Is it all in the hinge? A kryptoracemate and three of its alternative racemic polymorphs of an aminonitrile

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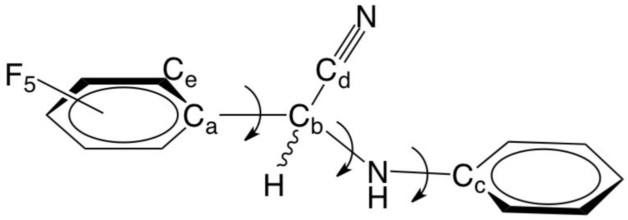
Fig. S1: Large *krypto*-**1** crystal obtained by very slow evaporation from a hexane solution: 1.75 cm and 13.01 mg

Table 1

	Z′	Torsion angle C_a-C_b-N-C_c (°)	Torsion angle C_c-N-C_b-C_d (°)	Torsion angle C_e- C_a -C_b-N (°)	Dihedral angle aryl rings (°)
krypto-**1**	2	166.37(14) 77.1(2)	69.2(2) -160.56(15)	-72.3(2) -111.76(19)	62.14(10) 85.95(9)
rac-**1a**	2	144.6(3) 159.3(3)	-89.6(4) -74.5(4)	-92.6(5) -77.1(5)	29.0(2) 31.2(2)
rac-**1b**	4	-161.8(8) 174.6(8) -168.9(8) 131.5(8)	73.8(10) -59.9(11) 66.9(11) -107.6(9)	-58.0(10) -114.9(10) -72.7(13) -116.5(9)	46.8(5) 42.6(5) 44.2(5) 34.8(5)
rac-**1c**	1	173.80(14)	-66.7(2)	-123.46(16)	58.90(8)



The kryptoracemate *krypto*-**1**, $C_{14}H_7F_5N_2$, crystallizes in the orthorhombic chiral space group $P2_12_12_1$ with one well-ordered enantiomeric pair in the asymmetric unit (Z'= 2) . As the chiral space group only allows proper symmetry operations, the only possibility for a racemic mixture to crystallize as a well-ordered structure in such a space group is to have both opposite enantiomers in the asymmetric unit. The two enantiomeric molecules of opposite chirality are depicted in Fig. 3. Unlike the majority of known kryptoracemates who show pseudosymmetry, ours consists of two molecules which differ significantly in conformation. Torsion angles C_a-C_b-N-C_c amount -166.37(14) and 77.1(2) for the two independent molecules. The first molecule adopts a twisted conformation in which the dihedral angles subtended by the aryl rings amount to 62.14(10)° whereas the second independent molecule reveals a bent conformation in which the two aryl rings form an angle of 85.95(9)°. One of the two independent moieties exhibits a classical[footnote ‡] heterogenous N-H...N hydrogen bond (Fig. S2, S3) with the donor- acceptor N-N distance amounting to 3.102(2) Å.

