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Amination and Hematological Study of Styrene Maleic Anhydride Copolymer with Amine and DMSO

Ravish S.Rajput[1]*, Singh A.[2]

[1]Applied Science Div. GCRG Memorial Trust Group of Institutions, Lucknow 226021 (U.P.), India
[2] Institute of Enginneing & Technology, Lucknow, 226001, India

***Corres. author: ravishrajput@gmail.com**

Abstract: SMA was modified with different amines and it was dissolv in DMSO some interesting results was obtain. For the different conversions of copolymers the propyl amine, aniline, 4-amino benzoic acid etc. was chosen for this work. Clearly it is observed that the conversion of Styrene maleic anhydride to amide by the treatment with amine derivatives and modified styrene maleic anhydride was treated with dimethyl sulphoxide. The heamatological profile was also be studied for modified amide.
Keywords: Styrene co-maleic anhydride, amine, haematological, amination,dimethyl sulfoxide.

Introduction

Exponential growth in the knowledge of polymer science and the applications there of witnessed in the recent past has prompted the author to look in to final details of SMA with emphasis on charge transfer interaction[1,2] with Dimethyl sulfoxide.

So far many reports available in literature deal with the interaction of Styrene maleic anhydride and amines[4] with dimethylsulphoxide. When SMA mixed with DMSO in 1:2 it forms a intermediate unstable complex[3].The author has investigated the interaction of amine modified SMA with dimethylsulphoxide,which has yielded very interesting results.

Styrene maleic anhydride co-polymer follows the complex radical polymerization of vinyl aromatic Styrene (Donor) and maleic anhydride (Acceptor) and it has interesting chemical and biological properties. The anhydride group can also easily react with amine containing compounds such as aminobenzoic acid[5] to obtain modified SMA polymer with high yield. SMA may be conveniently used as an intermediate in preparing functional polymers since active agents containing amino groups can be linked to it *via* ring-opening reaction.

Experimental

Material and methods

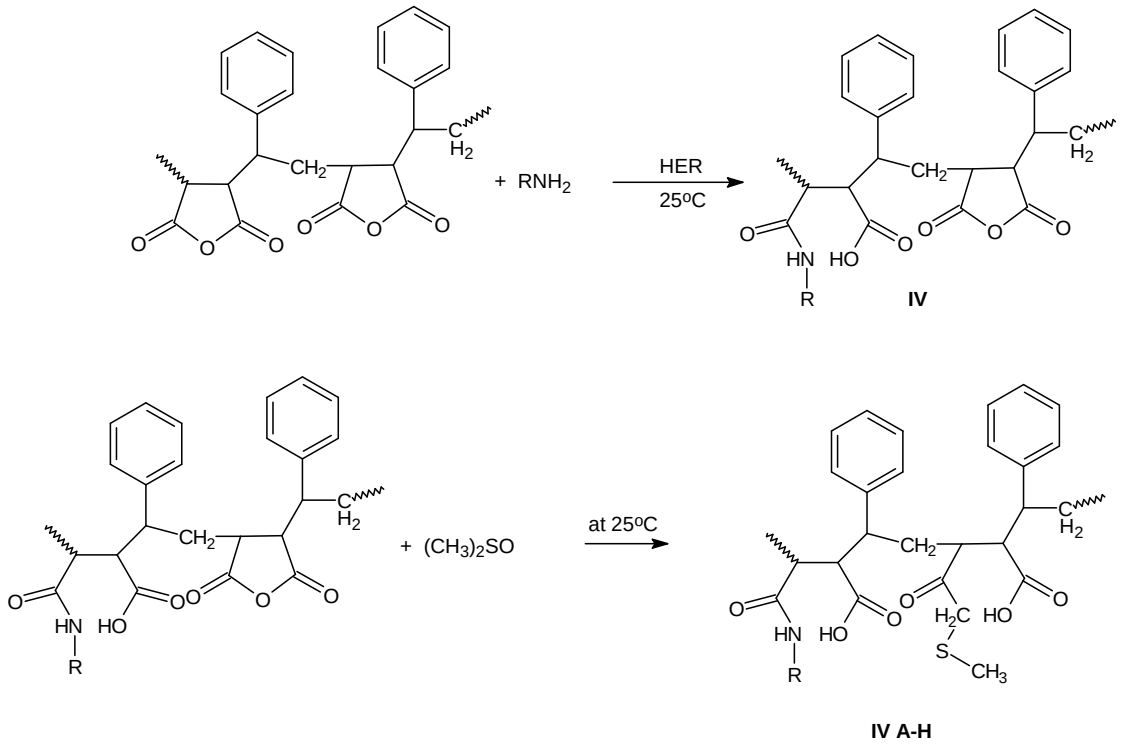
Styrene was purchased from S.d.fine and washed with aqueous NaOH solution then distilled water followed by drying over anhydrous calcium chloride and finally distilled under vacuum for further use. Maleic anhydride (99%) purchased from S.d.fine and purified before use by recrystallization from anhydrous benzene and sublimation in vacuum. Aniline(97%), and others amines, Pure DMSO(d6) also purchased from S.d.fine, was used for the synthesis, all the chemicals were purchased as analytical grade from S.d.fine. Infrared spectra of complex polymer were recorded on Perkin-Elmer Spectrum RX1 FTIR in range of 4000-450cm^{-1}, pellets were prepared by mixing of complex with KBr while ^{1}H NMR Spectra of the polymer complex was recorded on 500 MHZ-FT NMR spectrometer.

