(i) Supporting Information for the manuscript:

Title: “Syntheses and reactivities of non-symmetrical "active ester" bi-dentate cross-linking reagents having a phthalimidoyl and acid chloride, 2-benzothiazole, or 1-benzotriazole group”

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1. Experimental Section

1.1. General

All the melting points were uncorrected using a micro melting point apparatus. 1H NMR (400 MHz) and 13C NMR (100 MHz) spectra were recorded in CDCl3 using TMS as an internal standard. All the reactions were monitored with TLC and the products were separated by column chromatography using Silica Gel 60 and by preparative layer chromatography using Silica Gel 60 PF254 with UV or PMA and DNP detection. Mass spectra were obtained on a JEOL-JMS-D300 mass spectrometer. The elemental analyses were performed at Micro Analytical Laboratory of the Department of Material Systems Engineering and Life Science, University of Toyama. All the reagents were the highest quality and were further purified by distillation, or re-crystallization.

1.2. Preparation of Phthalimido 4-chloroformylbutanoate (9)

Method (A): Glutaryl dichloride 17 (1457.4 mg, 8.62 mmol) was added to a stirred solution of N-hydroxyphthalimide (469.8 mg, 2.87 mmol) and pyridine (749.0 µL, 2.87 mmol) in CH2Cl2 (7 mL) at rt under N2, and the reaction mixture was stirred for 3 h. Then, hexane was added to the reaction mixture and the precipitate was removed by glass funnel. The solution was concentrated by evaporation and purification by kugelrohr distillation and finally repeated re-crystallization from AcOEt/hexane to yield acid chloride 9 (373.8 mg, 44%) as a colorless solid; Method (B): Thionyl chloride (316.1 µL, 4.33 mmol) was added to a stirred solution of 10 (1.00 g, 3.60 mmol) in ClCH2CH2Cl (13 mL) under N2 and the reaction mixture was refluxed with stirring for 3 h. Then, the solvent was removed under vacuum. The residue was purified by repeated re-crystallization from AcOEt/hexane to yield acid chloride 9 (979.0 mg, 92%) as a colorless solid; Method (C): Compound 10 (50.0 mg, 0.18 mmol) was added to a stirred solution of dichloromethyl methyl ether (47.8 µL, 0.54 mmol) in CH2Cl2 (1 mL) and C6H6 (1 mL) at reflux under N2 and stirred for 5 h. Then, the solvent was removed under vacuum. The residue was purified by repeated re-crystallization from AcOEt/hexane to yield acid chloride 9 (46.8 mg, 88%) as a colorless solid; Method (D): Compound 10 (115.0 mg, 0.42 mmol) was added to a stirred solution of trichloroacetic acid ethyl ester (114.3 µL, 0.83 mmol) in the presence of Ph3P...
(217.7 mg, 0.83 mmol) in CHCl₃ (3 mL) at rt under N₂ and the reaction mixture was stirred for 5 h. Then, the solvent was removed under vacuum. The residue was purified by repeated recrystallization from AcOEt/hexane to yield acid chloride 9 (111.7 mg, 90%) as a colorless solid; mp 88-90 °C; ¹H NMR (CDCl₃, 400 MHz) δ 2.13-2.21 (m, 2H), 2.80 (t, J = 7.9 Hz, 2H), 3.13 (t, J = 7.2 Hz, 2H), 7.79-7.83 (m, 2H), 7.88-7.92 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 19.9, 29.2, 45.2, 123.9, 124.0, 128.7, 134.8, 161.7, 168.5, 173.1; IR (KBr) 1805, 1791, 1741 cm⁻¹. Anal. Calcd for C₁₃H₁₀ClNO₅: C, 55.89; H, 4.02; N, 5.18. Found: C, 53.02; H, 3.56; N, 4.78.

1.3. Preparation of Phthalimido 4-carboxybutanoate (10)

To a stirred solution of N-hydroxyphthalimide (1.00 g, 6.13 mmol) and 4-DMAP (898.6 mg, 7.36 mmol) in CH₂Cl₂ (8 mL) was added to a stirred solution of glutaric anhydride (768.7 mg, 6.74 mmol) in CH₂Cl₂ (4 mL) and the reaction mixture was stirred for 4 h under N₂ at 0 °C. Then, the reaction mixture was neutralized by 1N HCl solution and extracted with CH₂Cl₂ and H₂O, washed with 1N HCl (4 ×), dried over anhydrous MgSO₄, and concentrated under vacuum, to give 10 (1478 mg, 87%) as a colorless solid; mp 92-93 °C (from AcOEt-hexane); ¹H NMR (CDCl₃, 400 MHz) δ 2.09-2.16 (m, 2H), 2.58 (t, J = 7.2 Hz, 2H), 2.80 (t, J = 7.2 Hz, 2H), 7.77-7.82 (m, 2H), 7.86-7.91 (m, 2H), 8.40 (d, J = 8.8 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 19.5, 29.9, 32.3, 124.0, 124.0, 128.8, 134.7, 161.8, 168.9, 177.8; IR (KBr) 1736 cm⁻¹. Anal. Calcd for C₁₃H₁₀ClNO₅: C, 56.32; H, 4.00; N, 5.05. Found: C, 55.89; H, 4.02; N, 5.18.

1.4. Preparation of N-(3-Phenylpropionyloxy)benzotriazole (11)

DCC (892.9 mg, 4.32 mmol) was added to a stirred solution of hydrocinnamic acid (500.0 mg, 3.32 mmol) and 1-hydroxybenzotriazole (584.8 mg, 4.32 mmol) in CH₂Cl₂ (8 mL) at 0 °C under N₂ and stirred for 3 h. Then, the precipitate was filtered and washed with CH₂Cl₂. Purification by TLC on silica gel (AcOEt/hexane; 1:1) gave the title compound 11 (851.8 mg, 96%) as a colorless solid; mp 92-93 °C (from AcOEt-hexane); ¹H NMR (CDCl₃, 400 MHz) δ 3.17 (t, J = 7.6 Hz, 2H), 3.48 (t, J = 7.6 Hz, 2H), 7.22-7.31 (m, 5H), 7.54-7.58 (m, 1H), 7.75-7.79 (m, 1H), 8.00 (d, J = 8.4 Hz, 1H), 8.40 (d, J = 8.8 Hz, 1H); ¹³C NMR (CDCl₃, 100 MHz) δ 19.9, 29.2, 36.5, 115.5, 116.0, 126.5, 126.7, 128.3, 128.6, 132.5, 133.0, 139.4, 169.1; IR (KBr) 1736 cm⁻¹. Anal. Calcd for C₁₃H₁₀N₂O₂: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.68; H, 5.01; N, 15.80.

1.5. Preparation of N-(3-Phenylpropionyloxy)phthalimide (12)

DCC (1786.8 mg, 8.66 mmol) was added to a stirred solution of hydrocinnamic acid (1.00 g, 6.66 mmol) and N-hydroxyphthalimide (1412.2 mg, 8.66 mmol) in CH₂Cl₂ (15 mL) at 0 °C under N₂ and stirred for 3 h. Then, the precipitate was filtered and washed with CH₂Cl₂. Purification by TLC on silica gel (AcOEt/hexane; 1:1) gave the title compound 12 (1.81 g, 92%) as a colorless solid; mp 84-85 °C (from CH₂Cl₂-hexane); ¹H NMR (CDCl₃, 400 MHz) δ 2.96-3.00 (m, 2H), 3.11 (t, J = 7.2 Hz, 2H), 7.23-7.27 (m, 3H), 7.31-7.35 (m, 2H), 7.77-7.81 (m, 2H), 7.86-7.91 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 30.5, 32.7, 123.9, 126.7, 128.3, 128.7, 134.7, 139.1, 161.9, 168.8; IR (KBr) 1789, 1740 cm⁻¹. Anal. Calcd for C₁₇H₁₅N₂O₂: C, 69.15; H, 4.44; N, 4.74. Found: C, 69.14; H, 4.52; N, 4.69.

