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SYNTHESIS AND SPECTROSCOPIC STUDIES OF SOME FLUORINATED  
1,3,5-TRIAZINE DERIVATIVES

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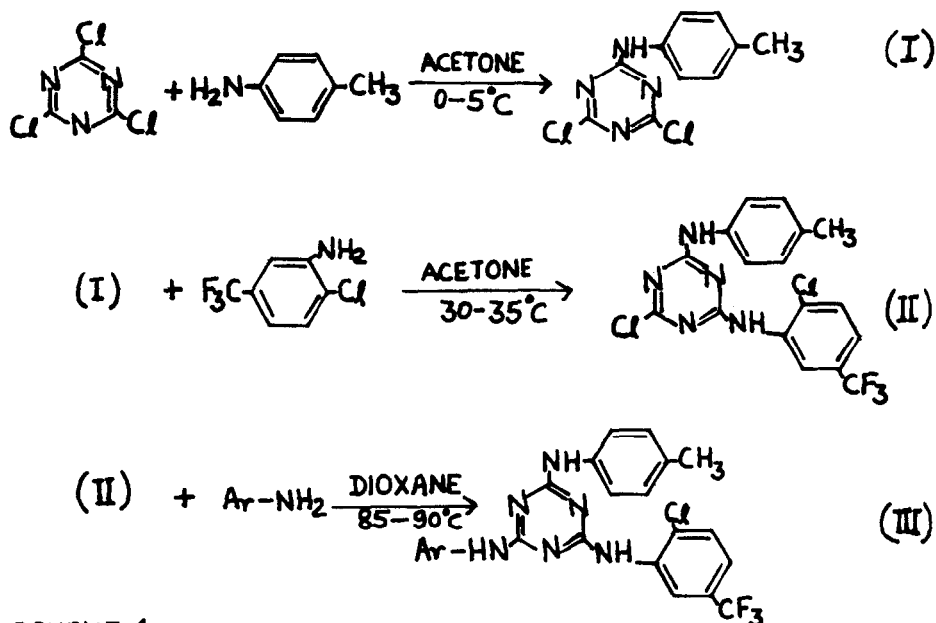
SUMMARY

Tri-substituted derivatives of 2,4,6-trichloro-1,3,5-triazine have been prepared in good yields by the reaction of 2,4,6-trichloro-1,3,5-triazine with various aromatic amines. These new type of products have been characterised by elemental analysis, IR,  $^1\text{H}$  and  $^{19}\text{F}$  NMR spectral studies.

INTRODUCTION

1,3,5-Triazine derivatives have been known for their biological activities such as antimalarial, anticancer, antiviral and antifungal [1-4]. Keeping in view the therapeutic importance of 1,3,5-triazine derivatives as revealed in the literature [5-10], new types of fluorinated derivatives of 1,3,5-triazine have been synthesized in the hope of finding better therapeutic value. The general method of preparation is described in Scheme 1.

The first chlorine of 2,4,6-trichloro-1,3,5-triazine was replaced with the help of p-toluidine at  $0-5^\circ\text{C}$  to produce 2,4-dichloro-6-(4-methylanilino)-1,3,5-triazine (I) which on treatment with 3-amino-4-chlorobenzotrifluoride at  $30-35^\circ\text{C}$  led to the formation of 2-chloro-4-(2-chloro-5-trifluoromethylanilino)-6-(4-methylanilino)-1,3,5-triazine (II). The condensation reaction of (II) with different aromatic amines was carried out at  $85-90^\circ\text{C}$  to produce 8 different derivatives of Type (III) in 60-90% yield.



## SCHEME 1

### SYNTHESIS

#### (I) Synthesis of 2,4-Dichloro-6-(4-methylanilino)-1,3,5-triazine

2,4,6-Trichloro-1,3,5-triazine (0.03 mol) was dissolved in acetone (30 ml). To this, the solution of p-toluidine (0.03 mol) in acetone (10 ml) was added slowly with stirring at  $0-5^{\circ}\text{C}$ , followed by the addition of NaOH solution (0.03 mol in 10 ml of water). The reaction mixture was stirred for further 3 hours at  $0-5^{\circ}\text{C}$ . The whole content was poured into ice-cold water and acidified with HCl. The product was filtered, washed and dried. It was recrystallised from ethanol m.p.,  $190^{\circ}$ ; yield 79%. Analysis : Found : C, 47.28; H, 3.29; N, 21.56.  $\text{C}_{10}\text{H}_8\text{Cl}_2\text{N}_4$  requires C, 47.06; H, 3.14; N, 21.96.  $\nu_{\text{max}} \text{ cm}^{-1}$  (KBr) 3490-3380 (br. N-H str.), 820 ( $\text{C}_3\text{N}_3$  str.), 795 (C-Cl str.),  $\delta_{\text{H}}$  ppm (DMSO- $d_6$  soln.) 2.26 (s ;  $\text{CH}_3$ ), 10.10 (s ; NH), and 6.92 - 7.82 (m ; ArH).

