ACS OMEGA

http://pubs.acs.org/journal/acsodf

Article

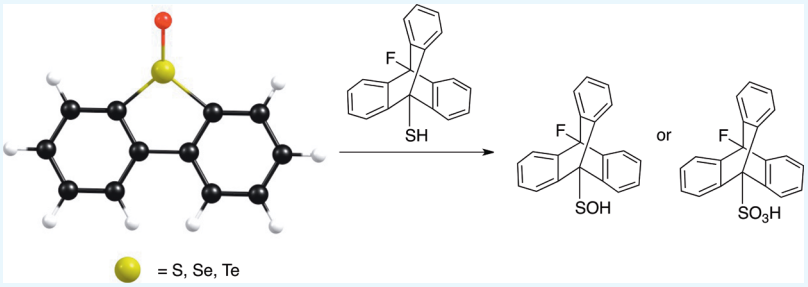
Photo-oxidation and Thermal Oxidations of Triptycene Thiols by Aryl Chalcogen Oxides

Satyanarayana M. Chintala, Peter F. Maness, John T. Petroff II, John C. Throgmorton, Miao Zhang, Sara M. Omlid, and Ryan D. McCulla*

Cite This: *ACS Omega* 2020, 5, 32349−32356

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information



ABSTRACT: Oxidation of thiols yield sulfenic acids, which are very unstable intermediates. As sulfenic acids are reactive, they form disulfides in the presence of thiols. However, sulfenic acids also oxidize to sulfinic acids ($-SO_2H$) and sulfonic acids ($-SO_3H$) at higher concentrations of oxidants. Hydrogen peroxide is a commonly used oxidant for the oxidation of thiols to yield sulfenic acids. However, hydrogen peroxide also oxidizes other reactive functional groups present in a molecule. In this work, the reaction intermediates arising from the oxidation of sterically hindered thiols by aryl chalcogen oxides, dibenzothiophene *S*-oxide (DBTO), dibenzoselenophene *Se*-oxide (DBSeO), and dibenzotellurophene *Te*-oxide (DBTeO), were investigated. Photodeoxygenation of DBTO produces triplet atomic oxygen [$O(^3P)$], which has previously shown to preferentially react with thiols over other functional groups. Similarly, aryl selenoxides have also shown that they can thermally react selectively with thiols at room temperature to yield disulfides. Conversely, aryl telluroxides have been reported to oxidize thiols to disulfides thermally with no selectivity toward thiols. The results from this study demonstrate that sulfenic acids are an intermediate in the oxidation of thiols by DBTeO and by photodeoxygenation of DBTO. The results also showed that the oxidation of thiols by DBSeO yields sulfonic acids. Triptycene-9-thiol and 9-fluorotriptycene-10-thiol were for the thiols used in this oxidation reaction. This work expands the list of oxidants that can be used to oxidize thiols to obtain sulfenic acids.

INTRODUCTION

Sulfenic acids are very reactive intermediates that are important in cell signaling pathways.[1−5] Due to the reactive nature of sulfenic acids, their formation has often been proven indirectly by trapping them using HCN, silyl enol ethers, dimedone, and derivatives of dimedone.[3,6−8] However, sulfenic acids can be stabilized by hydrogen bonding, sterics, and conjugation.[9−14] Triptycene-9-sulfenic acid is one of the stable sulfenic acids that have been isolated and characterized.[9] Steric hinderance because of the triptycene framework is the reason for the stability of triptycene-9-sulfenic acid. The structures of triptycene-9-thiol and triptycene-9-sulfenic acid are shown in Figure 1. Other small-molecule stable sulfenic acids include 1-anthraquinonesulfenic acid, 1-methyluracil-4-sulfenic acid, 1,3,6-trimethyllumazine-7-sulfenic acid, (*E*)-decalin-9-sulfenic acid, 4,6-dimethoxy-1,3,5-triazine-2-sulfenic acid, and azetidinone sulfenic acid.[3,11−14] Triptycene-9-thiol was used as the thiol for oxidation reactions in this study due to the stability of triptycene-9-sulfenic acid and the absence of reactive functional groups other than thiol in the structure of triptycene-9-thiol.

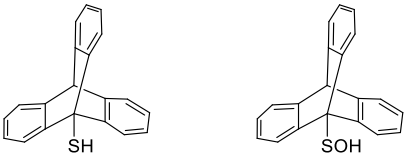


Figure 1. Structures of triptycene-9-thiol and triptycene-9-sulfenic acid.

Received: September 2, 2020
Accepted: December 2, 2020
Published: December 11, 2020

https://dx.doi.org/10.1021/acsomega.0c04293
ACS Omega 2020, 5, 32349−32356

Photodeoxygenation of dibenzothiophene *S*-oxide (DBTO), shown in Figure 2, is purported to produce $O(^3P)$ in

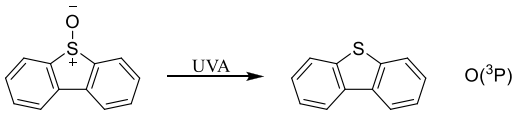


Figure 2. Photodeoxygenation of DBTO.

solution.[15] The other sources of $O(^3P)$ in solution are photodeoxygenation of aryl sulfoxides, dibenzoselenophene *Se*-oxide (DBSeO), pyridine *N*-oxide, and oxo-anions.[16−19] Aryl selenoxides, aryl telluroxides, and $O(^3P)$ have been previously used to oxidize thiols to disulfides.[20−22] However, the reaction intermediates of the thiol oxidation by aryl selenoxides, aryl telluroxides, and $O(^3P)$ have not been investigated in solution. Gas-phase studies of the reaction between methanethiol and $O(^3P)$ indicate a sulfenic acid intermediate.[23,24]

Although $O(^3P)$, aryl selenoxides, and aryl telluroxides oxidize thiols to disulfides, only $O(^3P)$ and aryl selenoxides have shown some selective reactivity with thiols. In a recent study, $O(^3P)$ has shown some selectivity to oxidize thiols compared to sulfides, alkenes, and aromatics.[22] In another study, the reaction kinetics data showed that polymer-bound aryl selenoxides could selectively oxidize thiols to disulfides compared to other reactive groups at room temperature.[21] The reaction kinetics data from the same study also showed that polymer-bound aryl telluroxide did not show any selective reactivity with thiols.

