Methane Formation by Reaction of a Methyl Thioether with a Photo-Excited Nickel Thiolate—A Process Mimicking Methanogenesis in Archaea

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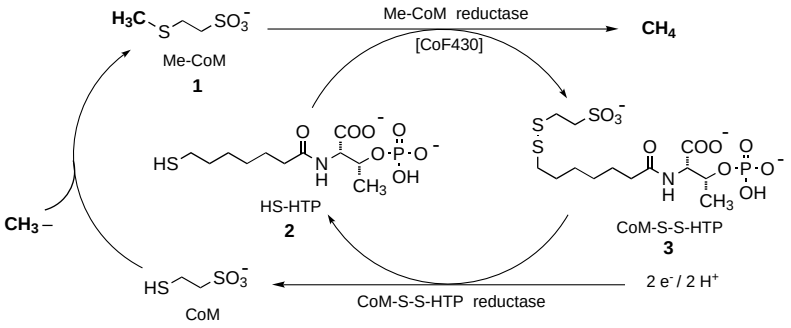
Abstract: The formation of a sulfuranyl radical intermediate followed by methyl transfer to the nickel(I) center of coenzyme F430 and generation of the disulfide has been proposed as a possible mechanism for the formation of methane catalyzed by methyl coenzyme M reductase in methanogenic archaea. In order to test this hypothesis, a sterically shielded, bifunctional model substrate that contained a methyl thioether and a sulfhydryl functional group, which could form a five-membered cyclic sulfuranyl radical according to the postulated mechanism, was synthesized. The corresponding thiolate reacted with Ni^{II} salts to give a diamagnetic, square-planar Ni^{II} dithiolate complex, which was characterized by X-ray diffraction. Upon irradiation of this complex with light of $\lambda >$ 300 nm, methane and the cyclic disulfide were formed, whereas irradiation of the thiolate in the absence of nickel gave only traces of methane and no cyclic disulfide. The observed products are consistent with the postulated mechanism via a sulfuranyl radical, and the role of light is interpreted as the formation of a Ni^{I}/thiyl radical pair upon excitation of a charge-transfer band of the Ni^{II} dithiolate. In the presence of a large excess of thiolate, the diamagnetic complex was transformed into a paramagnetic, five- or six-coordinate complex that proved to be more active in the generation of both methane and the cyclic disulfide, than the square-planar diamagnetic dithiolate.

Keywords: enzyme mimetics · methanogenesis · nickel · photochemistry · thiolate

Introduction

Methyl coenzyme M reductase (MCR) is the key enzyme in methane formation by methanogenic archaea.[1] It catalyzes the reaction between the thioether methyl coenzyme M (**1**, MeCoM) and the thiol *N*-(7-mercaptoheptanoyl)-*O*-phospho-L-threonine (**2**, HS-HPT, Coenzyme B) to give methane and the mixed disulfide CoM-S-S-HTP (**3**)[2] (Scheme 1). Each of the two symmetry-equivalent active sites of MCR contains one molecule of the hydroporphinoid nickel complex coenzyme F430 (**4**).[3–5] The nickel center of free coenzyme F430 and its penta-ester or penta-amide derivatives can be reduced reversibly to the Ni^{I} valence state, which exhibits a characteristic quasi-axial EPR spectrum and UV-visible absorption maxima at 380 and 750 nm.[6–8] Whereas conventional purification of MCR leads to an inactive enzyme that contains the metal in the Ni^{II} valence state, the first isolation of highly active enzyme preparations from reductively preconditioned cells[9, 10] and,



Scheme 1. The last step of biological methane formation in methanogenic archaea. Methyl coenzyme M reductase catalyzes the conversion of methyl coenzyme M (**1**) and *N*-(7-mercaptoheptanoyl)-*O*-phospho-L-threonine (**2**, HS-HTP) to methane and the mixed disulfide **3**.

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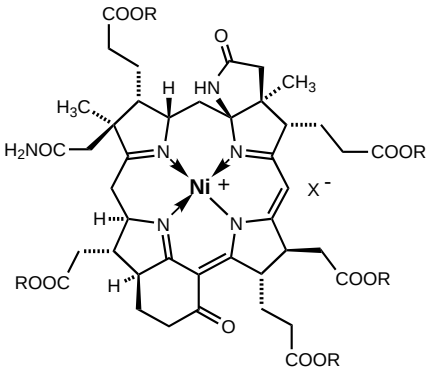
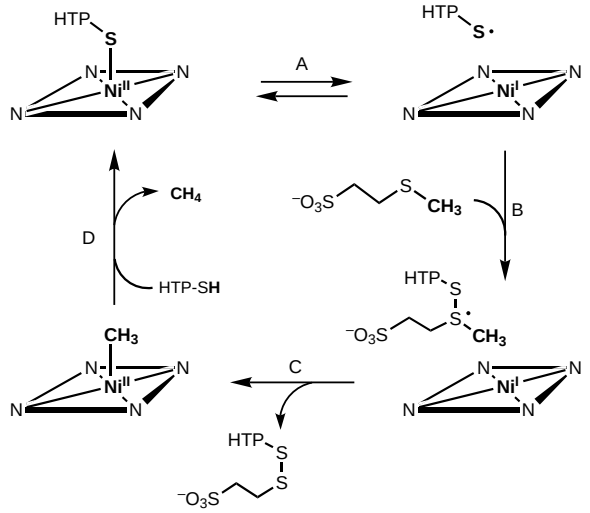


4 Coenzyme F430 (R = H)
5 F430M (R = CH_3, X = ClO_4)

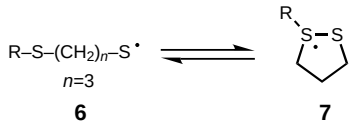
more recently, the reductive reactivation of the so-called MCR_{ox1} state to active enzyme (MCR_{red1})[11] by Thauer and co-workers demonstrated that the enzyme is active only if the metal center of coenzyme F430 is in the Ni^I form.

We have previously shown that the Ni^I form of coenzyme F430 pentamethyl ester (**5**) reacts with electrophilic methyl donors such as iodomethane, methyl tosylate, and methyl-dialkyl sulfonium ions according to a two-electron mechanism (SN_2 or oxidative addition) to give methane via a methyl-Ni^{II} F430M intermediate.[12–14] The natural substrate, methyl coenzyme M, or simple methyl thioethers, however, did not react with Ni^I F430M. This prompted us to propose and study a different catalytic mechanism in which the addition of a thiyl radical to the sulfur atom of the thioether giving a sulfuranyl radical intermediate is the central step (Scheme 2).[15] The same mechanism has been proposed independently by Berkessel.[16]



Scheme 2. The mechanism proposed by us[15] and independently by Berkessel.[16]

While this mechanistic proposal explains the activation of the carbon–sulfur bond towards attack by Ni^I as well as the formation of the disulfide, we found only one precedent for the crucial step in the literature. Anklam and Steenken observed the formation of a metastable intermediate, identified as the cyclic sulfuranyl radical **7**, when thiyl radicals of the

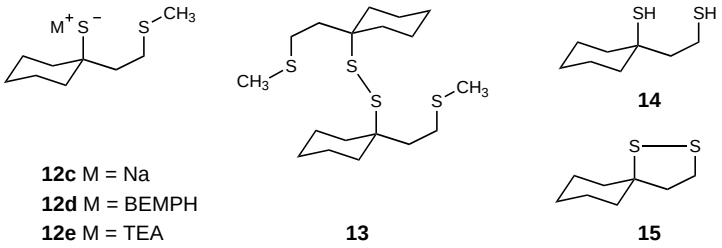


6 **7**

type **6** with $n = 3$ were generated by flash photolysis in acetonitrile.[17] We therefore decided to try to experimentally observe the reaction shown in Scheme 2 using a suitable bifunctional substrate and a nickel model complex. Here we describe the design and synthesis of a substrate that contains both an aliphatic thiol and a methyl thioether function, and the photo-induced cleavage of the corresponding nickel thiolates to give methane and the cyclic disulfide. During the course of our work, Tada and Masuzawa[18] reported a similar but bimolecular reaction between sodium *p*-toluene thiolate and thioanisole catalysed by the nickel complex **19**. We have repeated part of their work and will compare the results of the two systems in the discussion.

