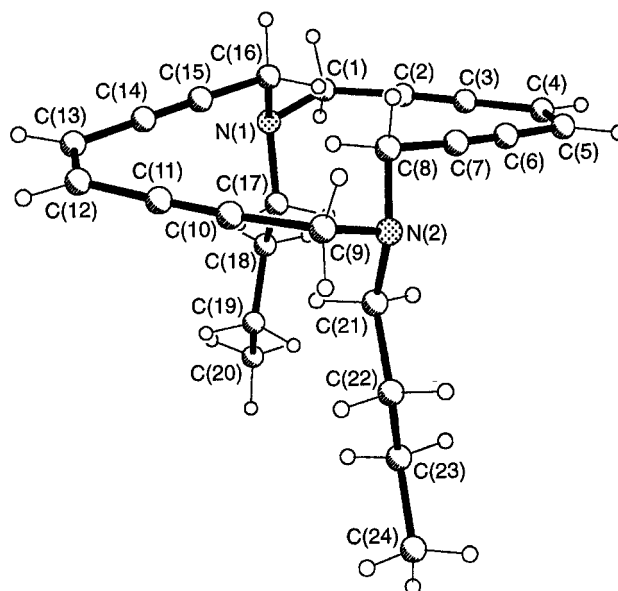


Fig. 1 Molecular structure of 1,10-dibutyl-1,10-diazacycloocta-5,14-diene-3,7,12,16-tetrayne (**3a**)

total of 5313 intensities (3799 unique, *R<sub>int</sub>* = 0.0431) were measured to 2θ 50°. The structure was solved by direct methods and refined anisotropically on *F*<sup>2</sup> (program SHELXL-93, G. M. Sheldrick, University of Göttingen). The final *wR*(*F*<sup>2</sup>) for all reflections was 0.19, with a conventional *R*(*F*) of 0.086, for 236 parameters. The high *R* values may be attributed to the appreciable thermal motion (or slight disorder) of the *n*-butyl side chains.

In summary, a one step procedure for the synthesis of very labile 18-membered macrocyclic diaza-bisenediynes *via* two-fold *N*-alkylation of amines has been described.

Techniques used: <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR, UV, MS, elemental analysis, X-ray diffraction

References: 4

Table 2: Atomic coordinates and equivalent isotropic displacement parameters for **3a**

Table 3: Intramolecular bond distances and angles for **3a**

Appendix: packing diagram for **3a** and Fig. 1 with thermal ellipsoids

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†Atomic coordinates, thermal parameters and bond lengths and angles are given in the full text and have also been deposited at the Cambridge Crystallographic Data Centre (CCDC). Any request to the CCDC for this material should quote the full literature citation and the reference number 423/2.