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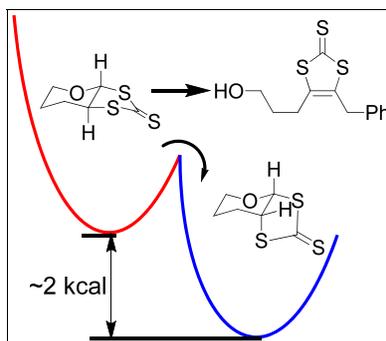
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The bicyclic pyran thiolone tetrahydro-3 $\alpha$ H-[1,3]dithiolo[4,5- $\beta$ ]pyran-2-thione (**3a**) engages in a highly unusual fragmentation in the presence of DDQ. The pyran thiolone, **3a**, was synthesized by chlorination of 3,4-dihydro-2H-pyran (**1**) followed by condensing with CS<sub>2</sub> and NaSH. Reaction of **3a** with DDQ generates the isomerized pyran thiolone tetrahydro-3 $\alpha$ H-[1,3]dithiolo[4,5- $\beta$ ]pyran-2-thione (**3b**) and 4-benzyl-5-(3-hydroxypropyl)-1,3-dithiole-2-thione (**4**) via a deep-seated rearrangement. The identity of **3b** was confirmed by single crystal X-ray analysis: P2<sub>1</sub>/c, a = 5.807(9) Å, b = 12.99(2) Å, c = 11.445(15),  $\beta$  = 113.23(6)°. Mechanistic experiments and computational insight is used to explain the likely sequence of events in the highly unusual formation of **4**. Collectively, these results establish fundamental reactivity patterns for further research in this area.

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## INTRODUCTION

The chemistry of vinyl disulfides, also known as dithiolenes (S–C=C–S), is as vast as it is transformative. Dithiolenes have a particularly rich coordination chemistry [1–4] with potential applications in material science [5,6], whereas their incorporation within organic metals afford superconducting materials. Dithiolenes have distinctive redox and structural features [7–12] that have shown promise as potential sensor materials with unparalleled optical and magnetic properties. [5,13–16] The luminescent properties of these dithiolene complexes have been used in developing sensors for molecular oxygen, [17] and the fluorescence properties have been utilized in developing sensors for metal ions such as Pb<sup>2+</sup> [18]. Dithiolene-based catalysts have also been used for separations of olefins [19].

The basic dithiolene unit is recognized to be at the heart of more than 50 molybdenum and tungsten enzymes [20,21]. These enzymes catalyze a wide variety of reactions that constitute important processes in all phyla of life including humans [22]. Here, the dithiolene ligand comprises a part of a more complicated three ring pterin cofactor, where the third pyran ring exists at times in an

open form exposing an alcohol [23,24]. In fact, the open pyran ring was initially thought to be the structure of the cofactor. In some cases, the metal ion is coordinated by endogenous ligands such as serine in DMSO reductase or cysteine in nitrate reductase [25]. Critical to understanding the basic chemistry of such systems is the ability to synthesize dithiolenes coupled with other molecular entities. We have been engaged in the design and synthesis of new pyranopterin dithiolenes as a part of our program to understand the structure–function relation of pyranopterin containing enzymes [18,24,26,27].

The importance of 1,2-dithiolenes has stimulated several syntheses. An established method of preparing an arene dithiolene is the reductive dealkylation of 1,2-C<sub>6</sub>H<sub>4</sub>(SR)<sub>2</sub> [28,29], or alternatively through directed lithiation of thiphenols followed by electrophilic addition [30]. Substitution on benzene rings provides an entry to different functionalized dithiolene derivatives [26,31]. 1,2-Alkene dithiolenes are generally prepared as salts or as latent precursors that can be deprotected before ligation to a metal ion. For example, the disodium salt of dimercapto maleonitrile has been synthesized by reacting CS<sub>2</sub> with NaCN. [32] The syntheses of

protected 1,2-dithiolene is expediently achieved by treating  $\alpha$ -haloketones with a xanthate salt followed by an acid catalyzed cyclization [33,34].

Synthetic strategies for accessing pyranodithiolene are less developed, and even less is known about the conditions pyran ring opening [35]. A conceptually attractive strategy for preparing pyranodithiolenes is to sulfurize a pyran ring followed by dehydrogenation to form a carbon–carbon double bond to the target compound. Herein, we report reactions of 1,2-dichloro-pyran with thionodithio carbonate as a bis-sulfur nucleophile, stereoselectively forming the *tetrahydropyran* dithiolane **6**. Subsequent dehydrogenation of **6** with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), affords a highly unusual product in which the pyran ring is cleaved accompanied by isomerization to a diastereoisomer via a deep-seated rearrangement. In addition to disclosing the synthetic details, we report characterization and provide a plausible mechanism to account for the highly unusual molecular transformation.

## RESULTS

**Chlorination of 3,4-dihydropyran.** Chlorination of 3,4-dihydro-2H-pyran (**1**) [36,37] was conducted in dry pentane at  $-78\text{ }^{\circ}\text{C}$  to yield 2,3-dichlorotetrahydropyran

(**2**) as a yellow liquid. The product was isolated as a mixture of isomers (~34 g, 91%) exhibiting identical spectra to that reported previously [36,37]. In non-polar solvents, the *cis*-isomer is the major product, whereas in polar solvents, the *trans*-isomer is the major product [36]. The *trans* isomer exists in a conformation with two equatorial chlorines; the axial–axial splitting is ~10 Hz in the  $^1\text{H}$  NMR spectrum [38]. On the basis of the NMR spectra, the *cis* isomers and the *trans* isomer are present in a ~55:45 ratio [36].

