

Electronic supplementary information for:

Valine Sulfonamidedecinnamic Acid Asymmetric Crystal Reactions

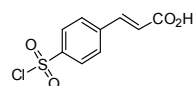
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Supporting Information

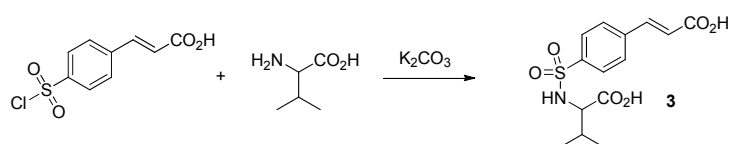
General Considerations. All chemicals and solvents were purchased from the Aldrich Chemical Co. or Acros Chemicals and used as received without further purification. ^1H NMR and ^{13}C NMR spectral data were recorded with a 400 MHz Bruker Avance spectrometer using TopSpin v.2.1. Melting point data were determined using a Melt-Temp apparatus and are uncorrected. Recrystallization experiments were conducted at room temperature using reagent-grade solvents.

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



4-Chlorosulfonylcinnamic acid was prepared using a previously reported literature procedure.¹

L-Valine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-



Preparation of racemic and homochiral **3** was carried out using a parallel procedure as described for sulfonamidecinnamic acids **1** and **2**.¹ To a 250 rd-bottom flask containing 100 mL of acetone and 25 mL of deionized water was added 4-chlorosulfonylcinnamic acid (1.01 g, 4.10 mmol, 1.0 eq.) and (*rac*)- or D-valine (4.10 mmol, 1.0 eq.). The reaction mixture was stirred in an ice bath (0°C) for 30 min while anhydrous K_2CO_3 (0.0123 mol) dissolved in 20 mL of deionized water was added dropwise. The light-yellow reaction mixture was allowed to stir at 0°C for an additional 1.75 hrs. Reaction progress was assessed via TLC (10:30:1; hexanes, EtOAc, AcOH) showing the presence of product (R_f = 0.61-0.63) and the absence of chloro sulfonylcinnamic acid (R_f = 0.82). The acetone from the reaction mixture was removed under *vacuo* and the resulting light-yellow homogenous aqueous layer acidified (pH = 2-3) using 6M HCl at 0°C and extracted with 3x25 mL EtOAc. The combined organic extracts were dried over anhydrous MgSO_4 and reduced under *vacuo* to give light-yellow solids in 37-41% yield. Crystals suitable for X-ray diffraction were grown from room temperature slow evaporation of acetone or 2-butanone solutions.

(*rac*)-3 (unreacted): 41% yield, Mp. 220 (dec). ^1H -NMR (400 MHz, acetone- d_6): δ 7.89 (d, J = 9.4 Hz, 2H, Ar-H); 7.68 (d, J = 9.4 Hz, 2H, Ar-H); 7.72 (d, J = 16.0 Hz, 1H, C_{sp^2} -H); 6.79 (d, J = 9.6 Hz, 1H, NH); 6.69 (d, J = 16.0 Hz, 1H, C_{sp^2} -H); 3.79-3.83 (m, 1H, CH); 1.98-2.02 (m, 1H, CH); 0.90-0.98 (m, 2H, CH_3). ^{13}C NMR: δ 171.9, 167.4, 141.2, 140.8, 137.5, 127.7, 127.7, 120.6, 60.5, 31.1, 18.5, 17.2.

(*R*)-3 (unreacted): 37% yield, Mp. 220 (dec). ^1H -NMR (400 MHz, acetone- d_6): δ 7.89 (d, J = 8.4Hz, 2H, Ar-H), 7.85 (d, J = 8.4Hz, 2H, Ar-H), 7.72 (d, J = 15.8Hz, 1H, C_{sp^2} - H), 6.76 (d, J = 9.5Hz, 1H, N-H), 6.67 (d, J = 16.0Hz, 1H, C_{sp^2} - H), 3.72 (dd, J = 9.5, 5.0 Hz, 1H, CH), 2.10 (ddq, J = 6.7, 5.0, 1.7 Hz, 1H, CH), 0.95 (dd, J = 6.7, 1.7 Hz, 3H, CH_3), 0.89 (dd, J = 6.7, 1.7 Hz, 3H, CH_3). ^{13}C NMR: δ 172.4, 167.5, 141.8, 140.9, 137.9, 127.7, 127.3, 121.3, 60.7, 30.7, 18.7, 17.0.

