Synthesis of Disulfides Containing a Corrinoid Head Group for Preparation of Self-Assembled Monolayers

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Abstract: The synthesis of three novel alkane disulfides with headgroups derived from vitamin B_{12}, **14a**, **14b** and **15**, is described. Self-assembled monolayers on gold are prepared from the symmetrical disulfide **15**, bearing two cobyrinate head groups. The coating of the gold surface is analyzed by TOF-SIMS and ESCA measurements.

Key words: disulfides, vitamin B_{12} derivatives, cobester disulfides, self-assembled monolayers

Novel surface characterization techniques at the nanometer scale and progress in organic synthesis have induced a remarkable growth in surface sciences in recent years.[1–5] Thus, a variety of nano- and mesoscale surface phenomena have been investigated, which advanced many industrial applications in chemistry and material sciences such as coatings, semiconductors, polymer surfaces and chemical sensors.[6–14] In particular, the field of chemical and biochemical sensors has advanced dramatically due to miniaturization and novel sensing elements.[15–17]

The combination of functional synthesis and electrochemical detection at a sensor surface is particularly intriguing as it allows to explore molecular processes and reactions. The three dimensional microenvironment at the surface of electrodes provides a solid structural basis for a detailed investigation of electronic processes occurring at the organic interphase between the electrode and the solution, and allows to investigate morphological changes during electrochemical processes including electrocatalytic reactions.

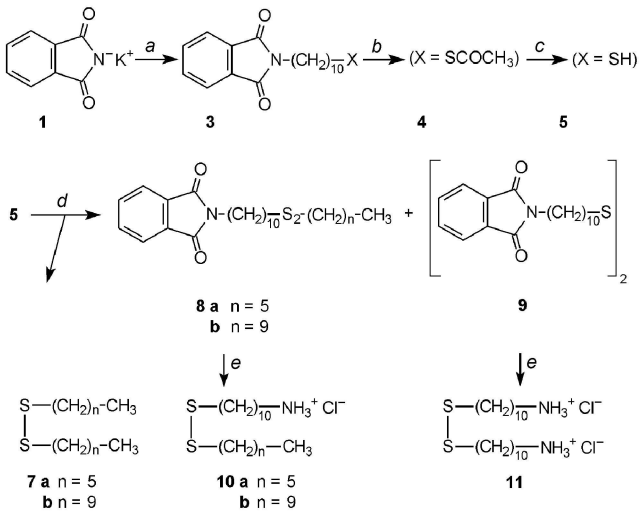
Vitamin B_{12} and the corrinoids as its congeners are key catalysts for a variety of unique biological transformations.[18–23] Their basic reactivities are known from many in vivo studies. Corrinoids derived from vitamin B_{12} have been used for a large variety of in vitro investigations.[24–31] These results led to mechanistic models for the enzymatic transformations with the in vitro studies simulating key features of some of the important steps of the catalytic cycles.

While most of the in vitro studies were performed in solution, in many cases using electrochemically induced redox reactions of the corrinoids, electrodes coated with B_{12} derivatives are of more recent interest.[32–42] The efficient redox reaction of corrinoids in solution is enhanced by grafting them to an electrode surface. Furthermore, such studies will provide the information necessary for an in depth understanding of their catalytic activity and may give additional clues for the biofunction of vitamin B_{12}.

In order to engineer the surface and its coating via SAMs (self-assembled monolayers), vitamin B_{12} derivatives bearing disulfide side chains were synthesized. Subsequently, self-assembled monolayers on crystalline gold electrode surfaces were prepared.

Synthesis of disulfides with B_{12}-derived head groups.

Disulfides bearing one or two corrinoid head groups were prepared as shown in Scheme 1 and Scheme 2. The procedures are based on our earlier results.[43] Due to varying results in the preparation of the disulfide **9** and the thiol thereof via the Bunte salt method we prepared the thiol **5** by selective cleavage of the thioacetate **4**. This approach gave reliable results and, in addition, readily allowed the formation of nonsymmetrical disulfides.



Scheme 1 *Reagents and conditions*: (a) $Br(CH_2)_{10}Br$ (**2**); (b) $CH_3COS^-K^+$, DMF; (c) Et_2NH, MeOH, reflux; (d) $C_6H_{13}SH$ (**6a**) or $C_{10}H_{21}SH$ (**6b**), I_2; (e) CH_3NH_2, HCl.

