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Meta-terphenyls as Building Blocks for Benzimidazolophanes

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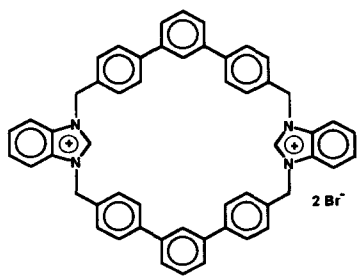
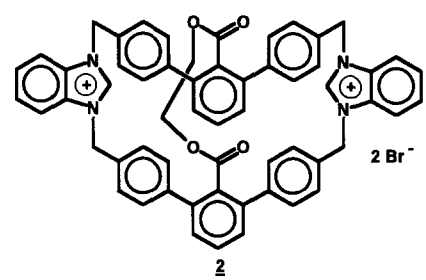
Abstract: Coupling of the dibromide **4** and the tetrabromide **6** with benzimidazole gave the benzimidazolophanes **1** and **2** respectively. © 1997 Elsevier Science Ltd.

Cyclophanes with large molecular cavity[2] and intra-annular functionality[3] can function as selective hosts. Recently, synthesis of cyclophanes with heterocyclic ring system like pyridinophanes,[4] ureaphanes[5] has gained additional impetus. We describe here a simple and short convergent synthesis to new benzimidazolophanes **1** and **2** that incorporate *m*-terphenyl moiety.

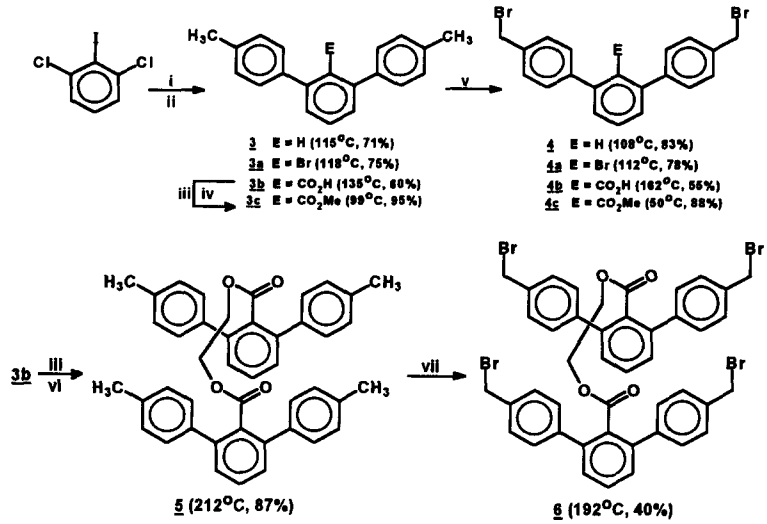


1



2

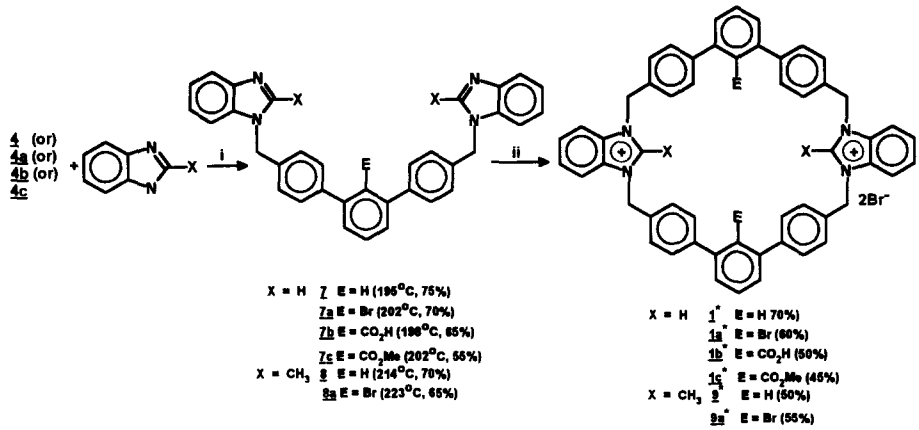
The *m*-terphenyl frame work in **1** and **2** is obtained by known tandem-aryne sequence.[6] Addition of three equivalents of *p*-tolylmagnesium bromide to 2,6-dichloroiodobenzene followed by quenching with aqueous acid or bromine or carbon dioxide resulted in the formation of **3, 3a,** and **3b (Scheme 1)**. **3c** was obtained from **3b** using diazomethane or thionyl chloride followed by refluxing with methanol. Two fold radical bromination of **3, 3a, 3b** and **3c** gave the dibromides **4, 4a, 4b** and **4c.** Reaction of the disodium salt of ethylene glycol with the acid chloride of **3b** gave ester **5**, which on four fold radical bromination afforded the tetrabromide **6.**



i. *p*-Tolylmagnesiumbromide (3 eq.), THF, reflux; ii. H_3O^+ or Br_2 or CO_2 and H_3O^+. iii. $SOCl_2$, C_5H_5N, CH_2Cl_2, rt. iv. CH_3OH, reflux, 10 min. v. NBS (2 eq.), CCl_4, Bz_2O_2, reflux. vi. $NaOCH_2CH_2ONa$, DMF, 55°C. vii. NBS (4 eq.), CCl_4, Bz_2O_2

