# A CONVENIENT SYNTHESIS OF 2-PHENYLBENZOFURAN DERIVATIVES WITH POTENT TESTOSTERONE 5α-REDUCTASE INHIBITORY ACTIVITIES

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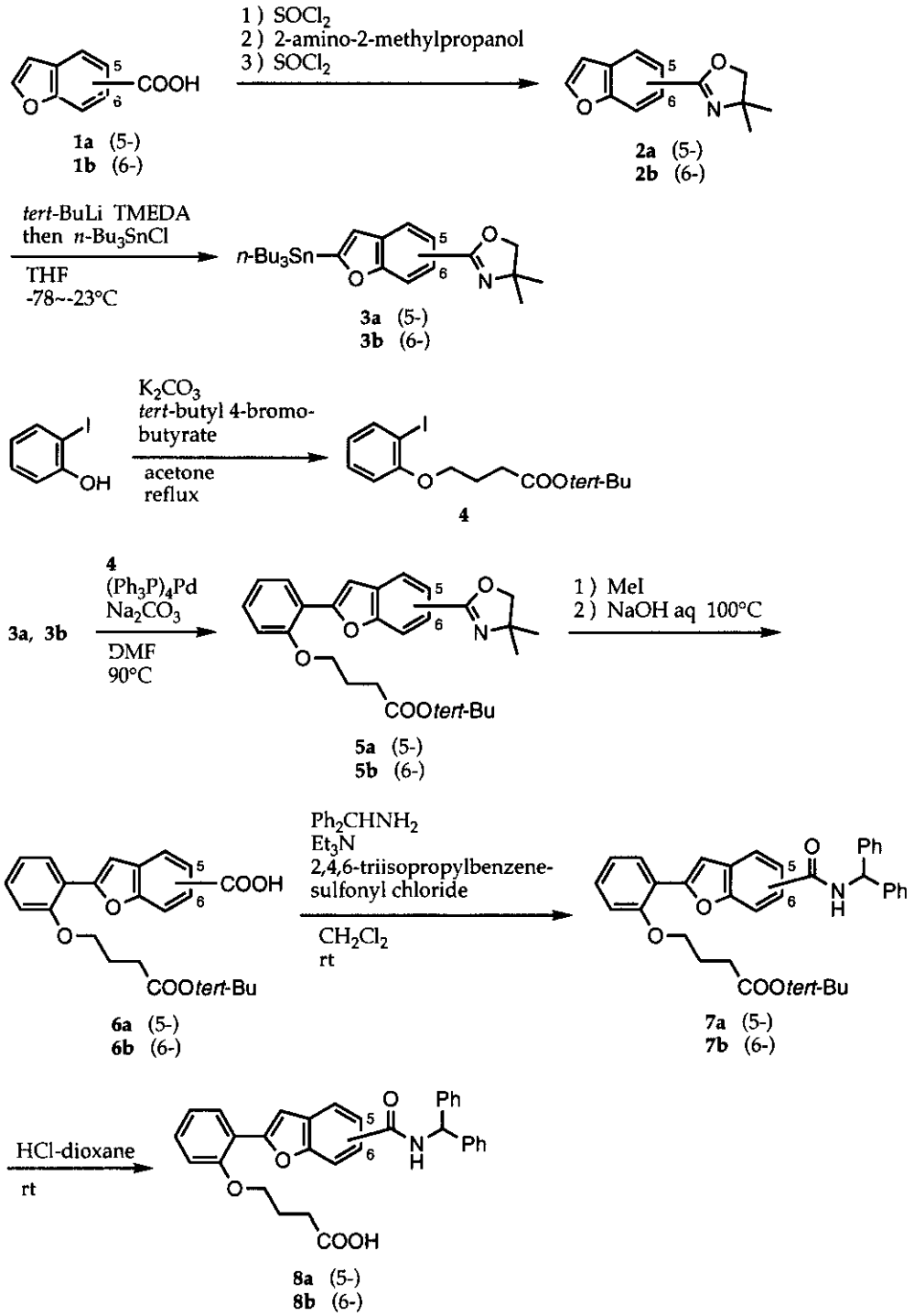
**Abstract** - A convenient method for the synthesis of 4-[2-(benzo[*b*]furan-2-yl)phenyloxy]butyric acid derivatives with a carbamoyl group at the 5 or 6 position of the benzofuran ring showing potent 5α-reductase inhibitory activities was developed. Oxazolin-2-ylbenzofuran derivatives were treated with *tert*-BuLi followed by tri(*n*-butyl)tin chloride, to give 2-tri(1-butyl)stannylbenzofuran derivatives. A palladium-catalyzed cross-coupling reaction of these benzofuran derivatives with *tert*-butyl 4-(2-iodophenyloxy)butyrate afforded the 2-phenyl benzofuran compounds in good yields.

