

## Polystyrene-supported hydroxamic dithiocarbonic anhydrides: A new class of acyl transfer reagents

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**Abstract.** Polystyrene-supported hydroxamic dithiocarbonic anhydrides were developed as a new class of regenerable solid phase reagents for acylating amino groups selectively. The reagent was prepared from crosslinked polystyrene support by a series of polymer analogous reactions. The crosslinking agents used were divinylbenzene (DVB) and ethyleneglycol dimethacrylate (EGDMA). The reagents were found to transfer their acyl groups to amines in solution at room temperature, yielding a solution of the corresponding amides. The influence of solvent, temperature, molar ratio and duration of reaction were studied to find out the optimum conditions. The spent reagent can be regenerated several times by a simple reaction, without significant loss in activity.

**Keywords.** Polystyrene-bound hydroxamic dithiocarbonic anhydrides; polymer analogous reaction; polymeric acyl transfer reagents.

### 1. Introduction

There has been increased interest in the application of functionalized polymers as participants in chemical reactions (Sreekumar and Pillai 1987; Hodge and Sherrington 1988; Devaky and Pillai 1990; Akelah and Moet 1991; Drtina *et al* 1996; Fruchtel and Jung 1996). These insoluble reagents have the advantages of easy separation from the reaction mixture and regenerability over their soluble counterparts. Investigations with various polymeric reagents have revealed that nature of the polymeric backbone does influence the kinetics and extent of functional group conversion in polymer-aided reactions (Morawetz 1978, 1985). The binding of a functional group to a polymer chain generally results in a new reagent with different structure, reactivity and selectivity (George and Pillai 1988; Sreekumar and Pillai 1989; Sudhakaran and Pillai 1990; Sophiamma and Sreekumar 1997).

Realizing the potential of the solid phase technique, a number of reagents were developed which were found to be very successful in acylating several organic substrates. Insoluble anhydrides prepared by the acylation of polymer-supported sulphonic acids and carbonic acids (Shambu and Digenis 1973, 1974) exhibited good shelf stability and acylating ability for simple and complex amines. Popcorn polymer prepared from styrene, *p*-vinyl benzoic acid and divinylbenzene has been used for preparing insoluble anhydrides. The insoluble anhydrides on reaction with aniline or ethanol gave benzanilide or ethyl benzoate in high yield (Gavina *et al* 1980).

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Polymer-bound mixed carboxylic dithiocarbamic anhydrides have been developed as reagents for the selective acylation of amino groups (Haridasan *et al* 1987). Polystyrene- and polyacrolein-bound oximino dithiocarbamic anhydrides were also developed as reagents for the selective acylation of amino groups (Aiswaryakumari *et al* 1995; Aiswaryakumari and Sreekumar 1996).

We report here the preparation of polymeric acyl transfer reagents, polystyrene-supported hydroxamic dithiocarbamic anhydrides and their use in the selective acylation of amino groups. Polystyrene-bound hydroxamic dithiocarbamic anhydrides were found to activate the carboxyl component for the formation of amide or peptide bonds.

## 2. Experimental

### 2.1 General

The monomers, styrene, DVB and EGDMA, were purified by low pressure distillation. Styrene-divinylbenzene (**1a**) and styrene-EGDMA (**1b**) copolymer supports were prepared by adopting procedures reported for parallel cases (Sherrington *et al* 1977). Chloromethylation of polystyrene was done according to literature procedure (Pepper *et al* 1953). Solvents were of reagent grade and were distilled and purified by standard procedures. Microanalyses were performed at the Regional Sophisticated Instrumentation Centre, Indian Institute of Technology, Chennai. IR spectra were recorded on a Perkin-Elmer 397 spectrophotometer using KBr pellets. Melting points were determined on a hot-stage melting point apparatus and are uncorrected. Thin layer chromatography was performed on pre-coated silica gel plates.

### 2.2 Preparation of 3-nitro-4-chloromethyl polystyrene

Chloromethylated polystyrene (10 g) was added to fuming nitric acid (100 ml). The reaction mixture was stirred at 0 °C for 1 h. The temperature was allowed to rise to 30 °C over a period of 2 h. The contents were poured into water (300 ml) containing crushed ice. The resin was washed with water, water-dioxan (1:1 v/v), ethanol and finally with methanol, filtered and dried at 70 °C in vacuum. IR (KBr): 1525 cm<sup>-1</sup>, 1350 cm<sup>-1</sup>, (NO<sub>2</sub> str), 1250 cm<sup>-1</sup> (C-CH<sub>2</sub> str), 650 cm<sup>-1</sup> (C-Cl str).