1.6. Preparation of 3-Phenylpropionyloxybenzothiazole (13)

DCC (44.3 mg, 0.21 mmol) was added to a stirred solution of hydrocinnamic acid (25.0 mg, 0.16 mmol) and 2-hydroxybenzothiazole (32.0 mg, 0.21 mmol) in CH₂Cl₂ (1 mL) at rt under N₂ and stirred for 3 h. Then, the precipitate was filtered and washed with CH₂Cl₂. Purification by TLC on
silica gel (CH$_2$Cl$_2$) gave the title compound 8 ($29.0$ mg, $64\%$) as a colorless solid; mp $83-84$ °C (from CH$_2$Cl$_2$-hexane); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.09 (t, $J = 7.4$ Hz, 2H), 3.45 (t, $J = 7.6$ Hz, 2H), 7.18-7.37 (m, 7H), 8.25-8.27 (dd, $J = 8.2$, 8.3 Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 30.4, 40.6, 117.7, 121.8, 125.4, 126.3, 126.9, 128.5, 128.5, 134.6, 140.2, 170.9, 173.3; IR (KBr) 1732 cm$^{-1}$. Anal. Calcd for C$_{16}$H$_{13}$NO$_3$: C, 67.82; H, 4.62; N, 6.83. Found: C, 67.89; H, 4.75; N, 4.98.

1.7. Preparation of N-(3-Phenylpropionyl)benzotriazole (14)

*Method A*: A mixture of hydrocinnamic acid (53.0 mg, 0.35 mmol) and 1-(methanesulfonyl)benzotriazole (70 mg, 0.35 mmol) and Et$_3$N (50 mg, 0.48 mmol) were refluxed in THF (2 mL) under N$_2$ for overnight. The solvent was evaporated and the residue was dissolved in CHCl$_3$. The organic layer was washed with water, dried over anhydrous MgSO$_4$, and evaporated to give a solid crude product, which was purified by TLC on silica gel (AcOEt/hexane; 1:1) gave the title compound mp 58-59 °C (from AcOEt-hexane); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 1.82 (s, 3H), 2.23-2.30 (m, 2H), 2.86 (t, $J = 7.4$ Hz, 2H), 3.45 (t, $J = 8.4$ Hz, 1H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 19.3, 29.9, 37.5, 117.8, 121.8, 121.9, 123.9, 125.5, 127.0, 128.8, 134.7, 161.8, 169.0, 172.9; IR (KBr) 1787, 1739, 1714 cm$^{-1}$. Anal. Calcd for C$_{20}$H$_{14}$NO$_3$: C, 67.82; H, 4.62; N, 6.94. Found: C, 67.89; H, 4.75; N, 4.98.

1.8. Modified procedure for the synthesis of Phthalimido 4-(2-benzothiazolylcarbonyl)butanoate (15)

DCC (96.5 mg, 0.46 mmol) was added to a stirred solution of 10 (100.0 mg, 0.36 mmol) and 2-hydroxybenzothiazole (54.4 mg, 0.36 mmol) in CH$_2$Cl$_2$ (2 mL) and the reaction mixture was stirred for 3 h under N$_2$ at 0 °C. Then, the reaction mixture was neutralized by dil. AcOH solution and extracted with CH$_2$Cl$_2$. Purification by TLC on silica gel (AcOEt/hexane; 1:1) gave the title compound 9 (220.5 mg, 66%) as a colorless solid. mp 58-59 °C (from AcOEt-hexane); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.23 (t, $J = 7.6$ Hz, 2H), 3.76 (t, $J = 3.0$ Hz, 2H), 7.19-7.32 (m, 5H), 7.47-7.51 (m, 1H), 7.62-7.66 (m, 1H), 8.11-8.13 (m, 1H), 8.28-8.31 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 30.1, 37.0, 114.3, 120.1, 126.1, 126.4, 128.4, 128.6, 130.3, 131.0, 139.7, 146.1, 171.5; IR (KBr) 1755 cm$^{-1}$.

1.9. Preparation of Phthalimido 4-(1-benzotriazolylcarbonyl)butanoate (16)

*Method A*: To a stirred solution of 26 (156.2 mg, 0.79 mmol) in CH$_2$Cl$_2$ (4 mL) was added to a solution of 10 (200.0 mg, 0.72 mmol) in CH$_2$Cl$_2$ (4 mL) in the presence of pyridine (75.5 µL, 0.93 mmol) at rt under N$_2$ and stirred for 9 h. Then, the solvent was removed under vacuum. The residue was purified after repeated recrystalization to yield 15 (115.1 mg, 78%) as a colorless solid; mp 150-151 °C (from CH$_2$Cl$_2$-hexane); $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 2.23-2.30 (m, 2H), 2.86 (t, $J = 7.4$ Hz, 2H), 3.32 (t, $J = 7.0$ Hz, 2H), 7.25-7.28 (m, 1H), 7.32-7.39 (m, 2H), 7.78-7.81 (m, 2H), 7.87-7.90 (m, 2H), 8.33 (d, $J = 8.4$ Hz, 1H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 19.3, 29.9, 37.5, 117.8, 121.8, 121.9, 123.9, 125.5, 127.0, 128.8, 134.7, 161.8, 169.0, 172.9; IR (KBr) 1787, 1739, 1714 cm$^{-1}$. Anal. Calcd for C$_{20}$H$_{14}$NO$_3$: C, 67.82; H, 4.34; N, 6.83. Found: C, 57.94; H, 3.52; N, 6.81.
product, which were purified by flash chromatography (AcOEt/hexane; 1:1) to yield 16 (1215.0 mg, 84%) as a colorless solid; mp 155.5-157 °C (from CH2Cl2/hexane); 1H NMR (CDCl3, 400 MHz) δ 2.37-2.44 (m, 2H), 2.95 (t, J = 7.2 Hz, 2H), 3.65 (t, J = 7.2 Hz, 2H), 7.50-7.54 (m, 1H), 7.65-7.69 (m, 1H), 7.78-7.82 (m, 2H), 7.87-7.90 (m, 2H), 8.12-8.15 (m, 1H), 8.29-8.31 (m, 1H); 13C NMR (CDCl3, 100 MHz) δ 19.1, 30.0, 34.1, 114.3, 120.2, 124.0, 126.2, 128.8, 130.5, 134.7, 146.1, 161.8, 168.8, 171.3; IR (KBr) 1812, 1785, 1752 cm⁻¹.


X-ray crystal data; Empirical formula: C19H14N4O4; Formula weight 362.34; Crystal system = triclinic; Space group Pī ( No. 2; Lattice parameters: a = 8.781(2) Å; b = 14.847(2) Å; c = 7.735(2) Å; α = 90.96(2)°, β = 114.70(2)°, γ = 74.50(1)°; V = 877.7(3) Å³; T = 23.0 °C; Z = 2; m (MoKα) = 0.99 cm⁻¹; 5427 reflections measured, 2839 unique (Rint = 0.048); final R value 0.066.

Crystallographic data has been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 751600

1.10. Bis(1,3-diphthalimidyl glutarate) (18)

Colorless solid; mp 216.5-217.5 °C (from CH2Cl2/hexane); 1H NMR (CDCl3, 400 MHz) δ 2.24-2.31 (m, 2H), 2.89 (t, J = 7.4 Hz, 2H), 7.78-7.82 (m, 2H), 7.87-7.92 (m, 2H); 13C NMR (CDCl3, 100 MHz) δ 19.7, 29.7, 124.0, 128.9, 134.8, 161.8, 168.7; IR (KBr) 1816, 1787, 1741 cm⁻¹. Anal. Calcd for C21H14N2O8: C, 59.72; H, 3.34; N, 6.63. Found: C, 59.77; H, 3.58; N, 6.66.

1.11. General procedure for the reaction of model “active ester” compound 11, 12, 13, and 14 with several nucleophiles (product 19 as an example)

Typical procedure: To a stirred solution of 4-DMAP (86.1 mg, 0.70 mmol) was added to a stirred solution of 4-methylbenzyl alcohol (86.1 mg, 0.70 mmol) and 13 (200.0 mg, 0.70 mmol) in CH2Cl2 (4 mL) under N2 at rt and stirred for 2 h. Then, the reaction mixture was neutralized by dil. AcOH solution and extracted with CH2Cl2. The organic layer was separated, successively washed with water and brine, and dried over anhydrous MgSO4. Removal of solvent in vacuum, to give oil crude product, which was purified by flash chromatography yielded 3-phenylpropionic acid 4-methylbenzyl ester 19 (159.7 mg, 89%) as a colorless liquid; 1H NMR (CDCl3, 400 MHz) δ 2.31 (s, 3H), 2.61-2.65 (m, 2H), 2.93 (t, J = 7.8 Hz, 2H), 5.04 (s, 2H), 7.11-7.26 (m, 9H); 13C NMR (CDCl3, 100 MHz) δ 21.0, 30.8, 35.7, 66.0, 126.1, 128.1, 128.2, 128.3, 129.0, 132.8, 137.8, 140.3, 172.5; IR (neat) 1735 cm⁻¹. HRMS (EI) calcd for C17H18O2: 254.1307; found: m/z 254.1304.

