Supplementary Information

Poly(*N*-protected ethylene imine-*alt*-ethylene sulfide) Block to Functionalize Polymeric Materials

Yoichi Hori, Na Pei, Ryota Kumagai, and Yuji Sasanuma*

Department of Applied Chemistry and Biotechnology, Faculty of Engineering, Chiba University, 1-33 Yayoi-cho, Inage-ku, Chiba 263-8522, Japan

Methods

Materials

Commercially available chemicals were used as received: ethanol (Japan Alcohol); silica gel (Merck); tetrahydrofuran (Nacalai Tesque); diethanolamine, 33% hydrobromic acid in acetic acid, potassium *tert*-butoxide, sodium hydroxide, and thiourea (Sigma-Aldrich); 2,2-dimethoxy-2-phenylacetophenone (abbreviated herein as DMPA) and *p*-toluenesulfonyl chloride (Tokyo Chemical Industry); acetic acid, acetone, *tert*-butanol, chloroform, chloroform-*d*, dichloromethane (abbreviated as DCM), diethyl ether, dimethyl sulfoxide, *n*-hexane, hydrochloric acid, methanol, phenol, sodium hydrogen carbonate, toluene, triethylamine, and thionyl chloride (Wako Pure Chemical Industries).

Synthesis of *N*,*N*-bis(2-hydroxyethyl)-4-methylbenzenesulfonamide (2): reaction I (see Fig. 1)

p-Toluenesulfonyl chloride (45.4 g, 0.238 mol), dissolved in DCM (100 mL), was added dropwise to diethanolamine (30.0 g, 0.285 mol) and triethylamine (72.7 g, 0.718 mol) in a flask cooled with ice water. While being stirred at room temperature for 4 h, the reaction mixture became viridescent and viscous. The solvent was removed using a rotary evaporator, and the residue underwent extraction with water and DCM. The organic layer was condensed and recrystallized from a mixed solvent of water and ethanol. White crystals were collected by filtration, washed with water, and dried in vacuo at 45 °C. The yield was 55.6 g (90%). ^{1}H NMR (500 MHz, $CDCl_3$, δ, see

Fig. S1): 7.70 (d, *ortho N*-tosyl, 2H), 7.33 (d, *meta N*-tosyl, 2H), 3.87 (br s, –CH_2OH, 4H), 3.23 (br s, –CH_2N–, 4H), 2.43 (s, –CH_3 *N*-tosyl, 3H).

Synthesis of *N,N*-bis(2-chloroethyl)-4-methylbenzenesulfonamide (3): reaction II[S1]

Compound **2** (50.0 g, 0.193 mol) was dissolved in DCM (120 mL) stirred in a three-necked flask equipped with a reflux condenser connected to a trap containing sodium hydroxide solution. Thionyl chloride (70.1 g, 0.589 mol) was dropwise added into the flask, with the trap bathed in ice water. The reaction mixture, foaming vigorously, was stirred at ambient temperature for 22 h and then heated gradually up to 95 °C to remove DCM. After the residual liquid was cooled to room temperature, water was added to quench excess thionyl chloride, and then sodium hydroxide solution was added to adjust the pH to about 10. The solution underwent extraction with water and DCM. The organic layer was condensed on a rotary evaporator and, furthermore, in a vacuum oven at 45 °C to yield green liquid (55.5 g, 97%), which quickly crystallized at ambient temperature. ^{1}H NMR (500 MHz, $CDCl_3$, δ, Fig. S2): 7.71 (d, *ortho N*-tosyl, 2H), 7.33 (d, *meta N*-tosyl, 2H), 3.67 (t, –CH_2N–, 4H), 3.43 (t, –CH_2OH, 4H), 2.43 (s, –CH_3 *N*-tosyl, 3H).

Synthesis of 4-methyl-*N,N*-divinylbenzenesulfonamide (4): reaction III[S2]

Compound **3** (11.1 g, 37.5 mmol) was dissolved in *tert*-butanol (64 mL) stirred in a three-necked flask equipped with a reflux condenser, and then potassium *tert*-butoxide (16.8 g, 150 mmol) was added. While standing stirred at 70 °C for 24 h, the solution gradually turned brown. Afterward, *tert*-butanol was removed, and the remaining liquid was subjected to extraction with water and DCM. The organic layer was condensed under reduced pressure overnight, purified by column chromatography on silica gel with a mixed eluting solvent (DCM : *n*-hexane = 4 : 1, Rf of the product = 0.60 ∼ 0.65), and condensed overnight to yield **4** as yellow liquid (3.78 g, 45%). ^{1}H NMR (500 MHz, $CDCl_3$, δ, Fig. S3): 7.64 (d, *ortho N*-tosyl, 2H), 7.28 (d, *meta N*-tosyl, 2H), 6.41 (q, –C*H*N–, 2H), 4.93 (d, *trans* C*H*=, 2H), 4.79 (d, *cis* C*H*=, 2H), 2.40 (s, –CH_3 *N*-tosyl, 3H).

