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Selective Modifications of Hydrophobic Vitamin B_{12} Derivatives at *c*-and *d*-Positions

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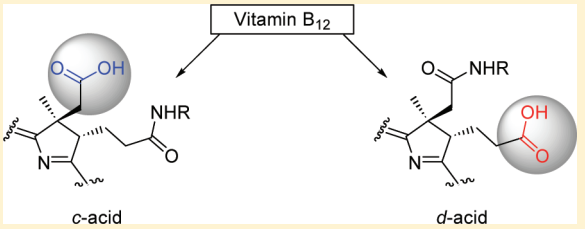
Supporting Information

ABSTRACT: The acid-sensitivity of vitamin B_{12} derived mono- and diamides was studied. It was found that the use of reductive ring-opening of the lactone moiety deactivated undesired decomposition of *c*-mono- and *c,d*-diamides under acidic conditions. As a result, reactions gave respectively *c*- or *d*-acids which were further functionalized via coupling with amino acids. Though mono- and diamides exhibited acid sensitivity, they were used for the preparation of several highly functionalized molecules showing their stability under various reaction conditions.



The importance of vitamin B_{12}, which stems from its diversified applications, is difficult to overestimate.[1] It has been investigated for many years as an oral delivery vehicle for therapeutic agents.[2−8] Most of these conjugates have been prepared via selective reactions on the cobalt center or at the 5′-hydroxy group on the ribose moiety (Figure 1).

Moreover, vitamin B_{12} derivatives have been effectively used as artificial enzymes and have been found to catalyze various organic reactions.[9] One of the most widely investigated derivatives was hydrophobic heptamethyl dicyanocobyrinate possessing terminal ester groups instead of original amides and the central cobalt atom being bound to two cyanide ligands. Hisaeda and co-workers have recently elaborated an efficient method for the dechlorination of di(4-chlorophenyl)trichloroethane (DDT) mediated by heptamethyl cobyrinate perchlorate in ionic liquids,[10] which mainly led to 1,1′-(ethylidene)bis(4-chlorobenzene) (DDO). Compounds of this type were also found to catalyze the nucleophilic addition of an alcohol to an olefin under mild conditions.[11] Moreover, to elucidate the role of potassium ion in vitamin B_{12} dependent enzymatic reactions Hisaeda's group has prepared a hydrophobic vitamin B_{12} bearing a benzo-18-crown-6 moiety.[12]

For vitamin B_{12} to realize its full potential, more efficient approaches toward selective modifications of both hydrophilic and hydrophobic derivatives have to be developed. Though various vitamin B_{12} derivatives have already been prepared and studied, there have been only a few reports describing selective preparation and use of cobalamin-derived acids. Syntheses of such compounds were usually based on vitamin B_{12} hydrolysis followed by partial esterification.[13] These approaches are non-selective, thus requiring laborious separation of regioisomers. Still, acids prepared in such a way have been successfully used in further reactions.[14,15] Selective formation of *c*-lactone and its reduction leading to either a carboxylic acid or an alcohol was reported by Keese and co-workers.[16] Therefore, further modifications of hydrophobic cobalamines have been rather limited

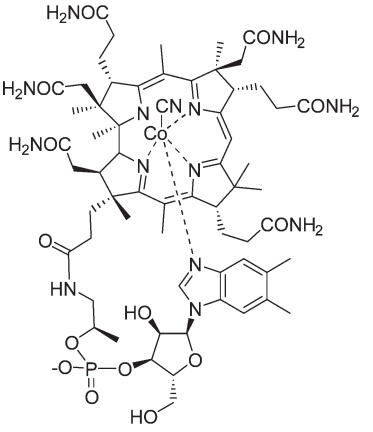


Figure 1. Vitamin B_{12}.

to reactions occurring at the *c*-position. There have been a multitude of reports detailing reactions at this site.[17,18]

Recently, we have undertaken comprehensive studies directed toward selective modifications of both hydrophilic and hydrophobic cobalamin derivatives.[19] It was shown that ring-opening of *c*-lactone **1** with various primary amines led selectively to either mono- or diamides (Scheme 1).

The goal of our research was to elaborate the vitamin B_{12} chemistry and to find superior approaches for the *regioselective* preparation of derivatives bearing complex and diversified functionalities. In particular, we were interested in strategies that could lead to bifunctional molecules under very mild conditions, thus enabling us to link a broad range of substrates to the vitamin B_{12} core.

The studies were initiated by evaluating the acid sensitivity of vitamin B_{12} derived *c*-mono- and *c,d*-diamides. When *c*-monoamides

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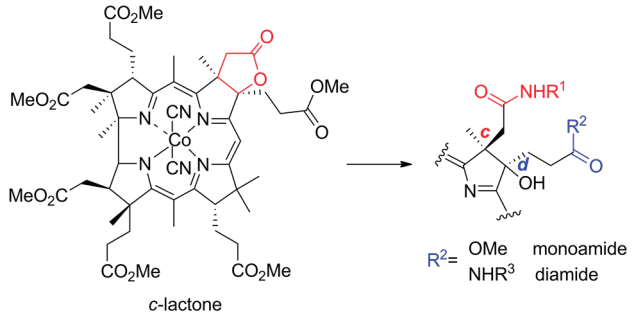
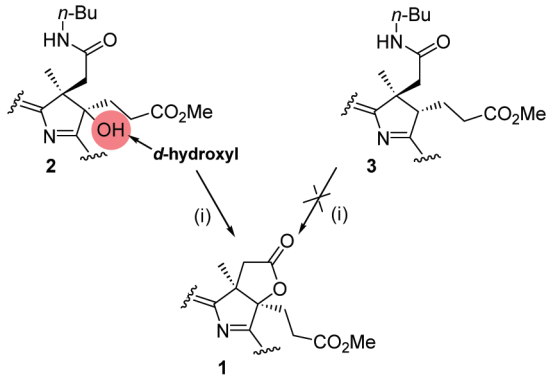
Scheme 1. Ring-opening of *c*-Lactone to Mono- and Diamides



Scheme 2. Investigation into Acid Sensitivity[a]



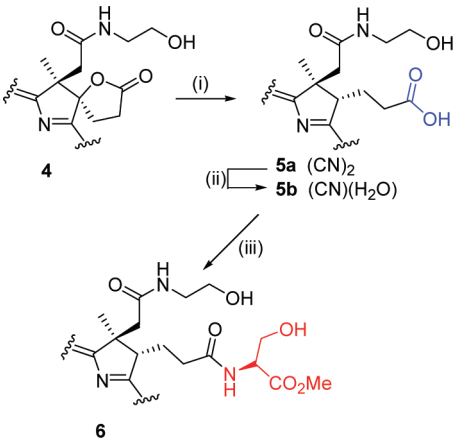
[a] Conditions: (i) 10% TFA in DCM.

were subjected to mild acidic conditions, the formation of only one specific compound was observed. ESIMS and ^{1}H NMR data revealed that *c*-monoamides had reverted back to the original *c*-lactone **1**. Thus, we assumed that the acid sensitivity was due to the presence of the hydroxyl group at the *d*-position. After ring-opening of either *c*- or *d*-lactone the hydroxyl group is always present at this position. Therefore, the acid sensitivity of amides **2**[19] and **3**, in which **3** lacked the *d*-hydroxyl group, were compared. Treatment of **2** and **3** with equal amounts of TFA clearly showed that **2** reverted back to *c*-lactone **1**, whereas **3** was completely stable (Scheme 2).

