J IRAN CHEM SOC
DOI 10.1007/s13738-016-0811-4

ORIGINAL PAPER

Synthesis of a novel class of chromophoric cross-linkers

Kamahldin Haghbeen[1] · Raymond L. Legge[2]

Received: 14 June 2015 / Accepted: 11 January 2016

Abstract Considering the special place of aromatic diazo compounds in photo-responsive materials and growing demand for materials with interesting optical properties, a new class of chromophoric cross-linkers was synthesized by acrylation of diazo derivatives of *m*-diaminobenzene. The cross-linkers are soluble in a wide variety of organic solvents as well as in mixtures of water and water miscible solvents. The chromophores of the cross-linkers are stable in protic and some certain aprotic solvents and remain stable after cross-linking. The chemical structure of this class allows one to have a cross-linker with tuned chemical reactivity and solubility with post-linking applicability. The cross-linkers are obtained from reactions with simple chemistry in high yields and are able to participate in radical and ionic polymerization as well as in nucleophilic addition reactions. Successful participation of these substances in acrylamide polymerization and sol–gel preparation is demonstrated.

Keywords Cross-linker · Diazo · Acrylation · *m*-Diaminobenzene · Hydrogel

Introduction

Cross-linkers are designed to bind covalently to at least two growing molecular chains during polymerization, a process that could create new materials with modified physical and mechanical properties [1]. Advances in different branches of science and technology expanded the concept and application of cross-linkers. In addition to the synthetic polymers [2], cross-linkers play key roles in interfacial and separation technologies [3], photo responding materials [4], protein science [5], genetic research [6], ligand and receptor interactions [7], immobilization techniques [8], cell biology [9], label transfer agents [10], sensor technology [4, 11], pharmaceutical and drug delivery [12]. There is also a growing demand for post-linking roles of cross-linkers such as responding to electromagnetic radiation [13], exhibiting fluorescence or luminescence activity [14], degradability [9, 15], and performing structural changes. Such expectations have led research for making versatile cross-linkers.

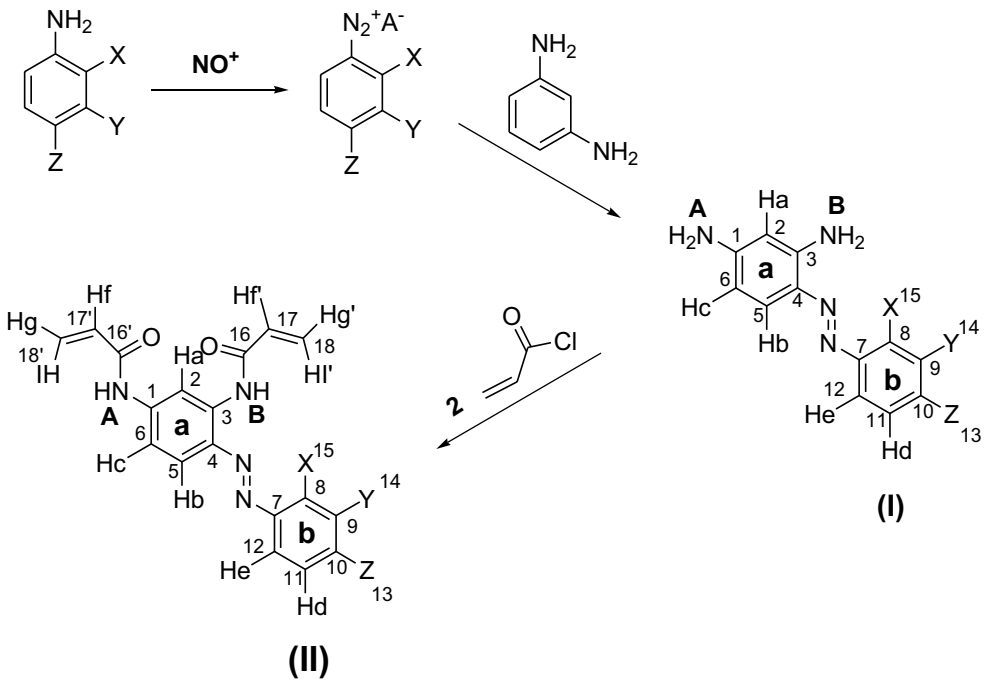
Photo aligning phenomenon was first described for the reversible *cis–trans* isomerization of azobenzene units attached to a substrate. It was also shown that the optical nonlinearity of nematic liquid crystals could be further enhanced by adding a small amount of dye impurities. Therefore, polymers with azobenzene side groups and materials containing pure photochemically stable azo dye layers were investigated [16, 17]. Research has demonstrated that aromatic diazo dyes can be inserted into different polymeric matrix and make them applicable in production of optical responsive materials such as liquid crystals [18]. These materials are employed in making electro-optical displays, optical storage devices, and muscle-like actuators [2, 4, 16]. Considering this important potential of aromatic diazo structure, a new class of chromophoric cross-linkers with general structure of **II** (illustrated in Scheme 1) was developed through a facile method which is described in this paper. These cross-linkers are anticipated to facilitate the association of various

✉ Kamahldin Haghbeen
kamahl@nigeb.ac.ir

[1] National Institute for Genetic Engineering and Biotechnology, P.O.Box: 14965/161, Tehran, Iran

[2] Department of Chemical Engineering, University of Waterloo, Waterloo, ON N2L 3G1, Canada

Published online: 28 January 2016



Scheme 1 Synthetic scheme for making diazo dyes of *meta*-diaminobenzene with general structure of **I** and their corresponding homofunctional cross-linkers (**II**)

diazo moieties into the polymer matrices with photo-responsive properties.

Results and discussion

Preparation of diazo derivatives of *meta*-diaminobenzene

To prepare the cross-linkers with the general structure of **II**, diazo dyes of *meta*-diaminobenzene were prepared first (Scheme 1). To make dyes with the general structure of **I**, diazonium salts of the desired amines had to be synthesized. The coupling reaction between diazonium salts and *meta*-diaminobenzene resulted in compounds of **I**. The chemistry of both reactions, diazotization and coupling, is well known [19]. The latter reaction is usually carried out in aqueous media, but the right medium for the former reaction, diazotization, is based on the solubility and susceptibility to oxidation of the selected amine. The efficiency of a diazotization reaction is heavily dependent on the chosen reaction medium and the nature of the substituents presents on the aromatic ring of the selected amine. Electron-withdrawing substituents usually decrease yield of the reaction [2].

