Primary amines undergo chloromethylation with CH2O/ SOCl2 to give RN(CH2Cl)2, which in turn react with Li2[Fe2S2(SR)2] to give Fe2[(SCH2)2NR]2(CO)6; in the case of R = CH2CH2CH2 and CH2CH2SMe, Me3NO-induced decarbonylation afforded pentacarbonyl derivatives wherein the pendant functionality is coordinated to Fe.

The Fe-only hydrogenases are a topical class of proteins with the pendant functionality is coordinated to Fe. Decarbonylation afforded pentacarbonyl derivatives wherein the first coordination shell of the diiron core, including high quality crystal structures of the dicyanides Fe2[(SCH2)2NR]2(CO)5L species. It has recently been proposed that the dithiolate ligand is an azadithiolate SCH2NHCH2S, and we have used (CICH2)3NMe to introduce this novel functionality (Scheme 1).

Because the azadithiolate cofactor defines an unprecedented coordination motif, we sought to explore its scope. The only known bis(chloromethyl)amine, (CICH2)3NMe, is however prepared via an uninviting degradation of triazine [CH2NMe]3 using PCls.

We have found that many primary amines undergo efficient chloromethylation upon treatment with a solution of paraformaldehyde followed by 2× excess of SOCl2 (Scheme 2). The reactions occur under mild conditions, and the chloromethylated amines are isolated as the free bases. In some cases the amines were further purified by vacuum distillation, but usually evaporation of ether extracts provided the targeted species. These compounds were identified by 1H NMR spectroscopy (characteristic NCH2Cl singlet at δ 5.5–5.2) as well as elemental analysis or high resolution mass spectrometry. The following derivatives were prepared: allyl (2a), tert-butyl (2b), methylcarboxylethyl (2c), benzyl (2d), 4-nitroaniline (2e), and 2-(methylthio)ethyl (2f). Compounds 2a–f are stable under anhydrous conditions at 0 °C.

Iron thiolate carbonyl dimers were prepared from bis(chloromethyl)amines 2a, 2b, 2c, 2f by treatment with Li2[Fe2-
characterization showed that the theioger is coordinated in 4f (Fig. 2). Pickett and coworkers have recently reported a similar complex Fe(μ-SCH2)2CHCH2SMel(CO)4.13 For 4a, and to an even greater extent, 4f, C–S distances are lengthened and C–N–C angles are increased due to the anemic effect.14

In summary, a new route to bis(chloromethyl)amines allows general access to a broad class of N-functionalized azadithiolato complexes. Independent of any biological relevance, azadithiolates could be applied more generally, especially as bridging ligands with functionality.14 This research was supported by the U.S. National Institute of Health.

Notes and references

1 Representative procedure: a mixture of 1.8 g (0.025 mol) BuNH2, 1.95 g (0.065 mol) paraformaldehyde, and 30 mL CH2Cl2 was stirred for ca. 3 h; the resulting suspension was treated dropwise with 11.9 g (0.1 mol) of SOCl2. After gas evolution had ceased, solvent and unreacted SOCl2 were handled cautiously.

2a Colorless oil; bp 40 °C (0.6 mm Hg); yield: 70%. Anal. Calc. for C4H6ClN2: C, 42.37; H, 7.70; N, 19.16. Found: C, 42.37; H, 7.70; N, 19.16.

3 Characteristic infrared data for the complexes: IR (hexanes): 32.62; H, 5.36; N, 7.67%. 1H NMR (CDCl3): 3.48 (2H, m, CHC=O); 3.76 (2H, s, CH2Cl); 3.76 (2H, s, CH2Cl); 3.07 and 2.40 (s, 4H, NCCH2); 4.77 and 4.66 (ddq, 2H, NCH2CH=); IR (hexanes): v(CO)= 202.0187, 1973, 1995 cm−1.

4a An orange solution of 0.150 g (0.35 mmol) 3a in 10 mL of MeCN was treated with 0.026 g (0.35 mmol) ONMe2 in MeCN. The resulting red–purple solution was evaporated and the product crystallized from cold hexane. Yield: 45%. Anal. Calc. for C4H6Cl2N2O2: C, 30.10; H, 2.27; N, 3.51. Found: C, 29.94; H, 2.10; N, 3.41%. 1H NMR (CDCl3): δ 4.17 (m, 1H, CH2CH=CHCl); 3.69 and 3.06 (dd, 2H, NCH2CH=CHCl); 3.07 and 2.40 (s, and AA′BB′, 4H, NCH2S); 2.77 and 1.48 (dd and dd, 2H, NCH2CH=CHCl). IR (hexanes): ν(CO)= 2062, 2009, 1998, 1982, 1967 cm−1. 4f Dark red crystals from hexane: yield: 32%. Anal. Calc. for C4H6Cl2N2O2: C, 32.53; H, 2.96; N, 3.16. Found: C, 32.42; H, 3.10; N, 3.07. 1H NMR (CDCl3): δ 4.10 and 4.01 (dd, 4H, SHCH2SCH3); 3.12 (b, 4H, NCH2CH2SMel), 2.66 (s, 3H, SCH3). IR (hexane): ν(CO)= 2053, 1990, 1970, 1943 cm−1.

5 Crystal data for 4a, C4H6Cl2N2O2S, M = 399.0, monoclinic, P21/n, a = 10.740(13), b = 9.4727(11), c = 14.1176(16) Å, β = 91.2324(2)°, V = 1436.63(6) Å3, T = 193 K, Z = 4, max. transmission: 0.9990, 0.7248, Dcalc = 1.845 g cm−3, 1996 reflections collected, 3222 unique, Rint = 0.0763, R = 0.0384, wR2 = 0.0548 [λ (2σ(λ))]. For 4f, C4H6Cl2N2O2S, M = 866.16, monoclinic, P21/n, a = 17.3411(11), b = 10.498(7), c = 18.338(12) Å, β = 110.020(12), V = 3134.3(3) Å3, T = 193 K, Z = 4, max. transmission: 0.9991, 0.7477, Dcalc = 1.863 g cm−3, 2854 reflections collected, 7566 unique, Rint = 0.0489, R = 0.322, wR2 = 0.0709 [λ (2σ(λ))].

CCDC reference numbers 163360 and 163361. See also http://www.rcsb.org/supr/cif/ or other electronic format.


9 D. Seyfert, R. S. Henderson and L. C. Song, Organometallics, 1982, 1, 125.


