HETEROCYCLES, Vol. 57, No. 12, 2002, pp. 2373 - 2381, Received, 1st August, 2002

PREPARATION AND STRUCTURE OF 3,4,8,9-TETRACHLORO-2,5,7,10-TETRAHYDRO[1,6]DITHIECINE

David L. Eaton, John P. Selegue*, John Anthony, and Brian O. Patrick

Department of Chemistry, University of Kentucky, Lexington, KY, 40506-0055, USA, selegue@uky.edu

Abstract – The reaction of *Z*-1,4-dibromo-2,3-dichlorobut-2-ene (**1**) with sodium sulfide leads to 3,4,8,9-tetrachloro-2,5,7,10-tetrahydro[1,6]dithiecine (**2**) as the principal product, rather than the anticipated 3,4-dichloro-2,5-dihydrothiophene (**3**). Compound (**2**) was characterized spectroscopically and its structure determined by X-Ray crystallography.

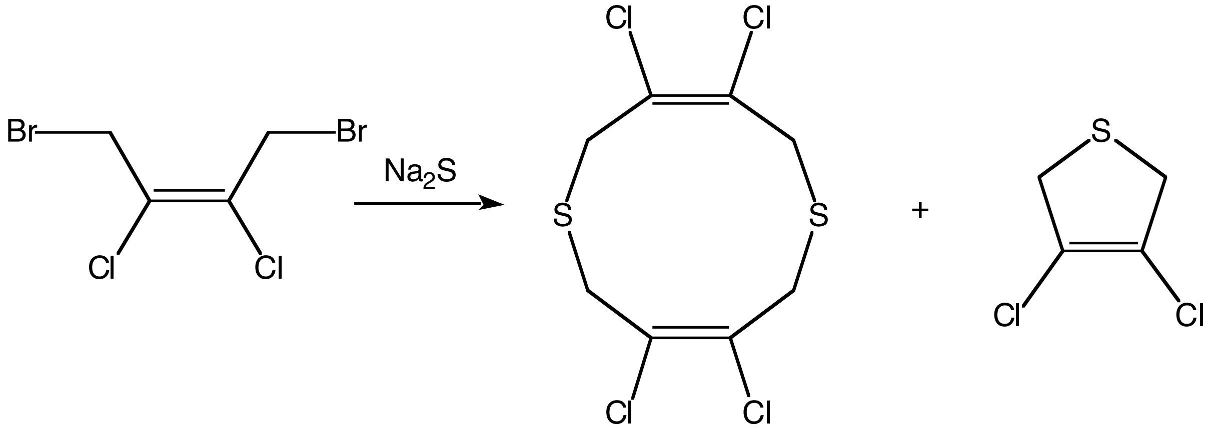
INTRODUCTION

In the course of a study of organometallic heterocycles, we desired a 3,4-dialkynyl-2,5-dihydrothiophene intermediate. A logical approach to such a compound is *via* Sonogashira coupling[1] of an alkyne with 3,4-dichloro-2,5-dihydrothiophene (**3**, Scheme 1). However, attempts to prepare **3** led instead to 3,4,8,9-tetrachloro-2,5,7,10-tetrahydro[1,6]dithiecine (**2**) in good yield. We report here the synthesis, spectroscopic characterization and crystal structure of **2**.

EXPERIMENTAL SECTION

General Procedures. Operations were carried out under a dry, oxygen-free nitrogen atmosphere. NMR spectra were recorded on Varian Gemini (^{1}H at 200 MHz), or INOVA (^{1}H at 400 MHz) spectrometers. ^{1}H and ^{13}C chemical shifts are referenced to solvent and reported in ppm downfield from TMS. *Z*-2,3-Dichlorobut-2-ene-1,4-diol was prepared by the published method.[2, 3] Other reagents were used as received from standard commercial sources. TLC was carried out on Merck Silica Gel 60 thin layer plates. Silica gel chromatography was performed on Fisher silica gel (170-400 mesh).