Scheme 1

Reaction of two equivalents of benzimidazole with one equivalent of *m*-terphenyl dibromide **4** in acetonitrile for 48 hours at room temperature afforded **7** after purification on alumina. ^{1}H NMR of **7** showed the -NCH_2- protons as a singlet at δ5.38 in addition to the aromatic protons. Refluxing **7** with one more equivalent of **4** for 5 days in acetonitrile afforded the cyclophane **1** as a colorless solid. ^{1}H NMR of **1**[7] displayed singlets at δ5.90 for -NCH_2- protons and at δ10.44 for the proton at C_2 carbon of imidazole in addition to aromatic protons. Similarly, imidazolophanes **1a, 1b,**[8] and **1c** were prepared form the dibromides **4a, 4b** and **4c** respectively (**Scheme 2**).[9] When the above reaction sequence applied to 2-methyl benzimidazole, *syn* and *anti* conformational isomers of **9** were detected (based on ^{1}H NMR). Variable temperature ^{1}H NMR measurements revealed that the conformers do not coalesce up to 170°C and are non-interconvertible. ^{1}H NMR of **9** showed two signals corresponding to methyl protons at δ2.89 and 3.28 and two signals for -NCH_2- at δ5.70 and 5.92 due to *syn* and *anti* isomers[10] in the ratio 2 : 3 respectively.

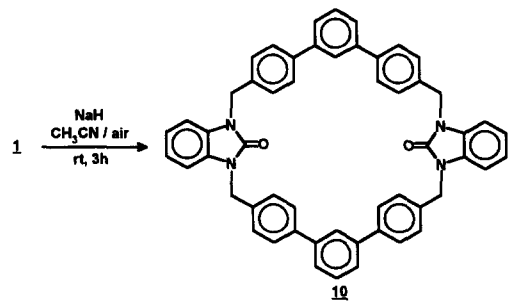


*All the cyclophanes decomposed at 290-300°C & did not melt and gave satisfactory elemental analysis. i. CH_3CN, 48h, rt. ii. **4** or **4a** or **4b** or **4c** (one eq.), CH_3CN, reflux, 5 days.

Scheme 2

Two fold coupling of the tetrabromide **6** with two equivalents of benzimidazole afforded the imidazolophane **2** in 45% yield. ^1H NMR of **2** showed singlets at δ3.65 for four protons ($-OCH_2-$) and at δ5.36 for eight protons ($-NCH_2-$). The C_2 protons on the imidazole ring appeared at δ10.2 in addition to the aromatic protons.

Cyclophane **1**, when treated with sodium hydride in acetonitrile afforded the ureaphane **10** as revealed by the appearance of carbonyl carbon at δ153.2 in ^{13}C NMR and the appearance of ν_{co} at 1684 cm^{-1} in IR spectrum (**Scheme 3**).



Scheme 3

Synthesis of criss-crossed benzimidazolophanes and their chemical transformations are under investigation.

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1. Present address: College of pharmacy, Seoul National University, Seoul 151-742, S. Korea.
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7. ^{1}H NMR (DMSO-d_6 ,400 MHz) for **1** : δ5.90 (*s*, 8H), 7.42 (*ABq*, 8H, 8.8 Hz), 7.65 (*m*, 8H), 7.94 (*ABq*, 8H, 8.8Hz), 7.97 (*bs*, 2H), 7.99 (*d*, 4H, 7.8Hz), 8.04 (*t*, 2H, 7.8Hz), 10.4 (*s*, 2H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ50.77, 115.28, 127.29, 128.05, 128.53, 129.62, 130.09, 131.99, 132.14, 134.45, 140.81, 141.10, 141.43. Anal.calcd. for $C_{54}H_{42}Br_2N_4$: C,71.52; H,4.64; Br,17.66; N,6.18. Found : C,71.50; H,4.66; Br,17.63; N,6.21.
8. ^{13}C NMR ($CDCl_3$, 100 MHz) for **1b**: δ49.80, 114.14, 121.50, 125.19, 126.76, 128.00, 128.48, 130.40, 130.40, 131.20, 133.60, 137.81, 142.55, 164.64 (CO).
9. Direct refluxing of the *m*-terphenyl dibromide and benzimidazole gave only insoluble polymeric material.
10. Structure of *syn* and *anti* conformers of **9** is being resolved by XRD as a collaborative work with Department of Crystallography and Bio-Physics, University of Madras, Guindy Campus, Madras 600 025, India, and will appear as a separate communication.

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