Results and Discussion

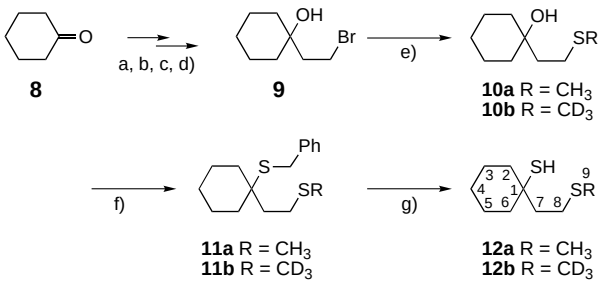
Design and synthesis of the model substrate: Since formation of cyclic sulfuranyl radicals has been observed only for five-membered rings, we selected the partial structure of an *S*-methyl-1,3-propanedithiol for the model substrate. In order to promote attack of the Ni^I center at the methyl carbon rather than at the divalent sulfur of the cyclic sulfuranyl radical, we selected structure **12** in which the cyclohexane ring was expected to shield the divalent sulfur against nucleophilic attack by Ni^I.



12c M = Na
12d M = BEMPH
12e M = TEA

13 **14** **15**

Starting from cyclohexanone, 1-[2-(methylthio)ethyl] cyclohexanethiol (**12a**) was synthesized in seven steps according to Scheme 3. Thiomethylation with $NaSCD_3$ gave the corre-



8 **9**
10a R = CH_3
10b R = CD_3
11a R = CH_3
11b R = CD_3
12a R = CH_3
12b R = CD_3

Scheme 3. Synthesis of componds **12a** and **12b**. a) *i*-Pr_2NH, *n*-BuLi, THF, −70 °C; EtOAc, THF, −70 °C; b) $LiAlH_4$, Et_2O, reflux; c) $PhSO_2Cl$, Py, 0 °C; d) KBr, 18-crown-6, acetone, 50 °C; e) $NaSCH_3$ (→**10a**), $NaSCD_3$ (→**10b**), MeOH, RT.; f) BnSH, $BF_3 \cdot OEt_2$; g) Na (1.1 equiv), NH_3(l), EtOH, −40 °C.

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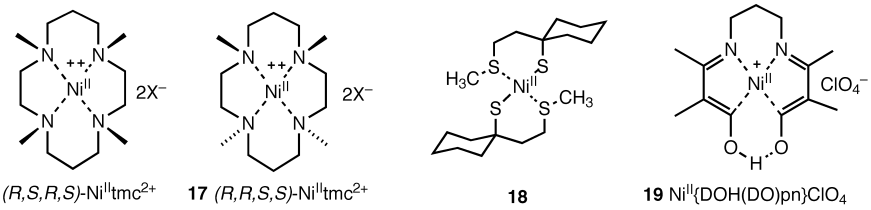
sponding trideuteromethylated compound **12b**. Thiol **12a** was oxidized to the symmetric disulfide **13** according to the method of Aida.[19]

For reference purposes, the cyclic disulfide 1,2-dithiaspiro-[4.5]decane (**15**) was synthesized from the benzyl-protected intermediate **11a** by exhaustive dealkylation in $Na/NH_3(l)$ at $-40\,^{\circ}C$, followed by oxidation of the resulting dithiol **14**.

Methane formation by photolysis of 12c in the presence of nickel complexes: According to Anklam and Steenken,[17] the lifetime of sulfuranyl radicals lies in the microsecond range. The thiyl radical should therefore be generated so close to the nickel that no diffusion step is necessary for the reaction of the sulfuranyl radical with Ni^{I}. Our approach was to try to generate a Ni^{I}/thiyl-radical pair by excitation of the ligand-to-metal charge-transfer band of a suitable Ni^{II} thiolate complex.

The two isomers of Ni^{II} tetramethylcyclam, [(*R*,*S*,*R*,*S*)-Ni^{II}(tmc)]$^{2+}$ (**16**) and [(*R*,*R*,*S*,*S*)-Ni^{II}(tmc)]$^{2+}$ (**17**), have been thoroughly studied by several groups.[20, 21] In terms of reactivity, they are surprisingly good models for coenzyme F430 despite the large differences in structure and charge of the macrocyclic ligand. The Ni^{II}/Ni^{I} redox potential of **17** is very close to that of F430 pentamethyl ester (**5**).[6, 22] Like coenzyme F430, both Ni^{II}-tmc isomers have a pronounced tendency to axially coordinate additional ligands to form high-spin complexes. Paramagnetic methyl-nickel(II) derivatives have been described for **5** as well as for **16** and **17**.[13, 23, 24] Ram et al. have reported the formation and X-ray structure of pentacoordinated thiophenolate complexes of both **16** and **17**.[22] We therefore planned to generate the Ni^{I}/thiyl radical pair from the five-coordinate complex between the thiolate derived from **12a** and **16**.



16 *(R,S,R,S)*-Ni^{II}tmc^{2+} **17** *(R,R,S,S)*-Ni^{II}tmc^{2+} **18** **19** Ni^{II}{DOH(DO)pn}ClO_4

When a fivefold excess of sodium 1-[2-(methylthio)ethyl] cyclohexane-thiolate (**12c**, prepared from **12a** by reaction with sodium metal) and **16**[ClO_4], both as suspensions in dry degassed tetraydrofuran, were mixed inside a Schlenck apparatus with an attached UV-visible cell, the salts dissolved slowly to give a clear, light orange solution with two strong UV bands at 316 and 370 nm. Upon irradiation of this solution at $-70\,^{\circ}C$ or at room temperature with a 200 W high-pressure mercury lamp through a 320 nm cut-off filter, both bands diminished with time and disappeared after approximately 1 h of irradiation. Analysis of the head-space gas by gas chromatography revealed the formation of about 15% of methane, based on nickel. Analysis of the liquid phase by gas liquid chromatography (glc) after workup demonstrated the formation of both the spirodisulfide **15** and the symmetric disulfide **13**.

