

Volume 72 (2016)

Supporting information for article:

Electron density, disorder and polymorphism: high-resolution diffraction studies of the highly polymorphic neuralgic drug Carbamazepine

Ioana Sovago, Matthias J. Gutmann, Hans Martin Senn, Lynne H. Thomas, Chick C. Wilson and Louis J. Farrugia

Supporting information

Figures S1-S6

Tables S1-S4

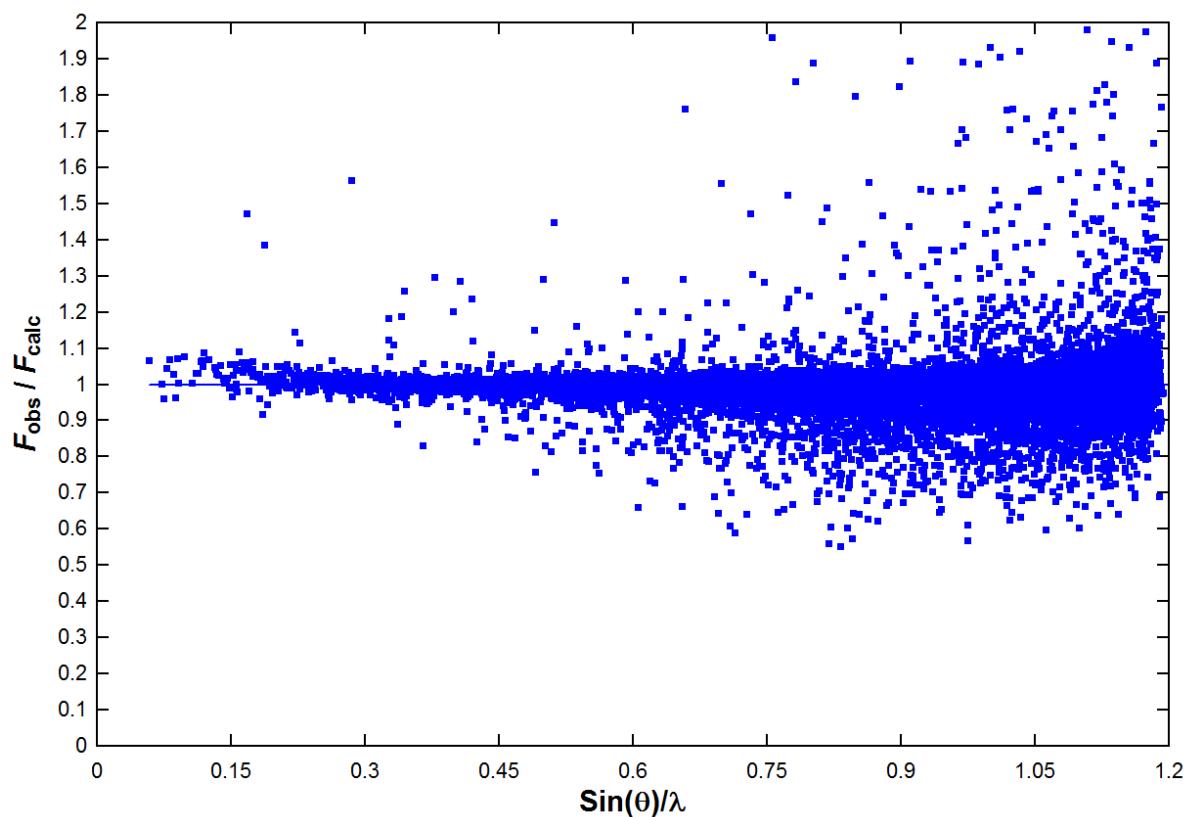


Figure S1 Scatter plot of the scale factor $F_{\text{obs}}/F_{\text{calc}}$ against $\sin(\theta)/\lambda$ for form III from final XD refinement.

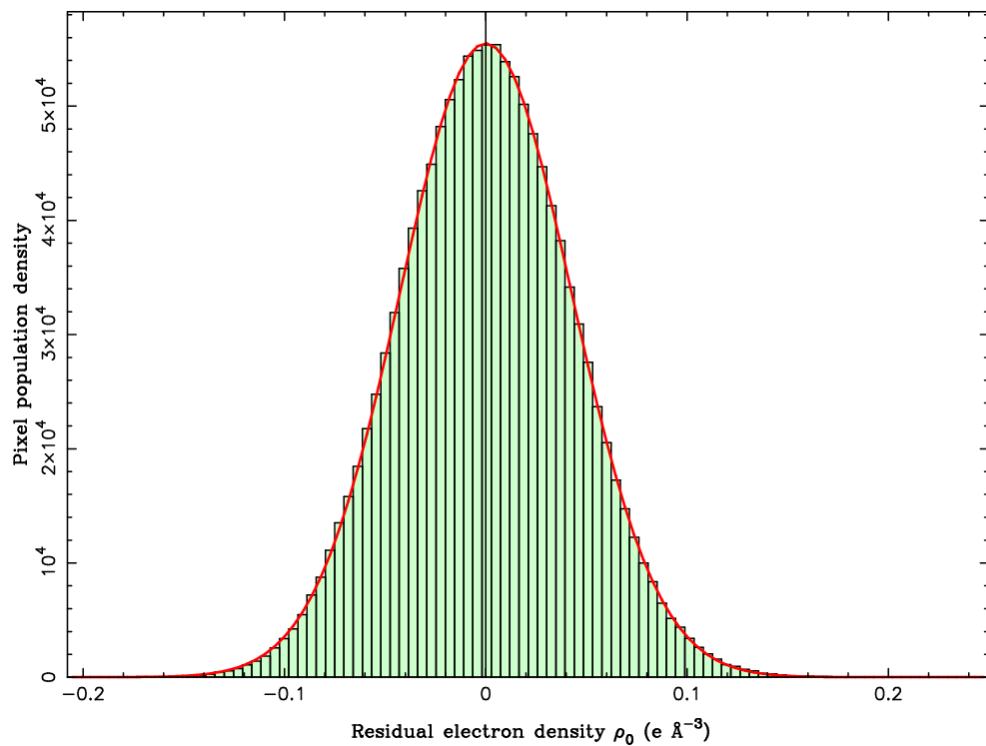


Figure S2 (a) Residual density histogram plot for form III from final XD refinement.

