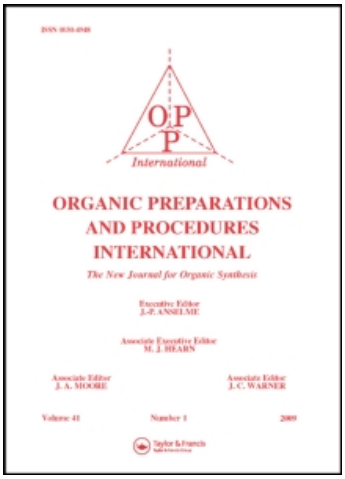

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CONVENIENT AND EFFICIENT SYNTHESIS OF IMIDAZOLIUM CYCLOPHANES

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CONVENIENT AND EFFICIENT SYNTHESIS OF IMIDAZOLIUM CYCLOPHANES

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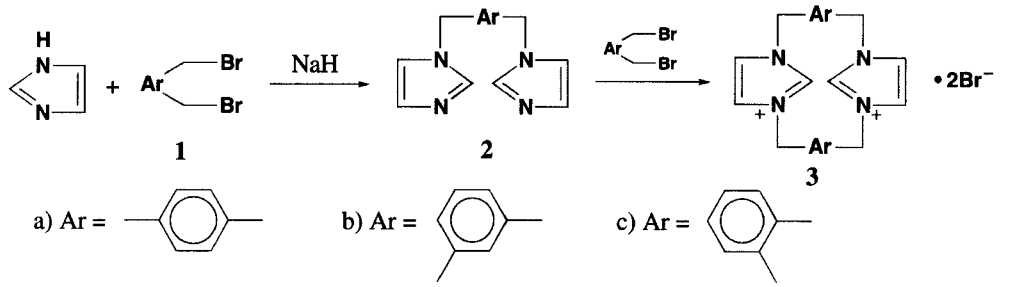
Recently, azaaromatic onium cyclophanes have been used in a variety of applications, such as in artificial enzymes and receptors, host-guest complexes, self-assembly and materials science.[1] Much effort has been directed toward their syntheses and properties.[2] To further develop and generalize onium cyclophane chemistry, it is important to study, design and synthesize imidazolium cyclophanes. A recent paper[3] described imidazolium cyclophanes containing aliphatic bridges. We now report a convenient and efficient synthesis for a type of water-soluble rigid imidazolium cyclophane.

The synthesis of imidazolium cyclophanes **3a-c** is outlined in Scheme 1. *bis*-(Imidazol-1-ylmethyl)benzenes **2a-c** were obtained in high yields by the reaction of imidazole with the corresponding *bis*-(bromomethyl)benzenes **la-c**. Cyclophanes **3a-c** were prepared in excellent yields by the



Scheme 1

dropwise addition of *bis*-(bromomethyl)benzenes **1a-c** to *bis*-imidazole **2a-c** in refluxing THF or acetonitrile. TLC analysis [silica gel: CH_3OH/H_2O/satd. aq. NH_4Br (16/3/1)] showed that this reaction produced few by-products such as the open-chain and other ring-closed types. The salts **3a-c** are soluble in H_2O and CH_3OH, and sparingly soluble in THF and CH_3CN. The structure of compounds **3a-c** was established on the basis of their elemental analyses and spectral data (Table 1). The EI mass spectra reveal fragmentation peaks at m/z 421 and 342 (343) corresponding to the loss of one and two Br^- counterions from the "molecular" ion respectively. The large downfield shift of the imidazolium ring 2-H results from the positive charge on **3a-c**.

TABLE 1. Yields, Mps, Analytical and Spectral Data of Cyclophanes **3a-c**

Cmpd	Yield[a] (%)	mp. (°C)	EI-MS M/Z (%)	^{1}H NMR (D_2O,DSS)[b] δ (ppm)	Anal. Calcd (Found) C	H	N
3a	85.3	>350	421 (8) [M^+ -Br] 342 (4) [M^+ -2Br] 239 (20) [M^+ +1- $BrCH_2C_6H_4CH_2Br$] 171 (50) [$ImCH_2C_6H_4CH_2^+$] 104 (100) [$CH_2C_6H_4CH_2^+$]	9. 15 (s, 2H, Im2-H) 7.59 (s, 12H, Ph-H, Im4-and 5-H) 5.55 (s, 8H, $PhCH_2Im$)	52.61 (52.91)	4.42 (4. 34)	11.56 (11.56)
3b	90.4	345-347	421 (5) [M^+ -Br] 342 (3) [M^+ -2Br] 238 (20) [M^+ - $BrCH_2C_6H_4CH_2Br$] 171 (65) [$ImCH_2C_6H_4CH_2^+$] 104 (100) [$CH_2C_6H_4CH_2^+$]	8. 92 (s, 2H, Im2-H) 7.68-7.62(m,10H, Ph-H, Im4- and 5-H) 6.80 (s, 2H, Ph 5-H) 5.52 (s, 8H, $PhCH_2Im$)	52.61 (52.42)	4.42 (4.41)	11.56 (11.39)
3c	89.1	>350	423 (2) [M^++Br^-] 343 (4) [M^++1- 2Br] 239 (41)[M^++1- $BrCH_2C_6H_4CH_2Br$] 171 (100) [$ImCH_2C_6H_4CH_2^+$] 104 (45) [$CH_2C_6H_4CH_2^+$]	8.72 (s, 2H, Im 2-H) 7.76 (s, 8H, Ph-H, Im4-and 5-H) 7.11 (s, 4H, Ph4- and 5-H) 5.50 (s, 8H, $PhCH_2Im$)	52.61 (52.83)	4.42 (4.51)	11.56 (11.61)

