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Chemistry of ecteinascidins. Part 3: Preparation of 2′-*N*-acyl derivatives of ecteinascidin 770 and evaluation of cytotoxicity

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ABSTRACT

A three-step transformation of ecteinascidin 770 (**1b**) into 2′-*N*-indole-3-carbonyl derivative **3** via 18,6′-*O*-bisallyl-protected derivative **4a**, which was shown to have higher cytotoxicity than **1b**, is presented. In addition, a number of 2′-*N* amide derivatives of **1b** have been prepared from **4a** and their in vitro cytotoxicity were determined by measuring IC_{50} values against human cell lines HCT116, QG56, and DU145. Benzoyl amide derivatives **7a–c** showed similar in vitro cytotoxicity to **1b**, whereas the nitrogen-containing heterocyclic derivatives **7d–h** and cinnamoyl derivatives **9a–b** showed higher cytotoxicity than **1b**. In contrast, the 18,6′-*O*-bisallyl protected derivatives **4a–c**, **6a–h**, and **8a–b** showed dramatic decreases in cytotoxicity relative to **1b**.

1. Introduction

Members of the tetrahydroisoquinoline family of natural products have attracted considerable interest for more than 30 years due to their novel structures and meager availability in nature, and for their potent antitumor activity (Fig. 1).[1] Of particular significance is ecteinascidin 743 (**1a**), which has been demonstrated to possess extremely potent in vitro cytotoxicity (0.1–1 ng/mL) in a variety of tumor cell lines.[2,3] Yondelis® (trabectedin, Et 743),[4] a marine anticancer agent, was the approved in 2007 for use in humans with soft tissue sarcoma in the European Union.

A common problem associated with the isolation of marine natural products is their low concentrations in the organisms that produce them. The complexity of their structures has attracted the attention of synthetic organic chemists worldwide. To date, three total syntheses have been accomplished by the groups of Corey,[5,6] Fukuyama,[7] and Zhu.[8] Formal total syntheses has been reported by Danishefsky[9] and Williams.[10] A semisynthetic process starting from cyanosafracin B, an antibiotic produced by the fermentation of *Pseudomonas fluorescens*,[11–17] has been developed by Pharma Mar in the synthesis of **1a**. Less than 30 steps,[18,19] this semisynthetic process for the preparation of **1a** will eventually be used for gram scale production. Many structure–activity relationship (SAR) studies including those of the related natural products saframycins and renieramycins, have been reported,[20–27] but few examples of SAR studies on ecteinascidins have been reported.[28]

As part of our search for new metabolites via the isolation and characterization of biologically active compounds from Thai marine animals, we were able to isolate ecteinascidin 770 (**1b**) on a large scale from the Thai tunicate *Ecteinascidia thurstoni* by pretreatment with potassium cyanide in buffer solution. During the course of this work we elucidated the structure of ecteinascidin 770 (**1b**).[29] We have reported the preparation 6′-*O*-acyl derivatives of ecteinascidin 770 (**2**) and determined their cytotoxicity in several human tumor cell lines (Fig. 2).[30] We found that the nitrogen-containing heterocyclic ester derivatives showed similar in vitro cytotoxicity to **1b**. We also discovered that the coupling of **1b** with indole-3-carboxylic acid in the presence of *N,N*′-dicyclohexylcarbodiimide (DCC) provided 2″-*N*-amide **3**, which exhibited high cytotoxicity relative to **1b**. The high cytotoxicity of **3** prompted us to explore a general method for the preparation of derivatives of **1b** and to evaluate their cytotoxicity. In this paper, we report a three-step transformation of **1b** into 2′-*N*-amides **7** and **9** via 18,6′-*O*-bisallyl protected derivative **4a**. We also report the in vitro cytotoxicity of the resulting 2′-*N*-amides.

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2. Chemistry

We first examined the preparation of **3** from **1b** in order to develop a general route to 2′-*N*-amides via a three-step protocol: (1) 18,6′-*O*-bisallyl protection leading to **4a**, (2) 2′-*N*-amide formation, and (3) deprotection of the ally group. A mixture of **1b** and 25 equiv of K_2CO_3 in acetone was treated with allyl bromide (20 equiv) at 25 °C for 10 h to generate the desired product **4a** (81%) along with 6′-*O*-allyl Et 770 **4b** (2.7%) and triallyl Et 770 **4c** (5.5%) (Scheme 1). The structure of **4c** was easily confirmed by NMR and MS data. The ^1H and ^{13}C NMR spectral data of **4a** and **4c** were very similar, the only major difference being the presence of additional signals attributable to the 2′-*N*-allyl group in **4c** [^1H NMR: δ 5.58 (1H, *N*–CH_2CH=CH_2), 5.13 and 5.04 (each 1H, *N*–CH_2CH=CH_2), 3.09 (2H, *N*–CH_2CH=CH_2); ^{13}C NMR: δ 138.0 (*N*–CH_2CH=CH_2), 115.3 (*N*-CH_2CH=CH_2), 54.2 (*N*–CH_2CH=CH_2)]. The assignment of the signals for the allyl substituents of **4b** was made by conducting further NMR experiments. All proton and carbon signals of **4b** were assigned by using H-H, H-C COSY and a series of ^1H detected two-dimensional heteronuclear multiple bond correlation (HMBC) experiments (see Experimental). The NOE spectra of compound **4b** showed a sharp phenolic OH signal at δ 5.73 with an NOE enhancement of the 17-OCH_3 methyl proton signal at 3.79. The data indicated that the OH group might be located at C18 in **4b**. This is consistent with the long-range correlations between 18-OH and C17 (δ 143.0), C18 (δ 147.8), and C19 (δ 118.1). Thus, the structure of **4b** was confirmed to be 6′-*O*-allyl Et 770.

The transformation of **1b** into the desired **4a** took place smoothly in 81% yield. It was desirable to recover **1b** from the fully allylated compound **4c**. Accordingly, reaction[31,32] of **4c** with tributyltin hydride, $(Ph_3P)_2PdCl_2$ and AcOH in THF at 25 °C for 6 h gave **1b** (33%) along with 2′-*N*-allyl Et 770 **4d** (28%). The ^1H NMR spectrum of **4d** showed two characteristic phenolic proton signals at δ 5.69 and 5.42.

Coupling of **4a** with indole-3-carboxylic acid in the presence of DCC at 25 °C for 6 h provided amide **5** in 90% yield. Deprotection of **5** at 25 °C for 1.5 h under the same conditions described above gave **3** in 42.9% yield,[33] which was identical in all respects with the authentic sample.[30]

Subsequently, we examined the transformation of **4a** into the corresponding aromatic ester derivatives. In contrast to the transformation of **1b** into 2′-*N*-indole-3-carboxylic acid **5** employing DCC, treatment of **1b** with 4-nitrobenzoic acid and DCC in CH_2Cl_2 under the same conditions gave only 6′-*O*-4″-nitrobenzoyl Et 770 **2** (R = $COC_6H_4NO_2$-4″) in 81.6% yield. No 2′-*N*-acyl derivative was produced. It is surprising that the attempted condensation of compound **4a** with a variety of carboxylic acids, such as pyridine-2-carboxylic acid, indole-5-carboxylic acid, 4-imidazolecarboxylic acid, and 4-pyrazolecarboxylic acid in the presence of DCC in CH_2Cl_2 failed and lead only to the recovery of the starting material. However, treatment of **4a** with the corresponding acid chloride and a catalytic amount of 4-dimethylaminopyridine (DMAP) in pyridine at 60 °C for several hours gave 2′-*N*-benzoyl derivatives 6a–**c** and **6i** in 80–92% yields (Fig. 3). In contrast, the condensation of **4a** with 2-bromobenzoyl chloride under the same conditions proceeded relatively slowly and the yield of a desired product **6j** was low (29%). Deprotection of **6a–c** using the same conditions described above afforded within 1 h the desired amides **7a–c** in moderate yields (48–51%). Attempted deprotection of **6i** or **6j** under the same conditions was unsuccessful and gave only polar polymeric materials.

Five nitrogen-containing heterocyclic aromatic amide derivatives **7d–h** were prepared by acylation (73–91% yield), followed by deallylation (65–98%). The ^1H NMR signals of **6f**, **6g**, **7f**, and **7g** revealed mixtures of rotational isomers are present. Finally, cinnamoyl amide derivatives **9a** and **9b** were prepared from **4a** via **8a** and **8b**, respectively. In this case, 18-*O*-allyl derivatives **10a** and **10b** were also obtained in 18.3% and 22.6% yields, respectively.

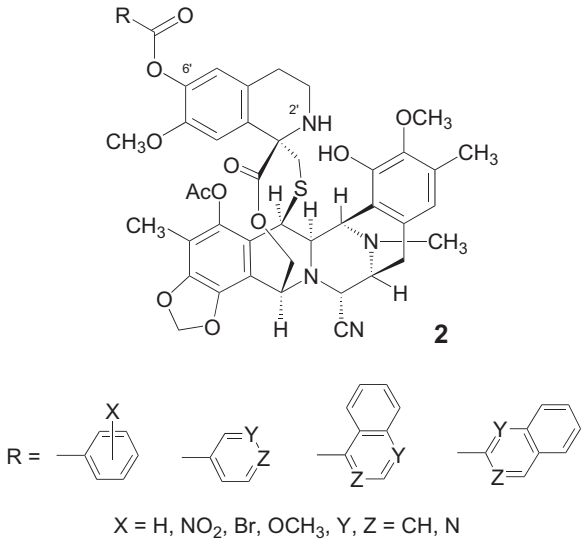


Figure 2. 6′-*O*-Acyl derivatives of ecteinascidin 770.

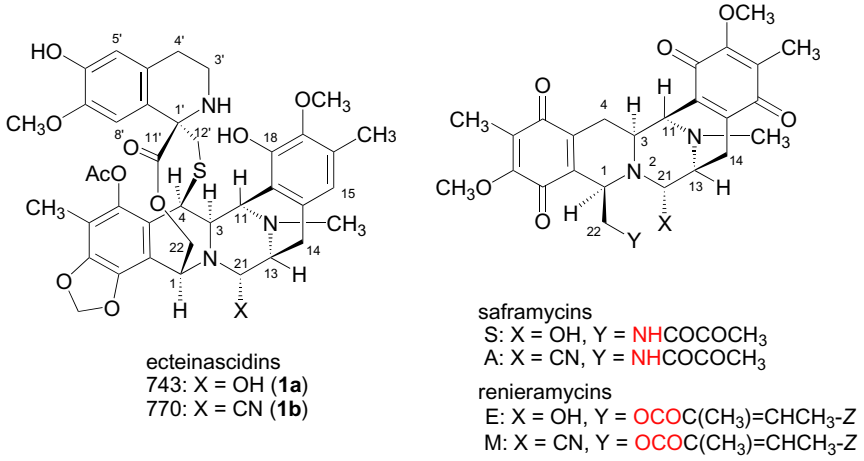
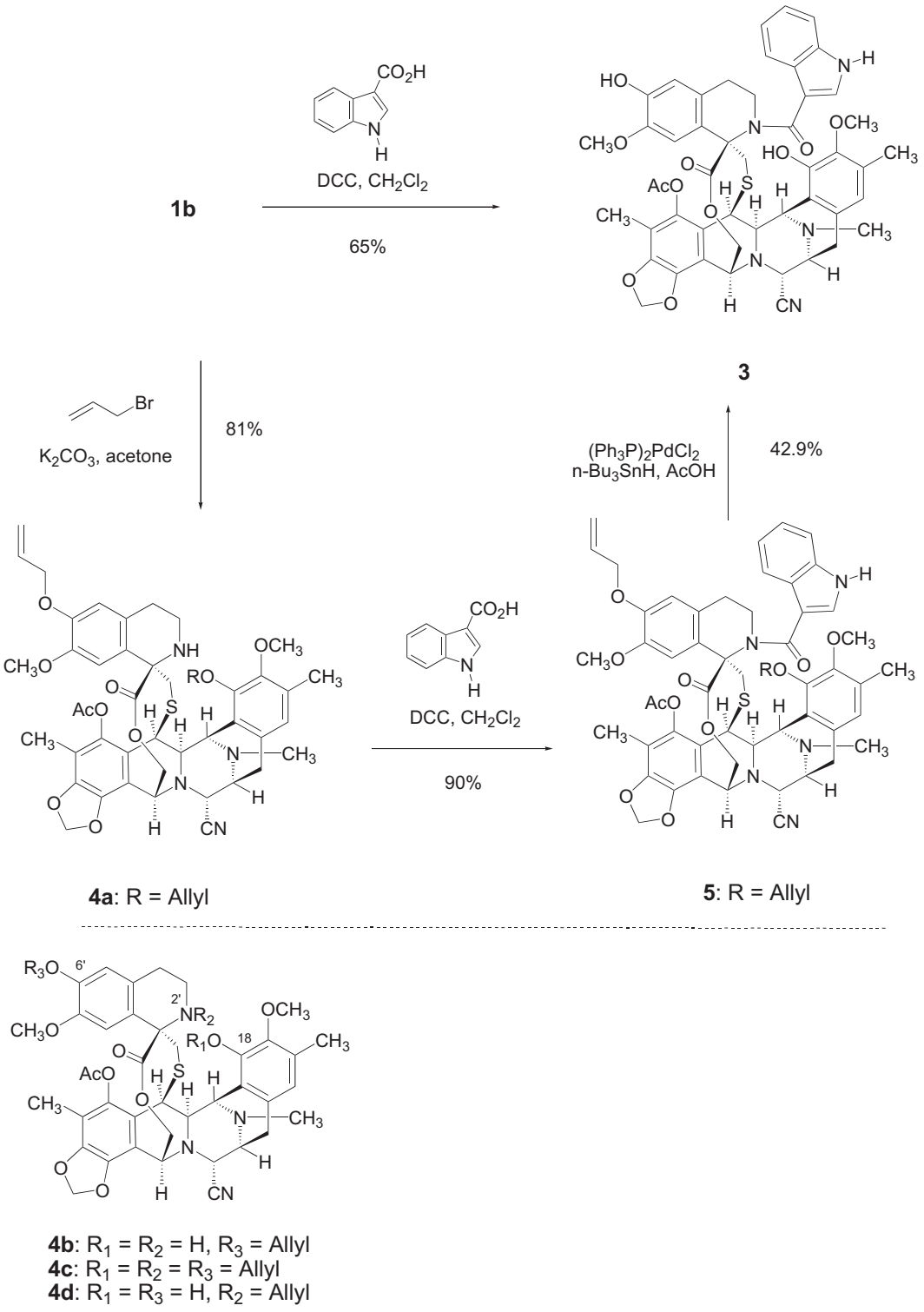


Figure 1. Structures of representative isoquinoline natural products.



Scheme 1. Preparation of compound **3**.

3. Biological evaluation

The analogues synthesized above, including ecteinascidin 770 (**1b**), were tested in vitro for cytotoxicity using three representative human solid tumor cell lines (HCT116 colon carcinoma, QG56 lung carcinoma, and DU145 prostate carcinoma) using the standard MTT method (Table 1). It can be seen from the data in Table 1 that the IC_{50} values of ecteinascidin 770 analogues were of nM order. Among the four allylated Et 770 derivatives **4a–d**, 2′-*N*-monoallylated Et 770 **4d** had similar cytotoxicity to **1b**, whereas 6′-*O*-monoallylated 770 **4b** showed five-hold lower cytotoxicity than **1b**. The 18-*O*-Protected Et 770 derivatives, such as **4a** and **4c**, showed decreased cytotoxicity as well. The aromatic carboxylic acid amide derivatives **6a–j**, including **5** and the two cinnamoyl amides **8a–b**, all of which had a 6′-*O*-allyl protecting group present, exhibited dramatically decreased cytotoxicity.

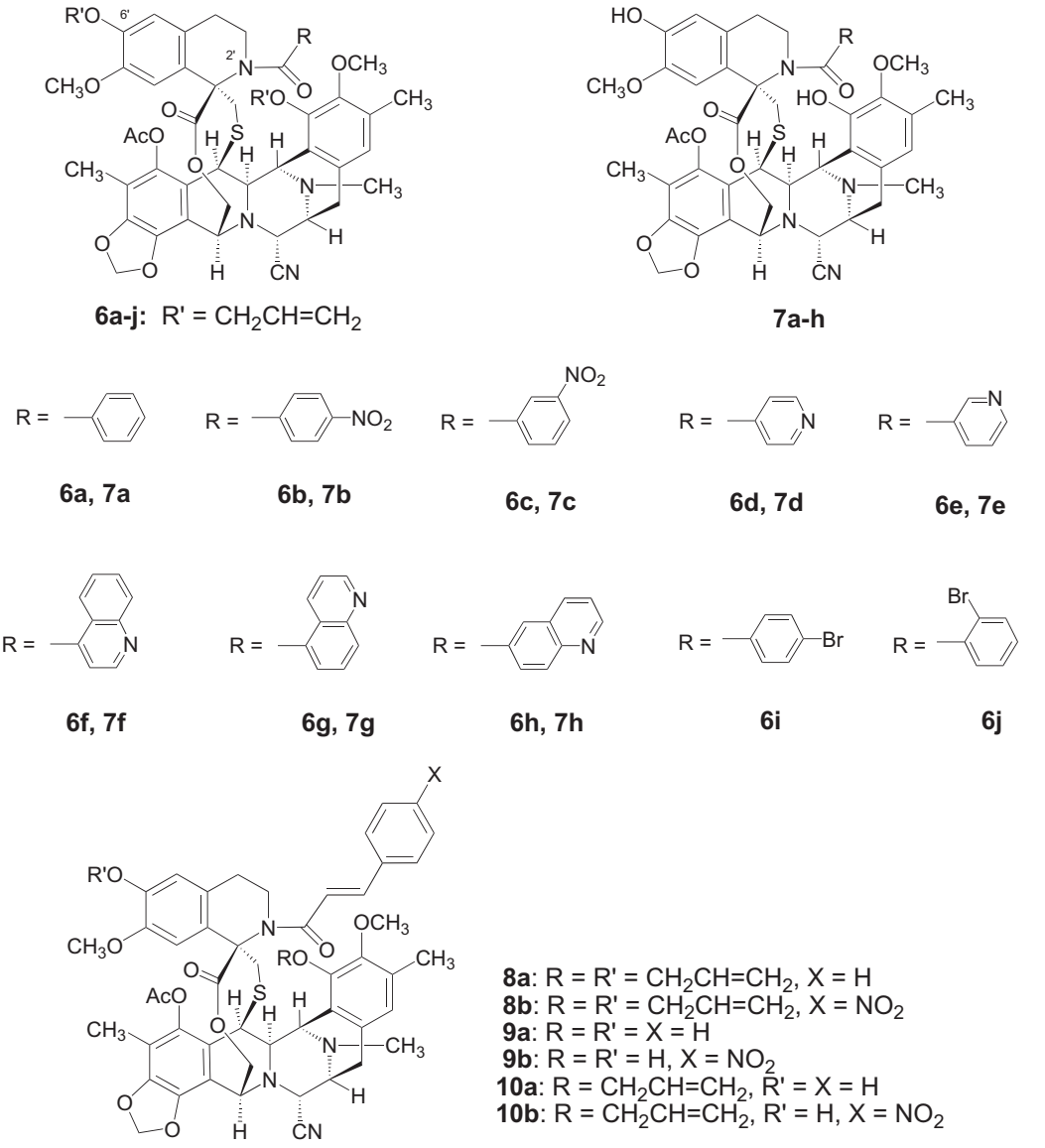


Figure 3. 2′-*N*-Acyl derivatives of ecteinascidin 770.

Of particular interest was compound **5** which showed highly specific cytotoxicity in the HCT116 cell line in contrast to most of the 2′-*N*-acyl derivatives of Et 770 that showed considerable cytotoxicity to all these three cell lines. On the other hand, nitrogen-containing heterocyclic amides (**3**, **7d–h**) exhibited higher cytotoxicity than **1b**. It is noteworthy that compound **7h** having a 6″-quinolinecarbonyl group, which was the most potent of the 30 compounds prepared, showed approximately 10- to 20-fold higher cytotoxicity than **1b**. It exhibited very potent inhibitory activity against HCT116 and DU145 cell lines with IC_{50} values of 0.045 nM and 0.043 nM, respectively.

From these results, we conclude that the 2′-*N*-acyl derivative of Et 770 having 18,6′-bishydroxy groups showed high cytotoxicity. These data show that the 2′-*N*-acyl group of the ecteinascidin 770 derivative warrant further biological activity.

4. Conclusion

Eleven 2′-*N*-amide analogues of **1b** were prepared from 18,6′-*O*-bisallyl-protected derivative **4a** in two steps and evaluated in vitro for their cytotoxicity in human HCT116 colon carcinoma, QG56 lung carcinoma, and DU145 prostate carcinoma cell lines. The protection of both 18- and 6′-phenolic hydroxyl groups resulted in diminished cytotoxicity, whereas the introduction of acyl groups at the 2′-*N* position enhanced cytotoxicity. We found that 2′-*N*-(6″-quinolinecarbonyl) Et 770 analogue **7h** was the most potent among all the analogues prepared exhibiting approximately 10- to 20-fold increase in cytotoxicity relative to **1b**.

Our findings indicate that the potent antitumor activity of our analogue **7h** is promising. Efforts to explore the therapeutic potential of other ecteinascidin analogues are under way and will be reported in due course.

