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A SYNTHETIC ROUTE TO POLY-N,N'-DIMETHYLETHYLENEDIAMINES

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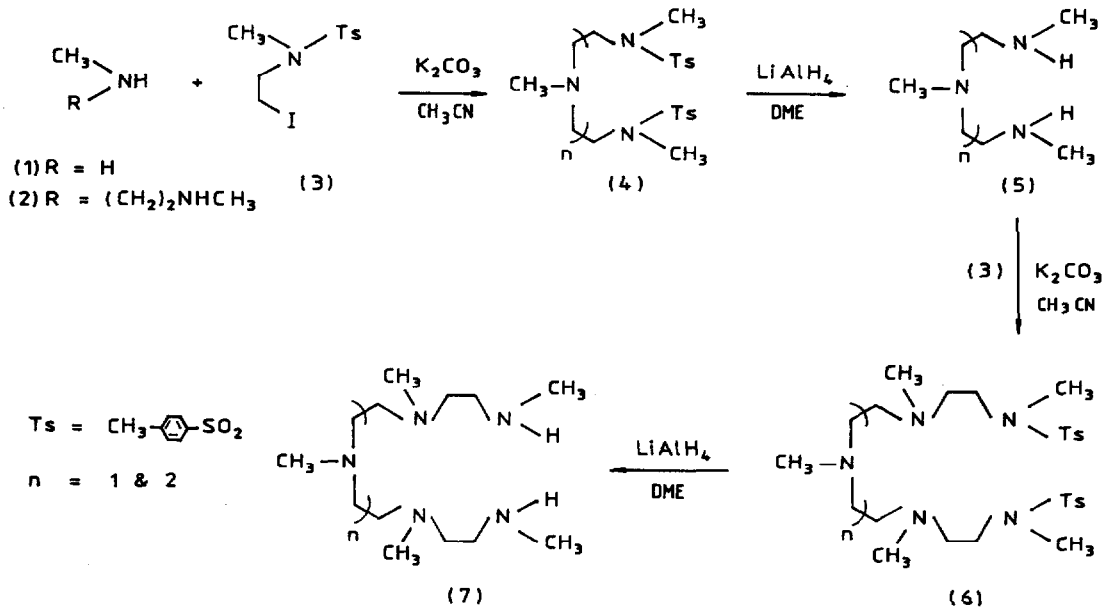
Abstract: A simple high yielding synthesis of poly-N,N'-dimethylethylenediamines has been achieved by the alkylation of readily available N-methylamine or N,N'-dimethylethylenediamine with N-methyl-N-(4-toluenesulphonyl)iodoethylamine.

As part of a continuing programme of investigations into molecular recognition[1-3] we required to synthesise macrocyclic polyamines such as 2-borono-1,3-xylyl-N-methyl aza-crown ethers. These aza-crown ethers were expected to form stable complexes with transition metal cations,[4] and have a higher stability towards air oxidation than the corresponding 2-borono-1,3-xylyl crown ethers[5] which form complexes with alkali and alkaline-earth metal cations.[6] To synthesise these xylyl aza-crown ethers using recently developed methods,[5] we needed to prepare aliphatic poly-N,N'-dimethylethylenediamine side chains (**5** and **7**, n = 1 & 2). Although polyethylenediamines are commercially available, the corresponding N-methyl derivatives of these amines are relatively inaccessible, and are very expensive, when commercially available. The preparation of 1,4,7-trimethyldiethylenetriamine (**5**, n = 1) and 1,4,7,10-tetramethyltriethylenetetramine (**5**, n = 2) from N-methylamine and 1,2-dichloro- or 1,2-dibromoethane was reported by Langenbeck et. al.[8] in very low yield. However, to the best of our knowledge, the synthesis of 1,4,7,10,13-pentamethyltetraethylenepentamine (**7**, n = 1) and 1,4,7,10,13,16-hexamethylpentaethylenehexamine (**7**, n = 2) has not been reported to date.