Synthesis of (tosylazanediyl)bis(ethane-2,1-diyl) bis(4-methylbenzene sulfonate) (5): reaction IV

p-Toluenesulfonyl chloride (92.8 g, 0.487 mol), dissolved in DCM (150 mL), was added dropwise into diethanolamine (16.0 g, 0.152 mol) and triethylamine (92.4 g, 0.913 mol) in a flask bathed in ice water, and the mixture was stirred at room temperature for 150 min. Afterward, the fluid components were removed under reduced pressure, and yellowish green solid remained. The crude product was washed with ethanol and dried overnight in a vacuum oven at 45 °C to yield **5** as white solid (85.4 g, 99%). ^{1}H NMR (500 MHz, $CDCl_3$, δ, Fig. S4): 7.76 (d, *ortho O*-tosyl, 4H), 7.64 (d, *ortho N*-tosyl, 2H), 7.36 (d, *meta O*-tosyl, 4H), 7.28 (d, *meta N*-tosyl, 2H), 4.11 (t, –CH_2O–, 4H), 3.38 (t, –CH_2N–, 4H), 2.46 (s, –CH_3 *O*-tosyl, 6H), 2.43 (s, –CH_3 *N*-tosyl, 3H).

Synthesis of *N,N*-bis(2-mercaptoethyl)-4-methylbenzenesulfonamide (6): reactions V_1 and V_2[S3]

Thiourea (2.95 g, 38.8 mmol) was added to absolute ethanol (100 mL) containing **5** (10.0 g, 17.6 mmol) in a three-necked flask equipped with a reflux condenser, the flask was kept at 70 °C in an oil bath for 24 h, and then ethanol was removed with a rotary evaporator. The residue was diluted with water (100 mL), and the mixture, stirred vigorously, was heated up to 70 °C. Sodium hydrogen carbonate (7.4 g, 88 mmol) was added, and the mixture was refluxed at 100 °C for 2 h. The reaction mixture, standing cooled to room temperature, was acidified with hydrochloric acid to pH $\approx$ 5 and subjected to extraction with water and DCM. The organic layer was condensed on a rotary evaporator and, furthermore, in a vacuum oven at 45 °C overnight to be viscous reddish oil. The crude product was purified by column chromatography on silica gel with a mixed eluting solvent (DCM : methanol = 199 : 1, Rf of the product = $0.5 - 0.75$) and condensed to yield **6** as colorless liquid, which gradually solidified at room temperature. The yield was 2.1 g (41%).

Air oxidation of **6** gives a cyclic compound, 5-tosyl-1,2,5-dithiazepane (**6s**: side product of **6**, see Fig. S5). The amount of **6s** increases with time; four months later, about 66% of **6** was changed to **6s**. Therefore, it is preferable that **6** should be used as soon as possible. Because **6** and **6s** are soluble in similar solvents, **6s** could not be separated from **6** even by column chromatography. Fortunately, however, **6s** was unreactive in the following copolymerization and could be removed thereafter. ^{1}H NMR (500 MHz,

$CDCl_3$, δ, Fig. S5) of **6**: 7.64 (d, *ortho N*-tosyl, 2H), 7.28 (d, *meta N*-tosyl, 2H), 3.28 (t, –CH_2N–, 4H), 2.72 (q, –CH_2S–, 4H), 2.43 (s, –CH_3 *N*-tosyl, 3H), 1.41 (t, –S*H*, 2H). ^{1}H NMR (500 MHz, $CDCl_3$, δ, Fig. S5) of 5-tosyl-1,2,5-dithiazepane **6s**: 7.72 (d, *ortho N*-tosyl, 2H), 7.32 (d, *meta N*-tosyl, 2H), 3.64 (t, –CH_2N–, 4H), 2.99 (t, –CH_2S–, 4H), 2.43 (s, –CH_3 *N*-tosyl, 3H).

Polymerization between 4 and 6: reaction VI

Compounds **4** (0.60 g, 2.69 mmol) and **6** (0.78 g, 2.68 mmol) were dissolved in chloroform in a 50-mL flask, DMPA (0.014 g, 1.0 wt%) was added,[S4] and the flask was shaken vigorously so that the mixture would be uniform. The common solvent, chloroform, was removed with a rotary evaporator, and the residue in the flask was dried in a vacuum oven at 45 °C for 1 h. The flask, being dipped in a water bath kept at 50 °C and rotated continuously on the evaporator with its inner pressure left atmospheric, was exposed for 10 min to ultraviolet light (wavelength = 375 nm),[S5] whose source was 41 light emitting diodes of an OptCode LED-41UV375N Black Light. As the irradiation time increased, the contents became more viscous and finally lost fluidity. The hardened product, dissolved in chloroform (20 mL), was poured into ethanol (250 mL) and kept still for 3 days to yield white precipitate. The deposit was collected by suction filtration with Advantec GS-25 glass fiber filters, washed with ethanol, and dried at 45 °C under reduced pressure to yield the final product **7** (0.29 g, 21%) as yellowish solid. ^{1}H NMR (500 MHz, $CDCl_3$, δ, Fig. 2): 7.69 (br s, *ortho N*-tosyl, 2H), 7.31 (br s, *meta N*-tosyl, 2H), 3.28 (br s, –CH_2N–, 4H), 2.73 (br s, –CH_2S–, 4H), 2.42 (br s, –CH_3 *N*-tosyl, 3H).

