

0040-4039(94)02345-X

Synthesis of Monomeric and Oligomeric Naphtho- and Biaryl-fused 1,8-Diaza-14-crown-4 Macrocycles

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Abstract: Efficient syntheses of naphtho- and biaryl-fused 1,8-diaza-14-crown-4 macrocycles 4a, 4b, 7a, and 7b and related oligometric systems 11 and 15 are described. An X-ray structure determination for the <u>N.N</u>-dicyanomethyl substituted macrocycle 8 is reported.

Macrocycles with coordination sites for metals and extended π -chromophores are candidates for the study of nonlinear optical properties.¹ Chemical enhancements of the intrinsically large third-order nonlinear susceptibilities of noble metal nanoparticles² have been achieved by the study of solid suspensions of silver colloids in cyanoalkyl functionalized polymeric systems.³

Herein we report a significant extension of the bimolecular cyclization process⁴ to the synthesis of monomeric and oligomeric naphtho- and biaryl-fused 1,8-diaza-14-crown-4 macrocycles **4a**, **4b**, **7a**, **7b**, **11** and **15**. The efficient formation of **4a** and **4b** to the apparent exclusion of monomolecular cyclization products (the benzoxazepinone ring system)^{4a} is particularly remarkable in light of the steric hindrance at C(1) of **3a** and **3b**. The tolerance of potentially reactive substituents (fluoride in **4b** and **7b**) to the conditions for bimolecular cyclization also is noteworthy. X-ray characterization of the <u>N</u>N-dicyanomethyl substituted macrocycle **8** suggests that composite formation with silver nanoparticles² should be possible.



The preparation of substrates for the bimolecular cyclization experiments was dependent on the outstanding ability of fluoride to direct <u>ortho</u>-metallation.⁵ To a solution of 1-fluoronaphthalene (1a) and TMEDA (1 equiv) in THF at -78 °C was added <u>sec</u>-BuLi (1.3 M in cyclohexane, 1 equiv). After 3 h at -78 °C the reaction mixture was added to dry ice in ether. Acidification, extractive workup and solvent evaporation provided crystalline 1-fluoronaphthalene-2-carboxylic acid (2a) in ~ quantitative yield (mp 192-3 °C; lit mp 193-4 °C⁶). An analogous procedure involving 1,5-difluoronaphthalene⁷ gave the previously unreported 1,5-difluoronaphthalene-2-carboxylic acid (2b, 212-4 °C) in 74% yield.

Naphthalene-2-carboxylic acids 2a and 2b were converted to 3a and 3b (product yields shown) and bimolecular cyclization with NaH in DMF at ambient temperature provided the <u>bis</u>-naphtho-fused macrocycles 4a (mp >292 °C; chemical ionization HRMS, m/z calc for M+1 $C_{26}H_{22}N_2O_4$ 427.1658, found 427.1649) and 4b (292-3 °C).

The conversions of commercially available 4-fluorobiphenyl and 4,4'-difluorobiphenyl to $5a^5$ and 5b enabled syntheses of macrocycles 7a (mp 252-3 °C) and 7b (mp 267-271 °C). Reduction of 7a with LiAlH4 in ether and benzene (1:1) provided the diamine (73%, mp 175-6 °C; chemical ionization HRMS, m/z calc for M+1 C₃₀H₃₀N₂O₂ 451.2385, found 451.2359) and <u>bis</u>-alkylation with NaH/BrCH₂CN in THF at ambient temperature gave the <u>N,N</u>-dicyanomethyl substituted macrocycle **8** (68%, mp 215-218 °C).



The X-ray determined molecular structure of 8 is shown in Figure 1; the minimum distance between nitrogen atoms of cyanomethyl substituents on adjacent molecules was found to be 3.96Å. Crystal growth experiments with 8 under conditions that facilitate the formation of solid suspensions of colloidal silver^{2,3} could provide materials with useful nonlinear optical properties.



Figure 1. Molecular structure of 8

The <u>bis</u>-carboxylations of 1b and 12 with excess <u>sec</u>-BuLi/TMEDA gave 9 (mp >287 °C dec) and 13 (mp >285 °C). The derived <u>bis</u>-carboxamides 10 and 14 were subjected to macrocyclization/oligomerization in DMF/NaH at ambient temperature. After four days at room temperature, DMF was removed by distillation at reduced pressure (<75 °C) and the resulting colorless solid material was washed several times with water and then methanol to remove unreacted monomer and low molecular weight materials. The residue was dried to give the highly insoluble (DMF, DMSO, THF) ladder-type oligomer 11 in 84% yield.⁸



An analogous procedure provided oligomer 15 in 89% isolated yield. ¹H NMR spectral data demonstrate that the oligomer structure is as shown rather than a chain; clearly defined resonances for CH₂N and CH₂O appear at δ 3.78 and 4.29 (D₆-DMSO) nearly superimposable with resonances for these protons in 7a rather than at ~3.3 and 3.5, which is characteristic of these protons in acyclic structures such as 14. Oligomer 15 is considerably more soluble in DMF and DMSO than 11 because of the relatively flexible biaryl connections. GPC analysis indicated that the average molecular weight of 15 is ~5000. It is probable that the moderate degree of polymerization of 14 (and presumably 10) is a result of insolubility of the growing oligomers or possibly termination as a result of intramolecular alkoxide displacement of fluoride; e.g., formation of an end-group benzoxazepinone ring.^{4a}



It should be clear from the chemistry reported in this note that the bimolecular cyclization method for construction of 1,8-diaza-14-crown-4 macrocycles will provide molecular systems with a wide range of π -chromophores, <u>bis</u>-fused to the macrocyclic core. The unprecedented synthesis of oligomers that contain alternating macrocyclic and aromatic units should provide interesting new molecular systems for nonlinear optical studies.⁹ It is expected that higher polymers will be obtainable by placement of substituents on monomeric substrates corresponding to <u>10</u> and <u>14</u> to increase solubility of the growing oligomer.

Acknowledgment. We thank Dr. F. S. Tham for the X-ray structure determination and the ICSC World Laboratory for a scholarship to Zihong Guo. We thank Professor J. Moore and Dr. S. Kaur for assistance with the GPC studies.

References and Notes

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(Received in USA 28 September 1994; revised 1 November 1994; accepted 1 December 1994)