

Supporting Information

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Supporting Information 1.

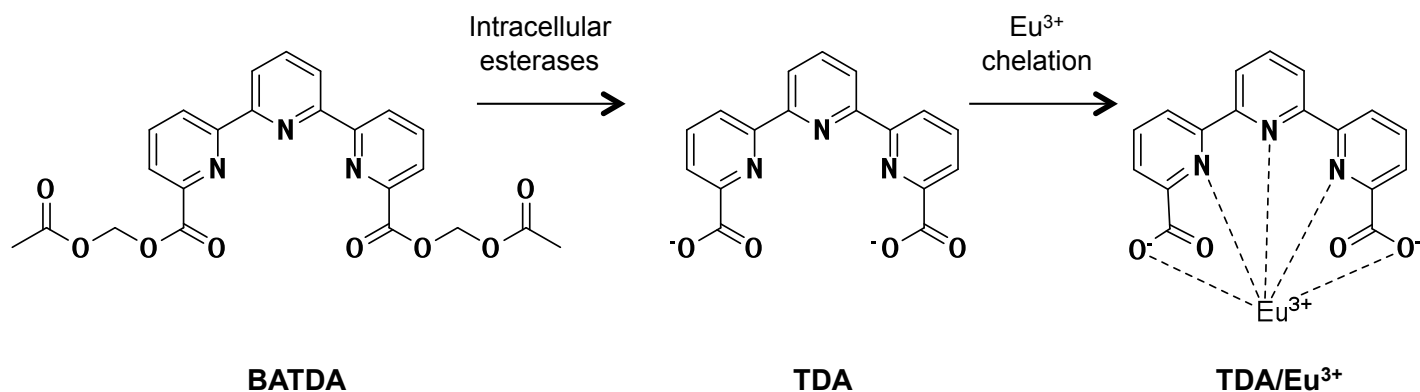
Figure S1. Schematic representation of a non-radioactive cellular cytotoxicity assay system using BATDA, a terpyridine derivative proligand.

Supporting Information 2.

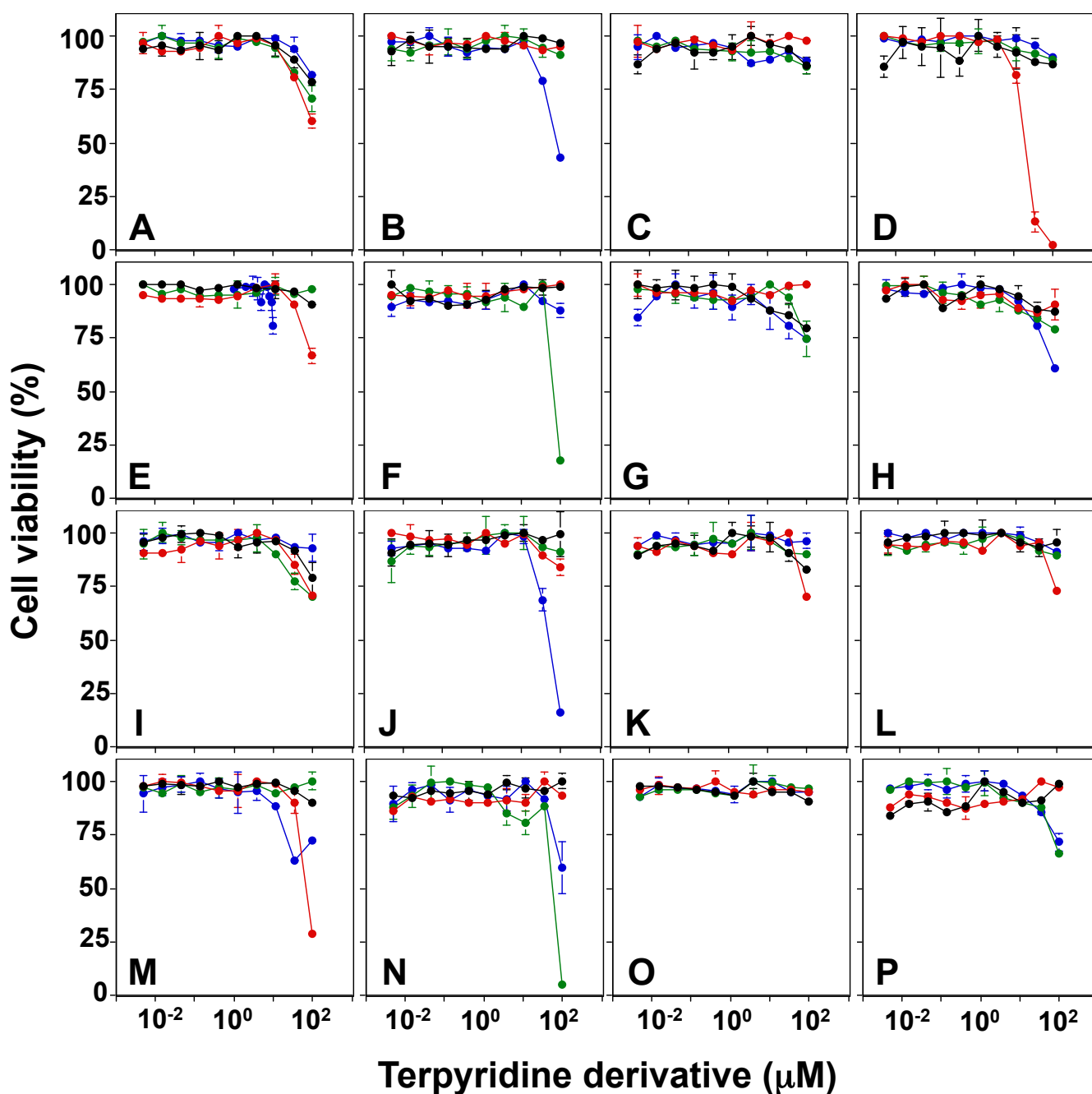
Figure S2. Effect of terpyridine derivatives on the viability of tumor cells.

Supporting Information 3.

General chemistry.



Supporting Information Figure S1. Schematic representation of a non-radioactive cellular cytotoxicity assay system using BATDA, a terpyridine derivative proligand. Bis(acetoxymethyl) 2,2':6',2''-terpyridine-6,6''-dicarboxylate (BATDA, **32**) is a proligand for Eu³⁺. When tumor cells are treated with BATDA, the proligand permeates into the tumor cells, where intracellular esterases hydrolyze it to yield 2,2':6',2''-terpyridine-6,6''-dicarboxylic acid (TDA). Because TDA is negatively charged, the membrane permeability of the negatively-charged ion is lower than that of its proform, resulting in the accumulation of TDA in the cytoplasm. When the labeled tumor cells are killed by immune effector cells, the cell membrane is perforated, resulting in the release of TDA in the culture medium. Upon addition of Eu³⁺ to the culture supernatant, TDA forms a complex with Eu³⁺ that can emit long-life fluorescence through excitation with laser pulses.



Supporting Information Figure S2. Effect of terpyridine derivatives on the viability of tumor cells. Tumor cells were treated with a series of newly synthesized terpyridine derivative for 2 h and the viability of the cells was examined using a CellGlo Titer kit. K562 erythrocytoma cells were treated with; A: black, compound 1; red, 2, green, 3; blue, 4, B: black, 5; red, 6, green, 7; blue, 8, C: black, 9; red, 10, green, 11; blue, 12, D: black, 13; red, 14, green, 15; blue, 16, E: black, 17; red, 18, green, 19; blue, 20, F: black, 21; red, 22, green, 23; blue, 24, G: black, 25; red, 26, green, 27; blue, 28 and H: black, 29; red, 30, green, 31; blue, BATDA. U937 histiocytoma cells were treated with; I: black, 1; red, 2, green, 3; blue, 4, J: black, 5; red, 6, green, 7; blue, 8, K: black, 9; red, 10, green, 11; blue, 12, L: black, 13; red, 14, green, 15; blue, 16, M: black, 17; red, 18, green, 19; blue, 20, N: black, 21; red, 22, green, 23; blue, 24, O: black, 25; red, 26, green, 27; blue, 28 and P: black, 29; red, 30, green, 31; blue, BATDA.

Supporting Information 3

General Chemistry

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1. General Information

All NMR spectra were recorded on Varian Gemini300, JEOL AL 400 and Varian 500PS spectrometers at 24°C. ¹H and ¹³C NMR spectra are reported as chemical shifts (δ) in parts per million (ppm) relative to the solvent peak using tetramethylsilane, (2, 2, 3, 3-D4) trimethylsilyl-3-propanoic acid, sodium salt (¹H and ¹³C) and trichlorofluoromethane (¹⁹F) as an internal standard. Chemical shifts (δ) are quoted in parts per million (ppm) and coupling constants (*J*) are measured in hertz (Hz). The following abbreviations are used to describe multiplicities s=singlet, d=doublet, t=triplet, q=quartet, quint.=quintet, sext.=sextet, sept.=septet br=broad, m=multiplet. NMR spectra were processed in ACD/SpecManager. High resolution mass spectra (HRMS, *m/z*) were obtained on JEOL JMS-700N for FAB using *m*-nitrobenzylalcohol as a matrix or on JEOL JMS-T100 TD for electrospray ionization (ESI+). All reactions were performed in apparatuses with magnetic stirring under an inert atmosphere. Flash column chromatography was performed over Fuji Silysia Chemical Ltd. silica gel C60 (50-200 μm) and CHROMATOREX DIOL (MB 100-40/75) using an eluent system as described for each experiment. Thin-layer chromatography was performed using TLC Silica gel 60 F₂₅₄ aluminum sheets (Merck) and silica gel F₂₅₄ glass plates (Merck).

Materials.

2,2':6',2''-Terpyridine-6,6''-dicarboxylic acid, halomethyl alkanooates and diethyl 1'-hydro-4'-oxo-2,2':6',2''-terpyridine-6,6''-dicarboxylate were known compounds and were prepared according to reported procedures.^[1-3] Unless otherwise stated, all starting materials and reagents were obtained

from commercial suppliers and were used without further purification. All chemicals were purchased from Aldrich, Nacalai Tesque, Tokyo Chemical Industry and Wako Pure Chemical Industries and used as received. All solvents were purchased from Nacalai Tesque.

2. Experimental Procedures and Characterization Data

2-1 Representative procedure for synthesis of bis (alkanoyloxymethyl) 2,2':6',2''-terpyridine-6,6''-dicarboxylate

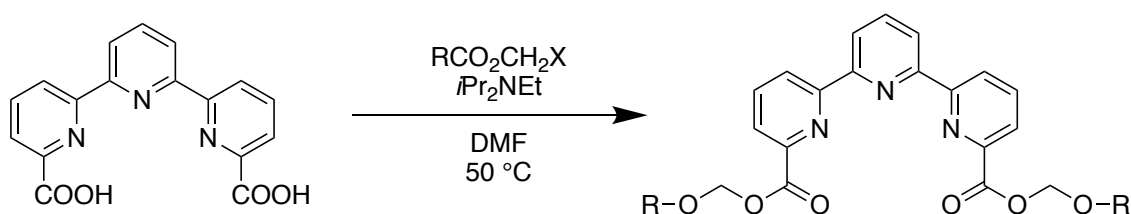


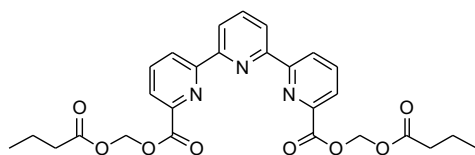
Table 1. The reaction of 2, 2':6',2''-terpyridine-6,6''-dicarboxylic acid with halomethyl alkanate

Entry	halomethyl alkanate		Product	
	X	R	yield (%) ^a	cpd. No.
1	Cl	butyryl	24	1
2	Cl	isobutyryl	28	2
3	I	pivaloyl	25	3

[a] isolated yield

To a solution of halomethyl alkanate (0.13 mmol) in DMF (1.0 ml) was added *N,N*-diisopropylethylamine (0.23 mmol) and 2,2':6',2''-terpyridine-6,6''-dicarboxylic acid (0.05 mmol). The reaction mixture was heated at 50°C. After stirring for 25 h, the solution was cooled to room temperature and the mixture was washed with a saturated solution of NH₄Cl and the aqueous phase was extracted with AcOEt (3 × 2.0 ml). The combined organic layer was washed with brine, then dried over MgSO₄, filtered and concentrated *in vacuo*. Purification by preparative TLC afforded the bis(alkanoyloxymethyl) 2,2':6',2''-terpyridine-6,6''-dicarboxylate.

***Bis*((butyryloxy)methyl) 2,2':6',2''-terpyridine-6,6''-dicarboxylate (1)**

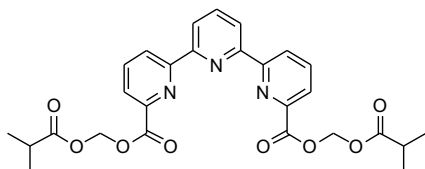


Synthesized following procedure (0.05 mmol scale). Purified by preparative TLC (mobile phase: hexane : AcOEt = 2 : 1) to give 6.4 mg (24 % yield) of the title compound as a yellow solid.

¹H NMR (500 MHz, CDCl₃) δ 0.98 (t, *J* = 7.5 Hz, 6H), 1.71 (sext, *J* = 7.5 Hz, 4H), 2.41 (t, *J* = 7.5

Hz, 4H), 6.12 (s, 4H), 8.01-8.04 (m, 3H), 8.18 (d, $J = 7.5$ Hz, 2H), 8.65 (d, $J = 8.0$, 2H), 8.83 (d, $J = 8.0$, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 13.5, 18.1, 35.8, 80.2, 122.3, 124.7, 125.6, 137.9, 138.3, 146.6, 154.3, 156.5, 163.9, 172.3; HRMS (FAB) m/z Calcd for $\text{C}_{27}\text{H}_{27}\text{N}_3\text{O}_8$ $[\text{M}+\text{H}]^+$ 522.1876, found 522.1880.

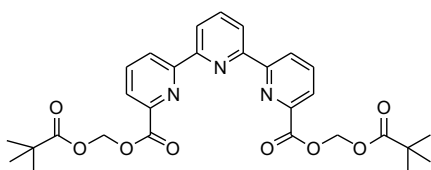
Bis(isobutyryloxy)methyl [2,2':6',2''-terpyridine]-6,6''-dicarboxylate (2)



Synthesized following procedure (0.05 mmol scale). Purified by preparative TLC (mobile phase: hexane : AcOEt = 2 : 1) to give 7.4 mg (28 % yield) of the title compound as a yellow solid.

^1H NMR (500 MHz, CDCl_3) δ : 1.23 (d, $J = 7.0$, 12H), 2.66 (sept., $J = 7.0$ Hz, 2H), 6.12 (s, 4H), 8.01-8.04 (m, 3H), 8.18 (dd, $J = 1.0$, 7.5 Hz, 2H), 8.65 (d, $J = 7.5$ Hz, 2H), 8.83 (dd, $J = 1.0$, 7.5 Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 18.7, 33.8, 80.4, 122.3, 124.7, 125.5, 137.9, 138.3, 146.6, 154.3, 156.5, 163.9, 175.7; HRMS (FAB) m/z Calcd for $\text{C}_{27}\text{H}_{27}\text{N}_3\text{O}_8$ $[\text{M}+\text{H}]^+$ 522.1876, found 522.1878.

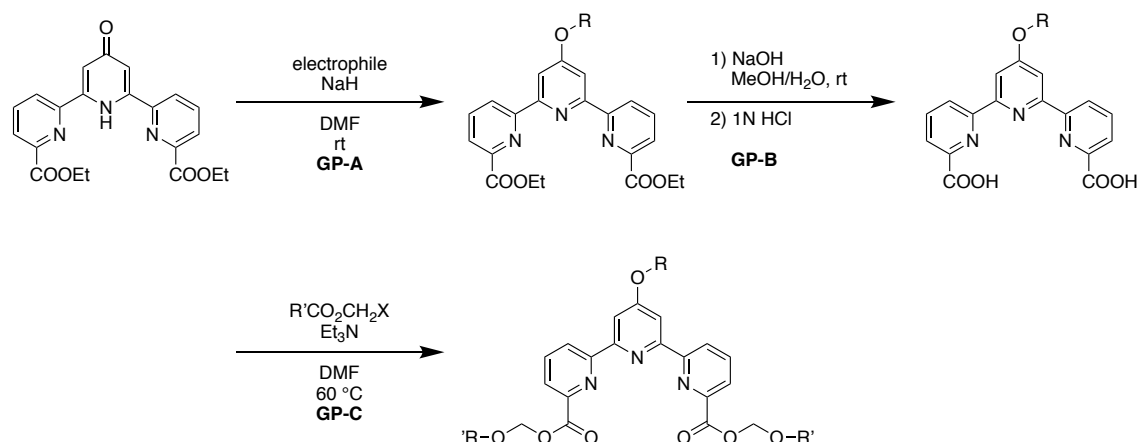
Bis(pivaloyloxy)methyl 2,2':6',2''-terpyridine-6,6''-dicarboxylate (3)



Synthesized following procedure (0.09 mmol scale). Purified by SiO_2 gel column chromatography (eluent: hexane : AcOEt = 1 : 0 ~ 4 : 1) to give 12.3 mg (25 % yield) of the title compound as a yellow solid.