**Nucleophilic substitution of chlorine with sulfur.** Reaction of **2** with a sulfide nucleophile such as  $\text{CS}_2/\text{NaSH}$  or  $\text{Na}_2\text{S}$  in DMF leads to the formation of carbon–sulfur bonds at the expense of carbon–chlorine bonds [39]. In the present case,  $\text{CS}_2/\text{NaSH}$  provided **3a** in 25% overall yield. Only the *cis*-isomer can afford **3a** in a stereoselective reaction reducing the overall yield of the compound. We anticipate that the reaction proceeds through an initial attack by a sulfur from the trithiocarbonate nucleophile replacing the chlorine at position 2. A second nucleophilic attack at position 3 by the second sulfur of the trithiocarbonate completes the cycloaddition reaction. The *cis*-isomer is energetically more favorable in this stereoselective reaction.

The  $^1\text{H}$  NMR spectrum of **3a** shows a doublet at 4.73 ppm assigned to H2 (Table 1); the 10.5 Hz coupling

**Table 1**

Room temperature NMR data for compound **3a** collected in  $\text{C}_6\text{D}_6$ .

Position	$^{13}\text{C}$ , $\delta$ , ppm	Position	$^1\text{H}$ $\delta$ , ppm	$J$ , Hz	Cross peaks in COSY	Cross peaks in HMQC
C2	94.66	H2 (ax)	4.73 (d)	10.5	H3 (ax)	H2 (ax)
C3	60.47	H3 (ax)	3.52 (ddd)	10.5, 12, 3.5	H2 (ax), H4 (ax), H4 (eq)	H3 (ax)
C6	69.19	H6 (eq)	3.45 (dddd)	11.5, 5, 1.5, 1.5	H6 (ax), H5 (eq), H5 (ax)	H6 (eq), H6 (ax)
C6	69.19	H6 (ax)	2.78 (ddd)	12, 12, 3	H6 (eq), H5 (eq), H5 (ax)	H6 (eq), H6 (ax)
C4	26.49	H4 (eq)	1.17–1.22 (m)		H3 (ax), H4 (ax), H5 (ax), H5 (eq)	H4 (eq), H4 (ax)
C5	24.86	H5 (eq)	0.96–1.06 (m)		H6 (eq), H6 (ax), H4 (eq), H4 (ax), H5 (ax)	H5 (eq), H5 (ax)
C4	26.49	H4 (ax)	0.88–0.95 (m)		H3 (ax), H4 (eq), H5 (ax), H5 (eq)	H4 (eq), H4 (ax)
C5	24.86	H5 (ax)	0.72–0.76 (m)		H6 (eq), H6 (ax), H4 (eq), H4 (ax), H5 (eq)	H5 (eq), H5 (ax)
C7	220.36					

**Table 2**

Room temperature NMR data for compound **3b** in  $\text{C}_6\text{D}_6$ .

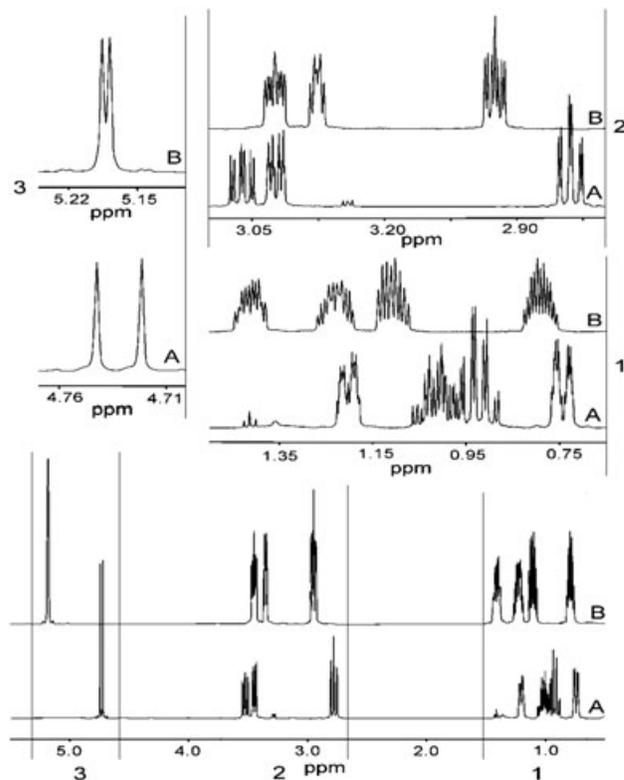
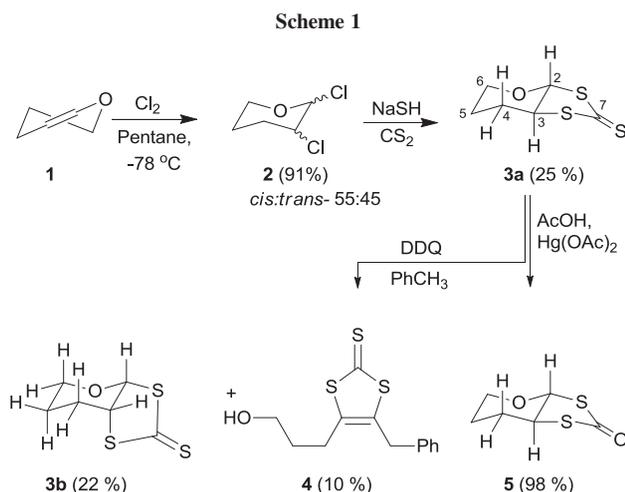
Position	$^{13}\text{C}$ , $\delta$ , ppm	Position	$^1\text{H}$ $\delta$ , ppm	$J$ , Hz	Cross peaks in COSY	Cross peaks in HMQC
C2	93.83	H2 (eq/ax)	5.18 (d)	4	H3 (eq/ax)	H2 (eq/ax)
C6	65.25	H6 (eq)	3.45 (ddd)	11, 7, 3	H6 (ax), H5 (ax), H5 (eq)	H6 (eq), H6 (ax),
C3	57.77	H3 (eq/ax)	3.35 (ddd)	6.5, 4.5, 4.5	H2 (eq/ax), H4 (eq), H4 (ax)	H3 (eq/ax)
C6	65.25	H6 (ax)	2.94 (ddd)	11, 7.5, 3	H6 (eq), H5 (eq), H5 (ax)	H6 (eq), H6 (ax),
C4	24.81	H4 (eq)	1.32–1.41 (m)		H4 (ax), H5 (ax), H5 (eq), H3 (eq/ax)	H4 (eq), H4 (ax)
C5	21.51	H5 (eq)	1.19–1.26 (m)		H5 (ax), H6 (ax), H6 (eq), H4 (eq), H4 (ax)	H5 (eq), H5 (ax)
C4	24.81	H4 (ax)	1.07–1.13 (m)		H4 (eq), H3 (eq/ax), H5 (eq), H5 (ax)	H4 (eq), H4 (ax)
C5	21.51	H5 (ax)	0.75–0.82 (m)		H5 (eq), H6 (eq), H6 (ax), H4 (eq), H4 (ax)	H5 (eq), H5 (ax)
C7	224.93					