Similar to *ortho* and *para*-dihydroxy benzenes, *ortho* and *para*-diaminobenzenes fall in oxidation during coupling reaction with diazonium salts [20]. In contrast, *meta*-diaminobenzene participates in coupling reactions with different diazonium salts and produces the corresponding dye. Amino substituents not only are activator of the aromatic ring in electrophilic substitution reactions, they are also *ortho*/*para* directing groups. As a result, the coupling reaction is highly regioselective and substitution happens mostly at position 4 shown in Scheme 1. The final yield of the diazo dyes hardly falls below 70 % and it is first merit of these cross-linkers as they are prepared through facile and high yield reactions. Data in Table 1 show the efficiency of this preparation method.

Table 1 Yields of the reactions introduced in Scheme 1

Compound	X	Y	Z	%Yield of I	%Yield of II
1	–H	–H	–H	100	85
2	–H	–H	$–OCH_3$	100	95
3	–H	–H	$–SO_2NH_2$	100	76
4	$–CH_3$	–H	–I	100	76
5	–H	–I	$–CH_3$	100	83
6	$–OCH_3$	–H	$–NO_2$	92	68
7	$–NO_2$	–H	$–OCH_3$	100	79

Preparation of the cross-linkers

All the cross-linkers described in this paper were obtained in excellent yield (Table 1). These results indicate that the

reaction of acryloyl chloride with the dyes carrying electron donating group(s) is better. It also appears that THF works as a proper reaction medium for the dyes with the general structure of **I**. However, solubility of some certain dye molecules might be problematic which necessitates a change of the reaction medium. Dimethylformamide is suggested for more hydrophilic precursors [21]. It is important to note that carrying a double bond in the vicinity of a conjugated carbonyl functional group renders these cross-linkers very reactive. This high reactivity is another advantage of these compounds as it facilitates their participation in various reactions; however, it also affects their susceptibility. NMR experiments confirmed high sensitivity of these compounds to light at room temperature especially in some certain solvents such as chloroform.

Structure and properties

Structure **II** consists of three distinct components: acrylamido moiety which is expected to give the whole molecule *homofunctional* cross-linking ability. Second, a benzene ring (**a**) conjugated to the acrylamido substituents. The benzene ring also functions as a docking terminal for the third part of the molecule, an aromatic diazo moiety. With acrylamido groups as the binding arms, it is assumed that the cross-linker will show the chemical activity of α-β-unsaturated carbonyl compounds. Therefore, it is anticipated that the cross-linker can take part in both radical and ionic reactions. However, there are two significant differences between the chemical structures of **II** and acrylamides. First, the "N" terminals of the acrylamido groups are conjugated to the benzene ring (**a**) and the conjugation has been extended to another aromatic moiety (**b**) through the double bond of a diazo functional group. As a result, the electronic transitions in the whole conjugated system shift toward visible region and make the molecule colorful (Fig. 1). This additional feature increases post-linking applications of the cross-linker especially where the chromophoric behavior of the material is important [22, 23].

Physical phenomena such as light, pressure and temperature can cause structural changes in dye molecules which result in color changes. One example of this type phenomenon is the reversible response of certain dyes to pH changes [24]. Figure 2a shows the change in the color solution of $\mathbf{I}_2$ upon a shift in pH. Comparing the λ_{max}(s) of compounds **I** with those of compounds **II** (Table 2) reveals a blue shift in the λ_{max}(s) of the dyes after acrylation (Fig. 1). Nonetheless, compounds **II** are still sensitive to pH changes (Fig. 2a). This feature is faded upon cross-linking (Fig. 2b). Therefore, if the cross-linkers **II** are expected to respond to pH changes, appropriate substituent/s have to be placed on the aromatic ring (**b**).

Second, conjugation makes it possible to control the reactivity of the double bond at the "C" terminals of the acrylamido groups. For instance, the reactivity of the cross-linker toward nucleophiles can be enhanced by adding an electron-withdrawing group to the second aromatic ring (**b**). This feature is important when the cross-linker is to be used to bind molecules containing moderate nucleophilic functional groups such as proteins.

The structural features of the second aromatic ring (**b**) in **I** and **II** not only influence the visible spectrum and chemical reactivity of the cross-linker but also affect the solubility. For example, adding a sulfonamide or sulfonic substitute to the second aromatic ring promotes both the chemical activity of the cross-linker toward nucleophiles and its solubility in aqueous media. The more soluble is the cross-linker, the higher amount of that can be used in reactions which are run in water. For instance, $\mathbf{II}_3$ was successfully used as cross-linker in acrylamide polymerization (Fig. 3a).

Polyacrylamide is obtained by radical polymerization of acrylamide in the presence of a cross-linker in aqueous medium [25]. In contrast, sol–gels do not need a cross-linker as they are produced by hydrolysis of orthosilanes followed by polymerization of the hydrolysis products through a nucleophilic condensation mechanism [26]. In comparison with hydrogels, sol–gels are robust materials which can be used for immobilization purposes where hydrogels may not

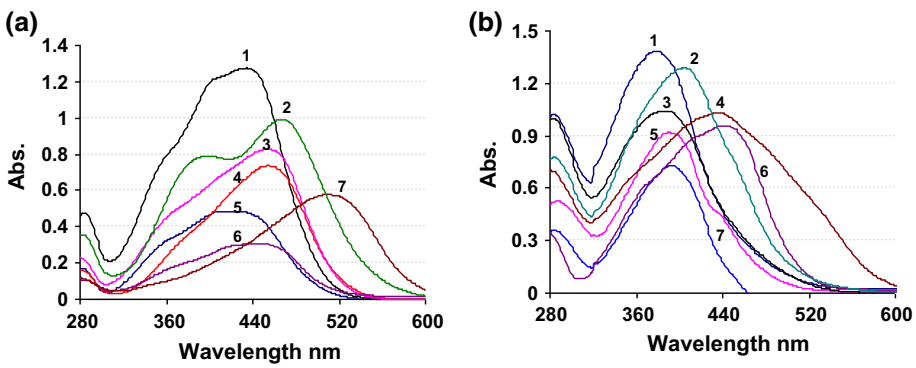


Fig. 1 The overlaid UV–visible spectra of compounds with general structure of **a I** including (1) $\mathbf{I}_2$, (2) $\mathbf{I}_7$, (3) $\mathbf{I}_5$, (4) $\mathbf{I}_3$, (5) $\mathbf{I}_1$, (6) $\mathbf{I}_4$, (7) $\mathbf{I}_6$ and **b II** including (1) $\mathbf{II}_1$, (2) $\mathbf{II}_7$, (3) $\mathbf{II}_3$, (4) $\mathbf{II}_6$, (5) $\mathbf{II}_2$, (6) $\mathbf{II}_5$, (7) $\mathbf{II}_4$ in ethanol at 20 °C

