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ORGANIC SYNTHESIS USING PTC-1: REACTIONS OF OXYBIS(BROMOMETHANE) WITH DIOLS UNDER LIQUID-LIQUID PHASE TRANSFER CONDITIONS

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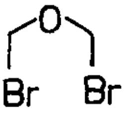
Abstract - Reaction of oxybis(bromomethane) with 1,2-dihydroxybenzene gives 1,3,5-benzotrioxepin and dibenzo [f,m][1,3,5,8,10,12] hexaoxacyclotetradecin[1] but 1,3-and 1,4-dihydroxybenzene derivatives furnish only polymeric products. 1,2-Bis(2-hydroxyethoxy) benezene with oxybis(bromomethane) 1 gives macrocyclics 6 and 7.

In recent years macrocyclic systems have attracted considerable attention due to their chemical and biological applications.[2] But for their synthesis the conventional techniques are used which often suffer from many drawbacks. Phase transfer catalysis has been used advantageously for the synthesis of a variety of organic compound.[3] To the best of our knowledge literature records only one such example where it has been applied to the synthesis of macrocyclic compounds.[4] The crown compounds which have been reported so far invariably incorporate an ethylene bridge between two heteroatoms.[5] It has been reported that if the ratio of heteroatoms to carbon atoms is increased in macrocyclic systems, a better complexing ability for metal ions may be envisaged.[6] On way of achieving this goal is to synthesise such compounds which contain methylene group instead of ethylene as a bridge between two heteroatoms. In the present communication we report the reactions of oxybis(bromomethane) with some diols under liquid-liquid PT conditions.

In the first instance we have studied the reactions of 1, with 1,2-dihydroxybenzene 2, using 50% aq. NaOH as base, benzene as solvent and triethylbenzylammonium chloride (TEBA) as catalyst at room temperature. The reaction of 1,2-dihydroxybenzene 2 after work-up gives a product mixture consisting of two components which have been isolated by column chromatography. The first component (37%) has been found to be identical with an authentic sample of 1,3,5-benzotrioxepin(3)(mixed mp 65-66°C)[7], m/z 152(M^+), ^{1}H nmr ($CDCl_3$) δ 5.0(s,4H,2x-O-CH_2-O-), 7.0(m,4H,ArH), ir($CHCl_3$): ν_{max} 2800, 1590 cm^{-1}. The second component (12%), mp 150-153°C has been assigned the structure dibenzo [f,m][1,3,5,8,10,12] hexaoxacyclotetradecin (4) on the basis following spectral data:[8] m/z 304(M^+). In its ^1H nmr spectrum it exhibits a signal at δ 5.50 due to four $-O-CH_2-O-$ groups and the eight aromatic protons appear as a multiplet at δ 6.7. Its ^{13}C nmr spectrum shows four signals at δ 95.90(t,$-OCH_2O-$), 107.00(d,=CH-), 111.20(d, = CH-) and 135.60(s, = C-O-).



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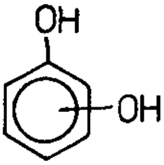

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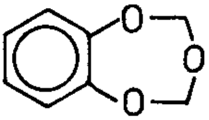

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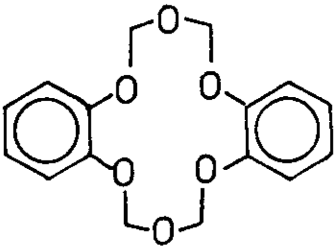

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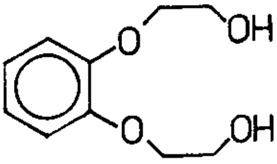

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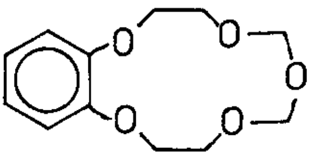

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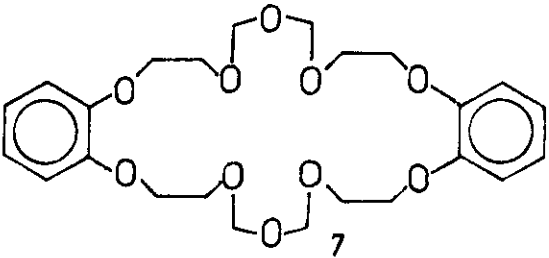

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This reaction has been performed under a variety of PT conditions and it has been found that the use of 60% aq. NaOH containing solid KBr constitutes the optimum reaction conditions for the synthesis of 4 (30%).

But the reaction of 1,3- and 1,4-dihydroxybenzene derivatives with 1 under the same reaction conditions furnish polymeric materials which have been found to be insoluble in most of the organic solvents and thus could not be characterised. Alternately, these reactions have been performed using Paderson's method[9] and high dilution technique[10], but under both these conditions, 4 is formed in very poor yields (2-3%).

In order to further investigate the synthetic utility of this technique we have carried out the reaction of 1,2-bis(hydroxyethoxy)benzene 5 with 1 under liquid-liquid PT conditions. After work-up the residue consisted of two components (tlc) which have been isolated by column chromatography. The first components (25%), mp 126-129°C, in its mass spectrum exhibits the parent ion peak at m/z (M^+) 240. ^{1}H nmr($CDCl_3$) δ 3.87(m,4H,2xArOCH$_2$$\underline{CH}_2OCH_2$-) 4.05(m,4H, 2xArO$\underline{CH}_2CH_2OCH_2$-), 4.87(s,4H,2x-OCH$_2$O-) and 7.0(s,4H,ArH). Ir($CHCl_3$) ν_{max}3250, 2800, 1600, 1460 cm^{-1}. On the basis of these spectral data it has been assigned the structure 2,3,9,10-tetrahydro-1,4,6,8,11-benzopentaxacyclotridecin (6). The second component (65%), a dense liquid in its mass spectrum exhibits the parent ion peak at m/z (M^+) 480. ^{1}H nmr($CDCl_3$) δ 3.87(m,8H,4xArOCH$_2$$\underline{CH}_2OCH_2$-), 4.05(m, 8H,4xArO$\underline{CH}_2CH_2OCH_2$-), 4.87(s,8H,4x-OCH$_2$O-) and 7.0(m,8H,ArH). Ir($CHCl_3$): ν_{max} 2800, 1500, 1140, 1040 cm^{-1}. On the basis of these spectral data it has been assigned the structure of 6,7,13,14,21,22,28,29-octahydrodibenzo[i.v][1,3,5, 8,11,14,16,18,21,24]-decaoxacyclohexacosin (7).

But on performing the reaction of 1,2-dihydroxybenzene and 5 with 1 under solid-liquid PT conditions using solid NaOH or KOH as base, a solid mass is obtained which is insoluble in most of the organic solvents but soluble in water and hence could not be characterised.

However, the present report on the synthesis of cyclic ethers under PT conditions is advantageous because of (i) milder reaction conditions, (ii) shorter reaction time, (iii) relatively cheaper materials, (iv) easier work-up and (v) relatively higher yields.

Similar reactions of oxybis(bromomethane) 1 and other activated dihalides with diols are being investigated under PTC.

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