We have already reported that the 4-[2-(benzo[*b*]furan-2-yl)phenyloxy]butyric acid derivatives with a carbamoyl group at the 5 or 6 position of the benzofuran ring showed potent inhibitory activities against rat and human testosterone 5α-reductase.[1] These 5-carbamoyl- and 6-carbamoyl-2-phenylbenzofuran derivatives were synthesized *via* 1-phenyloxyiminoethylbenzene analogues and diphenylacetylene analogues, respectively. To effectively conduct SAR studies on 2-phenylbenzofuran derivatives, a convenient and common synthetic method applicable for the preparation of 2-phenylbenzofuran derivatives with substituents at each position of the two phenyl groups is required. A method for the construction of the 2-phenylbenzofuran structure by a coupling reaction of a benzofuran boric acid with halobenzene has been developed,[2] and we thought this kind of method could be applied to a synthesis of 2-phenylbenzofuran derivatives with a carbamoyl group. In this report, we describe a convenient synthesis of the 5-carbamoyl- or 6-carbamoyl-2-phenylbenzofuran derivatives with a palladium-catalyzed cross-coupling reaction of tin-substituted benzofuran compounds with iodobenzene analogues.

The synthetic route to the 5-carbamoyl- or 6-carbamoyl-2-phenylbenzofuran derivatives is shown in Scheme 1. First, the carboxyl groups of benzofurancarboxylic acids (**1a**) and (**1b**) were protected. Benzofurancarboxylic acids (**1a**) and (**1b**)[3] were treated with thionyl chloride in benzene to give the acid chlorides, which were then reacted with 2-amino-2-methyl-1-propanol in $CH_2Cl_2$ to afford the amides. Treatment of the amides with thionyl chloride in the absence of solvent at room temperature induced a cyclization to an oxazoline ring giving the oxazolin-2-ylbenzofuran (**2a**) (99% yield) and (**2b**) (95%), respectively. Then tri(1-butyl)stannyl group was introduced. The compounds (**2a**) and (**2b**) were treated

## Scheme 1


1) $SOCl_2$
2) 2-amino-2-methylpropanol
3) $SOCl_2$
1a (5-)
1b (6-)
2a (5-)
2b (6-)
*tert*-BuLi TMEDA
then *n*-$Bu_3SnCl$
THF
-78~-23°C
3a (5-)
3b (6-)
$K_2CO_3$
*tert*-butyl 4-bromo-butyrate
acetone
reflux
4
3a, 3b
4
$(Ph_3P)_4Pd$
$Na_2CO_3$
DMF
90°C
1) MeI
2) NaOH aq 100°C
5a (5-)
5b (6-)
$Ph_2CHNH_2$
$Et_3N$
2,4,6-triisopropylbenzene-sulfonyl chloride
$CH_2Cl_2$
rt
6a (5-)
6b (6-)
7a (5-)
7b (6-)
HCl-dioxane
rt
8a (5-)
8b (6-)

