1	Supplementary information
2 3 4	Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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7	Mechanisms of hydrolysis of phenyl- and benzyl 4-nitrophenyl- sulfamate
8	esters
9	William J. Spillane,* ^a Sergio Thea, ^b Giorgio Cevasco ^{b,c} , Michael J. Hynes, ^a Cheryl J. A. McCaw ^a
10	and Neil P. Maguire ^a
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EMD 486019



betulinyl-bis-sulfamate



Compound	Exper. pK _a	Anal. λ (nm)	Hammett σ^{d}		
1a	7.32	302	0.778		
1b	7.40	283	0.71		
1c	7.45	253	0.66		
1d	7.50	228	0.75		
1e	7.66	240	0.56		
1f	7.88	229	0.227		
1g	7.92	210	0.232		
1h	8.15	210	0.062		
1i	8.24	216	0		
1j	8.34	222	-0.17		
Гаble S2 Е	xperimental ^a	pK _a s for the se	cond ionizatio	n ^b of compou	nds 1 in A
Fable S2 E Compound	Experimental ^a Exper. pK _a	pK _a s for the se Hammett σ ^c	cond ionizatio	n ^b of compou Exper. pK _a	nds 1 in A Hammett
Fable S2 E Compound 1a	Experimental ^a Exper. pK _a 21.38	pK _a s for the se Hammett σ ^c 0.778	cond ionizatio Compound 1h	n ^b of compou Exper. pK _a 22.69	nds 1 in A(Hammett 0.062
Fable S2 E Compound 1a 1f	Experimental ^a Exper. pK _a 21.38 22.48	pK _a s for the set Hammett σ^c 0.778 0.227	cond ionizatio Compound 1h 1i	n ^b of compou Exper. pK _a 22.69 22.41	nds 1 in A0 Hammett 0.062 0
Fable S2 E Compound 1a 1f 1g	Experimental ^a Exper. pK _a 21.38 22.48 22.35	pK _a s for the set Hammett σ^c 0.778 0.227 0.232	cond ionizatio Compound 1h 1i 1j	n ^b of compou Exper. pK _a 22.69 22.41 22.71	nds 1 in A Hammett 0.062 0 -0.17

