Electronic supplementary information for (C2CE26307F):

Solid-State Photodimerization Reactions of Racemic and Homochiral Phenylalanine Sulfonamidecinnamic Acids

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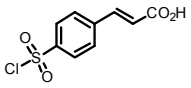
Supporting Information

General Considerations. All chemicals and solvents were purchased from the Aldrich Chemical Co. or Acros Chemicals and used as received without further purification unless stated otherwise. Chromatography purifications were performed using silica gel 60 (Sorbent Technologies 40-75 μm, 200 × 400 mesh). 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.2.1. Recrystallization experiments were conducted at room temperature using reagent-grade solvents. 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.

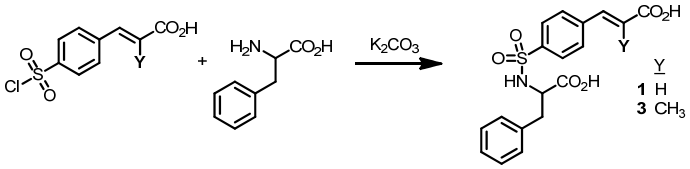
(2E)-3-[4-(Chlorosulfonyl)phenyl]-2-propenoic acid



The preparation of 4-Chlorosulfonylcinnamic acid and 4-Chlorosulfonyl-α-methylcinnamic acid were carried out using the general procedure described by Grove *et. al.*[1]

D- and DL-Phenylalanine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-

DL-Phenylalanine, N-[[4-(2-carboxy-2-methylethenyl)phenyl]sulfonyl]-



Preparation of (*rac*)-**1**, (*R*)-**1**, and (*rac*)-**3** 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 D- or DL-phenylalanine (8.92 mmol, 1.1 eqv.) and the appropriate 4-chlorosulfonyl derivative (8.09 mmol, 1.0 eqv.). The reaction mixture was stirred at 0°C for 10 min to give a light-orange heterogeneous mixture. A solution consisting of K_2CO_3 (3.3641g, 24.3 mmol) dissolved in 20 mL of distilled 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 orange homogeneous solution that was allowed to stir at 0°C for an additional four hours. Reaction progress was assessed via TLC (10:30:1; hexanes, EtOAc, AcOH) showing the presence of both product (R_f = 0.46 (*rac*- and *R*-**1**) and 0.52 (*rac*-**3**)) and phenylalanine (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* (rotvap, 30°C water bath). The resulting yellow homogenous aqueous layer was cooled to 0°C, acidified (*pH* = 2-3) using 6M HCl (~50 drops), and extracted with 2x20 mL EtOAc. The combined organic extracts were dried over anhydrous $MgSO_4$ and reduced under *vacuo* (rotovap, 30°C water bath) to give light-yellow solids.

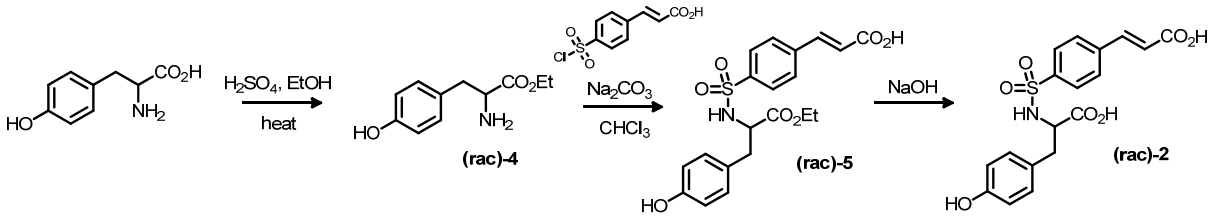
[1] R. C. Grove, S. H. Malehorn, M. E. Breen, K. A. Wheeler, *Chem. Comm.*, 2010, **46**, 7322.

DL-Phenylalanine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-. (*rac*)-1: 41.5% yield. ^{1}H-NMR (acetone-d_6): δ 7.75 (d, J = 8.6 Hz, 2H, Ar-H); 7.70 (d, J = 8.6 Hz, 2H, Ar-H); 7.68 (d, J = 16.1 Hz, 1H, Csp^2-H); 7.22-7.17 (m, 5H, Ar-H); 6.94 (d, J = 8.8 Hz, 1H, N-H); 6.65 (d, J = 16.1 Hz, 1H, Csp^2-H); 4.22-4.14 (m, 1H, CH), 3.15 (dd, J = 13.5, 5.5Hz, 1H, CH_2), 2.94 (dd, J = 13.5, 8.5Hz, 1H, CH_2). ^{13}C-NMR (acetone-d_6): δ172.5, 167.4, 143.7, 143.2, 139.1, 137.5, 130.5, 129.4, 129.2, 128.2, 127.6, 122.1, 58.3, 39.5.

