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*Article*

# Synthesis and Anti-HBV Activity of Novel 3′-*N*-phenylsulfonyl Docetaxel Analogs

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**Abstract:** Nine new 3′-*N*-phenylsulfonyl docetaxel analogs were synthesized in good yields from the key intermediate *N*-phenylsulfonyl oxazolidine via a six-step route. These analogs were tested for anti-hepatitis B virus (HBV) activity in vitro. Compounds **3e**, **3g** and **3j** showed more potent inhibitory activity against HBeAg secretion than the positive control lamivudine. Further extensive SAR and mechanistic studies will be reported in due course.

**Keywords:** 3′-*N*-phenylsulfonyl; docetaxel analogs; synthesis; anti-HBV

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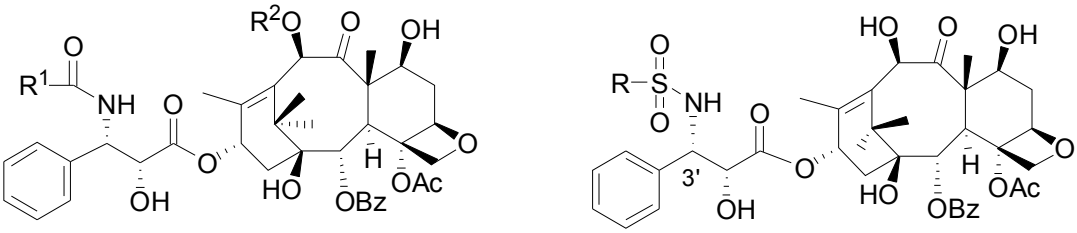
## 1. Introduction

Hepatitis B virus (HBV) is a major cause of acute and chronic hepatitis which can lead to liver cirrhosis, liver failure and hepatocellular carcinoma [1]. It was estimated there are 350 million chronic carriers and that about 2 billion people have been infected, and an estimated 600,000 to 1.2 million people die each year from HBV-associated illnesses [2,3]. Currently, therapies for HBV infection on market include immuno-modulators, interferons (interferon-alpha and pegylated interferon) and nucleoside analogues. However, these drugs still have their drawbacks. For example, immune-modulators (IFN-a and pegIFN-a) and polymerase inhibitors (lamivudine, entecavir, telbivudine and adefovir) are associated with a low cure rate, viral resistance, poor tolerability, and inefficiency in eradicating HBV [4–7]. Therefore, there is a need to search for new anti-HBV agents with novel antiviral targets and mechanisms of action.

Natural products and their derivatives have always played a pivotal role as leads in drug discovery. Paclitaxel (**1**, Figure 1) and its semi-synthetic derivative docetaxel (Taxotere, **2**), are currently considered to be the most important and promising anticancer agents in the treatment of refractory breast and ovarian cancers due to their unique mechanism of action by binding tubulin and stabilizing microtubule formation, which ultimately disrupts mitosis and causes cell death [8]. In our studies of docetaxel derivatives as anticancer agents [9,10], many analogs were synthesized, including one 3′-*N*-phenylsulfonyl docetaxel analog. It was found that this 3′-*N*-phenylsulfonyl docetaxel analog didn't show any potent antitumor activity [11,12]. However, it has been reported that a large number of structurally novel sulfonamide derivatives have shown substantial antiviral activity both *in vitro* and *in vivo* [13,14]. Accordingly, a series of novel 3′-*N*-phenylsulfonyl docetaxel analogs were designed, synthesized and investigated for their HBV inhibitory activity. It was hoped that a promising lead could be emerged from this type of structure.

**Figure 1.** Structure of paclitaxel, docetaxel and 3′-*N*-phenylsulfonyl docetaxel analogs.




**1** paclitaxel $R^1$ = Ph, $R^2$ = Ac
**2** docetaxel $R^1$ = *t*-BuO, $R^2$ = H

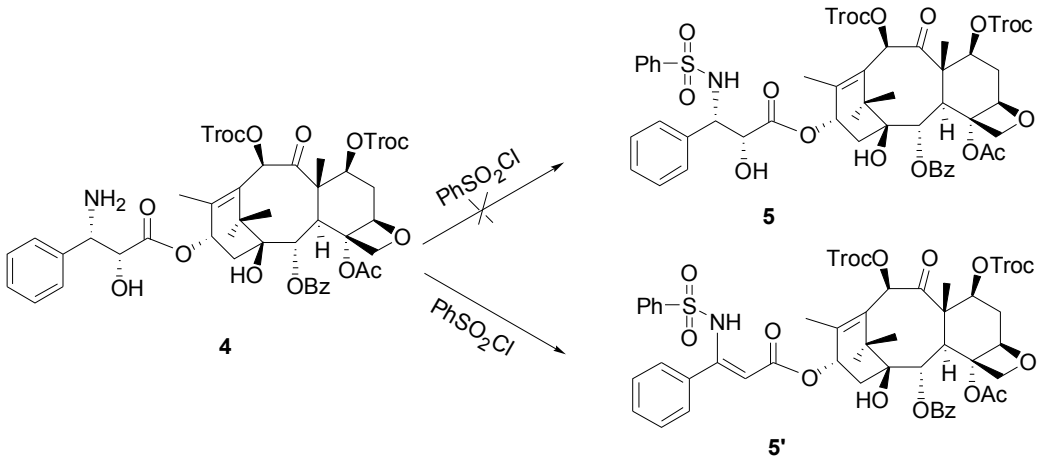
**3**

## 2. Results and Discussion

### *2.1. Chemistry*

In order to synthesize these 3′-*N*-phenylsulfonyl docetaxel analogues, several synthetic routes were approached. The first attempt was to couple the intermediate *N*-de-*tert*-butoxy-carbonyl-7,10-ditroc-docetaxel (**4**) with phenylsulfonyl chloride directly (Scheme 1).

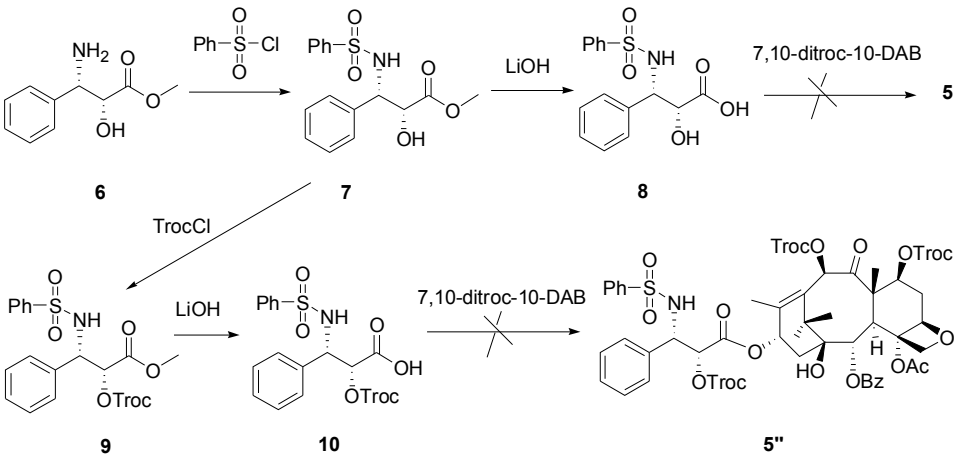
**Scheme 1.** Attempted synthesis of compound **5**.



However, ESIMS of the product showed a quasimolecular ion peak at m/z 852 $[M+Na]^+$, indicating a molecular weight of 829, or 18 Da lower than that of **5**. Since the H-3′ peak had disappeared in $^1$H-NMR spectrum, it was suggested that the dehydrated product **5′** was obtained rather than **5**. Obviously the elimation occurred quickly since the benzenesulfonate is a very good leaving group formed by phenylsulfonyl and hydroxyl groups.

The second attempt was to synthesize the side chain from (2*R*,3*S*)-3-amino-2-hydroxy-3-phenyl-propionic acid methyl ester (**6**), as illustrated in Scheme 2. Compound **6** was transformed into phenylsulfonamide **7** with phenylsulfonyl chloride, followed by saponification to afford acid **8**. However, the coupling reaction between **8** and the intermediate 7,10-ditroc-10-deacetylbaccatin failed to yield **5**, partially because **8** was more prone to undergo self-condensation due to the steric hindrance of the hydroxyl group in 10-DAB. Since the free hydroxyl group in **7** interfered with the reaction, we decided to protect it first. Thus, after protecting the hydroxyl group of **7** with 2,2,2-trichloroethyl chloroformate (TrocCl) followed by saponification, the carboxylic acid **10** was obtained as expected. However, the desired product **5″** was still not formed when **10** reacted with 7,10-ditroc-10-DAB.

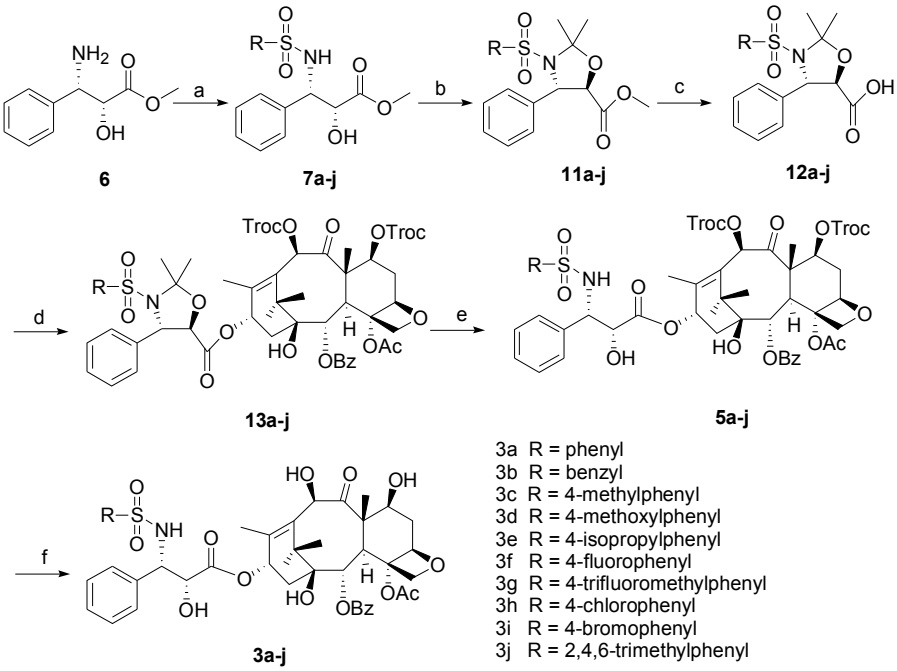
**Scheme 2.** Another attempted synthesis of compound **5**.




Ke *et al.* reported the synthesis of novel 3′-*N*-*tert*-butylsulfonyl analogs of docetaxel by asymmetric synthesis of the side chain oxazolidine and condensing this oxazolidine with 7,10-ditroc-10-DAB [12]. Unfortunately, the oxazolidine is only obtained as diastereomeric mixtures via five steps from (*R*)-*tert*-butylsulfinylimine. We previously reported the synthesis of fluorinated docetaxel derivatives from the enantiopure *N*-Boc oxazolidine side chain [9,10]. Therefore, *N*-phenylsulfonyl oxazolidine could be used as an important intermediate for this condensation reaction. Finally, compounds **3a**–**j** were synthesized via a new six-step route in good yields from (2*R*,3*S*)-3-amino-2-hydroxy-3-phenyl-propionic acid methyl ester (**6**), a commercially available starting material, as illustrated in Scheme 3. Compound **6** was first transformed into phenylsulfonamides **7a**–**j** with phenylsulfonyl chloride. Cyclic protection using methoxypropene in the presence of a catalytic amount of pyridinium *para*-toluenesulfonate (PPTS) followed by saponification of the formed intermediates **11a**–**j** afforded acids **12a**–**j** in 80%–95% yields. Then, key intermediates **12a**–**j** were coupled with 7,10-ditroc-10-DAB in the presence of dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP) to provide the corresponding intermediates **13a**–**j** in 85%–95% yields. After removing the acetonide protecting group of **13a**–**j** with 98% formic acid at room temperature**,** intermediates **5a**–**j** were obtained in 57%–85% yields. After further

deprotection of the 7,10-ditroc protecting groups on **5a**–**j** with zinc in acetic acid, 3′-*N*-phenylsulfonyl docetaxel analogs **3a**–**j** were synthesized in 53%–80% yields.

**Scheme 3.** Synthesis of compounds **3a**–**j**.




*Reagents and conditions:* (a) $RSO_2Cl/Et_3N$, $CH_2Cl_2$, 0 °C-r.t., 1 h; (b) $CH_2 = C(OCH_3)CH_3$, PPTs, toluene, 85 °C, 2 h; (c) LiOH, THF/$H_2O$, r.t., 1 h; (d) 7,10-ditroc-10-DAB, DCC, DMAP, toluene; 85 °C, 3 h; (e) HCOOH, r.t., 1.5 h; (f) Zn/HOAc, MeOH, 50 °C, 1 h.

## *2.2. Anti-HBV Activity*

With compounds **3a**–**j** in hand, they were tested for their antiviral activity against hepatitis B virus (HBV) *in vitro* [15], and the results are summarized in Table 1.

**Table 1.** Anti-HBsAg and anti-HBeAg effects of compounds **3a**–**j** in HepG2 2.2.15 cell line.

| | MNTC [b] (in μM or μg/mL) | HBsAg inhibition (%) | HBeAg inhibition (%) |
|---|---|---|---|
| **3a** | 7.4 (6.25) | 10.7 | 19.2 |
| **3b** | 14.5 (12.5) | 10.0 | 34.1 |
| **3c** | 14.5 (12.5) | 0 | 11.4 |
| **3d** | 28.5 (25) | 11.8 | 14.8 |
| **3e** | 14.1 (12.5) | 0 | **44.4** |
| **3f** | 28.9 (25) | 0 | 3.0 |
| **3g** | 13.7 (12.5) | 0 | **47.0** |
| **3h** | 14.2 (12.5) | 5.0 | 25.8 |
| **3i** | 13.5 (12.5) | 0 | 26.0 |
| **3j** | 14.1 (12.5) | 0 | **40.2** |
| **Docetaxel** | 7.7 (6.25) | 0 | **8.2** |
| **Paclitaxel** | 7.3 (6.25) | 0 | **5.3** |
| 3TC [a] | 873.4 (200) | 10.9 | 12.5 |

[a] Positive control (3TC = Lamivudine); [b] Maximum non-toxic concentration. Cell damage was assessed by means of the MTT assay; cell growth inhibition ≥25% was considered as cytotoxic.

Overall, the compounds showed only weak or no inhibitory activity on HBsAg secretion, except for compounds **3c** and **3f**, **3a**–**b**, **3d**–**e** and **3g**–**j** that exhibited more potency against HBeAg secretion than the positive control lamivudine (12.5% at 873.4 μM). Especially, **3e**, **3g** and **3j** showed inhibitory activity on HBeAg secretion by 44.4%, 47.0% and 40.2% at the maximum non-toxic concentration (12.5 μg/mL), respectively.

Preliminary structure-activity relationships (SAR) did not show a clear trend in terms of electron-withdrawing or electron-donating substituents on the phenyl ring. Only phenyl (**3a**), 4-methoxyl (**3d**), 4-chloro (**3h**) and benzyl (**3b**) analogs exihibited weaker inhibitory activity against both HBsAg secretion and HBeAg secretion. However, 4-isopropyl (**3e**), 4-trifluoromethyl (**3g**) and 2,4,6-trimethyl (**3j**) analogs demonstrated the most potent inhibitory activity against HBeAg secretion. Meanwhile, they were all inactive against HBsAg secretion. Accordingly, further extensive SAR study on the substituent pattern on phenyl ring and modification of the linker (based on the result of **3b**) will be continued in the near future.

## 3. Experimental

### *3.1. General*

Reagents were purchased from the Aldrich (Shanghai, China) and TCI Chemical (Shanghai, China) companies. All solvents are purified and dried in accordance with standard procedures, unless otherwise indicated. Reactions were monitored by TLC using Yantai (Yantai, China) GF254 silica gel plates (5 × 10 cm). Silica gel column chromatography was performed on silica gel (300–400 mesh) from Yantai. Melting points (mp) were determined using an X-4 microscope melting point apparatus and were uncorrected. All NMR spectra were recorded on a Bruker DRX-400 (400/100 MHz) spectrometer. Low-resolution mass spectra (ESI) were performed on a Shimadzu LCMS-2010EV and high-resolution mass spectra on a Bruker Daltonics, Inc. APEXIII7.0 TESLA FMS (ESI). Elemental analysis was carried out on an Elementar Vario EL instrument.

