Synthesis of triazine based dialdehyde Schiff’s base – new templates for Molecular Imprinting and study of their structural and photophysical properties

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Abstract Triazine based dialdehyde (DIPOD) and its Schiff’s base derivatives were designed and synthesized from cyanuric chloride as template for Molecular Imprinting. Density functional theory calculation results revealed that the distance between two aldehyde groups is 1.3 nm. Synthesized structurally the rigid template having 1,3,5-triazine as core moiety, has been used as template to introduce two appropriately spaced amino groups for substrate binding on the solid surface of silica. The structures of the synthesized DIPOD and its Schiff’s base were characterized by FT-IR, 1H NMR, 13C NMR, and UV–Vis spectral analysis. Thermogravimetric analysis showed that the compound has thermal stabilities above 300 °C.

1. Introduction

Molecular Imprinting techniques have a wide application in the field of molecular recognition (Pirkle and Pochapsky, 1989). They also find application in designing the three-helix bundled protein, analytical separations, enzyme-like catalysis, chemical sensors and drug delivery (Sasaki and Tahmassebi, 1998; Alexander et al., 2006; Nostrum, 2005; Hilt and Byrne, 2004; Ye and Mosbach, 2001; Byrne et al., 2002). Various inorganic (Sasaki and Lieberman, 1991; Ghadiri et al., 1992) as well as organic molecules (Sasaki and Kaiser, 1989) have been used as templates to organize peptide strands with defined secondary structure into bundled or coiled protein. The template can provide the correct spacing between the strands in the bundle so that maximum stability due to hydrophobic interaction can be achieved. The distance between the incorporating groups on the solid surface is defined by the structurally rigid trialdehyde (TRIPOD) and dialdehyde (DIPOD).

Molecular Imprinting has proven to be particularly successful for low molecular weight compounds (Sasaki and Tahmassebi, 1994; Flavin and Resmini, 2009; Huang et al., 2009; Lee et al., 2008; Maier and Lindner, 2007). Imprinting of larger more complex molecules such as proteins, DNA, whole cells and viruses has also been reported (Takatsy
et al., 2007; Bolisay et al., 2006; Seidler et al., 2009). The quantum of work in this area is relatively small. Till 2003, less than 10 research papers on imprinting of bio-macromolecules were published per year, which reflects the difficulties faced when trying to imprint large and sensitive biomolecules (Turner et al., 2006; Takeuchi and Hishiya, 2008; Verheyen et al., 2011). The current objective in this quest involves the development of multidentate template molecules to expand the repertoire of functional groups available at the binding site. As part of ongoing research to develop materials for high tech applications (Sekar et al., 2010; Padalkar et al., 2010), here we report the synthesis of dialdehyde and its Schiff’s bases as new templates for incorporation of amino groups on the solid silica surface and their structural and thermal stability studies.

2. Experimental

2.1. Materials and methods

Reagents and solvents were procured from S.D. fine chemicals (India) and were used without purification. Fracitol 500 was used for Molecular Imprinting. The reaction was monitored by TLC using on 0.25 mm E-Merck silica gel 60 F254 precoated plates, which were visualized with UV light. The FT-IR spectra were recorded on Perkin-Elmer 257 spectrometer using KBr discs. ¹H NMR and ¹³C NMR spectra were recorded on VXR 400-MHz instrument using TMS as an internal standard. Mass spectra were recorded on Finnigan mass spectrometer. The visible absorption spectra of the compounds were recorded on a Spectronic Genesys 2 UV–Vis spectrophotometer. TGA measurements were performed on SDT Q 600 v8.2 Build 100 model of TA instruments Waters (India) Pvt. Ltd.

2.2. Synthesis of compounds

2.2.1. Synthesis of 4-(4,6-dichloro-1,3,5-triazin-2-yl)-N,N-diethylaniline (3)

A mixture of N,N-diethylaniline (27 g, 0.2 mol) and cyanuric chloride (18.4 g, 0.1 mol) was heated at 70 °C for 8 h under a slow stream of dry nitrogen gas. Reaction was monitored by TLC and after completion the mixture was extracted with hot chloroform (200 mL) and the white crystalline hydrochloride salt of N,N-diethylaniline was removed by filtration. Slow cooling and evaporation of the chloroform extract to a volume of 50 mL yielded good crystals of the 4-(4,6-dichloro-1,3,5-triazin-2-yl)-N,N-diethylaniline. The obtained product was recrystallized two times from acetone. (Yield: 11.68 g, 40%) (Lit.156=C; Cowley et al., 1991).

