Ismayil A. Aliyev
Boris A. Trofimov
Lyudmila A. Oparina

Aromatic Thiols and Their Derivatives

Translated by Igor G. Grushin

Springer

Aromatic Thiols and Their Derivatives

Ismayil A. Aliyev • Boris A. Trofimov •
Lyudmila A. Oparina

Aromatic Thiols and Their Derivatives

Springer

Authors
Ismayil A. Aliyev
Baku State University
Baku, Azerbaijan

Boris A. Trofimov
A.E. Favorsky Irkutsk Institute of Chemistry
Irkutsk, Russia

Lyudmila A. Oparina
A.E. Favorsky Irkutsk Institute of Chemistry
Irkutsk, Russia

Translated by
Igor G. Grushin
A.E. Favorsky Irkutsk Institute of Chemistry
Irkutsk, Russia

ISBN 978-3-030-69620-7 ISBN 978-3-030-69621-4 (eBook)
https://doi.org/10.1007/978-3-030-69621-4

Translation from the Russian language edition: *ароматические тиолы и их производные* by I.A. Aliyev, L.A. Oparina, B.A. Trofimov, © The Authors, 2018. Published by Новосибирск, издательство "ГЕО". All Rights Reserved.
© The Editor(s) (if applicable) and The Author(s), under exclusive license to Springer Nature Switzerland AG 2021
This work is subject to copyright. All rights are solely and exclusively licensed by the Publisher, whether the whole or part of the material is concerned, specifically the rights of reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.
The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.
The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, expressed or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Switzerland AG
The registered company address is: Gewerbestrasse 11, 6330 Cham, Switzerland

Preface

The present monograph is devoted to one of the developing topical areas of the organosulfur compounds chemistry, i.e. to the synthesis, reactivity, and fundamental physical properties of aromatic thiols and their derivatives (aryl thiols, sulfides, sulfones, sulfoxides, their acylated derivatives, and thioacylates).

The necessity and timeliness of the monograph is quite obvious to everyone who is familiar with chemistry and technologies of organosulfur compounds and sulfur chemistry in general. At present, the huge reserves of elemental sulfur, released during hydrodesulfurization of petroleum products, have been accumulated and continue to increase. The need for their utilization is strongly dictated by both technological and environmental problems, the acuteness of which is steadily growing. Therefore, we believe that the summarizing of publications devoted to aromatic organosulfur derivatives is timely and useful. Of course, the authors do not in any way consider that the use of organosulfur compounds, such as aryl thiols and their derivatives can solve all the problems associated with the utilization of million tons of elemental sulfur.

Note that in the world scientific literature the flow of publications (original papers and reviews) on the chemistry of aromatic thiols increases year by year. However, a monograph summarizing the main achievements in this field, especially over the last decades, was lacking before the publication of this book.

The monograph covers, along with traditional (classical) methods for the synthesis of aromatic thiols and their derivatives, the newest approaches to the formation of the carbon-sulfur bonds based on the application of transition metals and their complexes. The examples of the synthesis of the most important and available representatives of aromatic thiol derivatives are given at the end of each chapter.

Over the last decades, the attention of researchers has attracted such an important property of thiols (especially aromatic ones), as the ease of their addition to the double and triple bonds. Such reactions, as a rule, occur in the presence of cheap radical initiators or under the action of ultraviolet irradiation and do not require sophisticated and expensive metal complex catalysts. Now, these reactions have found wide practical applications. No wonder that recently several reviews and dozens of original papers and patents have been dedicated to this issue. To this extensively developing research direction, which is now referred to as "ene-thiol chemistry," is given a significant place in the monograph.

The authors tried to focus their presentation on large series of aromatic thiols and their derivatives bearing different substitutes, which has allowed a correct comparative analysis of both reactivity and various physicochemical properties of the corresponding compounds. For this purpose, the relevant publications were chosen, in which the correlation analysis with reliable statistical processing was systematically and correctly applied. Accordingly, the monograph contains tables of physical and chemical properties of large series of compounds studied. These tables already in themselves represent a factual value and, naturally, increase the importance of the monograph as a reference manual.

