Electronic Supplementary Material (ESI) for CrystEngComm.

H-bond competition experiments in solution and the solid state

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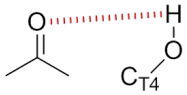
Supporting Information

Conquest searches of the CSD

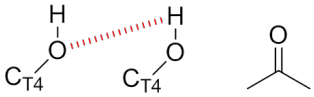
All CSD searches were performed using Conquest (version 1.17) to retrieve structures using the following settings: 3D coordinates determined, not disorder, no errors, not polymeric, no ions, no powder structures, only organics.

Retrieving crystal structures to study a given competition experiment was achieved by firstly creating two CSD queries for each of the potential H-bonds. For example, query 1 in Figure S1 will find structures containing a ketone and an alcohol that form an intermolecular interaction in the crystal structure (the subscript T4 specifies tetrahedral carbons to avoid the retrieval of phenols). Query 2 will find structures containing a ketone and an alcohol where an intermolecular interaction was formed between two alcohol groups. The H-bonds were specified using the contact tool in the Conquest structural editor and the criteria for a H-bond was a close contact which was less than the sum of the van der Waals radii of the interacting atoms. Finally to ensure that the retrieved structures only have a ketone and an alcohol, and only a variable hydrocarbon skeleton connecting them, a formula constraint was applied (Query 3) which states that any retrieved structure can have any number of carbon and hydrogen atoms greater than 0 and must have 2 oxygen atoms for the ketone and the alcohol. The formula constraint was applied to all molecules in the structure to allow for the inclusion of co-crystals and to make sure that no other heteroatoms are allowed in the structure. Using the 'combine queries' option in Conquest it is possible to retrieve structures which satisfy the criteria shown in multiple queries. An example of a structure retrieved as a result of combining query 1 and query 3 is shown in Figure S2, and a structure retrieved by combining query 2 and query 3 is shown in Figure S3.

Query 1



Query 2



Query 3

$C_{>0}H_{>0}O_2$

Figure S1 – Conquest queries used for a competition experiment between an alcohol-alcohol and an alcohol-ketone H- bond. Queries 1 and 2 specify the two types of H-bond, and query 3 ensures that only these two functional groups are present in the structures retrieved.

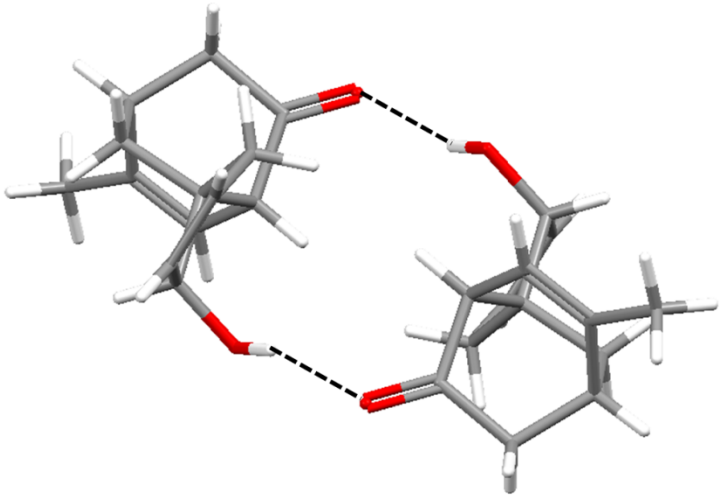


Figure S2 – An example of a crystal structure retrieved by combining queries 1 and 3 in Figure S1. (CSD refcode = BOPWAG)

