Supramolecular synthon hierarchy in cyclopropyl-containing peptide-derived compounds

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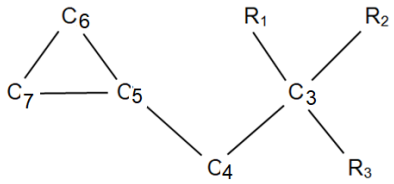
Scheme 1, Figures S1 to S26, Tables S1 to S21

Description of *Synthesis* and *Pharmacokinetic Measurements*, details of *Molecular Docking*

Contents



	R_1	R_2	R_3
1	- $CO–OC_2H_5$	- $CO–OC_2H_5$	- $NH–CO–CH_3$
2 (3)	- COOH	- COOH	- $NH–CO–CH_3$
4	- H	- COOH	- $NH–CO–CH_3$
5	- H	- COOH	- $NH–CO–CH_2–C_{13}H_9$

Scheme S1 Schematic representation moiety under quantum-chemical calculations.

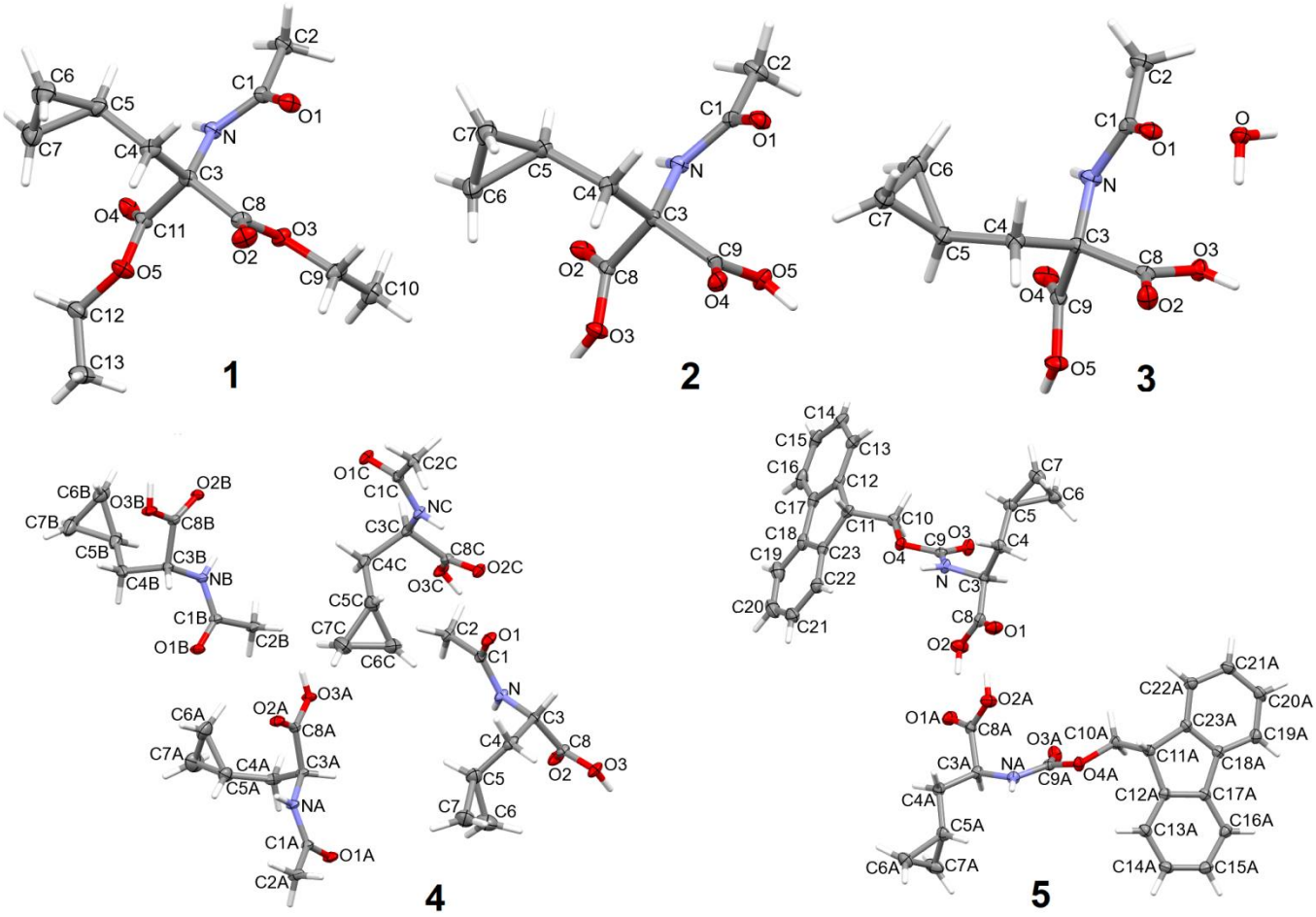


Fig. S1 The molecular structures of **1-5** showing the atom labellling schemes for non-hydrogen atoms. The displacement of ellipsoids is drawn at a probability level of 30 %.

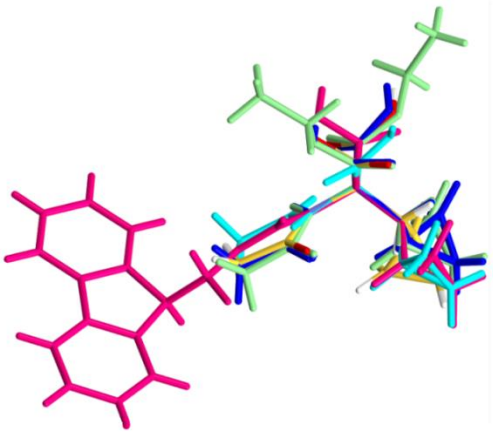


Fig. S2 Overlay (by N-C3-C4) of the studied molecules: **1** (green), **2** (dark blue), **3** (yellow), **4** (light blue), **5** (magenta)

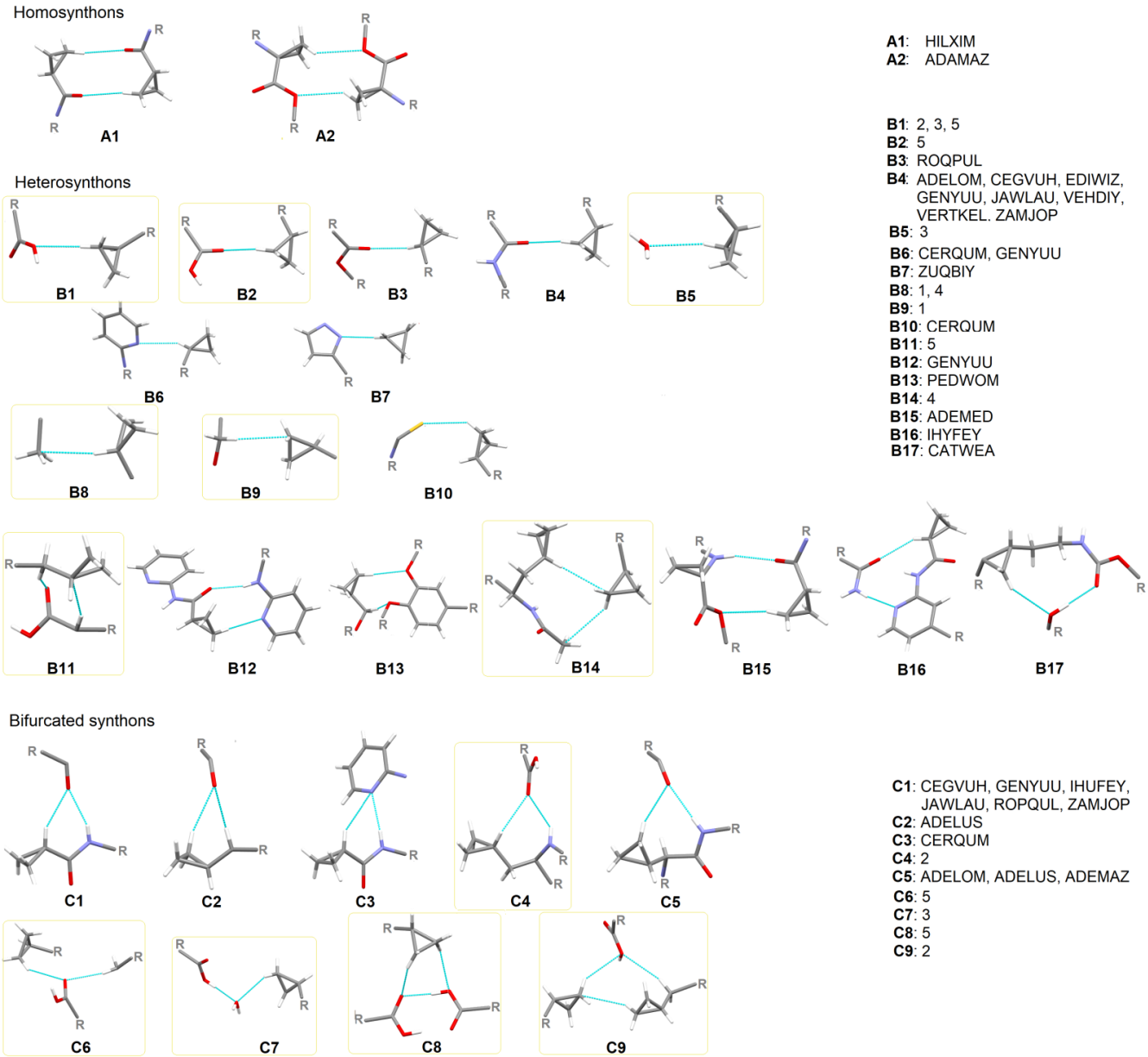


Fig. S3 Particular cyclopropyl-based supramolecular H-bonding patterns identified in **1**-**5** and those derived from the CSD (new motifs, realized for the first time, in yellow frames).

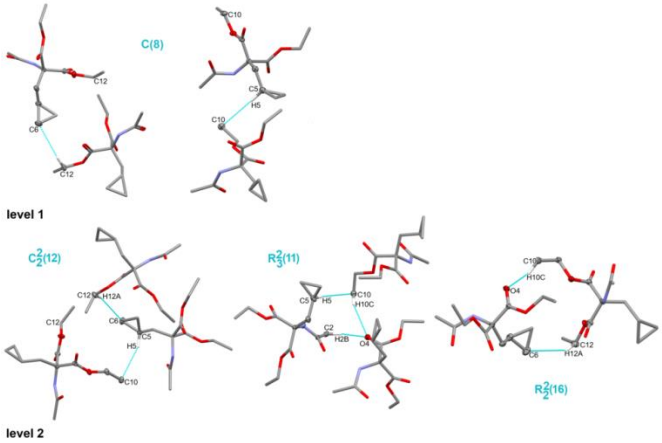


Fig. S4 Cyclopropyl-based H-bonding patterns in **1**

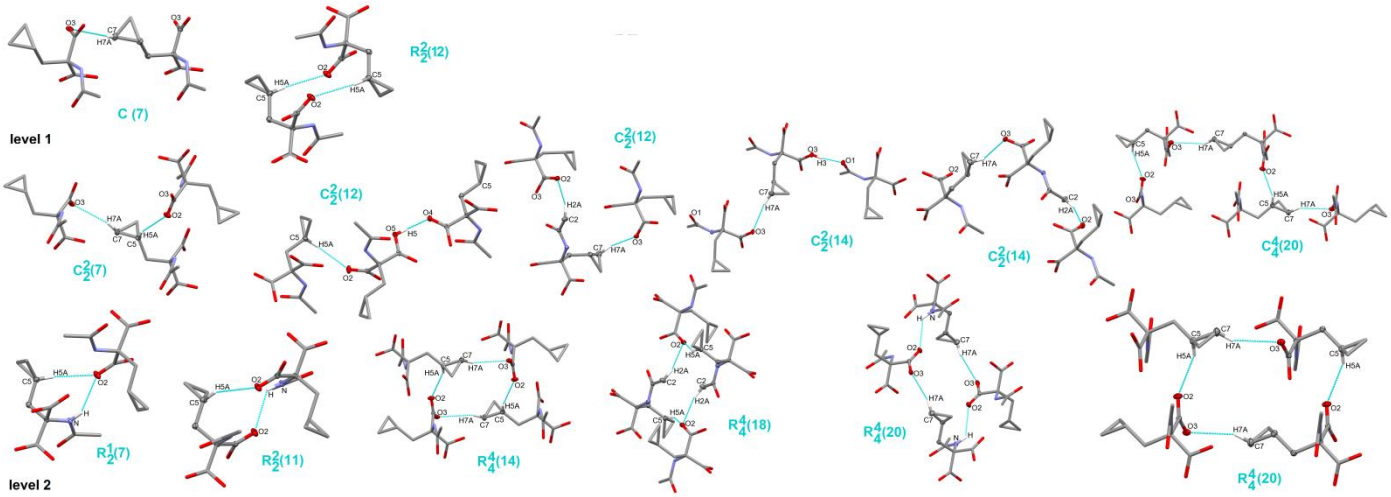


Fig. S5 Cyclopropyl-based H-bonding patterns in **2**

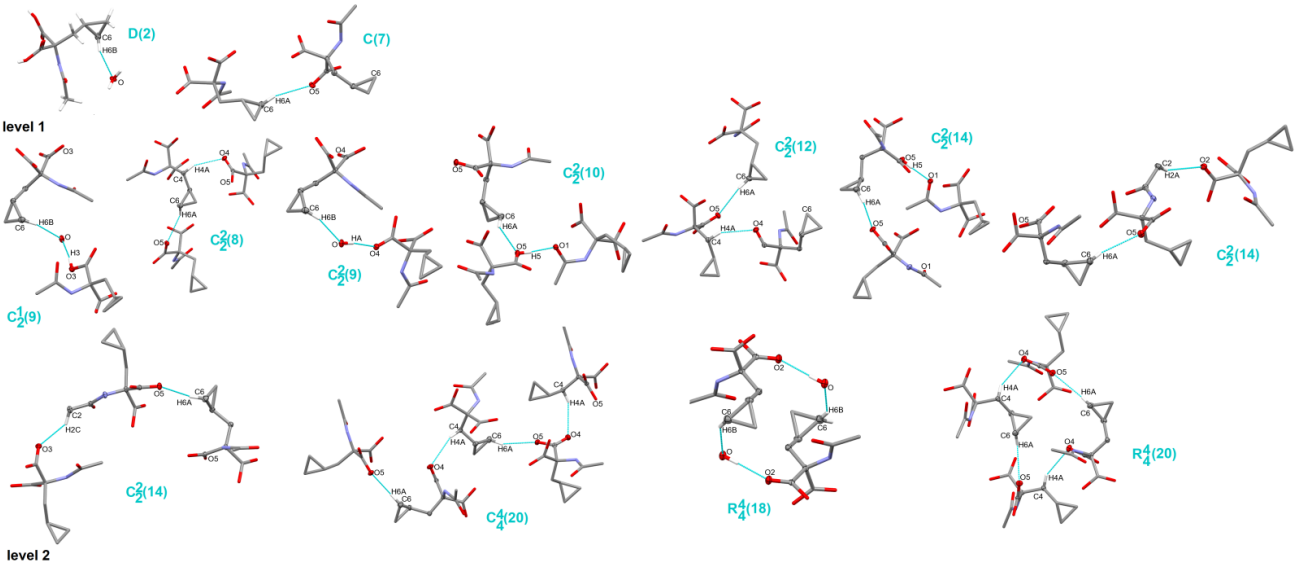


Fig. S6 Cyclopropyl-based H-bonding patterns in **3**

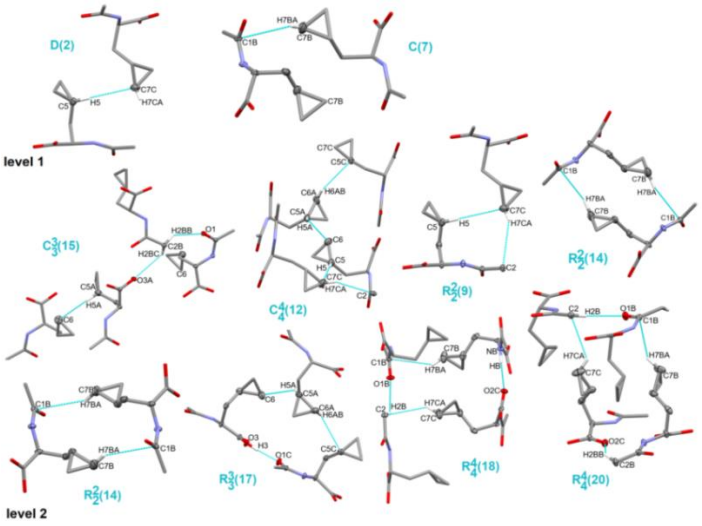


Fig. S7 Cyclopropyl-based H-bonding patterns in **4**

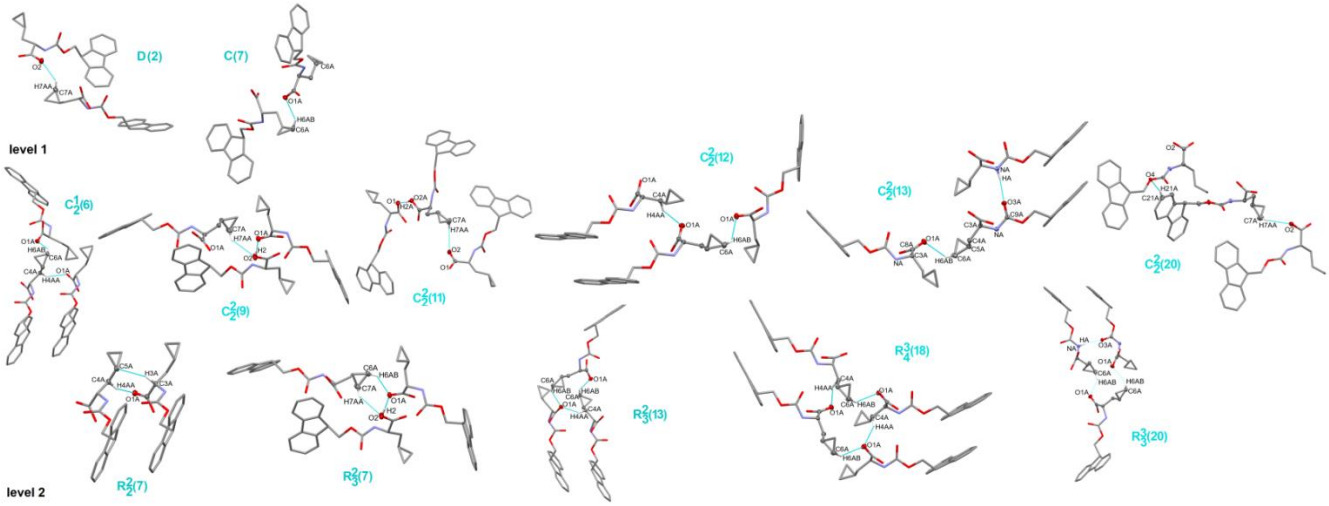


Fig. S8 Cyclopropyl-based H-bonding patterns in **5**

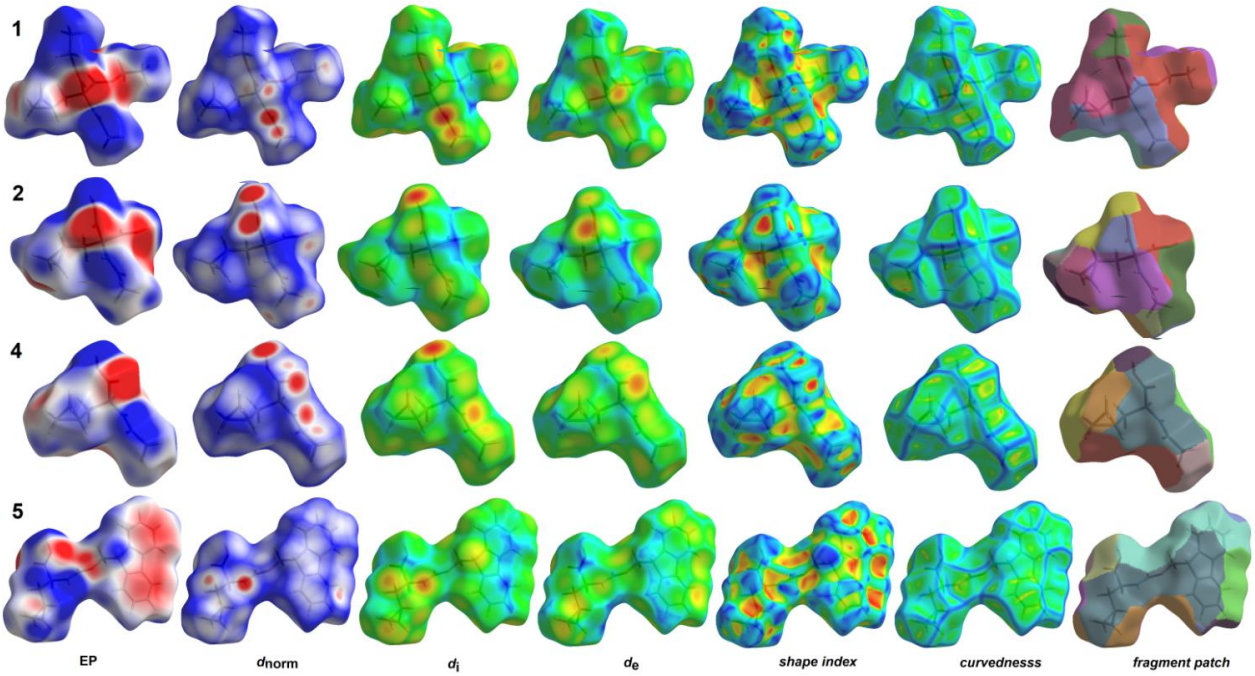


Fig. S9 Hirshfeld surfaces with different properties for **1**-**5**: the d_{norm} (−0.25 a.u. to 0.01 a.u.), d_i and d_e properties, *shape index*, *curvedness* and *fragment patch*.

