Electronic Supplementary Material (ESI) for RSC Advances

Electronic supplementary information for:

Chiral Transmission to Crystal Photodimerizations of Leucine-Methionine Quasiracemic Assemblies

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Electronic Supplementary Information

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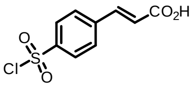
Supporting Information

S1. Experimental Details

General Considerations. All chemicals and solvents were purchased from the Aldrich Chemical Co. or Acros Chemicals and used as received without further purification unless stated otherwise. Thin-layer chromatography (TLC) was performed on silica-gel plate w/UV254 (200 µm). Chromatograms were visualized by UV-light. ^{1}H NMR and ^{13}C NMR spectral data were recorded with a 400 MHz Bruker Avance spectrometer using TopSpin v.3.2. They were referenced using the solvent residual signal as internal standard. The chemical shift values are expressed as δ values (ppm) and the value of coupling constants (*J*) in Hertz (Hz). The following abbreviations were used for signal multiplicities: s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; m, multiplet; and br, broad.

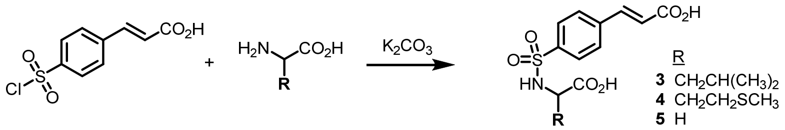
Synthetic Procedures

(2E)-3-[4-(Chlorosulfonyl)phenyl]-2-propenoic acid



The preparation of 4-chlorosulfonylcinnamic acid was carried out using the general procedure described by Grove *et. al.*[1]

Leucine/Methionine/Glycine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-



Preparation of *rac*-**3**, L-**3**, *rac*-**4**, D-**4**, and **5** were carried out using a parallel procedure as described previously for sulfonamidecinnamic acids.[1] To a 250 rd-bottom flask containing 100 mL of acetone and 25 mL of deionized water was added the appropriate amino acid (8.92 mmol, 1.1 eqv.) and (2E)-3-[4-(chlorosulfonyl)phenyl]-2-propenoic acid (8.09 mmol, 1.0 eqv.). The reaction mixture was stirred at 0°C for 15 min to give a light-yellow heterogeneous mixture. A solution consisting of anhydrous K_2CO_3 (3.3641g, 24.3 mmol) dissolved in 20 mL of deionized H_2O was then added to the reaction flask via an addition funnel at ~1 drop per second. Upon complete addition of the base, the reaction mixture appeared as a clear light-yellow homogeneous solution that was further stirred at 0°C for four hours. Reaction progress was assessed via TLC (10:30:1; hexanes, EtOAc, AcOH) showing the presence of both product ($R_f = 0.62$ (*rac*- and L-**3**), 0.68 (*rac*- and D-**4**) and 0.65 (**5**)) and leucine/methionine/glycine ($R_f = 0.0$) and the absence of sulfonyl chloride ($R_f = 0.76$-78). The acetone from the reaction mixture was removed under *vacuo* (rotary evaporator, 30°C water bath). The resulting yellow homogenous aqueous layer was cooled to 0°C, acidified (*pH* = 2-3) using 6M HCl, and extracted with 2×20 mL EtOAc. The combined organic extracts were dried over anhydrous $MgSO_4$ and reduced under *vacuo* (rotary evaporator, 30°C water bath) to give light-yellow solids.

DL-Leucine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-. *rac*-3: 46.5% yield. ^{1}H-NMR (400 MHz, acetone-d_6): δ 7.92 (d, $J = 8.7$ Hz, 2H, Ar-H); 7.88 (d, $J = 8.7$ Hz, 2H, Ar-H); 7.72 (d, $J = 16.1$ Hz, 1H, Csp2-H); 6.98 (d, $J = 8.8$ Hz, 1H, NH); 6.68 (d, $J = 16.1$ Hz, 1H, Csp2-H); 4.12-3.93 (m, 1H, CH); 1.90-1.78 (m, 2H, CH_2); 1.68-1.54 (m, 2H, CH_2); 0.91 (d, $J = 6.8$ Hz, 3H, CH_3); 0.85 (d, $J = 6.7$ Hz, 3H, CH_3). 13C-NMR (acetone-d_6): δ 173.8, 167.4, 143.8, 143.3, 139.4, 129.5, 128.5, 122.3, 55.6, 42.9, 25.2, 23.3, 21.8.