(Yield: 11.68 g, 40%); m.p.: 156 °C (Recrystallized from Acetone).

FT-IR (KBr) ν max cm⁻¹: 567, 715, 824, 839, 1164, 1232, 1515, 1610, 2967.


¹³C NMR (DMSO-d₆, 25 °C) (δ ppm): 15.6 (s, –CH₃), 49 (s, –CH₂), 114.6 (s, Ar-C), 125.6 (Ar-C), 130.7 (s, Ar-C), 154.2 (Substituted Ar-C), 172.3 (N=C), 179.5 (N=C).

HRMS: 299.032 (M + 1; 45%), 298.123 (40%), 161.221 (100%), 105.201 (80%); HRMS calculated: 297.1830.

2.2.2. 4,4’-[(6-(4-(Diethylamino) phenyl)-1,3,5-triazine-2,4 diyl)(bis(oxy)) dibenzaldehyde (5)

A Suspension of 4,4’-[(6-(4-(Diethylamino)phenyl)-1,3,5-triazine-2,4 diyl)(bis(oxy)) dibenzaldehyde (5) (1 g, 0.0023 mol) in 50 mL of methanol was added to a solution of aniline 6a (0.44 g, 0.0047 mol) in 20 mL of methanol, 3–4 drops conc. HCl. The mixture was stirred at reflux temperature for 4 h, after completion of Schiff’s base formation (monitored by TLC), the suspension becomes thicker as a white to buff white precipitate formed. The reaction mixture was filtered and solid residue washed with 20 mL methanol to obtain pure DIPOD Schiff’s bases 7a (Sekar et al., 2011).

(Yield: 1.07 g, 73%); m.p.: 195 °C. (Recrystallized from ethanol).

FT-IR (KBr) ν max cm⁻¹: 691, 803, 1142, 1159, 1368, 1497, 1547, 2975.

¹H NMR (CDCl₃, 25 °C) (δ ppm): 1.11 (t, 6H, –CH₃), 3.42 (q, 4H, –CH₂), 6.74 (dd, 2H, J = 8.8, 2.4 Hz, Ar-H), 7.29 (dd, 2H, J = 8.8, 2.4 Hz, Ar-H), 7.32 (dd, 2H, J = 8.4, 2.4 Hz, Ar-H), 7.46–7.50 (dd, 8H, J = 8.4, 1.8 Hz, Ar-H), 7.96–8.00 (dd, 4H, J = 8.8, 1.8 Hz, Ar-H), 10.04 (s, 2H, Aldehyde H).

¹³C NMR (DMSO-d₆, 25 °C) (δ ppm): 12.3 (CH₃), 43.9 (CH₂), 110.7 (Ar-C), 119.2 (Ar-C), 122.5 (Ar-C), 130.9 (Ar-C), 131.1 (Ar-C), 133.7 (Ar-C), 151.5 (Substituted Ar-C), 151.8 (Substituted Ar-C), 171.3 (N=C), 174.4 (N=C), 192.9 (Aldehyde C).

HRMS: 469.201 (M + 1; 76%), 440.109 (35%), 347.398 (15%), 322.234 (17%), 279.365 (100%), 175.423 (22%); HRMS calculated: 468.5038.
HRMS: 619.721 (M+1; 23%), 576.402 (20%), 422.437 (100%), 397.598 (80%), 354.409 (40%), 223.034 (10%); HRMS calculated: 618.7262.

2.2.4. Synthesis of DIPOD Schiff’s bases 7b
A Suspension of 4,4’-((6-(4-(diethylamino)phenyl)-1,3,5-triazine-2,4-diyi)bis(oxi)) dibenzaldehyde 5 (1 g, 0.0023 mol) in 50 mL of methanol was added to a solution of p-chloro aniline 6b (0.61 g. 0.0047 mol) in 20 mL of methanol, 3–4 drops conc. HCl. The mixture was stirred at reflux temperature for 4 h, after completion of Schiff’s base formation (monitored by TLC), the suspension becomes thicker as a white to buff white fluffily precipitate formed. The reaction mixture was filtered and solid residue washed with 20 mL methanol to obtain pure DIPOD Schiff’s bases 7b (Sekar et al., 2011).

(Yield: 1.38 g. 83%); m.p.: 230 °C (Recrystallized from ethanol)

FT-IR (KBr) νmax cm⁻¹: 804, 840, 1042, 1142, 1203, 1342, 1364, 1550, 2975.