Substitution of the sparingly soluble perchlorate by the more soluble triflate salt of **16**[OTf] and in situ generation of the thiolate **12d** by deprotonation of **12a** with the strong base BEMP[25] allowed for better control of the stoichiometry owing to the reaction between the two homogeneous solutions. Irradiation at room temperature, with or without a cut-off filter, and in the presence or absence of excess thiol **12a**, consistently gave methane and the two disulfides as the major products, although with different yields under varying conditions. In a series of parallel experiments, product analysis after different irradiation times (Table 1) showed that the yield of methane increased with irradiation time. On the other hand, the yield of spirodisulfide **15** was at its maximum when only 20% of methane (based on nickel) had been formed and diminished thereafter. This indicated that disulfide **15** is itself photolabile, which was confirmed by irradiation of the disulfide **15** alone under otherwise identical conditions (see Experimental Section).

Table 1. Results obtained with the system that exhibited the UV/Vis spectrum shown in Figure 1.[a]

	Ni catalyst added (c = [mM])	Thiolate (equiv)[b]	Thiol (equiv)[b]	Irrad. source[c]	Irrad. time [min]	Methane yield [%][b]	**15** yield [%][d]
1	**16**OTf (0.17)	**12d** (5)	**12a** (5)	Hg	4	20	84
2	**16**OTf (0.17)	**12d** (5)	**12a** (5)	Hg	60	48	14
3	**16**OTf (0.35)	**12b**/BEMP (5)	**12b** (5)	Hg	30	11[e]	n.d.[f]
4	**16**OTf (0.17)	**12d** (5)	**12a** (5)	Xe	290	6	43
5	**16**OTf (0.17)	**12d** (10)	**12a** (20)	Xe	650	16	13
6	$Ni(CF_3SO_3)_3$ (0.17)	**12d** (5)	**12a** (5)	Xe	740	2.5	83
7	$Ni(CF_3SO_3)_2$ (0.17)	**12d** (5)	none	Xe	305	12.5	30
8	**18** (0.17)	none	none	Ray	4	12	32
9	**18** (0.17)	none	**12a** (2)	Xe	250	4.5	82
Control experiments:							
10	**16**OTf (0.17)	**12d** (5)	**12a** (5)	none	0	not found	not found
11	none	**12d** (0.85 mM)	none	Xe	380	<0.5	not found
12	**16**OTf (0.17)	none	**12a** (5)	Hg	60	<0.5	not found
13	none	**12d** (0.85 mM)	none	Ray	180	<1.5	not found

[a] Conditions: in dry THF under vacuum, irradiation with stirring at RT. [b] Based on total Ni^{II}. [c] Hg: 200 W high-pressure mercury lamp with cut-off filter ≤ 320 nm; Xe: 150 W high-pressure xenon lamp with pyrex/H_2O filter ≤ 300 nm; Ray: Rayonett reactor with 350 nm lamps. [d] Yield based on the methane formed. [e] Glc/MS: $\geq 90\%$ CHD_3. [f] Not determined.

It was shown that the source of methane is indeed the methyl group bound to sulfur. The use of the *S*-trideuteromethyl derivative **12b** gave methane containing $>75\%$ CHD_3, as determined by GC/MS. In control experiments, in which either thiol **12a**, the thiolate generated in situ, or the nickel complex **16** were irradiated alone under otherwise identical conditions, only traces ($<0.4\%$) of methane and no cyclic disulfide were detected (Table 1).

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Identification, independent synthesis, and X-ray structure analysis of the photolytically active nickel thiolate species: When different nickel complexes were examined as potential catalysts in the newly discovered photo-induced reaction, we observed that plain nickel triflate reacted with the thiolate **12d** [generated from **12a** in situ with *tert*-butyliminodiethylaminodimethyl-perhydrodiazaphosphorine (BEMP)] or with preformed TEA-thiolate (TEA = tetraethylammonium) **12e** to give exactly the same characteristic UV-visible spectrum as observed with **16**. This demonstrated that the macrocyclic tetramethylcyclam ligand can not be a constituent of the photo-active species that exhibits this absorption spectrum. When the reaction between **16** and the thiolate was monitored by NMR spectroscopy in a vacuum-sealed reaction system with attached NMR tube and UV-visible cell, the signals of free tetramethylcyclam were indeed detectable in the ^{1}H NMR spectrum shortly after mixing the two solutions, and they increased with time in parallel with the development of the bands at 316 and 370 nm in the UV-visible spectrum. The same result was obtained with the (*R*,*R*,*S*,*S*)-stereoisomer **17**. Clearly, the thiolate had displaced the nickel ion from the macrocyclic complexes and a new nickel thiolate complex had been formed. Attempts to synthesize this complex by reaction of $NiCl_2 \cdot 6H_2O$ with thiol **12a** in methanol/triethylamine were successful and yielded a brown-orange, diamagnetic, oxygen-sensitive solid that was soluble in hexane; its UV-visible spectrum is shown in Figure 1 (solid trace). Recrystallization

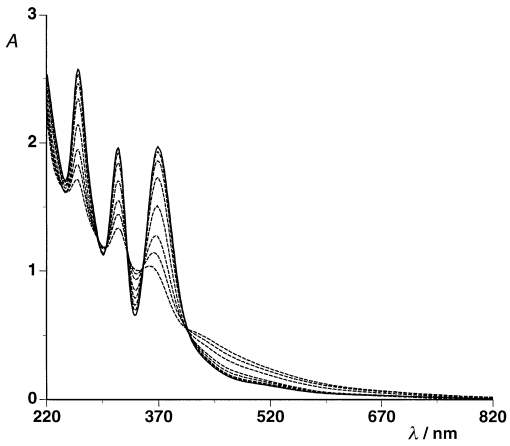


Figure 1. Solid line: UV-visible spectrum of complex **18** (0.23 mM in THF under vacuum). Broken lines: development of the spectrum during irradiation with a xenon lamp ($\lambda > 300$ nm, times of irradiation: 2, 15, 35, 75, 135, 190, 250 min).

from hexane gave crystals suitable for X-ray analysis, which confirmed the structure as the neutral square-planar complex **18** (Figure 2). In **18**, each of the two thiolate ligands is coordinated to the nickel through both, the thiolate and the methyl thioether sulfur atoms. Nickel alkyl thiolates are notoriously difficult to prepare because of their pronounced tendency to form refractory polynuclear aggregates. Only a small number of mononuclear complexes, mostly with tri- or tetradentate thioether/thiolate ligands bearing bulky alkyl substituents, have been described in the literature.[26–28] In complex **18**, the cyclohexane ring, which we incorporated into

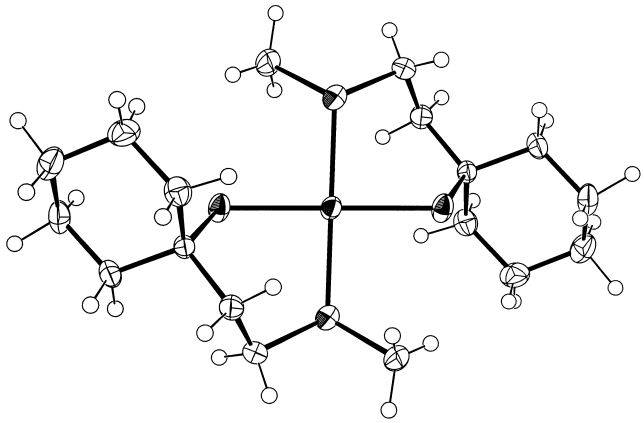


Figure 2. X-ray structure of bis{1-[2-(methylthio)ethyl]cyclohexanethiolato}nickel(II) (**18**). Plot generated with ORTEP.[38]

12 in order to sterically shield the sulfur from attack by Ni^I, is apparently bulky enough to prevent formation of bridged polynuclear aggregates and thus led to the fortuitous discovery of a new mononuclear, diamagnetic, nonpolar nickel(II) thiolate.