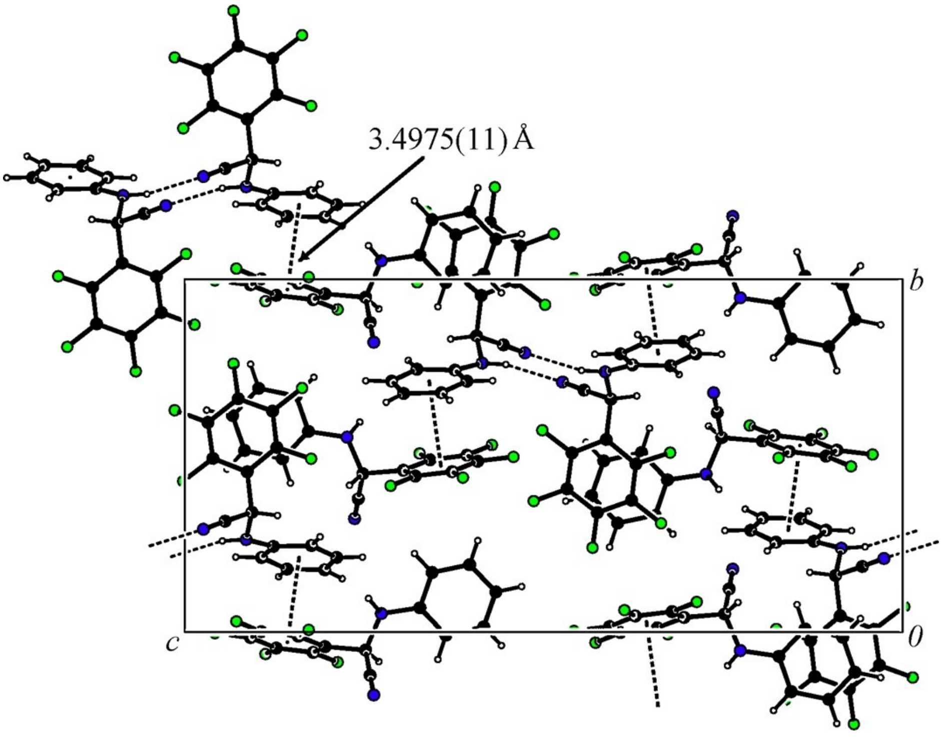


Fig. S2: Packing of the molecules by hydrogen bonding and π-π stacking interactions in *krypto*-**1**, view from the *a* direction in *krypto*-**1**

This leads to an infinite chain containing $C^2_2(10)$ motifs[1, footnote ‡‡] along the *a* direction (Fig. S3), while the second independent molecule is associated to this chain through π-π stacking interactions between the electronically different substituted aryl rings of the (*R*)- and (*S*)-enantiomers amounting to 3.4975(11) Å and no slippage (Fig. S2). Overall an one-dimensional structure is generated. Intra-molecular hydrogen bonds between the hydrogen attached to the chiral atom and the nearest fluorine neighboring atoms amount 2.8481(19) Å and 2.876(2) Å for the two independent molecules respectively.

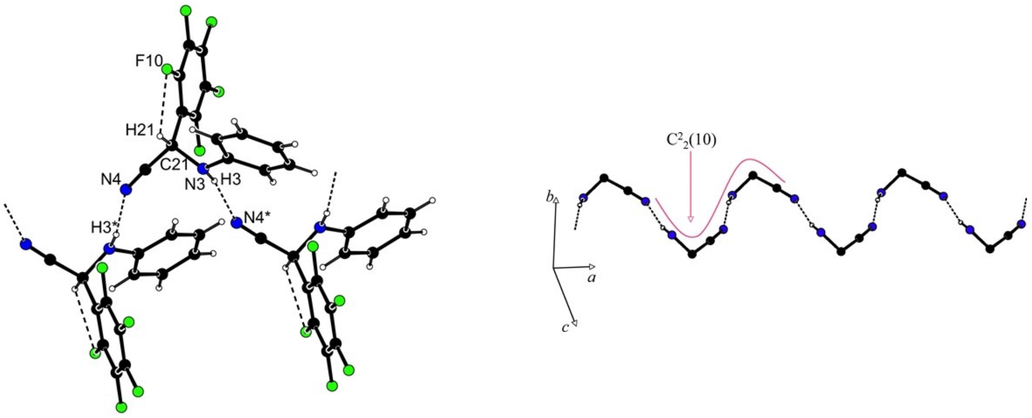


Fig S3. Classical N-H…N hydrogen bonds forming an infinite chain along a direction, containing $C^2_2(10)$ motifs in one independent molecule in the asymmetric unit of *krypto*-**1**

Non-classical hydrogen bonding interactions (NCHb)[2-3] formed between less electronegative donors such as C-H bonds and lone pair electron groups such as N, O, F and π systems as acceptors may be important in molecular and chiral recognition and crystal packing. Between the two independent moieties in the asymmetric unit a weak T- shaped stacking contact (F7- c_g) amounting to 3.3293(14) is present. There is also evidence of weak N…F possible contacts between the two independent residues (F10…N2* 2.994(2) Å, * = 2-x, -1/2+y, 3/2-z).

