organics

MDPI

Communication

An Unexpected Reaction between Diaryliodonium Salts and DMSO

Konrad Kepski and Wesley James Moran *

Department of Chemical Sciences, University of Huddersfield, Queensgate, Huddersfield HD1 3DH, UK
* Correspondence: w.j.moran@hud.ac.uk

Abstract: Diaryliodonium salts are useful arylating reagents that have been exploited widely. In this Communication, we demonstrate that heating diphenyliodonium triflate in the solvent DMSO leads to an unexpected arylation reaction. It is postulated that arylation of DMSO at oxygen, followed by a thia-Sommelet–Hauser rearrangement, leads to the formation of 2-thiomethylphenols. More substituted diaryliodonium salts and cyclic diaryliodonium salts are shown to be more stable and less likely to react with DMSO. In conclusion, when using iodonium salts dissolved in DMSO, beware of side-reactions.

Keywords: iodine; iodonium salt; Sommelet–Hauser rearrangement; arylation; sulfide; sulfoxide

Citation: Kepski, K.; Moran, W.J. An Unexpected Reaction between Diaryliodonium Salts and DMSO. *Organics* **2022**, *3*, 275–280. https://doi.org/10.3390/org3030020

Academic Editors: David StC Black and George Kokotos

Received: 10 June 2022
Accepted: 30 August 2022
Published: 31 August 2022

1. Introduction

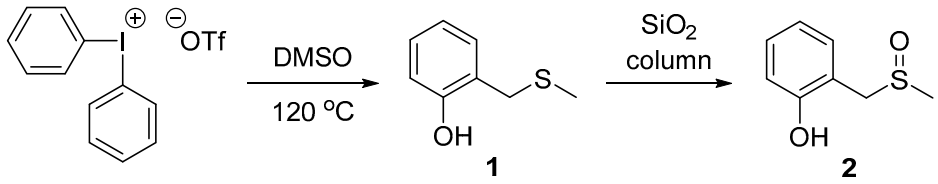
In recent years, diaryliodonium salts have found great utility in a wide range of catalyzed and non-catalyzed arylation reactions [1–4]. Typically, these compounds are stable, non-toxic, and readily available solids that are easy to handle. They possess high electrophilicity due to the superior leaving group ability of the constituent iodoarene moiety which enables its ability as an arylating agent for a wide range of nucleophiles.

The C-H arylation of arenes, heteroarenes, alkenes, and alkanes by diaryliodonium salts has been achieved using a variety of different metal salts as catalysts; representative examples with some or all of these substrates are known with Pd [5], Pt, Au, Cu, Fe, Ir, Ni, and Ru salts [6]. Diaryliodonium salts are also known to arylate a wide variety of nucleophiles such as enolates, carboxylates, amides, alkoxides, halides, etc. without the aid of any catalyst [7].

During the development of an arylation reaction using diaryliodonium salts with dimethylsulfoxide (DMSO) as solvent, we found a deleterious side-reaction. In 2016, we reported our findings that (2-(arylsulfonyl)vinyl)phenyliodonium salts undergo hydrolysis to aldehydes upon stirring in aqueous DMSO at room temperature [8]. Herein, we describe our latest findings that show that DMSO can be arylated by diaryliodonium salts at elevated temperatures.

2. Results and Discussion

Whilst investigating the use of diphenyliodonium triflate (Ph_2IOTf) as an arylating agent, we screened the use of DMSO as a solvent. Upon heating, the formation of a new compound was observed. Analysis led to the conclusion that arylation of DMSO had occurred and sulfide **1** had been formed (Scheme 1). Attempted purification on silica gel led to oxidation of the sulfide **1** to the sulfoxide **2**. The ability of diaryliodonium salts to arylate a wide range of nucleophiles is well documented, but we are not aware of any examples with sulfoxides. DMSO is a common polar aprotic solvent which can be used to assess the relative nucleophilicities of a range of compounds [9,10]. In the present case, DMSO itself is acting as the nucleophile; of course, this is the case in the Swern and Kornblum oxidations, as well as in other transformations [11,12].



Scheme 1. Unexpected reaction between diphenyliodonium triflate and DMSO.