Subsequently, the experiments on the photo-induced cleavage of the methyl thioether were repeated with pure compound **18**. Qualitatively, the same results described above with complex **16** as the starting material were obtained (Table 1). In these experiments, no excess thiol **12a** was present during the irradiation, and hence the yield of methane was consistently 13–15% based on the nickel complex. Methane formation, as followed by head-space analysis at different irradiation times, showed the same kinetics as the disappearance of the UV bands at 316 and 370 nm (Figure 3).

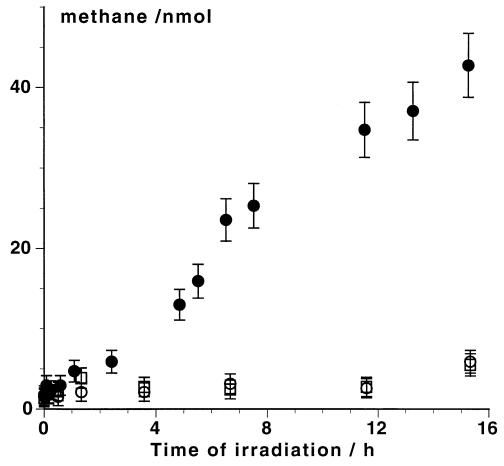
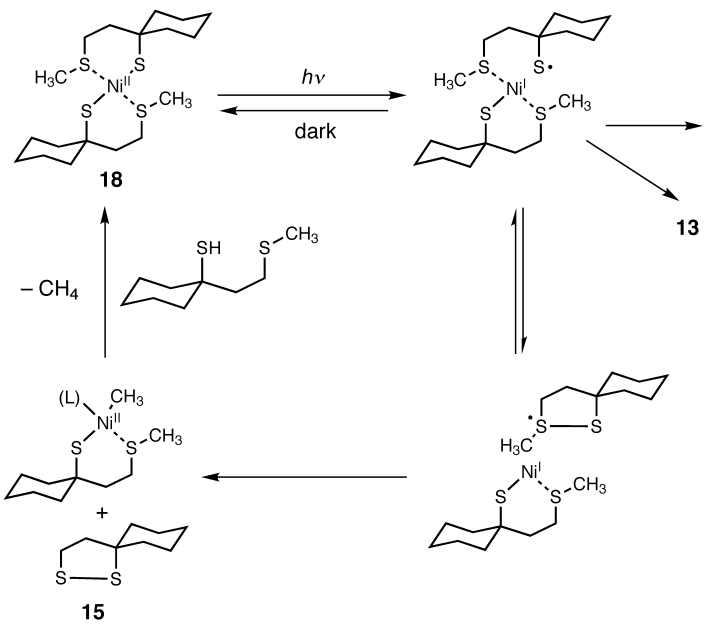


Figure 3. Kinetics of methane formation during irradiation with a xenon lamp ($\lambda > 300$ nm). a) $Ni^{II}(CF_3SO_3)_2$ (0.73mM), thiol **12a** (3.65 mM), BEMP (3.65 mM) (●); b) thiol **12a** (3.65 mM), BEMP (3.65 mM) (□); c) thiol **12a** (3.65 mM) (○). The total amounts of methane in the reactor are plotted versus the irradiation time.

In principle, the proposed mechanism would be compatible with a catalytic system as depicted in Scheme 4. In practice, however, we have not been able to obtain yields of methane larger than 100% (based on the nickel complex). No dark-



Scheme 4. Mechanistic interpretation of the photo-induced methane formation from complex **18**. Cyclisation of the photochemically generated thiyl radical to a sulfuranyl radical, followed by transfer of a methyl group to nickel(I). Competing side reactions of the thiyl radical reduce the methane yield and lead to irreversible destruction of the complex.

recovery of the UV bands at 316 and 370 nm, which should be expected for a regeneration of **18** according to Scheme 4, was observed when a large excess of free thiol **12a** was present. Either the kinetics of ligand exchange are too slow or, more likely, competing side reactions of the generated thiyl radical lead to irreversible destruction of the catalyst complex.

In situ generation of a more reactive species upon addition of excess thiolate to complex 18: Upon addition of a 10- to 20-fold excess of preformed tetraethylammonium thiolate **12e** to either nickel triflate or complex **18**, a new species with a UV-visible band at 420 nm was generated (see Figure 4, solid trace). This species proved to be extremely oxygen-sensitive,

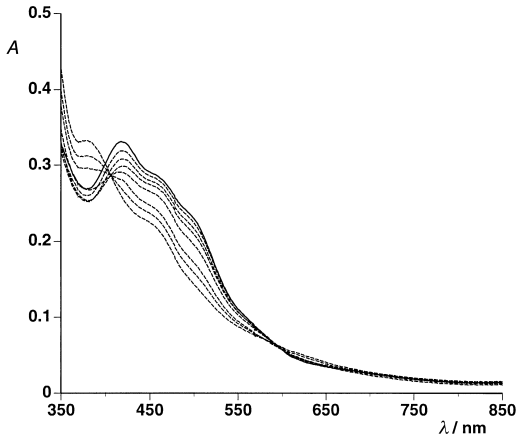


Figure 4. Solid line: UV-visible spectrum observed with nickel complex **18** (1.5 mM) in the presence of ten equivalents (15 mM) of thiolate **12e**. Broken lines: development of the spectrum during irradiation with a xenon lamp ($\lambda > 300$ nm, times of irradiation: 4, 9, 35, 21, 41, 86, 126, 186 min).

Table 2. X-ray data[a] for complex **18**.

formula	$C_{18}H_{34}NiS_4$
M_r	218.70
crystal system	monoclinic
space group	$P2_1/n$
a [Å]	8.975(2)
b [Å]	11.412(1)
c [Å]	9.984(2)
β [°]	92.002(1)
V [Å^3]	1021.9(3)
ρ_{calcd} [Mg m^{-3}]	1.422
μ [mm^{-1}]	5.143
Z	2
$F(000)$	468
crystal size [mm]	$0.10 \times 0.10 \times 0.10$
T [K]	180(2)
λ [Å]	1.54184
θ range	5.89 to 66.94
index ranges	$0 \le h \le 10$, $0 \le k \le 13$, $-11 \le l \le 11$
reflections collected	2044
independent reflections	1822 [R(int) = 0.0320]
absorption correction	PSI scan
transmission max/min	0.998/0.938
refinement method	full-matrix least-squares on F^2
goodness-of-fit (on F^2)	0.884
final R indices [$I > 3\sigma(I)$]	$R1 = 0.0292$, w$R2 = 0.0933$
R indices (all data)	$R1 = 0.0428$, w$R2 = 0.1054$
Largest diff. peak and hole [e Å^{-3}]	0.477; −0.387

[a] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-138626. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

but stable in solution if the glass reactors were sealed under high vacuum before mixing the previously well-degassed solutions of thiolate and nickel complex. When the addition of excess thiolate to complex **18** was monitored by NMR spectroscopy, the well-resolved ^{1}H NMR spectrum of diamagnetic **18** changed to a spectrum that exhibited large isotropic shifts and very broad lines as expected for a paramagnetic (high-spin) Ni^{II} complex. Although attempts to isolate and structurally characterize the species absorbing at 420 nm have not yet been successful, the observed paramagnetism and absorption spectrum point to a five- or six-coordinate complex with at least one axially coordinated thiolate.

