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Functionalization of hydroxyl terminated polybutadiene with biologically active fluorescent molecule

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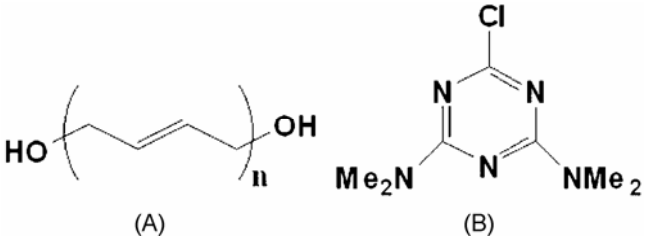
Abstract. **A biologically active molecule, 2-chloro-4,6-*bis*(dimethylamino)-1,3,5-triazine (CBDT), has been covalently attached at the terminal carbon atoms of the hydroxyl terminated polybutadiene (HTPB) backbone. The modification of HTPB backbone by CBDT molecule does not affect the unique physico-chemical properties such as fluidity, hydroxyl value and microstructure of the parent HTPB. The formation of hydrogen bonding between the terminal hydroxyl groups and the nitrogen atoms of triazine moiety is the driving force for the terminal attachment chemistry. The functionalized HTPB (HTPB–CBDT) shows a strong fluorescence emission at 385 nm.**

Keywords. **Hydroxyl terminated polybutadiene (HTPB); functionalization of polymers; intermolecular hydrogen bonding; fluorescent active hydroxyl terminated polybutadiene; biologically active HTPB.**

1. Introduction

Hydroxyl terminated polybutadiene (HTPB) (scheme 1) is a polymeric binder having molecular weight ranging between 2000 and 6000. Anionic or free radical polymerization methods are used to synthesize HTPB. The molecular weight, polydispersity and the hydroxyl functionality of the HTPB depends upon various factors such as type of initiator, solvent, polymerization temperature, polymerization time etc (Odian 2004). HTPB yields mechanically strong polyurethane when reacted with diisocyanides. This polyurethane has been used in the field of medical and bioengineering for several decades (Zhou and Yi 1999; Zhang *et al* 2000; Guan *et al* 2005) because of its outstanding mechanical properties. In case of HTPB, three different types of microstructures (e.g. *cis*, *trans* and *vinyl*) are possible because of the probability of addition of monomers in three different ways during polymerization. The quantity of microstructure present in HTPB sample dictates the flow characteristics of the sample and the mechanical properties of the corresponding polyurethane (Manjari *et al* 1993; Nazare *et al* 1993). The HTPB based polyurethanes have also been studied in the literature by several authors for the separation of organic compounds, selective adsorption of proteins and selective gas transport properties (Chen *et al* 2000; Yang and Lin 2001; Gupta *et al* 2002). Recently, HTPB has been successfully used for the fabrication of elastic conducting polymer micro particles with core-shell structure (Kuo *et al* 2003). Also HTPB based polyurethane has been used in drug capsules because of its excellent biodegradable properties. The aim of this article is to functionalize the HTPB with biologically active molecule such as 2-chloro-4,6-*bis*(dimethylamino)-1,3,5-triazine (CBDT) (Tseng *et al* 2005).

Here, we have functionalized HTPB by an important biologically active molecule called 2-chloro-4,6-*bis* (dimethylamino)-1,3,5-triazine (CBDT) (scheme 1). CBDT is known as an antitumour agent, which is effective against several human malignancies (Donald *et al* 1951; Atri *et al* 1984; Sanders and Ames 1985; Baliani *et al* 2005). The main objective of this work is to functionalize the HTPB backbone with CBDT molecule which upon further reaction with diisocyanides will produce CBDT functionalized polyurethane. This functionalized polyurethane will be selective and efficient towards various human malignancies. This kind of polyurethane will have excellent biodegradable properties. In this article, we are reporting the functionalization of HTPB backbone by covalently attaching biologically active molecule 2-chloro-



Scheme 1. (A) Hydroxyl terminated polybutadiene (HTPB) and (B) 2-chloro-4,6-*bis*(dimethylamino)-1,3,5-triazine (CBDT).

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4,6-*bis*(dimethylamino)-1,3,5-triazine (CBDT) at the terminal carbon atoms of the HTPB. We have characterized the functionalized HTPB using IR, NMR, and UV-vis fluorescence spectroscopic techniques.