Instead of chloroform, acetone was used as the common solvent, and the thiol-ene polymerization was conducted with a smaller amount (0.1 wt%) of the initiator, DMPA. Then, the UV irradiation of as long as 1 hr was needed to attain full gelation of the polymer. Its ^{1}H NMR spectrum was essentially identical with that in Fig. 2; therefore, no further characterization was carried out for this product.

When the polymer was collected by suction filtration, three pieces of glass fiber filters were laid in the funnel. Nevertheless, the filtrate was solidified after evaporation of the solvent. ^{1}H NMR showed that the residual solid included a significant amount of **7**, probably, of smaller molecular weights. Accordingly, the actual yield of the thiol-ene photopolymerization

must be higher than the above value (21%). Fractionations with good and poor solvents will give some fractions of different molecular weights.

Deprotection: reaction VII[S6]

Acetic acid solution (8 mL) of hydrobromic acid (33%) was added into phenol (0.18 g, 1.9 mmol) and **7** (0.20 g), and the mixture was gradually heated and kept at 90 °C for 12 h. Afterward, acetic acid solution of 33% HBr was added again by 8 mL, and the mixture was stirred at 90 °C for 24 h. The reaction mixture was condensed on a rotary evaporator and dried in vacuo overnight to yield dark solid, which was dissolved in chloroform and filtered. The filtrate was condensed and dried as above. The residual solid was subjected to washing and decantation with diethyl ether three times and dried in a vacuum oven at 45 °C. The yield was 0.11 g. ^{13}C NMR with ^{1}H broad-band decoupling (125.7 MHz, $CDCl_3$, δ) of **1S**: 49.0 (s, –CH_2N–), 34.7 (s, –CH_2S–)

According to the literature,[S7] it is desirable that the deprotected compound should be purified by ion exchange resin. However, insolubility of **1S** in water prevented us from employing this procedure. Although a ^{1}H NMR spectrum (not shown here) of the deprotected sample showed the presence of a small amount of impurities such as the eliminated tosyl group, we could characterize **1S** as described in the text.

NMR measurements

Proton (^{13}C) NMR spectra were measured at 500 (125.7) MHz on a JEOL JNM-ECA500 spectrometer in the Chemical Analysis Center of Chiba University. The free induction decays were accumulated 8 or 16 (256) times. The $\pi/2$ pulse width and recycle delay were 5.6 (5.0) μs and 2.0 (2.0) s, respectively. Here, the ^{13}C NMR parameters are given in the parentheses. The solvent was chloroform-*d*, and the chemical shifts were calibrated with respect to the tetramethylsilane signal.

Molecular orbital calculations of NMR chemical shifts

Density functional calculations were carried out at the B3LYP/6-311++G(3df, 3pd) level with the Gaussian03 program[S8] installed on an HPC 8000-Z500 computer. Geometrical parameters of *N*-ethyl-4-methyl-*N*-vinylbenzenesulfonamide, $CH_3CH_2N(Ts)CH{=}CH_2$, and **4** were fully optimized, and their

^{1}H NMR chemical shifts were calculated by the gauge-independent atomic orbital method[S9] and subtracted from that of tetramethylsilane to derive the δ values in ppm. All the self-consistent field calculations were conducted under the tight convergence.

Static light scattering

Static light scattering (SLS) experiments were carried out using a Photal DLS-8300CU photometer equipped with a He−Ne laser (wavelength, 632.8 nm). Five chloroform solutions of different polymer concentrations (0.260 − 0.977 mg mL^{-1}) of **7** were prepared. The solution was optically purified by filtration through a 0.45 μ m cellulose membrane filter. During the measurement, the sample temperature was maintained at 34.0±0.1 °C. The excess Rayleigh ratio was measured in a scattering angle range of $30 \leq \theta \leq 130$ ° at intervals of 5 °. The differential refractive index increment (dn/dc) was measured by a Photal DRM-3000 differential refractometer with the He−Ne laser. The sample temperature and concentrations were the same as in the SLS measurement. The dn/dc value was evaluated as 0.1309 mL g^{-1}. The weight-average molecular weight M_{w} of **7** was determined by a Zimm plot to be 2.77 $\times 10^4$.

Thermogravimetry (TG) and differential thermal analysis (DTA)

Thermal histories of **7** and **1S** on heating at a rate of 10 °C min^{-1} from room temperature to 500 °C under nitrogen atmosphere were investigated with a MAC Science TG−DTA2000 differential thermal analysis system. The recorded temperatures were calibrated with respect to the melting point of lead. TG/DTA curves of **7** and **1S** are shown in Fig. S6.

Solubility classification test

Solubilities of **7** and **1S** were investigated for a variety of solvents. For **7**, 10 mg of sample was mixed in a solvent of 2.0 mL and shaken vigorously at room temperature to visually distinguish the solubility into three degrees: (1) completely soluble, (2) partially soluble, or (3) insoluble. For **1S**, a smaller amount of sample was used.