### 2.3 Preparation of polystyrene carboxylic acid resin

Chloromethyl polystyrene or 3-nitro-4-chloromethyl polystyrene (10 g), pre-swollen in acetonitrile was treated with potassium permanganate (15 g) in the presence of anhydrous sodium carbonate (7 g) in distilled water (100 ml) at 90 °C for 15 h. After the reaction, the mixture was cooled and acidified with conc. HCl (10 ml) in the presence of sodium sulphite (7 g). The reaction mixture was filtered, washed successively with acetonitrile (10 ml × 3 times), water:dioxane (1:1) (20 ml × 6 times), dioxane (20 ml × 3 times), ethanol (20 ml × 2 times), and methanol (20 ml × 3 times), and finally dried in vacuum. IR (KBr): 1670 cm<sup>-1</sup> (C=O str), 2960 cm<sup>-1</sup> (O-H str), 1420 cm<sup>-1</sup> (C-O str).

### 2.4 Preparation of carbethoxy polystyrene resin

Polymeric carboxylic acid resin (10 g), was esterified using absolute ethanol (30 ml) in the presence of conc. H<sub>2</sub>SO<sub>4</sub> (2 ml) at 80 °C for 12 h. The mixture was filtered, washed

with water, ethanol, methanol and acetone (20 ml  $\times$  3 times each), and dried. IR (KBr): 1700  $\text{cm}^{-1}$  (C=O *str*), 1240  $\text{cm}^{-1}$  (C–O *str*).

### 2.5 Preparation of polystyrene hydroxamic acid resin

Hydroxylamine hydrochloride (9.2 g) in methanol (15 ml) was neutralized with methanolic potassium hydroxide (10.2 g). The mixture was cooled to 0 °C and the potassium chloride precipitated was filtered off. Carbethoxy polystyrene resin (10 gm), pre-swollen in dichloromethane (20 ml) was then added to the filtrate and stirred for 6 h. The polymeric potassium hydroxamate was heated at 80 °C with acetic acid (2 N, 50 ml) for 10 h to get the hydroxamic acid resin. It was filtered, and washed successively with water (20 ml  $\times$  5 times), ethanol, methanol and acetone (20 ml  $\times$  5 times each). The resin was then dried in vacuum. IR (KBr): 1735  $\text{cm}^{-1}$  (C=O *str*), 3400  $\text{cm}^{-1}$  (N–H *str*), 3500  $\text{cm}^{-1}$  (O–H *str*).

### 2.6 Preparation of polystyrene hydroxamic dithiocarbonate resin

Polystyrene hydroxamic acid resin (10 g) was added to a five-fold molar excess of an equimolar mixture of CS<sub>2</sub> (16 ml, 200 mmol) and NaOH (10 g, 200 mmol). The mixture was shaken for 10 h at room temperature. The resin was collected by filtration and washed with water, ethanol and methanol (25 ml  $\times$  1 min  $\times$  5 times each), and dried in vacuum to afford the dithiocarbonate resin. IR (KBr): 3400  $\text{cm}^{-1}$  (N–H *str*), 1040  $\text{cm}^{-1}$  (C=S *str*), 650  $\text{cm}^{-1}$  (C–S *str*).

### 2.7 Preparation of polystyrene hydroxamic dithiocarbonic anhydride resin

Polystyrene dithiocarbonate resin (10 g) was suspended in a mixture of acetonitrile and chloroform (1:1 v/v, 50 ml) and pyridine (5 ml). A 3-fold molar excess of acyl chloride (acetyl chloride, benzoyl chloride, N-*p*-nitrobenzoyl chloride) was added to the suspension and the mixture was stirred for 8 h. The reaction mixture was filtered to collect the resin, washed with acetonitrile, water, ethanol and methanol (20 ml  $\times$  2 min  $\times$  3 times each), and dried in vacuum. IR (KBr): 1040  $\text{cm}^{-1}$  (C=S *str*), 650  $\text{cm}^{-1}$  (C–S *str*), 1730 (C=O acetic *str*), 1690 (C=O benzoic *str*) and 1650 (C=O *p*-nitrobenzoic *str*).