with H3 (*vide infra*) suggests that both are in an axial orientation. Single frequency decoupling and COSY experiments of H3 ( $\delta=3.52$ , ddd) are consistent with this assignment. The two large couplings (11 Hz) of H3 are due to two axial-axial couplings assigned to H2 and H4, and the smaller coupling of 4 Hz is due to an axial-equatorial coupling. Collectively, the results are consistent with axial orientations of H2 and H3. Peaks at 2.78 ppm (ddd) and 3.45 ppm (dddd) are assigned to the axial and equatorial protons at C6 (H6ax and H6eq, respectively). The remaining four sets of multiplets in the upfield region are assigned to the four protons H4ax/H4eq and H5ax/H5eq, consistent with correlation and decoupling experiments.

A distinct resonance at 220.36 ppm in the  $^{13}\text{C}$  NMR spectrum is assigned to the thione group, and the resonance at 94.66 ppm is assigned to C2, which is attached to two electronegative atoms. Resonances at 69.19 and 60.47 ppm are assigned to carbons C3 and C6, respectively, whereas the resonances at 26.49 and 24.86 ppm are assigned to C4 and C5, respectively. The infrared spectrum of **3a** has a diagnostic signal at  $1093\text{ cm}^{-1}$  for the C=S stretch.

**Conversion of thione (3a) to ketone (5).** Conversion of the thione (**3a**) to ketone (**5**) occurred smoothly under standard conditions. The spectral data for **5** were very similar to those of **3a** as expected for sulfur to oxygen interchange. However, the carbonyl carbon of **5** resonates at 189.36 ppm,  $\sim 30$  ppm upfield from that of **3a**. The C=S stretch of **3a** that appeared at  $\sim 1093\text{ cm}^{-1}$  was replaced by C=O stretch at  $\sim 1720\text{ cm}^{-1}$  in **5**. The GC-MS showed a  $[\text{M}+\text{H}]^+$  peak at  $177\text{ m/z}$  with the isotope distribution identical to the theoretical pattern.

**Reaction of 3a with 2,3 dichloro 5,6-dicyano quinone.** Exposing **3a** to DDQ in toluene afforded dithiole-2-thione **4** (10% yield) and thione diastereoisomers **3a** (65%) and **3b** (22%). The spectroscopic data clearly established the structure of **4** (Scheme 1). Particularly, diagnostic was the  $^{13}\text{C}$  resonance due to the C=S at 227 ppm, the benzylic  $^1\text{H}$  NMR resonance at 4.8 ppm,



**Figure 1.** Room temperature  $^1\text{H}$  NMR spectra of compound **3a** (A) and compound **3b** (B) in  $\text{C}_6\text{D}_6$ . The expanded sections are shown in the insets. Assignments of the peaks are tabulated in Tables 1 and 2.

and the molecular ion peak ( $[\text{M}+\text{H}]^+$ ,  $283.0282\text{ m/z}$ ) in the high resolution mass spectrum.