References

S1 Partially based on P. M. Kushakova, A. N. Chernobroviy, V. A. Kuznetsov and A. V. Garabadgiu, *Chem. Heterocycl. Compd.*, 2004, **40,** 1546.

S2 Partially based on G. D. Modica and E. Angeletti, *Gazz. Chim. Ital.,* 1960, **90,** 434.

S3 Partially based on A. S. Craig, R. Kratky, R. C. Matthews, D. Parker, G. Ferguson, A. Lough, H. Adams, N. Bailey and H. Schneider, *J. Chem. Soc., Perkin Trans. 2.,* 1990, 1523.

S4 D. L. Kurdikar and N. A. Peppas, *Macromolecules,* 1994, **27,** 733.

S5 N. T. Brummelhuis, C. Diehl and H. Schlaad, *Macromolecules,* 2008, **41,** 9946.

S6 Partially based on D. I. Weisblat, B. J. Magerlein and D. R. Myers, *J. Am. Chem. Soc.,* 1953, **75,** 3630.

S7 B. Dietrich, M. W. Hosseini, J. M. Lehn, R. B. Sessions, *Hlelv. Chim. Acta,* 1983, **66,** 1262.

S8 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez and J. A. Pople, *GAUSSIAN 03, Revision D.01*, Gaussian, Inc., Wallingford CT, 2004.

S9 K. Wolinski, J. F. Hinton and P. Pulay, *J. Am. Chem. Soc.,* 1990, **112,** 8251.

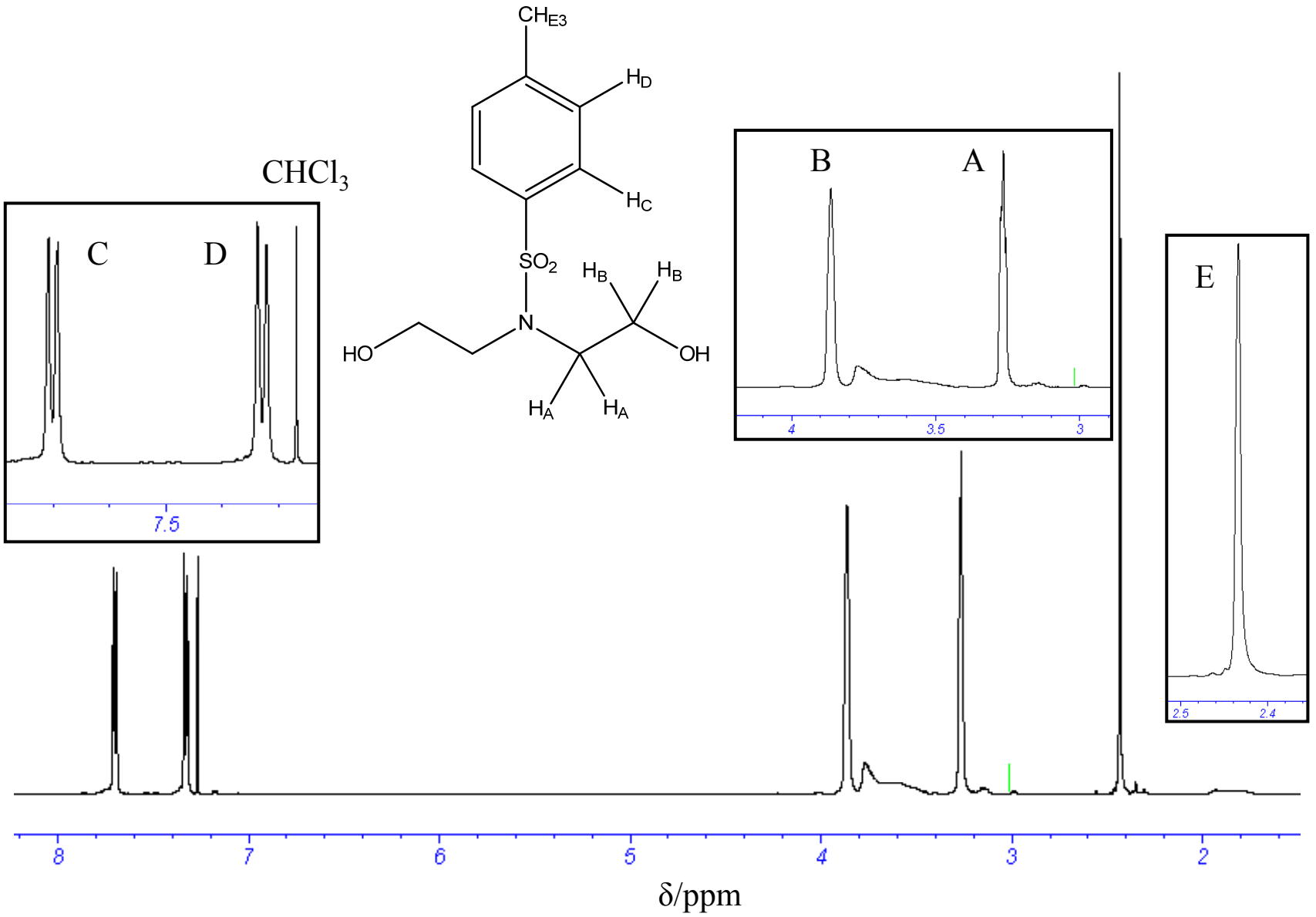

Fig. S1 ^{1}H NMR spectrum of *N,N*-bis(2-hydroxyethyl)-4-methylbenzenesulfonamide (**2**).