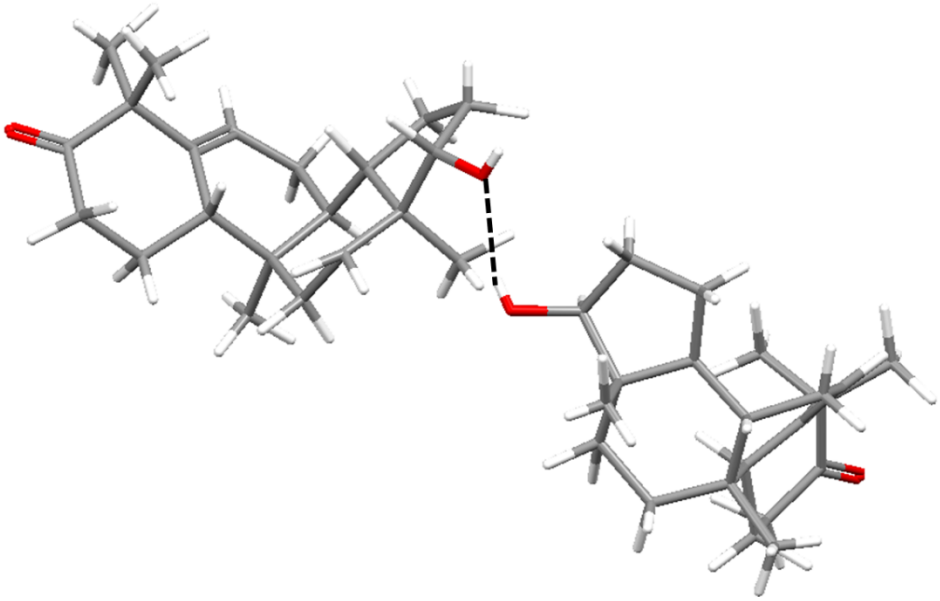


Figure S3 – An example of a crystal structure retrieved by combining queries 2 and 3 in Figure S1. (CSD refcode = CEMKAG)

Table S1 – Results of CSD searches and corresponding solution phase free energies for H-bond formation.

D	A1	A2	N_1	N_2	p_1	p_2	ε	ΔG^o / kJ mol^{-1}	ΔG^o error / kJ mol^{-1}
alcohol	alcohol	ketone	41	319	0.11	0.89	0.02	-1.0	2.6
alcohol	alcohol	tertiary amide	3	167	0.02	0.98	0.01	-5.4	2.9
alcohol	alcohol	nitrile	3	35	0.08	0.92	0.04	0.6	2.6
alcohol	alcohol	alkyl ether	41	125	0.25	0.75	0.03	-0.4	2.7
alcohol	alcohol	aryl ether	24	22	0.52	0.48	0.07	3.2	2.4
alcohol	alcohol	ester	57	298	0.16	0.84	0.02	-0.2	2.6
alcohol	alcohol	sulphonamide	5	41	0.11	0.89	0.05	-1.4	2.6
alcohol	alcohol	sulphone	7	37	0.16	0.84	0.06	-1.8	2.7
alcohol	alcohol	tertiary amine	17	78	0.18	0.82	0.04	-5	2.8
alcohol	alcohol	sulphoxide	0	38	0.00	1.00	0.16	-6.8	2.9
alcohol	alcohol	phosphine oxide	0	28	0.00	1.00	0.19	-10.8	3.3
alcohol	alcohol	pyridine	0	27	0.00	1.00	0.19	-4.2	3.0
alcohol	alcohol	akyl tertiary carbamate	1	42	0.02	0.98	0.02	-3.8	2.7
Phenol	phenol	Ketone	2	68	0.03	0.97	0.02	-8.1	1.7
Phenol	phenol	amide	0	23	0.00	1.00	0.21	-14.5	2.1
Phenol	phenol	aryl ether	0	21	0.00	1.00	0.22	-2.0	1.3
Phenol	phenol	ester	1	59	0.02	0.98	0.02	-7.0	1.6
Phenol	phenol	sulphonamide	0	15	0.00	1.00	0.26	-8.7	1.8
Phenol	phenol	tert amine	0	10	0.00	1.00	0.32	-13.9	2.0
alkyl amide	alkyl amide	Ketone	13	1	0.93	0.07	0.07	5.1	0.7

