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Chiral donor–π-acceptor azobenzene dyes

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ABSTRACT

Four chiral donor–π-acceptor azobenzene dye conjugates were synthesized and characterized. Chiral moieties, namely (*S*)-(+)-2-(6-methoxy-2-naphthyl)propionic acid (naproxen) and (*S*)-2-aminopropionic acid (L-alanine), were attached to either the donor end or the acceptor site of the azo compound using ester or amide bonds, respectively. The structures of the molecules were verified using ^{1}H NMR, ^{13}C NMR and ESI TOF mass spectrometry; spectral properties were evaluated with UV–vis and CD spectrometry whilst thermal stability was determined by TGA. The compounds displayed a broad absorption maximum in the visible region between 433 and 483 nm. All compounds showed relatively high thermal stability, decomposition temperatures being ~200 °C.

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1. Introduction

Azobenzenes are well-known compounds used primarily as synthetic colorants [1]. In addition to dyeing feature, azobenzenes possess interesting properties such as the reversible *cis–trans* photoisomerization about the azo bond when irradiated [2–4], and non-linear optical (NLO) effect [5,6] related to the donor–acceptor azobenzenes. NLO effects require either non-centrosymmetric or polar packing (space group) of the NLO active material. Controlling the organization/packing of an achiral NLO molecule is a very difficult task to accomplish, an easier way is to make the NLO candidate chiral and use its inherent chirality to prevent centrosymmetric packing.

In designing new materials for the needs of advanced technology, chiral azobenzene systems have proven to be useful candidates: in addition to attributes mentioned above, they also display optical activity, observed by circular dichroism (CD) measurements [7]. Recently, several studies of azobenzene systems with chiral functionality have been studied, since they provide properties useful in various research topics including molecular switches [8–10], optically active polymers [11–13], liquid crystals [14], and non-linear optics [15,16].

Herein we report the synthesis, structural and spectroscopic evaluation of four new chiral donor–acceptor azobenzene molecules that are potential NLO materials due to the known donor–acceptor functionality of the azobenzene part supplemented with the chiral unit controlling the intermolecular interactions. In this study we introduced the chirality to the azobenzene skeleton by attaching either (*S*)-(+)-2-(6-methoxy-2-naphthyl)propionic acid (naproxen) or (*S*)-2-aminopropionic acid (L-alanine) moieties into it. Through free carboxylic acid group present in the azobenzenes, they can be attached covalently to nearly any suitable counter part, one example being the periphery of the hydroxyl functionalized dendrimer [17,18] or focal point of the dendron [19] to make branched photoactive molecules. The synthesized azobenzene conjugates are given in Fig. 1.

2. Experimental

2.1. Materials and instrumentations

All starting materials were purchased from major suppliers and used without any further purification. Naproxen acid chloride [20] and L-alanine methyl ester hydrochloride [21] were synthesized following the published procedures.

Dichloromethane and dimethylformamide were dried over 4 Å sieves.

Column chromatography was performed with Merck 60 F_{254} silica gel, particle size 0.040–0.063 mm. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DRX 500 NMR (500.13 and 125.76 MHz) or on a Bruker Avance DPX 250 NMR (250.13 and 62.90 MHz) spectrometer in DMSO-d_6 or $CDCl_3$ solutions. The solvent signal was used as an internal standard. Mass spectral data was obtained with Micromass LCT Electronspray ionization time-of-flight (ESI TOF) instrument with positive-ion or negative-ion

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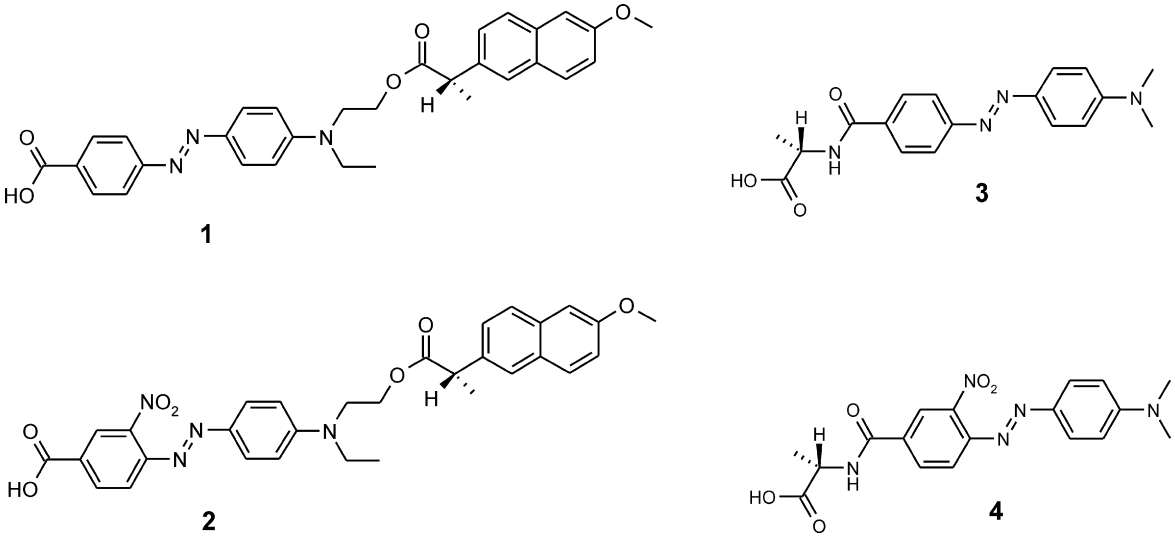

Fig. 1. Synthesized chiral azobenzene compounds.

mode. Absorption spectra were scanned on a Varian Cary100 UV–vis Spectrometer with 10 mm quartz cell in chloroform or dimethylformamide solutions. Circular dichroism spectra were recorded on a Jasco J-715 CD-spectrometer under the following conditions: temperature 20 °C; cuvette length 1 mm; wavelength area 200–650 mn; scan speed 50 mn/min. Decomposition temperatures were determined utilizing Perkin Elmer TGA7 Thermogravimetric Analyzer under following conditions: heating rate 10 °C/min; atmosphere, air at 60 mL/min; sample size of about 1.5 mg. Melting points were measured on a Metler Toledo FP62 apparatus at a heating rate 2 °C/min, and are uncorrected.