The monograph consists of seven chapters. The first five of them cover various aspects of the synthesis and reactivity of the studied objects. In Chap. 1, methods for the synthesis of aryl thiols are discussed. The Chap. 2 is devoted to aromatic sulfides and general approaches to their synthesis. Also, the issues related to the direct preparation of individual representatives of these compounds are analyzed. These representatives were needed to expand the scope of the series, which were subsequently used for the correlation analysis of the relationship between the reactivity, physical properties, and structure of the molecules studied. In particular, the nontrivial problem of aryl thiols alkylation with tertiary alkyl halides is considered in this chapter.

The Chap. 3 covers the methods for the synthesis of aromatic disulfides, sulfoxides, sulfones, and some other derivatives of aromatic thiols. In our opinion, the usage of selenium analogs of the studied derivatives, namely arylselenoacylates, for comparative analysis, is of particular value.

The Chap. 4 deals with the reactions of aromatic sulfides: the electrochemical oxidation of aryl thiols and their derivatives, the bromination of alkyl aryl and alkyl benzyl sulfides, the acylation of alkyl aryl sulfides, and some other reactions involving aromatic thiols and their derivatives.

Chapter 5 of the monograph is dedicated to the application of acylated aromatic sulfides in organic synthesis. In this chapter, the reader should pay attention to the original and simple synthesis of pyrroles and N-vinylpyrroles based on oximes of acylated aromatic sulfides and acetylene in superbasic catalytic systems such as alkali metal hydroxide/DMSO by the Trofimov reaction. In some cases, instead of free acetylene, its synthetic equivalents are used: vinyl chloride and dihaloalkanes, which increases the safety and technological feasibility of the method, and hence the availability of the compounds obtained.

“Of a special scientific significance is the chapter devoted to theoretical issues related to the interaction of the sulfur atom in various degrees of oxidation with neighboring aromatic systems. In this chapter, the ^{1}H, ^{13}C, ^{17}O, ^{19}F, NMR, NQR, IR, UV spectra, as well as X-ray fluorescence data are analyzed at a high professional level, often with correct employment of the correlation analysis. All these data represent a unique material for understanding the main problems of the electronic and conformational structure of aromatic sulfides that allows predicting their reactivity and possible directions of their practical application” (From the review of Academician O. N. Chupakhin on this monograph).

The last Chap. 7 of the monograph is devoted to practical applications of aromatic thiols and their derivatives. Naturally, it was difficult for the authors to encompass in sufficient detail in one chapter all areas, in which these compounds are applied or could be applied. But it seems to us that the above examples convincingly illustrate the almost inexhaustible possibilities of the organosulfur compounds of these series.

The authors hope that the synthetic methods and main reactions involving aromatic thiols and their derivatives summarized in the monograph, the formulated regularities and correlation dependences of the reactivity on their structure, as well as the above experimental procedures, will be of help to the experts working in the field of chemistry and technology of organosulfur compounds.

In general, the monograph can be useful not only to narrow specialists, i.e. synthetic chemists and physical chemists, but also to petrochemists, engineers, pharmacologists, biochemists, photochemists, and photophysicists, who create materials for high technologies, new drugs, and agricultural preparations. The book may be of interest to researchers, faculty staff, graduate students, and students of the chemical faculties of various universities. For many of them, the book can be a desk reference and a source of new ideas.

We express our sincere gratitude to the scientific editor of this monograph, Academician M. P. Yegorov, and to reviewers, Academician O. N. Chupakhin, Profs. N. K. Gusarova and S. V. Amosova for their useful constructive advice and comments. The authors are deeply grateful also to I. G. Grushin and D. N. Tomilin for their valuable help in preparing the manuscript. Any criticism and comments on the book will be accepted with gratitude.

Baku, Azerbaijan — Ismayil A. Aliyev
Irkutsk, Russia — Boris A. Trofimov
Irkutsk, Russia — Lyudmila A. Oparina

Introduction

The targeted search for synthetic routes to novel organosulfur compounds and investigations of their properties remain an urgent challenge in organic chemistry [1–8]. Interest in the structure and reactivity of organosulfur compounds, especially aromatic thiols and their derivatives, is due to their wide application in various fields of modern medicine and technology (pharmaceuticals [9–12], stimulators of biochemical processes [13–16], electroconductive complex-forming polymers [17], anticorrosion coatings [18], additives to lubricating oils and fuels [19], analytical reagents [20–22], agricultural pest control agents [23–24], etc.). Aromatic thiols and their derivatives also attract attention as models for theoretical studies. For example, the kinetics of the enzymatic oxidation of aryl thiols has been studied to better understand the metabolism of numerous drugs containing the thiol function [25].