### 2.8 Estimation of acyl group capacity

The polymeric acylating reagent (1 mmol, calculated from sulphur content) was suspended in chloroform (20 ml) along with aniline (0.5 mmol) and was shaken for 2 h when maximum conversion was noticed as judged by tlc. The reaction mixture was filtered and washed with chloroform. The excess aniline present in the filtrate was extracted with 2 N HCl, made up to 250 ml and estimated by iodometric titration.

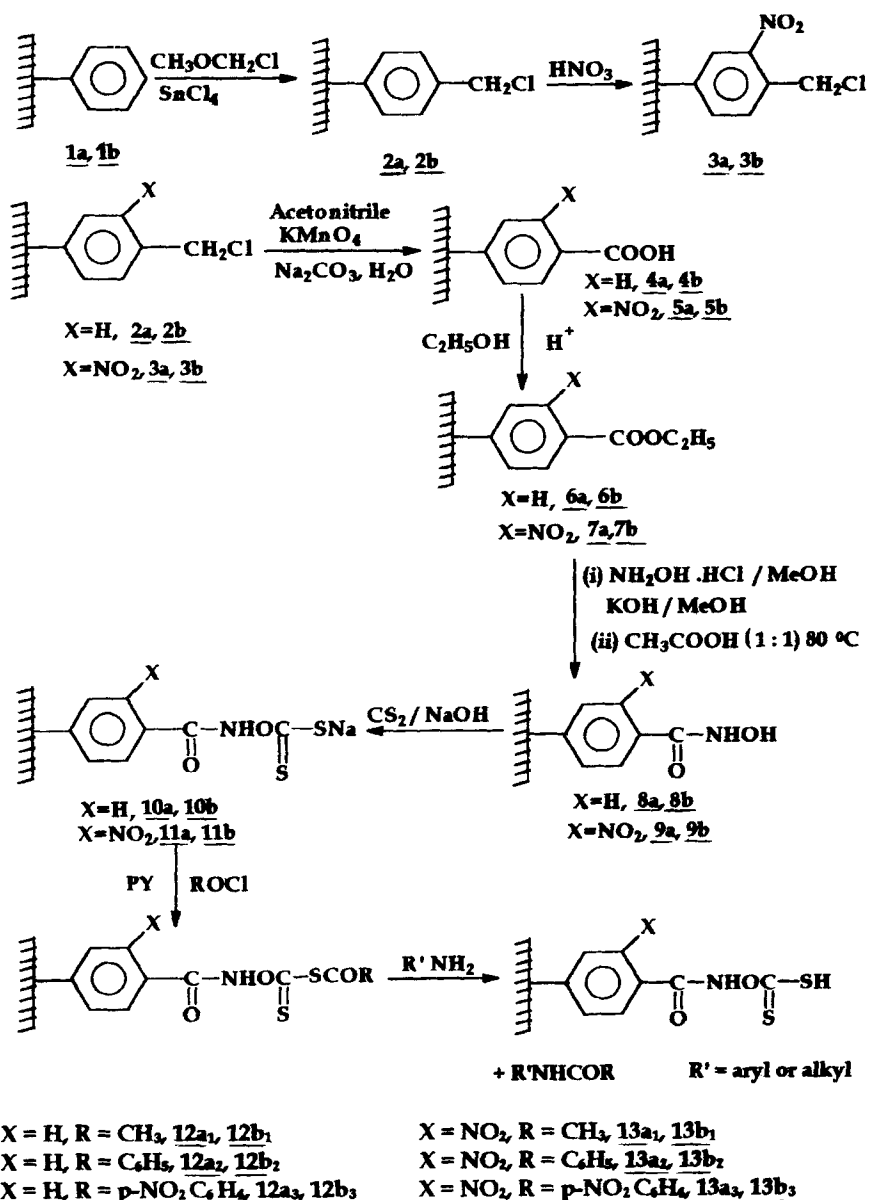
### 2.9 Acylation of amines using polystyrene bound hydroxamic dithiocarbonic anhydrides

A suspension of the polystyrene-based hydroxamic dithiocarbonic anhydride resin (1 mmol), amine (0.5 mmol) and chloroform (20 ml) was shaken for a definite time when maximum conversion was obtained as indicated by tlc. The mixture was filtered and washed with chloroform (20 ml  $\times$  3 times). The filtrate together with washings was collected, washed with HCl, (1:1, 20 ml) to remove any unreacted amine, followed by washing with water, and dried over anhydrous CaCl<sub>2</sub>. Evaporation of the solvent yielded the amide.