2.2. Synthesis

2.2.1. (E)-4-(((4-Ethyl(2-hydroxyethyl)amino)phenyl)diazenyl) benzoic acid (**5**)

4-Aminobenzoic acid (2.00 g, 14.6 mmol) in 18% HCl (30 ml) was cooled to 0 °C, and ice-cold aqueous solution of $NaNO_2$ (1.00 g, 14.6 mmol) was added dropwise to the mixture at below 4 °C. This diazonium solution was then added to the solution of *N*-ethyl-*N*-(2-hydroxy)aniline (2.41 g, 14.6 mmol) and 37% HCl (10 ml) at below 4 °C. The mixture was stirred for 1 h, and neutralized with saturated sodium acetate. Solid was filtered, washed several times with water and dried in vacuo to give 3.87 g (85%) of red solid.

^{1}H NMR (DMSO-d_6, 500 MHz): $\delta_{ppm} = 1.14$ (t, 3H, CH_3, $J = 7.0$ Hz), 3.48–3.53 (m, 4H, CH_2), 3.61 (t, 2H, CH_2OH, $J = 6.1$ Hz), 4.81 (br s, 1H, O*H*), 6.84 (d, 2H, *o*-Ar*H* to NCH_2, $J = 9.3$ Hz), 7.80 (d, 2H, *m*-Ar*H* to NCH_2, $J = 9.2$ Hz), 7.82 (d, 2H, *m*-Ar*H* to COOH, $J = 8.7$ Hz), 8.07 (d, 2H, *o*-Ar*H* to COOH, $J = 8.7$ Hz), 12.98 (br s, 1H, COO*H*). ^{13}C NMR (DMSO-d_6, 126 MHz): $\delta_{ppm} = 11.97$ (CH_3), 45.12 (NCH_2CH_3), 52.12 (NCH_2CH_2), 58.33 (NCH_2CH_2OH), 111.23 (*o*-Ar*C*H to NCH_2), 121.60 (*m*-Ar*C*H to COOH), 125.49 (*m*-Ar*C*H to NCH_2), 130.43 (*o*-Ar*C*H to COOH), 130.66 (Ar*C* next to COOH), 142.33 (*p*-Ar*C* to NCH_2), 151.19 (Ar*C* next to NCH_2), 155.13 (*p*-Ar*C* to COOH), 166.85 (*C*OOH). ESI TOF MS: *m*/*z* calcd for $C_{17}H_{19}N_3O_3$ 312.13 $[M - H]^-$, found 312.13 $[M - H]^-$.

2.2.2. (E)-4-((4-(Ethyl(2-hydroxyethyl)amino)phenyl)diazenyl)-3-nitrobenzoic acid (**6**)

Aqueous $NaNO_2$ (0.52 g, 7.58 mmol) was added stirring to conc. H_2SO_4 (12 ml) at 30 °C (cooled with ice-bath). The solution was heated to 70 °C, before cooling to <5 °C. 4-Amino-3-nitrobenzoic acid (1.38 g, 7.58 mmol) was added during 30 min, and the resulting mixture stirred at 5 °C for about 3 h. This diazonium solution was then added to the solution of *N*-ethyl-*N*-(2-hydroxy)aniline (1.25 g, 7.58 mmol) and ice-cold water (38 ml) containing 2 ml of conc. H_2SO_4. The reaction mixture was neutralized with saturated sodium acetate until precipitation occurred, and stirred at room temperature for 1 h. Solid was filtered, washed thoroughly with water and dried in vacuo to give 2.05 g (75%) of almost black solid.

^{1}H NMR (DMSO-d_6, 250 MHz): $\delta_{ppm} = 1.15$ (t, 3H, CH_3, $J = 6.9$ Hz), 3.40–3.62 (overlapped peaks, 6H, CH_2), 4.82 (br s, 1H, O*H*), 6.87 (d, 2H, *o*-Ar*H* to NCH_2, $J = 9.2$ Hz), 7.72–7.79 (overlapped peaks, 3H, *m*-Ar*H* to NCH_3 and *m*-Ar*H* to COOH), 8.22 (dd, 1H, *o*-Ar*H* to COOH, $J = 8.5$, 1.5 Hz), 8.40 (d, 1H, *o*-Ar*H* to COOH and NO_2, $J = 1.4$ Hz), 13.54 (br s, 1H, COO*H*). ^{13}C NMR (DMSO-d_6, 63 MHz): $\delta_{ppm} = 11.96$ (CH_3), 45.36 (NCH_2CH_3), 52.21 (NCH_2CH_2OH), 58.39 (NCH_2CH_2OH), 111.62 (*o*-Ar*C*H to NCH_3), 118.63 (*m*-Ar*C*H to COOH), 124.67 (*o*-Ar*C*H to COOH and NO_2), 126.52 (*m*-Ar*C*H to NCH_2), 130.61 (Ar*C* next to COOH), 133.43 (*o*-Ar*C*H to COOH), 142.70 (*p*-Ar*C* to NCH_3), 146.39 (Ar*C* next to NO_2), 147.20 (*p*-Ar*C* to COOH), 152.35 (Ar*C* next to NCH_2), 165.30 (*C*OOH). ESI TOF MS: *m*/*z* calcd for $C_{17}H_{18}N_4O_5$ 358.12 $[M - H]^-$, found 358.16 $[M - H]^-$.

2.2.3. (E)-4-((4-(Dimethylamino)phenyl)diazenyl)benzoic acid (**7**)

The procedure is the same as the synthesis of **5**. 4-Aminobenzoic acid (2.00 g, 14.6 mmol), $NaNO_2$ (1.00 g, 14.6 mmol) and *N*,*N*-dimethylaniline (1.77 g, 14.6 mmol) were used. Red solid. Yield: 3.61 g (92%).

^{1}H NMR (DMSO-d_6, 500 MHz): $\delta_{ppm} = 3.08$ (s, 6H, NCH_3), 6.84 (d, 2H, *o*-Ar*H* to NCH_3, $J = 9.2$ Hz), 7.82 (d, 2H, *m*-Ar*H* to NCH_3, $J = 9.1$ Hz), 7.83 (d, 2H, *m*-Ar*H* to COOH, $J = 8.5$ Hz), 8.07 (d, 2H, *o*-Ar*H* to COOH, $J = 8.5$ Hz). ^{13}C NMR (DMSO-d_6, 63 MHz): $\delta_{ppm} = 39.76$ (N*C*H$_3$), 111.53 (*o*-Ar*C*H to NCH_3), 121.66 (*m*-Ar*C*H to COOH), 125.21 (*m*-Ar*C*H to NCH_3), 130.44 (*o*-Ar*C*H to COOH), 130.87 (Ar*C* next to COOH), 142.65 (*p*-Ar*C* to NCH_3), 152.94 (Ar*C* next to NCH_2), 155.03 (*p*-Ar*C* to COOH), 166.86 (*C*OOH). ESI TOF MS: *m*/*z* calcd for $C_{15}H_{15}N_3O_2$ 268.11 $[M - H]^-$, found 268.04 $[M - H]^-$.