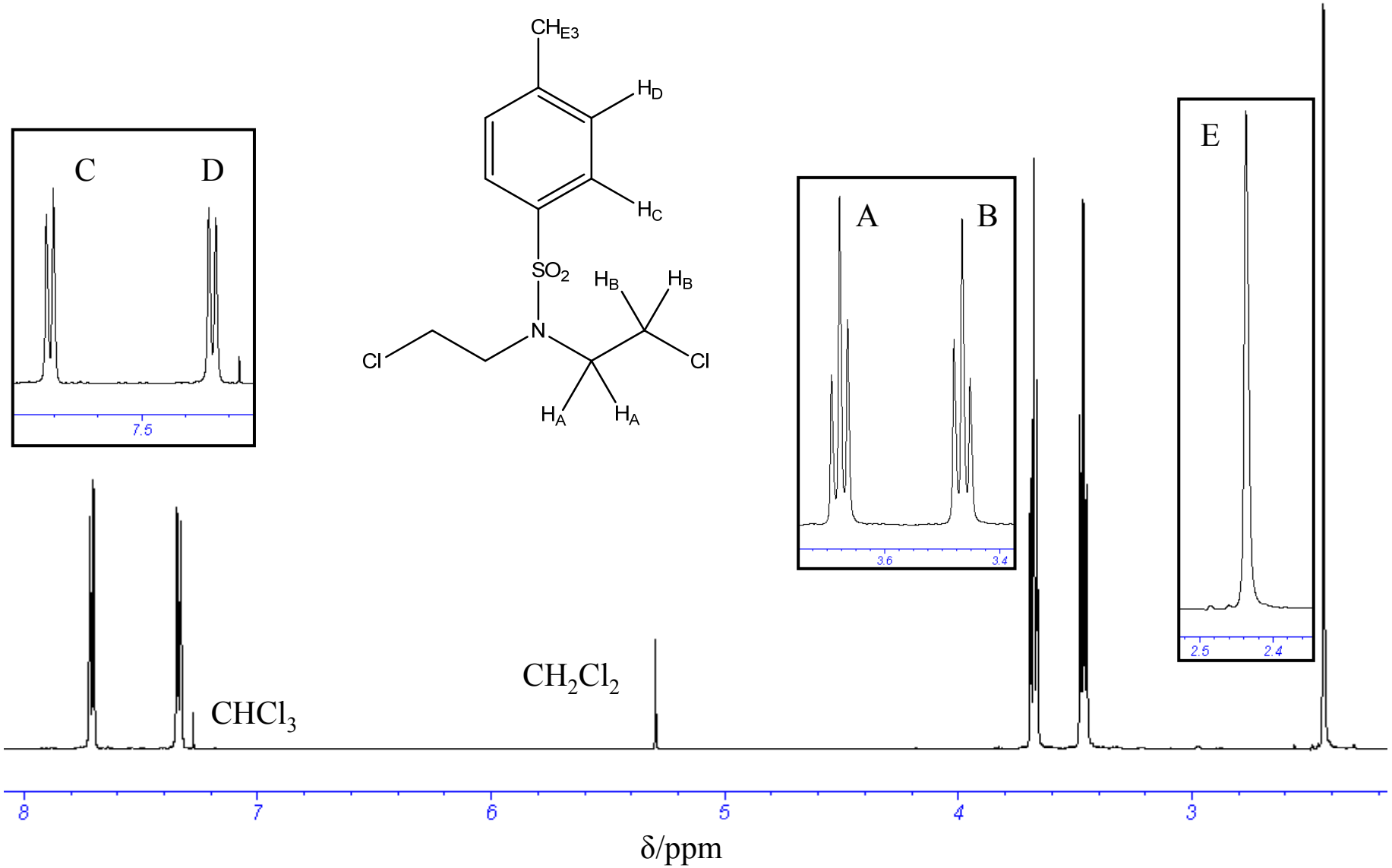

Fig. S2 ^{1}H NMR spectrum of *N,N*-bis(2-chloroethyl)-4-methylbenzenesulfonamide (**3**).