2. Experimental

2.1 *Materials*

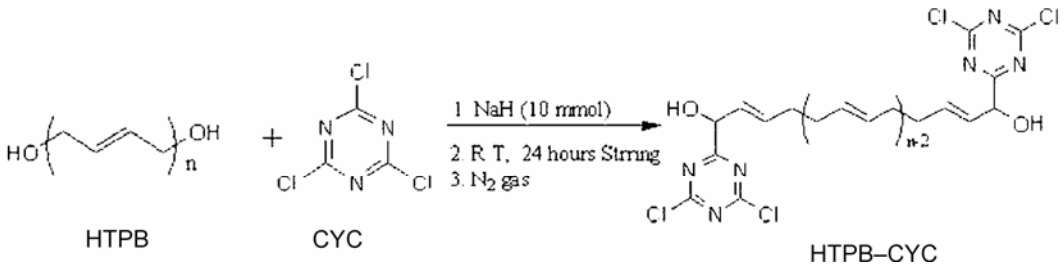
The hydroxyl terminated polybutadiene (HTPB) used in this work was prepared by free radical polymerization using hydrogen peroxide as initiator and was received from HEMRL Pune, India, as a gift sample. The molecular weight and polydispersity of the HTPB was determined by using gel permeable chromatography (GPC) technique. The number average molecular weight ($\bar{M}_n$) of HTPB was 5210 and the polydispersity index (PDI) was 2·53. Sodium hydride (NaH) was purchased from LOBA chemical, India and used as received. The cyanuric chloride (CYC) was purchased from Sigma-Aldrich and used as received. The solvents (dimethylformamide, dichloromethane) were dried and distilled before they were used. NMR solvents were obtained from Merck, India.

2.2 *Preparation of HTPB–CYC*

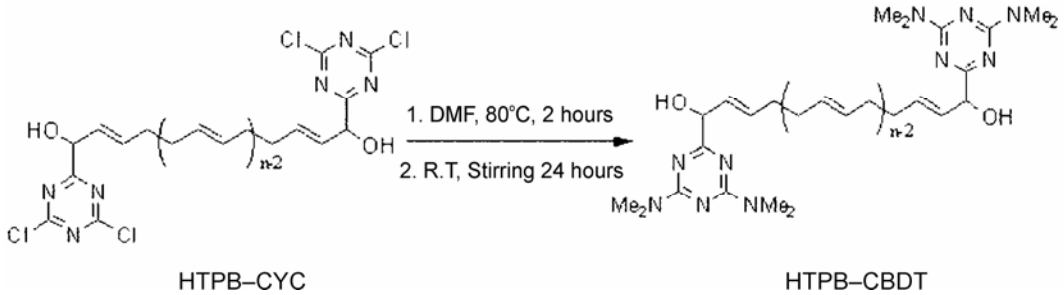
3·355 g (62 mmol, considering 54 as a molecular weight of HTPB repeat unit) of moisture free HTPB was taken in 10 ml of dichloromethane solvent in a three neck round bottom flask fitted with a guard-tube and continuous nitrogen purging inlet. HTPB was completely dissolved in dichloromethane solvent by stirring with the help of a magnetic stirrer. Then 0·223 g (10 mmol) of NaH was added to the HTPB solution in presence of continuous nitrogen gas purging. The mixture was stirred for 30 min and then the cyanuric chloride (CYC) (0·185 g, 1 mmol) was added to the reaction mixture. The stirring was continued for another 3 h in presence of nitrogen gas and then stirring was continued for overnight without nitrogen gas. The solvent was removed at 50°C in rotary evaporator. The resulting product was washed thoroughly and repeatedly with methanol followed by hexane to remove traces of NaH, unreacted CYC and excess HTPB. The final compound was milky white in colour which is different from the parent HTPB. The purity of the resulting sample was checked by thin layer chromatography (TLC) using 3 : 2 (V/V) mixture of hexane and ethyl acetate as a solvent. The reaction scheme for the modification of HTPB using CYC is presented in scheme 2.

2.3 *Preparation of HTPB–CBDT*

The moisture free HTPB–CYC was taken in 100 ml round bottom flask along with 10 ml dimethylformamide (DMF) and heated at 80°C for 2 h with continuous stirring. The reaction was further continued with continuous stirring at room temperature for overnight. A reddish brown colour compound was obtained. The compound obtained from the above reaction was extracted by using dichloromethane solvent. The final reddish brown product was achieved after evaporation of the dichloromethane and purified by washing several times with methanol solvent to remove the unreacted starting materials. The reaction scheme is presented in scheme 3.



Scheme 2. Preparation of HTPB–CYC.