2.2.4. (E)-4-((4-(Dimethylamino)phenyl)diazenyl)-3-nitrobenzoic acid (**8**)

The procedure is the same as the synthesis of **6**. $NaNO_2$ (345 mg, 5.00 mmol), 4-amino-3-nitrobenzoic acid (911 mg, 5.00 mmol) and *N*,*N*-dimethylaniline (641 mg, 5.29 mmol) were used. Dark red solid. Yield: 1.15 g (73%).

^{1}H NMR (DMSO-d_6, 500 MHz): $\delta_{ppm} = 3.11$ (s, 6H, NCH_3), 6.86 (d, 2H, *o*-Ar*H* to NCH_3, $J = 9.3$ Hz), 7.76 (d, 2H, *m*-Ar*H* to NCH_3, $J = 9.2$ Hz), 7.78 (d, 1H, *m*-Ar*H* to COOH, $J = 8.3$ Hz), 8.23 (dd, 1H,

o-Ar*H* to COOH, $J = 8.5, 1.8$ Hz), 8.41 (d, 1H, *o*-Ar*H* to COOH and NO_2, $J = 1.7$ Hz). ^{13}C NMR (DMSO-d_6, 126 MHz): $\delta_{ppm} = 39.76$ (NCH_3), 111.74 (*o*-Ar*C*H to NCH_3), 118.63 (*m*-Ar*C*H to COOH), 124.66 (*o*-Ar*C*H to COOH and NO_2), 126.23 (*m*-Ar*C*H to NCH_3), 130.91 (Ar*C* next to COOH), 133.47 (*o*-Ar*C*H to COOH), 142.90 (*p*-Ar*C* to NCH_3), 146.44 (Ar*C* next to NO_2), 147.07 (*p*-Ar*C* to COOH), 153.85 (Ar*C* next to NCH_3), 165.29 (*C*OOH). ESI TOF MS: *m*/*z* calcd for $C_{15}H_{14}N_4O_4$ 313.09 $[M - H]^-$, found 313.07 $[M - H]^-$.

2.2.5. (S,E)-4-((4-(Ethyl(2-(2-(6-methoxynaphthalen-2-yl)propanoyloxy)ethyl)amino)-phenyl) diazenyl)benzoic acid (**1**)

Compound **5** (1000 mg, 3.19 mmol), DMAP (4 mg) and pyridine (280 μl, 3.46 mmol) were dissolved in DMF (4 ml) and DCM (7 ml), cooled to 0 °C and naproxen acid chloride (802 mg, 3.22 mmol) in DCM (3 ml) was added. The mixture was stirred at 50 °C for 21 h, then washed with water (10 ml) and brine (10 ml). Organic phase was dried over $MgSO_4$, and evaporated to dryness. Crystallization from ethyl acetate and hexane gave 1.23 g (73%) of orange solid.

^1H NMR ($CDCl_3$, 500 MHz): $\delta_{ppm} = 1.09$ (t, 3H, C*H*$_3$, $J = 7.1$ Hz), 1.57 (d, 3H, CHC*H*$_3$, $J = 7.2$ Hz), 3.27–3.35 (m, 2H, NC*H*$_2$CH$_3$), 3.54–3.62 (m, 2H, NC*H*$_2$CH$_2$O), 3.84 (q, 1H, C*H*, $J = 7.1$ Hz), 4.25–4.35 (m, 2H, NCH$_2$C*H*$_2$O), 6.70 (d, 2H, *o*-Ar*H* to NCH_2, $J = 9.2$ Hz), 7.10 (d, 1H, Np*H* position 5, $J = 2.2$ Hz), 7.14 (dd, 1H, Np*H* position 7, $J = 8.9$, 2.4 Hz), 7.36 (dd, 1H, Np*H* position 3, $J = 8.4$, 1.6 Hz), 7.63 (s, 1H, Np*H* position 1), 7.68 (d, 2H, Np*H* positions 4 and 8), 7.83 (d, 2H, *m*-Ar*H* to NCH_2, $J = 9.1$ Hz), 7.90 (d, 2H, *m*-Ar*H* to COOH, $J = 8.6$ Hz), 8.23 (d, 2H, *o*-Ar*H* to COOH, $J = 8.6$ Hz). ^{13}C NMR ($CDCl_3$, 126 MHz): $\delta_{ppm} = 12.09$ (NCH$_2$*C*H$_3$), 18.38 (OCOCH*C*H$_3$), 45.28 (N*C*H$_2$CH$_3$), 45.47 (*C*H), 48.64 (N*C*H$_2$CH$_2$O), 55.30 (O*C*H$_3$), 61.91 (NCH$_2$*C*H$_2$O), 105.64 (Np*C*H position 5), 111.39 (*o*-Ar*C*H to NCH_2), 119.06 (Np*C*H position 7), 122.10 (*m*-Ar*C*H to COOH), 125.77 (*m*-Ar*C*H to NCH_2), 126.02 (Np*C*H position 3), 126.05 (Np*C*H position 1), 127.24 (Np*C*H position 4), 128.94 (Np*C* position 9), 129.15 (Ar*C* next to COOH), 129.24 (Np*C*H position 8), 131.23 (*o*-Ar*C*H to COOH), 133.75 (Np*C* position 10), 135.31 (Np*C* position 2), 143.84 (*p*-Ar*C* to NCH_2), 150.76 (Ar*C* next to NCH_2), 156.60 (*p*-Ar*C* to COOH), 157.73 (Np*C* position 6), 171.10 (*C*OOH), 174.62 (*C*OOCH$_2$). ESI TOF MS: *m*/*z* calcd for $C_{31}H_{31}N_3O_5$ 526.23 $[M + H]^+$, found 526.18 $[M + H]^+$.

2.2.6. (S,E)-4-((4-(Ethyl(2-(2-(6-methoxynaphthalen-2-yl) propanoyloxy)ethyl)amino)-phenyl)diazenyl)-3-nitrobenzoic acid (**2**)

Compound **6** (2.95 g, 8.23 mmol), DMAP (15 mg) and pyridine (700 μl, 8.69 mmol) were dissolved in DMF (10 ml) and DCM (30 ml), cooled to 0 °C, and naproxen acid chloride (2.15 g, 8.64 mmol) in DCM (10 ml) added dropwise. The mixture was stirred at 50 °C for 3 days, and poured to 100 ml acidic water. DCM was added, organic phase was separated, washed several times with 2 M HCl, twice with water, dried over Na_2SO_4, and evaporated to dryness. Crystallization from ethyl acetate and hexane gave 2.34 g (50%) of red solid.