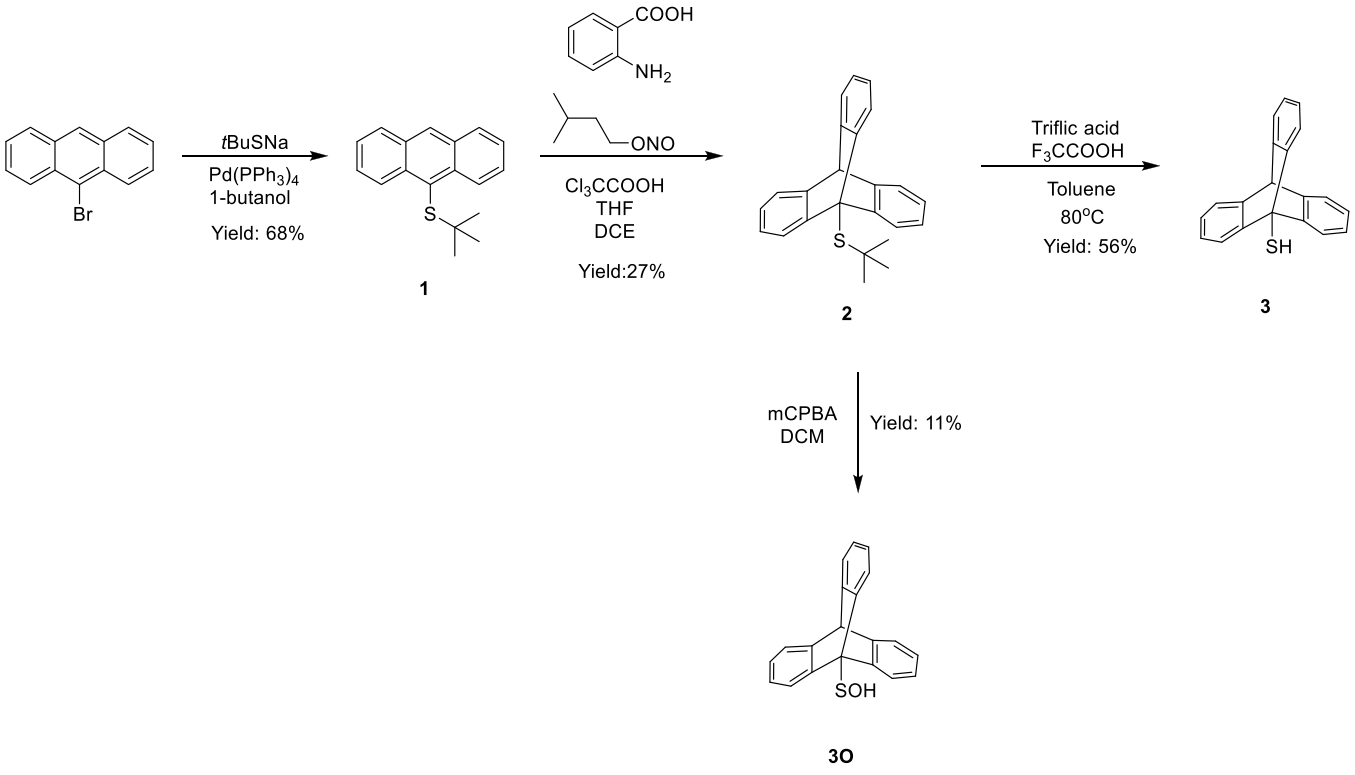
The objective of this work is to investigate the reaction intermediates of thiol oxidation by $O(^3P)$, DBSeO, and DBTeO. DBTO was used as the $O(^3P)$ precursor. Initially, triptycene-9-thiol (**3**) was the thiol chosen for the oxidation reaction as triptycene-9-sulfenic acid (**3O**) is stable under the reaction conditions. If in these experiments **3O** is observed, this would indicate that sulfenic acids are intermediates in the oxidation of thiol by the examined chalcogen oxides since typically sulfenic acid reacts rapidly with thiols to form disulfides.[1,3,4,6,7,25,26]

RESULTS AND DISCUSSION

Synthesis of Triptycene-9-thiol and Triptycene-9-sulfenic Acid. Compounds triptycene-9-thiol (**3**) and triptycene-9-sulfenic acid (**3O**) were synthesized according to the procedures in literature, as shown in Scheme 1.[27,28] The first step involved coupling of sodium *tert*-butyl thiolate and 9-bromoanthracene using $Pd(PPh_3)_4$ in anhydrous 1-butanol. The second step was a Diels−Alder reaction between compound **1** and in situ generated benzyne to yield compound **2**. Compound **3** was synthesized by heating compound **2** in the presence of triflic acid and trifluoroacetic acid in toluene. Oxidation of compound **2** by mCPBA in dichloromethane yielded **3O**.

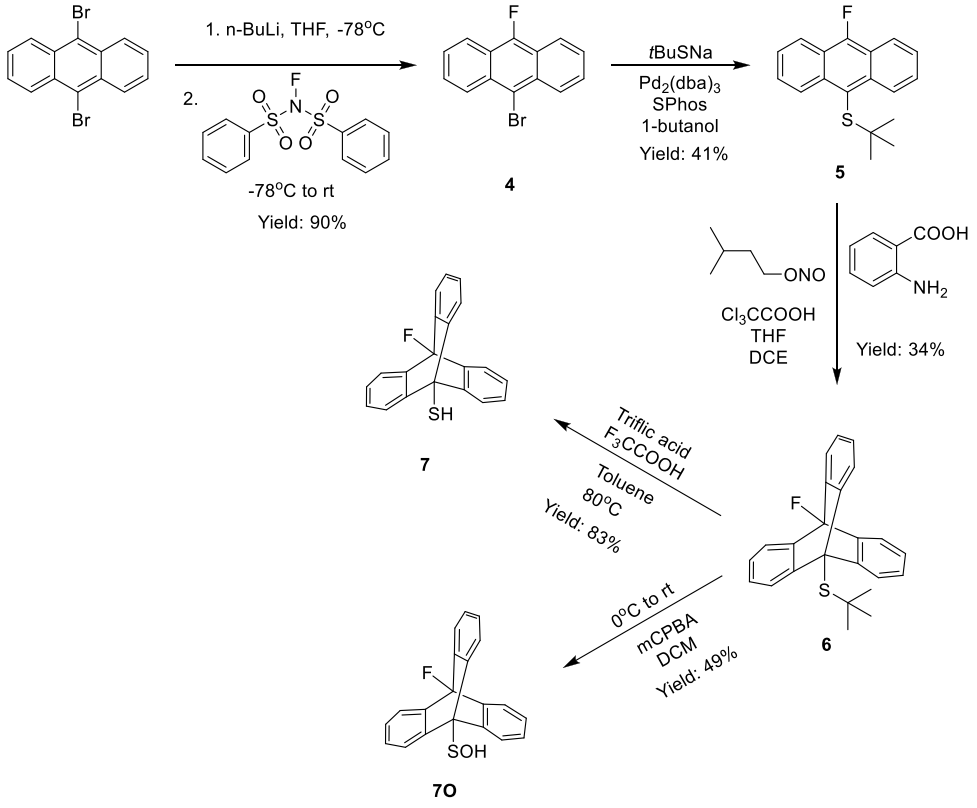
Oxidation of Triptycene-9-thiol by Photodeoxygenation of DBTO. One of the objectives of this work is to investigate the reaction intermediate of thiol oxidation by $O(^3P)$. To study the reaction intermediate, DBTO was used as the $O(^3P)$ precursor to oxidize **3**. A solution of 20 mM DBTO and 44 mM compound **3** was prepared in acetonitrile in a quartz test tube. The solution was degassed by argon purging and irradiated with UVA light for 4.5 h. The reaction products were characterized by HPLC. HPLC analysis showed formation of dibenzothiophene (DBT) but did not show any peak corresponding to **3O**. The control experiments showed that **3O** was stable in a solution containing compound **3**.