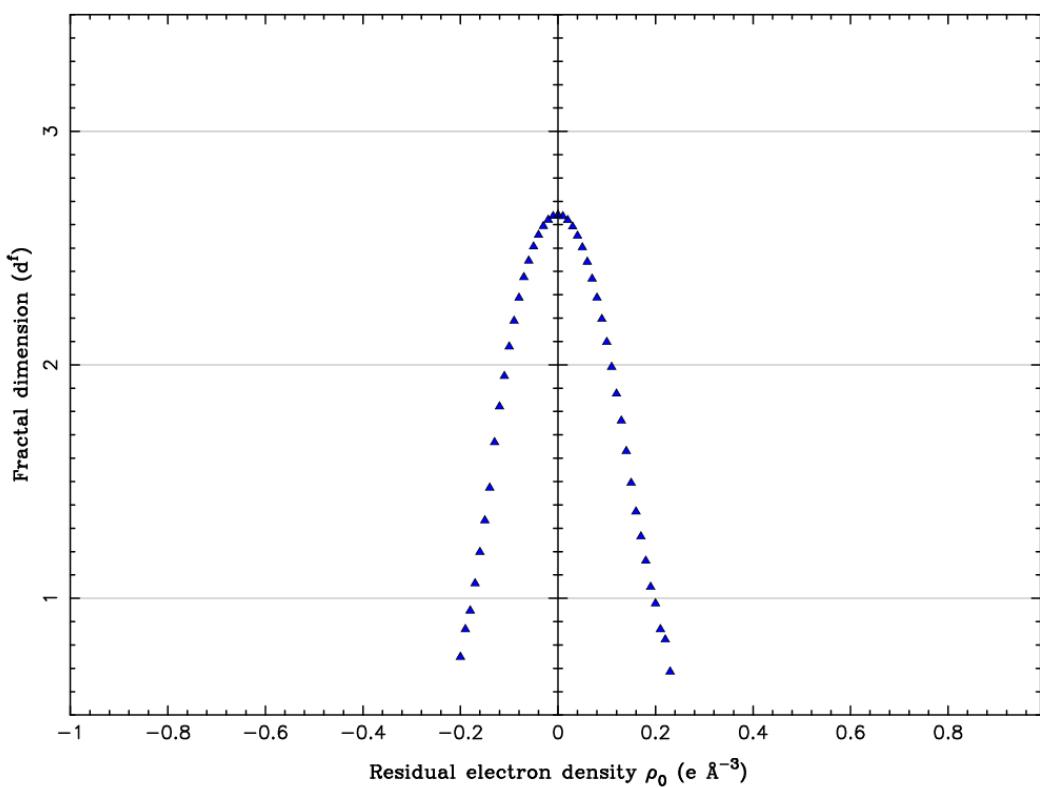


Figure S2 (b) Residual density fractal dimension plot for form III from final XD refinement.