Macrocyclic polyamines are conveniently synthesised using the Richman and Atkins[9] modification of the method of Koyamo and Yoshino.[4] This method involves the condensation of bis-sulfonamide sodium salts with compounds having tosylate ester leaving groups Attempts to employ a modification of this method to the preparation of aliphatic poly-N,N'-dimethylenediamine side chains failed due the low reactivity of the tosylate ester leaving group with substituted N-methylamines. The conversion of the tosylate group into an iodo leaving group, however proved more effective in alkyaltion reactions with N-methylamines and resulted in the efficient high yielding synthesis of poly-N,N'dimethyl-ethylenediamines which we now report here. The synthesis is accomplished by the alkylation of readily available N-methylamine or N,N'-dimethylethylene-diamine with N-methyl-N-(4-toluenesulphonyl)iodoethylamine as shown in Scheme 1.



Scheme 1.

bis -N-Alkylation of N-methylamine (**1, R = H**) (hydrochloride salt) with N-methyl-N-(4-toluene sulphonyl)iodoethylamine (**3**)[9] in the presence of anhydrous potassium carbonate in refluxing acetonitrile afforded 1,7-ditosyl-1,4,7-trimethyldiethylenetriamine (**4**, n = 1) in 95 % yield, m.p. 81-83°C (EtOAc). Under similar reaction conditions, N,N'-dimethylethylenediamine (**2, R = $(CH_2)_2NHCH_3$**) gave 1,10-ditosyl-1,4,7,10-tetramethyltriethylenetetramine (**4**, n = 2) in 99% yield, m.p. 76-77°C. Compound (**3**) was prepared in quantitative yield from N,O-ditosyl-N-methylethanolamine[10] by simple displacement of O-tosyl group with iodide anion using sodium iodide in refluxing acetone. Reductive N-detosylation of compounds (**4**, n = 1 and 2) with lithium aluminium hydride in refluxing 1,2-dimethoxyethane (DME) gave 1,4,7-trimethyldiethylenetriamine (**5**, n = 1) and 1,4,7,10-tetramethyltriethylenetetramine (**5**, n = 2) in 91 and 96% yields respectively. Further treatment of these amines (**5**, n = 1 and 2) with (**3**) under similar conditions produced 1,13-ditosyl-1,4,7,10,13-pentamethyltetraethylenepentamine (**6**, n = 1) and 1,16-ditosyl-1,4,7,10,13,16-hexamethylpentaethylenehexamine (**6**, n = 2) in quantitative yield. The subsequent removal of the tosyl group from (**6**, n = 1 and 2) gave the desired N-detosylated amines (**7**, n = 1 and 2) in 85 and 92% yields, respectively. These compounds were fully characterised by spectroscopic methods (IR, ^1H NMR and ^{13}C NMR) and the results presented in Table 1. Strong intramolecular hydrogen bonding was observed both by IR and NMR spectroscopies for all N-detosylated amines (**5** and **7**, n = 1 & 2). The scope of this reaction can be extended further by repeating the steps described to give 1,4,7,10,13,16,19-heptamethylhexaethyleneheptamine or 1,4,7,10,13,16,19,22-octamethylheptaethyleneoctamine, and so on.

Typical Procedure for N-Alkylation: A solution of N,N'-dimethylethylenediamine (**2, R = $(CH_2)_2NHCH_3$**) (2.0 gm, 22.7 mmole) and N-methyl-N-(4-toluenesulphonyl)iodoethylamine (**3**) (15.4 gm,

Table 1. Spectroscopic Data on Ditosyl-poly-N,N'dimethylethylenediamines (**4** & **6**, n = 1 & 2) and Poly-N,N'-dimethylethylenediamines (**5** & **7**, n = 1 & 2).