### 3. Results and discussion

#### 3.1 Preparation and characterization of polystyrene-based hydroxamic dithiocarbonic anhydrides

DVB crosslinked polystyrene (**1a**) and EGDMA crosslinked polystyrene (**1b**) were prepared by suspension polymerization technique and were used as the macromolecular supports. The preparation of polystyrene-bound hydroxamic dithiocarbonic anhydrides involved a series of polymer-analogous reactions (scheme 1).



Scheme 1. Preparation of polystyrene-based hydroxamic dithiocarbonic anhydrides and their acyl transfer reactions.

**Table 1.** Functional group capacities of different functionalized resins.

Resin	X	R	Functional group capacity (meq/g)	Resin	X	R	Functional group capacity (meq/g)
<u>2a</u>	H	—	4.2 <sup>a</sup>	2b	H	—	4.6 <sup>a</sup>
<u>4a</u>	H	—	3.7 <sup>b</sup>	4b	H	—	4.2 <sup>b</sup>
<u>6a</u>	H	—	3.4 <sup>a</sup>	6b	H	—	3.9 <sup>c</sup>
<u>8a</u>	H	—	3.1 <sup>d</sup>	8b	H	—	3.4 <sup>d</sup>
<u>10a</u>	H	—	4.0 <sup>e</sup>	10b	H	—	4.4 <sup>e</sup>
<u>12a<sub>1</sub></u>	H	CH <sub>3</sub>	1.0 <sup>f</sup>	12b <sub>1</sub>	H	CH <sub>3</sub>	1.8 <sup>f</sup>
<u>12a<sub>2</sub></u>	H	C <sub>6</sub> H <sub>5</sub>	1.3 <sup>f</sup>	12b <sub>2</sub>	H	C <sub>6</sub> H <sub>5</sub>	2.4 <sup>f</sup>
<u>12a<sub>3</sub></u>	H	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	1.5 <sup>f</sup>	12b <sub>3</sub>	H	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	2.9 <sup>f</sup>
<u>3a</u>	NO <sub>2</sub>	—	4.6 <sup>a</sup>	3b	NO <sub>2</sub>	—	5.1 <sup>a</sup>
<u>5a</u>	NO <sub>2</sub>	—	4.2 <sup>b</sup>	5b	NO <sub>2</sub>	—	4.6 <sup>b</sup>
<u>7a</u>	NO <sub>2</sub>	—	3.8 <sup>c</sup>	7b	NO <sub>2</sub>	—	4.2 <sup>c</sup>
<u>9a</u>	NO <sub>2</sub>	—	3.5 <sup>d</sup>	9b	NO <sub>2</sub>	—	4.0 <sup>d</sup>
<u>11a</u>	NO <sub>2</sub>	—	4.4 <sup>e</sup>	11b	NO <sub>2</sub>	—	4.7 <sup>e</sup>
<u>13a<sub>1</sub></u>	NO <sub>2</sub>	CH <sub>3</sub>	1.5 <sup>f</sup>	13b <sub>1</sub>	NO <sub>2</sub>	CH <sub>3</sub>	2.3 <sup>f</sup>
<u>13a<sub>2</sub></u>	NO <sub>2</sub>	C <sub>6</sub> H <sub>5</sub>	1.8 <sup>f</sup>	13b <sub>2</sub>	NO <sub>2</sub>	C <sub>6</sub> H <sub>5</sub>	3.0 <sup>f</sup>
<u>13a<sub>3</sub></u>	NO <sub>2</sub>	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	2.1 <sup>f</sup>	13b <sub>3</sub>	NO <sub>2</sub>	<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	3.4 <sup>f</sup>