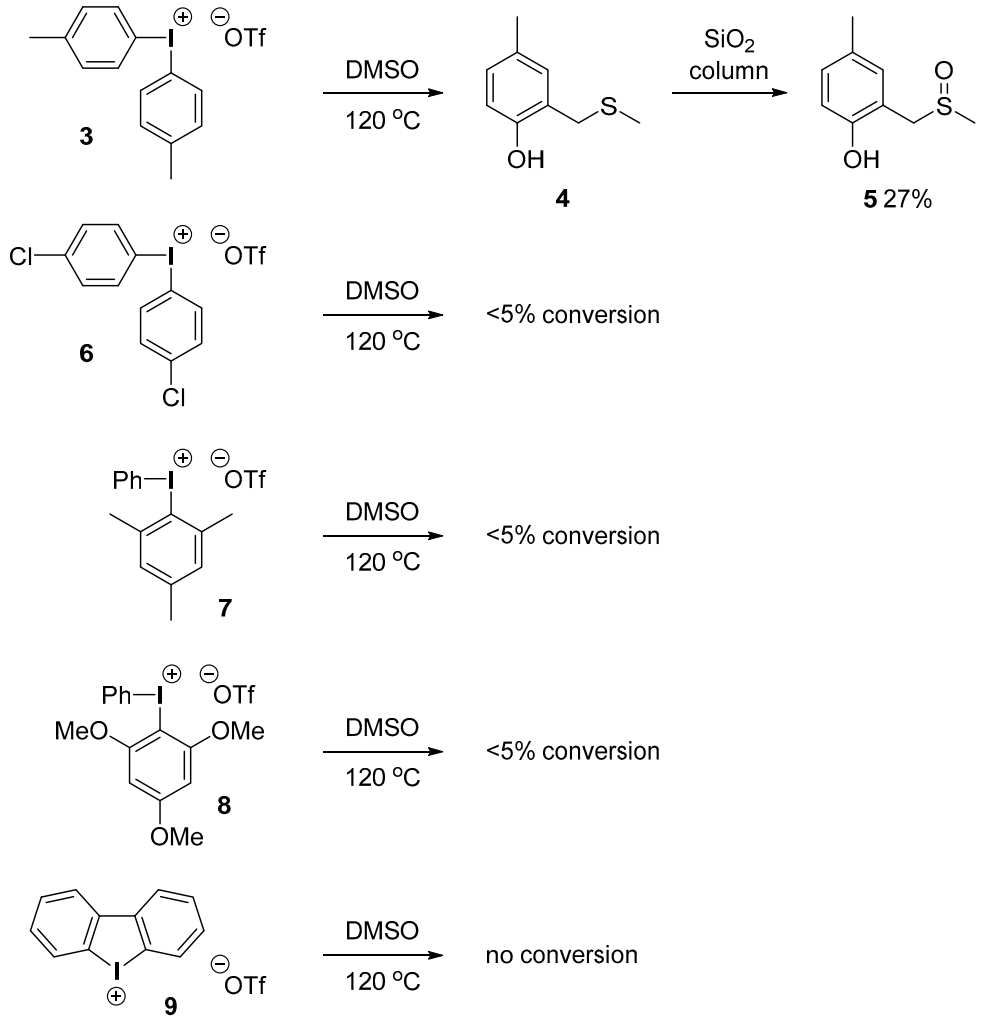
We decided to investigate this reaction with the initial aim of developing a synthetically useful preparation of sulfides (Table 1). Heating diphenyliodonium triflate in anhydrous DMSO for 24 h at 110 °C led to formation of sulfide **1** in a yield of about 8% (entry 1). Increasing the temperature to 120 °C led to an increase in yield to about 40% (entry 2). Further increasing the temperature to 130 and 140 °C led to similar yields whereas at 150 °C a sharp drop in yield was observed (entries 3–5). Increasing or decreasing the concentration also led to a drop in yield at 120 °C (entries 6–7). An increase in reaction time to 48 h led to a marginal increase in yield and, after chromatography, a 46% yield of the sulfoxide **2** was obtained (entry 8). Attempts to prevent oxidation to **2** and isolate the sulfide **1** by chromatography using different solvents or swapping silica gel for alumina all failed. Samples of **1** could be obtained, but containing varying amounts of **2**. Finally, repeating the reaction using non-anhydrous DMSO led to a diminished yield (entry 9).