In irradiation experiments, under the conditions used for complex **18**, the species absorbing at 420 nm proved to be more reactive than **18** (Figure 4 and Table 3).

Comparison of the reactivities of nickel complexes 18 and 19: During the course of our work, Tada and Masuzawa reported a similar, but bimolecular photo-induced reaction based on the nickel complex **19** and *p*-toluene thiolate/thioanisole reactants.[18] This prompted us to also investigate the activity of complex **19** with the bifunctional substrate **12a**. In addition, we were interested in checking whether the nickel ion in complex **19** would also be labile in the presence of an aliphatic thiolate. When excess thiolate **12d** was added to complex **19** under the same conditions described above, the UV-visible spectrum changed, and new absorption bands at 587, 460, and 340 nm, very similar to those described in ref. [18] were

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Table 3. Results obtained with the system that exhibits the UV/Vis spectrum shown in Figure 4.[a]

	Ni catalyst added (c = [mM])	Thiolate (equiv)[b]	Thiol (equiv)[b]	Irrad. source[c]	Irrad. time [min]	Methane yield [%][b]	Cyclic disulfide yield [%][d]
1	**16**OTf (0.17)	**12e** (60)	none	Xe	60	30	16
2	$Ni(CF_3SO_3)_2$ (0.73)	**12e** (10)	none	Xe	360	21	20
Control experiments:							
3	none	**12e** (7.3 mM)	none	Xe	360	< 4	not found
4	none	**12e** (15.0 mM)	none	none	0	< 0.1	not found

[a] Footnotes: see Table 1.

observed. However, no excess methane (compared with the traces found in the control reaction) and no disulfide **15** were formed upon irradiation of this solution in the rayonett with 350 nm light. Workup by reacidification led to the near-quantitative recovery of complex **19**. Hence, in contrast to **18**, complex **19** was stable towards decomplexation by thiolate, but inactive in methane formation.

Since the yield of methane had not been reported in the work of Tada and Masuzawa, we repeated their experiment with complex **19**, preformed sodium *p*-toluene thiolate, and thioanisole in degassed acetonitrile. Both methane and the mixed disulfide were found as described in ref. [18] (see Table 4). In our hands, however, the corresponding control reaction in the absence of the nickel complex consistently gave more methane and mixed disulfide than in the presence of the nickel complex **19** (Table 4).

Table 4. Results obtained with $[Ni^{II}\{(DOH)(DO)pn)\}]ClO_4$ (**19**)/thioanisole/sodium toluene *p*-thiolate.[a,d]

	Ni catalyst	Na toluene *p*-thiolate	Thioanisole	Irrad. source	Irrad. time [min]	Methane [mM] (yield [%])[b]	Mixed disulfide [mM][c]
1	**19** 0.5 mM	1.5 mM	1.5 mM	Ray	255	0.041 (0.27)	0.146
2	**19** 0.5 mM	1.5 mM	1.5 mM	Ray	255	0.216 (1.44)	0.674
Control experiments:							
3	none	1.5 mM	1.5 mM	Ray	255	10.89	0.539
4	none	1.5 mM	1.5 mM	Ray	255	16.05	0.716

[a] In acetonitrile under vacuum, irradiated with rayonett reactor (350 nm lamps). [b] Yield of CH_4 based on the Ni^{II} complex. [c] Phenyl *p*-tolyl disulfide. [d] Diphenyl disulfide, di-*p*-tolyl sulfide, and methyl *p*-tolyl sulfide were not detectable.

Conclusion

The formation of methane and, in particular, of spirodisulfide **15** upon irradiation of either nickel dithiolate **18** or the five- or six-coordinate species absorbing at 420 nm are consistent with the postulated reaction via a cyclic sulfuranyl radical. The moderate methane yields and the irreversible change in the UV-visible spectra upon irradiation indicate that no true catalytic turnover according to Scheme 4 takes place. Reaction channels, other than the postulated cyclization to the sulfuranyl radical followed by methyl transfer to nickel, evidently compete efficiently for the thiyl radicals formed upon irradiation. This interpretation is corroborated by the observed variations in methane yield under different conditions and by the degradation of complex **18** with a parallel increase of free thiol during irradiation, as observed by NMR spectroscopy.

The results presented here indicate that, once formed, a Ni^{I}/thiyl radical pair is reactive towards a methyl thioether functional group and gives methane and the disulfide. Our interpretation does not imply, however, that a state in which the thiolate of coenzyme B is coordinated to the Ni^{II} form of coenzyme F430 occurs in the catalytic cycle of the enzymatic reaction. If the X-ray structure of the enzyme in the inactive (Ni^{II}) $MCR_{ox1/silent}$ form is considered as a structural model for the active site, such a coordination would actually be impossible for geometric reasons. Scheme 2 reproduces the original mechanistic proposal as presented long before structural information on the active site was available.[15] While our experimental studies are consistent with steps B, C, and D in Scheme 2, the question of how the Ni^{I}/thiyl radical pair could be generated in vivo remains open. Experiments from our laboratory, which will be described elsewhere, in fact show that in homogeneous solution, coenzyme F430 is not reduced to the Ni^{I} form by aliphatic thiolates.

At present, we do not have an explanation for the different results obtained by Tada and Masuzawa, and by our laboratory for the blank experiments in which thioanisole and *p*-toluene thiolate were irradiated without nickel catalyst. Sulfur–carbon bonds in aliphatic methyl thioethers have bond dissociation energies that are approximately 4 kcal mol^{-1} higher than in aryl methyl sulfides such as thioanisole. In the experiments described here, the cleavage of the carbon–sulfur bond of aliphatic sulfide **12a** occurred only in the presence of nickel and after excitation of the Ni^{II} thiolate charge-transfer band. With thioanisole and *p*-toluene thiolate, the system used by Tada and Masuzawa, direct photolytic cleavage of the carbon sulfur–bond with light of wavelength > 300 nm occurred in the absence of nickel. Since methyl coenzyme M, the natural substrate of MCR, is an aliphatic thioether, the experiments with thiol **12** reported here constitute the most direct analogy to the enzymatic conversion found in homogeneous solution so far.

Whether a methyl-Ni^{II} species is indeed an intermediate in the observed reaction remains to be demonstrated. Methyl-Ni^{II}-L_n derivatives have been shown to dissociate to methane and Ni^{II}-L_n through protonation, whereas a free methyl radical would be expected to abstract a hydrogen atom from the solvent or from one of the reaction partners in the medium. Deuterium incorporation studies distinguishing between protonation and radical processes,[12] as well as laser flash photolysis experiments with the goal to directly observe the primary intermediates, are under way in our laboratory.