D-Phenylalanine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-. (*R*)-1: 54.1% yield. ^{1}H-NMR (400 MHz, acetone-d_6): δ 7.75 (d, J = 8.2Hz, 2H, Ar-H), 7.70 (d, J = 8.2Hz, 2H, Ar-H), 7.68 (d, J = 16.0 Hz, 1H, Csp^2-H); 7.22-7.18 (m, 5H, Ar-H); 6.97 (d, J = 9.2 Hz, 1H, N-H); 6.65 (d, J = 16.0 Hz, 1H, Csp^2-H); 4.22-4.14 (m, 1H, CH), 3.11 (dd, J = 13.8, 5.4Hz, 1H, CH_2), 2.92 (dd, J = 13.8, 8.5 Hz, 1H, CH_2). ^{13}C-NMR (acetone-d_6): δ172.5, 167.4, 143.7, 143.2, 139.1, 137.5, 130.5, 129.4, 129.2, 128.2, 127.6, 122.1, 58.3, 39.5.

DL-Phenylalanine, N-[[4-(2-carboxy-2-methylethenyl)phenyl]sulfonyl]-. (*rac*)-3: 81.3% yield. ^{1}H-NMR (400 MHz, acetone-d_6): δ 7.72 (d, J = 8.5Hz, 2H, Ar-H), 7.70 (br s, 3H, Csp^2-H), 7.68 (d, J = 8.5Hz, 2H, Ar-H), 7.20-7.19 (m, 5H, Ar–H), 6.94 (d, J = 9.27Hz, 1H, NH), 4.23-4.13 (m, 1H, CH), 3.12 (dd, J = 13.8, 5.4Hz, 1H, CH_2), 2.93 (dd, J = 13.8, 8.4Hz, 1H, CH_2), 2.10 (d, J = 1.5Hz, 3H, CH_3). ^{13}C-NMR (100 MHz, acetone-d$_6$): δ 172.6, 169.4, 141.6, 140.7, 137.7, 137.5, 131.8, 130.9, 130.4, 129.2, 127.8, 127.6, 58.3, 39.5, 14.4.

DL-Tyrosine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-



DL-Tyrosine ethyl ester. (***rac*)-4:** To a solution of DL-tyrosine (9.00 g, 49.7 mmol) and absolute ethyl alcohol (42 mL) was added dropwise 4.85 mL of concentrated sulfuric acid. The reaction mixture was refluxed for an additional 16 h, cooled to room temperature. The solution was poured over ice, and Na_2CO_3 was added portion wise until the solution was basic (pH ~ 8). This solution was extracted with 3 portions of 100 mL of ethyl acetate and the organic layers were combined and dried over $MgSO_4$. The solvent was removed under vacuum to give (*rac*)-**4** as an off-white solid (75.3%). The product was used in the next step without further purification. ^{1}H NMR (400 MHz, chloroform-*d*, 27 °C): δ = 6.90 (d, J = 8.4 Hz, 2H, Ar-H), 6.65 (d, J = 8.4 Hz, 2H, Ar-H), 4.05 (q, J = 7.2 Hz, 2H, CH_2), 3.53 (dd, J_1 = 7.6, 5.6 Hz, 1H, CH), 2.76 (dd, J = 13.4, 5.2 Hz, 1H, CH_2), 2.75 (dd, J = 13.4, 7.2 Hz, 1H, CH_2), 1.16 (t, J = 7.2 Hz, 3H, CH_3).