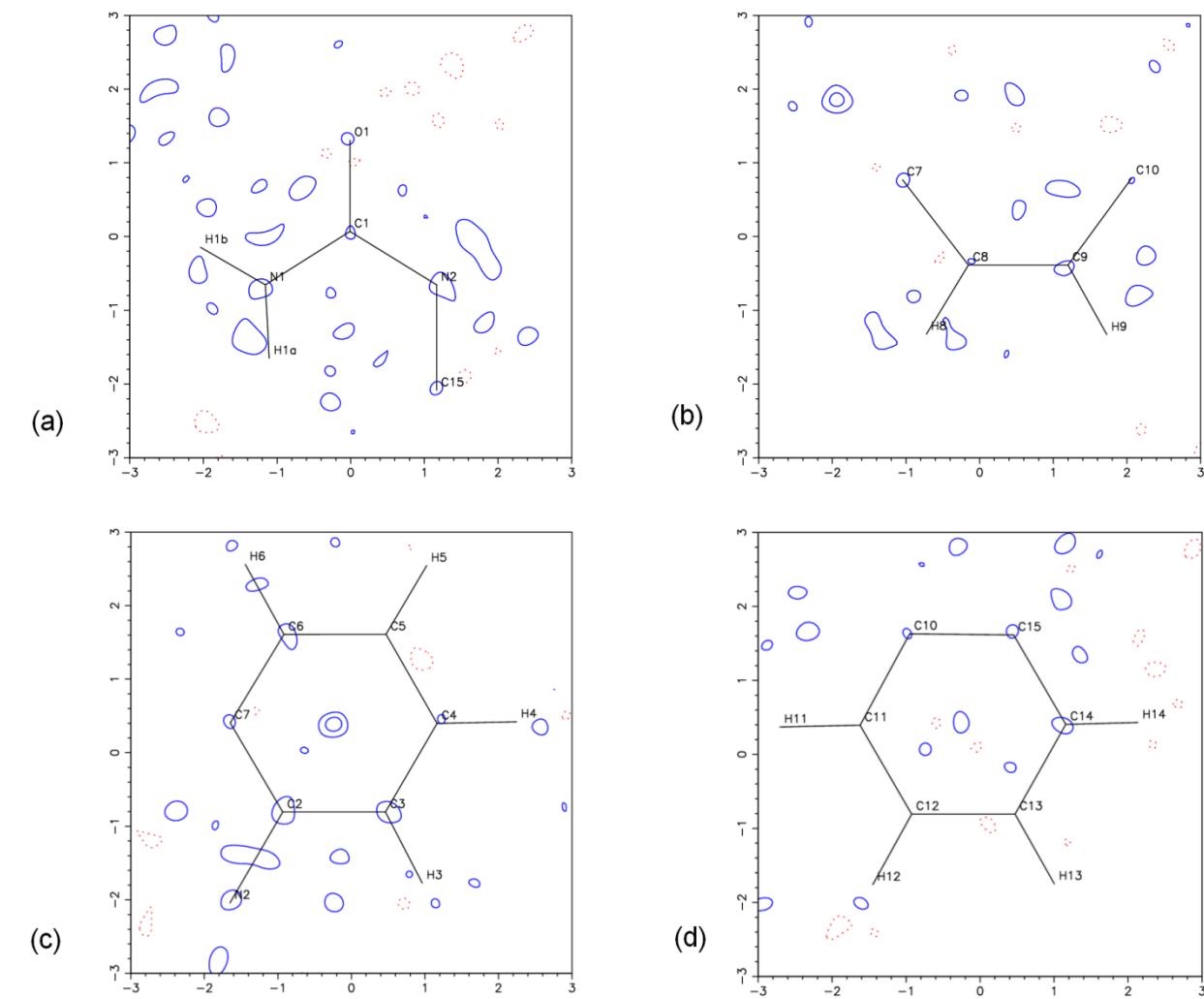


Figure S3 Residual electron density plots for form III in the planes of the (a) amide group (b) C(8)-C(9) double bond (c) benzene ring C(2)-C(7) and (d) benzene ring C(10)-C(15). Contours at $\pm 0.1 \text{ e}\text{\AA}^{-3}$, blue contours positive, red contours negative. All data included in the Fourier synthesis.

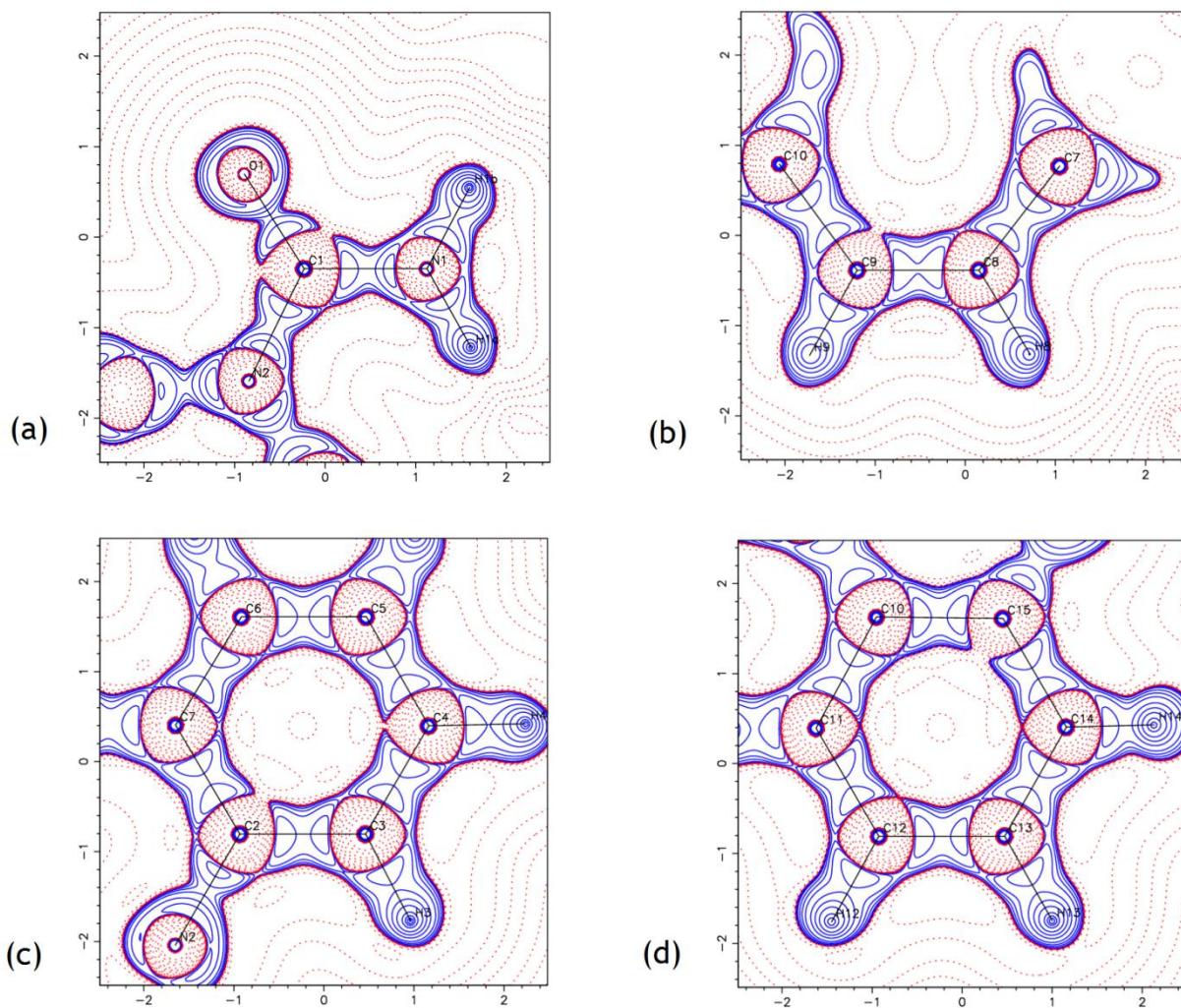


Figure S4 Plots of the experimental negative Laplacian, $L(\mathbf{r})$ for form III in the planes of the (a) amide group (b) C(8)-C(9) double bond (c) benzene ring C(2)-C(7) and (d) benzene ring C(10)-C(15). Positive contours – solid blue line; negative contours – red dotted line. The contour levels are at -1.0×10^{-3} , $\pm 2.0 \times 10^{-4}$, $\pm 4 \times 10^{-4}$, $\pm 8 \times 10^{-4}$ ($n = -3, -2, -1, 0, +1, +2$) e Å⁻⁵.