To eliminate the acid sensitivity, the removal of the hydroxyl group from the *d*-position was considered, as it should increase the robustness of these compounds and their reactivity toward more complex substrates. Keese showed that *c*-lactone could be reduced to either a carboxylic acid or an alcohol.[14] We assumed that this method would also remove the hydroxyl group from the *d*-position and simultaneously the acid sensitivity. The idea of acquiring *d*-acid is not completely foreign. Alberto and co-workers described hydrolysis of vitamin B_{12} followed by partial esterification.[20,21] The reaction afforded a mixture of esters, and the isolation of the *d*-acid required HPLC separation from other acids formed. Using these compounds, he successfully coupled histidine derivatives to the vitamin derivative and proceeded to effectively employ them in biological labeling. Thus, spirolactone **4**[19] was treated with zinc, affording *d*-acid **5a** (Scheme 3), which was used, without further purification, in coupling reactions.

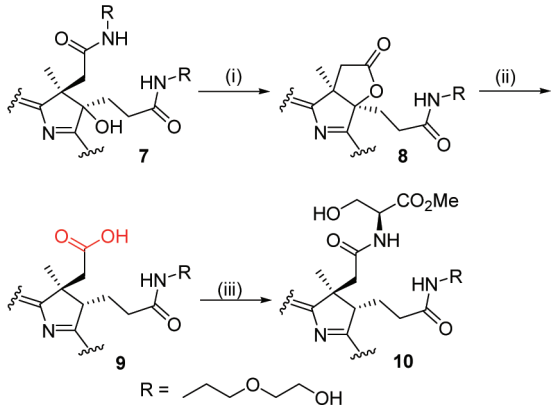
Compound **5a** turned out to be a very useful starting material, which allowed us to explore various reactions and the addition of more complex linkers. In previously attempted reactions, we

Scheme 3. Reduction of *d*-Lactone 4 to *d*-Acid[a]



[a] Conditions: (i) zinc dust, AcOH, toluene, 30 min, 65%; (ii) 30% $HClO_4$; (iii) serine methyl ester·HCl, DEPC (diethyl cyanophosphonate), Et_3N, DMF, 35% from **5a**, 80% from **5b**.

Scheme 4. Selective *c*-Lactone Formation From Diamide and Reduction to *c*-Acid[a]



[a] Conditions: (i) 50% TFA in DCM, 96%; (ii) zinc dust, AcOH, toluene, 53%; (iii) a) 30% $HClO_4$; b) serine methyl ester·HCl, DEPC, Et_3N, DMF, 56%.

envisaged the possibility of attaching amino acids to the vitamin via ring-opening of spirolactone **4**. Unfortunately, all efforts failed or gave extremely low yields. Therefore, we examined the coupling of serine methyl ester with acid **5a** (Scheme 3). When the reaction was first attempted with dicyano complex **5a**, desired product **6** was obtained in a low yield of 35%. In their report, Keese et al.[16] utilized the aqua complex form of a *c*-acid derivative in coupling reactions, which consists of one cyanide ligand being replaced by a water ligand. After treatment of **5a** with an aqueous solution of $HClO_4$, ligand exchange occurred to give **5b**. When it was used in our reaction, the yield showed a dramatic increase, giving amide **6** in 80% yield. The successful synthesis of **6** showed that it was now possible to couple complex moieties at the *d*-position by producing *d*-acid **5a**. It has been shown that the position of conjugation affects the manner in which the vitamin B_{12} derivative functioned. Wilbur proved this by examining various cobalamin—biotin conjugates and their effect in relation to location of attachment toward binding to transcobalamin II.[22]

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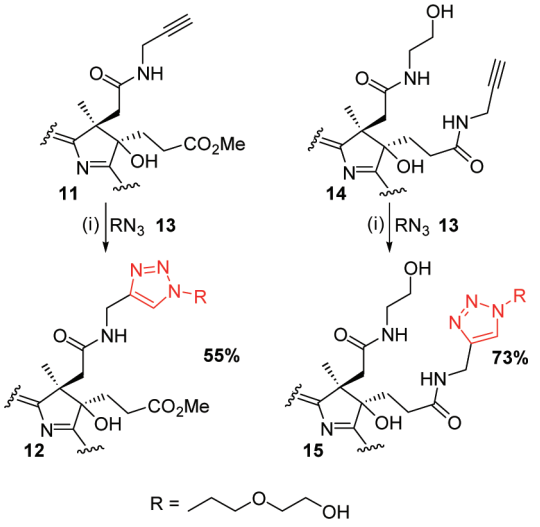
Scheme 5. Click Reaction of *c*- or *d*-Propargylamide Derivative[a]



[a] Conditions: (i) $CuSO_4 \cdot 5H_2O$, sodium ascorbate, *t*-BuOH, H_2O.

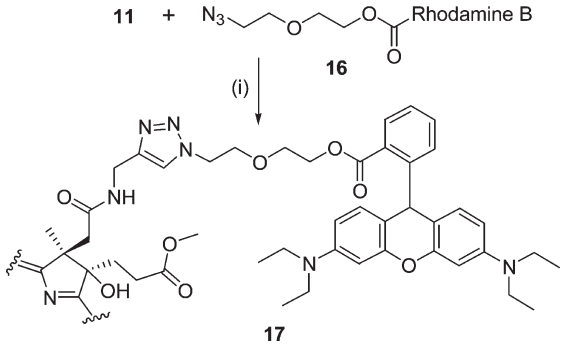
Therefore, the idea of creating a similar *c*-acid, while retaining the functionalized linker at the *d*-position, intrigued us. In order to obtain this type of compound, the acid sensitivity of these derivatives was used to our advantage. It was found that by treating diamide **7**[19] with an acidic solution *c*-lactone **8** was exclusively obtained in 96% yield (Scheme 4). At this stage of our research, it was not clear why *d*-spirolactone was not formed. It is important to note that this reaction must be closely monitored since over time byproducts begin to form because of the high concentration of acid used.

Once *c*-lactone **8** had reformed, it was converted to *c*-acid **9** using the procedure described by Keese.[14] In the form of the crude aqua complex **9** was coupled with serine methyl ester, producing **10** in 56% yield.

By verifying the cause of acid sensitivity, we focused on reactions that are compatible with our mono- and diamide derivatives. One of the most common reactions used for conjugation of biologically important molecules is copper-catalyzed [1,3]-dipolar cycloaddition.[23] The addition of a terminal acetylene to the azide group in the presence of a copper(I) source gives selectively 1,4-disubstituted 1,2,3-triazoles.[24] Reactions of azide **13** with previously synthesized derivatives **11**[19] and **14**[19] were catalyzed by copper sulfate and sodium ascorbate, giving conjugates **12** and **15** in good yields (Scheme 5). Even though the hydroxyl group was present at the *d*-position, no byproduct related to the decomposition of the starting material or product had been observed during these reactions.

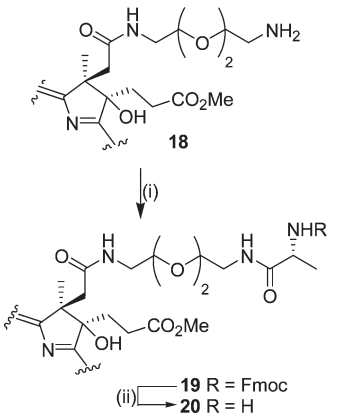
Having this proof-of-principle in hand, we set out to accomplish one of our key goals, which was to link vitamin B_{12} with molecules possessing beneficial properties. Grissom et al. reported that the addition of a fluorescent moiety to the hydrophilic vitamin B_{12} is a good approach to imaging of cobalamin receptors.[25,26] Therefore, linking of a well-known functional dye, rhodamine B, to cobalamin via CuAAC (copper-catalyzed alkyne−azide cycloaddition) was investigated. First, the azide-linked rhodamine **16** was prepared according to the procedure reported by Russell.[27] Then, under standard reaction conditions, azide **16** was reacted with alkyne **11** to give hybrid **17** (Scheme 6).