Scheme 1. Synthesis of Triptycene-9-thiol (3) and Triptycene-9-sulfenic acid (3O)



https://dx.doi.org/10.1021/acsomega.0c04293
ACS Omega 2020, 5, 32349−32356

Scheme 2. Synthesis of Compounds 7 and 7O



LCMS analysis showed a peak with an m/z value equal to 333 in negative ion mode, which is the same m/z value for triptycene-9-sulfonic acid. The LCMS analysis of this reaction is included in the Supporting Information.

The absence of **3O** after the photodeoxygenation reaction in HPLC analysis was not entirely unexpected as the concentration of pure acetonitrile is 19 M and the maximum concentration that could be achieved for compound **3** in acetonitrile was 44 mM. As the rate constant of the reaction between **3** and $O(^3P)$ is unknown, one can estimate the rate constant from the reaction between *tert*-butyl thiol and $O(^3P)$. The rate constants of oxidation of acetonitrile and *tert*-butyl thiol by $O(^3P)$ are 1×10^5 and 3.9×10^9 M^{-1} s^{-1}, respectively.[18,22] Therefore, the initial rate for compound **3** is at maximum expected to be ∼100 times faster than acetonitrile. However, compound **3** has three aromatic rings competing with the thiol functional group for oxidation. The relative rate constant of the oxidation of *tert*-butyl thiol by $O(^3P)$ with respect to benzene is 10.2.[22] Therefore, the thiol functional group in **3** is expected to react ∼30 times faster than acetonitrile and ∼3 times faster than ring oxidation. However, if the rate constant of the reaction between $O(^3P)$ and **3** is lower than the rate constant of oxidation of *tert*-butyl thiol, then the oxidation of the thiol functional group in **3** in this reaction would be much more minimal under these conditions.

Synthesis of 9-Fluorotriptycene-10-thiol and 10-Fluorotriptycene-9-sulfenic Acid. One of the alternate approaches that were considered was to incorporate a fluorine atom at the 9-position of compound **3** structure. This approach was previously used to monitor the thiol oxidation reaction by ^{19}F NMR.[10] Additionally, 9-fluorotriptycene-10-sulfenic acid (**7O**) is a stable sulfenic acid, which has been previously isolated and characterized.[10] Therefore, 9-fluorotriptycene-10-thiol (**7**) and the sulfenic acid **7O** were synthesized by using similar procedures reported in the literature.[10] The syntheses of compounds **7** and **7O** are shown in Scheme 2. The first step involved fluorination of 9,10-dibromoanthracene to yield compound **4**. Compound **4** was coupled with sodium *tert*-butyl thiolate to synthesize compound **5**. Compound **6** was obtained by performing a Diels−Alder reaction between **4** and in situ generation of benzyne. The reaction of compound **6** with triflic acid and trifluoroacetic acid yielded **7**. Compound **7O** was obtained by oxidation of **6** by mCPBA in DCM.

Oxidation of 9-Fluorotriptycene-10-thiol by Photodeoxygenation of DBTO. The addition of a fluoro substituent at the 9-position of **3** was advantageous as ^{19}F NMR could be used to monitor the oxidation reaction. Similar to oxidation of **3** by photodeoxygenation of DBTO, a solution of 40 mM compound **7** and 20 mM DBTO was prepared in acetonitrile-d_3. The solution was degassed using the freeze pump thaw technique and was irradiated by UVA wavelength light for 45 h, as shown in Figure 3. It should be noted that **7** was stable to UVA irradiation in the absence of DBTO. In another control experiment, no oxidation was observed if DBT was used instead of DBTO. In addition, the data of the control experiments also showed that the sulfenic acid **7O** was stable in

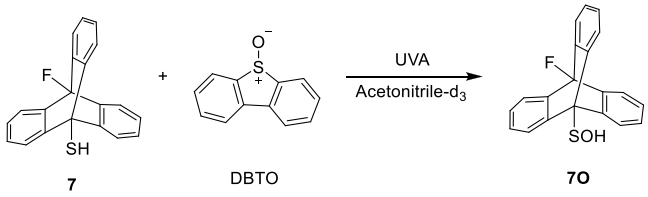


Figure 3. Oxidation of **7** by photodeoxygenation of DBTO.