^1H NMR ($CDCl_3$, 500 MHz): $\delta_{ppm} = 1.08$ (t, 3H, C*H*$_3$, $J = 7.0$ Hz), 1.56 (d, 3H, CHC*H*$_3$, $J = 7.1$ Hz), 3.22–3.33 (m, 2H, NC*H*$_2$CH$_3$), 3.53–3.64 (m, 2H, NC*H*$_2$CH$_2$O), 3.83 (q, 1H, C*H*, $J = 7.1$ Hz), 4.24–4.36 (m, 2H, NCH$_2$C*H*$_2$O), 6.66 (d, 2H, *o*-Ar*H* to NCH_2, $J = 9.1$ Hz), 7.11 (d, 1H, Np*H* position 5, $J = 2.6$ Hz), 7.14 (dd, 1H, Np*H* position 7, $J = 2.4$, 8.9 Hz), 7.33 (dd, 1H, Np*H* position 3, $J = 1.5$, 8.5 Hz), 7.61 (s, 1H, Np*H* position 2), 7.67 (d, 1H, Np*H* position 8, $J = 8.9$ Hz), 7.68 (d, 1H, Np*H* position 4, $J = 8.2$ Hz), 7.80 (overlapping peaks, 3H, *m*-Ar*H* to NCH_2 and *m*-Ar*H* to COOH), 8.31 (d, 1H, *o*-Ar*H* to COOH, $J = 8.3$ Hz), 8.56 (s, 1H, *o*-Ar*H* to COOH and NO_2). ^{13}C NMR ($CDCl_3$, 126 MHz): $\delta_{ppm} = 12.07$ (NCH$_2$*C*H$_3$), 18.35 (OCOCH*C*H$_3$), 45.38 (N*C*H$_2$CH$_3$), 45.45 (*C*H), 48.67 (N*C*H$_2$CH$_2$O), 55.31 (O*C*H$_3$), 61.78 (NCH$_2$*C*H$_2$O), 105.69 (Np*C*H position 5), 111.53 (*o*-Ar*C*H to NCH_2), 118.98 (*m*-Ar*C*H to COOH), 119.08 (Np*C*H position 7), 125.94 (*o*-ArCH to COOH and NO_2), 125.98 (Np*C*H position 3), 126.03 (Np*C*H position 1), 127.01 (*m*-Ar*C*H to NCH_2), 127.28 (Np*C*H position 4), 128.86 (Ar*C* next to COOH), 128.94 (Np*C* position 9), 129.23 (Np*C*H position 8), 133.78 (Np*C* position 10), 133.92 (*o*-Ar*C*H to COOH), 135.24 (Np*C* position 2), 144.21 (*p*-Ar*C* to NCH_2), 147.01 (Ar*C* next to NO_2), 149.07 (*p*-Ar*C* to COOH), 151.89 (Ar*C* next to NCH_2), 157.75 (Np*C* position 6), 169.20 (*C*OOH), 174.62 (*C*OOCH$_2$). ESI TOF MS: *m*/*z* calcd for $C_{31}H_{30}N_4O_7$ 569.20 $[M - H]^-$, found 569.29 $[M - H]^-$.

2.2.7. (E)-2,5-Dioxopyrrolidin-1-yl 4-((4-(dimethylamino) phenyl)diazenyl)benzoate (**11**)

Compound **7** (1.48 g, 5.50 mmol) and NHS (700 mg, 6.05 mmol) were dissolved in DMF (80 ml), and DCC (1.25 g, 6.05 mmol) in DMF (10 ml) was added. The reaction mixture was stirred at room temperature for 26 h. The precipitated urea was removed by filtration, and filtrate was evaporated. Residue was dissolved in DCM and filtered, again. Filtrate was evaporated, and residue dried in vacuo to give 1.65 g (82%) of orange solid.

^1H NMR ($CDCl_3$, 250 MHz): $\delta_{ppm} = 2.92$ (s, 4H, C*H*$_2$), 3.12 (s, 6H, C*H*$_3$), 6.75 (d, 2H, *o*-Ar*H* to NCH_3, $J = 9.3$ Hz), 7.92 (d, overlapping peaks, 4H, *m*-Ar*H* to NCH_3 and COON), 8.23 (d, 2H, *o*-Ar*H* to COON, $J = 8.8$ Hz). ^{13}C NMR ($CDCl_3$, 63 MHz): $\delta_{ppm} = 25.68$ (CH_2), 40.25 (NCH_3), 111.46 (*o*-Ar*C*H to NCH_3), 122.37 (*m*-Ar*C*H to COON), 124.61 (Ar*C* next to COON), 125.84 (*m*-Ar*C*H to NCH_3), 131.64 (*o*-Ar*C*H to COON), 143.74 (*p*-Ar*C* to NCH_3), 153.18 (Ar*C* next to NCH_3), 157.17 (*p*-Ar*C* to COON), 161.62 (*C*OON), 169.23 (CH_2*C*ON). ESI TOF MS: *m*/*z* calcd for $C_{19}H_{18}N_4O_4$ 367.14 $[M + H]^+$, found 367.14 $[M + H]^+$.

2.2.8. (S,E)-Methyl 2-(4-((4-(dimethylamino)phenyl)diazenyl) benzamido)propanoate (**12**)

Compound **11** (1.40 g, 3.82 mmol), L-alanine methyl ester hydrochloride (0.64 g, 4.59 mmol) and TEA (0.64 ml, 4.59 mmol) were dissolved in DMF (80 ml) and the mixture was stirred at room temperature for 17 h. DMF was removed, and the residue was dissolved in chloroform. Organic phase was washed twice with water and once with brine, dried with anhydrous $MgSO_4$ and evaporated to dryness to give 1.36 g (99%) of orange solid.