Table 1. Effect of reaction conditions on the formation of sulfide **1** by the reaction between diphenyliodonium triflate and anhydrous DMSO.

Entry	Temperature (°C)	Molarity (M)	Time (h)	Yield (%) [1]
1	110	0.14	24	8
2	120	0.14	24	40
3	130	0.14	24	40
4	140	0.14	24	40
5	150	0.14	24	2
6	120	0.28	24	21
7	120	0.056	24	21
8	120	0.14	48	(46)
9	120	0.14	24	5 [2]

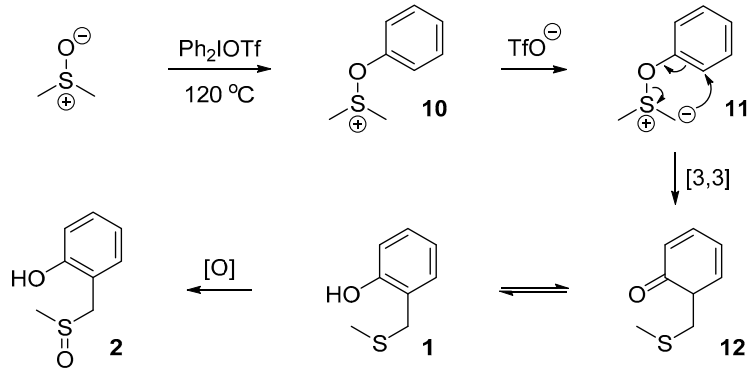
[1] NMR yield of **1** from an average of two or more experiments using 1,4-dinitrobenzene as an internal standard. [2] "Wet" DMSO used. Yield in parentheses is of sulfoxide **2** after flash chromatography.

Despite our best efforts, further improvements in yield could not be obtained. To determine if this process occurred with other diaryliodonium salts, di-*p*-tolyliodonium triflate **3**, phenyl(mesityl)iodonium triflate **5**, phenyl(2,4,6-trimethoxyphenyl)iodonium triflate **6**, and cyclic iodonium triflate **7** were heated in DMSO at 120 °C (Scheme 2). Similar to the diphenyl analog, tolyliodonium **3** underwent the arylation process and generated phenol **4**. Isolation of pure **4** proved difficult but sulfoxide **5** could be isolated with a yield of 27%. Careful purification enabled isolation of a small sample of **4** containing **5**. The yield of **4** (and **5**) is noticeably lower than the yield for **1** (and **2**). Bis(4-chlorophenyl)iodonium triflate **6** was similarly heated at 120 °C in DMSO for 16 h but only a trace of the arylated product was observed by NMR analysis of the crude reaction mixture. The mesityl iodonium salt **7** has been popularized due to its ability to selectively transfer one aromatic group in preference to the other [13–16]. In the present case, very low conversion of the iodonium salt was observed upon heating in DMSO. Similarly, phenyl(2,4,6-trimethoxyphenyl)iodonium triflate **8** has been shown to selectively transfer one aryl group over the other but this compound was also unreactive under heating in DMSO [17]. In addition, cyclic salt **9** did not undergo any conversion upon heating for 24 h. These results suggest that increasing the substitution on the aryl groups retards the reaction with DMSO and that using mesityliodonium or trimethoxyphenyliodonium salts prevents the reaction almost completely.



Scheme 2. Attempted arylations of DMSO with other iodonium salts.

This reaction with DMSO is envisaged to proceed through a mechanism related to the Pummerer [18] and interrupted-Pummerer [19] processes (Scheme 3). Arylation of the oxygen atom in DMSO leads to sulfonium **10**. Deprotonation leads to formation of ylide **11** which undergoes a thia-Sommelet–Hauser rearrangement to **12** [20]. Rearomatization provides the observed product **1**, which is readily oxidized to the sulfoxide **2** on silica. Formation of the isomeric 1,4-alkylated phenol is not observed, suggesting that this is a rearrangement process rather than elimination of phenol and readdition.



Scheme 3. Proposed mechanism for arylation process.