alkyl amide	alkyl amide	alkyl ether	18	0	1.00	0.00	0.24	6.0	1.1
alkyl amide	alkyl amide	Ester	75	8	0.90	0.10	0.03	6.2	0.7
alkyl amide	alkyl amide	aryl ether	14	0	1.00	0.00	0.27	10.1	0.4
alkyl amide	alkyl amide	tert aniline	13	0	1.00	0.00	0.28	8.1	1.6
aryl amide	aryl amide	Ketone	25	9	0.74	0.26	0.08	4.4	0.7
aryl amide	aryl amide	Nitrile	9	5	0.64	0.36	0.13	6.5	0.8
aryl amide	aryl amide	Ester	39	19	0.67	0.33	0.06	5.5	0.6
aryl amide	aryl amide	nitro	35	3	0.92	0.08	0.04	9.6	0.5
aryl amide	aryl amide	aryl ether	36	0	1.00	0.00	0.12	9.9	0.0
aryl amide	aryl amide	pyridine	39	28	0.58	0.42	0.06	0.3	1.6
cyclic amide	cyclic amide	Ketone	25	3	0.89	0.11	0.06	6.9	0.7
cyclic amide	cyclic amide	Nitrile	22	1	0.96	0.04	0.04	8.7	0.8
cyclic amide	cyclic amide	Alkyl ether	17	1	0.94	0.06	0.05	7.6	1.1
cyclic amide	cyclic amide	Ester	41	1	0.98	0.02	0.02	7.8	0.6
secondary alkyl aniline	secondary alkyl aniline	tert amine	0	11	0.00	1.00	0.30	-5.4	1.5
secondary alkyl aniline	secondary alkyl aniline	tert amide	0	20	0.00	1.00	0.22	-5.8	1.5
secondary alkyl aniline	secondary alkyl aniline	nitro alkane	0	13	0.00	1.00	0.28	1.4	1.4
secondary alkyl aniline	secondary alkyl aniline	pyridine	0	11	0.00	1.00	0.30	-4.8	1.8
secondary alkyl aniline	secondary alkyl aniline	ester	0	26	0.00	1.00	0.20	-1.4	1.5
secondary alkyl aniline	secondary alkyl aniline	ketone	1	36	0.03	0.97	0.03	-2.0	1.5
sulphonamide	sulphonamide	nitro	13	4	0.76	0.24	0.10	4.4	1.5
sulphonamide	sulphonamide	alkyl ether	7	5	0.58	0.42	0.14	0.8	1.9
sulphonamide	sulphonamide	aryl ether	16	0	1.00	0.00	0.25	4.6	1.4

sulphonamide	sulphonamide	ester	12	8	0.60	0.40	0.11	1.1	1.7
sulphonamide	sulphonamide	ketone	5	10	0.33	0.67	0.12	0.2	1.8
pyrrole	pyrrole	ester	0	28	0.00	1.00	0.19	-3.5	2.2
pyrrole	pyrrole	ketone	0	22	0.00	1.00	0.21	-4.4	2.2
carboxyic acid	carboxyic acid	nitro	25	0	1.00	0.00	0.20	3.2	2.5
carboxyic acid	carboxyic acid	alkyl ether	16	12	0.57	0.43	0.09	-1.7	3.2
carboxyic acid	carboxyic acid	aryl ether	86	0	1.00	0.00	0.11	3.5	2.5
carboxyic acid	carboxyic acid	pyridine	1	24	0.04	0.96	0.04	-7.3	4.0
carboxyic acid	carboxyic acid	tert carbamate	4	27	0.13	0.87	0.06	-6.7	3.5
carboxyic acid	carboxyic acid	amide	3	22	0.12	0.88	0.06	-9.0	3.9
carboxyic acid	carboxyic acid	sulphoxide	0	12	0.00	1.00	0.29	-11.0	4.0
carboxyic acid	carboxyic acid	phosphine oxide	0	12	0.00	1.00	0.29	-16.8	4.9
carboxyic acid	carboxyic acid	nitrile	10	2	0.83	0.17	0.11	-0.3	2.9
carboxyic acid	carboxyic acid	ester	75	21	0.78	0.22	0.04	-1.5	3.0
carboxyic acid	carboxyic acid	tert aniline	10	0	1.00	0.00	0.32	0.9	3.2
carboxyic acid	carboxyic acid	ketone	85	56	0.60	0.40	0.04	-2.6	3.1

‡Errors in ΔG^o are calculated from the propagation of errors in functional group H-bond parameters using the equations below.