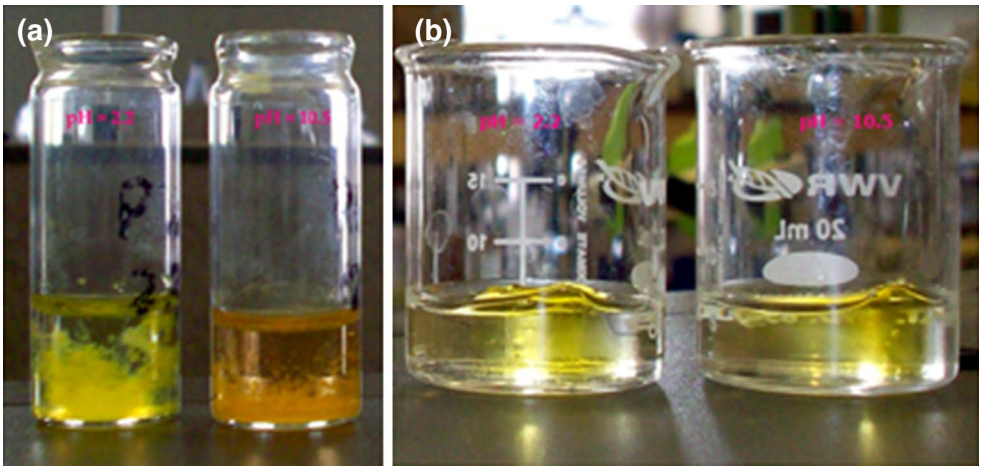


Fig. 2 **a** Cross-linker $\mathbf{II_2}$ in phosphate buffer solution at two different pH (left 2.2 and right 10.5). **b** Poly acrylamide hydrogel obtained by polymerization of acrylamide in the presence of bis-acrylamide and $\mathbf{II_2}$ as cross-linkers in phosphate buffer solution at two different pH (left 2.2 and right 10.5)

Table 2 UV-visible data of compounds **I** and **II** in ethanol at 20 °C

Dye	$\lambda_{max(EtOH)}$, nm	ε, M^{-1} cm^{-1}	Cross-linker	$\lambda_{max\ (EtOH),}$ nm
$\mathbf{I_1}$	418	20,920	$\mathbf{II_1}$	384
$\mathbf{I_2}$	430	19,770	$\mathbf{II_2}$	399
$\mathbf{I_3}$	450	30,700	**II3**	390
$\mathbf{I_4}$	441	26,180	$\mathbf{II_4}$	395
$\mathbf{I_5}$	449	30,800	$\mathbf{II_5}$	445
$\mathbf{I_6}$	503	38,880	$\mathbf{II_6}$	440
$\mathbf{I_7}$	462	25,590	$\mathbf{II_7}$	410

be applicable [27]. In addition; combining dyes with sol–gels through various methods is a hot topic in the on-going research on the sol–gels applications [28]. Figure 3c shows successful application of $\mathbf{II_2}$, $\mathbf{II_3}$, and $\mathbf{II_7}$ in xerogel preparation. The color stability of the obtained materials was confirmed by placing them in pure organic solvents such as acetone, ethanol and THF (Fig. 3b, d).

Experimental

Aniline, 1,3-diaminobenzene, *p*-nitroaniline, 2-methoxy-4-nitro-aniline, 4-methoxyaniline, 4-methoxy-2-nitro-aniline, 4-sulfonamidoaniline, 4-iodo-2-methyl-aniline, 3-iodo-4-methyl-aniline, acryloyl chloride and tetraethoxy orthosilicate (TEOS) were purchased from the Sigma-Aldrich (Oakville, ON, Canada). The organic solvents and the other chemicals were reagent grade. NMR spectra were recorded by a Brucker (Ultrashield, 300 MHz) spectrometer. Proton and carbon chemical shifts are relative to TMS. Multiplicity determinations and 2D NMR (COSY and HMQC) were conducted using standard pulse programs. CH3OD was used for proton exchange experiments. Infrared spectra were recorded by a Brucker (Tensor 27) FTIR. Electron impact mass spectra were acquired with a JEOL HX110 double focusing mass spectrometer operated at a mass resolution of ~1000. Typical source conditions were: source temp = 200 °C and electron energy of 70 eV. All samples were introduced by direct insertion. Molecules with the general structure of **II** were made through a three-step process illustrated in Scheme 1; diazonium salt preparation, diazo coupling reaction, and acrylation of the diazo dye.

Procedure for preparation of diazonium chloride solutions of aromatic amines

The desired aromatic amine (0.01 M) was dissolved in a mixture of concentrated HCl (5 ml) and distilled water (20 ml). A solution of sodium nitrite (0.83 g, 0.012 M) in distilled water (5 ml) was prepared in a test tube and added to the acidic solution of amine dropwise over 5 min at 0 °C. To complete the reaction, the overall mixture was stirred at the same temperature for 40 min.

Modified procedure for preparation of diazonium chloride solution of *p*-nitroaniline

Some aromatic amines, such as *p*-nitroaniline, are less soluble in water. As a result, a modified procedure was employed for preparation of the corresponding diazonium