***Z*-1,4-Dibromo-2,3-dichlorobut-2-ene** (**1**)**.** To a 250-mL round-bottom flask with a magnetic stir bar were added dichloromethane (60 mL) and triphenylphosphine (15.7 g, 60.0 mmol). The flask was cooled to 0 °C in an ice bath. Bromine (3.09 mL, 9.60 g, 60.0 mmol) was added dropwise *via* syringe. Ten minutes later, *Z*-2,3-dichlorobut-2-ene-1,4-diol (3.14 g, 20.0 mmol) was added in one portion and the



1 2 3

Scheme 1

flask was allowed to warm to room temperature. The solution was stirred for one hour, during which time the solution became clear. The solvent was removed *in vacuo*, and the residue dissolved in hexanes. The solution was eluted through a thin pad of silica gel with hexane. The hexane was removed *in vacuo* to yield **1** (5.24 g, 92.6%) as a yellow oil. **Caution: The product is a potent lachrymator and is used immediately**.

3,4,8,9-Tetrachloro-2,5,7,10-tetrahydro[1,6]dithiecine (**2**). **Method 1.** Ethanol (80 mL) was added to a 250-mL round-bottom flask containing **1** (5.24 g, 18.5 mmol). Sodium sulfide nonahydrate (4.8 g, 20 mmol) was added. After the mixture was heated at reflux overnight, GC/MS analysis revealed a single peak with m/z = 308. The solution was allowed to cool. Saturated brine was added, and the precipitate collected and washed with dichloromethane. The off-white precipitate was recrystallized from boiling benzene to yield **2** (2.01 g, 70%) as translucent, hexagonal prisms.

Method 2. Compound (**1**) (5.7 g, 20 mmol) was dissolved in benzene (60 mL) in a 250-mL round-bottom flask. After a solution containing sodium sulfide nonahydrate (4.8 g, 20 mmol) and two drops of Aliquat 336 in water (60 mL) was added, the mixture was stirred at room temperature for one hour then heated to reflux for three hours. After cooling to room temperature, the benzene layer was separated. The aqueous layer was washed with benzene and the combined benzene solution was analyzed by GC/MS to reveal two components, with m/z = 154 and 308. The product was isolated by removal of solvent *in vacuo*, followed by washing the oily residue with dichloromethane to yield **2** (1.6 g, 54%) as an off-white solid. GC/MS: M^+ for $^{12}C_8{}^1H_8{}^{32}S_2{}^{35}Cl_4$, m/z 308, isotope pattern matches calculated pattern. ^1H NMR (400 MHz, C_6D_6) δ 3.07 (s, 8H). ^{13}C (100 MHz, C_6D_6): δ_C 32.4 (CH_2), 128.4 (CCl). mp 190 °C (decomp). Anal. Calcd for $C_8H_8Cl_8S_2$: C 30.99, H 2.60. Found: C 30.62, H 2.17.

X-Ray crystal structure of 2. X-Ray-quality single crystals were obtained from benzene. A transparent, hexagonal prism was mounted on a glass fiber with epoxy. Data were collected at room temperature on a Nonius KappaCCD diffractometer. The main programs used were SCALEPACK for data reduction, SORTAV for absorption correction, SHELXS-86 for structure solution and SHELXL-93 for refinement. Data collection and crystal parameters are listed in Table 1. Hydrogen atoms were placed in geometrically calculated positions. Routine structure solution and refinement led to the structural parameters listed in Table 2.

RESULTS AND DISCUSSION

There is substantial precedent for the formation of 2,5-dihydrothiophenes *via* reactions of unsaturated 1,4-dihalides with sources of sulfide. Early reports of reactions of *Z*-1,4-dihalo-2-butene with sulfide were discouraging, resulting in less than 10% 2,5-dihydrothiophene along with uncharacterized oligomers and polymers.[4, 5] Everhardus *et al.* later improved the yield of 2,5-dihydrothiophene up to 38%, but also noted the formation of polymers and other byproducts.[6] In a recent review,[7] Shvekhgeimer cites several other preparative methods for dihydrothiophenes, including the metal-catalyzed ring-closing metathesis of diallyl sulfide.[8-11] We previously had good success in preparing 2,5-dihydrobenzo[3.4-c]thiophene[12, 13] by reacting 1,2-bis(chloromethyl)benzene with sodium sulfide under phase-transfer conditions,[14] so we tried a similar approach to 3,4-dichloro-2,5-dihydrothiophene (**3**).