5. Experimental section

Optical rotations were measured with a Horiba-SEPA polarimeter. IR spectra were obtained with a Shimadzu Prestige 21/IRA Affinity-1 FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL-JNM-ECA500 FT NMR spectrometer at 500 MHz for ^{1}H and 125 MHz for ^{13}C, on a JEOL-JNM-AL400 NMR spectrometer at 400 MHz for ^{1}H and 100 MHz for ^{13}C, and on a JEOL-JNM-AL300 NMR spectrometer at 300 MHz for ^{1}H and 75 MHz for ^{13}C

Table 1
Cytotoxicities of ecteinascidin 770 and related analogues to three carcinoma cell lines (IC_{50} nM)

Entry	Compound	Comments	Cytotoxicity		
			HCT116[a]	QG56[a]	DU145[a]
1	**1b**	Ecteinascidin 770	0.60	2.4	0.81
	1b[b]		0.40	1.8	0.66
2	**4a**	18,6′-*O*-Bisallyl Et 770	54	1.6×10^2	1.0×10^2
3	**4b**	6′-*O*-Allyl Et 770	2.4	12	7.1
4	**4c**	triallyl Et 770	6.2×10^2	$>1.0 \times 10^3$	$>1.0 \times 10^3$
5	**4d**	2′-*N*-Allyl Et 770	0.50	1.8	1.2
6	**5**	18,6′-*O*-Bisallyl-2′-*N*-indole-3-carbonyl Et 770	0.45	$>1.0 \times 10^3$	$>1.0 \times 10^3$
7	**3**	2′-*N*-Indole-3-carbonyl Et 770	0.16	0.46	0.45
	3[b]		0.07	0.53	0.37
8	**6a**	18,6′-*O*-Bisallyl-2′-*N*-Bz Et 770	1.9×10^2	6.9×10^2	5.4×10^2
9	**7a**	2′-*N*-Bz Et 770	0.37	1.0	1.1
10	**6b**	18,6′-*O*-Bisallyl-2′-*N*-(4-nitroBz) Et 770	2.6×10^2	7.9×10^2	5.9×10^2
11	**7b**	2′-*N*-(4-NitroBz) Et 770	0.38	1.1	1.0
12	**6c**	18,6′-*O*-Bisallyl-2′-*N*-(3-nitroBz) Et 770	1.8×10^2	5.2×10^2	2.7×10^2
13	**7c**	2′-*N*-(3-NitroBz) Et 770	0.14	0.43	0.73
14	**6d**	18,6′-*O*-Bisallyl-2′-*N*-(isonicotinyl) Et 770	2.8×10^2	7.9×10^2	5.9×10^2
15	**7d**	2′-*N*-(Isonicotinyl) Et 770	0.045	0.20	0.30
16	**6e**	18,6′-*O*-Bisallyl-2′-*N*-(nicotinyl) Et 770	3.9×10^2	$>1.0 \times 10^3$	6.8×10^2
17	**7e**	2′-*N*-(Nicotinyl) Et 770	0.13	0.40	0.72
18	**6f**[c]	18,6′-*O*-Bisallyl-2′-*N*-(4-quinolinecarbonyl) Et 770	3.1×10^2	4.2×10^2	4.2×10^2
19	**7f**[c]	2′-*N*-(4-Quinolinecarbonyl) Et 770	0.067	0.23	0.16
20	**6g**[c]	18,6′-*O*-Bisallyl-2′-*N*-(5-quinolinecarbonyl) Et 770	3.2×10^2	6.4×10^2	5.5×10^2
21	**7g**[c]	2′-*N*-(5-Quinolinecarbonyl) Et 770	0.086	0.36	0.92
22	**6h**	18,6′-*O*-Bisallyl-2′-*N*-(6-quinolinecarbonyl) Et 770	1.5×10^2	2.6×10^2	1.8×10^2
23	**7h**	2′-*N*-(6-Quinolinecarbonyl) Et 770	0.045	0.16	0.043
24	**8a**	18,6′-*O*-Bisallyl-2′-*N*-(cinnamoyl) Et 770	6.3×10^2	$>1.0 \times 10^3$	$>1.0 \times 10^3$
25	**9a**	2′-*N*-(Cinnamoyl) Et 770	0.053	0.33	0.24
26	**8b**	18,6′-*O*-Bisallyl-2′-*N*-(4-nitrocinnamoyl) Et 770	5.2×10^2	8.5×10^3	7.5×10^3
27	**9b**	2′-*N*-(4-Nitrocinnamoyl) Et 770	0.60	2.40	0.81
28	**10b**	18-*O*-Allyl-2′-*N*-(4-nitrocinnamoyl) Et 770	2.7	9.8	5.0
29	**6i**	18,6′-*O*-Bisallyl-2′-*N*-(4-bromoBz) Et 770	4.8×10^2	$>1.0 \times 10^3$	7.3×10^2
30	**6j**	18,6′-*O*-Bisallyl-2′-*N*-(2-bromoBz) Et 770	$>1.0 \times 10^3$	$>1.0 \times 10^3$	$>1.0 \times 10^3$

[a] HCT116: human colon carcinoma; QG56: human lung carcinoma. DU145: human prostate carcinoma.
[b] For previous cytotoxicity data, see Ref. 30.
[c] A mixture of rotational isomers.

(ppm, *J* in Hz with TMS as internal standard). All protons and carbon signals were assigned by extensive NMR measurements including correlation spectroscopy (COSY), ^{1}H-detected heteronuclear multiple bond coherence) HMBC, and ^{1}H-detected heteronuclear multiple-quantum coherence (HMQC) techniques. Mass spectra were recorded on a JEOL JMS 700 instrument with a direct inlet system operating at 70 eV.

5.1. Extraction and isolation of Et 770

Stocked frozen animals of *E. thurstoni* (22.5 kg, wet weight), which were collected in April 2009, were homogenized and phosphate buffer was added until pH reached 7, followed by the addition of 10% potassium cyanide solution. Stirring was continued for 5 h. The mixture was macerated with methanol (20 L × 5) and filtered, and the combined filtrates were concentrated in vacuo to an aqueous emulsion, that was partitioned with ethyl acetate to give a dark-brown oily residue. The residue was re-dissolved in methanol (100 mL) and the methanol solution was partitioned with hexane (100 mL × 3), dried, and concentrated in vacuo to afford a residue (26.62 g). After performing conventional purification procedure, 276.4 mg (1.23×10^{-3}% of wet weight) of Et 770 (**1b**) was obtained as colorless fine needles.

5.1.1. 18, 6′-*O*-Bisallyl Et 770 4a

Allyl bromide (0.69 mL, 8.0 mmol) was added to a mixture of Et 770 (**1b**: 308.0 mg, 0.4 mmol) and anhydrous K_2CO_3 (1.38 g, 10 mmol) in acetone (100 mL) for 5 min at 0 °C, and the resulting mixture was stirred for 10 h at 25 °C. After the reaction mixture was concentrated in vacuo, the residue was diluted with water (80 mL) and extracted with chloroform (80 mL × 3). The combined extracts were washed with brine, dried, and concentrated in vacuo to give a residue. Chromatography on a silica gel flash column using elution of a gradient of hexane–ethyl acetate 10:1 to 1:1 as eluent gave **4a** (275.6 mg, 81.1%) along with 6′-*O*-allyl Et 770 (**4b**: 9.0 mg, 2.7%) and triallyl Et 770 (**4c**: 19.5 mg, 5.5%).

5.1.1.1. Compound 4a. Colorless amorphous powder, $[\alpha]_D^{16}$ −55.3 (*c* 0.47, $CHCl_3$); IR (KBr) 3447, 2930, 2250w, 1769, 1742, 1518, 1485, 1458, 1445, 1431, 1369, 1323, 1261, 1221, 1194, 1167, 1144, 1125, 1107, 1089, 1069, 1055, 1028, 1101, 959, 914, 806 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.79 (1H, s, 15-H), 6.48 (1H, br s, 8′-H), 6.41 (1H, s, 5′-H), 6.10 (1H, ddd, *J* = 17.1, 10.4, 5.2 Hz, 18-OCH$_2$*CH*=CH$_2$), 6.05 (1H, d, *J* = 1.2 Hz, OCHO), 5.99 (1H, ddd, *J* = 17.1, 10.7, 5.2 Hz, 6′-OCH$_2$*CH*=CH$_2$), 5.98 (1H, d, *J* = 1.2 Hz, OCHO), 5.45 (1H, dd, *J* = 17.1, 1.5 Hz, 18-OCH$_2$CH=C*H*$_2$), 5.31 (1H, dd, *J* = 17.1, 1.3 Hz, 6′-OCH$_2$CH=C*H*$_2$), 5.25 (1H, dd, 1H, dd, *J* = 10.4, 1.5 Hz, 18-OCH$_2$CH=C*H*$_2$), 5.22 (1H, dd, *J* = 10.7, 1.3 Hz, 6′-OCH$_2$CH=C*H*$_2$), 5.02 (1H, d, *J* = 11.3 Hz, 22-H), 4.80 (1H, dd, *J* = 12.6, 5.2 Hz, 18-OC*H*CH), 4.54 (1H, br s, 4-H), 4.49 (2H, d, *J* = 5.2 Hz, 6′-OC*H*$_2$CH), 4.35 (1H, dd, *J* = 12.6, 5.2 Hz, 18-OC*H*CH), 4.33 (1H, br s, 1-H), 4.25 (1H, d, *J* = 4.0 Hz, 11-H), 4.19 (1H, d, *J* = 1.4 Hz, 21-H), 4.13 (1H, d, *J* = 11.3 Hz, 22-H), 3.83 (3H, s, 17-OCH$_3$), 3.61 (3H, s, 7′-OCH$_3$), 3.52 (1H, br d, *J* = 4.0 Hz, 3-H), 3.43 (1H, dd, *J* = 8.2, 1.4 Hz, 13-H), 3.12 (1H, m, 3′-H), 2.95 (2H, d, *J* = 8.2 Hz, 14-H$_2$), 2.81 (1H, br t, 3′-H), 2.63 (1H, m, 4′-H), 2.49 (1H, br t, *J* = 15.9 Hz, 4′-H), 2.33 (1H, br s, 12′-H), 2.29 (3H, s, 16-CH$_3$), 2.24 (3H, s, OCOCH$_3$), 2.20 (3H, s, *N*CH$_3$), 2.14 (1H, br d, 12′-H), 2.04 (3H, s, 6-CH$_3$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.5 (1′-CO), 168.1 (5-OCO), 150.6 (C-18), 148.9 (C-17), 147.0 (C-6′

and C-7′), 145.4 (C-7), 141.3 (C-5), 140.2 (C-8), 134.6 (18-$OCH_2CH{=}CH_2$), 133.2 (6′-$OCH_2CH{=}CH_2$), 131.3 (C-16), 130.3 (C-20), 128.3 (C-10′), 126.5 (C-9′), 124.7 (C-19), 124.5 (C-15), 121.2 (C-10), 118.1 (21-CN), 117.8 (6′-$OCH_2CH{=}CH_2$), 116.7 (18-$OCH_2CH{=}CH_2$), 114.0 (C-9), 113.3 (C-6), 113.2 (C-5′), 110.9 (C-8′), 101.9 (OCH_2O), 72.9 (18-OCH_2CH), 69.6 (6′-OCH_2CH), 64.6 (C-1′), 61.2 (C-1), 59.8 (C-3 and C-22), 59.4 (17-OCH_3), 59.3 (C-21), 55.2 (7′-OCH_3), 55.1 (C-11), 54.7 (C-13), 42.0 (C-12′), 41.9 (C-4), 41.7 (NCH_3), 39.6 (C-3′), 28.9 (C-4′), 24.2 (C-14), 20.3 ($COCH_3$), 15.8 (16-CH_3), 9.7 (6-CH_3); FABMS *m/z* 851 (MH^+); HRFABMS *m/z* 851.3328 (MH^+, calcd for $C_{46}H_{51}N_4O_{10}S$, 851.3326). CD $\Delta\varepsilon$ nm (*c* 11.7 μM, methanol, 23 °C) 8.0 (210), −89.3 (220), 0 (239), 23.4 (254), 0 (276), −10.8 (292), 0 (310).

5.1.1.2. Compound 4b. Colorless amorphous powder, $[\alpha]_D^{16}$ −25.1 (*c* 0.26, $CHCl_3$); IR (KBr) 3443, 2926, 2852, 2250w, 1763, 1744, 1517, 1458, 1431, 1369, 1261, 1223, 1194, 1167, 1125, 1107, 1055, 1028, 804 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.60 (1H, s, 15-H), 6.48 (1H, br s, 8′-H), 6.44 (1H, br, NH), 6.41 (1H, s, 5′-H), 6.05 (1H, d, *J* = 1.2 Hz, OCHO), 5.99 (1H, ddd, *J* = 17.4, 10.7, 5.2 Hz, 6′-$OCH_2CH{=}CH_2$), 5.98 (1H, d, *J* = 1.2 Hz, OCHO), 5.73 (1H, OH), 5.32 (1H, dd, *J* = 17.4, 1.2 Hz, 6′-$OCH_2CH{=}CH_2$), 5.22 (1H, dd, *J* = 10.7, 1.2 Hz, 6′-$OCH_2CH{=}CH_2$), 5.02 (1H, d, *J* = 11.3 Hz, 22-H), 4.56 (1H, br s, 4-H), 4.49 (2H, d, *J* = 5.4 Hz, 6′-OCH_2CH), 4.33 (1H, br s, 1-H), 4.28 (1H, d, *J* = 4.2 Hz, 11-H), 4.18 (1H, d, *J* = 2.7 Hz, 21-H), 4.12 (1H, d, *J* = 11.3 Hz, 22-H), 3.79 (3H, s, 17-OCH_3), 3.61 (3H, s, 7′-OCH_3), 3.51 (1H, br d, *J* = 4.2 Hz, 3-H), 3.42 (1H, dd, *J* = 6.1, 2.7 Hz, 13-H), 3.12 (1H, m, 3′-H), 2.79 (1H, br t, 3′-H), 2.78 (2H, d, *J* = 6.1 Hz, 14-H_2), 2.61 (1H, m, 4′-H), 2.47 (1H, br t, *J* = 15.6 Hz, 4′-H), 2.35 (1H, br s, 12′-H), 2.33 (3H, s, 16-CH_3), 2.27 (3H, s, $OCOCH_3$), 2.22 (3H, s, NCH_3), 2.22 (1H, m, 12′-H, the signals overlapped with the methyl signals), 2.04 (3H, s, 6-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 172.6 (1′-CO), 168.1 (5-OCO), 147.8 (C-18), 147.0 (C-6′ and C-7′), 145.4 (C-7), 143.0 (C-17), 141.3 (C-5), 140.1 (C-8), 133.2 (6′-$OCH_2CH{=}CH_2$), 130.8 (C-20), 129.3 (C-16), 128.4 (C-10′), 126.6 (C-9′), 121.2 (C-10), 120.7 (C-15), 118.1 (21-CN and C-19), 117.8 (6′-$OCH_2CH{=}CH_2$), 114.0 (C-9), 113.2 (C-5′), 113.2 (C-6), 110.0 (C-8′), 101.9 (OCH_2O), 69.6 (6′-OCH_2CH), 64.6 (C-1′), 61.1 (C-1), 60.4 (17-OCH_3), 60.0 (C-22), 59.6 (C-3 and C-21), 55.3 (7′-OCH_3), 54.7 (C-11), 54.5 (C-13), 42.1 (C-12′), 41.9 (C-4), 41.6 (NCH_3), 39.7 (C-3′), 29.0 (C-4′), 24.2 (C-14), 20.4 ($COCH_3$), 15.8 (16-CH_3), 9.7 (6-CH_3); FABMS *m/z* 811 (MH^+); HRFABMS *m/z* 811.3019 (MH^+, calcd for $C_{43}H_{47}N_4O_{10}S$, 811.3013). CD $\Delta\varepsilon$ nm (*c* 12.3 μM, methanol, 23 °C) 42.0 (210), −157.5 (221), 0 (240), 39.9 (253), 0 (269), −33.4 (287), 0 (317).

5.1.1.3. Compound 4c. Colorless amorphous powder, $[\alpha]_D^{16}$ −71.1 (*c* 0.97, $CHCl_3$); IR (KBr) 3435, 2928, 2250w, 1767, 1738, 1518, 1464, 1445, 1429, 1416, 1375, 1333, 1261, 1234, 1196, 1163, 1109, 1088, 1070, 1028, 1003, 914, 804 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.67 (1H, s, 15-H), 6.37 (1H, s, 5′-H), 6.24 (1H, s, 8′-H), 6.09 (1H, ddd, *J* = 17.3, 10.3, 5.1 Hz, 18-$OCH_2CH{=}CH_2$), 6.08 (1H, d, *J* = 1.2 Hz, OCHO), 5.99 (1H, ddd, *J* = 17.3, 10.5, 5.4 Hz, 6′-$OCH_2CH{=}CH_2$), 5.97 (1H, d, *J* = 1.2 Hz, OCHO), 5.58 (1H, ddd, *J* = 17.1, 10.3, 5.6 Hz, $NCH_2CH{=}CH_2$), 5.45 (1H, dd, *J* = 17.3, 1.5 Hz, 18-$OCH_2CH{=}CH_2$), 5.32 (1H, dd, *J* = 17.3, 1.3 Hz, 6′-$OCH_2CH{=}CH_2$), 5.25 (1H, dd, 1H, dd, *J* = 10.3, 1.5 Hz, 18-$OCH_2CH{=}CH_2$), 5.22 (1H, dd, *J* = 10.5, 1.3 Hz, 6′-$OCH_2CH{=}CH_2$), 5.13 (1H, dd, *J* = 17.1, 1.7 Hz, $NCH_2CH{=}CH_2$), 5.04 (1H, dd, *J* = 10.3, 1.7 Hz, $NCH_2CH{=}CH_2$), 4.95 (1H, d, *J* = 11.2 Hz, 22-H), 4.81 (1H, dd, *J* = 12.7, 5.1 Hz, 18-$OCHCH$), 4.60 (1H, br s, 4-H), 4.49 (2H, d, *J* = 5.4 Hz, 6′-OCH_2CH), 4.37 (1H, d, *J* = 1.2 Hz, 1-H), 4.33 (1H, dd, *J* = 12.7, 5.6 Hz, 18-$OCHCH$), 4.22 (1H, dd, *J* = 5.4, 1.5 Hz, 11-H), 4.12 (1H, d, *J* = 2.8 Hz, 21-H), 3.91 (1H, dd, *J* = 11.2, 2.6 Hz, 22-H), 3.80 (3H, s, 17-OCH_3), 3.55 (3H, s, 7′-OCH_3), 3.53 (1H, br, 3-H, the signals overlapped with the methyl signals), 3.43 (1H, br d, *J* = 9.2 Hz, 13-H), 3.09 (2H, m, NCH_2CH), 2.96 (1H, dd, *J* = 17.1, 9.2 Hz, 14-Hα), 2.96 (1H, m. 3′-H, signals overlapped with 14-Hα), 2.81 (1H, d, *J* = 17.1 Hz, 14-Hβ), 2.76 (1H, m, 3′-H), 2.59 (1H, ddd, *J* = 15.9, 10.5, 5.6 Hz, 4′-H), 2.44 (1H, m, 4′-H), 2.32 (1H, br dd, *J* = 16.1, 5.1 Hz, 12′-H), 2.26 (3H, s, $OCOCH_3$), 2.23 (3H, s, 16-CH_3), 2.12 (3H, s, NCH_3), 2.05 (1H, m, 12′-H), 2.03 (3H, s, 6-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.2 (1′-CO), 168.0 (5-OCO), 150.0 (C-18), 148.7 (C-17), 146.8 (C-6′), 146.4 (C-7′), 145.5 (C-7), 141.5 (C-5), 140.4 (C-8), 138.0 ($NCH_2CH{=}CH_2$), 134.5 (18-$OCH_2CH{=}CH_2$), 133.0 (6′-$OCH_2CH{=}CH_2$), 131.1 (C-16), 130.0 (C-20), 129.3 (C-10′), 128.0 (C-9′), 124.9 (C-15), 124.8 (C-19), 121.3 (C-10), 118.1 (21-CN), 117.7 (6′-$OCH_2CH{=}CH_2$), 116.7 (18-$OCH_2CH{=}CH_2$), 115.3 ($NCH_2CH{=}CH_2$), 114.2 (C-9), 112.6 (C-5′), 112.4 (C-6 and C-8′), 101.9 (OCH_2O), 72.9 (18-OCH_2CH), 71.0 (C-1′), 69.5 (6′-OCH_2CH), 61.1 (C-3), 60.6 (C-1 and C-22), 59.8 (C-21), 59.3 (17-OCH_3), 55.7 (7′-OCH_3), 55.4 (C-11), 54.8 (C-13), 54.2 (NCH_2CH), 43.8 (C-3′), 43.0 (C-4), 41.9 (NCH_3), 39.7(C-12′), 28.0 (C-4′), 25.0 (C-14), 20.3 ($COCH_3$), 16.4 (16-CH_3), 9.8 (6-CH_3); FABMS *m/z* 891 (MH^+); HRFABMS *m/z* 891.3636 (MH^+, calcd for $C_{49}H_{55}N_4O_{10}S$, 891.3639).