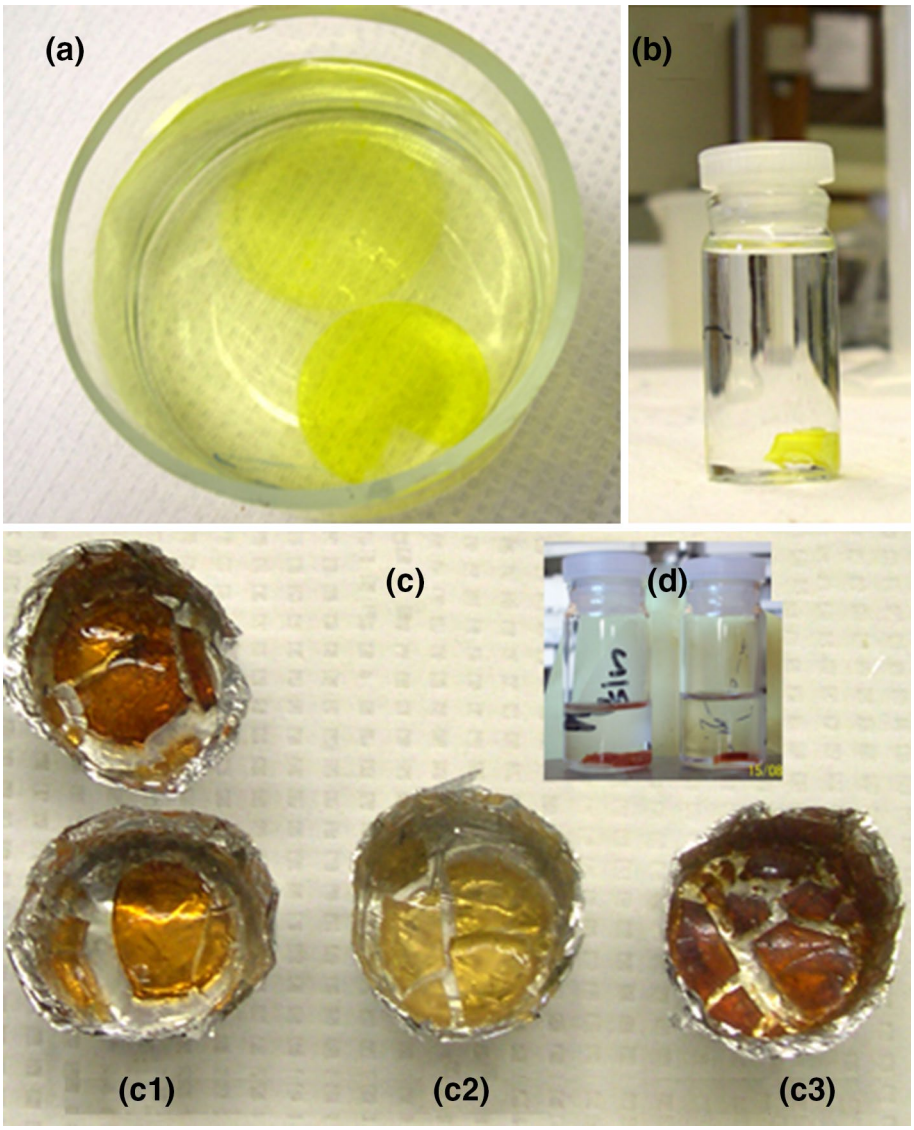


Fig. 3 Polyacrylamide hydrogel obtained by polymerization of acrylamide in the presence of bis-acrylamide and $\mathbf{II_3}$ as cross-linkers in **a** water and **b** acetone; **c** xerogels obtained by drying the sol–gels resulted from polymerization of TEOS sol in the presence of **c1** $\mathbf{II_2}$, **c2** $\mathbf{II_3}$, **c3** $\mathbf{II_7}$. **d** Samples **c1** and **c3** in ethanol and in acetone. See the "Experimental" section for the details of preparation

salts. *p*-Nitroaniline (1.38 g, 0.01 M) was dissolved in a mixture of methanol (20 ml) and concentrated HCl (5 ml). The isoamyl nitrite (1.34 ml, 0.01 M) was then added to this solution at 0 °C. A yellow precipitate gradually formed. The reaction mixture was kept stirring at the same temperature for 45 min to get completed.

General procedure for making diazo derivatives of 1,3-diaminobenzene with general structure of I in Scheme 1

The desired aryl diazonium chloride solution was added dropwise to a mixture of 1,3-diaminobenzene (0.01 M) in 15 ml of double-distilled water containing 1 ml of concentrated HCl at 0 °C. The reaction mixture was continuously stirred at 0 °C for 30 min. The pH was raised to 5 by adding sodium acetate and the resulting mixture was left to stir at <5 °C for an extra hour. The product appeared as a precipitate which was collected and recrystallized either from water or ethanol. The product can be increased completely, if the pH is raised to 7. Chemical structures for the compounds $\mathbf{I_1}$ to $\mathbf{I_7}$ were assigned by the following spectroscopic data. The star sign on some protons indicates overlapped ones.

I_1: (E)-4-(2-phenyldiazenyl)benzene-1,3-diamine

Light orange powder, IR in KBr: [(–NH_2 = 3473, 3379, 1619 cm^{-1}), (–CH_{Ar} = 3056 cm^{-1}), (–C=C_{Ar} = 1568 cm^{-1}), (–N=N– 1450 cm^{-1}), (–C–N– = 1331 cm^{-1})]; ^{1}HNMR in $CDCl_3$: δ [H_a(5.87, 1H, d, j–j = 2.4 Hz), H_b(7.63, 1H, d, j–j = 8.7 Hz), H_c*(6.12, 3H, q), H_d&Y(7.41, 2H, t), H_e&X(7.72, 2H, d, j–j = 7.8 Hz), Z(7.30, 1H, q), NH_2A(3.90, 2H, br), NH_2B*(overlapped by H_c)]; ^{13}CNMR

in $CDCl_3$: δ [C1(150.3), C2(99.4), C3(144.7), C4(131.4), C5(131.4), C6(106.1), C7(153.2), C8(121.4), C9(128.8), C10(128.4), C11(128.8), C12(121.4)].

I_2: (E)-4-(2-(4-methoxyphenyl)diazenyl) benzene-1,3-diamine

Yellow powder, IR in KBr: [(–NH_2 = 3473, 3432, 3375,3348, 1637 cm^{-1}), (–CH_{Ar} = 3000 cm^{-1}), (–CH = 2837, cm^{-1}), (–C=C_{Ar} = 1571 cm^{-1}), (–N=N– 1450 cm^{-1}), (–C–N– = 1330 cm^{-1})]; ^{1}HNMR in $CDCl_3$: δ [H_a(5.91, 1H, d, j–j = 2.4 Hz), H_b(7.59, 1H, d, j–j = 8.7 Hz), H_c(6.11, 1H, q), H_d&Y(6.93, 2H, q), H_e&X(7.70, 2H, q), Z(3.84, 3H, s), NH_2A(3.90, 2H, br), NH_2B(5.95, 2H, br)], ^{13}CNMR in $CDCl_3$: δ [C1(149.9), C2(99.8), C3(144.6), C4(131.5), C5(130.1), C6(106.0), C7(147.5), C8(123.0), C9(114.1), C10(160.2), C11(114.1), C12(123.0), C13(55.5)].