^1H NMR ($CDCl_3$, 500 MHz): $\delta_{ppm} = 1.55$ (d, 3H, CHC*H*$_3$, $J = 7.1$ Hz), 3.10 (s, 6H, NC*H*$_3$), 3.80 (s, 3H, OC*H*$_3$), 4.83 (quint, 1H, C*H*, $J = 7.2$ Hz), 6.76 (d, 2H, *o*-Ar*H* to NCH_3, $J = 9.2$ Hz), 6.79 (d, 1H, N*H*, $J = 7.1$ Hz), 7.87–7.92 (m, 6H, *m*-Ar*H* to NCH_3, *m*-Ar*H* to CONH, and *o*-Ar*H* to CONH). ^{13}C NMR ($CDCl_3$, 126 MHz): $\delta_{ppm} = 18.67$ (CH*C*H$_3$), 40.24 (N*C*H$_3$), 48.56 (*C*H), 52.55 (O*C*H$_3$), 111.48 (*o*-Ar*C*H to NCH_3), 122.25 (*m*-Ar*C*H to CONH), 125.41 (*m*-Ar*C*H to NCH_3), 127.93 (*o*-Ar*C*H to CONH), 133.88 (Ar*C* next to CONH), 143.72 (*p*-Ar*C* to NCH_3), 152.85 (Ar*C* next to NCH_3), 155.27 (*p*-Ar*C* to CONH), 166.33 (*C*ONH), 173.66 (*C*OOCH$_3$). ESI TOF MS: *m*/*z* calcd for $C_{19}H_{22}N_4O_3$ 377.16 $[M + Na]^+$, found 377.19 $[M + Na]^+$.

2.2.9. (S,E)-2-(4-((4-(Dimethylamino)phenyl)diazenyl)benzamido) propanoic acid (**3**)

Compound **12** (1.10 g, 3.10 mmol) was dissolved in 1:1 THF/MeOH (40 ml) and LiOH (149 mg, 6.21 mmol) in water (10 ml) was added. The reaction mixture was stirred at room temperature for 7 h, and evaporated to dryness. Residue was dissolved in THF, and 1 M HCl was added to make the solution slightly acidic. The precipitate was filtered, washed with water and dried in vacuo to give 743 mg (70%) of orange solid.

^1H NMR (DMSO-d_6, 500 MHz): $\delta_{ppm} = 1.42$ (d, 3H, CHC*H*$_3$, $J = 7.3$ Hz), 3.08 (s, 6H, NC*H*$_3$), 4.45 (quint, 1H, C*H*, $J = 7.3$), 6.85 (d, 2H, *o*-Ar*H* to NCH_3, $J = 9.2$ Hz), 7.83 (d, 4H, *m*-Ar*H* to NCH_3 and *m*-Ar*H* to CONH, $J = 8.9$ Hz), 8.03 (d, 2H, *o*-Ar*H* to CONH, $J = 8.5$ Hz), 8.74 (d, 1H, N*H*, $J = 7.2$ Hz). ^{13}C NMR ($CDCl_3$, 126 MHz): $\delta_{ppm} = 18.85$ (CH*C*H$_3$), 39.76 (N*C*H$_3$), 48.18 (*C*H), 111.53 (*o*-Ar*C*H to NCH_3), 121.40 (*m*-Ar*C*H to CONH), 125.03 (*m*-Ar*C*H to NCH_3), 128.52 (*o*-Ar*C*H to CONH), 134.17 (Ar*C* next to CONH), 142.63 (*p*-Ar*C* to NCH_3), 152.85 (Ar*C* next to NCH_3), 154.06 (*p*-Ar*C* to CONH), 165.50 (*C*ONH), 174.06

(COOH). ESI TOF MS: *m*/*z* calcd for $C_{18}H_{20}N_4O_3$ 339.15 $[M-H]^-$, found 339.09 $[M-H]^-$.

*2.2.10. (E)-2,5-Dioxopyrrolidin-1-yl 4-((4-(dimethylamino) phenyl)diazenyl)-3-nitro-benzoate (**13**)*

The procedure is the same as the synthesis of **11**. Compound **8** (726 mg, 2.31 mmol), NHS (292 mg, 2.54 mmol) and DCC (524 mg, 2.54 mmol) were used. Red solid. Yield: 938 mg (99%).

^{1}H NMR ($CDCl_3$, 250 MHz): $\delta_{ppm} = 2.93$ (s, 4H, CH_2), 3.15 (s, 6H, CH_3), 6.73 (dd, 2H, *o*-Ar*H* to NCH_2, $J = 9.3$ Hz), 7.84–7.92 (overlapping peaks, 3H, *m*-Ar*H* to NCH_2 and *m*-Ar*H* to COON), 8.30 (dd, 1H, *o*-Ar*H* to COON, $J = 8.5$, 1.9 Hz), 8.57 (d, 1H, *o*-Ar*H* to COOH and NO_2, $J = 1.8$ Hz). ^{13}C NMR ($CDCl_3$, 63 MHz): $\delta_{ppm} = 22.65$ (CH_2), 40.28 (NCH_3), 111.55 (*o*-ArCH to NCH_2), 119.21 (*m*-ArCH to COON), 124.24 (*o*-ArCH to COON and NO_2), 126.28 (*m*-ArCH to NCH_3), 127.20 (*o*-ArCH to COON), 134.13 (Ar*C* next to COON), 144.19 (*p*-Ar*C* to NCH_3), 146.93 (*p*-Ar*C* to COON), 149.66 (Ar*C* next to NO_2), 154.11 (Ar*C* next to NCH_3), 160.12 (COON), 168.81 (CH_2CON). ESI TOF MS: *m*/*z* calcd for $C_{19}H_{17}N_5O_6$ 412.13 $[M+H]^+$, found 412.15 $[M+H]^+$.

*2.2.11. (S,E)-Methyl 2-(4-((4-(dimethylamino)phenyl)diazenyl)-3-nitrobenzamido) propanoate (**14**)*

The procedure is the same as the synthesis of **12**. Compound **13** (892 mg, 2.17 mmol), L-alanine methyl ester hydrochloride (361 mg, 2.60 mmol) and TEA (0.63 ml, 2.60 mmol) were used. Red solid. Yield: 660 mg (76%).