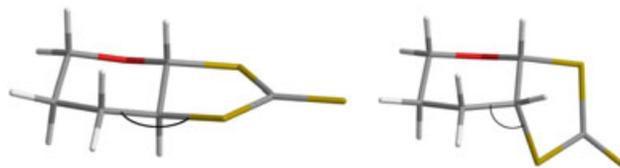
The  $^{13}\text{C}$  NMR spectra of **3a** and **3b** are very similar; however, the  $^1\text{H}$  NMR spectra differ in their chemical shift as well as splitting pattern (Fig. 1). The H2 resonance is shifted downfield from 4.73 ppm in **3a** to 5.18 ppm (d) in **3b** (Table 2). The large (10.5 Hz) coupling in **3a** indicates axial orientations of both H2 and H3, whereas the smaller coupling (4.0 Hz) constant in **3b** suggests an axial-equatorial interaction, which is consistent with the solid state structure. In order to understand whether the molecule is fluxional, the  $^1\text{H}$  NMR spectrum of **3b** in acetone was recorded at 180 K giving broad singlet peaks at 5.96 ppm and 5.03 ppm, respectively, for H2 and H3. In the same solvent, at room temperature, these resonances appear at 6.18 ppm (d,  $J \sim 3.8$  Hz) and 4.79 ppm (ddd, 6.2, 4.2, 4.8 Hz), respectively, for protons H2 and H3. Thus, the signal for H2 ( $\delta=5.18$ ) moved upfield whereas that for H3 moved downfield. We suggest that even at 180 K in acetone, a dynamic environment exists and the broadening of the peaks is due to an increase in viscosity and the compound's dynamic behavior.

In order to understand the driving force for rearrangement of compound **3a** into compound **3b** in the reaction with DDQ, DFT calculations were conducted at the

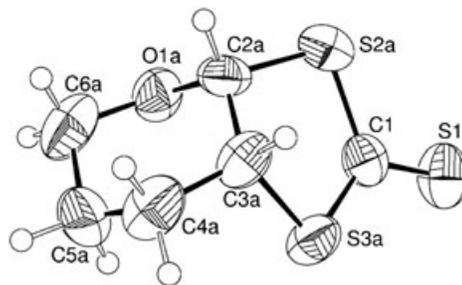
B3LYP/6-311+G(d) level (details are in the supporting information). Such a level of theory has provided reliable geometries, energies, and spectroscopic properties of sulfur containing thiols, disulfides, thiones, and thioamides [26,40–54]. The DFT structure is very similar to that determined by crystallographically, although the bond distances are longer (Table 3). We suggest that longer distances are due to the disorder in the crystal structure that required constraints, as well as the relaxed nature of the calculated structure in the gas phase. Compound **3b** was 1.84 kcal (2.03 kcal with zero-point energy correction) more stable than thione **3a**. We suggest that the increased stability of **3b** is due to the *cis*-fusion of the two rings that relieves the torsional strain in the *trans* thione **3a** (Fig. 2), similar to the reported steric strain in the all carbon system [55].

This steric strain is reflected in the bond angles. The  $\langle S(3)CC$  bond angles calculated from the optimized structures are:  $\langle SC3C2$ ,  $107.7^\circ$ ;  $\langle SC3C4$ ,  $112.6^\circ$  for **3b**, and  $106.1^\circ$  and  $116.4^\circ$  for the same angles in **3a**. Deviations from the idealized tetrahedral nature of the bridgehead carbon in **3a** impart strain making **3a** less stable than **3b**. Equilibration would therefore favor **3b** over **3a**.

**Crystal structure of 3b.** The unit cell of 7-dihydro-5H-[1,3]dithiolo[4,5-b]pyran-2-thione (**3b**) contains (R,R) and (S,S) enantiomers. The molecular structure of (R,R) **3** is shown in Figure 3, whereas selected geometric parameters are listed in Table 3. The bicyclic structure of **3b** is evident with the six and five-membered rings connected by a common single (C2a–C3a) bond. Although saturated five-membered [1,3]dithiolo-2-thione heterocycles connected via a single carbon–carbon bridge to saturated six-membered rings are known, the crystal structure is not. A search of the Cambridge Crystallographic Structure Database [56] indicates that dithione **3b** is the only example of such a bicyclic motif. The C=S double bond is significantly shorter ( $1.602(3)\text{ \AA}$ ) than that reported in a related compound ( $1.657\text{ \AA}$ ) [57], whereas the C–S single bonds ( $1.790(6)\text{ \AA}$ ,  $1.730(4)\text{ \AA}$ ) are close to those reported for similar thiones [58]. The six membered pyran ring adopts a typical "chair" conformation, the [1,3]-dithiolo-2-thione



**Figure 2.** Calculated structures of **3a** (left) and **3b** (right) differing in S–C–C bond angle (see text).



**Figure 3.** Thermal ellipsoid diagram (50% probability) of the R,R-**3b**.

fragment is essentially planar, whereas the five-membered C1–S2a–C2a–C3a–S3a heterocyclic moiety adopts a twist conformation. Specifically, large torsion angles for C(1)–S(2A)–C(2A)–C(3A) fragment ( $34.4(6)^\circ$ ) and C(1)–S(3A)–C(3A)–C(2A) fragment ( $31.1(6)^\circ$ ) exclude more a common "envelope" conformation.

## DISCUSSION

The chlorination of **1** and the subsequent sulfurization smoothly provide dithione **3a** (Scheme 1) [39]. Extrusion of oxygen using mercuric acetate and acid, quantitatively converts thioketone **3a** to ketone **5**, following the procedure for preparing dithiocarbonate ligands [18]. Treating **3a** with DDQ causes a deep-seated rearrangement to **3b** that is highly unusual. Control experiments demonstrate the requirement of DDQ, which presumably triggers the reaction through a sequence of proton and electron transfers [59–61]. Mechanistically, single electron transfer from toluene to DDQ and loss of a proton would yield a