Reaction of the phthalimido bromide **3**, prepared from **1** and **2** in 72% yield by an economical modification of our earlier procedure, gave with CH_3COSK the thioacetate **4**. Selective cleavage of the ester group was achieved by warming of **4** with Et_2NH in methanol whereas treatment with aqueous NaOH, MeONa or *n*-$C_4H_9NH_2$ in MeOH led

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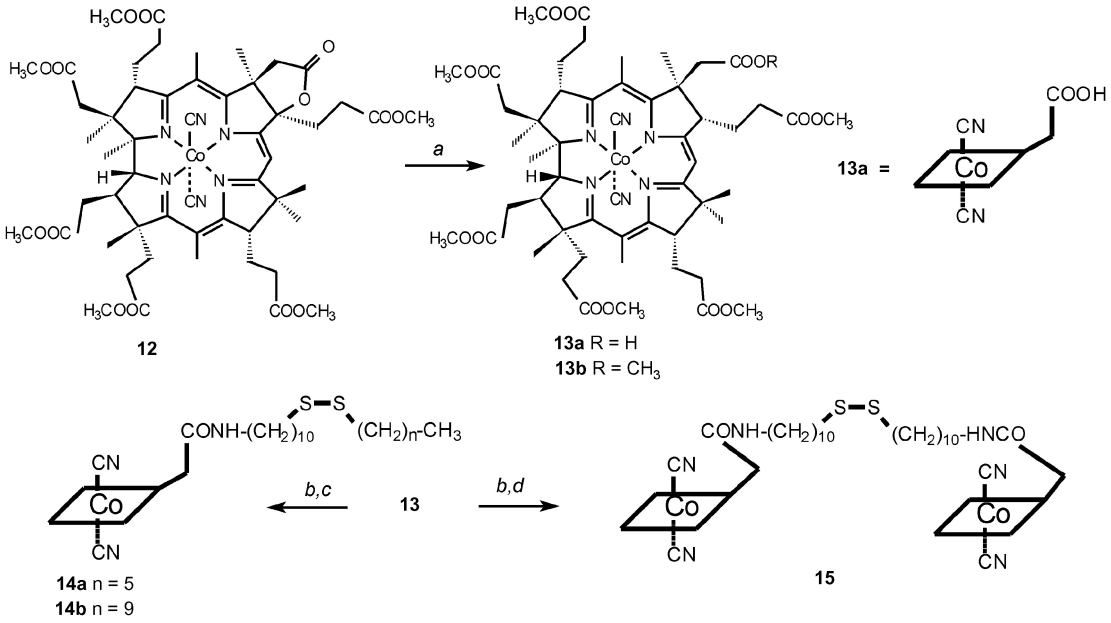

Scheme 2 *Reagents and conditions*: (a) Zn, CH_3COOH; (b) $Cl_3CC(CH_3)_2OCOCl$, Et_3N, CH_2Cl_2; (c) **10a** or **10b**, Et_3N; (d) **11**, Et_3N.

to lower yields and partial cleavage of the imide moiety. The nonsymmetrical disulfides **8a**,**b** were obtained by oxidative coupling of the phthalimido thiol **5** with the thiol **6a** and **6b** by treatment with I_2, respectively. We chose this method rather than the selective reaction of the thiols with the sulfenylchloride of **5**,[44,45] because we needed the symmetrical disulfides **7a**,**b** and **9** in addition to **8a**,**b**.

The phthalimido group was cleaved by aqueous methylamine rather than hydrazine.[46–48] This procedure led to the ammonium salts **10a**,**b** in an efficient way. The corrins **14a**,**b** and **15**, bearing a disulfide side chain, were prepared following our published procedure.[43]

Self-assembled monolayers on gold surfaces were obtained by immersing the gold substrates into solutions of the symmetrical cobyrinate alkane disulfide **15**. The surfaces of the coated gold electrodes were analyzed by TOF-SIMS (Time of flight – secondary ion mass spectroscopy) and ESCA (electron spectroscopy for chemical analysis).

TOF-SIMS analyses revealed clear mass signatures of the whole molecule at *m/e* = 2464.08, 2661.17, and 2687.90 reflecting the molecular ions of **15** – CN^-, – CN^-/+ Au and + Au, respectively. The signature of (**15** + Au)$^+$ at *m/z* = 2687.90 is important since it proves the strong interaction of **15** with the gold surface. In addition, several signals in the range below *m/z* = 2400 were attributed to Au and disulfide containing fragments of **15** indicating again the high affinity of disulfides to the gold surface.