^{1}H NMR ($CDCl_3$, 500 MHz): $\delta_{ppm} = 1.55$ (d, 3H, $CHCH_3$, $J = 7.2$ Hz), 3.12 (s, 6H, NCH_3), 3.81 (s, 3H, OCH_3), 4.80 (quint, 1H, *CH*, $J = 7.2$ Hz), 6.72 (d, 2H, *o*-Ar*H* to NCH_3, $J = 9.3$ Hz), 6.94 (d, 1H, N*H*, $J = 7.1$ Hz), 7.76 (d, 1H, *m*-Ar*H* to CONH, $J = 8.4$ Hz), 7.86 (d, 2H, *m*-Ar*H* to NCH_3, $J = 9.2$ Hz), 8.01 (dd, 2H, *o*-Ar*H* to CONH, $J = 8.4$, 1.9 Hz), 8.26 (d, 1H, *o*-Ar*H* to CONH and NO_2, $J = 1.8$ Hz). ^{13}C NMR ($CDCl_3$, 126 MHz): $\delta_{ppm} = 18.47$ ($CHCH_3$), 40.26 (NCH_3), 48.81 (*C*H), 52.72 (OCH_3), 111.48 (*o*-ArCH to NCH_2), 118.94 (*m*-ArCH to CONH), 122.91 (*o*-ArCH to CONH and NO_2), 126.68 (*m*-ArCH to NCH_3), 131.03 (*o*-ArCH to CONH), 133.53 (Ar*C* next to CONH), 144.00 (*p*-Ar*C* to NCH_3), 146.96 (*p*-Ar*C* to CONH), 147.72 (Ar*C* next to NO_2), 153.72 (Ar*C* next to NCH_3), 164.32 (CONH), 173.41 ($COOCH_3$). ESI TOF MS: *m*/*z* calcd for $C_{19}H_{21}N_5O_5$ 422.14 $[M+Na]^+$, found 422.16 $[M+Na]^+$.

*2.2.12. (S,E)-2-(4-((4-(Dimethylamino)phenyl)diazenyl)-3-nitrobenzamido)propanoic acid (**4**)*

The procedure is the same as the synthesis of **3**. Compound **14** (600 mg, 1.50 mmol) and LiOH (72 mg, 3.00 mmol) were used. Red solid. Yield: 527 mg (91%).

^{1}H NMR (DMSO-d_6, 500 MHz): $\delta_{ppm} = 1.43$ (d, 3H, $CHCH_3$, $J = 7.3$ Hz), 3.11 (s, 6H, NCH_3), 4.46 (quint, 1H, *CH*, $J = 7.3$ Hz), 6.87 (d, 2H, *o*-Ar*H* to NCH_3, $J = 9.3$ Hz), 7.76–7.80 (overlapping peaks, 3H, *m*-Ar*H* to CONH and *m*-Ar*H* to NCH_3), 8.24 (dd, 2H, *o*-Ar*H* to CONH, $J = 8.5$, 1.9 Hz), 8.49 (d, 1H, *o*-Ar*H* to CONH and NO_2, $J = 1.8$ Hz), 9.00 (d, 1H, N*H*, $J = 7.1$ Hz). ^{13}C NMR (DMSO-d_6, 126 MHz): $\delta_{ppm} = 16.80$ ($CHCH_3$), 39.67 (NCH_3), 48.45 (*C*H), 111.75 (*o*-ArCH to NCH_2), 118.52 (*m*-ArCH to CONH), 122.90 (*o*-ArCH to CONH and NO_2), 126.13 (*m*-ArCH to NCH_3), 132.03 (*o*-ArCH to CONH), 133.71 (Ar*C* next to CONH), 142.86 (*p*-Ar*C* to NCH_3), 146.21 (*p*-Ar*C* to CONH), 146.32 (Ar*C* next to NO_2), 153.77 (Ar*C* next to NCH_3), 163.67 (CONH), 177.88 (COOH). ESI TOF MS: *m*/*z* calcd for $C_{18}H_{19}N_5O_5$ 384.13 $[M-H]^-$, found 384.06 $[M-H]^-$.

*2.3. Preparation of the single crystal of compounds **3** and **4** and their single crystal X-ray determination*

2.3.1. Crystallization

Single crystals of compounds **3** and **4** were grown by vapor diffusion method. Compounds (~20 mg) were dissolved in THF in small open containers. The receptacles were then placed inside the bigger containers containing hexane, and sealed well. After about one week suitable orange crystals were selected for X-ray analysis.

*2.3.2. Crystal data for (S,E)-2-(4-((4-(dimethylamino) phenyl)diazenyl)benzamido)-propanoic acid (**3**)*

$C_{18}H_{20}N_4O_3$; Fw = 340.38; monoclinic system, $P2_1$ space group, $a = 6.4870(10)$ Å, $b = 10.582(3)$ Å, $c = 12.523(2)$ Å, $\beta = 99.810(10)$, $V = 847.1(3)$, $Z = 2$, $D_c = 1.334$ Mg m^{-3}, crystal size $0.20 \times 0.15 \times 10$ mm.

*2.3.3. Crystal data for (S,E)-2-(4-((4-(dimethylamino) phenyl)diazenyl)-3-nitrobenzamido)propanoic acid (**4**)*

$C_{44}H_{54}N_{10}O_{12}$, Fw = 914.97; monoclinic space group, $P2_1$ space group, $a = 9.9650(10)$ Å, $b = 8.7760(10)$ Å, $c = 26.479(2)$ Å, $\beta = 92.99(2)^\circ$, $V = 2312.5(4)$ Å^3, Z = 2, $D_c = 1.314$ Mg m^{-3}, crystal size $0.65 \times 0.20 \times 0.08$ mm.

2.3.4. Crystal structure determinations

Bruker Apex II CCD diffractometer with a graphite-monochromatted Mo Kα ($\lambda = 0.71073$ Å) radiation source and a CCD detector was used for recording the data for both compounds [22]. The cell refinement and data reduction were made with the program DENZO [23] and the structure solutions were made with the SHELX computer program [24]. The structures were analyzed using the WIN-GX [25] and SHELX computer programs and refined as a full matrix least square against F^2 for all data; all non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in calculated positions with thermal parameters, 1.2 or 1.5 (methyl) times those of the attached atoms. The CCDC reference numbers are 680360 for **3** and 600361 for **4**. The crystal structures of **3** and **4** are shown in Figs. 2 and 3.

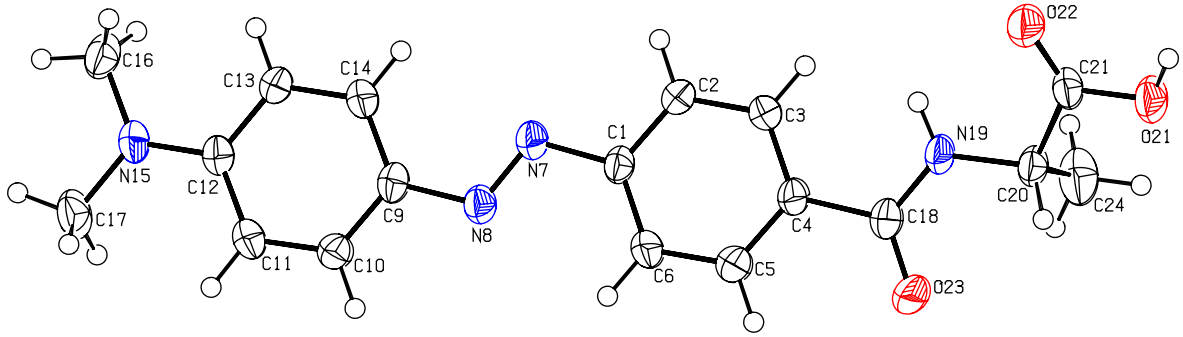

Fig. 2. X-ray crystal structure of **3** showing thermal ellipsoids in 30% probability level.