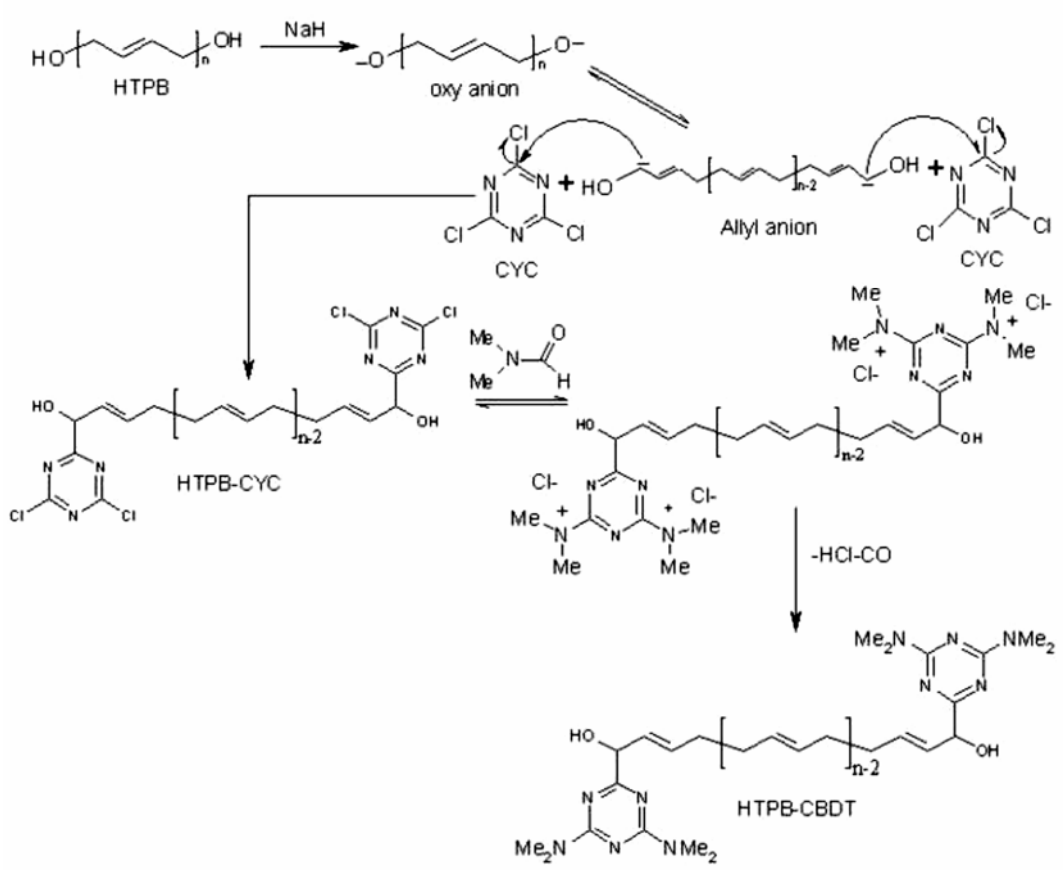
Scheme 3. Preparation of HTPB–CBDT.

2.4 *Characterization of materials*

FTIR spectra of HTPB, HTPB–CYC and HTPB–CBDT were recorded on a Nicolet 4700 FT–IR spectrometer. The spectra were taken using the neat samples in KBr crystal. The ^{1}H-NMR and ^{13}C-NMR of the samples were recorded on a Bruker 400 MHz spectrometer using $CDCl_3$ as NMR solvent. The UV-visible absorption spectra of the dilute solution of all the samples in THF solvent were recorded on a Cary-100Bio (VARIAN) spectrophotometer. Steady state fluorescence emission spectra of the dilute solution of all the samples in THF solvent were recorded on a Jobin Yvon Horiba spectrofluorimeter (model Fluoromax-4).

3. Results and discussion

Cyanuric chloride (CYC) is covalently attached at the terminal carbon atoms of HTPB polymer backbone (scheme 2). The modified HTPB (HTPB–CYC hereafter) has been further reacted with dimethylformamide (DMF) to get dimethylamine substitution at the 3,5 position of the attached cyanuric chloride by replacing the chlorine from the CYC moiety as shown in scheme 3 (Agarwal and Chauhan 2004). This dimethylamine substitution changes the CYC moiety to CBDT moiety which is our desired molecule. Hereafter we defined this molecule as HTPB–CBDT. The covalent attachment of CYC onto the HTPB backbone is carried out using NaH as a catalyst in CH_2Cl_2 solvent by taking appropriate moles of HTPB and CYC. After a careful and thorough purification, HTPB–CYC compound is subjected to various characterization processes and further reacted with DMF by heating at 80°C to get HTPB–CBDT. The catalyst, NaH, plays an important role for the covalent attachment of CYC molecule in the HTPB backbone. The absence of any kind of functional group at the terminal carbon atoms (except hydroxyl group) makes it difficult to carry out the attachment chemistry. We have proposed a mechanism (scheme 4) for the attachment of the CYC moiety at the terminal carbon atoms of the HTPB. Similar mechanism has been proposed by us for the terminal attachment/functionalization of the HTPB by various highly energetic molecules (Murali Sankar *et al* 2009a, b). The catalyst, NaH, readily yields oxy anion. Due to the instability of the oxy anion, it abstracts proton from the adjacent carbon atom and yields allyl anions. This allyl anion gets stability very easily due to the long conjugation of the π electron cloud of the polybutadiene chain. Allyl anion readily attacks the CYC molecule, which is a good elec-