https://dx.doi.org/10.1021/acsomega.0c04293
ACS Omega 2020, 5, 32349−32356

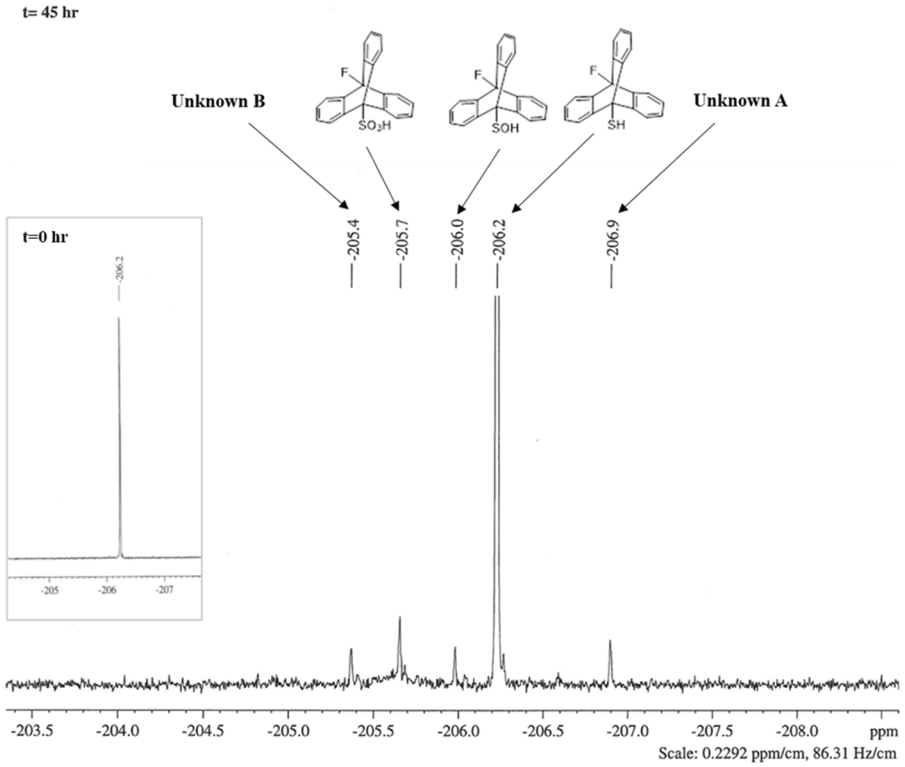


Figure 4. Comparison of ^{19}F NMR spectra of the reaction mixture of DBTO + 7 before and after irradiation of UVA light.

the presence of DBTO in acetonitrile without UVA irradiation. The ^{19}F NMR spectra of the control experiments are provided in the Supporting Information. The ^{19}F NMR spectrum of the reaction mixture with DBTO before photolysis, as shown in Figure 4, had one peak at −206.2 ppm, which corresponds to 7. The ^{19}F NMR spectrum of the reaction mixture with DBTO after UVA irradiation showed an additional four low intensity new peaks compared to t = 0 min ^{19}F NMR spectrum, as shown in Figure 4. The chemical shifts (in ppm) of the new peaks were −205.4, −205.7, −206.0, and −206.9.

The chemical shift −206.0 ppm matched with the chemical shift of the authentic sample of **7O**. The peak at −205.7 ppm was identified as 9-fluorotriptycene-10-sulfonic acid based on the analysis discussed later in the oxidation of thiol 7 by the DBSeO section. The peaks at −206.9 and −205.4 ppm are labeled as unknown A and unknown B, respectively. The areas of the 9-fluorotriptycene-10-sulfenic acid and 9-fluorotriptycene-10-sulfonic acid peaks in Figure 4 showed that the amount of sulfonic acid obtained was 2.4 times the amount of sulfenic acid. Additionally, the ratio of the sum of areas of the compound A and compound B peaks to the area of sulfenic acid obtained was 2.9 relative to **7O**. HPLC analysis of the reaction mixture showed that the concentration of dibenzothiophene (DBT) formed after the reaction was 15 mM. As the ratio of the peak areas of sulfenic acid **7O** to thiol 7 in ^{19}F NMR spectrum shown in Figure 4 is 1:57, the concentration of the obtained **7O** after the reaction can be estimated to be 0.7 mM, given that the concentration of the thiol 7 is 40 mM. Therefore, from the obtained concentrations of obtained DBT and sulfenic acid **7O**, the calculated yield of the formation of **7O** is 5%. However, if we assume that **7O** was an intermediate in the formation of 9-fluorotriptycene-10-sulfonic, then the yield of **7O** that could be achieved would be higher than the obtained 5%. In the ^{19}F NMR spectrum shown in Figure 4, the sum of the areas of the compounds **7O** and 9-fluorotriptycene-9-sulfonic acid is 0.06 relative to the area of the peak corresponding to 7. Therefore, given the obtained concentration of DBT, which is 15 mM, and the initial concentration of 7, which is 40 mM, the yield of **7O** could have been as high as 16%.

As mentioned earlier, the rate constant of oxidation of *tert*-butyl thiol by O(^{3}P) relative to benzene is 10.2.[22] Therefore, the aromatic rings in the structure of 7 are also likely susceptible to oxidation by O(^{3}P) to form hydroxy functional groups. Hence, unknown A was suspected of being aromatic ring oxidation products of 7. Our efforts to synthesize or isolate unknown A to confirm the ^{19}F NMR shifts were unsuccessful. In another experiment, **7O** was oxidized by photodeoxygenation of DBTO. The concentrations of **7O** and DBTO were 5 and 25 mM, respectively, and the reaction time was 45 h. ^{19}F NMR analysis showed that all the sulfenic acid **7O** was converted to unknown B. To obtain the mass of unknown B, the reaction mixture was analyzed by LCMS. The analysis showed an m/z = 367 peak in negative ion mode, which could correspond to the addition of three more oxygen atoms to **7O**. This suggests that unknown B could be 9-fluorotriptycene-10-sulfonic acid with oxidation of one ring position to a hydroxy group. Attempts to isolate and prepare unknown B were unsuccessful. These results indicated that **7O** was susceptible to further oxidation by O(^{3}P) to the sulfonic acid, and the triptycene unit was also susceptible to oxidation.