I_3: (E)-4-(2-(4-sulfonamido)diazenyl)benzene-1,3-diamine

Dark orange powder, IR in KBr: [(–NH_2 = 3481, 3418, 3387,3350, 1622 cm^{-1}), (–CH_{Ar} = 3043 cm^{-1}), (–C=C_{Ar} = 1559 cm^{-1}), (–N=N– 1464 cm^{-1}), (–C–N– = 1301 cm^{-1})]; ^{1}HNMR in $CDCl_3$: δ [H_a(5.89, 1H, d, j–j = 1.8 Hz), H_b(7.59, 1H, d, j–j = 8.7 Hz), H_c*(6.10, 3H, q), H_d&Y(7.37, 2H, d, j–j = 7.8 Hz), H_e&X(7.68, 2H, d, j–j = 8.1 Hz), Z(7.27, 2H, d, j–j = 7.2 Hz), NH_2A(4.0, 2H, br), NH_2B*(overlapped by H_c)], ^{13}CNMR in $CDCl_3$: δ [C1(150.4), C2(99.3), C3(144.7), C4(131.3), C5(128.3), C6(106.0), C7(153.2), C8(121.4), C9(128.7), C10(131.4), C11(128.7), C12(121.4)].

I_4: (E)-4-(2-(4-iodo-2-methylphenyl)diazenyl) benzene-1,3-diamine

Orange to dark red powder, IR in KBr: [(–NH_2 = 3430, 3373, 3199, 1620 cm^{-1}), (–CH_{Ar} = 3048 cm^{-1}), (–CH = 2903, 1364 cm^{-1}), (–C=C_{Ar} = 1570 cm^{-1}), (–N=N– 1465 cm^{-1}), (–C–N– = 1327 cm^{-1})]; ^{1}HNMR in $CDCl_3$: δ [H_a(5.89, 1H, d, j–j = 3 Hz), H_b(7.33, 1H, d, j–j = 8.4 Hz), H_c(6.14, 1H, q), H_d(7.52, 1H, q), H_e*(7.62, 2H, d, j–j = 8.7 Hz), X(2.50, 3H, s), Y(overlapped by H_e), NH_2A(3.99, 2H, br), NH_2B(6.24, 2H, br)], ^{13}CNMR in $CDCl_3$: δ [C1(150.9), C2(99.2), C3(144.3), C4(132.0), C5(116.9), C6(106.3), C7(150.5), C8(137.2), C9(139.5), C10(93.9), C11(135.6), C12(133.0), C15(17.8)].

I_5: (E)-4-(2-(3-iodo-4-methylphenyl)diazenyl) benzene-1,3-diamine

Orange to brown powder, IR in KBr: [(–NH_2 = 3432, 3356, 3206, 1617 cm^{-1}), (–CH_{Ar} = 3048 cm^{-1}), (–CH = 1370 cm^{-1}), (–C=C_{Ar} = 1575 cm^{-1}), (–N=N– 1469 cm^{-1}), (–C–N– = 1324 cm^{-1})]; ^{1}HNMR in $CDCl_3$: δ [H_a(5.87, 1H, s), H_b&H_e(7.59, 2H, t), H_c*(6.12, 3H, d, j–j = 8.4), H_d(7.25, 1H, d, j–j = 8.4), X(8.17, 1H, s), Z(2.44, 3H, s), NH_2A(3.99, 2H, br), NH_2B*(overlapped by H_c)], ^{13}CNMR in $CDCl_3$: δ [C1(150.6), C2(99.2), C3(144.8), C4(131.2), C5(131.6), C6(106.2), C7(152.0), C8(131.0), C9(101.20), C10(141.2), C11(129.7), C12(121.9), C13(27.8)].

I_6: (E)-4-(2-(2-methoxy-4-nitrophenyl)diazenyl) benzene-1,3-diamine

Dark metallic brown powder, IR in KBr: [(–NH_2 = 3462, 3370, 3335, 3212, 1621 cm^{-1}), (–CH_{Ar} = 3099 cm^{-1}), (–CH = 2997, 1370 cm^{-1}), (–C=C_{Ar} = 1579 cm^{-1}), (–N=N– 1416 cm^{-1}), (–C–N– = 1304 cm^{-1}), (–C–NO_2 = overlapped)]; ^{1}HNMR in $CDCl_3$: δ [H_a(5.85, 1H, d, j–j = 1.8 Hz), H_b(7.62, 1H, d, j–j = 8.7 Hz), H_c(6.16, 1H, q), H_d*(7.86, 2H, d, j–j = 9.9 Hz), H_e(7.75, 1H, d, j–j = 8.7 Hz), X(4.02, 3H, s), Y(overlapped by H_d), NH_2A(4.14, 2H, br), NH_2B(6.85, 2H, br)], ^{13}CNMR in $CDCl_3$: δ [C1(147.2), C2(98.4), C3(144.8), C4(132.9), C5(135.1), C6(106.9), C7(146.4), C8(154.6), C9(107.2), C10(151.3), C11(116.7), C12(115.7), C15(56.3)].

I_7: (E)-4-(2-(4-methoxy-2-nitrophenyl)diazenyl) benzene-1,3-diamine

Shiny brown powder, IR in KBr: [(–NH_2 = 3481, 3427, 3385, 3226, 1633 cm^{-1}), (–CH_{Ar} = 3009 cm^{-1}), (–CH = 2924, 1370 cm^{-1}), (–C=C_{Ar} = 1566 cm^{-1}), (–N=N– 1421 cm^{-1}), (–C–N– = 1308 cm^{-1}), (–C–NO_2 = overlapped)]; ^{1}HNMR in $CDCl_3$: δ [H_a(5.83, 1H, d, j–j = 2.1 Hz), H_b(7.54, 1H, d, j–j = 8.7 Hz), H_c(6.12, 1H, q), H_d(7.10, 1H, q), H_e(7.85, 1H, d, j–j = 9.3 Hz), Y(7.33, 1H, d, j–j = 2.4 Hz), Z(3.87, 1H, s), NH_2A(4.13, 2H, br), NH_2B(6.65, 2H, br)], ^{13}CNMR in $CDCl_3$: δ [C1(151.1), C2(98.6), C3(144.4), C4(131.9), C5(135.7), C6(106.4), C7(139.9), C8(146.2), C9(108.1), C10(158.8), C11(120.0), C12(118.6), C13(55.9)].