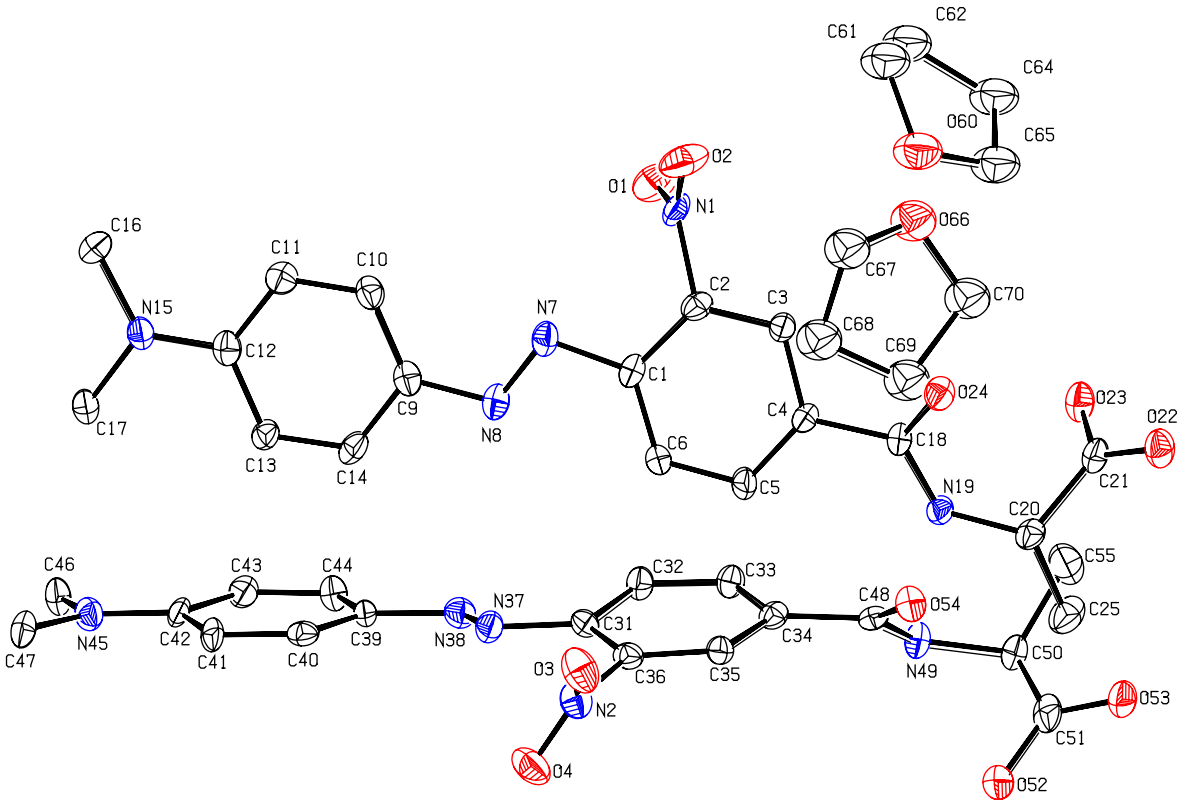

Fig. 3. X-ray crystal structure of **4** showing thermal ellipsoids in 30% probability level. Hydrogen atoms are omitted for clarity.

3. Results and discussion

3.1. Synthesis

Four chiral azobenzene conjugates with free carboxyl acid group were synthesized (Fig. 1). Compounds were constructed by synthesizing first azobenzene skeleton where chiral moieties were then attached to. Naproxen and L-alanine were chosen as chiral counterparts for the azobenzenes. In this work the chiral moieties were attached to the azobenzenes conjugates at a donor or an acceptor site through ester or amide bonds.

Azobenzenes **5** and **7** were synthesized by the typical diazotization reaction of diazonium salt of 4-aminobenzoic acid with *N*,*N*-dimethylaniline and *N*-ethyl-*N*-(2-hydroxy)aniline, performed in $NaNO_2$/HCl medium. In the case of very weakly basic 4-amino-3-nitrobenzoic acid diazotization was performed in concentrated sulphuric acid (compounds **6** and **8**).

Naproxen acid chloride [20] was attached to the free hydroxyl group of azobenzenes **5** and **6** in the presence of pyridine and catalytic amount of DMAP in dichloromethane. Due to the low solubility of the azo compounds in dichloromethane a small amount of dimethylformamide was added to dissolve the azobenzenes completely. Chiral azo conjugate **1** was afforded in 73% yields after purification by crystallization from ethyl acetate/hexane solution. Attempts to synthesize **2** in as high yield as **1** failed probably due to a less reactive starting material **6**. Compound **2** was achieved, nevertheless, in yields ranging from 14% to moderate 50% after purification.

In the synthesis of L-alanine functionalized azobenzenes, the building blocks **7** and **8** were allowed to react with *N*-hydroxysuccinimide (NHS) in the presence of *N*,*N*-dicyclohexylcarbodiimide (DCC) in DMF. The reaction side product, dicyclohexylurea (DCU), was removed by filtering, and DMF was evaporated off. The DCU impurities were further removed by dissolving the reaction product in dichloromethane and filtering off the insoluble DCU. The filtrate was evaporated to dryness to isolate azobenzene succinimide esters **11** and **13** in 82 and 99% yields, respectively. Compounds **11** and **13** were then reacted with L-alanine methyl ester hydrochloride [21] in the presence of triethylamine in DMF. After removal of DMF, resulting solid was dissolved in CH_2Cl_2 and washed with water and brine. Evaporation of solvent gave compound **12** in 99% yield, and compound **14** was obtained in 76% yield after chromatographic purification. Finally, removal of methyl ester functionality of compounds **12** and **14** in the presence of LiOH in MeOH/THF solution gave compounds **3** and **4** in 70 and 91% yields, respectively. In the case of compound **4**, the traces of DCU were found in the final product despite filtering and column chromatography. Due to a problematic purification of DCC by-products, other synthetic procedures have also been utilized for the synthesis of amino acid functionalized molecules [26].