Space filling for this structure is 70.1%.

The second polymorph, *rac*-**1a,** $C_{14}H_7F_5N_2$, is an ordered racemic structure crystallizing as a monoclinic twin with a *ß* angle of approximately 90° in the monoclinic space group $P2_1/c$ with two independent molecules of the same chirality and similar conformation in the asymmetric unit (Fig. 3 and Fig. S4 for an overlap of the two independent residues) with torsion angles C_a-C_b-N-C_c of 144.6(3) and 159.3(3) respectively.

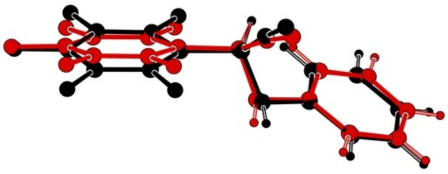


Fig. S4: Overlap of the two independent molecules in the asymmetric unit of *rac*-1a

Aryl rings are twisted at about 30° with respect to the perfluorophenyl rings. An infinite one-dimensional chain appear between the hydrogen atoms of the -NH group and the –CN groups of different residues with N-H ….N bonds which give rise to $C^2_2(10)$ motifs[1, footnote] ‡ which amount to 3.043(5) Å and 3.087(5) Å for the donor-acceptor distances. Adjacent chains are running parallel along the *c* axis (Fig. S5 and Fig. S6).

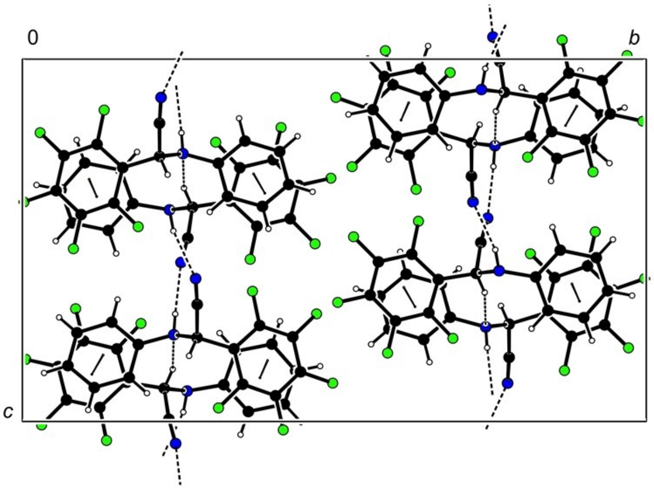


Fig S5. Packing with hydrogen bonding and π-π stacking interactions in *rac*-1a, view from the *a* direction

A short non-classical intramolecular hydrogen bond C7-H7…F5 amounts to 2.809(5) Å. π stacking interactions occur between electronically different substituted aryl rings with the shortest distances c_g-c_g up to 3.849(3) Å (Fig. S5).