1.11.1. 3-Phenylpropionic acid 4-chlorobenzyl ester (20)

Colorless liquid; 1H NMR (CDCl3, 400 MHz) δ 2.66 (t, J = 7.6 Hz, 2H), 2.94 (t, J = 7.6 Hz, 2H), 5.03 (s, 2H), 7.15-7.29 (m, 9H); 13C NMR (CDCl3, 100 MHz) δ 21.0, 30.8, 35.7, 66.0, 126.1, 128.1, 128.4, 128.5, 129.4, 133.9, 134.3, 140.1, 172.4; IR (neat) 1735 cm⁻¹. HRMS (EI) calcd for C16H15ClO2: 274.0761; found: m/z 274.0741.

1.11.2. 3-Phenyl propionic acid 2 phenylethyl ester (21)

Colorless liquid; 1H NMR (CDCl3, 400 MHz) δ 2.49-2.54 (m, 2H), 2.79-2.84 (m, 4H), 4.17-4.21 (m, 2H), 7.06-7.21 (m, 10H); 13C NMR (CDCl3, 100 MHz) δ 30.8, 35.0, 35.8, 64.8, 126.1, 126.4, 128.2, 128.4, 128.8, 137.7, 140.4, 172.7; IR (neat) 1734 cm⁻¹. HRMS (EI) calcd for C17H18O2: 254.1307; found: m/z 254.1282.
1.11.3. N-Benzyl-3-phenylpropionamide (22)

Colorless solid; mp 76.5-77.0 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 2.51 (t, J = 7.6 Hz, 2H), 2.99 (t, J = 6.8 Hz, 2H), 4.39 (d, J = 6.0 Hz, 2H), 5.62 (s, 1H), 7.13-7.31 (m, 10H); ¹³C NMR (CDCl₃, 100 MHz) δ 31.6, 38.5, 43.6, 126.2, 127.4, 127.7, 128.3, 128.5, 128.6, 138.1, 140.7, 171.8; IR (KBr) 3292, 1639 cm⁻¹. Anal. Calcd for C₁₆H₁₇NO: C, 80.30; H, 7.16; N, 5.85; found: C, 80.34; H, 7.16; N, 5.90.

1.11.4. N-4-Chlorobenzyl-3-phenylpropionamide (23)

Colorless solid; mp 114.5-115.5 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 2.48 (t, J = 7.8 Hz, 2H), 2.93 (t, J = 7.8 Hz, 2H), 4.28 (s, 2H), 6.11 (s, 1H), 6.96-6.99 (m, 2H), 7.00-7.27 (m, 7H); ¹³C NMR (CDCl₃, 100 MHz) δ 31.5, 38.1, 42.5, 126.1, 128.2, 128.4, 128.5, 128.7, 132.9, 136.6, 140.5, 172.0; IR (KBr) 3282, 1636 cm⁻¹. HRMS (EI) calcd for C₁₇H₁₆ClNO: 273.0920; found: m/z 273.0917.

1.11.5. 3-Phenylthiopropionic S-benzyl ester (24)

Colorless liquid; ¹H NMR (CDCl₃, 400 MHz) δ 2.85-2.89 (m, 2H), 2.99 (t, J = 7.6 Hz, 2H), 4.12 (s, 2H), 7.15-7.31 (m, 10H); ¹³C NMR (CDCl₃, 100 MHz) δ 31.3, 33.1, 45.2, 126.3, 127.2, 128.2, 128.5, 128.6, 128.7, 137.5, 139.9, 197.8; IR (neat) 1686 cm⁻¹. HRMS (EI) calcd for C₁₆H₁₆OS: 256.0922; found: m/z 256.0920.

1.12. N-(1-Methanesulphonyl)benzotriazole (26)

To a ice-cold solution of benzotriazole (1.00 g, 8.4 mmol) and pyridine (1215.1 µL, 15.1 mmol) in dry toluene (5 mL) was added dropwise methanesulfonyl chloride (977.4 µL, 12.6 mmol) in toluene (10 mL) and the reaction mixture was stirred at rt under N₂ for 12 h. Then, AcOEt and H₂O were added and organic layer was separated, successively washed with H₂O and brine, and dried over anhydrous MgSO₄. Removal of solvents in vacuum, to give a solid crude product which was separated by column (Hexane/AcOEt; 1:1) to give 26 (1538 mg, 93%) as a colorless solid; mp [9-10] 110-111.5 °C (from CH₂Cl₂/hexane).

1.13. General procedure for the reactions of linker 9, 15, or 16 with various nucleophiles in the present of 4-DMAP (product 27 as an example)

**Typical procedure:** To a stirred solution of 4-DMAP (29.3 mg, 0.24 mmol) and benzyl alcohol (25.3 µL, 0.24 mmol) in CH₂Cl₂ (1 mL) dropwise added to a stirred solution of 15 (100.0 mg, 0.24 mmol) in CH₂Cl₂ (1 mL) at rt under N₂ and stirred for 1 h. Then, the reaction mixture was neutralized by NaHCO₃ solution and extracted with CH₂Cl₂, and dried over anhydrous MgSO₄, and concentrated under vacuum, to give crude product which was purified by flash chromatography yielded, phthalimido 4-benzyloxycarbonylbutanoate 27 (69.6 mg, 79%) as a colourless solid; mp 93% 110-111.5 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 2.09-2.16 (m, 2H), 2.55 (t, J = 7.2 Hz, 2H), 2.76 (t, J = 7.2 Hz, 2H), 5.15 (s, 2H), 7.30-7.38 (m, 5H), 7.76-7.80 (m, 2H), 7.85-7.90 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 19.8, 29.9, 32.6, 66.3, 123.9, 128.1, 128.2, 128.5, 128.8, 134.7, 135.7, 161.8, 168.9, 172.3; IR (KBr) 1814, 1787, 1743 cm⁻¹. Anal. Calcd for C₂₀H₁₇NO₆: C, 65.39; H, 4.66; N, 3.81. Found: C, 65.71; H, 4.75; N, 3.72.

1.13.1. Phthalimido 4-(4-methylbenzyloxycarbonyl)butanoate (28)
Colorless liquid; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 1.54-1.61 (m, 3H), 2.08-2.13 (m, 2H), 2.50-2.54 (m, 2H), 2.69-2.75 (m, 2H), 5.88-5.91 (m, 1H), 7.25-7.37 (m, 5H), 7.77-7.80 (m, 2H), 7.87-7.90 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 19.8, 22.2, 29.9, 32.9, 72.6, 123.9, 126.0, 126.1, 127.9, 128.5, 128.6, 134.8, 141.5, 161.8, 169.0, 171.7; IR (neat) 1814, 1788, 1745 cm$^{-1}$. HRMS (EI) calcd for C$_{21}$H$_{19}$NO$_6$: 381.1212; found: m/z 381.1198.

1.13.2. Phthalimido 4-(1-methylbenzyloxycarbonyl)butanoate (29)

Colorless solid; mp 48.5-50.5 °C (from CH$_2$Cl$_2$/hexane); $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 1.98-2.05 (m, 2H), 2.25 (s, 3H), 2.44 (t, $J = 7.2$ Hz, 2H), 2.66 (t, $J = 7.2$ Hz, 2H), 7.05-7.08 (m, 2H), 7.12-7.17 (m, 2H), 7.67-7.70 (m, 2H), 7.75-7.79 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 19.7, 21.0, 29.8, 32.6, 66.2, 123.8, 128.3, 128.7, 129.0, 129.1, 132.7, 134.6, 138.0, 161.7, 168.9, 172.2; IR (KBr) 1817, 1787, 1738 cm$^{-1}$. HRMS (EI) calcd for C$_{21}$H$_{19}$NO$_6$: 381.1212; found: m/z 381.1220.