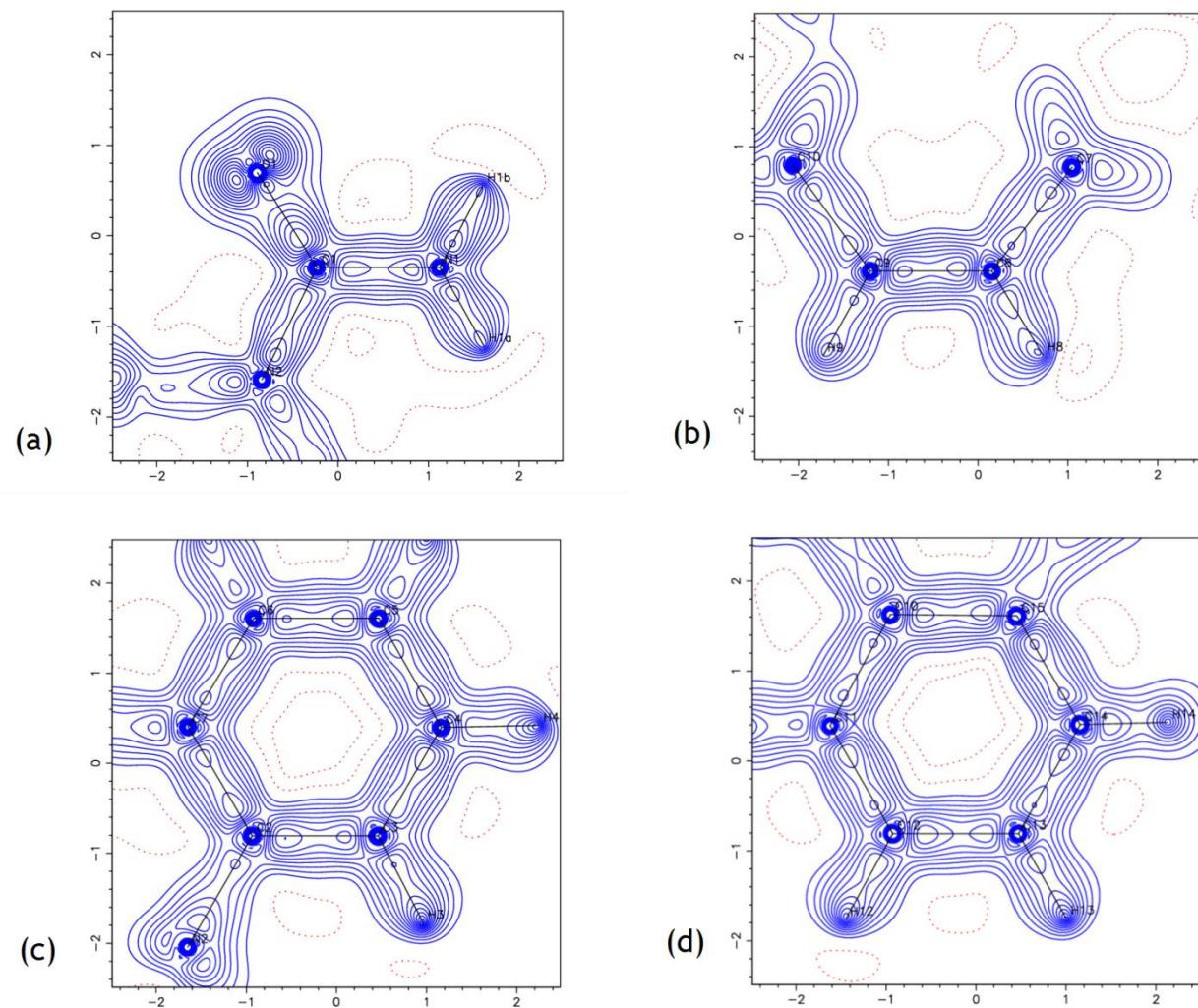


Figure S5 Plots of model deformation density maps for form III in the planes of the (a) amide group (b) C(8)-C(9) double bond (c) benzene ring C(2)-C(7) and (d) benzene ring C(10)-C(15). Positive contours – solid blue line; negative contours – red dotted line. The contour levels are at $0.1 \text{ e } \text{\AA}^{-3}$.