<sup>a</sup>Volhard's method; <sup>b</sup>alkalimetry; <sup>c</sup>saponification method; <sup>d</sup>acylation method; <sup>e</sup>elemental analysis; <sup>f</sup>titrimetric method

Chloromethylation of polystyrene, using chloromethyl methyl ether in the presence of anhydrous SnCl<sub>4</sub>, gave chloromethylated polystyrene (2a, 2b) (Pepper *et al* 1953). The chlorine capacity was determined using modified Volhard's method by digesting the resin with pyridine followed by determination of the displaced chlorine as silver chloride (Merrifield 1963). Nitration of chloromethyl polystyrene using fuming nitric acid of specific gravity 1.42 gave 3-nitro-4-chloromethyl polystyrene (3a, 3b) (Rich and Gurwara 1975). The presence of the nitro group was supported by elemental analysis; the results are given in table 1. The formation of the nitro group was also supported by IR spectra which showed strong absorption bands at 1525 cm<sup>-1</sup> and 1350 cm<sup>-1</sup>. Chloromethyl polystyrene or 3-nitro-4-chloromethyl polystyrene was converted to polystyrene carboxylic acid resin by oxidation using alkaline KMnO<sub>4</sub> [4a, 4b, 5a, 5b] (Haridasan 1988). The formation of carboxylic acid functional resin was confirmed by the presence of strong absorption bands at 1670 cm<sup>-1</sup> (C=O *str*), 2960 cm<sup>-1</sup> (O-H *str*) and 1420 cm<sup>-1</sup> (C-O *str*) in the IR spectrum. The acid content was determined by treatment of the resin with standard alkali. The excess alkali was back-titrated. Polystyrene resin bearing carboxylic acid function was converted to carbethoxy polystyrene resin (6a, 6b, 7a, 7b) by esterification reaction. The formation of ester function was supported by the occurrence of absorption bands at 1700 cm<sup>-1</sup> (C=O *str*) and 1240 cm<sup>-1</sup> (C-O *str*) in the IR spectrum. The ester content was determined by hydrolysis with standard NaOH. Results are given in table 1. The ester group of the polymer was easily converted to the hydroxamic acid function by reaction with hydroxylamine followed by acetic acid (Fieser and Fieser 1967). The formation of hydroxamic acid resin (8a, 8b, 9a, 9b) was supported by elemental and IR spectral analysis. When the ester group was converted to the hydroxamic acid resin, the IR band corresponding to the NH-OH [3400 cm<sup>-1</sup> (N-H *str*), 3500 cm<sup>-1</sup> (O-H *str*)] was

found to occur. The hydroxyl group capacity was determined by acetylation method (Siggia 1954). The hydroxamic acid resin was converted to the dithiocarbonate derivative [10a, 10b, 11a, 11b] by treatment with a five-fold molar excess (based on OH capacity) of an equimolar mixture of carbon disulphide and sodium hydroxide in aqueous medium. The dithiocarbonate resin on treatment with an acyl halide in the presence of pyridine gave the corresponding polystyrene-bound hydroxamic dithiocarbonic anhydride resin (12a, 12b, 13a, 13b).

The conversion of dithiocarbonate resin to dithiocarbonic anhydride resin was confirmed by the appearance of absorption peaks at  $1730\text{ cm}^{-1}$  (C=O, acetic),  $1690\text{ cm}^{-1}$  (C=O benzoic),  $1650\text{ cm}^{-1}$  (C=O *p*-nitrobenzoic) which are characteristic of the carbonyl absorption of the anhydride function. The acyl group content was determined by treating the anhydride resin with a standard solution of aniline and the unreacted aniline was estimated titrimetrically. The functional group capacities of the different resins are given in table 1.

### 3.2 Acylation of amines

The polystyrene-bound hydroxamic dithiocarbonic anhydride resin on reaction with an amine, transfers its acyl group to the amine forming an amide (scheme 1). The acyl transfer reaction was tried on different amines using the polystyrene-bound hydroxamic dithiocarbonic anhydride resin. Details are given in table 2. In cases where complete conversion of the amine did not take place, before evaporation of the solvent, the excess amine was extracted with dil. HCl. The products were recrystallized and characterized, and the values were compared with reported results (IR and melting points), with which they were in good agreement.

