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Letter

Dehydrogenative C−H Phenochalcogenazination

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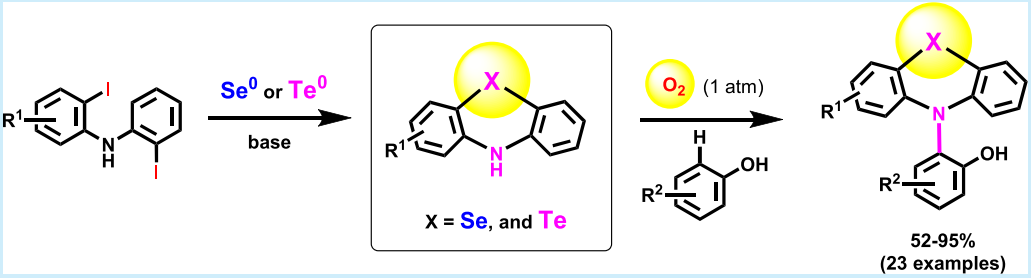

ABSTRACT: Heavy-atom-modified chalcogen-fused triarylamine organic materials are becoming increasingly important in the photochemical sciences. In this context, the general and direct dehydrogenative C−H phenochalcogenazination of phenols with the heavier chalcogens selenium and tellurium is herein described. The latter dehydrogenative C−N bond-forming processes operate under simple reaction conditions with highly sustainable O_2 serving as the terminal oxidant.

"I shall not decide whether that smell belongs to both, or whether tellurium is often associated with the new substance. Nevertheless, as a reminder of the *affinity* of the latter with tellurium, I have named it selenium."[1] Upon the discovery of the latter element in 1818, Berzelius had already noted the chemical similarity of newly found selenium with already known sulfur and tellurium. He also noted some important redox differences. Another essential difference within the chalcogen group lies with the variation of covalent radius, which approximatively doubles from oxygen to tellurium.[2]

Vast numbers of organic heterocyclic structures are known with oxygen and sulfur, yet considerably fewer with selenium and almost none with metalloid tellurium. However, the chemistry of selenium and tellurium is becoming increasingly important in the field of heterocyclic chemistry, associated to the emergence of novel properties.[2] The latter are becoming a research priority in the field of bioactive compounds[3] and, in particular, organic materials and catalysts (Figure 1).[4−8]

Meanwhile, the cross-dehydrogenative phenothiazination reaction has grown into a straightforward synthetic tool for the direct access to important triarylamine structures (Scheme 1).[9] Its most important conceptual feature is that it represents a rare case of intermolecular dehydrogenative amination reaction, wherein no catalyst nor additive is required, apart from a mild oxidant.[10] Importantly, even trivial O_2 can serve as an efficient oxidant in this reaction, conferring on it a highly sustainable character.[11] Its specificity is moreover excellent, in particular for phenothiazines as N−H substrates (**PSZH**, X = S) and phenols and related electron-rich arenes as C−H substrates.[9] Until now, however, this reaction has been mostly

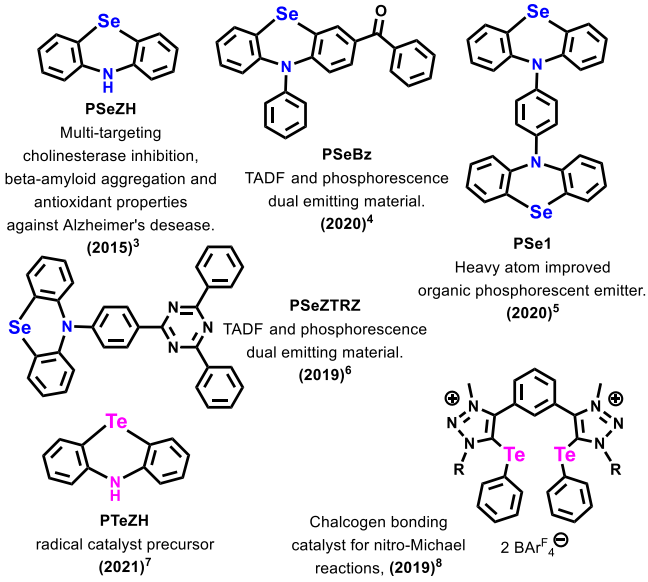

Figure 1. Recent selected Se- and Te-containing heterocyclic materials and catalysts.