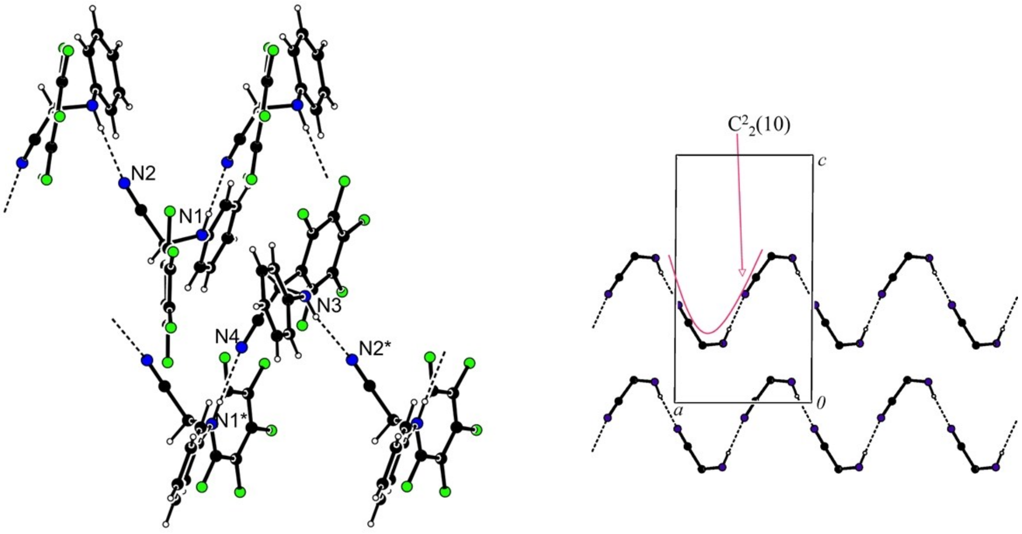


Fig S6. Classical N-H...N hydrogen bonds forming an infinite chain along *a* direction, containing $C^{2}_{2}(10)$ motifs in *rac*-**1a**

Although there are similarities between the lattice parameters of the *krypto*-**1** and *rac*-**1**, the two structures show no group-subgroup relationship, the independent molecules show different conformation and therefore the acentric structure *krypto*-**1** does not mimic the racemic structure. Space filling for this structure is 69.3 %.

A third polymorphic structure of **1** was only obtained in a very small amount in a crystallization experiment which resulted in 96% *krypto*-**1** as huge rod crystal and 4% *rac*-**1b** as very thin needle twinned crystals. This polymorph crystallizes as a racemic twin in the achiral polar space group $Pna2_1$ with four independent molecules in the asymmetric unit, two pairs of opposite enantiomers which show slightly different conformations. There is an elevated number of independent molecules in the asymmetric unit. Torsion angles C_a-C_b-N-C_c are within the range 131.5(8) and 174.6(8). Aryl rings are twisted with respect to the perfluorophenyl rings at angles varying between 34.8(5) and 46.8(5). The four independent molecules in the asymmetric unit of *rac*-**1b** are shown in Fig. 2. An overlap of the pairs of residues of the same chirality is ploted in Fig. S7.

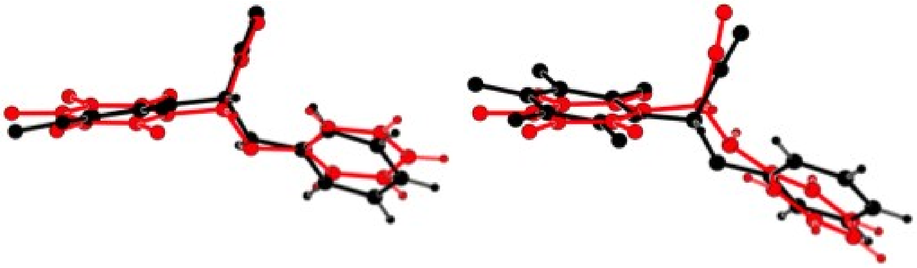


Fig. S7: Overlap of the independent molecules in *rac*-**1b** having same chirality and different conformations

The two enantiomeric molecules of the same chirality are associated through classical hydrogen bonds N - H...N amounting to 3.173(11) and 3.209(12) Å donor-acceptor distance for N1 - H1...N6 (the *R* enantiomers) and N3 - H3...N8 (the *S* enantiomers- Fig. S8) respectively. Between one residue and its symmetry equivalent N-H...F hydrogen bonds are formed with donor-acceptor distance of 2.918(9) Å (N1-H1...F5a, a = x, 1+y, z).