Polystyrene-bound hydroxamic dithiocarbonic anhydride resin is selective for acylating an amino group in the presence of a hydroxyl group or carboxyl group. The resin on prolonged reaction with *o*-aminophenol produced only *o*-hydroxybenzanilide and with glycine gave only benzoyl glycine. The resin did not react with ethanol to give the respective ester.

**Table 2.** Acyl transfer reactions using polystyrene-bound hydroxamic dithiocarbonic anhydride resin.

Amine	Solvent	Duration <sup>a</sup>	Yield (%)					
			12a <sub>1</sub>	12a <sub>2</sub>	12a <sub>3</sub>	12b <sub>1</sub>	12b <sub>2</sub>	12b <sub>3</sub>
Aniline	CHCl <sub>3</sub>	4.0	44	50	58	49	55	63
<i>o</i> -Toluidine	CHCl <sub>3</sub>	4.0	48	56	66	56	60	68
<i>m</i> -Toluidine	CHCl <sub>3</sub>	4.0	46	52	60	52	57	65
<i>p</i> -Toluidine	CHCl <sub>3</sub>	4.0	47	54	63	54	59	67
<i>m</i> -Chloroaniline	CHCl <sub>3</sub>	4.0	37	41	48	40	45	51
<i>p</i> -Chloroaniline	CHCl <sub>3</sub>	4.0	39	45	50	43	49	54
<i>o</i> -Aminophenol	CHCl <sub>3</sub>	4.0	45	52	60	48	54	63
Glycine	Dioxan: water (1.1)	4.5	44	49	54	46	50	56
Methylamine	Dioxan	4.5	55	64	73	59	69	78
2,4-Dimethylaniline	CHCl <sub>3</sub>	4.0	42	58	54	45	53	57
2,6-Dimethylaniline	CHCl <sub>3</sub>	4.0	44	50	57	49	56	60

<sup>a</sup>Indicates time for maximum conversion; temperature, 30°C

**Table 3.** Acyl transfer reactions using 3-nitropolystyrene-4-hydroxamic dithiobenzoic anhydrides.

Amine	Solvent	Duration <sup>a</sup> (h)	Yield (%)					
			13a <sub>1</sub>	13a <sub>2</sub>	13a <sub>3</sub>	13b <sub>1</sub>	13b <sub>2</sub>	13b <sub>3</sub>
Aniline	CHCl <sub>3</sub>	4.0	53	58	67	58	66	75
<i>o</i> -Toluidine	CHCl <sub>3</sub>	4.0	58	65	74	64	70	80
<i>m</i> -Toluidine	CHCl <sub>3</sub>	4.0	58	60	69	60	68	77
<i>p</i> -Toluidine	CHCl <sub>3</sub>	4.0	57	63	71	62	69	79
<i>m</i> -Chloroaniline	CHCl <sub>3</sub>	4.0	43	47	54	48	54	62
<i>p</i> -Chloroaniline	CHCl <sub>3</sub>	4.0	46	49	57	50	59	65
<i>o</i> -Aminophenol	CHCl <sub>3</sub>	4.0	50	56	62	55	60	70
Glycine	Dioxan: water (1:1)	4.5	48	54	62	43	58	68
Methylamine	Dioxan	4.5	60	70	79	68	76	84
2,4-Dimethylaniline	CHCl <sub>3</sub>	4.0	48	55	62	55	60	67
2,6-Dimethylaniline	CHCl <sub>3</sub>	4.0	50	58	65	58	63	69

<sup>a</sup>Indicates time for maximum conversion, temperature, 30 °C

Acylation studies revealed that the extent of acyl transfer was highly dependent on the structure of the substrate. Acylation of aniline using EGDMA-crosslinked polystyrene-bound hydroxamic dithiobenzoic anhydride gave 55% yield, whereas *o*-toluidine gave 60% and *p*-toluidine gave 59% yield. *p*-Chloroaniline gave 49% yield. The higher extent of acylation of toluidines may be due to their higher nucleophilicity when compared to aniline. The converse is true for the chloroanilines.