### *3.2. Synthesis*

#### 3.2.1. General Procedure for the Synthesis of **7a**–**j**

To a round-bottomed flask (2*R*,3S)-*3*-amino-2-hydroxy-3-phenyl-propionic acid methyl ester (**6**, 0.39 g, 2 mmol) was added into THF (15 mL), which was cooled to 0 $^{o}$C. To this suspension was added $Et_3N$ (1.11 mL, 8 mmol), followed by the dropwise addition of phenylsulfonyl chloride (2.2 mmol). After further stirred at this temperature for 1 h, it was diluted with DCM (30 mL). The organic layer was washed with brine, dried over anhydrous $Na_2SO_4$ and filtered. Then the filtrate was evaporated and the residue was purified by column chromatography using petroleum ether/EtOAc (2/1) to afford the products **7a**–**j** as white solids.

*2-Hydroxy-3-benzenesulfonylamino-3-phenyl-propionic acid methyl ester* (**7a**). Yield 59% (395 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 3.60 (s, 3H, $OCH_3$), 4.35 (d, 1H, $J$ = 3.2 Hz, 2-CH), 4.88 (d, 1H, $J$ = 3.2 Hz, 3-CH), 7.14 (m, 3H, 3-Ph), 7.27 (m, 2H, 3-Ph), 7.35 (t, 2H, $J$ = 7.6 Hz, *m*-$PhSO_2$), 7.46 (t, 1H, $J$ = 7.6 Hz, *p*-$PhSO_2$), 7.66 (t, 2H, $J$ = 7.6 Hz, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): $\delta$ 172.72, 142.67, 139.31, 132.76,

129.44, 128.72, 128.26, 128.07, 127.63, 75.45, 60.92, 52.52; ESI-MS (*m/z*): 336 [M + H]$^+$. HRMS (ESI) *m/z* calcd. for $C_{16}H_{17}NO_5SNa$ [M + Na]$^+$: 358.0725, found 358.0704.

*2-Hydroxy-3-phenylmethane sulfonylamino-3-phenyl-propionic acid methyl ester* (**7b**). Yield 59% (412 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 3.69 (s, 3H, $OCH_3$), 4.01 (d, 1H, $J$ = 13.2 Hz, $CH_2$ in Bn), 4.13 (d, 1H, $J$ = 14.0 Hz, $CH_2$ in Bn), 4.44 (d, 1H, $J$ = 4.0 Hz, 2-CH), 4.93 (d, 1H, $J$ = 3.6 Hz, 3-CH), 7.19 (m, 2H, 3-Ph), 7.27 (m, 3H, 3-Ph), 7.39 (m, 3H, Ph in Bn), 7.52 (m, 2H, Ph in Bn); $^{13}$C-NMR ($CD_3COCD_3$): 172.92, 140.33, 131.73, 130.88, 129.21, 129.03, 128.85, 128.66, 128.61, 75.63, 61.10, 60.41, 52.56; ESI-MS (*m/z*): 350 [M + H]$^+$. HRMS (ESI) *m/z* calcd. for $C_{17}H_{19}NO_5SNa$ [M + Na]$^+$: 372.0882, found 372.0859.

*2-Hydroxy-3-(4-methyl benzenesulfonylamino)-3-phenyl-propionic acid methyl ester* (**7c**). Yield 64% (448 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 2.31 (s, 3H, $CH_3$ in Tosyl), 3.60 (s, 3H, $OCH_3$), 4.34 (d, 1H, $J$ = 2.8 Hz, 2-CH), 4.84 (d, 1H, $J$ = 3.6 Hz, 3-CH), 7.27 (m, 5H, 3′-Ph), 7.26 (m, 2H, Ph in Tosyl), 7.53 (d, 2H, $J$ = 8.0 Hz, Ph in Tosyl); $^{13}$C-NMR ($CD_3COCD_3$): 172.73, 143.39, 139.45, 129.92, 128.70, 128.29, 127.96, 127.73, 75.45, 60.87, 52.50, 21.29; ESI-MS (*m/z*): 350 [M + H]$^+$. HRMS (ESI) *m/z* calcd. for $C_{17}H_{19}NO_5SNa$ [M + Na]$^+$: 372.0882, found 372.0869.

*2-Hydroxy-3-(4-methoxy benzenesulfonylamino)-3-phenyl-propionic acid methyl ester* (**7d**). Yield 59% (432 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 3.63 (s, 3H, 3′-$CH_3$), 3.81 (s, 3H, $OCH_3$), 4.33 (d, 1H, $J$ = 4.0 Hz, 2-CH), 4.83 (d, 1H, $J$ = 3.2 Hz, 3-CH), 6.85 (m, 2H, $PhSO_2$), 7.15 (m, 3H, 3-Ph), 7.26 (m, 2H, 3-Ph), 7.57 (m, 2H, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 172.74, 163.31, 139.38, 134.30, 129.78, 128.94, 128.70, 128.29, 114.52, 75.50, 60.86, 55.98, 52.53; ESI-MS (*m/z*): 366 [M + H]$^+$. HRMS (ESI) *m/z* calcd. for $C_{17}H_{19}NO_6SNa$ [M + Na]$^+$: 388.0831, found 388.0837.

*2-Hydroxy-3-(4-isopropyl benzenesulfonylamino)-3-phenyl-propionic acid methyl ester* (**7e**). Yield 59% (445 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.19 (d, 6H, $J$ = 3.2 Hz, 2$CH_3$ in *i*-PrPh), 2.89 (m, 1H, CH in *i*-PrPh), 3.61 (s, 3H, $OCH_3$), 4.34 (d, 1H, $J$ = 3.2 Hz, 2-CH), 4.85 (d, 1H, $J$ = 2.8 Hz, 3-CH), 7.12 (m, 3H, 3-Ph), 7.19 (d, 2H, $J$ = 8.4 Hz, $PhSO_2$), 7.23 (m, 2H, 3-Ph), 7.40 (m, 2H, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 172.74, 154.05, 139.99, 139.20, 128.66, 128.31, 127.97, 127.87, 127.38, 75.44, 60.91, 52.51, 34.74, 23.93; ESI-MS (*m/z*): 378 [M + H]$^+$. HRMS (ESI) *m/z* calcd. for $C_{19}H_{23}NO_5SNa$ [M + Na]$^+$: 400.1195, found 400.1180.

*2-Hydroxy-3-(4-fluoro benzenesulfonylamino)-3-phenyl-propionic acid methyl ester* (**7f**). Yield 49% (346 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 3.66 (s, 3H, $OCH_3$), 4.35 (d, 1H, $J$ = 2.8 Hz, 2-CH), 4.88 (d, 1H, $J$ = 3.2 Hz, 3-CH), 7.08 (t, 2H, $J$ = 8.8 Hz, $PhSO_2$), 7.15 (m, 3H, 3-Ph), 7.26 (m, 2H, 3-Ph), 7.68 (m, 2H, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 172.68, 166.54, 164.06, 138.94, 130.66, 130.57, 128.73, 128.37, 128.10, 116.41, 116.18, 75.41, 61.01, 52.53; ESI-MS (*m/z*): 354 [M + H]$^+$. HRMS (ESI) *m/z* calcd. for $C_{16}H_{16}FNO_5SNa$ [M + Na]$^+$: 376.0631, found 376.0618.

*2-Hydroxy-3-(4-trifluoromethyl benzenesulfonylamino)-3-phenyl-propionic acid methyl ester* (**7g**). Yield 19% (153 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 3.65 (s, 3H, $OCH_3$), 4.37 (d, 1H, $J$ = 3.2 Hz, 2-CH), 4.91 (d, 1H, $J$ = 3.2 Hz, 3-CH), 7.11 (m, 3H, 3-Ph), 7.23 (m, 2H, 3-Ph), 7.66 (d, 2H, $J$ = 8.4 Hz,

$PhSO_2$), 7.82 (d, 2H, $J$ = 8.0 Hz, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 172.62, 146.30, 138.65, 133.69, 133.37, 128.73, 128.54, 128.43, 128.16, 126.52, 126.48, 126.44, 125.90, 123.20, 75.33, 61.19, 52.51; ESI-MS (*m/z*): 404 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{17}H_{16}F_3NO_5SNa$ $[M + Na]^+$: 426.0599, found 426.0606.

*2-Hydroxy-3-(4-chloro benzenesulfonylamino)-3-phenyl-propionic acid methyl ester* (**7h**). Yield 32% (236 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 3.65 (s, 3H, $OCH_3$), 4.36 (d, 1H, $J$ = 3.2 Hz, 2-CH), 4.88 (d, 1H, $J$ = 3.2 Hz, 3-CH), 7.15 (m, 3H, 3-Ph), 7.26 (m, 2H, 3-Ph), 7.35 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$), 7.62 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 172.65, 141.42, 138.98, 138.36, 129.49, 128.74, 128.39, 128.10, 75.38, 61.05, 52.51; ESI-MS (*m/z*): 370 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{16}H_{16}ClNO_5SNa$ $[M + Na]^+$: 392.0335, found 392.0342.

*2-Hydroxy-3-(4-bromo benzenesulfonylamino)-3-phenyl-propionic acid methyl ester* (**7i**). Yield 35% (290 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 3.64 (s, 3H, $OCH_3$), 4.36 (d, 1H, $J$ = 3.2 Hz, 2-CH), 4.88 (d, 1H, $J$ = 3.2 Hz, 3-CH), 7.16 (m, 3H, 3-Ph), 7.26 (m, 2H, 3-Ph), 7.51 (m, 4H, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 172.65, 141.88, 138.98, 132.51, 129.60, 128.75, 128.40, 128.09, 126.87, 75.37, 61.06, 52.51; ESI-MS (*m/z*): 413 $[M + H]^+$. HRMS (ESI) *m/z* calcd. For $C_{16}H_{16}BrNO_5SNa$ $[M + Na]^+$: 435.9830, found 435.9807.

*2-Hydroxy-3-(2,4,6-trimethyl benzenesulfonylamino)-3-phenyl-propionic acid methyl ester* (**7j**). Yield 50% (377 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 2.23 (s, 3H, $CH_3$ in $PhSO_2$), 2.53 (s, 6H, $CH_3$ in $PhSO_2$), 3.45 (s, 3H, $OCH_3$), 4.32 (d, 1H, $J$ = 3.2 Hz, 2-CH), 4.72 (d, 1H, $J$ = 3.2 Hz, 3-CH), 6.90 (s, 2H, $PhSO_2$), 7.20 (m, 3H, 3-Ph), 7.31 (m, 2H, 3-Ph); $^{13}$C-NMR ($CD_3COCD_3$): 172.67, 142.56, 139.92, 139.49, 136.23, 132.43, 128.70, 128.11, 128.05, 75.18, 60.45, 52.37, 23.09, 20.74; ESI-MS (*m/z*): 378 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{19}H_{23}NO_5SNa$ $[M + Na]^+$: 400.1195, found 400.1180.

### 3.2.2. General Procedure for the Synthesis of **11a–j**

To a stirred solution of **7a–j** (0.45 mmol) and PPTs (113 mg, 0.045 mmol) in anhydrous toluene (8 mL) was added 2-methoxypropene (0.129 mL, 1.35 mmol). The reaction mixture was warmed to 85 °C , and further stirred for 2 h at this temperature. After cooled down to room temperature, the mixture was diluted with EtOAc (50 mL). The organic layer was washed with brine, dried over anhydrous $Na_2SO_4$ and filtered. The filtrate was evaporated and the residue was purified by silica gel column chromatography using petroleum ether/EtOAc (2/1) to obtain products **11a–j** as colorless liquids.

*2,2-Dimethyl-3-benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid methyl ester* (**11a**). Yield 97% (164 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.69 (s, 3H, *i*-Pr), 1.81 (s, 3H, *i*-Pr), 3.66 (s, 3H, $OCH_3$), 4.62 (d, 1H, $J$ = 4.8 Hz, 2-CH), 5.27 (d, 1H, $J$ = 4.8 Hz, 3-CH), 7.22 (m, 3H, 3′-Ph), 7.32 (m, 2H, 3′-Ph), 7.42 (t, 2H, $J$ = 7.6 Hz, *m*-$PhSO_2$), 7.55 (t, 1H, $J$ = 7.6 Hz, *p*-$PhSO_2$), 7.62 (t, 2H, $J$ = 7.6 Hz, *o*-$PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 171.03, 142.02, 139.51, 133.41, 129.60, 129.14, 128.76, 128.46, 128.32, 100.78, 82.50, 66.19, 52.76, 27.31; ESI-MS (*m/z*): 376 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{19}H_{21}NO_5SNa$ $[M + Na]^+$: 398.1038, found 398.1024.

*2,2-Dimethyl-3-phenylmethane sulfonyl-4-phenyl-oxazolidine-5-carboxylic acid methyl ester* (**11b**). Yield 92% (161 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.60 (s, 3H, *i*-Pr), 1.73 (s, 3H, *i*-Pr), 3.79 (s, 3H, $OCH_3$), 3.79 (d, 1H, $J$ = 14.0 Hz, $CH_2$ in Bn), 4.10 (d, 1H, $J$ = 13.6 Hz, $CH_2$ in Bn), 4.79 (d, 1H, $J$ = 4.0 Hz, 2-CH), 5.30 (d, 1H, $J$ = 4.4 Hz, 3-CH), 7.25 (m, 2H, 3-Ph), 7.33 (m, 3H, 3-Ph), 7.40 (m, 1H, Ph in Bn), 7.48 (m, 2H, Ph in Bn), 7.58 (m, 2H, Ph in Bn); $^{13}$C-NMR ($CD_3COCD_3$): 171.57, 140.54, 131.98, 130.12, 129.58, 129.30, 129.14, 128.97, 100.28, 82.18, 65.65, 61.03, 52.88, 28.95, 27.74; ESI-MS (*m/z*): 390 $[M + H]^+$; Anal. calcd. for $C_{20}H_{23}NO_5S$: C, 61.68; H, 5.95; N, 3.60. Found: C, 61.73; H, 6.05; N, 3.52.

*2,2-Dimethyl-3-(4-methyl)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid methyl ester* (**11c**). Yield 80% (140 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.68 (s, 3H, *i*-Pr), 1.79 (s, 3H, *i*-Pr), 2.36 (s, 3H, $CH_3$ in tosyl), 3.66 (s, 3H, $OCH_3$), 4.60 (d, 1H, $J$ = 4.8 Hz, 2-CH), 5.24 (d, 1H, $J$ = 4.8 Hz, 3-CH), 7.23 (m, 5H, 3′-Ph), 7.32 (m, 2H, Ph in tosyl), 7.50 (d, 2H, $J$ = 8.4 Hz, Ph in tosyl); $^{13}$C-NMR ($CD_3COCD_3$): 171.04, 144.23, 139.71, 139.12, 130.07, 129.10, 128.62, 128.43, 128.42, 100.68, 82.48, 66.20, 52.75, 27.22, 21.37; ESI-MS (*m/z*): 390 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{20}H_{23}NO_5SNa$ $[M + Na]^+$: 412.1195, found 412.1196.

*2,2-Dimethyl-3-(4-methoxy)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid methyl ester* (**11d**). Yield 99% (180 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.69 (s, 3H, *i*-Pr), 1.80 (s, 3H, *i*-Pr), 3.67 (s, 3H, 3-$CH_3$), 3.85 (s, 3H, $OCH_3$), 4.58 (d, 1H, $J$ = 4.8 Hz, 2-CH), 5.21 (d, 1H, $J$ = 4.8 Hz, 3-CH), 6.89 (m, 2H, $PhSO_2$), 7.22 (m, 3H, 3-Ph), 7.29 (m, 2H, 3-Ph), 7.53 (m, 2H, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 171.06, 163.73, 139.67, 133.52, 130.57, 129.08, 128.63, 128.38, 114.63, 100.65, 82.51, 66.12, 60.57, 56.09, 52.73, 27.15; ESI-MS (*m/z*): 406 $[M + H]^+$; Anal. calcd. for $C_{20}H_{23}NO_6S$: C, 59.24; H, 5.72; N, 3.45. Found: C, 59.21; H, 5.70; N, 3.49.

*2,2-Dimethyl-3-(4-isopropyl)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid methyl ester* (**11e**). Yield 97% (182 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.22 (d, 6H, $J$ = 7.4 Hz, 2$CH_3$ in *i*-PrPh), 1.71 (s, 3H, *i*-Pr), 1.83 (s, 3H, *i*-Pr), 2.94 (m, 1H, CH in *i*-PrPh), 3.66 (s, 3H, $OCH_3$), 4.59 (d, 1H, $J$ = 4.8 Hz, 2-CH), 5.21 (d, 1H, $J$ = 5.2 Hz, 3-CH), 7.19 (m, 3H, 3-Ph), 7.24 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$), 7.26 (m, 2H, 3-Ph), 7.49 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 170.14, 153.83, 138.44, 138.35, 128.18, 127.91, 127.68, 127.57, 126.60, 99.98, 81.68, 78.33, 65.24, 51.82, 33.87, 26.42, 23.03, 22.98; ESI-MS (*m/z*): 418 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{22}H_{27}NO_5SNa$ $[M + Na]^+$: 440.1508, found 440.1501.