ESCA investigations clearly revealed the presence of the cobester disulfide **15** on the gold substrates. The Co 2p signature was found only on sample surfaces exposed to the **15**, and not on substrates that had been exposed to the heptamethyl cobyrinate **13b**. This molecule was washed off the surface easily demonstrating that there were no or only weak interactions between the CN ligands of the Co center and the gold.

Angular dependent investigations did not allow for clear interpretations of the orientation of **15**, even though concentrations of Co and S did decrease and increase, respectively, with change of the incident angle. The overall atomic composition was in good agreement with theoretical calculations (cf. Table 1). The high levels of sulfur can be attributed to the omnipresence of sulfur containing contaminations that adsorb readily to any gold surface.

The highly angular dependency and strong Au 4f signature indicated that the organic layer was either very thin

Table 1 ESCA Results for **15** on Gold[a]

Biscobyrinate **15**	Carbon	Oxygen	Sulfur	Nitrogen	Cobalt
	C 1s	O 1s	S 2p	N 1s	Co 2p
Percentages calcd	74.12	15.29	1.17	8.25	1.17
Percentages obsd	74.70	15.44	2.75	6.21	0.90

[a] Atomic composition of the elements; calculated and observed percentages (for the angle of 55° and the orbitals given).

(monolayer), or that phase segregation and island formation occurred. Ellipsometric results also suggest a very low thickness.[40] Since no cobyrinate had been found on control surfaces, it was concluded that (Cob–C_{10}–S)$_2$ **15** formed a monolayer with the disulfide attached onto the gold substrates.

The synthesis of three novel alkane disulfides with cobyrinate head groups, **14a**,**b** and **15**, is described. The formation of self-assemblies on Au (100, 111 and polycrystalline) from the disulfide **15** with its bulky corrinoid head groups was established by TOF-SIMS and ESCA analyses. As a first result of the catalytic acitvity of the Au electrode coated with **15**, Abrantes and coworkers reported the reduction of O_2.[40] The STM (scanning tunneling microscopy) analysis of the surface coating will be reported elsewhere.[49]

Selected data:

Experimental and analytical data for compounds **4**, **5**, **8a**, **8b** (R_f, mp, IR, ^{1}H NMR, ^{13}C NMR, MS, correct elemental analysis), **10a** (IR, ^{1}H NMR, ^{13}C NMR, TOF-MS) and **10b** (^{1}H NMR, ^{13}C NMR) may be obtained from the author of correspondence.

Coα,Coβ-Di(cyano-κC)-*N*^{c}-(11,12-dithiooctadec-1-yl)cob(III)yrinic Acid-*c*-amide *a,b,d,e,f,g*-Hexamethyl Ester (14a)