Error in αβ :

$$\delta\alpha\beta = \alpha\beta\, x \sqrt{(\frac{\delta\alpha}{\alpha})^2 + (\frac{\delta\beta}{\beta})^2}$$

where δαβ is the error in an αβ value, δα and δβ are the errors in α and β which are twice the standard deviation in the experimental values (Tables S3 and S4).

Error in ΔG^o :

$$\delta_{(\Delta G)} = \sqrt{\delta^2_{(\alpha\beta_1)} + \delta^2_{(\alpha\beta_2)}}$$

where $\delta_{(\Delta G)}$ is the error in ΔG^o, $\delta_{(\alpha\beta 1)}$ and $\delta_{(\alpha\beta 2)}$ are the errors in $\alpha\beta_1$ and $\alpha\beta_2$ respectively.

Table S2 – Solution phase functional group H-bond interaction parameters with standard deviations (and number of experimental values used).

Functional Group	α	β
alcohol	2.7 ± 0.1 (12)	5.3 ± 0.4 (11)
phenol	3.6 ± 0.1 (25)	3.0 ± 0.1 (3)
Secondary alkyl amide	2.9 ± 0.0 (3)	8.1 ± 0.1 (3)
Secondary alkyl aniline	2.1 ± 0.0 (1)	4.4 ± 0.6 (6)
secondary sulphonamide	3.1 ± 0.1 (3)	5.9 ± 0.0 (1)
pyrrole	3.0 ± 0.0 (1)	3.9 ± 0.4 (2)
carboxylic acid	3.6 ± 0.2 (4)	4.9 ± 0.0 (2)
ketone		5.8 ± 0.3 (6)
tertiary alkyl amide		8.1 ± 0.3 (22)
nitrile		5.0 ± 0.2 (8)
alkyl ether		5.5 ± 0.3 (14)
aryl ether		3.1 ± 0.0 (1)
ester		5.4 ± 0.2 (18)
tertiary sulphonamide		6.0 ± 0.2 (4)
sulphone		6.2 ± 0.2 (4)
tertiary amine		7.8 ± 0.2 (6)
sulphoxide		8.6 ± 0.1 (3)
alkyl phosphine oxide		10.7 ± 0.4 (4)
pyridine		7.4 ± 0.5 (21)
tertiary alkyl carbamate		7.2 ± 0.2 (3)
tertiary aryl carbamate		6.1 ± 0.3 (3)
nitro alkane		3.8 ± 0.1 (6)
Tertiary alkyl aniline		4.6 ± 0.5 (2)
alkyl aldehyde		4.6 ± 0.1 (5)

Table S3 – Experimental solution phase H-bond donor parameters used to calculate average functional group parameters in Table S2.

Functional group	Compound	α	standard deviation
Alcohol	AVERAGE	2.7	0.1
	methanol	2.9	
	water	2.8	
	ethanol	2.7	
	butan-1-ol	2.7	
	hexan-1-ol	2.7	
	propan-2-ol	2.7	
	neopentanol	2.7	
	tert-butanol	2.7	
	tert-pentanol	2.6	
	propan-1-ol	2.6	
	cyclohexanol	2.6	
	butan-2-ol	2.5	
Phenol	AVERAGE	3.6	0.1
	2-naphthol	3.9	
	1-naphthol	3.8	
	phenol	3.8	
	4-phenylphenol	3.8	
	3-isopropylphenol	3.7	
	4-sec-butylphenol	3.7	
	3-methylphenol	3.7	
	4-methylphenol	3.7	