1.13.3. Phthalimido 4-(4-chlorobenzyloxycarbonyl)butanoate (30)

Colorless liquid; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 1.99-2.06 (m, 2H), 2.46 (t, $J = 7.4$ Hz, 2H), 5.01 (s, 2H), 7.18-7.24 (m, 5H), 7.67-7.71 (m, 2H), 7.75-7.79 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 19.7, 29.8, 32.4, 65.4, 123.8, 128.4, 128.6, 129.5, 134.0, 134.2, 134.7, 161.7, 168.8, 172.1; IR (neat) 1813, 1788, 1744 cm$^{-1}$. HRMS (EI) calcd for C$_{20}$H$_{16}$ClNO$_6$: 401.0666; found: m/z 401.0668.

1.13.4. Phthalimido 4-phenylethyloxycarbonylbutanoate (31)

Colorless liquid; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 2.03-2.12 (m, 2H), 2.45-2.49 (m, 2H), 2.68-2.72 (m, 2H), 2.95 (t, $J = 7.2$ Hz, 2H), 4.30-4.34 (m, 2H), 7.21-7.31 (m, 5H), 7.77-7.80 (m, 2H), 7.87-7.89 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 19.7, 29.8, 32.6, 35.0, 123.9, 126.5, 128.4, 128.7, 128.8, 134.7, 137.6, 161.8, 168.9, 172.3; IR (neat) 1814, 1788, 1745 cm$^{-1}$. HRMS (EI) calcd for C$_{21}$H$_{19}$NO$_6$: 381.1212; found: m/z 381.1194.

1.13.5. Phthalimido 4-phenyloxycarbonylbutanoate (32)

Colorless solid; mp 105-106 °C (from CH$_2$Cl$_2$/hexane); $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 2.19-2.26 (m, 2H), 2.73-2.78 (m, 2H), 2.86 (t, $J = 7.2$ Hz, 2H), 4.17-4.21 (m, 2H), 5.01 (s, 2H), 7.21-7.26 (m, 2H), 7.36-7.41 (m, 2H), 7.77-7.82 (m, 1H), 7.87-7.91 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 19.7, 29.9, 32.6, 121.5, 124.0, 125.8, 128.8, 129.4, 134.8, 150.5, 161.8, 168.9, 171.0; IR (KBr) 1808, 1781, 1751 cm$^{-1}$. Anal. Calcd for C$_{19}$H$_{15}$NO$_6$: C, 64.59; H, 4.28; N, 3.96. Found: C, 64.34; H, 4.33; N, 4.04. HRMS (EI) calcd for C$_{19}$H$_{15}$NO$_6$: 353.0899; found: m/z 353.0868.

1.13.6. Phthalimido 4-(S-benzyloxycarbonyl)butanoate (33)

Colorless solid; mp 49-50 °C (from CH$_2$Cl$_2$/hexane); $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 2.11-2.19 (m, 2H), 2.73-2.78 (m, 2H), 4.14 (s, 2H), 7.21-7.31 (m, 5H), 7.77-7.81 (m, 2H), 7.86-7.90 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$ 20.3, 29.9, 33.2, 41.9, 123.9, 127.3, 128.6, 128.7, 128.8, 134.7, 137.3, 161.8, 168.8, 197.5; IR (KBr) 1810, 1745, 1746 cm$^{-1}$. Anal. Calcd for C$_{20}$H$_{17}$NO$_5$S: C, 62.65; H, 4.47; N, 3.65. Found: C, 63.04; H, 4.54; N, 3.59.
1.13.7. Phthalimido 4-(N-benzyloxycarbonyl)butanoate (34)

Colorless solid; mp 149.0-149.5 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 2.14-2.21 (m, 2H), 2.40 (t, J = 7.2 Hz, 2H), 2.74 (t, J = 6.8 Hz, 2H), 4.46 (d, J = 5.6 Hz, 2H), 6.27 (s, 1H), 7.21-7.32 (m, 5H), 7.78-7.82 (m, 2H), 8.57-8.89 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 20.9, 29.9, 34.6, 43.6, 124.0, 127.4, 127.8, 128.6, 128.7, 134.8, 138.1, 162.0, 169.3, 171.5; IR (KBr) 3316, 1808, 1787, 1747 cm⁻¹. Anal. Calcd for C₂₀H₁₈N₂O₅: C, 65.57; H, 4.95; N, 7.65. Found: C, 65.13; H, 4.88; N, 7.52.

1.13.8. Phthalimido 4-(N-4-chlorobenzyloxycarbonyl)butanoate (35)

Colorless solid; mp 144.5-147 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 2.12-2.22 (m, 2H), 2.40 (t, J = 7.0 Hz, 2H), 2.74 (t, J = 6.6 Hz, 2H), 4.43 (d, J = 5.6 Hz, 2H), 6.33 (s, 1H), 7.21-7.27 (m, 4H), 7.80-7.83 (m, 2H), 7.86-7.89 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 20.9, 29.8, 34.3, 42.9, 123.5, 124.0, 128.7, 129.2, 134.3, 134.9, 171.6, 147.9; IR (KBr) 3293, 1807, 1783, 1743 cm⁻¹. HRMS (EI) calcd for C₂₀H₁₇ClN₂O₅: 400.0826; found: m/z 400.0868.

1.13.9. Phthalimido 4-(N-phenylethoxycarbonyl)butanoate (36)

Colorless solid; mp 100.5-102 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 1.99-2.06 (m, 2H), 2.22 (t, J = 7.0 Hz, 2H), 2.60 (t, J = 6.8 Hz, 2H), 2.75 (t, J = 7.0 Hz, 2H), 3.48 (q, J = 12.8 Hz, 2H), 6.00 (s, 1H), 7.03-7.19 (m, 5H), 7.70-7.77 (m, 2H), 7.78-7.81 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 20.8, 29.8, 34.4, 35.4, 40.4, 123.9, 126.3, 128.4, 128.6, 128.7, 133.9, 134.7, 134.8, 138.6, 161.9, 169.2, 171.6; IR (KBr) 3312, 1816, 1791, 1750 cm⁻¹. HRMS (EI) calcd for C₂₁H₂₀N₂O₅: 380.1372; found: m/z 380.1414.

1.13.10. Phthalimido 4-(N-phenylalaninocarbonyl methyl ester)butanoate (37)

Colorless solid; mp 94.5-95.5 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 2.04-2.12 (m, 2H), 2.33-2.37 (m, 2H), 2.59-2.75 (m, 2H), 3.06 (dd, J = 6.8 Hz, 14.0 Hz, 1H), 3.19 (dd, J = 5.6 Hz, 14.0 Hz, 1H), 3.73 (s, 3H), 4.93 (q, J = 13.6 Hz, 1H), 6.21 (d, J = 7.6 Hz, 1H), 7.13 (d, J = 7.2 Hz, 2H), 7.18-7.29 (m, 3H), 7.80-7.82 (m, 2H), 7.86-7.89 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 20.7, 29.8, 34.2, 37.8, 52.3, 53.0, 124.0, 127.0, 128.5, 128.8, 129.1, 134.3, 135.8, 135.8, 161.9, 169.2, 171.2, 172.0; IR (KBr) 3293, 1816, 1791, 1750 cm⁻¹. Anal. Calcd for C₂₃H₂₂N₂O₇: C, 63.01; H, 5.06; N, 6.39. Found: C, 63.02; H, 5.10; N, 6.40.

1.13.11. Phthalimido 4-(N-diphenylalaninocarbonyl benzyl ester)butanoate (38)

Colorless solid; mp 134-136 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 1.99-2.05 (m, 2H), 2.29 (t, J = 8.0 Hz, 2H), 2.57-2.64 (m, 2H), 2.97-3.10 (m, 4H), 4.64-4.70 (m, 1H), 4.78-4.85 (m, 1H), 5.10 (s, 2H), 6.34 (d, J = 8.0 Hz, 1H), 6.40 (d, J = 8.0 Hz, 1H), 6.93-6.96 (m, 2H), 7.16-7.37 (m, 13H), 7.80-7.83 (m, 2H), 7.83-7.91 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 20.6, 29.6, 29.8, 34.2, 37.8, 52.3, 54.2, 67.2, 124.0, 127.0, 127.0, 128.5, 128.8, 129.1, 134.8, 135.8, 135.8, 161.9, 169.2, 171.2, 172.0; IR (KBr) 3293, 1815, 1745, 1639 cm⁻¹. Anal. Calcd for C₂₃H₂₅N₃O₈: C, 63.01; H, 5.06; N, 6.39. Found: C, 63.02; H, 5.10; N, 6.40.