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Compound	pK_a^{spectr}	pK_a^{kin}	Ham	mett σ^{a}
4a	7.83	7.75	0.	73 ^e
4b	8.11	7.79	0.2	227
4c	7.89	7.80	0.5	50 ^e
4d	8.04	7.91	0.0	062
4e	8.26	8.01	0)
4f	8.22	8.07	-0.1	17
4g	8.26	8.12	-0.2	27
^h Measured sp	ectrophotometrical	lly in water at 2	5°C at constan	t ionic strength(µ
M KCl. Anal	ytical wavelength	was 302 nm fo	r all substrates.	^b Calculated by
the pH-rate p	rofile data to eqn 1	with the Fig.P	[®] program. ^c 44	≒5 . ^d Taken fror
McDaniel and	1 H. C. Brown, <i>J.</i> (Org. Chem., 19	58, 23 , 420-42'	7. ^e The σ value f
chloro is fron	M T Tribble and	1 I G Travnha	m J Am Cher	m Soc 1969 91
		a J. O. Mayima	in, <i>5</i> . <i>1m</i> . <i>Cher</i>	<i>n</i> . 500., 1707, 71
388. Table S4 pH	-Rate profile data ^a	^{,b} for the hydro	lysis of compo	und 4a in water a
388. Table S4 pH	-Rate profile data ^a	^{,b} for the hydro	lysis of compo	und 4a in water a $-\log k_{obs}/k$
388. Table S4 pH pH 5.37	-Rate profile data ^a - logk _{obs} /s 3.98	^{,b} for the hydro	lysis of compo pH 9.95	und 4a in water a - logk _{obs} / 2.58
Table S4 pH 6.37 7.10	-Rate profile data ^a - logk _{obs} /s 3.98 3.29	^{,b} for the hydro	lysis of compo pH 9.95 10.8	und 4a in water a - logk _{obs} // 2.58 2.58
Table S4 pH pH 6.37 7.10 7.62	-Rate profile data ^a - logk _{obs} /s 3.98 3.29 2.93	^{,b} for the hydro	lysis of compo pH 9.95 10.8 12.0	und 4a in water a - logk _{obs} // 2.58 2.58 2.55
Table S4 pH pH 6.37 7.10 7.62 8.15	-Rate profile data ^a - logk _{obs} /s 3.98 3.29 2.93 2.71	^{,b} for the hydro	lysis of compo pH 9.95 10.8 12.0 13.0	und 4a in water a - logk _{obs} // 2.58 2.58 2.55 2.56
Table S4 pH 6.37 7.10 7.62 8.15 8.47	-Rate profile data ^a - logk _{obs} /s 3.98 3.29 2.93 2.71 2.65	^{,b} for the hydro	lysis of compo pH 9.95 10.8 12.0 13.0 14.0	und 4a in water a - logk _{obs} // 2.58 2.58 2.55 2.55 2.56 2.47
Table S4 pH pH 6.37 7.10 7.62 8.15 8.47 9.14	-Rate profile data ^a - logk _{obs} /s 3.98 3.29 2.93 2.71 2.65 2.68	^{,b} for the hydro	lysis of compo pH 9.95 10.8 12.0 13.0 14.0	und 4a in water a - logk _{obs} // 2.58 2.58 2.55 2.56 2.47
Table S4 pH 6.37 7.10 7.62 8.15 8.47 9.14	-Rate profile data ^a - logk _{obs} /s 3.98 3.29 2.93 2.71 2.65 2.68 ectrophotometrical	^{,b} for the hydro	lysis of compo pH 9.95 10.8 12.0 13.0 14.0 5°C at (µ)=1.0	und 4a in water a - logk _{obs} // 2.58 2.58 2.55 2.56 2.47 M KCl. Analyt
Table S4 pH pH 6.37 7.10 7.62 8.15 8.47 9.14 ^a Measured sp wavelength w	-Rate profile data ^a - logk _{obs} /s 3.98 3.29 2.93 2.71 2.65 2.68 ectrophotometrical vas 400 nm. ^b The f	^{,b} for the hydro lly in water at 2 following buffe	lysis of compo pH 9.95 10.8 12.0 13.0 14.0 5°C at (μ)=1.0 rs were used to	und 4a in water a - logk _{obs} // 2.58 2.58 2.55 2.56 2.47 M KCl. Analytt
Table S4 pH pH 6.37 7.10 7.62 8.15 8.47 9.14 ^a Measured sp wavelength w ranges shown	-Rate profile data ^a - $\log k_{obs} / s$ 3.98 3.29 2.93 2.71 2.65 2.68 ectrophotometrical vas 400 nm. ^b The f	^{,b} for the hydro lly in water at 2 following buffe 52 phosphate (0	lysis of compo pH 9.95 10.8 12.0 13.0 14.0 5° C at (µ)=1.0 rs were used to .005 - 0.1 M);	und 4a in water a - logk _{obs} // 2.58 2.58 2.55 2.56 2.47 M KC1. Analytt o control pH in the pH 8.15-9.14 bc
Table S4 pH \overline{pH} $\overline{6.37}$ 7.10 7.62 8.15 8.47 9.14 ^a Measured sp wavelength w ranges shown $(0.01 - 0.2 \text{ M})$	-Rate profile data ^a - $\log k_{obs} / s$ 3.98 3.29 2.93 2.71 2.65 2.68 ectrophotometrical vas 400 nm. ^b The f : pH from 6.37-7.6 ; pH 9.95-10.8 car	^{,b} for the hydro lly in water at 2 following buffe 52 phosphate (0 bonate (0.05 –	lysis of compo pH 9.95 10.8 12.0 13.0 14.0 5° C at (µ)=1.0 rs were used to .005 – 0.1 M); 0.2 M) and pH	und 4a in water a - logk _{obs} // 2.58 2.58 2.55 2.56 2.47 M KCl. Analytt o control pH in th pH 8.15-9.14 bc 12-14 hydroxide
Table S4 pH \overline{pH} $\overline{6.37}$ 7.10 7.62 8.15 8.47 9.14 'Measured sp wavelength w $(0.01 - 0.2 \text{ M})$ $(0.01 - 0.1 \text{ M})$	-Rate profile data ^a - logk _{obs} /s 3.98 3.29 2.93 2.71 2.65 2.68 ectrophotometrical vas 400 nm. ^b The f : pH from 6.37-7.6 ; pH 9.95-10.8 car	^b for the hydro lly in water at 2 following buffe 52 phosphate (0 bonate (0.05 –	lysis of compo pH 9.95 10.8 12.0 13.0 14.0 5° C at (µ)=1.0 rs were used to .005 – 0.1 M); 0.2 M) and pH	und 4a in water a - logk _{obs} // 2.58 2.58 2.55 2.56 2.47 M KCl. Analyt o control pH in th pH 8.15-9.14 bc 12-14 hydroxide