Synthesis

Synthesis of Propyl Amine derived Styrene maleic anhydride and dimethyl Sulfoxide (1A)

A solution containing 2g (0.01 mole) styrene maleic anhydride, 0.82 ml. (0.01 mole) propyl amine in 50 ml of DMF at 25^{o}C for 8 hours, the solution was precipitated with toluene collected by filtration and washed with ether and dried *in vacuo* overnight. The modified SMA (T_g 137^{o}C) was checked by FTIR for determination of unreacted maleic anhydride moiety ,half esterification reation (HER). Now 0.46g (0.001mole) modified SMA mixed with 1 ml of dimethyl sulfoxide and kept in desiccator with P_2O_5 for 20 days at room temperature.Above synthesis follows scheme-1.

Scheme-1



R= 1A- C_3H_7, **1B-** C_4H_9, **1C**-C_5H_{11}, **1D**-C_6H_{13}, **1E**-C_6H_5, **1F**-C_6H_4-CH_3(O) **1G**-C_6H_4-CH_3 (m) **1H**-C_6H_4COOH(p) replace one by one, resulting in the formation of 8 unknown compounds denoted by 1A to 1H.

Synthesis of Aniline derived Styrene maleic anhydride and dimethyl Sulfoxide (1-E)

A solution composed of 2g (0.01 mole) styrene maleic anhydride,0.88 ml (0.01 mole) aniline in 50 ml of DMF at 25^{o}C for 8 hours, the solution was precipitated with toluene collected by filtration and washed with ether and dried *in vacuo* overnight. The modified SMA (T_g 110^{o}C) was checked by FTIR for determination of unreacted maleic anhydride moiety (Half esterification reaction). Now (0.50g) 0.001 mole, modified SMA mixed with 1 ml of pure dimethyl sulfoxide and kept in desiccator with P_2O_5 for 20 days at room temperature.

Synthesis of 4-aminobenzoic acid derived Styrene maleic anhydride and dimethyl Sulfoxide (1-H)

A solution composed of (2 g, 0.01 mole) styrene maleic anhydride, (0.01 mole) aminobenzoic acid in 50 ml. of DMF followed by triethylamine. The mixture was heated at 30^{o}C for 12 hours under nitrogen atmosphere, cooled at room temperature and the solution was precipitated with tetrahydrofurane. The precipitates was redissolved in DMF, and precipitated in to THF and collected by filtration and dried in vacuo overnight. The modified SMA (T_g 251^{o}C) was checked by FTIR for determination of unreacted maleic anhydride moiety (Half esterification reaction). Now 0.50g (0.001) mole, modified SMA mixed with 1 ml of dimethyl sulfoxide and kept in desiccator with P_2O_5 for 20 days at room temperature.