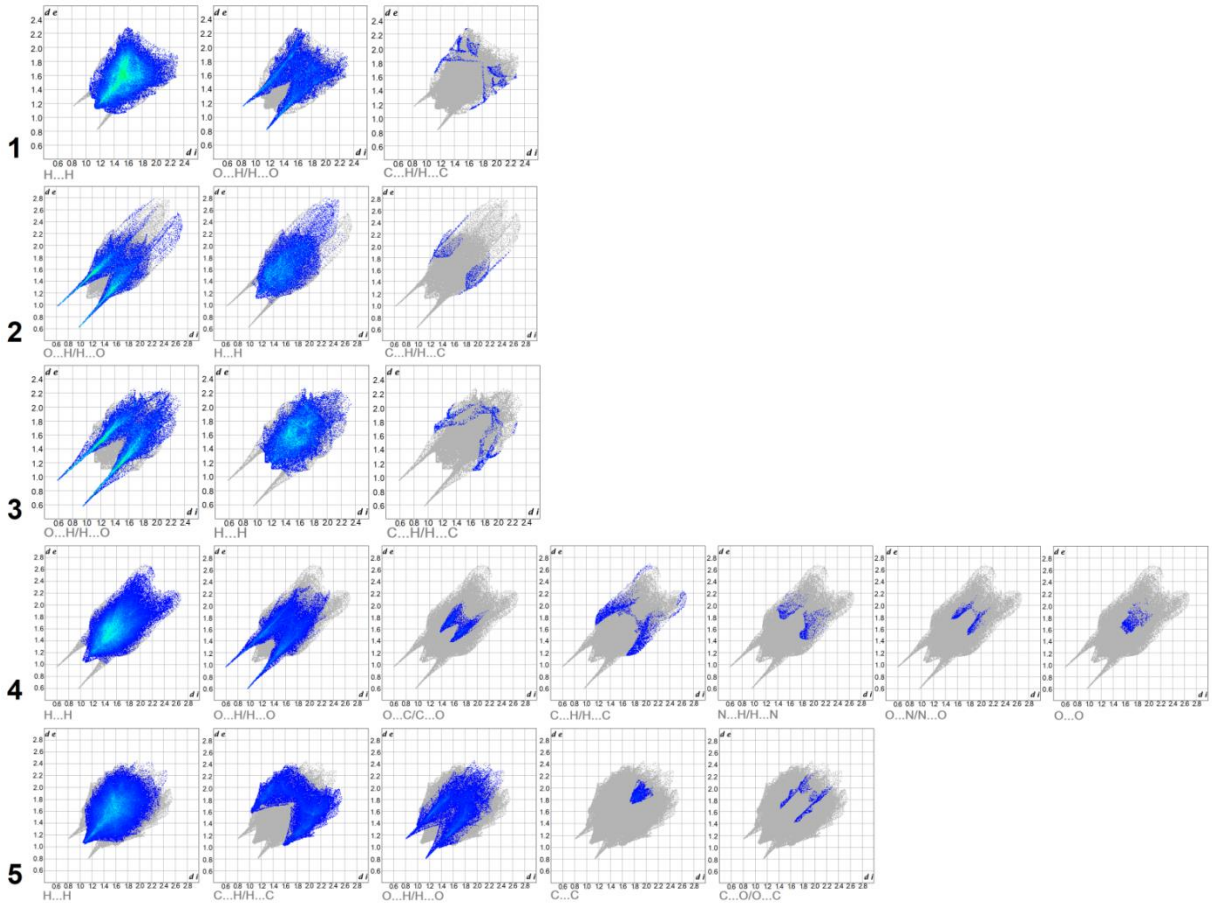


Fig. S10 Fingerprint plots delineated into the corresponding interactions in **1-5**

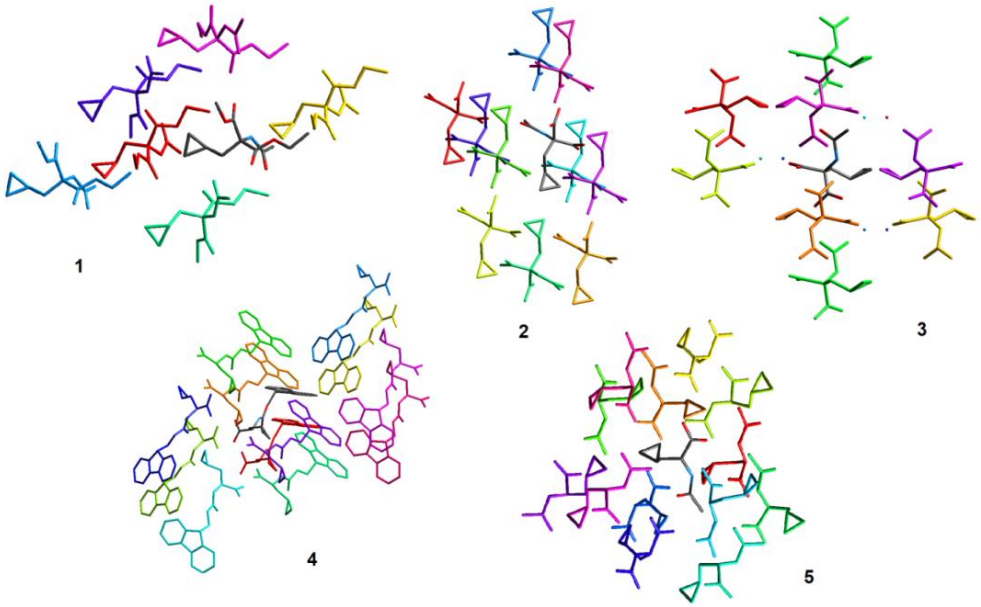


Fig. S11 The distribution of colour-coded total interaction energies between different molecules in **1-5**

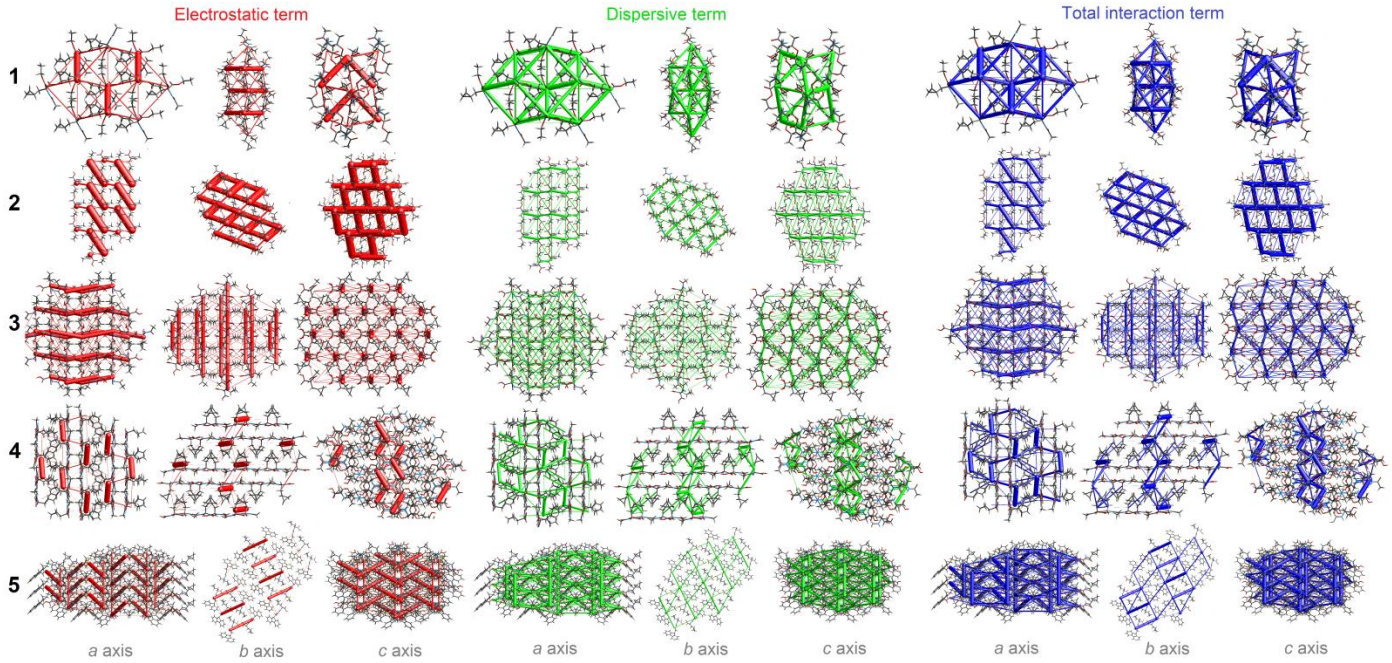


Fig. S12 Energy frameworks (calculated within a cluster of 3.8 Å radius related to a central molecule) of **1**-**5** corresponding to the electrostatic and dispersion energy components and the total energy framework along the *a*, *b* and *c*-axis. The strength of the energies for molecular pairs is visualized by tubes (size of 100).

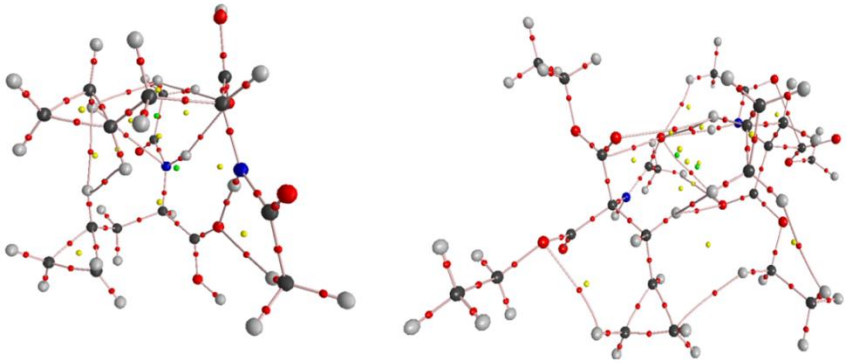


Fig. S13 On the left: Molecular graph of the **4** dimer (C – black, H – grey, O –red, N – blue, bond critical points – small red, ring critical points – yellow, cage critical points – green). On the right: Molecular graph of the **1** dimer (C – black, H – grey, O –red, N – blue, bond critical points – small red, ring critical points – yellow, cage critical points – green)

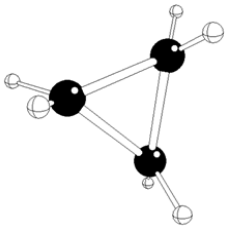


Fig. S14 M06/6-311++G(d,p) optimized structure of cyclopropane C_3H_6 (C – black, H – white)

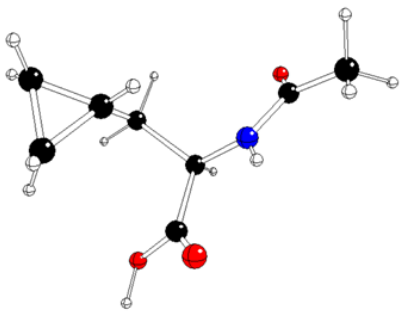


Fig. S15 M06/6-311++G(d,p) optimized structure of compound **4** (C – black, H – white, O – red, N- blue)

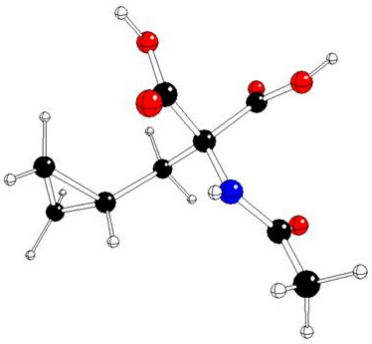


Fig. S16 M06/6-311++G(d,p) optimized structure of compound **2** (C – black, H – white, O – red, N- blue)

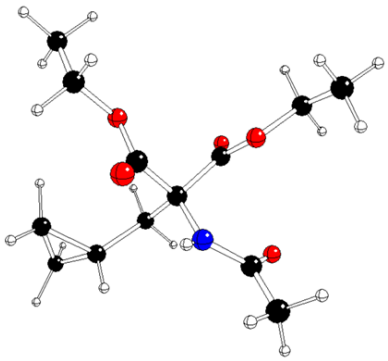


Fig. S17 M06/6-311++G(d,p) optimized structure of compound **1** (C – black, H – white, O – red, N- blue)

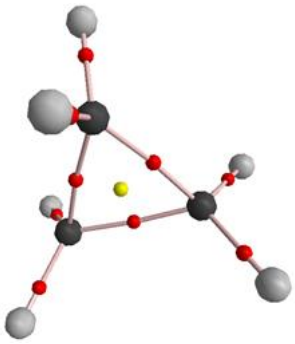


Fig. S18 Molecular graph of cyclopropane C_3H_6 (C – black, H – grey, bond critical points – red, ring critical point - yellow)

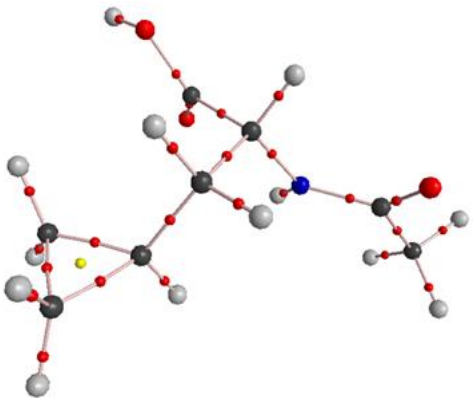


Fig. S19 Molecular graph of compound **4** (C – black, H – grey,O – red, N – blue, bond critical points – small red, ring critical point - yellow)

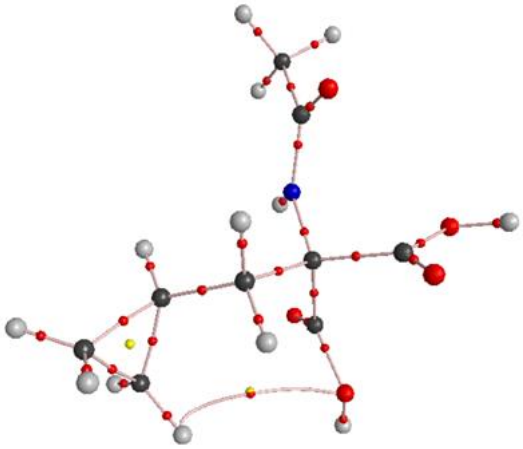


Fig. S20 Molecular graph of compound **2** (C – black, H – grey, O – red, N – blue, bond critical points – small red, ring critical point - yellow)

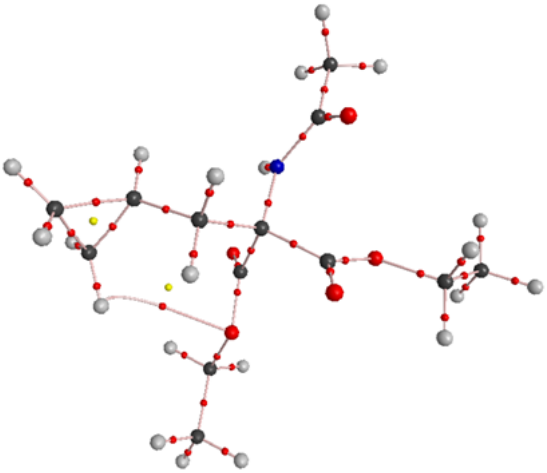


Fig. S21 Molecular graph of compound **1** (C – black, H – grey, O – red, N – blue, bond critical points – small red, ring critical point – yellow).

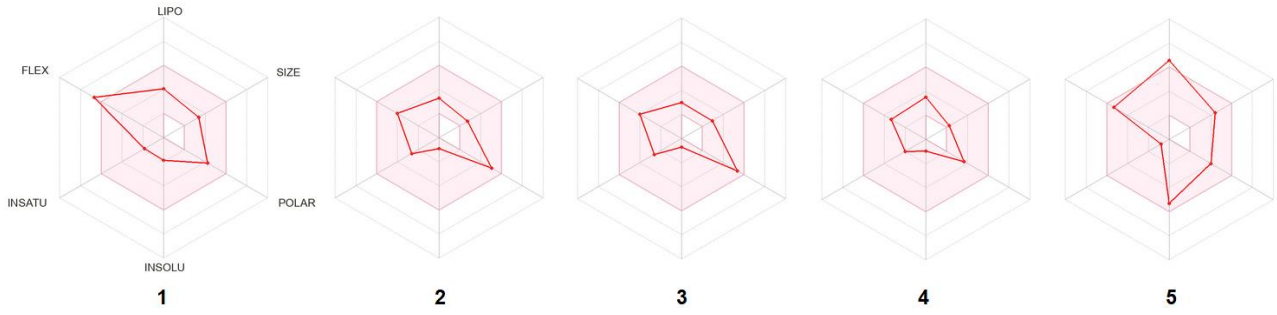


Fig. S22 Bioavailability radars of **1**-**5**.

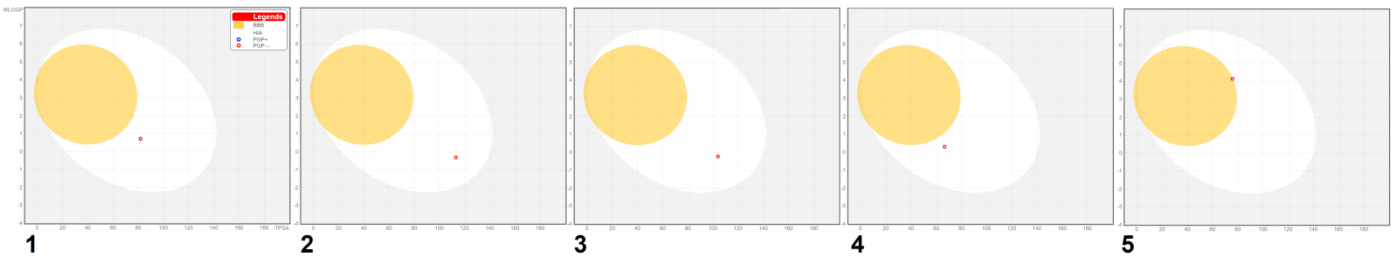


Fig. S23 BOILED-egg diagrams for **1**-**5**

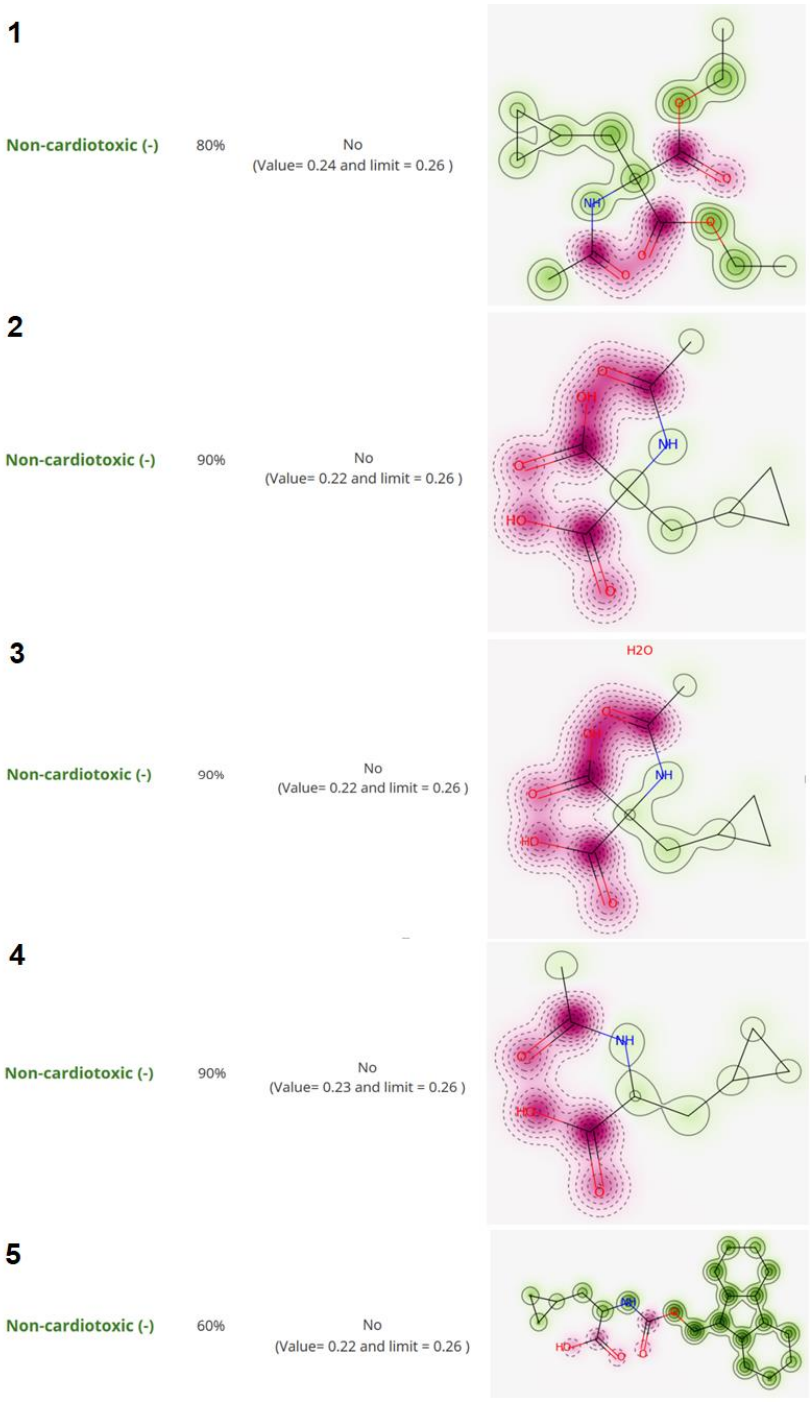


Fig. S24 Maps of cardiac toxicity for **1**-**5**

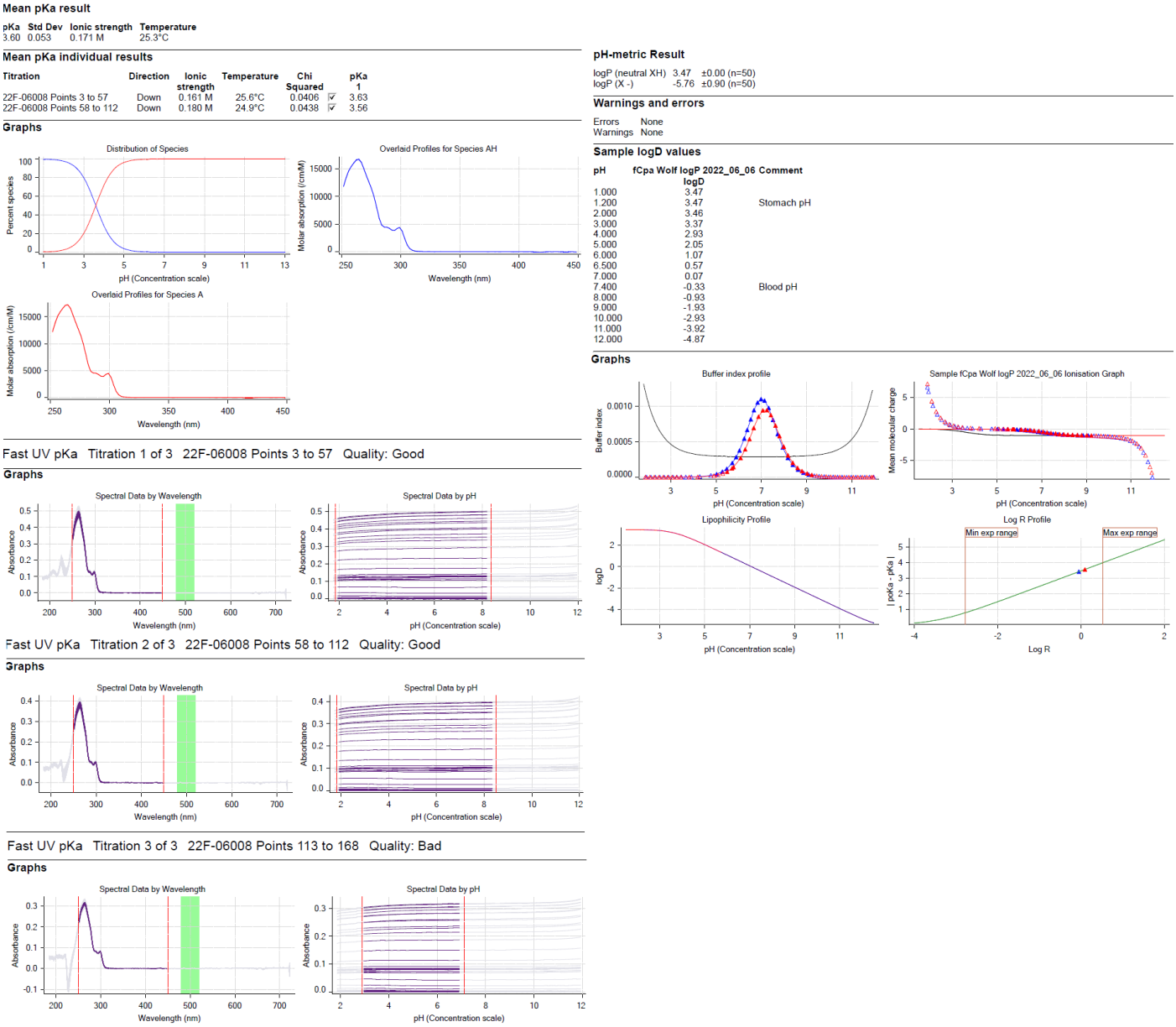


Fig. S25 Experimental pK_a and log $D_{oct/w}$ measurements for **5**

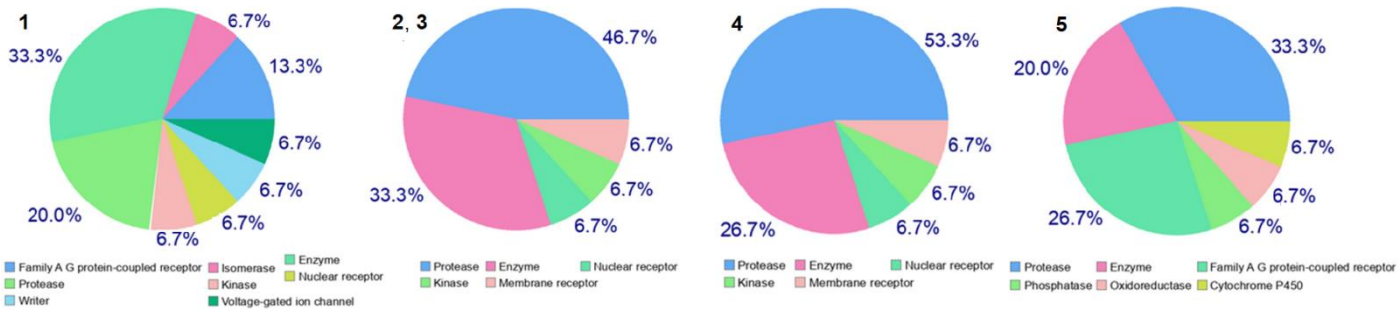
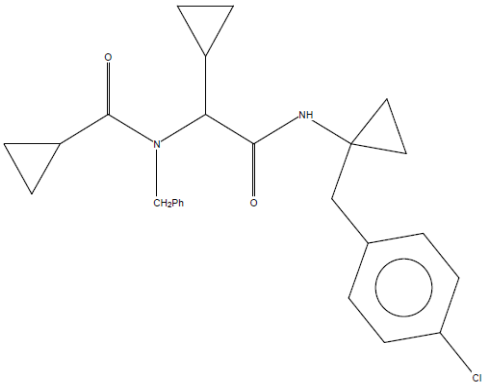
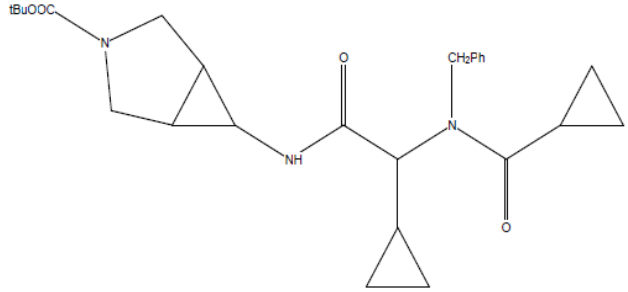
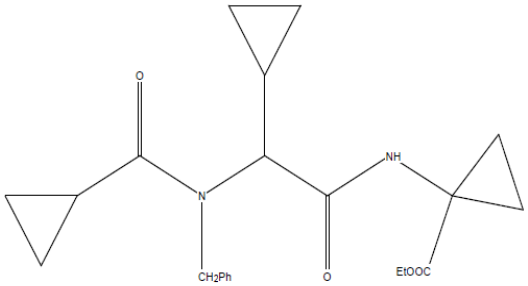