1.14. Typical procedure for the preparation of 3β-Cholesteryl 4-(phthalimidoyloxy carbonyl)butyrate (39)
To a stirred solution of 4-DMAP (59.8 mg, 0.48 mmol) and cholesterol (188.3 mg, 0.48 mmol) in CH$_2$Cl$_2$ (2 mL) was added dropwise to a stirred solution of 15 (200 mg, 0.48 mmol) in CH$_2$Cl$_2$ (2 mL) at rt under N$_2$ and stirred for 19 h. Then, the reaction mixture was neutralized by NaHCO$_3$ solution and extracted with CH$_2$Cl$_2$, and dried over anhydrous MgSO$_4$, and concentrated under vacuum, to give crude product which was purified by flash chromatography yielding 39 (248.4 mg, 79%) as a colorless solid; mp 83-85 °C (from CH$_2$Cl$_2$/hexane); $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$0.67 (s, 3H), 0.86 (dd, $J = 1.6$ Hz, 6.4 Hz, 6H), 0.91 (d, $J = 6.4$ Hz, 3H), 0.94-1.04 (m, 5H), 1.05-1.17 (m, 6H), 1.23-1.37 (m, 6H), 1.42-1.58 (m, 7H), 1.78-1.88 (m, 3H), 1.93-2.03 (m, 2H), 2.06-2.13 (m, 2H), 2.33 (d, $J = 7.6$ Hz, 2H), 2.47 (t, $J = 7.2$ Hz, 2H), 2.76 (t, $J = 7.2$ Hz, 2H), 4.60-4.68 (m, 1H), 5.38 (d, $J = 4$ Hz, 1H), 7.77-7.81 (m, 2H), 7.86-7.91 (m, 2H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$11.8, 18.7, 19.3, 19.9, 21.0, 22.5, 22.8, 23.8, 24.3, 27.8, 27.9, 28.2, 30.07, 31.8, 31.9, 33.1, 35.8, 36.2, 36.6, 36.9, 38.1, 39.5, 39.7, 42.3, 49.9, 56.1, 56.7, 74.2, 122.7, 123.9, 128.8, 134.8, 139.6, 161.8, 169.1, 171.9; IR (KBr) 1814, 1789, 1741 cm$^{-1}$. Anal. Calcd for C$_{36}$H$_{55}$NO$_6$: C, 74.38; H, 8.58; N, 2.17. Found: C, 74.79; H, 8.71; N, 2.12.

1.15. General procedure for the reaction of 39 with several amines (product 40 as an example)

**Typical procedure:** To a stirred solution of benzylamine (17 µL, 0.15 mmol) in CH$_2$Cl$_2$ (1 mL) was added dropwise to a stirred solution of 39 (100 mg, 0.15 mmol) in CH$_2$Cl$_2$ (1 mL) at rt under N$_2$ and stirred for 10.5 h. Then, the reaction mixture was neutralized by dil. AcOH solution and extracted with CH$_2$Cl$_2$, and dried over anhydrous MgSO$_4$, and concentrated under vacuum, to give solid crude product which was purified by flash chromatography yielded, 3β-cholesterol 4-(benzylaminocarbonyl)butyrate 40 (74.4 mg, 82%) as a colorless solid; mp 115-117 °C (from CH$_2$Cl$_2$/hexane); $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$0.67 (s, 3H), 0.86 (dd, $J = 1.6$ Hz, 7.2 Hz, 6H), 0.91 (d, $J = 6.4$ Hz, 3H), 0.94-1.04 (m, 5H), 1.08-1.21 (m, 6H), 1.24-1.39 (m, 6H), 1.42-1.61 (m, 7H), 1.78-1.87 (m, 3H), 1.94-2.02 (m, 4H), 2.25-2.29 (m, 4H), 2.35 (t, $J = 7.0$ Hz, 2H), 4.43 (d, $J = 5.6$ Hz, 1H), 4.55-4.63 (m, 1H), 5.36 (d, $J = 4.4$ Hz, 2H), 5.86 (s, 1H), 7.26-7.37 (m, 5H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$11.8, 18.6, 19.2, 20.9, 22.5, 22.8, 23.7, 24.2, 27.7, 27.9, 28.2, 31.8, 31.9, 33.6, 35.4, 35.7, 36.1, 36.5, 36.9, 38.1, 39.4, 39.6, 42.2, 43.6, 49.9, 56.0, 56.6, 74.0, 122.6, 127.5, 127.8, 128.7, 138.2, 139.5, 171.9, 172.5; IR (KBr) 3276, 1729, 1639 cm$^{-1}$. Anal. Calcd for C$_{39}$H$_{55}$NO$_6$: C, 79.41; H, 10.08; N, 2.37. Found: C, 78.93; H, 9.87; N, 2.35.

1.15.1. 3β-Cholesteryl 4-(4-chlorobenzylaminocarbonyl)butyrate (41)

Colorless solid; mp 122-124 °C (from CH$_2$Cl$_2$/hexane); $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$0.67 (s, 3H), 0.86 (dd, $J = 2.0$ Hz, 6.4 Hz, 6H), 0.91 (d, $J = 6.4$ Hz, 3H), 0.94-1.0 (m, 6H), 1.05-1.16 (m, 7H), 1.20-1.35 (m, 5H), 1.41-1.58 (m, 7H), 1.80-1.90 (m, 3H), 1.95-2.02 (m, 4H), 2.27-2.37 (m, 6H), 4.41 (d, $J = 5.6$ Hz, 1H), 4.40-4.61 (m, 1H), 5.36 (d, $J = 4.8$ Hz, 1H), 6.38 (s, 1H), 7.20-7.31 (m, 4H); $^{13}$C NMR (CDCl$_3$, 100 MHz) $\delta$11.8, 18.7, 19.2, 20.9, 21.0, 22.5, 22.8, 23.8, 24.2, 27.7, 27.9, 28.2, 31.8, 31.9, 33.4, 35.1, 35.7, 36.1, 36.5, 36.9, 38.0, 39.5, 39.7, 42.2, 43.1, 49.9, 56.1, 56.6, 74.3, 122.7, 128.8, 129.2, 133.4, 136.3, 139.4, 172.8; IR (KBr) 3262, 1724, 1638 cm$^{-1}$. HRMS (EI) calcd for C$_{39}$H$_{56}$ClNO$_6$: 623.4105; found: m/z 623.4081.

1.15.2. 3β-Cholesteryl 4-(2-phenylethylaminocarbonyl)butyrate (42)

Colorless solid; mp 128-129.5 °C; (from CH$_2$Cl$_2$/hexane); $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$0.67 (s, 3H), 0.86 (dd, $J = 1.6$ Hz, 6.6 Hz, 6H), 0.91 (d, $J = 6.4$ Hz, 4H), 0.92-1.03 (m, 6H), 1.04-1.20 (m, 7H), 1.20-1.34 (m, 4H), 1.40-1.58 (m, 7H), 1.78-1.99 (m, 7H), 2.19 (t, $J = 7.4$ Hz, 2H), 2.30 (t, $J = 7.4$ Hz, 4H), 2.81 (t, $J = 6.8$ Hz, 2H), 4.55-4.65 (m, 1H), 5.36 (d, $J = 3.6$ Hz, 2H), 5.65 (s, 1H),
1.15.3. 3β-Cholesteryl 4-(L-phenylalaninocarbonyl methyl ester)butyrate (43)

Colorless solid; mp 80-82 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 0.60 (s, 3H), 0.78 (dd, J = 1.6 Hz, 6.8 Hz, 6H), 0.84 (d, J = 6.4 Hz, 3H), 0.87-0.97 (m, 5H), 0.98-1.09 (m, 6H), 1.10-1.27 (m, 6H), 1.36-1.51 (m, 7H), 1.73-1.95 (m, 7H), 2.16 (t, J = 7.0 Hz, 2H), 2.19-2.24 (m, 4H), 2.98 (dd, J = 6.0 Hz, 14.2 Hz, 1H), 3.10 (dd, J = 6.0 Hz, 13.8 Hz, 1H), 3.65 (s, 3H), 4.49-4.57 (m, 1H), 4.79-4.84 (m, 1H), 5.30 (d, J = 4.4 Hz, 1H), 5.90 (d, J = 8.0 Hz, 2H), 7.01-7.03 (m, 2H), 7.15-7.24 (m, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 11.8, 18.6, 19.2, 20.7, 20.9, 22.5, 22.8, 24.2, 27.7, 27.9, 28.2, 31.8, 31.9, 33.5, 35.2, 36.1, 36.9, 37.8, 38.0, 39.4, 39.6, 42.2, 49.9, 52.3, 52.9, 56.0, 56.6, 73.9, 75.2, 75.6, 76.9, 122.5, 123.4, 127.1, 128.5, 128.6, 128.8, 129.1, 134.0, 135.8, 139.5, 171.7, 172.0, 172.4; IR (KBr) 3431, 1789, 1733, 1716 cm⁻¹. HRMS (EI) Calcd for C₄₀H₅₆NO₃: 661.4706; found: m/z 661.4717.