a) Yield of pure products by crystallization from THF or acetonitrile, based on **2**. b) Peak multiplicities are reported as s(singlet) and m(multiplet).

EXPERIMENTAL SECTION

Melting points were determined on a micro-melting point apparatus and are uncorrected. MS and ^{1}H NMR spectra were recorded on a Finnigan MAT4510 and a JNM-FX90Q respectively. Elemental analyses were performed with a Carlo-Erba-1106 instrument. Analytical TLC was performed on glass sheets coated with a 0.2 mm layer of silica gel. THF and acetonitrile were purified following standard purification methods. All other chemicals and reagents were obtained commercially and used without further purification.

1,4-*bis*-(Imidazol-1-ylmethyl)benzene (2a). -Imidazole (5 mmol) in 10 mL THF was added slowly to a stirred suspension of sodium hydride (2.0 mmol) in 5 mL THF. The resulting mixture was stirred for 20 min. A solution of 1,4-*bis*-(bromomethyl)benzene (2 mmol) in 15 mL THF was added dropwise over 3-5 hrs, then the reaction temperature was allowed to rise to 60°. After the reaction was complete (TLC, eluent: 60°-90° petroleum ether), the mixture was cooled to 0°, treated with 40 mL water and stirred. The resulting solution was extracted with chloroform (3 X 50 mL), and the combined organic phase was dried over anhydrous sodium sulfate. The solution was concentrated to a volume of 3-4 mL, and 10 mL 30-60° petroleum ether was added to the liquid residue. Compound **2a** crystallized slowly. Yield 85% (lit.[5] 55%). mp. 132-134° (lit.[4] 132-134°, 148-150°[5]). EI-MS: M/Z(%) =238 (40) [M^+], 171 (100) [M^+-Im], 104 (35) [M^+ -2Im].

1,3-*bis*-(Imidazol-1-ylmethyl)benzene (2b).- Compound **2b** was obtained in a manner analogous to **2a**, starting with 1,3-*bis*-(bromomethyl)benzene (2 mmol). The resulting product was recrystallized

from chloroform/hexane to yield 89% (lit.[5] 60%) of **2b**. mp. 83.5-84° (lit.[4] 85.5-86°, 146°[5]). EI-MS: M/Z(%) = 238 (45) [M^+], 170 (100) [M^+ -1-Im], 104 (50) [M^+ -2Im].

1,2-*bis*-(Imidazol-1-ylmethyl)benzene (2c).- Compound **2c** was prepared in the same manner as described for **2a**, starting with 1,2-*bis*-(bromomethyl)benzene (2 mmol) to yield 92% of **2c**. mp.153-155° (lit.[4] 154-156°). EI-MS: M/Z (%) = 239 (100) [M^++1], 171 (50) [M^+ -Im], 104 (15) [M^+ -2Im].

[1_4]paracyclo-*bis*-(1,3)Imidazolophanium Dibromide (3a).- To a stirred solution of 0.42 mmol of **2a** in 30 mL of dry THF or acetonitrile under reflux, 0. 42 mmol of 1,4-*bis*-(bromomethyl)benzene in 20 mL of dry THF or acetonitrile was added *dropwise* over 3-5 hrs. A white solid gradually formed. After the reaction was complete [TLC, eluent: acetone/ethanol (5/1)], the mixture was concentrated to a volume of about 10 mL and cooled to 0°. The white solid was filtered and washed with cold THF or acetonitrile. Imidazolium cyclophane **3a** was obtained in high purity by this procedure and could be recrystallized from methanol/acetonitrile (9/1) (Table 1).

[1_4]metacyclo-*bis*-(1,3)Imidazolophanium Dibromide (3b).- Cyclophane **3b** was synthesized starting with **2b** (0.42 mmol) and 1,3-*bis*-(bromomethyl)benzene (0.42 mmol) according to the experimental procedure described above for **3a** (Table 1).

[1_4]orthocyclo-*bis*-(1,3)Imidazolophanium Dibromide (3c).- Cyclophane **3c** was prepared starting with **2c** (0.42 mmol) and 1,2-*bis*-(bromomethyl)benzene (0.42 mmol) according to the experimental procedure described above for **3a** (Table 1).

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