71 **Table S3** Spectrophotometric^a and kinetic^b pK_{as} for the ionization^c of compounds **4a**-

1i

4.69

9.99

H _o /pH	-logk _{obs} /	s H_o/pH		-logk _{obs} /s
-1.05	3.87 ^b	5.00		3.37 ^{c,d}
-0.83	3.83 ^b	5.47		3.01 ^{c,d}
-0.69	3.82 ^b	6.05		2.64 ^{c,d}
-0.44	3.79 ^b	6.59		2.00 ^{c,d}
0	3.79 ^c	6.71		1.91 ^{c,d}
0.3	3.76 ^c	7.14		1.60 ^{c,d}
0.8	3.71 ^c	7.30		1.59 ^{c,d}
1.0	3.65 °	7.80		1.41 ^{c,d}
2.33	3.54 ^c	8.60		0.83 ^{c,d}
3.8	3.49 ^{c,d}	8.78		0.72 ^{c,d}
^a Conditions: Su	ubstrate concer	tration was 1 x 10	⁻⁴ M. Runs	s were followed by the
production of 4	I-nitrophenol a	t 265 nm or 4-nitr	ophenoxid	e at 410 nm and were
carried out for	at least 4 half-l	ives and done in t	riplicate.	Runs were generally
reproducible to	within \pm 5% e	except those at pH	s 7.8, 8.6 a	nd 8.78 which were
reproducible to	within \pm 9%.	^b Constant ionic st	rength (µ)	=3.0 M KCl. $^{c}(\mu)$ =1.0
KCl. ^d Carried of	out using 0.01	M TRIS-cacodyla	te buffer.	
Table S6 Log	k _{obs} for the hyd	rolysis ^a of compo	unds 1a an	d 1f-j in water at 50°C
pH = 2.0, the p	K _a of the leaving	ng phenols ^b and li	terature Ha	mmett σ value ^c
Compound	-logk _{obs} /s	Anal. λ (nm)	pKa	Hammett o
1a	3.60	325	7.15	0.778
1f	4.50	290	9.41	0.232
1g	4.46	275	9.37	0.227
11	1 70	200	0.00	0.060

Table S5 pH-Rate profile data^a for the hydrolysis of compound **1a** in water at 50°C.