Fig. S26 Target predictions for **1-5**

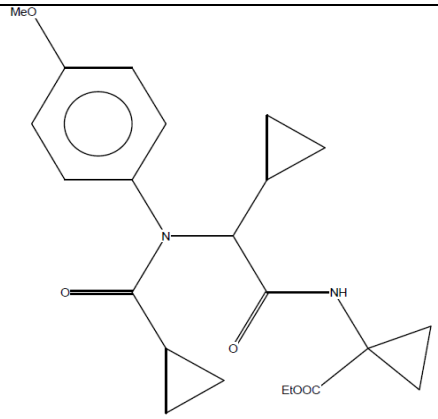
Table S1 Cyclopropyl-containing peptide-derived drugs, approved by the Food and Drug Administration (FDA) in the last decade

Drug name	*activity*	*Drug name*	*activity*
lenvatinib	thyroid cancer	tasimelteon	a regulator of sleep
cabozantinib	thyroid cancer	tezacaftor, lumacaftor	cystic fibrosis
trametinib	melanoma	naldemedine	opioid-induced constipation
olaparib	ovarian cancer	tecovirimat	smallpox
lemborexant	insomnia	combined imipenem-cilastatin/relebactam	hospital-acquired pneumonia
simeprevir	viral hepatitis		
paritaprevir			
grazoprevir			
glecaprevir, voxilaprevir, ledipasvir			

Table S2 CSD (including structural formulas and names) and PDB ref. codes

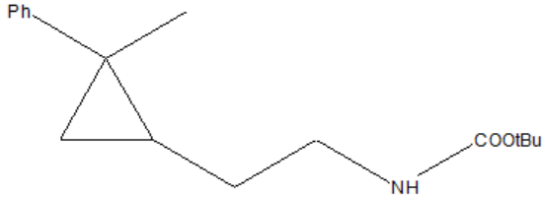
CSD ref. code	**Structural formula & chemical name**
ADELOM	 cyclopropanecarboxylic acid benzyl-([1-(4-chlorobenzyl)cyclopropylcarbamoyl]cyclopropyl-methyl)amide
ADELUS	 cyclopropanecarboxylic acid (benzyl)-[(3-tert-butoxycarbonyl-3-azabicyclo[3.1.0]hexylcarbamoyl)-cyclopropylmethyl]-amide
ADEMAZ	 1-[2-(benzylcyclopropanecarbonylamino)-2-cyclopropylacetamino]cyclopropanecarboxylic acidethyl ester

ADEMED



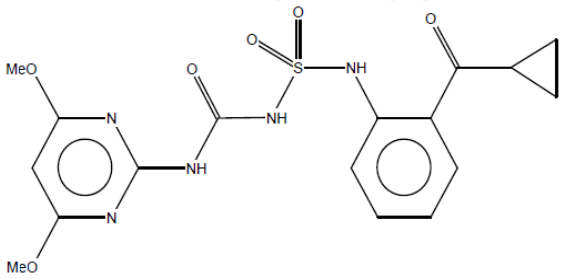
Ethyl 1-((cyclopropyl((cyclopropylcarbonyl)(4-methoxyphenyl)amino)acetyl)amino)cyclopropanecarboxylate

APOFOD



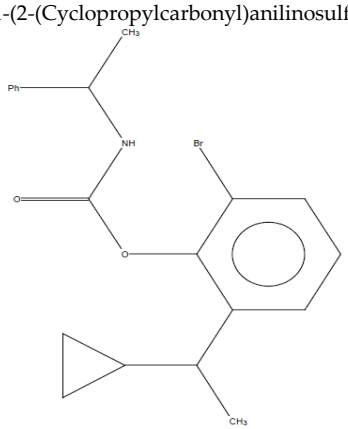
t-butyl (2-((1R,2S)-2-methyl-2-phenylcyclopropyl)ethyl)carbamate

BUTCIE



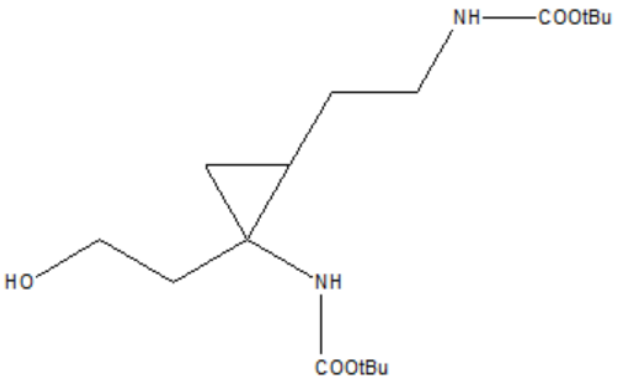
1-(2-(Cyclopropylcarbonyl)anilinosulfonyl)-3-(4,6-dimethoxypyrimidin-2-yl)urea

CARYAY



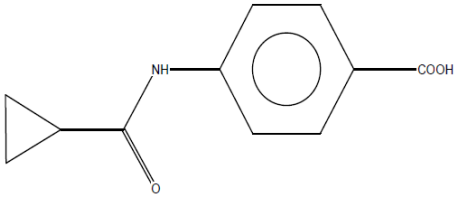
(S)-2-bromo-6-(1-cyclopropylethyl)phenyl (1-phenylethyl)carbamate

CATWEA



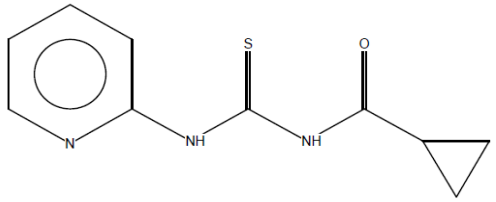
t-Butyl (E)-N-(2-(2-(N-t-butoxycarbonylamino)ethyl-1-(2-hydroxyethyl))cyclopropyl)carbamate

CEGVUH



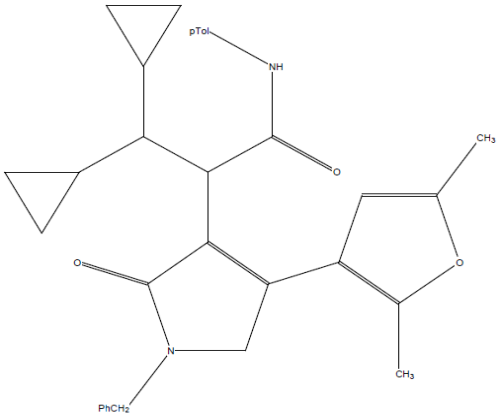
4-(Cyclopropanecarboxamido)benzoic acid]

CERQUM



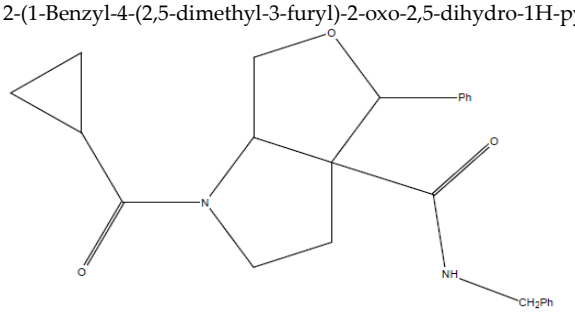
1-Cyclopropylcarbonyl-3-(2-pyridyl)thiourea

EDIWIZ



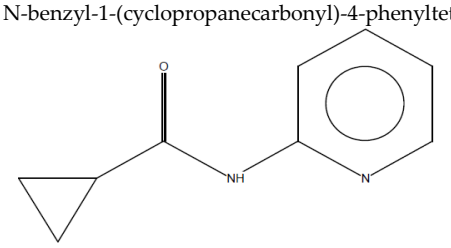
2-(1-Benzyl-4-(2,5-dimethyl-3-furyl)-2-oxo-2,5-dihydro-1H-pyrrol-3-yl)-3,3-dicyclopropyl-N-(4-methylphenyl)propanamide

FIJDIO



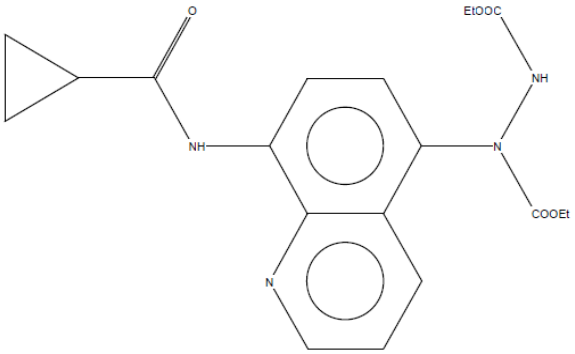
N-benzyl-1-(cyclopropanecarbonyl)-4-phenyltetrahydro-1H-furo[3,4-b]pyrrole-3a(4H)-carboxamide

GENYUU



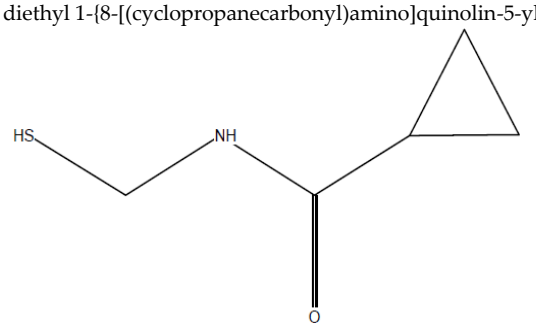
N-(2-Pyridyl)cyclopropanecarboxamide

HILXIM



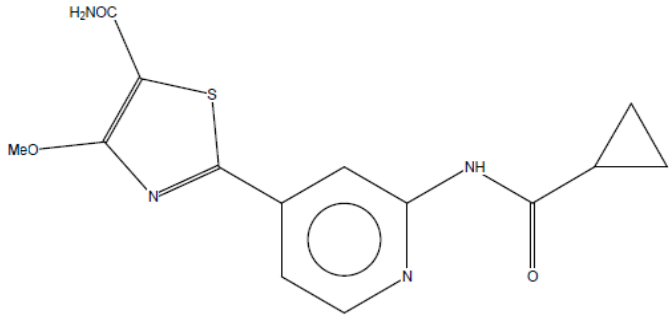
diethyl 1-{8-[(cyclopropanecarbonyl)amino]quinolin-5-yl}hydrazine-1,2-dicarboxylate

HORZEU



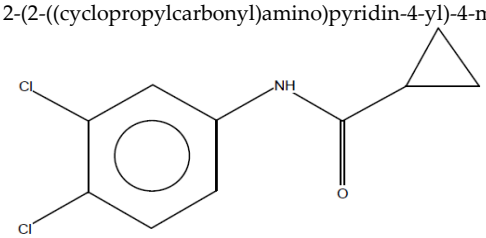
N-(Mercaptomethyl)cyclopropanecarboxamide

IHUFEY



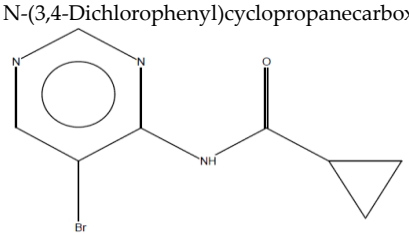
2-(2-((cyclopropylcarbonyl)amino)pyridin-4-yl)-4-methoxy-1,3-thiazole-5-carboxamide

JAWLAU



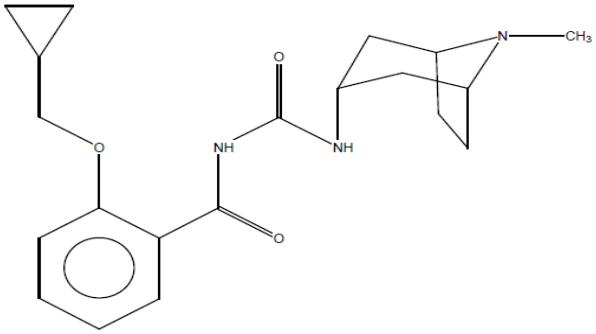
N-(3,4-Dichlorophenyl)cyclopropanecarboxamide

KEZNEJ



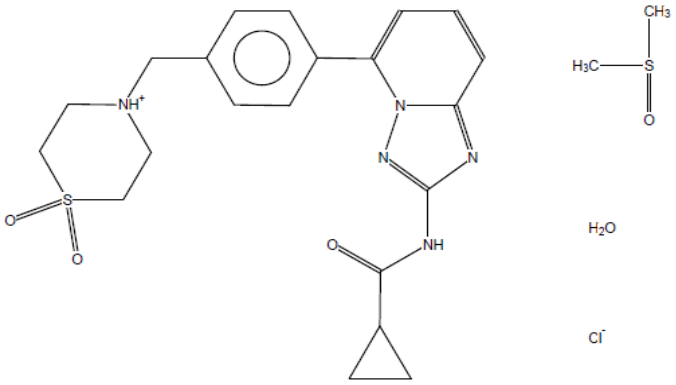
N-(5-Bromopyrimidin-4-yl)cyclopropanecarboxamide

KUDZIS



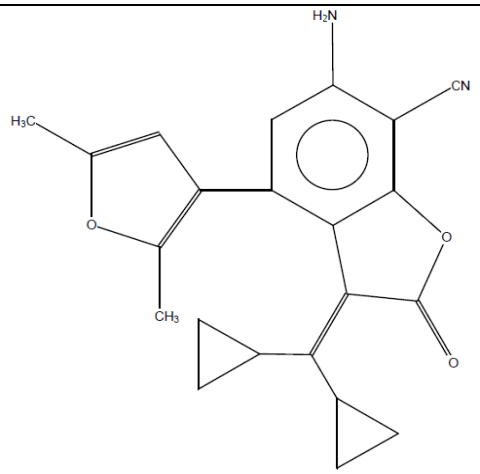
endo-N-(((8-Methyl-8-azabicyclo(3.2.1)octan-3-yl)amino)carbonyl)-2-(cyclopropylmethoxy)benzamide

LIKFIX



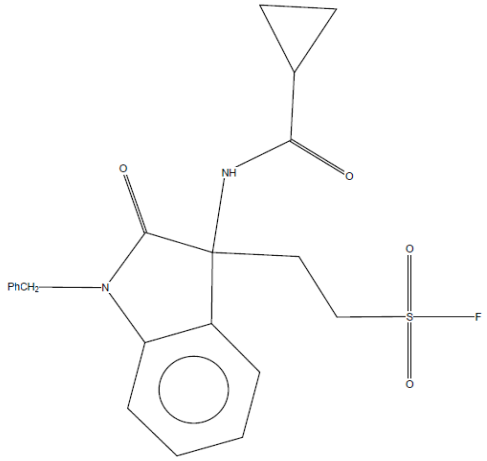
4-[(4-{2-[(cyclopropanecarbonyl)amino][1,2,4]triazolo[1,5-a]pyridin-5-yl}phenyl)methyl]-1,1-dioxo-1,4-thiazinan-4-ium chloride dimethyl sulfoxide solvate monohydrate

MENHIW



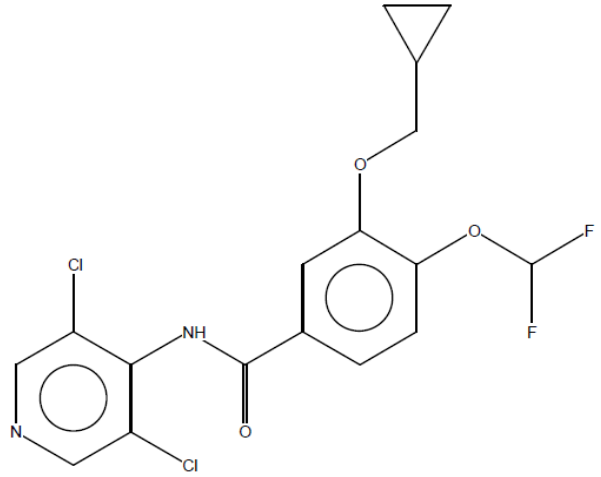
6-Amino-7-cyano-3-(dicyclopropylmethylene)-4-(2,5-dimethyl-3-furyl)-benzofuran-2(3H)-one

MOYSEB



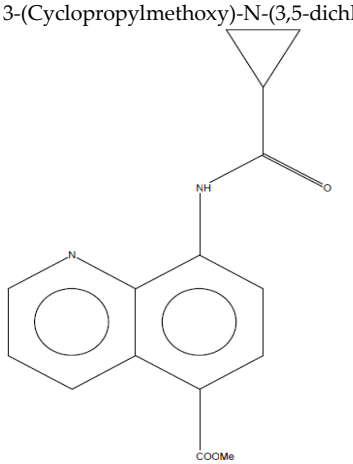
2-{1-benzyl-3-[(cyclopropanecarbonyl)amino]-2-oxo-2,3-dihydro-1H-indol-3-yl}ethane-1-sulfonyl fluoride

PEDWOM



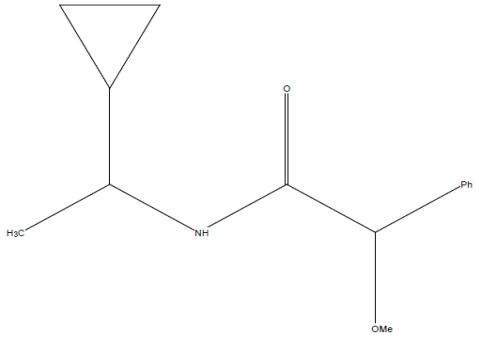
3-(Cyclopropylmethoxy)-N-(3,5-dichloropyridin-4-yl)-4-(difluoromethoxy)benzamide

ROPQUL



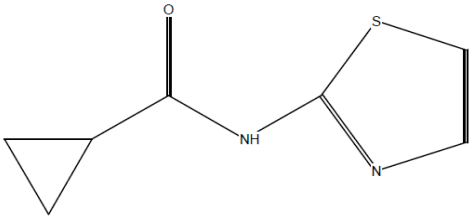
methyl 8-[(cyclopropanecarbonyl)amino]quinoline-5-carboxylate

VEHDIY



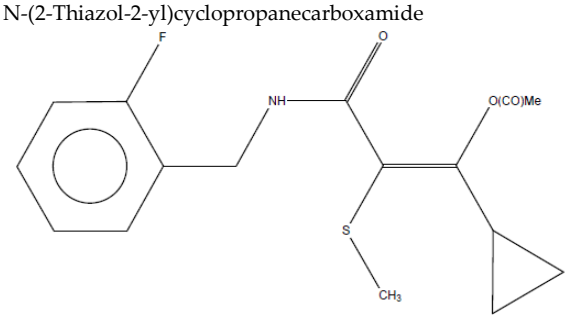
(2S)-N-((1S)-1-cyclopropylethyl)-2-methoxy-2-phenylacetamide

VETKEL



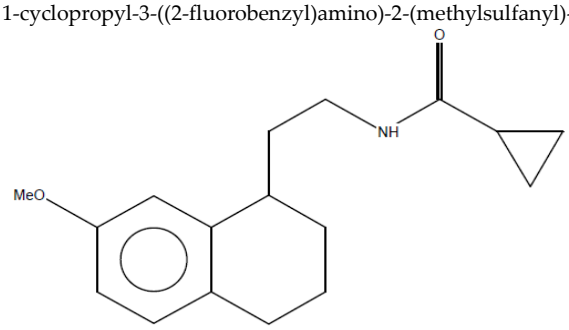
N-(2-Thiazol-2-yl)cyclopropanecarboxamide

WICMIH



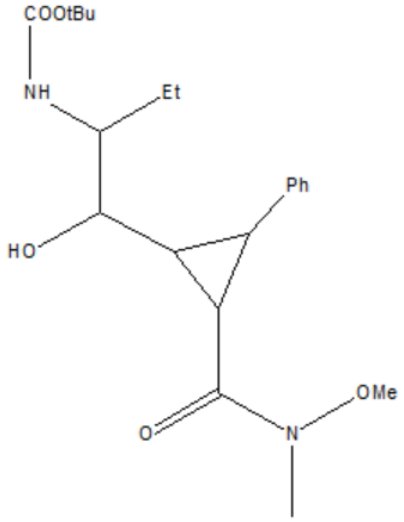
1-cyclopropyl-3-((2-fluorobenzyl)amino)-2-(methylsulfanyl)-3-oxoprop-1-en-1-yl acetate

WOVXAG



N-((-)-2-(7-methoxy-1,2,3,4-tetrahydronaphth-1-yl)ethyl)cyclopropylcarboxamide

XICRAC



t-butyl 1-(hydroxy[2-((methoxy(methyl)amino)carbonyl)-3-phenylcyclopropyl]methyl)propylcarbamate

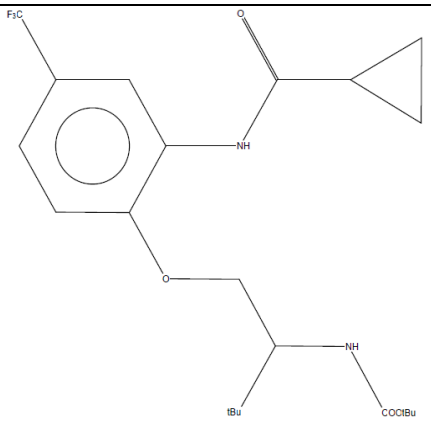
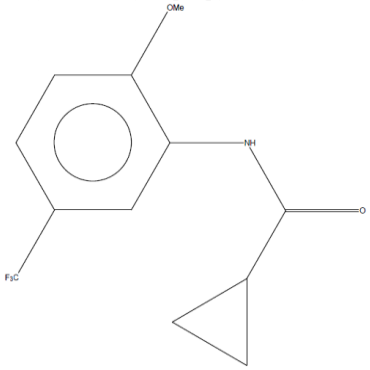
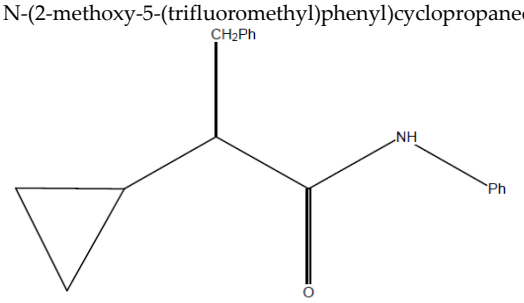
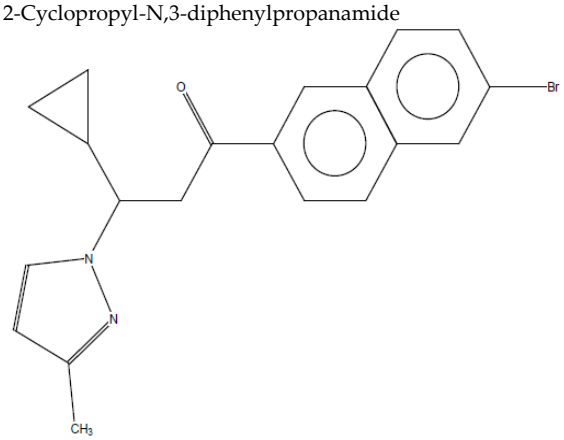
ZAMJEF	 t-butyl (1-(2-((cyclopropylcarbonyl)amino)-4-(trifluoromethyl)phenoxy)-3,3-dimethylbutan-2-yl)carbamate
ZAMJOP	 N-(2-methoxy-5-(trifluoromethyl)phenyl)cyclopropanecarboxamide
ZEGGEZ	 2-Cyclopropyl-N,3-diphenylpropanamide
ZUQBIY	 1-(6-bromo-2-naphthyl)-3-cyclopropyl-3-(3-methyl-1H-pyrazol-1-yl)propan-1-one
PDB ref.codes	7Z29, 7Z24, 7F9R, 7F99, 5SRV, 8CZX, 8CZV, 8CZU, 7Z54, 7TQ3, 7TQ4, 7x5u, 7ULM, 7V68,7Z8W, 7Z4U, 7R5W, 7BNU, 7BNS, 7TQ5, 7T2I, 7T36, 7LB3, 5SPJ, 5SPG, 8DGY, 7F9C, 7EVV, 7RVX, 7RVW, 7RVT, 7RVS, 7RVO, 7TTI, 7UAS, 7WYP, 7QK0, 7Q7V, 7Q7R, 7FIC, 7AZ0, 7AYZ, 7AYY, TTIA, 7R53, 7VUE, 7MMH, 7MM6, 7EVU, 7OY6, 7OY5, 7N3L, 7EVJ, 7SVR, 7SVD, 7SUJ, 7SUI, 7SUF, 7SLX

Table S3 Crystal data of structures derived from the CSD

CSD ref. code	formula	Sp. gr.	*Z*	Unit cell parameters		*R1* factor	T (K)
ADELOM	$C_{26}H_{29}ClN_2O_2$	$P2_1/c$	4	a=11.781(0) b=19.591(0) c=10.037(0)	α=90.00 β=95.03(1) γ=90.00	4.00	120

