Table S1. Identified compounds from *Agelas tubulata* extracts. Peak ID refers to the number assigned to individual peaks in LC chromatogram shown in Fig. 1. LC retention times, mass to charge (m/z) ratios from LC-MS, compound names, chemical formulas, published molecular masses (MM), published bioactivity and the associated references are included.

Peak ID	Retention Time (min)	m/z $[M+H]^+$	m/z $[M-H]^-$	Compound	MM	Chemical Formula	Activity	Publication
1	16.32-16.36	339.00	336.98	Agelongine	339.14	$C_{13}H_{11}BrN_2O_4$	antihistamine	Cafieri et al. 1997
							antiprotazoal	Scala et al. 2010
							antiserotonergic	Cafieri et al. 1995
2	17.24-17.49	557.14	555.12	Debromooxysceptrin	557.40	$C_{22}H_{25}BrN_{10}O_3$	antifouling	Keifer et al. 1991
3	18.72-18.89	--	417.9156	Dispacamide C	418.92	$C_{11}H_{11}Br_2N_5O_3$	antihistamine	Cafieri et al. 1997
4	19.01-19.23	635.05	--	Oxysceptrin	636.3	$C_{22}H_{24}Br_2N_{10}O_3$	antibacterial	Keifer et al. 1991
5	20.67-20.93	619.05	617.04	Sceptrin	620.30	$C_{22}H_{24}Br_2N_{10}O_2$	antibacterial	Walker et al. 1981
								Keifer et al. 1991
								Bernan et al. 1993
								Eder et al. 1999
								Richelle-Maurer et al. 2003
							antifungal	Walker et al. 1981
								Peng et al., 2003
								Richelle-Maurer et al. 2003
								Mohammed et al. 2006
							antihistaminic	Cafieri et al. 1997
							antimuscarinic	Rosa et al. 1992
							feeding deterrent	Assman et al. 2000
							inhibits cell motility	Cipres et al. 2010
6	21.36-21.44	387.94	385.93	Oroidin	389.05	$C_{11}H_{11}Br_2N_5O$	antibacterial	Mohammed et al. 2006
								Zidar et al. 2014
								Kovalerchik et al. 2020
							antibiofilm	Sun et al. 2017
								Kovalerchik et al. 2020
							antihistaminic	Cafieri et al. 1997
							antifungal	Hammami et al. 2010
								da Silva et al. 2011
								Erdogan-Orhan et al. 2012
							antifouling	Tsukamoto et al. 1996
							antimuscarinic	Rosa et al. 1992
							antiprotazoal	Konig et al. 1998
								Mohammed et al. 2006

								Scala et al. 2010
							cytotoxic	Konig et al. 1998
							feeding deterrent	Lindel et al. 2000
7	22.25-22.65	619.05	617.04	Ageliferin	620.30	$C_{22}H_{24}Br_{22}N_{10}O_2$	antibacterial	Eder et al. 1999
							antifouling	Keifer et al. 1991
8	22.87-22.97	696.96	694.95	Bromosceptrin	695.96	$C_{22}H_{23}Br_3N_{10}O_2$	antibacterial	Keifer et al. 1991
8	22.87-22.97	696.96	694.95	Bromoageliferin	695.96	$C_{22}H_{23}Br_3N_{10}O_2$	antibacterial	Keifer et al. 1991
								Melander et al. 2016
							antibiofilm	Melander et al. 2016
							disrupts calcium signaling	Bickmeyer 2005
9	25.92-26.08	--	--	Unknown 1	--	--		
10	25.92-26.08	--	265.85	4,5-Dibromo-1H-pyrrole-2-carboxylic acid	268.89	$C_5H_3Br_2NO_2$	antibacterial	Erdogan-Orhan et al. 2012
								Ponasik et al. 1998
							antifouling	Ponasik et al. 1998
							antifungal	Erdogan-Orhan et al. 2012
							feeding deterrent	Lindel et al. 2000
							antiprotazoal	Konig et al. 1998
							disrupts calcium signaling	Bickmeyer et al. 2005
							immunosuppressive	Gunasekera et al. 1989
11	27.33-27.50	774.87	772.86	Dibromoageliferin	778.09	$C_{22}H_{22}Br_4N_{10}O_2$	disrupts calcium signaling	Bickmeyer 2005

Table S2. Summary of Student's *t*-tests evaluating antibacterial activity of *Agelas tubulata* extracts collected from three sites in each of Belize and Grand Cayman (15 m depth), along a depth gradient of 15 - 61 m in Grand Cayman, and in a transplant experiment (22 to 61 m [SD], 61 to 22 m [DS], 22 to 22 m [SS], and 61 to 61 m [DD]). Note: the null hypothesis assumed that the ratio of bacterial growth in treated vs. untreated wells is equal to one if extracts exhibit no antibacterial activity. All P values were adjusted for multiple comparisons using Bonferroni corrections.