^a At μ=	=1.0 M K	Cl. ^o In v	water at 25	5°C. Values	were tal	ken from A.	Albert and E.
Serjear Londor	1094	elermina	Calvan from	$m D \amalg M_{2}$	nsiumis, Domial a	nd II C Dra	аршан ани па
1059 ~	1, 1964, j 13, 420, 4	p.145. 1	aken noi	п D. п. мс	Daniel a	па п. С. ыс	own, J. Org. C
1938, 4	23 , 420-4	ΕΖΤ.					
Tabla	67 Uydr	olygic of	aamnaun	d le in agu	aous ara	onia solvant	mixturos ^a of
identic	əl ionizir	ng power	(Vor.) bu	u Ta III aqu	nucleon	allicities (No	
			V		nucleopi		l's).
Solven	t system	INOTS	I OTs	logk _{obs} /s	1-		
44.00/	P OU	0.10	1.02	2.20	K _{solvent} m	xture/K97% TFE	or 97% HFIP
44.8%	EtOH	-0.19	1.83	-3.39		95°	
52.4%	MeOH	-0.17	1.83	-3.45		840	
36% A	CN	-1.16	1.83	-3.52		71 ⁶	
97% T	FE	-3.25	1.83	-5.37		-	
10% E	tOH	-0.41	3.78	-3.46		22^{c}	
10% M	ſeOH	-0.41	3.78	-3.47		21 ^c	
10% A	CN	-1.29	3.60	-3.47		21 ^c	
97% H	FIP	-4.27	3.60	-4.79		-	
^a At 50	°C using	v/v mixt	ures exce	pt for 97%	TFE and	97% HFIP	which were w
^b Comp	ared with	h the rate	in 97% T	FE. ^c Com	pared wit	th the rate in	97%HFIP.
Table	S8 Logk	k _{obs} for th	e hydrolys	sis of 1a in	50% aqu	eous ACN a	t 25°C at high
pН	logk _{ol}	_{bs} /s	Anal. λ n	m	pН	logk _{obs} /s	Anal. λ nm
8.7	-4.71		325 ^a		11.7	0.921	400 ^{b,c}
9.7	-4.46		400 ^b		12.7	2.068	400 ^{b,c}
10.7	-1.67		400 ^b				
a 🔒	arance of	4-nitrop	henol. ^b A	ppearance	of 4-nitro	ophenoxide.	^c Rates detern
Appea						-	

170	Table S9	Logkobs for the	e hydrolysis	of compounds	1a and 1g-j	j at pH =	11.7 at 25°	C
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171	in 50% aqueous ACN	I, the pK _a of the	leaving phenols and	literature Hammett σ
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172 values.