¹H NMR (CDCl₃, 25 °C) (δ ppm): 1.14 (t, 6H, –CH₃), 3.43 (q, 4H, –CH₂), 6.74 (dd, 2H, J = 9.0, 2.4 Hz, Ar-H), 7.31 (dd, 2H, J = 8.6, 2.4 Hz, Ar-H), 7.34 (dd, 2H, J = 8.6, 2.2 Hz, Ar-H), 7.48–7.51 (dd, 6H, J = 8.6, 2.0 Hz, Ar-H), 7.99–8.05 (dd, 4H, J = 8.0, 2.0 Hz, Ar-H), 8.13–8.19 (dd, 4H, J = 8.0, 2.4 Hz, Ar-H), 8.72 (s, 2H, CH=N).

¹³C NMR (DMSO-d₆, 25 °C): ppm: 12.5 (CH₃), 44.7 (CH₂), 113.6 (Ar-C), 120.0 (Ar-C), 124.7 (Ar-C), 131.7 (Ar-C), 132.7 (Ar-C), 134.9 (Ar-C), 150.0 (Ar-C), 151.3 (Ar-C), 152.7 (Substituted Ar-C), 157.9 (Substituted Ar-C), 160.1 (Substituted Ar-C), 174.0 (N-C), 175.8 (N=C), 179.7 (N=C).

HRMS: 690.613 (M+1; 20%), 644.087 (76%), 456.376 (100%), 431.475 (58%), 388.987 (96%), 257.098 (30%); HRMS calculated: 689.6322.

2.2.5. Synthesis of DIPOD Schiff’s bases 7e
A Suspension of 4,4’-((6-(4-(diethylamino)phenyl)-1,3,5-triazine-2,4-diyi)bis(oxi)) dibenzaldehyde 5 (1 g, 0.0023 mol) in 50 mL of methanol was added to a solution of p-methoxy aniline 6e (0.59 g, 0.0047 mol) in 20 mL of methanol, 3–4 drops conc. HCl. The mixture was stirred at reflux temperature for 4 h, after completion of Schiff’s base formation (monitored by TLC), the suspension becomes thicker as a white to buff white fluffily precipitate formed. The reaction mixture was filtered and solid residue washed with 20 mL methanol to obtain pure DIPOD Schiff’s bases 7e (Sekar et al., 2011).

(Yield: 1.27 g. 79%); m.p.: 235 °C (Recrystallized from ethanol)

FT-IR (KBr) νmax cm⁻¹: 805, 836, 1144, 1201, 1243, 1345, 1366, 1547, 2978.

¹H NMR (CDCl₃, 25 °C) (δ ppm): 1.09 (t, 6H, –CH₃), 3.41 (q, 4H, –CH₂), 3.53 (s, 6H, –OCH₃), 6.73 (dd, 2H, J = 8.8, 2.4 Hz, Ar-H), 7.28 (dd, 2H, J = 8.5, 2.4 Hz, Ar-H), 7.31 (dd, 2H, J = 8.5, 2.0 Hz, Ar-H), 7.45–7.48 (dd, 8H, J = 8.5, 2.0 Hz, Ar-H), 7.94–7.97 (dd, 2H, J = 7.9, 2.0 Hz, Ar-H), 8.01–8.04 (dd, 4H, J = 8.2, 2.4 Hz, Ar-H), 8.67 (s, 2H, CH=N).

¹³C NMR (DMSO-d₆, 25 °C): ppm: 12.2 (CH₃), 44.3 (CH₂), 59.4 (–OCH₃), 113.2 (Ar-C), 119.8 (Ar-C), 124.2 (Ar-C), 131.4 (Ar-C), 132.3 (Ar-C), 134.7 (Ar-C), 142.5 (Ar-C), 149.3 (Ar-C), 150.1 (Ar-C), 152.4 (Substituted Ar-C), 157.6 (Substituted Ar-C), 158.4 (Substituted Ar-C), 172.9 (N=C), 175.0 (N=C), 178.3 (N=C).

HRMS: 719.843 (40%), 590.698 (75%), 465.521 (100%), 360.403 (56%), 259.291 (70%); HRMS calculated: 718.8436.