^1H NMR (500 MHz, CDCl_3) δ : 1.26 (s, 18H), 6.11 (s, 4H), 8.02 (t, $J = 8.0$ Hz, 1H), 8.02 (t, $J = 7.5$ Hz, 2H), 8.17 (d, $J = 7.0$ Hz, 2H), 8.65 (d, $J = 7.5$ Hz, 2H), 8.83 (d, $J = 8.0$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ : 26.9, 38.9, 80.6, 122.3, 124.7, 125.5, 137.9, 138.3, 146.6, 154.3, 156.5, 163.8, 177.2; HRMS (FIAB) m/z Calcd for $\text{C}_{29}\text{H}_{31}\text{N}_3\text{O}_8$ $[\text{M}+\text{H}]^+$ 550.2189, found 550.2200.

2-2. General procedure for synthesis of 4'-O-substituted 2,2':6',2''-terpyridine



General procedure for 4'-O-substitution of diethyl 1'-hydro-4'-oxo-2,2':6',2''-terpyridine-6,6''-dicarboxylate (GP-A): To a suspension of NaH (60 mg, 60% 1.5 mmol) in DMF (5.0 ml) was added diethyl 1'-hydro-4'-oxo-2,2':6',2''-terpyridine-6,6''-dicarboxylate (393 mg, 1.0 mmol) and the reaction was allowed to stir for 30 min at room temperature. An electrophile (1.5 mmol) was added dropwise and the reaction mixture was stirred for 15 h. The reaction was quenched by the addition of a saturated solution of NH₄Cl. The aqueous phase was extracted with AcOEt (2 × 50 ml). The combined organic phases were washed with water (50 ml) and brine (50 ml), dried over MgSO₄, filtered and then concentrated *in vacuo*. Purification using SiO₂ gel column chromatography afforded 4'-O-substituted diethyl 1'-hydro-4'-oxo-2,2':6',2''-terpyridine-6,6''-dicarboxylate derivatives.

General procedure for the hydrolysis of 4'-O-substituted diethyl 1'-hydro-4'-oxo-2,2':6',2''-terpyridine-6,6''-dicarboxylate derivative (GP-B): A mixture of 4'-O-substituted diethyl 1'-hydro-4'-oxo-2,2':6',2''-terpyridine-6,6''-dicarboxylate derivatives (1.0 mmol) and NaOH (3.5 mmol) was stirred for 20 h at room temperature. The pH was adjusted to approximately 4 with 1 N HCl. The precipitate was collected by filtration, dried under *vacuo* affording 4'-O-substituted 1'-hydro-4'-oxo-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid.

General procedure for the synthesis of 4'-O-substituted bis(alkanoxy)methyl 1'-hydro-4'-oxo-2,2':6',2''-terpyridine-6,6''-dicarboxylate (GP-C): To a solution of 4'-O-substituted 1'-hydro-4'-oxo-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid (0.4 mmol) in DMF (10 ml) was added Et₃N (1.3 mmol) and chloromethyl alkanoate (1.1 mmol). The reaction mixture was heated at 60 °C. After stirring for 18 h, the solution was cooled to room temperature and the mixture was washed with H₂O (20 ml), and the aqueous phase was extracted with AcOEt (2 × 30 mL). The combined organic phases were washed with brine, then dried over MgSO₄, filtered and

concentrated *in vacuo*. Purification using SiO₂ gel column chromatography afforded 4'-*O*-substituted 1'-hydro-4'-oxo-2,2':6',2''-terpyridine-6,6''-dicarboxylate.

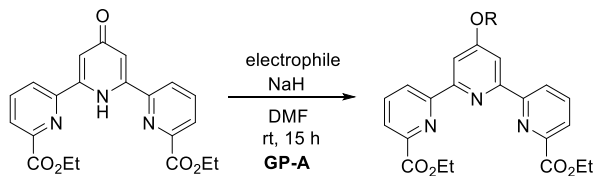
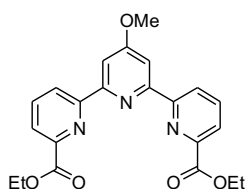


Table 2. Alkylation of diethyl 2,2':6',2''-terpyridine-4'-oxo-6,6''-dicarboxylate with a variety of electrophiles.

Entry	Electrophile	Product	
		R	Yield (%) ^a
1	MeI	Me	47
2	EtBr	Et	45
3	Br(CH ₂) ₁₀		46
4	Br(CH ₂) ₁₀ Br		31
5	BrCH ₂ CH ₂ OAc		41
6	BrCH ₂ CH ₂ OCH ₂ CH ₂ OAc		19
7	BrCH ₂ CO ₂ Me		56
8	Br(CH ₂) ₈ CO ₂ Me		61
9	BrCH ₂ CO ₂ NHCH ₂ CH ₂ CH ₃		70
10 ^b			84
11 ^b			40

[a] Isolated yield. [b] Electrophiles were prepared according to literature precedures.⁴

Diethyl 4'-methoxy-2,2':6',2''-terpyridine-6,6''-dicarboxylate

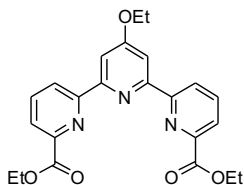


Synthesized following GP A (1.0 mmol scale). Purified by flash column chromatography (eluent: AcOEt) to give 190 mg (47 % yield) of the title compound as a yellow solid.

¹H NMR (500 MHz, CDCl₃) δ 1.50 (t, *J* = 7.1 Hz, 6H), 4.09 (s, 3H), 4.51 (q, *J* = 7.1 Hz, 4H), 7.99 (t, *J* = 7.9 Hz, 2H), 8.15 (dd, *J* = 0.8, 7.6 Hz, 2H), 8.19 (s, 2H), 8.80 (dd, *J* = 0.8, 7.8 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 14.3, 55.6, 61.8, 107.9, 124.4, 125.1, 137.7, 147.8, 156.2, 156.3, 165.3, 167.9; HRMS (FAB) *m/z* Calcd for C₂₂H₁₁N₃O₅ [M+H]⁺

408.1559, found 408.1559.

Diethyl 4'-ethoxy-2,2':6',2''-terpyridine-6,6''-dicarboxylate

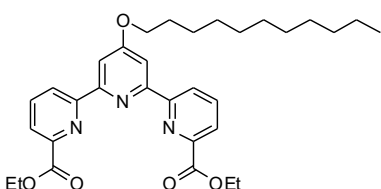


Synthesized following GP A (0.8 mmol scale). Purified by flash column chromatography (eluent: 50% *n*-hexane in AcOEt) to give 143 mg (45 % yield) of the title compound as a yellow solid.

¹H NMR (500 MHz, CDCl₃) δ 1.45–1.53 (m, 9H), 4.30–4.36 (m, 2H), 4.47–4.52 (m, 4H), 7.94–7.99 (m, 2H), 8.11–8.16 (m, 4H), 8.74 (m, 2H);

¹³C NMR (125 MHz, CDCl₃) δ 14.3, 14.6, 61.8, 63.9, 108.3, 124.3, 125.0, 137.6, 147.7, 156.2, 165.3, 167.2; **HRMS** (FAB) *m/z* Calcd for C₂₃H₂₃N₃O₅ [M+H]⁺ 422.716, found 422.717.

Diethyl 4'-undecyloxy-2,2':6',2''-terpyridine-6,6''-dicarboxylate

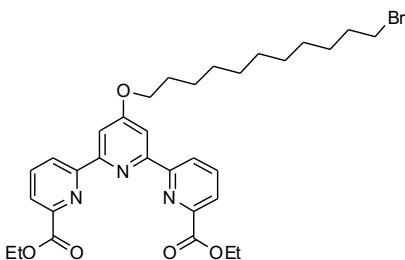


Synthesized following GP A (0.6 mmol scale). Purified by flash column chromatography (eluent: 50% *n*-hexane in AcOEt) to give 147 mg (45 % yield) of the title compound as a white solid.

¹H NMR (500 MHz, CDCl₃) δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.26–1.39 (m, 16H), 1.49 (t, *J* = 7.1 Hz, 6H), 1.50–1.54 (m, 2H),

1.85 (m, 2H), 4.27 (t, *J* = 6.6 Hz, 2H), 4.51 (q, *J* = 7.1 Hz, 4H), 7.97 (t, *J* = 7.9 Hz, 2H), 8.14 (dd, *J* = 1.2, 7.6 Hz, 2H), 8.16 (s, 2H), 8.79 (dd, *J* = 1.0, 7.8 Hz, 2H); **¹³C NMR** (125 MHz, CDCl₃) δ 14.1, 14.3, 22.7, 26.0, 29.0, 29.3, 29.3, 29.6, 29.6, 29.61, 31.9, 61.8, 68.3, 108.4, 124.4, 125.0, 137.7, 147.7, 156.2, 156.3, 165.3, 167.4; **HRMS** (FAB) *m/z* Calcd for C₃₂H₄₁N₃O₅ [M+H]⁺ 548.3124, found 548.3119.

Diethyl 4'-(11-bromoundecyloxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate



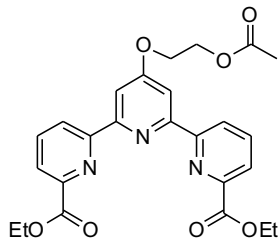
Synthesized following GP A (1.0 mmol scale). Purified by flash column chromatography (eluent: 50% *n*-hexane in AcOEt) to give 197 mg (31% yield) of the title compound as a white solid.

¹H NMR (500 MHz, CDCl₃) δ 1.29–1.45 (m, 12H), 1.48 (t, *J* = 7.1 Hz, 6H), 1.49–1.53 (m, 2H), 1.81 (m, 4H), 3.39 (t, *J* =

6.9 Hz, 2H), 4.26 (t, *J* = 6.4 Hz, 2H), 4.50 (q, *J* = 7.1 Hz, 4H), 7.97 (t, *J* = 7.8 Hz, 2H), 8.13 (d, *J* = 7.6 Hz, 2H), 8.16 (s, 2H), 8.77 (d, *J* = 8.0 Hz, 2H); **¹³C NMR** (125 MHz, CDCl₃) δ 14.3, 25.9, 28.1, 28.7, 29.0, 29.2, 29.4, 29.4, 29.4, 32.8, 34.0, 61.8, 68.2, 108.4, 124.3, 125.0, 137.6, 147.6, 156.1, 156.3, 165.3, 167.4; **HRMS** (FAB) *m/z* Calcd for C₃₂H₄₀⁷⁹BrN₃O₅ [M+H]⁺ 626.2230, found 626.2224.

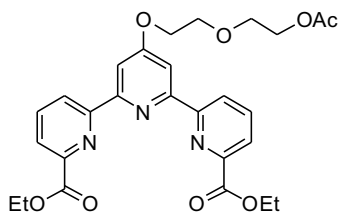
Diethyl 4'-(2-acethoxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate

Synthesized following GP A (2.5 mmol scale). Purified by flash column chromatography (eluent: 50% *n*-hexane in AcOEt) to give 494 mg (41 % yield) of the title compound as a orange solid.



¹H NMR (500 MHz, CDCl₃) δ 1.48 (t, *J* = 7.1 Hz, 6H), 2.14 (s, 3H), 4.49–4.54 (m, 4H), 4.52 (q, *J* = 7.1 Hz, 4H), 8.00 (t, *J* = 7.8 Hz, 2H), 8.16 (dd, *J* = 1.0, 7.6 Hz, 2H), 8.20 (s, 2H), 8.80 (dd, *J* = 1.0, 7.8 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 14.3, 20.9, 61.8, 62.4, 66.1, 108.3, 124.3, 125.1, 137.7, 147.8, 156.0, 156.4, 165.2, 166.8, 170.9; HRMS (FAB) *m/z* Calcd for C₂₅H₂₅N₃O₇ [M+H]⁺ 480.1771, found 480.1767.

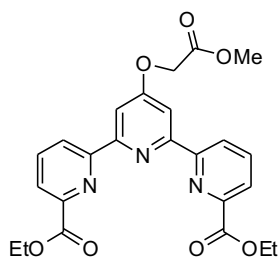
Diethyl 4'-(2-(2-acetoxyethoxy)ethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate



Synthesized following GP A (1.3 mmol scale). Purified by flash column chromatography (eluent: 50% *n*-hexane in AcOEt) to give 60 mg (9 % yield) of the title compound as a orange solid.

¹H NMR (400 MHz, CDCl₃) δ 1.49 (t, *J* = 7.1 Hz, 6H), 2.08 (s, 3H), 3.81–3.83 (m, 2H), 3.96–3.98 (m, 2H), 4.27 (t, *J* = 3.5 Hz, 2H), 4.43–4.46 (m, 2H), 4.50 (q, *J* = 7.1 Hz, 4H), 7.98 (t, *J* = 7.6 Hz, 2H), 8.13 (d, *J* = 7.6 Hz, 2H), 8.19 (s, 2H), 8.87 (d, *J* = 7.8 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 14.2, 20.8, 61.8, 63.5, 67.6, 69.3, 108.4, 124.4, 125.1, 137.7, 147.8, 156.2, 156.4, 165.4, 167.1, 171.1; HRMS (FAB) *m/z* Calcd for C₂₇H₂₉N₃O₈ [M+H]⁺ 524.2033, found 524.2037.

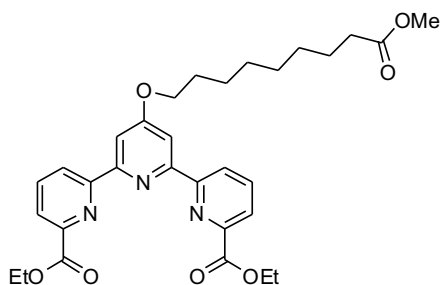
Diethyl 4'-(2-methoxy-2-oxoethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate



Synthesized following GP A (2.0 mmol scale). Purified by flash column chromatography (eluent: 50% *n*-hexane in AcOEt) to give 525 mg (56 % yield) of the title compound as a orange solid.

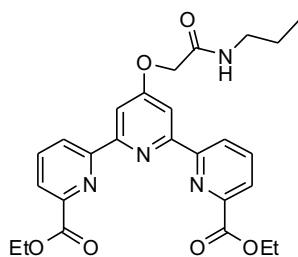
¹H NMR (500 MHz, CDCl₃) δ 1.49 (t, *J* = 7.1 Hz, 6H), 3.87 (s, 3H), 4.51 (q, *J* = 7.2 Hz, 4H), 4.93 (s, 2H), 7.99 (t, *J* = 7.9 Hz, 2H), 8.16 (d, *J* = 7.6 Hz, 2H), 8.21 (s, 2H), 8.78 (d, *J* = 7.8 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 14.4, 52.5, 61.9, 64.9, 108.3, 124.4, 125.2, 137.7, 147.8, 155.8, 156.6, 165.3, 166.1, 168.4; HRMS (FAB) *m/z* Calcd for C₂₄H₂₃N₃O₇ [M+H]⁺ 466.1641, found 466.1618.

Diethyl 4'-((9-methoxy-9-oxononyl)oxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate



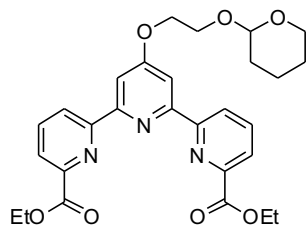
Synthesized following GP A (1.7 mmol scale). Purified by flash column chromatography (eluent: 50% *n*-hexane in AcOEt) to give 586 mg (61 % yield) of the title compound as a yellow solid. ¹H NMR (500 MHz, CDCl₃) δ 1.34–1.42 (m, 6H), 1.49 (t, *J* = 7.1 Hz, 6H), 1.50–1.54 (m, 2H), 1.61–1.66 (m, 2H), 1.85–1.89 (m, 2H), 2.32 (t, *J* = 7.4 Hz, 2H), 3.66 (s, 3H), 4.27 (t, *J* = 6.4 Hz, 2H), 4.51 (q, *J* = 7.1 Hz, 4H), 7.99 (t, *J* = 7.8 Hz, 2H), 8.14 (dd, *J* = 1.0, 7.6 Hz, 2H), 8.16 (s, 2H), 8.79 (dd, *J* = 1.0, 7.8 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 14.4, 25.0, 25.9, 29.0, 29.09, 29.14, 29.2, 34.1, 51.5, 61.9, 68.3, 108.4, 124.4, 125.0, 137.7, 147.7, 156.2, 156.3, 165.3, 167.4, 174.3; HRMS (FAB) *m/z* Calcd for C₃₁H₃₇N₃O₇ [M+H]⁺ 564.2710, found 564.2702.