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

(R)-3 (photodimerized): $^1\text{H-NMR}$ (400 MHz, acetone- d_6): δ 7.81 (d, $J = 8.2\text{ Hz}$, 2H, Ar-H), 7.60 (d, $J = 8.2\text{ Hz}$, 2H, Ar-H), 6.61 (d, $J = 9.2\text{ Hz}$, 1H, N-H), 4.53 (dd, $J = 10.3, 7.7\text{ Hz}$, 1H, CH), 4.10 (d, $J = 10.3, 7.7\text{ Hz}$, 1H, CH), 3.71 (dd, $J = 9.2, 5.1\text{ Hz}$, 1H, CH), 1.98-2.02 (m, 1H, CH), 0.95 (dd, $J = 6.6, 1.7\text{ Hz}$, 3H, CH_3), 0.90 (dd, $J = 6.6, 1.7\text{ Hz}$, 3H, CH_3).

Photodimerization reactions. UV illumination studies on single crystal of (*rac*)-**3** and (*R*)-**3** 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). Powdered (*R*)-**3** was exposed to unfiltered radiation for 1030 min (17 h), 2530 min (42 h), and 4020 min (67 h) with reaction conversion assessed by $^1\text{H-NMR}$ spectroscopy (acetone- d_6).

Crystallography. Crystallographic details for compounds (*rac*)-**3** and (*R*)-**3** are summarized in Table 1. X-ray data were collected on a Bruker APEX II CCD diffractometer using phi and omega scans with graphite monochromatic Cu Mo $K\alpha$ ($\lambda = 1.54178\text{ \AA}$) radiation. Data sets were corrected for Lorentz and polarization effects as well as absorption ((*rac*)-**3**, sadabs/multi-scan; (*R*)-**3**, twinabs). 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 for (*rac*)-**3** and TWINABS for (*R*)-**3**.² Structures solved by direct methods and refined by full-matrix least-squares analysis on F^2 using X-SEED³ equipped with SHELXS⁴. All non-hydrogen atoms for unreacted and reacted phases of (*rac*)- and (*R*)-**3** were refined anisotropically by full-matrix least-squares on F^2 using the SHELXL⁴ program. For photoreacted (*R*)-**3**, the minor component was restrained using the ISOR command in SHELXL. H atoms (for OH and NH) were located in difference Fourier synthesis and refined isotropically with $U_{\text{iso}} = 1.2U_{\text{eq}}$ and independent O/N-H distances or restrained to 0.85(2) Å. The remaining H atoms were included in idealized geometric positions with $U_{\text{iso}} = 1.2U_{\text{eq}}$ of the atom to which they were attached ($U_{\text{iso}} = 1.5U_{\text{eq}}$ for methyl groups). Molecular configurations were compared to both the known chirality of the valine components and estimated Flack parameters⁵ and where applicable, atomic coordinates were inverted to achieve correct structural configurations.

Inspection of X-ray data for photoreacted (*R*)-**3** in well dispersed reciprocal space revealed several twin components. The programs Cell_Now⁶ and ROTAX⁷ allowed indexing of the unreacted and reacted phases as a two-component twin. Since a ~60:40 ratio of reflections from these two phases were present, both sets of reflections were employed for further structure refinements (hklf5). Successful direct methods solutions were calculated for both phases which provided most of the non-hydrogen atoms from the E-maps. Several full-matrix least-squares/difference Fourier cycles were performed to locate the remainder of the non-hydrogen atoms.

² G. M. Sheldrick, SADABS and TWINABS—Program for Area Detector Absorption Corrections, University of Göttingen, Göttingen, Germany, 2010.

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, 876-881.

⁶ Sheldrick, G. M. CELL_NOW; University of Göttingen.

⁷ Cooper, R. I.; Gould, R. O.; Parsons, S.; Watkin, D. J. Acta Crystallogr. 2002, A35, 168-174.