Z-1,4-Dibromo-2,3-dichlorobut-2-ene (**1**) was prepared by treating *Z*-2,3-dichlorobut-2-ene-1,4-diol[2, 3] with triphenylphosphine and bromine in dichloromethane. Compound **1**, a volatile oil and a potent lachrymator, has been previously reported as part of a mixture of *E* and *Z* isomers.[15] GC/MS monitoring of the reaction of **1** with sodium sulfide (Scheme 1), initially in DMF, showed rapid consumption of **1** and formation of a product with a GC/MS (M+ for $^{12}C_4{}^{1}H_4{}^{32}S_1{}^{35}Cl_2$, m/z 154, isotope pattern matches calculated pattern) consistent with 3,4-dichloro-2,5-dihydrothiophene (**3**). Workup led to **3** as a brown oil in very low yield, never more than 30%, that we characterized only by its NMR spectrum (^{1}H NMR (200 MHz, $CDCl_3$) □3.06 (s)). We noticed an insoluble, flaky residue that resisted dissolution in organic solvents as well as in acidic or basic aqueous solution. We suspected that the reaction might be producing a polymer, but GC/MS revealed a component with m/z twice that of **3**. By working under phase-transfer conditions in benzene/water, the yield of dimer was increased to about 50%. In refluxing ethanol, the yield of **2** was increased to about 70%.

Although **2** is very insoluble in most solvents, it dissolves in boiling benzene. Upon cooling, the solution yielded millimeter-sized, hexagonal plates. X-Ray diffraction revealed the 10-membered cyclic structure of 3,4,8,9-tetrachloro-2,5,7,10-tetrahydro[1,6]dithiecine. Structural diagrams of **2** are shown in Figure 1, and crystallographic information is in Tables 1 and 2. Compound (**2**) is the first uncomplexed 2,5,7,10-tetrahydro[1,6]dithiecine to be structurally characterized. The molecule resides on a crystallographic inversion center. The S1-S1A distance is 5.356(1) Å. The four alkene carbon atoms (C3, C4, C3A and C4A) are crystallographically coplanar, and the two sulfur atoms (S1 and S1A) lie only 0.009(5) above and below this plane. The planes of the two alkenes (Cl1-Cl2-C3-C2-C1A and Cl1A-Cl2A-C3A-C2A-C1) are crystallographically parallel to one another and inclined 44.81(6)° from the C3-C4-S1A-C3A-C4A-S1. The sulfur atoms lie 1.398(2) Å and 1.362(2) Å from the alkene planes. As a result, two methylene carbon atoms, C1 and C2A, and two chlorine atoms, Cl1 and Cl2, lie respectively 0.878(4) Å, 0.0877(4) Å, 1.038(3) Å, and 1.020(4) Å below the C3-C4-C3A-C4 plane, while the other two methylene carbon atoms, C1A and C2, and two chlorine atoms, Cl1A and Cl2A, lie the corresponding distances above that plane. This unusual ring puckering is similar to that observed in the structure of the 2,5,7,10-tetrahydro[1,6]dithiecine ligand in its polymeric $(HgCl_2)_2$ complex.[16, 17] Benzo analogs of **2**, i.e. 2,11-dithia[3,3]orthocyclophanes, display a similar *anti* geometry.[18-23] The alkyne analog of **2**, 1,6-dithiacyclodeca-3,8-diyne, adopts a chair geometry with one sulfur atom above and the other below the mean plane of the ring,[24, 25] whereas the saturated ring 1,6-dithiacyclodecane displays a "boat-chair-boat" geometry with C_{2h} symmetry.[26] Tables of crystallographic details, atomic coordinates and displacement parameters, bond distances and angles, intermolecular contact distances, structure factors and a crystallographic information file (CIF) for the structure of **2** have been deposited with the Cambridge Crystallographic Data Centre.[27]