Table-1: Characterization data of Scheme -1 (1A-1H)

Comp. No.	R	Tg ^{o}C	Molecular Formula	Analysis % Cal. (Found)		
				C	H	N
1A	C_3H_7	137	$C_{29}H_{35}O_7SN$	64.31 (64.00)	6.50 (6.28)	2.58 (2.70)
1B	C_4H_9	132	$C_{30}H_{37}O_7SN$	64.85 (65.01)	6.70 (7.0)	2.52 (2.68)
1C	C_5H_{11}	118	$C_{31}H_{39}O_7SN$	65.36 (65.40)	6.89 (6.90)	2.45 (2.32)
1D	C_6H_{13}	100	$C_{32}H_{41}O_7SN$	65.85 (65.00)	7.07 (7.00)	2.39 (2.40)
1E	C_6H_5	110	$C_{32}H_{33}O_7SN$	66.77 (66.72)	5.77 (5.98)	2.43 (2.01)
1F	C_6H_4-CH_3(O)	192	$C_{33}H_{35}O_7SN$	67.11 (67.23)	6.13 (6.10)	2.37 (2.48)
1G	C_6H_4-CH_3(m)	192.8	$C_{33}H_{35}O_7SN$	67.11 (67.00)	6.13 (6.10)	2.37 (2.48)
1H	-C_6H_4-COOH	251	$C_{33}H_{33}O_9SN$	67.47 (65.91)	5.62 (5.63)	2.38 (2.40)

Table-.2: Spectral data of Scheme -1 (1A-1H)