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[1] R. C. Grove, S. H. Malehorn, M. E. Breen and K. A. Wheeler, *Chem. Commun.*, 2010, **46**, 7322.

L-Leucine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-. L-3: 52.0% yield. ^{1}H-NMR (400 MHz, acetone-*d*$_6$): δ 7.90 (d, *J* = 8.6 Hz, 2H, Ar-H); 7.86 (d, *J* = 8.6 Hz, 2H, Ar-H); 7.71 (d, *J* = 15.9 Hz, 1H, Csp^2-H); 6.92 (d, *J* = 9.5, 1H, N-H); 6.67 (d, *J* = 15.9 Hz, 1H, Csp^2-H); 4.05-3.88 (m, 1H, CH); 1.86-1.72 (m, 2H, CH$_2$), 1.65-1.50 (m, 2H, CH$_2$); 0.90 (d, *J* = 6.9 Hz, 3H, CH$_3$), 0.85 (d, *J* = 6.6 Hz, 3H, CH$_3$). ^{13}C-NMR (acetone-*d*$_6$): δ173.5, 167.4, 143.6, 143.4, 139.3, 129.5, 128.5, 122.3, 55.2, 42.7, 25.2, 23.2, 21.6

DL-Methionine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-. *rac*-4: 48.7% yield. ^{1}H-NMR(acetone-*d*$_6$): δ 7.91 (d, *J* = 8.8 Hz, 2H, Ar-H); 7.87 (d, *J* = 8.8 Hz, 2H, Ar-H); 7.73 (d, *J* = 16.1 Hz, 1H, Csp2-H); 6.97 (d, *J* = 8.9 Hz, 1H, NH); 6.68 (d, *J* = 16.1 Hz, 1H, Csp2-H); 4.22-4.08 (m, 1H, CH); 2.62-2.44 (m, 2H, CH$_2$); 2.12-1.98 (m, 1H, CH$_2$); 2.02 (s, 3H, CH$_3$); 1.98-1.86 (m, 1H, CH$_2$). ^{13}C-NMR(acetone-*d*$_6$): δ 172.7, 167.3, 143.8, 143.3, 139.4, 129.5, 128.4, 122.3, 55.6, 31.6, 29.6, 14.8.

D-Methionine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-. D-3: 54.1% yield. ^{1}H-NMR(acetone-*d*$_6$): δ 7.92 (d, *J* = 8.7 Hz, 2H, Ar-H); 7.88 (d, *J* = 8.7 Hz, 2H, Ar-H); 7.72 (d, *J* = 16.08 Hz, 1H, Csp2-H); 6.98 (d, *J* = 8.84 Hz, 1H, NH); 6.08 (d, *J* = 16.08 Hz, 1H, Csp2-H); 4.12-4.23 (m, 1H, CH); 2.45-2.65 (m, 2H, CH$_2$); 2.23-1.95 (m, 1H, CH$_2$); 2.02 (s, 3H, CH$_3$); 1.98-1.85 (m, 1H, CH$_2$). ^{13}C-NMR(acetone-*d*$_6$): δ 172.7, 167.3, 143.6, 143.3, 139.4, 129.5, 128.5, 122.3, 55.8, 33.3, 32.5, 15.1.

Glycine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-. 5: 58.7% yield. ^{1}H-NMR (400 MHz, acetone-*d*$_6$): δ 7.75 (d, *J* = 8.2 Hz, 2H, Ar-H), 7.67 (d, *J* = 8.2 Hz, 2H, Ar-H), 7.68 (d, *J* = 16.0 Hz, 1H, Csp^2-H); 6.67 (d, *J* = 16.0 Hz, 1H, Csp^2-H); 4.08 (s, 1H, CH). ^{13}C-NMR (acetone-*d*$_6$): δ172.6, 166.3, 143.6, 143.0, 139.2, 129.4, 128.5, 122.1, 45.5.

S2. Crystal Growth. Recrystallization experiments were conducted at room temperature using spectroscopic grade solvents to give X-ray quality crystals after 1-6 days.