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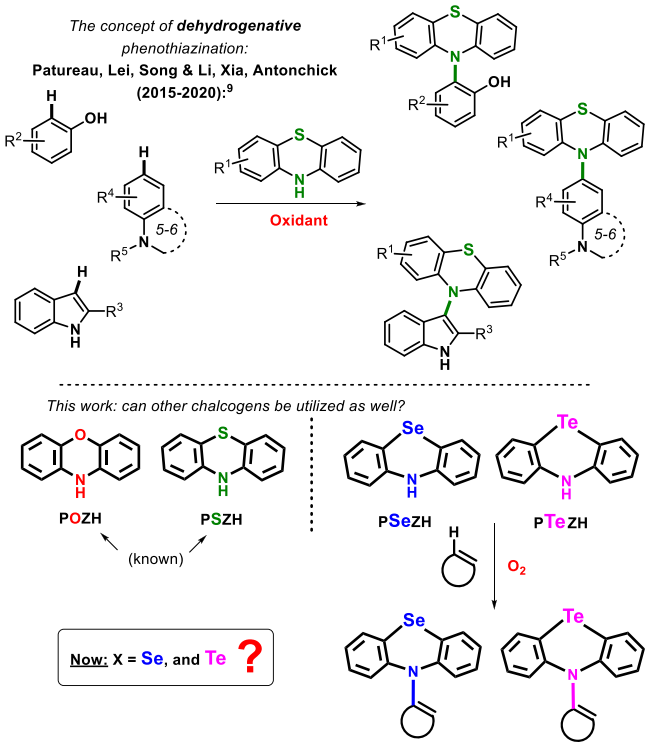
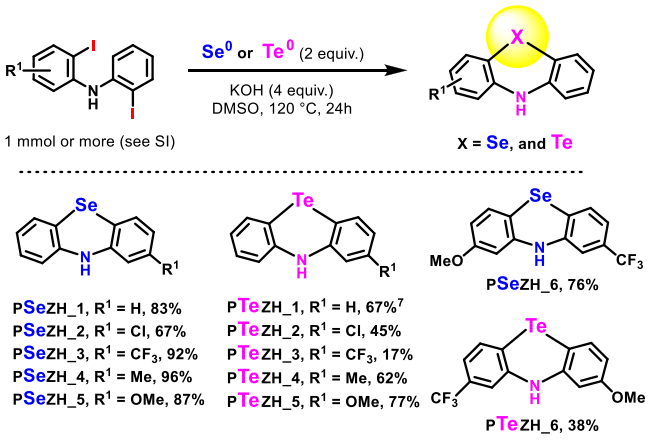
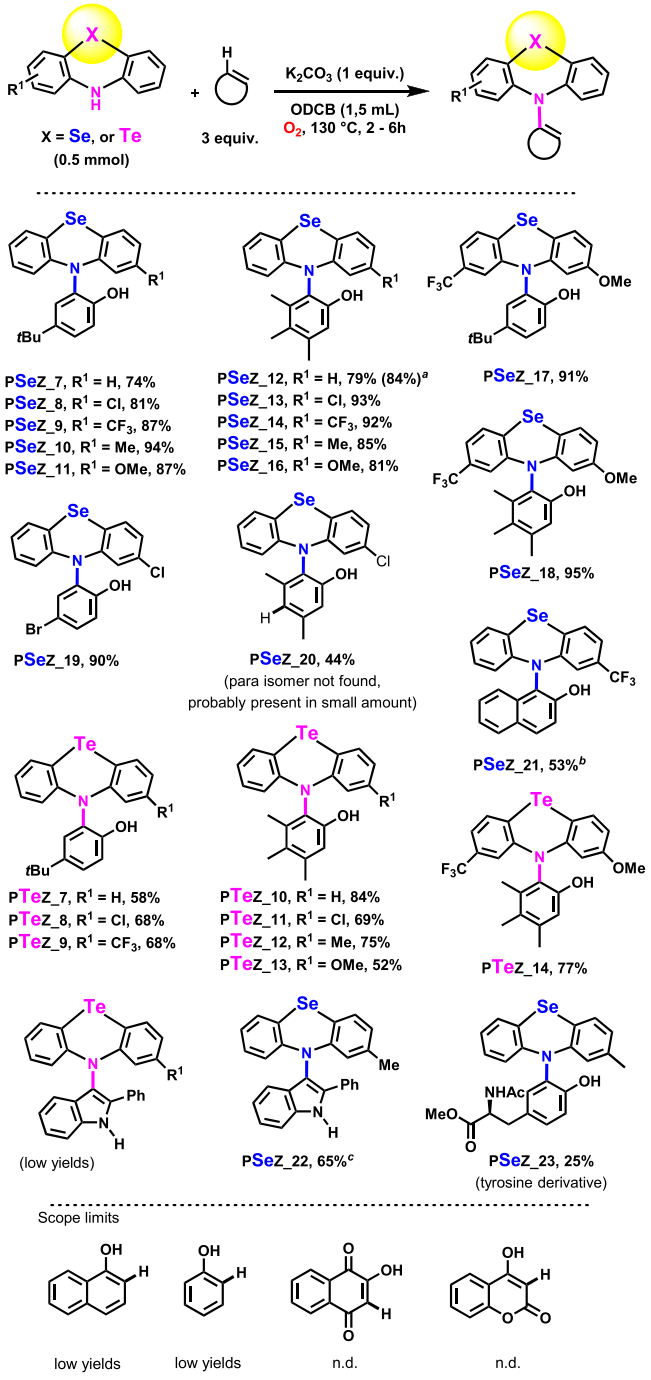
Scheme 1. Dehydrogenative Phenothiazination Reaction



