Electronic Supplementary Information (ESI) for:

Enzyme-like *Substrate*-Selectivity in C-H oxidation enabled by recognition

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Instruments and General Methods

Oxidation products related to the oxidation of all of the substrates were identified by comparison of GC retention times with that of commercially available standard samples or synthesized ones.[1] The products were quantified by GC analysis using biphenyl as an internal standard. GC analyses were carried out on a gas chromatograph equipped with a capillary methylsilicone column (30 m x 0.25 mm x 25 µm) Chrompack CP-Sil 5 CB. NMR spectra were recorded on either a BrukerDPX300 or a BrukerDPX400 spectrometer and were internally referenced to the residual proton solvent signal. Elemental analyses were performed using a CHNS-O EA-1108 elemental analyzer from Fisons. Electrospray ionization mass spectrometry (ESI-MS) experiments were performed on a Bruker Daltonics Esquire 3000 Spectrometer.

Materials

All reagents and solvents were purchased at Sigma Aldrich, Cymit, Scharlab or Fluorochem and used at the reagent grade unless otherwise stated. Solvents used for crystallizations were purchased from SDS and Scharlab and purified and dried by passing through an activated alumina purification system (M-Braun SPS-800). Sigma-Aldrich HPLC-grade acetonitrile was employed for oxidation reactions. Iron (II) bis (trifluoromethanesulfonate) bis (acetonitrile) was prepared according to a literature procedure from Fe(II) chloride (Sigma Aldrich).[2] Complexes **1**,[1] **2**,[3] $^{\mathbf{TIPS}}\mathbf{2}$[4] and $^{\mathbf{DMM}}\mathbf{2}$[3] were prepared according to previously reported procedures. Hexane (ScharLab), cyclohexane (Sigma Aldrich), cyclooctane (Sigma Aldrich), methylcyclohexane (TCI Chemicals), ethylbenzene (ScharLab), cumene (Sigma Aldrich), 1,2-*cis*-dimethyl cyclohexane (Sigma Aldrich), 1,2-*trans*-dimethylcyclohexane (Sigma Aldrich), *cis*-decaline (TCI Chemicals), *trans*-decaline (TCI Chemicals), (*d*)-menthyl acetate (Sigma Aldrich) were purchased and filtered over a short pad of SiO_2 prior to use. Trans-1,4-methylcyclohexyl pivalate was obtained as described previously.[5] Acetic acid, $Ba(ClO4)_2$ and (+)-sclareolide were purchased from Sigma Aldrich and used as received.

Undecylammonium tetrafluoroborate **3**, tetradecylammonium tetrafluoroborate, hexylammonium tetrafluoroborate and nonylammonium tetrafluoroborate were synthesized as previously described[1] by treatment of the corresponding amine with hydrofluoroboric acid diethyl ether complex (Sigma Aldrich) and purified by washing with ether and successive crystallization from CH_3CN.

Very Important: The ammonium substrate needs to be completely pure, otherwise significant alterations in yields and, sometimes, selectivity were observed. To achieve this purity, the salts were crystallized by slow evaporation of concentrated CH_3CN solution of the ammonium.

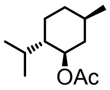
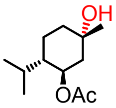
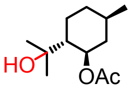
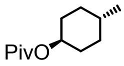
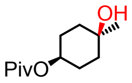
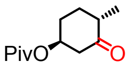
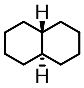
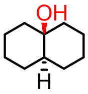
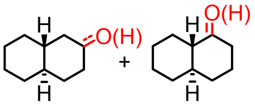
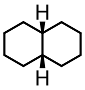
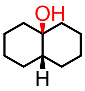
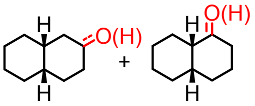
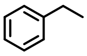
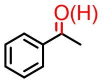
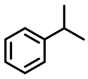
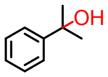
Oxidation Procedure

Catalyst (0.19 µmol, 1 mol%, added from a CH_3CN mother solution), acetic acid (22 µL, 418 µmol, 22 molar eq.), the appropriate ammonium salt (19 µmol, 1 molar eq., added from a CH_3CN mother solution) and the competing substrate(s) (19 µmol each, 1 molar eq. each, added from a CH_3CN mother solution) were dissolved in 400 µL of CH_3CN (HPLC grade, Sigma-Aldrich) at 0°C. Under stirring, a CH_3CN solution of H_2O_2 (28.5 µmol, 2.5 molar eq., mother solution roughly 0.55 M) was slowly added over 18 minutes by a syringe pump.

After two additional minutes of stirring, internal standard (biphenyl, 9.5 µmol, 50 mol%, added from a CH_3CN mother solution), Et_3N (200 µL) and Ac_2O (400 µL) were added and the mixture was stirred for 1 hour at 0°C. Then H_2O (500 µL) was added, and after 15 minutes, the mixture was extracted with CH_2Cl_2 (2 mL). The organic phase was washed with H_2SO_4 1 M (2 mL), $NaHCO_3$ sat. (2 mL), H_2O (2 mL), dried over $MgSO_4$ and analysed by GC (error ±5%).