with *tert*-BuLi in THF at -78°C in the presence of *N,N,N',N'*-tetramethylethylenediamine (TMEDA) and then reacted with tri(*n*-butyl)tin chloride at -23°C to give the 2-tri(1-butyl)stannylbenzofuran derivatives (**3a**) (74%) and (**3b**) (69%). On the other hand, 2-iodophenol was reacted with *tert*-butyl 4-bromobutyrate[4] in the presence of $K_2CO_3$ in acetone to give *tert*-butyl 4-(2-iodophenyloxy)butyrate (**4**) (82%). And then, a coupling reaction of the prepared benzofuran compounds with iodobenzene analogues was accomplished. The coupling reactions of **3a** with **4**, and **3b** with **4** catalyzed by $(Ph_3P)_4Pd$ in the presence of $Na_2CO_3$ in DMF at 90°C yielded the 2-phenylbenzofuran derivatives (**5a**) (85%) and (**5b**) (83%), respectively. The reaction of **3a** with **4** in a mixture of 1,2-dimethoxyethane and $H_2O$ slightly reduced the yield (**5a**: 70%). Finally, the substituents were modifed. The compounds (**5a**) and (**5b**) were reacted with MeI in DMF and then hydrolyzed with aqueous NaOH solution at 100°C to give the 2-phenylbenzofurancarboxylic acid derivatives (**6a**) (80%) and (**6b**) (83%).[5] The compounds (**6a**) and (**6b**) were reacted with diphenylmethylamine in the presence of 2,4,6-triisopropylbenzenesulfonyl chloride[6] and $Et_3N$ to afford the amide derivatives (**7a**) (97%) and (**7b**) (92%). Treatment of **7a** and **7b** with HCl-dioxane solution at room temperature gave the 4-[2-(benzo[*b*]furan-2-yl)phenyloxy]butyric acid derivatives (**8a**) (94%) and (**8b**) (89%).

The yield in every step of this synthetic method was good. This synthetic method is thought to be applicable to the synthesis of a 4- or 7-carbamoyl-2-phenylbenzofuran derivative from benzofuran-4- or 7-carboxylic acids.[3]

## EXPERIMENTAL

Melting points were taken on a micro melting point apparatus (Yanaco) and are uncorrected. $^1$H-NMR spectra were obtained on a JEOL JNM-GX270 or JNM-EX270 spectrometer (270 MHz) using tetramethylsilane as an internal standard. Chemical shifts are given in δ values (ppm). IR spectra were recorded on a JASCO FT/IR8300 or JASCO FT/IR8900 spectrophotometer. Silica gel 60 (E. Merck, 230-400 mesh) was used for column chromatography.

### 5-(4,4-Dimethyl-2-oxazolin-2-yl)benzo[*b*]furan (2a)

A solution of a mixture of benzofuran-5-carboxylic acid (**1a**)[3] (500 mg, 3.08 mmol) and thionyl chloride (0.563 mL, 7.71 mmol) in benzene (3.0 mL) was stirred under reflux for 3 h. The reaction mixture was concentrated under reduced pressure to give a solid. A solution of a mixture of the solid and 2-amino-2-methylpropanol (563 mg, 6.32 mmol) in $CH_2Cl_2$ (3.0 mL) was stirred at rt for 3 h. The reaction mixture was poured into water and extracted with $CH_2Cl_2$. The combined organic layer was washed with water and brine, and dried over $Na_2SO_4$. The solvent was removed under reduced pressure to give a residue. A mixture of the residue and thionyl chloride (0.675 mL, 9.25 mmol) was stired at rt for 12 h. The reaction mixture was diluted with water and extracted with $CH_2Cl_2$. The conbined organic layer was washed with saturated aqueous $NaHCO_3$ solution and brine, and dried over $Na_2SO_4$. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel. The fraction eluted with *n*-hexane-EtOAc (23:2-4:1) was concentrated under reduced pressure to give **2a** (658 mg, 99%) as an oil. $^1$H-NMR ($CDCl_3$) δ: 1.40 (6H, s), 4.14 (2H, s), 6.80 (1H, d, *J*=2 Hz), 7.51 (1H, d, *J*=9 Hz), 7.66 (1H, d, *J*=2 Hz), 7.93 (1H, dd, *J*=2, 9 Hz), 8.22 (1H, d, *J*=2 Hz). IR ($CHCl_3$): 2970, 2896, 1648 cm$^{-1}$. MS (EI) *m/z*:

215 ($M^+$). HR-MS (EI) *m/z*: Calcd for $C_{13}H_{13}NO_2$ ($M^+$): 215.0946. Found: 215.0960.

**6-(4,4-Dimethyl-2-oxazolin-2-yl)benzo[*b*]furan (2b)**

According to the similar method to that described for the preparation of **2a**, benzofuran-6-carboxylic acid (**1b**)[3] gave **2b** (95%) as an oil. $^1$H-NMR ($CDCl_3$) δ: 1.41 (6H, s), 4.14 (2H, s), 6.80 (1H, m), 7.60 (1H, d, *J*=8 Hz), 7.71 (1H, d, *J*=2 Hz), 7.87 (1H, m), 8.09 (1H, s). IR ($CHCl_3$): 2969, 2896, 1644 cm$^{-1}$. MS (EI) *m/z*: 215 ($M^+$). HR-MS (EI) *m/z*: Calcd for $C_{13}H_{13}NO_2$ ($M^+$): 215.0946. Found: 215.0958.