Diethyl 4'-((2-oxo-2-(propylamino)ethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate



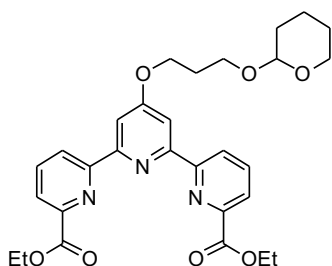
Synthesized following GP A (1.0 mmol scale). Purified by flash column chromatography (eluent: 50% *n*-hexane in AcOEt) to give 342 mg (70 % yield) of the title compound as a white solid. ¹H NMR (500 MHz, CDCl₃) δ 0.99 (t, *J* = 7.1 Hz, 3H), 1.50 (t, *J* = 7.4 Hz, 6H), 1.65 (sext, *J* = 7.3 Hz, 2H), 3.38 (q, *J* = 7.9 Hz, 2H), 4.53 (t, *J* = 7.1 Hz, 4H), 6.76 (br. t, NH), 8.01 (t, *J* = 7.9 Hz, 2H), 8.17 (dd, *J* = 1.0, 7.6 Hz, 2H), 8.22 (s, 2H), 8.79 (dd, *J* = 1.0, 7.9 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 11.3, 14.3, 22.8, 40.9, 61.9, 66.8, 108.2, 124.3, 125.3, 137.8, 147.8, 155.6, 156.7, 165.1, 165.3, 166.9; HRMS (FAB) *m/z* Calcd for C₂₆H₂₈N₄O₆ [M+H]⁺ 493.2087, found 493.2082.

Diethyl 4'-((2-((tetrahydro-2H-pyran-2-yl)oxy)ethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate



Synthesized following GP A (1.0 mmol scale). Purified by flash column chromatography (eluent: hexane : AcOEt = 2 : 1 ~ 1 : 1) to give 438 mg (84% yield) of the title compound as a white solid. ¹H NMR (500 MHz, CDCl₃) δ: 1.45-1.90 (m, 12H), 3.55-3.59 (m, 1H), 3.90-3.96 (m, 2H), 4.13-4.17 (m, 1H), 4.44-4.54 (m, 6H), 4.77 (t, *J* = 4.0 Hz, 1H), 7.99 (t, *J* = 8.0 Hz, 2H), 8.14 (d, *J* = 8.0 Hz, 2H), 8.21 (s, 2H), 8.78 (d, *J* = 8.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ: 14.3, 19.2, 25.4, 30.4, 61.8, 62.1, 65.5, 67.7, 98.9, 108.5, 124.3, 125.0, 137.7, 147.8, 156.2, 156.2, 165.3, 167.2; HRMS (FAB) *m/z* Calcd for C₂₈H₃₁N₃O₇ [M+H]⁺ 522.2240, found 522.2242.

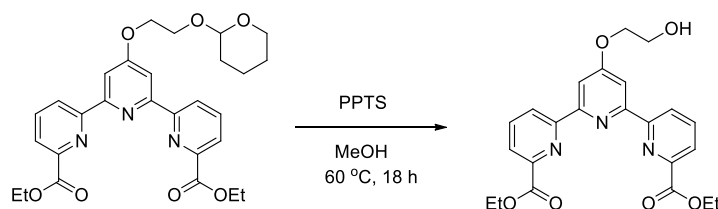
Diethyl 4'-((3-((tetrahydro-2H-pyran-2-yl)oxy)propoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate



Synthesized following GP A (0.5 mmol scale). Purified by flash column chromatography (eluent: hexane : AcOEt = 2 : 1 ~ 1 : 1) to give 110 mg (40% yield) of the title compound as a white solid.

¹H NMR (500 MHz, CDCl₃) δ: 1.49 (t, *J* = 7.0 Hz, 6H), 1.52-1.63 (m, 4H), 1.70-1.76 (m, 1H), 1.80-1.89 (m, 1H), 2.18 (quint., *J* = 6.0 Hz, 2H), 3.50-3.54 (m, 1H), 3.63-3.67 (m, 1H), 3.85-3.90 (m, 1H), 3.98-4.02 (m, 1H), 4.37-4.44 (m, 2H), 4.51 (q, *J* = 7.0 Hz, 4H), 4.63 (t, *J* = 4.5 Hz, 1H), 7.98 (t, *J* = 8.0 Hz, 2H), 8.14 (dd, *J* = 1.0, 8.0 Hz, 2H), 8.17 (s, 2H), 8.78 (dd, *J* = 1.0, 8.0 Hz, 2H); **¹³C NMR** (125 MHz, CDCl₃) δ: 14.3, 19.6, 25.4, 29.5, 30.6, 61.8, 62.3, 63.7, 65.2, 99.0, 108.3, 124.3, 125.0, 137.6, 147.7, 156.2, 156.2, 165.3, 167.3; **HRMS** (FAB) *m/z* Calcd for C₂₉H₃₃N₃O₇ [M+H]⁺ 536.2397, found 536.2396.

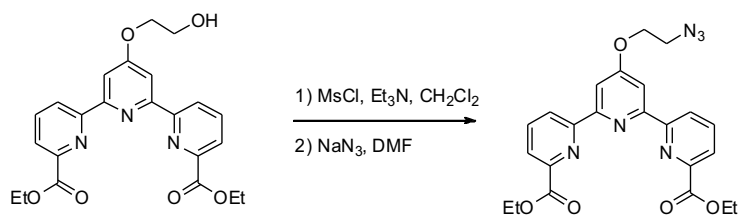
Diethyl 4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate



To a solution of Diethyl 4'-(2-((tetrahydro-2*H*-pyran-2-yl)oxy)ethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (287mg, 0.55mmol) in DMF was added PPTS (70mg, 0.28mmol) and the reaction mixture was heated at 60°C. After stirring for 18 h, the solution was cooled to room temperature and the mixture was added Et₃N (1.0 mL), concentrated *in vacuo*. The residue was purified by SiO₂ gel column chromatography (eluent: CHCl₃ : AcOEt = 1 : 0 ~ 1 : 1) afforded a title compound (211mg, 88% yield) as a white solid.

¹H NMR (500 MHz, CDCl₃) δ 1.49 (t, *J* = 7.0 Hz, 6H), 4.08 (t, *J* = 4.5 Hz, 2H), 4.42 (t, *J* = 4.5 Hz, 2H), 4.52 (q, *J* = 7.0 Hz, 4H), 7.98 (t, *J* = 8.0 Hz, 2H), 8.14 (d, *J* = 8.0 Hz, 2H), 8.19 (s, 2H), 8.76 (d, *J* = 8.0 Hz, 2H); **¹³C NMR** (125 MHz, CDCl₃) δ: 14.3, 61.1, 61.8, 69.5, 108.4, 124.3, 125.0, 137.6, 147.6, 156.0, 156.2, 165.3, 167.0; **HRMS** (FAB) *m/z* Calcd for C₂₃H₂₃N₃O₆ [M+H]⁺ 438.1665, found 438.1665.

Diethyl 4'-(2-azidoethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate



To a solution of diethyl 4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (206 mg, 0.47 mmol) in CH₂Cl₂ (4.7 ml) was added Et₃N (0.10 ml, 0.71 mmol) and MsCl (0.04 ml, 0.52 mmol) at 0 °C. After stirring for 15 h, the solution was cooled to room temperature and the mixture was added a saturated aqueous solution of NH₄Cl (5.0 mL), and the aqueous phase was extracted with CHCl₃ (2 × 5 ml). The combined organic layer was dried over MgSO₄, filtered and concentrated *in vacuo*. The crude product was used without further purification (254mg).

¹H NMR (500 MHz, CDCl₃) δ 1.49 (t, *J* = 7.0 Hz, 6H), 3.12 (s, 3H), 4.52 (q, *J* = 7.0 Hz, 4H), 4.57-4.58 (m, 2H), 4.67-4.68 (m, 2H), 8.00 (t, *J* = 8.0 Hz, 2H), 8.16 (dd, *J* = 1.0, 8.0 Hz, 2H), 8.79 (dd, *J* = 1.0, 8.0, 2H), 8.19 (s, 2H); ¹³C NMR (125 MHz, CDCl₃) δ: 14.3, 37.9, 61.9, 66.0, 67.3, 108.2, 124.4, 125.2, 137.8, 147.8, 155.9, 156.6, 165.2, 166.3.

To a solution of the crude product (37 mg, 0.07 mmol) in DMF (3.5 ml) was added NaN₃ (7.0 mg, 0.11 mmol) and reaction mixture was heated at 60 °C. After stirring for 13 h, the solution was cooled to room temperature and the mixture was added H₂O (3.5 ml), and the resulting mixture was extracted with AcOEt (2 × 5.0 ml). The combined organic layer was washed with brine and dried over MgSO₄. The mixture was filtered and concentrated *in vacuo* to give a title compound (30 mg, 92 %) as a white solid.

¹H NMR (500 MHz, CDCl₃) δ 1.49 (t, *J* = 7.0 Hz, 6H), 3.73 (t, *J* = 5.0 Hz, 2H), 4.45 (t, *J* = 5.0 Hz, 2H), 4.51 (q, *J* = 7.0 Hz, 4H), 7.99 (t, *J* = 8.0 Hz, 2H), 8.15 (dd, *J* = 8.0, 1.0 Hz, 2H), 8.19 (s, 2H), 8.77 (dd, *J* = 8.0, 1.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 14.3, 50.0, 61.8, 66.9, 108.2, 124.3, 125.1, 137.7, 147.7, 155.9, 156.4, 165.2, 166.5; HRMS (FI/EI) *m/z* Calcd for C₂₃H₂₂N₆O₅ [M+H]⁺ 463.1730, found 463.1733.

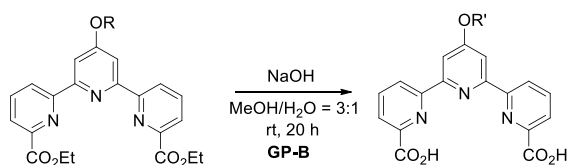
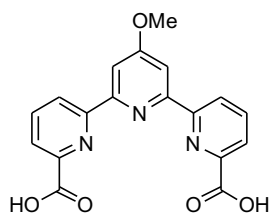


Table 3. Hydrolysis diethyl 4'-substituted-2,2':6',2''-terpyridine-6,6''-dicarboxylate

Entry	R	Product	
		R'	Yield (%) ^a
1	Me	Me	95
2	Et	Et	84
3			87
4			78
5			90
6			87
7			90
8			79
9			77
10			95

[a] Isolated yield.

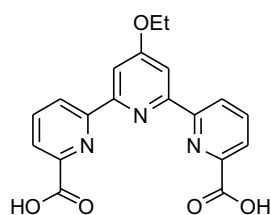
4'-Methoxy-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid



Synthesized following GP B (0.44 mmol scale) to give 149 mg (95 % yield) of the title compound as a yellow solid.

¹H NMR (500 MHz, d-DMSO) δ 4.06 (s, 3H), 8.14–8.21 (m, 6H), 8.85 (d, *J* = 7.6 Hz, 2H); ¹³C NMR (125 MHz, d-DMSO) δ 56.1, 107.7, 124.4, 125.3, 139.0, 147.9, 154.8, 155.9, 166.1, 167.9; HRMS (FAB) *m/z* Calcd for C₁₈H₁₃N₃O₅ [M+Na]⁺ 374.0753, found 374.0752.

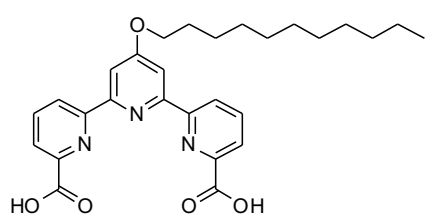
4'-Ethoxy-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid



Synthesized following GP B (0.24 mmol scale) to give 73 mg (84% yield) of the title compound as a yellow solid.

¹H NMR (400 MHz, d-DMSO) δ 1.43 (t, *J* = 6.4 Hz, 3H), 4.32 (q, *J* = 6.6 Hz, 2H), 8.13–8.22 (m, 6H), 8.80 (d, *J* = 6.8 Hz, 2H); ¹³C NMR (100Hz,d-DMSO) δ 14.4, 64.2, 108.0, 124.3, 125.2, 139.0, 147.9, 154.7, 155.8, 166.0, 167.3; HRMS (FAB) *m/z* Calcd for C₁₉H₁₅N₃O₅ [M+Na]⁺ 388.0909, found 388.0923.

4'-Undecyloxy-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid

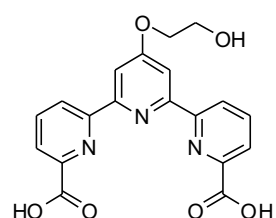


Synthesized following GP B (0.22 mmol scale) to give 104 mg (87 % yield) of the title compound as a white solid.

¹H NMR (500 MHz, d-DMSO) δ 0.82 (t, J = 7.1 Hz, 3H), 1.18–1.39 (m, 12H), 1.45–1.54 (m, 2H), 1.78–1.86 (m, 2H), 4.26–4.32 (m, 2H), 8.14–8.21 (m, 6H), 8.85 (d, J = 7.6 Hz,

2H); The peaks in ¹³C NMR analysis was not observed due to the poor solubility to d-DMSO; **HRMS** (FAB) m/z Calcd for C₂₈H₃₃N₃O₅ [M+Na]⁺ 514.2318, found 514.2324.

4'-(2-Hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid

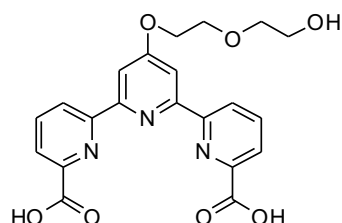


Synthesized following GP B (0.83 mmol scale) to give 248 mg (78% yield) of the title compound as a yellow solid.

¹H NMR (500 MHz, d-DMSO) δ 3.84 (t, J = 4.6 Hz, 2H), 4.32 (t, J = 4.6 Hz, 2H), 8.16 (d, J = 7.1 Hz, 2H), 8.19 (t, J = 7.8 Hz, 2H), 8.24 (s, 2H), 8.84 (d, J = 7.6 Hz, 2H); **¹³C NMR** (125 MHz, d-DMSO) δ 59.4, 70.2,

107.9, 123.6, 124.8, 138.7, 154.3, 155.9, 166.3, 167.3; **HRMS** (FAB) m/z Calcd for C₁₉H₁₅N₃O₆ [M+Na]⁺ 404.0859, found 404.0858.

4'-(2-(2-Hydroxyethoxy)ethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate

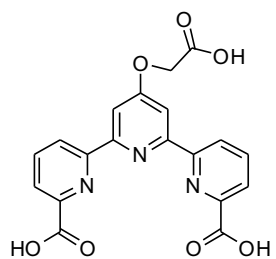


Synthesized following GP B (0.1 mmol scale) and concentrated in *vacuo* to give 30 mg (>90%) of the title compound as a white solid which was used without further purification.

¹H NMR (500 MHz, d-DMSO) δ 3.55 (m, 4H), 3.87 (t, J = 4.2 Hz, 2H), 4.44 (t, J = 3.9 Hz, 2H), 8.15 (dt, J = 1.3, 7.6 Hz, 2H), 8.20 (t, J = 7.6 Hz, 2H), 8.26 (d, J = 1.7 Hz, 2H), 8.86 (ddd, J = 1.3, 2.4, 7.8

Hz, 2H); **¹³C NMR** (125 MHz, d-DMSO) δ 60.7, 68.4, 69.1, 73.0, 108.5, 124.7, 125.6, 139.4, 148.2, 166.3, 167.5; **HRMS** (FAB) m/z Calcd for C₂₁H₁₉N₃O₇ [M+Na]⁺ 448.1121, found 448.1158.

4'-(carboxymethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid

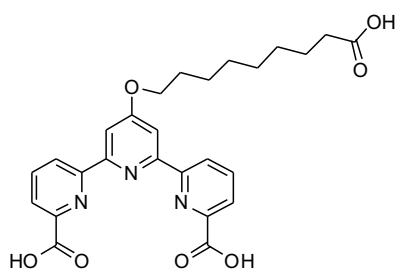


Synthesized following GP B (1.0 mmol scale) to give 345 mg (87 % yield) of the title compound as a yellow solid.