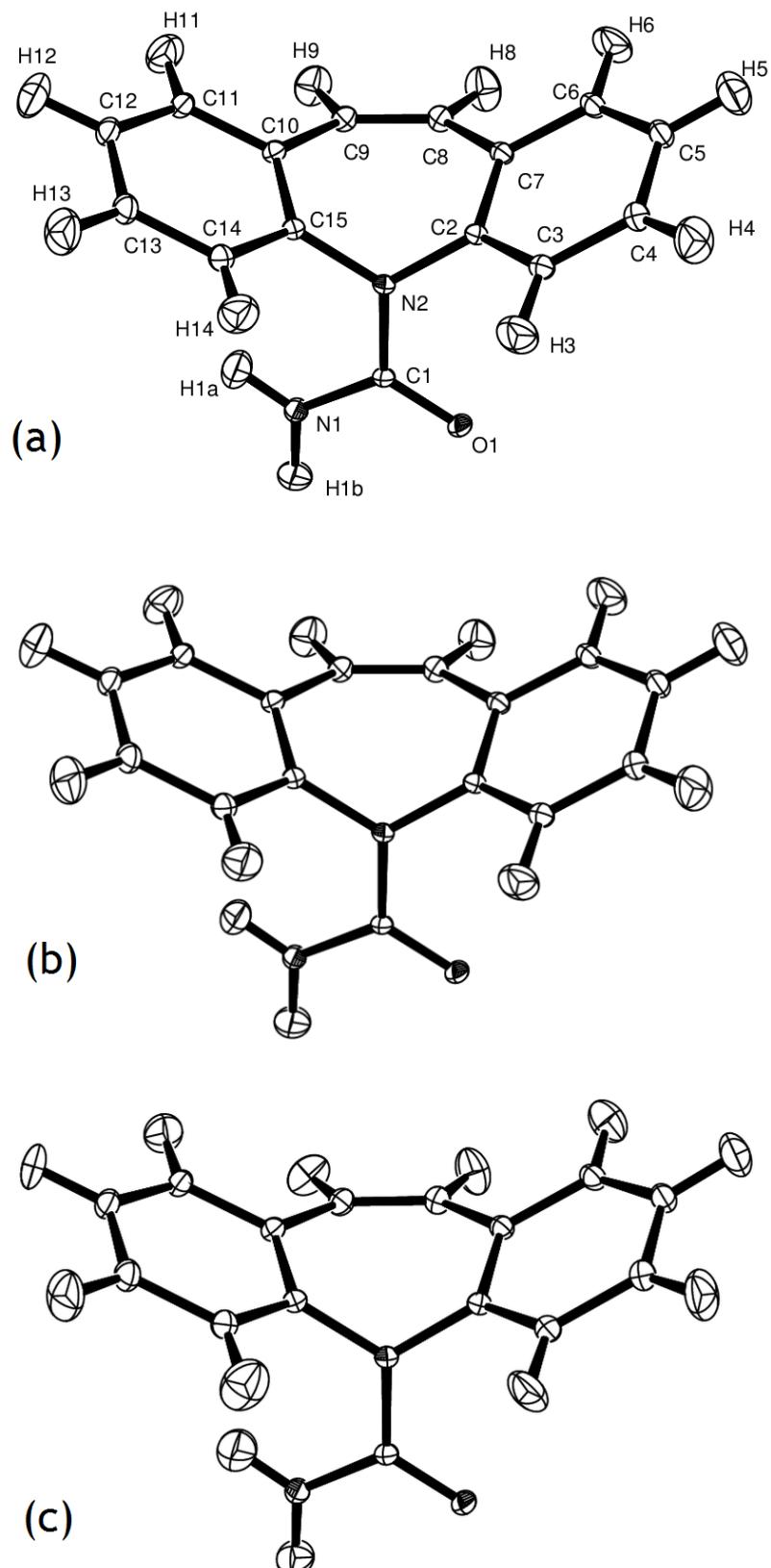


Figure S6 ORTEP plots of form III, showing the H atom anisotropic displacement parameters obtained from (a) the scaled neutron diffraction parameters (b) the SHADE procedure and (c) the Hirshfeld Atom Refinement (see text).

Table S1 Comparison of Atomic Anisotropic Displacement Parameters.¹

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0106(9)	0.0095(9)	0.0139(9)	-0.0032(7)	-0.0045(8)	0.0040(7)
	0.01198(6)	0.01160(6)	0.01428(6)	-0.00257(5)	-0.00242(5)	0.00400(5)
	0.0125(2)	0.0118(2)	0.0143(2)	-0.0040(1)	-0.0031(1)	0.0026(1)
N1	0.0141(7)	0.0128(7)	0.0140(6)	-0.0065(5)	-0.0042(5)	0.0055(5)
	0.01583(6)	0.01303(6)	0.01493(6)	-0.00576(5)	-0.00424(5)	0.00527(5)
	0.0164(2)	0.0133(2)	0.0151(2)	-0.0053(2)	-0.0048(2)	0.0055(2)
N2	0.0091(6)	0.0097(6)	0.0089(5)	-0.0024(4)	-0.0008(5)	0.0040(4)
	0.01142(5)	0.01054(5)	0.00965(5)	-0.00236(4)	-0.00068(4)	0.00393(4)
	0.0115(2)	0.0108(2)	0.0099(1)	-0.0038(1)	-0.0010(1)	0.0022(1)
C1	0.0078(7)	0.0081(8)	0.0087(7)	-0.0016(5)	0.0003(6)	0.0019(6)
	0.00915(4)	0.00895(4)	0.01018(5)	-0.00145(4)	0.00038(3)	0.00181(3)
	0.0093(2)	0.0091(2)	0.0104(2)	-0.0018(1)	0.0000(1)	0.0014(1)
C2	0.0095(8)	0.0077(8)	0.0079(7)	-0.0010(6)	0.0002(6)	0.0018(6)
	0.01035(5)	0.00952(5)	0.00923(5)	-0.00127(4)	0.00070(4)	0.00176(4)
	0.0105(2)	0.0096(2)	0.0094(2)	-0.0019(1)	0.0002(1)	0.0012(1)
C3	0.0094(8)	0.0128(9)	0.0114(8)	-0.0021(6)	-0.0001(7)	0.0014(6)
	0.01073(5)	0.01403(6)	0.01200(5)	-0.00232(5)	0.00095(4)	0.00048(4)
	0.0109(2)	0.0142(2)	0.0122(2)	-0.0006(1)	0.0003(1)	0.0023(2)
C4	0.0121(9)	0.0140(9)	0.0115(8)	-0.0028(6)	-0.0017(7)	0.0001(7)
	0.01360(6)	0.01459(6)	0.01309(6)	-0.00267(5)	-0.00091(5)	-0.00052(5)
	0.0139(2)	0.0148(2)	0.0133(2)	0.0004(2)	-0.0016(2)	0.0026(2)