Oxidation of 9-Fluorotriptycene-10-thiol by DBSeO. Aryl selenoxides have shown to thermally oxidize thiols to disulfides.[21] In this study, dibenzoselenophene *Se*-oxide (DBSeO) was used to oxidize 9-fluorotriptycene-10-thiol to investigate the reaction intermediate of thiol oxidation by aryl selenoxides. Although DBSeO is an O(^{3}P) precursor that has a higher quantum yield of photodeoxygenation compared to

https://dx.doi.org/10.1021/acsomega.0c04293
ACS Omega 2020, 5, 32349−32356

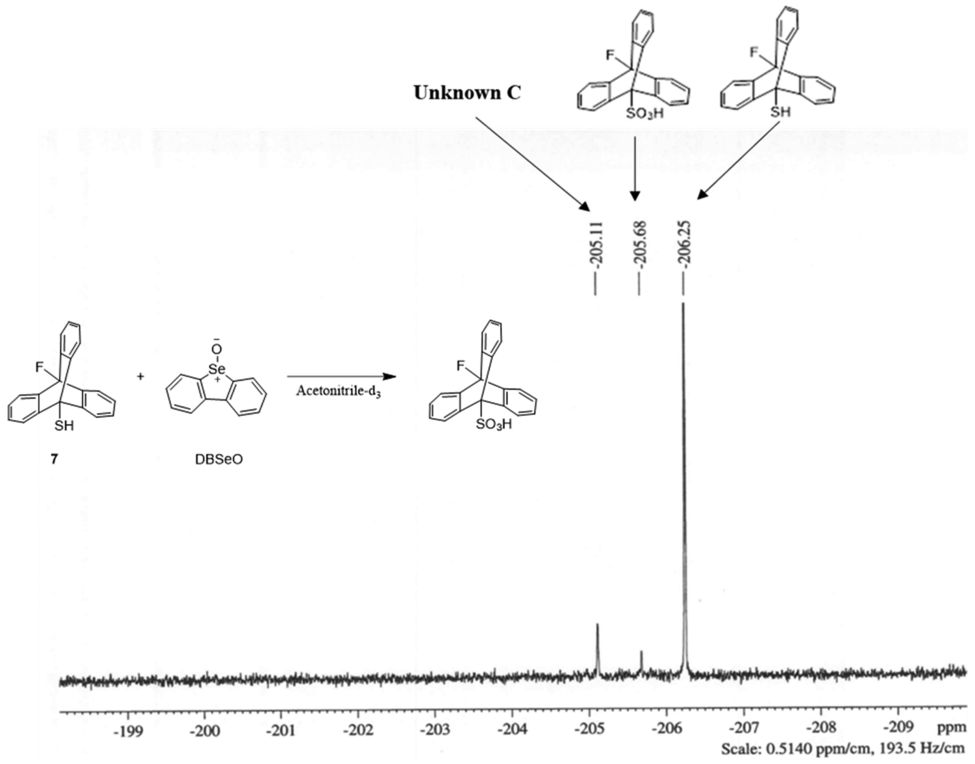


Figure 5. ^{19}F NMR spectrum of thermal oxidation of 7 by 0.25 equiv of DBSeO at t = 20 min.

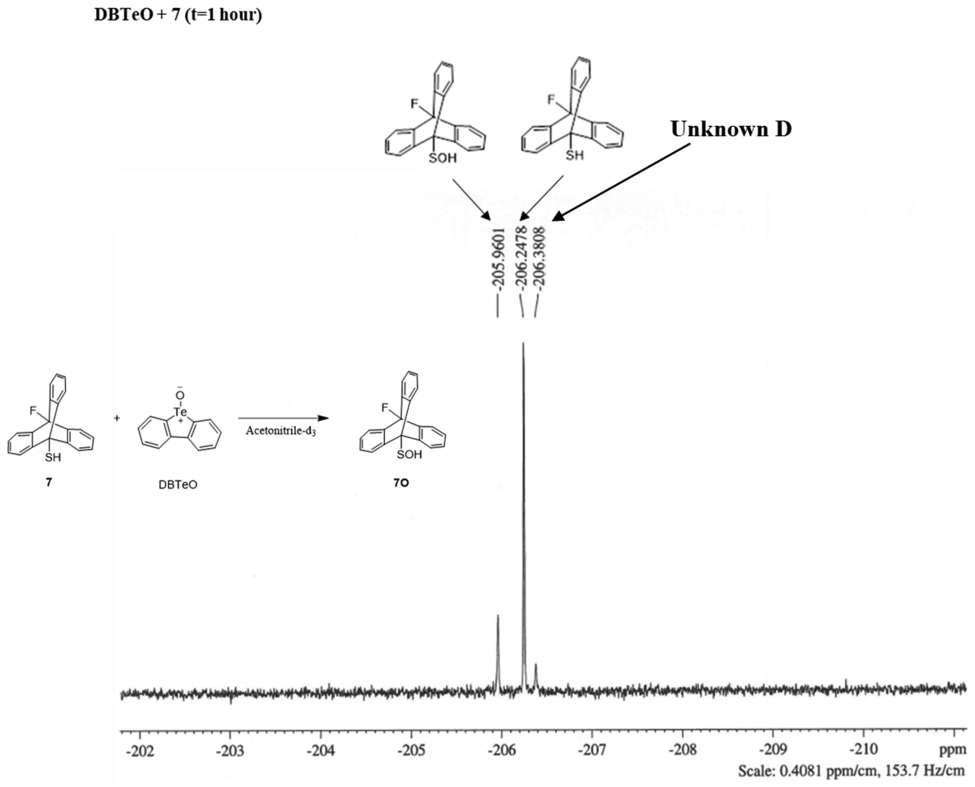


Figure 6. ^{19}F NMR spectrum of thermal oxidation of 7 by DBTeO at t = 1 h.

DBTO, it could not be used as the O(^{3}P) precursor for the oxidation of thiols because of rapid thermal oxidation of thiols by DBSeO.[15,16] The ^{19}F NMR spectrum of a solution of 7 and DBSeO prepared in acetonitrile-d_3 showed that DBSeO thermally reacted with 7, as shown in Figure 5.

For the oxidation of 7 by DBSeO, the ^{19}F NMR spectrum of the reaction mixture showed two new peaks with the chemical shifts (in ppm) of −205.1 and −205.7. For this experiment, 0.04 mmol of DBSeO was used to oxidize 0.04 mmol of 7 in 4 mL of acetonitrile-d_3. HPLC analysis showed the conversion of

https://dx.doi.org/10.1021/acsomega.0c04293
ACS Omega 2020, 5, 32349−32356

DBSeO to DBSe. A white precipitate was observed after the reaction. The precipitate was filtered and analyzed by ^{19}F NMR and LCMS. The ^{19}F NMR chemical shift of the precipitate was −205.7 ppm, and the LCMS had *m/z* that corresponds to10-fluorotriptycene-9-sulfonic acid in negative ion mode. The LCMS is provided in the Supporting Information.