Polyphenylene(arylene)sulfides are important high-temperature engineering thermoplastics possessing increased mechanical strength and elasticity, as well as useful electrical characteristics [26–27]. The method for their production (developed as back as 1948) by high-temperature condensation of polyhalobenzenes in the presence of sulfur and alkali metal carbonates did not find wide industrial application, and therefore, interest in these compounds is not faded to the date. Various reactions of aromatic thiols, sulfides, and disulfides are employed for the synthesis of such compounds. For instance, polyphenylene sulfides are prepared via the reaction of electron transfer involving diphenyl disulfide [28]. Polyphenylene disulfide is also obtained from diphenyl sulfide and sulfur chloride [29]. Catalytic oxidation of aromatic dithiols affords aromatic cyclic disulfide oligomers possessing good solubility and high glass transition temperature [30]. Cyclic disulfide oligomers are used for the construction of polythioarylenes having high thermostability [31]. High-molecular electrically conductive polyphenylene sulfide-phenyleneamine is utilized as a soluble model of polyaniline [32]. The synthesis and functionalization of soluble derivatives of bromomethylated polyphenylene sulfides have been implemented [33]. Macrocyclic arylthioesters (simple and complex oligomers) are synthesized from phthaloyldichloride and diatomic thiophenols [34]. In recent years, transition metals-catalyzed reactions are increasingly being used to prepare polyarylene sulfides. Thus, an approach to phenylene sulfide-sulfoxide oligomers via palladium-catalyzed cross-coupling of aryl iodides with bromothiophenol is described. Further growth of the polymer molecule occurs due to the addition of bromothiophenol to the obtained sulfide after copper-catalyzed substitution of bromine by iodine [35]. Monodisperse *para*-phenylene sulfide oligomers with a high degree of crystallinity are prepared by the Cu-catalyzed cross-coupling of Ar–S and the aromatic substitution of fluorine by aryl thiolates [36]. Oxidative polymerization of diphenyl disulfides in the presence of a vanadium complex has been realized [37].

Synthesis and functionalization of the closest derivatives of aromatic thiols (sulfides, disulfides, sulfoxides, sulfones) continue to command the research interest. The search for new reactions with the participation of these compounds and investigations of their valuable properties are progressing rapidly. The obtained chemical and biochemical data stimulate a comprehensive study of the electronic and spatial structure of organosulfur compounds, especially aromatic thiols and their derivatives. This is necessary to develop more rational, environmentally benign, energy saving, and atom-economical approaches for the synthesis of these important class of compounds.

The peculiarities of the electronic, conformational, and other spatial characteristics of aromatic thiols, sulfides, and their closest derivatives as a whole and their individual fragments, the localization of electron density on atoms and bonds, and the ease of its redistribution, symmetry, and molecular orbitals enable to correctly understand the participation of these molecules in chemical processes, to predict the direction, rate, and other physical-chemical characteristics of organic and bioorganic reactions involving the studied compounds.

Aromatic sulfur derivatives in II, IV, and VI valence states represent convenient objects for establishing the fundamental relationships between the physical-chemical properties of the most important organosulfur compounds, especially aromatic thiols and their derivatives, their structure, and reactivity. Much attention is paid to the conjugation in the series of sulfur compounds with different valencies, to the nature of the interaction between sulfur atom and π- or p-electrons of the substituents, to the rationalization of duality (π-donor or π-acceptor effect) of its electronic influence.

For a long time, the common point of view on the nature of the acceptor properties of the sulfur atom was based on the hypothesis of its participation in 3d–π-interaction. Later, it became clear that this effect had a much more complex character [38–42], since the conclusions about the manifestation of 3d-π-conjugation were often contradictory, and some results could not be explained at all using this hypothesis. A more correct understanding of this effect was hindered by the absence of systematic studies of compounds with a regularly changing structure, which began to appear only in the late 1980s [43–57]. In the present monograph, the analysis of these studies occupies a significant place.