¹H NMR (300 MHz, d-DMSO) δ 5.05 (s, 2H), 8.14–8.21 (m, 4H), 8.23 (s, 2H), 8.85 (dd, J = 1.7 Hz, 7.4 Hz, 2H); **¹³C NMR** (125 MHz, d-DMSO) δ 64.7, 108.1, 124.3, 125.2, 139.0, 147.8, 154.6, 155.9, 165.9, 166.5, 169.5;

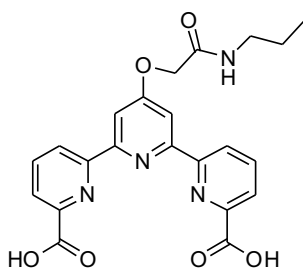
HRMS (FAB) m/z Calcd for C₁₉H₁₃N₃O₇ [M]⁺ 418.0651, found 418.0647.

4'-((8-carboxyoctyl)oxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid



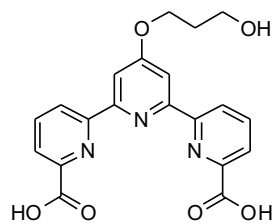
Synthesized following GP B (1.0 mmol scale) to give 437 mg (90% yield) of the title compound as a white solid. $^1\text{H NMR}$ (500 MHz, d-DMSO) δ 1.29–1.39 (m, 6H), 1.46–1.52 (m, 4H), 1.81 (quint, $J = 7.6$ Hz, 2H), 2.19 (t, $J = 7.4$ Hz, 2H), 4.25 (t, $J = 6.1$ Hz, 2H), 8.14 (d, $J = 7.6$ Hz, 2H), 8.18 (t, $J = 8.0$ Hz, 2H), 8.19 (s, 2H), 8.82 (d, $J = 7.6$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, d-DMSO) δ 25.0, 25.9, 29.0, 29.2, 34.1, 68.6, 108.2, 124.6, 125.5, 139.2, 148.2, 155.2, 156.2, 166.3, 167.5, 175.0; **HRMS** (FAB) m/z Calcd for $\text{C}_{26}\text{H}_{27}\text{N}_3\text{O}_7$ $[\text{M}+\text{Na}]^+$ 516.1747, found 516.01767.

4'-(2-oxo-2-(propylamino)ethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid



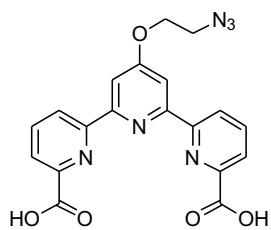
Synthesized following GP B (0.6 mmol scale) to give 210 mg (79% yield) of the title compound as a pale yellow solid. $^1\text{H NMR}$ (500 MHz, d-DMSO) δ 0.84 (t, $J = 7.6$ Hz, 3H), 1.48 (sext, $J = 7.1$ Hz, 2H), 3.13 (q, $J = 6.4$ Hz, 2H), 4.82 (s, 2H), 8.15 (dd, $J = 1.2$, 7.8 Hz, 2H), 8.20 (t, $J = 7.9$ Hz, 2H), 8.25 (s, 2H), 8.37 (br. t, $J = 5.9$ Hz, NH), 8.86 (dd, $J = 1.2$, 7.8 Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, d-DMSO) δ 11.4, 22.4, 40.2, 66.9, 108.1, 124.2, 125.2, 138.9, 147.9, 154.6, 155.8, 165.9, 166.2, 166.6; **HRMS** (FAB) m/z Calcd for $\text{C}_{22}\text{H}_{20}\text{N}_4\text{O}_6$ $[\text{M}+\text{Na}]^+$ 459.1281, found 459.1280

4'-(3-hydroxypropoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid



Synthesized following GP B (0.20 mmol scale) and concentrated in *vacuo* to give 61 mg (77% yield) of the title compound as a white solid which was used without further purification. $^1\text{H NMR}$ (500 MHz, d-DMSO) δ 1.93–1.99 (m, 2H), 3.62 (t, $J = 6.0$ Hz, 2H), 4.33 (t, $J = 6.0$ Hz, 2H), 8.11–8.19 (m, 6H), 8.78–8.84 (m, 2H); $^{13}\text{C NMR}$ (125 MHz, d-DMSO) δ 32.0, 57.2, 65.6, 108.0, 124.3, 125.3, 139.0, 147.9, 154.6, 155.6, 165.9, 167.4; **HRMS** (FAB) m/z Calcd for $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_6$ $[\text{M}+\text{Na}]^+$ 418.1015, found 418.0974.

4'-(2-azidoethoxy)-2,2':6,2''-terpyridine-6,6''-dicarboxylic acid



Synthesized following GP B (0.10 mmol scale) and concentrated *in vacuo* to give 27 mg (95% yield) of the title compound as a white solid which was used without further purification. ¹H NMR (500 MHz, d-DMSO) δ 3.78 (t, *J* = 4.5 Hz, 2H), 4.47 (t, *J* = 4.5 Hz, 2H), 8.13 (dd, *J* = 1.0, 8.0, 2H), 8.17 (t, *J* = 8.0 Hz, 2H), 8.19 (s, 2H), 8.80 (dd, *J* = 1.0, 8.0 Hz, 2H); ¹³C NMR (125 MHz, d-DMSO) δ 49.6, 67.5, 107.9, 124.3, 125.3, 139.0, 147.9, 154.6, 155.9, 165.9, 166.7; HRMS (FAB) *m/z* Calcd for C₁₉H₁₄N₆O₅ [M+Na]⁺ 429.0923, found 429.0930.

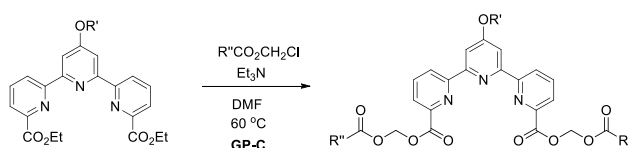
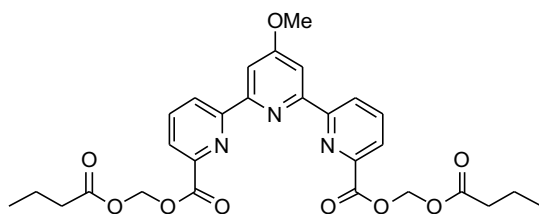


Table 4. The reactions of 4'-substituted-2,2':6,2''-terpyridine-6,6''-dicarboxylic acid with chloromethylalkoxylate

Entry	Substrate		Product		
	R'	R'	R''	Yield (%) ^a	compd. no
1	Me	Me	propyl	22	4
2	Et	Et	propyl	45	5
3			Me	85	6
4			Me	47	7
5			Et	13	8
6			i-Pr	50	9
7			propyl	45	10
8			hexyl	52	11
9			Ph	47	12
10			propyl	56	13
11			methyl	43	15
12			i-Pr	19	16
13			propyl	51	17
14			Me	49	18
			Me	36	19
15			Me	98	21
16			propyl	>99	22
17			propyl	51	23
18			propyl	45	26

[a] Isolated yield.

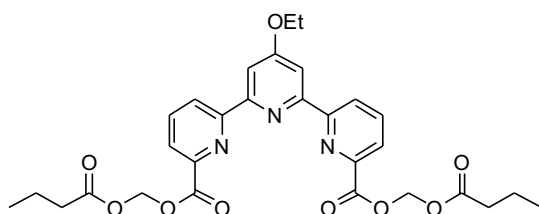
Bis(butyryloxymethyl) 4'-methoxy-2,2':6',2''-terpyridine-6,6''-dicarboxylate (4)



Synthesized following GP C (0.43 mmol scale). Purified by flash column chromatography (eluent: 70% *n*-hexane in AcOEt) to give 52 mg (21% yield) of the title compound as a white solid.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 0.98 (t, $J = 7.6$ Hz, 6H), 1.72 (sext. $J = 7.6$ Hz, 4H), 2.41 (t, $J = 7.6$ Hz, 4H), 4.08 (s, 3H), 6.12 (s, 4H), 8.02 (t, $J = 7.9$ Hz, 2H), 8.18 (dd, $J = 1.0$, 2H), 8.19 (s, 2H), 8.83 (dd, $J = 1.0$, 8.1 Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 13.5, 18.1, 35.8, 55.7, 80.2, 108.1, 124.9, 124.6, 137.8, 146.4, 156.1, 156.4, 163.9, 168.0, 172.2; **HRMS** (FAB) m/z Calcd for $\text{C}_{28}\text{H}_{29}\text{N}_3\text{O}_9$ $[\text{M}+\text{H}]^+$ 552.1982, found 552.1976.

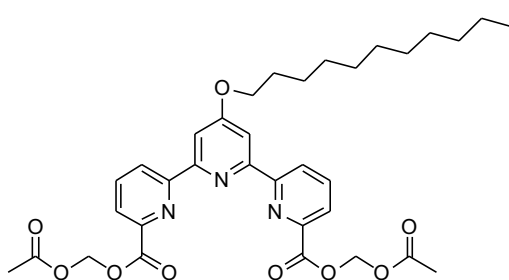
Bis(butyryloxymethyl) 4'-ethoxy-2,2':6',2''-terpyridine-6,6''-dicarboxylate (5)



Synthesized following GP C (0.19 mmol scale). Purified by flash column chromatography (eluent: 50% *n*-hexane in AcOEt) to give 48 mg (45% yield) of the title compound as a white solid.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 0.99 (t, $J = 7.6$ Hz, 6H), 1.53 (t, $J = 7.1$ Hz, 3H), 1.72 (sext. $J = 7.3$ Hz, 4H), 2.41 (t, $J = 7.3$ Hz, 4H), 4.35 (q, $J = 7.1$ Hz, 2H), 6.12 (s, 4H), 8.01 (t, $J = 7.8$ Hz, 2H), 8.17–8.19 (m, 4H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 13.6, 14.6, 18.1, 35.8, 64.1, 80.2, 108.5, 124.9, 125.6, 137.8, 146.4, 156.0, 156.5, 163.9, 167.3, 172.2; **HRMS** (FAB) m/z Calcd for $\text{C}_{29}\text{H}_{31}\text{N}_3\text{O}_9$ $[\text{M}+\text{H}]^+$ 566.2139, found 566.2152.

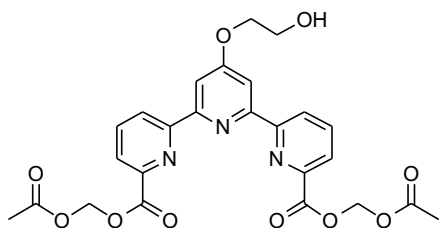
Bis(methoxyxymethyl) 4'-undecyloxy-2,2':6',2''-terpyridine-6,6''-dicarboxylate (6)



Synthesized following GP C (0.16 mmol scale). Purified by flash column chromatography (eluent: 50% *n*-hexane in AcOEt) to give 89 mg (85% yield) of the title compound as a white solid. $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 0.87 (t, $J = 7.2$ Hz, 3H), 1.24–1.39 (m, 14H), 1.53 (quint. $J = 7.9$ Hz, 2H), 1.86 (quint. $J = 6.3$ Hz, 2H), 2.16 (s, 6H), 4.25 (t, $J = 6.4$ Hz, 2H),

6.10 (s, 4H), 7.99 (t, $J = 7.8$ Hz, 2H), 8.15 (s, 2H), 8.16 (dd, $J = 1.0$, 7.8 Hz, 2H), 8.80 (dd, $J = 1.0$, 7.8 Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 14.1, 20.7, 22.6, 25.9, 29.0, 29.3, 29.3, 29.5, 29.6, 29.6, 31.8, 68.4, 80.2, 108.5, 124.9, 125.5, 137.7, 146.3, 155.9, 156.5, 163.8, 167.5, 169.5; **HRMS** (FAB) m/z Calcd for $\text{C}_{34}\text{H}_{41}\text{N}_3\text{O}_9$ $[\text{M}+\text{H}]^+$ 636.2921, found 636.2921.

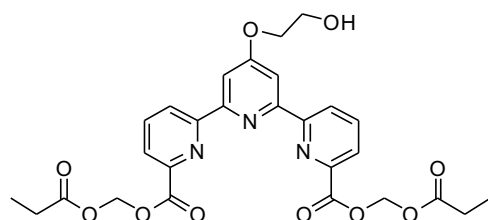
Bis(acetoxymethyl) 4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (7)



Synthesized following GP C (0.05 mmol scale). Purified by preparative TLC (mobile phase: CHCl₃ : Acetone = 4 : 1) to give 12 mg (47 % yield) of the title compound as a white solid.

¹H NMR (500 MHz, CDCl₃) δ 2.18 (s, 6H), 4.07-4.10 (m, 2H), 4.42 (t, *J* = 4.5 Hz, 2H), 6.11 (s, 4H), 8.01 (t, *J* = 8.0 Hz, 2H), 8.18 (d, *J* = 8.0 Hz, 2H), 8.21 (s, 2H), 8.81 (d, *J* = 8.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 20.8, 61.1, 65.6, 80.2, 108.5, 124.9, 125.7, 137.9, 146.4, 156.1, 156.3, 163.9, 165.5, 169.6; HRMS (FAB) *m/z* Calcd for C₂₅H₂₃N₃O₁₀ [M+H]⁺ 526.1462, found 526.1463.

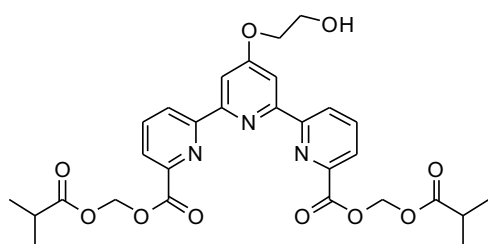
Bis(propionyloxy)methyl 4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (8)



Synthesized following GP C (0.05 mmol scale). Purified by preparative TLC (mobile phase: CHCl₃ : Acetone = 2 : 1) to give 4 mg (13 % yield) of the title compound as a white solid.

¹H NMR (500 MHz, CDCl₃) δ 1.19 (t, *J* = 8.0 Hz, 6H), 2.46 (q, *J* = 8.0 Hz, 4H), 4.07-4.10 (m, 2H), 4.41 (t, *J* = 4.5 Hz, 2H), 6.12 (s, 4H), 8.01 (t, *J* = 7.5 Hz, 2H), 8.18 (dd, *J* = 1.0, 7.5 Hz, 2H), 8.21 (s, 2H), 8.82 (dd, *J* = 1.0, 7.5 Hz, 2H); HRMS (FAB) *m/z* Calcd for C₂₇H₂₇N₃O₁₀ [M+H]⁺ 554.1775, found 554.1774.

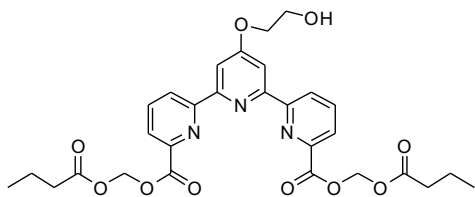
Bis(isobutyryloxy)methyl 4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (9)



Synthesized following GP C (0.05 mmol scale). Purified by preparative TLC (mobile phase: CHCl₃ : Acetone = 4 : 1) to give 14 mg (50 % yield) of the title compound as a white solid.

¹H NMR (500 MHz, CDCl₃) δ 1.23 (d, *J* = 7.0 Hz, 12H), 2.66 (sept., *J* = 7.0 Hz, 2H), 4.06-4.09 (m, 2H), 4.41 (t, *J* = 4.5 Hz, 2H), 6.11 (s, 4H), 8.01 (t, *J* = 8.0 Hz, 2H), 8.17 (d, *J* = 8.0 Hz, 2H), 8.21 (s, 2H), 8.81 (d, *J* = 8.0 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 18.7, 33.8, 61.1, 69.6, 80.3, 108.5, 124.9, 125.6, 137.9, 146.4, 156.1, 156.3, 163.9, 167.1, 175.8; HRMS (FAB) *m/z* Calcd for C₂₉H₃₁N₃O₁₀ [M+H]⁺ 582.2088, found 582.2086.

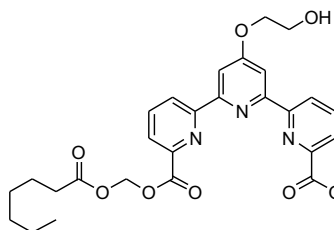
Bis(butyryloxymethyl) 4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (10)



Synthesized following GP C (0.39 mmol scale). Purified by flash column chromatography (eluent: 50% *n*-hexane in AcOEt) to give 101 mg (45% yield) of the title compound as a yellow solid.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 0.97 (t, $J = 7.4$ Hz, 6H), 1.70 (sext, $J = 7.6$ Hz, 4H), 2.41 (t, $J = 7.4$ Hz, 4H), 4.08 (t, $J = 4.4$ Hz, 2H), 4.41 (t, $J = 4.9$ Hz, 2H), 6.11 (s, 4H), 7.99 (t, $J = 7.8$ Hz, 2H), 8.16 (dd, $J = 1.2, 7.6$ Hz, 2H), 8.18 (s, 2H), 8.78 (dd, $J = 1.0, 7.9$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 13.5, 18.1, 35.8, 61.1, 69.6, 80.1, 108.5, 124.9, 125.6, 137.8, 146.3, 156.0, 156.2, 163.9, 167.1, 172.3; **HRMS** (FAB) m/z Calcd for $\text{C}_{29}\text{H}_{31}\text{N}_3\text{O}_{10}$ $[\text{M}+\text{H}]^+$ 582.2088, found 582.2084.