**5-(4,4-Dimethyl-2-oxazolin-2-yl)-2-tri(1-butyl)stannylbenzo[*b*]furan (3a)**

*tert*-BuLi (1.7 M *n*-pentane solution, 0.406 mL, 0.690 mmol) was added dropwise at -78°C to a solution of a mixture of **2a** (100 mg, 0.464 mmol) and *N,N,N',N'*-tetramethylethylenediamine (0.105 mL, 0.696 mmol) in dried THF (3.0 mL) and the mixture was stirred at -23°C for 1 h. Tri(*n*-butyl)tin chloride (0.189 mL, 0.697 mmol) was added to the reaction mixture at -78°C and the whole was stirred at -23°C for 2 h. The reaction mixture was poured into water and extracted with EtOAc. The combined organic layer was washed with water and brine, and dried over $Na_2SO_4$. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel. The fraction eluted with *n*-hexane-$Et_2O$ (4:1-7:3) was concentrated under reduced pressure to give **3a** (173 mg, 74%) as an oil. $^1$H-NMR ($CDCl_3$) δ: 0.90 (9H, t, *J*=7 Hz), 1.16 (6H, t, *J*=8 Hz), 1.29-1.45 (6H, m), 1.40 (6H, s), 1.42-1.71 (6H, m), 4.12 (2H, s), 6.89 (1H, s), 7.48 (1H, d, *J*=9 Hz), 7.85 (1H, dd, *J*=1, 9 Hz), 8.14 (1H, d, *J*=2 Hz). IR ($CHCl_3$): 2962, 2932, 1645 cm$^{-1}$. MS (FAB) *m/z*: 506 ((M+H)$^+$, calcd for $C_{25}H_{40}NO_2{}^{120}Sn$). HR-MS (FAB) *m/z*: Calcd for $C_{25}H_{40}NO_2{}^{120}Sn$ ((M+H)$^+$): 506.2081. Found: 506.2080.

**6-(4,4-Dimethyl-2-oxazolin-2-yl)-2-tri(1-butyl)stannylbenzo[*b*]furan (3b)**

According to the similar method to that described for the preparation of **3a**, **2b** gave **3b** (69%) as an oil. $^1$H-NMR ($CDCl_3$) δ: 0.90 (9H, t, *J*=7 Hz), 1.16 (6H, t, *J*=8 Hz), 1.27-1.46 (6H, m), 1.40 (6H, s), 1.49-1.71 (6H, m), 4.12 (2H, s), 6.90 (1H, m), 7.53 (1H, d, *J*=8 Hz), 7.81 (1H, dd, *J*=1, 8 Hz), 8.06 (1H, s). IR ($CHCl_3$): 2962, 2932, 1642 cm$^{-1}$. MS (FAB) *m/z*: 506 ((M+H)$^+$, calcd for $C_{25}H_{40}NO_2{}^{120}Sn$). HR-MS (FAB) *m/z*: Calcd for $C_{25}H_{40}NO_2{}^{120}Sn$ ((M+H)$^+$): 506.2081. Found: 506.2079.

***tert*-Butyl 4-(2-iodophenyloxy)butyrate (4)**

A suspension of a mixture of 2-iodophenol (5.02 g, 22.8 mmol), *t*-buthyl 4-bromobutyrate[4] (4.62 g, 20.7 mmol) and $K_2CO_3$ (9.45 g, 68.4 mmol) in acetone (70 mL) was stirred under reflux for 6 h. The reaction mixture was poured into water and extracted with EtOAc. The combined organic layer was washed with 1*N* NaOH aqueous solution, water and brine, and dried over $Na_2SO_4$. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel. The fraction eluted with *n*-hexane-$Et_2O$ (47:3-9:1) was concentrated under reduced pressure to give **4** (6.15 g, 82%) as an oil. $^1$H-NMR ($CDCl_3$) δ: 1.45 (9H, s), 2.06-2.16 (2H, m), 2.52 (2H, t, *J*=7 Hz), 4.05 (2H, t, *J*=6 Hz), 6.70 (1H, m), 6.80 (1H, m), 7.29 (1H, m), 7.76 (1H, dd, *J*=1, 8 Hz). IR ($CHCl_3$): 2982, 2936, 1721 cm$^{-1}$. MS (FAB) *m/z*: 363 ((M+H)$^+$). HR-MS (FAB) *m/z*: Calcd for $C_{14}H_{20}IO_3$ ((M+H)$^+$): 363.0457. Found: 363.0447.