Experimental Section

General:[29] Air- and/or moisture-sensitive reactions were performed under N_2 in oven-dried glassware and with standard syringe/septa techniques. THF was triply distilled from potassium directly prior to use. Synthetic reactions were monitored by thin-layer chromatography (TLC) on precoated silica gel 60 F254 plates (thickness = 0.25 mm, Merck) and visualized with UV light and aqueous $KMnO_4$ (1%). Commercial reagents were used as received, unless otherwise stated. Products were purified by flash chromatography on silica gel 60 (particle size 40–63 μm, Merck). ^1H and ^{13}C NMR spectra were recorded on Varian Gemini (200 MHz, 300 MHz) spectrometers at 25 °C with TMS as the internal standard. UV/Vis spectra were recorded on a Uvikon 860 spectrophotometer (Kontron Instruments). Electron ionisation (EI) mass spectra were recorded at 70 eV on a VG TRIBRID spectrometer. Microanalyses were carried out by the microanalytical laboratory at the ETH, Zürich.

Materials: THF (J. T. Baker, >99%), CH_3CN (Riedel de Häen, min. 99.5%). [(*R*,*S*,*R*,*S*)-Ni^{II}(tmc)][$(CF_3SO_3)_2$](**16**) and [Ni^{II}{DOH(DO)pn}]-ClO_4 (**19**) were synthesized as described in the literature.[20, 30] BEMP (2-*tert*-butylimino-2-diethylamino-1,3-dimethyl-perhydro-1,3,2-diazaphosphorine) (>98%), thioanisole (>99.0%), and *p*-thiocresol (>98.0) were purchased from Fluka Chemie (Switzerland). Di-*p*-tolyl disulfide (>98%) and methyl *p*-tolyl sulfide (>99%) were purchased from Aldrich Chemie (Switzerland). Phenyl *p*-tolyl disulfide and di-*p*-tolyl sulfide were synthesized according to literature procedures.[31, 32]

1-(2-Bromoethyl)cyclohexanol (9): Synthesized in four steps (71% overall) according to a slightly modified procedure of Kabalka et al.[33]

1-[2-(Methylthio)ethyl]cyclohexanol (10a): A solution of 1-(2-bromoethyl)cyclohexanol (**9**) (1.08 g, 4.9 mmol) and CH_3SNa (0.67 g, 9.5 mmol) in methanol (10 mL) was stirred at room temperature for 16 h. After addition of saturated aqueous NaCl (5 mL), the reaction mixture was extracted with *t*BuOMe (10 mL). The organic layer was dried over $MgSO_4$ and evaporated to dryness to give a yellow oil (0.814 g). Chromatography on silica gel (ethyl acetate/hexanes 1:9) gave **10a** as a colorless oil (0.80 g, 94%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.61$ (t, 2H; H_2C8), 2.12 (s, 3H; H_3C9), 1.76 (t, 2H; H_2C7), 1.73 (s, 1H; OH), 1.7–1.2 (m, 10H; cyclohexyl-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 71.4$ (C1), 40.8 (C7), 37.5 (C2,C6), 28.3 (C8), 25.7 (C4), 22.1 (C3,C5), 15.5 (C9); IR ($CHCl_3$): $\tilde{\nu} = 3597$, 3442, 3002, 2935, 1448, 1174, 966 cm^{-1}; MS (EI): *m*/*z* (%): 174 (13) $[M]^+$, 176 (0.8) $[M+2]^+$, 156 (36), 141 (29), 109 (23), 108 (23), 99 (52), 81 (72), 61 (100).

1-[2-([D_3]Methylthio)ethyl]cyclohexanol (10b): This compüound was prepared as described for **10a** by using CD_3SNa (prepared from CD_3I and thiourea according to a slightly modified procedure of Urquhart et al.[34]).^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.61$ (t, 2H; H_2C8), 1.76 (t, 2H; H_2C7), 1.73 (s, 1H; OH), 1.7–1.2 (m, 10H; cyclohexyl-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 71.4$ (C1), 40.8(C7), 37.5(C2,C6), 28.3 (C8), 25.7 (C4), 22.1 (C3,C5); MS (EI): *m*/*z* (%):177 (21) $[M]^+$, 179 (1.2) $[M+2]^+$, 159 (45).

Benzyl 1-[2-(methylthio)ethyl]cyclohexyl sulfide (11a): $BF_3 \cdot OEt_2$ (0.45 mL, 3.58 mmol) was added dropwise to a solution of **10a** (0.31 g, 1.78 mmol) and benzylmercaptan (0.21 mL, 1.79 mmol) in $CHCl_3$ (2 mL). The reaction mixture was heated at reflux with a preheated oil bath (60 °C) for 10 min, then rapidly cooled with ice to 0 °C. After the dropwise addition of saturated aqueous $NaHCO_3$ (12 mL), the reaction mixture was extracted with ethyl acetate. The combined organic layers were washed with water, dried over Na_2SO_4, and evaporated to give an oil (0.51 g) that contained benzylmercaptan (18%), 2-(methylthio)ethyl-1-cyclohexene (24%), and **11a** (48%) according to glc. This crude product was directly used for the next step. For characterization, **11a** was purified by chromatography on silica gel (CH_2Cl_2/hexanes 1:9 → 1:1) to give pure **11a** (210 mg). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.35–7.15$ (m, 5H; Ar-H), 3.59 (s, 2H; $ArCH_2S$), 2.66 (m, 2H; H_2C8), 2.10 (s, 3H; H_3C9), 1.82 (m, 2H; H_2C7), 1.8–1.2 (m, 10H; cyclohexyl-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 138.3$, 128.9, 128.5, 126.8 (Ar), 50.6 (C7), 39.8 (C1), 36.2 (C2,C6), 31.7 ($ArCH_2S$), 28.9 (C8), 25.9 (C4), 21.8 (C3,C5), 15.8 (C9); MS (EI): *m*/*z* (%): 280 (0.8) $[M]^+$, 265 (0.4), 189 (100), 157 (6), 141 (8), 109 (54), 91 (39), 67 (33).

Benzyl 1-[2-([D_3]methylthio)ethyl]cyclohexyl sulfide (11b): This compound was prepared by the procedure described for **11a**. ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.35–7.15$ (m, 5H; Ar-H), 3.59 (s, 2H; $ArCH_2S$), 2.66 (m, 2H; H_2C8), 1.82 (m, 2H; H_2C7), 1.8–1.2 (m, 10H; cyclohexyl-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 138.3$, 128.9, 128.5, 126.8 (Ar), 50.6 (C7), 39.8 (C1), 36.2 (C2,C6), 31.7 ($ArCH_2S$), 28.9 (C8), 25.9 (C4), 21.8 (C3,C5); MS (EI): m/z (%): 283 (1.0) $[M]^+$, 285 (0.1) $[M+2]^+$, 265 (0.5), 192 (100), 160 (4.5).

1-[2-(Methylthio)ethyl]cyclohexanethiol (12a): Na (85 mg) was dissolved in liquid NH_3 (ca. 15 mL) at −78 °C to give a dark blue solution. A solution of the crude product from the preceding step (0.51 g containing 0.87 mmol **11a**) in Et_2O/EtOH (2:1) was added to the sodamide solution. Within 2 min the reaction mixture had turned colorless. After the addition of another portion of Na (8 mg), the solution stayed blue for 5 min. The reaction mixture was worked up by the dropwise addition of aqueous HCl (2N, 5 mL), evaporation of NH_3, and extraction with ethyl acetate. The organic layer was washed with water, dried over Na_2SO_4, filtered, and evaporated to dryness. After chromatography on silica gel (pentane/CH_2Cl_2 30:1), pure **12a** (0.31 g, 0.68 mmol, >98.5% by glc) was obtained as a colorless oil (overall yield from **10a**: 38.4%). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.67$ (m, 2H; H_2C8), 2.13 (s, 3H; H_3C9), 1.88 (m, 2H; H_2C7), 1.75–1.2 (m, 11H; cyclohexyl-H, SH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 49.2$ (C7), 45.0 (C1), 40.0 (C2,C6), 29.0 (C8), 25.8 (C4), 22.3 (C3,C5), 15.6 (C9); IR ($CHCl_3$): $\tilde{\nu} =$ 2998, 2933, 2858, 1448, 1102 cm^{-1}; MS (EI): *m*/*z* (%):190 (94) $[M]^+$, 192 (9) $[M+2]^+$, 175 (14), 157 (41), 141 (33), 109 (100), 81 (51), 67 (94).