2.3. Molecular Imprinting of Fractosil 500 with DIPOD Schiff’s base 7a
Fractosil 500 was refluxed in 5% HNO₃ for 1 h and then washed with H₂O thoroughly and dried in a vacuum oven (120 °C) for 5 h before use. Into a suspension of oven-dried Fractosil 500 dissolving 7a (0.59 g, 0.0023 mol) in 20 mL of dry toluene was added DIPOD Schiff’s base 7a dissolved in a minimum amount of chloroform. The suspension was refluxed in a nitrogen atmosphere for 2 days, mixture was filtered and silica was washed thoroughly with toluene and then chloroform and dried under vacuum for 6 h. This modified silica gel was stirred in a solution of 5 N HCl in 5 mL 50% methanol for 5 h to remove DIPOD and separate out imprinted silica which contains free amine groups. After 5 h, the silica gel was filtered, washed with 5 mL methanol and 20% sodium bicarbonate solution followed by water (20 mL) to remove acidic content and dried under vacuum for 5 h. The filtrate was concentrated under reduced pressure to recover DIPOD and which was further confirmed by thin layer chromatography as well as with standard DIPOD samples. The imprinted silica gel was heated with 25% aqueous HF (40 mL) in 10 mL chloroform. After 1 h, 20 mL water was added and the organic layer was removed. The organic layer was washed with water and dried over sodium sulfate and concentrated up to dryness. The obtained amine confirmed by TLC, UV and FT-IR analysis with standard amines.
3. Results and discussion

The reaction of cyanuric chloride with N,N-diethyl aniline yielded the desired dichloro 1,3,5-triazine (3). 4-(4,6-Dichloro-1,3,5-triazin-2-yl)-N,N-diethylaniline (3) reacted with two equivalents of 4-hydroxybenzaldehyde in benzene to give the desired dialdehyde, 4,4’-(6-(4-(diethylamino)phenyl)-1,3,5-triazine-2,4-diyl)bis(oxy)) dibenzaldehyde (5), coded as DIPOD. Dialdehyde (5) was then reacted with different aromatic amines to afford the corresponding Schiff’s base DIPOD derivatives (7a–7d) Scheme 1.

Molecular Imprinting was carried out with DIPOD Schiff’s 7a on silica gel to yield imprinted silica. Porous silica gel, Frac-tosil 500, was refluxed in dry toluene for 2 days with an appropriate amount of the DIPOD Schiff’s bases 7a to get a substitution on silica gel as shown in Fig. 1. Primary experiments of DIPOD Schiff’s base Molecular Imprinting indicated that a partial degradation of DIPOD aldehyde takes place during Molecular Imprinting reaction. Refluxing of the DIPOD Schiff’s base in toluene for 2 days produced p-hydroxy benzaldehyde, suggesting that degradation was caused by the partial hydrolysis of the Schiff’s base and subsequent attack on the ether linkage of amine. DIPOD was separated from the modified imprinted silica by treatment with dilute hydrochloric acid to yield silica gel with free amines on the solid surface as shown in Fig. 1. In the $^1$H NMR spectra of DIPOD, the signal was detected at about 10.04 ppm confirming the formation of DIPOD. Further conversion of DIPOD into dipodal Schiff’s bases was confirmed by $^1$H NMR and Mass spectra. The recovered DIPOD was confirmed by TLC. The imprinted

Scheme 1 Synthesis of DIPOD (5) and DIPOD Schiff’s bases (7a–7d).
silica was treated with aqueous hydrogen fluoride to analyze the surface bonded molecules. Analysis of the product indicated that aniline 6a was released by the treatment of hydrogen fluoride, confirming the incorporation of amines group on the solid surface.

3.1. Density functional theory calculation

Density functional theory calculations were performed to optimize the geometry of compound 5. Ground state geometry was optimized with B3LYP level of theory and 6–31/G(d) basis set using Gaussian 03 W package (Frisch et al., 2004).

The optimized geometry has energy $-1563.23970829 \text{ Hartree} (\text{42537.93494877 eV})$ with PMS gradient norm approximately 0.00. The triazine ring and $N,N$-diethyl amino phenyl ring are in plane but due to the angular nature of C-O-C bonds (14–18–22) and (16–19–21) 4-formyl phenyl rings are out of plane. The distance between two formyl groups (C32–C34) is calculated to be 13.02846 Å and results are summarized in Table 1 and optimized structure is summarized in Fig. 2. The distance between incorporated groups on solid support depends on the distance between two formyl groups present in molecules, the calculated distance between two formyl groups in compound 5 is 13.02846 Å.

3.2. Thermal stability

In order to examine the thermal stability of these DIPOD Schiff's bases, Thermo gravimetric (TG) and differential scanning colorimeter (DSC) analyses were carried out between 40 and 600 °C under a nitrogen atmosphere. The TG curves of the compounds are shown in Fig. 3. The TG results indicate that the frame work of the synthesized compounds is stable up to 300 °C. Above 300 °C the thermo gravimetric curve of the synthesized compounds showed a major loss in weight for compounds 7a–7c, but compound 7d did not decompose even up to temperature 600 °C. The comparisons of the $T_d$ (decomposition temperature) showed that the thermal stability of the 7a–7d decreases in the order 7d > 7b > 7a > 7c. Thermal stability and their plausible degradation scheme are presented in, Fig. 3.