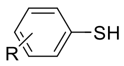
The main sections of the monograph are devoted to the following issues:

- Directed synthesis of aryl thiols, their derivatives; comprehensive physical-chemical study of properties of these compounds;
- Critical analysis of theoretical representations on the electronic structure and reactivity of aromatic thiols, sulfides, and their derivatives on the basis of available experimental data;
- Supplementing the scientific foundations of rational control of technological processes with the participation of the most practically important organosulfur compounds.

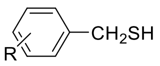
Also, the following issues are discussed in detail:

1. Methods for the synthesis of aromatic sulfur derivatives in II, IV, and VI valence states and (for comparison) their selenium analogs.
2. An original approach to the synthesis of (organylthio)phenylpyrroles by the Trofimov reaction [58–60].
3. Reactivity of aromatic sulfides on the basis of the results of chemical and physical-chemical studies.
4. Spatial and electronic structure, mutual effects of molecular fragments in the series of substituted aryl and benzyl sulfides, aryl sulfoxides, sulfones, and their oxygen and selenium analogs.
5. π-Donor and π-acceptor properties of sulfur, selenium, and oxygen compounds in the ground and excited electronic states and the substituents effect.
6. Some little-known areas of practical application of aromatic thiols, sulfides, and their derivatives.

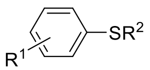
Specifically, the authors focused their attention on the following objects:



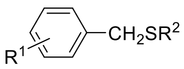
Substituted aromatic thiols



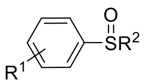
Substituted benzyl thiols



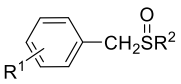
Substituted aromatic sulfides



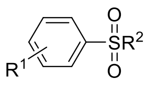
Substituted benzyl sulfides



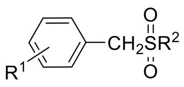
Substituted aromatic sulfoxides



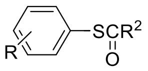
Substituted benzyl sulfoxides



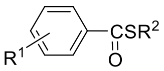
Substituted aromatic sulfones



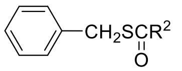
Substituted benzyl sulfones



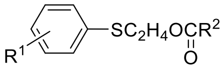
S-aryl thioacylates



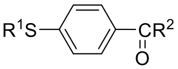
S-Organyl thiobenzoates



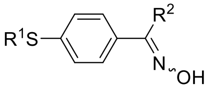
S-Benzyl thioacylates



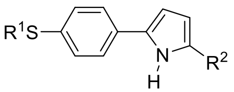
2-(Arylthio)ethyl carboxylates



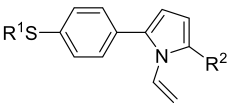
Alkyl 4-(organylthio)phenyl ketones



(Alkylthio)aryl ketoximes



(Organylthio)phenylpyrroles



(Organylthio)phenyl-*N*-vinylpyrroles

A number of monographs on chemistry [2–4, 8, 61–66], biochemistry [13, 67–69], and analysis of organosulfur compounds are known. The works by Prilezhaeva [70–71], Oae [2], Mangini [72–73], Voronkov [62], Chmutova [74], Trofimov [63, 65, 75], Guryanova [76], Kalabin [77], and others [64, 78] have given an insight into the character and strength of intramolecular electronic interactions in the ground and excited states of aromatic thiols, sulfides, and their derivatives. The total and partial effects of element-containing substituents relative to the aromatic ring, depending on the nature and the valence state of the heteroatom, the character of the non-aromatic radical, the nature and position of the secondary substituents in the aromatic nucleus, have been analyzed at both the empirical level and within the framework of correlation equations. These questions are briefly considered in this monograph.

The attention of researchers to these issues is not weakened. Temperature effects upon photolysis of aryl vinyl sulfides in comparison with aryl vinyl ethers are studied [79]. The behavior of aryl vinyl sulfides in reactions of tandem photocyclization and intramolecular addition is investigated [80]. It is assumed and confirmed by the data of *ab initio* calculations that the sulfonic cation acts as an active intermediate in the oxidative polymerization of diphenyl disulfide [81]. The photochemical study of aryl vinyl sulfides and aryl vinyl ethers proves the formation of thiocarbonyl and carbonyl ylides [82]. The investigation into non-oxidative Pummerer reaction, on the example of (*R*)-ethyl-*p*-tolylsulfoxide as an equivalent of chiral α-hydroxyethyl anion, evidences the stereoselectivity of S_N2 type. The mechanism for the formation of enantiomerically pure products, L-α-trifluoromethyltreoninate, and D-α-trifluoromethylallothreoninate is given [83]. It is reported on the unusual effect of the transition metal complexes on the catalytic formation of the C–S and C–Se bonds [84]. Zinc-promoted palladium catalysts are proposed for the formation of a carbon-sulfur bond [85]. Catalytic adaptive recognition of thiol and selenol groups in the synthesis of functionalized vinyl monomers is found [86]. Recently, the participation of transition metals in the activation and conversions of the C–S bond has also been considered [87]. Under the action of a silver catalyst, direct thiylation of quinones with aryl disulfide is implemented [88].