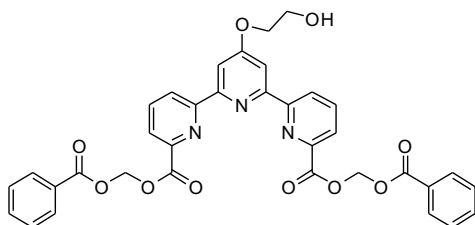
Bis((heptanoyloxy)methyl) 4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (11)



Synthesized following GP C (0.05 mmol scale). Purified by preparative TLC (mobile phase: CHCl_3 : Acetone = 4 : 1) to give 17 mg (52 % yield) of the title compound as a white solid.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 0.85 (t, $J = 7.0$ Hz, 6H), 1.25-1.36 (m, 12H), 1.67 (quint., $J = 7.5$ Hz, 4H), 2.42 (t, $J = 7.5$ Hz, 4H), 4.08 (t, $J = 4.5$ Hz, 2H), 4.41 (t, $J = 4.5$ Hz, 2H), 6.11 (s, 4H), 8.00 (t, $J = 8.0$ Hz, 2H), 8.14 (dd, $J = 1.0, 8.0$ Hz, 2H), 8.21 (s, 2H), 8.81 (dd, $J = 8.0, 1.0$, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 14.0, 22.4, 24.6, 28.6, 31.4, 34.0, 61.1, 69.6, 80.1, 108.5, 124.9, 125.7, 137.8, 146.4, 156.1, 156.3, 163.9, 167.1, 172.5; **HRMS** (FAB) m/z Calcd for $\text{C}_{35}\text{H}_{43}\text{N}_3\text{O}_{10}$ $[\text{M}+\text{H}]^+$ 666.3027, found 666.2955.

Bis((benzoyloxy)methyl) 4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (12)

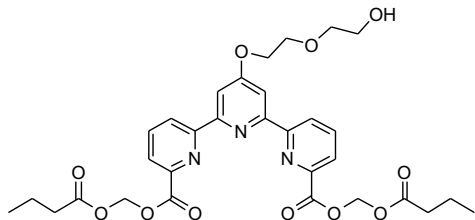


Synthesized following GP C (0.05 mmol scale). Purified by preparative TLC (mobile phase: CHCl_3 : Acetone = 5 : 1) to give 15 mg (47 % yield) of the title compound as a white solid.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 4.04 (t, $J = 4.5$ Hz, 2H), 4.36 (t, $J = 4.5$ Hz, 2H), 6.36 (s, 4H), 7.46 (t, $J = 7.5$ Hz, 4H), 7.60 (t, $J = 7.5$ Hz, 2H), 7.99 (t, $J = 8.0$ Hz, 2H), 8.12-8.20 (m, 8H), 8.79 (d, $J = 8.0$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 61.1, 69.5, 80.6, 108.5, 124.9, 125.7, 128.5, 128.9, 130.1, 133.8, 137.8, 146.4, 156.1, 156.3, 163.9, 165.2, 167.0; **HRMS** (FAB) m/z Calcd for $\text{C}_{35}\text{H}_{27}\text{N}_3\text{O}_{10}$ $[\text{M}+\text{H}]^+$ 650.1775, found 650.1772.

Bis(butyryloxymethyl)

4'-(2-(2-hydroxyethoxy)ethoxy)-2,2a':6',2''-terpyridine-6,6''-dicarboxylate (13)

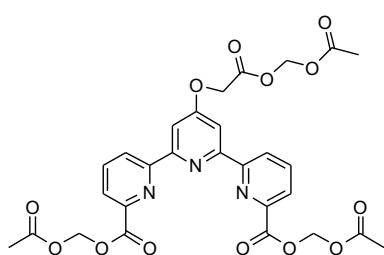


Synthesized following GP C (0.07 mmol scale). Purified by flash column chromatography (eluent: AcOEt) to give 21 mg (56% yield) of the title compound as a pale yellow solid.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 0.98 (t, $J = 7.6$ Hz, 6H), 1.71 (sext. $J = 7.6$ Hz, 4H), 2.41 (t, $J = 7.3$ Hz, 4H), 3.72 (dd, $J = 3.9, 5.6$ Hz, 2H), 3.80 (dd, $J = 4.2, 4.9$ Hz, 2H), 3.97–3.99 (m, 2H), 4.47–4.49 (m, 2H), 6.11 (s, 4H), 8.00 (t, $J = 7.6$ Hz, 2H), 8.17 (dd, $J = 1.0, 7.8$ Hz, 2H), 8.24 (s, 2H), 8.81 (dd, $J = 1.0, 7.8$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 13.5, 18.1, 35.8, 61.2, 67.7, 69.6, 72.7, 80.1, 108.7, 124.9, 125.6, 137.8, 146.4, 156.0, 156.4, 163.9, 167.2, 172.3; **HRMS** (FAB) m/z Calcd for $\text{C}_{31}\text{H}_{35}\text{N}_3\text{O}_{11}$ $[\text{M}+\text{H}]^+$ 626.2350, found 626.2357.

Bis(acetoxymethyl)

4'-(2-(acetoxymethoxy)-2-oxoethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (15)

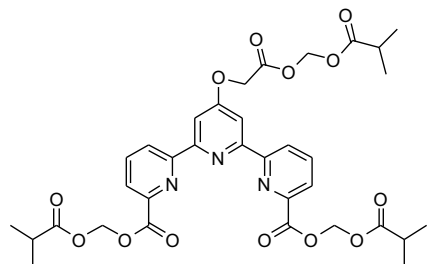


Synthesized following GP C (0.05 mmol scale). Purified by preparative TLC (mobile phase: hexane : AcOEt = 1 : 2) to give 13 mg (43 % yield) of the title compound as a white solid.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 2.12 (s, 3H), 2.18 (s, 6H), 4.98 (s, 2H), 5.90 (s, 2H), 6.10 (s, 4H), 8.01 (t, $J = 8.0$ Hz, 2H), 8.18 (dd, $J = 1.0, 8.0$ Hz, 2H), 8.21 (s, 2H), 8.81 (dd, $J = 1.0, 8.0$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 20.6, 20.7, 64.5, 79.5, 80.2, 108.4, 124.9, 125.8, 137.9, 146.4, 156.0, 156.4, 163.8, 165.9, 166.7, 169.4, 169.5; **HRMS** (FAB) m/z Calcd for $\text{C}_{28}\text{H}_{25}\text{N}_3\text{O}_{13}$ $[\text{M}+\text{H}]^+$ 612.1466, found 612.1459.

Bis(isobutyryloxy)methyl)

4'-(2-((isobutyryloxy)methoxy)-2-oxoethoxy) 2,2':6',2''-terpyridine-6,6''-dicarboxylate (16)



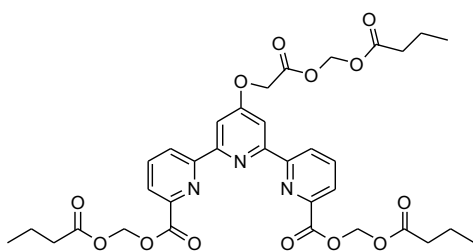
Synthesized following GP C (0.05 mmol scale). Purified by preparative TLC (mobile phase: hexane : AcOEt = 3 : 2) to give 7 mg (19 % yield) of the title compound as a white solid.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 1.17 (d, $J = 7.0$ Hz, 6H), 1.23 (d, $J = 7.0$ Hz, 12H), 2.60 (sept., $J = 7.0$ Hz, 1H), 2.66 (sept., $J = 7.0$ Hz, 2H), 4.97 (s, 2H), 5.92 (s, 2H), 6.11 (s, 4H), 8.01 (t, $J = 8.0$ Hz, 2H), 8.18 (d, $J = 8.0$ Hz, 2H), 8.21 (s, 2H), 8.81 (d, $J = 8.0$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 18.6, 18.7, 33.7, 33.8,

64.5, 79.7, 80.4, 108.4, 124.9, 125.7, 137.9, 146.5, 156.0, 156.4, 163.8, 165.9, 166.7, 175.5, 175.7;
HRMS (FAB) m/z Calcd for $C_{34}H_{37}N_3O_{13}$ $[M+H]^+$ 696.2405, found 696.2410.

Bis((butyryloxy)methyl)

4'-(2-((butyryloxy)methoxy)-2-oxoethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (17)

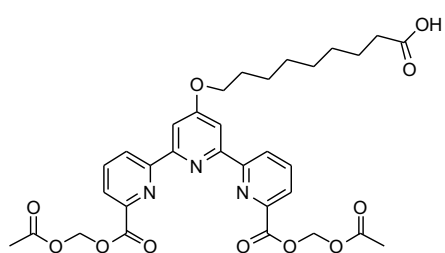


Synthesized following GP C (0.06 mmol scale) without purification of column chromatography to give 21 mg (51% yield) of the title compound as a white solid.

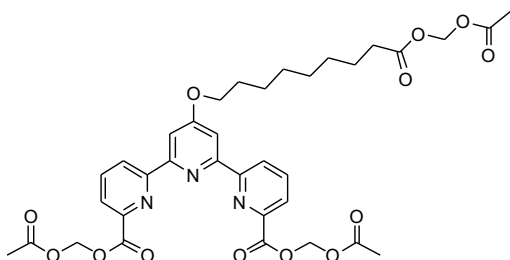
$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 0.94 (t, $J = 7.5$ Hz, 2H), 0.98 (t, $J = 7.5$ Hz, 4H), 1.65 (sext., $J = 7.5$ Hz, 2H), 1.71 (sext., $J = 7.5$ Hz, 4H), 2.35 (t, $J = 7.0$ Hz, 2H), 2.41 (t, $J = 7.0$ Hz, 4H), 4.97 (s, 2H), 5.92 (s, 2H), 6.12 (s, 4H), 8.01 (t, $J = 8.0$ Hz, 2H), 8.18 (d, $J = 7.0$ Hz, 2H), 8.20 (s, 2H), 8.81 (d, $J = 8.0$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ : 13.5, 13.6, 18.0, 18.1, 35.7, 35.8, 64.5, 79.6, 80.2, 108.4, 124.9, 125.8, 137.9, 146.5, 156.0, 156.4, 163.8, 166.0, 166.7, 172.1, 172.2; **HRMS** (FAB) m/z Calcd for $C_{34}H_{37}N_3O_{13}$ $[M+H]^+$ 696.2405, found 696.2405

9-((6,6''-Bis(acetoxymethoxycarbonyl)-2,2':6',2''-terpyridin-4'-yl)oxy)nonanoic acid (18) and Bis(acetoxymethyl)-4'-(9-((acetoxymethoxy)-9-oxononyl)oxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (19)

Synthesized following GP C (0.3 mmol scale). Purified by flash column chromatography (gradient: AcOEt/*n*-hexane = 1/1 to AcOEt) to give 69 mg (36% yield) of carboxylic acid (**18**) and 106 mg (49% yield) of the title compound as a white solid (**19**).



characterization data for **18**: $^1\text{H NMR}$ (500 MHz, *d*-DMSO) δ 1.27–1.41 (m, 6H), 1.46–1.53 (m, 4H), 1.84 (quint. $J = 7.1$ Hz, 2H), 2.14 (s, 6H), 2.19 (t, $J = 7.2$ Hz, 2H), 4.26 (t, $J = 6.4$ Hz, 2H), 6.02 (s, 4H), 8.01 (s, 2H), 8.18 (d, $J = 7.6$ Hz, 2H), 8.23 (t, $J = 7.8$ Hz, 2H), 8.88 (d, $J = 7.8$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, *d*-DMSO) δ 20.5, 25.4, 25.4, 28.4, 28.5, 28.7, 28.7, 33.7, 68.0, 80.2, 107.4, 124.7, 125.8, 138.9, 146.0, 155.0, 155.6, 163.1, 166.8, 169.3, 174.5; **HRMS** (FAB) m/z Calcd for $C_{32}H_{35}N_3O_{11}$ $[M+H]^+$ 638.2350, found 638.2354.



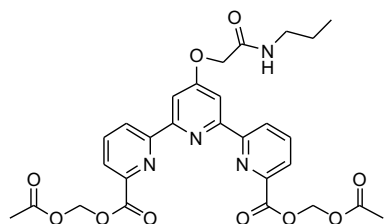
characterization data for **19**: $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 1.35–1.40 (m, 6H), 1.52 (quint. $J = 7.3$ Hz, 2H), 1.65 (quint. $J = 7.4$ Hz, 2H), 1.86 (quint. $J = 7.8$ Hz, 2H), 2.10 (s, 3H), 2.15 (s, 6H), 2.36 (t, $J = 7.6$ Hz, 2H), 4.24 (t, $J = 6.4$ Hz, 2H), 5.73 (s, 2H), 6.09

(s, 4H), 7.99 (t, $J = 7.9$ Hz, 2H), 8.13 (s, 2H), 8.15 (dd, $J = 0.8, 7.8$ Hz, 2H), 8.79 (dd, $J = 1.0, 7.8$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 20.7, 20.8, 24.6, 25.9, 28.9, 29.0, 29.1, 29.1, 68.2, 79.0, 80.1, 108.4, 124.9, 125.5, 137.7, 146.3, 155.8, 156.4, 163.8, 167.4, 169.4, 169.6, 172.4; **HRMS** (FAB) m/z Calcd for $\text{C}_{35}\text{H}_{39}\text{N}_3\text{O}_{13}$ $[\text{M}+\text{H}]^+$ 710.2561, found 710.2557.

Bis(acetoxymethyl)

4'-(2-oxo-2-(propylamino)ethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (21)

Synthesized following GP C (0.14 mmol scale) without purification of column chromatography to give 78 mg (98% yield) of the title compound as a white solid.

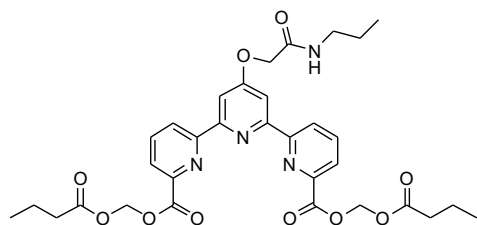


^1H NMR (500 MHz, CDCl_3) δ 1.00 (t, $J = 7.6$ Hz, 3H), 1.67 (sext, $J = 7.4$ Hz, 2H), 2.19 (s, 6H), 3.40 (q, $J = 7.3$ Hz, 2H), 4.79 (s, 2H), 6.11 (s, 4H), 6.78 (br. t, $J = 5.6$ Hz, NH), 8.03 (t, $J = 7.9$ Hz, 2H), 8.20 (d, $J = 7.4$ Hz, 2H), 8.22 (s, 2H), 8.82 (d, $J = 7.6$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 11.4, 20.8, 22.8,

40.9, 66.9, 80.3, 108.4, 125.0, 125.9, 138.0, 146.5, 155.9, 156.5, 163.8, 165.4, 166.8, 169.6; **HRMS** (FAB) m/z Calcd for $\text{C}_{28}\text{H}_{28}\text{N}_4\text{O}_{10}$ $[\text{M}+\text{H}]^+$ 581.1884, found 581.1882.

Bis(butyryloxymethyl)

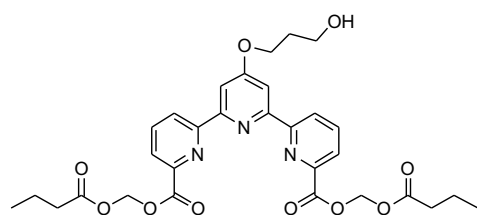
4'-(2-oxo-2-(propylamino)ethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (22)



Synthesized following GP C (0.32 mmol scale) without purification of column chromatography. ^1H NMR (500 MHz, CDCl_3) δ 0.98 (t, $J = 7.4$ Hz, 6H), 1.00 (t, $J = 7.4$ Hz, 3H), 1.62–1.74 (m, 6H), 2.42 (t, $J = 7.6$ Hz, 4H), 3.39 (q, $J = 7.1$ Hz, 2H), 4.78 (s, 2H), 6.13 (s, 4H), 6.77

(br. t, $J = 5.4$ Hz, NH), 8.03 (t, $J = 8.1$ Hz, 2H), 8.19 (d, $J = 7.6$ Hz, 2H), 8.22 (s, 2H), 8.81 (d, $J = 7.8$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 11.4, 13.5, 18.1, 22.9, 35.8, 40.9, 66.9, 80.3, 108.4, 124.9, 125.9, 138.0, 146.6, 155.9, 156.4, 163.8, 165.4, 166.7, 172.2; **HRMS** (FAB) m/z Calcd for $\text{C}_{32}\text{H}_{36}\text{N}_4\text{O}_{10}$ $[\text{M}+\text{H}]^+$ 637.2510, found 637.2516.

