Metal-Mediated Synthesis of Thiol Derivatives: Synthesis and Reactivity of the Thiatitanacyclopropane Complex [CpTi(SCHCH₂CH₂S)]₂

Yujin Huang, T. T. Nadasdi, and Douglas W. Stephan*

Department of Chemistry and Biochemistry
University of Windsor
Windsor, Ontario, Canada N9B 3P4

The viability of metal-mediated syntheses of organic compounds containing heteroatoms has prompted the study of reactive early metal reagents. Fagan et al.[1] and others[2] have demonstrated that zirconocene and titanocene metallacycles are effective reagents for the synthesis of main group metallacycles, while more recently interest has focused on early metal–heteroatom double bonds as vehicles to main-group organic derivatives.[3] Heteroatom–metallacycles present an alternate class of potential reagents. Buchwald et al. have employed azazirconacyclopropanes to stoichiometrically prepare allylic amines.[4] Livinghouse and co-workers[5] have shown that the diminished steric constraints about the metal center in monocyclopentadienyltitanium systems permit the use of transient azatitanetines in the catalytic synthesis of dihydropyrrole and tetrahydropyridine derivatives. Related sulfur metallacycles have drawn less attention although zirconocene thioaldehyde derivatives[6,7] undergo alkene insertion and subsequent transmetalation with antimony halides to yield stibathiolanes.[8] Studies of the similar Ti–S species Cp₂Ti(SCH₂)-(PMe₃) were found to be much less useful from a synthetic perspective, as attempted insertion reactions were unsuccessful.[9] In this communication we describe a facile route to the monocyclopentadienylthiatitanacyclopropane [CpTi(SCHCH₂-CH₂S)]₂. This highly reactive species undergoes reactions with a variety of unsaturated organic substrates resulting in exclusive functionalization of the carbon α to sulfur, thus providing a metal-mediated synthesis of dissymmetric propanedithiolate derivatives.

We have previously described the facile synthesis of the compound CpTi(SCH₂CH₂CH₂S)Cl, **1**, from CpTiCl₃.[10] The reaction of **1** with MeLi proceeded smoothly at −78 °C to yield dark brown microcrystalline material **2**. ¹H NMR data for this product are consistent with loss of a hydrogen from the carbon β to Ti within the propanedithiolate moiety, yielding thiatitana-

cyclopropane species of empirical formula CpTi(SCHCH₂CH₂S), **2**. The compound **2** is also readily prepared in 81% yield from the reaction of **1** with AlMe₃. X-ray crystallographic data confirmed that **2** is a centrosymmetric dimer in the solid state.[11] The two Ti centers adopt distorted square-pyramidal coordination spheres in which the thiolato–sulfur atoms bridge the two metal centers. A second sulfur atom, the carbon α to it, and a cyclopentadienyl ring complete the coordination spheres of each Ti center. The ring strain in the thiatitanacyclopropane ring as evidenced by the S–Ti–C angle of 46.1(1)°, together with the known lability of dimeric Ti thiolate-bridged complexes, foreshadows the reactivity described below.

Reaction of **2** with benzophenone proceeded smoothly at 25 °C in THF to give product **3** which was subsequently isolated in 90% yield. ¹H and ¹³C{¹H} NMR data were consistent with the formation of an addition product in which benzophenone inserts into the Ti–C bond in **2** forming the mononuclear product CpTi-(SCH(CPh₂O)CH₂CH₂S), **3**. Furthermore, the NMR data implied that the alkoxide carbon adopts a position axial to the six-membered ring formed by the chelating dithiolate moiety. This conformation was subsequently confirmed by X-ray crystallographic study of **3**.[11]

In a similar manner compound **2** reacted cleanly with imines. Reaction with PhN=CH(C₆H₄-p-OMe) at 25 °C in THF yielded the purple-black product **4** in 80% yield. From NMR data, **4** contained a 70:30 mixture of the two diastereomers, **4a** and **4b**, with formula CpTi(SCH(CH(C₆H₄-p-OMe)NPh)CH₂CH₂S), which were derived from imine insertion into the Ti–C bond of **2**. A 9% NOE between the methine protons indicated a *trans* disposition and thus the *erythro* geometry of the S₂N ligand in the major isomer **4a**. Crystals of the *erythro* isomer were obtained from the reaction mixture and characterized by X-ray crystallography.[11] The structure of **4a**, similar to **3**, is best described as a "three-legged piano stool". In the case of **4a**, the planarity at N and the Ti–N distance of 1.939(9) Å are typical of early metal amides.[12] Reaction of **2** with PrN=CHPh affords the similar species CpTi(SCH(CHPhNPr)CH₂CH₂S), **5**, in 87% yield. The observation of a 6% NOE between the methine protons and a 5% NOE between the methine imine proton and the axial proton of the γ-methylene group are consistent with the exclusive formation of the *threo* isomer. This is in contrast to the geometry of **4a**, and investigations of factors controlling stereoselectivity are ongoing.