3. Materials and Methods

Diaryliodonium salts were prepared using literature methods: PhI_2OTf [21], **3** [22], **6** [22], **7** [23], **8** [24], **9** [21]. NMR spectra were obtained using a Bruker 400 MHz Avance spectrometer. Chemical shifts δ (in ppm) for ^1H and ^{13}C NMR are referenced to the residual protio-solvent. For ^1H NMR: $CDCl_3$, 7.26 ppm. For ^{13}C NMR: $CDCl_3$, 77.16 ppm. Coupling constants (*J*) are expressed in Hertz (Hz). HRMS analyses were obtained using an Agilent 1290 Infinity II HPLC + 6545 QTOF operating with the electrospray ionization technique; only the mass ion is reported.

3.1. General Method for Arylation Process

Diaryliodonium triflate (0.28 mmol) was dissolved in anhydrous DMSO (2 mL) under a N_2 atmosphere. The mixture was heated to 120 °C and stirred for 48 h. Water (10 mL) was added followed by addition of EtOAc (10 mL). The mixture was stirred rapidly for 20 min until the layers were clear. The resulting mixture was transferred to a separating funnel and the aqueous layer was run off. The organic layer was washed with water (4 × 10 mL), dried with Na_2SO_4 and filtered. All volatiles were removed under vacuum and the crude was purified by flash chromatography using a petrol/ethyl acetate gradient.

Characterization Data

2-((Methylthio)methyl)phenol **1** and 2-((methylsulfinyl)methyl)phenol **2** were obtained as colorless oils (22 mg combined, 46% yield). 2-((Methylthio)methyl)phenol **1**: ^1H NMR ($CDCl_3$, 400 MHz): δ 1.99 (3H, s, Me), 3.78 (2H, s, -CH_2-), 6.54 (1H, s, OH), 6.86 (1H, t, *J* = 7.4 Hz, Ar), 6.90 (1H, d, *J* = 8.0 Hz, Ar), 7.08 (1H, d, *J* = 7.6 Hz Ar), 7.20 (1H, t, *J* = 7.7 Hz Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 34.7, 117.3, 120.7, 122.4, 129.3, 130.8, 155.5. 2-((Methylsulfinyl)methyl)phenol **2**: ^1H NMR ($CDCl_3$, 400 MHz): δ 2.50 (3H, s, Me), 3.78 (1H, d, *J* = 14.3 Hz, H^a), 4.47 (1H, d, *J* = 14.3 Hz, H^b), 6.90 (1H, t, *J* = 7.4 Hz, Ar), 7.01 (1H, d, *J* = 7.4 Hz, Ar), 7.05 (1H, d, *J* = 8.1 Hz, Ar), 7.27 (1H, t, *J* = 8.0 Hz, Ar), 9.19 (1H, s, OH); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 36.0, 55.2, 117.7, 119.3, 120.7, 130.7, 132.3, 156.8; IR: 992 (s), 1096 (m), 1277 (s), 1456 (s), 1594 (m), 2922 (m). HRMS $[M+H]^+$ calc'd for $C_8H_{11}O_2S^+$: 171.0474, found: 171.0477.

4-Methyl-2-((methylthio)methyl)phenol **4** and 4-methyl-2-((methylsulfinyl)methyl)phenol **5** were obtained as colorless oils (14 mg combined, 27% yield). 4-Methyl-2-((methylthio)methyl) phenol **4**: ^1H NMR ($CDCl_3$, 400 MHz): δ 1.99 (3H, s, Me), 2.25 (3H, s, SMe), 3.74 (2H, s, -CH_2-), 6.35 (1H, s, OH), 6.79 (1H, d, *J* = 8.2 Hz, Ar), 6.88 (1H, s, Ar), 6.99 (1H, d, *J* = 8.1 Hz, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 14.4, 20.6, 34.7, 117.0, 122.1, 129.7, 129.9, 131.3, 153.2. 4-Methyl-2-((methylsulfinyl)methyl)phenol **5**: ^1H NMR ($CDCl_3$, 400 MHz): δ 2.27 (3H, s, Me), 2.50 (3H, s, SOMe), 3.75 (1H, d, *J* = 14.2 Hz, H^a), 4.41 (1H, d, *J* = 14.2 Hz, H^b), 6.81 (1H, s, Ar), 6.93 (1H, d, *J* = 8.2 Hz, Ar), 7.05 (1H, dd, *J* = 1.7, 8.1 Hz, Ar), 8.89 (1H, brs, OH); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 20.5, 36.1, 55.3, 117.5, 119.2, 130.0, 131.3, 132.7, 154.5; IR: 993 (s), 1111 (m), 1277 (s), 1423 (m), 1511 (m), 2915 (m). HRMS $[M+H]^+$ calc'd for $C_9H_{12}NaO_2S^+$: 207.0450, found: 207.0456.