1-[2-([D_3]Methylthio)ethyl]cyclohexanethiol (12b): This compound was prepared by the procedure described for **12a**. ^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.67$ (m, 2H; H_2C8), 1.88 (m, 2H; H_2C7), 1.75–1.2 (m, 11H; cyclohexyl-H, SH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 49.2$ (C7), 45.0 (C1), 40.0 (C2,C6), 29.0 (C8), 25.8 (C4), 22.3 (C3,C5); MS (EI): *m*/*z* (%):193 (74) $[M]^+$, 195 (7) $[M+2]^+$, 175 (10), 160 (30).

Tetraethylammonium{1-[2-(methylthio)ethyl]cyclohexanethiolate} (12e): Et_4NOH (1.05 mmol, 700 μL of a 25% sol. in MeOH; 1.5M) was added to **12a** (200 mg, 1.05 mmol) under N_2 and the solution was stirred for 30 min. The methanol was evaporated under vacuum and the residue dried at 10^{-2} Torr overnight to give the pure tetraethylammonium thiolate as a pale-yellow oil. ^1H NMR (300 MHz, CD_3OD): $\delta = 1.32$ (tt, H;*J* = 1.86, 7.26 Hz, 12H; 4-CH_3 of Et_4N^+), 1.20–1.7 (m, 10H; cyclohexyl-H), 1.79 (m, 2H; CH_2-7), 2.09 (s, 3H; CH_3-9), 2.79 (m, 2H; CH_2-8), 3.33 (q, H; *J* = 7.26 Hz, 8H; CH_2 of Et_4N^+); ^1H NMR (300 MHz, [D_8]THF): $\delta = 1.31$ (tt, *J* = 1.66; 7.26 Hz, 12H; 4-CH_3 of Et_4N^+), 1.20–1.62 (m, 10H; cyclohexyl ring-H), 1.68 (m, 2H; CH_2-7), 2.02 (s, 3H; CH_3-9), 2.90 (m, 2H; CH_2-8), 3.47 (q, *J* = 7.26 Hz, 8H; 4-CH_2 of Et_4N^+); ^{13}C NMR (75 MHz, CD_3OD): $\delta = 8.01$ (CH_3 of Et_4N^+); 15.89 (C9); 24.51 (C3,C5); 28.02 (C4); 31.44 (C8); 44.87 (C2,C6), 47.07 (C1), 47.50 (C7), 53.59 (CH_2 of Et_4N^+); ^{13}C NMR (50 MHz, [D_8]THF): $\delta = 4.33$ (CH_3 of Et_4N^+), 11.88 (C9), 20.65 (C3,C5), 24.77 (C4), 27.93 (C8), 41.65 (C2,C6), 43.02 (C1), 45.79 (C7), 49.72 (CH_2 of Et_4N^+).

Bis{1-[2-(methylthio)ethyl]cyclohexyl} disulfide (13): DMSO (1.8 mL, 25 mmol) and I_2 (13 mg, 51 μmol) was added to a solution of **12a** (0.811 g, 4.3 mmol) in dry benzene (10 mL). After stirring at room temperature for 18 h, the reaction mixture was purified by chromatography on silica gel (hexanes/CH_2Cl_2 4:1) to give **13** (0.771 g, 95%) as a colorless oil which crystallized upon standing at 5 °C.

1-[2-(Mercaptoethyl)cyclohexanethiol (14): Benzyl 1-[2-(methylthio)-ethyl]cyclohexyl sulfide (**11a**) (0.133 g, 0.47 mmol) was dissolved in liquid NH_3 (4 mL) at −40 °C. Addition of Na metal (30 mg, 1.3 mmol) gave a deep blue solution which slowly faded upon stirring. Further portions of Na (10 mg, 0.4 mmol after 1 h; 15 mg, 0.7 mmol after 1.5 h) were added. After the disappearance of the blue color, the ammonia was allowed to evaporate by warming to room temperature overnight. The residue was diluted with HCl (2N, 10 mL) and extracted with *t*BuOMe. The combined organic layers were washed with water, dried over $MgSO_4$, and evaporated to dryness. Chromatography on silica gel (hexane/CH_2Cl_2 9:1) gave a colorless oil (73 mg, 81%) that contained the dithiol and approximately 9% of the corresponding cyclic disulfide **15**.

1,2-Dithiaspiro[4.5]decane (15): The dithiol was oxidized to the spirodisulfide **15** as described above for **13**. Yield after chromatography on silica gel (hexanes): 81%. ^1H NMR (300 MHz, $CDCl_3$): $\delta = 3.18$ (t, 2H; CH_2-8), 2.09 (t, 2H; CH_2-7), 2.0–1.85 (m, 2H; cyclohexyl-H), 1.68–1.51 (m, 7H; cyclohexyl-H), 1.35–1.20 (m, 1H; cyclohexyl-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 66.9$ (C1), 47.5 (C7), 37.5 (C2,C6), 37.3 (C8), 25.8 (C4), 25.1 (C3,C5); MS (EI): *m*/*z* (%): 174 (35) $[M]^+$, 176 (3.2) $[M+2]^+$, 141 (2.7), 109 (84), 81 (19), 67 (100).

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Bis{1-[2-(methylthio)ethyl]cyclohexanethiolato}nickel(II) (18): Compound **12a** (123 mg, 100 μL, 0.648 mmol) was added dropwise to a stirred solution of $NiCl_2 \cdot 6H_2O$ (77 mg, 0.324 mmol) in MeOH (2 mL) under N_2 at RT. Upon addition of Et_3N (90.3 μL, 0.648 mmol), the greenish solution turned dark-brown. After stirring at room temperature for 40 min, the solvent was evaporated, and the dark-brown residue extracted with toluene. The extract was filtered and evaporated to dryness giving crude **18** (96.8 mg). Recrystallization from warm *n*-hexane gave dark brown prismatic crystals (47.3 mg, 0.108 mmol, 33 %), some of which were selected for X-ray analysis. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.392$ (m, 4H; CH_2-8), 2.263 (s, 6H; CH_3-9), 1.85 (m, 4H; CH_2-7), 1.80–1.05 (m, 20H; cyclohexyl ring-H); ^{1}H NMR (500 MHz, [D_8]THF): $d = 2.42$ (m, 4H;CH_2-8), 2.30 (s, 6H; CH_3-9), 1.89 (m, 4H; CH_2-7), 1.85–1.00 (m, 20H; cyclohexyl-H); ^{13}C NMR (125 MHz, [D_8]THF): $\delta = 43.31$ (C1), 42.49 (C7), 42.31 (C2,C6), 31.577 (C8), 26.48 (C4), 22.74 (C3,C5), 18.88 (C9); UV/Vis (THF): λ_{max} (ε) = 370 (8472), 316 (7889), 262 nm (10362); elemental analysis calcd (%) for $C_{18}H_{34}S_4Ni$: C 49.43, H 7.83, S 29.32; found C 49.40, H 7.73, S 29.34; MS (ESI): calcd for $C_{18}H_{34}S_4Ni$ $[M+H]^+$ 437.0974; found 437.1 (100 %), 439.0 (61.2 %), 441.0 (20.1 %).