*2,2-Dimethyl-3-(4-fluoro)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid methyl ester* (**11f**). Yield 81% (143 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.71 (s, 3H, *i*-Pr), 1.83 (s, 3H, *i*-Pr), 3.69 (s, 3H, $OCH_3$), 4.62 (d, 1H, $J$ = 4.8 Hz, 2-CH), 5.23 (d, 1H, $J$ = 4.8 Hz, 3-CH), 7.14 (t, 2H, $J$ = 8.8 Hz, $PhSO_2$), 7.22 (m, 3H, 3-Ph), 7.29 (m, 2H, 3-Ph), 7.63 (m, 2H, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 171.02, 166.85, 164.35, 139.09, 138.26, 131.43, 131.33, 129.17, 128.82, 128.60, 116.63, 116.40, 100.97, 82.52, 66.07, 52.77, 27.38; ESI-MS (*m/z*): 394 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{19}H_{20}FNO_5SNa$ $[M + Na]^+$: 416.0944, found 416.0936.

*2,2-Dimethyl-3-(4-trifluoromethyl)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid methyl ester* (**11g**). Yield 99% (197 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.74 (s, 3H, *i*-Pr), 1.87 (s, 3H, *i*-Pr), 3.69 (s, 3H, $OCH_3$), 4.65 (d, 1H, $J$ = 5.2 Hz, 2-CH), 5.26 (d, 1H, $J$ = 4.8 Hz, 3-CH), 7.19 (m, 3H, 3-Ph), 7.26 (m, 2H, 3-Ph), 7.70 (d, 2H, $J$ = 8.4 Hz, $PhSO_2$), 7.76 (d, 2H, $J$ = 8.0 Hz, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 170.90, 145.58, 138.51, 134.14, 129.21, 129.17, 128.95, 128.78, 126.71, 126.68, 126.64, 126.60, 101.24, 82.49, 66.11, 52.79, 27.67; ESI-MS (*m/z*): 444 $[M + H]^+$; Anal. calcd. for $C_{20}H_{20}F_3NO_5S$: C, 54.17; H, 4.55; N, 3.16. Found: C, 54.31; H, 4.51; N, 3.22.

*2,2-Dimethyl-3-(4-chloro)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid methyl ester* (**11h**). Yield 93% (171 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.71 (s, 3H, *i*-Pr), 1.83 (s, 3H, *i*-Pr), 3.69 (s, 3H, $OCH_3$), 4.63 (d, 1H, $J$ = 5.2 Hz, 2-CH), 5.24 (d, 1H, $J$ = 5.2 Hz, 3-CH), 7.24 (m, 3H, 3-Ph), 7.29 (m, 2H, 3-Ph), 7.41 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$), 7.56 (d, 2H, $J$ = 8.0 Hz, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 170.99, 140.73, 139.10, 139.02, 130.15, 129.69, 129.21, 128.83, 128.66, 101.01, 82.50, 66.11, 52.79, 27.46; ESI-MS (*m/z*): 410 $[M + H]^+$. HRMS (ESI) *m/z* calcd for $C_{19}H_{20}ClNO_5SNa$ $[M + Na]^+$: 432.0648, found 432.0653.

*2,2-Dimethyl-3-(4-bromo)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid methyl ester* (**11i**). Yield 99% (202 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.71 (s, 3H, *i*-Pr), 1.83 (s, 3H, *i*-Pr), 3.69 (s, 3H, $OCH_3$), 4.63 (d, 1H, $J$ = 5.2 Hz, 2-CH), 5.23 (d, 1H, $J$ = 4.8 Hz, 3-CH), 7.24 (m, 3H, 3-Ph), 7.29 (m, 2H, 3-Ph), 7.49 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$), 7.57 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$): 170.96, 141.17, 138.99, 132.70, 130.20, 129.21, 128.81, 128.65, 127.67, 101.00, 82.48, 66.10, 52.78, 27.46; ESI-MS (*m/z*): 455 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{19}H_{20}BrNO_5SNa$ $[M + Na]^+$: 476.0143, found 476.0156.

*2,2-Dimethyl-3-(2,4,6-trimethyl)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid methyl ester* (**11j**). Yield 81% (152 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.82 (s, 3H, *i*-Pr), 1.92 (s, 3H, *i*-Pr), 2.10 (s, 3H, $CH_3$ in $PhSO_2$), 2.51 (s, 6H, $CH_3$ in $PhSO_2$), 3.74 (s, 3H, $OCH_3$), 4.47 (d, 1H, $J$ = 5.6 Hz, 2-CH), 4.99 (d, 1H, $J$ = 6.0 Hz, 3-CH), 6.63 (s, 2H, $PhSO_2$), 7.01 (m, 5H, 3-Ph); $^{13}$C-NMR ($CD_3COCD_3$): 171.11, 144.03, 140.69, 138.39, 134.00, 132.53, 128.67, 128.25, 127.46, 102.10, 83.12, 66.06, 52.72, 27.12, 23.21, 20.67; ESI-MS (*m/z*): 418 $[M + H]^+$; Anal. calcd. for $C_{22}H_{27}NO_5S$: C, 63.29; H, 6.52; N, 3.35. Found: C, 63.42; H, 6.48; N, 3.39.

### 3.2.3. General Procedure for the Synthesis of **12a–j**

To a stirred solution of **11a–j** (0.437 mmol) in a mixture of solvent (THF:$H_2O$ = 6 mL:2 mL) at 0 °C was added LiOH•$H_2O$ (37 mg, 0.87 mmol). The resulting mixture was warmed to room temperature and further stirred for 1 h. Then the pH of the mixture was adjusted to 2~3 by adding 1N HCl solution. After extracted with $CH_2Cl_2$ three times, the combined organic phase was dried over anhydrous $Na_2SO_4$ and evaporated to afford the colorless liquid products **12a–j**.

*2,2-Dimethyl-3-benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid* (**12a**). Yield 97% (154 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.71 (s, 3H, *i*-Pr), 1.83 (s, 3H, *i*-Pr), 4.56 (d, 1H, $J$ = 4.8 Hz, 2-CH), 5.25 (d, 1H, $J$ = 4.4 Hz, 3-CH), 7.21 (m, 3H, 3′-Ph), 7.31 (m, 2H, 3′-Ph), 7.39 (t, 2H, $J$ = 7.6 Hz, *m*-$PhSO_2$),

7.53 (t, 1H, $J$ = 7.6 Hz, $p$-$PhSO_2$), 7.60 (t, 2H, $J$ = 7.6 Hz, $o$-$PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 171.48, 142.04, 139.68, 133.34, 129.55, 129.12, 128.69, 128.50, 128.305, 100.72, 82.50, 66.24, 27.41; ESI-MS (*m/z*): 362 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{18}H_{19}NO_5SNa$ $[M + Na]^+$: 384.0882, found 384.0888.

*2,2-Dimethyl-3-phenylmethane sulfonyl-4-phenyl-oxazolidine-5-carboxylic acid* (**12b**). Yield 97% (160 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.61 (s, 3H, *i*-Pr), 1.76 (s, 3H, *i*-Pr), 3.79 (d, 1H, $J$ = 14.0 Hz, $CH_2$ in Bn), 4.10 (d, 1H, $J$ = 14.0 Hz, $CH_2$ in Bn), 4.76 (d, 1H, $J$ = 4.0 Hz, 2-CH), 5.30 (d, 1H, $J$ = 4.0 Hz, 3-CH), 7.24 (m, 3H, 3-Ph), 7.33 (m, 2H, 3-Ph), 7.40 (m, 2H, Ph in Bn), 7.59 (m, 3H, Ph in Bn); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 172.03, 140.75, 131.99, 131.74, 130.93, 130.15, 129.56, 129.24, 129.15, 129.04, 129.00, 128.83, 128.62, 128.55, 100.23, 82.12, 75.05, 65.72, 27.81; ESI-MS (*m/z*): 376 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{19}H_{21}NO_5SNa$ $[M + Na]^+$: 398.1038, found 398.1031.

*2,2-Dimethyl-3-(4-methyl)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid* (**12c**). Yield 96% (158 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.70 (s, 3H, *i*-Pr), 1.82 (s, 3H, *i*-Pr), 2.35 (s, 3H, $CH_3$ in Tosyl), 4.55 (d, 1H, $J$ = 5.2 Hz, 2-CH), 5.22 (d, 1H, $J$ = 5.2 Hz, 3-CH), 7.22 (m, 5H, Ph in Tosyl), 7.30 (m, 2H, Ph in Tosyl), 7.48 (d, 2H, Ph in Tosyl); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 171.47, 144.15, 139.91, 139.12, 130.04, 129.09, 128.55, 128.45, 128.44, 100.63, 82.49, 66.23, 27.31, 21.37; ESI-MS (*m/z*): 376 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{19}H_{21}NO_5SNa$ $[M + Na]^+$: 398.1038, found 398.1031.

*2,2-Dimethyl-3-(4-methoxy)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid* (**12d**). Yield 99% (170 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.74 (s, 3H, *i*-Pr), 1.88 (s, 3H, *i*-Pr), 3.70 (s, 3H, 3-$CH_3$), 4.67 (d, 1H, $J$ = 4.8 Hz, 2-CH), 5.29 (d, 1H, $J$ = 5.2 Hz, 3-CH), 7.21 (m, 3H, 3-Ph), 7.29 (m, 2H, 3-Ph), 7.80 (d, 2H, $J$ = 9.2 Hz, $PhSO_2$), 8.19 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 170.87, 150.65, 147.26, 138.47, 129.81, 129.30, 129.06, 128.9, 124.68, 101.32, 82.43, 66.12, 52.85, 27.78; ESI-MS (*m/z*): 392 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{19}H_{21}NO_6SNa$ $[M + Na]^+$: 414.0987, found 414.0998.

*2,2-Dimethyl-3-(4-isopropyl)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid* (**12e**). Yield 95% (168 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.21 (d, 3H, $J$ = 1.6 Hz, $CH_3$ in *i*-PrPh), 1.22 (d, 3H, $J$ = 1.2 Hz, $CH_3$ in *i*-PrPh), 1.74 (s, 3H, $CH_3$ in *i*-Pr), 1.85 (s, 3H, $CH_3$ in *i*-Pr), 2.92 (m, 1H, CH in *i*-PrPh), 4.53 (d, 1H, $J$ = 5.2 Hz, 2-CH), 5.19 (d, 1H, $J$ = 5.2 Hz, 3-CH), 7.16 (m, 3H, 3-Ph), 7.20 (d, 2H, $J$ = 8.4 Hz, $PhSO_2$), 7.23 (m, 2H, 3-Ph), 7.46 (m, 2H, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 171.48, 154.64, 139.36, 139.33, 129.06, 128.64, 128.55, 128.54, 127.45, 100.83, 82.59, 66.20, 34.76, 27.46, 23.95, 23.86; ESI-MS (*m/z*): 404 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{21}H_{25}NO_5SNa$ $[M + Na]^+$: 426.1351, found 426.1339.

*2,2-Dimethyl-3-(4-fluoro)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid* (**12f**). Yield 81% (135 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.73 (s, 3H, *i*-Pr), 1.84 (s, 3H, *i*-Pr), 4.58 (d, 1H, $J$ = 5.2 Hz, 2-CH), 5.23 (d, 1H, $J$ = 5.2 Hz, 3-CH), 7.12 (t, 2H, $J$ = 8.8 Hz, $PhSO_2$), 7.22 (m, 3H, 3-Ph), 7.28 (m, 2H, 3-Ph), 7.63 (m, 2H, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 171.45, 166.83, 164.32, 139.32, 138.29, 138.26, 131.43, 131.33, 129.16, 128.76, 128.62, 116.60, 116.38, 100.93, 82.50, 66.12, 27.47; ESI-MS (*m/z*): 380 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{18}H_{18}FNO_5SNa$ $[M + Na]^+$: 402.0787, found 402.0782.

*2,2-Dimethyl-3-(4-trifluoromethyl)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid* (**12g**). Yield 78% (147 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.77 (s, 3H, *i*-Pr), 1.88 (s, 3H, *i*-Pr), 4.64 (d, 1H, $J$ = 5.2 Hz, 2-CH), 5.29 (d, 1H, $J$ = 4.8 Hz, 3-CH), 7.21 (m, 3H, 3-Ph), 7.30 (m, 2H, 3-Ph), 7.81 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$), 8.18 (d, 2H, $J$ = 9.2 Hz, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 171.32, 150.62, 147.27, 138.73, 129.82, 129.28, 128.99, 128.89, 124.68, 101.26, 82.38, 66.18, 27.83; ESI-MS (*m/z*): 430 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{19}H_{18}F_3NO_5SNa$ $[M + Na]^+$: 452.0755, found 452.0737.

*2,2-Dimethyl-3-(4-chloro)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid* (**12h**). Yield 100% (173 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.73 (s, 3H, *i*-Pr), 1.84 (s, 3H, *i*-Pr), 4.59 (d, 1H, $J$ = 5.2 Hz, 2-CH), 5.24 (d, 1H, $J$ = 4.8 Hz, 3-CH), 7.23 (m, 3H, 3-Ph), 7.29 (m, 2H, 3-Ph), 7.39 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$), 7.56 (d, 2H, $J$ = 8.0 Hz, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 171.40, 140.74, 139.26, 139.04, 130.14, 129.66, 129.19, 128.76, 128.67, 100.95, 82.46, 66.14, 27.54; ESI-MS (*m/z*): 396 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{18}H_{18}ClNO_5SNa$ $[M + Na]^+$: 418.0492, found 418.0504.

*2,2-Dimethyl-3-(4-bromo)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid* (**12i**). Yield 99% (191 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.73 (s, 3H, *i*-Pr), 1.84 (s, 3H, *i*-Pr), 4.59 (d, 1H, $J$ = 4.8 Hz, 2-CH), 5.23 (d, 1H, $J$ = 5.2 Hz, 3-CH), 7.23 (m, 3H, 3-Ph), 7.29 (m, 2H, 3-Ph), 7.48 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$), 7.55 (d, 2H, $J$ = 8.8 Hz, $PhSO_2$); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 171.40, 141.20, 139.22, 132.67, 130.20, 129.20, 128.73, 128.70, 127.62, 100.93, 82.45, 66.14, 27.54; ESI-MS (*m/z*): 439 $[M + H]^+$. HRMS (ESI) *m/z* calcd. for $C_{18}H_{18}BrNO_5SNa$ $[M + Na]^+$: 461.9987, found 461.9997.

*2,2-Dimethyl-3-(2,4,6-trimethyl)benzenesulfonyl-4-phenyl-oxazolidine-5-carboxylic acid* (**12j**). Yield 99% (175 mg); $^1$H-NMR ($CD_3COCD_3$): $\delta$ 1.85 (s, 3H, *i*-Pr), 1.93 (s, 3H, *i*-Pr), 2.09 (s, 3H, $CH_3$ in $PhSO_2$), 2.52 (s, 6H, $CH_3$ in $PhSO_2$), 4.44 (d, 1H, $J$ = 5.6 Hz, 2-CH), 5.02 (d, 1H, $J$ = 5.6 Hz, 3-CH), 6.63 (s, 2H, $PhSO_2$), 7.01 (m, 5H, 3-Ph); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 171.58, 143.99, 140.68, 138.84, 134.01, 132.52, 128.65, 128.15, 127.39, 102.05, 83.10, 66.04, 27.20, 23.21, 20.68. ESI-MS (*m/z*): 404 $[M + H]^+$. HRMS (ESI) *m/z* calcd for $C_{21}H_{25}NO_5SNa$ $[M + Na]^+$: 426.1351, found 426.1345.

### 3.2.4. General Procedure for the Synthesis of **13a–j**

To a solution of anhydrous toluene (60 mL) were added **12a–j** (0.49 mmol), 7,10-ditroc-10-DAB (0.23 g, 0.24 mmol), DCC (0.15 g, 0.75 mmol) and DMAP (15 mg, 0.13 mmol). The resulting mixture was stirred at 85 °C for 3 h. After the completion, the reaction mixture was washed with brine (30 mL × 3), dried over $Na_2SO_4$, filtered and concentrated *in vacuo*. The obtained residue was purified by silica gel flash chromatography column (petroleum ether/ethyl acetate: 4/1) to afford **13a–j** as white solids.