Scheme 6. Addition of Rhodamine B via CuAAC[a]



[a] Conditions: (i) CuI, TBTA, DMF, rt, 24 h, 74%.

Scheme 7. Coupling of Amine Derivative 11 with Fmoc Alanine and Deprotection[a]



[a] Conditions: (i) Fmoc-L-Ala-CO_2H, DEPC, Et_3N, DMF, 18 h, 54%; (ii) 20% piperidine in DMF, 2 h, 76%.

Unfortunately, the use of the $CuSO_4$ method proved low yielding (22% after 48 h), and prolongation of the reaction time did not dramatically affect the outcome of this reaction. However, by using CuI and TBTA (*tris*-(benzyltriazoylmethyl)amine)[28] in degassed DMF the yield increased to a satisfactory 74%.

One of the most essential reactions in vitamin B_{12} chemistry involves amide bond formation for the purpose of linking active peptides. In 2007, Petrus et al. showed that a vitamin B_{12}−insulin bioconjugate had potential as an insulin carrier; in its synthesis the crucial step relied on the coupling of the vitamin B_{12} derivative.[3,29] In this context, having access to a range of amides derived not only from simple amines but also from bifunctional ones[19] is vital. Therefore, we have conducted an investigation into peptide bond formation. As an example, monoamide **18**,[19] possessing a linker with terminal amine functionality, was coupled with an amino acid in order to prove its capability and stability in peptide synthesis. Crude **18** was coupled with Fmoc-Ala-OH, using DEPC as the coupling reagent, giving **19** in 54% yield. Then, the Fmoc protecting group was removed using 20% piperidine in DMF, affording **20** in 76% yield (Scheme 7).

In conclusion, we have discovered facile methods for the selective formation of both vitamin B_{12} *c*- and *d*-acids. It was found that the presence of the *d*-hydroxyl group in amides

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obtained via ring-opening of the *c*-lactone causes their acid sensitivity. An increase in the reactivity and robustness of the cobalamine derivative was achieved via the reduction of spirolactone **4** which gave *d*-acid **5**. By reforming the *c*-lactone from diamide **8** it was possible to further reduce the lactone to *c*-acid **10** with the amide functionality present at the *d*-position. Subsequently both *c*- and *d*-acids were successfully coupled with serine methyl ester. Furthermore, our cobalamine derivative was successfully attached to rhodamine B via CuAAC, as well as to amino acids via classical peptide methodology.

These results are not only of theoretical significance, in that they provide new insight into factors influencing the course of the reactions of vitamin B_{12} derivatives, but they also contribute to a better understanding of vitamin B_{12} chemistry, particularly toward the reactivity and regioselectivity of such a complex molecule.

We are currently applying similar strategies to related hydrophilic vitamin B_{12} derivatives, the synthesis of which will be reported in due course.

EXPERIMENTAL SECTION

General Methods. Analytical grade solvents were used as received. ^{1}H and ^{13}C NMR spectra were recorded at rt on a 500 MHz instrument. DCVC (dry column vacuum chromatography) was performed using silica gel (200−300 mesh). Flash column chromatography was performed using silica gel (60 mesh). Thin-layer chromatography (TLC) was performed using silica gel GF254, 0.20 mm thickness. UV/vis absorption and fluorescence emission spectra were recorded in DCM at room temperature.

$(CN)_2$Cob(III)6C1(*n*-butylamide) (3). $[(CN)(H_2O)$Cob(III)-C1$(CO_2H)]^+ClO_4^-$[16] (26 mg, 0.02 mmol) and *n*-butylamine (5.0 μL, 0.1 mmol) were dissolved in dry DMF (1 mL) under an argon atmosphere. DEPC (10 μL) and Et_3N (10 μL) were then added and the mixture was stirred at room temperature for 18 h. It was then diluted with DCM, washed with water and NaCN aq, dried over Na_2SO_4, filtered, and concentrated in vacuo. Compound **3** was then purified using DCVC (2.5% EtOH in DCM). Recrystallization from Hex/AcOEt gave **3** as a purple solid (18 mg, 67%): mp 97−100 °C; R_f 0.32 (10% EtOH in DCM); ^{1}H NMR (500 MHz, toluene-d_8) δ (ppm) 7.46 (t, J = 2.6 Hz, 1H), 5.59 (s, 1H), 3.72−3.69 (m, 2H), 3.65−3.58 (m, 1H), 3.39 (s (br), 3H), 3.37 (s (br), 9H), 3.31 (s (br), 6H), 2.98−2.97 (m, 1H), 2.81−2.77 (m, 2H), 2.68−2.49 (m, 5H), 2.42 (dd, J = 2.8 and 2.8 Hz, 1H), 2.35−2.33 (m, 5H), 2.26 −2.23 (m, 3H), 2.19 (s, 3H), 2.61 (s, 3H), 2.08−2.06 (m, 3H), 2.04−2.01 (m, 1H), 1.28−1.24 (m, 3H), 1.15 (s, 3H), 1.12 (s, 3H), 1.04 (s (br), 2H), 0.96 (s, 3H), 0.88 (s, 3H), 0.82 (t, J = 4.4 Hz, 4H) (because of overlapping of the toluene peak in the spectra, the number of assigned protons is lower than the value stated in the molecular formula); ^{13}C NMR (125 MHz, toluene-d_8) δ (ppm) 175.8, 175.6, 175.5, 173.7, 173.1, 172.6, 172.1, 172.0, 171.7, 171.5, 169.1, 163.6, 161.9, 107.5, 102.4, 91.5, 82.9, 75.0, 59.4, 58.6, 57.0, 53.9, 51.9, 51.7, 51.4, 51.3, 51.2, 51.0, 50.9, 47.4, 46.6, 46.5, 42.0, 39.7, 33.7, 32.9, 31.9, 31.8, 31.1, 30.9, 30.5, 29.8, 27.2, 26.1, 25.8, 25.6, 24.8, 22.2, 19.5, 19.1, 18.0, 16.9, 15.6, 15.5, 13.8; HRMS ESI (m/z) calcd for $C_{56}H_{80}CoN_6O_{13}$ $[M - CN]^+$ 1103.5109, found 1103.5104; UV/vis CH_2Cl_2, λ_{max}, ε ($L \cdot mol^{-1} \cdot cm^{-1}$) 549 ($8.20 \times 10^3$), 423 ($2.63 \times 10^3$), 371 ($2.67 \times 10^4$), 317 ($9.11 \times 10^3$), 279 ($1.04 \times 10^4$). Anal. Calcd for $C_{57}H_{80}CoN_7O_{13} + 2H_2O$: C, 58.70; H, 7.26; N, 8.41. Found: C, 59.04; H, 7.19; N, 8.26.