C5	0.0147(10)	0.0125(9)	0.0107(8)	-0.0030(6)	-0.0014(7)	0.0011(7)
	0.01703(7)	0.01314(6)	0.01070(5)	-0.00249(5)	-0.00041(5)	0.00069(5)
	0.0174(2)	0.0133(2)	0.0108(2)	-0.0009(2)	-0.0010(2)	0.0025(2)
C6	0.0154(10)	0.0111(9)	0.0090(7)	-0.0012(6)	0.0008(7)	0.0012(7)
	0.01567(6)	0.01264(6)	0.00936(5)	-0.00111(4)	0.00194(4)	0.00117(5)
	0.0157(2)	0.0128(2)	0.0096(2)	-0.0013(2)	0.0015(1)	0.0011(2)
C7	0.0097(8)	0.0091(8)	0.0079(7)	0.0002(6)	0.0016(6)	0.0013(6)
	0.01190(5)	0.00985(5)	0.00906(5)	-0.00014(4)	0.00147(4)	0.00100(4)
	0.0120(2)	0.0100(2)	0.0092(2)	-0.0011(1)	0.0010(1)	0.0001(1)
C8	0.0105(8)	0.0113(9)	0.0121(8)	0.0017(6)	0.0014(7)	-0.0006(6)
	0.01311(6)	0.01320(6)	0.01169(6)	0.00173(5)	0.00194(4)	-0.00089(4)
	0.0132(2)	0.0133(2)	0.0119(2)	0.0009(2)	0.0014(1)	-0.0017(2)
C9	0.0087(8)	0.0119(9)	0.0137(9)	0.0014(6)	0.0011(7)	-0.0007(6)
	0.01159(5)	0.01285(6)	0.01377(6)	0.00098(5)	0.00075(4)	-0.00055(4)
	0.0117(2)	0.0130(2)	0.0141(2)	0.0006(2)	0.0000(2)	-0.0010(2)
C10	0.0092(8)	0.0085(8)	0.0102(8)	-0.0003(6)	-0.0007(7)	0.0022(6)
	0.01060(5)	0.01036(5)	0.01158(5)	-0.00040(4)	-0.00048(4)	0.00176(4)
	0.0109(2)	0.0105(2)	0.0117(2)	-0.0018(1)	-0.0011(1)	0.0004(1)
C11	0.0101(8)	0.0125(9)	0.0141(8)	-0.0010(7)	-0.0029(7)	0.0028(7)
	0.01187(6)	0.01362(6)	0.01411(6)	-0.00085(5)	-0.00232(5)	0.00255(5)
	0.0124(2)	0.0137(2)	0.0143(2)	-0.0026(2)	-0.0031(2)	0.0010(2)
C12	0.0136(9)	0.0113(9)	0.0127(8)	-0.0010(6)	-0.0045(7)	0.0029(7)
	0.01647(7)	0.01251(6)	0.01368(6)	-0.00012(5)	-0.00409(5)	0.00313(5)
	0.0172(2)	0.0126(2)	0.0139(2)	-0.0031(2)	-0.0049(2)	0.0001(2)

C13	0.0169(10)	0.0130(9)	0.0102(8)	0.0012(6)	-0.0017(7)	0.0022(7)
	0.01855(7)	0.01433(6)	0.01145(6)	0.00164(5)	-0.00151(5)	0.00221(5)
	0.0190(3)	0.0145(2)	0.0116(2)	-0.0021(2)	-0.0022(2)	-0.0017(2)
C14	0.0136(9)	0.0129(9)	0.0099(8)	0.0009(6)	0.0002(7)	0.0022(7)
	0.01450(6)	0.01414(6)	0.01053(5)	0.00084(5)	0.00081(4)	0.00215(5)
	0.0147(2)	0.0143(2)	0.0108(2)	-0.0021(2)	0.0003(2)	-0.0008(2)
C15	0.0092(8)	0.0096(8)	0.0078(7)	-0.0005(5)	-0.0001(6)	0.0028(6)
	0.01092(5)	0.01013(5)	0.00957(5)	-0.00053(4)	-0.00001(4)	0.00261(4)
	0.0112(2)	0.0102(2)	0.0098(2)	-0.0027(1)	-0.0005(1)	0.0006(1)
H1A	0.027(3)	0.032(3)	0.028(2)	-0.0088(19)	-0.012(2)	0.011(2)
	0.02654	0.027262	0.025115	0.008263	-0.007414	-0.003396
	0.0380	0.0414	0.0356	-0.0060	-0.0073	0.0123
H1B	0.025(2)	0.018(2)	0.026(2)	-0.0067(16)	-0.0015(19)	0.0079(16)
	0.032312	0.023882	0.031647	0.011651	-0.003924	-0.009613
	0.0307	0.0222	0.0278	-0.0037	-0.0005	0.0031
H3	0.024(3)	0.038(3)	0.026(2)	-0.007(2)	0.007(2)	-0.001(2)
	0.022393	0.03504	0.024566	-0.002482	0.007919	-0.005216
	0.0252	0.0424	0.0207	0.0058	0.0063	0.0116
H4	0.022(3)	0.037(3)	0.032(3)	-0.005(2)	-0.001(2)	-0.010(2)
	0.023908	0.033426	0.032522	-0.008591	-0.001495	-0.007657
	0.0234	0.0438	0.0318	0.0095	-0.0039	0.0045
H5	0.038(3)	0.033(3)	0.022(2)	-0.0105(19)	-0.003(2)	-0.004(2)
	0.037268	0.035152	0.021132	-0.002965	-0.000768	-0.011924

	0.0321	0.0356	0.0221	-0.0003	-0.0060	0.0089
H6	0.029(3)	0.038(3)	0.021(2)	-0.008(2)	0.010(2)	-0.002(2)
	0.030538	0.038973	0.021545	-0.001397	0.010254	-0.004584
	0.0393	0.0324	0.0217	0.0087	0.0039	0.0001
H8	0.031(3)	0.041(3)	0.020(2)	0.004(2)	0.005(2)	-0.010(2)
	0.03039	0.037615	0.020463	-0.0052	0.006942	0.005478
	0.0364	0.0397	0.0244	0.0104	0.0032	0.0002
H9	0.020(2)	0.031(3)	0.032(3)	0.006(2)	0.000(2)	-0.0084(19)
	0.018589	0.035937	0.033233	-0.007089	0.00154	0.003073
	0.0215	0.0320	0.0401	0.0046	0.0042	-0.0054
H11	0.015(2)	0.043(3)	0.034(3)	0.003(2)	0.000(2)	0.002(2)
	0.017233	0.037334	0.035976	0.000842	-0.000361	0.003506
	0.0200	0.0407	0.0305	-0.0001	0.0020	0.0002
H12	0.029(3)	0.030(3)	0.030(3)	0.0048(19)	-0.013(2)	0.005(2)
	0.029124	0.03872	0.028747	0.007058	-0.010896	0.005384
	0.0297	0.0380	0.0252	-0.0060	-0.0138	-0.0046
H13	0.036(3)	0.041(3)	0.019(2)	0.011(2)	0.000(2)	0.003(2)
	0.038544	0.039469	0.018716	0.002614	0.000873	0.008351
	0.0351	0.0467	0.0193	-0.0008	0.0014	-0.0112
H14	0.022(2)	0.037(3)	0.027(2)	0.004(2)	0.003(2)	0.001(2)
	0.021355	0.037352	0.025322	0.000575	0.005026	0.003126
	0.0237	0.0451	0.0333	-0.0010	0.0046	-0.0123