***rac*-3, L-3, and *rac*-4**. Colorless or light-yellow plates were grown from slow evaporation of acetone solutions.

L-3/D-4. Light-yellow plate-like crystals of quasiracemate L-**3**/D-**4** were grown from recrystallization of an equimolar mixture of L-**3** and D-**4** via slow evaporation from acetone.

5. Colorless needles were grown form the vapor diffusion technique by dissolving **5** in a minimal amount of MeOH and using dichloromethane as the diffusion solvent (**5**-I). Dissolution of **5** in a 15:15:1 methanol:acetone:H_2O mixture followed by slow evaporation gave colorless plates (**5**-II).

S3. Photodimerization Reactions. UV illumination studies on single crystals of *rac*-**3**, L-**3**, *rac*-**4**, and L-**3**/D-**4** were carried out at room temperature (296 K) using a focused 200 W Xe(Hg) arc lamp (Newport Corp., 67005, 6292) equipped with a 360 nm optical edge filter (Newport Corp., CGA-360). Photodimerization conversions were assessed via X-ray diffraction of irradiated single crystals. Due to significant crystal fracturing of L-**3** during UV exposure, evaluation of this transformation was only practical to ~20% conversion. Further investigation of this photodimerization was conducted using polycrystalline samples L-**3** and unfiltered radiation. During the illumination period, samples were periodically ground (~ once every hour) and reaction progress assessed with ^{1}H NMR spectroscopy after 10, 19, and 29 hours (Fig. S1).

Photodimerization product of UV irradiated L-3: ^{1}H-NMR (400 MHz, acetone-*d*$_6$/DMSO-*d*$_6$ 8:1 v/v): δ 7.82 (d, *J* = 8.4 Hz, 2H, Ar-H); 7.60 (d, *J* = 8.4 Hz, 2H, Ar-H); 7.01 (d, *J* = 9.8 Hz, 1H, N-H); 4.51 (m, 1H, CH); 4.04 (m, 1H, CH); 3.89 (m, 1H, CH); 1.77 (m, 1H, CH); 1.52 (m, 2H, CH2); 0.90 (d, *J* = 6.6

Hz, 3H, CH_3); 0.85 (d, $J = 6.6$ Hz, 3H, CH_3). Reaction progressed was assessed using NMR integrals after 10, 19, 29 hours of UV exposure to give 50, 81, and 92 % conversions, respectively.

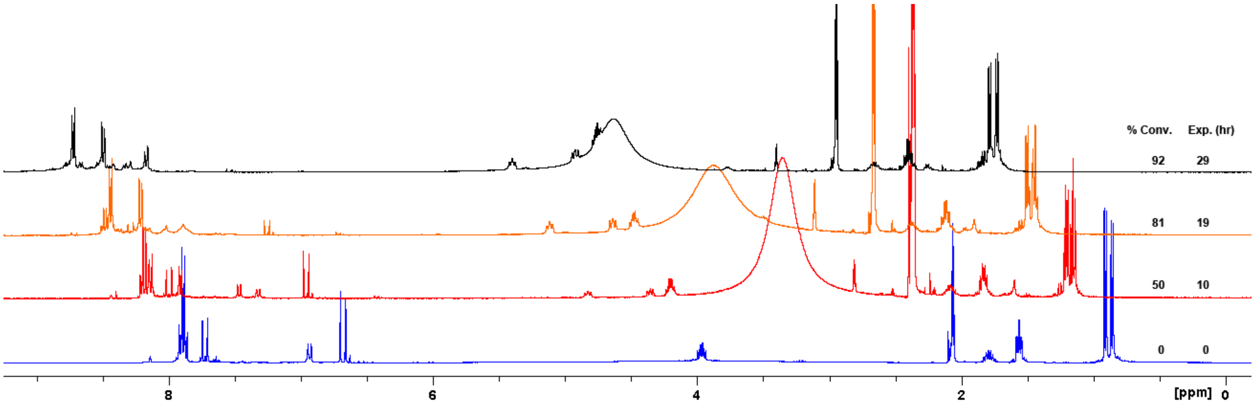

Fig. S1 ^{1}H-NMR spectra of L-**3** UV illuminated for 0, 10, 19, and 29 hours.