ADELUS	$C_{26}H_{35}N_3O_4$	*P*-1	2	a=8.080(0) b=9.947(1) c=15.668(2)	α=94.70(0) β=91.89(0) ɣ=92.20(0)	3.98	200
ADEMAZ	$C_{22}H_{28}N_2O_4$	*P*-1	2	a=9.736(0) b=9.831(0) c=12.265(0)	α=70.08(0) β=71.43(0) ɣ=82.39(0)	4.07	120
ADEMED	$C_{22}H_{28}N_2O_5$	*P*-1	4	a=11.324(0) b=13.817(0) c=14.257(0)	α=90.01(0) β=93.74(0) ɣ=111.30(0)	4.10	120
APOFOD	$C_{17}H_{25}NO_2$	$P2_1$	2	a=5.336(1) b=10.032(1) c=15.105(1)	α=90.00 β=95.90 ɣ=90.00	3.92	room
BUTCIE	$C_{17}H_{19}N_5O_6S$	$P2_1/n$	4	a=12.702(0) b=9.622(0) c=15.621(0)	α=90.00 β=93.62(0) ɣ=90.00	3.87	173
CARYAY	$C_{20}H_{22}BrNO_2$	$P2_12_12_1$	4	a=9.933(0) b=9.966(0) c=19.578(1)	α=90.00 β=90.00 ɣ=90.00	4.56	293
CATWEA	$C_{17}H_{32}N_2O_5$	$P2_1/c$	8	a=34.625(1) b=11.034(1) c=10.550(1)	α=90.00 β=98.66 ɣ=90.00	4.69	110
CEGVUH	$C_{11}H_{11}NO_3$	$P2_1/n$	4	a=13.243(1) b=4.770(0) c=16.798(1)	α=90.00 β=111.23(0) ɣ=90.00	4.11	293
CERQUM	$C_{10}H_{11}N_3OS$	$P2_1/c$	4	a=8.457(3) b=12.178(4) c=10.998(4)	α=90.00 β=96.96(0) ɣ=90.00	3.76	293
ECULOG	$C_{35}H_{43}N_3O_7S$, H_2O	$P2_1$	2	a=11.411(0) b=8.930(0) c=17.321(0)	α=90.00 β=107.36(0) ɣ=90.00	4.22	173
EDIWIZ	$C_{33}H_{36}N_2O_3$	$P2_1/c$	4	a=9.514(2) b=14.447(1) c=20.694(4)	α=90.00 β=99.98(2) ɣ=90.00	3.81	293
FIJDIO	$C_{24}H_{26}N_2O_3$	*P*bcn	8	a=28.952(0) b=13.022(0) c=10.602(0)	α=90.00 β=90.00 ɣ=90.00	3.51	120
GENYUU	$C_9N_{10}N_2O$	*P*bca	16	a=9.475(4) b=9.844(4) c=36.821(15)	α=90.00 β=90.00 ɣ=90.00	4.46	294
HILXIM	$C_{19}H_{22}N_4O_5$	*P*-1	2	a=8.697(0) b=9.899(0) c=12.559(0)	α=105.06(0) β=98.53(0) ɣ=111.72(0)	3.64	293
HORZEU	C_5H_9NOS	$P2_1$	2	a=6.237(0) b=4.863(0) c=11.096(1)	α=90.00 β=94.71(0) ɣ=90.00	3.39	200
IHUFEY	$C_{14}H_{14}N_4O_3S$	$Pna2_1$	4	a=18.184(0) b=11.767(0) c=6.736(0)	α=90.00 β=90.00 ɣ=90.00	2.59	296
JAWLAU	$C_{10}H_9Cl_2NO$	$P2_1/c$	4	a=5.025(1) b=22.051(5) c=9.615(2)	α=90.00 β=101.53(2) ɣ=90.00	3.80	295
KEZNEJ	$C_8H_8BrN_3O$	$P2_1/c$	4	a=13.623(0) b=4.889(0) c=13.128(0)	α=90.00 β=94.06(0) ɣ=90.00	2.24	120
KUDZIS	$C_{20}H_{27}N_3O_3$	$P2_1/a$	4	a=19.432(4) b=7.481(2) c=13.370(2)	α=90.00 β=101.89(1) ɣ=90.00	3.72	295
LIKFIX	$C_{21}H_{24}N_5O_3S^+$, C_2H_6OS, H_2O, Cl^-	*P*-1	2	a=9.573(0) b=11.240(0) c=13.126(0)	α=97.64(0) β=101.98(0) ɣ=104.22(0)	3.26	130
MENHIW	$C_{22}H_{20}N_2O_3$	$P2_1/c$	4	a=9.372(8) b=11.198(7) c=17.679(7)	α=90.00 β=101.07(4) ɣ=90.00	3.80	295
MOYSEB	$C_{21}H_{21}FN_2O_4S$	*P*43	4	a=11.151(0) b=11.151(0) c=16.058(0)	α=90.00 β=90.00 ɣ=90.00	2.56	100
PEDWOM	$C_{17}H_{14}Cl_2F_2N_2O_3$	$P2_1/n$	12	a=5.571(0) b=28.983(0) c=31.253(0)	α=90.00 β=92.77(0) ɣ=90.00	4.80	100
ROPQUL	$C_{15}H_{14}N_2O_3$	$P2_12_12_1$	4	a=4.937(0) b=14.761(0)	α=90.00 β=90.00	2.87	100

				c=17.102(0)	ɣ=90.00		
VEHDIY	$C_{14}H_{19}NO_2$	$P2_1$	2	a=10.546(0)	α=90.00	2.67	100
				b=5.132(0)	β=105.35(0)		
				c=12.372(0)	ɣ=90.00		
VETKEL	$C_7H_8N_2OS$	$P2_1/c$	4	a=5.707(3)	α=90.00	3.10	294
				b=9.170(4)	β=96.78(0)		
				c=15.453(7)	ɣ=90.00		
WICMIH	$C_{16}H_{18}FNO_3S$	$P2_1/n$	4	a=5.271(0)	α=90.00	4.37	293
				b=14.255(1)	β=91.65(0)		
				c=21.578(1)	ɣ=90.00		
WOVXAG	$C_{17}H_{23}NO_2$	$P2_1$	2	a=6.655(0)	α=90.00	3.60	295
				b=5.077(0)	β=95.26(0)		
				c=22.615(2)	ɣ=90.00		
XICRAC	$C_{21}H_{32}N_2O_5$	$P2_1$	2	a=12.370(8)	α=92.44	9.87	198
				b=5.470(4)	β=90.00		
				c=15.800(20)	ɣ=90.00		
ZAMJEF	$C_{22}H_{31}F_3N_2O_4$	*P*-1	2	a=10.211(0)	α=72.89(0)	3.94	150
				b=10.903(0)	β=82.14(0)		
				c=11.751(0)	ɣ=67.90(0)		
ZAMJOP	$C_{12}H_{12}F_3NO_2$	*P*bcn	8	a=12.872(0)	α=90.00	3.55	150
				b=9.766(0)	β=90.00		
				c=18.392(0)	ɣ=90.00		
ZEGGEZ	$C_{18}H_{19}NO$	$P2_1/c$	4	a=9.775(0)	α=90.00	4.76	100
				b=17.601(1)	β=113.84(0)		
				c=9.562(0)	ɣ=90.00		
ZUQBIY	$C_{20}H_{19}BrN_2O$	$P2_12_12_1$	4	a=8.843(0)	α=90.00	3.22	200
				b=10.226(0)	β=90.00		
				c=19.740(1)	ɣ=90.00		

Table S4 Geometrical parameters (in Å and angles in °) for the π-stacking moieties involved in the π···π interactions for crystal **5**

Rings Cg(I)-Cg(J) [a]	symmetry	Cg···Cg [b]	Cg(I)-perp [c]	Cg(J)-perp [d]	α [e]	β [f]	ɣ [g]
Cg(2)···Cg(3)	x, 1+y, z	3.9579(1)	3.5133	3.5363	1	26.7	27.4
Cg(2)···Cg(4)	x, -1+y, z	4.7029(1)	3.4782	3.4978	2	41.9	42.3
Cg(3)···Cg(4)	x, -1+y, z	4.4811(1)	3.5413	3.4529	2	39.6	37.8
Cg(9)···Cg(11)	x, 1+y, z	4.1947(1)	3.5017	3.5578	2	32.0	33.4

[a] Cg···Cg distance is below 5 Å; Cg(2): centroid of the ring C11-C12-C17-C18-C23; Cg(3): C12-C13-C14-C15-C16-C17; Cg(4): C18-C19-C20-C21-C22-C23; Cg(9): C11A-C12A-C17A-C18A-C23A; Cg(11): C18A-C19A-C20A-C21A-C22A-C23A

[b] distance between ring centroids [Å], [c] perpendicular distance of Cg(I) on ring J [Å], [d] perpendicular distance of Cg(J) on ring I [Å], [e] dihedral angle between planes I and J [°], [f] angle between the centroid vector Cg(I)···Cg(J) and normal to plane I [°], [g] angle between the centroid vector Cg(I)···Cg(J) and normal to plane J [°].

Table S5 C-H···π intermolecular interactions in structure **5**

X···H-Cg(J) [a]	symmetry	H···Cg	X···Cg [b]	X-H···Cg [c]	γ [d]	H-perp [e]	X-H, π [f]
C10A-H10B···Cg(9)	x, y, z	2.53	2.4488(1)	74	33.48	-2.11	49
C10-H10C···Cg(2)	x, y, z	2.63	2.5130(1)	72	38.24	-2.07	55
C11-H11···Cg(3)	x, 1+y, z	2.80	3.6190(1)	140	12.65	-2.73	55
C11A-H11A···Cg(11)	x, 1+y, z	2.83	3.7069(1)	147	7.48	2.81	49

[a] Cg(J) – center of gravity of ring J; H···Cg below 3.0 Å, [b] X···Cg – distance [Å], [c] X-H···Cg – angle [°], [d] γ – angle between Cg-H vector and ring J normal, [e] H-perp – perpendicular distance of H to ring plane J, [f] X-H, π – angle of the X-H bond with the π-plane (perpendicular = 90 °, parallel = 0 °).

Table S6 H-bonding motifs (up to 20-membered patterns) in **1**-**5** and structures derived from the CSD (cyclopropyl-based interactions in blue)

Motif	Interactions
1	
C(4)	(NH)N-H···O1(C=O)
C(4)	(CH3)C2-H2A···O1(C=O)
C(6)	(CH2)C10-H10A···O2(C=O)
C(7)	(CH3)C2-H2B···O4(C=O)
C(8)	(CH2)C10-H10C···O4(C=O)
C(8)	(CH-cyclopropyl)C5-H5···C10(CH3)
C(8)	(CH2)C12-H12A···C6 (CH-cyclopropyl)
level2	
$R^1_2(6)$	(NH)N-H···O1(C=O) & (CH3)C2-H2A···O1(C=O)
$R^2_2(9)$	(NH)N-H···O1(C=O) & (CH3)C2-H2B···O4(C=O)
$R^2_2(11)$	(CH3)C2-H2A···O1(C=O) & (CH3)C2-H2B···O1(C=O)
$R^2_2(16)$	(CH3)C10-H10C···O4(C=O) & (CH2)C12-H12A···C6(CH-cyclopropyl)
$R^2_3(11)$	(CH3)C10-H10C···O4(C=O) & (CH-cyclopropyl)C5-H5···C10(CH3) & (CH3)C2-H2B···O4(C=O)
$R^3_3(12)$	(CH2)C12-H12A···C6(cyclopropyl) & (CH-cyclopropyl)C5-H5···C10(CH3) & (CH2)C13-H13A···O2(C=O)
$C^1_2(11)$	(CH3)C2-H2B···O4(C=O) & (CH3)C10-H10C···O4(C=O)
$C^2_2(8)$	(NH)N-H···O1(C=O) & (CH3)C2-H2A···O1(C=O)
$C^2_2(8)$	(CH3)C10-H10A···O2(C=O) & (CH3)C10-H10C···O4(C=O)
$C^2_2(9)$	(CH3)C2-H2A···O1(C=O) & (CH3)C2-H2B···O4(C=O)
$C^2_2(11)$	(NH)N-H···O1(C=O) & (CH3)C2-H2B···O4(C=O)
$C^2_2(12)$	(CH-cyclopropyl)C5-H5···C10(CH3) & (CH2)C12-H12A···C6 (CH-cyclopropyl)
$C^2_2(14)$	(NH)N-H···O1(C=O) & (CH3)C10-H10A···O2(C=O)
$C^2_2(14)$	(NH)N-H···O1(C=O) & (CH3)C10-H10C···O4(C=O)
$C^2_2(14)$	(CH3)C10-H10A···O2(C=O) & (CH3)C10-H10C···O4(C=O)
$C^2_2(15)$	(CH3)C2-H2B···O4(C=O) & (CH3)C10-H10A···O2(C=O)
$C^2_2(15)$	(CH3)C2-H2B···O4(C=O) & (CH3)C10-H10C···O4(C=O)
$C^2_2(16)$	(CH3)C2-H2A···O1(C=O) & (CH3)C10-H10A···O2(C=O)
$C^2_2(16)$	(CH3)C2-H2A···O1(C=O) & (CH3)C10-H10C···O4(C=O)
2	
C(7)	(OH)O3-H3···O1(C=O)
C(7)	(CH3)C2-H2A···O2(C=O)
C(7)	(CH2-cyclopropyl)C7-H7A···O3(OH)
$R^2_2(8)$	[(OH)O5-H5···O4(C=O)]2
$R^2_2(10)$	[(NH)N-H···O2(C=O)]2
$R^2_2(12)$	[(CH-cyclopropyl)C5-H5A···O2(C=O)]2
level 2	
$C^2_2(7)$	(OH)O3-H7A···C7(C=O) & (CH2-cyclopropyl)C5-H5A···O2(OH)
$C^2_2(10)$	(OH)O3-H3···O1(C=O) & (CH2-cyclopropyl)C7-H7A···O3(OH)
$C^2_2(11)$	(OH)O5-H5···O4(C=O) & (NH)N-H···O2(C=O)
$C^2_2(12)$	(OH)O5-H5···O4(C=O) & (CH2-cyclopropyl)C5-H5A···O2(C=O)
$C^2_2(12)$	(CH3)C2-H2A···O2(C=O) & (CH2-cyclopropyl)C7-H7A···O3(OH)
$C^2_2(14)$	(OH)O3-H3···O1(C=O) & (CH3)C2-H2A···O2(C=O)
$C^2_2(14)$	(OH)O3-H3···O1(C=O) & (CH2-cyclopropyl)C7-H7A···O3(OH)
$C^2_2(14)$	(CH3)C2-H2A···O2(C=O) & (CH2-cyclopropyl)C7-H7A···O3(OH)
$C^3_4(18)$	(NH)N-H···O2(C=O) & (CH3)C2-H2A···O2(C=O)
$C^4_4(20)$	[(OH)O3-H3···O1(C=O)]2 & [(NH)N-H···O2(C=O)]2
$C^4_4(20)$	[(CH2-cyclopropyl)C5-H5A···O2(C=O)]2 & [(CH2-cyclopropyl)C7-H7A···O3(OH)]2
$R^1_2(7)$	(NH)N-H···O2(C=O) & (CH2-cyclopropyl)C5-H5A···O2(C=O)
$R^2_2(8)$	(OH)O3-H3···O1(C=O) & (CH3)C2-H2A···O2(C=O)
$R^2_2(11)$	(NH)N-H···O2(C=O) & (CH2-cyclopropyl)C5-H5A···O2(C=O)
$R^2_2(12)$	(CH)C4-H···O3(C=O) & (CH2-cyclopropyl)C6-H6A···O4(C=O)
$R^2_4(12)$	[(NH)N-H···O2(C=O)]2 & [(CH3)C2-H2A···O2(C=O)]2
$R^3_3(11)$	(CH-cyclopropyl)C7-H···O3(C=O) & (CH2-cyclopropyl)C6-H6A···O4(C=O) & CH2-cyclopropyl)C7-H···C7(CH-cyclopropyl)
$R^3_3(8)$	(CH-cyclopropyl)C7-H···O3(C=O) & (CH)C4-H···O3(C=O) & CH2-cyclopropyl)C7-H···C7(CH-cyclopropyl)
$R^4_4(14)$	[(CH2-cyclopropyl)C5-H5A···O2(C=O)]2 & [(CH2-cyclopropyl)C7-H7A···O3(OH)]2
$R^2_4(18)$	[(CH3)C2-H2A···O2(C=O)]2 & (CH2-cyclopropyl)C5-H5A···O2(C=O)
$R^3_4(18)$	[(NH)N-H···O2(C=O)]2 & [(CH3)C2-H2A···O2(C=O)]2
$R^4_4(16)$	[(OH)O3-H3···O1(C=O)]2 & [(NH)N-H···O2(C=O)]2
$R^4_4(20)$	[(OH)O3-H3···O1(C=O)]2 & [(NH)N-H···O2(C=O)]2
$R^4_4(20)$	[(NH)N-H···O2(C=O)]2 & [(CH2-cyclopropyl)C7-H7A···O3(OH)]2
$R^4_4(20)$	[(CH2-cyclopropyl)C5-H5A···O2(C=O)]2 & [(CH2-cyclopropyl)C7-H7A···O3(OH)]2
3	
D(2)	(H2O)O-HA···O4(C=O)
D(2)	(H2O)O-HB···O2(C=O)
D(2)	(OH)O3-H3···O(H2O)
D(2)	(CH2cyclopropyl)C6-H6B···O(H2O)
C(5)	(CH2)C4-H4A···O4(C=O)
C(7)	(OH)O5-H5···O1(C=O)

C(7)	(CH3)C2-H2A···O2(C=O)
C(7)	(CH2cyclopropyl)C6-H6A···O5(OH)
R^2_2(14)	[(CH3)C2-H2C···O3(OH)]2
level 2	
C^1_2(9)	(OH)O3-H3···O(H2O) & (CH2-cyclopropyl)C6-H6B···O(H2O)
C^2_2(6)	(H2O)O-HB···O2(C=O) & (OH)O3-H3···O(H2O)
C^2_2(6)	(CH3)C2-H2A···O2(C=O) & (CH3)C2-H2C···O3(OH)
C^2_2(8)	(H2O)O-HA···O4(C=O) & (H2O)O-HB···O2(C=O)
C^2_2(8)	(H2O)O-HA···O4(C=O) & (OH)O3-H3···O(H2O)
C^2_2(8)	(CH2)C4-H4A···O4(C=O) & (CH2-cyclopropyl)C6-H6A···O5(OH)
C^2_2(9)	(H2O)O-HA···O4(C=O) & (CH2-cyclopropyl)C6-H6B···O(H2O)
C^2_2(10)	(OH)O5-H5···O1(C=O) & (CH3)C2-H2A···O2(C=O)
C^2_2(10)	(OH)O5-H5···O1(C=O) & (CH3)C2-H2C···O3(OH)
C^2_2(10)	(OH)O5-H5···O1(C=O) & (CH2-cyclopropyl)C6-H6A···O5(OH)
C^2_2(12)	(CH3)C2-H2A···O2(C=O) & (CH2)C4-H4A···O4(C=O)
C^2_2(12)	(CH3)C2-H2C···O3(OH) & (CH2)C4-H4A···O4(C=O)
C^2_2(12)	(CH2)C4-H4A···O4(C=O) & (CH2-cyclopropyl)C6-H6A···O5(OH)
C^2_2(14)	[(OH)O5-H5···O1(C=O) & (CH3)C2-H2A···O2(C=O)
C^2_2(14)	(OH)O5-H5···O1(C=O) & (CH2-cyclopropyl)C6-H6A···O5(OH)
C^2_2(14)	(CH3)C2-H2A···O2(C=O) & (CH3)C2-H2C···O3(OH)
C^2_2(14)	(CH3)C2-H2C···O2(C=O) & (CH2-cyclopropyl)C6-H6A···O5(OH)
C^2_2(14)	(CH3)C2-H2C···O3(OH) & (CH2-cyclopropyl)C6-H6A···O5(OH)
C^4_4(20)	[(CH3)C2-H2A···O2(C=O)]2 & [(CH3)C2-H2C···O3(OH)]2
C^4_4(20)	[(CH2)C4-H4A···O4(C=O)]2 & [(CH2-cyclopropyl)C6-H6A···O5(OH)]2
R^3_4(8)	(H2O)O-HB···O2(C=O) & (OH)O3-H3···O(H2O) & (CH3)C2-H2C···O2(C=O) & (CH3)C2-H2C···O3(OH)
R^2_3(14)	(OH)O3-H3···O(H2O) & (CH3)C2-H2C···O2(C=O) & (CH2-cyclopropyl)C6-H6B···O(H2O)
R^3_3(14)	(OH)O3-H3···O(H2O) & (H2O)O-HA···O4(C=O) &(CH2-cyclopropyl)C6-H6A···O5(OH)
R^3_4(13)	(OH)O3-H3···O(H2O) & (OH)O5-H5···O1(C=O) & (CH2-cyclopropyl)C6-H6A···O5(OH) & (CH2-cyclopropyl)C6-H6B···O(H2O)
R^4_4(18)	[(H2O)O-HB···O2(C=O)]2 & [(CH2-cyclopropyl)C6-H6B···O(H2O)]2
R^4_4(20)	[(OH)O5-H5···O1(C=O)]2 & [(CH2)C4-H4A···O4(C=O)]2
R^4_4(20)	[(CH2)C4-H4A···O4(C=O)]2 & [(CH2-cyclopropyl)C6-H6A···O5(OH)]2
D^2_3(8)	[(OH)O-HA···O4(C=O)]2 & (CH2)C4-H4A···O4(C=O)
D^2_3(9)	[(H2O)O-HB···O2(C=O)]2 & (CH2)C2-H2A···O2(C=O)
D^3_3(12)	(OH)O5-H5···O1(C=O) & [(H2O)O-HA···O4(C=O)]2
D^3_3(16)	(OH)O5-H5···O1(C=O) & [(OH)O3-H3···O(H2O)]2
D^3_3(12)	[(H2O)O-HB···O2(C=O)]2 & (CH2)C2-H2C···O3(OH)
D^3_3(12)	[(H2O)O-HB···O2(C=O)]2 & (CH2)C4-H4A···O4(C=O)
D^3_3(12)	[(OH)O3-H3···O(H2O)]2 & (CH3)C2-H2C···O3(OH)
D^3_3(12)	(CH2-cyclopropyl)C6-H6A···O5(OH) & [(CH2-cyclopropyl)C6-H6B···O(H2O)]2
D^3_3(14)	[(H2O)O-HB···O2(C=O)]2 & (OH)O5-H5···O1(C=O)
D^3_3(14)	[(OH)O3-H3···O(H2O)]2 & (CH2)C2-H2A···O2(C=O)
D^3_3(14)	[(OH)O3-H3···O(H2O)]2 & (CH2)C4-H4A···O4(C=O)
D^3_3(14)	(H2O)O-HA···O4(C=O) & (CH2)C2-H2A···O2(C=O)
D^3_3(14)	[(H2O)O-HA···O4(C=O)]2 & (CH2)C2-H2C···O3(OH)
D^3_3(14)	[(H2O)O-HB···O2(C=O)]2 & (CH2-cyclopropyl)C6-H5A···O5(OH)
D^3_3(14)	(CH2)C4-H4A···O4(C=O) & [(CH2-cyclopropyl)C6-H6A···O5(OH)]2
D^3_3(16)	[(OH)O3-H3···O(H2O)]2 & (CH2-cyclopropyl)C6-H6A···O5(OH)
D^3_3(18)	(OH)O5-H5···O1(C=O) & [(CH2-cyclopropyl)C6-H6B···O(H2O)]2
D^3_3(18)	(CH2)C2-H2A···O2(C=O) & [(CH2-cyclopropyl)C6-H6B···O(H2O)]2
D^3_3(18)	(CH3)C2-H2C···O3(OH) & [(CH2-cyclopropyl)C6-H6B···O(H2O)]2
4	
C(7)	(CH3)C2A-H2C···O3A(OH)
C(7)	(CH-cyclopropyl)C7B-H7BA···C1B(CH)
D(2)	(OH)O3-H3···O1C(C=O)
D(2)	(OH)O3A-H3A···O1B(C=O)
D(2)	(OH)O3B-H3B···O1A(C=O)
D(2)	(C=O)O3C-H3C···O1(C=O)
D(2)	(NH)N-H···O2A(C=O)
D(2)	(NH)NA-HA···O2(C=O)
D(2)	(NH)NB-HB···O2C(C=O)
D(2)	(NH)NC-HC···O2B(C=O)
D(2)	(CH3)C2-H2B···O1B(C=O)
D(2)	(CH3)C2-H2C···O1B(C=O)
D(2)	(CH3)C2A-H2AB···O1C(C=O)
D(2)	(CH3)C2A-H2AB···O2(C=O)
D(2)	(CH3)C2B-H2B···O2C(C=O)
D(2)	(CH3)C2B-H2B···O1(C=O)
D(2)	(CH3)C2C-H2CA···O2(C=O)
D(2)	(CH3)C2C-H2CA···O2A(C=O)
D(2)	(CH3)C2C-H2CB···O2B(C=O)
D(2)	(CH-cyclopropyl)C5-H5···C7C(CH-cyclopropyl)