Scheme 4. Proposed mechanism for the terminal functionalization of HTPB by CBDT.

trophile because of the presence of strong chloride leaving groups. The detailed mechanism is explained in scheme 4.

3.1 *IR studies*

All the samples (HTPB, HTPB–CYC and HTPB–CBDT) are characterized by FT–IR, ^{1}H, ^{13}C-NMR spectroscopy techniques. The presence of C=C vibration (1640 cm^{-1}) and the microstructures (968 cm^{-1} for 1,4-*trans*, 911 cm^{-1} for 1,2-vinyl and 723 cm^{-1} for 1,4-*cis*) of HTPB are clearly visible in all three cases (figure 1). These observations hint that the double bond and the microstructures of the butadiene have not been disturbed even after the modification of the polymer backbone. The peak at 1708 cm^{-1} in case of HTPB–CYC is due to C–Cl vibration and the absence of C–Cl vibration in case of HTPB–CBDT indicates that both the Cl atoms in the HTPB–CYC have been replaced successfully by the dimethyl amine groups. Also the presence of dimethyl amine group is evident from the peaks at 1275 cm^{-1} which is absent in case of HTPB–CYC. The O–H frequency due to terminal hydroxyl group comes at 3407 cm^{-1} for HTPB, 3463 cm^{-1} for HTPB–CYC and HTPB–CBDT. Therefore, it is clearly evident that the free terminal hydroxyl groups are present even after the modification of HTPB backbone. The calculated hydroxyl values for HTPB, HTPB–CYC and HTPB–CBDT are 43, 41 and 37·2 mg KOH/g, respectively. Hence the almost similar hydroxyl values of the modified HTPB with the parent HTPB once again strengthens our observation from the IR studies that the free OH groups are available in the modified HTPB (HTPB–CYC, HTPB–CBDT) for further reaction. The free hydroxyl groups are essential because of the fact that these free OH groups need to be used for the polyurethane formation, where OH groups react with isocyanides to form polyurethane.

Our FT–IR results discussed in the previous section demonstrate the presence of free OH at the two terminals of the HTPB and double bond in the HTPB backbone. Our proposed mechanism (scheme 4) suggests the attachment of CYC molecules at the two terminal carbon atoms of the HTPB chain. Despite our proposed mechanism, the most important question regarding the feasibility of the terminal attachment chemistry still remain and it deserves experimental evidence. We have analysed FT–IR spectra (figure 2) of HTPB and the modified HTPB samples very closely to prove our terminal attachment chemistry argument. The stretching of the free OH is expected at 3600 cm^{-1} (Silverstein and Webster 2002) but in case of HTPB the terminal OH stretching appears at 3407 cm^{-1} which is much lower than expected. This indicates that in HTPB a strong intermolecular hydrogen bonding between the OH groups of different polymer chains exists. The HTPB–CYC and HTPB–CBDT samples show OH stretching at 3463 cm^{-1} (figure 2). This proves that CYC and CBDT molecules are able to break