5.1.2. Deallylation of 4c: 2′-*N*-allyl Et 770 4d

Tributyltin hydride (0.16 mL, 0.61 mmol) was added dropwise over 10 min to a vigorously stirred solution of **4c** (32.9 mg, 37.0 μmol), $(Ph_3P)_2PdCl_2$ (15.6 mg, 22.2 μmol), and AcOH (79.4 μL, 1.39 mmol) in THF (10 mL) at 25 °C, and the mixture was stirred for 6 h at 25 °C. The mixture was diluted with water (10 mL), made alkaline with 5% aqueous $NaHCO_3$, and extracted with chloroform (30 mL × 3). The combined extracts were washed with 5% aqueous $NaHCO_3$, dried, and concentrated in vacuo to give a residue. Chromatography on a silica gel column with hexane–ethyl acetate (5:1) to gave **1b** (9.5 mg, 33.4%) as a colorless solid, whose spectral data were in complete agreement with those of the authentic sample. Further elution with hexane–ethyl acetate (2:1) afforded 2′-*N*-Allyl Et 770 (**4d**: 8.3 mg, 27.8%). $[\alpha]_D^{22}$ −80.1 (*c* 0.25, $CHCl_3$); IR (KBr) 3447br, 2930, 2250w, 1749, 1508, 1458, 1375, 1234, 1196, 1161, 1107, 1086, 1005, 914 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 6.47 (1H, s, 15-H), 6.45 (1H, s, 5′-H), 6.22 (1H, s, 8′-H), 6.08 (1H, d, *J* = 1.2 Hz, OCHO), 5.97 (1H, d, *J* = 1.2 Hz, OCHO), 5.69 (1H, s, 18-OH), 5.57 (1H, ddt, *J* = 17.0, 10.2, 6.3 Hz, $NCH_2CH{=}CH_2$), 5.42 (1H, br s, 6′-OH), 5.11 (1H, dd, *J* = 17.0, 1.7 Hz, $NCH_2CH{=}CH_2$), 5.02 (1H, dd, *J* = 10.2, 1.7 Hz, $NCH_2CH{=}CH_2$), 4.96 (1H, d, *J* = 11.4 Hz, 22-H), 4.62 (1H, br s, 4-H), 4.37 (1H, d, *J* = 2.3 Hz, 1-H), 4.26 (1H, dd, *J* = 5.1, 1.2 Hz, 11-H), 4.11 (1H, d, *J* = 2.9 Hz, 21-H), 3.91 (1H, dd, *J* = 11.4, 2.9 Hz, 22-H), 3.76 (3H, s, 17-OCH_3), 3.56 (3H, s, 7′-OCH_3), 3.53 (1H, d, *J* = 5.1 Hz, 3-H), 3.42 (1H, br d, *J* = 9.0 Hz, 13-H), 3.08 (2H, br d, NCH_2CH), 2.95 (1H, dd, *J* = 17.0, 9.1 Hz, 14-Hα), 2.94 (1H, m. 3′-H), 2.80 (1H, d, *J* = 17.0 Hz, 14-Hβ), 2.74 (1H, dt, *J* = 12.5, 4.5 Hz, 3′-H), 2.56 (1H, ddd, *J* = 15.8, 10.2, 5.1 Hz, 4′-H), 2.56 (1H, br, 12′-H), 2.49 (1H, m, 12′-H), 2.34 (1H, dt, *J* = 15.8, 3.9 Hz, 4′-H), 2.30 (3H, s, $OCOCH_3$), 2.25 (3H, s, 16-CH_3), 2.11 (3H, s, NCH_3), 2.03 (3H, s, 6-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.6 (1′-CO), 168.4 (5-OCO), 147.3 (C-18), 145.5 (C-7), 144.5 (C-6′), 144.1 (C-7′), 142.9 (C-17), 141.8 (C-5), 140.6 (C-8), 138.1 ($NCH_2CH{=}CH_2$), 130.7 (C-20), 130.2 (C-10′), 129.4 (C-16), 127.4 (C-9′), 121.6 (C-10), 121.2 (C-15), 118.4 (C-19), 118.3 (21-CN), 115.4 ($NCH_2CH{=}CH_2$), 114.5 (C-9), 113.9 (C-5′), 112.5 (C-6), 110.9 (C-8′), 102.0 (OCH_2O), 71.1 (C-1′), 61.1 (C-3), 60.7 (C-22), 60.4 (C-1), 60.1 (17-OCH_3), 60.0 (C-21), 55.4 (7′-OCH_3), 54.9 (C-11), 54.7 (C-13), 54.2 (NCH_2CH), 43.7 (C-3′), 43.0 (C-4), 41.8 (NCH_3), 39.7(C-12′), 27.8 (C-4′), 24.9 (C-14), 20.3 ($COCH_3$), 16.1 (16-CH_3), 9.7 (6-CH_3); FABMS *m/z* 811 (MH^+); HRFABMS *m/z* 811.3011 (MH^+, calcd for $C_{43}H_{47}N_4O_{10}S$, 811.3013), CD $\Delta\varepsilon$ nm (*c* 12.3 μM, methanol, 32 °C) −29.4 (210), −66.7 (218), 0 (244), 9.6 (253), 0 (270), −13.8 (286), 0 (320).

5.1.3. 18, 6′-*O*-Bisallyl-2′-*N*-3″-indolecarbonyl Et 770 5

Indole-3-carboxylic acid (14.5 mg, 90 μmol) was added to a stirred solution of **4a** (15.3 mg, 18.0 mmol) and DCC (92.8 mg, 0.45 mmol) in CH_2Cl_2 (2.0 mL) and the reaction mixture was stirred at 25 °C for 6 h. After the reaction mixture was concentrated in vacuo, the residue was subjected to chromatography with CH_2Cl_2–ethyl acetate (9:1) as the eluent to afford **5** (16.0 mg, 90.0%) as a colorless amorphous powder. $[\alpha]_D^{16}$ −0.14 (*c* 0.61, $CHCl_3$); IR (KBr) 3393, 2932, 2250w, 1749, 1636, 1518, 1458, 1429, 1375, 1339, 1260, 1244, 1194, 1169, 1109, 1086, 997, 895, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.69 (1H, br s, NH), 8.13 (1H, d, *J* = 7.9 Hz, 4″-H), 7.58 (1H, d, *J* = 2.5 Hz, 2″-H), 7.46 (1H, d, *J* = 8.3 Hz, 7″-H), 7.41 (1H, ddd, *J* = 7.9, 7.0, 1.1 Hz, 5″-H), 7.34 (1H, ddd, *J* = 8.3, 7.0, 1.1 Hz, 6″-H), 6.47 (1H, br s, 8′-H), 6.33 (1H, s, 5′-H), 6.08 (1H, d, *J* = 1.2 Hz, OCHO), 6.03 (1H, ddd, *J* = 17.1, 10.7, 5.4 Hz, 18-$OCH_2CH=CH_2$), 5.99 (1H, d, *J* = 1.2 Hz, OCHO), 5.97 (1H, ddd, *J* = 17.1, 10.7, 5.5 Hz, 6′-$OCH_2CH=CH_2$), 5.69 (1H, br s, 15-H), 5.40 (1H, dd, *J* = 17.3, 1.5 Hz, 18-$OCH_2CH=CH_2$), 5.30 (1H, ddd, *J* = 17.3, 3.1, 1.7 Hz, 6′-$OCH_2CH=CH_2$), 5.20 (2H, m, 18-$OCH_2CH=CH_2$ and 6′-$OCH_2CH=CH_2$), 4.74 (1H, br d, *J* = 11.4 Hz, 22-H), 4.72 (1H, dt, *J* = 12.8, 5.4 Hz, 18-OCHCH), 4.62 (1H, br s, 4-H), 4.47 (2H, dt, *J* = 5.4, 1.5 Hz, 6′-OCH_2CH), 4.44 (1H, dd, *J* = 11.4, 2.0 Hz, 22-H), 4.37 (1H, br s, 1-H), 4.22 (1H, dt, *J* = 11.3, 5.4 Hz, 18-OCHCH), 4.21 (1H, d, *J* = 1.4 Hz, 21-H), 4.18 (1H, dd, *J* = 5.5, 1.3 Hz, 11-H), 4.06 (1H, dd, *J* = 14.3, 3.1 Hz, 3′-H), 3.93 (1H, d, *J* = 14.7 Hz, 12′-H), 3.69 (3H, s, 17-OCH_3), 3.66 (3H, s, 7′-OCH_3), 3.55 (1H, br d, *J* = 5.5 Hz, 3-H), 3.53 (1H, m, 3′-H), 3.43 (1H, br d, *J* = 7.9, 1.4 Hz, 13-H), 2.95 (1H, d, *J* = 17.4 Hz, 14-Hβ), 2.84 (1H, dd, *J* = 17.4, 9.1 Hz, 14-Hα), 2.50 (1H, ddd, *J* = 16.5, 10.9, 6.2 Hz, 4′-H), 2.50 (1H, m, 12′-H, the signals overlapped with 4′-H), 2.30 (3H, s, $OCOCH_3$), 2.27 (1H, br d, *J* = 16.5 Hz, 4′-H), 2.08 (3H, s, NCH_3), 2.06 (3H, s, 6-CH_3), 1.09 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 170.5 (1′-CO), 168.4 (5-OCO), 168.1 (*N*CO), 150.8 (C-18), 148.5 (C-17), 147.3 (C-7′), 147.1 (C-6′), 145.5 (C-7), 141.2 (C-8), 141.1 (C-5), 135.8 (C-8″), 134.9 (18-$OCH_2CH=CH_2$), 133.3 (6′-$OCH_2CH=CH_2$), 131.6 (C-16), 129.5 (C-20 and C-2″), 128.4 (C-9′), 127.0 (C-10′), 125.2 (C-15), 125.1 (C-9″), 123.9 (C-19), 122.9 (C-6″), 122.8 (C-10), 122.6 (C-4″), 121.4 (C-5″), 118.4 (21-CN), 117.9 (6′-$OCH_2CH=CH_2$), 116.7 (18-$OCH_2CH=CH_2$), 114.3 (C-3″), 113.5 (C-9), 112.8 (C-6 and C-5′), 111.5 (C-7″), 111.3 (C-8′), 102.1 (OCH_2O), 73.0 (18-OCH_2CH), 70.5 (C-1′), 69.7 (6′-OCH_2CH), 61.1 (C-3), 60.9 (C-1), 60.4 (C-22), 59.5 (C-21 and 17-OCH_3), 55.4 (C-11), 55.3 (7′-OCH_3), 55.0 (C-13), 46.7 (C-3′), 42.1 (C-4), 41.8 (NCH_3), 38.5 (C-12′), 29.4 (C-4′), 24.8 (C-14), 20.4 ($COCH_3$), 14.3 (16-CH_3), 9.9 (6-CH_3); FABMS *m/z* 851 (MH^+); HRFABMS *m/z* 994.3696 (MH^+, calcd for $C_{55}H_{56}N_5O_{11}S$, 994.3697). CD Δε nm (*c* 10.0 μM, methanol, 32 °C) −173.1 (210), −29.3 (222), −20.2 (228), 0 (235), 53.9 (252), 0 (276), −5.0 (292), 0 (300).

5.1.4. Deallylation of compound 5

Tributyltin hydride (0.07 mL, 0.61 μmol) was added dropwise over 10 min to a vigorously stirred solution of **5** (15.2 mg, 15.3 μmol), $(Ph_3P)_2PdCl_2$ (6.4 mg, 9.2 μmol), and AcOH (32.8 μL, 0.57 mmol) in THF (10 mL) at 25 °C, and the mixture was stirred for 1.5 h at 25 °C. The mixture was diluted with water (10 mL), made alkaline with 5% aqueous $NaHCO_3$, and extracted with chloroform (30 mL × 3). The combined extracts were washed with 5% aqueous $NaHCO_3$, dried, and concentrated in vacuo to give a residue. Chromatography on a silica gel column with hexane–ethyl acetate (3:2) afforded **3** (6.0 mg, 42.9%) as a colorless solid, whose spectral data were in complete agreement with those of the authentic sample. $[\alpha]_D^{22}$ +5.3 (*c* 0.20, $CHCl_3$); IR (KBr) 3420, 2928, 2855, 2250w, 1749, 1616, 1522, 1508, 1458, 1435, 1375, 1261, 1234, 1196, 1171, 1109, 1085, 1028 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.52 (1H, br s, NH), 8.06 (1H, d, *J* = 7.0 Hz, 4″-H), 7.56 (1H, d, *J* = 2.7 Hz, 2″-H), 7.51 (1H, d, *J* = 7.0 Hz, 7″-H), 7.39 (1H, td, *J* = 7.0, 1.1 Hz, 5″-H), 7.34 (1H, td, *J* = 7.0, 1.1 Hz, 6″-H), 6.48 (1H, br s, 8′-H), 6.40 (1H, s, 5′-H), 6.09 (1H, d, *J* = 1.3 Hz, OCHO), 6.00 (1H, d, *J* = 1.2 Hz, OCHO), 5.65 (1H, br s, 18-OH), 5.47 (2H, br s, 15H and 6′-OH), 4.67 (1H, br d, *J* = 11.4 Hz, 22-H), 4.66 (1H, br s, 4-H), 4.54 (1H, dd, *J* = 11.4, 2.2 Hz, 22-H), 4.36 (1H, br s, 1-H), 4.21 (1H, dd, *J* = 5.3, 1.4 Hz, 11-H), 4.19 (1H, d, *J* = 2.7 Hz, 21-H), 4.06 (1H, dd, *J* = 14.3, 3.1 Hz, 3′-H), 3.95 (1H, d, *J* = 14.8 Hz, 12′-H), 3.71 (3H, s, 17-OCH_3), 3.59 (3H, s, 7′-OCH_3), 3.55 (1H, br d, *J* = 4.8 Hz, 3-H), 3.53 (1H, m, 3′-H), 3.47 (1H, m, 12′-H), 3.42 (1H, m, 13-H), 2.85 (2H, d, *J* = 5.1 Hz, 14-H_2), 2.49 (2H, m, 3′-H and 4′-H), 2.34 (3H, s, $OCOCH_3$), 2.29 (1H, m, 4′-H), 2.09 (3H, s, NCH_3), 2.06 (3H, s, 6-CH_3), 1.13 (3H, s, 16-CH_3); FABMS *m/z* 914 (MH^+); HRFABMS *m/z* 914.3064 (MH^+, calcd for $C_{47}H_{48}N_5O_{11}S$, 914.3071). CD Δε nm (*c* 10.9 μM, methanol, 32 °C) −154.1 (210), −30.2 (222), −30.5 (226), 0 (235), 46.4 (252), 0 (276), −10.5 (288), 0 (305).

18-*O*-Allyl-2′-*N*-indole-3-carbonyl Et 770: IR (KBr) 3387, 2932, 2250w, 1749, 1620, 1518, 1458, 1431, 1391, 1375, 1337, 1319, 1304, 1261, 1234, 1196, 1170, 1109, 1086, 1028, 960, 930, 912, 895, 868, 806 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.44 (1H, br s, NH), 8.11 (1H, d, *J* = 7.7 Hz, 4″-H), 7.59 (1H, d, *J* = 2.6 Hz, 2″-H), 7.48 (1H, d, *J* = 7.7 Hz, 7″-H), 7.35 (1H, td, *J* = 7.0, 1.5 Hz, 5″-H), 7.34 (1H, td, *J* = 7.0, 1.5 Hz, 6″-H), 6.45 (1H, br s, 8′-H), 6.40 (1H, s, 5′-H), 6.09 (1H, s, OCHO), 6.04 (1H, ddd, *J* = 17.6, 10.3, 5.4 Hz, 18-$OCH_2CH=CH_2$), 6.00 (1H, s, OCHO), 5.63 (1H, br s, 15-H), 5.44 (1H, s, 6′-OH), 5.40 (1H, dd, *J* = 17.6, 1.5 Hz, 18-$OCH_2CH=CH_2$), 5.19 (1H, dd, *J* = 10.3, 1.5 Hz, 18-$OCH_2CH=CH_2$), 4.72 (1H, dd, *J* = 12.6, 5.4 Hz, 18-OCHCH), 4.69 (1H, br d, *J* = 11.2 Hz, 22-H), 4.64 (1H, br s, 4-H), 4.51 (1H, dd, *J* = 11.2, 1.9 Hz, 22-H), 4.36 (1H, br s, 1-H), 4.21 (1H, d, *J* = 2.2 Hz, 21-H), 4.20 (1H, dd, *J* = 12.6, 5.4 Hz, 18-OCHCH), 4.17 (1H, d, *J* = 5.3 Hz, 11-H), 4.03 (1H, dd, *J* = 14.5, 3.7 Hz, 3′-H), 3.93 (1H, d, *J* = 14.8 Hz, 12′-H), 3.70 (6H, s, 17-OCH_3 and 7′-OCH_3), 3.55 (1H, br d, *J* = 4.9 Hz, 3-H), 3.53 (1H, m, 3′-H), 3.48 (1H, m, 12′-H), 3.42 (1H, m, 13-H), 2.86 (2H, d, *J* = 8.4 Hz, 14-H_2), 2.43 (2H, m, 3′-H and 4′-H), 2.31 (3H, s, $OCOCH_3$), 2.30 (1H, m, 4′-H), 2.09 (3H, s, NCH_3), 2.06 (3H, s, 6-CH_3), 1.10 (3H, s, 16-CH_3); FABMS *m/z* 954 (MH^+); HRFABMS *m/z* 954.3383 (MH^+, calcd for $C_{52}H_{52}N_5O_{11}S$, 954.3384).

5.2. Condensation of Et 770 1b and 4-nitrobenzoic acid with DCC

4-Nitrobenzoic acid (14.5 mg, 90 μmol) was added to a stirred solution of **1b** (7.6 mg, 0.1 mmol) and DCC (103.1 mg, 0.5 mmol) in CH_2Cl_2 (2.0 mL) and the reaction mixture was stirred at 25 °C for 17 h. The reaction mixture was quenched with 2.5% $NaHCO_3$ solution, and extracted with CH_2Cl_2 (10 mL × 3). The combined extracts were washed with brine, dried, and concentrated in vacuo to give a residue. Chromatography on a silica gel column afforded 6′-*O*-4″-nitrobenzoyl Et 770 **2** (R = $COC_6H_4NO_2$-4″: 7.4 mg, 81.6%) as colorless amorphous powder, which was identical in all respects to the authentic sample.

5.3. General procedure for the preparation of *N*-acyl derivatives of 4a

Compound **4a** (15.3 mg, 0.018 mmol) and DMAP (1.1 mg) were dissolved in pyridine (1.5 mL), and 15 equimolar quantity of various acid chlorides was added to this mixture at 0 °C. The reaction mixture was heated at 60 °C for 2 h. After the solvent was removed in vacuo, the residue was diluted with water (10 mL), and extracted with chloroform (15 mL × 3). The combined extracts were washed with brine (15 mL), dried, and concentrated in vacuo to give a residue. This residue was purified by silica gel column chromatography using an appropriate eluent to give the corresponding purified product.

5.3.1. 18, 6′-*O*-Bisallyl-2′-*N*-benzoyl Et 770 6a (yield 79.8%)

$[\alpha]_D^{21}$ −55.4 (*c* 0.82, $CHCl_3$); IR (KBr) 3447, 2928, 2855, 2250w, 1763, 1657, 1518, 1447, 1375, 1260, 1196, 1142, 1109, 1086, 1070, 1028, 993, 802 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.47 (5H, m, ArH), 6.61 (1H, br s, 15-H), 6.60 (1H, br s, 8′-H), 6.34 (1H, s, 5′-H), 6.10 (1H, d, *J* = 1.2 Hz, OCHO), 6.09 (1H, ddd, *J* = 17.1, 10.5, 5.4 Hz, 18-OCH_2CH=CH_2), 6.02 (1H, d, *J* = 1.2 Hz, OCHO), 5.98 (1H, ddd, *J* = 17.1, 10.5, 5.4 Hz, 6′-OCH_2CH=CH_2), 5.44 (1H, dd, *J* = 17.2, 1.6 Hz, 18-OCH_2CH=CH_2), 5.32 (1H, dd, *J* = 17.2, 1.2 Hz, 6′-OCH_2CH=CH_2), 5.23 (1H, dd, *J* = 10.5, 1.5 Hz, 18-OCH_2CH=CH_2), 5.22 (1H, dd, *J* = 10.5, 1.5 Hz, 6′-OCH_2CH=CH_2), 4.79 (1H, dt, *J* = 12.4, 5.4 Hz, 18-O*CH*CH), 4.61 (1H, br s, 4-H), 4.61 (1H, br s, 22-H), 4.48 (2H, dt, *J* = 5.2, 1.5 Hz, 6′-OCH_2CH), 4.39 (1H, br s, 22-H), 4.31 (1H, s, 1-H), 4.30 (1H, dd, *J* = 12.4, 5.2 Hz, 18-O*CH*CH), 4.23 (1H, d, *J* = 4.0 Hz, 11-H), 4.10 (1H, br s, 21-H), 3.73 (3H, s, 17-OCH_3), 3.66 (3H, s, 7′-OCH_3), 3.61 (1H, br d, *J* = 5.5 Hz, 3-H), 3.54 (1H, m, 3′-H), 3.50 (1H, m, 12′-H), 3.50 (1H, m, 3′-H), 3.44 (1H, br d, *J* = 8.4 Hz, 13-H), 2.98 (1H, dd, *J* = 17.6, 9.6 Hz, 14-Hα), 2.83 (1H, d, *J* = 17.6 Hz, 14-Hβ), 2.38 (2H, m, 4′-H), 2.32 (1H, m, 12′-H), 2.29 (3H, s, $OCOCH_3$), 2.15 (3H, s, NCH_3), 2.04 (3H, s, 6-CH_3), 1.85 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.7 (1′-CO), 169.2 (*N*CO), 168.0 (5-OCO), 150.3 (C-18), 148.4 (C-17), 147.1 (C-7′), 146.8 (C-6′), 145.3 (C-7), 141.4 (C-8), 140.9 (C-5), 136.6 (C-1″), 134.5 (18-OCH_2CH=CH_2), 133.0 (6′-OCH_2CH=CH_2), 131.1 (C-16), 130.1 (C-4″), 129.9 (C-20), 128.3 (C-10′), 128.2 (C-3″), 128.1 (C-2″), 125.6 (C-9′), 124.5 (C-15), 124.1 (C-19), 122.1 (C-10), 118.1 (21-CN), 117.7 (6′-OCH_2CH=CH_2), 116.6 (18-OCH_2CH=CH_2), 113.0 (C-9), 112.8 (C-5′), 112.4 (C-6), 111.2 (C-8′), 102.0 (OCH_2O), 73.0 (18-OCH_2CH), 69.6 (C-1′), 69.6 (6′-OCH_2CH), 61.0 (C-3), 60.4 (C-22), 60.3 (C-1), 59.7 (C-21), 59.4 (17-OCH_3), 55.5 (C-11), 55.2 (7′-OCH_3), 54.9 (C-13), 45.4 (C-3′), 41.9 (C-4), 41.9 (NCH_3), 39.9 (C-12′), 29.8 (C-4′), 25.1 (C-14), 20.4 ($COCH_3$), 15.7 (16-CH_3), 9.8 (6-CH_3); FABMS *m/z* 955 (MH^+); HRFABMS *m/z* 955.3593 (MH^+, calcd for $C_{53}H_{55}N_4O_{11}S$, 955.3588), CD Δε nm (*c* 10.0 μM, methanol, 23 °C) −60.9 (210), −79.8 (216), 0 (241), 10.8 (254), 0 (279), −6.1 (294), 0 (310).