To verify if this reaction occurred via a sulfenic acid intermediate, the reaction was performed using different equivalents of DBSeO. The reaction was performed using 0.25, 0.5, 0.75, and 1 equiv of DBSeO. Figure 5 shows the F^{19} NMR spectrum of 0.25 equiv of DBSeO with **7**. ^{19}F NMR analysis did not show the formation of **7O** during the oxidation of **7** using any of the equivalents of DBSeO mentioned. Figure 5 shows the ^{19}F NMR spectra of the oxidation of **7** using 0.25 equiv of DBSeO. The peak at −205.7 ppm, as discussed earlier, was identified as 9-fluorotriptycene-10-sulfonic acid, and the peak at −205.1 ppm was unknown, which was labeled as unknown C in Figure 5. To obtain the mass of unknown C, the reaction mixture was injected into an LCMS. However, only the 9-fluorotriptycene-10-sulfonic acid peak was observed in the LCMS analysis. Additionally, to investigate if 9-fluorotriptycene-10-sulfonic acid was formed via a **7O** intermediate during the oxidation of compound **7** by DBSeO, sulfenic acid **7O** was oxidized using 1 equiv of DBSeO. ^{19}F NMR analysis showed that oxidation of **7O** by DBSeO yielded 9-fluorotriptycene-10-sulfonic acid. While this result indicates **7O** could be an intermediate in the oxidation of **7** to 9-fluorotriptycene-10-sulfonic acid by DBSeO, more mechanistic studies are required to prove this conclusively.

Oxidation of 10-Fluorotriptycene-9-thiol by DBTeO. Oxidation of thiols by aryl telluroxides yields disulfides similar to aryl selenoxides.[20,21] The intermediate of the oxidation of thiol functional group by dibenzotellurophene *Te*-oxide (DBTeO) was investigated in this study. Oxidation of **7** by DBSeO yielded 10-fluorotriptycene-9-sulfonic acid. The same reaction was performed using DBTeO to study the intermediate of thiol oxidation by DBTeO. A solution of 17 mM DBTeO and 17 mM **7** was prepared in acetonitrile-d_3 and allowed to react for 1 h. The reaction yielded **7O**, as shown in Figure 6. The ^{19}F NMR spectrum of the reaction mixture before the reaction only contained one peak at −206.2 ppm, which corresponds to **7**. The ^{19}F NMR of the reaction mixture after 1 h showed two new peaks with chemical shifts (in ppm) of −206.0 and −206.4 (unknown D), as shown in Figure 6. The chemical shift −206.0 ppm corresponds to **7O**. Furthermore, the peak at −206.4 ppm is much smaller in intensity compared to the **7O** peak. To test if DBTeO can oxidize **7** to 10-fluorotriptycene sulfinic acid or 10-fluorotriptycene-9-sulfonic acid, one more equivalent of DBTeO was added to the reaction mixture and allowed to react for 37 h. The ^{19}F NMR spectrum showed that DBTeO did not oxidize **7** to 10-fluorotriptycene sulfinic acid or 10-fluorotriptycene-9-sulfonic acid, as shown in Figure 7. However, an increase in the **7O** peak was observed and the peak with a chemical shift of −206.4 ppm disappeared.

Oxidation of 7 with Hydrogen Peroxide. Given the common use of peroxides in the oxidation of thiols to sulfenic acids, the oxidation of **7** by H_2O_2 was attempted under a variety of conditions. In acetonitrile-d_3, a reaction of 13 mM H_2O_2 and 13 mM **7** at room temperature was followed by NMR at 0, 5, 10, and 300 min. These NMR spectra showed no changes or new peaks. The reaction was also carried out in methanol for 8 h; however, again no reaction was observed. Thus, **7** was unreactive toward H_2O_2 under these conditions.

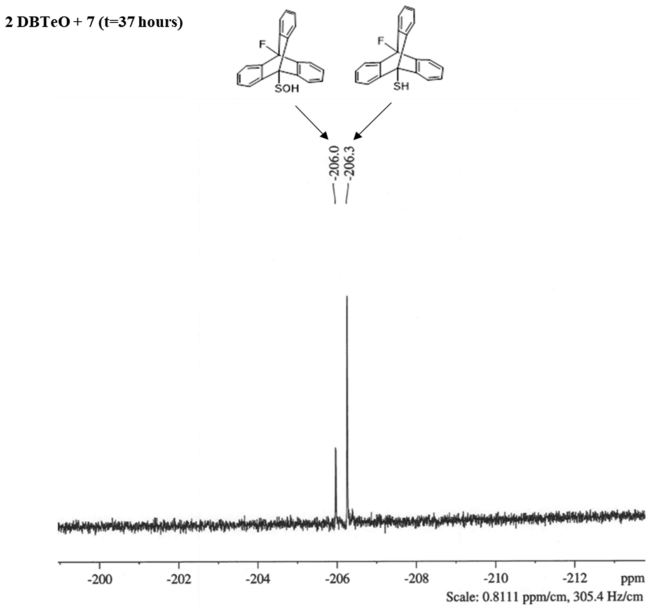


Figure 7. ^{19}F NMR spectrum of the reaction mixture after adding one more equivalent of DBTeO and allowed to react for 37 h.

Comparison of Oxidation by Chalcogen Oxides and Mechanistic Implications. Of the three chalcogen oxides examined, only DBTO was thermally stable in the presence of the triptycene thiols. Irradiation of DBTO is postulated to generate $O(^3P)$, which oxidizes **7** to **7O**. The resulting formation of 10-fluorotriptycene-9-sulfonic acid presumably arises from the further oxidation of **7O**. Unknown A likely arises from the oxidation of one of the $C(sp^2)$−H bonds to the corresponding hydroxy by $O(^3P)$ as indicated by +16 in the MS. Additionally, it was shown that $O(^3P)$ oxidizes **7O** further to the sulfonic acid. Speculation of the unknown's identity is based on the oxidation of benzene by $O(^3P)$ to phenol in good yields and proceeds at a similar rate to the oxidation *tert*-butyl thiol by $O(^3P)$.[22] The photodeoxygenation of DBTO is a relatively low quantum yield process, and thus, it takes much longer to achieve appreciable yields compared to the thermal oxidations by DBSeO and DBTeO discussed below.