Compound no.	IR[a] cm^{-1}	^1H NMR[b] (250 MHz)	^{13}C NMR[b] (63 MHz)
4, n = 1	1165, 1340, 1460, 1600.	2.29 (3H, s), 2.43 (6H, s), 2.60 (4H, t), 2,76 (6H, s) 3.08 (4H, t), 7.49 (8H, dd).	21.48, 35.52, 42.20, 47.99, 55.70, 127.35, 129.69, 134.48, 143.34.
4, n = 2	1160, 1340, 1465, 1600.	2.26 (6H, s), 2.39 (6H, s), 2.48 (4H, s), 2.57 (4H, t), 2.74 (6H, s), 3.08 (4H, t), 7.40 (8H, dd).	21.46, 35.50, 42.60, 48.01, 55.50, 55.99, 127.36, 129.64, 134.57, 143.27.
5, n = 1	1460, 3260, 3390.	2.20 (3H, s), 2.41 (6H, s), 2.49 (4H, t), 2.65 (4H, t), 2.88 (2H, br s).	35.91, 42.45, 48.87, 56.75.
5, n = 2	1465, 3255, 3410.	2.20 (6H, s), 2.26 (2H, br s), 2.39 (6H, s), 2.45 (4H, s), 2.48 (4H, t), 2.62 (4H, t).	36.30, 42.55, 49.22, 55.86, 57.15.
6, n = 1	1160, 1340, 1460, 1600.	2.23 (9H, s), 2.40 (6H, s), 2.47 (8H, s), 2.56 (4H, t), 2.74 (6H, s), 3.07 (4H, t), 7.48 (8H, dd).	22.16, 36.19, 43.28, 43.56, 48.70, 56.26, 56.54, 56.72, 128.03, 130.32, 135.20, 143.95.
6, n = 2	1170, 1340, 1465, 1600.	2.23 (12H, s), 2.37 (6H, s), 2 45 (12H, s), 2.54 (4H, t), 2.73 (6H, s), 3.07 (4H, t), 7.47 (8H, dd).	21.35, 35.37, 42.48, 42.72, 47.88, 55.41, 55.49, 55.78, 55.85, 127.22, 129.51, 134.40, 143.14.
7, n = 1	1465, 3260, 3400.	2.20 (3H, s), 2.28 (8H, s), 2.30 (6H, s), 2.45 (6H + 2H, merged br s), 2.53 (4H, merged t), 2.71 (4H, t).	35.57, 42.53, 42.94, 48.52, 54.61, 55.56, 55.91.
7, n = 2	1465, 3255, 3400.	2.20 (6H, s), 2.22 (6H, s), 2.42 (6H, s), 2.49 (8H, s), 2.50 (4H, s), 2.51 (4H, merged t), 2.62 (4H, t).	36.96, 43.20, 43.43, 49.86, 56.29, 56.56, 57.92.

[a]Recorded as neat or in nujol in AgCl plates using Mattson GALAXY 2020 FT-IR spectrometer.
[b]Recorded in $CDCl_3$ with Brucker AC-250 spectrometer operating in the FT mode.

45.4 mmole) was refluxed in the presence of anhydrous powdered potassium carbonate (15.7gm, 113.6 mmole) in dry acetonitrile (150 ml) for 10 hours (monitored by t.l.c.). The reaction mixture was then filtered and the filtrate concentrated in vacuo. The residue dissolved in ethyl acetate (100 ml) was further filtered and evaporated in vacuo to give 1,10-ditosyl-1,4,7,10-tetramethyltriethylenetetramine (**4**, n =2) (11.5 gm, 99%) as a colourless viscous oil which solidified on standing. Recrystallisation from ethyl acetate gave analytically pure compound, m.p. 76-77°C. (see Table 1 for spectroscopic data).

Typical Procedure for N-Detosylation: To a refluxing suspension of lithium aluminium hydride (6.0 gm, 158.1 mmole) in 1,2-dimethoxyethane (DME) (100 ml) was added dropwise a solution of 1,10-ditosyl-1,4,7,10-tetramethyltriethylenetetramine (**4**, n = 2) (5.0 gm, 9.8 mmole) in DME (50 ml). After complete addition, the reaction mixture was refluxed for 20h then the cooled reaction mixture treated with 3N NaOH until white granules were formed. The solvent was decanted and the residue further extracted with benzene (3 x 50 ml), and the combined organic extracts dried with potassium hydroxide pellets, filtered and evaporated in vacuo to give 1,4,7,10-tetramethyltriethylenetetramine (**5**, n = 2) (1.9 gm, 96%), as a colourless oil. Table 1 summarises the spectroscopic data.

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8. The compound (**3**) has m.p. 88-89°C (methanol); IR V_{max} (nujol): 1160, 1335, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ : 2.44 (3H, s), 2.81 (3H, s), 3.26 (2H, t), 3.39 (2H, t), 7.51 (4H, dd); ^{13}C NMR ($CDCl_3$) δ :1.11, 21.44, 35.45, 52.70, 127.19, 129.76, 134.39, 143.64; MS: m/e 339 (M^+), 212, 198, 155, 91.
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