level 2	
$C^2_2(8)$	(OH)O3-H3···O1C(C=O) & (CH3)C2-H2CA···O2(C=O)
$C^2_2(8)$	(OH)O3C-H3C···O1(C=O) & (CH3)C2-H2C···O2C(C=O)
$C^2_2(8)$	(CH3)C2-H2B···O1B(C=O) & (CH3)C2B-H2BB···O1(C=O)
$C^2_2(11)$	(CH3)C2A-H2AB···O1C(C=O) & (CH3)C2C-H2CA···O2A(C=O)
$R^2_2(14)$	[(CH-cyclopropyl)C7B-H7BA···C1B(CH)]2
$C^2_2(14)$	(OH)O3-H3···O1C(C=O) & (OH)O3-H3C···O1(C=O)
$C^2_2(14)$	(OH)O3A-H3AA···O1B(C=O) & (OH)O3B-H3B···O1A(C=O)
$C^2_2(14)$	(OH)O3-H3···O1C(C=O) & (CH3)C2-H2C···O2C(C=O)
$C^2_2(14)$	(OH)O3C-H3C···O1(C=O) & (CH3)C2C-H2CA···O2(C=O)
$C^3_3(15)$	cyclopropyl)C5A-H5A···C6(CH-cyclopropyl) & (CH3)C2B-H2BC···O3A(C=O) & (CH3)C2B-H2BB···O1(C=O)
$C^4_4(12)$	(CH-cyclopropyl)C7C-H7CA···C2(CH) & (CH-cyclopropyl)C5-H5···C7C(CH-cyclopropyl) & (CH-cyclopropyl)C5-H5A···C6(CH-cyclopropyl) & (CH-cyclopropyl)C6A-H6AB···C5C(CH-cyclopropyl)
$R^1_2(6)$	(NH)N-H···O2A(C=O) & (CH3)C2-H2B···O2A(C=O)
$R^1_2(6)$	(NH)NA-HA···O2(C=O) & (CH3)C2A-H2AB···O2(C=O)
$R^1_2(6)$	(NH)NB-HB···O2C(C=O) & (CH3)C2B-H2BB···O2C(C=O)
$R^1_2(6)$	(NH)NC-HC···O2B(C=O) & (CH3)C2C-H2CB···O2B(C=O)
$R^2_2(6)$	(OH)O3A-H···O1B(C=O) & (CH3)C2-H···O2A(C=O) & (CH3)C2-H···O1B(C=O)
$R^2_2(9)$	(CH-cyclopropyl)C5-H5···C7C(CH-cyclopropyl) & (CH-cyclopropyl)C7C-H7C···C2(CH2)
$R^2_2(10)$	(NH)N-H···O2A(C=O) & (NH)NA-HA···O2(C=O)
$R^2_2(10)$	(NH)NB-HB···O2C(C=O) & (NH)NC-HC···O2B(C=O)
$R^2_2(12)$	(NH)N-H···O2A(C=O) & (CH3)C2B-H2AB···O2(C=O)
$R^2_2(12)$	(NH)NA-HA···O2(C=O) & (CH3)C2-H2B···O2A(C=O)
$R^2_2(12)$	(NH)NB-HB···O2C(C=O) & (CH3)C2C-H2CB···O2B(C=O)
$R^2_2(12)$	(NH)NC-HC···O2B(C=O) & (CH3)C2B-H2BB···O2C(C=O)
$R^2_2(14)$	(CH3)C2-H2B···O2A(C=O) & (CH3)C2A-H2AB···O2(C=O)
$R^2_2(14)$	(CH3)C2-H2C···O2C(C=O) & (CH3)C2C-H2CA···O2(C=O)
$R^2_2(14)$	(CH3)C2B-H2BB···O2C(C=O) & (CH3)C2C-H2CB···O2B(C=O)
$R^3_3(14)$	(CH-cyclopropyl)C5A-H5A···C6(CH-cyclopropyl) & (CH-cyclopropyl)C7C-H7CA···C2(CH) & (NH)N-H···O2A(C=O)
$R^3_3(17)$	(CH-cyclopropyl)C5A-H5A···C6(CH-cyclopropyl) & (CH-cyclopropyl)C6A-H6AB···C5C(CH-cyclopropyl) & (OH)O3-H3···O1C(C=O)
$R^4_4(18)$	(CH-cyclopropyl)C5B-H7BA···C1B(CH) & (CH-cyclopropyl)C7C-H7CA···C2(CH) & (CH)C2-H2B···O1B(C=O) & (NH)NB-HB···O2C(C=O)
$R^4_4(20)$	(CH-cyclopropyl)C7B-H7BA···C1B(CH) & (CH)C2-H2B···O1B(C=O) & (CH-cyclopropyl)C7C-H7CA···C2(CH) & (CH)C2B-H2BB···O2C(C=O)
$D^1_2(3)$	(OH)O3-H3···O1C(C=O) & (CH3)C2A-H2AB···O1C(C=O)
$D^1_2(3)$	(OH)O3A-H3AA···O1B(C=O) & (CH3)C2-H2B···O1B(C=O)
$D^1_2(3)$	(OH)O3A-H3C···O1(C=O) & (CH3)C2B-H2BB···O1(C=O)
$D^1_2(3)$	(NH)N-H···O2A(C=O) & (CH3)C2B-H2CA···O2A(C=O)
$D^1_2(3)$	(NH)NB-HB···O2C(C=O) & (CH3)C2C-H2C···O2C(C=O)
$D^1_2(3)$	(CH3)C2-H2B···O1B(C=O) & (CH3)C2-H2B···O2A(C=O)
$D^1_2(3)$	(CH3)C2-H2B···O2A(C=O) & (CH3)C2C-H2CA···O2A(C=O)
$D^1_2(3)$	(CH3)C2-H2C···O2C(C=O) & (CH3)C2B-H2BB···O2C(C=O)
$D^2_1(3)$	(CH3)C2B-H2BB···O2C(C=O) & (CH3)C2B-H2BB···O1(C=O)
$D^2_2(5)$	(CH3)C2-H2B···O1B(C=O) & (CH3)C2-H2C···O2C(C=O)
$D^2_2(5)$	(CH3)C2-H2B···O2A(C=O) & (CH3)C2-H2C···O2C(C=O)
$D^2_2(6)$	(OH)O3-H3···O1C(C=O) & (NH)NA-HA···O2(C=O)
$D^2_2(6)$	(OH)O3-H3C···O1C(C=O) & (NH)NC-HC···O2B(C=O)
$D^2_2(6)$	(OH)O3A-H3A···O1B(C=O) & (NH)N-H···O2A(C=O)
$D^2_2(6)$	(OH)O3B-H3B···O1A(C=O) & (NH)NA-HA···O2(C=O)
$D^2_2(6)$	(OH)O3B-H3B···O1A(C=O) & (NH)NC-HC···O2B(C=O)
$D^2_2(6)$	(OH)O3C-H3C···O1(C=O) & (NH)N-H···O2A(C=O)
$D^2_2(6)$	(OH)O3A-H3A···O1B(C=O) & (CH3)C2-H2B···O2A(C=O)
$D^2_2(6)$	(OH)O3-H3C···O1(C=O) & (CH3)C2-H2B···O2A(C=O)
$D^2_2(6)$	(OH)O3-H3···O1C(C=O) & (CH3)C2A-H2AB···O2(C=O)
$D^2_2(6)$	(OH)O3-H3···O1C(C=O) & (CH3)C2C-H2CA···O2A(C=O)
$D^2_2(6)$	(OH)O3-H3···O1C(C=O) & (CH3)C2C-H2CB···O2B(C=O)
$D^2_2(6)$	(OH)O3B-H3B···O1A(C=O) & (CH3)C2A-H2AB···O2(C=O)
$D^2_2(6)$	(OH)O3B-H3B···O1A(C=O) & (CH3)C2C-H2CB···O2B(C=O)
$D^2_2(6)$	(OH)O3C-H3C···O1(C=O) & (CH3)C2-H2B···O1B(C=O)
$D^2_2(6)$	(NH)N-H···O2A(C=O) & (CH3)C2B-H2BB···O1(C=O)
$D^2_2(6)$	(NH)NB-HB···O2C(C=O) & (CH3)C2-H2A···O1B(C=O)
$D^2_2(6)$	(CH3)C2-H2B···O1B(C=O) & (CH3)C2B-H2BB···O2C(C=O)
$D^2_2(6)$	(CH3)C2-H2B···O2A(C=O) & (CH3)C2B-H2BB···O1(C=O)
$D^2_2(6)$	(CH3)C2-H2C···O2C(C=O) & (CH3)C2B-H2BB···O1 (C=O)
$D^2_2(7)$	(OH)O3B-H3B···O1A(C=O) & (NH)N-H···O2A(C=O)
$D^2_2(7)$	(NH)N-H···O2A(C=O) & (CH3)C2-H2B···O1B(C=O)
$D^2_2(7)$	(NH)N-H···O2A(C=O) & (CH3)C2-H2C···O2C(C=O)
$D^2_2(7)$	(NH)N-H···O2A(C=O) & (CH3)C2C-H2CA···O2(C=O)
$D^2_2(7)$	(NH)NC-HC···O2B(C=O) & (CH3)C2-H2C···O2C(C=O)
$D^2_2(8)$	(OH)O3-H3···O1C(C=O) & (NH)N-H···O2A(C=O)
$D^2_2(8)$	(OH)O3-H3···O1C(C=O) & (NH)NB-HB···O2(C=O)
$D^2_2(8)$	(OH)O3-H3···O1C(C=O) & (CH3)C2B-H2BB···O2C(C=O)
$D^2_2(8)$	(OH)O3B-H3B···O1A(C=O) & (NH)NB-HB···O2C(C=O)

$D^2_2(8)$	(OH)O3B-H3B···O1A(C=O) & (CH3)C2-H2BB···O2A(C=O)
$D^2_2(8)$	(OH)O3B-H3B···O1A(C=O) & (CH3)C2C-H2CA···O2A(C=O)
$D^2_2(8)$	(NH)NC-HC···O2B(C=O) & (CH3)C2-H2B···O1B(C=O)
$D^2_2(8)$	(CH3)C2-H2C···O2C(C=O) & (CH3)C2A-H2AB···O1C(C=O)
$D^2_2(8)$	(CH3)C2-H2B···O1B(C=O) & (CH3)C2C-H2CB···O2B(C=O)
$D^2_2(9)$	(OH)O3-H3···O1C(C=O) & (CH3)C2B-H2BB···O1(C=O)
$D^2_2(9)$	(OH)O3B-H3B···O1A(C=O) & (CH3)C2-H2B···O1B(C=O)
$D^2_2(9)$	(NH)N-H···O2A(C=O) & (CH3)C2A-H2AB···O1C(C=O)
$D^2_2(9)$	(NH)NA-HA···O2(C=O) & (CH3)C2-H2B···O1B(C=O)
$D^2_2(9)$	(NH)NA-HA···O2(C=O) & (CH3)C2-H2C···O2C(OH)
$D^2_2(9)$	(CH3)C2A-H2B···O1B(C=O) & (CH3)C2C-H2C···O2(C=O)
$D^2_2(9)$	(CH3)C2-H2B···O1B(C=O) & (CH3)C2A-H2AB···O2(C=O)
$D^2_2(9)$	(CH3)C2-H2B···O2A(C=O) & (CH3)C2A-H2AB···O1C(C=O)
$D^2_2(9)$	(CH3)C2-H2B···O2A(C=O) & (CH3)C2C-H2C···O2(C=O)
$D^2_2(9)$	(CH3)C2-H2C···O2C(C=O) & (CH3)C2C-H2CA···O2A(C=O)
$D^2_2(9)$	(CH3)C2-H2C···O2C(C=O) & (CH3)C2C-H2CB···O2B(C=O)
$D^2_2(9)$	(CH3)C2-H2C···O2C(C=O) & (CH3)C2C-H2AB···O2(C=O)
$D^2_2(10)$	(OH)O3-H3···O1C(C=O) & (CH3)C2-H2B···O1B(C=O)
$D^2_2(10)$	(OH)O3-H3···O1C(C=O) & (CH3)C2-H2B···O2A(C=O)
$D^2_2(10)$	(OH)O3B-H3B···O1A(C=O) & (CH3)C2B-H2BB···O2C(C=O)
$D^2_2(10)$	(OH)O3B-H3B···O1A(C=O) & (CH3)C2B-H2BB···O1(C=O)
$D^3_3(12)$	(OH)O3B-H3B···O1A(C=O) & (CH3)C2A-H2AC···O3A(OH)
$D^3_3(12)$	(NH)N-H···O2A(C=O) & (CH3)C2A-H2AC···O3A(OH)
$D^3_3(12)$	(CH3)C2-H2B···O2A(C=O) & (CH3)C2A-H2AC···O3A(OH)
5	
$D(2)$	(OH)O2-H2···O1A(C=O)
$D(2)$	(OH)O2-H2A···O1(C=O)
$D(2)$	(CH2-cyclopropyl)C7-H7AA···O2(OH)
$D(2)$	(CH)C21-H21···O4(C-O-C)
$C(4)$	(NH)N-H···O3(C=O)
$C(4)$	(NH)NA-HA···O3A(C=O)
$C(5)$	(CH2)C4A-H4A···O1A(C=O)
$C(6)$	(CH2)C4-H4A···O3(C=O)
$C(7)$	(CH2-cyclopropyl)C6A-H6AB···O1A(C=O)
level 2	
$C^1_2(6)$	(CH2)C4A-H4AA···O1A(C=O) & (CH2-cyclopropyl)C6A-H6AB···O1A(C=O)
$C^2_2(9)$	[(OH)O2-H2···O1A(C=O)]2 & (CH2-cyclopropyl)C7-H7A···O2(OH)
$C^2_2(10)$	(NH)N-H···O3(C=O) & (CH2)C4-H4A···O3(C=O)
$C^2_2(11)$	(OH)O2A-H2A···O1(C=O) & (CH2-cyclopropyl)C7A-H7A···O2(OH)
$C^2_2(11)$	(NH)NA-HA···O3A(C=O) & (CH2)C4-H4A···O1A(C=O)
$C^2_2(12)$	(CH2)C4A-H4A···O1A(C=O) & (CH2-cyclopropyl)C6A-H6AB···O1A(C=O)
$C^2_2(13)$	(NH)NA-HA···O3A(C=O) & (CH2-cyclopropyl)C6-H6AB···O1A(C=O)
$C^2_2(20)$	(CH)C21-H21A···O4(C-O-C) & (CH2-cyclopropyl)C7A-H7A···O2(OH)
$R^1_2(6)$	(NH)N-H···O3(C=O) & (CH2)C4-H4A···O3(C=O)
$R^2_2(8)$	[(OH)O2A-H2A···O1(C=O)]2
$R^2_2(7)$	(CH2)C4A-H4A···O1A(C=O) & (CH)C3A-H3A…C5A(CH-cyclopropryl)
$R^2_2(11)$	(NH)NA-HA···O3A(C=O) & (CH2)C4-H4A···O1A(C=O)
$R^2_3(7)$	(CH2-cyclopropyl)C7A-H7AA···O2(OH) & (OH)O2-H2···O1A(C=O) & (CH2-cyclopropyl)C6A-H6AB···O1A(C=O)
$R^2_3(13)$	(CH2)C4A-H4A···O1A(C=O) & [(CH2-cyclopropyl)C6A-H6AB···O1A(C=O)]2
$R^3_3(20)$	(NH)NA-HA···O3A(C=O) & [(CH2-cyclopropyl)C6A-H6AB···O1A(C=O)]2
$R^3_4(18)$	[(CH2)C4A-H4A···O1A(C=O)]2 & [(CH2-cyclopropyl)C6A-H6AB···O1A(C=O)]2
$D^2_3(8)$	[(OH)O2-H2···O1A(C=O)]2 & (CH2)C4A-H4A···O1A(C=O)
$D^2_3(10)$	[(OH)O2-H2···O1A(C=O)]2 & (CH2-cyclopropyl)C6A-H6AB···O1A(C=O)
$D^3_3(9)$	(NH)N-H···O3(C=O) & [(CH)C21-H21A···O4(C-O-C)]2
$D^3_3(11)$	(CH2)C4-H4A···O3(C=O) & [(CH)C21-H21A···O4(C-O-C)]2
$D^3_3(12)$	[(OH)O2A-H2A···O1(C=O)]2 & (CH2)C4-H4A···O1(C=O)
$D^3_3(13)$	[(OH)O2A-H2A···O1(C=O)]2 & (NH)N-H···O3(C=O)
$D^3_3(13)$	[(OH)O2A-H2···O1A(C=O)]2 & (NH)NA-HA···O3A(C=O)
$D^3_3(13)$	[(OH)O2A-H2A···O1(C=O)]2 & (CH2)C4-H4A···O3(C=O)
$D^3_3(13)$	(NH)N-H···O3(C=O) & [(CH2-cyclopropyl)C7-H7A···O2(OH)]2
$D^3_3(13)$	(CH2)C4-H4A···O3(C=O) & [(CH2-cyclopropyl)C7-H7A···O2(OH)]2
$D^3_3(13)$	(CH2-cyclopropyl)C6A-H6AB···O1A(C=O) & [(CH2-cyclopropyl)C7A-H7A···O2(OH)]2
$D^3_3(14)$	[(OH)O2A-H2A···O1(C=O)]2 & (CH2-cyclopropyl)C6A-H6AB···O1A(C=O)
$D^3_3(15)$	[(OH)O2-H2A···O1(C=O)]2 & (OH)O2A-H2A···O1(C=O)
$D^3_3(15)$	[(OH)O2-H2···O1A(C=O)]2 & (NH)N-H···O3(C=O)
$D^3_3(15)$	[(OH)O2-H2···O1A(C=O)]2 & (CH2)C4-H4A···O3(C=O)
$D^3_3(17)$	(NH)NA-HA···O3A(C=O) & [(CH2-cyclopropyl)C7-H7A···O2(OH)]2
ADELOM	
$C(6)$	(CH-cyclopropyl)C26-H28···O2(C=O)
level 2	
$R^1_2(8)$	(CH-cyclopropyl)C26-H28···O2(C=O) & (NH)N2-H1···O2(C=O)

$C^2_2(10)$	(CH-cyclopropyl)C26-H28···O2(C=O) & (NH)N2-H1···O2(C=O)
ADELUS	
level 2	
$R^2_2(12)$	[(CH-cyclopropyl)C25-H32···O3(C=O)]2
$R^2_2(14)$	[(CH-cyclopropyl)C25-H33···O4(C=O)]2
$C^2_2(11)$	(NH)N2-H5…O4(C=O) & (CH-cyclopropyl)C25-H32···O3(C=O)
$C^2_2(13)$	(NH)N2-H5···O4(C=O) & (CH-cyclopropyl)C25-H32···O3(C=O)
$R^1_2(8)$	(CH-cyclopropyl)C25-H33···O4(C=O) & (NH)N2-H5···O4(C=O)
$R^2_2(14)$	(CH-cyclopropyl)C25-H33···O4(C=O) & & (NH)N2-H5···O4(C=O)
$C^2_2(11)$	(CH-cyclopropyl)C25-H32···O3(C=O) & (CH)C12-H18…O4(C=O)
$R^1_2(6)$	(CH-cyclopropyl)C25-H33···O4(C=O) & (CH)C12-H18···O4(C=O)
$R^2_2(12)$	(CH-cyclopropyl)C25-H33···O4(C=O) & (CH)C12-H18···O4(C=O)
$R^2_2(20)$	(CH-cyclopropyl)C26-H28···O2(C=O) & (arom)C21-H28···O2(C=O)
$C^1_2(10)$	(CH-cyclopropyl)C26-H28···O2(C=O) & (arom)C23-H30···O3(C=O)
$C^2_2(14)$	(CH-cyclopropyl)C25-H33···O4(C=O) & (arom)C23-H30···O3(C=O)
$C^2_2(13)$	(CH-cyclopropyl)C25-H33···O4(C=O) & (arom)C23-H30···O3(C=O)
$C^2_2(15)$	(CH-cyclopropyl)C25-H33···O4(C=O) & (arom)C23-H30···O3(C=O)
$C^2_2(9)$	(CH-cyclopropyl)C25-H33···O4(C=O) & (CHcyclopropyl)C25-H32···O3(C=O)
$C^2_2(13)$	(CHcyclopropyl)C25-H32···O3(C=O) & (CH-cyclopropyl)C25-H33···O4(C=O)
ADEMAZ	
$R^2_2(10)$	[CHcyclopropyl)C3-H2···O1(c-o-c)]2
$R^2_2(14)$	[(CHcyclopropyl)C22-H27···O3(C=O)]2
level 2	
$C^2_2(14)$	(CHcyclopropyl)C3-H2···O1(c-o-c) & (NH)N1-H1···O3(C=O)
$R^1_2(8)$	(NH)N1-H1···O3(C=O) & (CHcyclopropyl)C22-H27···O3(C=O)
$R^2_2(14)$	(NH)N1-H1···O3(C=O) & (CHcyclopropyl)C22-H27···O3(C=O)
$C^2_2(8)$	(CHcyclopropyl)C3-H2···O1(c-o-c) & (CHcyclopropyl)C5-H7···O2(C=O)
$C^2_2(10)$	(CHcyclopropyl)C3-H2···O1(c-o-c) & (CH2)C5-H7…O2(C=O)
$C^4_4(18)$	(CHcyclopropyl)C3-H2···O1(c-o-c) & (CHcyclopropyl)C5-H7···O2(C=O)
$C^2_2(15)$	(CHcyclopropyl)C3-H2···O1(c-o-c) & (CH2)C11-H17…O4(C=O)
$C^2_2(15)$	(CHcyclopropyl) C3-H2···O1(c-o-c) & (arom)C16-H21…O2(C=O)
$C^2_2(17)$	(CHcyclopropyl) C3-H2···O1(c-o-c) & (arom)C16-H21…O2(C=O)
$C^2_2(18)$	(CHcyclopropyl) C3-H2···O1(c-o-c) & (CHcyclopropyl)C22-H27···O3(C=O)
$C^2_2(20)$	(CH2)C5-H7…O2(C=O) & (CHcyclopropyl)C22-H27···O3(C=O)
$C^2_2(20)$	(CH2)C5-H7…O2(C=O) & (CHcyclopropyl)C22-H27···O3(C=O)
$C^2_2(11)$	(CH2)C11-H17…O4(C=O) & (CHcyclopropyl)C22-H27···O3(C=O)
$C^2_2(13)$	(CH2)C11-H17…O4(C=O) & (CHcyclopropyl)C22-H27···O3(C=O)
$C^2_2(17)$	(arom)C16-H21…O2(C=O) & (CHcyclopropyl)C22-H27···O3(C=O)
$C^2_2(19)$	(arom)C16-H21…O2(C=O) & (CHcyclopropyl)C22-H27···O3(C=O)
ADEMED	
$D(2)$	(CHcyclopropyl)C9-H13…O10(C=O)
$D(2)$	(CHcyclopropyl)C31-H41…O5(C=O)
level 2	
$D^3_3(16)$	[(CHcyclopropyl)C9-H13…O10(C=O)]2 & (NH)N1-H1…O3(C=O)
$D^3_3(12)$	[(CHcyclopropyl)C31-H41…O5(C=O)]2 & & (NH)N1-H1…O3(C=O)
$C^2_2(19)$	(CHcyclopropyl)C9-H13···O10(C=O) & (CH2) C5-H7···O7(C-O-C)
$C^2_2(19)$	(CHcyclopropyl)C31-H41…O5(C=O) & (CH2) C5-H7···O7(C-O-C)
$D^2_3(14)$	(CHcyclopropyl)C32-H42…O7(C=O) & [(CH2) C5-H7···O7(C-O-C)]2
$C^1_2(15)$	(CHcyclopropyl)C9-H13…O10(C=O) & (CH2)C6-H9…O10(C=O)
$C^2_2(17)$	(CHcyclopropyl)C31-H41…O5(C=O) &(CH3)C6-H9…O10(C=O)
$D^3_3(16)$	(CHcyclopropyl)C32-H42…O7(C=O) & [(CH3)C6-H9…O10(C=O)]2
$D^3_3(14)$	[(CHcyclopropyl)C9-H13…O10(C=O)]2 & (CH)C19-H23…O3(C=O)
$D^3_3(12)$	[(CHcyclopropyl)C9-H13…O10(C=O)]2 & (NH)N3-H29…O8[C=O]
$C^2_2(17)$	(CHcyclopropyl)C9-H13…O10(C=O) & (CH3)C28-H38…O5(C=O)
$R^2_2(16)$	(CHcyclopropyl)C31-H41…O5(C=O) & (CHcyclopropyl)C9-H13…O10(C=O)
$D^3_3(16)$	[(CHcyclopropyl)C9-H13…O10(C=O)]2 & (CHcyclopropyl)C32-H42…O7(C=O)
$D^3_3(16)$	(CHcyclopropyl)C32-H42…O7(C=O) & [(arom)C13-H19…O6(C=O)]2
$D^3_3(12)$	[(CHcyclopropyl)C31-H41…O5(C=O)]2 & (CH)C19-H23…O3(C=O)
$D^3_3(16)$	[(CHcyclopropyl)C31-H41…O5(C=O)]2 & (NH)N3-H29…O8(C=O)
$R^2_2(10)$	(CHcyclopropyl)C32-H42…O7(C=O) & (NH)N3-H29…O8(C=O)
$R^2_2(18)$	(CHcyclopropyl)C32-H42…O7(C=O) & (NH)N3-H29…O8(C=O)
$C^1_2(15)$	(CHcyclopropyl)C31-H41…O5(C=O) & (CH3)C28-H38…O5(C=O)
$D^3_3(20)$	(CHcyclopropyl)C32-H42…O7(C=O) & [(CH3)C28-H38…O5(C=O)]2
$D^3_3(17)$	(CHcyclopropyl)C32-H42…O7(C=O) & [(CHcyclopropyl)C31-H41…O5(C=O)]2
$D^3_3(20)$	(CHcyclopropyl)C32-H42…O7(C=O) & (arom)C39-H50…O1(C=O)
BUTCIE	
$R^2_2(18)$	[(CHcyclopropyl)C2-H7…O2(C=O)]2
$R^2_2(20)$	[(CHcyclopropyl)C3-H8…O4(C=O)]2
level 2	
$C^1_2(13)$	(CHcyclopropyl)C2-H7…O2(C=O) & (NH)N3-H3…O2(C=O)
$C^2_2(15)$	(CHcyclopropyl)C2-H7…O2(C=O) & (NH)N3-H3…O2(C=O)