1.15.4. 3β-Cholesteryl 4-(diphenylalaninocarbonyl benzyl ester)butyrate (44)

Colorless solid; mp 145.5-147 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 0.67 (s, 3H), 0.86 (dd, J = 2.0 Hz, 6.8 Hz, 6H), 0.91 (d, J = 6.4 Hz, 3H), 0.93-1.04 (m, 6H), 1.05-1.21 (m, 7H), 1.20-1.34 (m, 5H), 1.41-1.58 (m, 7H), 1.80-1.87 (m, 5H), 1.90-2.02 (m, 2H), 2.16-2.22 (m, 4H), 2.30 (d, J = 8.0 Hz, 2H), 2.99 (d, J = 6.8 Hz, 3H), 3.08 (dd, J = 14.0 Hz, 6.0 Hz, 1H), 4.55-4.65 (m, 2H), 4.77 (q, J = 6.4 Hz, 1H), 5.09 (s, 2H), 5.36 (d, J = 4.4 Hz, 1H), 6.31 (s, 1H), 6.42 (s, 1H), 6.94 (t, J = 3.4 Hz, 2H), 7.13-7.27 (m, 10H), 7.34-7.36 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 11.8, 18.6, 19.2, 20.7, 21.0, 22.5, 23.8, 24.2, 27.7, 27.9, 28.2, 31.8, 31.9, 33.4, 35.0, 35.7, 36.1, 36.9, 37.7, 38.0, 38.1, 39.4, 39.6, 42.2, 49.9, 53.5, 54.4, 56.1, 56.6, 67.2, 74.0, 122.7, 127.0, 127.1, 128.5, 128.6, 129.2, 129.3, 135.0, 135.4, 136.2, 139.5, 170.5, 170.6, 172.4; IR (KBr) 3295, 1728, 1638 cm⁻¹. HRMS (FAB) Calcd for C₄₂H₆₃NO₅ (M+1): 885.5703; found (M+1): 885.6105.

1.16. General procedure for the reaction of 37 with various nucleophiles (product 45 as an example)

4-DMAP (55.7 mg, 0.45 mmol) was added to a stirred solution of 37 (200 mg, 0.45 mmol) and benzyl alcohol (47.1 µL, 0.45 mmol) in CH₂Cl₂ (2 mL) at rt under N₂ and stirred for 32 h. Then, the reaction mixture was neutralized by dil. AcOH solution and extracted with CH₂Cl₂ and dried over anhydrous MgSO₄. and concentrated under vacuum, to give oil crude product which was purified by flash column chromatography yield, O-benzyl 4-(L-phenylalaninocarbonyl methyl ester)butyrate (45) (130.8 mg, 75%) as a colorless oil; ¹H NMR (CDCl₃, 400 MHz) δ 1.89-1.97 (m, 2H), 2.21 (t, J = 7.2 Hz, 2H), 2.34-2.40 (m, 2H), 3.05 (dd, J = 6.0 Hz, 14.0 Hz, 1H), 3.14 (dd, J = 5.6 Hz, 14.0 Hz, 1H), 3.72 (s, 3H), 4.85-4.90 (m, 1H), 5.10 (s, 2H), 5.92 (d, J = 7.6 Hz, 1H), 7.07-7.09 (m, 2H), 7.20-7.38 (m, 8H); ¹³C NMR (CDCl₃, 100 MHz) δ 20.6, 33.1, 35.0, 37.8, 52.3, 52.9, 66.2, 127.1, 128.2, 128.2, 128.5, 128.6, 129.1, 135.7, 135.8, 171.5, 172.0, 172.8; IR (neat) 3301, 1814, 1787, 1743 cm⁻¹. HRMS (EI) Calcd for C₃₂H₂₆NO₃: 383.1733; found: m/z 383.1734.

1.16.1. O-4-Methylbenzyl 4-(L-phenylalaninocarbonyl methyl ester)butyrate (46)
Colorless solid; mp 53.5-55 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 1.88-1.96 (m, 2H), 2.21 (t, J = 7.0 Hz, 2H), 2.30-2.39 (m, 2H), 2.33 (s, 3H), 3.05 (dd, J = 6.0 Hz, 13.8 Hz, 1H), 3.14 (dd, J = 6.0 Hz, 13.8 Hz, 1H), 3.72 (s, 3H), 4.85-4.90 (m, 1H), 5.06 (s, 2H), 5.91 (d, J = 7.2 Hz, 1H), 7.06-7.08 (m, 2H), 7.16 (d, J = 7.2 Hz, 2H), 7.23-7.29 (m, 5H); ¹³C NMR (CDCl₃, 100 MHz) δ 20.6, 21.1, 33.1, 35.1, 37.8, 52.3, 52.9, 66.1, 127.1, 128.3, 128.5, 129.1, 129.2, 132.8, 135.7, 138.1, 171.6, 172.0, 172.9; IR (KBr) 3299, 1733, 1652 cm⁻¹. HRMS (EI) Calcd for C₂₃H₂₇NO₃: 397.1889; found: m/z 397.1886.

1.16.2. O-Phenyl 4-(L-phenylalaninocarbonyl methyl ester)butyrate (47)

Colorless solid; mp 43-45 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 2.00-2.07 (m, 2H), 2.30-2.33 (m, 2H), 2.55-2.59 (m, 2H), 3.07 (dd, J = 6.0 Hz, 13.8 Hz, 1H), 3.17 (dd, J = 5.6 Hz, 14.0 Hz, 1H), 3.73 (s, 3H), 4.88-4.93 (m, 1H), 5.97 (d, J = 7.6 Hz, 1H), 7.04-7.11 (m, 4H), 7.20-7.30 (m, 4H), 7.35-7.39 (m, 2H); ¹³C NMR (CDCl₃, 100 MHz) δ 20.5, 33.1, 34.9, 37.8, 52.3, 52.9, 121.4, 125.7, 127.1, 128.5, 129.1, 129.3, 135.7, 150.5, 171.5, 171.6, 172.0; IR (KBr) 3315, 1749, 1646 cm⁻¹. HRMS (EI) Calcd for C₂₁H₂₃NO₃: 369.1576; found: m/z 369.1579.

1.16.3. N-Benzyl 4-(L-phenylalaninocarbonyl methyl ester)butanamide (48)

Colorless solid; mp 100-101 °C (from CH₂Cl₂/hexane); ¹H NMR (CDCl₃, 400 MHz) δ 1.90-1.98 (m, 2H), 2.14-2.25 (m, 4H), 2.92 (dd, J = 7.2 Hz, 14.0 Hz, 1H), 3.09 (dd, J = 5.6 Hz, 14.0 Hz, 1H), 3.72 (s, 3H), 4.33-4.45 (m, 2H), 4.83 (q, J = 6.9 Hz 1H), 5.92 (d, J = 7.6 Hz, 1H), 6.28 (s, 1H), 7.07 (d, J = 6.8 Hz, 2H), 7.20-7.35 (m, 8H); ¹³C NMR (CDCl₃, 100 MHz) δ 21.7, 34.8, 34.9, 37.6, 43.4, 52.4, 52.9, 127.1, 127.5, 128.5, 128.6, 128.7, 129.0, 135.8, 138.5, 172.2, 172.3, 172.4; IR (KBr) 3289, 1747, 1643, 1546 cm⁻¹. Anal. Calcd for C₂₂H₂₆N₂O₄: C, 69.09; H, 6.85; N, 7.32; found: C, 68.81; H, 6.64; N, 7.23.