The interest in various aspects of chemistry and physical chemistry of aromatic thiols and their derivatives continues to increase, as evidenced by the publication of numerous relevant reviews. For instance, the review [89] covers the C–S bond forming reactions, including the addition of aromatic thiols to unsaturated compounds catalyzed by metal complexes. Similar reactions of thiols and selenols are also summarized [90]. In a later review [91], the formation of aryl–S bond under the action of copper compounds is surveyed. The reactions of fluorine-containing alkyl (aryl)vinyl sulfides and their interaction with electrophilic and nucleophilic reagents are systematically analyzed [92]. The problems of carbon-sulfur bond formation, including transition metals-catalyzed syntheses of aryl sulfides, continue to be the focus of the researchers [87, 93–97]. Particular attention is paid to these issues in the comprehensive reviews of Beletskaya et al. [95–96]. A chapter in the monograph is devoted to transition metals-catalyzed addition of S–H compounds, including aromatic thiols, to alkynes and allenes and related compounds [97]. Regular coverage of achievements in the synthesis of aryl alkyl- and dialkyl sulfides continues even now [98–99].

References

[1] Mashkina, A.V.: Catalytic synthesis of sulfides, sulfoxides and sulfones. Sulfur Rep. **10**, 279–388 (1991)

[2] Oae, S., Okuyama, T.: In: *Organic sulfur chemistry: Biochemical aspects.* CRC Press, p. 288 (1992)

[3] Metzner, P., Thuillier, A.: Sulfur reagents in organic synthesis. Academic Press, p. 200 (1994)

[4] Cremlyn, R.J.: An introduction to organosulfur chemistry. Wiley, p. 262 (1996)

[5] Vogel, P., Turks, M., Bouchez, L., Marković, D., Varela-Álvarez, A., Sordo J.A.: New organic chemistry of sulfur dioxide. Acc. Chem. Res. **40**, 931–942 (2007)

[6] Nakayama, J.: More than 30 years with organic chemistry of sulfur. J. Sulf. Chem. **30**, 393–468 (2009)

[7] Chung, W.J., Griebel, J.J., Kim, E.T., Yoon, H., Simmonds, A.G., Ji, H.J., Dirlam, P.T., Glass, R.S., Wie, J.J., Nguyen, N.A., Guralnick, B.W., Park, J., SomogyiÁrpád, Theato, P., Mackay, M.E., Sung, Y.-E., Char, K., Pyun, J.: The use of elemental sulfur as an alternative feedstock for polymeric materials. Nat. Chem. **5**, 518–524 (2013)

[8] Kutney, G.: Sulfur. History, technology, applications & industry. ChemTec Publishing, Oxford, p. 260 (2013)

[9] Kung, A.L., Wang, S., Klco, J.M., Kaelin, W.G., Livingston, D.M.: Suppression of tumor growth through disruption of hypoxia-inducible transcription. Nat. Med. **6**, 1335–1340 (2000)

[10] Jayakanthan, K., Mohan, S., Pinto, B.M.: Structure proof and synthesis of Kotalanol and de-O-sulfonated Kotalanol, glycosidase inhibitors isolated from an herbal remedy for the treatment of type-2 diabetes. J. Am. Chem. Soc. **131**, 5621–5626 (2009)

[11] Peng, J., Clive, D.L.J.: Asymmetric synthesis of the ABC-ring system of the antitumor antibiotic MPC1001. J. Org. Chem. **74**, 513–519 (2009)