5.3.2. 18, 6′-*O*-Bisallyl-2′-*N*-4″-nitrobenzoyl Et 770 6b (yield 89.0%)

$[\alpha]_D^{16}$ −38.6 (*c* 0.64, $CHCl_3$); IR (KBr) 3468, 2926, 2853, 2250w, 1748, 1663, 1522, 1460, 1348, 1319, 1302, 1260, 1234, 1196, 1144, 1107, 1086, 1070, 1028, 999, 914, 866, 856, 802 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.37 (2H, d, *J* = 8.4 Hz, 3″-H), 7.46 (2H, d, *J* = 8.4 Hz, 2″-H), 6.55 (1H, br s, 15-H), 6.45 (1H, br s, 8′-H), 6.35 (1H, s, 5′-H), 6.09 (1H, br s, OCHO), 6.07 (1H, ddd, *J* = 16.8, 10.4, 5.4 Hz, 18-OCH_2CH=CH_2), 6.01 (1H, br s, OCHO), 5.98 (1H, ddd, *J* = 17.1, 10.5, 5.4 Hz, 6′-OCH_2CH=CH_2), 5.43 (1H, dd, *J* = 17.2, 1.6 Hz, 18-OCH_2CH=CH_2), 5.33 (1H, dd, *J* = 17.2, 1.4 Hz, 6′-OCH_2CH=CH_2), 5.23 (2H, d, *J* = 10.4 Hz, 18-OCH_2CH=CH_2 and 6′-OCH_2CH=CH_2), 4.78 (1H, dd, *J* = 12.8, 5.2 Hz, 18-O*CH*CH), 4.65 (1H, br s, 4-H), 4.63 (1H, br, 22-H), 4.49 (2H, d, *J* = 5.2 Hz, 6′-OCH_2CH), 4.38 (1H, br, 22-H), 4.36 (1H, s, 1-H), 4.29 (1H, dd, *J* = 12.8, 5.2 Hz, 18-O*CH*CH), 4.22 (1H, d, *J* = 4.4 Hz, 11-H), 4.14 (1H, br s, 21-H), 3.70 (3H, s, 17-OCH_3), 3.64 (3H, s, 7′-OCH_3), 3.58 (1H, dd, *J* = 9.6, 4.4 Hz, 3-H), 3.58 (1H, m, 12′-H), 3.46 (3H, m, 3′-H_2 and 13-H), 3.00 (1H, dd, *J* = 17.6, 9.6 Hz, 14-Hα), 2.87 (1H, d, *J* = 17.6 Hz, 14-Hβ), 2.47 (1H, m, 4′-H), 2.36 (1H, m, 4′-H), 2.30 (3H, s, $OCOCH_3$), 2.13 (3H, s, NCH_3), 2.05 (1H, m, 12′-H, signals overlapped with 6-CH_3), 2.05 (3H, s, 6-CH_3), 1.73 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.6 (*N*CO), 168.8 (1′-CO), 168.0 (5-OCO), 150.3 (C-18), 148.6 (C-17), 148.4 (C-4″), 147.3 (C-7′), 147.1 (C-6′), 145.4 (C-7), 143.1 (C-1″), 141.2 (C-8), 141.0 (C-5), 134.4 (18-OCH_2CH=CH_2), 132.9 (6′-OCH_2CH=CH_2), 130.8 (C-16), 130.0 (C-20), 128.8 (C-2″), 127.5 (C-9′), 125.5 (C-10′), 124.6 (C-19), 123.7 (C-15), 123.6 (C-3″), 122.1 (C-10), 118.0 (21-CN), 117.8 (6′-OCH_2CH=CH_2), 116.7 (18-OCH_2CH=CH_2), 113.2 (C-9), 112.7 (C-5′), 112.6 (C-6), 111.0 (C-8′), 102.0 (OCH_2O), 72.9 (18-OCH_2CH), 69.9 (C-1′), 69.6 (6′-OCH_2CH), 61.0 (C-3), 60.8 (C-22), 60.6 (C-1), 59.6 (C-21), 59.4 (17-OCH_3), 55.5 (C-11), 55.2 (7′-OCH_3), 54.9 (C-13), 45.9 (C-3′), 42.2 (C-4), 41.9 (NCH_3), 39.2 (C-12′), 29.3 (C-4′), 24.2 (C-14), 20.4 ($COCH_3$), 15.9 (16-CH_3), 9.9 (6-CH_3); FABMS *m/z* 1000 (MH^+); HRFABMS *m/z* 1000.3434 (MH^+, calcd for $C_{53}H_{54}N_5O_{13}S$, 1000.3439), CD Δε nm (*c* 10.0 μM, methanol, 23 °C) −54.0 (210), −102.4 (216), 0 (246), 7.5 (255), 0 (283), −4.6 (292), 0 (300).

5.3.3. 18, 6′-*O*-Bisallyl-2′-*N*-3″-nitrobenzoyl Et 770 6c (yield 91.8%)

$[\alpha]_D^{16}$ −56.0 (*c* 0.32, $CHCl_3$); IR (KBr) 3456, 2926, 2250w, 1761, 1748, 1663, 1610, 1533, 1521, 1447, 1435,1412, 1350, 1258, 1196, 1109, 1086, 1069, 1028, 999, 808 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.37 (1H, dt, *J* = 7.6, 1.2 Hz, 4″-H), 8.34 (1H, t, *J* = 1.2 Hz, 2″-H), 7.83 (1H, dt, *J* = 7.6, 1.2 Hz, C-5″), 7.67 (1H, t, *J* = 7.6 Hz, 5″-H), 6.60 (1H, br s, 15-H), 6.42 (1H, br s, 8′-H), 6.39 (1H, s, 5′-H), 6.09 (1H, d, *J* = 1.2 Hz, OCHO), 6.07 (1H, ddd, *J* = 17.2, 10.5, 5.4 Hz, 18-OCH_2CH=CH_2), 6.00 (1H, d, *J* = 1.2 Hz, OCHO), 5.99 (1H, ddd, *J* = 17.2, 10.5, 5.4 Hz, 6′-OCH_2CH=CH_2), 5.42 (1H, dd, *J* = 17.2, 1.2 Hz, 18-OCH_2CH=CH_2), 5.32 (1H, dd, *J* = 17.2, 1.2 Hz, 6′-OCH_2CH=CH_2), 5.22 (2H, dt, *J* = 10.5, 1.2 Hz 18-OCH_2CH=CH_2 and 6′-OCH_2CH=CH_2), 4.77 (1H, dd, *J* = 13.2, 5.4 Hz, 18-O*CH*CH), 4.71 (1H, br s, 4-H), 4.67 (1H, br, 22-H), 4.51 (2H, dt, *J* = 5.4, 1.2 Hz, 6′-OCH_2CH), 4.38 (1H, s, 1-H), 4.35 (1H, br, 22-H), 4.27 (1H, dt, *J* = 13.2, 5.4 Hz, 18-O*CH*CH), 4.22 (1H, dd, *J* = 5.2, 1.2 Hz, 11-H), 4.20 (1H, br s, 21-H), 3.69 (3H, s, 17-OCH_3), 3.66 (1H, m, 12′-H, signals overlapped with 7′-OCH_3), 3.65 (3H, s, 7′-OCH_3), 3.56 (1H, d, *J* = 5.2 Hz, 3-H), 3.53 (1H, m, 3′-H), 3.49 (1H, m, 3′-H), 3.48 (1H, br d, *J* = 10.8 Hz, 13-H), 3.01 (1H, dd, *J* = 17.2, 8.8 Hz, 14-Hα), 2.93 (1H, d, *J* = 17.2 Hz, 14-Hβ), 2.50 (1H, ddd, *J* = 16.6, 10.3, 6.4 Hz, 4′-H), 2.50 (1H, m, 12′-H, signals overlapped with 4′-H), 2.33 (1H, m, 4′-H), 2.31 (3H, s, $OCOCH_3$), 2.12 (3H, s, NCH_3), 2.05 (3H, s, 6-CH_3), 1.51 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.1 (*N*CO), 169.1 (1′-CO), 168.0 (5-OCO), 150.1 (C-18), 148.7 (C-17), 147.9 (C-3″), 147.3 (C-7′), 147.1 (C-6′), 145.3 (C-7), 141.2 (C-5), 140.9 (C-8), 139.0 (C-1″), 134.5 (18-OCH_2CH=CH_2), 133.9 (C-6″), 132.9 (6′-OCH_2CH=CH_2), 130.8 (C-16), 130.0 (C-20), 129.5 (C-5″), 127.5 (C-9′), 125.7 (C-10′), 124.6 (C-4″), 124.4 (C-19), 124.1 (C-15), 123.1 (C-2″), 122.2 (C-10), 118.1 (21-CN), 117.8 (6′-OCH_2CH=CH_2), 116.6 (18-OCH_2CH=CH_2), 113.3 (C-9), 112.8 (C-6), 112.5 (C-5′), 111.0 (C-8′), 102.0 (OCH_2O), 72.9 (18-OCH_2CH), 70.6 (C-1′), 69.6 (6′-OCH_2CH), 60.9 (C-3), 60.8 (C-1), 60.6 (C-22), 59.4 (C-21), 59.4 (17-OCH_3), 55.4 (C-11), 55.3 (7′-OCH_3), 54.9 (C-13), 46.6 (C-3′), 42.3 (C-4), 41.9 (NCH_3), 38.7 (C-12′), 29.2 (C-4′), 24.8 (C-14), 20.4 ($COCH_3$), 15.5 (16-CH_3), 9.9 (6-CH_3); FABMS *m/z* 1000 (MH^+); HRFABMS *m/z* 1000.3441 (MH^+, calcd for $C_{53}H_{54}N_5O_{13}S$, 1000.3439), CD Δε nm (*c* 10.0 μM, methanol, 23 °C) −45.2 (210), −75.5 (216), 0 (241), 14.6 (254), 0 (284), −5.8 (294), 0 (309).

5.3.4. 18, 6′-*O*-Bisallyl-2′-*N*-4″-pyridinecarbonyl Et 770 6d (yield 90.9%)

$[\alpha]_D^{16}$ −50.0 (*c* 0.66, $CHCl_3$); IR (KBr) 3447, 2930, 2855, 2250w, 1761, 1749, 1662, 1519, 1458, 1446, 1410, 1375, 1321, 1288, 1259, 1234, 1196, 1146, 1109, 1086, 1069, 1028, 999 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.77 (2H, d, *J* = 5.2 Hz, 2″-H), 7.34 (2H, d, *J* = 5.2 Hz, 3″-H), 6.57 (1H, br s, 15-H), 6.43 (1H, br s, 8′-H), 6.35 (1H, s, 5′-H), 6.09 (1H, d, *J* = 1.2 Hz, OCHO), 6.08 (1H, ddd, *J* = 16.8, 10.4, 5.4 Hz, 18-OCH_2CH=CH_2), 6.00 (1H, d, *J* = 1.2 Hz, OCHO), 5.99 (1H, ddd, *J* = 17.1, 10.5, 5.4 Hz, 6′-OCH_2CH=CH_2), 5.44 (1H, dd, *J* = 17.2, 1.6 Hz, 18-OCH_2CH=CH_2), 5.32 (1H, dd, *J* = 17.2, 1.4 Hz, 6′-OCH_2CH=CH_2), 5.23 (2H, d, *J* = 10.4, 18-OCH_2CH=CH_2 and 6′-OCH_2CH=CH_2), 4.78 (1H, dd, *J* = 12.4, 5.2 Hz, 18-O*CH*CH), 4.65 (1H, br s, 4-H), 4.63 (1H, br, 22-H), 4.49 (2H,

dd, J = 5.6, 1.2 Hz, 6′-OCH_2CH), 4.38 (1H, br, 22-H), 4.36 (1H, s, 1-H), 4.30 (1H, dd, J = 12.4, 5.6 Hz, 18-OC*H*CH), 4.23 (1H, d, J = 5.6 Hz, 11-H), 4.14 (1H, d, J = 2.4 Hz, 21-H), 3.71 (3H, s, 17-OCH_3), 3.64 (3H, s, 7′-OCH_3), 3.58 (1H, br s, 3-H), 3.56 (1H, br d, 12′-H), 3.47 (3H, m, 3′-H_2 and 13-H), 2.99 (1H, dd, J = 17.2, 9.2 Hz, 14-Hα), 2.94 (1H, d, J = 17.2 Hz, 14-Hβ), 2.51 (1H, dd, J = 16.8, 5.2 Hz, 4′-H), 2.48 (1H, dd, J = 16.8, 8.0 Hz, 4′-H), 2.30 (3H, s, OCOCH_3), 2.13 (3H, s, *N*CH_3), 2.05 (1H, m, 12′-H, signals overlapped with 6-CH_3), 2.05 (3H, s, 6-CH_3), 1.77 (3H, s, 16-CH_3); ^{13}C NMR (CDCl_3, 100 MHz) δ 169.2 (*N*CO), 168.7 (1′-CO), 167.5 (5-OCO), 150.2 (C-18), 149.9 (C-2″), 148.6 (C-17), 147.3 (C-7′), 147.0 (C-6′), 145.3 (C-7), 144.8 (C-4″), 141.2 (C-5), 140.9 (C-8), 134.5 (18-OCH_2*C*H=CH_2), 132.8 (6′-OCH_2*C*H=CH_2), 131.0 (C-16), 129.9 (C-20), 127.5 (C-9′), 125.6 (C-10′), 124.5 (C-19), 124.4 (C-15), 122.1 (C-10), 121.9 (C-3″), 118.0 (21-CN), 117.8 (6′-OCH_2CH=*C*H_2), 116.6 (18-OCH_2CH=*C*H_2), 113.2 (C-9), 112.7 (C-6), 112.5 (C-5′), 111.0 (C-8′), 102.0 (OCH_2O), 72.9 (18-O*C*H_2CH), 69.9 (C-1′), 69.6 (6′-O*C*H_2CH), 61.0 (C-3), 60.7 (C-22), 60.6 (C-1), 59.6 (C-21), 59.4 (17-OCH_3), 55.5 (C-11), 55.2 (7′-OCH_3), 54.8 (C-13), 45.7 (C-3′), 42.2 (C-4), 41.9 (*N*CH_3), 39.2 (C-12′), 29.3 (C-4′), 25.0 (C-14), 20.4 (COCH_3), 15.9 (16-CH_3), 9.9 (6-CH_3); FABMS m/z 956 (MH$^+$); HRFABMS m/z 956.3534 (MH$^+$, calcd for $C_{52}H_{54}N_5O_{11}S$, 956.3541), CD $\Delta\varepsilon$ nm (c 10.0 μM, methanol, 23 °C) −49.6 (210), −93.5 (217), 0 (245), 12.1 (254), 0 (275), −7.6 (293), 0 (308).

5.3.5. 18, 6′-*O*-Bisallyl-2′-*N*-3″-pyridinecarbonyl Et 770 6e (yield 90.9%)

$[\alpha]_D^{16}$ −50.0 (c 0.61, $CHCl_3$); IR (KBr) 3451, 2930, 2250w, 1761, 1748, 1659, 1520, 1447, 1430, 1412, 1393, 1375, 1260, 1234, 1196, 1146, 1109, 1086, 1067, 1028, 999 cm^{-1}; ^{1}H NMR (CDCl_3, 400 MHz) δ 8.76 (1H, d, J = 4.4 Hz, 6″-H), 8.73 (1H, s, 2″-H), 7.79 (1H, d, J = 7.7 Hz, 4″-H), 7.42 (1H, dd, J = 7.7, 4.4 Hz, 5″-H), 6.61 (1H, br s, 15-H), 6.51 (1H, br s, 8′-H), 6.35 (1H, s, 5′-H), 6.09 (1H, s, OCHO), 6.07 (1H, ddd, J = 17.1, 10.5, 5.4 Hz, 18-OCH_2C*H*=CH_2), 6.01 (1H, s, OCHO), 5.98 (1H, ddd, J = 17.3, 10.5, 5.4 Hz, 6′-OCH_2C*H*=CH_2), 5.43 (1H, dd, J = 17.3, 1.4 Hz, 18-OCH_2CH=C*H*$_2$), 5.32 (1H, dd, J = 17.2, 1.3 Hz, 6′-OCH_2CH=C*H*$_2$), 5.22 (2H, dd, J = 10.5, 1.4 Hz, 18-OCH_2CH=C*H*$_2$ and 6′-OCH_2CH=C*H*$_2$), 4.77 (1H, dd, J = 12.8, 5.1 Hz, 18-O*C*HCH), 4.64 (1H, br s, 4-H), 4.56 (1H, br d, J = 11.4 Hz, 22-H), 4.49 (2H, d, J = 5.4 Hz, 6′-OCH_2CH), 4.48 (1H, br d, J = 11.4 Hz, 22-H), 4.34 (1H, s, 1-H), 4.29 (1H, dd, J = 12.8, 5.6 Hz, 18-O*C*HCH), 4.23 (1H, d, J = 5.1 Hz, 11-H), 4.15 (1H, br s, 21-H), 3.71 (3H, s, 17-OCH_3), 3.66 (3H, s, 7′-OCH_3), 3.60 (1H, d, J = 10.3 Hz, 12′-H), 3.58 (1H, s, 3-H), 3.52 (1H, m, 3′-H), 3.47 (1H, m, 3′-H), 3.45 (1H, br d, J = 8.3 Hz, 13-H), 2.99 (1H, dd, J = 17.5, 9.2 Hz, 14-Hα), 2.87 (1H, d, J = 17.5 Hz, 14-Hβ), 2.48 (1H, dd, J = 16.4, 7.1 Hz, 4′-H), 2.42 (1H, m, 12′-H), 2.38 (1H, dd, J = 16.4, 4.9 Hz, 4′-H), 2.30 (3H, s, OCOCH_3), 2.15 (3H, s, *N*CH_3), 2.05 (3H, s, 6-CH_3), 1.70 (3H, s, 16-CH_3); ^{13}C NMR (CDCl_3, 100 MHz) δ 169.7 (*N*CO), 169.1 (1′-CO), 168.0 (5-OCO), 150.6 (C-6″), 150.2 (C-18), 149.1 (C-2″), 148.5 (C-17), 147.3 (C-7′), 147.0 (C-6′), 145.3 (C-7), 141.1 (C-5), 141.1 (C-8), 135.8 (C-4″), 134.5 (18-OCH_2*C*H=CH_2), 132.9 (6′-OCH_2*C*H=CH_2), 132.8 (C-3″), 131.2 (C-16), 129.9 (C-20), 127.7 (C-9′), 125.5 (C-10′), 124.5 (C-15), 124.2 (C-19), 123.0 (C-5″), 122.1 (C-10), 118.0 (21-CN), 117.8 (6′-OCH_2CH=*C*H_2), 116.7 (18-OCH_2CH=*C*H_2), 113.1 (C-9), 112.7 (C-6), 112.6 (C-5′), 111.0 (C-8′), 102.0 (OCH_2O), 72.9 (18-O*C*H_2CH), 69.6 (6′-O*C*H_2CH), 69.5 (C-1′), 60.9 (C-3), 60.5 (C-22), 60.5 (C-1), 59.5 (C-21), 59.4 (17-OCH_3), 55.4 (C-11), 55.2 (7′-OCH_3), 54.9 (C-13), 46.1 (C-3′), 42.1 (C-4), 41.9 (*N*CH_3), 39.2 (C-12′), 29.2 (C-4′), 25.0 (C-14), 20.4 (COCH_3), 15.5 (16-CH_3), 9.9 (6-CH_3); FABMS m/z 956 (MH$^+$); HRFABMS m/z 956.3543 (MH$^+$, calcd for $C_{52}H_{54}N_5O_{11}S$, 956.3541), CD $\Delta\varepsilon$ nm (c 10.0 μM, methanol, 23 °C) −81.6 (210), −128.5 (217), 0 (242), 20.7 (253), 0 (282), −9.4 (292), 0 (309).