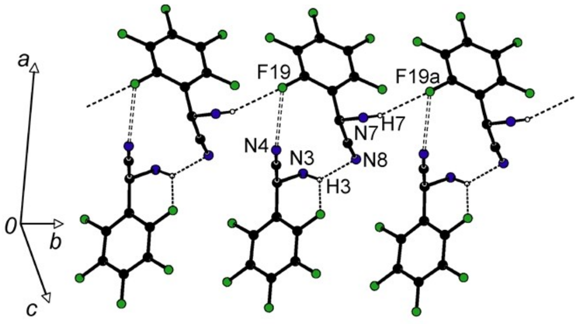


Fig. **S8**: Hydrogen bonding between the (*S*)- enantiomers. Aryl rings have been excluded for clarity. Symmetry operations a = x,1+y,z,

Besides, there are N...F halogen contacts present (N4...F19; N2...F15b) giving rise to infinite chains along *b*-axis. The two chains are further associated by weak π - π stacking interactions with the shortest c_g...c_g distance of 3.624(7) Å. No pseudosymmetry between the enantiomers of opposite chirality are present. Space filling for this structure is 70.9%.

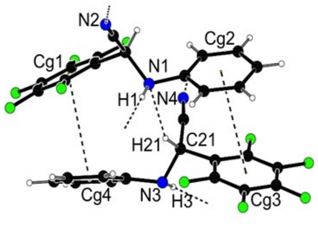


Fig. **S9**: Hydrogen bonding and π - π stacking interactions in *rac*-1b

A fourth polymorphic structure for **1** was lately obtained by evaporation of a hexane solution over a week. Crystals are hexagonal plates, very well diffracting. Note that up to that event, we did not observe such crystals in our multiple crystallization experiments. This polymorph crystallizes trivially in the monoclinic space group $P2_1/c$ with one molecule in the asymmetric unit. The two perfluophenyl and phenyl rings are twisted with respect to the other and subtend an dihedral angle of 58.90(8)° (Fig. 2, Table 1). Classical hydrogen N-H…N bonds with donor-acceptor distance of 3.087(2) Å occur between the molecules within the molecular packing forming infinite one-dimensional chains in the *c* direction (Fig. S9 and Fig. S10). c_g...c_g distance of 3.8629(10) Å are rather large. Space filling for this structure amounts to 72.8 %, slightly larger that for the other polymorphs but not extraordinary.

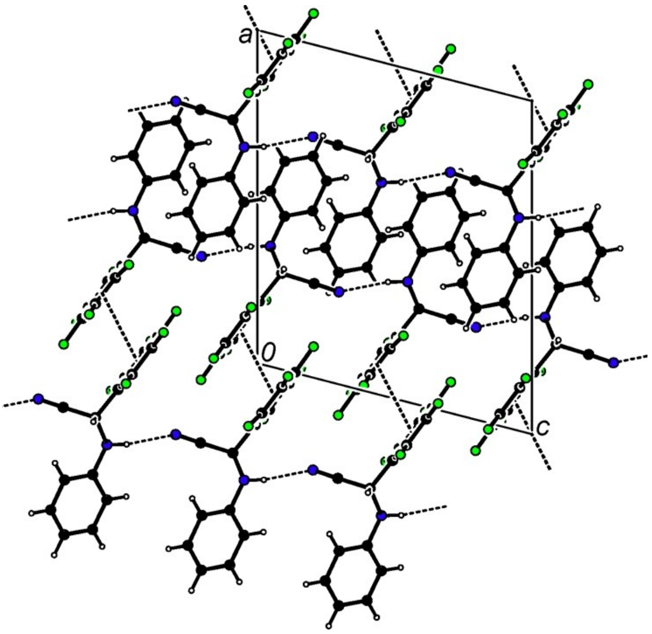


Fig. S9: Hydrogen bonding and packing in *rac*-**1c**, view from the *b* direction