$(CN)_2$Cob(III)5C1(ethanolamide)(propionic acid) (5a). Spirolactone **4** (46 mg, 0.04 mmol) was added to a degassed solution of toluene/acetic acid (2 mL/0.3 mL) under an argon atmosphere. Activated zinc dust (80 mg, 1.2 mmol) was then added, and the reaction was monitored by TLC until full conversion was observed (20−60 min). The reaction was then neutralized using $NaHCO_3$ and zinc removed by filtration. The filtrate was then washed with NaCN aq, dried over Na_2SO_4, filtered, and concentrated in vacuo. The product was crudely purified using DCVC (2−20% MeOH in DCM). Recrystallization from Hex/AcOEt gave **5a** as a purple solid (30 mg) and was used without further purification: R_f 0.31 (10% EtOH in DCM); HRMS ESI (m/z) calcd for $C_{54}H_{74}CoN_7O_{14}$ $[M]^+$ 1103.4616, found 1103.4620.

The broadening of peaks in the ^{1}H NMR spectrum (see the Supporting Information) made it impossible to decipher, and consequently, high-resolution ^{13}C spectra could not be obtained. This was caused by the presence of the acid group.

$[(H_2O)(CN)$Cob(III)5C1(ethanolamide)(propionic acid)$]^+ClO_4^-$ (5b). Compound **5b** was prepared using a procedure described by Keese.[16] Compound **5a** in DCM was washed with an solution of aqueous 30% perchloric acid until the organic layer turned from violet to red. The organic layer was separated, dried over Na_2SO_4, and concentrated in vacuo to give **5b** as a red solid. The compound was used without any further purification since the resulting complex was very labile.

$(CN)_2$Cob(III)C1(ethanolamide)(NH-Serine-OMe) (6). Compound **5b** (15 mg, 0.01 mmol) and serine methyl ester hydrochloric acid (14 mg, 0.05 mmol) were dissolved in dry DMF (1.0 mL) under an argon atmosphere. To the solution were added DEPC (10 μL, 0.05 mmol) and Et_3N (8 μL, 0.06 mmol). The mixture was stirred at room temperature for 18 h and then diluted with DCM. The solution was then washed with water and NaCN aq, dried over Na_2SO_4, and concentrated in vacuo to afford a purple residue. The crude product **6** was purified by DCVC (2.5% EtOH in DCM). Recrystallization from AcOEt/Hex gave **6** as a purple solid (13 mg, 80%): mp 117−119 °C; R_f 0.13 (5% EtOH in DCM); ^{1}H NMR (500 MHz, CD_2Cl_2) δ (ppm); 6.86 (d, J = 6.8 Hz, 1H), 6.79 (t, J = 4.8 Hz, 1H), 5.62 (s, 1H), 4.27 (dd, J = 2.9 and 3.9 Hz, 1H), 3.75 (s, 7H), 3.70 (s, 3H), 3.68 (s, 3H), 3.67 (s, 3H), 3.65 (s, 3H), 3.57 (s, 4H), 3.47−3.40 (m, 3H), 3.25−3.19 (m, 1H), 3.15−3.12 (m, 1H), 3.09 (t, J = 4.9 Hz, 1H), 2.87−2.79 (m, 1H), 2.67 (dd, 1H, J = 4.3 and 2.2 Hz), 2.64−2.63 (m, 2H), 2.62−2.55 (m, 2H), 2.54−2.51 (m, 1H), 2.48−2.35 (m, 4H), 2.30 (d, J = 14.6 Hz, 1H), 2.25 (s, 5H), 2.20 (s, 2H), 2.12 (s, 7H), 2.11−2.05 (m, 3H), 1.87−1.82 (m, 1H), 1.78 (s, 3H), 1.45 (s, 3H), 1.38 (s, 3H), 1.36 (s, 3H), 1.26 (s, 3H), 1.20 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ (ppm); 177.1, 176.9, 176.4, 173.8, 173.0, 172.8, 172.7, 172.5, 172.0, 171.9, 171.2, 170.8, 170.1, 163.4, 161.3, 107.3, 103.1, 91.6, 83.3, 74.9, 62.5, 61.5, 60.6, 58.8, 57.1, 55.3, 53.4, 52.6, 52.3, 52.1, 51.9, 51.8, 51.1, 48.1, 47.0, 46.3, 43.6, 41.9, 39.9, 33.9, 32.5, 32.3, 31.9, 31.8, 30.5, 29.9, 27.3, 25.7, 25.1, 22.1, 19.6, 19.1, 18.3, 17.1, 15.6, 15.5; HRMS ESI (m/z) calcd for $C_{58}H_{81}CoN_8O_{16}$ $[M + Na]^+$ 1227.5000, found 1227.4994; UV/vis CH_2Cl_2, λ_{max}, ε ($L \cdot mol^{-1} \cdot cm^{-1}$) 586 ($8.34 \times 10^3$), 545 ($7.33 \times 10^3$), 422 ($2.55 \times 10^3$), 370 ($2.50 \times 10^4$), 316 ($8.44 \times 10^3$), 279 ($8.96 \times 10^3$). Anal. Calcd for $C_{58}H_{81}CoN_8O_{16} + 2H_2O$: C, 56.12; H, 6.90; N, 9.04. Found: C, 56.41; H, 6.91; N, 8.74. *See the Supporting Information for full ^{1}H and ^{13}C NMR assignments.

$(CN)_2$Cob(III)C1(lactone)(diglycolamide) (8). Compound **7** (24 mg, 0.02 mmol) was dissolved in DCM (2 mL). TFA was added until the reaction turned a dark red color. The reaction was monitored by TLC until complete conversion was observed. Water was then added and the mixture neutralized using $NaHCO_3$. The organic layer was then washed with NaCN aq, dried over Na_2SO_4, filtered, and concentrated in vacuo to produce a purple oil. The crude product was purified by DCVC (2.5−5% EtOH in DCM). Recrystallization from Hex/AcOEt gave **8** as a purple solid (21 mg, 96%): mp 117−118 °C; R_f 0.32 (5% EtOH in DCM); ^{1}H NMR (500 MHz, CD_2Cl_2) δ (ppm) 7.00 (t, J = 5.0 Hz, 1H), 5.70 (s, 1H), 3.84 (d, J = 10.8 Hz, 1H), 3.76−3.74 (m, 4H), 3.69 (s, 7H), 3.68 (s, 3H), 3.59 (s, 3H), 3.50−3.32 (m, 7H), 3.15−3.10 (m, 1H), 3.06 (dd, J = 4.5 and 1.4 Hz, 1H), 2.86−2.82 (m, 1H), 2.79 (d, J = 5.9 Hz, 2H), 2.70−2.65 (m, 1H), 2.63 (d, J = 6.2 Hz, 2H), 2.59−2.53 (m, 4H),

2.50−2.39 (m, 2H), 2.30 (d, J = 15.8 Hz, 1H), 2.26 (s, 3H), 2.21−2.15 (m, 7H), 2.11−2.02 (m, 3H), 1.99−1.91 (m, 1H), 1.84−1.74 (m, 2H), 1.65 (s, 3H), 1.46 (s, 3H), 1.37 (s, 6H), 1.26 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ (ppm) 178.9, 176.8, 176.0, 173.7, 173.05, 173.01, 172.9, 171.9, 171.1, 166.7, 163.3, 160.2, 133.8, 128.0, 104.3, 95.1, 88.2, 83.2, 75.4, 72.9, 69.6, 61.4, 58.7, 57.1, 54.0, 52.6, 52.1, 52.0, 51.9, 51.8, 50.4, 47.8, 45.9, 43.3, 41.3, 39.7, 39.4, 33.7, 32.9, 31.9, 31.0, 30.8, 30.4, 29.9, 29.8, 25.9, 25.0, 22.1, 19.7, 19.3, 18.5, 17.2, 16.9, 15.6; HRMS ESI (m/z) calcd for $C_{56}H_{76}CoN_7O_{15}$ $[M + Na]^+$ 1168.4623, found 1168.4603; UV/vis CH_2Cl_2, λ_{max}, ε ($L \cdot mol^{-1} \cdot cm^{-1}$) 591 ($1.17 \times 10^4$), 552 ($1.01 \times 10^4$), 421 ($3.13 \times 10^3$), 369 ($3.32 \times 10^4$), 307 ($9.06 \times 10^3$), 279 ($1.14 \times 10^4$). Anal. Calcd for $C_{56}H_{76}CoN_7O_{15} + H_2O$: C, 57.77; H, 6.75; N, 8.42. Found: C, 57.91; H, 6.81; N, 8.46. *See the Supporting Information for full ^{1}H and ^{13}C NMR assignments.