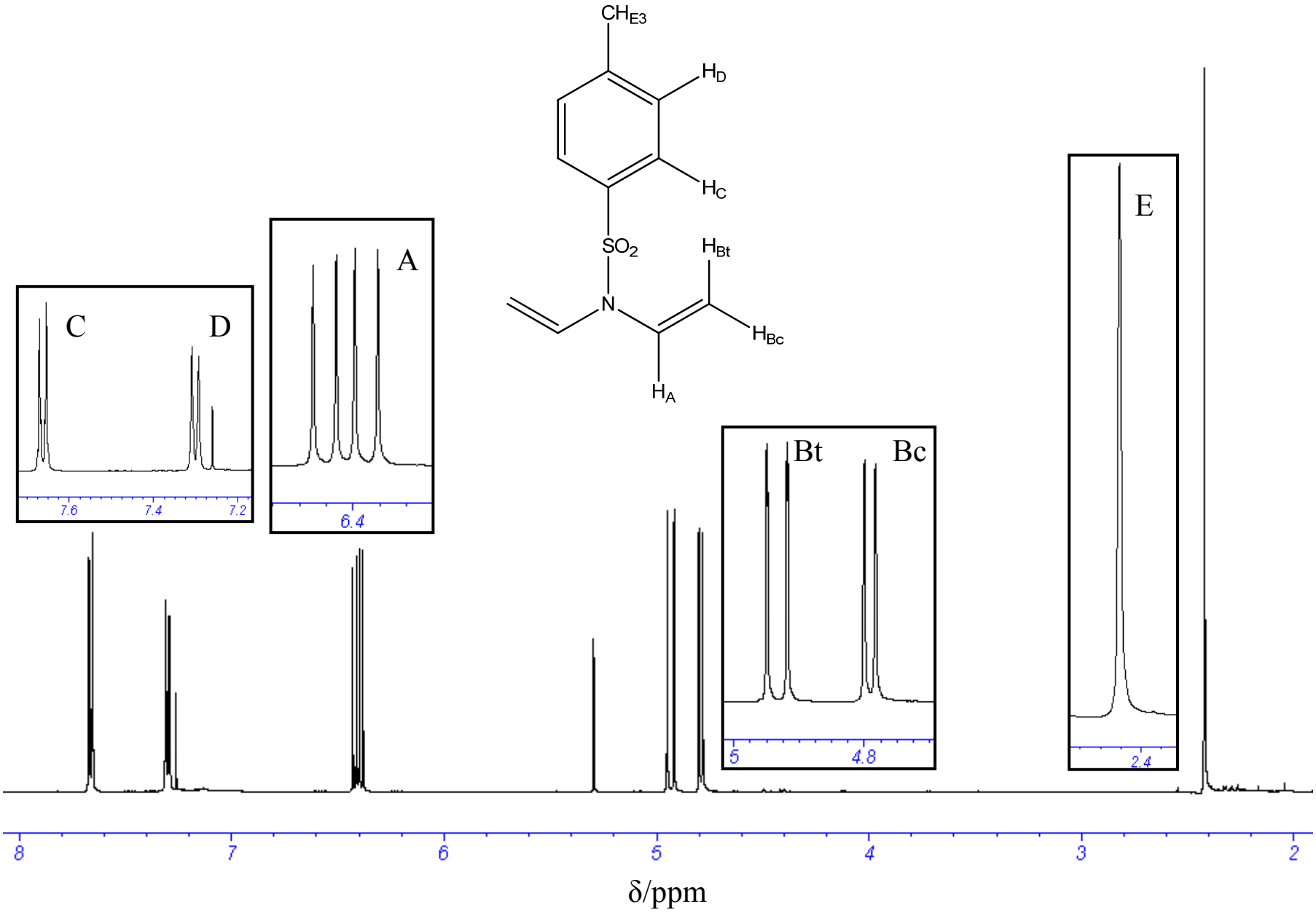

Fig. S3 ^{1}H NMR spectrum of 4-methyl-*N,N*-divinylbenzenesulfonamide (**4**).