Experiment		***A. coralicida***			***S. marcescens***			***V. coralliilticus***			***Y. enterocolitica***		
		df	***t***	**P**	**df**	***t***	**P**	**df**	***t***	**P**	**df**	***t***	**P**
Site	Carrie Bow Cay, Belize	9	-8.61	< 0.0001	9	-10.9	< 0.0001	9	-14.57	< 0.0001	8	-16.98	< 0.0001
	Curlew Cay, Belize	4	-2.45	0.04	4	-12.49	0.0004	4	-74.42	< 0.0001	4	-8.36	0.002
	Southwater Cay, Belize	4	-4.86	0.004	4	-8.46	0.002	4	-39.11	< 0.0001	4	-8.97	0.001
	Kittiwake Anchor Chain, Grand Cayman	9	-4.95	0.0004	9	-18.77	< 0.0001	9	-34.1	< 0.0001	9	-7.66	< 0.0001
	Sentinel, Grand Cayman	3	-10.91	0.0008	2	-5.69	0.04	2	-19.69	0.004	1	-28.35	0.03
	Wall Street, Grand Cayman	4	-31.64	< 0.001	4	-19.94	< 0.0001	3	-65.39	< 0.0001	3	-8.16	0.006
Depth (m)	15	18	-10.13	< 0.0001	17	-21.83	< 0.0001	16	-49.92	0.004	15	-11.19	< 0.0001
	22	4	-20.22	< 0.0001	4	-7.48	0.003	4	-8.80	0.001	3	-21.55	0.0003
	30	4	-4.52	0.005	4	-4.61	0.01	4	-3.87	0.03	4	-7.29	0.009
	46	4	-6.12	0.002	4	-10.17	0.0008	4	-44.33	< 0.0001	4	-9.41	0.001
	61	4	-10.00	0.0003	4	-7.93	0.002	2	-7.54	0.03	3	-9.88	0.003
Transplant	SS	4	-15.40	< 0.0001	4	-9.45	0.001	4	-15.71	0.0001	3	-5.21	0.02
	SD	2	-13.94	0.003	2	-8.5	0.02	2	-30.38	0.002	2	-3.97	0.09
	DS	3	-5.58	0.006	3	-7.07	0.009	3	-23.08	0.0003	2	-5.38	0.05
	DD	4	-11.17	0.0002	3	-6.15	0.01	4	-13.94	0.0002	4	-10.61	0.0007