$C^2_2(12)$ (CHcyclopropyl)C3-H8…O4(C=O) & (NH)N3-H3…O2(C=O)
$C^2_2(16)$ (CHcyclopropyl)C3-H8…O4(C=O) & (NH)N3-H3…O2(C=O)
$C^2_2(9)$ (CHcyclopropyl)C2-H7…O2(C=O) & (CHcyclopropyl)C3-H8…O4(C=O)
$C^2_2(19)$ (CHcyclopropyl)C2-H7…O2(C=O) & (CHcyclopropyl)C3-H8…O4(C=O)
$C^2_2(12)$ (CHcyclopropyl)C2-H7…O2(C=O) & (arom)C8-H11…O3(C=O)
$C^2_2(16)$ (CHcyclopropyl)C2-H7…O2(C=O) & & (arom)C8-H11…O3(C=O)
$C^2_2(20)$ (CHcyclopropyl)C2-H7…O2(C=O) & (CH3)C16-H16…O3(C=O)
$C^2_2(20)$ (CHcyclopropyl)C2-H7…O2(C=O) & (CH3)C16-H16…O3(C=O)
$C^2_2(13)$ (CHcyclopropyl)C3-H8…O4(C=O) & (arom)C8-H11…O3(C=O)
$C^2_2(17)$ (CHcyclopropyl)C3-H8…O4(C=O) & (arom)C8-H11…O3(C=O)
$C^2_2(17)$ (CHcyclopropyl)C3-H8···O4(C=O) & (CH3)C16-H16…O3(C=O)

CATWEA

$R^2_2(12)$ [(CHcyclopropyl)C3-H6···O5(OH)]2 {[CH(cyclopropyl)C20-H38···O10(OH)]2}

level 2

$R^2_2(10)$ (CHcyclopropyl)C3-H6···O5(OH) & (OH)O5-H1···O3(C=O)
$R^2_2(17)$ (CHcyclopropyl)C3-H6···O5(OH) & (OH)O5-H1···O3(C=O)
$C^1_2(6)$ (CHcyclopropyl)C3-H6···O5(OH) & (NH)N1-H2···O5(OH)
$C^2_2(12)$ (CHcyclopropyl)C3-H6···O5(OH) & (NH)N1-H2···O5(OH)
$C^3_4(18)$ [(CHcyclopropyl)C3-H6···O5(OH)]2 & [(NH)N1-H2···O5(OH)]2
$C^2_2(14)$ (CHcyclopropyl)C3-H6···O5(OH) & (NH)N2-H3···O1(C=O)
$C^2_2(15)$ (CHcyclopropyl)C3-H6···O5(OH) & (NH)N2-H3···O1(C=O)
$R^2_2(10)$ (CHcyclopropyl)C20-H38···O10(OH) & (OH)O10-H33···O8(C=O)
$R^2_2(17)$ (CHcyclopropyl)C20-H38···O10(OH) & (OH)O10-H33···O8(C=O)
$C^1_2(6)$ (CHcyclopropyl)C20-H38···O10(OH) &(NH)N3-H34···O10(OH)
$C^2_2(12)$ (CHcyclopropyl)C20-H38···O10(OH) &(NH)N3-H34···O10(OH)
$C^3_4(18)$ [(CHcyclopropyl)C20-H38···O10(OH)]2 &[(NH)N3-H34···O10(OH)]2
$C^2_2(14)$ (CHcyclopropyl)C20-H38···O10(OH) & (NH)N4-H35···O6(C=O)
$C^2_2(15)$ (CHcyclopropyl)C20-H38···O10(OH) & (NH)N4-H35···O6(C=O)

CEGVUH

$C(4)$ (CHcyclopropyl)C2-H1···O1(C=O)

level 2

$R^1_2(6)$ (CHcyclopropyl)C2-H1···O1(C=O) & (NH)N1-H10···O1(C=O)
$C^2_2(8)$ (CHcyclopropyl)C2-H1···O1(C=O) & (NH)N1-H10···O1(C=O)
$C^1_2(13)$ (CHcyclopropyl)C3-H3···O2(C=O) & (OH)O3-H11···O2(C=O)
$C^2_2(15)$ (CHcyclopropyl)C3-H3···O2(C=O) & O) & (OH)O3-H11···O2(C=O)

CERQUM

$C(8)$ (CHcyclopropyl)C8-H7···N1(arom)
C(7) (CHcyclopropyl)C9-H8···S1

level 2

$R^1_2(6)$ (CHcyclopropyl)C8-H7···N1(arom) & (NH)N3-H2···N1(arom)
$C^2_2(14)$ (CHcyclopropyl)C8-H7···N1(arom) & (NH)N3-H2···N1(arom)
$R^4_4(14)$ [(CHcyclopropyl)C8-H7···N1(arom)]2 & (arom)C2-H3···O1(C=O)
$C^2_2(12)$ (CHcyclopropyl)C9-H8···S1 & (arom)C2-H3···O1(C=O)
$C^2_2(16)$ (CHcyclopropyl)C9-H8···S1 & (arom)C2-H3···O1(C=O)
$R^4_4(18)$ (CHcyclopropyl)C9-H8···S1 & [(CHcyclopropyl)C8-H7···N1(arom)]2

EDIWIZ

$C(7)$ (CHcyclopropyl)C12-H12···O1(C=O)

level 2

$C^2_2(17)$ (CHcyclopropyl)C12-H12···O1(C=O) & (CH3)C1-H3···O2(C=O)
$C^2_2(19)$ (CHcyclopropyl)C12-H12···O1(C=O) & (CH3)C1-H3···O2(C=O)

GENYUU

$C(4)$ (CHcyclopropyl)C7-H7···O1(C=o)
$C(7)$ (CHcyclopropyl)C8-H8···N1(arom)

level 2

$R^1_2(6)$ (CHcyclopropyl)C7-H7···O1(C=o) & (NH)N2-H1···O1(C=O)
$C^2_2(8)$ (CHcyclopropyl)C7-H7···O1(C=o) & (NH)N2-H1···O1(C=O)
$R^2_2(9)$ (CHcyclopropyl)C8-H8···N1(arom) & (NH)N2-H1···O1(C=O)
$C^2_2(11)$ (CHcyclopropyl)C8-H8···N1(arom) & (NH)N2-H1···O1(C=O)
$C^2_2(9)$ (CHcyclopropyl)C8-H8···N1(arom) & (CHcyclopropyl)C7-H7···O1(C=o)
$R^2_2(11)$ (CHcyclopropyl)C8-H8···N1(arom) & (CHcyclopropyl)C7-H7···O1(C=o)

HILXIM

$R^2_2(10)$ [(CHcyclopropyl)C2-H3···O5(C=O)]2
$C(12)$ (CHcyclopropyl)C2-H4···O1(C=O)

level 2

$C^2_2(20)$ [(CHcyclopropyl)C2-H3···O5(C=O) & (arom)C7-H7···O3(C=o)
$C^1_2(16)$ (CHcyclopropyl)C2-H3···O5(C=O) & (CH3)C18-H16···O5(C=O)
$C^2_2(18)$ CHcyclopropyl)C2-H3···O5(C=O) & (CH3)C18-H16···O5(C=O)
$C^2_2(13)$ (CHcyclopropyl)C2-H4···O1(C=O) & (arom)C12-H9···O5(C=O)

IHUFEY

$C(12)$ (CHcyclopropyl)C12-H10···O1(C=O)

level 2

$R^2_2(10)$	(CHcyclopropyl)C12-H10···O1(C=O) & (NH2)N1-H1···N3(arom)
$R^1_2(6)$	(CHcyclopropyl)C12-H10···O1(C=O) & (NH)N4-H3···O1(C=O)
$C^2_2(11)$	(CHcyclopropyl)C12-H10···O1(C=O) & (CH3)C5-H5···O3(C=O)
JAWLAU	
C(4)	(CHcyclopropyl)C8-H5···O1(C=O)
level 2	
$R^1_2(6)$	(CHcyclopropyl)C8-H5···O1(C=O) & (NH)N1-H1···O1(c=O)
$C^2_2(8)$	(CHcyclopropyl)C8-H5···O1(C=O) & NH)N1-H1···O1(c=O)
PEDWOM	
$R^2_2(20)$	[(CHcyclopropyl)C15-H10···F1]2
D(2)	(CHcyclopropyl)C16-H12···N5(arom)
C(5)	(CHcyclopropyl)C49-H38···O8(C-O-C)
D(2)	(CHcyclopropyl)C50-H40···F3
$D^2_2(13)$	(CHcyclopropyl) C16-H12···N5(arom) & (NH)N2-H1···O4(C=O)
level 2	
$D^2_2(11)$	(CHcyclopropyl)C50-H40···F3 & (NH)N2-H1···O4(C=O)
$D^3_3(18)$	(CHcyclopropyl)C49-H38···O8(C-O-C) & [(CH)C1-H2···F6]2
$D^2_2(12)$	(CHcyclopropyl)C50-H40···F3 & (CH)C1-H2···F6
$D^3_3(17)$	(CHcyclopropyl)C15-H10···F1 &[(arom)C8-H4···Cl6]2
$C^2_2(12)$	(CHcyclopropyl)C16-H12···N5(arom) & (arom)C8-H4···Cl6
$D^2_2(15)$	(CHcyclopropyl)C50-H40···F3 & (arom)C8-H4…Cl6
$D^3_3(16)$	[(CHcyclopropyl)C16-H12···N5(arom)]2 & (CHcyclopropyl)C15-H10···F1
$C^2_2(8)$	(CHcyclopropyl)C15-H10···F1 & (CH)C170H14···O2(C-O-C)
$C^2_2(16)$	(CHcyclopropyl)C15-H10···F1 & (CH)C17-H14···O2(C-O-C)
$C^2_2(11)$	(CHcyclopropyl)C15-H10···F1 & (CH)C17-H14···O3(C-O-C)
$C^2_2(13)$	(CHcyclopropyl)C15-H10···F1 & (CH)C17-H14···O3(C-O-C)
$D^3_3(17)$	[(CHcyclopropyl)C16-H12···N5(arom)]2 & (CH)C17-H14···O2(C-O-C)
$D^3_3(20)$	[(CHcyclopropyl)C16 -H12···N5(arom)]2 & (CH)C17-H14···O3(C-O-C)
$D^2_2(9)$	(CHcyclopropyl)C16 -H12···N5(arom) & (NH)N4-H15···O7(C=O)
$D^2_2(15)$	(CHcyclopropyl)C16 -H12···N5(arom) & (arom)C25-H18···Cl2
$D^2_2(6)$	(CHcyclopropyl)C16 -H12···N5(arom) & (arom)C28-H19···Cl5
$D^2_2(9)$	(CHcyclopropyl)C16 -H12···N5(arom) & (arom)C29-H20···O7(C=O)
$R^2_2(16)$	(CHcyclopropyl)C16 -H12···N5(arom) & (NH)N6-H29···O1(C=O)
$D^2_2(11)$	(CHcyclopropyl)C16 -H12···N5(arom) & (arom)C42-H32···Cl3
$D^2_2(16)$	(CHcyclopropyl)C16 -H12···N5(arom) & (CHcyclopropyl)C50-H40···F3
$D^3_3(18)$	(CHcyclopropyl)C49-H38···N3(arom) & (NH)N4-H15···O7(C=O) & (NH)N4-H15···O7(C=O)
$C^2_2(20)$	(NH)N4-H15···O7(C=O) & (CHcyclopropyl)C50-H40···F3
$D^2_2(9)$	(CHcyclopropyl)C50-H40···F3 & (arom)C25-H18···Cl2
$C^2_2(19)$	(CHcyclopropyl)C50-H40···F3 & (arom)C28-H19···Cl5
$D^3_3(18)$	(CHcyclopropyl)C49-H38···O8(C-O-C) & [(arom)C29-H20···O7(C=O)]2
$C^2_2(17)$	(CHcyclopropyl)C50-H40···F3 & (arom)C29-H20···O7(C=O)
$D^3_3(20)$	(CHcyclopropyl)C49-H38···O8(C-O-C) & [(NH)N6-H29···O1(C=O)]2
$D^2_2(13)$	(CHcyclopropyl)C50-H40···F3 & (NH)N6-H29···O1(C=O)
$C^2_2(20)$	(CHcyclopropyl)C50-H40···F3 &(arom)C42-H32···Cl3
$D^3_3(16)$	(CHcyclopropyl)C49-H38···O8(C-O-C) & [(arom)C45-H33···Cl1]2
$D^2_2(11)$	(CHcyclopropyl)C50-H40···F3 & (arom)C45-H33···Cl1
$R^2_2(9)$	(CHcyclopropyl)C49-H38···O8(C-O-C) & (CH2)C47-H36···O9(C=O)
$C^2_2(11)$	(CHcyclopropyl)C49-H38···O8(C-O-C) & (CH2)C47-H36···O9(C=O)
$D^3_3(15)$	[(CHcyclopropyl)C50-H40···F3]2 & (CH2)C47-H36···O9(C=O)
$D^3_3(11)$	(CHcyclopropyl)C49-H38···O8(C-O-C) & [(CHcyclopropyl)C50-H40···F3]2
$D^3_3(18)$	(CHcyclopropyl)C49-H38···O8(C-O-C) & [(CH)C51-H42···N1(arom)]2
$D^2_2(12)$	(CHcyclopropyl)C50-H40···F3 & (CH)C51-H42···N1(arom)
ROPQUL	
C(10)	(CHcyclopropyl)C3-H6···O2(C=O)
level 2	
$R^1_2(6)$	(CHcyclopropyl)C3-H6···O2(C=O) & (NH)N1-H1···O2(C=O)
$C^2_2(18)$	(CHcyclopropyl)C3-H6···O2(C=O) & (NH)N1-H1···O2(C=O)
$C^2_2(12)$	(CHcyclopropyl)C3-H6···O2(C=O) & (arom)C12-H11···O1(C=O)
$C^2_2(18)$	(CHcyclopropyl)C3-H6···O2(C=O) & (arom)C12-H11···O1(C=O)
$C^2_2(9)$	(CHcyclopropyl)C3-H6···O2(C=O) & (arom)C15-H12···O1(C=O)
$R^2_2(12)$	(CHcyclopropyl)C3-H6···O2(C=O) & (arom)C15-H13···N2(arom)
$C^2_2(18)$	(CHcyclopropyl)C3-H6···O2(C=O) & (arom)C15-H13···N2(arom)
VEHDIY	
C(6)	(CHcyclopropyl)C12-H15···O2(C=O)
level 2	
$R^1_2(6)$	*(CHcyclopropyl)C12-H15···O2(C=O) & (NH)N1-H1···O2(C=O)
	*(CHcyclopropyl)C12-H15···O2(C=O) & (CH3)C10-H13···O2(C=O)
$C^2_2(10)$	(CHcyclopropyl)C12-H15···O2(C=O) & (NH)N1-H1···O2(C=O)
$C^2_2(12)$	(CHcyclopropyl)C12-H15···O2(C=O) & (CH3)C10-H13···O2(C=O)
VETKEL	
C(4)	(CHcyclopropyl)C1-H2···O1(C=O)

C(5)	(CHcyclopropyl)C3-H5···O1(C=O)
level 2	
C^2_2(10)	(CHcyclopropyl)C1-H2···O1(C=O) & (NH)N1-H1···N2(arom)
C^4_4(20)	[(CHcyclopropyl)C1-H2···O1(C=O)]2 & [(NH)N1-H1···N2(arom)]2
C^1_2(5)	(CHcyclopropyl)C1-H2···O1(C=O) & (CHcyclopropyl)C3-H5···O1(C=O)
C^2_2(9)	(CHcyclopropyl)C1-H2···O1(C=O) & (CHcyclopropyl)C3-H5···O1(C=O)
C^3_4(14)	[(CHcyclopropyl)C1-H2···O1(C=O)]2 & [(CHcyclopropyl)C3-H5···O1(C=O)]2
R^3_4(14)	[(CHcyclopropyl)C1-H2···O1(C=O)]2 & [(CHcyclopropyl)C3-H5···O1(C=O)]2
C^1_2(10)	(CHcyclopropyl)C3-H5···O1(C=O) & (arom)C6-H7···O1(C=O)
C^2_2(12)	(CHcyclopropyl)C3-H5···O1(C=O) & (arom)C6-H7···O1(C=O)
WICMIH	
C(11)	(CHcyclopropyl)C5-H3···F1
level 2	
C^2_2(13)	(CHcyclopropyl)C5-H3···F1 & (NH)N1-H18···O1(C=O)
$C^2$2(15)	(CHcyclopropyl)C5-H3···F1 & (NH)N1-H18···O1(C=O)
$C^2$2(19)	(CHcyclopropyl)C5-H3···F1 & (CH3)C15-H13···O2(C=O)
ZAMJEF	
S(12)	(CHcyclopropyl)C20-H30···O2(C=O)
level 2	
C^2_2(12)	(CHcyclopropyl)C22-H28···O2(C=O) & (arom)C4-H2···O3(C-O-C)
ZAMJOP	
C(4)	(CHcyclopropyl)C10-H12···O2(C=O)
level 2	
R^1_2(6)	(CHcyclopropyl)C10-H12···O2(C=O) & (NH)N1-H11···O2(C=O)
C^2_2(8)	(CHcyclopropyl)C10-H12···O2(C=O) & (NH)N1-H11···O2(C=O)
ZUQBIY	
C(6)	(CHcyclopropyl)C20-H18···N2(arom)
level 2	
C^2_2(18)	(CHcyclopropyl)C20-H18···N2(arom) & (arom)C8-H4···O1(C=O)
C^1_2(12)	(CHcyclopropyl)C20-H18···N2(arom) & (arom)C9-H5···N2(arom)
R^2_2(16)	(CHcyclopropyl)C20-H18···N2(arom) & (arom)C9-H5···N2(arom)

Table S7 Relative percentage contributions of main inter-contacts in **1**-**5**, relatively to the whole HS area (contributions below 0.5 % is not included)

	1	**2**	**3**	**4**	**5**
H···H	71	47.7	48.1	66.8	56.2
O···**H**/H···O	27.2 (**14.5**/12.7)	49.7 (**26.6**/23.1)	48.9 (**26.5**/22.4)	25.3 (**13.4**/11.9)	18.1 (**9.5**/8.6)
C···**H**/H···C	1.6 (**0.8**/0.8)	2.5 (**1.4**/1.1)	2.3 (**1.2**/1.1)	2.5 (**1.3**/1.2)	22.5 (**12.9**/9.6)
N···**H**/H···N				0.9 (**0.4**/0.5)	
O···O				0.6	
O···**C**/C···O				3.3 (**1.6**/1/7)	0.8 (**0.4**/0.4)
C···C					1.5
O···**N**/N···O				0.7 (**0.3**/0.4)	

Table S8 Enrichment ratios in **1**-**5**

	1			**2**			**3**		
	H	O	C	H	O	C	H	O	C
H	71			*47.7*			*48.1*		
O	27.2			*49.7*			*48.9*		
C	1.6			*2.5*			*2.3*		
Sx	85.4	13.6	0.8	73.8	24.85	1.25	73.7	24.45	1.15
Random contacts							Random contacts		
H	72.93			54.46			54.32		
O	23.23			36.68			36.04		
C	1.37			1.85			1.7		
Enrichment ratio							Enrichment ratio		
H	**0.97**			0.88			0.89		
O	**1.17**			**1.35**			**1.36**		
C	**1.17**			**1.35**			**1.35**		

4				**5**		
H	O	C	N	H	O	C

H	*66.8*				*56.2*		
O	*25.3*	*0.6*	*3.3*	*0.7*	*18.1*		
C	*2.5*				*22.5*	*0.8*	*1.5*
N	*0.9*						
Sx	81.15	15.25	2.9	0.8	76.5	9.45	13.15
Random contacts					Random contacts		
H	68.85				58.52		
O	24.75	2.33	0.88	0.24	14.46		
C	4.71				20.12	2.49	1.73
N	1.3						
Enrichment ratio					Enrichment ratio		
H	**1.01**				**0.96**		
O	**1.02**	0.26	**3.75**	**2.92**	**1.25**		
C	0.53				**1.12**	0.32	0.87
N	0.69						

Table S9 Inter-contacts energy values (kJ/mol) for **1**-**5**

	Symmetry code	*R*	E_{ele}	E_{pol}	E_{dis}	E_{rep}	E_{tot}
1							
	-x+1/2, y+1/2, z+1/2	8.68	-6.4	-1.4	-25.1	13.8	-21.1
	-x+1/2, y+1/2, z+1/2	8.68	-4.9	-0.6	-28.3	20.1	-17.9
	x+1/2, -y+1/2, z	6.80	-39.8	-11.3	-28.4	46.9	-46.2
	-x, -y, z+1/2	8.26	-7.6	-3.3	-17.4	11.1	-18.7
	x, y, z	11.78	0.3	-0.0	-2.5	0.2	-1.7
	-x, -y, z+1/2	7.27	-6.3	-2.5	-36.3	23.4	-25.6
	x+1/2, -y+1/2, z	9.19	-2.4	-2.1	-9.3	4.3	-9.5
	Total		***-67.1***	***-21.2***	***-147.3***	***119.8***	***-140.7***
2							
	x, y, z	7.50	-82.5	-19.4	-13.6	94.1	-55.2
	x, y, z	8.87	2.8	-1.6	-8.7	2.0	-4.7
	x, y, z	8.09	-2.7	-0.5	-11.7	7.8	-8.6
	-x,- y, -z	5.57	-8.5	-7.5	-28.3	16.8	-28.8
	-x,- y, -z	10.23	-2.9	-0.1	-9.2	7.7	-6.4
	-x,- y, -z	5.34	-23.9	-5.8	-41.2	44.4	-38.1
	-x,- y, -z	8.12	-1.5	-0.4	-9.8	3.4	-8.3
	-x,- y, -z	7.67	-3.7	-1.0	-21.8	11.8	-16.4
	-x,- y, -z	6.36	-9.1	-4.5	-26.7	18.6	-24.8
	-x,- y, -z	7.39	-120.6	-26.7	-14.3	138.3	-74.3
	Total		***-252.6***	***-67.5***	***-185.3***	***344.9***	***-265.6***
3							
	x+1/2, -y+1/2, -z	7.98	-7.7	-2.8	-8.3	8.9	-12.0
	-x, y+1/2, -z+1/2	6.51	-0.7	-1.4	-19.3	9.5	-12.7
	X+1/2, y, -z+1/2	7.70	-6.6	-1.3	-8.8	4.1	-13.1
	-x+1/2, y+1/2, z	9.38	-2.9	-0.4	-1.3	0.0	-4.5
	-x, -y, -z	5.96	-9.1	-6.7	-20.6	9.6	-26.5
	x, -y+1/2, z+1/2	7.49	-90.2	-24.2	-17.3	113.7	-58.1
	---	5.09	0.00	-	0.0	0.0	-
	---	4.20	0.00	0.0	0.00	0.0	0.0
	---	5.10	-6.6	-1.3	-8.8	4.1	-13.1
	---	4.55	-2.9	-0.4	-1.3	0.0	-4.5
	---	6.50	-0.7	-1.4	-19.3	9.5	-12.7
	-x+1/2, y+1/2, z	8.18	-6.1	-1.2	-17.3	11.4	-15.4
	-x, -y, -z	7.64	-7.3	-1.0	-20.4	19.9	-13.9
	---	6.73	-7.3	-1.0	-20.4	19.9	-13.9
	Total		***-148.1***	***-43.1***	***-163.1***	***210.6***	***-175***
4							
	---	6.49	-4.9	-2.8	-16.9	8.2	-16.9
	---	7.32	0.0	-	0.0	0.0	-
	---	7.81	0.0	-	0.00	0.0	-
	---	10.94	0.2	-0.0	-0.00	0.0	0.2
	-x, -y, -z	7.70	-1.5	-0.3	-10.4	4.9	-7.9
	---	4.92	-41.9	-9.5	-27.1	59.2	-38.4
	---	7.64	0.0	-0.0	0.0	0.0	-0.0
	-x, y+1/2, -z+1/2	7.58	-0.7	-0.3	-7.1	4.3	-4.6
	---	7.19	-1.5	-0.3	-10.4	4.9	-7.9
	---	6.23	-0.7	-0.3	-7.1	4.3	-4.6
	---	7.72	-0.6	-0.0	-0.1	0.0	-0.7

---	7.53	-2.3	-0.2	-3.6	0.0	-5.6
---	8.84	-1.5	-0.3	-10.4	4.9	-7.9
Total		***-55.4***	***-14***	***-93.1***	***90.7***	***-94.3***
5						
---	7.98	-7.7	-1.8	-40.9	21.8	-31.7
x, y, z	5.05	-48.3	-12.4	-76.1	75.2	-80.1
-x, y, -z	14.29	-0.5	-0.7	-3.9	0.0	-4.4
---	8.82	-3.7	-1.4	-37.6	20.0	-25.3
---	10.77	5.1	-1.1	-8.9	1.2	-2.4
---	12.63	-5.2	-0.7	-20.6	0.0	-23.9
---	12.19	7.8	-0.7	-20.8	0.0	-10.5
-x+1/2, y+1/2, -z+1/2	11.90	-2.0	-0.2	-8.4	4.7	-6.7
---	8.17	-1.7	-1.5	-30.7	15.0	-20.3
---	8.84	-7.4	-1.6	-40.9	31.2	-25.3
-x, y, -z	13.37	-4.5	-1.1	-20.1	0.0	-23.0
---	11.43	-118.6	-27.5	-14.0	136.4	-73.7
Total		***-186.7***	***-50.7***	***-322.9***	***305.5***	***-327.3***

R – distance [Å] between molecular centroids (mean atomic position)

Scale factors for *Etot`* k_{ele} = 1.057, k_{pol} = 0.740, k_{disp} = 0.871, k_{rep} = 0.618*

* C.F. MacKenzie, P.R. Spackman, D. Jayatilaka, M.A. Spackman. *IUCrJ* 2017, **4**(5), 575-587.