X-ray structure determination of 18: From a crystal of size 0.10 × 0.10 × 0.10 mm, 2044 reflections were measured on an Enraf–Nonius CAD-4 diffractometer[35] with $Cu_{K\alpha}$ radiation (graphite monochromator, λ = 1.54184 Å). The structure was solved by direct methods with SHELXS-96.[36] The non-H atoms were refined anisotropically with SHELXL-97.[36] H-atoms were obtained from a difference Fourier map and refined isotropically. Drawings of the molecule were done with PLUTO, ORTEP.[37, 38] For final R values and experimental data see Table 2.

Photolysis experiments: For concentrations, irradiation times, and light sources in the individual experiments, see tables and legends to figures. Typically, the photolysis experiments were run in a pyrex-glass reactor consisting of two cylindrical, round-bottomed arms joined at the top (total volume ca. 20 mL). The outlet was equipped with a Young valve. A UV-quartz cell sealed to the reactor allowed for the UV/Vis spectral changes to be followed. Solutions of the Ni^{II} complexes (**16** or **19**) and the thiol–thioether substrates (**12** or thioanisole and *p*-thiocresol) were introduced into one of the side-arms, and a solution of the base BEMP was introduced into the other. The solutions in both arms were thoroughly degassed by four freeze-pump-thaw cycles (10^{-5} to 5×10^{-6} Torr), and, after closing the valve and warming to room temperature, the two solutions were mixed to give a total volume of liquid of approximately 3 mL. Photolysis was carried out with the system under the partial pressure of the solvent, except for the experiments in which the CH_4 formation was monitored during the irradiation, where the system was flushed with N_2 before starting the irradiation.

Photochemical irradiation: Photolysis experiments were carried out at room temperature with continuous stirring. The following lamps were used as excitation sources: a) high-pressure Xenon lamp (OSRAM XBO 150W/1); b) high-pressure Mercury lamp (OSRAM HBO 200 W); c) Rayonett photoreactor equipped with 350 nm lamps (Srinivasan–Griffin, The Southern New England Ultraviolet Company, USA). With the xenon or mercury lamps, the light beam was focused through a quartz lens and passed through a double-walled pyrex cut-off filter filled with circulating water. The irradiated area on the reaction vessel was approximately 3 cm^2. For irradiations with the rayonett (circular array of rod-shaped lamps), the reaction vessel was positioned in the center of the rayonett and cooled with a stream of air generated by a fan.

Product analysis: In order to determine the thiol (**12**), the spirodisulfide (**15**), and the disulfide (**13**) at the end of the photochemical irradiation, the reaction mixture was worked up as follows. A standard solution of *n*-octadecane (3.93 mM, 50 μL) was added as the internal standard. The solvent was evaporated with a slow stream of N_2 until the volume of the sample had been reduced to about one third. After the addition of *n*-hexane (5 mL) and aqueous HCl (10 mM, 3 mL) the two-phase system was vigorously stirred for 1 h. The organic phase was separated and passed through a silica gel microcolumn (100 mg, SiOH-Chromabond, Macherey–Nagel, Germany) and the column was eluted with *n*-hexane/EtOAc (4:1, 6 mL). The solvents were evaporated with a stream of N_2 and the residue dissolved in *n*-hexane (500 μL). Aliquots (2 μL) of this solution were injected into the capillary gas chromatograph for analysis.

Capillary gas-liquid chromatography (glc): Hewlett Packard HP-5890A; FID-detector; integrator: Hewlett Packard HP-3396A, H_2 = 140 KPa, synthetic air = 230 KPa, carrier = 200 KPa, column head-pressure = 50 KPa; column: Supelco 2-4034, stationary-phase: SPB-5 (bonded; poly [5 % diphenyl/95 % dimethylsiloxane]), 30 m, diameter = 0.25 mm, film thickness = 0.25 μm. Measurement conditions: injector temperature = 180 °C, detector temperature = 250 °C, initial temperature 60 °C (1 min), temperature gradient = from 60 to 250 °C (10 °C min^{-}), final temperature = 250 °C (30 min), volume of sample injected = 2 μL (split-mode). Retention times (min): **15**: 13.5, **12a**: 15.4, *n*-octadecane: 17.6, **13**: 44.6.

Determination of methane in the head-space by gas chromatography: At the end of the photochemical irradiation, the outlet of the Young valve was closed with a septum cap and the dead volume flushed with N_2 through two fine needles. The valve was then opened, and the vacuum was broken with N_2 through a fine needle. The head-space gas was sampled with a 250 μL gastight syringe (Hamilton—Bonaduz, Switzerland). Samples (50 μL) were injected into the gas-chromatograph (Carlo Erba Fractovap Mod. G1 with electrometer Mod. 180, FID-detector; N_2 = 0.8 kg cm^{-2}; H_2 = 0.6 kg cm^{-2}; synthetic air: 1 kg cm^{-2}; column: packed pyrex-column, l = 60 cm, diameter = 2 mm; stationary phase: Porapak Type R, 80–100 mesh, Waters Associates). The column was preconditioned overnight at 200 °C and held at 100 °C for the measurements. The response factors of the detector were determined from a calibration curve obtained with a methane/ethane (1:1) standard mixture. The distribution of methane between the gas phase and the solution was determined by a series of calibration experiments in which the concentration of CH_4 in the solution was measured relative to an internal standard (C_6H_6) by NMR spectroscopy. The distribution coefficient [μmol CH_4 per mL (gasphase) per μmol CH_4 per mL (THF solution)] was 1.05 ± 0.05 over two orders of magnitude in total CH_4. The yields given in the tables and in Figure 3 are corrected for the methane in solution and were calculated based on the total volume of the reactor as determined by filling with water and weighing.

Determination of [D_3]methane after irradiation of the Ni thiolate formed from 12b: The head-space gas was analysed by GC/MS and compared with samples of natural abundance methane and of trideuteromethane (synthesized from CD_3I [> 99.5 % D] by reduction with Zn powder in CH_3COOH). Using the ratio of *m*/*z* 19 to total ion current for the range *m*/*z* 14–20, and assuming that the reference sample was > 98 % CHD_3, the CHD_3 content of the head-space sample was calculated to be $> 75.2 \pm 5$ % (average over 3 samples). For the natural abundance sample, the peak at *m*/*z* = 19 was below the detection limit.

Degradation of 15 under irradiation: A degassed solution of spirodisulfide (**15**) in [D_8]THF was irradiated with the Xenon lamp in a sealed NMR tube and the decay of the signals of **15** with irradiation time was followed by ^{1}H NMR spectroscopy. *I* [% of the initial signal] (total irradiation time in min): 100 (0), 91.7 (20), 65.9 (60), 36.6 (120), 16 (180), 7.2 (270).

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