Bis((butyryloxy)methyl) 4'-(3-hydroxypropoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (23)

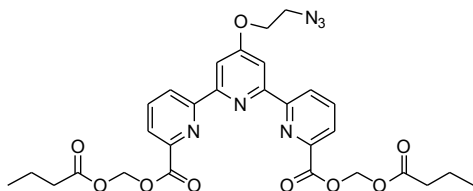


Synthesized following GP C (0.05 mmol scale). Purified by preparative TLC (mobile phase: hexane : EtOAc = 2 : 1) to give 15 mg (51% yield) of the title compound as a white solid.

^1H NMR (500 MHz, CDCl_3) δ 0.98 (t, $J = 7.5$ Hz, 6H), 1.71 (sext., $J = 7.5$ Hz, 4H), 2.16 (quint., $J = 6.0$ Hz, 2H), 2.41 (t, $J = 7.5$ Hz, 4H), 3.93 (t, $J = 6.0$ Hz,

2H), 4.46 (t, $J = 6.0$ Hz, 2H), 6.11 (s, 4H), 8.01 (t, $J = 8.0$ Hz, 2H), 8.17 (d, $J = 8.0$ Hz, 2H), 8.22 (s, 2H), 8.81 (d, $J = 8.0$ Hz, 2H); 13.5, 18.1, 31.9, 35.8, 59.6, 65.7, 80.1, 108.6, 124.9, 125.6, 137.8, 146.4, 156.1, 156.4, 163.9, 167.3, 172.4; **HRMS** (FAB) m/z Calcd for $C_{30}H_{33}N_3O_{10}$ $[M+H]^+$ 596.2244, found 596.2244.

Bis((butyryloxy)methyl) 4'-(2-azidoethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (26)

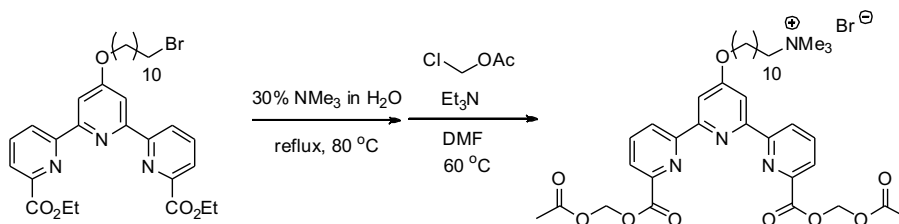


Synthesized following GP C (0.05 mmol scale). Purified by preparative TLC (mobile phase: hexane : EtOAc = 5 : 2) to give 19 mg (61% yield) of the title compound as a white solid.

1H NMR (500 MHz, $CDCl_3$) δ 0.98 (t, $J = 7.5$ Hz, 6H), 1.71 (sext., $J = 7.5$ Hz, 4H), 2.41 (t, $J = 7.5$ Hz, 4H), 3.75 (t, $J = 5.0$ Hz, 2H), 4.45 (t, $J = 5.0$ Hz, 2H), 6.12 (s, 4H), 8.18 (dd, $J = 1.0, 8.0$ Hz, 2H), 8.19 (s, 2H), 8.81 (dd, $J = 1.0, 8.0$ Hz, 2H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 13.5, 18.1, 35.8, 50.0, 67.0, 80.2, 108.4, 124.9, 125.7, 137.9, 146.5, 156.2, 156.2, 163.9, 166.6, 172.2; **HRMS** (FAB) m/z Calcd for $C_{29}H_{30}N_6O_9$ $[M+H]^+$ 607.2153, found 607.2145.

2-3. Synthesis of 4'-substituted-2,2':6',2''-terpyridine-6,6''-dicarboxylate derivatives (14, 20, 24, 25, 27, 28, 29, 30, 31)

11-((6,6''-bis((acetoxymethoxy)carbonyl)-2,2':6',2''-terpyridin-4'-yl)oxy)-N,N,N-trimethylundecan-1-aminium bromide (20)

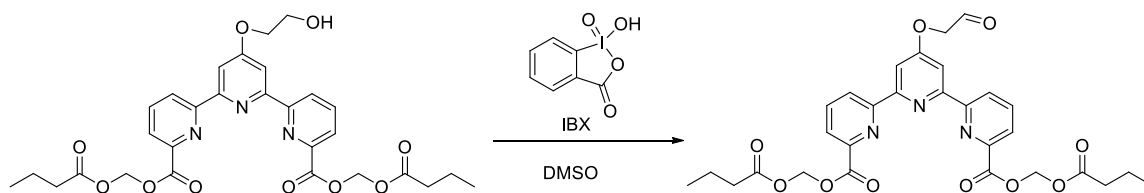


A suspension of Diethyl 4'-(11-bromoundecyloxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (200 mg, 0.32 mmol) in aqueous solution of NMe_3 (30%, 3.0 ml) was heated at $80^\circ C$ for 5 h. After cooling to room temperature, the solution was lyophilized to remove the excess NMe_3 and water. The residue was dissolved in DMF (8.0 ml), and Et_3N (102 μ l, 0.73 mmol) and chloromethyl acetoxylate (0.63 mmol). The reaction mixture was heated at $60^\circ C$. After stirring for 18 h, the solution was cooled to room temperature and the mixture was washed with H_2O (20 ml), and the aqueous phase was extracted with dichloromethane (2×30 ml). The combined organic phases were washed with brine, then dried over $MgSO_4$, filtered and concentrated *in vacuo*. To the residue was added a mixture of

AcOEt and *n*-hexane (1/1), the precipitate was collected by the filtration, dried *in vacuo* to yield as a white solid (87 mg, 37% yield).

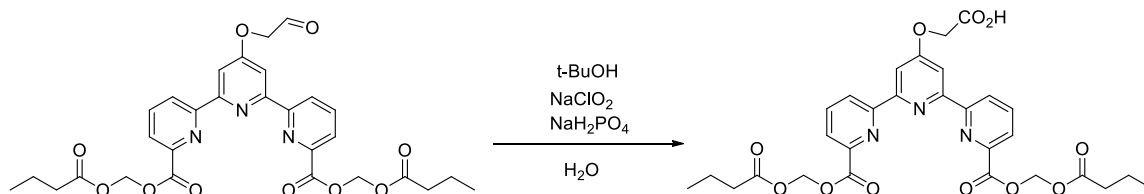
$^1\text{H NMR}$ (300 MHz, CDCl_3) δ 1.26–1.53 (m, 16H), 1.70–1.82 (m, 2H), 1.82 (m, 1.95 (m, 2H), 2.17 (s, 6H), 3.42 (m, 9H), 3.49–3.54 (m, 2H), 4.26 (t, $J = 7.6$ Hz, 2H), 6.10 (s, 4H), 8.02 (t, $J = 7.6$ Hz, 2H), 8.15 (s, 2H), 8.16 (d, $J = 7.6$ Hz, 2H), 8.82 (d, $J = 8.0$ Hz, 2H); $^{13}\text{C NMR}$ (100 MHz, CDCl_3) δ 8.5, 20.6, 23.0, 25.8, 26.0, 28.9, 29.0, 29.1, 29.2, 45.8, 53.2, 66.8, 68.3, 80.1, 108.4, 125.0, 125.6, 137.9, 146.3, 156.0, 156.5, 163.9, 167.5, 169.6; **HRMS** (FAB) m/z Calcd for $\text{C}_{37}\text{H}_{49}\text{BrN}_4\text{O}_9$ $[\text{M}]^+$ 693.3494, found 693.3499.

***Bis*(butyryloxymethyl) 4'-(2-oxoethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (24)**



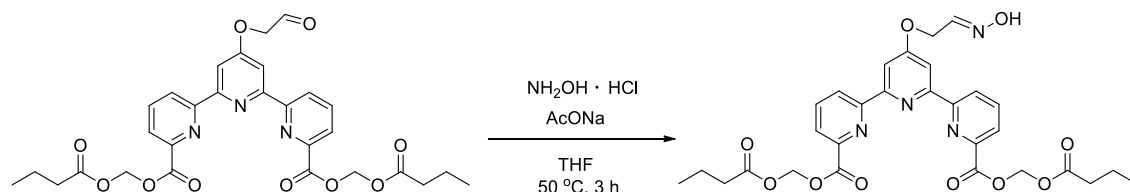
To a suspension of 1-hydroxy-1,2-benziodoxol-3(*1H*)-one 1-oxide: IBX (60 mg, 0.21 mmol) in DMSO was added (2 ml) bis(butyryloxymethyl) 4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (25 mg, 0.04 mmol) at room temperature. The mixture was stirred for 24 h before being quenched with water. The organic phase was separated, and the aqueous phase was extracted with AcOEt (2×10 ml). The combined organic phases were washed with brine, then dried over MgSO_4 , filtered and concentrated *in vacuo*. The crude was purified by column chromatography on SiO_2 gel (eluent: AcOEt) to give the product (19 mg, 74%) as a white solid. $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 0.98 (t, $J = 7.4$ Hz, 6H), 1.71 (sext, $J = 7.3$ Hz, 4H), 2.42 (t, $J = 7.6$ Hz, 4H), 4.93 (s, 2H), 6.12 (s, 4H), 8.02 (t, $J = 8.1$ Hz, 2H), 8.18–8.21 (m, 4H), 8.81 (d, $J = 7.8$ Hz, 2H), 9.96 (s, 1H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 13.5, 18.1, 35.8, 72.4, 80.1, 108.3, 124.9, 125.8, 137.9, 146.4, 163.8, 172.3, 172.5, 197.0; **HRMS** (FAB) m/z Calcd for $\text{C}_{29}\text{H}_{29}\text{N}_3\text{O}_{10}$ $[\text{ML}+\text{H}]^+$ 579.1931, found 579.1931.

2-((6,6''-Bis(((butyryloxy)methoxy)carbonyl)-2,2':6',2''-terpyridin-4'-yl)oxy)acetic acid (14)



Synthesized according to a literature procedure⁵: Bis(butyryloxymethyl) 4'-(2-oxoethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (30 mg, 0.05 mmol) dissolved in *tert*-butyl alcohol (1.5 ml) followed by addition of a solution of 2-methyl-2-butene (274 μ l, 26 mmol, 2M in THF). To the mixture at room temperature was added dropwise aliquots (810 μ l) of stock solution (NaClO₂ (1.76 g, 19.4 mmol) and NaH₂PO₄ (1.81 g, 15.1 mmol) in H₂O (27 ml). The reaction mixture was stirred at room temperature for 30 min and partitioned with H₂O, and the layers were separated. The aqueous layer was extracted with AcOEt (3 \times 10 ml). The combined organic layers were dried over MgSO₄, filtered and concentrated in *vacuo* to give the title compound as white solid (31 mg, 99% yield). ¹H NMR (500 MHz, CDCl₃) δ 0.96 (t, *J* = 7.4 Hz, 6H), 1.70 (sext, *J* = 7.4 Hz, 4H), 2.41 (t, *J* = 7.4 Hz, 4H), 4.95 (s, 2H), 6.11 (s, 4H), 7.99 (t, *J* = 7.8 Hz, 2H), 8.15 (d, *J* = 7.9 Hz, 2H), 8.17 (s, 2H), 8.74 (d, *J* = 7.8 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 13.5, 18.1, 35.8, 64.8, 80.1, 108.6, 125.0, 125.7, 137.9, 146.3, 163.9, 170.0, 172.6; HRMS (FAB) *m/z* Calcd for C₂₉H₂₉N₃O₁₁ [M+H]⁺ 596.1880, found 596.1880.

Bis(butyryloxymethyl) 4'-((2-hydroxyimino)ethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (25)

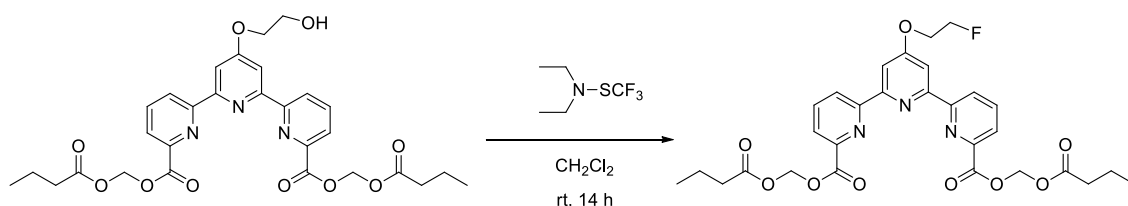


To a solution of Bis(butyryloxymethyl) 4'-(2-oxoethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (140 mg, 0.24 mmol) in tetrahydrofuran (5.0 ml) was added hydroxyamine (20 mg, 0.48 mmol) and AcOK (35 mg, 0.36 mmol) at room temperature. The reaction mixture was allowed to warm to 60°C, stirred for 3 h. H₂O was added and the aqueous layer was extracted with AcOEt (2 \times 10 ml). The combined organic layers were washed with H₂O and brine, dried over MgSO₄, filtered and concentrated in *vacuo*. The crude was purified by column chromatography on silica-gel (eluent: 50 % *n*-hexane in AcOEt) to give the title compound as white solid (60 mg, 42% yield).

characterization data for isomers (cis/trans = 1/1)

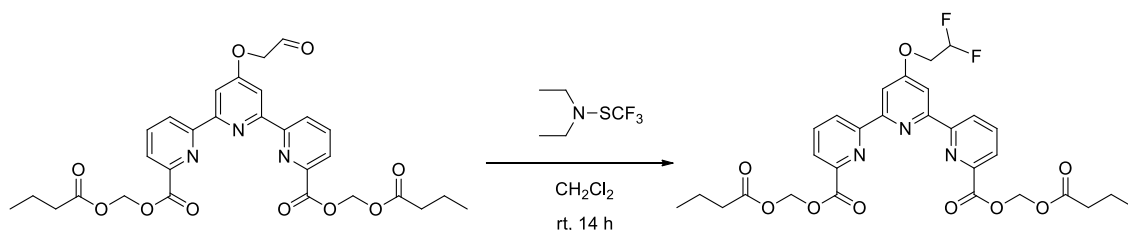
¹H NMR (500 MHz, CDCl₃) δ 0.97 (t, *J* = 7.1 Hz, 6H), 1.68–1.73 (m, 4H), 2.42 (t, *J* = 7.1 Hz, 4H), 4.96 (d, *J* = 5.6 Hz, 1H), 5.18 (d, *J* = 4.4 Hz, 1H), 6.11 (s, 4H), 6.99 (t, *J* = 4.4 Hz, 1H), 7.97–8.01 (m, 2H), 8.17 (d, *J* = 7.1 Hz, 2H), 8.24–8.25 (m, 2H), 8.76–8.79 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 13.4, 18.0, 60.6, 65.5, 80.0, 108.4, 108.8, 124.8, 124.8, 125.6, 125.6, 137.7, 137.8, 145.8, 146.1, 146.2, 147.4, 156.0, 156.1, 156.1, 164.0, 164.0, 166.3, 172.7, 172.7; HRMS (FAB) *m/z* Calcd for C₂₉H₃₀N₄O₁₀ [M+H]⁺ 595.2040, found 595.2048.

Bis(butyryloxymethyl) 4'-(2-fluoroethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (27)



To a solution of Bis(butyryloxymethyl) 4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (58 mg, 0.10 mmol) in dichloromethane (3.0 ml) was added diethylaminosulfur trifluoride (24 μ L, 0.18 mmol) at 0°C. The reaction mixture was allowed to warm to room temperature, stirred for 14 h before quenching with sat. NaHCO₃. The aqueous layer was extracted with dichloromethane (2 \times 10 ml). The combined organic layers were washed with H₂O and brine, dried over MgSO₄, filtered and concentrated in *vacuo*. The crude was purified by column chromatography on silica-gel (eluent: 50 % *n*-hexane in AcOEt) to give the title compound as white solid (26 mg, 45% yield). ¹H NMR (500 MHz, CDCl₃) δ 0.98 (t, J = 7.4 Hz, 6H), 1.71 (sext, J = 7.4 Hz, 4H), 2.41 (t, J = 2.41 Hz, 4H), 4.53 (ddd, J = 2.4, 3.9, 27.6 Hz, 2H), 4.96 (ddd, J = 2.7, 4.2, 47.3 Hz, 2H) 6.12 (s, 4H), 8.02 (t, J = 7.9 Hz, 3H), 8.18 (dd, J = 1.2, 7.6 Hz, 2H), 8.23 (s, 2H), 8.83 (dd, J = 1.2, 8.1 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 13.5, 18.1, 35.8, 67.3 (d, J = 20.6 Hz), 80.2, 108.5, 124.9, 125.7, 136.9, 146.5, 156.2, 163.9, 166.8, 172.3; ¹⁹F NMR (470 MHz, CDCl₃) δ -224.1 (tt, J = 27.4, 47.2 Hz, 1F); HRMS (FAB) m/z Calcd for C₂₉H₃₀FN₃O₉ [M+H]⁺ 584.2044, found 584.2047.