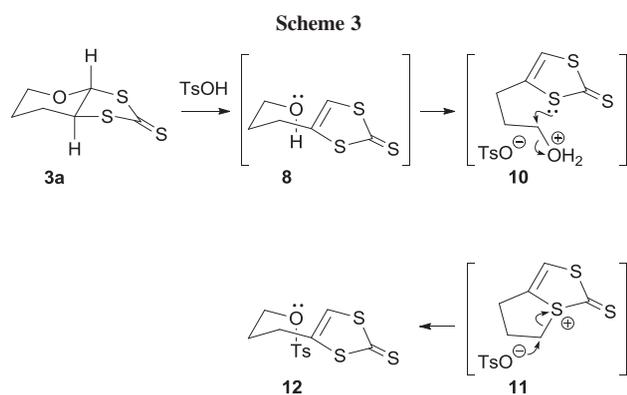
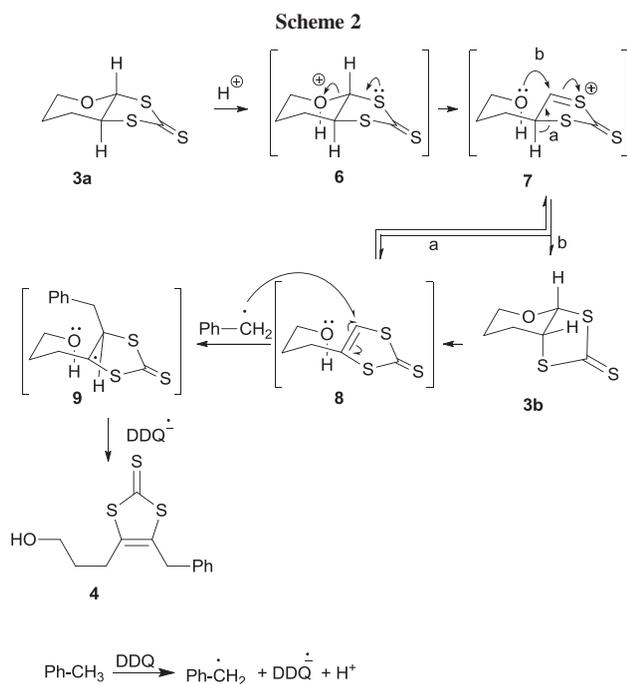
**Table 3**

Selected bond distances ( $\text{\AA}$ ) and angles ( $^\circ$ ) for **3b** from X-ray structure and those obtained from the DFT calculation are in parenthesis [].

S1–C1	1.602(3)	[1.638]	C1–S2a–C2a	95.8(3)	[97.31]
S2a–C1	1.730(4)	[1.773]	C1–S3a–C3a	97.9(3)	[97.19]
S2a–C2a	1.755(7)	[1.826]	O1a–C2a–C3a	112.6(6)	[113.67]
S3a–C1	1.642(3)	[1.762]	O1a–C2a–S2a	107.3(5)	[108.1]
S3a–C3a	1.790(6)	[1.847]	C3a–C2a–S2a	108.6(5)	[108.14]
C2a–O1a	1.380(8)	[1.408]	C2a–C3a–S3a	107.0(5)	[107.72]
C2a–C3a	1.473(8)	[1.536]	C4a–C3a–S3a	112.3(5)	[112.59]
C3a–C4a	1.480(8)	[1.537]	C2a–O1a–C6a	113.4(7)	[113.21]
C4a–C5a	1.475(14)	[1.533]	S1–C1–S3a	127.7(2)	[123.72]
C5a–C6a	1.478(10)	[1.524]	S1–C1–S2a	117.7(2)	[122.67]
C6a–O1a	1.418(13)	[1.433]	S3a–C1–S2a	114.6(2)	[113.61]

relatively stable benzyl radical (Scheme 2). Protonation of the pyran oxygen in **3a** likely generates oxonium ion (**6**) that triggers the pyran ring opening, analogous to the proposed pyran ring opening in the pyranopterin cofactor [62]. The resulting sulfenyl cation **7** could eliminate proton to form **8** (path a, Scheme 2) or recyclize by attack of the alcohol on the more accessible  $\alpha$ -face leading to **3b** (path b, Scheme 2). The preferential formation of **3b** is consistent with the greater calculated stability of **3b** over **3a**. Subjecting **3a** to formic acid in refluxing toluene generates **3b** with 30% conversion, consistent with a slow equilibrium from **3a** to **3b**.

A likely intermediate in this sequence is the hydroxy-dithione, **8**. In acidic media, **8** can equilibrate to **3a** and **3b** but in the presence of DDQ the benzyl radical intercepts **8** to form sulfur-stabilized radical **9**. Subsequent hydrogen atom abstraction by DDQH $\cdot$  would afford **4** and the



reduced form of DDQ. Consistent with this mechanistic scenario, when the reaction was conducted in deuterated toluene, isotope enrichment was only observed in the benzylic functionality of **4**. The deuterium labeling experiment demonstrates the incorporation of solvent and indirectly supports an initial deuterium abstraction by DDQ.

Consistent with the key role of hydroxy dithione, **8**, exposing **3a** to *p*-toluenesulfonic acid in refluxing toluene affords the tosylate **12**. Presumably, protonation of **3a** generates **8** that subsequently protonates to afford **10** that then cyclizes to afford sulfenyl cation **11** (Scheme 1). Opening of the thiophene ring by nucleophilic attack of the tosylate yields **12**. Trapping the tosylate **12** under these conditions provides supports for the presence of **8** in the rearrangement mechanism.