General procedure for acrylation of diazo derivatives of 1,3-diaminobenzene

The desired diazo derivative of 1,3-diaminobenzene (0.01 M) was dissolved in dried THF (25 ml) in a round-bottom flask equipped with a separatory funnel. The flask was put on ice with mixing. An excess amount of acryloyl chloride (0.04 M) in dry THF (15 ml) was prepared and poured into the separatory funnel. The content of the funnel was slowly added to the flask while the mixture was mixed until the ice melted and the temperature of the resulting water

reached the room temperature. The content of the reaction flask was then added to a saturated solution of ammonium bicarbonate (50 ml) and the resulting mixture left under a fume hood overnight. THF evaporation resulted in precipitation. The product was washed with hot water and reprecipitated from acetone. Chemical structures for the compounds **II_1** to **II_7** were assigned by the following spectroscopic data.

II_1: N,N′-{4-[(E)-phenyldiazenyl]benzene-1,3-diyl} bisprop-2-enamide

Dark orange powder, melting point (120 °C). IR in KBr: [(–NH = 3279, 1603 cm^{-1}), (–CH_{Ar} = 3055 cm^{-1}), (–C=O=1666 cm^{-1}), (–C=C_{Ar} = 1527 cm^{-1}), (–N=N– overlapped cm^{-1}), (–C–N– = 1331 cm^{-1})]; ^{1}HNMR in DMSO-d^6: δ [H_a(8.68, 1H, s), H_b&H_c*(7.75, 2H, d, j–j = 4.5 Hz), H_d&Y*(7.56, 3H, m), H_e&X(7.97, 2H, d, j–j = 7.8 Hz), Z*(7.50, 1H, m, overlapped by H_d), NH_A(10.34, 1H, s), NH_B(10.52, 1H, s), H_f(6.45, 1H, q), $H_{f'}$(6.7, 1H, q), H_g&$H_{g'}$(5.79, 2H, q), H_I&$H_{I'}$(6.27, 2H, q)]; ^{13}CNMR [C1(142.8), C2(112.1), C3(137.0), C4(137.5), C5(117.8), C6(115.1), C7(152.2), C8&C12(122.9), C9&C11(129.3), C10(131.1), C16(163.4), C16′(163.5), C17(131.6), C17′(132.1), C18(127.5), C18′(127.7)]. Mass spectrum (Mw) ion m/z 320. Elemental analysis (%) calcd for $C_{18}N_4O_2H_{16}$ (320.35): C 67.49, H 5.03, N 17.49; found: C 67.32, H 5.05, N 17.43.

II_2: N,N′-{4-[(E)-(4-methoxyphenyl)diazenyl] benzene-1,3-diyl}bisprop-2-enamide

Orange powder, melting point (159 °C). IR in KBr: [(–NH = 3432, 3297, 1597 cm^{-1}), (–CH_{Ar} = 3093 cm^{-1}), (–CH = 2940, 2838 cm^{-1}), (–C=O = 1675 cm^{-1}), (–C=C_{Ar} = 1527 cm^{-1}), (–N=N– = 1465 cm^{-1}), (–C–N– = 1339 cm^{-1})]; ^{1}HNMR in DMSO-d^6: δ [H_a(8.64, 1H, d, j–j = 1.8 Hz), H_b(7.68, 1H, d, j–j = 8.7 Hz), H_c(7.61, 1H, q), H_d&Y(7.07, 2H, d, j–j = 8.7 Hz), H_e&X(7.93, 2H, d, j–j = 8.7 Hz), Z(3.84, 3H, s), NH_A(10.25, 1H, s), NH_B(10.46, 1H, s), H_f(6.40, 1H, q), $H_{f'}$(6.64, 1H, q), H_g&$H_{g'}$(5.75, 2H, m), H_I&$H_{I'}$(6.24, 2H, oct)]; ^{13}CNMR in DMSO-d^6: [C1(142.4), C2(112.5), C3(137.3), C4(137.4), C5(117.8), C6(115.5), C7(146.9), C8&C12(125.3), C9&C11(114.9), C10(162.2), C13(56.0), C16(163.7), C16′(163.8), C17(131.0), C17′(132.6), C18(127.7), C18′(127.9)]. Mass spectrum (Mw) ion m/z 350. Elemental analysis (%) calcd for $C_{19}N_4O_3H_{18}$ (350.38): C 65.13, H 5.18, N 15.99; found: C 64.93, H 5.16, N 15.93.

II_3: N,N′-{4-[(E)-(4-sulfamoylphenyl)diazenyl] benzene-1,3-diyl}bisprop-2-enamide

Orange-reddish powder, melting point (225 °C). IR in KBr: [(–NH = 3305, 3231, 1598 cm^{-1}), (–CH_{Ar} = 3077 cm^{-1}), (–C=O = 1673 cm^{-1}), (–C=C_{Ar} = 1519 cm^{-1}), (–N=N– 1464 cm^{-1}), (–C–N– = 1326 cm^{-1})]; ^{1}HNMR in DMSO-d^6: δ [H_a(8.73, 1H, s), H_b(7.78, 1H, d, j–j = 9 Hz), H_c(7.73, 1H, d, j–j = 9 Hz), H_d&Y(7.98, 2H, d, j–j = 8.4 Hz), H_e&X(8.12, 2H, d, j–j = 8.4 Hz), Z(7.51, 2H, s), NH_A(10.38, 1H, s), NH_B(10.62, 1H, s), H_f(6.46, 1H, q), $H_{f'}$(6.71, 1H, q), H_g&$H_{g'}$(5.80, 2H, m), H_I&$H_{I'}$(6.28, 2H, q)], ^{13}CNMR in DMSO-d^6: [C1(143.7), C2(112.0), C3(137.0), C4(138.2), C5(117.9), C6(115.1), C7(153.7), C8&12(123.3), C9&C11(126.8), C10(145.5), C16(163.5), C16′(163.6), C17(131.5), C17′(132.1), C18(127.7), C18′(127.9)]. Mass spectrum (Mw) ion m/z 399. Elemental analysis (%) calcd for $C_{18}N_5O_4SH_{17}$ (399.43): C 54.13, H 4.29, N 17.53, S 8.03; found: C 54.00, H 4.28, N 17.47, S 7.99.