Both DBSeO and DBTeO thermally oxidized **7** within minutes, which is much faster than the photodeoxygenation of these compounds. The significant difference between these two oxidants is their selective production of different oxidation states of sulfur. While DBSeO fully oxidizes the triptycene thiol **7** to the sulfonic acid, DBTeO appears capable of only partial oxidation to the sulfenic acid (**7O**). Both of these compounds generate an observed unknown compound that appears to convert to the final oxidation product. Presumably, DBSeO oxidizes **7** to **7O**, and **7O** rapidly reacts with DBSeO that oxidizes to higher oxidation states, which was verified experimentally. The preparation of an authentic sample of unknown C was unsuccessful. For DBTeO, unknown D is potentially a tautomer of the RSOH, such as RS(O)H, since over time, unknown D appears to convert to **7O**.

CONCLUSIONS

The reaction intermediate of the oxidation of the thiol functional group by potential $O(^3P)$ donors was investigated in

https://dx.doi.org/10.1021/acsomega.0c04293
ACS Omega 2020, 5, 32349−32356

this work. Oxidation of 9-fluorotriptycene-10-thiol by photodeoxygenation of DBTO yielded 9-fluorotriptycene-10-sulfenic acid as one of the products. However, 9-fluorotriptycene-10-sulfenic acid was not the major product of this reaction since it was susceptible to further oxidation. One of the other products obtained was 9-fluorotriptycene-10-sulfonic acid, and the rest of the observed products were expected to be ring oxidation products. These undesired products were obtained either by oxidation of formed sulfenic acid during the reaction or oxidation of the triptycene rings. Therefore, it can be construed that oxidation of thiol functional group by photodeoxygenation of DBTO yields sulfenic acid. In addition, 9-fluorotriptycene-10-thiol was thermally oxidized to its corresponding sulfenic acid by dibenzotellurophene *Te*-oxide at room temperature. Dibenzoselenophene *Se*-oxide thermally reacted with 9-fluorotriptycene-10-thiol to its corresponding sulfonic acid.

EXPERIMENTAL SECTION

Materials. All chemicals were purchased from Sigma Aldrich, Fisher, Arctom Chemicals, Oakwood Chemicals, or Ark Pharm and used without further purification except as specified. 1-Butanol obtained from Sigma Aldrich was further dried using 3 Å molecular sieves. HPLC-grade acetonitrile was used for photoreactions. DBTO, DBSeO, and DBTeO were prepared according to the procedures reported in the literature.[16,29−31] All the synthetic procedures are reported in the Supported Information.

General Methods. A Bruker DRX-400 NMR was used to obtain ^{19}F NMR, ^{1}H NMR, and ^{13}C NMR spectra. HPLC analysis was conducted using an Agilent 1200 Series HPLC with a quaternary pump, diode-array detector, and a Higgins Analytical CLIPEUS C18 column (5 μm, 150 × 4.6 4.6 mm). A Shimadzu GCMS equipped with a QP2010S was used from GC−MS analysis. LCMS was carried out using a Shimadzu LCMS-2020. For the photodeoxygenation reaction of DBTO, 14 Luzchem UVA bulbs (LZC-UVA) centered at 350 nm were used.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.0c04293.

^{1}H NMR, ^{13}C NMR, GCMS, HPLC traces, and HRMS (PDF)

AUTHOR INFORMATION

Corresponding Author

Ryan D. McCulla − *Department of Chemistry, Saint Louis University, St. Louis, Missouri 63103, United States*; Email: ryan.mcculla@slu.edu

Authors

Satyanarayana M. Chintala − *Department of Chemistry, Saint Louis University, St. Louis, Missouri 63103, United States*

Peter F. Maness − *Department of Chemistry, Saint Louis University, St. Louis, Missouri 63103, United States*

John T. Petroff II − *Department of Chemistry, Saint Louis University, St. Louis, Missouri 63103, United States*

John C. Throgmorton − *Department of Chemistry, Saint Louis University, St. Louis, Missouri 63103, United States*

Miao Zhang − *Department of Chemistry, Saint Louis University, St. Louis, Missouri 63103, United States*

Sara M. Omlid − *Department of Chemistry, Saint Louis University, St. Louis, Missouri 63103, United States*

Complete contact information is available at: https://pubs.acs.org/10.1021/acsomega.0c04293

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

This work was supported by the National Science Foundation under CHE-1900417.

REFERENCES

(1) Beedle, A. E. M.; Lynham, S.; Garcia-Manyes, S. Protein S-Sulfenylation Is a Fleeting Molecular Switch That Regulates Non-Enzymatic Oxidative Folding. *Nat. Commun.* **2016**, *7*, 12490−12410.

(2) Amorati, R.; Lynett, P. T.; Valgimigli, L.; Pratt, D. A. The Reaction of Sulfenic Acids with Peroxyl Radicals: Insights into the Radical-Trapping Antioxidant Activity of Plant-Derived Thiosulfinates. *Chem. - Eur. J.* **2012**, *18*, 6370−6379.

(3) Gupta, V.; Carroll, K. S. Sulfenic Acid Chemistry, Detection and Cellular Lifetime. *Biochim. Biophys. Acta - Gen. Subj.* **2014**, *1840*, 847−875.

(4) Davis, F. A.; Jenkins, R. H., Jr. Chemistry of Sulfenic Acids. 2. Formation of Hydrogen Peroxide from Sulfenic Acids. *J. Am. Chem. Soc.* **1980**, *102*, 7967−7969.

(5) Billiet, L.; Geerlings, P.; Messens, J.; Roos, G. The Thermodynamics of Thiol Sulfenylation. *Free Radical Biol. Med.* **2012**, *52*, 1473−1485.

(6) Brewer, T. F.; Garcia, F. J.; Onak, C. S.; Carroll, K. S.; Chang, C. J. Chemical Approaches to Discovery and Study of Sources and Targets of Hydrogen Peroxide Redox Signaling Through NADPH Oxidase Proteins. *Annu. Rev. Biochem.* **2015**, *84*, 765−790.

(7) Paulsen, C. E.; Carroll, K. S. Orchestrating Redox Signaling Networks through Regulatory Cysteine Switches. *ACS Chem. Biol.* **2010**, *5*, 47−62.

(8) Kumar, M. R.; Farmer, P. J. Trapping Reactions of the Sulfenyl and Sulfinyl Tautomers of Sulfenic Acids. *ACS Chem. Biol.* **2017**, *12*, 474−478.

(9) Nakamura, N. A Stable Sulfenic Acid, 9-Triptycenesulfenic Acid: Its Isolation and Characterization. *J. Am. Chem. Soc.* **1983**, *105*, 7172−7173.