Compound	$logk_{obs}/s$	Anal. λ (nm)	рК _а	Hammett σ
1 a	0.921	325	7.15	0.778
1g	-2.39	275	9.37	0.232
1h	-3.47	280	9.89	0.062
1i	-3.52	275	9.99	0
1j	-4.26	280	10.26	-0.17
^a In water at 25 th	°C. Values we	re taken from A. A	lbert and E	E. P. Serjeant, The
Determination	of Ionization (Constants, 3rd ed.,	Chapman	and Hall, London, 1984,
p.145. ^b Taken	from D. H. M	cDaniel and H. C.	Brown, J.	Org. Chem., 1958, 23 , 42
427.				
Table S10 Lo	gk _a for the hyd	rolysis of compour	nds 4a-g i r	n water ^a at 25°C and
Hammett σ val	lues ^b			
Comp	ound	-logk _a /s		Hammett o
4	a	2.57		0.73 ^c
4	la Ib	2.57 2.46		0.73° 0.227
4 4 4	la lb lc	2.57 2.46 2.56		0.73° 0.227 0.50°
4 4 4 4	la lb lc ld	2.57 2.46 2.56 2.43		0.73° 0.227 0.50° 0.062
4 4 4 4 4	la lb lc ld le	2.57 2.46 2.56 2.43 2.40		0.73° 0.227 0.50° 0.062 0
4 4 4 4 4 4	la lb lc ld le lf	2.57 2.46 2.56 2.43 2.40 2.33		0.73° 0.227 0.50° 0.062 0 -0.17
4 4 4 4 4 4 4	ka Ib Ic Id Ie If	2.57 2.46 2.56 2.43 2.40 2.33 2.33		0.73° 0.227 0.50° 0.062 0 -0.17 -0.27
4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4 4	la lb lc ld le lf Cl). Analytical	2.57 2.46 2.56 2.43 2.40 2.33 2.33 I wavelength was 4	400 nm for	0.73° 0.227 0.50° 0.062 0 -0.17 -0.27 each substrate. ^b See Tal
4 4 4 4 4 4 4 4 4 4 53, footnote d.	la lb lc ld le lf C1). Analytical °The σ value	2.57 2.46 2.56 2.43 2.40 2.33 2.33 I wavelength was 4 for 2-chloro is from	400 nm for m M. T. Tr	0.73° 0.227 0.50° 0.062 0 -0.17 -0.27 each substrate. ^b See Tal ibble and J. G. Traynham
4 4 4 4 4 4 4 4 4 4 53, footnote d. <i>J. Am. Chem. S</i>	la lb lc ld le ff f g C1). Analytical ^c The σ value Soc., 1969, 91 ,	2.57 2.46 2.56 2.43 2.40 2.33 2.33 1 wavelength was 4 for 2-chloro is from 379-388.	400 nm for n M. T. Tr	0.73° 0.227 0.50° 0.062 0 -0.17 -0.27 each substrate. ^b See Tal ibble and J. G. Traynham
4 4 4 4 4 4 4 4 53, footnote d. <i>J. Am. Chem. S</i>	la lb lc ld le ff C1). Analytical ^c The σ value Soc., 1969, 91 ,	2.57 2.46 2.56 2.43 2.40 2.33 2.33 I wavelength was 4 for 2-chloro is from 379-388.	400 nm for m M. T. Tr	0.73° 0.227 0.50° 0.062 0 -0.17 -0.27 each substrate. ^b See Tal ibble and J. G. Traynham
4 4 4 4 4 4 4 4 53, footnote d. <i>J. Am. Chem. S</i>	la lb lc ld le C1). Analytical ^c The σ value Soc., 1969, 91 ,	2.57 2.46 2.56 2.43 2.40 2.33 2.33 I wavelength was 4 for 2-chloro is from 379-388.	400 nm for m M. T. Tr	0.73° 0.227 0.50° 0.062 0 -0.17 -0.27 each substrate. ^b See Tal ibble and J. G. Traynham
4 4 4 4 4 4 4 4 4 53, footnote d. <i>J. Am. Chem. S</i>	la lb lc ld le Cl). Analytical ^c The σ value Soc., 1969, 91 ,	2.57 2.46 2.56 2.43 2.40 2.33 2.33 I wavelength was 4 for 2-chloro is from 379-388.	400 nm for m M. T. Tr	0.73° 0.227 0.50° 0.062 0 -0.17 -0.27 each substrate. ^b See Tal ibble and J. G. Traynham
4 4 4 4 4 4 4 5 4 5 3, footnote d. <i>J. Am. Chem. S</i>	la lb lc ld le 21). Analytical ^c The σ value Soc., 1969, 91 ,	2.57 2.46 2.56 2.43 2.40 2.33 2.33 I wavelength was 4 for 2-chloro is from 379-388.	400 nm for m M. T. Tr	0.73° 0.227 0.50° 0.062 0 -0.17 -0.27 each substrate. ^b See Tal ibble and J. G. Traynham

