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SYNTHESIS OF SOME 1,3,5-TRIAZINE DERIVATIVES

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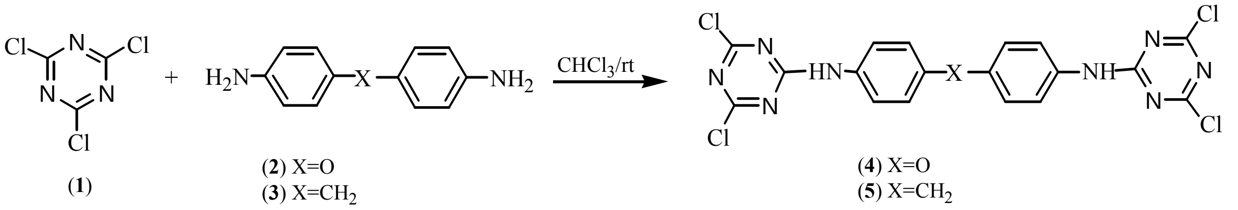
Abstract- Some derivatives of 1,3,5-triazine were prepared with excellent yields by nucleophilic reactions between cyanuric chloride and some nucleophiles under mild conditions.

Available data on 2,4,6-trichloro-1,3,5-triazine, or cyanuric chloride (**1**), suggest that it is a highly reactive halogen compound, almost like an acid chloride.[1] It is of great synthetic importance in the preparation of 1,3,5-triazine derivatives,[2] and industrially important in forming the basis of a wide range of complex dyestuffs (Procoin and Cibacron dyes) as an stable unit to which can be attached two or three dyestuffs, and which can even be covalently linked to fiber cellulose.[3,4] Cyanuric chloride has also been widely employed in organic synthesis as a versatile reagent to effect various transformations such as the conversion of carboxylic acids to their different derivatives,[5,6] oxidation of alcohols,[7] and dehydration of amides[8] and aldoximes to nitriles under very mild conditions.[9] Also, aryl sulfoxides have been subjected to deoxygenation to aryl sulfides by cyanuric chloride in dioxane under reflux condition.[10] Polymers containing the 1,3,5-triazine moieties exhibit an unusual combination of properties such as high softening temperature and thermal stability together with higher solubility.[11]

Electron-accepting property of the 1,3,5-triazine, that could be altered upon substitution with nucleophiles,[12] has made it to be so valuable as a bridging agent in synthetic reactive dyes,[13,14] and other biologically active compounds.[15-17] It has been shown that, the substitution of the first chlorine atom in the cyanuric chloride by most nucleophiles usually occurs under very mild conditions, whereas the second and third chlorine atoms are replaced increasingly more severely.[11,18]