[12] Wada, Y., Otani, K., Endo, N., Harayama, Y., Kamimura, D., Yoshida, M., Fujioka, H., Kita, Y.: Synthesis of antitumor marine alkaloid Discorhabdin A oxa analogues. Org. Lett. **11**, 4048–4050 (2009)

[13] Hatahet, D., Boyd, D., Beckwith, J.: Disulfide bond formation in prokaryotes: history, diversity and design. Biochem. Biophys. Acta. **1844**, 1402–1414 (2014)

[14] Mortimer, A.J.P., Aliev, A.E., Tocher, D.A., Porter, M.J.: Synthesis of the Tagetitoxin core via photo-Stevens rearrangement. Org. Lett. **10**, 5477–5480 (2008)

[15] Iijima, Y., Munakata, A., Shinya, K. Ganesan, A., Doi, T., Takahashi, T.: A solid-phase total synthesis of the cyclic depsipeptide HDAC inhibitor spiruchostatin A. Tetrahedron Lett. **50**, 2970–2972 (2009)

[16] Studentsov, E.P., Ramsh, S.M., Kazurova, N.G. Neporozhneva, O.V., Garabagiu, A.V., Kochina, T.A., Voronkov, M.G., Kuznetsov, V.A., Krivorotov, D.V.: Adaptogens and related groups of drugs: 50 years of research. Reviews on clinical pharmacology and drug therapy. **11**, 41 (2013)

[17] Brembilla, A., Collard, A., Henry, B., Jadamiec, M., Lapkowski, M., Matlengiewicz, M., Rodehüser, L.: Synthesis of functionalized thiophenes for the preparation of conducting polymer films with complexing properties. Phosphorus Sulfur Silicon Relat. Elem. **182**, 723–734 (2007)

[18] Ireni, N.G., Narayan, R., Basak, P., Raju, K.V.S.: Functional polyurethane-urea coatings from sulfur rich hyperbranched polymers and an evaluation of their anticorrosion and optical properties. New J. Chem. **40**, 8081–8092 (2016)

[19] Kuliyev, A.M. Chemistry and technology of additives to oils and fuels. Khimiya, Leningrad, p. 312 (1985)

[20] Gevorgyan, A.M., Yakhshieva, Z.Z., Sultonov, M.M., Daminov, G.N.: *Thioacetamide as an analytical reagent for noble metals*. Djizak, p. 122 (2010)

[21] Makki, M.S.T., Abdel-Rahman, R.M., El-Shahawi, M.S. Synthesis of new bioactive sulfur compounds bearing heterocyclic moiety and their analytical applications. Int. J. Chem. **3**, 181–192 (2011)

[22] Reddy, S.A.N., Reddy, K.J., Duk, L.K., Reddy, A.V.: Evaluation of 2,6-diacetylpyridinebis-4-phenyl-3-thiosemicarbazone as complexing reagent for zinc in food and environmental samples. J. Saudi Chem. Soc. **20**, S271–S279 (2016)

[23] Mel'nikov, N.N.: *Pesticides. Chemistry, technology and application*. M.: Khimiya, p. 712 (1987)

[24] Soldatenkov, A.T., Kolyadina, N.M., Le Tuan, A.: *Pesticides and growth regulators. Applied Organic Chemistry*. M.: Binom. Laboratory of Knowledge, p. 223 (2013)

[25] Burner, U., Jantschko, W., Obinger, C.: Kinetics of oxidation of aliphatic and aromatic thiols by myeloperoxidase compounds I and II. FEBS Lett. **443**, 290–296 (1999)

[26] Wang, Z.Y., Hay, A.S.: Synthesis of poly(p-phenylene sulfide) by thermolysis of bis (4-halophenyl) disulfides. Macromolecules. **24**, 333–335 (1991)

[27] Tsuchida, E., Yamamoto, K., Oyaizu, K., Suzuki, F., Hay, A.S., Wang, Z.Y.: Synthesis of reactive functionalized oligo(p-phenylene sulfide)s. Macromolecules. **28**, 409–416 (1995)

[28] Tsuchida, E., Yamamoto, K., Nishide, H.: New Synthesis of poly(phenylenesulfide)s through an electron transfer. J. Macromol. Sci., Chem. **27**, 1119–1131 (1990)

[29] Miyatake, K., Jikei, M., Yamamoto, K., Nishide, H., Tsuchida, E.: Sulfur-containing polymers by the reaction of diphenyl sulfide with sulfur chlorides. Polym. Adv. Technol. **3**, 401–405 (1992)