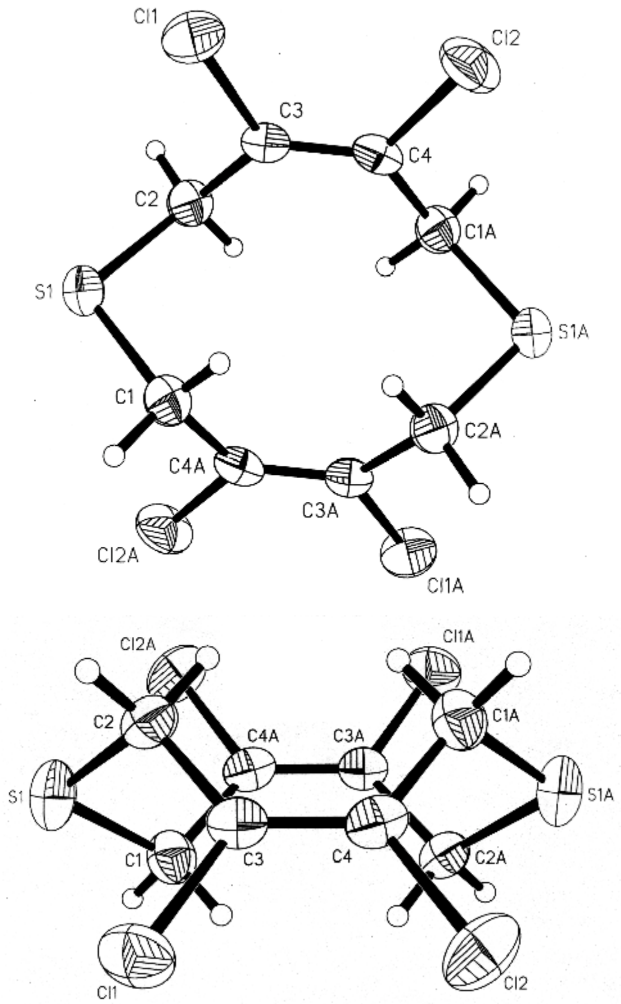


Figure 1. SHELXL-93 perspective drawings of **2**. The ellipsoids correspond to 50% probability contours of atomic displacement.

Table 1. Selected Crystal Data and Details of the Structure Determination of 3,4,8,9-Tetrachloro-2,5,7,10-tetrahydro[1,6]dithiecine (**2**)

Crystal Data	
Empirical Formula	$C_8H_8Cl_4S_2$
Formula Weight	310.08
Crystal System	Monoclinic
Space group	$P2_1/c$
a, b, c [Å]	7.685(2), 7.1270(10), 10.749(2)
α, β, γ [°]	90, 90.17(3), 90
Z	2
Crystal Size [mm^3]	0.11 x 0.26 x 0.32
Data Collection	
Temperature (K)	293
Radiation [Å]	$Mo_{K\alpha}$, 0.71073
Theta Min-Max [°]	3.4, 27.9
Data Set	-9 to 9; -9 to 0; -14 to 13
Tot., Uniq. Data, R(int)	2521, 1358, 0.019
Observed data [I > 2.0 sigma(I)]	1214
Refinement	
N_{ref}, N_{par}	1358, 65
R, wR, S	0.0307, 0.0778, 1.10
Max. and Av. Shift/Error	0.00, 0.00
Min. and Max. resd. dens. [e/$Å^3$]	-0.40, 0.34

Table 2. Selected Bond Distances and Angles of 3,4,8,9-Tetrachloro-2,5,7,10-tetrahydro[1,6]dithiecine (**2**)

Atoms	Distance (Å)	Atoms	Angle (°)
Cl1–C3	1.7381(17)	C1–S1–C2	101.63(10)
Cl2–C4	1.734(2)	S1–C1–C4A	115.28(15)
S1–C1	1.809(2)	S1–C2–C3	114.69(14)
S1–C2	1.805(2)	Cl1–C3–C2	113.16(13)
C1–C4A	1.494(3)	Cl1–C3–C4	120.89(16)
C2–C3	1.494(3)	C2–C3–C4	125.91(17)
C3–C4	1.326(3)	Cl2–C4–C3	120.67(16)
		Cl2–C4–C1A	113.62(16)
		C1A–C4–C3	125.64(19)