S4. X-ray Crystallography. Crystallographic details for compounds **3** - **5** are summarized in Table S1. X-ray data were collected on a Bruker APEX II and P4 CCD diffractometers using phi and omega scans with graphite monochromatic Cu $K\alpha$ (λ = 1.54178 Å) and Mo $K\alpha$ (λ = 0.71073 Å) radiation, respectively. Data sets were corrected for Lorentz and polarization effects as well as absorption - SADABS/multi-scan. The criterion for observed reflections is $I > 2\sigma(I)$. Lattice parameters were determined from least-squares analysis and reflection data. Empirical absorption corrections were applied using SADABS.[2] Structures solved by direct methods and refined by full-matrix least-squares analysis on F^2 using X-SEED[3] equipped with SHELX-2013/3-XS[4]. All non-hydrogen atoms for unreacted crystal phases were refined anisotropically by full-matrix least-squares on F^2 by the use of the SHELXL[4] program. For photoreacted *rac*-**3**, *rac*-**4**, L-**3** and L-**3**/D-**4** the reaction proceeds with an increasing amount of truxillic acid derivative generated within the reactant lattice. The relative amounts of the two species in the lattice were determined from the occupancies of the two parts. The occupancy of the cinnamic acid fragment and the corresponding truxillic acid fragment were constrained to sum to 1.0. H atoms (for OH and NH), where possible, were located in difference Fourier synthesis and refined isotropically with restrained O/N-H distances of 0.85(2) Å and U_{iso}=1.2U_{eq} of the attached O/N atom. The remaining H atoms were included in idealized geometric positions with U_{iso}=1.2U_{eq} of the atom to which they were attached (U_{iso}=1.5U_{eq} for methyl groups). For L-**3**/D-**4** and L-**3**, molecular configurations were compared to both the known chirality of the leucine/methionine components and estimated Flack parameters[5], where applicable, atomic coordinates were inverted to achieve correct structural configurations. Crystallographic assessment of *rac*-**3** (unreacted) and quasiracemate L-**3**/D-**4** were processed as two-component twinned datasets using TWINABS.[6] The diffuse electron density () in the crystal lattice of **5**-II corresponding to 60 electrons and 1.5 water molecules was removed with the SQUEEZE[7] function in PLATON[8].

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[2] G. M. Sheldrick, SADABS —Program for Area Detector Absorption Corrections, University of Göttingen, Göttingen, Germany, 2013.

[3] L. J. Barbour, *J. Supramol. Chem*., 2001, **1**, 189.

[4] G. M. Sheldrick, *Acta Crystallogr., Sect. A: Fundam. Crystallogr.*, 2008, **64**, 112.

[5] H. D. Flack, *Acta Crystallogr.,* 1983, **39**, 876.

[6] G. M. Sheldrick, TWINABS —Program for Area Detector Absorption Corrections of Twinned Data, University of Göttingen, Göttingen, Germany, 2013.

[7] A. L.Spek, *Acta Cryst*., 2009, **D65**, 148.

[8] A. L. Spek, *J. Appl. Crystallogr*., 2003, **36**, 7.