## SUMMARY

DDQ triggers a highly unusual rearrangement of the pyran dithiolate **3a**. Although **3a** is readily prepared, no unusual rearrangements or isomerizations have been reported for this type of substrate. A series of mechanistic probes provides strong evidence for an equilibrium radical trapping sequence. Refluxing **3a** in formic acid equilibrates the *trans*-fused pyran dithiolate **3a** to the corresponding *cis*-fused pyran dithiolate, **3b**. In the presence of DDQ, the ring opening is accompanied by formation of a benzylic radical capable of trapping the hydroxy dithione **8** to ultimately afford **4**. Using deuterium labeled toluene leads to incorporation of a deuterated benzylic group with no additional deuterium label. Collectively, these mechanistic experiments provide insight into pyran ring opening and closing reactions of potentially general relevance for pterin-containing molybdenum enzymes during catalytic turnover [62].

## EXPERIMENTAL

**Materials and instrumentation.** The chemicals were purchased from Aldrich Chemical Company or ACROS Chemical Company and were used without further purification. Commercial grade solvents were dried and purified using a solvent purification system (SP-105) by LC Technology Solutions Inc. before use. Toluene was dried and distilled over Na-benzophenone, chloroform and pentane were dried and distilled over CaH $_2$ . NMR spectra were collected on Bruker ACP-300, Bruker Avance 400, or 500 and Varian Unity 500 spectrometers. Mass spectra were obtained with a Waters LCQ ESI/APCI. High resolution mass spectra (HRMS) were collected on an Agilent 6200 time of flight LC MS system using a nano ESI-TOF interface. IR spectra were recorded either on a Perkin-Elmer FT-IR 1760X spectrometer or a Nicolet 380 FTIR (Thermo) spectrometer. Melting points were determined on a Mel-Temp II apparatus. GC-MS were recorded on a Varian Saturn II instrument.

### Synthesis.

**Synthesis of 2,3-dichlorotetrahydro-2H-pyran (2).** A Schlenk flask was charged with 3,4-dihydro-2H-pyran, (**1**),

(20 g, 238 mmol) and pentane (65 mL) under an Ar-atmosphere. The contents were cooled to  $-78^{\circ}\text{C}$  using an acetone-dry ice bath and using Teflon tubing, chlorine gas was slowly bubbled through the solution with stirring until a yellow color persisted ( $\sim 25$  min). Chlorine gas was then passed for an additional 10 min to ensure completion of the reaction. Argon gas was then bubbled through the solution to remove excess chlorine gas, and then the solvent was removed under reduced pressure. The resulting colorless liquid was purified by distillation at  $\sim 55^{\circ}\text{C}$  ( $\sim 30$  mmHg) to yield **2** as a colorless liquid. Yield: 92% (33.9 g, 219 mmol).

$^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ )  $\delta$ , ppm: 0.84 (d, 1H, 13 Hz), 1.04 (d, 1H, 13 Hz), 1.16–1.25 (m, 1H), 1.45 (d, 1H, 14 Hz), 1.53 (d, 1H, 12 Hz), 1.85–1.99 (m, 2H), 2.06–2.12 (m, 1H), 3.23–3.26 (m, 1H), 3.40 (dd, 1H, 11 Hz, 4.5 Hz), 3.60–3.62 (m, 1H), 3.67 (qd, 2H 3 Hz, 1 Hz), 3.84 (s, 1H), 5.87 (d, 1H, 3 Hz), 5.93 (s, 1H).  $^{13}\text{C}$  NMR ( $\text{C}_6\text{D}_6$ )  $\delta$ , ppm: 19.00, 24.92 (C4) 25.60, 27.75 (C5) 57.68, 58.20 (C3), 60.75, 61.99 (C6), 94.42, 96.47 (C2); ESI MS<sup>+</sup> ( $m/z$ ): 119 (calculated for  $\text{C}_5\text{H}_8\text{ClO} [\text{M} - \text{Cl}]^+$ , 119); IR (neat),  $\text{cm}^{-1}$ : 2949, 2929, 2876, 1070, 976, 874, 436.

**Synthesis of tetrahydro-3 $\alpha$ H-[1,3]dithiolo[4,5- $\beta$ ]pyran-2-thione (3a).** Sodium hydrosulfide hydrate (1.10 g, 19.69 mmol) was dissolved in DMF (15 mL) and neat carbon disulfide (1.49 g, 19.69 mmol) was added at room temperature over 30 min. The mixture was then warmed to  $40^{\circ}\text{C}$ . A DMF solution (2 mL) of 2,3-dichloropyran (**2**) (2 g, 13.00 mmol) was added to the reaction mixture. After 2 h, water (100 mL) and then chloroform (75 mL) were added, and then the target compound was extracted with chloroform and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . Evaporation of the organic phase afforded a yellow colored liquid, which was purified by silica gel column chromatography (hexanes/chloroform, 2:1). The first yellow band was collected and evaporated to yield **3a** as a yellow solid, mp:  $73\text{--}74^{\circ}\text{C}$ . Yield 25% (0.61 g, 3.21 mmol). NMR data are presented in Table 1. IR (KBr): 1093 (C=S)  $1084\text{ cm}^{-1}$ ; IR (neat),  $\text{cm}^{-1}$ : 2945, 2917, 2847, 1442, 1082, 1046, 1021, 477; HRMS ESI<sup>+</sup> ( $m/z$ ): 192.9812 [calculated for  $\text{C}_6\text{H}_9\text{S}_3\text{O} (\text{M} + \text{H}^+)$ , 192.9810]; (GC-MS): 191.8 (calculated for  $\text{C}_6\text{H}_8\text{S}_3\text{O} (\text{M}^+)$  192); HRMS ESI<sup>+</sup> with 0.1% HCOOH ( $m/z$ ): 190.9651 (calculated for  $\text{C}_6\text{H}_8\text{S}_3\text{O} (\text{M} - 2\text{H} + \text{H}^+)$ , 190.9659).