	3,5-dimethylphenol	3.7	
	4-methyl-2-tert-butylphenol	3.7	
	3,4-dimethylphenol	3.6	
	4-tert-butylphenol	3.6	
	3-methyl-6-tert-butylphenol	3.6	
	3-ethylphenol	3.6	
	4-octylphenol	3.6	
	4-ethylphenol	3.6	
	4-propylphenol	3.6	
	3,4,5-trimethylphenol	3.6	
	2,4-di-tert-butylphenol	3.6	
	2,5-dimethylphenol	3.6	
	2,3-dimethylphenol	3.5	
	2,4-dimethylphenol	3.5	
	4-methylpyrazole	3.5	
	2,3,5-trimethylphenol	3.5	
	2-methylphenol	3.5	
	2-tert-butylphenol	3.4	
Secondary alkyl amide	AVERAGE	3.0	0.2
	acetanilide	3.3	
	N-methylacetamide	2.9	
	N-methylformamide	2.9	
	N-methyl-tert-butamide	2.9	
Secondary alkyl aniline	AVERAGE	2.4	0.4

	diphenylaniline	2.7	
	aniline	2.4	
	N-methylaniline	2.1	
Carboxylic acid	AVERAGE	3.6	0.2
	benzoic acid	3.8	
	ethanoic acid	3.6	
	tert-butanoic acid	3.5	
	hexanoic acid	3.3	
Secondary sulphonamide	AVERAGE	3.1	0.1
	N-(2-naphthyl) toluene-p-sulfonamide	3.2	
	toluene-p-sulfonamide	3.2	
	N-benzyl toluene-p-sulfonamide	3.0	
Pyrrole	AVERAGE	3.0	0.0
	pyrrole	3.0	

Table S4 – Experimental solution phase H-bond acceptor parameters used to calculate average functional group parameters in Table S2.

Functional Group	Compound	β	standard deviation
Nitro alkane	AVERAGE	3.8	0.1
	2-methyl-2-nitropropane	4.0	
	2-nitropropane	4.0	
	4-nitrotoluene	3.8	
	nitroethane	3.8	
	nitrobenzene	3.7	
	nitromethane	3.7	
Ester	AVERAGE	5.4	0.2
	sec-butyl acetate	5.6	
	propyl ethanoate	5.6	
	isopropyl ethanoate	5.6	
	isobutyl acetate	5.6	
	(E)-ethyl cinnamate	5.6	
	butyl acetate	5.6	
	ethyl isovalerate	5.5	
	ethyl butyrate	5.5	
	tert-butyl ethanoate	5.5	
	ethyl isobutyrate	5.5	
	ethyl propionate	5.5	
	ethyl ethanoate	5.4	
	ethyl 4-methylbenzoate	5.4	
	ethyl phenylacetate	5.4	
	ethyl 3-methylbenzoate	5.3	

	tert-butyl benzoate	5.2	
	ethyl benzoate	5.2	
	methyl benzoate	5.0	
Tertiary aniline	AVERAGE	4.1	0.9
	N,N-diethylaniline	4.9	
	N,N-dimethylaniline	4.2	
	diphenylaniline	3.2	
Aniline	AVERAGE	4.4	0.6
	4-methylaniline	4.9	
	3-methylaniline	4.7	
	2-methylaniline	4.5	
	aniline	4.5	
	N,N-diethylaniline	4.9	
	N,N-dimethylaniline	4.2	
	diphenylaniline	3.2	
Ketone	AVERAGE	5.8	0.3
	dicyclopropyl ketone	6.1	
	methyl cyclopropyl ketone	6.0	
	1-adamantyl methyl ketone	6.0	
	cyclohexyl methyl ketone	5.8	
	di-(1-adamantyl)ketone	5.7	
	methyl isopropyl ketone	5.6	
	1-adamantyl tert-butyl ketone	5.5	