To a degassed solution of freshly prepared **13**[50–51] (0.282 g, 0.262 mmol) in 15 mL CH_2Cl_2 was added 0.12 g (0.28 mmol) 2,2,2-trichloro-*tert*-butylchloroformate in 1.2 mL CH_2Cl_2 and 0.04 mL Et_3N (0.4 mmol) at –10 °C. After 2 h, a suspension of 0.119 g (0.3 mmol) **10a** and 0.14 g Et_3N in 5 mL CH_2Cl_2 was added. The mixture was stirred overnight at r.t., worked up, and the residue was dissolved in CH_2Cl_2 and adsorbed on 7 g silica gel. Flash chromatography with CH_2Cl_2-MeOH (0.1% HCN) = 50:1 gave 0.191 g (53.5%) **14a**. Residual heptamethyl cobyrinate was removed by TLC with toluene–*i*-PrOH–MeOH (0.1% HCN) = 10:1:1 as eluent. R_f [CH_2Cl_2–MeOH (0.1% HCN) = 40:1] 0.25; [toluene–*i*-PrOH–MeOH (0.1% HCN = 10:1:1] 0.38. IR (KBr): 3551m, 3416m, 2953m, 2928s, 2855m, 2120w, 1737s, 1661m, 1581s, 1503s, 1437m, 1199s, 1148s cm^{-1}. UV/Vis (1.981×10^{-5} M in CH_2Cl_2, λ_{max}, log ε): 590 (3.83) 550 (3.72). 513 (3.51), 424 (3.26), 372 (4.25), 356 (sh, 3.93), 3.16 (3.78), 280 (3.83). ^{1}H NMR: δ = 0.85 (t, *J* = 7.0, 3 H), 1.10–1.40 (stack, 33 H), 1.47 (s, 3 H), 1.52–1.90 (stack, 12 H), 1.9–2.3 (stack, 15 H), 2.32–2.79 (stack, 16 H), 3.0 (m, 1 H), 3.25–3.35 (m, 1 H), 3.6–3.78 (6s, 18 H), 5.50 (s, 1 H), 6.96 (t, 1 H). ^{13}C NMR: δ = 13.9 (q), 15.28 (q), 15.31 (q), 16.87 (q), 18.41 (q), 19.23 (q), 19.72 (q), 21.99 (q), 22.49 (t), 24.81(t), 25.68 (t), 25.77 (t), 26.98 (t), 28.14 (t), 28.46 (t), 29.15 (t), 29.17 (t), 29.20 (t), 29.22 (t), 29.28 (t), 29.45 (t), 29.56 (t), 29.66 (t), 29.68 (t), 30.72 (t), 30.84 (t), 31.39 (t), 31.43 (q), 31.76 (t), 32.39 (t), 33.65 (t), 39.08 (t), 39.11 (t), 39.14 (q), 39.77 (t), 41.59 (t), 46.05 (s), 46.89 (s), 47.23 (t), 51.36 (s), 51.62 (q), 51.84 (q), 51.86 (q), 51.87 (q), 52.41 (q), 53.49 (q), 56.56 (q), 58.43 (s), 58.65 (d), 74.61 (d), 82.59 (s), 91.34 (d), 102.17 (s), 106.67 (s), 129 (s), 135.16 (s), 161.30 (s), 163.53 (s), 169.46 (s), 171.32 (s), 171.49 (s), 171.62 (s), 172.51 (s), 172.86 (s), 173.59 (s), 173.84 (s), 175.32 (s), 175.74 (s), 175.88 (s). ESI-MS (CH_3OH + 0.1% HCN) $C_{69}H_{104}CoN_7O_{13}S_2$ (MW 1362.67): 1337.71 (38), 1336.76 (74 [M – CN^-]$^+$), 1335.8 (100), 679.51 (28, [M – CN^- + Na^+]$^{2+}$), 668.58 (0.2, [M – CN^- + H^+]$^{2+}$), 655.11 (20, [M – 2CN^-]$^{2+}$).

Coα,Coβ-Di(cyano-κC)-*N*^{c}-(11,12-dithiodocosan-1-yl)cob(III)yrinic Acid-*c*-amide *a,b,d,e,f,g*-Hexamethyl Ester (14b)

Yield: 36%; R_f [toluene–MeOH (0.1% HCN) = 10:1]: 0.40. IR (KBr): 3443w, 3303w, 2925s, 2121w, 1737s, 1662m, 1581s, 1502s cm^{-1}. UV/Vis (1.13×10^{-5} M, CH_2Cl_2, λ_{max}, log ε): 590 (3.2), 550 (3.81), 516 (3.63), 422 (3.38), 371 (4.29), 356 (sh, 4.02), 318 (3.92), 280 (3.95). ^{1}H NMR: δ = 0.83 (t, 3 H), 1.15–1.40 (stack, 39 H), 1.49–1.85 (stack, 14 H), 1.95–2.35 (stack, 13 H), 2.40–3.85 (stack, 14 H), 3.01 (m, 1 H), 3.28 (m, 1 H), 3.62–3.80 (stack , 18 H), 5.51 (s, 1 H), 6.97 (m, 1 H); ^{13}C NMR: δ = 14.33 (q), 15.57 (q), 15.58 (q), 17.14 (q), 18.68 (q), 19.51 (q), 20.01 (q), 22.25 (q), 22.90 (t), 25.11 (t), 25.97 (t), 26.04 (t), 27.26 (t), 28.74 (t), 29.39 (t), 29.44 (t), 29.51 (t), 29.52 (t), 29.68 (t), 29.73 (t), 29.89 (t), 31.71 (t), 31.71 (q), 32.11 (t), 32.69 (t), 33.94 (t), 39.38 (t), 39.15 (t), 39.17 (q), 39.79 (t), 41.62 (t), 46.12 (s), 46.93 (s), 47.29 (t), 51.41 (s), 51.86 (q), 51.87 (q), 52.09 (q), 52.11 (q), 52.13 (q), 52.66 (q), 53.79 (q), 56.62 (q), 58.47 (s), 58.95 (d), 74.67 (d), 82.63 (s), 91.64 (d), 101.8 (s), 106.3 (s), 161.35 (s), 163.59 (s), 169.47 (s), 171.39 (s), 171.51 (s), 171.63 (s), 172.51 (s), 172.86 (s), 173.59 (s), 173.83 (s), 175.36 (s), 175.77 (s), 175.89 (s). ESI-MS (CH_3OH + 0.1% HCN): $C_{73}H_{112}CoN_7O_{13}S_2$ (1418.78) 1440.78 {[M + Na^+]$^+$, (3)}, 1393.7 (43), 1392.80 (77), 1391.83 {[M – CN^-]$^+$, (100)}, 707.56 {[M – CN^- + Na^+]$^{2+}$, (60)}, 696.57{([M – CN^- + H^+]$^{2+}$ (11)}, 683.13 {[M – 2 CN^-]$^{2+}$ (50)}.