Table S1. Crystallographic data for 3 – 5

	(*rac*)-**3**	(*rac*)-**3**-reacted	(*rac*)-**4**	(*rac*)-**4**-reacted
Crystal data				
CCDC deposit no.	CCDC-974965	CCDC-974966	CCDC-974967	CCDC-974968
Empirical formula	$C_{15}H_{19}NO_6S$	$C_{18}H_{17}NO_6S$	$C_{14}H_{17}NO_6S_2$	$C_{18}H_{17}NO_6S_2$
Crystal System, space group	Monoclinic *P*-1	Monoclinic *P*-1	triclinic $P2_1/n$	Monoclinic $P2_1/n$
M_r	341.37	341.37	359.41	359.41
a, Å	7.0006(3)	7.0252(15)	8.2440(3)	8.0832(2)
b, Å	7.8988(4)	8.1514(16)	7.4617(3)	7.1669(2)
c, Å	14.9207(7)	14.875(3)	27.2752(11)	27.7096(6)
α, deg	92.055(3)	97.853(11)	90	90
β, deg	102.842(3)	103.477(8)	96.372(2)	96.214(1)
γ, deg	97.201(3)	100.951(8)	90	90
V, (Å^3)	796.34(6)	798.6(3)	1667.45(11)	1595.83(7)
Z, *Z'*	2, 1	4, 1	4, 1	4, 1
D_{calc} (g cm^{-3})	1.424	1.420	1.432	1.496
μ (mm^{-1}), rad. type	2.092, Cu $K\alpha$	2.086, Cu $K\alpha$	3.168, Cu $K\alpha$	3.310, Cu $K\alpha$
F_{000}	360	360	752	752
temp (K)	100(2)	296(2)	298(2)	100(2)
Crystal form, color	plate, colorless	plate, colorless	plate, light-yellow	plate, light-yellow
Crystal size, mm	0.19×0.16×0.03	0.19×0.16×0.03	0.31×0.29×0.08	0.31×0.29×0.08
Data collection				
Diffractometer	Bruker Apex II	Bruker Apex II	Bruker Apex II	Bruker Apex II
T_{min}/ T_{max}	0.691/0.942	0.452/0.723	0.435/0.790	0.423/0.782
No. of refls. (meas., uniq., and obs.)	7101/5223/3562	14209/2700/1686	20611/3003/2260	22047/2882/2294
R_{int}	0.0494	0.1137	0.0355	0.0818
θ_{max} (^{o})	67.98	67.97	67.81	67.71
Refinement				
R/R^2_{ω} (obs data)	0.0638/0.1459	0.1915/0.4683	0.0511/0.1289	0.0553/0.1315
R/R^2_{ω} (all data)	0.1089/0.1713	0.2373/0.4959	0.0696/0.1398	0.0714/0.1402
S	0.965	1.09	1.03	1.12
No. of refls.	5223	2700	3003	2882
No. of parameters	221	239	219	358
$\Delta\rho_{max/min}$ (e·Å^{-3})	0.304/-0.348	0.442/-0.370	0.532/-0.252	0.508/-0.290
flack	-	-	-	-

Table S1. Crystallographic data for 3 – 5 (continued)

	(*L*)-**3**/(*D*)-**4**	(*L*)-**3**/(*D*)-**4**-reacted UV 4 hrs	(*L*)-**3**/(*D*)-**4**-reacted UV 11 hrs	(*L*)-**3**/(*D*)-**4**-reacted UV 22 hrs
Crystal data				
CCDC deposit no.	CCDC-974969	CCDC-974970	CCDC-974971	CCDC-974972
Empirical formula	$C_{29}H_{36}N_2O_{12}S_3$	$C_{29}H_{36}N_2O_{12}S_3$	$C_{29}H_{36}N_2O_{12}S_3$	$C_{29}H_{36}N_2O_{12}S_3$
Crystal System, space group	Monoclinic *P*1	triclinic *P*1	triclinic *P*1	triclinic *P*1
M_r	700.78	700.78	700.78	700.78
a, Å	6.9045(2)	6.8872(3)	6.9686(5)	6.8789(6)
b, Å	7.9441(2)	7.9769(4)	8.0453(5)	8.1405(7)
c, Å	15.2565(4)	15.0753(7)	14.9788(10)	14.5005(13)
α, deg	82.911(1)	93.167(3)	93.118(3)	92.437(5)
β, deg	77.052(2)	102.378(3)	101.808(3)	98.960(5)
γ, deg	81.884(1)	98.319(3)	98.412(3)	99.960(5)
V, (Å^3)	803.71(4)	797.26(7)	810.11(9)	788.25(12)
Z, Z'	1, 1	1, 1	1, 1	1, 1
D_{calc} (g cm^{-3})	1.448	1.460	1.436	1.476
μ (mm^{-1}), rad. type	2.679, Cu $K\alpha$	2.701, Cu $K\alpha$	2.658, Cu $K\alpha$	2.732, Cu $K\alpha$
F_{000}	368	368	368	368
temp (K)	100(2)	296(2)	296(2)	296(2)
Crystal form, color	plate, light-yellow	plate, light-colorless	plate, colorless	plate, colorless
Crystal size, mm	0.41×0.31×0.11	0.45×0.36×0.10	0.45×0.36×0.10	0.45×0.36×0.10
Data collection				
Diffractometer	Bruker Apex II	Bruker Apex II	Bruker Apex II	Bruker Apex II
T_{min}/ T_{max}	0.419/0.753	0.297/0.763	0.302/0.767	0.292/0.761
No. of refls. (meas., uniq., and obs.)	11931/4571/4522	14944/4722/4394	14694/4755/3278	24878/2680/2263
R_{int}	0.0276	0.0454	0.0581	0.0733
θ_{max} (°)	68.22	67.130	67.679	67.553
Refinement				
R/R^2_ω (obs data)	0.0379/0.1035	0.0840/0.2339	0.1133/0.2823	0.0748/0.1970
R/R^2_ω (all data)	0.0382/0.1037	0.0890/0.2389	0.15.01/0.3106	0.0858/0.2121
S	1.07	1.11	1.05	1.07
No. of refls.	4571	4722	4755	2680
No. of parameters	436	518	499	438
$\Delta\rho_{max/min}$ (e·Å^{-3})	0.514/-0.310	0.806/-0.526	0.387/-0.298	0.542/-0.317
flack	0.111(8)	0.169(16)	0.22(2)	0.05(4)