(CN)$_2$Cob(III)C1(ethanoic acid)(diglycolamide) (9). Compound **8** (45 mg, 0.04 mmol) was in a degassed solution of toluene/acetic acid (2 mL/0.3 mL) under an argon atmosphere. Activated zinc dust (80 mg, 1.2 mmol) was then added, and the reaction was monitored by TLC until complete conversion was observed. Workup as described for compound **5a**. The product was crudely purified using DCVC (2−20% MeOH in DCM). Recrystallization from Hex/AcOEt gave **9** as a purple solid (24 mg) and was used without further purification: R_f 0.23 (10% EtOH in DCM); HRMS ESI (m/z) calcd for $C_{56}H_{78}CoN_7O_{15}$ $[M - CN]^+$ 1221.4820, found 1221.4851.

The broadening of peaks in the ^{1}H NMR spectrum made it impossible to decipher and consequently high resolution ^{13}C spectra could not be obtained. This was caused by the presence of the acid group.

(CN)$_2$Cob(III)5C1(NH-serine-OMe)(diglycolamide) (10). Compound **9** (8 mg, 7.2 μmol) and serine methyl ester hydrochloric acid (5 mg, 0.02 mmol) were dissolved in dry DMF (0.5 mL) under an argon atmosphere. To the solution were added DEPC (4 μL, 0.02 mmol) and Et_3N (3 μL, 0.02 mmol). The mixture was stirred at room temperature for 18 h and then worked up according to the procedure of **6**. Compound **10** was isolated as a purple solid (5 mg, 56%): mp 108−110 °C; R_f 0.24 (5% EtOH in DCM); ^{1}H NMR (500 MHz, CD_2Cl_2) δ (ppm); 7.02 (t, J = 4.9 Hz, 1H), 6.82 (d, J = 7.7 Hz, 1H), 5.62 (s, 1H), 4.26−4.24 (m, 1H), 3.80−3.77 (m, 1H), 3.75 (s, 4H), 3.71 (s, 4H), 3.68 (s, 4H), 3.67 (s, 3H), 3.65 (s, 3H), 3.59 (s, 3H), 3.52−3.45 (m, 4H), 3.43−3.38 (m, 5H), 3.33−3.27 (m, 1H), 3.17−3.11 (m, 1H), 3.09−3.07 (m, 1H), 2.82−2.78 (m, 1H), 2.63−2.62 (m, 2H), 2.61−2.51 (m, 4H), 2.48−2.38 (m, 5H), 2.30 (d, J = 15.3 Hz, 1H), 2.25 (s, 4H), 2.20−2.07 (m, 7H), 2.05 (s, 3H), 1.87−1.81 (m, 2H), 1.78 (s, 3H), 1.46 (s, 3H), 1.38 (s, 3H), 1.37 (s, 3H), 1.27 (s, 3H), 1.21 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ (ppm); 176.8, 176.7, 176.3, 173.9, 173.0, 172.9, 172.0, 171.8, 170.8, 169.9, 163.6, 161.3, 107.0, 102.9, 91.8, 83.2, 74.9, 72.9, 72.8, 69.7, 62.0, 61.4, 61.2, 58.7, 56.8, 56.0, 53.8, 52.6, 52.4, 52.2, 52.1, 52.0, 51.9, 51.8, 47.2, 47.0, 46.4, 42.0, 39.7, 39.6, 33.9, 33.7, 32.6, 32.1, 31.8, 30.0, 29.8, 28.0, 25.7, 25.1, 22.1, 19.6, 18.8, 18.2, 17.1, 15.6, 15.4; HRMS ESI (m/z) calcd for $C_{60}H_{85}CoN_8O_{17}$ $[M - CN]^+$ 1222.5311, found 1222.5328; UV/vis CH_2Cl_2, λ_{max}, ε ($L \cdot mol^{-1} \cdot cm^{-1}$) 587 ($9.59 \times 10^3$), 548 ($7.87 \times 10^3$), 423 ($2.52 \times 10^3$), 370 ($2.85 \times 10^4$), 316 ($9.01 \times 10^3$), 279 ($9.97 \times 10^3$). Anal. Calcd for $C_{60}H_{85}CoN_8O_{17} + H_2O$: C, 56.86; H, 6.92; N, 8.84. Found: C, 57.00; H, 6.91; N, 8.78. *See the Supporting Information for full ^{1}H and ^{13}C NMR assignments.

(CN)$_2$Cob(III)6C1(2-{1-[2-(2-hydroxyethoxy)ethyl]-1*H*-[1,2,3]-triazol-4-yl}amide) (12). Compounds **11** (10 mg, 8.8 μmol) and **13** (5.0 mg, 35.2 μmol) were dissolved in *t*BuOH/H_2O (1:1) and treated with 30 mol % of $CuSO_4 \cdot 5H_2O$ and sodium ascorbate. The mixture was stirred at room temperature for 18 h and then diluted with DCM, washed with brine and NaCN aq, dried over Na_2SO_4, filtered, and concentrated in vacuo. Compound **12** was then purified using DCVC (2.5−5.0% EtOH in DCM). Recrystallization from pentane/AcOEt gave **12** as a purple solid (6.0 mg, 55%): mp 110−112 °C; R_f 0.45 (10% EtOH in DCM); ^{1}H NMR (500 MHz, CD_2Cl_2) δ (ppm) 7.70 (s(br), 1H), 7.58 (s(br), 1H), 6.10 (s(br), 1H), 5.75 (s, 1H), 4.52 (dd, J = 5.7 and 9.2 Hz, 1H), 4.48−4.38 (m, 3H), 4.08 (dd, J = 4.6 and 10.0 Hz, 1H), 3.84 (d, J = 10.7 Hz, 1H), 3.75 (s, 4H), 3.69 (s, 4H), 3.68 (s, 5H), 3.67 (s, 3H), 3.62 (s, 3H), 3.56−3.53 (m, 2H), 3.48−3.42 (m, 2H), 3.07 (dd, J = 3.8 and 2.8 Hz, 1H), 2.82−2.78 (m, 1H), 2.74−2.66 (m, 3H), 2.63−2.39 (m, 9H), 2.35 (d, J = 13.1 Hz, 1H), 2.26 (s, 3H), 2.23−2.08 (m, 8H), 2.06 (s, 3H), 1.88−1.80 (m, 1H), 1.79−1.67 (m, 2H), 1.64 (s, 3H), 1.47 (s, 3H), 1.40 (s, 3H), 1.37 (s, 3H), 1.29 (s, 3H), 1.20 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ (ppm); 176.7, 176.3, 176.0, 175.8, 173.9, 173.1, 172.9, 172.5, 172.1, 172.0, 171.7, 163.4, 159.5, 144.9, 124.4, 106.3, 103.0, 90.0, 85.4, 83.1, 74.9, 73.0, 69.5, 61.6, 58.8, 57.1, 56.1, 52.5, 52.3, 52.2, 52.0, 51.9, 51.8, 50.3, 47.1, 42.7, 42.1, 38.7, 35.5, 33.9, 32.6, 32.5, 31.6, 30.9, 29.9, 29.8, 25.8, 25.2, 22.2, 19.6, 18.1, 17.4, 17.1, 15.6, 15.5; HRMS ESI (m/z) calcd for $C_{59}H_{83}CoN_9O_{16}$ $[M - CN]^+$ 1232.5285, found 1232.5284; UV/vis CH_2Cl_2, λ_{max}, ε ($L \cdot mol^{-1} \cdot cm^{-1}$) 556 ($8.45 \times 10^3$), 368 ($2.19 \times 10^4$), 320 ($8.33 \times 10^3$), 310 ($8.30 \times 10^3$), 281 ($9.34 \times 10^3$). Anal. Calcd for $C_{60}H_{83}CoN_{10}O_{16} + 2H_2O$: C, 56.33; H, 6.85; N, 10.95. Found: C, 56.57; H, 6.79; N, 10.70.