**Synthesis of 4-benzyl-5-(3-hydroxypropyl)-1,3-dithiole-2-thione (4) and tetrahydro-3 $\alpha$ H-[1,3]dithiolo[4,5- $\beta$ ]pyran-2-thione (3b).** A toluene solution (10 mL) of tetrahydro-3 $\alpha$ H-[1,3]dithiolo[4,5- $\beta$ ]pyran-2-thione (**3a**) (0.17 g, 0.88 mmol) in dry and DDQ (0.22 g, 0.975 mmol) was heated to reflux for 48 h. The reaction was then cooled, the solvent was removed, and then the crude product was purified by silica gel chromatography (hexanes/chloroform, 2:1) to afford 24 mg (0.08 mmol, 10%) of **4** as an oily liquid; 110 mg (65%) of **3a**, and 37 mg (22%) of **3b** as a crystalline solid.

Characterization of **4**.  $^1\text{H}$  NMR ( $\text{C}_6\text{D}_6$ )  $\delta$ , ppm: 1.31 (q, 2H, 6.3 Hz), 2.02 (td, 2H, 6.3 Hz, 1.6 Hz), 3.43 (t, 2H, 5 Hz), 4.38 (s, 2H), 6.94–7.01 (m, 3H, Ar-H), 7.06 (d, 2H, 8 Hz, Ar-H).  $^{13}\text{C}$  NMR ( $\text{CD}_3\text{Cl}$ )  $\delta$ , ppm: 227.42 (C=S), 154.9 (C=C), 135.21 (C=C), 129.5, 128.6, 128.01 (aromatic ring), 104.17 (aromatic ring, bridging carbon), 66.18 (alcoholic carbon) 42.13 (methylene carbon) 26.05, 22.92 (methylene carbon); IR (KBr): 1613 (C=C), 1093 (C=S); IR (neat),  $\text{cm}^{-1}$ : 3391 (broad), 2912, 2847, 1799, 1609, 1156, 1050, 914; HRMS ESI<sup>+</sup> ( $m/z$ ): 283.0280 [calculated for  $\text{C}_{13}\text{H}_{15}\text{S}_3\text{O} (\text{M} + \text{H}^+)$ , 283.0282].

Characterization of **3b**. NMR data are tabulated in Table 2. IR (C=S)  $1078\text{ cm}^{-1}$ ; HRMS ESI<sup>+</sup> ( $m/z$ ): 192.9810 [calculated for  $\text{C}_6\text{H}_9\text{S}_3\text{O} (\text{M} + \text{H}^+)$ , 192.9810]; mp:  $73\text{--}74^{\circ}\text{C}$ . IR (neat),  $\text{cm}^{-1}$ : 2937, 2913, 2847, 1425, 1301, 1033, 874, 502, 461.

**The reaction of 3a with DDQ in toluene- $d_8$ .** A dry toluene- $d_8$  solution (2 mL) of tetrahydro-3 $\alpha$ H-[4,5- $\beta$ ]pyran-2-thione (**3a**) (0.015 g, 0.078 mmol) and DDQ (0.022 g 0.097 mmol) was refluxed for 53 h. The reaction was monitored by thin layer chromatography (silica, dichloromethane-hexane: 2:1); and purified by preparative TLC (silica, dichloromethane/hexanes: 2:1). The first yellow fraction is isotopically labeled **4** (or **4a**); compound **3a** and **3b** eluted as the second and third fractions, respectively. Yields were not calculated.

Characterization of **4a**.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ , ppm: 2.01 (qd, 2H, 6.3 Hz, 10.5 Hz), 2.36 (td, 2H, 1.4 Hz, 6.3 Hz), 4.07 (t, 2H, 5.3 Hz); HRMS ESI<sup>+</sup> ( $m/z$ ): 290.0706 [calculated for  $\text{C}_{13}\text{H}_8\text{D}_7\text{S}_3\text{O} (\text{M} + \text{H}^+)$ , 290.0722].

**The reaction of 3a with formic acid in toluene.** A dry toluene solution (2 mL) of **3a** (3.0 mg, 0.015 mmol) containing 5 drops of formic acid (95%) was heated to reflux. After 10 h, the reaction mixture was allowed to cool to room temperature, 30 mL of a saturated solution of  $\text{NaHCO}_3$  was added, and then the mixture was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 5$  mL). The combined organic phase was dried over  $\text{Na}_2\text{SO}_4$ , separated and the solvent was then removed under reduced pressure.  $^1\text{H}$  NMR spectroscopic analysis identified the product to be **3b** (30% conversion).

**The reaction of 3a with *p*-TsOH in toluene.** A toluene solution (2 mL) of **3a** (5 mg, 0.026 mmol) and *p*-toluenesulfonic acid monohydrate (0.2 g 1.05 mmol) was heated to reflux. After 3.5 h, the reaction mixture was allowed to cool to room temperature, 30 mL of saturated aqueous  $\text{NaHCO}_3$  was added, and then the mixture was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 5$  mL). The combined organic phase was dried over  $\text{Na}_2\text{SO}_4$ , the organic solvent was removed, and the resulting brown gummy material was purified by preparative TLC (silica,  $\text{CH}_2\text{Cl}_2$ ) to afford 4.1 mg (0.011 mmol, 45%) of 3-(2-thioxo-1,3-dithiole-4-yl)propyl 4-methylbenzenesulfonate (**12**) as a pale yellow oil.