**5-(4,4-Dimethyl-2-oxazolin-2-yl)-2-[2-[3-(*tert*-butyl)oxycarbonyl-1-propyloxy]phenyl]-benzo[*b*]furan (5a)**

A solution of **3a** (700 mg, 1.39 mmol), **4** (554 mg, 1.53 mmol), $Na_2CO_3$ (222 mg, 2.09 mmol), and $(Ph_3P)_4Pd$ (33.0 mg, 0.0286 mmol) in DMF (15 mL) was stirred at 90°C for 3 h. The reaction mixture was diluted with EtOAc and filtered through celite. The filtrate was diluted with water and the organic layer was separated. The aqueous layer was extracted with EtOAc and the combined organic layer was washed with water and brine, and dried over $Na_2SO_4$. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel. The fraction eluted with *n*-hexane-$Et_2O$ (4:1-7:3) was concentrated under reduced pressure to give **5a** (528 mg, 85%) as a pale yellow solid. $^1$H-NMR ($CDCl_3$) δ: 1.41 (6H, s), 1.46 (9H, s), 2.04-2.27 (2H, m), 2.52 (2H, t, *J*=7 Hz), 4.14 (2H, s), 4.20 (2H, t, *J*=6 Hz), 7.00 (1H, d. *J*=8 Hz), 7.08 (1H, t, *J*=8 Hz), 7.29-7.35 (2H, m), 7.50 (1H, d, *J*=8 Hz), 7.90 (1H, dd, *J*=2, 8 Hz), 8.05 (1H, dd, *J*=2 Hz), 8.21 (1H, d, *J*=2 Hz). IR ($CHCl_3$): 2973, 2934, 1722, 1645, 1605 cm$^{-1}$. MS (FAB) *m/z*: 450 ((M+H)$^+$). HR-MS (FAB) *m/z*: Calcd for $C_{27}H_{32}NO_5$ ((M+H)$^+$): 450.2280. Found: 450.2282.

**6-(4,4-Dimethyl-2-oxazolin-2-yl)-2-[2-[3-(*tert*-butyl)oxycarbonyl-1-propyloxy]phenyl]-benzo[*b*]furan (5b)**

According to the similar method to that described for the preparation of **5a**, **3b** gave **5b** (83%) as an oil. $^1$H-NMR ($CDCl_3$) δ: 1.41 (6H, s), 1.46 (9H, s), 2.20-2.54 (2H, m), 2.52 (2H, t, *J*=7 Hz), 4.14 (2H, s), 4.20 (2H, t, *J*=6 Hz), 7.00 (1H, d, *J*=8 Hz), 7.09 (1H, t, *J*=8 Hz), 7.28-7.37 (2H, m), 7.59 (1H, d, *J*=8 Hz), 7.86 (1H, dd, *J*=1, 8 Hz), 8.05-8.10 (2H, m). IR ($CHCl_3$): 2959, 2932, 2859, 1721, 1642, 1612 cm$^{-1}$. MS (FAB) *m/z*: 450 ((M+H)$^+$). HR-MS (FAB) *m/z*: Calcd for $C_{27}H_{32}NO_5$ ((M+H)$^+$): 450.2280. Found: 450.2274.