Comp. No.	R	IR (ν_{max} cm^{-1}) KBr	^{1}H NMR (δ ppm) d_6 DMSO
1A	C_3H_7	3340(N-H *str*.) H-bond, 3018 (C-H *str*.) aromatic, 1260 (C-N*str*.),1630 (C=C*str*.) aromatic, 1740 (C=O *str*.) ester,1480 (C-H bend) methylene, 3310 (O-H *str*.) H bond, 648 (C=O*str*) amide I band, 1775 (C=O) anhydride.	1.3 (t, 6H), 1.4 (sextent, 2H), 3.5 (q, 2H), 6.5 (t, 1H), 2.2 (d, 1H), 10.6 (s, 2H) H bond, 7.36 (s, 10H, Ar) over lap, 2.4 (q, 3H), 3.4 (s, 2H), 1.7 (s, 3H), 1.6 (d, 3H)
1B	C_4H_9	3350(N-H *str*.) H-bond, 3020 (C-H *str*.) aromatic, 1030 (C-N*str*.),1630 (C=C*str*.)aroma tic, 1748 (C=O *str*.) ester, 1468 (C-H bend) methylene, 3510 (O-H *str*.) H bond 1660 (C=O *str*.) amide.	0.9 (t, 3H),1.4(multi., 4H), 3.4 (q, 2H), 5.8 (t, 1H), 2.1 (d, 1H), 1.2 (t, 3H), 9.8 (s, 2H) H bond, 7.1 (s, 10H, Ar) overlap, 2.3 (q, 3H), 3.4 (s, 2H), 1.7 (s, 3H), 1.6 (d, 1H), 1.3 (d, 2H)
1C	C_5H_{11}	3002(C-H*str*.)aromatic, 1035 (C-N *str*.), 1640 (C=C*str*.) aromatic, 1750 (C=O *str*.) ester,3350(N-H *str*.) H-bond, 1470 (C-H bend) methylene, 3510 (O-H *str*.) H bond 1612 (CO)	1.0 (t,3H),1.5(multi., 6H), 3.5 (q, 2H), 5.3 (t, 1H), 2.1 (d, 1H), 10.1(s,2H) H bond, 7.3 (s, 10H, Ar) overlap, 2.3 (q, 3H), 3.4 (s, 2H),1.7(s, 3H), 1.6 (d, 3H), 1.3 (t, 3H)
1D	C_6H_{13}	3010(C-H*str*.)aromatic, 1040 (C-N *str*.), 1664 (C=C *str*.) aromatic, 1764 (C=O *str*.) ester, 3610 (N-H *str*.) H-bond, 1480 (C-H bend) methylene, 1635 (C=O), 3340 (O-H *str*.) H bond	1.1 (t,3H),1.4 (multi.,8H),3.2 (q,2H), 6.0(t, 1H),10.1 (s,2H) Hbond,7.2(s,10H, Ar) overlap, 2.3 (d, 1H), 3.4 (s, 2H), 1.8 (s, 3H), 1.6 (d, 3H),1.3 (t, 3H), 2.5 (q, 3H).
1E	C_6H_5	3018(C-H*str*.)aromatic,1175 (CN*str*.),1600(C=C*str*.)aromatic, 1745 (C=O *str*.) ester, 3340, 3450 (N-H *str*.) H-bond, 1400 (C-H bend) methylene, 3210 (O-H *str*.) H bond, 1660 (C=O *str*.) amide band I	3.8(s,1H),1.6(d,3H) 2.5(q, 3H), 3.4 (s, 2H), 6.9 (s, 15H, Ar) overlap, 10.2 (s, 2H) H bond, 2.4 (d, 1H), 1.3 (t, 3H), 1.8 (s, 3H),
1F	$C_6H_4CH_3O$)	3002(C-H*str*.) aromatic, 1240 (C-N*str*.), 1640 (C=C*str*.) aromatic, 1764 (C=O *str*.) ester,3448(N-H *str*.) H-bond, 1470 (C-H bend) methylene, 3312 (O-H *str*.) H bond, 735 (ortho substituted).	2.2 (s, 3H, ortho substi.), 3.8 (s, 1H), 1.8 (s, 3H), 1.3 (t, 3H), 2.4 (d, 1H), 9.6 (s, 2H) H bond, 6.8(s, 14H, Ar) overlap, 3.45 (s, 2H), 2.5 (q, 3H), 1.6 (d, 3H)
1G	C_6H_4-CH_3(m)	3030(C-H*str*.)aromatic, 1363 (C-N *str*.), 1682 (C=C*str*.) aromatic, 1748(C=O*str*.) ester,3445 (N-H *str*.) H-bond, 1420 (C-H bend) methylene, 3312 (O-H *str*.) H bond, 742 (meta substituted), 1580 (C=O *str*.) amide.	7.1 (s,14H,Ar) overlap, 1.5 (s, 3H),1.3 (t,3H), 2.6 (d, 1H), 10.1 (s, 2H) H bond,3.8 (s, 1H), 3.45 (s,2H),2.44 (q,3H), 1.6 (d, 3H), 2.23 (s, 3H)
1H	C_6H_4COO(p)	3348,(N-H*str*.)H-Bond, 3002 (C-H *str*.) aromatic, 1363 (C-N*str*.),1680 (C=C*str*.) aroma tic,1764 (C=O*str*.) ester, 1478 (C-H bend) methylene, 3200 (O-H *str*.) H bond 1665 (C=O *str*.) amide, 840 para disubstituted.	1.5(s,3H),1.3(t,3H),2.64(q,3H),14 (d,3H), 2.4 (d,1H), 3.4 (s, 3H),7.1 (s,14H, Ar) overlap, 9.6 (s, 3H) H bond