Acylation of aniline using EGDMA-crosslinked polystyrene-bound hydroxamic dithiobenzoic anhydride resin gave 55% yield, and the corresponding hydroxamic dithioacetic anhydride gave 49% and hydroxamic dithio-*p*-nitrobenzoic anhydride gave 63% yield. *p*-Nitrobenzoyl group is found to be a better leaving group compared to benzoyl and acetyl groups. Thus the extent of acyl transfer is higher for *p*-nitrobenzoic anhydride resin.

The reaction efficiencies of DVB-crosslinked polystyrene-based reagents were compared with that of EGDMA-crosslinked polystyrene-based reagents and it is clear that the latter are more reactive. The enhanced reactivity of the styrene-EGDMA resin can be attributed to the presence of ester-COO groups in the crosslinks which could form hydrogen bonds with the substrate. It may also be due to the highly flexible nature of the crosslinks and the higher polarity of the matrix. This favours hydrogen bonds involving the carboxy groups of the EGDMA crosslinks and the substrates, and thereby promotes better interaction between the substrate and the reactive centre.

### 3.3 Effect of neighbouring nitro group

Polystyrene-bound hydroxamic dithiocarbonic anhydride resins with a nitro group at the 3-position of the phenyl residue of the polystyrene backbone were prepared and used as acyl transfer reagents for various amines. The results are given in table 3.

It was observed that the extent of acylation was higher in the case of resins having a nitro group at the 3-position of the phenyl ring of the polystyrene matrix. The percentage yield of benzamide obtained after 4 h was 55% in the case of

**Table 4.** Effect of solvents on the acylation of aniline using polystyrene-bound hydroxamic dithiobenzoic anhydride resin<sup>a</sup>.

Resin	Yield of anilide formed in						
	CHCl <sub>3</sub>	CH <sub>2</sub> Cl <sub>2</sub>	CCl <sub>4</sub>	CH <sub>3</sub> CN	THF	C <sub>6</sub> H <sub>6</sub>	Dioxan
<u>12a<sub>2</sub></u>	50	35	45	27	40	49	47
<u>12b<sub>2</sub></u>	55	40	50	38	45	47	51

<sup>a</sup>Substrate to resin ratio, 1:2; temperature 30 °C; time, 4 h

EGDMA-crosslinked polystyrene-bound hydroxamic dithiobenzoic anhydride resin, where there was no nitro group, whereas, in the case of the corresponding 3-nitro derivative, 66% conversion was observed after the same duration of the reaction. The higher values of acyl group capacity and the extent of acyl transfer in the presence of a nitro group at the 3-position of the phenyl residue of the polystyrene backbone, presumably arise from the increased electrophilicity of the acylating function (Devaky 1989).

#### 3.4 Reaction conditions and extent of acyl transfer

The acylation reaction using polystyrene-bound hydroxamic dithiocarbonic anhydride resin was found to be affected by the nature of the solvent, temperature, duration of reaction and the effective concentration of the reagent function. It has been observed that only when there is an effective interaction between the reagent function, substrate and the reaction medium, does reaction take place with reasonable extent of functional group conversion.

**3.4a Effect of solvent:** A major factor influencing the efficiency of polymer-supported reactions is the type of solvent used for the reaction. Solvents that are capable of swelling the polymer network and are also able to dissolve the low molecular substrates are found to be suitable for carrying out acylation reactions. In order to investigate the effect of the nature of the solvent on the reactivity of acylating reagents, acyl transfer reactions with aniline were conducted using polystyrene-bound hydroxamic dithiobenzoic anhydrides in different solvents with varying polarities. Percentage conversion after a specified period was noted and the results are given in table 4.

The studies reveal that chloroform is the most effective solvent. The higher reactivity of polystyrene-supported acylating reagents in chloroform is due to the greater extent of swelling of polymeric reagents in chloroform. Polar solvents like acetonitrile and tetrahydrofuran do not have much effect on the extent of acylation of polystyrene-supported acylating reagents due to the hydrophobic nature of the resin.

**3.4b Effect of temperature:** Influence of temperature on the extent of acyl transfer was studied by carrying out the reaction at different temperatures ranging from 10 °C to 60 °C. It was found that as the temperature was increased, the percentage yield of anilide obtained from polystyrene-bound hydroxamic dithiobenzoic anhydride increased gradually. The results are given in table 5.