Table S1

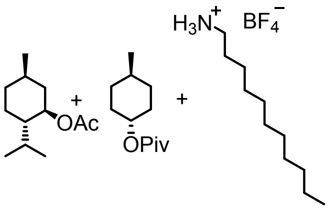
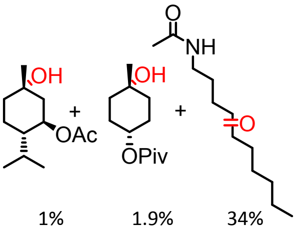
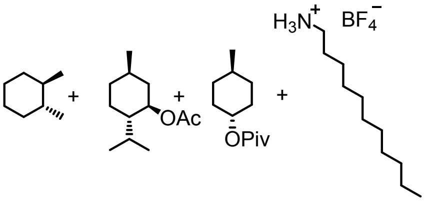
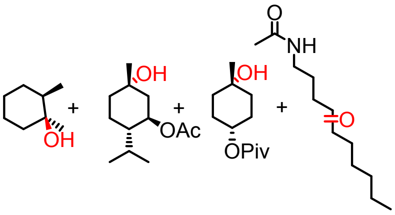
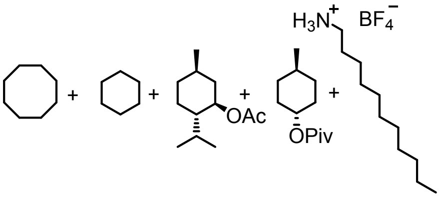
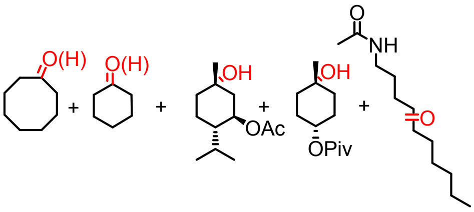
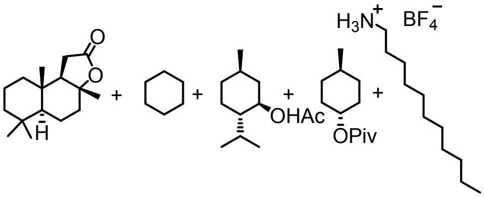
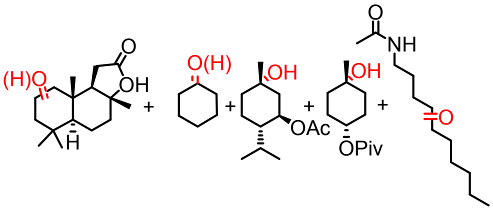
Table S1: Competitive, pairwise oxidation of undecylammonium **3** and a series of substrates[a]

Entry	Cat.	Substrate and Conversion	Substrate Oxidation	Other products	**3** Conversion	**3** Oxidation	(C8+C9) selectivity[b]	Product ratio[c]
								
1	**1**	8%	0.7%	traces	50%	40%	61%	57 : 1
2	**2**	34%	21%	4%	8%	6%	25%	1 : 4
								
3	**1**	17%	0.8%	-	39%	24%	60%	30 : 1
4	**2**	30%	15%	2%	26%	2%	32%	1 : 8
								
5	**1**	31%	0.5%	2.5%	55%	42%	60%	14 : 1
6	**2**	39%	2%	27%	15%	1%	33%	1 : 29
								
7	**1**	40%	14%	<1%	51%	31%	64%	2 : 1
8	**2**	76%	53%	2%	18%	0.6%	30%	1 : 92
								
9	**1**	18%	14%		43%	32%	58%	1 : 2.3
10	**2**	60%	56%		94%	0.3%	28%	190 : 1
								
11	**1**	8%	5.5%		30%	13%	61%	1 : 2.4
12	**2**	66%	60%		91%	0.2%	32%	300 : 1

[a]Conditions as in the oxidation procedure. GC analysis with biphenyl as internal standard (error ±5%; this impliesthat the error is high with low yields). [b]Site-selectivity for C8 and C9 oxidation (over the total yield of **3** oxidation). [c]Ratio of undecylammonium **3** oxidation : substrate oxidation.

Table S2

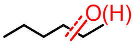
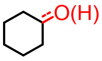
Table S2: Competitive, pairwise oxidation of undecylammonium **3** and mixtures of substrates.[a]

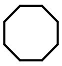
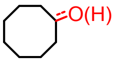
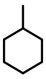
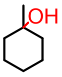
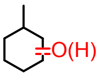
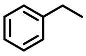
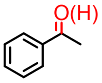
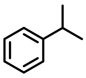
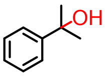
Entry	Cat.	Competing substrates and conversions	Oxidation product yields *product ratio*	Sel. for **3** oxid.
				