**2-[2-[3-*tert*-Butyloxycarbonyl-1-propyloxy]phenyl]benzo[*b*]furan-5-carboxylic acid (6a)**

A solution of a mixture of **5a** (450 mg, 1.00 mmol) and MeI (12.0 mL) in DMF (3.0 mL) was stirred at 70°C for 1 d. The reaction solution was concentrated under reduced pressure. 1*N* aqueous NaOH solution (8.0 mL) and DMF (9.0 mL) were added to the residue and the whole was stirred at 100°C for 12 h. The reaction mixture was acidified with 1*N* HCl and extracted with EtOAc. The combined organic layer was washed with water and brine, and dried over $Na_2SO_4$. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel. The fraction eluted with $CH_2Cl_2$ containing 0.5% formic acid and 10% MeOH was concentrated under reduced pressure to give a residue, which was recrystallized from EtOAc-*n*-hexane to afford **6a** (316 mg, 80%) as a white powder. mp 163-164°C. $^1$H-NMR ($CDCl_3$) δ: 1.47 (9H, s), 2.22-2.31 (2H, m), 2.54 (2H, t, *J*=7 Hz), 4.22 (2H, t, *J*=6 Hz), 7.02 (1H, d, *J*=8 Hz), 7.10 (1H, t, *J*=8 Hz), 7.31-7.42 (2H, m), 7.57 (1H, d, *J*=9 Hz), 8.05-8.11 (2H, m), 8.43 (1H, d, *J*=1 Hz). IR (KBr): 2979, 2932, 2650, 1726, 1688, 1613, 1590 cm$^{-1}$. MS (FAB) *m/z*: 396 (M$^+$). *Anal.* Calcd for $C_{23}H_{24}O_6$: C, 69.68; H, 6.10. Found: C, 69.72; H, 6.18.

**2-[2-[3-*tert*-Butyloxycarbonyl-1-propyloxy]phenyl]benzo[*b*]furan-6-carboxylic acid (6b)**

According to the similar method to that described for the preparation of **6a**, **5b** gave **6b** (83%) as a white powder. mp 151-152°C (EtOAc-*n*-hexane). $^1$H-NMR ($CDCl_3$) δ: 1.47 (9H, s), 2.22-2.31 (2H, m), 2.53 (2H, t, *J*=7 Hz), 4.22 (2H, t, *J*=6 Hz), 7.02 (1H, d, *J*=8 Hz), 7.11 (1H, t, *J*=8 Hz), 7.30-7.41 (2H, m), 7.66 (1H, d, *J*=8 Hz), 8.01 (1H, dd, *J*=1, 8 Hz), 8.11 (1H, dd, *J*=2, 8 Hz), 8.27 (1H, s). IR (KBr): 2977, 2936, 2582, 1729, 1685, 1618, 1604 cm$^{-1}$. MS (FAB) *m/z*: 396 (M$^+$). *Anal.* Calcd for $C_{23}H_{24}O_6$:

C, 69.68; H, 6.10. Found: C, 69.74; H, 6.12.

**N-Diphenylmethyl-2-[2-[3-*tert*-butyloxycarbonyl-1-propyloxy]phenyl]benzo[*b*]furan-5-carboxamide (7a)**

2,4,6-Triisopropylbenzenesulfonyl chloride (115 mg, 0.380 mmol) was added in three portions every 30 min to a solution of a mixture of **6a** (100 mg, 0.252 mmol), $Et_3N$ (70.0 μL, 0.504 mmol), diphenylmethylamine (70 mg, 0.382 mmol), and 4-dimethylaminopyridine (3.0 mg) in $CH_2Cl_2$ (3.0 mL). The whole was stirred at rt for 3 h. The reaction mixture was poured into water and extracted with $CH_2Cl_2$. The combined organic layer was washed with 1*N* HCl, water and brine, and dried over $Na_2SO_4$. The solvent was removed under reduced pressure and the residue was chromatographed on silica gel. The fraction eluted with $CH_2Cl_2$-EtOAc (99:1-97:3) was concentrated under reduced pressure to give a residue, which was recrystallized from EtOAc-*n*-hexane to afford **7a** (138 mg, 97%) as a white powder. mp 182-184°C. $^1$H-NMR ($CDCl_3$) δ: 1.45 (9H, s), 2.21-2.29 (2H, m), 2.51 (2H, t, *J*=7 Hz), 4.20 (2H, t, *J*=6 Hz), 6.50 (1H, d, *J*=8 Hz), 6.70 (1H, d, *J*=8 Hz), 7.01 (1H, d, *J*=8 Hz), 7.09 (1H, t, *J*=8 Hz), 7.26-7.42 (12H, m), 7.54 (1H, d, *J*=9 Hz), 7.79 (1H, dd, *J*=2, 9 Hz), 8.04-8.08 (2H, m). IR (KBr): 3326, 2978, 2934, 1725, 1637, 1612, 1588 cm$^{-1}$. MS (FAB) *m/z*: 562 ((M+H)$^+$). *Anal.* Calcd for $C_{36}H_{35}NO_5$: C, 76.98; H, 6.28; N, 2.49. Found: C, 77.02; H, 6.34; N, 2.51.