*7,10-Di(2,2,2-trichloroethyloxycarbonyl)-10-deacetylbaccatin III-13-O-[2,2-dimethyl-3-benzene sulfonyl-4-phenyl-oxazolidine-5-carboxylate]* (**13a**). Yield 96% (285 mg); mp 155–157 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.17 (s, 3H, 17-$CH_3$), 1.24 (s, 3H, 16-$CH_3$), 1.82 and 1.87 (2s, 6H, *i*-Pr), 1.95 (s, 3H, 19-$CH_3$), 1.97 (s, 3H, 18-$CH_3$), 1.99 (s, 3H, OAc), 2.13 (m, 2H, 14-$CH_2$), 2.03 and 2.59 (2m, 2H, 6-$CH_2$), 3.87 (d, 1H, $J$ = 7.2 Hz, 3-CH), 4.11 and 4.27 (2d, 2H, $J$ = 8.6 Hz, 20-$CH_2$), 4.50 (d, 1H, $J$ = 6.0 Hz, 2′-CH), 4.60 and 4.91 (2d, 2H, $J$ = 12.0 Hz, Troc), 4.78 (s, 2H, Troc), 4.90 (d, 1H, $J$ = 7.6 Hz, 5-CH), 5.23 (d, 1H, $J$ = 6.4 Hz, 3′-CH), 5.56 (dd, 1H, $J$ = 10.8, 7.2 Hz, 7-CH), 5.65 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.21

(t, 1H, $J$ = 8.4 Hz, 13-CH), 6.23 (s, 1H, 10-CH), 7.15 (m, 2H, 3′-Ph), 7.21 (m, 3H, 3′-Ph), 7.26 (t, 2H, $J$ = 7.6 Hz, *m*-$PhSO_2$), 7.41 (t, 1H, $J$ = 7.6 Hz, *p*-$PhSO_2$), 7.46 (d, 2H, $J$ = 7.2 Hz, *o*-$PhSO_2$), 7.47 (t, 2H, $J$ = 7.6 Hz, *m*-OBz), 7.62 (t, 1H, $J$ = 7.6 Hz, *p*-OBz), 8.01 (d, 2H, $J$ = 7.2 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.65, 170.14, 169.78, 166.84, 153.21, 142.48, 140.58, 136.95, 133.87, 132.41, 132.02, 130.05, 129.00, 128.67, 128.58, 128.46, 128.33, 128.00, 127.50, 100.95, 94.19, 83.68, 81.99, 80.43, 79.01, 78.88, 74.23, 71.49, 65.27, 58.46, 56.09, 49.21, 46.90, 43.07, 35.38, 33.91, 33.17, 28.73, 27.18, 26.23, 25.60, 24.92, 21.58, 21.03, 18.43, 14.81, 10.72. Anal. calcd. for $C_{53}H_{55}Cl_6NO_{18}S$: C, 51.39; H, 4.48; N, 1.13. Found: C, 51.52; H, 4.51; N, 1.15.

*7,10-Di(2,2,2-trichloroethyloxycarbonyl)-10-deacetylbaccatin III-13-O-[2,2-dimethyl-3-phenyl methane sulfonyl-4-phenyl-oxazolidine-5-carboxylate]* (**13b**). Yield 94% (282 mg); mp 154–156 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.20 (s, 3H, 17-$CH_3$), 1.28 (s, 3H, 16-$CH_3$), 1.61 (s, 3H, 19-$CH_3$), 1.84 and 1.85 (2s, 6H, *i*-Pr), 2.08 (s, 3H, 18-$CH_3$), 2.10 (s, 3H, OAc), 2.22 (m, 2H, 14-$CH_2$), 2.04 and 2.62 (2m, 2H, 6-$CH_2$), 3.73 (2d, 2H, $J$ = 13.6 Hz, 3″-$CH_2$), 3.93 (d, 1H, $J$ = 7.2 Hz, 3-CH), 4.15 and 4.32 (2d, 2H, $J$ = 8.4 Hz, 20-$CH_2$), 4.70 (d, 1H, $J$ = 5.2 Hz, 2′-CH), 4.62 and 4.94 (2d, 2H, $J$ = 12.0 Hz, Troc), 4.80 (dd, 2H, $J$ = 12.8, 12.0 Hz, Troc), 4.94 (d, 1H, $J$ = 9.2 Hz, 5-CH), 5.29 (d, 1H, $J$ = 5.2 Hz, 3′-CH), 5.61 (dd, 1H, $J$ = 10.6, 7.0 Hz, 2-CH), 5.69 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.27 (t, 1H, $J$ = 8.6 Hz, 13-CH), 6.27 (s, 1H, 10-CH), 7.21 (m, 2H, 3′-Ph), 7.35 (m, 3H, 3′-Ph), 751 (t, 2H, $J$ = 8.0 Hz, *m*-OBz), 7.51 (m, 2H, 3″-Ph), 7.56 (m, 2H, 3″-Ph), 7.65 (t, 1H, $J$ = 7.6 Hz, *p*-OBz), 8.05 (d, 2H, $J$ = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.67, 171.18, 170.18, 170.04, 166.86, 153.22, 153.19, 142.43, 138.48, 133.91, 132.07, 130.99, 130.07, 129.21, 129.14, 128.99, 128.80, 128.71, 128.59, 128.50, 128.17, 100.50, 94.19, 83.70, 81.67, 80.48, 79.02, 78.91, 74.24, 71.66, 64.89, 61.36, 60.41, 56.10, 49.31, 46.94, 43.10, 35.45, 33.83, 33.19, 29.70, 27.98, 27.77, 26.23, 25.57, 24.89, 2, 21.65, 21.06, 21.03, 14.96, 14.21, 10.74. Anal. calcd. for $C_{54}H_{57}Cl_6NO_{18}S$: C, 51.77; H, 4.59; N, 1.12. Found: C, 51.88; H, 4.65; N, 1.18.

*7,10-Di(2,2,2-trichloroethyloxycarbonyl)-10-deacetylbaccatin III-13-O-[2,2-dimethyl-3-(4-methyl) benzene sulfonyl-4-phenyl-oxazolidine-5-carboxylate]* (**13c**). Yield 85% (255 mg); mp 154–156 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.19 (s, 3H, 17-$CH_3$), 1.27 (s, 3H, 16-$CH_3$), 1.84 and 1,87 (2s, 6H, *i*-Pr), 1.94 (s, 3H, 19-$CH_3$), 1.99 (s, 3H, 18-$CH_3$), 2.00 (s, 3H, OAc), 2.16 (m, 2H, 14-$CH_2$), 2.36 (s, 3H, 4″-$CH_3$), 2.05 and 2.61 (2m, 2H, 6-$CH_2$), 3.89 (d, 1H, $J$ = 6.8 Hz, 3-CH), 4.13 and 4.29 (2d, 2H, $J$ = 8.4 Hz, 20-$CH_2$), 4.52 (d, 1H, $J$ = 6.8 Hz, 2′-CH), 4.62 and 4.93 (2d, 2H, $J$ = 12.0 Hz, Troc), 4.80 (dd, 2H, $J$ = 14.4, 12.0 Hz, Troc), 4.92 (d, 1H, $J$ = 7.6 Hz, 5-CH), 5.21 (d, 1H, $J$ = 6.8 Hz, 3′-CH), 5.58 (dd, 1H, $J$ = 10.8, 7.2 Hz, 7-CH), 5.67 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.22 (t, 1H, $J$ = 8.8 Hz, 13-CH), 6.25 (s, 1H, 10-CH), 7.07 (d, 2H, $J$ = 8.4 Hz, *m*-$PhSO_2$), 7.20 (m, 2H, 3′-Ph), 7.26 (m, 3H, 3′-Ph), 7.39 (d, 2H, $J$ = 8.4 Hz, *o*-$PhSO_2$), 7.50 (t, 2H, $J$ = 7.6 Hz, *m*-OBz), 7.65 (t, 1H, $J$ = 7.4 Hz, *p*-OBz), 8.04 (d, 2H, $J$ = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.65, 171.15, 169.81, 166.85, 153.21, 153.20, 143.32, 142.51, 137.57, 133.88, 131.99, 130.06, 129.10, 128.99, 130.06, 129.10, 128.99, 128.68, 128.53, 128.16, 127.92, 100.81, 94.21, 94.19, 83.67, 81.94, 80.42, 79.02, 78.90, 74.23, 71.45, 65.33, 60.39, 56.08, 46.90, 43.07, 35.37, 33.10, 33.17, 29.70, 28.90, 26.99, 26.23, 25.51, 24.82, 21.57, 21.44, 21.03, 14.78, 14.20, 10.72. Anal. calcd. for $C_{54}H_{57}Cl_6NO_{18}S$: C, 51.77; H, 4.59; N, 1.12. Found: C, 51.93; H, 4.63; N, 1.16.

*7,10-Di(2,2,2-trichloroethyloxycarbonyl)-10-deacetylbaccatin III-13-O-[2,2-dimethyl-3-(4-methoxy) benzene sulfonyl-4-phenyl-oxazolidine-5-carboxylate]* (**13d**). Yield 95% (288 mg); mp 159–161 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.19 (s, 3H, 17-$CH_3$), 1.26 (s, 3H, 16-$CH_3$), 1.83 and 1.87 (2s, 6H, *i*-Pr), 1.94 (s, 3H, 19-$CH_3$), 1.99 (s, 3H, 18-$CH_3$), 2.01 (s, 3H, OAc), 2.15 (m, 2H, 14-$CH_2$), 2.05 and 2.61 (2m, 2H, 6-$CH_2$), 3.82 (s, 3H, $OCH_3$), 3.89 (d, 1H, $J$ = 6.8 Hz, 3-CH), 4.13 and 4.28 (2d, 2H, $J$ = 8.4 Hz, 20-$CH_2$), 4.51 (d, 1H, $J$ = 6.8 Hz, 2′-CH), 4.62 and 4.93 (2d, 2H, $J$ = 11.6 Hz, Troc), 4.80 (dd, 2H, $J$ = 14.0, 12.0 Hz, Troc), 4.92 (d, 1H, $J$ = 8.0 Hz, 5-CH), 5.20 (d, 1H, $J$ = 6.4 Hz, 3′-CH), 5.58 (dd, $J$ = 10.8, 7.2 Hz, 7-CH), 5.67 (d, 1H, $J$ = 7.6 Hz, 2-CH), 6.22 (t, 1H, $J$ = 9.2 Hz, 13-CH), 6.25 (s, 1H, 10-CH), 6.72 (d, 2H, $J$ = 8.8 Hz, *o*-3″-Ph$OCH_3$), 7.23 (m, 5H, 3′-Ph), 7.41 (d, $J$ = 9.2 Hz, *m*-3″-Ph$OCH_3$), 7.50 (t, 2H, $J$ = 7.6 Hz, *m*-OBz), 7.64 (t, 1H, $J$ = 7.6 Hz, *p*-OBz), 8.03 (d, 2H, $J$ = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.66, 171.15, 170.16, 169.86, 166.82, 162.70, 153.21, 153.19, 142.51, 137.31, 133.87, 132.00, 132.19, 132.00, 130.05, 129.75, 129.01, 128.67, 128.55, 128.20, 127.93, 113.64, 100.84, 94.21, 94.19, 83.67, 81.98, 80.41, 79.02, 78.88, 74.24, 71.45, 65.28, 60.39, 56.08, 55.58, 49.23, 46.90, 43.07, 35.39, 33.86, 33.17, 28.89, 26.96, 26.23, 25.59, 24.90, 21.57, 21.04, 14.80, 14.20, 10.72. Anal. calcd. for $C_{54}H_{57}Cl_6NO_{19}S$: C, 51.12; H, 4.53; N, 1.10. Found: C, 51.33; H, 4.55; N, 1.14.

*7,10-Di(2,2,2-trichloroethyloxycarbonyl)-10-deacetylbaccatin III-13-O-[2,2-dimethyl-3-(4-isopropyl) benzene sulfonyl-4-phenyl-oxazolidine-5-carboxylate]* (**13e**). Yield 87% (267 mg); mp 165–167 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.18 (s, 3H, 17-$CH_3$), 1.22 (d, 3H, $J$ = 1.6 Hz, 2″-$CH_3$), 1.24 (d, 3H, $J$ = 1.6 Hz, 2″-$CH_3$), 1.26 (s, 3H, 16-$CH_3$), 1.83 and 1.89 (2s, 6H, *i*-Pr), 1.96 (s, 3H, 19-$CH_3$), 1.99 (s, 3H, 18-$CH_3$), 2.00 (s, 3H, OAc), 2.15 (m, 2H, 14-$CH_2$), 2.05 and 2.61 (2m, 2H, 6-$CH_2$), 2.89 (m, 1H, 2″-CH), 3.89 (d, 1H, $J$ = 7.2 Hz, 3-CH), 4.12 and 4.28 (2d, 2H, $J$ = 8.4 Hz, 20-$CH_2$), 4.51 (d, 1H, $J$ = 6.4 Hz, 2′-CH), 4.62 and 4.93 (2d, 2H, $J$ = 12.0 Hz, Troc), 4.80 (dd, 2H, $J$ = 14.4, 12.0 Hz, Troc), 4.92 (d, 1H, $J$ = 8.0 Hz, 5-CH), 5.24 (m, 1H, 3′-CH), 5.58 (dd, 1H, $J$ = 10.8, 7.2 Hz, 7-CH), 5.66 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.22 (t, 1H, $J$ = 9.2 Hz, 13-CH), 6.24 (s, 1H, 10-CH), 7.08 (d, 2H, $J$ = 8.0 Hz, 3″-Ph), 7.14 (m, 2H, 3′-Ph), 7.20 (m, 3H, 3′-Ph), 7.39 (d, 2H, $J$ = 8.8 Hz, 3″-Ph), 7.49 (t, 2H, $J$ = 7.6 Hz, *m*-OBz), 7.64 (t, 1H, $J$ = 7.6 Hz, *p*-OBz), 8.03 (d, 2H, $J$ = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.66, 171.15, 170.15, 169.88, 166.82, 153.91, 153.20, 153.19, 142.51, 137.01, 133.87, 131.99, 130.05, 129.01, 128.67, 128.47, 128.18, 127.97, 127.73, 126.52, 100.94, 94.22, 94.20, 83.67, 82.01, 80.41, 79.01, 78.88, 74.24, 71.46, 65.30, 60.39, 56.07, 53.43, 46.89, 43.07, 35.39, 34.09, 33.16, 28.82, 27.06, 26.23, 23.67, 23.58, 21.55, 21.03, 14.81, 14.20, 10.72. Anal. calcd. for $C_{56}H_{61}Cl_6NO_{18}S$: C, 52.51; H, 4.80; N, 1.09. Found: C, 52.75; H, 4.88; N, 1.15.

*7,10-Di(2,2,2-trichloroethyloxycarbonyl)-10-deacetylbaccatin III-13-O-[2,2-dimethyl-3-(4-fluoro) benzene sulfonyl-4-phenyl-oxazolidine-5-carboxylate]* (**13f**). Yield 89% (268 mg); mp 166–168 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.19 (s, 3H, 17-$CH_3$), 1.27 (s, 3H, 16-$CH_3$), 1.84 and 1.90 (2s, 6H, *i*-Pr), 1.97 (s, 3H, 19-$CH_3$), 2.01 (s, 3H, 18-$CH_3$), 2.04 (s, 3H, OAc), 2.16 (m, 2H, 14-$CH_2$), 2.05 and 2.62 (2m, 2H, 6-$CH_2$), 3.90 (d, 1H, $J$ = 6.8 Hz, 3-CH), 4.13 and 4.29 (2d, 2H, $J$ = 8.8 Hz, 20-$CH_2$), 4.52 (d, 1H, $J$ = 6.4 Hz, 2′-CH), 4.62 and 4.94 (2d, 2H, $J$ = 11.6 Hz, Troc), 4.80 (dd, 2H, $J$ = 13.0, 11.8 Hz, Troc), 4.93 (d, 1H, $J$ = 9.2 Hz, 5-CH), 5.25 (d, 1H, $J$ = 6.4 Hz, 3′-CH), 5.59 (dd, 1H, $J$ = 10.8, 7.2 Hz, 5-CH), 5.67 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.24 (t, 1H, $J$ = 8.4 Hz, 13-CH), 6.25 (s, 1H, 10-CH), 6.90 (t, 2H, $J$ = 8.4 Hz, -PhF), 7.20 (m, 4H, 3′-Ph), 7.26 (m, 1H, 3′-Ph), 7.45 (m, 2H, -PhF), 7.49 (t, 2H, $J$ = 7.6 Hz,

*m*-OBz), 7.64 (t, 1H, *J* = 7.6 Hz, *p*-OBz), 8.03 (d, 2H, *J* = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.65, 171.17, 170.13, 169.77, 166.84, 166.02, 163.49, 153.21, 142.42, 136.71, 133.90, 132.05, 130.30, 130.20, 130.05, 128.97, 128.68, 128.65, 128.46, 128.11, 115.70, 115.47, 101.12, 94.18, 83.68, 82.03, 80.44, 79.00, 78.89, 74.21, 71.55, 65.15, 60.40, 56.08, 46.91, 43.07, 35.36, 33.17, 28.59, 27.26, 26.22, 21.59, 21.06, 21.02, 14.85, 14.21, 10.73. Anal. calcd. for $C_{53}H_{54}Cl_6FNO_{18}S$: C, 50.65; H, 4.33; N, 1.11. Found: C, 50.82; H, 4.37; N, 1.18.