(CN)$_2$Cob(III)5C1(ethanolamide)(2-{1-[2-(2-hydroxyethoxy)-ethyl]-1*H*-[1,2,3]triazol-4-yl}amide) (15). Following the procedure described in the synthesis of **12**, **14** (13.4 mg, 0.01 mmol) and **13** (6.8 mg, 40.1 μmol) were dissolved in *t*BuOH/H_2O (1:1) and treated with 30 mol % of $CuSO_4 \cdot 5H_2O$ and sodium ascorbate. Compound **15** was isolated as a purple solid (11 mg, 73%): mp 111−113 °C; R_f 0.40 (10% EtOH in DCM); ^{1}H NMR (500 MHz, CD_2Cl_2) δ (ppm); 7.78 (s, 1H), 7.48 (t, J = 4.4 Hz, 1H), 6.92 (t, J = 4.7 Hz, 1H), 6.65 (s, 1H), 5.78 (s, 1H), 4.49 (t, J = 4.8 Hz, 2H), 4.39 (dq, J = 5.0, 10.7, and 15.2 Hz, 2H), 3.82−3.77 (m, 3H), 3.76 (s, 3H), 3.74−3.72 (m, 1H), 3.70 (s, 3H), 3.69 (s, 3H), 3.68 (s, 3H), 3.58 (s, 3H), 3.57−2.55 (m, 1H), 3.49−3.43 (m, 4H), 3.20−3.16 (m, 1H), 3.08−3.07 (m, 1H), 2.82−2.78 (m, 1H), 2.66 (d, J = 6.1 Hz, 2H), 2.62−2.52 (m, 3H), 2.50−2.45 (m, 4H), 2.43−2.39 (m, 1H), 2.34−2.30 (m, 2H), 2.28 (s, 3H), 2.23−2.12 (m, 5H), 2.09 (s, 4H), 2.05−1.96 (m, 5H), 1.87−1.74 (m, 3H), 1.68 (s, 3H), 1.45 (s, 3H), 1.38 (s, 3H), 1.32 (s, 3H), 1.28 (s, 3H), 1.19 (s, 3H); C NMR (125 MHz, CD_2Cl_2) δ (ppm); 176.3, 176.2, 175.6, 174.5, 173.7, 173.6, 172.6, 172.5, 172.2, 171.6, 171.5, 163.0, 159.4, 144.4, 134.9, 131.2, 123.8, 106.6, 102.5, 89.8, 85.4, 82.7, 74.4, 72.6, 69.1, 58.4, 56.4, 56.3, 53.6, 52.2, 51.8, 51.7, 51.6, 51.5, 50.1, 46.6, 46.0, 43.4, 43.3, 41.6, 39.2, 35.5, 33.5, 32.6, 32.1, 31.7, 31.4, 31.3, 30.6, 29.5, 25.3, 24.8, 21.6, 19.0, 17.8, 16.7, 16.2, 15.2, 15.1; HRMS ESI (m/z) calcd for $C_{61}H_{86}CoN_{11}O_{16}$ $[M + Na]^+$ 1310.5478, found 1310.5456; UV/vis CH_2Cl_2, λ_{max}, ε ($L \cdot mol^{-1} \cdot cm^{-1}$) 590 ($9.51 \times 10^3$), 552 ($7.74 \times 10^3$), 425 ($2.80 \times 10^3$), 371 ($2.62 \times 10^4$), 318 ($8.8 \times 10^3$), 282 ($8.62 \times 10^3$). Anal. Calcd for $C_{61}H_{86}CoN_{11}O_{16} + H_2O$: C, 56.08; H, 6.79; N, 11.76. Found: C, 55.88; H, 6.80; N, 11.63.

Rhodamine 2-(2-Azidoethoxy)ethyl Ester (16). Rhodamine B (56 mg, 0.11 mmol) and **13** (22 mg, 0.16 mmol) were dissolved in dry DCM and stirred under an argon atmosphere. EDC (32 mg, 0.16 mmol) and DMAP (13 mg, 0.11 mmol) were then added and the mixture stirred at room temperature for 18 h. The mixture was diluted with DCM, washed with water, dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification using flash column chromatography (2.5−10% EtOH in DCM). Recrystallization from THF/Et_2O gave **16** as a purple solid (55 mg, 79%): R_f 0.53 (10% EtOH in DCM); HRMS ESI (m/z) calcd for $C_{32}H_{39}N_5O_4$ $[M - H]^+$ 556.2942, found 556.2918; UV/vis CH_2Cl_2, λ_{max}, ε ($L \cdot mol^{-1} \cdot cm^{-1}$) 557 ($1.17 \times 10^5$), 521 ($3.03 \times 10^4$), 400 ($2.97 \times 10^3$), 352 ($7.81 \times 10^3$), 282 ($1.60 \times 10^4$), 256 ($2.94 \times 10^4$); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm); δ 8.33 (d, J = 7.6 Hz, 1H), 7.79 (t, J = 7.5 Hz, 1H), 7.72 (t, J = 7.4 Hz, 1H), 7.05 (d, J = 9.6 Hz, 2H), 6.88 (d, J = 2.4 Hz, 1H), 6.86 (d, J = 2.4 Hz, 1H), 6.79 (d, J = 2.4 Hz, 2H), 4.17 (t, J = 4.6 Hz, 2H), 3.62 (q, J = 7.2 Hz, 8H), 3.58−3.53 (m, 6H), 3.29 (t, J = 4.8 Hz, 2H), 1.30 (t, J = 7.2 Hz, 12H); ^{13}C NMR (100 MHz,

$CDCl_3$) δ (ppm); δ 164.8, 157.6, 155.4, 133.5, 133.1, 131.5, 131.2, 130.3, 130.0, 114.1, 113.4, 96.1, 69.9, 68.5, 64.3, 50.4, 46.0, 12.5.