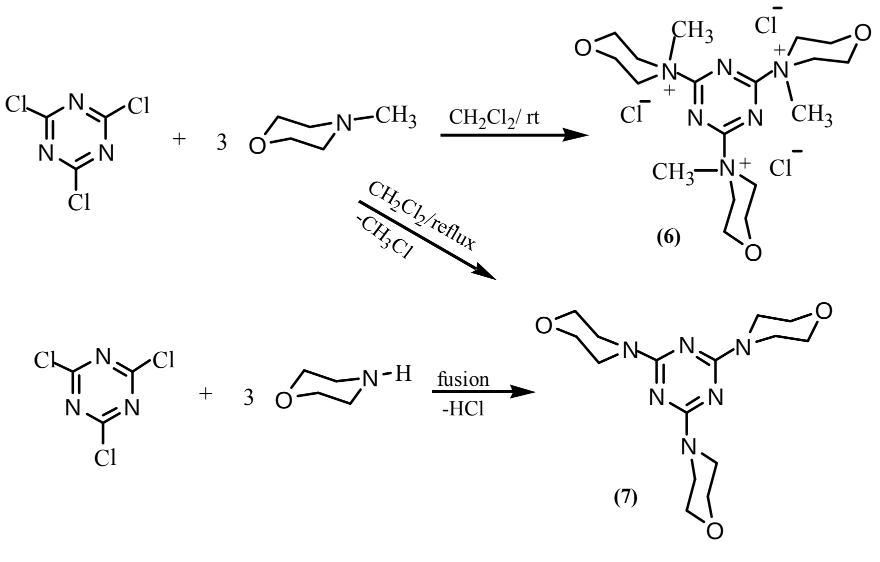
In continuation of our previously reported work on the nucleophilic reactions of the cyanuric chloride with various nucleophiles,[19] we have observed that the reactions of cyanuric chloride with 4-aminophenyl ether (**2**) and 4,4′-methylenedianiline (**3**) occur in CH_2Cl_2 under very mild conditions at room temperature to produce (4,6-dichloro-1,3,5-triazin-2-yl)-4-aminophenyl ether (**4**) and 4,4'-methylenedi[*N*-(4,6 dichloro-1,3,5-triazin-2-yl)]aniline (**5**) respectively in high yields (**Scheme 1**). All attempts to substitute the remaining chlorines on the 1,3,5-triazine ring of these products by different nucleophiles such as imidazole, pyrazole, piperidine and morpholine under various conditions resulted in the formation of several mixed products in very low yields, so that they couldn't be characterized.

Scheme 1



In addition, it was shown that the cyanuric chloride can readily undergo reactions with *N*-methylmorpholine in CH_2Cl_2 at room temperature to afford 1,3,5-triazine-2,4,6-tris(*N*-methylmorpholinium) chloride **(6)** as an insoluble product in high yield, whereas the reaction with morpholine to produce 2,4,6-tris(1-morpholino)-1,3,5-triazine (7) required more vigorous condition (**Scheme 2**). The greater reactivity of the cyanuric chloride towards *N* - methylmorpholine compared with morpholine itself is possibly attributed to the positive charge generated on morpholine nitrogen atom upon its attachment to the 1,3,5-triazine ring which renders the remaining chlorine atoms more reactive towards the subsequent replacements. It is, however, interesting to note that when cyanuric chloride is refluxed with *N*-methylmorpholine for almost one hour, demethylation occurs to produce 2,4,6-tris(1-morpholino)-1,3,5-triazine (7) in quantitative yield. This is evidenced by disappearance of the methyl group signals shown in the ^{1}H-NMR and ^{13}C-NMR spectra of the compound (**6**).

Scheme 2



EXPERIMENTAL

Chemicals were purchased from Fluka, Merck and Aldrich chemical companies and purified prior to use.^{1}H NMR and ^{13}CNMR spectra were recorded with JEOL FX 90Q (90 MHz) and Bruker DRX 500 AVANCE (500 MHz) spectrometer. IR spectra were recorded using a Perkin Elmer GX FT-IR spectrophotometer. Melting points were determined on a Stuart SMP3 apparatus and reported uncorrected. Elemental analyses were performed on a Perkin Elmer 2400 microanalyser. MS spectra were recorded on a GCMS-QP 1100 EX spectrometer.

(4,6-Dichloro-1,3,5-triazin-2-yl)-4-aminophenyl ether (4): A mixture of 4-aminophenyl ether (0.2 g, 1 mmol), cyanuric chloride (0.369 g, 2 mmol) and sodium carbonate (0.26 g, 2.5 mmol) in chloroform (30 mL) was stirred at rt. The reaction was completed in 10 min as monitored by TLC. The resulting reaction mixture was evaporated, the residue was dissolved in acetone (30 mL) and filtered. Then the filtrate was dried over anhydrous $MgSO_4$, filtered and evaporated to leave a solid product which was recrystallized from ethanol, yield 0.46 g (93%); mp 232-233 ºC; ^{1}H-NMR ($CDCl_3$): δ 7-7.55 (8H, dd, J=9.8 and 31.9 Hz, Ar), 7.46-7.55 (2H, 2NH); ^{13}C-NMR ($CDCl_3$): δ 119.56 (C3), 123.19 (C2), 131.23 (C4), 154.78 (C1), 164.16 (C *ipso* triazine), 172.55 (C-Cl) ; IR (KBr): 3278 (N-H), 1615, 1497 (Ar), 1551 (N-H) (cm^{-1}); MS (EI): m/z 496 (M^+); Anal. Calcd for $C_{18}H_{10}N_8OCl_4$: C, 43.58; H, 2.01; N, 22.58; Found: C, 43.61; H, 1.98; N, 22.65.