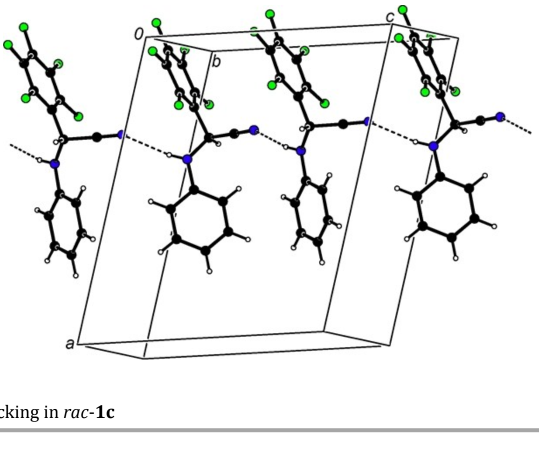


Fig. S10: Hydrogen bonding and packing in *rac*-**1c**

Footnote ‡: The expressions "classical" hydrogen bonding refers to a bond subtended by two kinds of electronegative atoms. The "non-classical" hydrogen bonds are defines as C-H...X bonds, where X = N, O, Cl, etc..

Footnote ‡‡: Graph set assignment of hydrogen bond motifs according to Etter[1]: A graph set $G^{a}_{d}(r)$ is specified using the pattern designator (G), its degree (r), and the number of donors (d) and acceptors (a). G is a descriptor referring to the pattern of hydrogen bonding. It has four different assigmnements based on whether hydrogen bonds are inter- or intramoleculer: S, C, R and D. S standing for self, C standing for chain, R standing for rings, D refers to noncyclic dimers and other finite hydrogen-bonded sets.

Experimental

General Methods and Instrumentation. Until completeness of the Strecker-type synthesis all steps were carried out under argon atmosphere using standard Schlenk techniques. Dichloromethane was purified and dried by conventional methods. 2,3,4,5,6-Pentafluorobenzaldehyde and gallium(III) trifluoromethane-sulfonate were obtained from abcr, trimethylsilyl cyanide was obtained from Sigma-Aldrich and stored in an argon atmosphere. All other reagents and solvents were commercially available and used as received. NMR analyses were carried out with a Bruker AVANCE II 400 or 500 spectrometer. ^{1}H NMR shifts were referenced to the residual proton signals of the deuterated solvent ($CHDCl_2$ at $\delta = 5.32$ ppm). HR-ESI-MS analyses were carried out with a Micromass Q-TOF II spectrometer.

General procedure for synthesis of the 2-(perfluorophenyl)-2-(phenylamino)acetonitrile

The Strecker-type synthesis was performed analogue as described in the literature[4]. Pentafluorobenzaldehyde (2 mmol) and the corresponding amine (2 mmol) dissolved in 4 mL of CH_2Cl_2 was added to $Ga(OTf)_3$ (5 mol%). TMSCN (3 mmol) was then added and the reaction mixture was stirred at room temperature until the reaction was finished with monitoring by ^{1}H and ^{19}F NMR spectroscopy (ca. 2 days). The mixture was then filtered and the solvent of the filtrate was removed under reduced pressure to isolate the desired product as a colourless solid. Further purification could be achieved by washing the residue with *n*-hexane. 50% yield; elemental analysis (%) calc. for $C_{14}H_7F_5N_2$ (298.21): C 56.39, H 2.37, N 9.39 and found: C 56.07, H 2.36, N 9.16; HR-ESI-MS ([**1**-H]$^{-}$, m/z): calc.: 297.0451 and found: 297.0453; ^{1}H NMR (400.1 MHz, CD_2Cl_2): $\delta = 7.18$ (m, 2H, *meta*-Ar), 6.95 (m, 1H, *para*-Ar), 6.81 (m, 2H, *ortho*-Ar), 5.79 (d, ^{3}J(H,H) = 11 Hz, 1H, C*H*NH), 4.39 ppm (d, ^{3}J(H,H) = 11 Hz, 1H, CHN*H*); ^{19}F NMR (470.6 MHz, CD_2Cl_2): $\delta = -142.3$ (m, 2F, *ortho*-Ar), -151.3 (m, 1F, *para*-Ar), -160.4 ppm (m, 2F, *meta*-Ar).