pН			- log	gk _{obs} /s		
6.37	3.82	3.82	3.96	3.92	3.96	4.03
7.10	3.27	3.38	3.31	3.44	3.39	3.40
7.62	2.91	2.99	2.92	2.95	2.96	2.97
8.15	2.65	2.74	2.65	2.66	2.63	2.64
8.47	2.55	2.65	2.54	2.54	2.48	2.50
9.14	2.47	2.59	2.45	2.43	2.37	2.35
9.95	2.45	2.55	2.42	2.40	2.32	2.32
10.77	2.47	2.57	2.44	2.41	2.34	2.35
12.0	2.45	2.54	2.42	2.38	2.31	2.30
13.0	2.42	2.52	2.41	2.37	2.31	2.30
14.0	2.33	2.44	2.33	2.29	2.23	2.19
Table S12	Effect of a	me as thos	fer on the	in Table 2	of 1a in wat	nd 4a . ter at 25°C
Table S12	Effect of a	acetate buf	fer on the (M)	in Table 2 hydrolysis pH	of 1a in wat $10^5 k_{obs}/s$	nd 4a .
Table S12 Buffer Acetate	Effect of a	acetate buf	e reported	in Table 2 hydrolysis pH 4.63	of 1a in wat $10^5 k_{obs}/s$ 1.21	ter at 25°C
Table S12 Buffer Acetate Acetate	Effect of a	acetate buf affer conc. 0.09 0.018	fer on the (M)	in Table 2 hydrolysis pH 4.63 4.65	of 1a in wat $10^5 k_{obs}/s$ 1.21 1.28	ter at 25°C
Table S12 Buffer Acetate Acetate Acetate	Effect of a	acetate buf affer conc. 0.09 0.018 0.036	fer on the	in Table 2 hydrolysis pH 4.63 4.65 4.65	of 1a in wat $10^5 k_{obs}/s$ 1.21 1.28 1.27	ter at 25°C
Table S12 Buffer Acetate Acetate Acetate Table S13 Compound	Effect of a Bu Physical m.p. (°C	acetate buf affer conc. 0.09 0.018 0.036 and analyt	fer on the (M)	in Table 2 hydrolysis pH 4.63 4.65 4.65 or compoun d (%)	of $1a$ in wat $10^5 k_{obs}/s$ 1.21 1.28 1.27 nds $4a-g$	rer at 25°C
Table S12 Buffer Acetate Acetate Acetate Table S13 Compound	Effect of a Bu Physical m.p. (°C	acetate buf affer conc. 0.09 0.018 0.036 and analyt:	fer on the (M) (M) ical data fo Calculated	in Table 2 hydrolysis pH 4.63 4.65 4.65 or compoun d (%) N	of $1a$ in wat $10^5 k_{obs}/s$ 1.21 1.28 1.27 hds $4a-g$	rer at 25°C

204 **Table S11** pH-rate profile data for the hydrolysis of compounds **4b–g**.^a

Supplementary Material (ESI) for Organic & Biomolecular Chemistry This journal is (c) The Royal Society of Chemistry 2010

106 - 107	45.56	3.23	8.17	45.79	3.21	8.28
84 - 85	45.56	3.23	8.17	45.56	3.21	8.08
100 - 101	47.85	3.40	8.56	48.02	3.42	8.68
109 - 110	50.64	3.92	9.09	50.81	3.87	9.10
113 - 114	52.17	4.38	8.69	52.58	4.54	8.75
103 - 104	49.70	4.17	8.30	50.64	4.22	8.25
	106 - 107 84 - 85 100 - 101 109 - 110 113 - 114 103 - 104	106 - 107 45.56 $84 - 85$ 45.56 $100 - 101$ 47.85 $109 - 110$ 50.64 $113 - 114$ 52.17 $103 - 104$ 49.70	106 - 107 45.56 3.23 $84 - 85$ 45.56 3.23 $100 - 101$ 47.85 3.40 $109 - 110$ 50.64 3.92 $113 - 114$ 52.17 4.38 $103 - 104$ 49.70 4.17	106 - 107 45.56 3.23 8.17 $84 - 85$ 45.56 3.23 8.17 $100 - 101$ 47.85 3.40 8.56 $109 - 110$ 50.64 3.92 9.09 $113 - 114$ 52.17 4.38 8.69 $103 - 104$ 49.70 4.17 8.30	106 - 107 45.56 3.23 8.17 45.79 $84 - 85$ 45.56 3.23 8.17 45.56 $100 - 101$ 47.85 3.40 8.56 48.02 $109 - 110$ 50.64 3.92 9.09 50.81 $113 - 114$ 52.17 4.38 8.69 52.58 $103 - 104$ 49.70 4.17 8.30 50.64	106 - 107 45.56 3.23 8.17 45.79 3.21 $84 - 85$ 45.56 3.23 8.17 45.56 3.21 $100 - 101$ 47.85 3.40 8.56 48.02 3.42 $109 - 110$ 50.64 3.92 9.09 50.81 3.87 $113 - 114$ 52.17 4.38 8.69 52.58 4.54 $103 - 104$ 49.70 4.17 8.30 50.64 4.22