¹ Top entry in list from neutron diffraction, second from multipole modelling of X-ray data and third from Hirshfeld Atom Refinement using X-ray data. For the H atoms, the second entry is the fixed contribution estimated by SHADE procedure. The estimated errors for the third entry (HAR values) for H atoms are typically 0.01 – 0.02 Å²

Table S2 Bond Critical Point Properties for H-Atom Model a, see text.¹

24	(3,-1)	C(10)	-C(15)	0.7017	0.7041	2.19	-16.32	-17.94	-13.77	15.39	0.30	2.21	1.01	-
5.56				5.56	-3.35									
25	(3,-1)	H(11)	-C(11)	0.3836	0.7047	1.94	-18.98	-19.04	-18.31	18.37	0.04	1.53	0.79	-
4.40				4.40	-2.86									
26	(3,-1)	C(12)	-C(11)	0.6847	0.7039	2.24	-18.14	-18.40	-14.75	15.02	0.25	2.23	1.00	-
5.73				5.73	-3.50									
27	(3,-1)	H(12)	-C(12)	0.3735	0.7159	1.95	-19.17	-19.47	-18.44	18.74	0.06	1.56	0.80	-
4.46				4.46	-2.90									
28	(3,-1)	C(13)	-C(12)	0.6825	0.7146	2.17	-16.11	-17.20	-14.14	15.24	0.22	2.18	1.00	-
5.49				5.49	-3.31									
29	(3,-1)	C(13)	-C(14)	0.6919	0.7014	2.19	-16.53	-17.27	-14.45	15.19	0.20	2.19	1.00	-
5.53				5.53	-3.35									
30	(3,-1)	H(13)	-C(13)	0.3698	0.7126	1.93	-18.90	-19.33	-18.40	18.83	0.05	1.52	0.79	-
4.35				4.35	-2.84									
31	(3,-1)	H(14)	-C(14)	0.3036	0.6745	1.95	-14.92	-20.43	-19.50	25.02	0.05	1.75	0.90	-
4.54				4.54	-2.79									
32	(3,-1)	C(14)	-C(15)	0.6883	0.7104	2.23	-17.54	-18.53	-14.32	15.30	0.29	2.25	1.01	-
5.72				5.72	-3.48									

¹ d₁/d₂ are nearest two distances (Å) to bcp; σ in units e Å⁻³; ∇²(σ), λ₁, λ₂, λ₃ in units e Å⁻⁵; kinetic energy densities (G_b) estimated according to Abramov [Abramov, Y. A. (1997) Acta Cryst. A53, 264] ; G_b, V_b, Eb in units Hartree Å⁻³.

Table S3 Bond Critical Point Properties for H-Atom Model b, see text.¹

24	(3,-1)	C(10)	-C(15)	0.7016	0.7043	2.16	-16.35	-17.62	-13.38	14.65	0.32	2.14	0.99	-
5.43				5.43	-3.29									
25	(3,-1)	H(11)	-C(11)	0.3776	0.7108	1.92	-18.82	-19.10	-18.36	18.64	0.04	1.50	0.78	-
4.33				4.33	-2.82									
26	(3,-1)	C(12)	-C(11)	0.6874	0.7008	2.22	-18.59	-18.30	-14.56	14.27	0.26	2.17	0.98	-
5.64				5.64	-3.47									
27	(3,-1)	H(12)	-C(12)	0.3724	0.7168	1.97	-19.00	-19.68	-18.62	19.31	0.06	1.61	0.82	-
4.56				4.56	-2.94									
28	(3,-1)	C(13)	-C(12)	0.6782	0.7191	2.16	-16.69	-17.08	-14.02	14.41	0.22	2.13	0.98	-
5.43				5.43	-3.30									
29	(3,-1)	C(13)	-C(14)	0.6930	0.7002	2.19	-17.79	-17.53	-14.57	14.31	0.20	2.15	0.98	-
5.54				5.54	-3.39									
30	(3,-1)	H(13)	-C(13)	0.3676	0.7148	1.92	-20.09	-19.67	-18.78	18.36	0.05	1.46	0.76	-
4.32				4.32	-2.86									
31	(3,-1)	H(14)	-C(14)	0.2994	0.6795	1.92	-15.07	-20.47	-19.55	24.95	0.05	1.67	0.87	-
4.40				4.40	-2.73									
32	(3,-1)	C(14)	-C(15)	0.6914	0.7071	2.21	-18.23	-18.53	-14.19	14.49	0.31	2.18	0.98	-
5.63				5.63	-3.45									

¹ d₁/d₂ are nearest two distances (Å) to bcp; σ in units e Å⁻³; ∇²(σ), λ₁, λ₂, λ₃ in units e Å⁻⁵; kinetic energy densities (G_b) estimated according to Abramov [Abramov, Y. A. (1997) Acta Cryst. A53, 264] ; G_b, V_b, Eb in units Hartree Å⁻³.