Table S10 Relevant bond angles (in degrees) of the optimized structures under study (see Scheme S1 for atom notation)

Bond	C_3H_6	**1**	**2**	**4**	**5**
C6-C7-C5	60.0	59.7	60.3	59.8	59.9
C6-C5-C7	60.0	60.0	60.0	60.0	60.1
C7-C6-C5	60.0	60.3	59.8	60.2	60.0
C6-C5-C4	-	119.2	120.2	119.4	119.1
C7-C5-C4	-	119.9	119.1	120.3	118.2
C5-C4-C3	-	112.8	112.9	113.2	112.7
H6-C6-H6	114.3	114.5	114.6	114.4	114.4
H7-C7-H7	114.3	114.7	114.5	114.5	114.5
H6-C6-C7	118.0(2×)	117.5	118.6	117.5	118.3
		118.4	117.1	118.4	117.7
H6-C6-C5	118.0(2×)	1172	118.4	117.2	118.5
		118.6	117.6	118.6	117.5
H7-C7-C6	118.0(2×)	117.0	118.4	117.2	117.7
		118.6	117.5	118.4	118.4
H7-C7-C5	118.0(2×)	117.5	118.5	117.8	117.2
		118.5	117.2	118.5	118.6
H5-C5-C4	-	115.1	115.1	114.7	115.6
H5-C5-C6	118.0(2×)	115.8	115.8	115.9	116.4
H5-C5-C7	118.0(2×)	115.7	115.7	115.8	116.1
H4-C4-H4	-	106.7	106.7	107.1	106.5
H4-C4-C3	-	106.8	108.8	108.9	109.2
		108.5	106.4	106.6	107.7
H4-C4-C5	-	111.5	110.4	109.9	111.0
		110.3	111.4	110.9	109.5

Table S11 Relevant natural charges in the systems under study (see Scheme S1 for atom notation)

Atom	C_3H_6	**1**	**2**	**4**	**5**
C6	-0.404	-0.387	-0.406	-0.390	-0.392
C7	-0.404	-0.407	-0.387	-0.405	-0.399
C5	-0.404	-0.243	-0.245	-0.246	-0.239
C4	-	-0.387	-0.393	-0.382	-0.377
C3	-	-0.024	-0.033	-0.113	-0.111
H6	0.202(2×)	0.206	0.211	0.204	0.209
		0.208	0.204	0.209	0.204
H7	0.202(2×)	0.201	0.209	0.203	0.206
		0.210	0.206	0.210	0.211
H5	0.202(2×)	0.214	0.214	0.214	0.213
H4	-	0.235	0.228	0.210	0.198
		0.228	0.241	0.229	0.222

Table S12 Relevant Wiberg bond indices in the systems under study (see Scheme S1 for atom notation)

Bond	C_3H_6	**1**	**2**	**4**	**5**
C6-C5	1.002	0.984	0.980	0.984	.983
C7-C5	1.002	0.980	0.983	0.981	.982
C6-C7	1.002	0.991	0.992	0.991	.993
C5-C4	-	1.012	1.013	1.013	.012
C4-C3	-	0.966	0.964	0.975	.987
C6-H6	0.934(2×)	0.932(2×)	0.931	0.933	.932
			0.933	0.932	.933
C7-H7	0.934(2×)	0.933	0.932(2×)	0.933	.932
		0.931		0.931	.931
C5-H5	0.934(2×)	0.909	0.909	0.922	.911
C4-H4	-	0.904	0.912	1.013	.920
		0.912	0.900	0.922	.917

Table S13 Natural hybrid orbital deviations from line of cyclopropyl nuclear centers in the systems under study (see Scheme S1 for atom notation)

Bond	Atom	C_3H_6	**1**	**2**	**4**	**5**
C6-C5	C6	23.5	23.0	23.7	23.1	23.4
	C5	23.5	22.7	24.0	22.6	22.1
C7-C5	C7	23.5	23.7	23.0	23.8	23.5
	C5	23.5	23.8	22.6	23.9	22.7
C6-C7	C6	23.5	23.2	23.2	23.3	23.3
	C7	23.5	23.3	23.2	23.3	23.4

Table S14 Bond bending at cyclopropyl nuclear centers in the systems under study (see Scheme S1 for atom notation)

Atom	C_3H_6	**1**	**2**	**4**	**5**
C6	107.0	106.5	106.7	106.6	106.7
C7	107.0	106.7	106.5	106.9	106.8
C5	107.0	107.1	106.6	106.5	104.9

Table S15 Relevant QTAIM charges in the systems under study (see Scheme S1 for atom notation)

Atom	C_3H_6	**1**	**2**	**4**	**5**
C6	0.00	-0.01	-0.02	-0.01	-0.01
C7	0.00	-0.02	-0.01	-0.02	-0.01
C5	0.00	-0.01	-0.01	-0.00	0.00
C4	-	0.06	0.03	0.06	0.06
C3	-	0.35	0.34	0.07	0.38
H6	0.03(2×)	0.03(2×)	0.03	0.03(2×)	0.03(2×)
			0.02[a)]		
H7	0.03(2×)	0.01[a)]	0.03(2×)	0.02	0.03
		0.03		0.03	0.04
H5	0.03(2×)	0.02	0.02	0.02	0.02
H4	-	0.05	0.04	0.02	0.00
		0.04	0.06	0.04	0.03

[a)]additional bond path to oxygen (see Figs. S15-16)

Table S16 Relevant atomic volumes (in $Bohr^3$) in the systems under study (see Scheme S1 for atom notation)

Atom	C_3H_6	**1**	**2**	**4**	**5**
C6	74.7	73.6	72.6	73.7	73.9
C7	74.7	72.3	73.6	73.2	73.5
C5	74.7	58.3	58.7	59.1	59.9
C4	-	53.2	53.4	55.3	55.0
C3	-	37.6	37.5	43.8	43.2
H6	49.5(2×)	49.4(2×)	49.3	49.7	49.3

			48.3[a)]	49.3	49.4
H7	49.5(2×)	48.4[a)]	49.1	49.0	49.4
		49.6	49.3	49.3	49.1
H5	49.5(2×)	48.5	48.3	48.4	48.6
H4	-	45.5	44.6	47.6	50.9
		44.2	44.1	46.3	46.5

[a)]additional bond path to oxygen (see Figs. S15-16)

Table S17 BCP electron density (in e/Bohr^3) of relevant bonds in the systems under study (see Scheme S1 for atom notation)

Bond	C_3H_6	**1**	**2**	**4**	**5**
C6-C5	0.2376	0.2401	0.2359	0.2400	0.2391
C7-C5	0.2376	0.2360	0.2399	0.2362	0.2386
C6-C7	0.2376	0.2364	0.2368	0.2364	0.2364
C5-C4	-	0.2525	0.2524	0.2523	0.2522
C4-C3	-	0.2397	0.2387	0.2387	0.2431
C6-H6	0.2749(2×)	0.2739	0.2748	0.2736	0.2751
		0.2750	0.2736	0.2750	0.2738
C7-H7	0.2749(2×)	0.2730	0.2751	0.2734	0.2732
		0.2745	0.2739	0.2749	0.2752
C5-H5	0.2749(2×)	0.2746	0.2749	0.2748	0.2752
C4-H4	-	0.2725	0.2726	0.2703	0.2675
		0.2727	0.2733	0.2728	0.2717

Table S18 BCP Laplacian of electron density (in e/Bohr^5) of relevant bonds in the systems under study (see Scheme S1 for atom notation)

Bond	C_3H_6	**1**	**2**	**4**	**5**
C6-C5	-0.4057	-0.4207	-0.3942	-0.4196	-0.4129
C7-C5	-0.4057	-0.3948	-0.4193	-0.3962	-0.4099
C6-C7	-0.4057	-0.4000	-0.4026	-0.4001	-0.3988
C5-C4	-	-0.5924	-0.5914	-0.5910	-0.5906
C4-C3	-	-0.5288	-0.5288	-0.5280	-0.5528
C6-H6	-0.8944(2×)	-0.8880	-0.8936	-0.8858	-0.8956
		-0.8946	-0.8862	-0.8948	-0.9096
C7-H7	-0.8944(2×)	-0.8840	-0.8953	-0.8849	-0.8838
		-0.8916	-0.8880	-0.8941	-0.8960
C5-H5	-0.8944(2×)	-0.8918	-0.8938	-0.8931	-0.8964
C4-H4	-	-0.8856	-0.8867	-0.8732	-0.8550
		-0.8878	-0.9048	-0.8871	-0.8815

Table S19 BCP ellipticity of relevant bonds in the systems under study (see Scheme S1 for atom notation)

Bond	C_3H_6	**1**	**2**	**4**	**5**
C6-C5	0.5283	0.4975	0.5551	0.4994	0.5228
C7-C5	0.5283	0.5522	0.5013	0.5484	0.5237
C6-C7	0.5283	0.5294	0.5232	0.5278	0.5314
C5-C4	-	0.0231	0.0251	0.0245	0.0178
C4-C3	-	0.0285	0.0327	0.0294	0.0751
C6-H6	0.0277(2×)	0.0280	0.0279	0.0287	0.0268
		0.0269	0.0298	0.0275	0.0280
C7-H7	0.0277(2×)	0.0306	0.0268	0.0295	0.0282
		0.0286	0.0279	0.0279	0.0271
C5-H5	0.0277(2×)	0.0339	0.0348	0.0339	0.0355
C4-H4	-	0.0126(2×)	0.0143	0.0130	0.0145
			0.0129	0.0119	0.0092

Table S20 Angles between carbon atoms and BCPs of cyclopropyl ring bonds in the systems under study (see Scheme S1 for atom notation)

Angle	C_3H_6	**1**	**2**	**4**	**5**

C5-C6-BCP$_{C6/C5}$	9.3	9.6	9.5	9.6	9.4
C6-C5-BCP$_{C6/C5}$	9.3	9.7	9.4	9.7	9.8
C5-C7-BCP$_{C7/C5}$	9.3	9.6	9.6	9.5	9.6
C7-C5-BCP$_{C7/C5}$	9.3	9.4	9.8	9.4	9.7
C7-C6-BCP$_{C6/C7}$	9.3	9.0	9.2	9.1	9.1
C6-C7-BCP$_{C6/C7}$	9.3	9.2	9.1	9.1	9.1
BCP$_{C6/C7}$-C6-BCP$_{C6/C5}$	78.6	78.9	78.5	78.9	78.5
BCP$_{C6/C7}$-C7-BCP$_{C7/C5}$	78.6	78.5	79.0	78.5	78.6
BCP$_{C6/C5}$-C5-BCP$_{C7/C5}$	78.6	79.1	79.2	79.1	79.6

Table S21 ADMET profiles for **1-5**

	1	**2**	**3**	**4**	**5**
Physicochemical properties					
Mol. weight [g/mol]	271.31	215.20	233.22	171.19	363.49
Num. heavy atoms	19	15	16	12	26
Num. arom. heavy atoms	0	0	0	0	0
Fraction Csp3	0.77	0.67	0.67	0.75	0.90
Num. rotatable bonds	10	6	6	5	8
Num. H-bond acceptors	5	5	6	3	4
Num. H-bonds donors	1	3	4	2	2
Molar refractivity	68.10	49.85	52.89	43.23	100.85
TPSA [Å^2]	81.70	103.70	112.93	66.40	75.63
Lipophilicity					
Log *P*$_{o/w}$ (iLOGP)	2.82	0.56	0.80	1.42	2.76
Log *P*$_{o/w}$ (XLOGP3)	1.61	0.23	-0.25	0.64	5.99
Log *P*$_{o/w}$ (WLOGP)	0.72	-0.23	-0.30	0.31	4.15
Log *P*$_{o/w}$ (MLOGP)	0.67	-0.47	-1.27	0.13	3.52
Log *P*$_{o/w}$ (SILICOS-IT)	1.60	-0.29	-0.29	0.45	2.77
Consensus Log *P*$_{o/w}$	1.48	-0.04	-0.26	0.59	3.84
Water solubility					
Log *S* (ESOL)	-1.88	-0.92	-0.73	-0.97	-5.34
solubility	3.61e+00 mg/ml; 1.33e-02 mol/l	2.57e+01; 1.19e-01	4.32e+01; 1.85e-01	1.82e+01; 1.06e-01	1.66e-03; 4.58e-06
class	Very soluble	Very soluble	Very soluble	Very soluble	Moderately soluble
Log *S* (Ali)	-2.94	-1.97	-1.66	-1.61	-7.36
solubility	3.13e-01 mg/ml; 1.15e-03 mol/l	2.32e+00; 1.08e-02	5.06e+00; 2.17e-02	4.20e+00; 2.46e-02	1.60e-05; 4.41e-08
class	soluble	Very soluble	Very soluble	Very soluble	Poorly soluble
Log *S* (SILICOS-IT)	-2.28	-0.08	-0.08	-0.69	-2.86
solubility	1.41e+00 mg/ml; 5.20e-03 mol/l	1.81e+02; 8.39e-01	1.96e+02; 8.39e-01	3.50e+01; 2.05e-01	5.05e-01; 1.39e-03
class	soluble	soluble	soluble	soluble	soluble
Pharmacokinetics					
GI absorption	high	high	high	high	High
BBB permeant	No	No	No	No	Yes
P-gp substrate	No	No	No	No	No
CYP1A2 inhibitor	No	No	No	No	No
CYP2C19 inhibitor	No	No	No	No	No
CYP2C9 inhibitor	No	No	No	No	Yes
CYP2D6 inhibitor	No	No	No	No	No
CYP3A4 inhibitor	No	No	No	No	Yes
Log *Kp* (skin permeability) [cm/s]	-6.81	-7.45	-7.90	-6.89	-4.26
Druglikeness					
Lipinski	-	Yes, 0 violation	Yes, 0 violation	Yes, 0 violation	Yes, 0 violation
Ghose	-	Yes	Yes	Yes	Yes
Veber	-	Yes	Yes	Yes	Yes
Egan	-	Yes	Yes	Yes	Yes
Muegge	-	yes	yes	No, 1 violation: MW<200	No, 1 violation: XLOGP3>5
Bioavailability score	-	0.56	0.56	0.85	0.56
Medicinal chemistry					
PAINS	0 alert	0 alert	0 alert	0 alert	0 alert

Brenk	2 alerts: beta-keto-anhydride, more than 2 esters	1 alert: beta-keto-anhydride	1 alert: beta-keto-anhydride	0 alert	0 alert
Leadlikeness	No, 1 violation: rotors>7	No, 1 violation: MW<250	No, 1 violation: MW<250	No, 1 violation: MW<250	No, 3 violations: MW>350, rotors>7, XLOGP3>3.5
Synthetic accessibillity	2.35	1.60	1.70	1.83	4.71

Synthesis of 1-5

Chemicals and solvents for the synthesis were obtained from the Sigma-Aldrich, FLUKA, IRIS and Chem-Impex. Based on the literature and our experience we have chosen the following strategy for the synthesis of **5**: - C-alkylation of diethyl acetamidomalonate with cyclopropylmethyl bromide yielding **1**, synthesis of racemic **4** in one pot three-step conversion of aminomalonate (base hydrolysis of the diester, careful neutralization/acidification and decarboxylation of **2** (**3**), enzymatic hydrolysis of the acetyl group by acylase yielding mixture of H-β-cyclopropyl-(*S*)-Ala-OH and Ac-β-cyclopropyl-(*R*)-Ala-OH, separation of enantiometrically pure free (S)-amino acid from **3** not hydrolyzed by the enzyme, contaminated with a few per cent of racemic mixture **4**, introduction of N-protecting Fmoc group yielding final product **5**. The first step required cyclopropylmethyl bromide, which was unavailable – thus we synthesized this reagent via treatment of cyclopropylmethanol by phosphorus tribromide. The next three steps were performed with good yield, but decarboxylation required careful control of pH of the refluxing reaction solution, as cyclopropyl ring is not stable at pH 1 or below at 100 °C.

In order to the synthesis of **1**, to the solution of 118.7 g (0.546 mole) of 2-acetylaminomalonic acid diethyl ester in 400 mL anhydrous DMF, equimolar amount of NaH (60% suspension in oil) was added in a several portions at a T < 30 °C (ice/water bath). When an evolution of a hydrogen gas ceased, cyclopropylmethyl bromide containing some diethyl ether (88.7g, 0.547 mole, 5:1 w/w, NMR). The reaction mixture was stirred overnight under argon, then the reaction was quenched by a few mL of glacial acetic acid. After dilution DMF with 5%of water (v/v) resulting mixture was extracted hexanes (2x50mL) to remove remaining oil from NaH suspension and then diluted with water to ~ 1.75 L and left overnight at rt. The first crop (colorless crystals) was collected on a funnel and washed twice with water. Crude wet yield 108g (72.5%) with purity 99%, MH+ 273.4 (HPLC-MS). The mother liquor was diluted with more water and left for growing crystals for X-ray analysis.

In order to obtain compound **4**, wet intermediate product **1** was suspended in 600 mL water and 44 g (1.1. mole, 2.77 eq.) sodium hydroxide in granules was added. The mixture was heated to reflux for 4 hours. HPLC analysis was performed from small acidified sample of reaction solution taken for, showing conversion approximately 90 %. Next portion of NaOH (5g, 0.125 mole) was then added and reaction solution was refluxed for 1 hour more. After cooling down reaction mixture was acidified to pH 1.2 with 6N HCl in water (200 mL). The solution of **2** was refluxed for 2 hours, then evolution of CO_2 ceased. HPLC analysis of a sample taken from reaction mixture had shown ~ 95 % decarboxylation product **4**, but pH of reaction solution raised to 2.5. After acidification back to pH 1.2 with small portion of aqueous concentrated hydrochloric acid, reflux was prolonged for 1 hour. Repeated HPLC analysis of a sample taken from solution had shown more than 99.5 % product **4**. Warm solution was treated with charcoal (1-2 g), heated to reflux for 5` and after cooling down to ~ 60 °C was filtered through cellite, then left overnight for o/n on large Petri dish for crystallization. Colorless crystals of 4 were collected, washed with small amount of cold water and dried on air. Colorless crystals 35.64 g, purity > 99 % (HPLC). Mother liquor was concentrated to half of volume and poured again on Petri dish for slow evaporation to obtain the second crop of product. After filtration, washing with small amount of water and drying yield was 23.84 g (>99% purity by HPLC). Total yield of intermediate product **4** was 59.48 g (0.348 mole, 93.8 %), for the first and second crop m.p. 118-200 °C and 117-119 °C, respectively.

For the synthesis of **3**, enzymatic hydrolysis of the acetyl group **4** by acylase (water, pH 7.5, 37 °C) yield a mixture of H-*b*-cyclopropyl-(*S*)-Ala-OH and Ac-*b*-cyclopropyl-(*R*)-Ala-OH. Acetyl-(*R*) enantiomer was separated from free (*S*)-enantiomer by crystallization from partially concentrated reaction solution (water) after acidification to pH ~ 0.5. Free (*S*) amino acid was crystallized from water after adjusting pH to ~ 6 and slow evaporation. Starting from 59.48 g (0.348 mole) of racemate **4**, acetyl-(*R*) enantiomer, 20.21 g (118.1 milimole, 68%, m.p. 120-122° C), and free (*S*)-enantiomer, 14.69 g, 113.7 milimole, 65.5%, m.p. 260-270° C (decomposition). Finally, Fmoc-*b*-cyclopropyl-(*S*)-Ala-OH **5** was synthesized from H-*b*-cyclopropyl-(*S*)-Ala-OH by standard method using Fmoc-OSu (0.95 equivalent) in water-

dioxane solution in the presence of 3 equivalents of $KHCO_3$. On the scale of 6.900 g (53.4 milimole) compound **5** was obtained in 94.6% yield (16.85g, 50.7 milimole, m.p. 140-142° C.

Pharmacokinetic measurements

The p*K*a and log Poct/w measurements* for **5** were performed on the Pion SiriusT3 system (Pion Inc. Ltd., Forest Row, UK) using the potentiometric procedure and the spectrometric technique.141-143 All the obtained data were processed using the Pion software SiriusT3 v.2.0.0. The acidity constants, p*K*a values, were determined by titration of the fully dissolved drug using the spectroscopic (UV-metric) and the logD values by potentiometric (pH-metric) technique. UV-metric titrations were performed for UV-active ionisable groups between pH 2 and 12 at concentration 2 mM of compound 5 obtained by adding 5 µL of 10 mM stock solution to 25 µL of Neutral Linear Buffer (which contains a mixture of acids and bases to be able to obtain a buffered solution between pH 2-12) into a 5 mL vial containing 1.5 mL of the media). Spectrometric p*K*a values were obtained from UV absorption measurements as a pH function applying the Target Factor Analysis methodology following the the Lambert-Beer Law.143 Potentiometric p*K*a values were derived from titration curves by applying charge and mass balance equations and the p*K*a value that provides the best fit of the calculated titration data to the measured ones is taken as the final p*K*a value. The p*K*a value corresponds to the average p*K*a from a minimum of three individual results. Partition values, log Poct/w, were obtained by potentiometric titrations as described for the aqueous p*K*a determination but in the presence of a partition solvent (octanol) performed between pH 2.0 and 12.0 at concentrations of the 0.65 to 1.35 mM weighing sample powder into a glass vial. The log Poct/w was calculated by the difference between the aqueous p*K*a and the apparent po*K*a (p*K*a measured in the presence of a partition solvent) at several phase ratios (octanol:water) 1:1, 1:0.3 and 1:0.01 depending on the expected partition value. All measurements were taken at 25◦C, under an inert gas atmosphere of argon, and at least three titrations were made for each compound.141-144

*A. Avdeef, *Anal. Chim. Acta*, 1983, **148**, 237–244; A. Avdeef, J. Comer, *J. Pharm. Sci.*, 1993, **82**, 183–190; K. Y. Tam, K. Takacs-Novak, *Anal. Chim. Acta*, 2001, **434**, 157–167; A. Avdeef, J. Comer, S. J. Thomson, *Anal. Chem*., 1993, **65**, 42–49.