The NMR spectra of **2** display a single ^{1}H NMR resonance at δ 3.07 and two ^{13}C NMR resonances at δ_C 32.4 and 128.4 for the CH_2 and CCl carbons. The single ^{1}H resonance particularly indicates that the fluxional ten-membered ring is at its high-temperature limit at room temperature. Feigenbaum and Lehn observed that the vinyl-deuterated compound d_4-2,5,7,10-tetrahydro[1,6]dithiecine also displays a high-temperature limiting ^{1}H NMR spectrum at 33.0 °C, which coalesces at –24 °C and shows an AB pattern with $\Delta\nu_{AB}$ = 43.1 Hz at –57 °C.[28, 29] Unfortunately, the low solubility of **2** prevents us from collecting low-temperature NMR spectra for comparison.

There are few well-characterized 2,5,7,10-tetrahydro[1,6]dithiecines. The mixtures of oligomers and polymers mentioned in early reports of reactions of *Z*-1,4-dihalo-2-butenes with sulfide probably contain the poorly soluble cyclic dimer.[4-6] Eglinton specifically mentioned that a reaction of ammonium sulfide with *Z*-1,4-dichloro-2-butene gave an intractable mixture of " malodorous oils."[24] More successful is the partial hydrogenation of 1,6-dithiacyclodeca-3,8-diyne, which gives 2,5,7,10-tetrahydro[1,6]dithiecine in reasonable yield.[24] Feigenbaum and Lehn used this method to prepare 2,5,7,10-tetrahydro[1,6]dithiecine for their NMR study.[28, 29] The synthesis and chemistry of several benzo-annellated 2,5,7,10-tetrahydro[1,6]dithiecines have been studied.[18-23, 30-32] Gleiter *et al.* also studied the chemistry of related 1,6-dithiacyclodeca-3,8-diynes.[25, 33-35] We believe that the high isolated yield of a tetrahydro[1,6]dithiecine (**2**) rather than a 2,5-dihydrothiophene (**3**) can be attributed to the reluctant closure of the moderately strained five-membered alkene ring of **3** compared to the rather unstrained ten-membered ring of **2**. The geometry of the *Z*-dichloroalkene linkage apparently overcomes entropic constraints, favoring cyclization rather than oligomerization. The low solubility and high crystallinity of **2** lead to its isolation in high yield. The present result helps to explain the low yields of 2,5-dihydrothiophenes reported for previous reactions of *Z*-1,4-dihaloalkenes with sulfide.[4-6, 24]

CONCLUSION

Although the reaction of sulfide with *Z*-1,4-dibromo-2,3-dichlorobut-2-ene (**1**) does not provide the facile route to 3,4-dichloro-2,5-dihydrothiophene (**3**) that we hoped for, the reaction gives a high yield of 3,4,8,9-tetrachloro-2,5,7,10-tetrahydro[1,6]dithiecine (**2**) after a simple workup. Compound (**2**) may be a useful starting material for other 2,5,7,10-tetrahydro[1,6]dithiecines if its low solubility can be overcome. In particular, the chlorides may be amenable to substitution with solubilizing groups.

ACKNOWLEDGMENT

We thank the National Science Foundation (MRSEC DMR-9809686) and the US Department of Energy (DE-FG02-00ER45847 and subcontract 10186-00-23) for partial support of this research, the University of Kentucky for a Kentucky Opportunity Fellowship to David L. Eaton, and Sean R. Parkin and Carolyn P. Brock for crystallographic help.

REFERENCES

1. K. Sonogashira, in 'Comprehensive Organic Synthesis', Vol. 3, ed. by B. M. Trost and I. Fleming, Pergamon Press, Oxford, 1991, p. 521.

2. J. Anthony, A. M. Boldi, Y. Rubin, M. Hobi, V. Gramlich, C. B. Knobler, P. Seiler, and F. Diederich, *Helv. Chim. Acta*, 1995, **78**, 13.