Scheme 2. PXZH Synthesis, Isolated Yields



Scheme 3. Dehydrogenative C−H Phenochalcogenazination with Selenium and Tellurium: Isolated Yields



[a]Two mmol scale. [b]K_2HPO_4 was utilized instead of K_2CO_3. [c]150 °C, 18 h.

limited to phenothiazines as the N−H coupling partners. The reason for this high specificity is well-understood: **PSZHs** combine a low N−H bond dissociation energy (BDE)[12] and low oxidation potential with N-centered radical persistency.[13] These features facilitate their oxidative interception with phenols or/and phenol radicals into a C−N bond-forming cross-dehydrogenative coupling process. But how exactly limited are the **PSZHs** backbones as coupling partners? Can the bridging chalcogen atom X be varied? Some authors have already noted in earlier works that phenoxazine **POZH** (X = O) is also a competent N−H substrate in the dehydrogenative C−H chalcogenazination reaction.[9] This finding, along with the rising interest for heavy-atom-modified chalcogen-fused triarylamine organic materials (Figure 1),[3−8] encouraged us to investigate the larger chalcogens. Thus, the aim of the present work is to explore whether or not phenoselenazines (**PSeZHs**, X = Se) and phenotellurazines (**PTeZHs**, X = Te) can also act as efficient N−H substrates.

After investigating several synthetic routes from the literature, we selected a simple 2,2′-diododiarylamine pathway under basic conditions with elemental selenium or tellurium to furnish the desired **PXZH** azines in high yields.[7] This approach is inexpensive, easy, mild, versatile in terms of functional group tolerance, and importantly, scalable. The synthetic results are summarized in Scheme 2 (see also the Supporting Information (SI)). Generally, the yields are excellent for the selenium

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analogues and encouraging for the tellurium ones, which is presumably due to the larger and more-strained heterocyclic structure of the latter. Typical functional groups such as chloro, methoxy, methyl, and CF_3 were otherwise well-tolerated.