1	**1**	8% 9% 49%	1% 1.9% 34% 1 : 2 : 34	92%
2	**2**	24% 17% 13%	22% 10% 3.5% 6 : 3 : 1	10%
				
3	**1**	30% 2.5% 5% 40%	4.5% 1.3% 0.7% 22% 6.4 : 1.9 : 1 : 32	78%
4	**2**	65% 20% 11% 3%	45% 17% 6.7% 3% 15 : 5.7 : 2.2 : 1	4%
				
5	**1**	22% [b] 7% 13% 58%	13% 3.8% 2.2% 1.1% 35% 12 : 3.5 : 2 : 1 : 32	64%
6	**2**	51% [b] 15% 16% 18%	34% 24% 7% 2.4% 0.9% 38 : 27 : 8 : 2.7 : 1	1.3%
				
7	**1**	3% [b] 2% 17% 60%	1.5% 8% 1.3% 0.8% 39% 1.9 : 10 : 2 : 1 : 49	77%
8	**2**	22% [b] 17% 15% 14%	20% 31% 17% 6.2% 2.3% 8.7 : 14 : 7.3 : 2.7 : 1	3%

[a] Conditions as in the oxidation procedure, except for the number of competing substrates (each at 100 molar eq with respect to the catalyst) and the H_2O_2 loading (fixed at 300 molar eq with respect to the catalyst). [b] Conversion was not determined due to extensive substrate evaporation during the workup (total 1 hour and half). Control experiments confirmed such near quantitative evaporation in catalysis and workup conditions.

Table S3

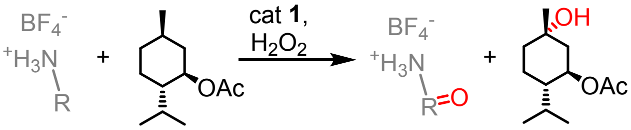
Table S3: Competitive, pairwise oxidation of undecylammonium **3** and a series of substrates with different C-H bond strength and value of ψ used in Figure 3.

Entry	Cat.	Substrate	BDE[b] (kcal/mol) (and number of C-H bonds)	Substrate Oxidation	Other products	**3** Oxidation	product ratio[c]	Ψ[d]
			99.1					
1	**1**	[e]	“	0.7%		27%	39 : 1	43
2	**2**	[e]	“	14%		1.3%	1 : 11	0.06
			98.5					

3	**1**	[e]	“	3.4%		34%	10 : 1	19
4	**2**	[e]	“	43%		1.7%	1 : 25	0.04
			95.5					
5	**1**	19%		8.5%		27%	3 : 1	8
6	**2**	75%	“	60%		0.5%	<1 : 99	0.01
			94.3					
7	**1**	86%		0.9%	1.5 %	22%	9 : 1	4
8	**2**	84%	“	14%	19%	1.3%	1 : 30	7x10^{-3}
			85.4					
9	**1**	18%		16%		31%	2.3 : 1	0.6
10	**2**	60%	“	56%		0.3%	<1 : 99	4x10^{-4}
			83.5					
11	**1**	8%		5.5%		9%	2 : 1	0.3
12	**2**	66%	“	60%		0.2%	<1 : 99	2.5 x10^{-4}

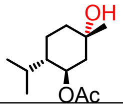
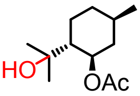
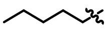
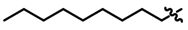
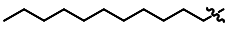
[a] Conditions as in the oxidation procedure. Reactions carried out in triplicate, and the values in this Table are the average of the three experiments (error ± 5%). For values <0.5%, the error is higher (± 30%) due to the difficulty of an accurate integration of such small peaks. [b] BDE taken from ref.[6]. [c] Ratio of undecylammonium **3** oxidation : hydrocarbon oxidation. [d] Ψ defined as the ratio between the sum of the yields of **3** oxidation on positions C8 and C9 and the sum of the yields of the hydrocarbon oxidation at its most reactive C-H bond, each normalized for the number of C-H bonds considered. The selectivity for C8 and C9 positions is always 58-66% with catalyst **1** and 27-31% with catalyst **2**. [e] Conversion was not determined due to extensive substrate evaporation during the workup (total 1 hour and half). Control experiments confirmed such near quantitative evaporation in catalysis and workup conditions.

Table S4



4

Table S4: Effect of the length of the ammonium chain on the substrate-selectivity.

Entry	Cat.	R		 + ketones	Ammonium Oxidation	product ratio[c]
		 (C6)				
1	**1**		21%	8%	-	-
2	**2**	"	21%	4%	-	-
		 (C9)				
3	**1**		0.8%	<0.2%	13%	16 : 1
4	**2**	"	21%	1.5%	3.5%	1 : 12
		 (C11)				
5	**1**		0.7%	<0.2%	40%	57 : 1
6	**2**	"	25%	4%	2%	1 : 4
		 (C14)				
7	**1**		0.5%	<0.2%	41%	82 : 1
8	**2**	"	30%	2.5%	15%	1 : 2

[a] Conditions as in the oxidation procedure. Reactions carried out in triplicate, and the values in this Table are the average of the three experiments (error ± 5%). For values <0.5%, the error is higher (± 30%) due to the difficulty of an accurate integration of such small peaks.
[c] Ratio of ammonium oxidation : **4** oxidation (if possible).