Single Crystal X-ray diffraction

The data were collected with a BRUKER D8 VENTURE area detector, Cu-*K*α radiation (λ = 1.54178 Å) for *krypto*-**1**, *rac*-**1a** and *rac*-**1b** and Mo-*K*α radiation (λ = 0.71073 Å) for *rac*-**1c** crystal structures. Multi-scan absorption corrections implemented in SADABS[5] were applied to the data. The structures were solved by intrinsic phasing method (SHELXT-2013) and refined by full-matrix least square procedures based on *F*2 with all measured reflections (SHELXL-2013) with anisotropic temperature factors for all non-hydrogen atoms.[6, 7] All hydrogen atoms were added geometrically and refined by using a riding model except for the aminic hydrogen atoms and the hydrogen atoms attached to the chiral carbon atom which were found in the electron density map and freely refined. Crystallographic data are given below. CCDC 1414258 (*krypto*-**1**), CCDC 1414259 (*rac*-**1a**), CCDC 1414260 (*rac*-**1b**), CCDC 1414261 (*rac*-**1c**) contain the supplementary crystallographic data for this paper.

These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

Crystal data

Compound	*krypto*-**1**	*rac*-**1a**	*rac*-**1b**	*rac*-**1c**
Formula	$C_{14}H_7F_5N_2$	$C_{14}H_7F_5N_2$	$C_{14}H_7F_5N_2$	$C_{14}H_7F_5N_2$
M_r /g·mol^{-1}	298.22	298.22	298.22	298.22
Cryst. system	orthorhombic	monoclinic	orthorhombic	monoclinic
Space group	$P2_12_12_1$	$P2_1/c$	$Pna2_1$	$P2_1/c$
a /Å	7.6294(5)	7.6779(2)	25.3241(16)	13.9748(10)
b /Å	12.6995(8)	23.7528(6)	6.5350(5)	7.4518(5)
c /Å	25.8239(17)	13.8443(3)	29.874(2)	11.8994(8)
α /°	90	90	90	90
β /°	90	90.3699(9)	90	104.487(2)
γ /°	90	90	90	90
V /Å^3	2502.1(3)	2524.75(11)	4943.9(6)	1199.77(14)
Z	8	8	16	4
Z'	2	2	4	1
Density / g·cm^{-3}	1.583	1.569	1.603	1.651
F(000)	1200	1200	2400	600
R_{int}	0.0366	0.0738	0.1811	0.0406
Total nr. of refl.	15750	15505	44264	13284
Indep. refl.	4872	4349	8260	2202
Refl. with $I>2\sigma(I)$	4677	4077	4789	1822
Parameters	387	396	787	198
Radiation	Cu	Cu	Cu	Mo
Θ-range (°)	3.88- 74.68	3.19- 67.68	2.96- 67.68	3.01- 25.47
R_1	0.0256	0.0697	0.0607	0.0340
wR_2	0.0669	0.1686	0.1090	0.0790
R_1 (all data)	0.0272	0.0750	0.1362	0.0468
wR_2 (all data)	0.0684	0.1740	0.1381	0.0854
GoF	1.031	1.093	1.014	1.007
Completness	100 %	99 %	100 %	100 %
Largest diff. peak and hole /e·Å	-0.17/ 0.14	-0.29/ 0.50	-0.29/ 0.26	-0.19/ 0.23
CCDC	1414258	1414259	1414260	1414261

Matrix of root mean square deviation (rms) [8]

	mol 1	mol 2	mol 3	mol 4	mol 5	mol6	mol 7	mol 8	mol 9
	krypto-1		**rac-1a**		**rac-1b**				**rac-1c**
krypto-1									
mol 1		0.96	1.0	0.66	0.20	0.28	0.27	0.84	0.30
mol 2			0.86	1.04	0.91	1.16	0.96	0.71	1.15
rac-1a									
mol 3				0.26	0.61	0.67	0.57	0.34	0.87
mol 4					0.97	0.67	0.57	0.56	0.90
rac-1b									
mol 5						0.31	0.32	0.49	0.33
mol 6							0.13	0.65	0.29
mol 7								0.57	0.38
mol 8									0.76

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