These new **PSeZHs** and **PTeZHs** were then evaluated as N−H coupling partners in the O_2-mediated cross-dehydrogenative phenochalcogenazination of some characteristic phenols. For this, we utilized a basic aerobic method recently developed for phenothiazines (**PSZH**).[7] To our satisfaction, the method afforded high yields with almost identical conditions than required for **PSZHs** and **POZH** (X = S and O, respectively), moreover with excellent functional group tolerance (Scheme 3; see also the SI). Indeed, electron-donating (methyl, methoxy) and electron-withdrawing groups (chloro, bromo, CF_3) were well-accommodated. Even a tyrosine derivative[14] could be obtained (**PSeZ_23**), albeit in low yield. The method is moreover easily scalable. For instance, **PSeZ_12** was obtained in 84% yield on a 2 mmol scale.

We were then able to obtain an X-ray structure of one of these heavy-chalcogen-fused triarylamine structures, that of **PSeZ_7** (Figure 2, Scheme 4). Very similar to that observed in

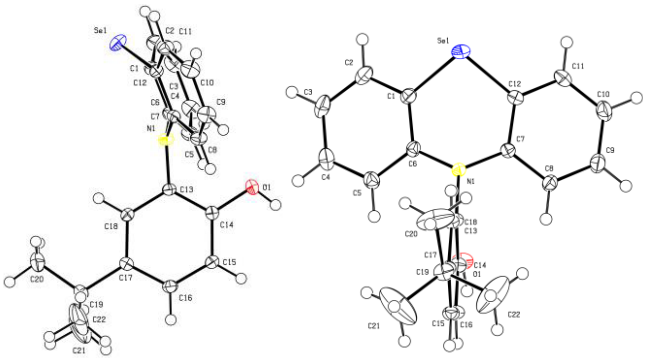
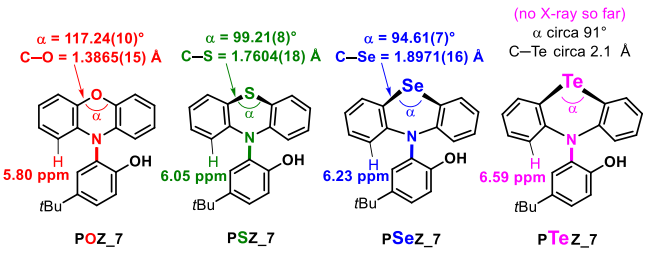


Figure 2. X-ray structure of **PSeZ_7**, 50% probability level, side and front view. Compound **PSeZ_7** crystallized with one diisopropyl ether molecule. The solvent molecule has been omitted for clarity (see the SI).

Scheme 4. Characteristic Differences from X = O to Te[a]



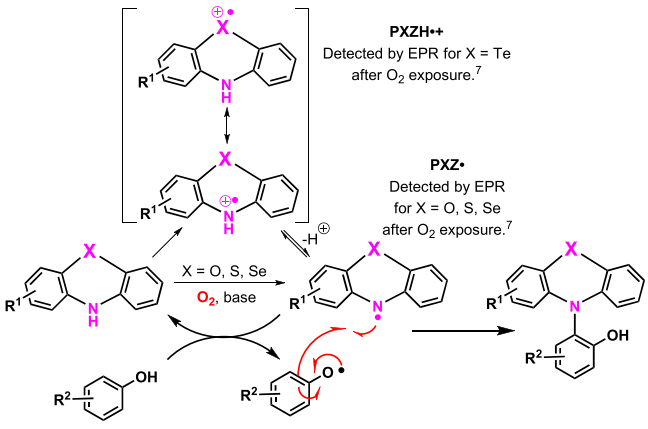
[a]Characteristic ^{1}H NMR signals in DMSO-d_6. X-ray structure of **POZ_7** and **PSZ_7**: see ref 13. X-ray structure of most resembling **PTeZH**: see ref 15.

the known cases of oxygen and sulfur, the **PSeZ** moiety sits mostly perpendicular to the plane of the phenol moiety. Surprisingly, however, the potential and characteristic intramolecular OH···N hydrogen bond does not seem to take place within this crystal. Indeed, the pyramidal-shaped triarylamine moiety is pointing in the opposite direction, with respect to the OH group, which itself is pointing toward a solvent molecule.