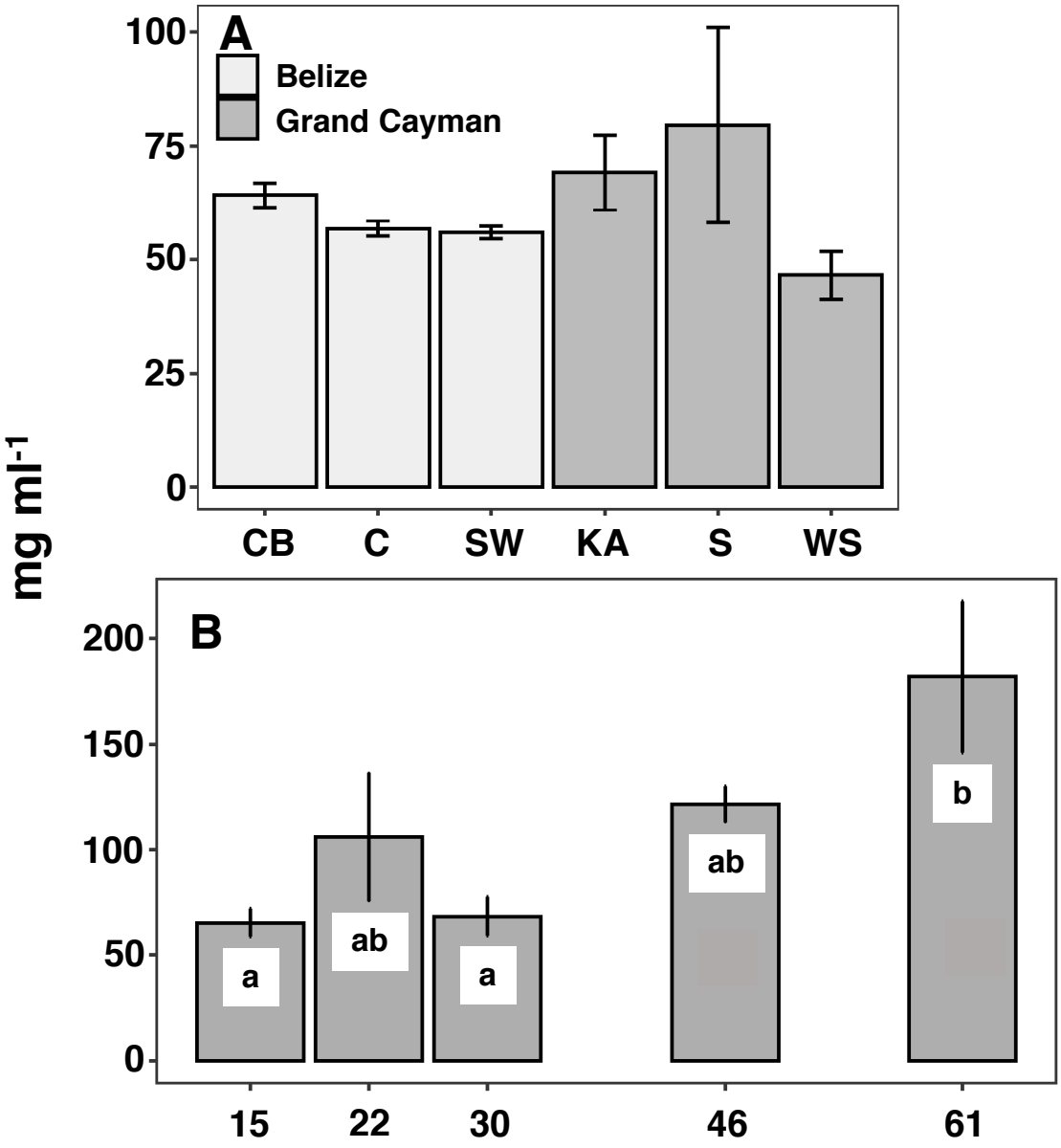

Figure S1. Total extract concentration of *Agelas tubulata* by (A) collection site [Belize- CB: Carrie Bow Cay, C: Curlew Cay, SW: Southwater Cay, and Grand Cayman- KA: Kittiwake Anchor Chain, S: Sentinel, WS: Wall Street] and (B) depth (15- 61 m). Barplots represent the mean (± SE) concentration (n = 5- 20 individuals per site or depth). There was no signficant difference in extract concentrations among sites. Lower case letters refer to significant differences ($P < 0.05$) between depths by Tukey's *post-hoc* tests.