$(CN)_2$Cob(III)6C1(2-{1-[rhodamine-2-(2-azidoethoxy)ethyl ester]-1*H*-[1,2,3]triazol-4-yl}amide) (17). CuI (2.0 mg, 0.012 mmol) and TBTA (6.0 mg, 0.012 mmol) were dissolved in degassed dry DMF (2.5 mL) and stirred for 30 min under an argon atmosphere. Compounds **16** (36 mg, 0.07 mmol) and **11** (42 mg, 0.04 mmol) were added, and the mixture was stirred for a further 24 h at room temperature. The mixture was then diluted with DCM, washed with water and NaCN aq, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by DCVC (2.5−5% EtOH in DCM). Recrystallization from Hex/AcOEt gave **17** as a purple solid (46 mg, 74%): mp 140−145 °C; R_f 0.30 (5% EtOH in DCM); ^{1}H NMR (500 MHz, CD_2Cl_2) δ (ppm); 8.27 (d, J = 4.5 Hz, 1H), 8.04 (s(br), 0.7H), 7.94 (s(br), 0.3H), 7.84−7.80 (m, 2H), 7.59 (s, 0.7H), 7.48 (s, 0.3H), 7.31 (d, J = 1.8 Hz, 1H), 7.10−7.08 (m, 2H), 6.87−6.80 (m, 4H), 6.42 (s(br), 0.7H), 6.18 (s(br), 0.3H), 5.82 (s, 1H), 4.48 (dd, J = 3.7 and 9.1 Hz, 1H), 4.31−4.29 (m, 2H), 4.09−4.07 (m, 3H), 3.77 (s, 1H), 3.75 (s, 2H), 3.71−3.68 (m, 10H), 3.65 (s, 5H), 3.61 (s, 6H), 3.60 (s, 3H), 3.41−3.39 (m, 2H), 3.23−3.22 (m, 0.3H), 3.06−3.04 (m, 0.7H), 2.98−2.94 (m, 0.3H), 2.83−2.78 (m, 0.7H), 2.67−2.56 (m, 6H), 2.49−2.46 (m, 4H), 2.33−2.30 (m, 3H), 2.24 (s, 3H), 2.21−2.15 (m, 5H), 2.07 (s, 3H), 2.00 (s, 2H), 1.83 (s, 5H), 1.75−1.70 (m, 2H), 1.65 (s, 3H), 1.48 (s, 3H), 1.40 (s, 2H), 1.38 (s, 2H), 1.31−1.21 (m, 17H), 1.18 (s, 2H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ (ppm); 176.5, 176.1, 175.8, 174.0, 173.9, 173.2, 173.1, 173.0, 172.9, 172.8, 172.3, 172.2, 172.1, 172.0, 171.8, 165.2, 163.6, 159.8, 159.4, 158.2, 156.0, 133.8, 133.4, 131.8, 131.7, 130.9, 130.4, 130.2, 123.6, 114.53, 114.50, 113.9, 106.5, 102.7, 96.53, 96.50, 90.2, 85.5, 83.1, 75.0, 74.9, 69.4, 68.9, 64.4, 60.5, 58.7, 58.5, 57.5, 57.2, 56.0, 52.6, 52.2, 52.1, 52.0, 51.97, 51.95, 51.7, 50.1, 47.2, 47.1, 46.44, 46.40, 42.6, 42.1, 39.7, 37.5, 34.1, 34.0, 32.7, 32.6, 31.9, 31.8, 31.6, 31.0, 30.8, 30.1, 30.0, 29.9, 29.7, 25.9, 25.5, 25.3, 23.6, 22.2, 21.1, 19.9, 19.7, 18.3, 18.2, 17.2, 17.1, 15.8, 15.6, 15.5, 14.3, 12.7. HRMS ESI (m/z) calcd for $C_{87}H_{112}CoN_{12}O_{18}$ $[M - H + Na]^{2+}$ 853.3724, found 1706.7436; UV/vis CH_2Cl_2, λ_{max}, ε ($L \cdot mol^{-1} \cdot cm^{-1}$) 557 ($1.28 \times 10^5$), 423 ($5.13 \times 10^3$), 371 ($2.71 \times 10^4$), 354 ($1.98 \times 10^4$), 308 ($2.06 \times 10^4$), 281 ($2.51 \times 10^4$); fluorescence CH_2Cl_2, λ_{max} 581. Anal. Calcd for $C_{88}H_{113}CoN_{12}O_{18} + 4H_2O$: C, 60.13; H, 6.94; N, 9.56. Found: C, 60.14; H, 6.72; N, 9.34.

$(CN)_2$Cob(III)6C1(*N*-[2-(2-aminoethoxy)ethoxylethyl]amide) (18). Compound **1** (38 mg, 0.04 mmol) and 2,2′-(ethylenedioxy)-diethylamine (52 μL, 0.35 mmol) were dissolved in dioxane (3 mL). The mixture was stirred at room temperature under argon atmosphere for 16 h. It was then diluted with DCM, washed with brine and NaCN aq, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude product was purified by DCVC (5−20% EtOH in DCM). Recrystallization from Hex/AcOEt gave **18** as a purple solid (31 mg, 71%): mp 114−116 °C; R_f 0.28 (20% EtOH in DCM); ^{1}H NMR (500 MHz, CD_2Cl_2) δ (ppm); 7.93 (s(br), 0.1H), 7.71 (s(br), 0.8H), 7.52 (s(br), 0.1H), 7.16 (s(br), 0.1H), 6.31 (s(br), 0.1H), 6.18 (s(br), 0.1H), 5.82 (s, 0.7H), 5.53 (s(br), 0.1H), 3.75 (s, 0.9H), 3.74 (s, 3H), 3.70 (s, 2H), 3.68 (s, 2H), 3.67 (s, 3H), 3.66 (s, 3H), 3.62 (s, 3H), 3.60 (s, 3H), 3.58−3.57 (m, 3H), 3.56−3.50 (m, 2H), 3.47−3.44 (m, 2H), 3.05−3.04 (m, 1H), 2.98−2.91 (m, 2H), 2.83−2.77 (m, 1H), 2.69−2.24 (m, 17H), 2.23 (s, 3H), 2.20−2.16 (m, 3H), 2.12 (s, 3H), 2.10−2.01 (m, 3H), 1.83−1.66 (m, 5H), 1.62 (s, 2.4H), 1.58 (s, 0.6H), 1.48 (s, 3H), 1.42−1.34 (m, 6H), 1.25 (s, 3H), 1.18 (s, 3H); HRMS ESI (m/z) calcd. for $C_{58}H_{85}CoN_7O_{16}$ $[M - CN]^+$ 1221.5488, found 1221.5497; UV/vis CH_2Cl_2, λ_{max}, ε ($L \cdot mol^{-1} \cdot cm^{-1}$) 552 ($7.95 \times 10^3$), 422 ($2.63 \times 10^3$), 370 ($2.48 \times 10^4$), 318 ($8.65 \times 10^3$), 279 ($9.09 \times 10^3$). Anal. Calcd for $C_{59}H_{85}CoN_8O_{16} + 3H_2O$: C, 55.56; H, 7.19; N, 8.79. Found: C, 55.38; H, 7.31; N, 8.81. Due to severe splitting of peaks in these spectra, caused by the presence of the terminal amine, the ^{1}H NMR spectra are very complicated, which made it difficult to obtain high-resolution ^{13}C spectra.