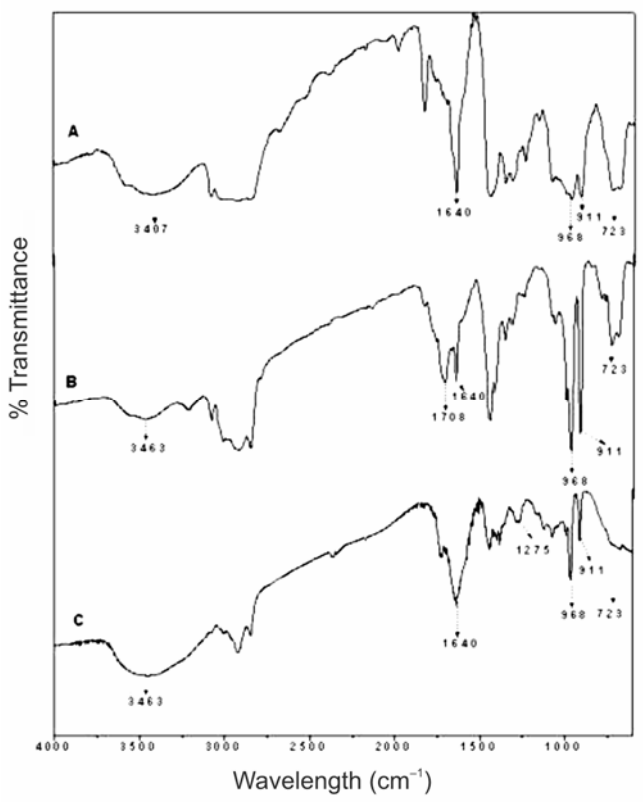


Figure 1. FT–IR spectra of (A) HTPB, (B) HTPB–CYC and (C) HTPB–CBDT.

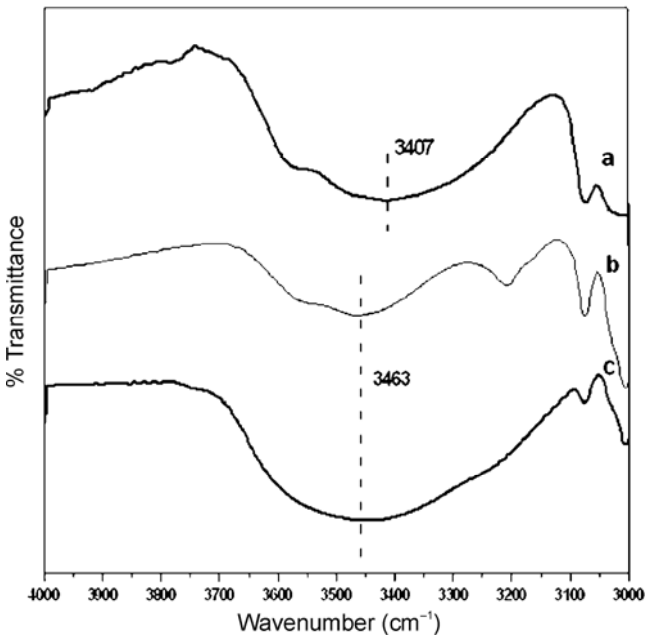


Figure 2. FT–IR of the hydroxyl region of (a) HTPB, (b) HTPB–CYC and (C) HTPB–CBDT.