4. Conclusions

Herein, we describe the arylation of DMSO with diphenyliodonium triflate and bis(*p*-tolyl)iodonium triflate. This method provides a simple access to a substituted phenol; however, diaryliodonium salts are popular and useful reagents and DMSO is a popular and useful solvent, therefore this reaction could be an undesirable side-reaction in many instances. More substituted aryliodonium salts and cyclic diaryliodonium salts appear to be more stable and do not react with DMSO at high temperatures to any appreciable extent.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/org3030020/s1, ^1H and ^{13}C NMR spectra for **1**, **2**, **4** and **5**.

Author Contributions: Conceptualization, W.J.M.; investigation, K.K.; writing—original draft preparation, W.J.M.; writing—review and editing, W.J.M. and K.K.; supervision, W.J.M.; funding acquisition, W.J.M. All authors have read and agreed to the published version of the manuscript.

Funding: A PhD studentship (K.K.) was funded by an EPSRC Doctoral Training Partnership, grant number EP/T51813X/1.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available in the Supplementary Material.

Acknowledgments: We thank the University of Huddersfield for supporting this work and Neil McLay for NMR assistance.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

References

1. Pacheco-Benichou, A.; Besson, T.; Fruit, C. Diaryliodoniums Salts as Coupling Partners for Transition-Metal Catalyzed *C*- and *N*-Arylation of Heteroarenes. *Catalysts* **2020**, *10*, 483. [CrossRef]
2. Zhichao, X.; Chengfeng, X. Progresses of Diaryliodonium Salts in Organic Reactions. *Chin. J. Org. Chem.* **2013**, *33*, 2119–2130.
3. Merritt, E.A.; Olofsson, B. Diaryliodonium Salts: A Journey from Obscurity to Fame. *Angew. Chem. Int. Ed.* **2009**, *48*, 9052–9070. [CrossRef] [PubMed]
4. Grushin, V.V. Cyclic diaryliodonium ions: Old mysteries solved and new applications envisaged. *Chem. Soc. Rev.* **2000**, *29*, 315–324. [CrossRef]
5. Shetgaonkar, S.E.; Mamgain, R.; Kikushima, K.; Dohi, T.; Singh, F.V. Palladium-Catalyzed Organic Reactions Involving Hypervalent Iodine Reagents. *Molecules* **2022**, *27*, 3900. [CrossRef]
6. Shetgaonkar, S.E.; Raju, A.; China, H.; Takenaga, N.; Dohi, T.; Singh, F.V. Non-Palladium-Catalyzed Oxidative Coupling Reactions Using Hypervalent Iodine Reagents. *Front. Chem.* **2022**, *10*, 909250. [CrossRef] [PubMed]
7. Stuart, D.R. Aryl Transfer Selectivity in Metal-Free Reactions of Unsymmetrical Diaryliodonium Salts. *Chem. Eur. J.* **2017**, *23*, 15852–15863. [CrossRef]
8. Zawia, E.; Moran, W.J. Aqueous DMSO Mediated Conversion of (2-(Arylsulfonyl)vinyl)iodonium Salts to Aldehydes and Vinyl Chlorides. *Molecules* **2016**, *21*, 1073. [CrossRef]
9. Breugst, M.; Corral Bautista, F.; Mayr, H. Nucleophilic Reactivities of the Anions of Nucleobases and Their Subunits. *Chem. Eur. J.* **2012**, *18*, 127–137. [CrossRef]