**N-Diphenylmethyl-2-[2-[3-*tert*-butyloxycarbonyl-1-propyloxy]phenyl]benzo[*b*]furan-6-carboxamide (7b)**

According to the similar method to that described for the preparation of **7a**, **6b** gave **7b** (92%) as a white powder. mp 192-194°C (EtOAc-*n*-hexane). $^1$H-NMR ($CDCl_3$) δ: 1.46 (9H, s), 2.21-2.30 (2H, m), 2.52 (2H, t, *J*=7 Hz), 4.21 (2H, t, *J*=6 Hz), 6.50 (1H, d, *J*=8 Hz), 6.72 (1H, d, *J*=8 Hz), 7.01 (1H, d, *J*=8 Hz), 7.09 (1H, t. *J*=8 Hz), 7.25-7.40 (12H, m), 7.63 (1H, d, *J*=8 Hz), 7.70 (1H, dd, *J*=1, 8 Hz), 8.03 (1H, s), 8.07 (1H, dd, *J*=2, 8 Hz). IR (KBr): 3343, 2976, 2934, 1727, 1634, 1603, 1582 cm$^{-1}$. MS (FAB) *m/z*: 562 ((M+H)$^+$). *Anal.* Calcd for $C_{36}H_{35}NO_5$: C, 76.98; H, 6.28; N, 2.49. Found: C, 77.06; H, 6.32; N, 2.44.

**4-[2-[5-(*N*-Diphenylmethylcarbamoyl)benzo[*b*]furan-2-yl]phenyloxy]butyric acid (8a)**

A solution of **7a** (20.0 mg, 0.0356 mmol) in 4*N* HCl-dioxane solution (1.0 mL) was stirred at rt for 2 h. The solvent was removed under reduced pressure and $Et_2O$ was added to the residue. The solvent was again removed under reduced pressure and the residue was triturated with $Et_2O$ to give **8a** (17.0 mg, 94%) as a white powder. mp 256-258°C. $^1$H-NMR ($CDCl_3$+$CD_3OD$) δ: 2.26-2.33 (2H, m), 2.61 (2H, t, *J*=7 Hz), 4.19-4.28 (2H, m), 6.48 (1H, s), 7.05 (1H, d, *J*=8 Hz), 7.09 (1H, t, *J*=8 Hz), 7.27-7.44 (12H, m), 7.56 (1H, d, *J*=8 Hz), 7.81 (1H, dd, *J*=2, 8 Hz), 8.06 (1H, dd, *J*=2, 8 Hz), 8.13 (1H, d, *J*=2 Hz). IR (KBr): 3301, 3063, 3033, 2947, 1715, 1636, 1612, 1586 cm$^{-1}$. MS (EI) *m/z*: 505 (M$^+$). *Anal.* Calcd for $C_{32}H_{27}NO_5 \cdot 4/5H_2O$: C, 73.92; H, 5.54; N, 2.69. Found: C, 73.75; H, 5.43; N, 2.68.

**4-[2-[6-(*N*-Diphenylmethylcarbamoyl)benzo[*b*]furan-2-yl]phenyloxy]butyric acid (8b)**

According to the similar method to that described for the preparation of **8a**, **7b** gave **8b** (89%) as a white powder. mp 195-197° (EtOAc-*n*-hexane). $^1$H-NMR ($CDCl_3$+$CD_3OD$) δ: 2.25-2.33 (2H, m), 2.62 (2H, t, *J*=7 Hz), 4.23 (2H, t, *J*=6 Hz), 6.49 (1H, m), 7.02 (1H, d, *J*=8 Hz), 7.09 (1H, t, *J*=8 Hz), 7.27-7.40 (13H, m), 7.64 (1H, d, *J*=8 Hz), 7.70 (1H, dd, *J*=1, 8 Hz), 8.02 (1H, s), 8.06 (1H, dd, *J*=2, 8 Hz). IR

(KBr): 3327, 3062, 3030, 2931, 1709, 1630, 1602, 1582 $cm^{-1}$. MS (EI) *m/z*: 505 ($M^+$). *Anal.* Calcd for $C_{32}H_{27}NO_5 \cdot 1/5H_2O$: C, 75.49; H, 5.42; N, 2.75. Found: C, 75.41; H, 5.32; N, 2.69.

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