5.3.6. 18, 6′-*O*-Bisallyl-2′-*N*-4″-quinolinecarbonyl Et 770 6f (yield 73.0%)

$[\alpha]_D^{25}$ −76.1 (c 0.41, $CHCl_3$); IR (KBr) 3443, 2933, 2870, 2808, 2250w, 1761, 1660, 1518, 1508, 1464, 1447, 1429, 1412, 1318, 1321, 1256, 1234, 1194, 1109, 1086, 1069, 1028, 997, 775 cm^{-1}; ^{1}H NMR (CDCl_3, 500 MHz, this compound was a mixture of rotational isomers, ratio 7:3, and only the signals of major isomer are presented) δ 8.98 (7/10H, d, J = 4.3 Hz, 2″-H), 8.38 (7/10H, d, J = 7.7 Hz, 5″-H), 8.21 (7/10H, d, J = 7.7 Hz, 8″-H), 7.86 (7/10H, t, J = 7.7 Hz, 7″-H), 7.79 (7/10H, t, J = 7.7 Hz, 6″-H), 7.26 (7/10H, d, J = 4.3 Hz, 3″-H), 6.38 (7/10H, br s, 8′-H), 6.34 (7/10H, s, 5′-H), 6.24 (7/10H, br s, 15-H), 6.09 (7/10H, d, J = 1.1 Hz, OCHO), 6.08 (7/10H, ddd, J = 17.2, 10.5, 5.3 Hz, 18-OCH_2C*H*=CH_2), 6.00 (7/10H, d, J = 1.1 Hz, OCHO), 5.99 (7/10H, ddd, J = 17.2, 10.5, 5.4 Hz, 6′-OCH_2C*H*=CH_2), 5.44 (7/10H, d, J = 17.0 Hz, 18-OCH_2CH=C*H*$_2$), 5.32 (7/10H, dd, J = 17.2, 1.2 Hz, 6′-OCH_2CH=C*H*$_2$), 5.23 (7/5H, d, J = 10.5, 1.2 Hz, 18-OCH_2CH=C*H*$_2$ and 6′-OCH_2CH=C*H*$_2$), 4.78 (1H, dd, J = 12.8, 5.3 Hz, 18-O*C*HCH), 4.78 (7/10H, br, 22-H), 4.71 (7/10H, br s, 4-H), 4.49 (7/5H, d, J = 5.4 Hz, 6′-OCH_2CH), 4.44 (7/10H, s, 1-H), 4.42 (7/10H, br, 22-H), 4.29 (7/10H, dd, J = 12.8, 5.3 Hz, 18-O*C*HCH), 4.24 (7/10H, d, J = 5.1 Hz, 11-H), 4.20 (7/10H, d, J = 2.6 Hz, 21-H), 3.76 (21/10H, s, 17-OCH_3), 3.63 (21/10H, s, 7′-OCH_3), 3.59 (7/10H, br d, J = 4.5 Hz, 3-H), 3.54 (7/10H, br, 12′-H), 3.49 (7/10H, br, 13-H), 3.29 (7/5H, m, 3′-H_2), 3.03 (7/10H, dd, J = 17.6, 8.3 Hz, 14-Hα), 2.97 (7/10H, d, J = 17.6 Hz, 14-Hβ), 2.68 (7/10H, br, 12′-H), 2.41 (7/10H, dd, J = 15.8, 5.7 Hz, 4′-H), 2.31 (21/10H, s, OCOCH_3), 2.28 (7/10H, dd, J = 15.8, 8.5 Hz, 4′-H), 2.13 (21/10H, s, *N*CH_3), 2.06 (21/10H, s, 6-CH_3), 1.34 (21/10H, s, 16-CH_3); ^{13}C NMR (CDCl_3, 125 MHz) δ 168.9 (1′-CO), 168.4 (5-OCO), 166.5 (*N*CO), 150.3 (C-2″), 150.2 (C-18), 149.5 (C-9″), 148.7 (C-17), 147.6 (C-7′), 147.4 (C-6′), 144.8 (C-4″), 145.5 (C-7), 141.5 (C-5), 140.0 (C-8), 134.7 (18-OCH_2*C*H=CH_2), 133.0 (6′-OCH_2*C*H=CH_2), 130.9 (C-16), 130.5 (C-20), 130.0 (C-6″), 129.5 (C-8″), 127.8 (C-7″), 127.5 (C-9′), 126.6 (C-5″), 125.4 (C-10′), 124.8 (C-19), 124.4 (C-15), 123.9 (C-10″), 122.8 (C-10), 119.1 (C-3″), 118.2 (21-CN), 118.0 (6′-OCH_2CH=*C*H_2), 116.7 (18-OC$H_{2CH=}$CH_2), 113.6 (C-9), 112.7 (C-6), 112.5 (C-5′), 111.3 (C-8′), 102.1 (OCH_2O), 72.8 (18-O*C*H_2CH), 71.0 (C-1′), 69.6 (6′-O*C*H_2CH), 61.6 (C-22), 61.4 (C-3), 60.5 (C-1), 59.8 (C-21), 59.3 (17-OCH_3), 55.4 (C-11), 55.4 (7′-OCH_3), 54.9 (C-13), 45.3 (C-3′), 42.4 (C-4), 41.8 (*N*CH_3), 39.7 (C-12′), 29.6 (C-4′), 24.9 (C-14), 20.3 (COCH_3), 15.0 (16-CH_3), 9.8 (6-CH_3); FABMS m/z 1006 (MH$^+$); HRFABMS m/z 1006.3701 (MH$^+$, calcd for $C_{56}H_{56}N_5O_{11}S$, 1006.3697), CD $\Delta\varepsilon$ nm (c 10.0 μM, methanol, 21 °C) −18.8 (210), −63.6 (217), −18.2 (235), 0 (248), 10.3 (256), 0 (277), −5.6 (293), 0 (299), 1.2 (304), 0 (320).

5.3.7. 18, 6′-*O*-Bisallyl-2′-*N*-5″-quinolinecarbonyl Et 770 6g (yield 75.2%)

$[\alpha]_D^{25}$ −76.1 (c 0.46, $CHCl_3$); IR (KBr) 3447, 2934, 2808, 2250w, 1761, 1748, 1655, 1518, 1501, 1487, 1458, 1447, 1429, 1414, 1375, 1319, 1260, 1194, 1109, 1086, 1070, 1028 cm^{-1}; ^{1}H NMR (CDCl_3, 500 MHz, this compound was a mixture of rotational isomers, ratio 7:3, and only the signals of major isomer are presented) δ 9.04 (7/10H, d, J = 2.5 Hz, 2″-H), 8.76 (7/10H, br d, J = 6.2 Hz, 4″-H), 8.21 (7/10H, d, J = 8.2 Hz, 8″-H), 7.77 (7/10H, dd, J = 8.2, 7.1 Hz, 7″-H), 7.60 (7/10H, d, J = 2.5 Hz, 3″-H), 7.51 (7/10H, d, J = 7.1 Hz, 6″-H), 6.43 (7/10H, s, 8′-H), 6.33 (7/10H, s, 5′-H), 6.18 (7/10H, br s, 15-H), 6.10 (7/10H, d, J = 1.1 Hz, OCHO), 6.06 (7/10H, ddd, J = 17.0, 10.4, 5.8 Hz, 18-OCH_2C*H*=CH_2), 6.02 (7/10H, d, J = 1.1 Hz, OCHO), 5.98 (7/10H, ddd, J = 17.3, 10.5, 5.4 Hz, 6′-OCH_2C*H*=CH_2), 5.44 (7/10H, d, J = 17.0 Hz, 18-OCH_2CH=C*H*$_2$), 5.32 (7/10H, dd, J = 17.3, 1.2 Hz, 6′-OCH_2CH=C*H*$_2$), 5.23 (7/5H, d, J = 10.4, 1.2 Hz, 18-OCH_2CH=C*H*$_2$ and 6′-OCH_2CH=C*H*$_2$), 4.77 (1H, dd, J = 12.8, 5.3 Hz, 18-O*C*HCH), 4.68 (7/10H, br s, 4-H), 4.64 (7/10H, br, 22-H), 4.48 (7/5H, d, J = 5.4 Hz, 6′-OCH_2CH), 4.46 (7/10H, br, 22-H), 4.41 (7/10H, s, 1-H), 4.29 (7/10H, dd, J = 12.8, 5.3 Hz,

18-OCHCH), 4.24 (7/10H, d, J = 4.3 Hz, 11-H), 4.17 (7/10H, br s, 21-H), 3.76 (21/10H, s, 17-OCH_3), 3.66 (21/10H, s, 7′-OCH_3), 3.60 (7/10H, br, 3-H), 3.54 (7/10H, br, 12′-H), 3.47 (7/10H, br, 13-H), 3.27 (7/5H, br t, 3′-H_2), 2.97 (7/5H, br d, J = 7.6 Hz, 14-H_2), 2.56 (7/10H, br, 12′-H), 2.39 (7/10H, dd, J = 15.8, 5.7 Hz, 4′-H), 2.31 (21/10H, s, $OCOCH_3$), 2.28 (7/10H, m, 4′-H), 2.13 (21/10H, s, NCH_3), 2.06 (21/10H, s, 6-CH_3), 1.41 (21/10H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.5 (1′-CO), 168.9 (*N*CO), 168.3 (5-OCO), 150.7 (C-2″), 150.4 (C-18), 148.6 (C-17), 147.7 (C-5″), 147.5 (C-7′), 147.3 (C-6′), 145.5 (C-7), 141.4 (C-5), 141.2 (C-8), 135.5 (C-9″), 135.1 (C-4″), 134.7 (18-$OCH_2CH{=}CH_2$), 133.0 (6′-$OCH_2CH{=}CH_2$), 131.2 (C-8″), 130.8 (C-16), 129.4 (C-20), 128.9 (C-7″), 127.9 (C-9′), 126.5 (C-6″), 126.1 (C-10′), 125.2 (C-15), 125.0 (C-10″), 124.3 (C-19), 122.6 (C-10), 122.1 (C-3″), 118.2 (21-CN), 117.9 (6′-$OCH_2CH{=}CH_2$), 116.7 (18-$OCH_2CH{=}CH_2$), 113.6 (C-9), 112.7 (C-6), 112.5 (C-5′), 111.3 (C-8′), 102.1 (OCH_2O), 72.9 (18-OCH_2CH), 70.0 (C-1′), 69.6 (6′-OCH_2CH), 61.5 (C-22), 61.4 (C-3), 60.4 (C-1), 60.0 (C-21), 59.3 (17-OCH_3), 55.4 (C-11), 55.3 (7′-OCH_3), 54.9 (C-13), 45.2 (C-3′), 42.1 (C-4), 41.8 (NCH_3), 40.0 (C-12′), 29.6 (C-4′), 25.0 (C-14), 20.3 ($COCH_3$), 15.0 (16-CH_3), 9.8 (6-CH_3); FABMS m/z 1006 (MH^+); HRFABMS m/z 1006.3702 (MH^+, calcd for $C_{56}H_{56}N_5O_{11}S$, 1006.3697), CD $\Delta\varepsilon$ nm (c 10.0 μM, methanol, 21 °C) −45.8 (210), −82.9 (217), 0 (238), 12.9 (252), 0 (275), −5.7 (293), 0 (306), 1.2 (304), 0 (320).

5.3.8. 18, 6′-*O*-Bisallyl-2′-*N*-6″-quinolinecarbonyl Et 770 6h (yield 88.4%)

$[\alpha]_D^{25}$ −58.1 (c 0.47, $CHCl_3$); IR (KBr) 3447, 2934, 2250w, 1761, 1749, 1655, 1518, 1508, 1487, 1458, 1447, 1429, 1375, 1319, 1260, 1234, 1194, 1132, 1107, 1086, 1049, 1028, 999, 914, 787 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.03 (1H, dd, J = 4.7, 1.7 Hz, 2″-H), 8.29 (1H, dd, J = 8.2, 1.7 Hz, 4″-H), 8.27 (1H, dd, J = 8.5, 1.4 Hz, 8″-H), 8.01 (1H, d, J = 1.4 Hz, 5″-H), 7.82 (1H, dd, J = 8.5, 1.4 Hz, 7″-H), 7.53 (1H, dd, J = 8.2, 4.5 Hz, 3″-H), 6.54 (2H, br s, 8′-H and 15-H), 6.35 (1H, s, 5′-H), 6.10 (1H, d, J = 1.3 Hz, OCHO), 6.06 (1H, ddd, J = 17.0, 10.5, 5.4 Hz, 18-$OCH_2CH{=}CH_2$), 6.02 (1H, d, J = 1.3 Hz, OCHO), 5.98 (1H, ddd, J = 17.3, 10.5, 5.4 Hz, 6′-$OCH_2CH{=}CH_2$), 5.43 (1H, dd, J = 17.0, 1.4 Hz, 18-$OCH_2CH{=}CH_2$), 5.32 (1H, dd, J = 17.3, 1.4 Hz, 6′-$OCH_2CH{=}CH_2$), 5.22 (2H, d, J = 10.4, 1.4 Hz, 18-$OCH_2CH{=}CH_2$ and 6′-$OCH_2CH{=}CH_2$), 4.76 (1H, dt, J = 12.7, 5.1 Hz, 18-OCHCH), 4.65 (1H, br s, 4-H), 4.58 (1H, br, 22-H), 4.52 (1H, br, 22-H), 4.49 (2H, dt, J = 5.4, 1.4 Hz, 6′-OCH_2CH), 4.36 (1H, s, 1-H), 4.28 (1H, ddd, J = 12.7, 5.4, 1.4 Hz, 18-OCHCH), 4.23 (1H, dd, J = 5.3, 1.3 Hz, 11-H), 4.16 (1H, br s, 21-H), 3.74 (3H, s, 17-OCH_3), 3.70 (3H, s, 7′-OCH_3), 3.65 (1H, d, J = 15.8 Hz, 12′-H), 3.64 (1H, br d, J = 15.8 Hz, 3′-H), 3.60 (1H, d, J = 5.1 Hz, 3-H), 3.52 (1H, m, 3′-H), 3.47 (1H, d, J = 8.8 Hz, 13-H), 3.02 (1H, dd, J = 17.3, 9.3 Hz, 14-Hα), 2.91 (1H, d, J = 17.3 Hz, 14-Hβ), 2.46 (1H, ddd, J = 16.2, 8.5, 6.0 Hz, 4′-H), 2.46 (1H, m, 12′-H, signals overlapped with 4′-H), 2.36 (1H, dt, J = 16.2, 4.3 Hz, 4′-H), 2.31 (3H, s, $OCOCH_3$), 2.13 (3H, s, NCH_3), 2.05 (3H, s, 6-CH_3), 1.49 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.6 (*N*CO), 169.5 (1′-CO), 168.3 (5-OCO), 151.3 (C-2″), 150.4 (C-18), 148.6 (C-17), 148.5 (C-9″), 147.4 (C-7′), 147.1 (C-6′), 145.5 (C-7), 141.3 (C-8), 141.3 (C-5), 137.0 (C-4″), 135.5 (C-6″), 134.7 (18-$OCH_2CH{=}CH_2$), 133.1 (6′-$OCH_2CH{=}CH_2$), 131.2 (C-16), 130.0 (C-20), 129.2 (C-8″), 129.2 (C-7″), 128.4 (C-5″), 128.1 (C-9′), 127.9 (C-10″), 125.9 (C-10′), 124.5 (C-19), 124.4 (C-15), 122.3 (C-10), 121.8 (C-3″), 118.2 (21-CN), 117.9 (6′-$OCH_2CH{=}CH_2$), 116.8 (18-$OCH_2CH{=}CH_2$), 113.2 (C-9), 112.8 (C-6), 112.8 (C-5′), 111.3 (C-8′), 102.1 (OCH_2O), 72.9 (18-OCH_2CH), 69.6 (C-1′), 69.6 (6′-OCH_2CH), 60.9 (C-3), 60.5 (C-22), 60.5 (C-1), 59.5 (C-21), 59.4 (17-OCH_3), 55.4 (C-11), 55.2 (7′-OCH_3), 54.8 (C-13), 45.8 (C-3′), 42.0 (C-4), 41.8 (NCH_3), 39.3 (C-12′), 29.1 (C-4′), 24.9 (C-14), 20.2 ($COCH_3$), 15.3 (16-CH_3), 9.7 (6-CH_3); FABMS m/z 1006 (MH^+); HRFABMS m/z 1006.3693 (MH^+, calcd for $C_{56}H_{56}N_5O_{11}S$, 1006.3697), CD $\Delta\varepsilon$ nm (c 10.0 μM, methanol, 21 °C) −33.3 (210), −53.5 (216), 0 (245), 6.6 (256), 0 (281), −3.6 (293), 0 (299), 0.9 (311), 0 (327).

5.3.9. 18, 6′-*O*-Bisallyl-2′-*N*-4″-bromobenzoyl Et 770 6i (yield 84.5%)

$[\alpha]_D^{16}$ −38.2 (c 0.45, $CHCl_3$); IR (KBr) 3470, 2961, 2928, 2854, 2250w, 1763, 1746, 1659, 1520, 1462, 1445, 1432, 1412, 1396, 1375, 1260, 1234, 1194, 1175, 1142, 1107, 1086, 1069, 1028, 1013, 802 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.60 (2H, d, J = 8.4 Hz, 3″-H), 7.35 (2H, d, J = 8.4 Hz, 2″-H), 6.55 (1H, br s, 15-H), 6.53 (1H, br s, 8′-H), 6.34 (1H, s, 5′-H), 6.09 (1H, d, J = 1.2 Hz, OCHO), 6.07 (1H, ddd, J = 16.9, 10.7, 5.1 Hz, 18-$OCH_2CH{=}CH_2$), 6.01 (1H, d, J = 1.2 Hz, OCHO), 5.98 (1H, ddd, J = 17.3, 10.5, 5.4 Hz, 6′-$OCH_2CH{=}CH_2$), 5.43 (1H, dd, J = 16.9, 1.6 Hz, 18-$OCH_2CH{=}CH_2$), 5.32 (1H, dd, J = 17.3, 1.6 Hz, 6′-$OCH_2CH{=}CH_2$), 5.22 (2H, dd, J = 10.8, 1.4 Hz 18-$OCH_2CH{=}CH_2$ and 6′-$OCH_2CH{=}CH_2$), 4.78 (1H, dd, J = 12.8, 5.2 Hz, 18-OCHCH), 4.62 (1H, br s, 22-H), 4.51 (1H, br s, 4-H), 4.51 (1H, br s, 22-H), 4.48 (2H, d, J = 5.6 Hz, 6′-OCH_2CH), 4.32 (1H, s, 1-H), 4.29 (1H, dd, J = 12.8, 5.2 Hz, 18-OCHCH), 4.22 (1H, d, J = 5.2 Hz, 11-H), 4.11 (1H, d, J = 2.0 Hz, 21-H), 3.71 (3H, s, 17-OCH_3), 3.65 (3H, s, 7′-OCH_3), 3.60 (1H, dd, J = 9.0, 4.4 Hz, 3-H), 3.57 (1H, d, J = 15.4 Hz, 12′-H), 3.50 (2H, t, J = 5.6 Hz, 3′-H_2), 3.45 (1H, dd, J = 9.6, 2.0 Hz, 13-H), 2.98 (1H, dd, J = 17.2, 9.6 Hz, 14-Hα), 2.82 (1H, d, J = 17.2 Hz, 14-Hβ), 2.39 (1H, m, 4′-H), 2.36 (1H, d, J = 15.4 Hz, 12′-H), 2.32 (1H, m, 4′-H), 2.29 (3H, s, $OCOCH_3$), 2.13 (3H, s, NCH_3), 2.04 (3H, s, 6-CH_3), 1.82 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.4 (*N*CO), 169.2 (1′-CO), 168.9 (5-OCO), 150.3 (C-18), 148.5 (C-17), 147.2 (C-7′), 146.9 (C-6′), 145.4 (C-7), 141.2 (C-8), 141.0 (C-5), 135.6 (C-1″), 134.5 (18-$OCH_2CH{=}CH_2$), 132.9 (6′-$OCH_2CH{=}CH_2$), 131.5 (C-3″), 131.1 (C-16), 129.9 (C-20), 129.9 (C-2″), 127.9 (C-9′), 125.6 (C-10′), 125.6 (C-15), 124.5 (C-4″), 124.4 (C-19), 122.1 (C-10), 118.0 (6′-$OCH_2CH{=}CH_2$), 117.8 (21-CN), 116.7 (18-$OCH_2CH{=}CH_2$), 113.0 (C-9), 112.7 (C-5′), 112.5 (C-6), 111.1 (C-8′), 102.0 (OCH_2O), 73.0 (18-OCH_2CH), 69.6 (6′-OCH_2CH), 68.9 (C-1′), 61.0 (C-3), 60.5 (C-22), 60.4 (C-1), 59.6 (C-21), 59.4 (17-OCH_3), 55.5 (C-11), 55.2 (7′-OCH_3), 54.9 (C-13), 45.7 (C-3′), 42.0 (C-4), 41.9 (NCH_3), 39.5 (C-12′), 29.2 (C-4′), 25.1 (C-14), 20.4 ($COCH_3$), 15.8 (16-CH_3), 9.9 (6-CH_3); FABMS m/z 1033 (MH^+); HRFABMS m/z 1033.2697 (MH^+, calcd for $C_{53}H_{54}N_4O_{11}SBr$, 1033.2693), CD $\Delta\varepsilon$ nm (c 60.0 μM, methanol, 23 °C) −99.1 (210), −149.8 (216), 0 (243), 19.9 (254), 0 (282), −7.7 (292), 0 (325).

5.3.10. 18, 6′-*O*-Bisallyl-2′-*N*-2″-bromobenzoyl Et 770 6j (yield 29.0%)

$[\alpha]_D^{22}$ −57.5 (c 0.34, $CHCl_3$); IR (KBr) 3446, 2932, 2250w, 1761, 1668, 1518, 1458, 1430, 1396, 1261, 1194, 1148, 1109, 1086, 1028, 999, 920 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.57 (1H, d, J = 7.4 Hz, 3″-H), 7.44 (1H, t, J = 7.4 Hz, 4″-H), 7.33 (1H, d, J = 7.4 Hz, 6″-H), 7.27 (1H, t, J = 7.4 Hz, 2″-H), 6.58 (1H, br s, 15-H), 6.37 (1H, s, 8′-H), 6.37 (1H, s, 5′-H), 6.08 (1H, d, J = 0.8 Hz, OCHO), 6.07 (1H, ddd, J = 17.0, 10.5, 5.4 Hz, 18-$OCH_2CH{=}CH_2$), 5.99 (1H, d, J = 0.8 Hz, OCHO), 5.99 (1H, ddd, J = 17.3, 10.5, 5.1 Hz, 6′-$OCH_2CH{=}CH_2$), 5.43 (1H, br d, J = 17.0 Hz, 18-$OCH_2CH{=}CH_2$), 5.32 (1H, dd, J = 17.3, 1.3 Hz, 6′-$OCH_2CH{=}CH_2$), 5.22 (2H, dd, J = 10.7, 1.3 Hz, 18-$OCH_2CH{=}CH_2$ and 6′-$OCH_2CH{=}CH_2$), 4.80 (1H, dd, J = 12.7, 5.1 Hz, 18-OCHCH), 4.76 (1H, d, J = 11.4 Hz, 22-H), 4.64 (1H, br s, 4-H), 4.49 (2H, dd, J = 5.5, 1.4 Hz, 6′-OCH_2CH), 4.40 (1H, s, 1-H), 4.32 (1H, dd, J = 12.7, 5.2 Hz, 18-OCHCH), 4.30 (1H, d, J = 5.2 Hz, 11-H), 4.23 (1H, d, J = 11.4 Hz, 22-H), 4.22 (1H, s, 21-H), 3.77 (1H, d, J = 15.3 Hz, 12′-H), 3.76 (3H, s, 17-OCH_3), 3.63 (3H, s, 7′-OCH_3), 3.55 (1H, dd, J = 9.6, 2.0 Hz, 13-H), 3.60 (1H, dd, J = 9.0, 4.4 Hz, 3-H), 3.47 (1H, ddd, J = 14.2, 5.4, 3.1 Hz, 3′-H), 3.28 (1H, ddd, J = 14.2, 10.9, 4.2 Hz, 3′-H), 2.99 (2H, br s, 14-H_2), 2.78(1H, ddd, J = 16.0, 10.9, 5.6 Hz, 4′-H), 2.57 (1H, d, J = 15.3 Hz, 12′-H), 2.34 (1H, m, 4′-H), 2.30 (3H, s, $OCOCH_3$), 2.18 (3H, s,

NCH_3), 2.05 (3H, s, 6-CH_3), 1.77 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.2 (1′-CO), 168.3 (*N*CO), 168.2 (5-OCO), 150.4 (C-18), 148.9 (C-17), 147.3 (C-7′), 147.2 (C-6′), 145.5 (C-7), 141.5 (C-5), 141.0 (C-8), 139.3 (C-1″), 134.6 (18-$OCH_2CH{=}CH_2$), 133.2 (C-3″), 133.1 (6′-$OCH_2CH{=}CH_2$), 131.9 (C-16), 129.9 (C-4″), 129.3 (C-20), 128.9 (C-6″), 127.9 (C-9′), 127.4 (C-5″), 126.8 (C-10′), 124.6 (C-15), 123.8 (C-19), 122.5 (C-10), 119.9 (C-2″), 117.9 (6′-$OCH_2CH{=}CH_2$), 117.9 (21-CN), 117.0 (18-$OCH_2CH{=}CH_2$), 113.3 (C-9), 113.1 (C-6), 112.6 (C-5′), 111.4 (C-8′), 102.0 (OCH_2O), 72.9 (18-OCH_2CH), 70.9 (C-1′), 69.6 (6′-OCH_2CH), 61.0 (C-3), 60.7 (C-22), 60.7 (C-1), 59.7 (17-OCH_3), 59.4 (C-21), 55.6 (C-11), 55.3 (7′-OCH_3), 54.9 (C-13), 46.0 (C-3′), 42.2 (C-4), 41.8 (NCH_3), 38.8 (C-12′), 29.8 (C-4′), 25.3 (C-14), 20.3 ($COCH_3$), 15.8 (16-CH_3), 9.8 (6-CH_3); FABMS *m/z* 1033 (MH^+); HRFABMS *m/z* 1033.2693 (MH^+, calcd for $C_{53}H_{54}N_4O_{11}SBr$, 1033.2693), CD $\Delta\varepsilon$ nm (*c* 60.0 μM, methanol, 23 °C) −22.2 (210), −54.0 (216), 0 (242), 8.3 (252), 0 (278), −75.2 (293), 0 (315).