*7,10-Di(2,2,2-trichloroethyloxycarbonyl)-10-deacetylbaccatin III-13-O-[2,2-dimethyl-3-(4-trifluoro methyl) benzene sulfonyl-4-phenyl-oxazolidine-5-carboxylate]* (**13g**). Yield 100% (312 mg); mp 165–167 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.19 (s, 3H, 17-$CH_3$), 1.27 (s, 3H, 16-$CH_3$), 1.84 and 1.92 (2s, 6H, *i*-Pr), 1.99 (s, 3H, 19-$CH_3$), 2.02 (s, 3H, 18-$CH_3$), 2.03 (s, 3H, OAc), 2.16 (m, 2H, 14-$CH_2$), 2.05 and 2.62 (2m, 2H, 6-$CH_2$), 3.90 (d, 1H, *J* = 6.8 Hz, 3-CH), 4.13 and 4.29 (2d, 2H, *J* = 8.0 Hz, 20-$CH_2$), 4.54 (d, 1H, *J* = 6.4 Hz, 2′-CH), 4.63 and 4.94 (2d, 2H, *J* = 12.0 Hz, Troc), 4.80 (dd, 2H, *J* = 13.6, 12.0 Hz, Troc), 4.93 (d, 1H, *J* = 7.6 Hz, 5-CH), 5.29 (dd, 1H, *J* = 6.0 Hz, 3′-CH), 5.59 (dd, 1H, *J* = 10.8, 6.8 Hz, 7-CH), 5.67 (d, 1H, *J* = 6.8 Hz, 2-CH), 6.24 (t, 1H, *J* = 9.2 Hz, 13-CH), 6.26 (s, 1H, 10-CH), 7.14 (m, 1H, 3′-Ph), 7.23 (m, 4H, 3′-Ph), 7.47 (d, 2H, *J* = 8.4 Hz, -Ph$CF_3$), 7.53 (d, 2H, *J* = 8.4 Hz, -Ph$CF_3$), 7.49 (t, 2H, *J* = 8.0 Hz, *m*-OBz), 7.37 (t, 1H, *J* = 7.6 Hz, *p*-OBz), 8.02 (d, 2H, *J* = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.64, 171.17, 170.10, 169.66, 166.84, 153.21, 144.07, 142.32, 136.19, 134.04, 133.90, 133.71, 132.11, 130.05, 128.96, 128.68, 128.60, 127.94, 125.49, 125.45, 124.47, 121.76, 101.32, 94.18, 83.67, 82.00, 80.46, 78.98, 74.20, 71.62, 65.16, 60.40, 56.08, 46.92, 43.08, 35.36, 33.17, 28.42, 27.55, 26.22, 21.60, 21.06, 21.00, 14.85, 14.20, 10.72. Anal. calcd. for $C_{54}H_{54}Cl_6F_3NO_{18}S$: C, 49.63; H, 4.17; N, 1.07. Found: C, 49.85; H, 4.22; N, 1.13.

*7,10-Di(2,2,2-trichloroethyloxycarbonyl)-10-deacetylbaccatin III-13-O-[2,2-dimethyl-3-(4-chloro) benzene sulfonyl-4-phenyl-oxazolidine-5-carboxylate]* (**13h**). Yield 91% (277 mg); mp 169–171 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.19 (s, 3H, 17-$CH_3$), 1.27 (s, 3H, 16-$CH_3$), 1.84 and 1.89 (2s, 6H, *i*-Pr), 1.96 (s, 3H, 19-$CH_3$), 2.01 (s, 3H, 18-$CH_3$), 2.03 (s, 3H, OAc), 2.16 (m, 2H, 14-$CH_2$), 2.05 and 2.61 (2m, 2H, 6-$CH_2$), 3.90 (d, 1H, *J* = 7.2 Hz, 3-CH), 413 and 4.29 (2d, 2H, *J* = 8.4 Hz, 20-$CH_2$), 4.53 (d, 1H, *J* = 6.4 Hz, 2′-CH), 4.62 and 4.94 (2d, 2H, *J* = 11.6 Hz, Troc), 4.80 (dd, 2H, *J* = 13.6, 11.6 Hz, Troc), 4.93 (d, 1H, *J* = 8.0 Hz, 5-CH), 5.25 (d, 1H, *J* = 6.4 Hz, 3′-CH), 5.58 (dd, 1H, *J* = 10.8, 7.2 Hz, 2-CH), 5.67 (d, 1H, *J* = 7.2 Hz, 2-CH), 6.24 (t, 1H, *J* = 9.2 Hz, 13-CH), 6.25 (s, 1H, 10-CH), 7.20 (d, 2H, *J* = 9.2 Hz, -PhCl), 7.20 (m, 4H, 3′-Ph), 7.28 (m, 1H, 3′-Ph), 7.36 (d, 2H, *J* = 8.8 Hz, -PhCl), 7.49 (t, 2H, *J* = 7.6 Hz, *m*-OBz), 7.64 (t, 1H, *J* = 7.6 Hz, *p*-OBz), 8.03 (d, 2H, *J* = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.65, 171.18, 170.13, 169.73, 166.84, 153.21, 142.40, 139.11, 138.95, 136.66, 133.90, 138.95, 136.66, 133.90, 132.06, 130.05, 128.97, 128.92, 128.68, 128.46, 128.14, 101.10, 94.20, 94.18, 83.67, 81.98, 80.44, 78.99, 78.89, 74.21, 71.55, 65.18, 60.41, 56.08, 46.91, 43.07, 35.37, 33.17, 28.58, 27.31, 26.23, 21.60, 21.06, 21.02, 14.84, 14.21, 10.73. Anal. calcd. for $C_{53}H_{54}Cl_7NO_{18}S$: C, 50.00; H, 4.27; N, 1.10. Found: C, 50.23; H, 4.34; N, 1.15.

*7,10-Di(2,2,2-trichloroethyloxycarbonyl)-10-deacetylbaccatin III-13-O-[2,2-dimethyl-3-(4-bromo) benzene sulfonyl-4-phenyl-oxazolidine-5-carboxylate]* (**13i**). Yield 98% (309 mg); mp 166–168 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.19 (s, 3H, 17-$CH_3$), 1.27 (s, 3H, 16-$CH_3$), 1.84 and 1.89 (2s, 6H, *i*-Pr), 1.96 (s,

3H, 19-$CH_3$), 2.01 (s, 3H, 18-$CH_3$), 2.03 (s, 3H, OAc), 2.16 (m, 2H, 14-$CH_2$), 2.06 and 2.62 (2m, 2H, 6-$CH_2$), 3.90 (d, 1H, $J$ = 6.8 Hz, 3-CH), 4.13 and 4.29 (2d, 2H, $J$ = 8.4 Hz, 20-$CH_2$), 4.53 (d, 1H, $J$ = 6.0 Hz, 2′-CH), 4.62 and 4.94 (2d, 2H, $J$ = 11.8 Hz, Troc), 4.80 (dd, 2H, $J$ = 13.8, 11.8 Hz, Troc), 4.93 (d, 1H, $J$ = 8.0 Hz, 5-CH), 5.25 (d, 1H, $J$ = 6.0 Hz, 3′-CH), 5.59 (dd, 1H, $J$ = 10.8, 7.2 Hz, 7-CH), 5.67 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.24 (t, 1H, $J$ = 9.2 Hz, 13-CH), 6.25 (s, 1H, 10-CH), 7.20 (m, 4H, 3′-Ph), 7.28 (m, 1H, 3′-Ph), 7.29 (d, 2H, $J$ = 8.8 Hz, -PhBr), 7.37 (d, 2H, $J$ = 8.8 Hz, -PhBr), 7.50 (t, 2H, $J$ = 7.8 Hz, *m*-OBz), 7.64 (t, 1H, $J$ = 7.4 Hz, *p*-OBz), 8.03 (d, 2H, $J$ = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.65, 170.12, 169.73, 166.85, 153.21, 142.39, 139.64, 136.63, 133.90, 132.06, 131.66, 130.06, 129.00, 128.96, 128.71, 128.46, 128.13, 127.49, 101.10, 94.18, 83.67, 81.97, 80.44, 78.99, 78.90, 74.20, 71.56, 65.20, 60.41, 56.08, 46.91, 43.08, 35.36, 33.17, 28.58, 27.32, 26.23, 21.60, 21.01, 14.84, 14.21, 10.73. Anal. calcd. for $C_{53}H_{54}BrCl_6NO_{18}S$: C, 48.31; H, 4.13; N, 1.06. Found: C, 48.53; H, 4.23; N, 1.14.

*7,10-Di(2,2,2-trichloroethyloxycarbonyl)-10-deacetylbaccatin III-13-O-[2,2-dimethyl-3-(2,4,6-trimethyl) benzene sulfonyl-4-phenyl-oxazolidine-5-carboxylate]* (**13j**). Yield 81% (248 mg); mp 167–169 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.19 (s, 3H, 17-$CH_3$), 1.28 (s, 3H, 16-$CH_3$), 1.84 and 1.96 (2s, 6H, *i*-Pr), 1.98 (s, 3H, 19-$CH_3$), 2.03 (s, 3H, 18-$CH_3$), 2.08 (s, 3H, OAc), 2.12 (s, 3H, *p*-3″-$CH_3$), 2.14 (m, 2H, 14-$CH_2$), 2.05 and 2.62 (2m, 2H, 6-$CH_2$), 2.54 (s, 6H, *o*-3″-$CH_3$), 3.91 (d, 1H, $J$ = 7.2 Hz, 3-CH), 4.13 and 4.28 (2d, 2H, $J$ = 8.4 Hz, 20-$CH_2$), 4.44 (d, 1H, $J$ = 6.8 Hz, 2′-CH), 4.63 and 4.94 (2d, 2H, $J$ = 11.8 Hz, Troc), 4.80 (s, 2H, Troc), 4.93 (d, 1H, $J$ = 8.0 Hz, 5-CH), 5.15 (d, 1H, $J$ = 6.8 Hz, 3′-CH), 5.59 (dd, 1H, $J$ = 10.8, 7.2 Hz, 7-CH), 5.67 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.27 (t, 1H, $J$ = 8.2 Hz, 13-CH), 6.27 (s, 1H, 10-CH), 6.55 (s, 2H, 3″-Ph), 6.95–7.09 (m, 5H, 3′-Ph), 7.49 (t, 2H, $J$ = 7.8 Hz, *m*-OBz), 7.63 (t, 1H, $J$ = 7.6 Hz, *p*-OBz), 8.02 (d, 2H, $J$ = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.72, 171.18, 170.17, 170.09, 166.83, 153.21, 153.19, 143.12, 142.62, 140.07, 136.70, 133.85, 132.93, 131.91, 131.69, 130.07, 129.00, 128.65, 128.00, 127.66, 126.91, 102.19, 94.20, 83.70, 82.46, 80.38, 79.02, 78.94, 74.23, 71.45, 65.32, 60.41, 56.06, 46.90, 43.06, 35.38, 33.17, 29.70, 29.05, 26.89, 26.33, 23.04, 21.53, 21.04, 20.72, 14.90, 14.21, 10.73. Anal. calcd. for $C_{56}H_{61}Cl_6NO_{18}S$: C, 52.51; H, 4.80; N, 1.09. Found: C, 52.75; H, 4.88; N, 1.17.

### 3.2.5. General Procedure for the Synthesis of **5a**–**j**

To a round-bottomed flask (25 mL) were added **13a**–**j** (0.218 mmol) and HCOOH (>98%, 5 mL). The reaction mixture was stirred at room temperature for 4 h. Then the resulting solution was neutralized by addition of saturated $NaHCO_3$. After extracted with EtOAc three times, the combined organic phase was washed with brine, dried over $Na_2SO_4$, filtered, and concentrated *in vacuo*. The obtained residue was purified by silica gel flash chromatography column (acetone/petroleum ether: 1/3) to afford **5a**–**j** as white solids.

*N-De-tert-butoxycarbonyl-N-phenylsulfonyl 7,10-di(2,2,2-trichloroethyloxycarbonyl)-docetaxel* (**5a**). Yield 72% (188 mg); mp 156–158 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.19 (s, 3H, 17-$CH_3$), 1.25 (s, 3H, 16-$CH_3$), 1.86 (s, 3H, 19-$CH_3$), 1.90 (s, 3H, 18-$CH_3$), 2.25 (m, 2H, 14-$CH_2$), 2.34 (s, 3H, OAc), 2.06 and 2.61 (2m, 2H, 6-$CH_2$), 3.86 (d, 1H, $J$ = 6.8 Hz, 3-CH), 4.20 and 4.31 (2d, 2H, $J$ = 8.4 Hz, 20-$CH_2$), 4.54 (d, 1H, $J$ = 3.2 Hz, 2′-CH), 4.60 and 4.91 (2d, 2H, $J$ = 12.0 Hz, Troc), 4.78 (s, 2H, Troc), 4.93 (d, 1H,

*J* = 9.6 Hz, 5-CH), 4.93 (m, 1H, 3′-CH), 5.52 (m, 1H, 7-CH), 5.67 (d, 1H, *J* = 6.8 Hz, 2-CH), 5.79 (m, 1H, -CONH-), 6.16 (t, 1H, *J* = 8.8 Hz, 13-CH), 6.21 (s, 1H, 10-CH), 7.09 (m, 2H, 3′-Ph), 7.18 (m, 3H, 3′-Ph), 7.28 (t, 2H, *J* = 8.0 Hz, *m*-$PhSO_2$), 7.42 (t, 1H, *J* = 7.6 Hz, *p*-$PhSO_2$), 7.48 (t, 2H, *J* = 7.6 Hz, *m*-OBz), 7.61 (t, 1H, *J* = 7.6 Hz, *p*-OBz), 7.62 (d, 2H, *J* = 7.6 Hz, *o*-$PhSO_2$), 8.08 (d, 2H, *J* = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.62, 170.61, 166.78, 153.22, 142.02, 140.18, 136.31, 133.88, 132.62, 132.30, 130.13, 129.04, 128.81, 128.72, 128.65, 128.36, 127.05, 126.91, 94.17, 83.60, 80.95, 79.12, 78.61, 74.62, 74.12, 72.10, 60.42, 59.50, 56.27, 46.92, 43.02, 35.53, 33.28, 26.50, 22.46, 20.73, 14.91, 14.20, 10.73. Anal. calcd. for $C_{50}H_{51}Cl_6NO_{18}S$: C, 50.10; H, 4.29; N, 1.17. Found: C, 50.33; H, 4.43; N, 1.23.

*N-De-tert-butoxycarbonyl-N-phenylmethylsulfonyl 7,10-di(2,2,2-trichloroethyloxycarbonyl)-docetaxel* (**5b**). Yield 79% (208 mg); mp 149–151 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.20 (s, 3H, 17-$CH_3$), 1.27 (s, 3H, 16-$CH_3$), 1.76 (s, 3H, 19-$CH_3$), 1.91 (s, 3H, 18-$CH_3$), 2.29 (m, 2H, 14-$CH_2$), 2.35 (s, 3H, OAc), 2.07 and 2.62 (2m, 2H, 6-$CH_2$), 3.89 (d, 1H, *J* = 7.2 Hz, 3-CH), 4.04 (s, 2H, 3″-$CH_2$), 4.22 and 4.32 (2d, 2H, *J* = 8.6 Hz, 20-$CH_2$), 4.54 (br s, 1H, 2′-CH), 4.61 and 4.92 (2d, 2H, *J* = 11.6 Hz, Troc), 4.79 (s, 2H, Troc), 4.88 (m, 1H, 3′-CH), 4.95 (d, 1H, *J* = 9.2 Hz, 5-CH), 5.53 (dd, 1H, *J* = 10.8, 7.2 Hz, 2-CH), 5.69 (d, 1H, *J* = 7.2 Hz, 2-CH), 6.22 (s, 1H, 10-CH), 6.25 (t, 1H, *J* = 8.0 Hz, 13-CH), 7.07 (d, 2H, *J* = 7.2 Hz, 3″-Ph), 7.22 (t, 2H, *J* = 7.2 Hz, 3′-Ph), 7.35 (d, 2H, *J* = 7.6 Hz, 3″-Ph), 7.42 (m, 3H, 3′-Ph), 7.48 (t, 2H, *J* = 8.0 Hz, *m*-OBz), 7.63 (t, 1H, *J* = 7.4 Hz, *p*-OBz), 8.10 (d, 2H, *J* = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.65, 171.53, 170.52, 166.75, 153.22, 153.17, 142.17, 137.52, 133.82, 132.20, 130.71, 130.16, 129.08, 129.02, 128.83, 128.68, 128.59, 128.44, 127.48, 94.18, 83.62, 80.89, 79.12, 78.61, 74.68, 74.19, 72.15, 60.41, 60.25, 59.57, 58.47, 56.24, 46.87, 43.04, 35.54, 33.81, 33.26, 29.69, 26.45, 25.57, 24.89, 22.47, 21.05, 20.84, 18.40, 14.79, 14.20, 10.73. Anal. calcd. for $C_{51}H_{53}Cl_6NO_{18}S$: C, 50.51; H, 4.40; N, 1.15. Found: C, 50.73; H, 4.53; N, 1.16.