Molecular Docking Preparation

Molecular docking studies to establish favorable ligand binding geometries for **2**, namely 2-(cyclopropylmethyl)-2-acetamidopropanedioic acid, were carried out on a four CPUs-based desktop PC computer equipped with AMD Phenom™ II X4 965 Processor 3.40 GHz and 32 GB of RAM on a Microsoft Windows 10 Professional 64-bit operating system using AutoDock Vina vs. 1.1.2 program for Windows (http://autodock.scripps.edu/) [Trrot, 2010]. The respective ligand molecule **2** in non-ionizable form was prepared with ChemAxon MarvinSketch vs. 14.9.1.0 (http://www.chemaxon.com/marvin/) using a general "Cleaning in 3D" option to assign with proper 3D orientation and then calculating conformers with MMFF94 force field parameters and saved as .pdb files. To obtain the minimum-energy conformation of ligands for docking studies, the initial geometries of the afore-pretreated ligands were additionally optimized in Avogadro vs. 1.2.0. (http://avogadro.cc/), after adding all the hydrogens to the structure and saved as .mol2 files. The same procedure as above was performed toward metribolone (R1881) and 2-methyl-*N*-[4-nitro-3-(trifluoromethyl)phenyl]propanamide (flutamide). The energy of the ligand molecules was minimized using the built-in feature of Avogadro, including General Amber Force Field (GAFF) [Wang, 2004] with Steepest Descent Algorithm (100 steps). The minimum conformation energies obtained for each ligand were as follows: $E_{calc.2}$ = –136.679 kJ/mol, $E_{calc.(metribolone)}$ = –264.109 kJ/mol, and $E_{calc.(flutamide)}$ = –86.1747 kJ/mol. The visualization of the optimized geometries was performed using molecular visualization software, POV-Ray for Windows v3.7.0. msvc10.win64 licensed under the GNU Affero General Public License (AGPL3) (see **Figure A1**). Next, the Gasteiger partial charges were calculated with AutoDock Tools vs. 1.5.6 (ADT, S3 http://mgltools.scripps.edu/),[1] while all torsion angles for each ligand molecule were considered flexible. All the possible rotatable bonds [7 out of 32 for 2-(cyclopropylmethyl)-2-acetamidopropanedioic acid **2**, 1 out of 32 for metribolone, and 4 out of 32 for flutamide] and non-polar hydrogen atoms were also determined using AutoDock Tools 1.5.6 package. Next, the final ligands' files were saved as PDBQT files (.pdbqt format) and further used in docking. The crystallographic structure of the human androgen receptor (hAR, PDB code: 1E3G)[i][ii] was downloaded from Brookhaven RCSB Protein Data Bank (PDB database, http://www.rcsb.org/pdb/). To avoid steric clashes within the protein model, the crude target protein was prepared as .pdb file using UCSF Chimera vs. 1.11.2 package (http://www.cgl.ucsf.edu/chimera/)[iii] by removing all nonstandard molecules, including conserved crystal water molecules (HOH), and small non-protein ligand

[metribolone (R1881)]. Next, the polar hydrogen atoms were added, and Gasteiger charges were calculated with AutoDock Tools 1.5.6 package using its standard utility scripts. Then the final protein file was saved as a .pdbqt file. Next, a searching "grid box" was set by using AutoGrid function to perform docking in a (60 × 60 × 60 Å)-unit grid box (final size space dimensions x = 60 Å, y = 60 Å, z = 60 Å), centered on the catalytic cavity as target coordinate (center_x = 0.802; center_y = 29.745; center_z = 3.780) with a grid spacing of 0.375 Å and exhaustiveness-value reaching 48.

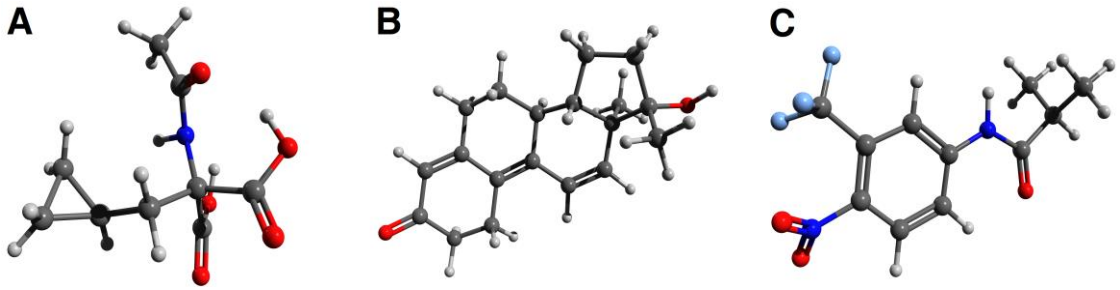


Figure A1. The geometries of (**A**) **2**-(cyclopropylmethyl)-2-acetamidopropanedioic acid, (**B**) metribolone, and (**C**) flutamide optimized in Avogadro – Version 1.2.0. The figures were prepared by rendering them using molecular visualization software, POV-Ray – Version 3.7.0. Nitrogen atoms are presented with blue color, oxygen atoms with red color, fluorine atoms with light blue color, whereas hydrogen atoms are expressed as light-grey balls.

Molecular Docking Procedure and Validation

The molecular docking protocol was validated by re-docking of the co-crystallized metribolone (R1881) into a human androgen receptor (hAR; PDB access code: 1E3G). The docked complexes were superimposed on the original crystal structure showing that the accommodation of the docked ligand in the binding pocket is identical to that present in a co-crystallized small molecule ligand. The overlaps between the docked pose of R1881 in hAR and the X-ray structure for the hAR-R1881 complex are shown in **Figure A2**. Docking was performed into a rigid protein and using advanced protein flexibility options after specifying flexible side chains. Each docking was performed with an exhaustiveness level of 48 concerning global search. In turn, for each ligand molecule, 100 independent runs were performed using the Lamarckian Genetic Algorithm (GA) with at most 106 energy evaluations and a maximum number of generations of >27,000 $Å^3$ (the search space volume). The rest of the docking parameters, including the remaining Lamarckian GA parameters, were set as default using the standard values for genetic Vina algorithms (the posed dockings were below 5.00 Å rmsd). The docking modes of each ligand that is: 2-(cyclopropylmethyl)-2-acetamidopropanedioic acid **2**, metribolone (R1881), and flutamide were clustered and ranked based on a mutual ligand-protein affinity expressed as absolute free binding energies [ΔG_{calc} (kcal/mol)] as well as the rmsd-values in both modes regarding rmsd lower bound (l.b.) and rmsd upper bound (u.b.), respectively. The rmsd were computed referring to the input structure submitted to docking simulations. For hAR the used random seed amounted to: (i) +1243584512 for 2-(cyclopropylmethyl)-2-acetamidopropanedioic acid **2**, (ii) –948142568 for metribolone (R1881), and (iii) –806635708 flutamide, respectively. The best nine binding poses (modes) were selected according to AutoDock Vina scoring functions mainly based on binding energies and showed mutual ligand-protein affinity (kcal/mol). Each binding mode was manually inspected to select only those conformations of the ligand molecule, which were accommodated in the hAR catalytic cavity in the highest possible proximity to the substrate-binding site according to the crystal structure of hAR co-crystallized with metribolone (R1881) deposited as PDB: 1E3G. The results of docking scoring of the respective ligands to hAR are collected in **Table A1**. The results generated by AutoDock Vina include optimized binding poses of all ligands in hypothetical complexes with the h-AR as well as critical polar contacts between the respective atoms of those ligands and the receptor molecule (h-AR, PDB code: 1E3G). The docking scoring was visualized using the PyMOL Molecular Graphics System software vs. 1.3 (Schrödinger, LLC; https://www.pymol.org/). Additional data, including the most important amino acid residues of hAR (PDB: 1E3G) involved in a hydrogen bonding to the respective ligands, and the results of the measurements of their distances given in Ångströms (Å) are depicted in **Figure A3**. In addition, visualization of the protein-ligand interactions was analyzed using freeware for academia BIOVIA Discovery Studio Visualizer vs. 20.1.0.19295 software (Dassault Systèmes Biovia Corp.; https://www.3ds.com) (**Figures A4–A8**).

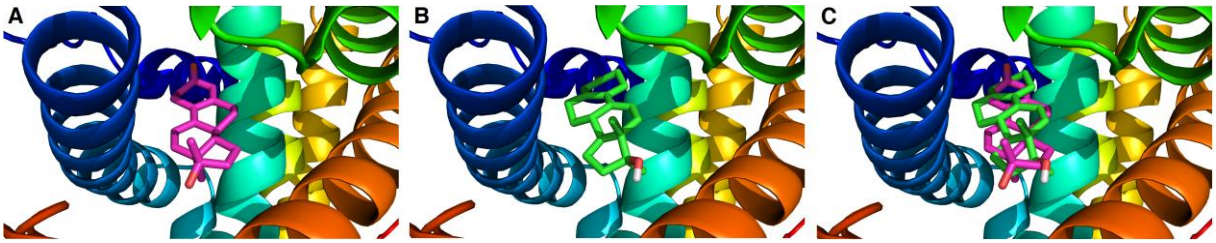


Figure A2. (**A**) X-ray structure for the complex of human androgen receptor and metribolone (R1881) (hAR, PDB ID: 1E3G), (**B**) binding mode of R1881 to hAR using standard docking protocol, (**C**) the overlaps between the docked pose of R1881 in hAR and hAR-R1881 complex deposited as 1E3G. The overall receptor structure (target protein) is shown as a cartoon diagram, whereas the ligand molecules are shown as stick representations. The carbon atoms are presented with a magenta color (in the case of R1881 ligand co-crystallized with hAR) or green color (in the case of R1881 ligand docked to hAR). The oxygen atoms are presented with red color, whereas polar hydrogen atoms with white color. The rest of the hydrogens were omitted for clarity.

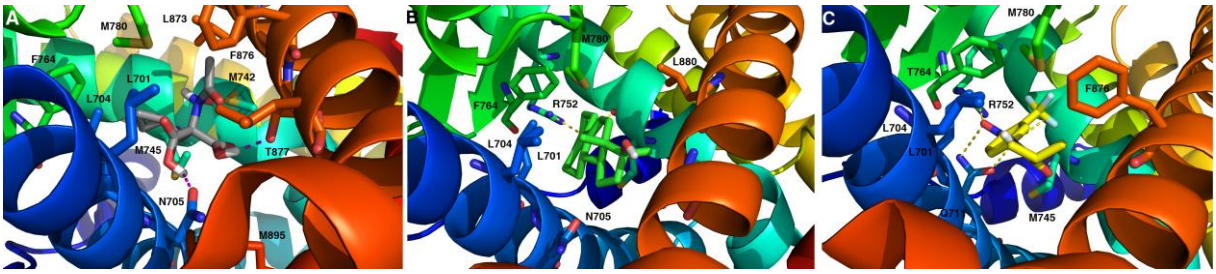


Figure A3. Predominant conformations of (**A**) 2-(cyclopropylmethyl)-2-acetamidopropanedioic acid (**2**, gray sticks), (**B**) metribolone (R1881, green sticks), and (**C**) flutamide (yellow sticks) docked in human androgen receptor (hAR, PDB ID: 1E3G). The overall enzyme structure is shown as a cartoon diagram (see **A**–**C**). The most significant amino acid residues contributing to the stabilization of the ligand molecules are shown with stick representation. Nitrogen atoms are presented with blue color, the oxygen atoms with red color, fluorine atoms with light blue color, and the polar hydrogen atoms with white color. The formation of potential intermolecular hydrogen bonds is represented by magenta (in the case of **2**) or yellow (in the case of R1881 and flutamide) dashed lines.

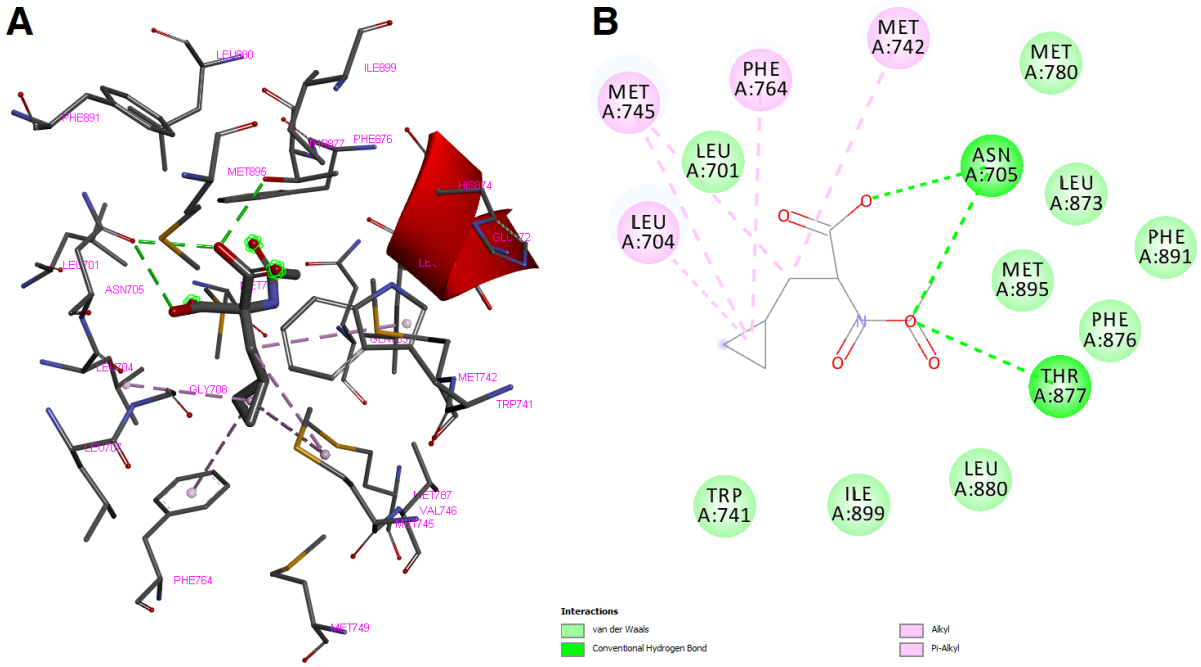


Figure A4. The protein-ligand interactions between hAR (PDB ID: 1E3G) and the top-scoring pose of 2-(cyclopropylmethyl)-2-acetamidopropanedioic acid **2**. (**A**) Receptor-ligand interactions in the 3D binding pocket; ligand with interacting amino acid residues is shown as sticks and lines representations, respectively. (**B**) The receptor-ligand interactions on a 2D diagram; ligand molecule is shown as a stick representation, while interacting amino acid residues are shown as circular stamps.

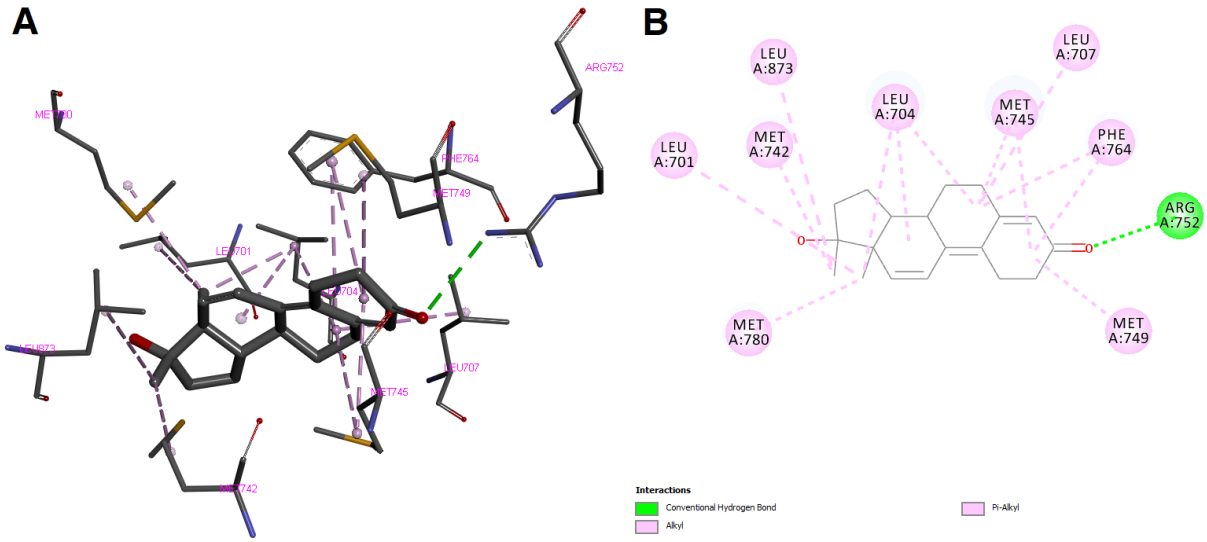


Figure A5. The protein-ligand interactions between hAR (PDB ID: 1E3G) and the top-scoring pose of metribolone (R1881). (**A**) Receptor-ligand interactions in the 3D binding pocket; ligand with interacting amino acid residues is shown as sticks and lines representations, respectively. (**B**) The receptor-ligand interactions on a 2D diagram; ligand molecule is shown as stick representation, while interacting amino acid residues are shown as circular stamps.

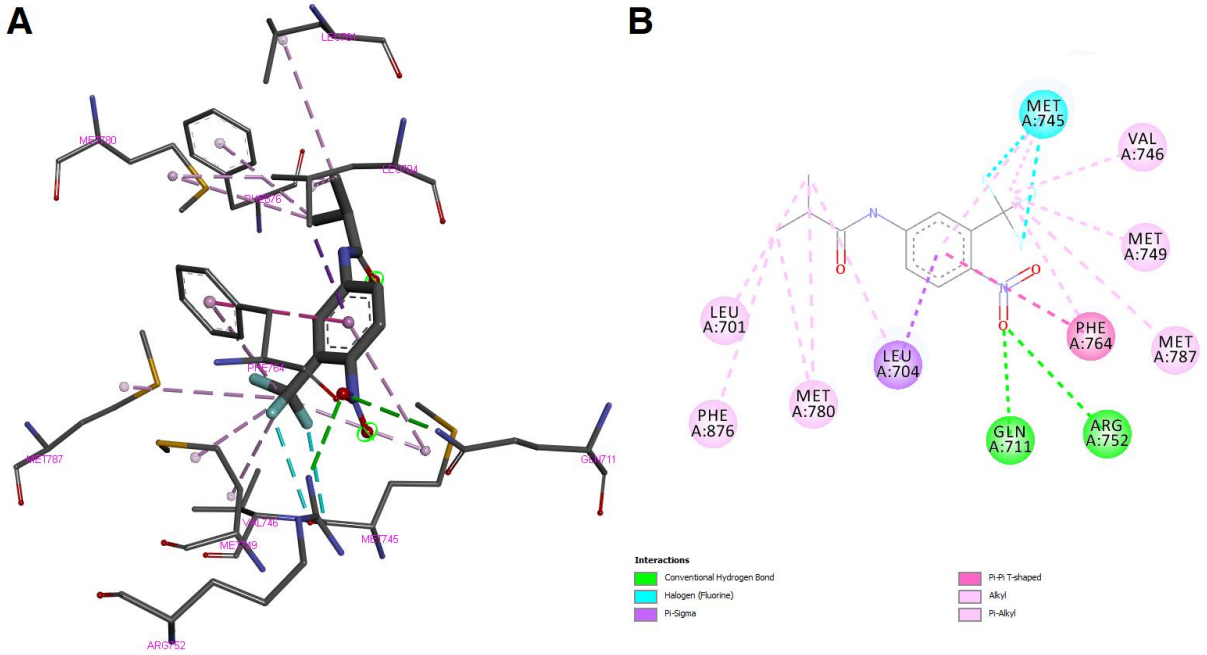


Figure A6. The protein-ligand interactions between hAR (PDB ID: 1E3G) and the top-scoring pose of flutamide. (**A**) Receptor-ligand interactions in the 3D binding pocket; ligand with interacting amino acid residues is shown as sticks and lines representations, respectively. (**B**) The receptor-ligand interactions on a 2D diagram; ligand molecule is shown as a stick representation, while interacting amino acid residues are shown as circular stamps.

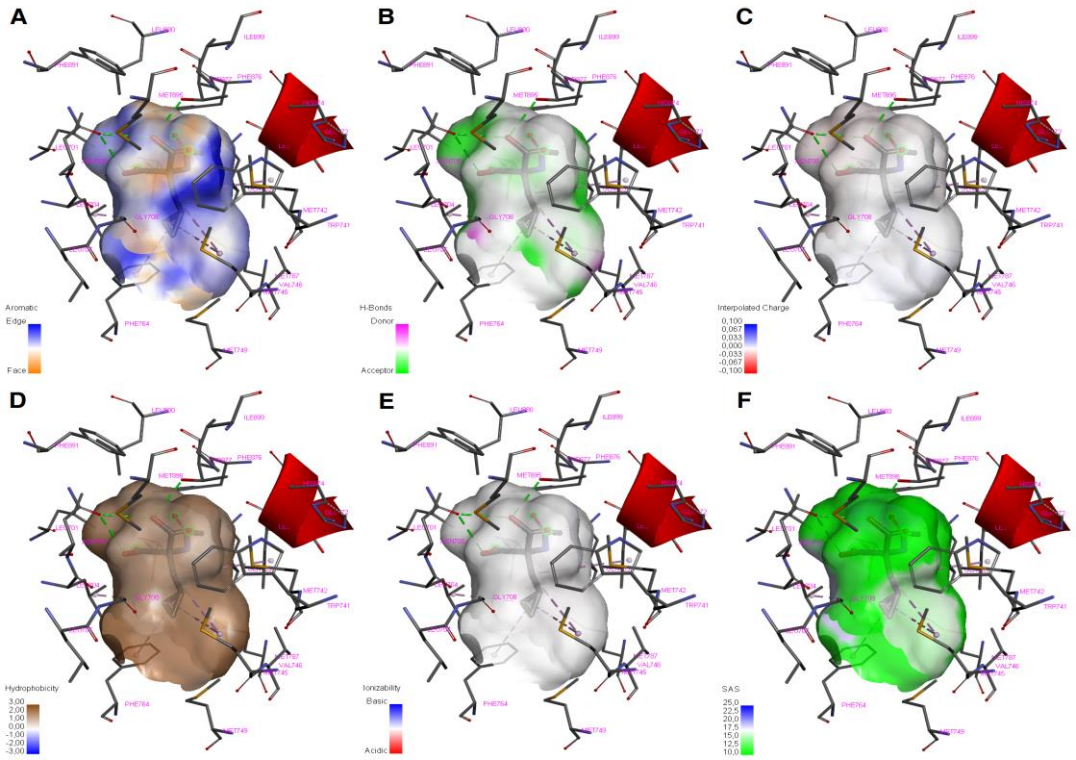
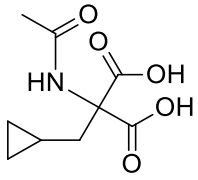
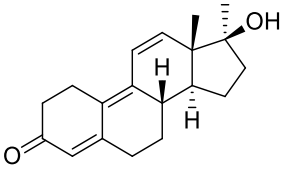
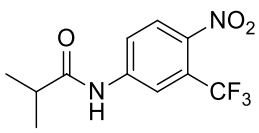


Figure A7. The protein-ligand interactions between hAR (PDB ID: 1E3G) and the top-scoring pose of 2-(cyclopropylmethyl)-2-acetamidopropanedioic acid 2 displaying receptor surfaces depending on their (**A**) aromaticity, (**B**) H-bonding, (**C**) charge, (**D**) hydrophobicity, (**E**) ionizability, and (**F**) SAS, respectively.

Docking scoring of the respective ligands complexed with human androgen receptor (hAR, PDB access code: 1E3G).

Table A1. Docking results of 2-(cyclopropylmethyl)-2-acetamidopropanedioic acid **2**, metribolone (R1881), and flutamide to human androgen receptor (hAR) (PDB: 1E3G).

Entry	Ligand	Pose[a]	Affinity (kcal/mol)[b]	Distance from best mode[c]	
				rmsd l.b.	rmsd u.b.
1		S1	–5.9	0.000	0.000
2		S2	–5.9	1.473	4.207
3		S3	–5.8	2.449	4.304
4		S4	–5.8	2.614	4.519
5		S5	–5.7	1.638	2.422
6		S6	–5.7	1.968	3.779
7		S7	–5.7	1.616	2.816
8		S8	–5.6	1.821	3.663
9		S9	–5.4	3.243	4.828
10		S1	–8.0	0.000	0.000
11		S2	–7.6	11.157	15.008
12		S3	–7.6	12.160	15.826
13		S4	–7.3	12.999	14.525
14		S5	–7.1	13.589	18.242
15		S6	–6.9	23.680	26.648
16		S7	–6.8	22.897	25.366
17	Metribolone (R1881)	S8	–6.6	15.928	19.329
18		S9	–6.6	12.487	14.374
19		S1	–7.9	0.000	0.000
20		S2	–7.6	2.992	6.408
21		S3	–7.5	3.396	6.568
22		S4	–7.4	3.678	6.776
23		S5	–7.1	2.273	3.083
24		S6	–7.0	11.887	13.533
25	Flutamide	S7	–6.8	10.697	12.577
26		S8	–6.8	11.193	13.057
27		S9	–6.7	12.603	14.891

[a] The pose S1 represents the lowest value of ΔG_{calc} (kcal/mol), which means that ligand-binding affinity to receptor (hAR site) is the highest, and in contrary, the S9 mode represent the lowest ligand-binding affinity.

[b] Average ΔG_{calc} (kcal/mol) for the respective ligand is as follows: –5.72 (in the case of **2**), –7.17 (in the case of R1881), and –7.20 (in the case of flutamide).

[c] The values <2.000 rmsd represent the closest distance between the ligand and the receptor (hAR) binding site.

*Trott and A. J. Olson, J. Comput. Chem., 2010, **31**, 455–461. * Wang, R. M. Wolf, J. W. Caldwell, P. A. Kollman and D. A. Case, J. Comput. Chem., 2004, **25**, 1157–1174.