$(CN)_2$Cob(III)C1(1-{2-[2-(aminomethoxy)ethoxy]ethylcarbamoyl}ethyl)carbamic Acid 9*H*-Fluoren-9-yl Methyl Ester (19). Compound **18** (29 mg, 0.02 mmol) and Fmoc-L-Ala-OH (28 mg, 0.09 mmol) were dissolved in dry DMF (1.5 mL) under an argon atmosphere. To the solution were added DEPC (15 μL, 0.08 mmol) and Et_3N (12 μL, 0.1 mmol). The mixture was stirred at room temperature for 16 h and then diluted using DCM. It was then washed with water and NaCN aq, dried over Na_2SO_4, filtered, and concentrated in vacuo producing a purple oil. The crude product was purified by DCVC (2.5−10% EtOH in DCM). Recrystallization from Hex/AcOEt gave **19** as a purple solid (19 mg, 54%): mp 79−82 °C; R_f 0.25 (10% EtOH in DCM); ^{1}H NMR (500 MHz, CD_2Cl_2) δ (ppm) 7.80 (d, J = 7.5 Hz, 2H), 7.63 (d, J = 7.3 Hz, 2H), 7.42 (t, J = 7.5 Hz, 2H), 7.32 (t, J = 7.5 Hz, 2H), 7.25 (s(br), 1H), 6.97 (s(br), 1H), 5.97−5.92 (m, 1H), 5.76 (s, 1H), 4.36 (s(br), 3H), 4.23 (dd, J = 7.3 and 6.7 Hz, 1H), 4.16 (q, J = 7.5 and 7.0 Hz, 1H), 3.80−3.76 (m, 1H), 3.72 (s(br), 3H), 3.68 (s, 4H), 3.67 (s, 4H), 3.65 (s, 3H), 3.62 (s, 3H), 3.50−3.45 (m, 6H), 3.42−3.40 (m, 2H), 3.34−3.31 (m, 3H), 3.06 (dd, J = 3.9 and 2.6 Hz, 2H), 2.82−2.77 (m, 1H), 2.64 (d, J = 5.9 Hz, 2H), 2.60−2.32 (m, 10H), 2.24 (s, 3H), 2.22−2.14 (m, 4H), 2.12 (s, 3H), 2.10−2.01 (m, 3H), 1.87−1.81 (m, 1H), 1.79−1.71 (m, 2H), 1.67−1.64 (m, 3H), 1.48 (s, 3H), 1.39 (s, 3H), 1.36 (s, 3H), 1.33−1.25 (m, 5H), 1.23 (s, 3H), 1.18 (s, 3H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ (ppm) 173.5, 173.4, 172.7, 172.6, 172.59, 172.54, 172.4, 172.3, 172.2, 172.1, 171.7, 171.68, 171.66, 171.61, 164.9, 163.1, 163.0, 159.6, 159.3, 155.5, 144.0, 141.2, 127.6, 127.5, 127.0, 125.1, 119.8, 105.9, 104.0, 103.8, 102.6, 93.8, 88.2, 85.0, 82.7, 82.6, 71.1, 74.4, 70.4, 70.2, 69.9, 69.4, 69.1, 66.7, 58.3, 56.7, 56.6, 55.6, 52.2, 52.1, 51.8, 51.7, 51.6, 51.5, 51.4, 50.5, 47.4, 47.1, 46.7, 46.1, 45.7, 42.5, 42.3, 41.7, 41.0, 39.5, 39.2, 33.5, 33.4, 32.4, 32.1, 31.5, 31.4, 31.2, 30.7, 30.5, 29.7, 29.6, 29.5, 28.3, 25.6, 25.4, 24.8, 22.3, 21.8, 21.7, 19.4, 19.35, 19.30, 19.0, 18.6, 18.1, 17.7, 16.8, 16.79, 16.72, 16.6, 15.5, 15.2, 13.7; LRMS ESI (m/z) calcd for $C_{76}H_{100}CoN_8O_{19}$ $[M - CN]^+$ 1487.5, found 1487.6 (the measured spectra is in agreement with the isotopic profile); UV/vis CH_2Cl_2, λ_{max}, ε ($L \cdot mol^{-1} \cdot cm^{-1}$) 554 ($6.77 \times 10^3$), 425 ($2.67 \times 10^3$), 372 ($2.26 \times 10^4$), 319 ($7.69 \times 10^3$), 309 ($7.39 \times 10^3$), 300 ($1.03 \times 10^4$), 278 ($1.65 \times 10^4$), 267 ($1.98 \times 10^4$), 257 ($1.98 \times 10^4$). Anal. Calcd for $C_{77}H_{100}CoN_9O_{19}$: C, 61.06; H, 6.65; N, 8.32. Found: C, 61.00; H, 6.77; N, 8.02.

$(CN)_2$Cob(III)C1(*N*-{2-[2-(aminomethoxy)ethoxy]ethyl}-2-aminopropionamide) (20). Compound **19** (10 mg, 6.6 μmol) was dissolved in 20% piperidine in DMF (1 mL) and stirred at room temperature for 3 h. It was then diluted with DCM, washed with water and NaCN aq, dried over Na_2SO_4, filtered, and then concentrated in vacuo. The crude product was purified by DCVC (5−20% EtOH in DCM). Recrystallization from Hex/AcOEt gave **20** as a purple solid (7 mg, 74%): mp 115−117 °C; R_f 0.35 (20% EtOH in DCM); ^{1}H NMR (500 MHz, CD_2Cl_2) δ (ppm) 8.02−7.95 (m, 0.5H), 7.83−7.82 (m, 0.3H), 7.66 (d, J = 4.5 Hz, 0.7H), 7.17 (d, J = 4.5 Hz, 0.5H), 6.20 (s, 0.4H), 5.82 (s, 0.6H), 4.21−4.19 (m, 1H), 3.97−3.90 (m, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 3.68−3.67 (m, 8H), 3.62 (s, 2H), 3.61 (s, 1H), 3.59 (s, 1H), 3.52−3.48 (m, 9H), 3.25−3.24 (m, 1H), 3.12−3.06 (m, 1H), 2.98−2.90 (m, 1H), 2.79−2.40 (m, 13H), 2.35 (s, 1H), 2.32 (s, 3H), 2.24 (s, 3H), 2.17−2.07 (m, 7H), 1.85−1.79 (m, 3H), 1.71 (s(br), 3H), 1.64−1.62 (m, 4H), 1.47 (s, 6H), 1.39 (s, 4H), 1.28−1.21 (m, 6H), 1.18 (s, 2H); HRMS ESI (m/z) calcd for $C_{61}H_{90}CoN_8O_{17}$ $[M - CN]^+$ 1265.5751, found 1265.5750; UV/vis CH_2Cl_2, λ_{max}, ε ($L \cdot mol^{-1} \cdot cm^{-1}$) 555 ($7.86 \times 10^3$), 419 ($3.25 \times 10^3$), 368 ($1.96 \times 10^4$), 321 ($8.72 \times 10^3$), 279 ($1.09 \times 10^4$). Anal. Calcd for $C_{62}H_{90}CoN_9O_{17} + 3H_2O$: C, 55.31; H, 7.19; N, 9.36. Found: C, 55.19; H, 6.90; N, 9.45. Due to severe splitting of peaks in these spectra, caused by the presence of the terminal amine, the ^{1}H NMR spectra are very complicated, which made it difficult to obtain high-resolution ^{13}C spectra.

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■ ASSOCIATED CONTENT

Supporting Information. All experimental details and complete analytical data of new products. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ DEDICATION

This paper is dedicated to Prof. J. Jurczak on the occasion of his 70th birthday.

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