Other characteristic features are the expected longer C−X bonds (from 1.3865(15) Å for X = O to 1.8971(16) Å for X = Se), and the considerably shorter C−X−C angles, from 117.24(10)° for X = O (quasi-regular and flat hexagonal heterocycle) to 94.61(7)° for X = Se (heavily distorted heterocyclic ring). While no X-ray structure of a tellurium congener could be obtained at this stage, the heterocyclic distortion therein is expected to be even greater, with a C−Te−C angle expected at ca. 91°, and a C−Te distance expected at ca. 2.1 Å.[15]

Based on literature precedents with X = S,[13] the dehydrogenative C−H phenochalcogenazination reaction is expected to run along a radical mechanism, as depicted in Scheme 5. The phenochalcogenazine **PXZH** undergoes

Scheme 5. Proposed Mechanism



hydrogen atom abstraction (HAT) upon reaction with O_2 under basic conditions to generate a persistent **PXZ**$^\bullet$ mostly nitrogen centered neutral radical. The latter key species can accumulate, eventually triggering HAT from the phenol. The phenol radical generated in this manner is then intercepted by **PXZ**$^\bullet$ to form the cross-dehydrogenative C−N coupling product. In support of this mechanism, a recently published study demonstrated that all phenochalcogenazines (X = O, S, Se, Te) have a similarly low oxidation potential (determined by cyclic voltammetry), associated with a mostly N-centered neutral radical persistency (determined by EPR spectroscopy after O_2 exposure).[7] Although some small differences were observed in the case of the larger **PTeZH** congener, which seems, according to its EPR profile, to accommodate a mostly protonated radical cation intermediate **PTeZH**$^{\bullet+}$, these altered features do not seem to forbid the C−N cross-dehydrogenative coupling reactivity, as illustrated in Scheme 3.

In summary, we demonstrated that the dehydrogenative C−H phenochalcogenazination reaction is a general concept, which can be extended to include selenium and tellurium. The latter afford the corresponding heavy-atom chalcogen-fused triarylamine materials in good yields, while utilizing only O_2 as a most sustainable terminal oxidant. This new synthetic tool should facilitate the development of heavy-atom-based fused organic materials.

■ ASSOCIATED CONTENT

Supporting Information

CCDC 2063310 contains the supplementary crystallographic data for this paper (compound **PSeZ_7**). These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by

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contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: + 44 1223 336033. The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c00573.

Experimental procedures and characterization of new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Original quote: "Je ne déciderai point si cette odeur leur appartient à tous les deux, ou si le tellure est souvent accompagné de la substance nouvelle. Cependant, pour rappeler *les rapports* de cette dernière avec le tellure, je l'ai nommée sélénium." Berzelius, J. J. Lettre de M. Berzelius à Mr. Berthollet sur deux Métaux nouveaux. *Ann. Chim. Phys.*, Tome 7 (1818), p 199.

(2) (a) Chinchilla, R.; Najera, C.; Yus, M. Metalated Heterocycles and Their Applications in Synthetic Organic Chemistry. *Chem. Rev.* **2004**, *104*, 2667. (b) Banerjee, B.; Koketsu, M. Recent developments in the synthesis of biologically relevant selenium-containing scaffolds. *Coord. Chem. Rev.* **2017**, *339*, 104. (c) Detty, M. R.; O'Regan, M. B. *Tellurium-Containing Heterocycles*; John Wiley & Sons, 1994.

(3) Tin, G.; Mohamed, T.; Gondora, N.; Beazely, M. A.; Rao, P. P. N. Tricyclic phenothiazine and phenoselenazine derivatives as potential multi-targeting agents to treat Alzheimer's disease. *MedChemComm* **2015**, *6*, 1930.

(4) Kim, C. L.; Jeong, J.; Lee, D. R.; Jang, H. J.; Kim, S.-T.; Baik, M.-H.; Lee, J. Y. Dual Mode Radiative Transition from a Phenoselenazine Derivative and Electrical Switching of the Emission Mechanism. *J. Phys. Chem. Lett.* **2020**, *11*, 5591.