The higher reactivities of polymeric acyl transfer reagents at higher temperatures may be due to the attainment of the required activation energy by many more



**Table 5.** Effect of temperature on the acylation of aniline using polystyrene bound hydroxamic dithiobenzoic anhydride resin<sup>a</sup>.

Resin	Yield of anilide formed at (°C)					
	10°	20°	30°	40°	50°	60°
<u>12a<sub>2</sub></u>	44	47	50	53	56	58
<u>12b<sub>2</sub></u>	47	50	55	58	61	64

<sup>a</sup>Substrate to resin ratio, 1:2; Solvent, chloroform; time, 4 h

**Table 6.** Acylation of aniline using polystyrene-bound hydroxamic dithiobenzoic anhydride resin with different resin to amine ratios<sup>a</sup>.

Resin	% Conversion when the molar ratio is				
	1:1	2:1	3:1	4:1	5:1
<u>12a<sub>2</sub></u>	25	50	53	56	58
<u>12b<sub>2</sub></u>	30	55	62	65	68

<sup>a</sup>Solvent, chloroform; temperature, 30 °C; time, 4 h

molecules. As the number of molecules with required activation energy increases, the acyl group transfer capacity also increases. The optimum temperature is 60 °C. Thereafter the amount of anilide obtained remains constant.

**3.4c Effect of molar ratio:** Acylation reactions using polystyrene-bound hydroxamic dithiocarbonic anhydride resins were found to be dependent on the effective concentration of the reagent function. Acylation of aniline was carried out at different molar ratios. The ratios (resin:amine) studied were 1:1, 2:1, 3:1, 4:1, and 5:1. When molar equivalents were used, the reactions did not go to completion in any case irrespective of the duration of the reaction. As the molar ratio was increased, the percentage yield of the product also increased. Maximum yield was obtained at a molar ratio of 5:1. A levelling-off effect is expected after that. The results are given in table 6.

**3.4d Effect of duration of reaction:** Acylation reactions with aniline were carried out at 30 °C with chloroform using polystyrene-bound hydroxamic dithiobenzoic anhydride resins and the percentage yields of anilide obtained were determined at fixed time intervals. The yield of anilide was found to increase up to a period of 4 h when the maximum yield was obtained. After that, there was a slight decrease in the percentage yield. This could be due to the possible adsorption of the product on the spent resin. The reaction proceeded rapidly in the initial stages until more than half of the substrate was converted to the product. Afterwards, the speed of the reaction was found to decrease gradually as more and more of the acylating function was consumed. The results are given in table 7.

### 3.5 Recyclability of the polystyrene-bound hydroxamic dithiocarbonic anhydride resin

The spent resin from the acylation step was treated with an equimolar mixture of carbon disulphide and sodium hydroxide to afford the sodium dithiocarbonate resin,

**Table 7.** Acylation of aniline using polystyrene-bound hydroxamic dithiobenzoic anhydride resin at various time intervals<sup>a</sup>.

Resin	% Conversion after (h)					
	1	2	3	4	5	6
<u>12a<sub>2</sub></u>	27	34	40	50	47	45
<u>12b<sub>2</sub></u>	30	42	49	55	52	50

<sup>a</sup>Substrate to resin ratio 1:2; Solvent, chloroform; temperature, 30°C

**Table 8.** Regeneration of EGDMA-crosslinked polystyrene-bound hydroxamic dithiobenzoic anhydride resin<sup>a</sup>.

No. of cycles	Benzoyl group capacity (meq/g)	Isolated yield (%)
1	2.4	55
2	2.3	54
3	2.3	54
4	2.3	54
5	2.2	53

<sup>a</sup>Acylation of aniline in chloroform at room temperature; Yield noted after 4 h; aniline to resin ratio, 1:2

which on subsequent acylation gave the original hydroxamic dithiocarbonic anhydride resin. The acyl group capacity as well as the extent of acyl transfer using these resins were found to be slightly lower even after several repeated recycling steps. The change in the capacity of the resin and the percentage of acylation in the course of the recyclization steps are presented in table 8.

The foregoing studies reveal that polystyrene-bound hydroxamic dithiocarbonic anhydride resins can be used as solid phase reagents for the selective acylation of amines. These have the advantages of increased shelf-life and operational simplicity, and also the possibility of regeneration and reuse.

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