II_4: N,N′-{4-[(E)-(4-iodo-2-methylphenyl)diazenyl] benzene-1,3-diyl}bisprop-2-enamide

Orange-brown powder, melting point (290 °C). IR in KBr: [(–NH = 3272, 3199, 1600 cm^{-1}), (–CH_{Ar} = 3055 cm^{-1}), (–CH = 2946 cm^{-1}), (–C=O = 16,666 cm^{-1}), (–C = C_{Ar} = 1520 cm^{-1}), (–N=N– 1466 cm^{-1}), (–C–N– = 1329 cm^{-1})]; ^{1}HNMR in DMSO-d^6: δ [H_a(8.54, 1H, d, j–j = 1.5 Hz), H_b(7.59, 1H, d, j–j = 9 Hz), H_c&H_d(7.53, 2H, t), H_e(7.41, 1H, d, j–j = 8.4 Hz), X(2.6, 3H, s), Y(7.69, 1H, s), NH_A(10.15, 1H, s), NH_B(10.42, 1H, s), H_f(6.30, 1H, q), $H_{f'}$(6.53, 1H, q), H_g(5.64, 1H, q), $H_{g'}$(5.67, 1H, q), H_I(6.12, 1H, q), $H_{I'}$(6.18, 1H, q)]; ^{13}CNMR in DMSO-d^6: [C1(137.6), C2(112.2), C3(137.6), C4(142.9), C5(117.9), C6(115.2), C7(149.7), C8(139.7), C9(139.8), C10(98.5), C11(135.4), C12(117.8), C15(16.7), C16(163.4), C16′(163.5), C17(131.6), C17′(132.0), C18(127.5), C18′(127.7)]. Mass spectrum (Mw) ion m/z 460. Elemental analysis (%) calcd for $C_{19}N_4O_2IH_{17}$ (460.27): C 49.58, H 3.72, N 12.17, I 27.57; found: C 49.47, H 3.71, N 12.13.

II_5: N,N′-{4-[(E)-(3-iodo-4-methylphenyl)diazenyl] benzene-1,3-diyl}bisprop-2-enamide

Orange powder, melting point (117 °C). IR in KBr: [(–NH = 3270, 3199, 1601 cm^{-1}), (–CH_{Ar} = 3048 cm^{-1}), (–CH = 2910 cm^{-1}), (–C = O = 1664 cm^{-1}), (–C=C_{Ar} = 1523 cm^{-1}), (–N=N– = 1471 cm^{-1}), (–C–N– = 1328 cm^{-1})]; ^{1}HNMR in DMSO-d^6: δ [H_a(8.66, 1H, d, j–j = 1.8 Hz), H_b&H_c (7.72, 2H, m), H_e(7.92, 1H, q), H_d(7.52, 1H, d, j–j = 8.4 Hz), X(8.40, 1H, d, j–j = 1.8 Hz), Z(3.32, 3H, s), NH_A(10.35, 1H, s), NH_B(10.52, 1H, s), H_f(6.45, 1H, q), $H_{f'}$(6.70, 1H, q), H_g&$H_{g'}$(5.78, 2H, q), H_I(6.27, 1H, q), $H_{I'}$(6.32, 1H, q)]; ^{13}CNMR in DMSO-d^6: [C1(143.0), C2(112.3), C3(137.0), C4(137.6), C5(117.7), C6(115.1), C7(151.0), C8(131.6), C9(101.8), C10(143.9), C11(130.3), C12(123.9) C13(27.5), C16(163.5),

C16′(163.5), C17(127.7), C17′(132.1), C18&C18′(127.5)]. Mass spectrum (Mw) ion m/z 460. Elemental analysis (%) calcd for $C_{19}N_4O_2IH_{17}$ (460.27): C 49.58, H 3.72, N 12.17, I 27.57; found: C 49.43, H 3.71, N 12.12.

II_6: N,N′-{4-[(E)-(2-methoxy-4-nitrophenyl)diazenyl] benzene-1,3-diyl}bisprop-2-enamide

Dark red brownish powder, melting point (225 °C). IR in KBr: [(–NH = 3428, 3245, 1608 cm^{-1}), (–CH_{Ar} = 3017 cm^{-1}), (–CH = 2940 cm^{-1}), (–C=O = 1667 cm^{-1}), (–C=C_{Ar} = 1517 cm^{-1}), (–N=N– = 1466 cm^{-1}), (–C–N– = 1336 cm^{-1}), (–C–NO_2 = overlapped)]; ^{1}HNMR in DMSO-d^6: δ [H_a(8.78, 1H, s), H_b&H_c(7.89, 2H, s), H_d&H_e(7.77, 2H, d, j–j = 3.9 Hz), X(4.08, 3H, s), Y(7.99, 1H, s), NH_A(10.67, 1H, s), NH_B(11.05, 1H, s), H_f(6.44, 1H, q), $H_{f'}$(6.54, 1H, q), H_g&$H_{g'}$(5.78, 2H, q), H_I&$H_{I'}$(6.26, 2H, q)]; ^{13}CNMR [C1(144.4), C2(111.4), C3(136.6), C4(136.9), C5(117.5), C6(116.1), C7(overlapped by C10), C8(156.3), C9(108.4), C10(149.4), C11(115.2), C12(124.2), C15(56.8), C16&C16′(163.8), C17(131.5), C17′(132.1), C18&C18′ (128.1)]. Mass spectrum (Mw) ion m/z 395. Elemental analysis (%) calcd for $C_{19}N_5O_5H_{17}$ (395.37): C 57.72, H 4.33, N 17.71; found: C 57.56, H 4.30, N 17.07.