Dicyclohexylcarbodiimide reacted with **2** in a similar fashion at 25 °C to yield a purple-black product. This species, formulated as CpTi(SC=(C(NHCy)NCy)CH₂CH₂S), **6**, was isolated in 93% yield. Enolization of the methine proton to the exocyclic N was confirmed by the presence of the amido ¹H NMR resonance, and the resulting C=C double bond was established by ¹³C NMR data. A similar enolization was observed in the product of nitrile addition to zirconocene thioaldehyde.[4] Structural data for **6**[11] revealed that in addition to the cyclopentadienyl ring, the nitrogen, and two sulfur atoms, the enolic double bond also coordinates to Ti as evidenced by the Ti–C(8) and Ti–C(9) distances of 2.27(1) and 2.47(1) Å, respectively, and is consistent with the Lewis acidic nature of the Ti center.

Acidolysis of the above insertion products permits the utilization of this chemistry in the formation of propanedithiol derivatives. Treatment of **3** with dry gas HCl in ether resulted in the liberation of the tridentate ligand HSCH(Ph₂COH)CH₂CH₂SH, **7**, and

(1) (a) Fagan, P. J.; Nugent, W. A. *J. Am. Chem. Soc.* **1988**, *110*, 2310. (b) Fagan, P. J.; Ward, M. D.; Caspar, J. V.; Calabrese, J. C.; Krusic, P. J. *J. Am. Chem. Soc.* **1988**, *110*, 2981.
(2) Doxsee, K. M.; Dhen, G. S.; Knobler, C. B. *J. Am. Chem. Soc.* **1989**, *111*, 9129.
(3) (a) Walsh, P. J.; Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1988**, *110*, 8729. (b) Walsh, P. J.; Carney, M. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1991**, *113*, 6343. (c) Walsh, P. J.; Hollander, F. J.; Bergman, R. G. *J. Organomet. Chem.* **1992**, *428*, 13. (d) Parkin, G.; Bercaw, J. E. *J. Am. Chem. Soc.* **1989**, *111*, 391. (e) Carney, M. J.; Walsh, P. J.; Hollander, F. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1989**, *111*, 8751. (f) Whinnery, L. L.; Hening, L. M.; Bercaw, J. E. *J. Am. Chem. Soc.* **1991**, *113*, 7575. (g) Carney, M. J.; Walsh, P. J.; Bergman, R. G. *J. Am. Chem. Soc.* **1990**, *112*, 6426. (h) Hou, Z.; Stephan, D. W. *J. Am. Chem. Soc.* **1992**, *114*, 10088. (i) Hou, Z.; Breen, T. L.; Stephan, D. W. *Organometallics*, **1993**, *12*, 3158. (j) Cummins, C. C.; Schrock, R. R.; Davis, W. M. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 756. (k) de With, J.; Horton, A. D. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 903.
(4) Buchwald, S. L.; Watson, B. T.; Wannamaker, W. M.; Dewan, J. C. *J. Am. Chem. Soc.* **1989**, *111*, 4486.
(5) McGrane, P. L.; Jensen, M.; Livinghouse, T. *J. Am. Chem. Soc.* **1992**, *114*, 5459.
(6) Buchwald, S. L.; Nielsen, R. B.; Dewan, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 1590.
(7) Buchwald, S. L.; Nielsen, R. B. *J. Am. Chem. Soc.* **1988**, *110*, 3171.
(8) (a) Buchwald, S. L.; Fisher, R. A.; Davis, W. M. *Organometallics* **1989**, *8*, 2082. (b) Fisher, R. A.; Nielsen, R. B.; Davis, W. M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1991**, *113*, 165.
(9) Park, J. W.; Henling, L. M.; Schaefer, W. P.; Grubbs, R. H. *Organometallics* **1990**, *9*, 1650.
(10) Nadasdi, T. T.; Huang, Y.; Stephan, D. W. *Inorg. Chem.* **1993**, *32*, 347.

(11) Crystal data: **2**, *P*2₁/*n*, *a* = 8.233(4) Å, *b* = 8.889(1) Å, *c* = 12.686-(3) Å, *β* = 103.61(3)°, *V* = 902.3(5) Å³, *Z* = 4; **3**, *P*1, *a* = 10.817(2) Å, *b* = 11.042(2) Å, *c* = 8.909(2) Å, *α* = 94.21(1)°, *β* = 111.35(1)°, *γ* = 80.15-(1)°, *V* = 1056.0(3) Å³, *Z* = 2; **4a**, *P*1, *a* = 11.759(4) Å, *b* = 12.900(3) Å, *c* = 8.786(2) Å, *α* = 91.51(2)°, *β* = 111.98(2)°, *γ* = 85.66(2)°, *V* = 1232.4(6) Å³, *Z* = 2; **6**: *P*2₁/*n*, *a* = 9.766(4) Å, *b* = 11.031(2) Å, *c* = 20.711(3) Å, *β* = 93.97(2)°, *V* = 2226(1) Å³, *Z* = 4.
(12) Dick, D. G.; Rousseau, R.; Stephan, D. W. *Can. J. Chem.* **1991**, *69*, 357 and references therein.