4,4′-Methylenedi[*N*-(4,6-dichloro-1,3,5-triazin-2-yl)]aniline (5): A mixture of 4,4'-methylenedianiline (0.198 g, 1 mmol), cyanuric chloride (0.369 g, 2 mmol) and sodium carbonate (0.26 g, 2.5 mmol) in chloroform (20 mL), was stirred at rt. The reaction was completed in 5 min as monitored by TLC. Then the resulting reaction mixture was filtered, the filtrate was dried over anhydrous $NaSO_4$, filtered and evaporated to yield a solid residue which was recrystallized from ethanol, yield 0.47 g (95%); mp 248-249 ºC; ^{1}H-NMR ($CDCl_3$): δ 3.96 (2H, s, CH_2), 7.24 (8H, m, Ar), 7.66 (2H, s, 2NH); ^{13}C-NMR ($CDCl_3$): δ 40.80 (CH_2), 121.58 (C3), 129.72 (C2), 133.99 (C4), 138.46 (C1), 164.10 (C *ipso* triazine), 171.39 (C-Cl) ; IR (KBr): 3361 (N-H), 1613, 1507 (Ar), 1560 (N-H) (cm^{-1}); MS (EI): m/z 494 (M^+); Anal. Calcd for $C_{19}H_{12}N_8Cl_4$: C, 46.19; H, 2.43; N, 22.67; Found: C, 46.24; H, 2.38; N, 22.74.

1,3,5-Triazine-2,4,6-tris(*N*-methylmorpholinium) chloride (6): A mixture of cyanuric chloride (0.369 g, 2 mmol) and *N*-methylmorpholine (0.8 mL, 7 mmol) in methylene chloride (15 mL) was stirred at rt for 1 h. After the reaction was completed (TLC), the resulting mixture was filtered, the filtrate was dried over anhydrous $MgSO_4$ and filtered. Evaporation of the filtrate gave a solid which was recrystallized from ethanol, yield 1.0 g (93%); mp 130-131 ºC; ^{1}H-NMR (D_2O): δ 3.53 (3H, s, CH_3), 3.92 (6H, m, 2-OCH_2-, 2-NCH-), 4.50 (2H, d, J=8.6 Hz, 2-NCH-); ^{13}C-NMR (D_2O): δ 55.12 (CH_3), 59.66 (CH_2O), 62.08 (CH_2N), 169.69 (C triazine) ; IR (KBr): 1589, 1506, 1461, 1361, 1386, 1267, 1114 (cm^{-1}); Anal. Calcd for $C_{16}H_{33}N_3O_3Cl_3$: C, 45.59; H, 7.83; N, 9.96. Found: C, 45.65; H, 7.79; N, 10.08.

2,4,6-Tris(1-morpholino)-1,3,5-triazine (7): A mixture of cyanuric chloride (0.369 g, 2 mmol) and *N* -

methylmorpholine (1.2 mL, 10 mmol) in CH_2Cl_2 (20 mL) was refluxed for 1 h. The resulting mixture was let to cool to rt and then evaporated to yield a solid which was recrystallized from ethanol to give white solid product (**7**), yield 1.26 g (91%); mp 283-285 ºC (decomp) [lit.,[20] mp 284-285 ºC (decomp)].

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