5.3.11. *N*-Benzoyl derivative of Et 770 7a

Tributyltin hydride (0.064 mL, 0.237 mmol) was added dropwise over 10 min to a vigorously stirred solution of **6a** (13.7 mg, 14.4 μmol), $(Ph_3P)_2PdCl_2$ (6.0 mg, 8.6 μmol), and AcOH (0.03 mL, 0.54 mmol) in THF (4 mL) at 25 °C, and the mixture was stirred for 1 h at 25 °C. The mixture was diluted with water (10 mL), made alkaline with 5% aqueous $NaHCO_3$, and extracted with chloroform (30 mL × 3). The combined extracts were washed with 5% aqueous $NaHCO_3$, dried, and concentrated in vacuo to give a residue. Chromatography on a silica gel column with benzene–ethyl acetate (6:1) gave **7a** (6.4 mg, 51.0%) as a colorless amorphous powder. $[\alpha]_D^{28}$ +2.0 (*c* 0.33, $CHCl_3$); IR (KBr) 3447, 2926, 2853, 2361, 2344, 1749, 1653, 1508, 1456, 1447, 1431, 1375, 1258, 1234, 1196, 1109, 1085 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.43 (5H, m, ArH), 6.59 (1H, br s, 8′-H), 6.41 (1H, br s, 15-H), 6.41 (1H, s, 5′-H), 6.10 (1H, s, OCHO), 6.01 (1H, s, OCHO), 5.78 (1H, s, 18-OH), 5.49 (1H, s, 6′-OH), 4.68 (2H, br s, 4-H and 22-H), 4.42 (2H, br s, 22-H and 11-H), 4.36 (1H, s, 1-H), 4.28 (1H, br s, 21-H), 3.76 (3H, s, 17-OCH_3), 3.76 (1H, br, 3-H, signals overlapped with 17-OCH_3), 3.70 (3H, s, 7′-OCH_3), 3.65 (1H, br, 13-H, signals overlapped with 7′-OCH_3), 3.58 (1H, d, *J* = 15.3 Hz, 12′-H), 3.51 (1H, m, 3′-H), 3.42 (1H, m, 3′-H), 3.00 (1H, dd, *J* = 17.3, 9.5 Hz, 14-Hα), 2.83 (1H, d, *J* = 17.3 Hz, 14-Hβ), 2.40 (2H, m, 4′-H), 2.36 (1H, m, 12′-H), 2.32 (3H, s, $OCOCH_3$), 2.27 (3H, s, NCH_3), 2.03 (3H, s, 6-CH_3), 1.81 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.9 (*N*CO), 169.8 (1′-CO), 168.3 (5-OCO), 147.6 (C-18), 145.6 (C-7), 144.8 (C-7′), 144.7 (C-6′), 143.7 (C-17), 141.6 (C-8), 141.1 (C-5), 136.9 (C-1″), 130.2 (C-4″), 128.8 (C-16), 128.5 (C-20), 128.3 (C-3″), 128.2 (C-2″), 127.5 (C-9′), 126.6 (C-10′), 122.8 (C-10), 120.9 (C-15), 117.6 (C-19), 117.6 (21-CN), 113.9 (C-5′), 112.8 (C-9), 112.7 (C-6), 111.0 (C-8′), 102.3 (OCH_2O), 68.6 (C-1′), 60.6 (C-1), 60.6 (C-22), 60.2 (17-OCH_3), 59.4 (C-21), 59.4 (C-3), 59.3 (7′-OCH_3), 55.2 (C-11), 54.8 (C-13), 45.6 (C-3′), 41.5 (C-4), 41.5 (NCH_3), 39.7 (C-12′), 28.8 (C-4′), 25.6 (C-14), 20.4 ($COCH_3$), 15.2 (16-CH_3), 9.8 (6-CH_3); FABMS *m/z* 875 (MH^+); HRFABMS *m/z* 875.2964 (MH^+, calcd for $C_{47}H_{47}N_4O_{11}S$, 875.2962), CD $\Delta\varepsilon$ nm (*c* 11.4 μM, methanol, 23 °C) −60.9 (210), −71.9 (217), 0 (242), 11.0 (254), 0 (271), −8.6 (287), 0 (311).

5.3.12. *N*-4″-Nitrobenzoyl derivative of Et 770 7b

Tributyltin hydride (0.07 mL, 0.264 mmol) was added dropwise over 10 min to a vigorously stirred solution of **6b** (16.0 mg, 16.0 μmol), $(Ph_3P)_2PdCl_2$ (6.7 mg, 9.6 μmol), and AcOH (34 μL, 0.38 mmol) in THF (4 mL) at 25 °C, and the mixture was stirred for 30 min at 25 °C. The mixture was diluted with water (10 mL), made alkaline with 5% aqueous $NaHCO_3$, and extracted with chloroform (30 mL × 3). The combined extracts were washed with 5% aqueous $NaHCO_3$, dried, and concentrated in vacuo to give a residue. Chromatography on a silica gel column with hexane–ethyl acetate (2:1) gave **7b** (7.3 mg, 49.7%) as a colorless amorphous powder. $[\alpha]_D^{28}$ −25.0 (*c* 0.43, $CHCl_3$); IR (KBr) 3524, 3447, 2936, 2250w, 1749, 1653, 1522, 1508, 1456, 1348, 1260, 1234, 1198, 1107, 1086 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.32 (2H, d, *J* = 8.7 Hz, 3″-H), 7.58 (2H, d, *J* = 8.4 Hz, 2″-H), 6.45 (1H, br s, 8′-H), 6.43 (1H, s, 5′-H), 6.36 (1H, br s, 15-H), 6.10 (1H, d, *J* = 1.3 Hz, OCHO), 6.00 (1H, d, *J* = 1.3 Hz, OCHO), 5.74 (1H, br s, 18-OH), 5.50 (1H, s, 6′-OH), 4.70 (1H, br s, 4-H), 4.59 (1H, br d, *J* = 9.9 Hz, 22-H), 4.47 (1H, br d, *J* = 9.9 Hz, 22-H), 4.38 (1H, s, 1-H), 4.33 (1H, br s, 11-H), 4.19 (1H, br s, 21-H), 3.69 (3H, s, 17-OCH_3), 3.64 (3H, s, 7′-OCH_3), 3.63 (2H, br, 3-H and 13-H, signals overlapped with 7′-OCH_3), 3.59 (1H, d, *J* = 15.3 Hz, 12′-H), 3.41 (3H, m, 3′-H_2), 3.03 (1H, dd, *J* = 16.9, 9.6 Hz, 14-Hα), 2.89 (1H, d, *J* = 16.9 Hz, 14-Hβ), 2.46 (1H, dd, *J* = 16.2, 8.2 Hz, 4′-H), 2.37 (1H, dt, *J* = 16.2, 4.8 Hz, 4′-H), 2.36 (1H, br d, *J* = 15.3 Hz, 12′-H), 2.33 (3H, s, $OCOCH_3$), 2.18 (3H, s, NCH_3), 2.05 (3H, s, 6-CH_3), 1.75 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.8 (*N*CO), 169.3 (1′-CO), 168.4 (5-OCO), 148.6 (C-4″), 147.7 (C-18), 145.6 (C-7), 145.0 (C-7′), 144.9 (C-6′), 143.2 (C-17), 143.2 (C-1″), 141.3 (C-8), 141.3 (C-5), 130.3 (C-20), 129.4 (C-16), 128.9 (C-2″), 126.9 (C-9′), 126.4 (C-10′), 123.8 (C-3″), 122.0 (C-10), 120.7 (C-15), 117.9 (C-19), 117.9 (21-CN), 113.8 (C-5′), 113.1 (C-9), 112.8 (C-6), 111.3 (C-8′), 102.1 (OCH_2O), 69.6 (C-1′), 61.0 (C-22), 60.8 (C-3), 60.3 (C-1), 60.1 (17-OCH_3), 59.6 (C-21), 55.3 (7′-OCH_3), 55.1 (C-11), 54.7 (C-13), 45.8 (C-3′), 41.9 (C-4), 41.7 (NCH_3), 39.2 (C-12′), 28.9 (C-4′), 25.2 (C-14), 20.4 ($COCH_3$), 15.7 (16-CH_3), 9.8 (6-CH_3); FABMS *m/z* 920 (MH^+); HRFABMS *m/z* 920.2812 (MH^+, calcd for $C_{47}H_{45}N_5O_{13}S$, 920.2813), CD $\Delta\varepsilon$ nm (*c* 11.4 μM, methanol, 23 °C) −18.7 (210), −32.4 (217), 0 (247), 1.5 (252), 0 (263), −3.6 (288), 0 (325).

5.3.13. *N*-3″-Nitrobenzoyl derivative of Et 770 7c

Tributyltin hydride (58 μL, 0.215 mmol) was added dropwise over 10 min to a vigorously stirred solution of **6c** (13.0 mg, 13.0 μmol), $(Ph_3P)_2PdCl_2$ (5.5 mg, 7.8 μmol), and AcOH (30 μL, 0.49 mmol) in THF (3.5 mL) at 25 °C, and the mixture was stirred for 1 h at 25 °C. The mixture was diluted with water (10 mL), made alkaline with 5% aqueous $NaHCO_3$, and extracted with chloroform (30 mL × 3). The combined extracts were washed with 5% aqueous $NaHCO_3$, dried, and concentrated in vacuo to give a residue. Chromatography on a silica gel column with benzene–ethyl acetate (5:1) gave **7c** (5.8 mg, 48.7%) as a colorless amorphous powder. $[\alpha]_D^{28}$ −13.9 (*c* 0.42, $CHCl_3$); IR (KBr) 3524, 3447, 2934, 2250w, 1749, 1653, 1533, 1508, 1458, 1437, 1396, 1375, 1350, 1254, 1234, 1198, 1150, 1109, 1086, 1062, 1028 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.37 (1H, ddd, *J* = 8.3, 2.3, 1.2 Hz, 4″-H), 8.31 (1H, dd, *J* = 2.3, 1.2 Hz, 2″-H), 7.77 (1H, dt, *J* = 7.8, 1.2 Hz, C-5″), 7.67 (1H, dd, *J* = 8.3, 7.6 Hz, 5″-H), 6.44 (1H, br s, 8′-H), 6.43 (1H, s, 5′-H), 6.22 (1H, br s, 15-H), 6.10 (1H, d, *J* = 1.3 Hz, OCHO), 6.00 (1H, d, *J* = 1.3 Hz, OCHO), 5.74 (1H, s, 18-OH), 5.51 (1H, s, 6′-OH), 4.72 (1H, br s, 4-H), 4.67 (1H, br d, *J* = 10.9 Hz, 22-H), 4.47 (1H, br d, *J* = 10.9 Hz, 22-H), 4.41 (1H, s, 1-H), 4.35 (1H, br s, 11-H), 4.27 (1H, br s, 21-H), 3.70 (3H, s, 17-OCH_3), 3.70 (1H, d, *J* = 15.3 Hz, 12′-H), 3.56 (1H, d, *J* = 5.2 Hz, 3-H), 3.61 (3H, s, 7′-OCH_3), 3.61 (1H, br, 13-H, signals overlapped with 7′-OCH_3), 3.52 (1H, ddd, *J* = 14.4, 6.0, 4.0 Hz, 3′-H), 3.40 (1H, ddd, *J* = 14.4, 10.2, 4.0 Hz, 3′-H), 3.06 (1H, dd, *J* = 17.3, 7.4 Hz, 14-Hα), 2.97 (1H, d, *J* = 17.3 Hz, 14-Hβ), 2.57 (1H, br d, *J* = 15.3 Hz, 12′-H), 2.48 (1H, ddd, *J* = 16.2, 10.2, 6.40 Hz, 4′-H), 2.35 (1H, dt, *J* = 16.2, 4.0, 4′-H), 2.34 (3H, s, $OCOCH_3$), 2.20 (3H, s, NCH_3), 2.05 (3H, s, 6-CH_3), 1.53 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.6 (1′-CO), 169.4 (*N*CO), 168.3 (5-OCO), 148.1 (C-3″), 147.6 (C-18), 145.6 (C-17), 145.0 (C-7′), 144.9 (C-6′), 143.1 (C-7), 141.3 (C-5), 141.3 (C-8), 139.0 (C-1″), 134.0 (C-6″), 130.1 (C-20), 129.8 (C-16), 129.7 (C-5″), 126.9 (C-9′), 126.5 (C-10′), 124.8 (C-4″), 123.2 (C-2″), 122.2 (C-10), 120.5 (C-15), 117.8 (21-CN), 117.8 (C-19), 113.7 (C-5′), 113.1

(C-9), 112.9 (C-6), 110.3 (C-8′), 102.8 (OCH_2O), 70.4 (C-1′), 60.8 (C-22), 60.8 (C-3), 60.5 (C-1), 60.1 (17-OCH_3), 59.3 (C-21), 55.4 (7′-OCH_3), 55.0 (C-11), 54.8 (C-13), 46.6 (C-3′), 41.9 (C-4), 41.6 (NCH_3), 38.7 (C-12′), 28.8 (C-4′), 25.1 (C-14), 20.4 ($COCH_3$), 15.2 (16-CH_3), 9.9 (6-CH_3); FABMS *m/z* 920 (MH^+); HRFABMS *m/z* 920.2812 (MH^+, calcd for $C_{47}H_{45}N_5O_{13}S$, 920.2813), CD $\Delta\varepsilon$ nm (*c* 10.8 μM, methanol, 27 °C) −18.1 (210), −31.5 (218), 0 (242), 6.2 (253), 0 (274), −3.8 (291), 0 (314).

5.3.14. *N*-4″-Pyridinecarbonyl derivative of Et 770 7d

Tributyltin hydride (71 μL, 0.264 mmol) was added dropwise over 10 min to a vigorously stirred solution of **6d** (15.3 mg, 16.0 μmol), $(Ph_3P)_2PdCl_2$ (6.7 mg, 9.6 μmol), and AcOH (34 μL, 0.60 mmol) in THF (4.0 mL) at 25 °C, and the mixture was stirred for 1 h at 25 °C. The mixture was diluted with ethyl acetate (10 mL) and extracted with 2 N aqueous HCl solution (20 mL × 3). The combined extracts were made alkaline with saturated Na_2CO_3, and extracted with chloroform (30 mL × 3). The combined extracts were washed with brine, dried, and concentrated in vacuo to give a residue (14.4 mg). Chromatography on a silica gel column with CH_2Cl_2–MeOH (50:1) gave **7d** (12.1 mg, 86.4%) as a colorless amorphous powder. $[\alpha]_D^{28}$ −43.3 (*c* 0.45, $CHCl_3$); IR (KBr) 3435, 2931, 2250w, 1751, 1655, 1595, 1516, 1458, 1418, 1375, 1304, 1260, 1234, 1198, 1148, 1109, 1086, 1065, 1028, 960 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.76 (2H, d, *J* = 5.5 Hz, 2″-H), 7.33 (2H, d, *J* = 5.5 Hz, 3″-H), 6.44 (1H, br s, 8′-H), 6.43 (1H, s, 5′-H), 6.38 (1H, s, 15-H), 6.10 (1H, d, *J* = 1.2 Hz, OCHO), 6.00 (1H, d, *J* = 1.2 Hz, OCHO), 5.75 (1H, s, 18-OH), 5.57 (1H, s, 6′-OH), 4.69 (1H, br s, 4-H), 4.60 (1H, br d, *J* = 10.0 Hz, 22-H), 4.43 (1H, br d, *J* = 10.0 Hz, 22-H), 4.36 (1H, s, 1-H), 4.27 (1H, dd, *J* = 4.9, 1.2 Hz, 11-H), 4.19 (1H, d, *J* = 2.1 Hz, 21-H), 3.68 (3H, s, 17-OCH_3), 3.63 (3H, s, 7′-OCH_3), 3.58 (1H, br s, 3-H), 3.58 (1H, br d, *J* = 16.8 Hz, 12′-H), 3.46 (1H, br d, *J* = 10.3 Hz, 13-H), 3.43 (2H, dd, *J* = 9.5, 5.2 Hz, 3′-H_2), 2.99 (1H, dd, *J* = 17.3, 9.5 Hz, 14-Hα), 2.85 (1H, d, *J* = 17.3 Hz, 14-Hβ), 2.47 (1H, dd, *J* = 16.5, 7.6 Hz, 4′-H), 2.37 (1H, dd, *J* = 16.5, 10.0 Hz, 4′-H), 2.37 (1H, br d, *J* = 16.8 Hz, 12′-H), 2.33 (3H, s, $OCOCH_3$), 2.13 (3H, s, NCH_3), 2.05 (3H, s, 6-CH_3), 1.80 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.4 (*N*CO), 169.1 (1′-CO), 168.3 (5-OCO), 150.0 (C-2″), 147.6 (C-18), 145.5 (C-7), 145.2 (C-4″), 145.0 (C-6′), 144.9 (C-7′), 143.1 (C-17), 141.3 (C-5), 141.2 (C-8), 130.5 (C-20), 129.2 (C-16), 126.9 (C-9′), 126.6 (C-10′), 122.2 (C-10), 122.1 (C-3″), 120.8 (C-15), 118.1 (21-CN), 118.0 (C-19), 113.8 (C-5′), 113.3 (C-9), 112.7 (C-6), 111.3 (C-8′), 102.1 (OCH_2O), 69.8 (C-1′), 60.9 (C-3), 60.9 (C-22), 60.4 (C-1), 60.1 (17-OCH_3), 59.8 (C-21), 55.3 (7′-OCH_3), 55.0 (C-11), 54.8 (C-13), 45.6 (C-3′), 42.0 (C-4), 41.7 (NCH_3), 39.2 (C-12′), 29.0 (C-4′), 25.0 (C-14), 20.4 ($COCH_3$), 15.6 (16-CH_3), 9.8 (6-CH_3); FABMS *m/z* 876 (MH^+); HRFABMS *m/z* 876.2909 (MH^+, calcd for $C_{46}H_{45}N_5O_{11}S$, 876.2914), CD $\Delta\varepsilon$ nm (*c* 11.4 μM, methanol, 23 °C) −68.3 (210), −123.9 (216), 0 (245), 17.3 (255), 0 (270), −16.5 (287), 0 (305).