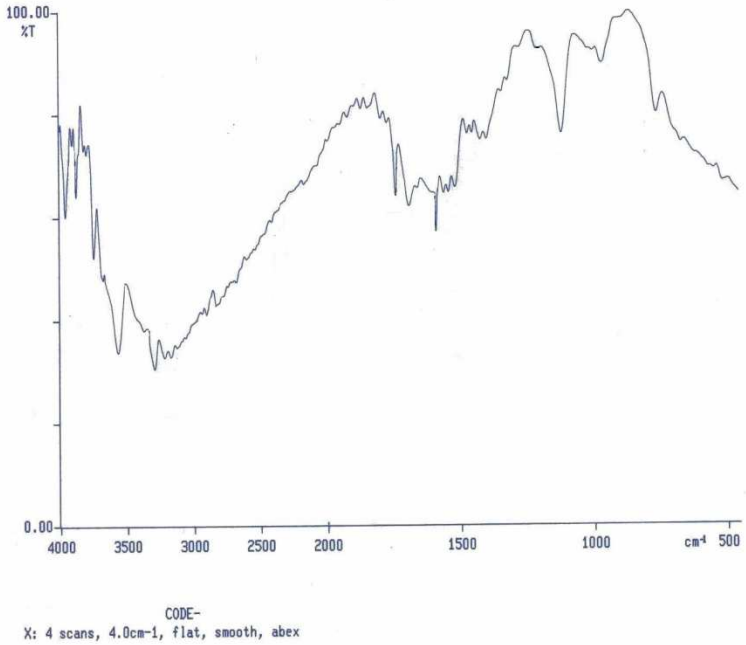


Fig. 1 IR SPECTRA (1A)

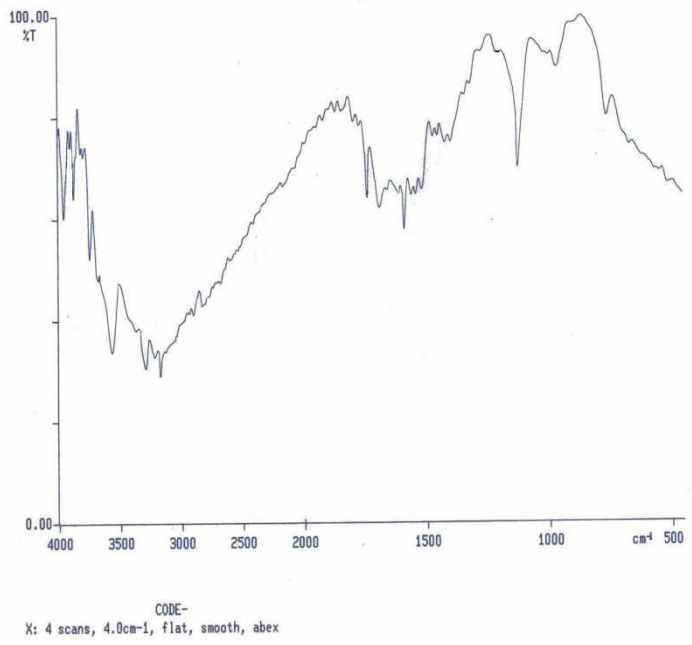


Fig. 2: IR SPECTRA (1E)