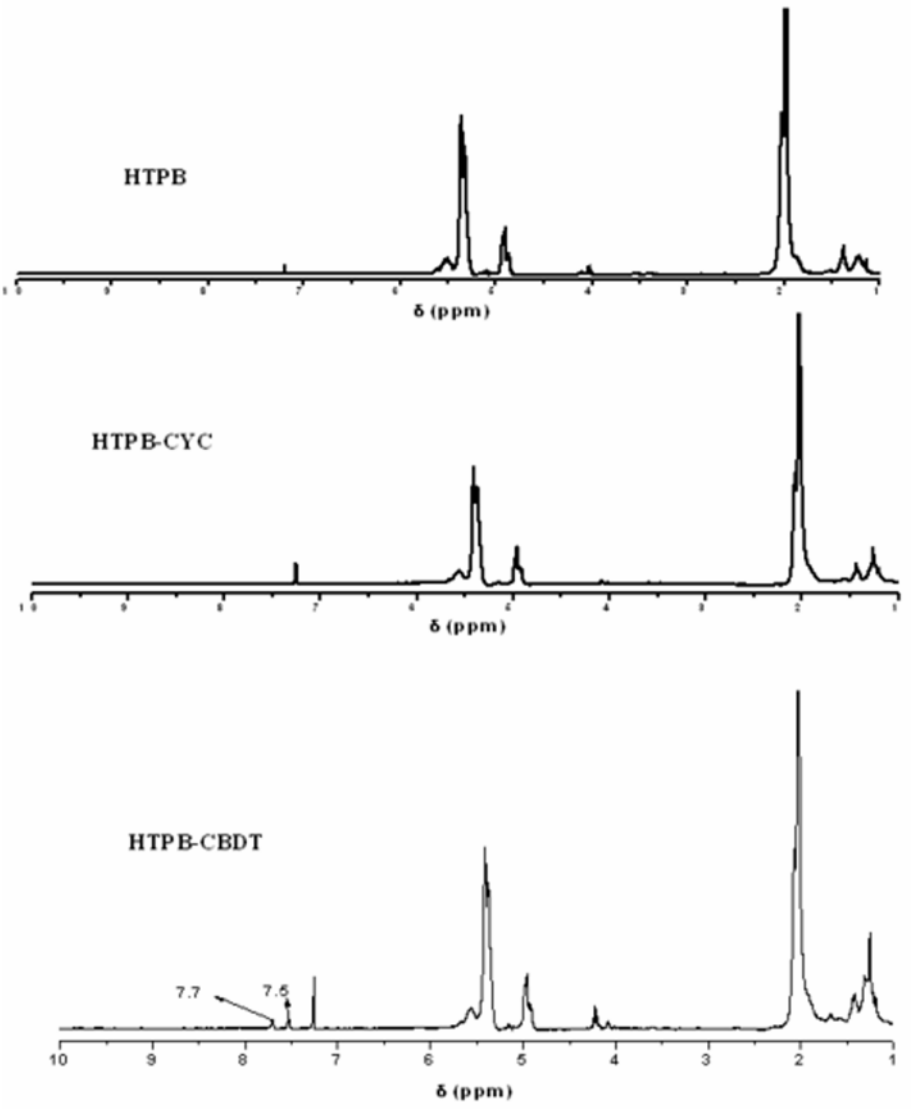


Figure 3. Proton NMR spectra of HTPB, HTPB–CYC and HTPB–CBDT. Spectra are recorded using $CDCl_3$ as NMR solvent.

the intermolecular hydrogen bonding between the terminal hydroxyls of HTPB chains and as a result OH stretching for the modified HTPB observed at higher wave number than the parent HTPB. It is important to note that the OH stretching frequency of HTPB–CYC and HTPB–CBDT have not shifted completely to the expected stretching of the free OH at 3600 cm^{-1}, the OH stretching of these compounds move towards higher wavenumber (3463 cm^{-1}) compared to the parent HTPB. This attributes the formation of hydrogen bonding between the OH groups of HTPB and CYC or CBDT molecules. The hydrogen bonding between the terminal OH and the nitrogen atom of triazine ring is possible. Because of this hydrogen bonding the OH frequency in case of modified HTPB samples move to 3463 cm^{-1} and not to 3600 cm^{-1}. Thus the existence of the hydrogen bonding between terminal OH and N and breaking of intermolecular hydrogen bonding of HTPB chains are proved from the IR study. Therefore, for successful hydrogen bonding between N and OH, the CYC or CBDT molecules have to be in the adjacent carbon atoms of the OH groups. Thus the terminal attachments of CYC and CBDT molecules are expected and obvious. Hence our proposed mechanism given in scheme 4 is justified.

3.2 *NMR studies*

The ^{1}H-NMR chemical shift regions of the HTPB–CYC and HTPB–CBDT are at δ = 1·2–1·4, 2–2·1 and 4·9–5·4 and these are exactly identical with the parent HTPB (figure 3). This reveals that the microstructure of HTPB present in HTPB–CYC and HTPB–CBDT are identical with the parent HTPB. Also the HTPB–CBDT has two new peaks at 7·5 and 7·7 (figure 3) which correspond to