Table S4 Bond Critical Point Properties for H-Atom Model c, see text.¹

V_b	E_b	A - B	d_1	d_2	σ	$-\nabla^2(\sigma)$	λ_1	λ_2	λ_3	ε	G_b	G_b/f
1	(3,-1)	C(1) - O(1)	0.4740	0.7637	3.10 9.71	-38.78 -6.21	-29.29	-26.43	16.94	0.11	3.50	1.13
2	(3,-1)	C(1) - N(1)	0.5982	0.7588	2.46 6.72	-21.39 -4.11	-21.69	-18.20	18.50	0.19	2.61	1.06
3	(3,-1)	H(1A) - N(1)	0.2672	0.7174	2.56 6.82	-37.69 -4.73	-36.46	-34.88	33.66	0.05	2.09	0.82
4	(3,-1)	H(1B) - N(1)	0.2674	0.7206	2.44 6.34	-33.17 -4.33	-33.97	-32.58	33.37	0.04	2.01	0.82
5	(3,-1)	C(1) - N(2)	0.6053	0.7770	2.24 5.75	-17.03 -3.47	-19.16	-15.99	18.12	0.20	2.28	1.02
6	(3,-1)	C(2) - N(2)	0.6361	0.7942	1.99 4.83	-10.86 -2.79	-15.78	-14.34	19.26	0.10	2.03	1.02
7	(3,-1)	C(15) - N(2)	0.6375	0.7939	2.04 5.00	-11.48 -2.90	-16.15	-14.90	19.57	0.08	2.10	1.03
8	(3,-1)	C(3) - C(2)	0.6855	0.7109	2.21 5.64	-17.02 -3.41	-18.09	-13.76	14.83	0.31	2.22	1.01
9	(3,-1)	C(7) - C(2)	0.6984	0.7075	2.08 5.08	-15.79 -3.09	-16.72	-13.14	14.08	0.27	1.99	0.96
10	(3,-1)	H(3) - C(3)	0.4029	0.6706	1.96 4.49	-19.56 -2.93	-18.47	-17.54	16.45	0.05	1.56	0.79

11	(3,-1)	C(3)	-C(4)	0.6803	0.7128	2.22	-18.26	-18.01	-14.73	14.48	0.22	2.19	0.99	-
						5.67	-3.47							
12	(3,-1)	H(4)	-C(4)	0.3872	0.6997	1.94	-21.43	-19.55	-18.10	16.22	0.08	1.43	0.73	-
						4.35	-2.93							
13	(3,-1)	H(5)	-C(5)	0.3667	0.7205	1.94	-20.06	-19.80	-18.16	17.89	0.09	1.49	0.77	-
						4.39	-2.90							
14	(3,-1)	C(4)	-C(5)	0.6948	0.7028	2.09	-16.30	-16.62	-13.51	13.83	0.23	1.98	0.95	-
						5.09	-3.12							
15	(3,-1)	C(6)	-C(5)	0.6918	0.6969	2.21	-18.19	-18.23	-14.31	14.35	0.27	2.17	0.98	-
						5.62	-3.45							
16	(3,-1)	H(6)	-C(6)	0.4111	0.6726	1.89	-19.70	-17.93	-16.98	15.20	0.06	1.40	0.74	-
						4.18	-2.78							
17	(3,-1)	C(6)	-C(7)	0.7038	0.7038	2.19	-17.50	-17.69	-14.39	14.58	0.23	2.14	0.98	-
						5.51	-3.37							
18	(3,-1)	C(8)	-C(7)	0.7312	0.7321	1.90	-12.66	-14.65	-12.61	14.60	0.16	1.76	0.92	-
						4.41	-2.65							
19	(3,-1)	C(8)	-C(9)	0.6755	0.6766	2.49	-22.59	-20.94	-16.23	14.57	0.29	2.63	1.06	-
						6.85	-4.22							
20	(3,-1)	H(9)	-C(9)	0.3819	0.7031	1.92	-20.05	-18.85	-18.14	16.94	0.04	1.45	0.76	-
						4.31	-2.86							
21	(3,-1)	H(8)	-C(8)	0.4082	0.6767	1.95	-19.52	-18.24	-17.59	16.31	0.04	1.53	0.79	-
						4.43	-2.90							
22	(3,-1)	C(9)	-C(10)	0.7262	0.7360	1.88	-12.56	-14.42	-12.54	14.40	0.15	1.72	0.92	-
						4.33	-2.60							
23	(3,-1)	C(11)	-C(10)	0.7011	0.7054	2.24	-18.19	-18.45	-14.65	14.91	0.26	2.24	1.00	-
						5.76	-3.52							

24	(3,-1)	C(15)	-C(10)	0.7010	0.7046	2.10	-15.53	-16.95	-13.01	14.42	0.30	2.05	0.97	-
						5.18	-3.13							
25	(3,-1)	H(11)	-C(11)	0.4235	0.6731	1.92	-19.74	-17.81	-17.31	15.38	0.03	1.47	0.76	-
						4.32	-2.85							
26	(3,-1)	H(14)	-C(14)	0.3803	0.7025	1.92	-19.51	-18.75	-17.97	17.21	0.04	1.47	0.77	-
						4.30	-2.83							
27	(3,-1)	C(12)	-C(11)	0.6902	0.6985	2.19	-17.46	-17.82	-14.09	14.45	0.26	2.15	0.98	-
						5.51	-3.37							
28	(3,-1)	H(12)	-C(12)	0.3537	0.7316	2.00	-21.09	-20.66	-19.22	18.78	0.08	1.57	0.78	-
						4.61	-3.04							
29	(3,-1)	H(13)	-C(13)	0.3830	0.6997	1.93	-19.98	-19.06	-18.05	17.12	0.06	1.47	0.76	-
						4.35	-2.87							
30	(3,-1)	C(13)	-C(12)	0.6947	0.7023	2.06	-15.01	-15.98	-13.28	14.25	0.20	1.99	0.96	-
						5.03	-3.04							
31	(3,-1)	C(13)	-C(14)	0.6891	0.7040	2.26	-18.51	-18.39	-14.86	14.74	0.24	2.26	1.00	-
						5.81	-3.55							
32	(3,-1)	C(14)	-C(15)	0.6928	0.7057	2.17	-16.95	-17.87	-13.61	14.54	0.31	2.13	0.98	-
						5.44	-3.31							

¹ d₁/d₂ are nearest two distances (Å) to bcp; σ in units e Å⁻³; ∇²(σ), λ₁, λ₂, λ₃ in units e Å⁻⁵; kinetic energy densities (G_b) estimated according to Abramov [Abramov, Y. A. (1997) Acta Cryst. A53, 264] ; G_b, V_b, Eb in units Hartree Å⁻³.