*N-De-tert-butoxycarbonyl-N-(4-methyl)-phenylsulfonyl 7,10-di(2,2,2-trichloroethyloxycarbonyl)-docetaxel* (**5c**). Yield 85% (224 mg); mp 157–159 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.20 (s, 3H, 17-$CH_3$), 1.26 (s, 3H, 16-$CH_3$), 1.88 (s, 3H, 19-$CH_3$), 1.91 (s, 3H, 18-$CH_3$), 2.26 (m, 2H, 14-$CH_2$), 2.34 (s, 3H, OAc), 2.35 (s, 3H, $CH_3$ in 4-methylphenyl), 2.08 and 2.63 (2m, 2H, 6-$CH_2$), 3.88 (d, 1H, *J* = 6.8 Hz, 3-CH), 4.22 and 4.32 (2d, 2H, *J* = 8.4 Hz, 20-$CH_2$), 4.56 (d, 1H, *J* = 3.2 Hz, 2′-CH), 4.62 and 4.93 (2d, 2H, *J* = 12.0 Hz, Troc), 4.80 (s, 2H, Troc), 4.91 (m, 1H, 3′-CH), 4.94 (d, 1H, *J* = 9.2 Hz, 5-CH), 5.54 (m, 1H, 7-CH), 5.69 (d, 1H, *J* = 6.8 Hz, 2-CH), 5.84 (m, 1H, -CONH-), 6.18 (t, 1H, *J* = 9.0 Hz, 13-CH), 6.22 (s, 1H, 10-CH), 7.08 (d, 2H, *J* = 8.4 Hz, *m*-$PhSO_2$), 7.13 (m, 2H, 3′-Ph), 7.21 (m, 3H, 3′-Ph), 7.50 (t, 2H, *J* = 7.6 Hz, *m*-OBz), 7.53 (d, 2H, *J* = 8.4 Hz, *o*-$PhSO_2$), 7.64 (t, 1H, *J* = 7.4 Hz, *p*-OBz), 8.10 (d, 2H, *J* = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.64, 170.58, 166.78, 153.22, 153.20, 143.51, 142.10, 137.25, 136.58, 133.87, 132.22, 130.14, 129.40, 129.07, 128.72, 128.62, 128.24, 127.08, 126.96, 94.17, 83.61, 80.90, 79.11, 78.63, 74.60, 74.17, 72.06, 59.51, 56.24, 46.90, 43.02, 35.50, 26.44, 22.46, 21.45, 20.79, 14.85, 10.73. Anal. calcd. for $C_{51}H_{53}Cl_6NO_{18}S$: C, 50.51; H, 4.40; N, 1.15. Found: C, 50.75; H, 4.51; N, 1.19.

*N-De-tert-butoxycarbonyl-N-(4-methoxyl)-phenylsulfonyl 7,10-di(2,2,2-trichloroethyloxycarbonyl)-docetaxel* (**5d**). Yield 79% (210 mg); mp 152–154 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.21 (s, 3H, 17-$CH_3$),

1.27 (s, 3H, 16-$CH_3$), 1.86 (s, 3H, 19-$CH_3$), 1.92 (s, 3H, 18-$CH_3$), 2.22 (m, 2H, 14-$CH_2$), 2.36 (s, 3H, OAc), 2.08 and 2.64 (2m, 2H, 6-$CH_2$), 3.80 (s, 3H, $OCH_3$), 3.89 (d, 1H, *J* = 7.2 Hz, 3-CH), 4.22 and 4.34 (2d, 2H, *J* = 8.4 Hz, 20-$CH_2$), 4.55 (d, 1H, *J* = 3.2 Hz, 2′-CH), 4.62 and 4.93 (2d, 2H, *J* = 12.0 Hz, Troc), 4.80 (s, 2H, Troc), 4.91 (m, 1H, 3′-CH), 4.96 (d, 1H, *J* = 9.2 Hz, 5-CH), 5.54 (dd, *J* = 10.8, 7.2 Hz, 7-CH), 5.69 (d, 1H, *J* = 6.8 Hz, 2-CH), 5.74 (m, 1H, -CONH-), 6.16 (t, 1H, *J* = 8.8 Hz, 13-CH), 6.23 (s, 1H, 10-CH), 6.76 (m, 2H, *o*-$PhOCH_3$), 7.15 (m, 2H, 3′-Ph), 7.23 (m, 3H, 3′-Ph), 7.51 (t, 2H, *J* = 7.6 Hz, *m*-OBz), 7.58 (d, 2H, *J* = 8.8 Hz, *m*-$PhOCH_3$), 7.64 (t, 1H, *J* = 7.2 Hz, *p*-OBz), 8.10 (d, 2H, *J* = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.64, 171.18, 170.57, 166.77, 162.83, 153.22, 136.72, 133.87, 132.22, 131.87, 130.13, 129.12, 128.72, 128.66, 128.27, 127.09, 113.94, 94.18, 83.60, 80.92, 79.12, 78.62, 74.13, 72.00, 60.40, 56.27, 55.57, 46.91, 43.02, 35.53, 33.80, 33.29, 26.43, 25.56, 24.88, 22.44, 21.05, 20.74, 14.90, 14.20, 10.72. Anal. calcd. for $C_{51}H_{53}Cl_6NO_{19}S$: C, 49.85; H, 4.35; N, 1.14. Found: C, 49.99, H, 4.43, N, 1.21.

*N-De-tert-butoxycarbonyl-N-(4-isopropyl)-phenylsulfonyl 7,10-di(2,2,2-trichloroethyloxycarbonyl)-docetaxel* (**5e**). Yield 77% (208 mg); mp 165–167 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.20 (br s, 6H, 2$CH_3$ in *i*-Pr), 1.21 (s, 3H, 17-$CH_3$), 1.27 (s, 3H, 16-$CH_3$), 1.88 (s, 3H, 19-$CH_3$), 1.92 (s, 3H, 18-$CH_3$), 2.29 (m, 2H, 14-$CH_2$), 2.37 (s, 3H, OAc), 2.08 and 2.64 (2m, 2H, 6-$CH_2$), 2.88 (m, 1H, CH in *i*-Pr), 3.89 (d, 1H, *J* = 6.4 Hz, 3-CH), 4.23 and 4.32 (2d, 2H, *J* = 8.4 Hz, 20-$CH_2$), 4.56 (d, 1H, *J* = 3.6 Hz, 2′-CH), 4.62 and 4.93 (2d, 2H, *J* = 11.6 Hz, Troc), 4.80 (s, 2H, Troc), 4.93 (m, 1H, 3′-CH), 4.94 (d, 1H, *J* = 9.2 Hz, 5-CH), 5.54 (dd, 1H, *J* = 10.6, 7.4 Hz, 7-CH), 5.70 (d, 1H, *J* = 6.8 Hz, 2-CH), 6.23 (s, 1H, 10-CH), 6.23 (t, 1H, *J* = 9.0 Hz, 13-CH), 7.01-7.15 (m, 8H, 3′-Ph and *i*-PrPh), 7.52 (m, 2H, *i*-PrPh), 7.52 (t, 2H, *J* = 7.6 Hz, *m*-OBz), 7.63 (t, 1H, *J* = 7.2 Hz, *p*-OBz), 8.11 (d, 2H, *J* = 7.6 Hz, *o*-OBz). $^{13}$C-NMR (100 MHz, $CDCl_3$) $\delta$ 200.65, 171.23, 170.63, 166.74, 154.17, 153.22, 142.15, 137.36, 136.21, 133.82, 132.22, 130.15, 129.13, 128.71, 128.51, 128.21, 127.09, 126.84, 94.18, 83.62, 80.88, 79.12, 78.62, 74.66, 74.21, 72.06, 60.41, 59.63, 56.22, 46.91, 43.02, 35.62, 34.08, 33.27, 26.45, 23.65, 23.60, 22.47, 21.05, 20.87, 14.83, 14.20, 10.75. Anal. calcd. for $C_{53}H_{57}Cl_6NO_{18}S$: C, 51.30; H, 4.63; N, 1.13. Found: C, 51.53; H, 4.72; N, 1.18.

*N-De-tert-butoxycarbonyl-N-(4-fluoro)-phenylsulfonyl 7,10-di(2,2,2-trichloroethyloxycarbonyl)-docetaxel* (**5f**). Yield 50% (132 mg); mp 162–164 °C;$^1$H-NMR ($CDCl_3$): $\delta$ 1.21 (s, 3H, 17-$CH_3$), 1.26 (s, 3H, 16-$CH_3$), 1.88 (s, 3H, 19-$CH_3$), 1.92 (s, 3H, 18-$CH_3$), 2.27 (m, 2H, 14-$CH_2$), 2.36 (s, 3H, OAc), 2.08 and 2.63 (2m, 2H, 6-$CH_2$), 3.88 (d, 1H, *J* = 6.8 Hz, 3-CH), 4.22 and 4.33 (2d, 2H, *J* = 8.6 Hz, 20-$CH_2$), 4.56 (d, 1H, *J* = 3.6 Hz, 2′-CH), 4.62 and 4.93 (2d, 2H, *J* = 11.6 Hz, Troc), 4.80 (s, 2H, Troc), 4.95 (d, 1H, *J* = 9.6 Hz, 3′-CH), 4.96 (d, 1H, *J* = 9.2 Hz, 5-CH), 5.53 (dd, 1H, *J* = 10.6, 7.4 Hz, 5-CH), 5.69 (d, 1H, *J* = 7.2 Hz, 2-CH), 5.92 (d, 1H, *J* = 9.2 Hz, -CONH-), 6.20 (t, 1H, *J* = 8.0 Hz, 13-CH), 6.23 (s, 1H, 10-CH), 6.94 (t, 2H, *J* = 8.4 Hz, -PhF), 7.11 (m, 2H, 3′-Ph), 7.21 (m, 3H, 3′-Ph), 7.50 (t, 2H, *J* = 7.6 Hz, *m*-OBz), 7.62 (m, 2H, -PhF), 7.63 (t, 1H, *J* = 7.6 Hz, *p*-OBz), 8.10 (d, 2H, *J* = 8.0 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.58, 171.21, 171.08, 170.66, 166.77, 166.16, 163.63, 153.22, 141.91, 136.30, 136.12, 133.90, 132.40, 130.12, 129.71, 129.62, 129.02, 128.71, 128.69, 128.47, 127.13, 126.89, 116.05, 115.82, 94.16, 83.58, 81.01, 79.10, 78.58, 74.62, 74.10, 72.11, 60.42, 59.57, 58.48, 56.29, 46.94, 43.02, 35.51, 33.28, 26.47, 22.45, 21.05, 20.67, 18.41, 14.94, 14.20, 10.72. Anal. calcd. for $C_{50}H_{50}Cl_6FNO_{18}S$: C, 49.36; H, 4.14; N, 1.15. Found: C, 49.58; H, 4.22; N, 1.16.

*N-De-tert-butoxycarbonyl-N-(4-trifluoromethyl)-phenylsulfonyl 7,10-di(2,2,2-trichloroethyloxy carbonyl)-docetaxel* (**5g**). Yield 56% (154 mg); mp 159–161 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.21 (s, 3H, 17-$CH_3$), 1.27 (s, 3H, 16-$CH_3$), 1.89 (s, 3H, 19-$CH_3$), 1.90 (s, 3H, 18-$CH_3$), 2.29 (m, 2H, 14-$CH_2$), 2.36 (s, 3H, OAc), 2.09 and 2.64 (2m, 2H, 6-$CH_2$), 3.88 (d, 1H, $J$ = 6.8 Hz, 3-CH), 4.23 and 4.33 (2d, 2H, $J$ = 8.6 Hz, 20-$CH_2$), 4.58 (d, 1H, $J$ = 2.4 Hz, 2′-CH), 4.62 and 4.93 (2d, 2H, $J$ = 11.6 Hz, Troc), 4.80 (s, 2H, Troc), 4.96 (d, 1H, $J$ = 9.6 Hz, 5-CH), 5.01 (dd, 1H, $J$ = 9.2, 7.2 Hz, 3′-CH), 5.53 (dd, 1H, $J$ = 10.6, 7.4 Hz, 7-CH), 5.69 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.00 (d, 1H, $J$ = 9.6 Hz, -CONH-), 6.22 (t, 1H, $J$ = 8.2 Hz, 13-CH), 6.23 (s, 1H, 10-CH), 7.07 (m, 2H, 3′-Ph), 7.17 (m, 3H, 3′-Ph), 7.50 (d, 2H, $J$ = 8.4 Hz, -Ph$CF_3$), 7.50 (t, 2H, $J$ = 7.6 Hz, *m*-OBz), 7.64 (t, 1H, $J$ = 7.6 Hz, *p*-OBz), 7.70 (d, 2H, $J$ = 8.4 Hz, -Ph$CF_3$), 8.09 (d, 2H, $J$ = 7.2 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.54, 170.86, 170.76, 166.78, 153.24, 143.76, 141.74, 135.70, 133.93, 132.53, 130.11, 128.98, 128.72, 128.68, 128.54, 127.41, 127.17, 125.79, 94.15, 83.55, 81.10, 79.10, 78.54, 74.57, 74.03, 72.12, 59.60, 58.49, 56.33, 46.97, 43.02, 35.50, 33.30, 26.52, 22.46, 21.05, 20.56, 18.42, 15.00, 14.20, 10.71. Anal. calcd. for $C_{51}H_{50}Cl_6F_3NO_{18}S$: C, 48.36; H, 3.98; N, 1.11. Found: C, 48.59; H, 4.11; N, 1.15.

*N-De-tert-butoxycarbonyl-N-(4-chloro)-phenylsulfonyl 7,10-di(2,2,2-trichloroethyloxycarbonyl)-docetaxel* (**5h**). Yield 67% (180 mg); mp 162–164 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.21 (s, 3H, 17-$CH_3$), 1.27 (s, 3H, 16-$CH_3$), 1.88 (s, 3H, 19-$CH_3$), 1.90 (s, 3H, 18-$CH_3$), 2.27 (m, 2H, 14-$CH_2$), 2.35 (s, 3H, OAc), 2.08 and 2.64 (2m, 2H, 6-$CH_2$), 3.88 (d, 1H, $J$ = 6.8 Hz, 3-CH), 4.22 and 4.33 (2d, 2H, $J$ = 8.8 Hz, 20-$CH_2$), 4.57 (br s, 1H, 2′-CH), 4.62 and 4.93 (2d, 2H, $J$ = 12.0 Hz, Troc), 4.80 (s, 2H, Troc), 4.96 (d, 1H, $J$ = 9.6 Hz, 5-CH), 4.97 (d, 1H, $J$ = 9.2 Hz, 3′-CH), 5.53 (dd, 1H, $J$ = 10.4, 7.0 Hz, 2-CH), 5.69 (d, 1H, $J$ = 7.2 Hz, 2-CH), 5.92 (d, 1H, $J$ = 9.2 Hz, -CONH-), 6.19 (t, 1H, $J$ = 8.8 Hz, 13-CH), 6.23 (s, 1H, 10-CH), 7.12 (m, 2H, -PhCl), 7.23 (m, 5H, 3′-Ph), 7.50 (t, 2H, $J$ = 7.6 Hz, *m*-OBz), 7.53 (d, 2H, $J$ = 8.8 Hz, -PhCl), 7.64 (t, 1H, $J$ = 7.6 Hz, *p*-OBz), 8.09 (d, 2H, $J$ = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.57, 171.01, 170.68, 166.77, 153.22, 141.85, 139.09, 138.78, 136.12, 133.92, 132.43, 130.12, 129.00, 128.72, 128.48, 128.36, 127.14, 94.17, 83.57, 81.03, 79.10, 78.57, 74.58, 74.07, 72.12, 60.42, 59.55, 56.30, 46.95, 43.02, 35.51, 33.29, 26.49, 22.46, 20.64, 14.95, 14.20, 10.72. Anal. calcd. for $C_{50}H_{50}Cl_7NO_{18}S$: C, 48.70; H, 4.09; N, 1.14. Found: C, 48.95; H, 4.11; N, 1.18.