DL-Tyrosine ethyl ester, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-. (*rac*)-5: To a suspension of (*rac*)-**4** (1.000 g, 4.78 mmol) and $CHCl_3$ (7.2 mL) was added in a solution of Na_2CO_3 (0.558 g, 5.26 mmol) in H_2O (2.8 mL). The mixture was stirred for 10 minutes and a solution of (E)-4-cholorsulfonylcinnamic acid (1.144 g, 4.64 mmol) in $CHCl_3$ (22.0 mL) was added at room temperature. The mixture was stirred for 2 h. Then a solution of Na_2CO_3 (0.558 g, 5.26 mmol) in H_2O (2.8 mL) was added. The mixture was stirred for further 4 h, then it was cooled to 0°C and acidified to pH 2-3 with 5M HCl. The resulting off-

white solid was filtered, and further purified by column chromatography (SiO_2, Hexanes/Ethyl Acetate/Acetic Acid = 30:30:1) to afford (*rac*)-**5 (** 0.3598 g, 18.1%) as a pale yellow solid. ^{1}H NMR (400 MHz, acetone-d_6, 27 ^{o}C): δ = 7.78 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.72 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.69 (d, *J* = 16.0 Hz, 1H, C_{sp2}-H), 6.97 (d, *J* = 8.6 Hz, 2H, Ar-H), 6.67 (d, *J* = 8.6 Hz, 2H, Ar-H), 6.65 (d, *J* = 16.0 Hz, 1H, C_{sp2}-H), 4.06 (dd, *J* = 8.0, 6.4 Hz, 1H, CH), 3.86 (q, *J* = 7.2 Hz, 2H, CH_2), 2.92 (dd, *J* = 14.0, 6.4 Hz, 1H, CH_2), 2.75 (dd, *J* = 14.0, 8.0 Hz, 1H, CH_2), 1.03 (t, *J* = 7.2 Hz, 3H, CH_3).

DL-Tyrosine, N-[[4-(2-carboxyethenyl)phenyl]sulfonyl]-. (*rac*)-2: Compound (*rac*)-**5** (0.5106 g, 1.22 mmol) was suspended in a 5*M* NaOH solution (7 mL) and warmed in a 80 ^{o}C water bath for 30 minutes. Water (15 mL) was added and the dark green mixture was acidified to pH 2-3 with 5*M* HCl and warmed for further 5 min, then cooled in an ice bath. Stirring was continued for 10 min and the product was vacuum-filtered to afford 0.2011 g (42.0%) of (*rac*)-**2**, a white solid. ^{1}H NMR (400 MHz, acetone-d_6, 27 ^{o}C): δ = 7.74 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.69 (d, *J* = 8.4 Hz, 2H, Ar-H), 7.68 (d, *J* = 14.8 Hz, 1H, C_{sp2}-H), 7.00 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.66 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.64 (d, *J* = 14.8 Hz, 1H, C_{sp2}-H), 4.09 (dd, *J* = 8.4, 5.2 Hz, 1H, CH), 3.00 (dd, *J* = 14.0, 5.2 Hz, 1H, CH_2), 2.82 (dd, J_1 = 14.0 Hz, J_2 = 8.4 Hz, 1H, CH_2).

Photodimerization reactions. UV illumination studies on single crystals of (*rac*)-**1**-I and (*R*)-**1** 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 during the UV illumination process, evaluation of these transformations was only practical to 32% [(*rac*)-**1**-I, 8.0 hrs] and 19% [(*R*)-**1**, 1.0 hr] conversion. Further investigation of the photodimerizations was conducted using polycrystalline samples and unfiltered radiation. During the illumination period, samples were periodically ground (~ once every hour) and reaction progress assessed with ^{1}H NMR spectroscopy after 7.5, 12.0, 21.5, 27.25, and 35.0 hours. The photodimerization reactions using polycrystalline samples of (*rac*)-**1**-II and (*R*)-**1** converged to 74% (27.25 hours) and 50% (21.5 hours), respectively.

Cyclobutane photoproduct from UV irradiation of (*rac*)-1-I [74% conversion (27.25 hrs)] and (*R*)-1 [**74% conversion (27.25 hrs)**]: ^{1}H-NMR (400 MHz, acetone-d_6/DMSO-d_6 8:1 v/v): δ 7.61 (d, *J* = 8.6Hz, 2H, Ar-H), 7.47 (d, *J* = 8.6 Hz, 2H, Ar-H); 7.22-7.17 (m, 5H, Ar-H); 4.45 (dd, *J* = 10.2, 7.2 Hz, 1H, CH); 4.18-3.90 (m, 1H, CH); 3.98 (dd, *J* = 10.2, 7.3 Hz, 1H, CH); 3.03 (dd, *J* = 13.7, 5.4 Hz, 1H, CH_2); 2.85 (dd, *J* = 13.7, 8.7Hz, 1H, CH_2).