3.3. Photophysical properties

The UV–Vis absorption and emission spectra of compounds 7a–7d were recorded in dimethyforamide (DMF), to find out the role of Schiff's base functionality for electron communication in DIPOD system between the electron donating and acceptor terminals on photophysical properties at room temperature and compound concentration was 1 × 10⁻⁶ M. The $\lambda_{\text{max}}$ (absorbance) values of compounds 7a–7d were obtained as 372 (1.554), 375 (1.106), 372 (0.801) and 335 (0.421) nm, respectively and $\lambda_{\text{max}}$ (emission) values of compounds 7a–7d were obtained as 434 (179), 428 (97), 428 (25), 411 (19) nm, respectively. As can be seen the absorption characteristics of compounds 7a–7d are nearly similar. The absorption and emission spectra of compounds 7a–7d are shown in Figs. 4 and 5.

![Figure 1 Molecular imprinting technique.](image)
Figure 2  Optimized structure of compound 5.

Figure 3  Thermogravimetric analysis of compounds 7a–7d.

Figure 4  UV–Vis absorption spectra of compounds 7a–7d.
Figure 5  Fluorescence emission spectra of compounds 7a–7d.

4. Conclusions

In this study, we illustrated the synthesis of a new DIPOD and DIPOD Schiff’s base template for Molecular Imprinting on silica surface. The imprinted surface provides a site of two organized amino groups which can be further modified with various functional groups. Density functional theory calculation results show the distance between two formyl groups in DIPOD and Schiff’s base to be approximately 1.3 nm. Thermal stability results showed that synthesized DIPOD derivatives have good thermal stability. The structure of synthesized dipodal derivatives was confirmed by FT-IR, $^1$H NMR, Mass spectra and UV–Vis analysis.

References


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Acknowledgment

Table 2  Absorption, emission and quantum yield of synthesized compounds 7a–7d.

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Absorption (Intensity a.u.)</th>
<th>Emission (Intensity a.u.)</th>
<th>Stoke’s shift</th>
<th>Quantum yield</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\lambda_{max}$ (nm)</td>
<td>$\lambda_{max}$ (nm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7a</td>
<td>372 (1.554)</td>
<td>434 (179)</td>
<td>62</td>
<td>0.1075</td>
</tr>
<tr>
<td>7b</td>
<td>375 (1.106)</td>
<td>428 (097)</td>
<td>53</td>
<td>0.0819</td>
</tr>
<tr>
<td>7c</td>
<td>372 (0.807)</td>
<td>428 (025)</td>
<td>56</td>
<td>0.0171</td>
</tr>
<tr>
<td>7d</td>
<td>335 (0.421)</td>
<td>411 (019)</td>
<td>76</td>
<td>0.0672</td>
</tr>
</tbody>
</table>

respectively. Electron donating group on Schiff’s causes a blue shift.

Quantum yield of compounds 7a–7d were determined by using anthracene as standard. Absorption and emission characteristics of standard as well as unknown samples were measured at different concentrations of unknown samples and standard at 2, 4, 6, 8 and 10 ppm levels. Absorbance intensity values were plotted against emission intensity values. A linear plot was observed. Gradients were calculated for each compound and for standards. All the measurements were done by keeping the parameters constant such as same solvent and constant slit width. Relative quantum yield of all synthesized DIPOD derivatives 7a–7d were calculated by using Formula (1) (Padalkar et al., 2012)

Relative fluorescence quantum yield

$$\phi_\lambda = \phi_{ST} \frac{\text{Grad} \lambda / \text{Grad} \lambda_{ST}}{(n^2 / n^2_{ST})}$$

where $\phi_\lambda$ = Quantum yield of unknown sample; $\phi_{ST}$ = Quantum yield of standard used; $\text{Grad} \lambda$ = Gradient of unknown sample; $\text{Grad} \lambda_{ST}$ = Gradient of standard used; $n^2 \lambda$ = Refractive index of solvent for unknown sample; $n^2_{ST}$ = Refractive index of solvent for sample.

The fluorescence quantum yields of 7a–7d in ethanol at room temperature are obtained and presented in Table 2. It is observed that the quantum yield values for 7b–7d were much lower than those for 7a. Furthermore the fluorescence quantum yield of 7a is about 10 times higher than that of 7b and all compounds showed similar fluorescence behavior.