*N-De-tert-butoxycarbonyl-N-(4-bromo)-phenylsulfonyl 7,10-di(2,2,2-trichloroethyloxycarbonyl)-docetaxel* (**5i**). Yield 57% (158 mg); mp 155–157 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.21 (s, 3H, 17-$CH_3$), 1.27 (s, 3H, 16-$CH_3$), 1.88 (s, 3H, 19-$CH_3$), 1.91 (s, 3H, 18-$CH_3$), 2.27 (m, 2H, 14-$CH_2$), 2.35 (s, 3H, OAc), 2.08 and 2.63 (2m, 2H, 6-$CH_2$), 3.88 (d, 1H, $J$ = 7.2 Hz, 3-CH), 4.22 and 4.33 (2d, 2H, $J$ = 8.6 Hz, 20-$CH_2$), 4.60 (t, 1H, $J$ = 3.6 Hz, 2′-CH), 4.62 and 4.93 (2d, 2H, $J$ = 11.6 Hz, Troc), 4.80 (s, 2H, Troc), 4.96 (d, 1H, $J$ = 9.6 Hz, 5-CH), 4.97 (d, 1H, $J$ = 9.2 Hz, 3′-CH), 5.53 (dd, 1H, $J$ = 10.8, 7.2 Hz, 7-CH), 5.69 (d, 1H, $J$ = 7.2 Hz, 2-CH), 5.92 (d, 1H, $J$ = 9.2 Hz, -CONH-), 6.20 (t, 1H, $J$ = 8.8 Hz, 13-CH), 6.23 (s, 1H, 10-CH), 7.11 (m, 2H, 3′-Ph), 7.24 (m, 3H, 3′-Ph), 7.40 (m, 2H, -PhBr), 7.46 (m, 2H, -PhBr), 7.50 (t, 2H, $J$ = 7.8 Hz, *m*-OBz), 7.64 (t, 1H, $J$ = 7.6 Hz, *p*-OBz), 8.09 (d, 2H, $J$ = 7.6 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.57, 171.21, 171.02, 170.67, 166.77, 153.22, 141.85, 139.33, 136.12, 133.91, 132.43, 131.98, 130.12, 129.01, 128.72, 128.43, 127.55, 127.15, 126.96, 94.16, 83.57, 81.03, 79.10, 78.57, 74.57, 74.08, 72.11, 60.42, 59.57, 58.48, 56.30, 53.43, 46.95, 43.03, 35.52, 33.29, 26.51, 22.46, 21.05,

20.64, 18.42, 14.95, 14.20, 10.72. Anal. calcd. for $C_{50}H_{50}BrCl_6NO_{18}S$: C, 47.00; H, 3.94; N, 1.10. Found: C, 47.30; H, 4.03; N, 1.17.

*N-De-tert-butoxycarbonyl-N-(2,4,6-trimethyl)-phenylsulfonyl 7,10-di(2,2,2-trichloroethyloxy carbonyl)-docetaxel* (**5j**). Yield 68% (183 mg); mp 151–153 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.21 (s, 3H, 17-$CH_3$), 1.26 (s, 3H, 16-$CH_3$), 1.87 (s, 3H, 19-$CH_3$), 1.92 (s, 3H, 18-$CH_3$), 2.29 (m, 2H, 14-$CH_2$), 2.23 (s, 3H, *p*-3″-$CH_3$), 2.32 (s, 3H, OAc), 2.08 and 2.63 (2m, 2H, 6-$CH_2$), 2.50 (s, 6H, *o*-3″-$CH_3$), 3.88 (d, 1H, $J$ = 6.8 Hz, 3-CH), 4.21 and 4.33 (2d, 2H, $J$ = 8.6 Hz, 20-$CH_2$), 4.54 (d, 1H, $J$ = 3.6 Hz, 2′-CH), 4.62 and 4.93 (2d, 2H, $J$ = 11.6 Hz, Troc), 4.75 (m, 1H, 3′-CH), 4.80 (s, 2H, Troc), 4.96 (d, 1H, $J$ = 9.6 Hz, 5-CH), 5.53 (dd, 1H, $J$ = 10.4, 7.2 Hz, 7-CH), 5.66 (d, 1H, $J$ = 8.8 Hz, -CONH-), 5.70 (d, 1H, $J$ = 6.8 Hz, 2-CH), 6.12 (t, 1H, $J$ = 8.8 Hz, 13-CH), 6.23 (s, 1H, 10-CH), 6.78 (s, 2H, 3″-Ph), 7.10-7.22 (m, 5H, 3′-Ph), 7.53 (t, 2H, $J$ = 7.8 Hz, *m*-OBz), 7.67 (t, 1H, $J$ = 7.2 Hz, *p*-OBz), 8.10 (d, 2H, $J$ = 7.2 Hz, *o*-OBz). $^{13}$C-NMR ($CDCl_3$) $\delta$ 200.63, 171.51, 170.31, 166.77, 153.22, 153.18, 142.38, 142.09, 138.60, 136.74, 134.20, 133.90, 132.26, 131.83, 130.08, 129.05, 128.71, 128.54, 128.35, 126.94, 94.17, 83.61, 80.90, 79.11, 78.59, 74.34, 74.10, 72.24, 59.39, 58.48, 56.24, 46.86, 43.05, 35.26, 33.27, 31.92, 29.68, 26.43, 22.87, 22.48, 20.85, 18.42, 14.73, 10.71. Anal. calcd. for $C_{53}H_{57}Cl_6NO_{18}S$: C, 51.30; H, 4.63; N, 1.13. Found: C, 51.53; H, 4.65; N, 1.17.

3.2.6. General Procedure for the Synthesis of **3a**–**j**

To a solution of **5a**–**j** (0.19 mmol) in methanol (10 mL) were added glacial acetic acid (4.60 mL) and zinc powder (0.46 g, 7.08 mmol). After stirred at 50 °C for 1 h, the reaction mixture was filtered to remove the zinc and solid formed. The filtrate was evaporated by distillation to give a white solid. The obtained solid was then dissolved in ethyl acetate (60 mL), which was washed with saturated $NaHCO_3$, brine, dried over $Na_2SO_4$, and concentrated *in vacuo*. The obtained residue was further purified by silica gel flash chromatography column (petroleum ether/acetone: 2/1) to give **3a**–**j**.

*N-De-tert-butoxycarbonyl-N-phenylsulfonyl docetaxel* (**3a**). White powder; Yield 75% (121 mg); mp 174–175 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.09 (s, 3H, 17-$CH_3$), 1.19 (s, 3H, 16-$CH_3$), 1.73 (s, 3H, 19-$CH_3$), 1.81 (s, 3H, 18-$CH_3$), 2.15 (m, 2H, 14-$CH_2$), 2.30 (s, 3H, OAc), 1.82 and 2.51 (2m, 2H, 6-$CH_2$), 3.84 (d, 1H, $J$ = 7.2 Hz, 3-CH), 4.20 and 4.26 (2d, 2H, $J$ = 8.4 Hz, 20-$CH_2$), 4.23 (m, 1H, 7-CH), 4.50 (d, 1H, $J$ = 4.0 Hz, 2′-CH), 4.89 (d, 1H, $J$ = 9.6 Hz, 5-CH), 4.89 (m, 1H, 3′-CH), 5.22 (s, 1H, 10-CH), 5.63 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.14 (t, 1H, $J$ = 8.8 Hz, 13-CH), 6.35 (d, 1H, $J$ = 6.0 Hz, -CONH-), 7.09 (m, 2H, 3′-Ph), 7.14 (m, 3H, 3′-Ph), 7.24 (t, 2H, $J$ = 8.0 Hz, *m*-$PhSO_2$), 7.40 (t, 1H, $J$ = 7.6 Hz, *p*-$PhSO_2$), 7.46 (t, 2H, $J$ = 7.6 Hz, *m*-OBz), 7.58 (t, 1H, $J$ = 7.6 Hz, *p*-OBz), 7.59 (d, 2H, $J$ = 7.6 Hz, *o*-$PhSO_2$), 8.07 (d, 2H, $J$ = 7.6 Hz, *o*-OBz); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 210.54, 171.85, 170.02, 165.73, 141.70, 137.67, 137.40, 136.71, 133.15, 131.98, 130.50, 130.00, 128.56, 128.48, 128.03, 127.57, 127.54, 126.77, 84.16, 80.86, 77.87, 77.76, 75.97, 75.23, 74.92, 74.28, 71.52, 71.26, 60.51, 57.63, 54.08, 46.52, 46.52, 43.25, 36.68, 36.10, 26.27, 22.17, 20.62, 13.55, 9.52; HRMS (ESI) *m/z* calcd. for $C_{44}H_{49}NO_{14}SNa^+$ [M+Na$^+$]: 870.2771, found 870.2802.

*N-De-tert-butoxycarbonyl-N-phenylmethylsulfonyl docetaxel* (**3b**). White powder; Yield 74% (121 mg); mp 168–170 °C; $^1$H-NMR ($CDCOCD_3$): $\delta$ 1.14 (s, 3H, 17-$CH_3$), 1.21 (s, 3H, 16-$CH_3$), 1.74 (s,

3H, 19-$CH_3$), 1.89 (s, 3H, 18-$CH_3$), 2.17 (m, 2H, 14-$CH_2$), 2.41 (s, 3H, OAc), 1.85 and 2.46 (2m, 2H, 6-$CH_2$), 3.89 (s, 1H, 2′-OH), 3.92 (d, 1H, *J* = 7.2 Hz, 3-CH), 4.09 and 4.22 (2d, 2H, *J* = 14.0 Hz, $CH_2$Ph), 4.16 and 4.19 (2d, 2H, *J* = 8.4 Hz, 20-$CH_2$), 4.32 (m, 1H, 7-CH), 4.36 (br s, 1H, 10-OH), 4.64 (t, 1H, *J* = 5.2 Hz, 2′-CH), 4.97 (d, 1H, *J* = 9.2 Hz, 5-CH), 5.00 (d, 1H, *J* = 5.6 Hz, 3′-CH), 5.12 (m, 1H, -CONH-), 5.24 (d, 1H, *J* = 2.0 Hz,10-CH), 5.67 (d, 1H, *J* = 7.6 Hz, 2-CH), 6.22 (t, 1H, *J* = 8.8 Hz, 13-CH), 7.25-7.36 (m, 6H, 3′-Ph and 3″-Ph), 7.47 (t, 2H, *J* = 7.2 Hz, *m*-OBz), 7.55 (m, 4H, 3″-Ph), 7.66 (t, 1H, *J* = 7.2 Hz, *p*-OBz), 8.10 (d, 2H, *J* = 7.2 Hz, *o*-OBz); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 210.54, 172.23, 170.07, 165.76, 138.92, 137.38, 136.73, 133.15, 130.94, 130.45, 130.05, 129.98, 128.55, 128.51, 128.19, 128.14, 128.00, 127.93, 84.18, 80.83, 77.83, 75.98, 75.20, 75.00, 74.28, 71.52, 71.16, 60.70, 59.68, 57.63, 54.09, 46.48, 43.24, 36.67, 35.98, 26.22, 22.29, 20.61, 18.00, 13.52, 9.52; HRMS (ESI) *m/z* calcd. for $C_{45}H_{51}NO_{14}SNa^+$ [M+$Na^+$]: 884.2928, found 884.2944.

*N-De-tert-butoxycarbonyl-N-(4-methyl)-phenylsulfonyl docetaxel* (**3c**). White powder; Yield 80% (131 mg); mp 172–174 °C; $^1$H-NMR ($CDCl_3$): $\delta$ 1.10 (s, 3H, 17-$CH_3$), 1.19 (s, 3H, 16-$CH_3$), 1.73 (s, 3H, 19-$CH_3$), 1.78 (s, 3H, 18-$CH_3$), 2.14 (m, 2H, 14-$CH_2$), 2.30 (s, 3H, OAc), 2.30 (s, 3H, $CH_3$ in 4-methylphenyl), 1.83 and 2.52 (2m, 2H, 6-$CH_2$), 3.84 (d, 1H, *J* = 6.8 Hz, 3-CH), 4.20 and 4.27 (2d, 2H, *J* = 8.4 Hz, 20-$CH_2$), 4.21 (m, 1H, 7-CH), 4.50 (d, 1H, *J* = 3.6 Hz, 2′-CH), 4.89 (d, 1H, *J* = 9.2 Hz, 5-CH), 4.89 (m, 1H, 3′-CH), 5.20 (s, 1H, 10-CH), 5.63 (d, 1H, *J* = 7.6 Hz, 2-CH), 6.12 (m, 1H, -CONH-), 6.13 (t, 1H, *J* = 9.2 Hz, 13-CH), 7.04 (d, 2H, *J* = 8.0 Hz, *m*-$PhSO_2$), 7.11 (m, 2H, 3′-Ph), 7.16 (m, 3H, 3′-Ph), 7.47 (t, 2H, *J* = 8.0 Hz, *m*-OBz), 7.49 (d, 2H, *J* = 8.4 Hz, *o*-$PhSO_2$), 7.59 (t, 1H, *J* = 7.6 Hz, *p*-OBz), 8.07 (d, 2H, *J* = 7.6 Hz, *o*-OBz); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 210.55, 171.86, 170.05, 165.75, 142.66, 138.85, 137.93, 137.44, 136.66, 133.17, 130.48, 130.00, 129.08, 128.92, 128.50, 128.20, 128.03, 127.79, 127.59, 127.43, 126.92, 126.84, 84.17, 80.86, 77.88, 77.77, 75.98, 75.23, 74.92, 74.29, 71.53, 71.26, 60.44, 57.64, 46.52, 43.24, 36.67, 36.09, 26.25, 22.16, 20.61, 20.47, 17.99, 13.55, 9.53; HRMS (ESI) *m/z* calcd. for $C_{45}H_{51}NO_{14}SNa^+$ [M+$Na^+$]: 884.2928, found 884.2942.

*N-De-tert-butoxycarbonyl-N-(4-methoxyl)-phenylsulfonyl docetaxel* (**3d**). White powder; Yield 73% (122 mg); mp 172–174 °C; $^1$H-NMR ($CDCOCD_3$): $\delta$ 1.16 (s, 3H, 17-$CH_3$), 1.23 (s, 3H, 16-$CH_3$), 1.74 (s, 3H, 19-$CH_3$), 1.89 (s, 3H, 18-$CH_3$), 2.25 (m, 2H, 14-$CH_2$), 2.40 (s, 3H, OAc), 1.86 and 2.45 (2m, 2H, 6-$CH_2$), 3.82 (s, 3H, $OCH_3$), 3.93 (d, 1H, *J* = 6.8 Hz, 3-CH), 3.93 (s, 1H, 2′-OH), 4.16 and 4.22 (2d, 2H, *J* = 8.2 Hz, 20-$CH_2$), 4.31 (m, 1H, 7-CH), 4.37 (br s, 1H, 10-OH), 4.56 (d, 1H, *J* = 4.0 Hz, 2′-CH), 4.91 (m, 1H, 3′-CH), 4.87 (m, 1H, -CONH-), 4.97 (d, 1H, *J* = 9.2 Hz, 5-CH), 5.24 (s, 1H, 10-CH), 5.69 (d, 1H, *J* = 6.8 Hz, 2-CH), 6.17 (t, 1H, *J* = 9.0 Hz, 13-CH), 6.85 (d, 2H, *J* = 8.8 Hz, *o*-$PhOCH_3$), 7.16 (t, 1H, *J* = 7.2 Hz, 3′-Ph), 7.22 (t, 2H, *J* = 7.2 Hz, 3′-Ph), 7.28 (d, 1H, *J* = 7.2 Hz, 3′-Ph), 7.57 (t, 2H, *J* = 7.2 Hz, *m*-OBz), 7.60 (d, 2H, *J* = 8.8 Hz, *m*-$PhOCH_3$), 7.67 (t, 1H, *J* = 7.2 Hz, *p*-OBz), 8.13 (d, 2H, *J* = 7.6 Hz, *o*-OBz); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 210.55, 171.88, 170.04, 165.75, 162.51, 137.88, 137.42, 136.69, 133.36, 133.16, 130.49, 130.01, 128.92, 128.50, 128.04, 127.61, 127.47, 113.69, 84.17, 80.85, 77.88, 75.97, 75.23, 74.95, 74.28, 71.53, 71.26, 60.44, 57.63, 55.12, 46.52, 43.24, 36.68, 36.11, 26.24, 22.17, 20.62, 13.57, 9.52; HRMS (ESI) *m/z* calcd. for $C_{45}H_{51}NO_{15}SNa^+$ [M+$Na^+$]: 900.2877, found 900.2889.