Table 1. Crystallographic data for 3

	(+/-)-3 (unreacted)	(+/-)-3 (UV-irradiated)	(R)-3 (unreacted)	(R)-3 (UV-irradiated)
Crystal data				
CCDC deposit no.	CCDC-838809	CCDC-838810	CCDC-838811	CCDC-838812
Empirical formula	C ₁₄ H ₁₇ NO ₆ S	C ₂₈ H ₃₄ N ₂ O ₁₂ S ₂	C ₁₄ H ₁₇ NO ₆ S	C ₂₈ H ₃₄ N ₂ O ₁₂ S ₂
Crystal System, space group	triclinic <i>P</i> -1	triclinic <i>P</i> -1	triclinic <i>P</i> 1	triclinic <i>P</i> 1
<i>M</i> _r	327.35	654.71	327.35	654.71
<i>a</i> , Å	7.2401(1)	7.4391(3)	7.9008(2)	7.8647(3)
<i>b</i> , Å	7.2996(1)	7.6719(3)	8.0121(2)	8.0522(3)
<i>c</i> , Å	15.8742(3)	15.0529(7)	11.8061(3)	11.7930(5)
<i>α</i> , deg	88.734(1)	88.371(3)	83.617(1)	83.951(2)
<i>β</i> , deg	87.853(1)	85.421(3)	77.774(2)	77.725(2)
<i>γ</i> , deg	64.951(1)	61.552(2)	88.744(2)	89.754(2)
<i>V</i> , (Å ³)	759.49(2)	752.91(5)	725.87(3)	725.57(5)
<i>Z</i> , <i>Z'</i>	2, 1	1, 1	2, 2	1, 1
<i>D</i> _{calc} (g cm ⁻³)	1.431	1.444	1.498	1.498
<i>μ</i> , (Mo Kα) (mm ⁻¹)	2.169	2.188	2.269	2.270
<i>F</i> ₀₀₀	344	344	344	344
temp (K)	100(2)	100(2)	100(2)	100(2)
Crystal form, color	lathe, colorless	lathe, colorless	rhomboid, colorless	Plate, colorless
Crystal size, mm	0.43 x 0.35 x 0.06	0.43 x 0.35 x 0.06	0.48 x 0.31 x 0.18	0.34 x 0.29 x 0.13
Data collection				
Diffractometer	Bruker Apex II	Bruker Apex II	Bruker Apex II	Bruker Apex II
<i>T</i> _{min} / <i>T</i> _{max}	0.459/0.815	0.459/0.815	0.408/0.691	0.458/0.738
No. of refls. (meas., uniqu., and obs.)	15072/2710/2566	13224/2563/2133	4857/4857/4664	4698/4698/4326
<i>R</i> _{int}	0.0467	0.0623	0.0461	0.0581
<i>θ</i> _{max} (°)	68.24	66.77	67.57	67.32
Refinement				
<i>R</i> / <i>R</i> ² _ω (obs data)	0.0485/0.1270	0.0751/0.1959	0.0423/0.1077	0.0499/0.1250
<i>R</i> / <i>R</i> ² _ω (all data)	0.509/0.1290	0.0888/0.2093	0.0475/0.1108	0.0555/0.1292
<i>S</i>	1.12	1.15	1.08	1.03
No. of refls.	2710	2563	4857	4698
No. of parameters	211	264	410	549
<i>Δρ</i> _{max/min} (e·Å ⁻³)	0.635/-0.344	0.606/-0.317	0.457/-0.326	0.528/-0.290
<i>flack</i>	-	-	0.54(6)	0.09(2)

Hydrogen-bond geometries for reactant and product phases of 3.				
Compound	D-H···A (Å)	D···A (Å)	D-H···A (°)	Symmetry operator
(rac)-3 (unreacted)	O1-H···O4	2.663(2)	170(3)	-x, 2-y, l-z
	O3-H···O2	2.648(2)	173(3)	-x, 2-y, l-z
	N1-H···O2	2.929(3)	162(2)	-x, l-y, l-z
	C5-H···O6	3.207(3)	150.9	x, y+1, z
(rac)-3 (photodimerized)	O1-H···O4	2.732(4)	157.3	l-x, 2-y, -z
	O3-H···O2	2.738(4)	169.1	l-x, 2-y, -z
	N1-H···O4	3.164(5)	154(5)	2-x, l-y, -z
	C5-H···O6	3.092(12)	164.1	x-l, y+1, z
	C5A-H···O6	3.32(3)	171.8	x-l, y+1, z
(R)-3 (unreacted)	O1A-H···O4B	2.673(4)	175.0	x,y,z
	O1B-H···O4a	2.636(4)	168.5	x,y,z
	O3A-H···O2B	2.685(4)	172.2	x,y,z
	O3B-H···O2A	2.659(4)	171.3	x,y,z
	N1A-H···O3B	3.038(4)	146(4)	x, y+1, z
	N1B-H···O2A	3.066(4)	149(4)	x-l, y-1, z+2
	C5A-H···O6A	3.325(5)	149.2	x, y+1, z
	C5B-H···O6B	3.194(5)	152.1	x, y-1, z
(R)-3 (photodimerized)	O1A-H···O4B	2.662(3)	175(4)	x,y,z
	O2B-H···O3A	2.683(3)	178(4)	x,y,z
	O4A-H···O1B	2.624(3)	163(4)	x,y,z
	O3B-H···O2A	2.652(3)	168(4)	x,y,z
	N1A-H···O3B	3.075(4)	142(3)	x-1, y-1, z+2
	N1B-H···O2A	3.080(4)	155(3)	x, y+1, z