Bis[Coα,Coβ-di(cyano-κC)-*N*^{c},*N*$^{c'}$-(dithiodidecan-10,1-diyl)]bis[cob(III)yrinic Acid-*c*-amide *a,b,d,e,f,g*-Hexamethyl Ester] (15)

Yield: 7.4%; R_f [toluene–*i*-PrOH–MeOH (+0.1% HCN) = 10:1:1]: 0.38; [CH_2Cl_2–MeOH (+0.1% HCN) = 10:1]: 0.66. IR: 3413w, 2927m, 2854m, 2124w, 1794m, 1736s, 1660m cm^{-1}. ^{1}H NMR: δ = 1.10-1.39 (stack, 54 H), 1.49 (s, 6 H), 1.55–1.85 (stack, 18 H), 1.95–2.87 (stack, 60 H), 3.01(m, 2 H), 3.29 (m, 2 H), 3.58–3.77 (stack, 36 H), 5.52 (s, 2 H), 6.97 (m, 2 H); ^{13}C NMR: δ = 15.61 (2q), 15.63 (2q), 17.19 (2q), 18.73 (2q), 19.56 (2q), 20.05 (2q), 22.31 (2q), 25.16 (2t), 26.01 (2t), 26.12 (2t), 27.31 (2t), 28.79 (2t), 29.44 (2t), 29.47 (2t), 29.49 (2t), 29.55 (2t), 29.73 (2t), 29.83 (2t), 29.94 (2t), 31.06 (2t), 31.18 (2t), 31.76 (2q), 32.07 (2t), 32.73 (2t), 33.99 (2t), 39.36 (2t), 39.48 (2d), 40.08 (2t), 41.90 (2t), 46.09 (2s), 46.90 (2s), 47.54 (2t), 51.36 (2s), 51.92 (2q), 51.93 (2q), 52.15 (4q), 52.18 (2q), 52.72 (2q), 53.84 (2d), 56.89 (2d), 58.45 (2s), 58.97 (2d), 74.95 (2d), 82.61 (2s), 91.67 (2d), 102.16 (2s), 106.67 (2s), 129.21 (s), 134.97 (s), 161.35 (2s), 163.56 (2s), 169.46 (2s), 171.37 (2s), 171.49 (2s), 171.61 (2s), 172.49 (2s), 172.85 (2s), 173.57 (2s), 173.81 (2s), 175.35 (2s), 175.76 (2s), 175.88 (2s). UV/Vis (8.03×10^{-6} M, λ_{max}, log ε, CH_2Cl_2): 590 (4.17), 550 (4.11), 515 (3.92), 423 (3.7), 371 (4.62), 356 (sh, 4.33), 318 (4.24), 280 (4.32). ESI-MS (CH_3OH + 0.1% HCN) $C_{106}H_{182}Co_2N_{14}O_{26}S_2$ (2490.89): × 10: 2463.12 {[M – CN–]$^+$, (3)}; 1243.8 {[M – CN^- + Na^+]$^{2+}$, (12)}, 1218.85 {[M – 2 CN^-]$^{2+}$, (100)}, 820.3 {[M – 2CN^- + Na^+]$^{3+}$, (20)}, 812.9 {[M – 2CN^- + H^+]$^{3+}$, (39)}, 804.1 {[M – 3CN^-]$^{3+}$, (9)}.

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