5.3.15. *N*-3″-Pyridinecarbonyl derivatives of Et 770 7e

Tributyltin hydride (73 μL, 0.273 mmol) was added dropwise over 10 min to a vigorously stirred solution of **6e** (15.8 mg, 16.5 μmol), $(Ph_3P)_2PdCl_2$ (6.9 mg, 9.9 μmol), and AcOH (35 μL, 0.62 mmol) in THF (4.0 mL) at 25 °C, and the mixture was stirred for 1 h at 25 °C. The mixture was diluted with ethyl acetate (10 mL), and extracted with 2 N aqueous HCl solution (20 mL × 3). The combined extracts were made alkaline with saturated Na_2CO_3, and extracted with chloroform (30 mL × 3). The combined extracts were washed with brine, dried, and concentrated in vacuo to give a residue (16.4 mg). Chromatography on a silica gel column with CH_2Cl_2–MeOH (60:1) gave **7e** (12.7 mg, 87.6%) as a colorless amorphous powder. $[\alpha]_D^{28}$ −49.6 (*c* 0.45, $CHCl_3$); IR (KBr) 3447, 2934, 2250w, 1749, 1734, 1717, 1699, 1684, 1653, 1636, 1558, 1541, 1522, 1508, 1456, 1418, 1375, 1304, 1260, 1234, 1148, 1109, 1086 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.76 (1H, dd, *J* = 5.1, 1.7 Hz, 6″-H), 8.70 (1H, d, *J* = 1.4 Hz, 2″-H), 7.79 (1H, d, *J* = 7.6 Hz, 4″-H), 7.43 (1H, dd, *J* = 7.6, 5.1 Hz, 5″-H), 6.52 (1H, br s, 8′-H), 6.43 (1H, s, 15-H), 6.43 (1H, s, 5′-H), 6.10 (1H, d, *J* = 1.3 Hz, OCHO), 6.00 (1H, d, *J* = 1.3 Hz, OCHO), 5.74 (1H, br s, 18-OH), 5.56 (1H, br s, 6′-OH), 4.68 (1H, br s, 4-H), 4.54 (2H, br s, 22-H_2), 4.49 (2H, d, *J* = 5.4 Hz, 6′-OCH_2CH), 4.34 (1H, s, 1-H), 4.28 (1H, d, *J* = 4.3 Hz, 11-H), 4.14 (1H, br s, 21-H), 3.70 (3H, s, 17-OCH_3), 3.64 (3H, s, 7′-OCH_3), 3.60 (2H, br, 12′-H and 3-H), 3.47 (2H, br, 3′-H_2), 3.46 (1H, br d, *J* = 8.2 Hz, 13-H), 3.00 (1H, dd, *J* = 17.6, 9.6 Hz, 14-Hα), 2.85 (1H, d, *J* = 17.6 Hz, 14-Hβ), 2.47 (1H, dd, *J* = 16.7, 7.3 Hz, 4′-H), 2.42 (1H, m, 12′-H), 2.38 (1H, dd, *J* = 16.7, 5.9 Hz, 4′-H), 2.33 (3H, s, $OCOCH_3$), 2.15 (3H, s, NCH_3), 2.04 (3H, s, 6-CH_3), 1.74 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.7 (*N*CO), 169.4 (1′-CO), 168.3 (5-OCO), 150.5 (C-6″), 148.9 (C-2″), 147.5 (C-18), 145.5 (C-7), 145.9 (C-6′), 144.8 (C-7′), 143.0 (C-17), 141.4 (C-8), 141.2 (C-5), 136.3 (C-4″), 133.1 (C-3″), 130.4 (C-20), 129.5 (C-16), 127.1 (C-9′), 126.4 (C-10′), 123.6 (C-5″), 122.1 (C-10), 120.9 (C-15), 118.1 (21-CN), 117.6 (C-19), 113.9 (C-5′), 113.1 (C-9), 112.7 (C-6), 111.3 (C-8′), 102.1 (OCH_2O), 69.5 (C-1′), 60.7 (C-22), 60.9 (C-3), 60.3 (C-1), 60.1 (17-OCH_3), 59.7 (C-21), 55.3 (7′-OCH_3), 54.9 (C-11), 54.7 (C-13), 46.1 (C-3′), 41.9 (C-4), 41.7 (NCH_3), 39.2 (C-12′), 28.8 (C-4′), 24.9 (C-14), 20.4 ($COCH_3$), 15.3 (16-CH_3), 9.8 (6-CH_3); FABMS *m/z* 876 (MH^+); HRFABMS *m/z* 876.2922 (MH^+, calcd for $C_{46}H_{45}N_5O_{11}S$, 876.2914), CD $\Delta\varepsilon$ nm (*c* 11.4 μM, methanol, 23 °C) −44.1 (210), −70.8 (216), 0 (242), 11.4 (253), 0 (270), −18.7 (291), 0 (332).

5.3.16. *N*-4″-Quinolinecarbonyl derivative of Et 770 7f

Tributyltin hydride (52 μL, 0.191 mmol) was added dropwise over 10 min to a vigorously stirred solution of **6f** (11.7 mg, 11.6 μmol), $(Ph_3P)_2PdCl_2$ (4.9 mg, 7.0 μmol), and AcOH (25 μL, 0.44 mmol) in THF (4.0 mL) at 25 °C, and the mixture was stirred for 5 h at 25 °C. The mixture was diluted with ethyl acetate (10 mL), and extracted with 2 N aqueous HCl solution (20 mL × 3). The combined extracts were made alkaline with saturated Na_2CO_3, and extracted with chloroform (30 mL × 3). The combined extracts were washed with brine, dried, and concentrated in vacuo to give a residue (9.5 mg). Chromatography on a silica gel column with CH_2Cl_2–MeOH (60:1) gave **7f** (7.0 mg, 65.0%) as a colorless amorphous powder. $[\alpha]_D^{25}$ −65.7 (*c* 0.17, $CHCl_3$); IR (KBr) 3447, 2930, 2853, 2810, 2250w, 1749, 1655, 1508, 1431, 1420, 1375, 1261, 1194, 1107, 1086, 1063, 1028, 802 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz, this compound was a mixture of rotational isomers, ratio 7:3, and only the signals of major isomer are presented) δ 8.98 (7/10H, d, *J* = 4.2 Hz, 2″-H), 8.36 (7/10H, d, *J* = 7.7 Hz, 5″-H), 8.25 (7/10H, d, *J* = 7.7 Hz, 8″-H), 7.88 (7/10H, t, *J* = 7.7 Hz, 7″-H), 7.80 (7/10H, t, *J* = 7.7 Hz, 6″-H), 7.26 (7/10H, d, *J* = 4.3 Hz, 3″-H), 6.43 (7/10H, s, 5′-H), 6.35 (7/10H, br s, 8′-H), 6.11 (7/10H, d, *J* = 0.8 Hz, OCHO), 6.03 (7/10H, br s, 15-H), 6.00 (7/10H, d, *J* = 0.8 Hz, OCHO), 5.75 (7/10H, s, 18-OH), 5.59 (7/10H, br s, 6′-OH), 4.77 (7/10H, d, *J* = 10.2 Hz, 22-H), 4.76 (7/10H, br s, 4-H), 4.44 (7/10H, s, 1-H), 4.34 (7/10H, d, *J* = 10.2 Hz, 22-H), 4.27 (7/10H, d, *J* = 4.5 Hz, 11-H), 4.19 (7/10H, br s, 21-H), 3.67 (21/10H, s, 7′-OCH_3), 3.65 (21/10H, s, 17′-OCH_3), 3.58 (7/10H, br d, *J* = 4.2 Hz, 3-H), 3.55 (7/10H, br d, *J* = 12.5 Hz, 12′-H), 3.47 (7/10H, br, 13-H), 3.25 (7/5H, m, 3′-H_2), 2.98 (7/5H, d, *J* = 8.3 Hz, 14-H_2), 2.68 (7/10H, br d, *J* = 12.5 Hz, 12′-H), 2.40 (7/10H, dd, *J* = 15.8, 5.7 Hz, 4′-H), 2.35 (21/10H, s, $OCOCH_3$), 2.30 (7/10H, dd, *J* = 15.8, 8.5 Hz, 4′-H), 2.14 (21/10H, s, NCH_3), 2.06 (21/10H, s, 6-CH_3), 1.35 (21/10H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.0 (1′-CO), 168.5 (5-OCO), 166.8 (*N*CO), 149.8 (C-2″), 147.6 (C-9″), 147.4 (C-18), 145.5 (C-7), 145.1 (C-7′), 145.5 (C-4″), 145.0 (C-6′), 143.0 (C-17), 141.5 (C-5), 141.1 (C-8), 130.3 (C-6″), 129.9 (C-20), 129.4 (C-8″), 129.0 (C-16), 128.1 (C-7″), 127.1 (C-9′), 126.8 (C-10′),

126.6 (C-5″), 123.8 (C-10″), 122.8 (C-10), 121.6 (C-15), 119.1 (C-3″), 118.2 (21-CN), 117.7 (C-19), 113.8 (C-5′), 113.6 (C-9), 112.6 (C-6), 110.4 (C-8′), 102.0 (OCH_2O), 70.8 (C-1′), 61.6 (C-22), 61.3 (C-3), 60.4 (C-1), 60.1 (17-OCH_3), 59.8 (C-21), 55.4 (7′-OCH_3), 55.0 (C-11), 54.8 (C-13), 45.3 (C-3′), 42.2 (C-4), 41.7 (*N*CH_3), 39.8 (C-12′), 29.6 (C-4′), 25.0 (C-14), 20.4 ($COCH_3$), 15.0 (16-CH_3), 9.9 (6-CH_3); FABMS *m/z* 926 (MH^+); HRFABMS *m/z* 926.3062 (MH^+, calcd for $C_{50}H_{48}N_5O_{11}S$, 926.3071), CD $\Delta\varepsilon$ nm (*c* 10.8 μM, methanol, 21 °C) −9.8 (210), −36.1 (218), −18.0 (231), −14.2 (237), 0 (247), 4.8 (255), 0 (271), −5.0 (288), 0 (300), 1.2 (304), 0 (320).

5.3.17. *N*-5″-Quinolinecarbonyl derivative of Et 770 7g

Tributyltin hydride (60 μL, 0.223 mmol) was added dropwise over 10 min to a vigorously stirred solution of **6g** (13.6 mg, 13.5 μmol), $(Ph_3P)_2PdCl_2$ (5.7 mg, 8.1 μmol), and AcOH (29 μL, 0.51 mmol) in THF (4.0 mL) at 25 °C, and the mixture was stirred for 1 h at 25 °C. The mixture was diluted with ethyl acetate (10 mL) and extracted with 2 N aqueous HCl solution (20 mL × 3). The combined extracts were made alkaline with saturated Na_2CO_3, and extracted with chloroform (30 mL × 3). The combined extracts were washed with brine, dried, and concentrated in vacuo to give a residue (16.4 mg). Chromatography on a silica gel column with CH_2Cl_2–MeOH (60:1) gave **7g** (12.2 mg, 97.7%) as a colorless amorphous powder. $[\alpha]_D^{26}$ −61.2 (*c* 0.39, $CHCl_3$); IR (KBr) 3443, 2936, 2250w, 1749, 1653, 1593, 1503, 1458, 1449, 1431, 1420, 1375, 1261, 1237, 1236, 1196, 1142, 1109, 1086, 1063, 1028, 1005, 810 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz, this compound was a mixture of rotational isomers, ratio 3:2, and only the signals of major isomer are presented) δ 9.03 (3/5H, d, *J* = 2.9 Hz, 2″-H), 8.76 (3/5H, br d, *J* = 6.2 Hz, 4″-H), 8.21 (3/5H, d, *J* = 8.5 Hz, 8″-H), 7.75 (3/5H, dd, *J* = 8.5, 7.1 Hz, 7″-H), 7.60 (3/5H, d, *J* = 2.5 Hz, 3″-H), 7.49 (3/5H, d, *J* = 7.1 Hz, 6″-H), 6.47 (3/5H, s, 8′-H), 6.41 (3/5H, s, 5′-H), 6.10 (3/5H, s, OCHO), 6.02 (3/5H, s, OCHO), 5.97 (73/5H, s, 15-H), 5.77 (3/5H, s, 18-OH), 5.63 (3/5H, s, 6′-OH), 4.72 (3/5H, br s, 4-H), 4.59 (3/5H, br, 22-H), 4.55 (3/5H, br, 22-H), 4.40 (3/5H, s, 1-H), 4.26 (3/5H, d, *J* = 4.3 Hz, 11-H), 4.16 (3/5H, br s, 21-H), 3.70 (9/5H, s, 17-OCH_3), 3.65 (9/5H, s, 7′-OCH_3), 3.60 (3/5H, br, 3-H), 3.57 (3/5H, br d, *J* = 15.3 Hz, 12′-H), 3.47 (3/5H, br, 13-H), 3.24 (6/5H, br t, 3′-H_2), 2.96 (3/5H, dd, *J* = 17.3, 7.9 Hz, 14-Hα), 2.90 (3/5H, d, *J* = 17.3 Hz, 14-Hβ), 2.58 (3/5H, br d, *J* = 15.3 Hz, 12′-H), 2.38 (3/5H, dd, *J* = 15.8, 5.7 Hz, 4′-H), 2.35 (9/5H, s, $OCOCH_3$), 2.27 (3/5H, m, 4′-H), 2.14 (9/5H, s, *N*CH_3), 2.06 (9/5H, s, 6-CH_3), 1.43 (9/5H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.6 (1′-CO), 169.0 (*N*CO), 168.4 (5-OCO), 150.7 (C-2″), 147.6 (C-18), 147.5 (C-5″), 145.5 (C-7), 145.0 (C-6′), 144.9 (C-7′), 143.0 (C-17), 141.4 (C-5), 141.3 (C-8), 135.4 (C-9″), 135.1 (C-4″), 131.3 (C-8″), 129.8 (C-20), 128.9 (C-16), 128.9 (C-7″), 127.9 (C-9′), 126.9 (C-10′), 126.6 (C-6″), 125.0 (C-10″), 122.6 (C-10), 122.1 (C-3″), 121.5 (C-15), 118.2 (21-CN), 117.7 (C-19), 113.9 (C-5′),113.2 (C-9), 112.5 (C-6), 110.4 (C-8′), 102.1 (OCH_2O), 70.0 (C-1′), 61.7 (C-22), 61.5 (C-3), 60.3 (C-1), 60.3 (C-21), 60.1 (17-OCH_3), 55.4 (7′-OCH_3), 55.0 (C-11), 54.8 (C-13), 45.3 (C-3′), 42.0 (C-4), 41.7 (*N*CH_3), 40.1 (C-12′), 29.4 (C-4′), 25.1 (C-14), 20.4 ($COCH_3$), 14.9 (16-CH_3), 9.8 (6-CH_3); FABMS *m/z* 926 (MH^+); HRFABMS *m/z* 926.3069 (MH^+, calcd for $C_{50}H_{48}N_5O_{11}S$, 926.3071), CD $\Delta\varepsilon$ nm (*c* 10.8 μM, methanol, 21 °C) −9.8 (210), −36.1 (218), −18.0 (231), −14.2 (237), 0 (247), 4.8 (255), 0 (271), −5.0 (288), 0 (300), 1.2 (304), 0 (320).

5.3.18. *N*-6″-Quinolinecarbonyl derivative of Et 770 7h

Tributyltin hydride (71 μL, 0.262 mmol) was added dropwise over 10 min to a vigorously stirred solution of **6h** (16.0 mg, 15.9 μmol), $(Ph_3P)_2PdCl_2$ (6.7 mg, 9.6 μmol), and AcOH (34 μL, 0.60 mmol) in THF (4.0 mL) at 25 °C, and the mixture was stirred for 1 h at 25 °C. The mixture was diluted with ethyl acetate (10 mL) and extracted with 2 N aqueous HCl solution (20 mL × 3). The combined extracts were made alkaline with saturated Na_2CO_3, and extracted with chloroform (30 mL × 3). The combined extracts were washed with brine, dried, and concentrated in vacuo to give a residue (14.4 mg). Chromatography on a silica gel column with hexane–ethyl acetate (3:7) gave **7h** (12.5 mg, 85.0%) as a colorless amorphous powder. $[\alpha]_D^{25}$ −43.9 (*c* 0.44, $CHCl_3$); IR (KBr) 3447, 2932, 2855, 2808, 2250w, 1749, 1734, 1653, 1624, 1593, 1516, 1508, 1458, 1449, 1429, 1420, 1395, 1375, 1261, 1238, 1194, 1107, 1086, 1063, 1028 cm^{-1}; ^1H NMR (500 MHz) δ 9.02 (1H, dd, *J* = 4.3, 1.4 Hz, 2″-H), 8.26 (1H, dd, *J* = 8.5, 1.7 Hz, 4″-H), 8.22 (1H, d, *J* = 8.5, 8″-H), 7.97 (1H, d, *J* = 1.4 Hz, 5″-H), 7.65 (1H, dd, *J* = 8.5, 1.4 Hz, 7″-H), 7.51 (1H, dd, *J* = 8.5, 4.3 Hz, 3″-H), 6.57 (1H, br s, 8′-H), 6.42 (1H, s, 5′-H), 6.36 (1H, s, 15-H), 6.11 (1H, d, *J* = 1.3 Hz, OCHO), 6.02 (1H, d, *J* = 1.3 Hz, OCHO), 5.74 (1H, br s, 18-OH), 5.59 (1H, s, 6′-OH), 4.68 (1H, br s, 4-H), 4.58 (1H, br, 22-H), 4.53 (1H, br, 22-H), 4.35 (1H, s, 1-H), 4.26 (1H, dd, *J* = 4.8, 1.4 Hz, 11-H), 4.14 (1H, br s, 21-H), 3.71 (3H, s, 17-OCH_3), 3.64 (1H, d, *J* = 15.3 Hz, 12′-H), 3.61 (3H, s, 7′-OCH_3), 3.61 (1H, br, 3-H, signals overlapped with 7′-OCH_3), 3.56 (1H, m, 3′-H), 3.49 (1H, m, 3′-H), 3.46 (1H, d, *J* = 8.5 Hz, 13-H), 3.01 (1H, dd, *J* = 17.2, 9.4 Hz, 14-Hα), 2.88 (1H, d, *J* = 17.2 Hz, 14-Hβ), 2.45 (1H, dd, *J* = 16.2, 8.5 Hz, 4′-H), 2.39 (2H, m, 12′-H and 4′-H), 2.31 (3H, s, $OCOCH_3$), 2.13 (3H, s, *N*CH_3), 2.05 (3H, s, 6-CH_3), 1.51 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.8 (*N*CO), 169.7 (1′-CO), 168.4 (5-OCO), 151.6 (C-2″), 148.8 (C-9″), 147.5 (C-18), 144.9 (C-7′), 144.8 (C-6′), 145.5 (C-7), 143.0 (C-17), 141.5 (C-8), 141.2 (C-5), 136.7 (C-4″), 135.2 (C-6″), 130.4 (C-20), 129.5 (C-8″), 129.3 (C-16), 129.0 (C-7″), 128.4 (C-5″), 127.8 (C-10″), 127.3 (C-9′), 126.7 (C-10′), 122.2 (C-10), 121.8 (C-3″), 120.8 (C-15), 118.2 (21-CN), 117.8 (C-19), 113.9 (C-5′), 113.2 (C-9), 112.6 (C-6), 110.4 (C-8′), 102.1 (OCH_2O), 69.2 (C-1′), 61.0 (C-3), 60.7 (C-22), 60.3 (C-1), 60.1 (17-OCH_3), 59.8 (C-21), 55.3 (7′-OCH_3), 55.0 (C-13), 54.8 (C-11), 45.8 (C-3′), 41.9 (C-4), 41.7 (*N*CH_3), 39.5 (C-12′), 29.7 (C-4′), 25.0 (C-14), 20.4 ($COCH_3$), 15.3 (16-CH_3), 9.8 (6-CH_3); FABMS *m/z* 926 (MH^+); HRFABMS *m/z* 926.3074 (MH^+, calcd for $C_{50}H_{48}N_5O_{11}S$, 926.3071), CD $\Delta\varepsilon$ nm (*c* 10.8 μM, methanol, 21 °C) −39.9 (210), −68.8 (218), 0 (247), 7.7 (254), 0 (273), −7.1 (288), 0 (302), 1.2 (310), 0 (337).

5.3.19. 18,6′-*O*-Bisallyl-2′-*N*-cinnamoyl Et 770 8a

Compound **4a** (15.3 mg, 0.018 mmol) and DMAP (1.1 mg) were dissolved in pyridine (1.5 mL), and a THF solution of cinnamoyl chloride (1 M, 0.27 mL, 0.27 mmol) was added to this mixture at 0 °C. The reaction mixture was heated at 60 °C for 1 h. After the solvent was removed in vacuo, the residue was diluted with 5% aqueous $NaHCO_3$ solution (20 mL) and extracted with chloroform (15 mL × 3). The combined extracts were washed with brine (15 mL), dried, and concentrated in vacuo to give a residue (49.4 mg). Chromatography on a silica gel column with hexane–ethyl acetate (4:1) gave **8a** (15.6 mg, 88.4%) as a colorless amorphous powder. $[\alpha]_D^{22}$ −35.4 (*c* 0.51, $CHCl_3$); IR (KBr) 3447, 3082, 2934, 2835, 2806, 2250w, 1759, 1659, 1616, 1518, 1487, 1449, 1414, 1375, 1321, 1260, 1238, 1194, 1109, 1086, 1069, 1028, 999, 974, 935, 914, 895, 862 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.54 (2H, d, *J* = 7.1 Hz, 2″-H), 7.40 (4H, m, 3″-H, 4″-H, *N*COCH=C*H*Ar), 6.77 (1H, d, *J* = 15.6 Hz, *N*COC*H*=CHAr), 6.61 (1H, s, 15-H), 6.37 (1H, s, 5′-H), 6.34 (1H, br s, 8′-H), 6.08 (1H, ddd, *J* = 17.3, 10.5, 5.7 Hz, 18-OCH_2CH=CH_2), 6.06 (1H, d, *J* = 0.8 Hz, OCHO), 5.98 (1H, d, *J* = 0.8 Hz, OCHO), 5.97 (1H, ddd, *J* = 17.3, 11.1, 5.4 Hz, 6′-OCH_2CH=CH_2), 5.44 (1H, dd, *J* = 17.0, 1.5 Hz, 18-OCH_2CH=CH_2), 5.31 (1H, dd, *J* = 17.2, 1.4 Hz, 6′-OCH_2CH=CH_2), 5.23 (1H, dd, *J* = 10.3, 1.5 Hz, 18-OCH_2CH=CH_2), 5.22 (1H, dd, *J* = 10.5, 1.4 Hz, 6′-OCH_2CH=CH_2), 4.79 (1H, ddt, *J* = 12.8, 5.3, 1.0 Hz, 18-OCHCH), 4.61 (1H, br, 22-H), 4.60 (1H, br s, 4-H), 4.48 (2H, dt, *J* = 5.4, 1.0 Hz, 6′-OCH_2CH), 4.32 (1H, s, 1-H), 4.31 (1H, dd, *J* = 12.8, 5.3 Hz, 18-OCHCH), 4.30 (1H, br, 22-H), 4.22 (1H, d, *J* = 4.0 Hz,

11-H), 4.11 (1H, d, J = 2.9 Hz, 21-H), 3.84 (3H, s, 17-OCH_3), 3.72 (2H, m, 3′-H_2), 3.61 (3H, s, 7′-OCH_3), 3.57 (1H, br d, J = 5.1 Hz, 3-H), 3.48 (1H, d, J = 15.0 Hz, 12′-H), 3.41 (1H, br, 13-H), 2.92 (2H, d, J = 5.7 Hz, 14-H_2), 2.57 (2H, t, J = 6.0 Hz, 4′-H_2), 2.30 (3H, s, $OCOCH_3$), 2.30 (1H, br, 12′-H, signals overlapped with $OCOCH_3$), 2.15 (3H, s, NCH_3), 2.04 (3H, s, 6-CH_3), 1.99 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.1 (1′-CO), 168.3 (5-OCO), 167.5 (*N*CO), 150.3 (C-18), 148.5 (C-17), 147.4 (C-7′), 147.0 (C-6′), 145.3 (C-7), 141.4 (*N*COCH=CHAr), 141.3 (C-5), 140.8 (C-8), 135.4 (C-1″), 134.7 (18-OCH_2*C*H=CH_2), 133.1 (6′-OCH_2*C*H=CH_2), 131.0 (C-16), 130.2 (C-20), 129.5 (C-4″), 128.8 (C-3″), 128.7 (C-9′), 127.6 (C-2″), 126.3 (C-10′), 124.3 (C-19), 124.5 (C-15), 122.4 (C-10), 120.9 (*N*COCH=*C*HAr), 118.3 (21-CN), 117.9 (6′-OCH_2CH=*C*H_2), 116.6 (18-OCH_2CH=*C*H_2), 113.6 (C-9), 112.8 (C-5′), 112.7 (C-6), 110.7 (C-8′), 102.0 (OCH_2O), 72.9 (18-O*C*H_2CH), 69.6 (6′-O*C*H_2CH), 69.5 (C-1′), 60.9 (C-22), 60.8 (C-3), 60.2 (C-1), 59.7 (C-21), 59.4 (17-OCH_3), 55.3 (C-11), 55.1 (7′-OCH_3), 54.8 (C-13), 43.7 (C-3′), 41.9 (C-4), 41.8 (NCH_3), 39.1 (C-12′), 29.1 (C-4′), 24.7 (C-14), 20.5 ($COCH_3$), 16.1 (16-CH_3), 9.7 (6-CH_3); FABMS m/z 981 (MH^+); HRFABMS m/z 981.3748 (MH^+, calcd for $C_{55}H_{57}N_4O_{11}S$, 981.3744), CD $\Delta\varepsilon$ nm (c 10.2 μM, methanol, 21 °C) −31.5 (210), −56.9 (215), −2.1 (243), 0 (247), 4.4 (254), 0 (272), −1.7 (286), 0 (295), 3.2 (303), 0 (333).