1.16.4. S-Benzyl 4-(L-phenylalaninocarbonyl methyl ester)butyrate (49)

Colorless syrup; ¹H NMR (CDCl₃, 400 MHz) δ 1.92-1.99 (m, 2H), 2.18-2.22 (m, 2H), 2.50-2.62 (m, 2H), 3.05 (dd, J = 6.0 Hz, 13.8 Hz, 1H), 3.15 (dd, J = 5.6 Hz, 14.0 Hz, 1H), 3.72 (s, 3H), 4.11 (s, 2H), 4.85-4.90 (m, 1H), 5.96 (d, J = 8 Hz, 1H), 7.07-7.20 (m, 2H), 7.20-7.31 (m, 8H); ¹³C NMR (CDCl₃, 100 MHz) δ 21.3, 21.9, 21.7, 33.1, 34.8, 37.8, 42.3, 52.3, 52.9, 127.1, 127.2, 128.5, 128.6, 128.7, 129.1, 135.7, 137.4, 171.3, 172.0, 198.2; IR (KBr) 3291, 1743, 1683, 1652 cm⁻¹. Anal. Calcd for C₂₂H₂₆N₂O₄S: C, 66.14; H, 6.31; N, 3.51. Found: C, 66.35; H, 6.10; N, 3.61. HRMS (EI) Calcd for C₂₂H₂₆N₂O₄S: 399.1504; found: m/z 399.1519.

References and Notes


\(^1\)H and \(^{13}\)C NMR Spectrum:

Phthalimido 4-chloroformylbutanoate (9) (\(^1\)H-NMR)
Phthalimido 4-chloroformylbutanoate (9) (13C-NMR)
Phthalimido 4-carboxybutanoate (10) (\(^1\)H-NMR)
Phthalimido 4-carboxybutanoate (10) (\(^{13}\)C-NMR)

S16
Phenylpropionyloxy)benzotriazole (11) (\(^1\)H-NMR)
Phenylpropionyloxy)benzotriazole (11) (13C-NMR)
Phenylpropionyloxy)phthalimide (12) (\(^1\)H-NMR)
Phenylpropionyloxyphthalimide (12) ($^{13}$C-NMR)
(ii) Supporting Information for the manuscript:

Title: “Syntheses and reactivities of non-symmetrical "active ester" bi-dentate cross-linking reagents having a phthalimidoyl and acid chloride, 2-benzothiazole, or 1-benzotriazole group”

\(^{1}H\text{-NMR and }^{13}C\text{-NMR)}

3-Phenylpropionyloxy)benzothiazole (13) \((^{1}H\text{-NMR)}

![NMR spectrum](image-url)
3-Phenylpropionyloxy)benzoazole (13) ($^{13}$C-NMR)
N-(3-Phenylpropionyl)benzotriazole (14) (1H-NMR)
N-(3-Phenylpropionyl)benzotriazole (14) \(^{13}\text{C-}\text{NMR}\)
Phthalimido 4-(2-benzothiazolyl)oxycarbonyl)butanoate (15) (1H-NMR)
Phthalimido 4-(2-benzothiazolyloxycarbonyl)butanoate (15) ($^{13}$C-NMR)
Phthalimido 4-(1-benzotriazolylcarbonyl)butanoate (16) (1H-NMR)
Phthalimido 4-(1-benzotriazolylcarbonyl)butanoate (16) (\(^{13}\)C-NMR)
Bis-(1,3-diphthalimidyl glutarate) (18) ($^1$H-NMR)
Bis-(1,3-diphthalimidyl glutarate) (18) (\(^{13}\)C-NMR)
(iii) Supporting Information for the manuscript:

Title: “Syntheses and reactivities of non-symmetrical "active ester" bi-dentate cross-linking reagents having a phthalimidoyl and acid chloride, 2-benzothiazole, or 1-benzotriazole group”

($^1$H –NMR and $^{13}$C-NMR)

3-phenylpropionic acid 4-methylbenzyl ester (19) ($^1$H-NMR)
3-phenylpropionic acid 4-methylbenzyl ester (19) \(^{13}\text{C-NMR}\)
Supplementary Material (ESI) for Organic & Biomolecular Chemistry
This journal is (c) The Royal Society of Chemistry 2011
3-phenylpropionic acid 4-chlorobenzyl ester (20) (1H-NMR)
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample</td>
<td>con-155 (rmh) p-33, r-2</td>
</tr>
<tr>
<td>Experiment Conditions</td>
<td></td>
</tr>
<tr>
<td>Temperature</td>
<td>20.8 °C</td>
</tr>
<tr>
<td>Spin Rate</td>
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</tr>
<tr>
<td>Field Strength</td>
<td>8.0 ppm</td>
</tr>
<tr>
<td>SF</td>
<td>0.12 Hz</td>
</tr>
</tbody>
</table>

For more detailed analysis, refer to the supplementary material (ESI) for Organic & Biomolecular Chemistry.
3-phenylpropionic acid 4-chlorobenzyl ester (20) ($^{13}$C-NMR)
3-phenyl propionic acid 2 phenylethyl ester (21) ($^1$H-NMR)
3-phenyl propionic acid 2 phenylethyl ester (21) ($^{13}$C-NMR)
N-benzyl-3-phenylpropionamide (22) ($^1$H-NMR)
**N-benzyl-3-phenylpropionamide (22) \(^{13}C\)-NMR**
(iv) Supporting Information for the manuscript:

Title: “Syntheses and reactivities of non-symmetrical "active ester" bi-dentate cross-linking reagents having a phthalimidoyl and acid chloride, 2-benzothiazole, or 1-benzotriazole group”

($^1$H –NMR and $^{13}$C–NMR)

$N$-4-chlorobenzyl-3-phenylpropionamide (23) ($^1$H–NMR)
N-4-chlorobenzyl-3-phenylpropionamide (23) ($^{13}$C–NMR)

**Supplementary Material (ESI) for Organic & Biomolecular Chemistry**
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3-phenylthiopropionic S-benzyl ester (24) (1H–NMR)
3-phenylthiopropionic S-benzyl ester (24) (13C–NMR)

(Diagram of 13C–NMR spectra)
1-(methanesulfonyl)benzotriazole (26) (\(^1H\)-NMR)

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
This journal is © The Royal Society of Chemistry 2011
1-(methanesulfonyl)benzotriazole (26) ($^{13}$C–NMR)

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Phthalimido 4-benzyloxycarbonylbutanoate (27) ($^1$H–NMR)
Phthalimido 4-benzyloxy carbonylbutanoate (27) ($^{13}$C–NMR)
Phthalimido 4-(4-methylbenzyl oxycarbonyl)butanoate (28) (1H–NMR)

S12
Phthalimido 4-(4-methylbenzyl)oxycarbonyl)butanoate (28) ($^{13}$C–NMR)

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Phthalimido 4-(1-methylbenzyloxycarbonyl)butanoate (29) ($^1$H–NMR)

**NMR Spectra**

The figure displays NMR spectra for the compound Phthalimido 4-(1-methylbenzyloxycarbonyl)butanoate (29). The spectra are shown for both proton ($^1$H) and carbon ($^13$C) nuclei, with peaks indicating the chemical shifts and multiplicities of the protons and carbons present in the molecule. The spectra are a typical representation of the chemical structure, showing the resonance positions across the spectrum.

The NMR data includes information such as chemical shifts, multiplicities, and coupling constants, which are characteristic of the molecule's structure.

**Supplementary Material (ESI) for Organic & Biomolecular Chemistry**

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Phthalimido 4-(1-methylbenzyloxycarbonyl)butanoate (29) (^13C–NMR)

**S17**

**Supplementary Material (ESI) for Organic & Biomolecular Chemistry**

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Phthalimido 4-(4-chlorobenzyloxy carbonyl) butanoate (30) (1H-NMR)

<table>
<thead>
<tr>
<th>Component</th>
<th>ppm</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.28</td>
<td>4.00</td>
<td></td>
</tr>
<tr>
<td>2.34</td>
<td>1.30</td>
<td></td>
</tr>
</tbody>
</table>

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Phthalimido 4-(4-chlorobenzyloxycarbonyl)butanoate (30) ($^{13}$C–NMR)
Phthalimido 4-phenylethoxycarbonylbutanoate (31) (1H–NMR)

S21
Phthalimido 4-phenylethoxycarbonylbutanoate (31) ($^{13}$C–NMR)

<table>
<thead>
<tr>
<th>ppm</th>
<th>200</th>
<th>175</th>
<th>150</th>
<th>125</th>
<th>100</th>
<th>75</th>
<th>50</th>
<th>25</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Value</td>
<td>71.80</td>
<td>76.87</td>
<td>64.36</td>
<td>35.00</td>
<td>32.80</td>
<td>29.40</td>
<td>19.78</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Note:** The table contains the chemical shifts in ppm for various carbon atoms in the compound 31. The spectrum shows the distribution of carbon signals across different ppm values, indicating the presence of multiple carbon isotopes and their relative intensities.