(II) Synthesis of 2-Chloro-4-(2-chloro-5-trifluoromethylanilino)-6-(4-methylanilino)-1,3,5-triazine

2,4-Dichloro-6-(4-methylanilino)-1,3,5-triazine (I) (0.012 mol) was dissolved in acetone (40 ml). To this, the solution of 3-amino-4-chlorobenzotrifluoride (0.012 mol) in acetone (10 ml) was added with continuous stirring followed by the addition of NaOH solution (0.012 mol in 10 ml of water). The reaction mixture was stirred for 3 hours at 30-35 °C. After cooling, the reaction mixture was poured into ice-cold water and acidified with HCl. It was filtered, washed, dried and recrystallised from ethanol m.p. 192 °C; yield 80%. Analysis: Found : C,49.58; H,3.10; N,16.50.  $C_{17}H_{12}Cl_2F_3N_5$  requires C,49.28; H,2.90; N,16.91  $\nu_{\max} \text{ cm}^{-1}$  (KBr) 3480 - 3300 (br.N-H str.), 810( $C_3N_3$  str.), 785 (C-Cl str.), 1170 (C-F str.),  $\delta_H$  ppm (DMSO- $d_6$  soln.) 2.25 (s;  $CH_3$ ), 9.99-10.20 (m; NH), and 6.97-7.92 (m; ArH).  $\delta_F$  ppm (DMSO- $d_6$  soln.)-56.06 (s;  $CF_3$ ).

(III) Synthesis of 2-(Arylanilino)-4-(2-chloro-5-trifluoromethylanilino)-6-(4-methylanilino)-1,3,5-triazines

2-Chloro-4-(2-chloro-5-trifluoromethylanilino)-6-(4-methylanilino)-1,3,5-triazine (II) (0.003 mol) was dissolved in 1,4-dioxane (6ml). The solution of different types of aromatic amines (0.003 mol) in dioxane (6 ml) was added slowly in the above solution, followed by the addition of NaOH solution (0.003 mol in 5 ml of water). The whole content was heated for 3 hours at 85-90 °C. After cooling, it was poured into ice-cold water. The products were filtered, washed, dried and recrystallised from ethanol.

The characterisation and analytical data of tri-substituted derivatives of 2,4,6-trichloro-1,3,5-triazine are given in Table 1.

TABLE I

Characterisation and analytical data of compounds(III) (New compounds)

| S.No. | - Ar                                              | Molecular Formula                                                              | M.P. <sup>a</sup><br>°C | Yield<br>% | Analysis % Calcd.<br>(Found) |                |                   |
|-------|---------------------------------------------------|--------------------------------------------------------------------------------|-------------------------|------------|------------------------------|----------------|-------------------|
|       |                                                   |                                                                                |                         |            | C                            | H              | N                 |
| 1.    | p-COOH.C <sub>6</sub> H <sub>4</sub>              | C <sub>24</sub> H <sub>18</sub> ClF <sub>3</sub> N <sub>6</sub> O <sub>2</sub> | 200                     | 65         | 55.98<br>(55.75)             | 3.50<br>(3.40) | 16.33<br>( 16.15) |
| 2.    | m-COOH.C <sub>6</sub> H <sub>4</sub>              | C <sub>24</sub> H <sub>18</sub> ClF <sub>3</sub> N <sub>6</sub> O <sub>2</sub> | 185                     | 89         | 55.98<br>(56.32)             | 3.50<br>(3.39) | 16.33<br>(16.73)  |
| 3.    | m-Cl.C <sub>6</sub> H <sub>4</sub>                | C <sub>23</sub> H <sub>17</sub> Cl <sub>2</sub> F <sub>3</sub> N <sub>6</sub>  | 170                     | 79         | 54.65<br>(54.97)             | 3.37<br>(3.38) | 16.63<br>(17.11)  |
| 4.    | o-NO <sub>2</sub> .C <sub>6</sub> H <sub>4</sub>  | C <sub>23</sub> H <sub>17</sub> ClF <sub>3</sub> N <sub>6</sub> O <sub>2</sub> | 171                     | 90         | 53.54<br>(53.23)             | 3.30<br>(3.20) | 19.01<br>(18.66)  |
| 5.    | o-OCH <sub>3</sub> .C <sub>6</sub> H <sub>4</sub> | C <sub>24</sub> H <sub>20</sub> ClF <sub>3</sub> N <sub>6</sub> O              | 310                     | 89         | 57.54<br>(57.82)             | 4.00<br>(3.64) | 16.78<br>(16.38)  |
| 6.    | -C <sub>10</sub> H <sub>7</sub>                   | C <sub>27</sub> H <sub>20</sub> ClF <sub>3</sub> N <sub>6</sub>                | 185                     | 58         | 62.25<br>(62.50)             | 3.84<br>(4.20) | 16.14<br>(15.94)  |
| 7.    | m-CH <sub>3</sub> .C <sub>6</sub> H <sub>4</sub>  | C <sub>24</sub> H <sub>20</sub> ClF <sub>3</sub> N <sub>6</sub>                | 125                     | 62         | 59.44<br>(59.24)             | 4.13<br>(4.33) | 17.34<br>(16.84)  |
| 8.    | p-NO <sub>2</sub> .C <sub>6</sub> H <sub>4</sub>  | C <sub>23</sub> H <sub>17</sub> ClF <sub>3</sub> N <sub>6</sub> O <sub>2</sub> | 180                     | 84         | 53.54<br>(53.89)             | 3.30<br>(3.50) | 19.01<br>(19.41)  |

<sup>a</sup> Melting points are uncorrected.