*N-De-tert-butoxycarbonyl-N-(4-isopropyl)-phenylsulfonyl docetaxel* (**3e**). White powder; Yield 77% (130 mg); mp 171–173 °C; $^1$H-NMR ($CDCOCD_3$): $\delta$ 1.17 (s, 3H, 17-$CH_3$), 1.20 (s, 3H, 16-$CH_3$), 1.22 (s, 3H, $CH_3$ in *i*-Pr), 1.25 (s, 3H, $CH_3$ in *i*-Pr), 1.75 (s, 3H, 19-$CH_3$), 1.91 (s, 3H, 18-$CH_3$), 2.29 (m, 2H, 14-$CH_2$), 2.43 (s, 3H, OAc), 1.86 and 2.47 (2m, 2H, 6-$CH_2$), 2.90 (m, 1H, CH in *i*-Pr), 3.95 (d, 1H, $J$ = 7.2 Hz, 3-CH), 3.96 (s, 1H, 2′-OH), 4.17 and 4.24 (2d, 2H, $J$ = 8.2 Hz, 20-$CH_2$), 4.32 (m, 1H, 7-CH), 4.38 (br s, 1H, 10-OH), 4.57 (d, 1H, $J$ = 4.8 Hz, 2′-CH), 4.93 (d, 1H, $J$ = 4.4 Hz, 3′-CH), 4.98 (d, 1H, $J$ = 9.2 Hz, 5-CH), 5.25 (s, 1H, 10-CH), 5.69 (d, 1H, $J$ = 7.6 Hz, 2-CH), 6.25 (t, 1H, $J$ = 9.0 Hz, 13-CH), 7.17 (m, 8H, 3′-Ph and *i*-PrPh), 7.55 (d, 2H, $J$ = 8.0 Hz, *i*-PrPh), 7.56 (t, 2H, $J$ = 7.6 Hz, *m*-OBz), 7.66 (t, 1H, $J$ = 7.2 Hz, *p*-OBz), 8.14 (d, 2H, $J$ = 7.2 Hz, *o*-OBz); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 210.56, 171.93, 170.08, 165.79, 153.27, 138.97, 137.49, 137.40, 136.69, 133.15, 130.50, 130.03, 128.49, 128.21, 127.96, 127.76, 127.64, 127.45, 127.06, 127.00, 126.51, 126.39, 84.19, 80.87, 77.91, 77.80, 75.99, 75.27, 74.91, 74.29, 71.52, 71.30, 60.48, 57.64, 46.51, 43.27, 36.67, 36.13, 33.84, 26.30, 23.13, 23.05, 22.21, 20.68, 17.99, 15.37, 13.58, 9.56; HRMS (ESI) *m/z* calcd. for $C_{47}H_{55}NO_{14}SNa^+$ [M+Na$^+$]: 912.3241, found 912.3239.

*N-De-tert-butoxycarbonyl-N-(4-fluoro)-phenylsulfonyl docetaxel* (**3f**). White powder; Yield 53% (87 mg); mp 173–175 °C; $^1$H-NMR ($CDCOCD_3$): $\delta$ 1.16 (s, 3H, 17-$CH_3$), 1.23 (s, 3H, 16-$CH_3$), 1.74 (s, 3H, 19-$CH_3$), 1.90 (s, 3H, 18-$CH_3$), 2.24 (m, 2H, 14-$CH_2$), 2.41 (s, 3H, OAc), 1.85 and 2.46 (2m, 2H, 6-$CH_2$), 3.93 (d, 1H, $J$ = 7.2 Hz, 3-CH), 3.93 (s, 1H, 2′-OH), 4.16 and 4.22 (2d, 2H, $J$ = 8.0 Hz, 20-$CH_2$), 4.31 (m, 1H, 7-CH), 4.37 (br s, 1H, 10-OH), 4.57 (d, 1H, $J$ = 4.8 Hz, 2′-CH), 4.95 (d, 1H, $J$ = 4.8 Hz, 3′-CH), 4.97 (d, 1H, $J$ = 9.0 Hz, 5-CH), 5.24 (s, 1H, 10-CH), 5.69 (d, 1H, $J$ = 7.6 Hz, 2-CH), 6.19 (t, 1H, $J$ = 8.8 Hz, 13-CH), 7.09 (t, 2H, $J$ = 7.2 Hz, 3′-Ph), 7.18 (d, 1H, $J$ = 7.2 Hz, 3′-Ph), 7.21 (d, 2H, $J$ = 6.8 Hz, -PhF), 7.27 (d, 2H, $J$ = 6.8 Hz, 3′-Ph), 7.57 (t, 2H, $J$ = 8.0 Hz, *m*-OBz), 7.67 (t, 1H, $J$ = 7.6 Hz, *p*-OBz), 7.71 (dd, 2H, $J$ = 8.8, 5.2 Hz, -PhF), 8.12 (d, 2H, $J$ = 8.0 Hz, *o*-OBz); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 210.53, 171.84, 170.05, 165.74, 165.71, 163.21, 138.03, 138.00, 137.45, 137.37, 136.74, 133.17, 130.48, 130.00, 129.79, 129.70, 128.49, 128.07, 127.68, 127.60, 115.59, 115.36, 84.17, 80.86, 77.87, 75.97, 75.23, 74.90, 74.27, 71.52, 71.23, 60.64, 57.63, 46.51, 43.25, 36.67, 36.12, 26.23, 22.18, 20.63, 13.56, 9.53; HRMS (ESI) *m/z* calcd. for $C_{44}H_{48}FNO_{14}SNa^+$ [M+Na$^+$]: 888.2677, found 888.2700.

*N-De-tert-butoxycarbonyl-N-(4-trifluoromethyl)-phenylsulfonyl docetaxel* (**3g**). White powder; Yield 57% (99 mg); mp 168–170 °C; $^1$H-NMR ($CDCOCD_3$): $\delta$ 1.16 (s, 3H, 17-$CH_3$), 1.23 (s, 3H, 16-$CH_3$), 1.74 (s, 3H, 19-$CH_3$), 1.91 (s, 3H, 18-$CH_3$), 2.24 (m, 2H, 14-$CH_2$), 2.42 (s, 3H, OAc), 1.86 and 2.47 (2m, 2H, 6-$CH_2$), 3.93 (s, 1H, 2′-OH), 3.93 (d, 1H, $J$ = 6.0 Hz, 3-CH), 4.16 and 4.23 (2d, 2H, $J$ = 8.0 Hz, 20-$CH_2$), 4.32 (m, 1H, 7-CH), 4.37 (br s, 1H, 10-OH), 4.59 (d, 1H, $J$ = 4.8 Hz, 2′-CH), 4.97 (d, 1H, $J$ = 8.8 Hz, 5-CH), 4.98 (d, 1H, $J$ = 4.4 Hz, 3′-CH), 5.24 (s, 1H, 10-CH), 5.69 (d, 1H, $J$ = 6.8 Hz, 2-CH), 6.23 (t, 1H, $J$ = 9.0 Hz, 13-CH), 7.16 (m, 3H, 3′-Ph), 7.24 (d, 1H, $J$ = 6.8 Hz, 3′-Ph), 7.56 (t, 2H, $J$ = 7.6 Hz, *m*-OBz), 7.66 (t, 1H, $J$ = 7.6 Hz, *p*-OBz), 7.66 (d, 2H, $J$ = 8.0 Hz, -Ph$CF_3$), 7.84 (d, 2H, $J$ = 8.0 Hz, -Ph$CF_3$), 8.12 (d, 2H, $J$ = 8.0 Hz, *o*-OBz); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 210.51, 171.79, 170.06, 165.75, 145.38, 137.35, 137.03, 136.77, 133.16, 132.87, 132.55, 130.48, 130.00, 128.48, 128.06, 127.75, 127.66, 125.67, 125.63, 125.00, 122.30, 84.17, 80.87, 77.87, 75.97, 75.24, 74.82, 74.27, 71.52, 71.23, 60.81, 57.63, 46.51, 43.25, 36.66, 36.13, 26.24, 22.20, 20.65, 13.55, 9.53; HRMS (ESI) *m/z* calcd. for $C_{45}H_{48}F_3NO_{14}SNa^+$ [M+Na$^+$]: 938.2645, found 938.2651.

*N-De-tert-butoxycarbonyl-N-(4-chloro)-phenylsulfonyl docetaxel* (**3h**). White powder; Yield 65% (109 mg); mp 178–180 °C; $^1$H-NMR ($CDCOCD_3$): $\delta$ 1.16 (s, 3H, 17-$CH_3$), 1.23 (s, 3H, 16-$CH_3$), 1.74 (s, 3H, 19-$CH_3$), 1.90 (s, 3H, 18-$CH_3$), 2.24 (m, 2H, 14-$CH_2$), 2.41 (s, 3H, OAc), 1.86 and 2.47 (2m, 2H, 6-$CH_2$), 3.93 (d, 1H, $J$ = 6.0 Hz, 3-CH), 3.93 (s, 1H, 2′-OH), 4.16 and 4.22 (2d, 2H, $J$ = 8.0 Hz, 20-$CH_2$), 4.32 (m, 1H, 7-CH), 4.38 (br s, 1H, 10-OH), 4.58 (d, 1H, $J$ = 4.8 Hz, 2′-CH), 4.95 (d, 1H, $J$ = 4.8 Hz, 3′-CH), 4.97 (d, 1H, $J$ = 10.2 Hz, 5-CH), 5.25 (s, 1H, 10-CH), 5.69 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.20 (t, 1H, $J$ = 9.0 Hz, 13-CH), 7.21 (m, 3H, 3′-Ph), 7.28 (d, 1H, $J$ = 6.8 Hz, 3′-Ph), 7.36 (d, 2H, $J$ = 8.4 Hz, -PhCl), 7.57 (t, 2H, $J$ = 7.6 Hz, *m*-OBz), 7.65 (d, 2H, $J$ = 8.8 Hz, -PhCl), 7.67 (t, 1H, $J$ = 7.2 Hz, *p*-OBz), 8.12 (d, 2H, $J$ = 7.2 Hz, *o*-OBz); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 210.53, 171.83, 170.07, 165.76, 140.49, 137.60, 137.44, 137.39, 136.74, 133.19, 130.47, 130.00, 128.67, 128.62, 128.50, 128.09, 127.70, 127.60, 84.18, 80.86, 77.88, 75.98, 75.24, 74.86, 74.28, 71.53, 71.25, 60.67, 57.64, 46.51, 43.26, 36.66, 36.12, 26.27, 22.20, 20.65, 13.57, 9.55; HRMS (ESI) *m/z* calcd. for $C_{44}H_{48}ClNO_{14}SNa^+$ [M+Na$^+$]: 904.2382, found 904.2359.

*N-De-tert-butoxycarbonyl-N-(4-bromo)-phenylsulfonyl docetaxel* (**3i**). White powder; Yield 61% (107 mg); mp 179–181 °C; $^1$H-NMR ($CDCOCD_3$): $\delta$ 1.16 (s, 3H, 17-$CH_3$), 1.24 (s, 3H, 16-$CH_3$), 1.74 (s, 3H, 19-$CH_3$), 1.90 (s, 3H, 18-$CH_3$), 2.24 (m, 2H, 14-$CH_2$), 2.41 (s, 3H, OAc), 1.86 and 2.46 (2m, 2H, 6-$CH_2$), 3.93 (s, 1H, 2′-OH), 3.93 (d, 1H, $J$ = 6.0 Hz, 3-CH), 4.16 and 4.22 (2d, 2H, $J$ = 8.0 Hz, 20-$CH_2$), 4.32 (m, 1H, 7-CH), 4.37 (br s, 1H, 10-OH), 4.58 (t, 1H, $J$ = 5.0 Hz, 2′-CH), 4.95 (d, 1H, $J$ = 5.2 Hz, 3′-CH), 4.95 (m, 1H, -CONH-), 4.97 (d, 1H, $J$ = 7.6 Hz, 5-CH), 5.24 (d, 1H, $J$ = 2.0 Hz,10-CH), 5.69 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.20 (t, 1H, $J$ = 9.0 Hz, 13-CH), 7.22 (m, 3H, 3′-Ph), 7.28 (d, 1H, $J$ = 6.8 Hz, 3′-Ph), 7.53 (t, 2H, $J$ = 7.6 Hz, *m*-OBz), 7.58 (d, 4H, $J$ = 8.4 Hz, -PhBr), 7.67 (t, 1H, $J$ = 7.2 Hz, *p*-OBz), 8.12 (d, 2H, $J$ = 7.2 Hz, *o*-OBz); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 210.52, 171.81, 170.04, 165.74, 140.96, 137.43, 137.34, 136.76, 133.17, 131.68, 130.48, 130.00, 128.71, 128.49, 128.10, 127.71, 127.58, 126.11, 84.16, 80.86, 77.87, 75.97, 75.23, 74.86, 74.27, 71.52, 71.24, 60.67, 57.64, 46.51, 43.26, 36.68, 36.13, 26.28, 22.19, 20.63, 13.55, 9.53; HRMS (ESI) *m/z* calcd. for $C_{44}H_{48}BrNO_{14}SNa^+$ [M+Na$^+$]: 948.1877, found 948.1870.

*N-De-tert-butoxycarbonyl-N-(2,4,6-trimethyl)-phenylsulfonyl docetaxel* (**3j**). White powder; Yield 65% (110 mg); mp 165–167 °C; $^1$H-NMR ($CDCOCD_3$): $\delta$ 1.13 (s, 3H, 17-$CH_3$), 1.21 (s, 3H, 16-$CH_3$), 1.73 (s, 3H, 19-$CH_3$), 1.87 (s, 3H, 18-$CH_3$), 2.16 (m, 2H, 14-$CH_2$), 2.20 (s, 3H, *p*-3″-$CH_3$), 2.36 (s, 3H, OAc), 1.84 and 2.45 (2m, 2H, 6-$CH_2$), 2.55 (s, 6H, *o*-3″-$CH_3$), 3.83 (s, 1H, 2′-OH), 3.90 (d, 1H, $J$ = 7.2 Hz, 3-CH), 4.16 and 4.19 (2d, 2H, $J$ = 8.0 Hz, 20-$CH_2$), 4.30 (m, 1H, 7-CH), 4.35 (br s, 1H, 10-OH), 4.53 (t, 1H, $J$ = 4.0 Hz, 2′-CH), 4.75 (d, 2H, $J$ = 4.8 Hz, -CONH-), 4.96 (d, 1H, $J$ = 9.6 Hz, 5-CH), 5.00 (m, 1H, 3′-CH), 5.23 (d, 1H, $J$ = 2.0 Hz,10-CH), 5.68 (d, 1H, $J$ = 7.2 Hz, 2-CH), 6.09 (t, 1H, $J$ = 8.4 Hz, 13-CH), 6.85 (s, 2H, 3″-Ph), 7.17-7.28 (m, 5H, 3′-Ph), 7.61 (t, 2H, $J$ = 8.0 Hz, *m*-OBz), 7.71 (t, 1H, $J$ = 7.4 Hz, *p*-OBz), 8.11 (d, 2H, $J$ = 7.6 Hz, *o*-OBz); $^{13}$C-NMR ($CD_3COCD_3$) $\delta$ 210.52, 171.94, 169.86, 165.72, 141.79, 138.47, 137.86, 137.33, 136.77, 135.17, 133.22, 131.57, 130.46, 129.91, 128.52, 127.97, 127.61, 127.36, 84.13, 80.86, 77.77, 77.67, 75.93, 75.13, 74.77, 74.29, 71.52, 71.32, 60.19, 57.63, 46.50, 43.24, 36.67, 35.82, 26.21, 22.36, 22.21, 20.49, 19.91, 13.46, 9.47. HRMS (ESI) *m/z* calcd. for $C_{47}H_{55}NO_{14}SNa^+$ [M+Na$^+$]: 912.3241, found 912.3264.

### *3.3. Biological Assays: Anti-HBV Tests*

Drug stock solutions were prepared in DMSO and stored at −70 °C. Upon dilution into culture medium, the final DMSO concentration was <1% DMSO (v/v), a concentration without effect on cell replication. Cell culture and other procedures were the same as those reported previously [15]. A HepG2-derived human hepatablastoma cell line, 2.2.15, was used in this study, which was transfected with cloned HBV DNA to produce HBV particles. All stock cultures were grown in T-25 flasks containing the DMEM supplemented with 10% (v/v) fetal bovine serum, 0.03% (v/v) L-glutamine, 100 μg/mL penicillin, 100 μg/mL streptomycin, and 380 μg/mL G418 at 37 °C in a humidified atmosphere containing 5% $CO_2$. After the HepG2 2.2.15 cell suspensions seeded in 24-well microtiter plates were cultured for 48 h, they were incubated at 37 °C for 9 d in the presence of various concentrations of drugs (200, 100, 50, 25, 12.5 and 6.25 μg/mL respectively) from DMSO-diluted stock, and the medium was refreshed every 3 d. Then the culture supernatants were harvested to detect the HBsAg and HBeAg secretion using diagnostic ELISA kits (Shanghai SIIC KEHUA Biotech Co., Ltd., Shanghai, China) as described in triplicate, and the standard error of the mean (SEM) of inhibition values varied no more than 5%. Cell damage was assessed using the MTT assay.

## 4. Conclusions

In conclusion, we have provided a convenient route for the synthesis in high yields of 3′-*N*-phenylsulfonyl docetaxel analogs from the key intermediate *N*-phenylsulfonyl oxazolidine. Among them, compounds **3e**, **3g** and **3j** showed more potent inhibitory activity against HBeAg secretion than the positive control lamivudine.

## Supplementary Materials

Supplementary materials can be accessed at: http://www.mdpi.com/1420-3049/18/9/10189/s1.

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## Conflicts of Interest

The authors declare no conflict of interest.

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*Sample Availability*: Samples of the compounds are available from the authors.