(5) Lee, D. R.; Lee, K. H.; Shao, W.; Kim, C. L.; Kim, J.; Lee, J. Y. Heavy Atom Effect of Selenium for Metal-Free Phosphorescent Light-Emitting Diodes. *Chem. Mater.* **2020**, *32*, 2583.

(6) de Sa Pereira, D.; Lee, D. R.; Kukhta, N. A.; Lee, K. H.; Kim, C. L.; Batsanov, A. S.; Lee, J. Y.; Monkman, A. P. The effect of a heavy atom on the radiative pathways of an emitter with dual conformation, thermally-activated delayed fluorescence and room temperature phosphorescence. *J. Mater. Chem. C* **2019**, *7*, 10481.

(7) Cremer, C.; Goswami, M.; Rank, C. K.; de Bruin, B.; Patureau, F. W. Tellurium(II)/Tellurium(III)-Catalyzed Cross-Dehydrogenative C−N Bond Formation. *Angew. Chem., Int. Ed.* **2021**, *60*, 6451.

(8) (a) Wonner, P.; Dreger, A.; Vogel, L.; Engelage, E.; Huber, S. M. Chalcogen Bonding Catalysis of a Nitro-Michael Reaction. *Angew. Chem., Int. Ed.* **2019**, *58*, 16923. (b) Wonner, P.; Steinke, T.; Vogel, L.; Huber, S. M. Carbonyl Activation by Selenium- and Tellurium-Based Chalcogen Bonding in a Michael Addition Reaction. *Chem. - Eur. J.* **2020**, *26*, 1258. (c) Kolb, S.; Oliver, G. A.; Werz, D. B. Chemistry Evolves, Terms Evolve, but Phenomena Do Not Evolve: From Chalcogen−Chalcogen Interactions to Chalcogen Bonding. *Angew. Chem., Int. Ed.* **2020**, *59*, 22306. (d) Haberhauer, G.; Gleiter, R. The Nature of Strong Chalcogen Bonds Involving Chalcogen Containing Heterocycles. *Angew. Chem., Int. Ed.* **2020**, *59*, 21236.

(9) (a) Louillat-Habermeyer, M.-L.; Jin, R.; Patureau, F. W. O_2-mediated dehydrogenative amination of phenols. *Angew. Chem., Int. Ed.* **2015**, *54*, 4102. (b) Jin, R.; Patureau, F. W. Mild, Periodate-Mediated, Dehydrogenative C−N Bond Formation with Phenothiazines and Phenols. *Org. Lett.* **2016**, *18*, 4491. (c) Zhao, Y.; Huang, B.; Yang, C.; Xia, W. Visible-Light-Promoted Direct Amination of Phenols via Oxidative Cross-Dehydrogenative Coupling Reaction. *Org. Lett.* **2016**, *18*, 3326. (d) Zhao, Y.; Huang, B.; Yang, C.; Li, B.; Gou, B.; Xia, W. Photocatalytic Cross-Dehydrogenative Amination Reactions between Phenols and Diarylamines. *ACS Catal.* **2017**, *7*, 2446. (e) Tang, S.; Wang, S.; Liu, Y.; Cong, H.; Lei, A. Electrochemical Oxidative C−H Amination of Phenols: Access to Triarylamine Derivatives. *Angew. Chem., Int. Ed.* **2018**, *57*, 4737. (f) Tang, S.; Zeng, L.; Lei, A. Oxidative R^1−H/R^2−H Cross-Coupling with Hydrogen Evolution. *J. Am. Chem. Soc.* **2018**, *140*, 13128. (g) Bering, L.; D'Ottavio, L.; Sirvinskaite, G.; Antonchick, A. P. Nitrosonium ion catalysis: aerobic, metal-free cross-dehydrogenative carbon−heteroatom bond formation. *Chem. Commun.* **2018**, *54*, 13022. (h) Jin, R.; Bub, C. L.; Patureau, F. W. Phenothiazinimides: Atom-Efficient Electrophilic Amination Reagents. *Org. Lett.* **2018**, *20*, 2884. (i) Liu, K.; Tang, S.; Wu, T.; Wang, S.; Zou, M.; Cong, H.; Lei, A. Electrooxidative *para*-selective C−H/N−H cross-coupling with hydrogen evolution to synthesize triarylamine derivatives. *Nat. Commun.* **2019**, *10*, 639. (j) Wu, Y.-C.; Jiang, S.-S.; Song, R.-J.; Li, J.-H. A metal- and oxidizing-reagent-free anodic *para*-selective amination of anilines with phenothiazines. *Chem. Commun.* **2019**, *55*, 4371. (k) Vemuri, P. Y.; Wang, Y.; Patureau, F. W. *Para*-Selective Dehydrogenative Phenothiazination of Hydroquinolines and Indolines. *Org. Lett.* **2019**, *21*, 9856. (l) Patureau, F. W. The Phenol-Phenothiazine Coupling: an Oxidative Click Concept. *ChemCatChem* **2019**, *11*, 5227.