5.3.20. 18,6′-*O*-Bisallyl-2′-*N*-4″-nitrocinnamoyl Et 770 8b

Compound **4a** (15.3 mg, 0.018 mmol) and DMAP (1.1 mg) were dissolved in pyridine (1.5 mL), and a THF solution of 4-nitrocinnamoyl chloride (0.2 M, 1.35 mL, 0.27 mmol) was added to this mixture at 0 °C. The reaction mixture was heated at 60 °C for 1 h. After the solvent was removed in vacuo, the residue was diluted with 5% aqueous $NaHCO_3$ solution (20 mL) and extracted with chloroform (15 mL × 3). The combined extracts were washed with brine (15 mL), dried, and concentrated in vacuo to give a residue (45.0 mg). Chromatography on a silica gel column with hexane–ethyl acetate (4:1) gave **8b** (17.7 mg, 95.9%) as a colorless amorphous powder. $[\alpha]_D^{22}$ −13.8 (c 0.10, $CHCl_3$); IR (KBr) 3447, 3078, 2934, 2808, 2250w, 1759, 1661, 1597, 1520, 1487, 1456, 1447, 1418, 1395, 1373, 1344, 1321, 1260, 1244, 1194, 1109, 1086, 1069, 1028, 999, 975, 935, 841 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 8.28 (2H, d, J = 8.8 Hz, 3″-H), 7.67 (2H, d, J = 8.8 Hz, 2″-H), 7.39 (1H, d, J = 15.5 Hz, *N*COCH=*CH*Ar), 6.92 (1H, d, J = 15.5 Hz, *N*COC*H*=CHAr), 6.58 (1H, s, 15-H), 6.38 (1H, s, 5′-H), 6.30 (1H, br s, 8′-H), 6.08 (1H, ddd, J = 17.3, 10.5, 5.1 Hz, 18-OCH_2C*H*=CH_2), 6.06 (1H, d, J = 1.1 Hz, OCHO), 5.99 (1H, ddd, J = 17.3, 10.5, 5.4 Hz, 6′-OCH_2C*H*=CH_2), 5.98 (1H, d, J = 1.1 Hz, OCHO), 5.45 (1H, dd, J = 17.3, 1.4 Hz, 18-OCH_2CH=C*H*$_2$), 5.32 (1H, dd, J = 17.2, 1.4 Hz, 6′-OCH_2CH=C*H*$_2$), 5.24 (1H, dd, J = 10.5, 1.5 Hz, 18-OCH_2CH=C*H*$_2$), 5.22 (1H, dd, J = 10.5, 1.4 Hz, 6′-OCH_2CH=C*H*$_2$), 4.79 (1H, ddt, J = 12.8, 5.3, 1.0 Hz, 18-O*CH*CH), 4.68 (1H, br d, J = 11.4 Hz, 22-H), 4.62 (1H, br s, 4-H), 4.49 (2H, dt, J = 5.4, 1.0 Hz, 6′-O*C*H_2CH), 4.34 (1H, s, 1-H), 4.32 (1H, dd, J = 12.8, 5.3 Hz, 18-O*CH*CH), 4.23 (1H, br, 22-H), 4.22 (1H, d, J = 5.1 Hz, 11-H), 4.12 (1H, d, J = 2.9 Hz, 21-H), 3.84 (3H, s, 17-OCH_3), 3.74 (2H, m, 3′-H_2), 3.61 (3H, s, 7′-OCH_3), 3.56 (1H, br d, J = 5.1 Hz, 3-H), 3.50 (1H, d, J = 15.5 Hz, 12′-H), 3.42 (1H, br, 13-H), 2.92 (2H, d, J = 5.6 Hz, 14-H_2), 2.59 (2H, t, J = 6.0 Hz, 4′-H_2), 2.41 (1H, br, 12′-H), 2.30 (3H, s, $OCOCH_3$), 2.15 (3H, s, NCH_3), 2.04 (3H, s, 6-CH_3), 1.95 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 168.8 (1′-CO), 168.2 (5-OCO), 166.2 (*N*CO), 150.3 (C-18), 148.6 (C-17), 148.4 (C-4″), 147.6 (C-7′), 147.2 (C-6′), 145.4 (C-7), 141.6 (C-1″), 141.4 (C-5), 140.7 (C-8), 138.3 (*N*COCH=CHAr), 134.7 (18-OCH_2*C*H=CH_2), 133.1 (6′-OCH_2*C*H=CH_2), 130.7 (C-16), 130.3 (C-20), 128.3 (C-10′), 128.0 (C-2″), 126.1 (C-9′), 125.6 (*N*COCH=*C*HAr), 124.6 (C-19), 124.3 (C-15), 124.2 (C-3″), 122.3 (C-10), 118.2 (21-CN), 117.9 (6′-OCH_2CH=*C*H_2), 116.7 (18-OCH_2CH=*C*H_2), 113.9 (C-9), 112.7 (C-5′), 112.7 (C-6), 110.7 (C-8′), 102.0 (OCH_2O), 72.9 (18-O*C*H_2CH), 70.1 (C-1′), 69.7 (6′-O*C*H_2CH), 61.0 (C-22), 60.8 (C-3), 60.4 (C-1), 59.7 (C-21), 59.4 (17-OCH_3), 55.3 (C-11), 55.1 (7′-OCH_3), 54.7 (C-13), 44.0 (C-3′), 42.0 (C-4), 41.8 (NCH_3), 38.9 (C-12′), 29.2 (C-4′), 24.6 (C-14), 20.53 ($COCH_3$), 16.3 (16-CH_3), 9.7 (6-CH_3); FABMS m/z 1026 (MH^+); HRFABMS m/z 1026.3595 (MH^+, calcd for $C_{55}H_{56}N_5O_{13}S$, 1026.3595), CD $\Delta\varepsilon$ nm (c 10.2 μM, methanol, 21 °C) −60.4 (210), −99.4 (215), 0 (241), 9.7 (252), 0 (268), −10.4 (286), 0 (299), 5.5 (318), 0 (376).

5.3.21. 2′-*N*-Cinnamoyl Et 770 9a

Tributyltin hydride (64 μL, 0.24 mmol) was added dropwise over 10 min to a vigorously stirred solution of **8a** (14.2 mg, 14.5 μmol), $(Ph_3P)_2PdCl_2$ (6.1 mg, 8.7 μmol), and AcOH (31 μL, 0.54 mmol) in THF (4.0 mL) at 25 °C, and the mixture was stirred for 2 h at 25 °C. The mixture was diluted with water (10 mL), made alkaline with 5% aqueous $NaHCO_3$, and extracted with chloroform (30 mL × 3). The combined extracts were washed with 5% aqueous $NaHCO_3$, dried, and concentrated in vacuo to give a residue (88.0 mg). The residue was subjected to chromatography on a silica gel with hexane–ethyl acetate (1:1) to afford **9a** (6.0 mg, 46.0%) and **10a** (2.5 mg, 18.3%).

5.3.21.1. Compound 9a. A colorless amorphous powder, $[\alpha]_D^{22}$ −13.8 (c 0.1, $CHCl_3$); IR (KBr) 3447, 2934, 2250w, 1757, 1653, 1616, 1593, 1514, 1449, 1431, 1420, 1402, 1395, 1373, 1304, 1263, 1196, 1107, 1086, 1065, 1028, 1005, 974, 962, 862 cm^{-1}; ^1H NMR (500 MHz) δ 7.52 (2H, dd, J = 8.2, 1.2 Hz, 2″-H), 7.46–7.40 (4H, m, 3″-H, 4″-H, *N*COCH=C*H*Ar), 6.75 (1H, d, J = 15.5 Hz, *N*COC*H*=CHAr), 6.44 (1H, s, 5′-H), 6.42 (1H, s, 15-H), 6.36 (1H, br s, 8′-H), 6.07 (1H, d, J = 1.3, OCHO), 5.98 (1H, d, J = 1.3 Hz, OCHO), 5.71 (1H, s, 18-OH), 5.45 (1H, s, OH), 4.61 (1H, br s, 4-H), 4.59 (1H, br d, J = 11.1 Hz, 22-H), 4.34 (1H, br d, J = 11.1 Hz, 22-H), 4.32 (1H, s, 1-H), 4.25 (1H, dd, J = 4.7, 1.4 Hz, 11-H), 4.10 (1H, d, J = 2.6 Hz, 21-H), 3.77 (3H, s, 17-OCH_3), 3.68 (2H, br t, 3′-H_2), 3.65 (3H, s, 7′-OCH_3), 3.56 (1H, br d, J = 4.8 Hz, 3-H), 3.51 (1H, d, J = 15.5 Hz, 12′-H), 3.40 (1H, br, 13-H), 2.93 (1H, dd, J = 17.5, 8.5 Hz, 14-Hα), 2.88 (1H, d, J = 17.5 Hz, 14-Hβ), 2.56 (2H, t, J = 6.0 Hz, 4′-H_2), 2.33 (3H, s, $OCOCH_3$), 2.32 (1H, br d, J = 15.5 Hz, 12′-H), 2.15 (3H, s, NCH_3), 2.04 (3H, s, 6-CH_3), 2.01 (3H, s, 16-CH_3); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 169.2 (1′-CO), 168.4 (5-OCO), 167.5 (*N*CO), 147.5 (C-18), 144.8 (C-7′), 144.8 (C-6′), 147.7 (C-17), 141.4 (*N*COCH=CHAr), 141.3 (C-5), 140.9 (C-7), 140.9 (C-8), 135.3 (C-1″), 130.6 (C-20), 129.5 (C-4″), 129.2 (C-16), 128.9 (C-3″), 128.0 (C-9′), 127.6 (C-2″), 127.2 (C-10′), 122.3 (C-10), 120.9 (*N*COCH=*C*HAr), 120.7 (C-15), 118.3 (21-CN), 117.9 (C-19), 113.8 (C-5′), 113.6 (C-9), 112.6 (C-6), 1109.9 (C-8′), 102.0 (OCH_2O), 69.5 (C-1′), 61.1 (C-22), 60.9 (C-3), 60.2 (C-21), 60.2 (17-OCH_3), 60.0 (C-1), 55.3 (7′-OCH_3), 54.9 (C-11), 54.8 (C-13), 43.8 (C-3′), 41.9 (C-4), 41.7 (NCH_3), 39.3 (C-12′), 28.9 (C-4′), 24.7 (C-14), 20.4 ($COCH_3$), 16.1 (16-CH_3), 9.8 (6-CH_3); FABMS m/z 901 (MH^+); HRFABMS m/z 901.3124 (MH^+, calcd for $C_{49}H_{49}N_4O_{11}S$, 901.3119), CD $\Delta\varepsilon$ nm (c 10.8 μM, methanol, 21 °C) −37.6 (210), −60.7 (218), 0 (244), 5.8 (254), 0 (267), −9.1 (287), 0 (297), 3.2 (303), 0 (339).

5.3.21.2. Compound 10a. A colorless amorphous powder, IR (KBr) 3424, 2928, 2853, 2808, 2250w, 1759, 1655, 1616, 1514, 1449, 1418, 1375, 1321, 1263, 1236, 1194, 1107, 1085, 1068, 1028, 993, 974, 912, 895, 866 cm^{-1}; ^1H NMR (300 MHz) δ 7.53 (2H, dd, J = 7.8, 1.2 Hz, 2″-H), 7.43–7.35 (4H, m, 3″-H, 4″-H, *N*COCH=C*H*Ar), 6.75 (1H, d, J = 15.6 Hz, *N*COC*H*=CHAr), 6.61 (1H, s, 5′-H), 6.44 (1H, s, 15-H), 6.40 (1H, br s, 8′-H), 6.09 (1H, ddd, J = 17.3, 10.5, 5.1 Hz, 18-OCH_2C*H*=CH_2), 6.07 (1H, d, J = 1.3, OCHO), 5.98 (1H, d, J = 1.3 Hz, OCHO), 5.45 (1H, dd, J = 17.4, 1.7 Hz, 18-OCH_2CH=C*H*$_2$), 5.43 (1H, s, 6′-OH), 5.23 (1H, dd, J = 10.4, 1.7 Hz, 18-OCH_2CH=C*H*$_2$), 4.79 (1H, dd, J = 12.6, 5.0 Hz, 18-OCH_2CH=C*H*$_2$), 4.58 (1H, br s, 4-H), 4.58 (1H, br d, J = 11.1 Hz, 22-H), 4.34 (1H, br d,

J = 11.1 Hz, 22-H), 4.34 (1H, dd, J = 12.6, 1.7 Hz, 18-OCH_2CH=CH_2), 4.32 (1H, s, 1-H), 4.22 (1H, dd, J = 5.0, 1.6 Hz, 11-H), 4.11 (1H, d, J = 2.7 Hz, 21-H), 3.84 (3H, s, 17-OCH_3), 3.67 (2H, br t, 3′-H_2), 3.65 (3H, s, 7′-OCH_3), 3.56 (1H, br d, J = 4.6 Hz, 3-H), 3.49 (1H, d, J = 14.7 Hz, 12′-H), 3.41 (1H, br, 13-H), 2.91 (2H, br d, J = 7.9 Hz, 14-H_2), 2.58 (2H, t, J = 5.7 Hz, 4′-H_2), 2.41 (1H, br d, J = 15.5 Hz, 12′-H), 2.33 (3H, s, $OCOCH_3$), 2.15 (3H, s, NCH_3), 2.04 (3H, s, 6-CH_3), 1.98 (3H, s, 16-CH_3); FABMS m/z 941 (MH^+); HRFABMS m/z 941.3428 (MH^+, calcd for $C_{52}H_{53}N_4O_{11}S$, 941.3432).

5.3.22. 2′-*N*-4″-Nitrocinnamoyl Et 770 9b

Tributyltin hydride (77 μL, 0.29 mmol) was added dropwise over 10 min to a vigorously stirred solution of **8b** (17.7 mg, 17.3 μmol), $(Ph_3P)_2PdCl_2$ (7.3 mg, 8.7 μmol), and AcOH (37 μL, 0.65 mmol) in THF (4.0 mL) at 25 °C, and the mixture was stirred for 1 h at 25 °C. The mixture was diluted with water (10 mL), made alkaline with 5% aqueous $NaHCO_3$, and extracted with chloroform (30 mL × 3). The combined extracts were washed with 5% aqueous $NaHCO_3$, dried, and concentrated in vacuo to give a residue (98.2 mg). The residue was subjected to chromatography on a silica gel with hexane–ethyl acetate (1:1) to afford **9b** (3.3 mg, 20.2%) and **10b** (3.7 mg, 22.6%).

5.3.22.1. Compound 9b. A pale yellow amorphous powder, IR (KBr) 3447, 2934, 2855, 2808, 2250w, 1757, 1751, 1655, 1618, 1597, 1520, 1458, 1420, 1373, 1344, 1263, 1236, 1196, 1086, 1065, 1028, 862 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.28 (2H, d, J = 8.8 Hz, 3″-H), 7.65 (2H, d, J = 8.8 Hz, 2″-H), 7.36 (1H, d, J = 15.5 Hz, *N*COCH=C*H*Ar), 6.89 (1H, d, J = 15.5 Hz, *N*COC*H*=CHAr), 6.46 (1H, s, 15-H), 6.40 (1H, s, 5′-H), 6.32 (1H, br s, 8′-H), 6.07 (1H, d, J = 1.1 Hz, OCHO), 5.98 (1H, d, J = 1.1 Hz, OCHO), 5.70 (1H, s, 18-OH), 5.47 (1H, s, 6′-OH), 4.66 (1H, br d, J = 10.8 Hz, 22-H), 4.65 (1H, br s, 4-H), 4.34 (1H, s, 1-H), 4.23 (1H, br, 22-H), 4.25 (1H, dd, J = 4.9, 1.2 Hz, 11-H), 4.11 (1H, d, J = 2.7 Hz, 21-H), 3.77 (3H, s, 17-OCH_3), 3.70 (2H, m, 3′-H_2), 3.65 (3H, s, 7′-OCH_3), 3.55 (1H, d, J = 6.2 Hz, 3-H), 3.50 (1H, d, J = 14.5 Hz, 12′-H), 3.42 (1H, br, 13-H), 2.91 (2H, d, J = 6.2 Hz, 14-H_2), 2.58 (2H, t, J = 5.7 Hz, 4′-H_2), 2.41 (1H, br, 12′-H), 2.33 (3H, s, $OCOCH_3$), 2.15 (3H, s, NCH_3), 2.04 (3H, s, 6-CH_3), 1.98 (3H, s, 16-CH_3); FABMS m/z 946 (MH^+); HRFABMS m/z 946.2964 (MH^+, calcd for $C_{49}H_{48}N_5O_{13}S$, 946.2970), CD $\Delta\varepsilon$ nm (c 10.1 μM, methanol, 21 °C) −37.8 (210), −57.6 (215), 0 (242), 6.0 (251), 0 (264), −10.3 (287), 0 (308), 2.6 (314), 0 (385).

5.3.22.2. Compound 10b. A pale yellow amorphous powder, IR (KBr) 3447, 2934, 2853, 1808, 2250w, 1751, 1655, 1618, 1597, 1520, 1447, 1418, 1373, 1344, 1321, 1265, 1236, 1196, 1109, 1086, 1069, 1028, 999 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.28 (2H, d, J = 8.8 Hz, 3″-H), 7.67 (2H, d, J = 8.8 Hz, 2″-H), 7.38 (1H, d, J = 15.7 Hz, *N*COCH=C*H*Ar), 6.90 (1H, d, J = 15.7 Hz, *N*COC*H*=CHAr), 6.58 (1H, s, 15-H), 6.45 (1H, s, 5′-H), 6.31 (1H, br s, 8′-H), 6.09 (1H, ddd, J = 17.3, 10.5, 5.1 Hz, 18-OCH_2CH=CH_2), 6.07 (1H, d, J = 1.1 Hz, OCHO), 5.98 (1H, d, J = 1.1 Hz, OCHO), 5.45 (1H, ddd, J = 17.3, 10.5, 5.1 Hz, 18-OC*H*$_2$CH=CH_2), 5.45 (1H, s, 6′-OH), 5.24 (1H, ddd, J = 17.3, 10.5, 1.5 Hz, 18-OC*H*$_2$CH=CH_2), 4.79 (1H, ddt, J = 12.8, 5.1, 1.5 Hz, 18-OCH_2CH=C*H*$_2$), 4.63 (1H, br d, J = 11.5 Hz, 22-H), 4.62 (1H, br s, 4-H), 4.36 (1H, dd, J = 12.8, 5.1 Hz, 18-OCH_2CH=C*H*$_2$), 4.33 (1H, s, 1-H), 4.26 (1H, br, 22-H), 4.23 (1H, dd, J = 4.9, 1.3 Hz, 11-H), 4.12 (1H, d, J = 2.7 Hz, 21-H), 3.84 (3H, s, 17-OCH_3), 3.71 (2H, t, J = 5.7 Hz, 3′-H_2), 3.65 (3H, s, 7′-OCH_3), 3.55 (1H, d, J = 4.9 Hz, 3-H), 3.51 (1H, d, J = 14.5 Hz, 12′-H), 3.42 (1H, br, 13-H), 2.91 (2H, d, J = 5.3 Hz, 14-H_2), 2.58 (2H, t, J = 5.8 Hz, 4′-H_2), 2.38 (1H, br d, J = 15.6 Hz, 12′-H), 2.30 (3H, s, $OCOCH_3$), 2.15 (3H, s, NCH_3), 2.05 (3H, s, 6-CH_3), 1.95 (3H, s, 16-CH_3); FABMS m/z 986 (MH^+); HRFABMS m/z 986.3284 (MH^+, calcd for $C_{52}H_{52}N_5O_{13}S$, 986.3283), CD $\Delta\varepsilon$ nm (c 10.1 μM, methanol, 21 °C) −35.7 (210), −52.7 (215), 0 (242), 5.1 (253), 0 (268), −5.8 (292), 0 (308), 2.8 (312), 0 (380).

6. Cell growth inhibition assay (IC_{50})

A single-cell suspension (2×10^3 cells/well) was added to serially diluted test compounds in a microplate. The cells were then cultured for 4 d. Cells were enumerated with a cell counting kit (DOJINDO, Osaka, Japan). IC_{50} was expressed as the concentration at which cell growth was inhibited by 50% compared with the untreated control.

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