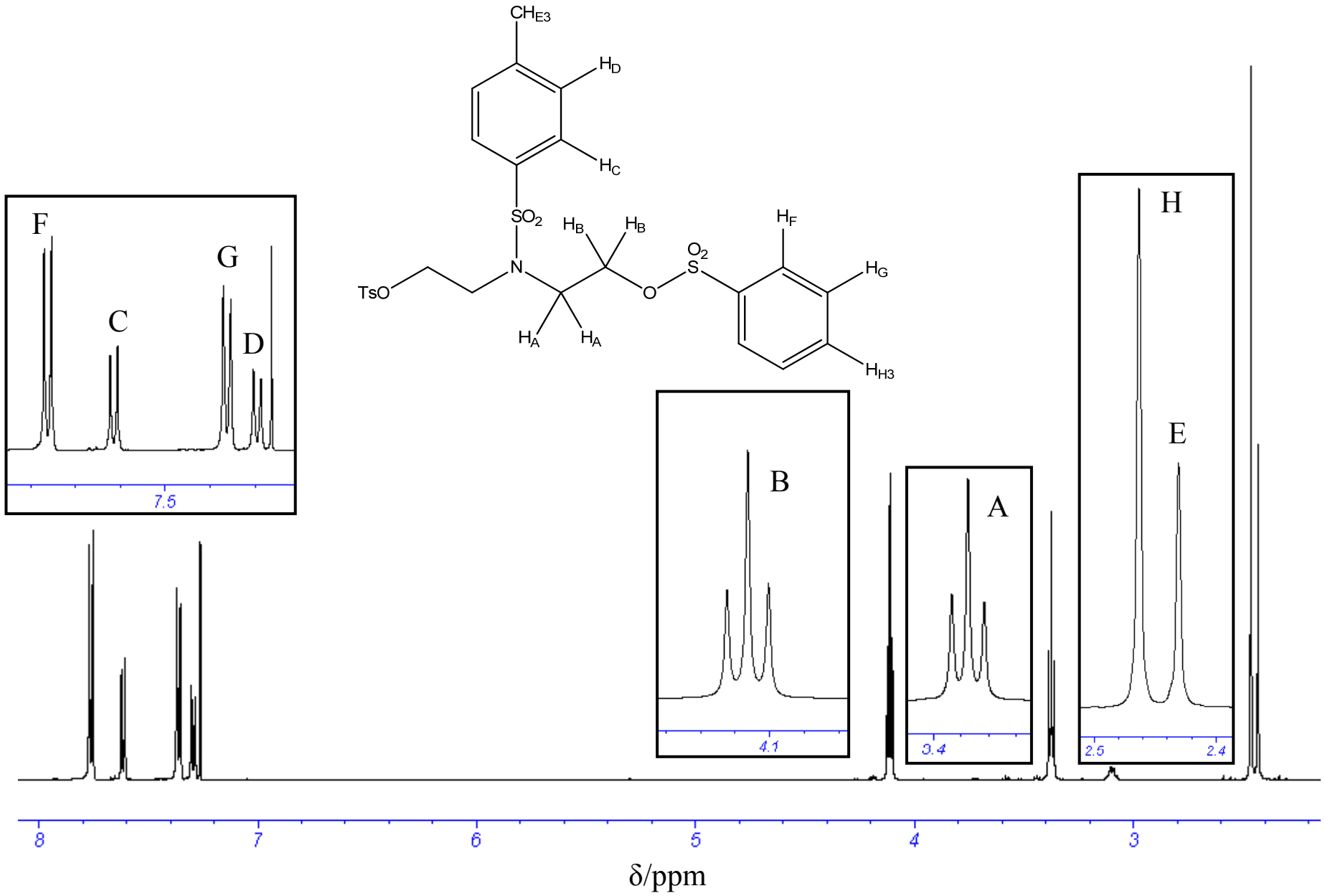

Fig. S4 ^{1}H NMR spectrum of (tosylazanediyl)bis(ethane-2,1-diyl) bis(4-methylbenzenesulfonate) (**5**).