10. Appel, R.; Mayr, H. Nucleophilic Reactivities of Sulfur Ylides and Related Carbanions: Comparison with Structurally Related Organophosphorus Compounds. *Chem. Eur. J.* **2010**, *16*, 8610–8614. [CrossRef]
11. Mancuso, A.J.; Swern, D. Activated Dimethyl Sulfoxide: Useful Reagents for Synthesis. *Synthesis* **1981**, *1981*, 165–185. [CrossRef]
12. Wan, C.; Shi, J.; Li, Y. Reactions of Sulfoxides with Benzynes. *Synlett* **2022**, *33*, 721–727.
13. Sundalam, S.; Nilova, A.; Seidl, T.L.; Stuart, D.R. A Selective C−H Deprotonation Strategy to Access Functionalized Arynes by Using Hypervalent Iodine. *Angew. Chem. Int. Ed.* **2016**, *55*, 8431–8434. [CrossRef] [PubMed]
14. Wang, M.; Huang, Z. Transition metal-free *N*-arylation of secondary amides through iodonium salts as aryne precursors. *Org. Biomol. Chem.* **2016**, *14*, 10185–10188. [CrossRef] [PubMed]
15. Stuart, D.R. Unsymmetrical Diaryliodonium Salts as Aryne Synthons: Renaissance of a C−H Deprotonative Approach to Arynes. *Synlett* **2017**, *28*, 275–279. [CrossRef]
16. Nilova, A.; Sibbald, P.A.; Valente, E.J.; Gonzalez-Montiel, G.A.; Richardson, H.C.; Brown, K.S.; Cheong, P.H.-Y.; Stuart, D.R. Regioselective Synthesis of 1,2,3,4-Tetrasubstituted Arenes by Vicinal Functionalization of Arynes Derived from Aryl(Mes)iodonium Salts. *Chem.—Eur. J.* **2021**, *27*, 7168–7175. [CrossRef]
17. Saikia, R.A.; Hazarika, N.; Biswakarma, N.; Deka, R.C.; Thakur, A.J. Metal-free *S*-arylation of 5-mercaptotetrazoles and 2-mercaptopyridine with unsymmetrical diaryliodonium salts. *Org. Biomol. Chem.* **2022**, *20*, 3890–3896. [CrossRef]
18. Bur, S.K.; Padwa, A. The Pummerer Reaction: Methodology and Strategy for the Synthesis of Heterocyclic Compounds. *Chem. Rev.* **2004**, *104*, 2401–2432. [CrossRef]
19. Higuchi, K.; Tayu, M. The Interrupted Pummerer Reaction: Design of Sulfoxides and their Utility in Organic Synthesis. *Heterocycles* **2021**, *102*, 783–824. [CrossRef]
20. Lin, X.; Yang, W.; Yang, W.; Liu, X.; Feng, X. Asymmetric Catalytic [2,3] Stevens and Sommelet–Hauser Rearrangements of α-Diazo Pyrazoleamides with Sulfides. *Angew. Chem. Int. Ed.* **2019**, *58*, 13492–13498. [CrossRef]
21. Elsherbini, M.; Moran, W.J. Scalable electrochemical synthesis of diaryliodonium salts. *Org. Biomol. Chem.* **2021**, *19*, 4706–4711. [CrossRef] [PubMed]

22. Li, F.; Thevenon, A.; Rosas-Hernández, A.; Wang, Z.; Li, Y.; Gabardo, C.M.; Ozden, A.; Dinh, C.T.; Li, J.; Wang, Y.; et al. Molecular tuning of CO_2-to-ethylene conversion. *Nature* **2020**, *577*, 509–513. [CrossRef] [PubMed]
23. Mayer, R.J.; Ofial, A.R.; Mayr, H.; Legault, C.Y. Lewis Acidity Scale of Diaryliodonium Ions toward Oxygen, Nitrogen and Halogen Lewis Bases. *J. Am. Chem. Soc.* **2020**, *142*, 5221–5233. [CrossRef] [PubMed]
24. Koseki, D.; Aoto, E.; Shoji, T.; Watanabe, K.; In, Y.; Kita, Y.; Dohi, T. Efficient *N*-arylation of azole compounds utilizing selective aryl-transfer TMP-iodonium(III) reagents. *Tetrahedron Lett.* **2019**, *60*, 1281–1286. [CrossRef]