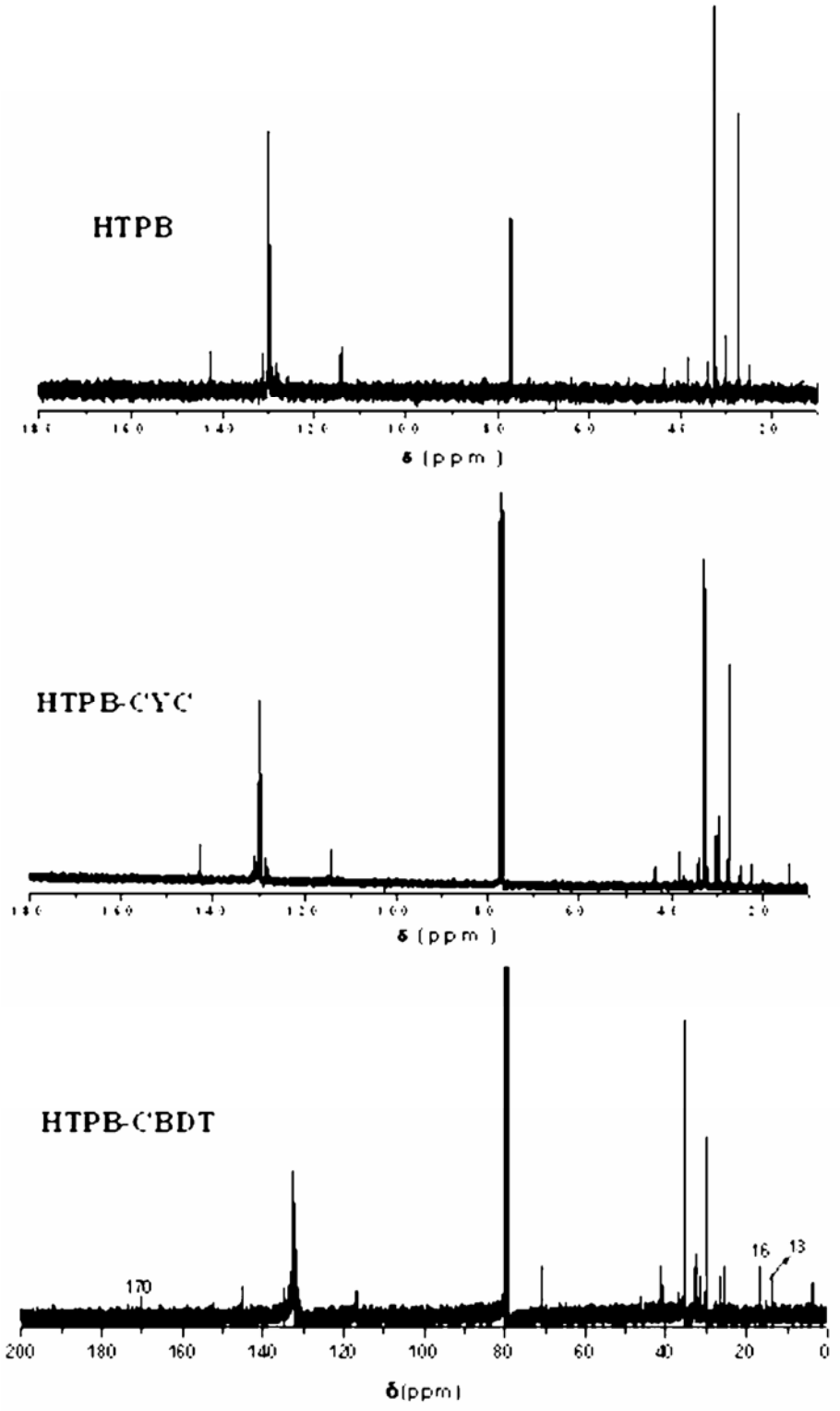


Figure 4. ^{13}C-NMR spectra of HTPB, HTPB–CYC and HTPB–CBDT. $CDCl_3$ are used as NMR solvent.

methyl protons of N–Me_2 groups; this clearly shows the presence of CBDT moiety and absence of chloride groups. These 7·5, 7·7 peaks are shifted a bit downfield because of the electron withdrawing nature of the three nitrogen atoms of the triazine ring (figure 3). The ^{13}C-NMR spectra of HTPB–CYC, HTPB–CBDT and HTPB are also

similar (figure 4). The peaks at the δ 25–42 region corresponds to aliphatic carbons of HTPB and the peaks at δ 114–142 region belongs to olefinic carbons of HTPB. A new peak at δ 170 in HTPB–CBDT is clearly seen corresponding to the carbon atoms which are attached to the N–Me_2 groups and the peaks at δ 16, 13 resemble the presence of methyl groups for the N–Me_2 which are shifted upfield because of the triazine ring nitrogen atoms (figure 4).

3.3 *UV-Vis studies*

We have carried out the UV visible studies for HTPB, CYC, HTPB–CYC and HTPB–CBDT from their dilute solution in THF and all the spectra are presented in figure 5. The absorption peak at 280 nm in case of HTPB is due to the $\pi \rightarrow \pi^*$ transition of trans microstructure of HTPB (Murali Sankar *et al* 2009a, b). CYC molecule has a sharp distinct peak at 247 nm. HTPB–CYC shows two distinct sharp peaks at 239 nm and 280 nm. HTPB–CBDT shows two distinct peaks at 230 and 280 nm. The UV spectra clearly show that the absorption maxima due to triazine moiety have blue shifted in case of HTPB–CYC and HTPB–CBDT. However, the $\pi \rightarrow \pi^*$ transition maxima at HTPB is not disturbed at all in both the cases. These observations indicate that the electron delocalizations of the triazine are influenced by the HTPB π electrons. This is possible only when the triazine moiety is covalently attached to the HTPB backbone. Therefore, our UV results also prove that triazine moiety is covalently attached with the HTPB. The larger blue shift in case of HTPB–CBDT (figure 5) is due to the electron donating NMe_2 functional groups. Thus we can summarize that FT–IR, ^{1}H-NMR, ^{13}C-NMR and UV visible analysis demonstrate the covalent attachment of CYC and further modification to dimethyl amine moiety is successful without disturbing the microstructure, other essential and unique physico-chemical properties of HTPB.