	dibenzyl ketone	5.3	
Tertiary sulphonamide	AVERAGE	5.8	0.4
	N,N-dimethyltoluene-p-sulphonamide	6.2	
	N,N-dimethylmethanesulphonamide	6.0	
	N-methylmethanesulphonamide	5.9	
	N,N-dimethylbenzenesulphonamide	5.7	
	N-methyl_N-benzylsulfonamide	5.2	
N,N-dialkyl carbamate	AVERAGE	6.6	0.7
	ethyl diethylcarbamate	7.4	
	ethyl dimethylcarbamate	7.1	
	methyl dimethylcarbamate	7.1	
	ethyl diphenylcarbamate	6.3	
	methyl diphenylcarbamate	6.2	
	phenyl diphenylcarbamate	5.7	
Tertiary amine	AVERAGE	7.7	0.2
	N-methylpyrrolidine	7.9	
	N,N-dimethylethylamine	7.9	
	cyclohexyldimethylamine	7.8	
	trimethylamine	7.8	
	N-methylpiperidine	7.7	
	triethylamine	7.5	
	N,N-dimethylallylamine	7.3	

Tertiary amide	AVERAGE	8.3	0.4
	1-methyl-2-piperidone	8.8	
	N,N-diethylacetamide	8.5	
	N,N-dimethylacetamide	8.5	
	N,N-dicyclohexylacetamide	8.4	
	N,N-dimethylpropionamide	8.3	
	N,N-dimethyl-4-methylbenzamide	8.1	
	N,N-dicyclohexylbenzamide	8.0	
	N,N-dimethylbenzamide	8.0	
	N,N-dicyclohexylpropionamide	8.0	
	N,N-diethylnonamide	7.9	
Tertiary urea	AVERAGE	8.1	0.7
	N,N'-dimethyl N,N'-trimethyleneurea	9.3	
	N,N'-dimethyl N,N'-ethyleneurea	8.5	
	1,1,3,3-tetramethylurea	8.5	
	1,1,3,3-tetraethylurea	8.5	
	1,3-diphenyl-1,3-diethylurea	7.9	
	1,1-diphenyl-3,3-dimethylurea	7.7	
	1,1-diphenyl-3,3-diethylurea	7.7	
	1,1,3,3-tetraphenylurea	6.9	
Sulfoxide	AVERAGE	8.3	0.6
	diisopropyl sulphoxide	8.7	
	dibutyl sulphoxide	8.7	
	dimethyl sulphoxide	8.6	

	di(p-tolyl) sulphoxide	7.8	
	diphenyl sulphoxide	7.5	
Trialkyl phosphine oxide	AVERAGE	10.6	0.4
	triethylphosphine oxide	11.1	
	tripropylphosphine oxide	10.8	
	trimethylphosphine oxide	10.7	
	tributylphosphine oxide	10.2	
	triphenylphosphine oxide	10.1	
Aryl ether	AVERAGE	3.2	0.14
	anisole	3.3	
	diphenyl ether	3.1	
Alcohol	AVERAGE	5.3	0.4
	adamantan-1-ol	5.9	
	tert-butanol	5.7	
	cyclohexanol	5.6	
	propan-2-ol	5.5	
	octan-1-ol	5.4	
	phenylethanol	5.3	
	propan-1-ol	5.3	
	ethanol	5.2	
	benzyl alcohol	4.9	
	allylalcohol	4.8	
	methanol	4.8	

Phenol	AVERAGE	3.0	0.1
	3-methylphenol	3.1	
	4-methylphenol	3.1	
	phenol	2.9	
Pyrrole	AVERAGE	3.9	0.4
	pyrrole	4.1	
	1-methylpyrrole	3.6	
Carboxylic acid	AVERAGE	4.9	0.0
	benzoic acid	4.9	
	butanoic acid	4.9	
Tertiary sulphonamide	AVERAGE	5.9	0.0
	N-methyl methanesulphonamide	5.9	
Furan	AVERAGE	2.2	0.0
	furan	2.2	
Thioamide	AVERAGE	6.1	0.7
	ε-thiocaprolactam	6.6	
	N-methyl thioacetamide	5.6	