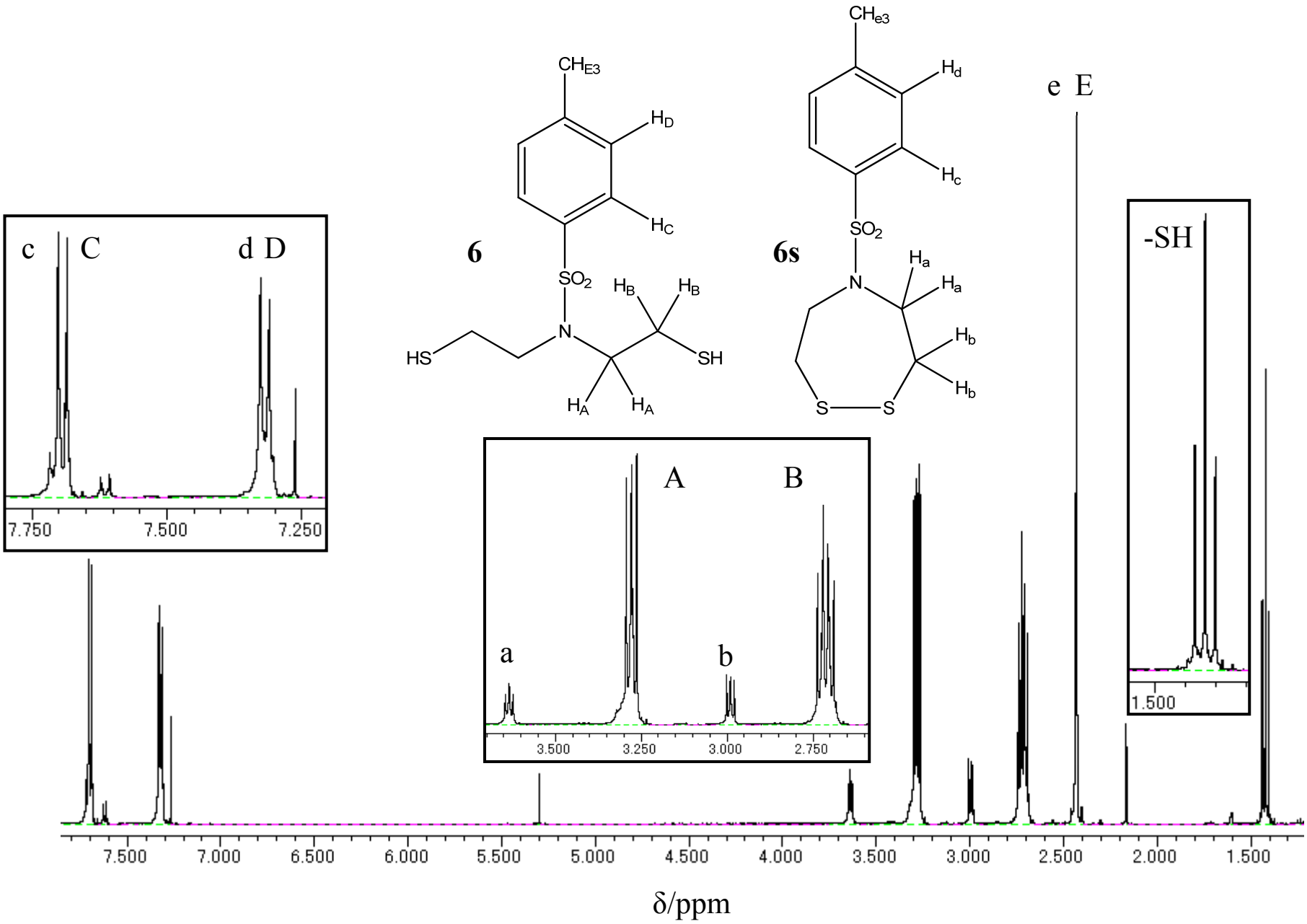

Fig. S5 ^{1}H NMR spectrum observed from a mixture of *N,N*-bis(2-mercaptoethyl)-4-methylbenzenesulfonamide (**6**) and 5-tosyl-1,2,5-dithiazepane (**6s**).

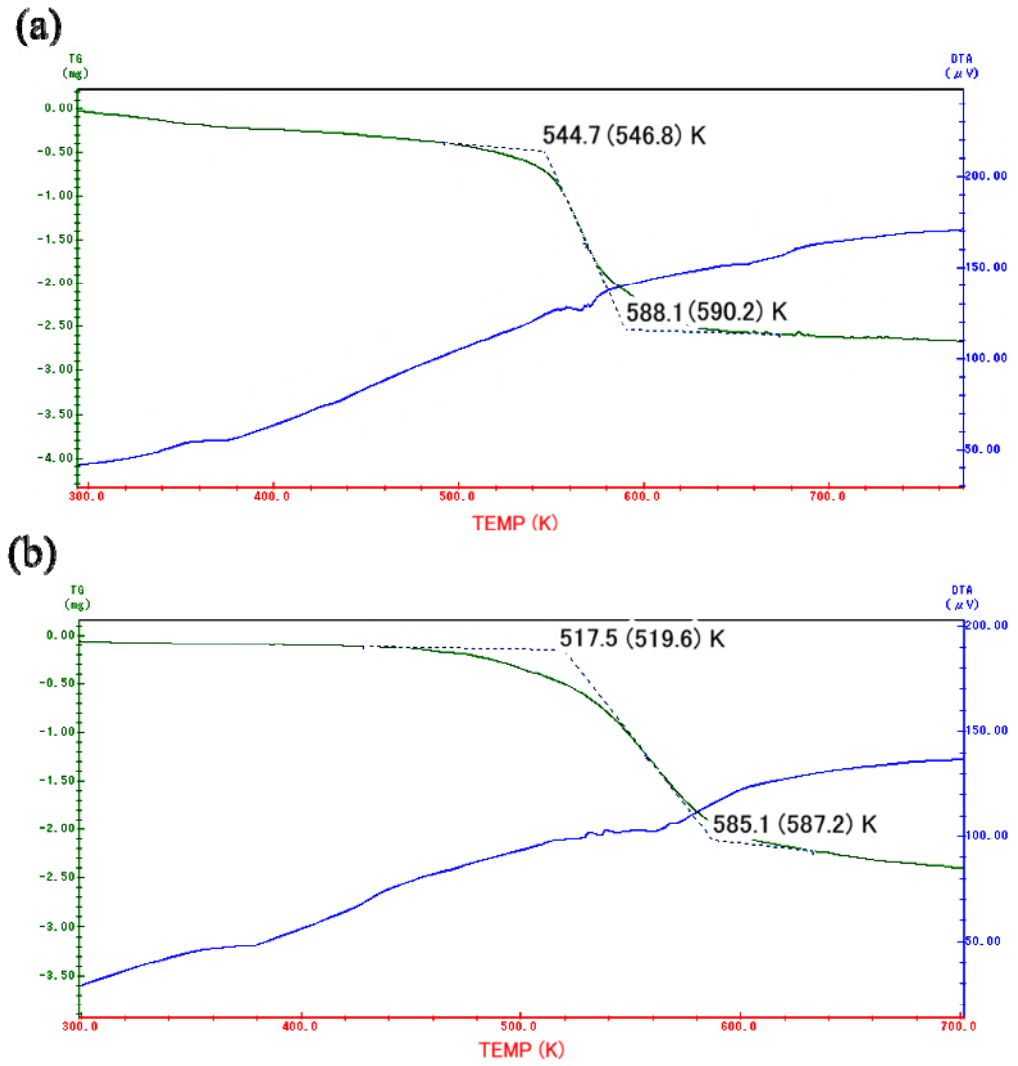

Fig. S6 TG/DTA curves of (a) **7** and (b) **1S**. As-recorded and calibrated temperatures are given in and outside the parentheses, respectively.