Bis(butyryloxymethyl) 4'-(2,2-difluoroethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (28)

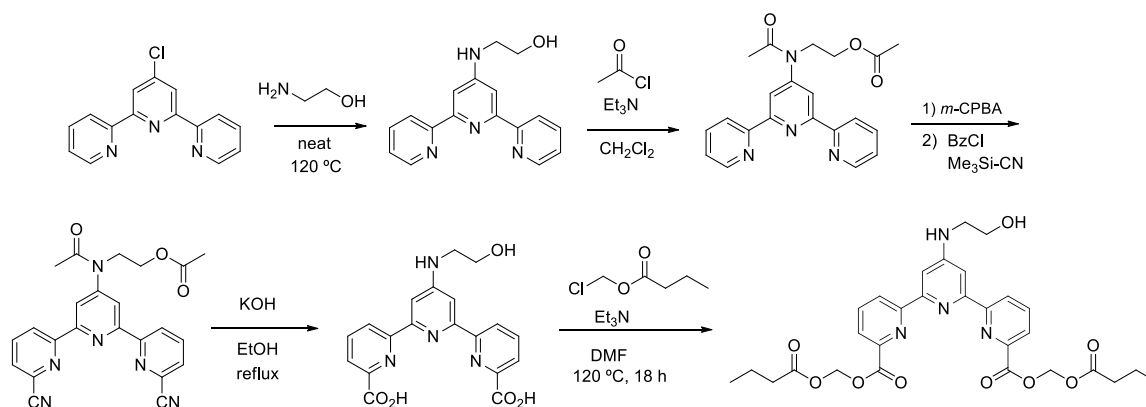


To a solution of Bis(butyryloxymethyl) 4'-(2-oxoethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (70 mg, 0.12 mmol) in dichloromethane (5.0 ml) was added diethylaminosulfur trifluoride (57 μ L, 0.43 mmol) at 0°C. The reaction mixture was allowed to warm to room temperature, stirred for 6 h before quenching with sat. NaHCO₃. The aqueous layer was extracted with dichloromethane (2 \times 10 ml). The combined organic layers were washed with H₂O and brine, dried over MgSO₄, filtered and concentrated in *vacuo*. The crude was purified by column chromatography on silica-gel (eluent: 30 % *n*-hexane in AcOEt) to give the title compound as white solid (38 mg, 52% yield).

¹H NMR (500 MHz, CDCl₃) δ 0.98 (t, J = 7.3 Hz, 6H), 1.71 (sext, J = 7.3 Hz, 4H), 2.41 (t, J = 7.4

Hz, 4H), 4.49 (dt, $J = 4.2, 12.7$ Hz, 1H), 6.12 (s, 4H), 6.20 (tt, $J = 4.2, 54.7$ Hz, 2H), 8.02 (t, $J = 7.9$ Hz, 2H), 8.18 (d, $J = 7.8$ Hz, 2H), 8.20 (s, 2H), 8.80 (d, $J = 8.1$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 13.5, 18.1, 35.8, 67.0 (t, $J = 30.3$ Hz), 80.2, 108.3, 113.2 (t, $J = 240$ Hz), 124.9, 125.8, 137.9, 146.5, 163.8, 172.2; HRMS (FAB) m/z Calcd for $\text{C}_{29}\text{H}_{29}\text{F}_2\text{N}_3\text{O}_9$ $[\text{M}+\text{H}]^+$ 602.1950, found 602.1963.

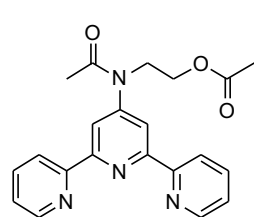
Synthesis of bis(butyryloxymethyl) 4'-(*N*-2-hydroxyethylamino)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (29)



4'-(*N*-2-Hydroxyethylamino)-2,2':6',2''-terpyridine

4'-chloro-2,2':6',2''-terpyridine (4'-chlorototterpyridine) (300 mg, 1.12 mmol) was suspended in tris(ethyleneglycol)-1,8-diamine (2.0 ml). The mixture was heated at 120°C for 12 h. After cooling to room temperature, H_2O (50 ml) was added and extracted with AcOEt (2×50 ml). The combined organic layers were washed with brine, dried over MgSO_4 filtered, and concentrated *in vacuo* to yield the title compound as a white solid (200 mg, 68% yield). ^1H NMR (500 MHz, CDCl_3) δ 2.05 (br. s, OH), 3.35 (q, $J = 5.2$ Hz, 2H), 3.91 (t, $J = 5.2$ Hz, 2H), 4.76 (br. t, NH), 7.31 (ddd, $J = 1.0, 4.7, 7.3$ Hz, 2H), 7.70 (s, 2H), 7.83 (dt, $J = 2.0, 7.8$ Hz, 2H), 8.60 (d, $J = 7.8$ Hz, 2H), 8.66 (d, $J = 4.6$ Hz, 2H). Characterization data correspond to a literature data.^[6]

2-(*N*-([2,2':6',2''-terpyridin]-4'-yl)acetamide)ethyl acetate

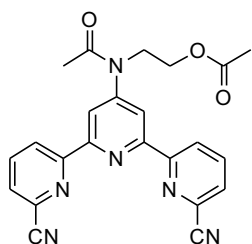


2-(*N*-([2,2':6',2''-terpyridin]-4'-yl)acetamide)ethyl acetate (200 mg, 0.68 mmol) was dissolved in dichloromethane (4.0 ml). Et_3N (229 μl , 1.6 mmol) and acetyl chloride (117 μl , 1.6 mmol) were sequentially added at room temperature. The mixture was stirred for 24 h before being quenched with water. The organic phase was separated, and the aqueous phase was extracted with dichloromethane (10 ml). The combined organic phases were washed with brine, then dried over MgSO_4 , filtered and concentrated *in vacuo* to yield the title compound as a sticky oil (256

mg, >99%) which was used without further purification.

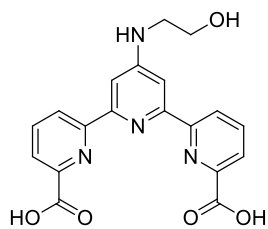
¹H NMR (500 MHz, CDCl₃) δ 2.01 (s, 3H), 2.16 (s, 3H), 4.11 (t, *J* = 5.4 Hz, 2H), 4.28 (t, *J* = 5.4 Hz, 2H), 7.35 (dt, *J* = 2.2, 6.6 Hz, 2H), 7.42 (dt, *J* = 1.3, 8.0 Hz, 2H), 8.30 (dd, *J* = 2.2, 8.0 Hz, 2H), 8.24 (dd, *J* = 1.0, 6.6 Hz, 2H), 9.00 (s, 2H); **¹³C NMR** (125 MHz, CDCl₃) δ 22.7, 22.9, 48.3, 62.2, 119.4, 121.3, 124.4, 137.0, 149.2, 155.0, 157.5, 169.9, 170.9; **HRMS** (FAB) *m/z* Calcd for C₂₁H₂₀N₄O₃ [M+H]⁺ 377.1614, found 377.1611.

4'-(*N*-(2-acetoxyethyl)acetamide)-2,2':6',2''-terpyridine-6,6''-dicyanitrile



To a suspension of *m*-chloroperbenzoic acid (626 mg, 75%, 2.7 mmol) in dichloromethane (3.0 ml) was slowly added a solution of 2-(*N*-([2,2':6',2''-terpyridin]-4'-yl)acetamide)ethyl acetate (256 mg, 0.68 mmol) in dichloromethane (1 ml) at room temperature. After stirring for 24 h, the mixture was washed with 10% aq. Na₂CO₃ (2 × 20 ml), and the aqueous phase was extracted with dichloromethane (20 ml). The combined organic phases were washed with brine, then dried over MgSO₄, filtered and concentrated *in vacuo*. The residue was dissolved in dichloromethane (5.0 ml). To the solution was added Me₃SiCN (563 μl, 4.5 mmol) at room temperature. After stirring for 1 h, benzoyl chloride (204 μl, 1.8 mmol) was added dropwise, and the solution was stirred at room temperature for 24 h. The solution was evaporated to halve volume, to the residue was added 10% aq. Na₂CO₃ (10 ml). The aqueous phase extracted with dichloromethane (5 × 10 ml). The combined organic layers were dried over MgSO₄, filtered and concentrated *in vacuo*. The crude was purified by column chromatography on SiO₂ gel (gradient: AcOEt/*n*-hexane = 1/2 to AcOEt/MeOH = 10/1) to give the product (183 mg, 63%) as a brown solid. **¹H NMR** (500 MHz, CDCl₃) δ 2.11 (s, 3H), 2.14 (s, 3H), 4.09 (t, *J* = 5.1 Hz, 2H), 4.37 (t, *J* = 5.1 Hz, 2H), 7.89 (dd, *J* = 1.0, 7.6 Hz, 2H), 8.05 (t, *J* = 7.6 Hz, 2H), 8.49 (s, 2H), 8.84 (dd, *J* = 1.0, 8.1 Hz, 2H); **¹³C NMR** (125 MHz, CDCl₃) δ 20.8, 22.9, 48.7, 61.9, 116.9, 120.8, 124.4, 128.9, 133.3, 138.3, 155.5, 156.2, 170.0, 171.0; **HRMS** (FAB) *m/z* Calcd for C₂₃H₁₈N₆O₃ [M+H]⁺ 427.1519, found 427.1518.

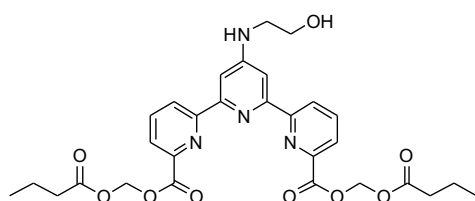
4'-(2-aminoethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid



To a solution of 4'-(*N*-(2-acetoxyethyl)acetamide)-2,2':6',2''-terpyridine-6,6''-dicyanitrile (100 mg, 0.23 mmol) in ethanol (6.0 ml) and dist. H₂O (1.5 ml) was added KOH (132 mg, 2.3 mmol). The reaction mixture was refluxed for 12 h, and then the solvent was evaporated to remove the solvent. The residue was dissolved in H₂O (3.0 ml), and the pH was adjusted to approximate 4 with 1N HCl. The precipitate was collected by the filtration affording the product (50 mg, 63% yield) as a yellow solid.

$^1\text{H NMR}$ (500 MHz, d-DMSO) δ 3.20–3.37 (m, 2H), 4.51–4.59 (m, 2H), 8.14 (d, $J = 7.6$ Hz, 2H), 8.19 (t, $J = 7.6$ Hz, 2H), 8.22 (s, 2H), 8.84 (d, $J = 7.6$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, d-DMSO) δ 57.5, 64.9, 107.9, 124.2, 125.3, 138.9, 148.0, 154.6, 155.9, 165.9, 166.4; **HRMS** (FAB) m/z Calcd for $\text{C}_{19}\text{H}_{16}\text{N}_5$ $[\text{M}+\text{Na}]^+$ 403.1018, found 403.0984.

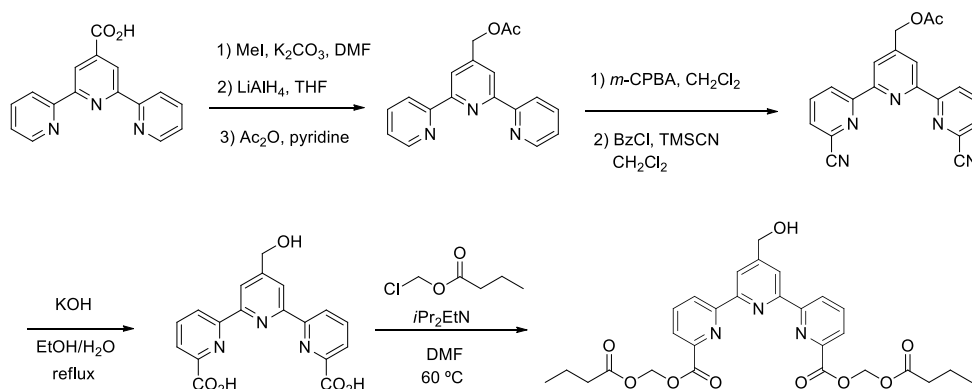
Bis(butyryloxymethyl) 4'-(N-2-hydroxyethylamino)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (29)



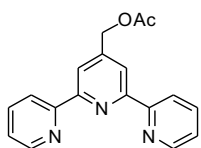
To a solution of 4'-(*N*-(2-acetoxyethyl)acetamide)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid (80.0 mg, 0.21 mmol) in DMF (5.0 ml) was added Et_3N (106 μl , 1.1 mmol) and chloromethyl butylate (80 μl , 0.63 mmol). The reaction mixture was heated at 50°C. After stirring for 18 h, the solution was cooled to room temperature and the mixture was washed with H_2O (20 ml), and the aqueous phase was extracted with AcOEt (2×30 ml). The combined organic phases were washed with brine, then dried over MgSO_4 , filtered and concentrated *in vacuo*. The crude was purified by column chromatography on SiO_2 gel (gradient: AcOEt/*n*-hexane = 1/2 to AcOEt/MeOH = 10/1) to give the product (41 mg, 31%) as a white solid.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 0.96 (t, $J = 7.3$ Hz, 6H), 1.70 (q, $J = 7.3$ Hz, 4H), 2.41 (q, $J = 7.3$ Hz, 4H), 3.56 (q, $J = 5.4$ Hz, 2H), 3.93 (t, $J = 5.6$ Hz, 2H), 5.11 (br. s, NH), 6.11 (s, 4H), 7.81 (s, 2H), 7.94 (t, $J = 7.8$ Hz, 2H), 8.12 (dd, $J = 1.0, 7.6$ Hz, 2H), 8.74 (d, $J = 7.6$ Hz, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ 13.5, 18.1, 35.8, 44.9, 61.0, 78.0, 105.8, 124.9, 125.2, 137.6, 146.0, 164.0, 172.4; **HRMS** (FAB) m/z Calcd for $\text{C}_{29}\text{H}_{32}\text{N}_4\text{O}_9$ $[\text{M}+\text{H}]^+$ 581.2248, found 581.2244..

Synthesis of *Bis(butyryloxymethyl) 4'-(hydroxymethyl)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (31)*



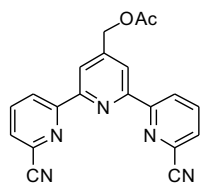
(2,2':6',2''-terpyridin-4'-yl)methyl acetate



To a solution of 2,2':6',2''-terpyridine-4'-carboxylic acid (200 mg, 0.72 mmol) in DMF (3.6 ml) was added K_2CO_3 (20 mg, 1.4 mmol) and methyl iodide (0.07 ml, 1.1 mmol). The reaction mixture was stirred for 16 h at rt. The reaction mixture was added brine and the aqueous phase was extracted with AcOEt (3 X 5.0 mL), washed with brine and dried over MgSO_4 . The mixture was filtered and concentrated *in vacuo* to give a crude material which was used to the next reaction without further purification. To a solution of above crude material (0.72 mmol) in tetrahydrofuran (7.2 ml) was added lithium aluminum hydride (28 mg, 0.7 mmol) at 0 °C. After stirring for 3 h, reaction mixture was added sodium sulfate $10 \cdot \text{H}_2\text{O}$ and then stirred one hour at rt. The resulting mixture was filtered through celite pad and the filtrate was concentrated *in vacuo*. After the residue was dissolved in pyridine (3.6 ml), the solution was added acetic anhydride (0.14 ml, 1.4 mmol). After stirring for 16 h, the mixture was added toluene and concentrated *in vacuo*. The crude mixture was purified by column chromatography on CHROMATOREX Diol SiO_2 gel (eluent: *n*-hexane : EtOAc = 1 : 0~1:1) to give the desired product (88 mg, 40 % yield in 3 steps) as a white solid.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 2.20 (s, 3H), 5.28 (s, 2H), 7.32-7.35 (m, 2H), 7.85 (dt, $J = 2.0, 8.0$ Hz, 2H), 8.43 (s, 2H), 8.61 (td, $J = 1.0, 8.0$ Hz, 2H), 8.70-8.71 (m, 2H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) δ ; 20.9, 64.8, 119.2, 121.3, 123.9, 136.8, 146.9, 149.1, 155.8, 155.8, 170.6; **HRMS** (ESI) m/z Calcd for $\text{C}_{18}\text{H}_{16}\text{N}_3\text{O}_2$ $[\text{M}+\text{H}]^+$ 306.1243, found 306.1203.