TABLE 2

The IR,  $^1\text{H}$  and  $^{19}\text{F}$  spectral data of compounds (III)

| Comp. -Ar<br>No. | IR(KBr : $\nu$ max $\text{cm}^{-1}$ )                             | $^{13}\text{C}$ NMR |      | $^1\text{H}$ NMR (DMSO- $d_6$ :ppm from TMS) |                                     | $^{19}\text{F}$ NMR<br>(ppm) |
|------------------|-------------------------------------------------------------------|---------------------|------|----------------------------------------------|-------------------------------------|------------------------------|
|                  |                                                                   | C-Cl                | C-F  | -NH-<br>CH <sub>3</sub>                      | -Ar H<br>-COOH<br>-OCH <sub>3</sub> |                              |
| 1. p             | -COOH.C <sub>6</sub> H <sub>4</sub><br>3470-3290(br)              | 800                 | 1155 | 2.26(s)                                      | 9.76-10.0(m)<br>6.82-8.14(m)        | 10.47(s)<br>-57.57           |
| 2. m             | -COOH.C <sub>6</sub> H <sub>4</sub><br>3400-3100(br)              | 810                 | 1170 | 2.28(s)                                      | 9.32-9.59(m)<br>6.95-7.83(m)        | 10.40(s)<br>-57.57           |
| 3. m             | -Cl.C <sub>6</sub> H <sub>4</sub><br>3300-3100(br)                | 810                 | 1170 | 2.24(s)                                      | 9.37-9.54(m)<br>6.73-7.74(m)        | -<br>-57.57                  |
| 4. o             | -NO <sub>2</sub> .C <sub>6</sub> H <sub>4</sub><br>3300-3090(br)  | 810                 | 1170 | 2.28(s)                                      | 9.61-10.22(m)<br>6.4-8.16(m)        | -<br>-55.71                  |
| 5. o             | -OCH <sub>3</sub> .C <sub>6</sub> H <sub>4</sub><br>3300-3000(br) | 820                 | 1170 | 2.26(s)                                      | 9.15-10.20(m)<br>6.6-8.3(m)         | 3.8(s)<br>-57.61             |
| 6. —             | C <sub>10</sub> H <sub>7</sub><br>3450-3100(br)                   | 805                 | 1165 | 2.27(s)                                      | 9.85-10.45(m)<br>6.64-7.91(m)       | -<br>-57.54                  |
| 7. m             | -CH <sub>3</sub> .C <sub>6</sub> H <sub>4</sub><br>3400-3100(br)  | 810                 | 1165 | 2.28(s)                                      | 8.99-10.05(m)<br>6.62-8.20(m)       | -<br>-56.06                  |
| 8. p             | -NO <sub>2</sub> .C <sub>6</sub> H <sub>4</sub><br>3350-3100(br)  | 815                 | 1175 | 2.26(s)                                      | 9.58-10.92(m)<br>6.24-8.24(m)       | -<br>-57.68                  |

br = broad

s=singlet m=multiplet

## SPECTROSCOPIC ANALYSIS

The IR spectra were recorded by using KBr pellets. The  $C_3N_3$  group frequency was obtained at  $820-805\text{ cm}^{-1}$ , and a broad band in the region  $3470-3100\text{ cm}^{-1}$  corresponded to NH-stretching. The absorptions due to the C-F linkage were observed in the region  $1175-1150\text{ cm}^{-1}$  and those due to the C-Cl linkage at  $795-780\text{ cm}^{-1}$ .

The  $^1\text{H}$  NMR spectra were recorded in  $\text{DMSO-d}_6$  using TMS as an internal standard. The chemical shifts are given in ppm downfield from tetramethylsilane. In trisubstituted compounds, a singlet appearing in the range of  $\delta$  2.20-2.28 ppm was assigned to  $\text{CH}_3$  protons. Aromatic protons occurred as a multiplet in the range  $\delta$  6.24-8.36 ppm, whereas the -NH peak was assigned at  $\delta$  8.99-10.92 ppm. The integration ratios followed the ratio of chemically different types of protons present in the molecules.

In the  $^{19}\text{F}$  NMR spectra, a characteristic signal was observed in the range of  $\delta$  -55.71 to -57.68 ppm assigned to the trifluoromethyl group carried on the phenyl ring. The  $^{19}\text{F}$  NMR spectra were recorded in  $\text{DMSO-d}_6$  and the values are relative to hexafluorobenzene used as external standard. The spectroscopic data are given in Table 2.

IR spectra were recorded on a Perkin - Elmer 577 grating infrared spectrophotometer.  $^1\text{H}$  and  $^{19}\text{F}$  NMR spectra were scanned on FX 90 Q JEOL type spectrometer (at 90 MHz).

## ACKNOWLEDGEMENT

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