Crystallography. Crystallographic details for compounds **1** - **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 $K\alpha$ (λ = 1.54178 Å) radiation. 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 -SEED[3] equipped with SHELXS[4]. All non-hydrogen atoms for unreacted crystal phases were refined anisotropically by full-matrix least-squares on F^2 by the use of

[2] G. M. Sheldrick, SADABS —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.

the SHELXL[3] program. For photoreacted (*rac*)-**1**-I and (*R*)-**1**, the photochemical 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) 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 (*R*)-**1**, the molecular configuration was compared to both the known chirality of the phenylalanine component and estimated Flack parameter[5] and where applicable, atomic coordinates were inverted to achieve correct structural configurations.

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

Table 1. Crystallographic data for 1-3

	(*rac*)-**1**-I	(*rac*)-**1**-I (reacted)	(*rac*)-**1**-II	(*R*)-**1**
Crystal data				
CCDC deposit no.	CCDC-895728	CCDC-895729	CCDC-895730	CCDC-895731
Empirical formula	$C_{18}H_{17}NO_6S$	$C_{18}H_{17}NO_6S$	$C_{18}H_{17}NO_6S$	$C_{18}H_{17}NO_6S$
Crystal System, space group	Monoclinic *P*21/*n*	Monoclinic *P*21/*n*	Triclinic P-1	Monoclinic *P*21
M_r	375.39	375.39	375.39	375.39
a, Å	15.5367(3)	15.3346(8)	7.3283(2)	10.2820(5)
b, Å	7.2065(1)	7.2910(4)	7.7161(2)	14.1275(6)
c, Å	15.8326(3)	16.1284(9)	16.2329(4)	11.8374(5)
α, deg	90	90	90.860(1)	90
β, deg	106.567(1)	104.857(4)	97.774(2)	96.725(2)
γ, deg	90	90	112.116(2)	90
V, (Å^3)	1699.11(5)	1742.94(16)	840.38(4)	1707.66(13)
Z, *Z'*	4, 1	4, 1	2, 1	2, 2
D_{calc} (g cm^{-3})	1.467	1.431	1.483	1.460
μ, (Mo Kα) (mm^{-1})	2.024	1.973	2.046	2.014
F_{000}	784	784	392	784
temp (K)	100(2)	100(2)	100(2)	100(2)
Crystal form, color	lathe, colorless	lathe, colorless	plate, colorless	plate, colorless
Crystal size, mm	0.44×0.38×0.08	0.48×0.39×0.18	0.19×0.10×0.04	0.18×0.15×0.02
Data collection				
Diffractometer	Bruker Apex II	Bruker Apex II	Bruker Apex II	Bruker Apex II
T_{min}/ T_{max}	0.469/0.861	0.452/0.723	0.679/0.921	0.697/0.970
No. of refls. (meas., uniq., and obs.)	23203/3054/2717	10334/3003/1693	17267/2950/2671	22936/5821/2989
R_{int}	0.0384	0.0704	0.0334	0.0808
θ_{max} (°)	67.60	66.67	67.34	67.46
Refinement				
R/R^2_ω (obs data)	0.0435/0.1091	0.0664 /0.1650	0.0355/0.0943	0.0681/0.0893
R/R^2_ω (all data)	0.487/0.1129	0.1180/0.2032	0.0405/0.1069	0.1690/0.1143
S	1.08	1.02	1.03	1.00
No. of refls.	2717	3003	2950	5821
No. of parameters	244	303	284	488
$\Delta\rho_{max/min}$ (e·Å^{-3})	0.481/-0.265	0.325/-0.185	0.306/-0.332	0.261/-0.238
flack	-	-	-	0.03(3)

Table 1. Crystallographic data for 1-3 (continued)