Characterization of **12**.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$ , ppm: 1.92–1.98 (m, 2H), 2.47 (s, 3H, Ar- $\text{CH}_3$ ), 2.71 (td, 2H, 1.1 Hz, 7.4 Hz), 4.07 (t, 2H, 5.6 Hz), 6.58 (s, 2H), 7.37 (d, 2H, 8 Hz, Ar-H), 7.79 (d, 2H, 8 Hz, Ar-H); IR (neat),  $\text{cm}^{-1}$ : 3101, 2958, 1728, 1356, 1180, 1066, 927; HRMS ESI<sup>+</sup> ( $m/z$ ): 346.9896 [calculated for  $\text{C}_{13}\text{H}_{15}\text{S}_4\text{O}_3 (\text{M} + \text{H}^+)$ , 346.9904].

**Synthesis of tetrahydro-3 $\alpha$ H-[1,3] dithiolo[4,5- $\beta$ ]pyran-2-one (5).** A room temperature Schlenk flask was charged with tetrahydro-3 $\alpha$ H-[1,3]dithiolo[4,5- $\beta$ ]pyran-2-thione (**3a**) (0.10 g, 0.52 mmol), dry dichloromethane (10 mL), acetic acid (1 mL) and mercuric acetate (0.20 g, 0.62 mmol). After 1 h, the color of the reaction mixture changed from yellow to white with precipitation of a white solid. After an additional 2 h, the solvent was removed, the residue was then dissolved in chloroform, the organic solution was filtered, and was then purified by passing through a silica gel column to afford 88 mg (98%) of **5** as a white solid (mp,  $46\text{--}48^{\circ}\text{C}$ ).  $^1\text{H}$  NMR ( $\text{C}_6\text{H}_6$ )  $\delta$ , ppm: 0.72–0.78 (m, 1H), 0.85–0.96 (m, 1H), 1.06–1.16 (m, 1H), 1.18–1.25 (m, 1H), 2.79–2.88 (m, 1H), 3.26–3.28 (m, 1H), 3.42–3.48 (m, 1H), 4.66 (d, 1H, 10 Hz);  $^{13}\text{C}$  NMR ( $\text{C}_6\text{D}_6$ )  $\delta$ , ppm: 189.36, 91.49, 69.73, 55.69, 26.90, 25.93; IR (KBr): 1653 (C=O); GC-MS ( $m/z$ ): 177 (25%) (calculated for  $\text{C}_6\text{H}_9\text{S}_2\text{O}_2 (\text{M} + \text{H})$ , 177).

**X-ray crystallography.** X-ray quality crystals were obtained by slow evaporation of an acetonitrile solution of **3b**. Experimental data were collected at room temperature on a Bruker SMART Apex II diffractometer using a graphite monochromator and Mo- $\text{K}\alpha$  ( $\lambda = 0.071073 \text{ \AA}$ ) radiation (0.8 mm collimator). Semi-empirical "Multi-Scan" absorption correction

**Table 4**  
Crystal data for **3b**.

Empirical formula	C <sub>6</sub> H <sub>8</sub> OS <sub>3</sub>
Mr	192.30
Temperature (°K)	296(2)
Crystal system	Monoclinic
Space group, Z	P2 <sub>1</sub> /c, 4
a, Å	5.807(9)
b, Å	12.99(2)
c, Å	11.445(15)
β, °	113.23(6)
V, Å <sup>3</sup>	793(2)
Crystal size, mm	0.7 × 0.3 × 0.1
ρ <sub>calc</sub> , g cm <sup>-3</sup>	1.610
2θ <sub>max</sub>	51.58
μ(Mo–Kα), cm <sup>-1</sup>	8.58
R <sub>int</sub>	0.0240
Reflections collected/unique	6563/1513
GooF	1.055
R <sub>1</sub> /wR <sub>2</sub> (I > 2σ(I))	0.035/0.090
R <sub>1</sub> /wR <sub>2</sub> (all data)	0.0485/0.0977
ρ <sub>max</sub> /ρ <sub>min</sub> , e <sup>-</sup> Å <sup>-3</sup>	0.227/–0.177

was performed using SADABS software [63]. Analysis of the systematic absences identified the P2<sub>1</sub>/c space group with the structure being solved by the direct method implemented in SHELXS and then refined by SHELXL program [64]. All non-hydrogen atoms were located on a difference Fourier-map and refined anisotropically. Hydrogen atoms were placed at idealized positions (C–H distances were constrained at 0.98 Å) and then refined using the Riding model approximation (U(H) = 1.2U<sub>eq</sub>(C)). The molecules of **3b** in the crystal lattice were found to be disordered through rotation around the S=C bond. The disorder was successfully resolved by using SAME/DFIX restraint of SHELXL and occupations of 0.58 and 0.42 for the first and second disordered components, respectively. The C–C bonds of the main disordered component were fixed to 1.54 Å with a deviation of 0.02 Å. Final anisotropic parameters for C4b were unreasonably low and O1b were unreasonably high compared with the neighboring atoms. On the basis of the thermal parameters and crystallization conditions, two different conformations (enantiomers) are proposed. Oxygen atom O1b of one enantiomer overlaps with carbon atom C4b of the other enantiomer. Such positional disorder was resolved by constraining coordinates and thermal displacement parameters to be same for both positions. Occupations were fixed at 0.5. The refined parameters are summarized in Table 4.

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