3.4 *Emission spectroscopy studies*

The fluorescence emission spectra of HTPB, CYC and modified HTPB (HTPB–CYC and HTPB–CBDT) are studied from their dilute solution in THF solvent. The emission spectra of the HTPB–CBDT and HTPB–CYC in THF solvent (concentrations of the solutions are 5×10^{-5} g dl^{-1}) are shown in figure 6. HTPB–CBDT shows a very strong emission band at 385 nm whereas HTPB–CYC shows emission at 370 nm and the HTPB–CYC emission is much weaker than HTPB–CBDT emission (figure 6). The HTPB and CYC do not show any emission from their solution in THF solvent. The peak at 385 nm region in the emission spectra clearly shows that the HTPB–CBDT molecule is fluorescence active. The fluorescence activity of HTPB–CBDT is due to the electron donating properties of NMe_2 groups which are attached on the HTPB backbone. Hence, the fluorescence spectra once again strengthen our claims (i) that the triazine molecules are covalently attached and (ii) the Cl atoms are completely substituted with NMe_2 groups. A thorough understanding of the emission spectra may help us to find out the chain conformation and microstructure of HTPB. This work is under progress.

4. Conclusions

We have covalently attached a biologically active molecule at the terminal carbon atoms of the HTPB without

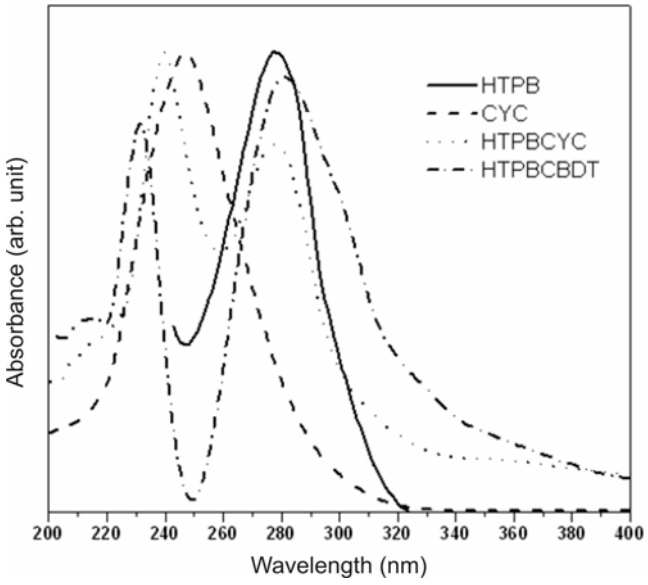


Figure 5. Absorption spectra of HTPB, HTPB–CYC, HTPB–CBDT and CYC from their dilute solution in THF.

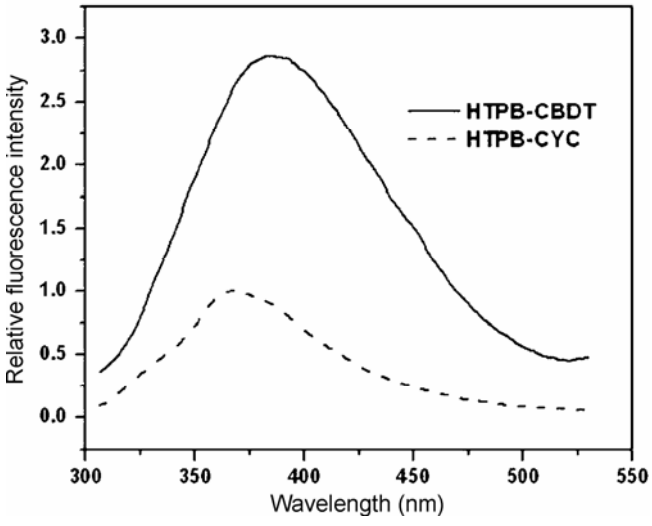


Figure 6. Emission spectra of HTPB–CBDT and HTPB–CYC in THF solvent (concentrations of the solutions are 5×10^{-5} g dl^{-1}); excited wavelength in both the cases are 280 nm.

destroying the unique physico-chemical properties of the parent HTPB. The disruption of the intermolecular hydrogen bonding between HTPB chains and the formation of hydrogen bonding between the terminal OH group of the HTPB and the N atom of the triazine ring are the driving forces for the covalent attachment of CBDT at the terminal carbon atoms of HTPB. The π electron delocalization of the butadiene backbone influenced the electron delocalization of the triazine moiety. The newly synthesized modified HTPB (HTPB–CBDT) is a fluorescent active molecule in solution. This property may help us to find out the chain conformation and microstructure of HTPB and this modified HTPB may play a vital role in bioengineering and drug delivery applications.

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