(10) Chauvin, J.-P. R.; Pratt, D. A. On the Reactions of Thiols, Sulfenic Acids, and Sulfinic Acids with Hydrogen Peroxide. *Angew. Chem., Int. Ed.* **2017**, *56*, 6255−6259.

(11) Fries, K. α-Anthraquinonesulfenic Acid. *Chem. Ber.* **1913**, *45*, 2965−2973.

(12) Chou, T. S.; Burgtorf, J. R.; Ellis, A. L.; Lammert, S. R.; Kukolja, S. P. Azetidinone Sulfenic Acids. Isolation of Crystalline Sulfenic Acids from Penicillin Sulfoxides and a Study of Their Reactivities. *J. Am. Chem. Soc.* **1974**, *96*, 1609−1610.

(13) Tripolt, R.; Belaj, F.; Edgar, N. Unexpectedly Stable Sulfenic Acid: 4,6-Dimethoxy-1,3,5-Triazine-2-Sulfenic Acid; Synthesis, Properties, Molecular and Crystal Structure. *Z. Naturforsch.. B* **2014**, *48*, 1212−1222.

(14) Yoshimura, T.; Tsukurimichi, E.; Yamazaki, S.; Soga, S.; Shimasaki, C.; Hasegawa, K. Synthesis of a Stable Sulfenic Acid{,} *Trans*-Decalin-9-Sulfenic Acid. *J. Chem. Soc., Chem. Commun.* **1992**, 1337−1338.

(15) Gregory, D. D.; Wan, Z.; Jenks, W. S. Photodeoxygenation of Dibenzothiophene Sulfoxide: Evidence for a Unimolecular S-O Cleavage Mechanism[1]. *J. Am. Chem. Soc.* **1997**, *119*, 94−102.

(16) McCulla, R. D.; Jenks, W. S. Deoxygenation and Other Photochemical Reactions of Aromatic Selenoxides. *J. Am. Chem. Soc.* **2004**, *126*, 16058−16065.

(17) Rockafellow, E. M.; McCulla, R. D.; Jenks, W. S. Deoxygenation of Dibenzothiophene-*S*-Oxide and Dibenzoselenophene-Se-Oxide: A Comparison of Direct and Sensitized Photolysis. *J. Photochem. Photobiol., A* **2008**, *198*, 45−51.
(18) Bucher, G.; Scaiano, J. C. Laser Flash Photolysis of Pyridine N-Oxide: Kinetic Studies of Atomic Oxygen [O(3P)] in Solution. *J. Phys. Chem.* **1994**, *98*, 12471−12473.
(19) Zheng, X.; Baumann, S. M.; Chintala, S. M.; Galloway, K. D.; Slaughter, J. B.; Mcculla, R. D. Photodeoxygenation of Dinaphthothiophene, Benzophenanthrothiophene, and Benzonaphthothiophene *S*-Oxides. *Photochem. Photobiol. Sci.* **2016**, *15*, 791−800.
(20) Lutkus, L. V.; Irving, H. E.; Davies, K. S.; Hill, J. E.; Lohman, J. E.; Eskew, M. W.; Detty, M. R.; McCormick, T. M. Photocatalytic Aerobic Thiol Oxidation with a Self-Sensitized Tellurorhodamine Chromophore. *Organometallics* **2017**, *36*, 2588−2596.
(21) Hu, N. X.; Aso, Y.; Otsubo, T.; Ogura, F. Polymer-Supported Diaryl Selenoxide and Telluroxide as Mild and Selective Oxidizing Agents. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 879−884.
(22) Omlid, S. M.; Zhang, M.; Isor, A.; McCulla, R. D. Thiol Reactivity toward Atomic Oxygen Generated during the Photodeoxygenation of Dibenzothiophene *S*-Oxide. *J. Org. Chem.* **2017**, *82*, 13333−13341.
(23) Nip, W. S.; Singleton, D. L.; Cvetanovic, R. J. Gas-Phase Reactions of O(3P) Atoms with Methanethiol, Ethanethiol, Methyl Sulfide, and Dimethyl Disulfide. 1. Rate Constants and Arrhenius Parameters. *J. Am. Chem. Soc.* **1981**, *103*, 3526−3530.
(24) Cvetanovic, R. J.; Singleton, D. L.; Irwin, R. S. Gas-Phase Reactions of O(3P) Atoms with Methanethiol, Ethanethiol, Methyl Sulfide, and Dimethyl Disulfide. 2. Reaction Products and Mechanisms. *J. Am. Chem. Soc.* **1981**, *103*, 3530−3539.
(25) Roos, G.; Messens, J. Protein Sulfenic Acid Formation: From Cellular Damage to Redox Regulation. *Free Radical Biol. Med.* **2011**, *51*, 314−326.
(26) Forman, H. J. Use and Abuse of Exogenous H2O2 in Studies of Signal Transduction. *Free Radical Biol. Med.* **2007**, *42*, 926−932.
(27) McGrath, A. J.; Garrett, G. E.; Valgimigli, L.; Pratt, D. A. The Redox Chemistry of Sulfenic Acids. *J. Am. Chem. Soc.* **2010**, *132*, 16759−16761.
(28) Jennings, W. B.; Kochanewycz, M. J.; Lunazzi, L. Conformation and Stereodynamics of Alkyl 9-Anthryl Sulfoxides. *J. Chem. Soc., Perkin Trans. 2* **1997**, *7*, 2271−2274.
(29) Chintala, S. M.; Petroff, J. T., II; Barnes, A.; McCulla, R. D. Photodeoxygenation of Phenanthro[4,5- *Bcd*]Thiophene *S* -Oxide, Triphenyleno[1,12- *Bcd*]Thiophene *S* -Oxide and Perylo[1,12- *Bcd*]Thiophene *S* -Oxide. *J. Sulfur Chem.* **2019**, *40*, 503−515.
(30) McCullough, J. D. Dibenzotellurophene. New Synthesis by Way of 2-Biphenylyltellurium Trichloride. *Inorg. Chem.* **2002**, 2285−2286.
(31) Product Class 12: Dibenzotellurophenes. In *Category 2, Hetarenes and Related Ring Systems*; Thomas, Ed.; Georg Thieme Verlag: Stuttgart, 2000.

https://dx.doi.org/10.1021/acsomega.0c04293
ACS Omega 2020, 5, 32349−32356