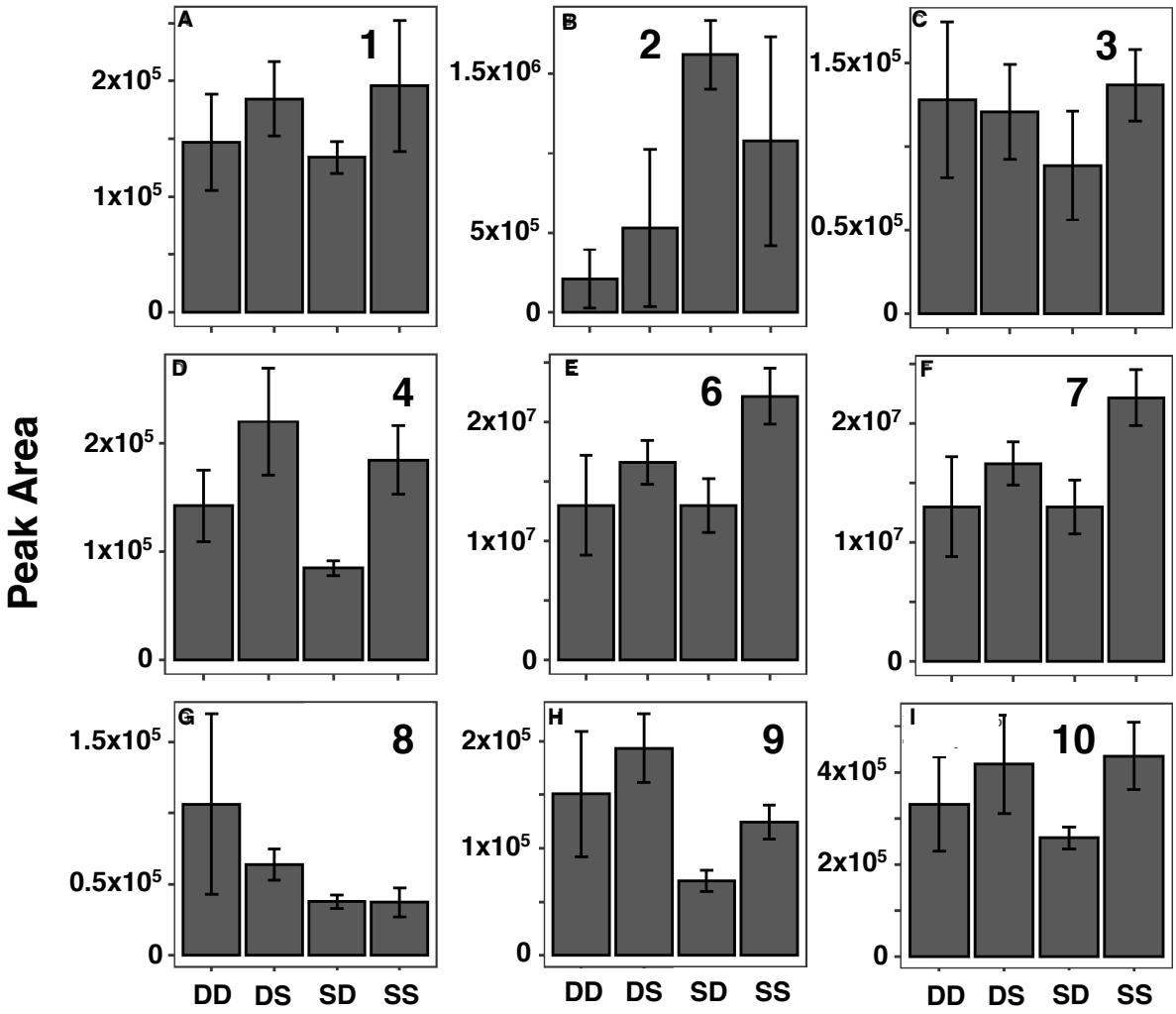

Figure S2. Relative concentration of individual compounds within *Agelas tubulata* extracts by transplant treatment. Barplots represent the mean (± SE) peak area of individual compounds within extracts from sponges transplanted from 22 to 61 m (SD; N=3), 61 to 22 m (DS; N=4), 22 to 22 m (SS; N=5), or 61 to 61 m (DD; N=5) in Grand Cayman. Numbers in the upper right of each panel represent specific compounds; refer to Figure 1 for compound names and structures. Note the difference in scales among panels.