The structures were fully characterized by ^1H and ^{13}C NMR spectroscopy and ESI TOF mass spectrometry. NMR methods such as HMQC (Heteronuclear Multiple Quantum Coherence), HMBC (Heteronuclear Multiple Bond Correlation), DEPT (Distortionless Enhancement by Polarization Transfer) and COSY (Correlation Spectroscopy) experiments were performed to facilitate characterizing the structures.

3.2. Thermal stability

High thermal stability is an important feature of dyes in order to be usable in applications. The onset decomposition temperatures (T_d) of the azobenzenes were determined by thermogravimetric analysis (TG) from ambient temperature to 700 °C in an air atmosphere at a heating rate of 10 °C/min. Melting points and decomposition temperatures are listed in Table 1. The thermal decomposition of the studied molecules proceeded in two noticeable stages. Compounds were thermally stable up to temperatures

Table 1
Thermal data of compounds **1**–**4**

Compound	T_m (°C)[a]	T_d (°C)[b]
1	157	222
2	134	213
3	211	235
4	172	193

[a] Melting point (T_m) is measured at a heating rate of 2 °C/min.
[b] Decomposition temperatures (T_d) are onset temperatures at a heating rate of 10 °C/min under air.

around 200 °C, at where first stage of decomposition started, probably by the splitting of azo group [27]. Compound **3** had highest T_d of 235 °C, whilst lowest $T_{d,}$ 193 °C, was measured for compound **4**. At 300 °C weight loss of 30–50% had occurred. Slow weight loss continued to around 500 °C at which decomposition accelerated and all compounds were completely decomposed at 700 °C. Small weight losses below decomposition temperatures are probably due to the loss of water or solvents.

3.3. Absorption and circular dichroism spectra

UV–vis absorption data of the molecules **1**–**4** are collected in Table 2. All donor–acceptor azo compounds exhibited a characteristic broad absorption band in the visible region, related to the $\pi \rightarrow \pi^*$ transition of azobenzene moiety which overlaps the weak $n \rightarrow \pi^*$ transition. Compounds **1** and **2** also showed absorption bands at around 275 and 325 nm corresponding to the absorption of naproxen moiety. Introduction of the strong electron withdrawing nitro group at the *ortho* position of azo compounds **2** and **4** gives rise to significant bathochromic shift in the absorption due to enhanced delocalization of electrons. The bathochromic shift of the absorption maximum of the compound **2** was 41 nm with respect to the compound **1**. Corresponding red shift of 46 nm was observed in the absorption maximum of alanine functionalized azobenzene **4** compared to the λ_{max} of relative compound **3**.

Circular dichroism (CD) spectra of the compounds **1**–**4** were measured to confirm the chirality of the molecules. The CD signals correlate with the UV–vis absorption bands of the relative compounds. Azo compounds **1** and **2**, functionalized with naproxen, exhibit negative cotton effect at the $\pi \rightarrow \pi^*$ transition bands of the azobenzene moieties at around 430 and 480 nm, respectively. Positive CD signals at around 275 and 325 nm correlate with the absorption of naproxen moiety. In the case of molecules **3** and **4**, functionalized with alanine moieties, both compounds show positive cotton effects throughout the absorption range.

3.4. Single crystal analysis

3.4.1. Structure of (S,E)-2-(4-((4-(dimethylamino)phenyl)diazenyl)benzamido)-propanoic acid (**3**)

The asymmetric unit consists of one dye molecule (Fig. 2). The dimethyl aminoazobenzene dye unit is essentially planar with dihedral angle of 2.7(2)°. The absolute configuration was not possible to determined reliable due to lack of a heavy atom (Si<) in the molecule, but the configuration of the chiral center (*S*) was taken from the synthesis route. In packing, the molecular pairs that formed as a result of intermolecular H-bond (O21(D)···O23(A) 2.592(3) Å) are partly stacked one on each other in such a way that they form a stacked array of interlayer associations by means of aromatic π–π-stacking, of 3.7–3.9 Å.

Table 2
Absorption data of compounds **1**–**4**

Compound	λ_{max} (nm)	ε_{max} ($cm^{-1}\,M^{-1}$)
1[a]	433	30,200
2[a]	474	35,600
3[b]	437	23,200
4[b]	483	30,400

[a] λ_{max} measured in chloroform.
[b] λ_{max} measured in dimethylformamide.

3.4.2. Structure of (S,E)-2-(4-((4-(dimethylamino)phenyl)diazenyl)-3-nitrobenzamido)propanoic acid (**4**)

The asymmetric unit consists of two dye molecules (**A** and **B**) and two tetrahydrofuran (THF) as trapped solvent (Fig. 3). Two dye molecules differ slightly from each other. The absolute configuration was not possible to determined reliable due to lack of a heavy atom (Si<) in the molecule, but the configuration of the chiral center (*S*) in both molecules was taken from the synthesis route. The dimethylazobenzene framework of each dye is nearly planar with angles of 8.9(3)° and 11.3(3)° and there are not significant differences in the bond lengths when molecules were compared. There are intramolecular interactions from nitro-group oxygen (O4···N37, 2.864 Å and O1···N7, 2.890 Å) to the free electron pair of the second nitrogen of azo group.

In packing, the molecules build up channels by strong (N49···O24, 2.785(7), 144.3°; N19···O54, 2.975(7), 152.1°; O23···O23, 2.633(9), 175.6°; O52···O22, 2.651(9), 176.1°) and weak hydrogen bonding and partial π–π-stacking. In these channels THF solvent molecules are located.

4. Conclusions

The chiral azobenzene conjugates **1**–**4** composed of donor–acceptor azo compounds and either naproxen or L-alanine moieties were synthesized, and characterized with ^1H and ^{13}C NMR, ESI TOF MS, thermogravimetric analysis, UV–vis spectrophotometer and CD-spectrometer. Thermal stability was evaluated and the decomposition temperatures of the molecules ranged from 193 to 235 °C.

All compounds showed absorption bands at visible region from 433 to 483 nm. Circular dichroism signals verifying the chirality of the compounds were found at absorption wavelengths. Compounds **1** and **2** showed negative CD signals at absorption wavelengths of azobenzenes, while positive CD signals were observed throughout the absorption range for compounds **3** and **4**. Crystal structures of compounds **3** and **4** were resolved. In the structure of **3**, there is one dye molecule in the asymmetric unit and the diaminoazobenzene skeleton is almost planar. The asymmetric unit of **4** comprises two dye molecules and two tetrahydrofuran solvent molecules. Both dimethyl aminoazobenzene frameworks are nearly planar and differ slightly and the packing diagram shows channels where THF molecules are located.

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