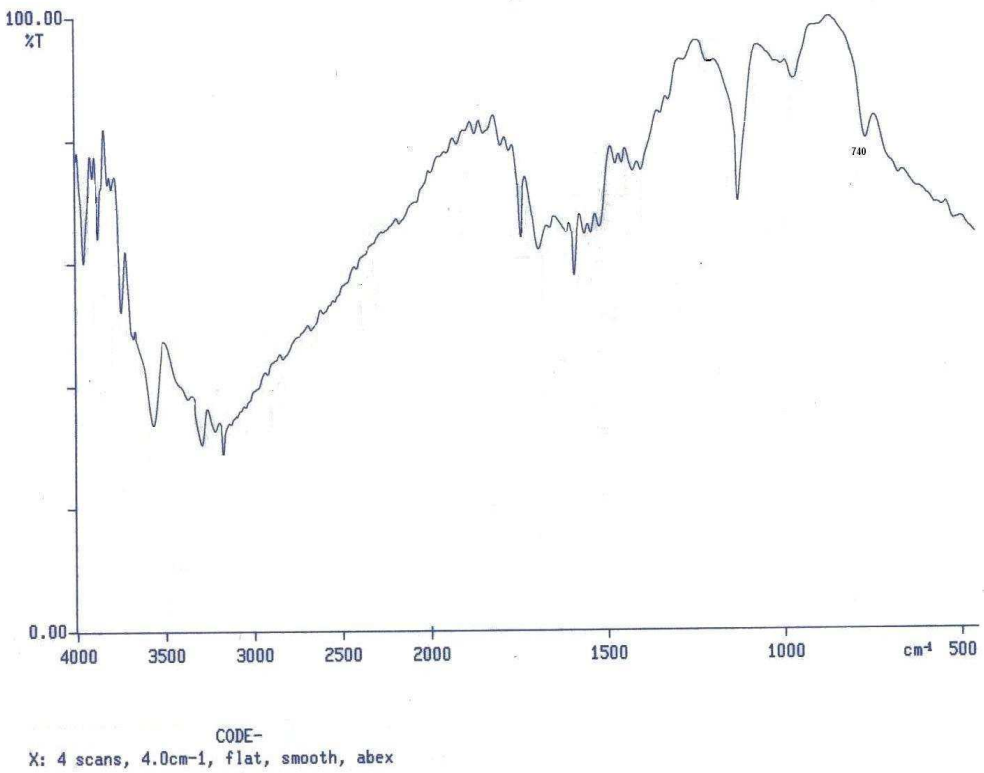


Fig. 3: IR Spectra (1H)

Haematology

For histopathological investigations 10 male Charles foster stain of albino rat of about 175-200g body weight were used for the study.10 days quarantined (acclimatized) rats were kept in husbandry condition of 22-25^{0}C room temperature, 50-70% relative humidity and 12hr. light and 12 hr. dark photoperiod. The animals were kept in identical environmental condition and were mentioned in pellet diet and water (24hrs.).The selected 8 male rats were divided into 4 groups of 2 rats, II, III, IV group served as treated, while Ist group served as control group. For implantation of the complex, lower abdominal area was chosen, minor incision with the help of sharp sterile blade was given of the size 0.5cm. The derived styrene maleic anhydride- amine polymer complex was injected into the lumen. Different doses of complex as stated in (Table-3) were given and skin wound was stitched, dressed up neosprin antibiotic powder, all the rats were kept under strict watch till the healing was completed. Different hematological parameters were recorded in the control as well as the complex treated rats as follows: Total leukocyte count (103/cumm), Total Erythrocyte count (RBC) (106cumm), Hb gm%., Platelet count (10 3 cumm) (Table-3). Liver was removed for histological examination. All readings were obtained by standard methods of histopathology.

Table 3- Heamatological profile for (1A-H)

No.	Dose	Body Wt(gm.)			R.B.C x 10^6 cumm			W.B.Cx10^3			Hb % gm			PLts x 10^3cumm		
		Initial	Mid term	Final Term	Initial	Mid term	Final term	Initial	Mid term	Final term	Initial	Mid term	Final term	Initial	Mid term	Final term
1A	L	185	220	240	6.27	6.14	6.1	12.9	13	13.5	12.56	13.34	14.73	619	612	622
	H	190	195	240	6.19	6.43	6.65	7.5	12.5	15.2	13.25	14.48	15.26	582	705	694
1B	L	180	195	225	6.57	6.2	6.18	9.0	9.5	9.8	12.65	13.43	14.73	622	624	632
	H	185	210	245	5.18	5.78	6.1	7.0	8.2	13.1	10.9	11.8	12.2	650	680	700
1C	L	190	200	230	6.05	6.1	6.0	14.0	14.5	14.2	12.5	12.48	12.96	582	594	601
	H	200	215	260	5.1	5.85	6.12	13.6	14.1	14	12.5	12.9	12.8	610	645	690
1D	L	195	200	220	6.2	6.12	6.02	7.3	7.5	7.8	13.35	13.5	13.7	585	596	610
	H	185	210	245	5.03	5.38	6.1	13.4	13.5	12.4	12.4	12.6	13.8	600	610	680
1E	L	195	200	220	6.2	6.12	6.02	7.3	7.5	7.8	13.35	13.5	13.7	585	596	610
	H	185	210	245	5.03	5.38	6.1	13.4	13.5	12.4	12.4	12.6	13.8	600	610	680
1F	L	175	215	245	6.29	6.2	6.14	8.1	8.7	8.9	12.88	12.8	12.94	715	722	732
	H	220	235	265	5.01	5.24	6.35	13.1	13.8	14.9	12.3	11.24	12.4	650	659	676