(6,6''-dicyano-2,2':6',2''-terpyridin-4'-yl)methyl acetate

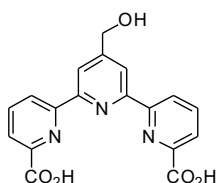


To a solution of (2,2':6',2''-terpyridin-4'-yl)methyl acetate (88 mg, 0.28 mmol) in dichloromethane (2.8 ml) was added *m*-chloroperbenzoic acid (170 mg, 75%, 0.74 mmol) at 0 °C. After stirring for 19 h, the mixture was washed with saturated aqueous solution of $\text{Na}_2\text{S}_2\text{O}_3$ (20 ml), and the aqueous phase was extracted with CHCl_3 (2 X 20 ml). The combined organic layer was washed with saturated aqueous solution of NaHCO_3 and brine. The organic layer was dried over MgSO_4 , filtered and concentrated *in vacuo*. The residue was dissolved in dichloromethane (2.8 ml). To the solution was added benzoyl chloride (0.10 ml, 0.86 mol) at room temperature. After stirring for 20 min, was added dropwise Me_3SiCN (0.11 ml, 0.87 mmol), and the solution was stirred at room temperature for 19 h. The solution was added saturated aqueous solution of NaHCO_3 (5.0 ml). The aqueous phase extracted with CHCl_3 (3 \times 5.0 ml). The combined organic layer washed with brine and dried over MgSO_4 , concentrated *in vacuo*. The crude was purified by column chromatography on SiO_2 gel (eluent: CHCl_3 /acetone = 1/0 to 15/1) to give the title compound (92 mg, 92%) as a white solid.

$^1\text{H NMR}$ (500 MHz, CDCl_3) δ 2.26 (s, 3H), 5.33 (s, 2H), 7.76 (d, $J = 7.5$ Hz, 2H), 8.02 (t, $J = 7.5$

Hz, 2H), 8.52 (s, 2H), 8.81 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR (125MHz, CDCl_3) δ 20.9, 64.4, 117.2, 120.7, 124.3, 128.5, 133.4, 138.0, 148.1, 154.0, 157.0, 170.6; HRMS (ESI) m/z Calcd for $\text{C}_{20}\text{H}_{13}\text{N}_5\text{NaO}_2$ $[\text{M}+\text{Na}]^+$ 378.0967, found 378.0966.

4'-(hydroxymethyl)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid

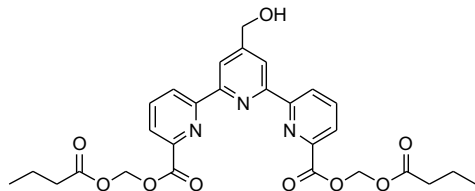


To a solution of (6,6''-dicyano-2,2':6',2''-terpyridin-4'-yl)methyl acetate (80 mg, 0.23 mmol) in ethanol (6.9 ml) and dist. H_2O (1.8 ml) was added KOH (200 mg, 3.9 mmol). The reaction mixture was refluxed for 11 h, and then the mixture was cooled to rt. The pH was adjusted to approximate 4 with 1N HCl. The precipitate was collected by the filtration affording the

product as a pale brown solid which was used to the next reaction without further purification.

^1H NMR (500 MHz, d-DMSO) δ 4.77 (s, 2H), 8.12 (d, $J = 7.5$ Hz, 2H), 8.17 (t, $J = 7.5$ Hz, 2H), 8.57 (s, 2H), 8.83 (d, $J = 7.5$ Hz, 2H); ^{13}C NMR (125 MHz, d-DMSO) ; 62.0, 124.0, 125.0, 138.8, 148.1, 154.0, 154.6, 155.2, 166.0 ; HRMS (ESI) m/z Calcd for $\text{C}_{18}\text{H}_{13}\text{N}_3\text{NaO}_5$ $[\text{M}+\text{Na}]^+$ 374.0753, found 374.0703.

Bis(butyryloxymethyl) 4'-(hydroxymethyl)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (31)



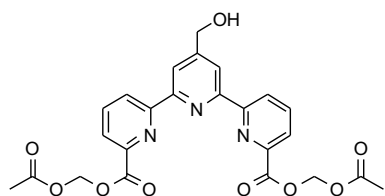
To a solution of 4'-(hydroxymethyl)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid (18 mg, 0.05 mmol) in DMF (1.0 ml) was added $i\text{-Pr}_2\text{EtN}$ (0.05 ml, 0.29 mmol) and chloromethyl butylate (0.03 ml, 0.24 mmol). The

reaction mixture was heated at 50°C . After stirring for 15 h, the solution was cooled to room temperature and the mixture was washed with saturated solution of NH_4Cl (2.0 ml), and the aqueous phase was extracted with AcOEt (3×5.0 ml). The combined organic layer was washed with brine and dried over MgSO_4 , filtered and concentrated *in vacuo*. The crude material was purified by column chromatography on SiO_2 gel (eluent: $n\text{-hexane} : \text{AcOEt} = 2 : 1 \sim 1 : 1$) to give the product (10.1 mg, 36%) as a white solid.

^1H NMR (500 MHz, CDCl_3) δ 0.98 (t, $J = 7.5$ Hz, 6H), 1.71 (sext., $J = 8.0$ Hz, 4H), 2.41 (t, $J = 7.5$ Hz, 4H), 2.45 (brt, $J = 6.0$ Hz, 1H), 4.9d (brd, $J = 6.0$ Hz, 2H), 6.12 (s, 4H), 8.01 (t, $J = 7.5$ Hz, 2H), 8.17 (dd, $J = 1.0, 7.5$ Hz, 2H), 8.61 (s, 2H), 8.80 (dd, $J = 1.0, 7.5$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 13.5, 18.1, 35.8, 63.9, 80.2, 119.7, 124.9, 125.6, 137.9, 146.5, 152.6, 154.5, 156.5, 163.9, 172.3; HRMS (ESI) m/z Calcd for $\text{C}_{28}\text{H}_{29}\text{N}_3\text{NaO}_9$ $[\text{M}+\text{Na}]^+$ 574.1802, found 574.1808.

Bis(acetoxymethyl) 4'-(hydroxymethyl)-2,2':6',2''-terpyridine-6,6''-dicarboxylate (30)

Synthesized following GP-C (0.05 mmol scale). Purified by SiO_2 column chromatography (mobile



phase: hexane : EtOAc = 2 : 1 ~ 1 : 3) to give 5.2 mg (20 % yield) of the title compound as a white solid.

¹H NMR (500 MHz, CDCl₃) δ 2.18 (s, 6H), 4.96 (brs, 2H), 6.11 (s, 4H), 8.02 (t, *J* = 7.5 Hz, 2H), 8.19 (d, *J* = 7.5 Hz, 2H), 8.62 (s, 2H), 8.82 (d, *J* = 7.5 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 20.8, 63.9, 80.2, 119.7, 125.0, 125.7, 137.9, 138.9, 146.5, 154.6, 156.5, 169.6; HRMS (ESI) *m/z* Calcd for C₂₄H₂₁N₃O₉ [M+Na]⁺ 518.1176, found 518.1151.

2-4. Photophysical properties of lanthanide metal/terpyridine ligand complex

UV-Vis absorption spectra were recorded on a JASCO V-670 spectrophotometer. Emission spectra ($\lambda_{\text{ex}} = 340 \text{ nm}$) for 5-10 μM ligand in water with 1.0 equiv. of Eu(OTf)₃ were recorded on a Shimadzu RF-1500 spectrofluorophotometer. The excitation wavelengths, molar absorptivities at the excitation wavelengths and luminescence of the Eu(OTf)₃ chelates were measured. From these results, luminescence quantum yields of compounds (Ligand + Eu(III)) were calculated by a relative method using Ru(bpy)₃Cl₂ in water under air ($\Phi = 4.0\%$, $\lambda_{\text{ex}} = 450 \text{ nm}$)⁷ as a standard according to literature procedure where the excitation.⁸

The relative quantum yield can be calculated from eq. 1:

$$\frac{f_i}{f_s} = \frac{F_i \cdot f_s \cdot n_i^2 \cdot D_i}{F_s \cdot f_i \cdot n_s^2 \cdot D_s} \quad (1)$$

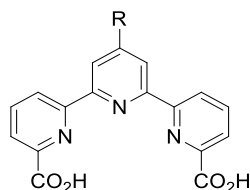
F : integrated intensity (area)

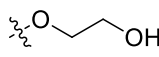

f : absorption factor

n : refractive index

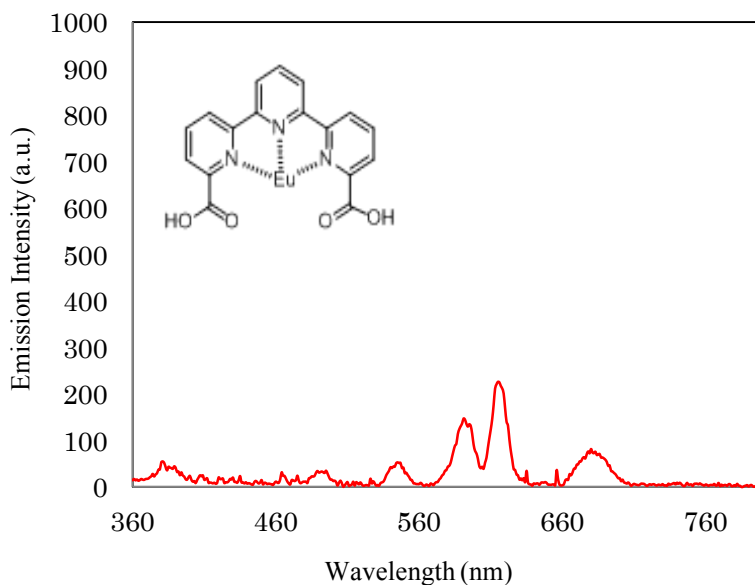
D: dilution ratio

Table 5. Luminescent properties of synthesized terpyridine ligands with Eu^{3+} .

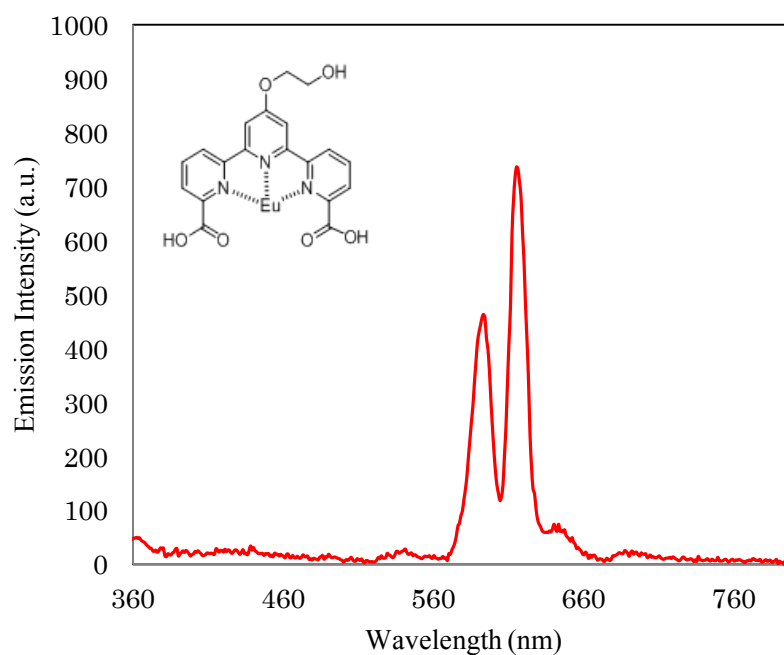


Ligand R	Solvent	Eu(III) Chelates		λ_{em} (nm)
		λ_{ex} (nm), ϵ ($\text{M}^{-1}, \text{cm}^{-1}$)		
H	10 μM in water	330, 7040	592, 615	0.34
	10 μM in water	323, 13075	592, 615	0.58
	5 μM in water	333, 12240	592, 615	1.02

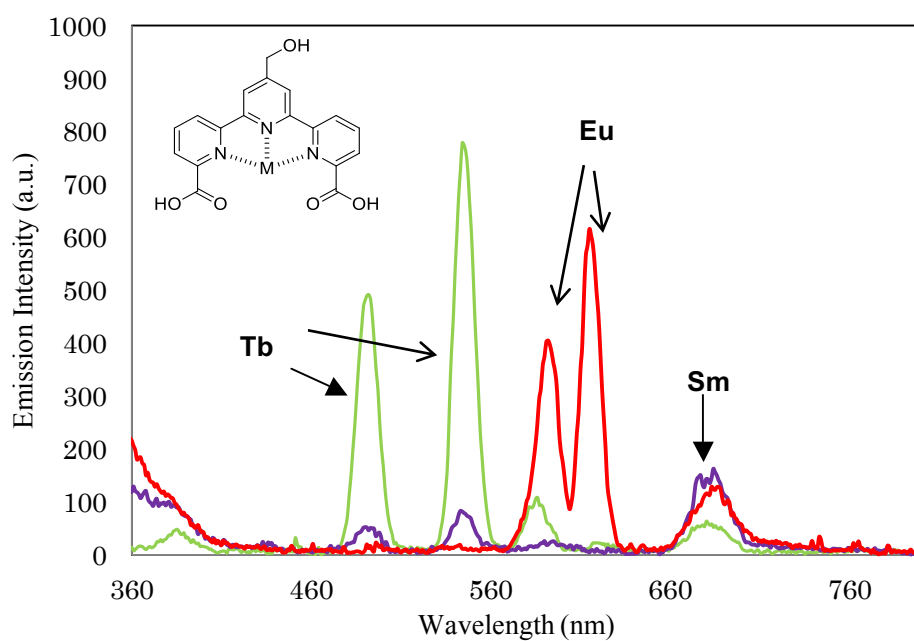
Corrected emission spectra of 1×10^{-5} M solution of 2,2':6',2''-terpyridine-6,6''-dicarboxylic acid with 1.0 equiv. of $\text{Eu}(\text{OTf})_3$ in water.



Corrected emission spectra of 1×10^{-5} M solution of 4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid with 1.0 equiv. of $\text{Eu}(\text{OTf})_3$ in water.



Corrected emission spectrum of 5×10^{-6} M solution of 4'-(hydroxymethyl)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid with 1.0 equiv. of $\text{Eu}(\text{OTf})_3$ in water (red solid line), 1×10^{-5} M of the ligand with 1.0 equiv. of $\text{Tb}(\text{OTf})_3$ in water (green solid line) and 1×10^{-5} M of the ligand with 1.0 equiv. $\text{Sm}(\text{OTf})_3$ (purple solid line).



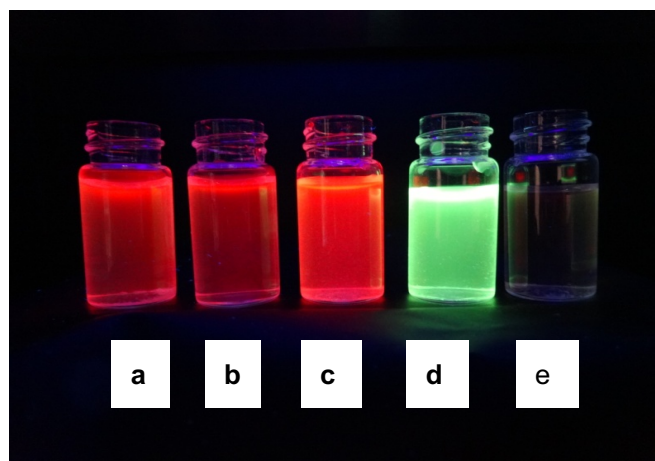


Figure 1. Emission of 2×10^{-5} M solution of lanthanide metal/ligand in H₂O under 365 nm UV lamp

- (a) Eu(OTf)₃/2,2':6',2''-terpyridine-6,6''-dicarboxylic acid
 (b) Eu(OTf)₃/4'-(2-hydroxyethoxy)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid
 (c) Eu(OTf)₃/4'-(hydroxymethyl)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid
 (d) Tb(OTf)₃/4'-(hydroxymethyl)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid
 (e) Sm(OTf)₃/4'-(hydroxymethyl)-2,2':6',2''-terpyridine-6,6''-dicarboxylic acid

3. References

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