

Table S1. Primers for *notI* and *notI'* intron removal and amplification

Name	Sequence	Function
<i>notI</i> _F	GGAGTTCCATATGGCTATAGACGGATCT	amplification
<i>notI</i> _F	CAATGAAGCTTTCAACCAACCGGTATACC	amplification
<i>notI'</i> _F_NdeI	GGAATTCCATATGGCTATAGACGCATCTGGTGCTG	amplification
<i>notI'</i> _R	ATAAGAATGCGGCCGCTTAATCCACCGGTATACCACCGAAG	amplification
<i>notI'</i> _MBP_F	CTAGTGAGAATCTCTACTTCCAAGGCGCTATGGCTATAGACGCATCTGGTGC	amplification
<i>notI'</i> _MBP_R	GGTGGTGCTCGAGTGCGGCCGCAAGTTAATCCACCGGTATACCACCG	amplification
<i>notI'</i> _Int1_F	CAAGAGCTACCGTTTGGG AGACTTGATCAATGTGACCGGG	intron removal
<i>notI'</i> _Int1_R	CCCGGTCACATTGATCAAGTCTCCCAAACGGTAGCTCTTG	intron removal
<i>notI'</i> _Int2_F	CGAGTGACAGAGAAGCTAAGGTACCAAAGGGTTGCTGCAA	intron removal
<i>notI'</i> _Int2_R	TTGCAGCAACCCTTTGGTACCTTAGCTTCTCTGTCACCTCG	intron removal

Table S2. ^{13}C -NMR, ^1H -NMR, gHMBCAD, and gCOSY correlations recorded at 700 MHz in $(\text{CD}_3)_2\text{SO}-d_6$ for notoamide TI (**18**) isolated from *in vitro* reaction with NotI. HRMS (ESI-QTOF): m/z $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{26}\text{H}_{31}\text{N}_3\text{O}_4 = 450.2393$, experimental = 450.2414. Data were measured on a Varian Vnmrs 700 spectrometer.

Position	$\delta^{13}\text{C}$	$\delta^1\text{H}$ (m, J [Hz])	gHMBCAD	gCOSY
1	43.37	3.38 obs		
2	29.03	1.78 (m)		
		2.50 obs	1,3,4,21	3
3	24.34	1.78 (m)	5	2
		1.99 (m)		
4	68.08			
5	29.57	1.72 (dd, 12.8, 8.3)	4,6,7,21	
		1.92 (m)		6
6	55.39	3.24 (m)	7,18	
7	44.92			
8	61.36			
9	120.29			
10	107.49	6.41 (d, 8.0)	9,14	11
11	123.64	6.81 (d, 8.0)	12,13	10
12	141.35			
13	155.27			
14	110.05			
15	NH	8.51		
16	183.39			
17	33.34	2.14 (d, 14.1)	7,8,16,18,19	
		2.78 (d, 14.2)	6,8,9,16,18,19	
18	65.53			
19	169.48			
20				
21	173.13			
22	NH	9.07	4	
23	23.46	3.17 (m)	12,13,14,24,25	24
24	122.66	5.13 (t, 7.0)		25
25	130.43			
26	25.57	1.61 (d, 10.1)	24,25,27	
27	17.83	1.69 (s)	24,25,26	
28	23.09	0.68 (s)	6,7,8,29	
29	19.56	0.70 (s)	28	

*obs: These peaks are obscured by the solvent and water in the sample.

Table S3. Percent identity matrix of NotI/NotI' homologs including AuaG,^[1] PhqK,^[2] OxaD,^[3] asperlicin C monooxygenase (GenBank: GBF62818.1), FMO from *Penicillium griseofulvum* (GenBank: KXG49074.1), NotI, NotI', NotB,^[4] and BvnB^[5] (generated using Clustal2.1).^[6]

	AuaG	PhqK	OxaD	Asperlicin C FMO	<i>P. griseofulvum</i>	NotI	NotI'	NotB	BvnB
AuaG	100.00	25.33	25.86	22.75	20.37	25.20	26.26	23.48	24.40
PhqK	25.33	100.00	33.71	35.78	33.55	34.91	33.96	31.82	32.34
OxaD	25.86	33.71	100.00	35.43	41.14	36.72	37.88	36.20	35.57
Asperlicin C FMO	22.75	35.78	35.43	100.00	44.30	42.13	41.44	38.48	35.51
<i>P. griseofulvum</i>	20.37	33.55	41.14	44.30	100.00	40.51	39.81	44.15	42.95
NotI	25.20	34.91	36.72	42.13	40.51	100.00	84.99	45.03	42.92
NotI'	26.26	33.96	37.88	41.44	39.81	84.99	100.00	43.42	41.76
NotB	23.48	31.82	36.20	38.48	44.15	45.03	43.42	100.00	62.14
BvnB	24.40	32.34	35.57	35.51	42.95	42.92	41.76	62.14	100.00

Table S4. Average percent conversions for NotI and NotI' with natural substrates (+)-stephacidin A (**9**), (-)-stephacidin A (**4**), (+)-6-*epi*-stephacidin A (**6**), and (-)-6-*epi*-stephacidin A (**7**). Reactions were performed in triplicate and conversions were calculated via substrate and product standard curves.

Substrate	Product	NotI conv (%)	NotI' conv (%)
(+)-Stephacidin A (9)	(-)-Notoamide B (10)	11	9
(-)-Stephacidin A (4)	(+)-Notoamide B (5)	68	52
(+)-6- <i>epi</i> -Stephacidin A (6)	(+)-Versicolamide B (8)	13	7
(-)-6- <i>epi</i> -Stephacidin A (7)	(-)-Versicolamide B (11)	0	0