II_7: N,N′-{4-[(E)-(4-methoxy-2-nitrophenyl)diazenyl] benzene-1,3-diyl}bisprop-2-enamide

Shiny metallic red brownish powder, melting point (192 °C). IR in KBr: [(–NH = 3415, 3262, 1606 cm^{-1}), (–CH_{Ar} = 3027 cm^{-1}), (–CH = 2836 cm^{-1}), (–C=C–C=O = 1697, 1677 cm^{-1}), (–C=C_{Ar} = 1526 cm^{-1}), (–N=N– = 1467 cm^{-1}), (–C–N– = 1340 cm^{-1}), (–C–NO_2 = overlapped)]; ^{1}HNMR in DMSO-d^6: δ [H_a(8.73, 1H, s), H_b*(7.63, 2H, t), H_c(7.56, 1H, d, j–j = 9 Hz), H_d(7.34, 1H, q), H_e(8.03, 1H, d, j–j = 9.3 Hz), Y*(overlapped by H_b), Z(3.91, 3H, s), NH_A(10.23, 1H, s), NH_B(11.62, 1H, s), H_f(6.43, 1H, q), $H_{f'}$(6.64, 1H, q), H_g&$H_{g'}$ (5.79, 2H, t), H_I&$H_{I'}$(6.27, 2H, q)]; ^{13}CNMR in DMSO-d^6: [C1(143.8), C2(112.4), C3(137.4), C4(137.6), C5(118.6), C6(115.6), C7(138.1), C8(149.8), C9(108.5), C10(161.7), C11(119.3), C12(120.6), C13(56.9), C16(163.9), C16′(164.0), C17(131.8), C17′(132.1), C18(128.3), C18′(128.4)]. Mass spectrum (Mw) ion m/z 395. Elemental analysis (%) calcd for $C_{19}N_5O_5H_{17}$ (395.37): C 57.72, H 4.33, N 17.71; found: C 57.60, H 4.34, N 17.08.

Sol–gel and acrylamide hydrogel preparation

A homogenous stock solution of TEOS was prepared as previously described [26]. To an appropriate volume of the sol, an equivalent volume of phosphate buffer solution (0.1 M, pH 7) containing the desired cross-linker **II** (10 mM, prepared in ethanol) was added and mixed. The final mixture was cast in a disposable aluminum cap at room temperature.

Cross-linked poly acrylamide polymers were prepared as previously described [25] except that half of the cross-linker (bis-acrylamide) concentration was replaced by the desired cross-linker **II**. The reaction mixture contained acrylamide (1.69 M), bis-acryl amide (10 mM), the desired cross-linker **II** (10 mM). Polymerization was carried out in the presence of constant amounts of TEMED (6.6 mM) and ammonium persulfate (2.2 mM) in 10 ml phosphate buffer (0.01 M) at pH 6.8 and room temperature.

Conclusions

The cross-linkers introduced in this paper are prepared in high yields using facile procedures. The chemical structure of these cross-linkers allows to tune solubility and chemical reactivity of the cross-linker through choosing the desired starting materials. The cross-linkers are anticipated to participate in various types of ionic and radical polymerization as well as nucleophilic addition reactions. The photochromic properties and trans–cis isomerization of the diazo motif of these cross-linkers can be used for post-linking purposes.

Acknowledgments This work was supported by the Natural Sciences and Engineering Research Council (NSERC) in the form of a Discovery Grant to RLL. Sincere collaboration of Dr Richard W. Smith manager of Mass Spectrometry Facility of University of Waterloo is appreciated.

References

1. V. Percec, Chem. Rev. **101**, 3579 (2001)
2. D.B. Otts, M.W. Urban, Polymer **46**, 2699 (2005)
3. M.R. Buchmeiser, J. Chromatogr. A **918**, 233 (2001)
4. S. Al-Kindy, R. Badía, J.L. Suárez-Rodríguez, M.E. Díaz-García, Crit. Rev. Anal. Chem. **30**, 291 (2000)
5. F. Falvo, L. Fiebig, M. Schäfer, Int. J. Mass Spectrom. **354**, 26 (2013)
6. K. Sato, K. Hosokawa, M. Maeda, Anal. Sci. **23**, 17 (2007)
7. S.A. Piletsky, T.L. Panasyuk, E.V. Piletskaya, I.A. Nicholls, M. Ulbricht, J. Membr. Sci. **157**, 263 (1999)
8. W.E. Hennink, C.F. van Nostrum, Adv. Drug Deliv. Rev. **54**, 13 (2002)
9. G. Leriche, L. Chisholm, A. Wagner, Bioorg. Med. Chem. **20**, 571 (2012)
10. M. Suchanek, A. Radzikowska, C. Thiele, Nat. Methods **2**, 261 (2005)
11. W. Wu, A.D. Li, Nanomedicine **2**, 523 (2007)
12. D.A. Spivak, Adv. Drug Deliv. Rev. **57**, 1779 (2005)
13. M.W. Gardner, L.A. Vasicek, S. Shabbir, E.V. Anslyn, J.S. Brodbelt, Anal. Chem. **80**, 4807 (2008)
14. R.N. Wine, J.M. Dial, K.B. Tomer, C.H. Borchers, Anal. Chem. **74**, 1939 (2002)

15. D. Filpula, H. Zhao, Adv. Drug Deliv. Rev. **60**, 29 (2008)
16. S. Rouhani, S. Salimi, K. Haghbeen, Dyes Pigm. **77**, 363 (2008)
17. D. Wang, X. Wang, Prog. Polym. Sci. **38**, 271 (2013)
18. A. Priimagi, C.J. Barrett, A. Shishido, J. Matter Chem. C **2**, 7155 (2014)
19. H. Gao, K. Matyjaszewski, Prog. Polym. Sci. **34**, 317 (2009)
20. K. Haghbeen, E.W. Tan, J. Org. Chem. **63**, 4503 (1998)
21. M. Constantin, G. Fundueanu, M. Nichifor, Rev. Roum. Chem. **53**(9), 753 (2008)
22. L. Chi, O. Sadovski, G.A. Woolley, Biocon. Chem. **17**, 670 (2006)
23. F. Mirazizi, A. Bahrami, K. Haghbeen, H.S. Zahiri, M. Bakavoli, R.L. Legge, J. Enzyme Inhib. Med. Chem. Online (2015). doi:10.3109/14756366.2015.1103234
24. M. Shamsipura, B. Maddah, B. Hemmateenejad, S. Rouhani, K. Haghbeen, K. Alizadeh, Spectrochimica Acta Part A **70**, 1–6 (2008)
25. K. Haghbeen, R. Agharafeie, S. Maghsoudi, Iran. Polym. J. **14**, 729 (2005)
26. K. Haghbeen, R.L. Legge, Chem. Eng. J. **150**, 1 (2009)
27. R. Haag, S. Roller, in Immobilized Catalysts, ed. (Springer, Berlin Heidelberg) (2004)
28. R. Mutneja, R. Singh, V. Kaur, J. Wagler, E. Kroke, Dyes Pigm. **108**, 41 (2014)