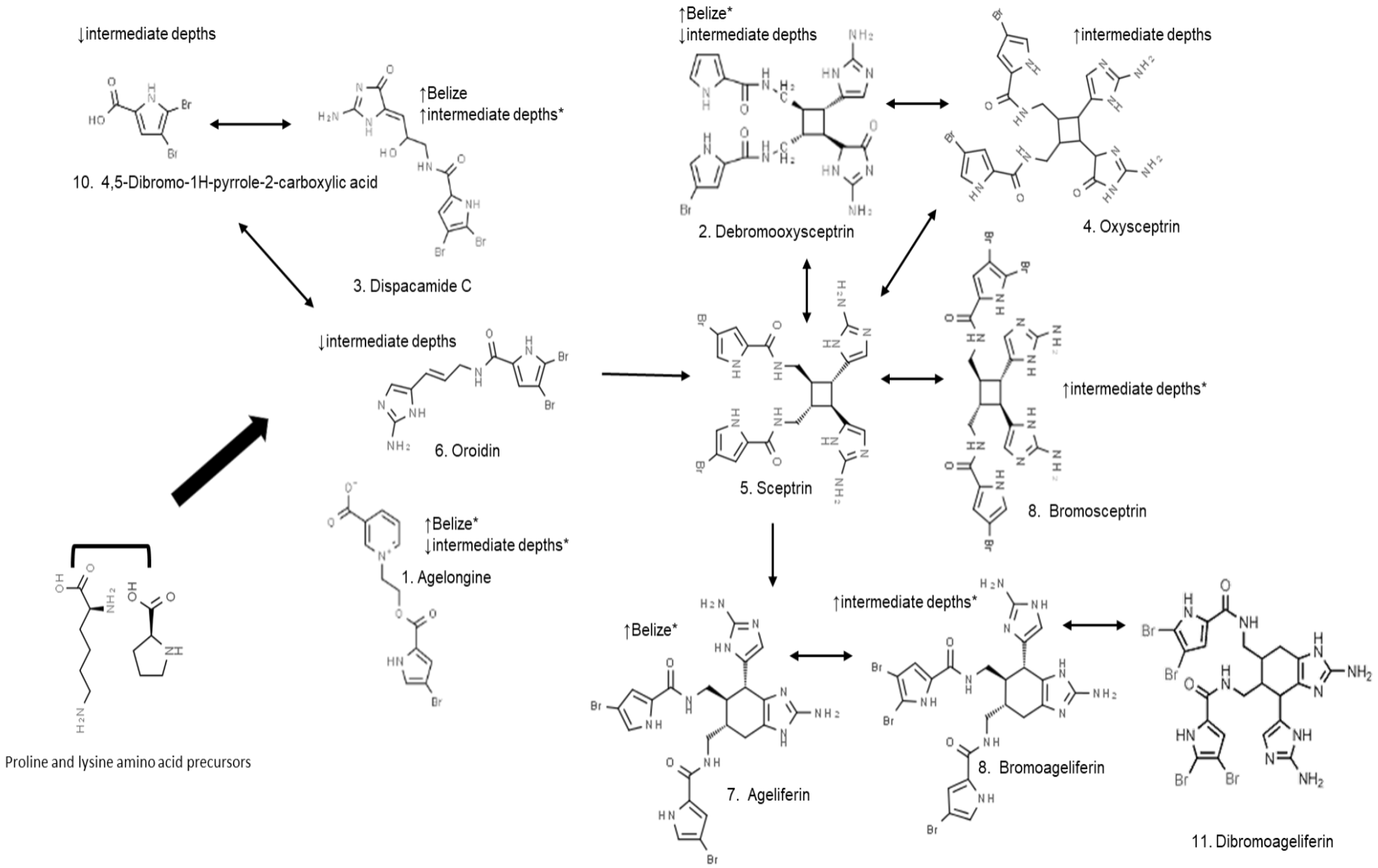
↓intermediate depths
↑Belize
↑intermediate depths*
10. 4,5-Dibromo-1H-pyrrole-2-carboxylic acid
3. Dispacamide C
↓intermediate depths
6. Oroidin
↑Belize*
↓intermediate depths*
1. Agelongine
Proline and lysine amino acid precursors
↑Belize*
↓intermediate depths
2. Debromooxysceptrin
↑intermediate depths
4. Oxysceptrin
5. Sceptrin
↑intermediate depths*
8. Bromosceptrin
↑Belize*
7. Ageliferin
↑intermediate depths*
8. Bromoageliferin
11. Dibromoageliferin

Figure S3. Proposed biosynthetic relationships between bromopyrrole alkaloids that occur in *A. tubulata.* Dimeric compounds sceptrin, bromosceptin, debromooxysceptrin, oxysceptrin, ageliferin, bromoageliferin, and dibromoageliferin are all derived from the monomeric precursor oroidin (Rane et al. 2013, Baran et al. 2004). Dispacamide C represents an oroidin analogue (Rane et al. 2013), while agelongine is related to oroidin and its analogues, but the imidazole ring has been replaced by pyridinium ring. The compound 4,5-dibromo-1H-pyrrole-2-carboxylic acid is a chemical derivative of oroidin, dispacamide C, and represents a possible precursor of these compounds. Oroidin, dispacamide C, agelongine, and 4,5-dibromo-1H-pyrrole-2-carboxylic acid, are all derived from proline and/or lysine amino acid precursors (Gente-Jouve et al. 2011). Up (↑) and down (↓) arrows indicate that a compound was relatively more or less concentrated in the tissue of sponges collected from sites within Belize as compared to Grand Cayman or at intermediate depths (30- 46 m) compared to shallow (15- 22 m) or deep (61 m) extremes. Asterisks (*) indicate that differences in tissue concentrations of individual compounds between sponges that occur along these geographical or depth gradients are statistically significant ($P < 0.05$) by ANOVA and Tukey's *post-hoc* tests. Numbers next to compound names indicate the order of a compound peak along the time axis in our HPLC analysis.