---

**Figure:**

The figure depicts a 1D NMR spectrum of Phthalimido 4-phenylethoxycarbonylbutanoate (31) with carbon signals ranging from 200 to 0 ppm. The peaks are labeled with their respective chemical shifts, providing a visual representation of the compound's chemical structure.
Phthalimido 4-phenyloxycarbonylbutanoate (32) ($^1$H–NMR)

**1H–NMR**

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Phthalimido 4-phenyloxycarbonylbutanoate (32) ($^{13}$C–NMR)
Phthalimido 4-(S-benzyloxy carbonyl)butanoate (33) (13C–NMR)

S29
(v) Supporting Information for the manuscript:

Title: “Syntheses and reactivities of non-symmetrical "active ester" bi-dentate cross-linking reagents having a phthalimidoyl and acid chloride, 2-benzothiazole, or 1-benzotriazole group”

($^1$H–NMR and $^{13}$C–NMR)

Phthalimido 4-(N-benzyloxycarbonyl)butanoate (34) ($^1$H-NMR)
Phthalimido 4-(N-benzyloxycarbonyl)butanoate (34) ($^{13}$C-NMR)

13C-NMR

S3
Phthalimido 4-(N-4-chlorobenzoylcarbonyl)butanoate (35) (1H-NMR)

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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Phthalimido 4-(N-4-chlorobenzyloxy carbonyl)butanoate (35) ($^{13}$C-NMR)

$^{13}$C-NMR spectra for the compound 35.
Phthalimido 4-(N-phenylethoxycarbonyl)butanoate (36) (1H-NMR)

S7
Phthalimido 4-(N-phenylethoxy carbonyl)butanoate (36) \(^{13}\)C-NMR

EFILE: SBI0411023E33
CONMT: MNC.p-53.p-2
DATUM: Mon Jan 11 15:55
GENUC: 35C
EMXR: SINGL

CDB  100.46 MHz
DBSET: 0.00 MHz
OMIT: 138.8900, 0.00 Hz
PDNT: 227.86
FREQU: 27100, 27 Hz
SCANE: 6000
ACQTM: 1.2091 sec
FD: 1.7500 sec
FP1: 0.00 sec
DEGR: 1H
CTMP: 18.2 c

ELN: 77.00 ppm
EF: 0.12 Hz
NRBN: 35
Phthalimido 4-(N-phenylalaninocarbonyl methyl ester)butanoate (37) (¹H-NMR)
Phthalimido 4-(N-phenylalaninocarbonyl methyl ester)butanoate (37) ($^{13}$C-NMR)

13C-NMR

13C-NMR
Phthalimido 4-(N-diphenylalaninocarbonyl benzyl ester)butanoate (38) \(^{1}H\)-NMR

PTLC
S14
Phthalimido 4-(N-diphenylalaninocarbonyl benzyl ester)butanoate (38) ($^{13}$C-NMR)
3β-cholesteryl 4-(phthalimidoxyloxy carbonyl)butyrate (39) ($^1$H-NMR)

RAW, p=43, n=3
$3\beta$-cholesteryl 4-(phthalimidoyloxy carbonyl)butyrate (39) ($^{13}$C-NMR)

13C-NMR
3β-cholesteryl 4-(benzylaminocarbonyl)butyrate (40) (1H-NMR)
$3\beta$-cholesteryl 4-(benzylaminocarbonyl)butyrate (40) ($^{13}$C-NMR)

$^{13}$C-NMR

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3β-cholesteryl 4-(4-chlorobenzylaminocarbonyl)butyrate (41) (1H-NMR)

**1H-NMR Spectra**

The image shows the 1H-NMR spectra for the compound 3β-cholesteryl 4-(4-chlorobenzylaminocarbonyl)butyrate (41). The spectra are used to identify the chemical shifts and other NMR parameters for the compound, which are essential for understanding its structure and properties.
3β-cholesteryl 4-(4-chlorobenzylaminocarbonyl)butyrate (41) (13C-NMR)

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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(vi) Supporting Information for the manuscript:

Title: “Syntheses and reactivities of non-symmetrical "active ester" bi-dentate cross-linking reagents having a phthalimidoyl and acid chloride, 2-benzothiazole, or 1-benzotriazole group”

\(^{1}H\text{-NMR and }^{13}C\text{-NMR}\)

3β-cholesteryl 4-(2-phenylethylaminocarbonyl)butyrate (42) \(^{1}H\text{-NMR}\)

![NMR Spectrum Image]

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**3β-cholesteryl 4-(2-phenylethylaminocarbonyl)butyrate (42) \(^{13}\text{C}-\text{NMR}\)**

<table>
<thead>
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<th>Value</th>
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<tbody>
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<tr>
<td>\text{ACQ}</td>
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<tr>
<td>\text{F3}</td>
<td>1.780 s</td>
</tr>
<tr>
<td>\text{F1}</td>
<td>0.00 usec</td>
</tr>
<tr>
<td>\text{EPRD}</td>
<td>77.00 ppm</td>
</tr>
<tr>
<td>\text{EF}</td>
<td>0.12 Hz</td>
</tr>
<tr>
<td>\text{AGAIN}</td>
<td>55</td>
</tr>
</tbody>
</table>

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3β-cholesteryl 4-(L-phenylalaninocarbonyl methyl ester) butyrate (43) (1H-NMR)
$3\beta$-cholesteryl 4-(L-phenylalaninocarbonyl methyl ester)butyrate (43) ($^{13}$C-NMR)

**ESI**

**1H NMR**

- **Chemical shifts**
- **Coupling constants**
- **Integration**

**COSY**

- **Correlation peaks**

**HMQC**

- **Correlation with nuclei**
- **Spin order**

**HMBC**

- **Correlation with long-range**
- **Coupling orders**

**2D NMR**

- **Spectral analysis**
- **Assignment**

**Supplementary Material (ESI)** for Organic & Biomolecular Chemistry

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**3β-cholesteryl 4-(diphenylalaninocarbonyl benzyl ester)butyrate (44) (1H-NMR)**

**Formula:** C\textsubscript{38}H\textsubscript{44}N\textsubscript{2}O\textsubscript{5}S

**CAS Number:** 153-81-5

**Notes:**
- IR (KBr): 3080, 2920, 1740, 1260, 720 cm\textsuperscript{-1}
- 

---

**S7**
3β-cholesteryl 4-(diphenylalaninocarbonyl benzyl ester)butyrate (44) (13C-NMR)

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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O-benzyl 4-(L-phenylalaninocarbonyl methyl ester)butyrate (45) (\textsuperscript{1}H-NMR)
O-benzyl 4-(L-phenylalaninocarbonyl methyl ester)butyrate (45) (^13C-NMR)

S12
**O-4-methylbenzyl 4-(L-phenylalaninocarbonyl methyl ester)butyrate (46) (**H-NMR)**

![NMR spectrum for compound 46](image)

**Supplementary Material (ESI) for Organic & Biomolecular Chemistry**

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O-4-methylbenzyl 4-(L-phenylalaninocarbonyl methyl ester)butyrate (46) (¹³C-NMR)

S15
O-phenyl 4-\((L\)-phenylalaninocarbonyl methyl ester\)butyrate (47) (\(^1\text{H-NMR}\))
O-phenyl 4-(L-phenylalaninocarbonyl methyl ester)butyrate (47) (\^{13}C-NMR)

Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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N-benzyl 4-(L-phenylalaniocarbonyl methyl ester)butanamide (48) (1H-NMR)
N-benzyl 4-(L-phenylalaninocarbonyl methyl ester)butanamide (48) ($^{13}$C-NMR)

$^{13}$C-NMR
S-benzyl 4-(L-phenylalaminocarbonyl methyl ester)butyrate (49) (1H-NMR)
S-benzyl 4-(L-phenylalaminocarbonyl methyl ester)butyrate (49) (13C-NMR)