Table S1. Crystallographic data for 3 – 5 (continued)

	(*L*)-**3**	(*L*)-**3**-reacted	**5**-I	**5**-II
Crystal data				
CCDC deposit no.	CCDC-974973	CCDC-974974	CCDC-974975	CCDC-974976
Empirical formula	$C_{15}H_{19}NO_6S$	$C_{15}H_{19}NO_6S$	$C_{11}H_{11}NO_6S\cdot CH_2Cl_2$	$C_{11}H_{11}NO_6S\cdot 1.5H_2O$
Crystal System, space group	Monoclinic $P2_1$	Monoclinic $P2_1$	Triclinic P-1	Monoclinic $P2_1/n$
M_r	341.37	341.37	370.19	294.28
a, Å	7.7603(1)	7.8661(4)	5.0738(1)	5.1963(1)
b, Å	6.9346(1)	7.1700(4)	8.1430(2)	29.5944(6)
c, Å	15.1225(1)	14.9612(8)	18.6485(4)	9.2515(2)
α, deg	90	90	91.867(1)	90
β, deg	93.392(1)	91.665(4)	93.641(1)	99.075(1)
γ, deg	90	90	97.715(1)	90
V, (Å^3)	812.385(17)	843.45(8)	761.31(3)	1404.90(5)
Z, Z'	2, 1	2, 1	2, 1	4, 1
D_{calc} (g cm^{-3})	1.396	1.363	1.615	1.391
μ (mm^{-1}), rad. type	2.050, Cu $K\alpha$	0.222, Mo $K\alpha$	5.394, Cu $K\alpha$	2.311, Cu $K\alpha$
F_{000}	360	364	380	612
temp (K)	100(2)	298(2)	100(2)	100(2)
Crystal form, color	plate, colorless	plate, colorless	plate, colorless	needle, colorless
Crystal size, mm	0.40×0.33×0.11	0.40×0.33×0.11	0.12×0.11×0.01	0.35×0.08×0.07
Data collection				
Diffractometer	Bruker Apex II	Bruker P4 CCD	Bruker Apex II	Bruker Apex II
T_{min}/ T_{max}	0.495/0.803	0.916/0.976	0.561/0.938	0.848/0.439
No. of refls. (meas., uniq., and obs.)	11646/2871/2819	7978/3084/1369	13623/2669/2051	30432/2557/2343
R_{int}	0.0249	0.0556	0.0597	0.0506
θ_{max} (^{o})	68.212	25.350	67.922	68.239
Refinement				
R/R^2_{ω} (obs data)	0.0245/0.0637	0.0728/0.1787	0.0619/0.1825	0.0446/0.1098
R/R^2_{ω} (all data)	0.049/0.0641	0.1746/0.2291	0.0804/0.1989	0.0490/0.1123
S	1.05	1.01	1.06	1.07
No. of refls.	2871	3084	2669	2557
No. of parameters	219	239	208	211
$\Delta\rho_{max/min}$ (e·Å^{-3})	0.234/-0.269	0.320/-0.186	0.632/-0.784	1.139/-0.297
flack	0.047(5)	0.07(7)	-	-