(10) (a) Li, C.-J. Cross-Dehydrogenative Coupling (CDC): Exploring C−C Bond Formations beyond Functional Group Transformations. *Acc. Chem. Res.* **2009**, *42*, 335. (b) Yeung, C. S.; Dong, V. M. Catalytic Dehydrogenative Cross-Coupling: Forming Carbon−Carbon Bonds by Oxidizing Two Carbon−Hydrogen Bonds. *Chem. Rev.* **2011**, *111*, 1215. (c) Morofuji, T.; Shimizu, A.; Yoshida, J.-i. Metal- and Chemical-Oxidant-Free C-H/C-H Cross-Coupling of Aromatic Compounds: The Use of Radical-Cation Pools. *Angew. Chem., Int. Ed.* **2012**, *51*, 7259. (d) Girard, S. A.; Knauber, T.; Li, C.-J. The cross-dehydrogenative coupling of C(sp3)-H bonds: a versatile strategy for C-C bond formations. *Angew. Chem., Int. Ed.* **2014**, *53*, 74. (e) Yi, H.; Zhang, G.; Wang, H.; Huang, Z.; Wang, J.; Singh, A. K.; Lei, A. Recent Advances in Radical C−H Activation/Radical Cross-Coupling. *Chem. Rev.* **2017**, *117*, 9016. (f) Huang, C.-Y.; Kang, H.; Li, J.; Li, C.-J. En Route to Intermolecular Cross-Dehydrogenative Coupling Reactions. *J. Org. Chem.* **2019**, *84*, 12705.

(11) Gulzar, N.; Schweitzer-Chaput, B.; Klussmann, M. Oxidative coupling reactions for the functionalisation of C−H bonds using oxygen. *Catal. Sci. Technol.* **2014**, *4*, 2778.

(12) Lucarini, M.; Pedrielli, P.; Pedulli, G. F.; Valgimigli, L.; Gigmes, D.; Tordo, P. Bond Dissociation Energies of the N-H Bond and Rate Constants for the Reaction with Alkyl, Alkoxyl, and Peroxyl Radicals of Phenothiazines and Related Compounds. *J. Am. Chem. Soc.* **1999**, *121*, 11546.

(13) Goswami, M.; Konkel, A.; Rahimi, M.; Louillat-Habermeyer, M.-L.; Kelm, H.; Jin, R.; de Bruin, B.; Patureau, F. W. Mechanism of the dehydrogenative phenothiazination of phenols. *Chem. - Eur. J.* **2018**, *24*, 11936.
(14) Song, C.; Liu, K.; Wang, Z.; Ding, B.; Wang, S.; Weng, Y.; Chiang, C.-W.; Lei, A. Electrochemical oxidation induced selective tyrosine bioconjugation for the modification of biomolecules. *Chem. Sci.* **2019**, *10*, 7982.
(15) Junk, T.; Irgolic, K. J.; Reibenspies, J. H.; Meyers, E. A. Structure of phenotellurazine. *Acta Cryst., Sect. C: Cryst. Struct. Commun.* **1993**, *C49* (5), 938−940.

https://doi.org/10.1021/acs.orglett.1c00573
Org. Lett. 2021, 23, 3243−3247