3. B. A. Arbuzov, E. N. Klimovitskii, and M. B. Timirbaev, *Zh. Obshch. Khim.*, 1986, **13**, 150.

4. W. Reppe, *Justus Liebigs Ann. Chem.*, 1955, **596**, 96.

5. Y. M. Slobodin, *J. Gen. Chem. USSR*, 1938, **3**, 714.

6. R. H. Everhardus, R. Grafing, and L. Brandsma, *Recl. Trav. Chim. Pays-Bas*, 1976, **95**, 153.

7. M. G. A. Shvekhgeimer, *Chem. Heterocycl. Compd. (Engl. Transl.)*, 1999, **34**, 1101.

8. J. E. O'Gara, J. D. Portmess, and K. B. Wagener, *Macromolecules*, 1993, **26**, 2837.

9. M. P. S. Leconte, A. Mutch, F. Lefebvre, and J. M. Basset, *Bull. Soc. Chim. Fr.*, 1995, **132**, 1069.

10. J. L. Couturier, K. Tanaka, M. Leconte, J. M. Basset, and J. Ollivier, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 112.

11. J. L. Couturier, K. Tanaka, M. Leconte, J. M. Basset, and J. Ollivier, *Phosphorus, Sulfur Silicon Relat. Elem.*, 1993, **74**, 383.

12. M. P. Cava, N. M. Pollack, O. A. Mamer, and M. J. Mitchell, *J. Org. Chem.*, 1971, **36**, 3932.

13. M. P. Cava and M. V. Lakshmikantham, *Acc. Chem. Res.*, 1975, **8**, 139.

14. J. P. Selegue and K. A. Swarat, *J. Am. Chem. Soc.*, 1993, **115**, 6448.

15. K. Griesbaum, K. Schlindwein, and M. Hilss, *Chem. Ber.*, 1993, **126**, 1843.

16. K. K. Cheung and G. A. Sim, *J. Chem. Soc.*, 1965, 5988.

17. K. K. Cheung, R. S. McEwen, and G. A. Sim, *Nature*, 1965, **205**, 383.

18. P. Kus and P. G. Jones, *Polish J. Chem.*, 2000, **74**, 649.

19. L. R. Hanton and T. Kemmitt, *Inorg. Chem.*, 1993, **32**, 3648.

20. G. Bodwell, L. Ernst, H. Hopf, and P. G. Jones, *Tetrahedron Lett.*, 1989, **30**, 6005.

21. P. G. Jones and P. Kus, *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.*, 1997, **C53**, 786.

22. T. Okajima, Z. H. Wang, and Y. Fukazawa, *Tetrahedron Lett.*, 1989, **30**, 1551.

23. J. J. H. Edema, H. T. Stock, J. Buter, R. M. Kellogg, W. J. J. Smeets, and A. L. Spek, *Tetrahedron*, 1993, **49**, 4355.

24. G. Eglinton, I. A. Hardy, R. A. Raphael, and G. A. Sim, *J. Chem. Soc.*, 1964, 1154.

25. R. Gleiter, S. Rittinger, and H. Irngartinger, *Chem. Ber.*, 1991, **124**, 365.

26. W. N. Setzer, G. S. Wilson, and R. S. Glass, *Tetrahedron*, 1981, **37**, 2735.

27. CCDC-00000 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk)

28. A. Feigenbaum and J. M. Lehn, *Bull. Soc. Chim. Fr.*, 1973, 198.

29. A. Feigenbaum and J. M. Lehn, *Bull. Soc. Chim. Fr.*, 1969, 3724.

30. O. M. Behr, G. Eglinton, I. A. Lardy, and R. A. Raphael, *J. Chem. Soc.*, 1964, 1151.

31. M.-K. Au, T. C. W. Mak, and T.-L. Chan, *J. Chem. Soc., Perkin Trans. 1*, 1979, 1475.

32. M.-K. Au, T.-W. Siu, T. C. W. Mak, and T.-L. Chan, *Tetrahedron Lett.*, 1978, 4269.

33. R. Gleiter, M. Karcher, B. Nuber, and M. L. Ziegler, *Angew. Chem., Int. Ed. Engl.*, 1987, **26**, 763.

34. R. Gleiter and S. Rittinger, *Tetrahedron Lett.*, 1988, **29**, 4529.

35. R. Gleiter, S. Rittinger, and H. Langer, *Chem. Ber.*, 1991, **124**, 357.