Scheme 1
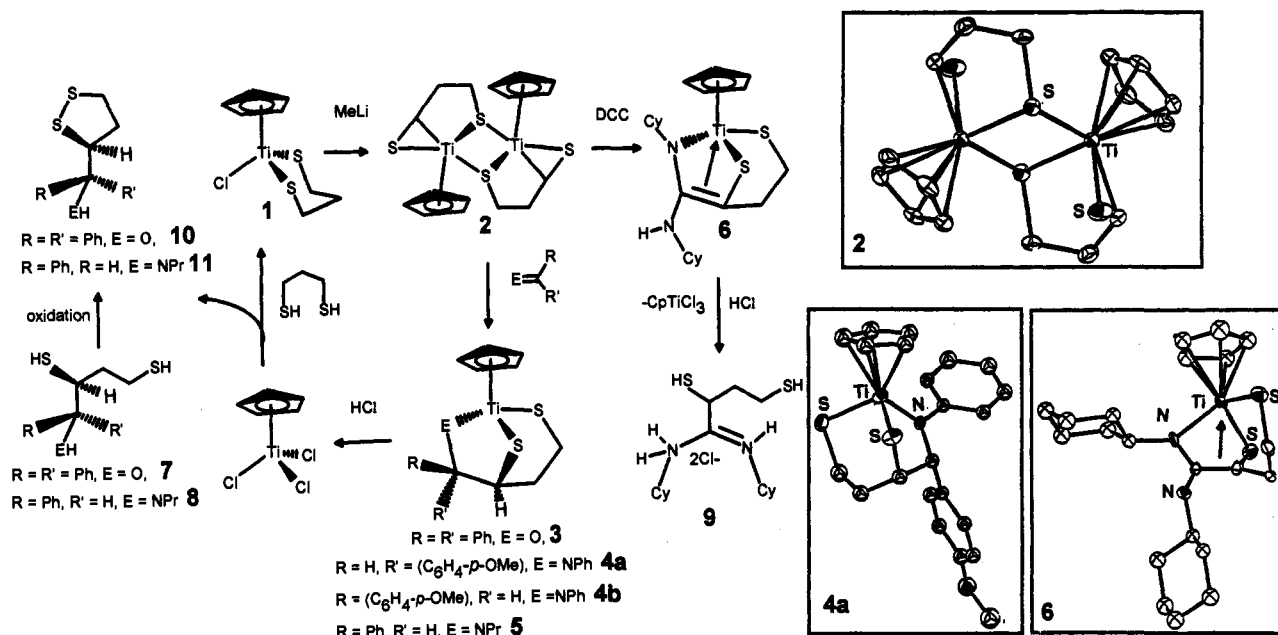
the regeneration of CpTiCl₃ (Scheme 1). Extraction of the products into benzene and/or CH₂Cl₂ and subsequent chromatography on alumina afforded 7 in 88% yield. In a similar fashion, 5 gave the amino dithiol *threo*-HSCH(CH(Ph)NPrH)CH₂CH₂-SH, 8, in 80% yield, while acidolysis of 6, and subsequent hydrolysis of the liberated organic product afforded (HSCH-(C(NCy)NHCy)CH₂CH₂SH)·2HCl, 9·2HCl, in 90% isolated yield. Compounds 7 and 8 underwent facile oxidation by air or I₂ to give the related disulfide derivatives 10 and 11, respectively. Recovery of CpTiCl₃ from aqueous acidolysis of 5 was modest (42%). In contrast, treatment of 6 with ethereal HCl generates CpTiCl₃ and 9·2HCl, permitting a facile separation and recovery of the titanium starting material in 85% yield.

The study of the reactivity of 2 is continuing with a view toward synthetic applications. Preliminary results have established that while the species CpTiCl₂(SCH₂Ph), 12, is unstable with respect to disproportation it does reacts with *t*-BuLi and subsequently with PMe₃ to generate the thiatitanacyclopropane complex CpTiCl(SCHPh)(PMe₃), 13.[13] These results augur well for general applications of this chemistry in the functionalization of thiols. Other system modifications are being explored, including those aimed at the production of optically pure thiol derivatives.

Supplementary Material Available: Tables of NMR, analytical and crystallographic data, positional, thermal and hydrogen atom parameters, selected bond distances and angles (33 pages); tables of observed and calculated structure factors (23 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(13) Compound **12** was isolated from the reaction of NaSCH₂Ph and CpTiCl₃ with subsequent recrystallization from pentane. This compound undergoes ligand disproportionation on standing in solution for 24 h. However, reaction of **12** with *t*-BuLi in THF was followed by addition of 1 equiv of PMe₃ and generates **13** quantitatively. However this species also proved to be thermally unstable in solution over a 24-h period.