	(*R*)-**1** (reacted)	(*rac*)-**2**	(*rac*)-**3**
Crystal data			
CCDC deposit no.	CCDC-895732	CCDC-895733	CCDC-895734
Empirical formula	$C_{18}H_{17}NO_6S$	$C_{18}H_{17}NO_7S \cdot C_3H_6O$	$C_{19}H_{19}NO_6S$
Crystal System, space group	Monoclinic *P*21	Triclinic *P*-1	Monoclinic *P*21/*n*
M_r	375.39	449.46	389.41
a, Å	10.3597(5)	9.6186(3)	9.6628(1)
b, Å	13.9938(7)	11.3663(4)	12.9705(2)
c, Å	11.8314(6)	11.7792(6)	15.2675(2)
α, deg	90	61.273(2)	90
β, deg	97.721(3)	76.368(3)	108.034(1)
γ, deg	90	67.977(2)	90
V, (Å^3)	1699.67(15)	1044.45(7)	1819.49(4)
Z, *Z'*	2, 2	2, 1	4, 1
D_{calc} (g cm^{-3})	1.467	1.429	1.422
μ, (Mo Kα) (mm^{-1})	2.023	1.815	1.910
F_{000}	784	472	816
temp (K)	296(2)	100(2)	100(2)
Crystal form, color	plate, colorless	plate, colorless	rhomboid, colorless
Crystal size, mm	0.33×0.33×0.04	0.48×0.36×0.13	0.26×0.18×0.09
Data collection			
Diffractometer	Bruker Apex II	Bruker Apex II	Bruker Apex II
T_{min}/ T_{max}	0.559/0.927	0.475/0.805	0.634/0.847
No. of refls. (meas., uniq., and obs.)	22398/5905/4578	19333/3626/2647	25034/3271/2672
R_{int}	0.0625	0.0864	0.0465
θ_{max} (°)	67.34	66.54	67.80
Refinement			
R/R^2_ω (obs data)	0.0542/0.1225	0.0645/0.1488	0.0374/0.0946
R/R^2_ω (all data)	0.0773/0.1364	0.0925/0.1622	0.0501/0.1019
S	1.03	1.15	1.04
No. of refls.	5905	3626	3271
No. of parameters	633	335	254
$\Delta\rho_{max/min}$ (e·Å^{-3})	0.545/-0.209	0.542/-0.317	0.342/-0.243
flack	0.01(2)	-	-

Hydrogen-bond geometries for reactant and product phases of 1-3.

Compound	D-H···A (Å)	D···A (Å)	D-H···A (º)	Symmetry operator
(*rac*)-1-I (unreacted)	O1-H···O4	2.678(2)	176(3)	*-x,1-y,1-z*
	O3-H···O2	2.603(2)	174(3)	*-x,1-y,1-z*
	N1-H···O6	2.914(2)	161(2)	*1-x,-y,1-z*
	O1-H···O4	2.731(5)	101(4)	*1-x,2-y,-z*
(*rac*)-1-I (reacted)	O2-H···O3	2.604(3)	167(2)	*-x,2-y,-z*
	O4-H···O1	2.701(3)	158(3)	*-x,2-y,-z*
	N1-H···O6	2.946(4)	152(3)	*1-x*, 2-*y*, *z*
(*rac*)-1-II	O1-H···O4	2.721(2)	166(2)	*2-x,2-y,-z*
	O3-H···O2	2.655(2)	172(2)	*2-x,2-y,-z*
	N1-H···O2	3.015(2)	169(2)	*2-x, y+1, z*
	C9-H···O6	3.137(2)	157	*x, y+1, z*
(*R*)-1 (unreacted)	O6A-H···O1B	2.661(2)	157(7)	*x,y,z*
	O2B-H···O5A	2.668(2)	174(7)	*x,y,z*
	O6B-H···O2A	2.643(2)	166(7)	*x,y,z*
	O1A-H···O5B	2.617(2)	148(7)	*x,y,z*
	N1A-H···O4B	2.976(6)	152(6)	*x*-1, *y*, *z*-1
	N1B-H···O1B	2.984(7)	168(6)	*2+x*, *y*, *z*
(*R*)-1 (reacted)	O1A-H···O4B	2.637(4)	169(6)	*x,y,z*
	O3B-H···O2A	2.667(4)	176(5)	*x,y,z*
	O2B-H···O3A	2.659(4)	176(2)	*x,y,z*
	O4A-H···O1B	2.656(4)	169(5)	*x,y,z*
	N1B-H···O1B	3.017(5)	173(5)	*1+x*, *y*, *z*
	N1A-H···O5B	2.971(4)	166(5)	*x-1*, *y*, *z-1*
(*rac*)-2	O7-H···O8	2.726(3)	178(4)	*x,y,z*
	O3-H···O2	2.602(3)	172(4)	*1-x, 2-y, -z*
	O1-H···O4	2.695(3)	169(3)	*1-x, 2-y, -z*
	N1-H···O6	2.973(4)	161(3)	*-x, 1-y, 1-z*
(*rac*)-3	O1-H···O4	2.635(2)	172(2)	*x-3/2, -y+1/2, z-1/2*
	O3-H···O2	2.603(2)	169(3)	*x+3/2, y+1/2, z+1/2*
	N1-H···O4	2.945(2)	163(2)	*2+x ,y, z*