L –Low, H- High

Dose Schedule- Group-I Control: 0.03ml DMSO , Group -II Low Dose: 0.5mg. modified ester + 0.03ml DMSO Group-III Mid Dose: 2.0mg. modified ester + 0.03ml.DMSO, Group-IV High Dose 4.0mg. modified ester + 0.03ml.DMSO

Result and Discussion

According to Scheme 1, the conversion of Styrene maleic anhydride to amide by the treatment with amine derivatives and modified styrene maleic anhydride was treated with dimethyl sulphoxide, they were identified on the basis of, Infra red spectroscopy analysis[7], and ^{1}H NMR spectra.

Reaction of an alkylamine with anhydride moiety ring opening of the anhydride was controlled such that the reaction stopped at amide formation by half amidation reaction. The leaving residual anhydride moiety group was identified by infrared spectroscopy. The unreacted anhydride moiety follow the partially half esterification reaction of copolymer which are very useful in the invention may be provided in various ways. The partial half esterified copolymers are formed from maleic anhydride copolymers having low molecular weight.

In the FTIR spectrum of copolymer products 1(A-H) peaks due to unreacted cyclic anhydride groups (C=O *str*.) 1855-1775 cm^{-1} are clearly seen which proved that one anhydride moiety is free from amidation reaction and this moiety is responsible fo the half esterification reaction[6] with dimethyl sulfoxide. The FTIR spectrum of (1A-H) show peaks at 3610 cm^{-}1- 3340 due to H-bond N-H *str*etching while peaks at 1040-1363 cm^{-1} show C-N *str*etching. As expected, the higher conversion of anhydride to amide group after the reaction with amine containing compounds the lower the residual anhydride absorption intensities of the peaks with 1855-1775 cm^{-1} region. In all the reaction products (1A-H) the characteristic absorption peak at 1764-1740 cm^{-1} which represents that C=O *str*etching of ester carbonyl.

In the ^{1}H NMR of the products (1A-H) narrow overlapping peaks fall between 0.9-2.4δ ppm and multiplet peaks between 6.9-7.3δ ppm are due to methylene/methane and aromatic ring hydrogen respectively. The product of (1A-H) shows a peak due to the carboxylic group at 9.6-10.6 δ ppm and peaks between 2.2-3.8 due to Ar-C-CH_2.The unreacted anhydride group reacts with dimethylsulfoxide by the charge transfer interaction to form a new ester product as is shown by the IR spectra. Alkyl amnie derivatives of styrene maleic anhydride were prepared by ring opening, out of the different chain length alkylamines. It has been tested, by butylamine and pentylamine derivatives which are specifically pH sensitive[8].

Conclusion

Product 1A-H were synthesis successfully by reacting SMA- amine derivatives-DMSO. The Tgs of the polymers were higher than that of SMA because of H-Bonding interaction between the polymer chains. The polymers became cross linked and insoluble in organic solvents on heating at about 300^0C. For the SMA–DMSO interaction is more efficient in pure DMSO, and probably further transformation of charge- transfer complexes takes place. The sulfur (S) moiety of pure DMSO is highly reactive. When styrene maleic anhydride (SMA) is mixed with this particular form of DMSO the sulphur moiety of DMSO interacts with the etheric oxygen (-O-) of the maleic anhydride moiety of the SMA thereby leading to the formation of an intermediate unstable complex of SMA and DMSO. The carbonyl oxygen of SMA being resonance stabilized, is not affected. FTIR studies proved that reality of the reaction between modified (SMA) and DMSO as it follows from above scheme1, the reaction results in the increase of the local concentration of COO- group in unit of transformed polymer, Hence the relative intensity at 1644cm-1 increases, and the intensities of the peaks at 1777cm-1and 1709cm-1due to C=O(str.) decrease. We believe that the results obtained fully agree with the mechanism.

The longer the aliphatic chain shows the greater the mobility of the chain and the more easily amide formed. If we compare aryl group containing amine like aniline the produce amide conversion was lower about 10-15% of amide.

Acknowledgements

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