[30] Ding, Y., Hay, A.S.: Cyclic aromatic disulfide oligomers: Synthesis and characterization. Macromolecules. **29**, 6386–6392 (1996)

[31] Ding, Y., Hay, A.S.: Preparation of poly(thioarylene)s from cyclic disulfide oligomers. Macromolecules. **30**, 2527–2531 (1997)

[32] Leuninger, J., Uebe, J., Salbeck, J., Gherghel, L., Wang, C., Müllen, K.: Poly(phenylene sulfide–phenyleneamine–phenyleneamine) (PPSAA) - a soluble model for polyaniline. Synth. Met. **100**, 79–88 (1999)

[33] Miyatake, K., Hara, H., Tsuchida, E.: Synthesis and functionalization of bromomethylated poly(phenylene sulfide). Macromol. Chem. Phys. **200**, 1930–1934 (1999)

[34] Qi, Y., Chen, T., Jiang, H., Bo, S, Xing, Y., Lin, Y., Xu, J.: Novel macrocyclic aryl thioether ester oligomers: structure characterization and free-radical ring opening polymerization. Macromol. Chem. Phys. **200**, 2407–2410 (1999)

[35] Vicente, J., Abad, J.A., López-Nicolás, R.M.: Synthesis of molecular chains: phenylene thioether and sulfoxide oligomers. Tetrahedron. **64**, 6281–6288 (2008)

[36] Goyot, O., Gingras, M.: p-Phenylene sulfide oligomers and their properties. Ar–S couplings mediated by copper or by fluorine substitutions. Tetrahedron Lett. **50**, 1977–1981 (2009)

[37] Aida, F., Takatori, Y., Kiyokawa, D., Nagamatsu, K., Oyaizu, K., Nishide, H.: Enhanced catalytic activity of oxovanadium complexes in oxidative polymerization of diphenyl disulfide. Polym. Chem. **7**, 2087–2091 (2016)

[38] Trofimov, B.A., Kositsyna, É.I., Shergina, N.I., Shevchenko, S.G., Vyalykh, E.P.: Comparative estimate of p-π interaction in vinyl ethers and sulfides. Bull. Acad. Sci. USSR, chem. sci. **20**, 1486–1487 (1971)

[39] Trofimov, B.A., Shergina, N.I., Kositsyna, E.I., Vyalykh, E.P., Amosova, S.V., Gusarova, N.K., Voronkov, M.G.: On the contributions of p-π- and π-d-bonding to the basicity of α, β-unsaturated sulfides. Reactivity of organic compounds. **10**, 757–768 (1973)

[40] Trofimov, B.A. Kalabin, G.A., Brzezovsky, V.M., Gusarova, N.K., Kushnarev, D.F., Amosova, S.V.: ^{13}C NMR spectra and conjugation effects in alkoxy and alkylthioenes. II. Correlation of *13*C chemical shifts with the constants of substituents. Reactivity of organic compounds. **11**, 365–379 (1974)

[41] Bernardi, F., Csizmadia, I.G., Mangini, A., Schlegel, H.B., Whangbo, M.H., Wolfe, S.: The irrelevance of d-orbital conjugation. I. The alpha-thiocarbon. A comparative quantum chemical study of the static and dynamic properties and proton affinities of carbonions adjacent to oxygen and to sulfur. J. Am. Chem. Soc. **97**, 2209–2218 (1975)

[42] Bernardi, F., Csizmadia, I.G., Schlegel, H.B., Wolfe, S.: On the π-donating abilities of sulfur and oxygen. A comparative quantum chemical investigation of the static and dynamic properties and gas phase acidities of $^{+}CH_2OH$ and $^{+}CH_2SH$. Can. J. Chem. **53**, 1144–1153 (1975)

[43] Bzhezovskii, V.M., Kalabin, G.A., Aliyev, I.A., Trofimov, B.A., Shakhgel'diyev, M.A., Guliyev, A.M.: Application of NMR spectroscopy to the study of coupling effects. Bull. Acad. Sci. USSR, chem. sci. **25**, 1878–1881 (1976)

[44] Bzhezovskii, V.M., Pestunovich, V.A., Kalabin, G.A., Aliyev, I.A., Trofimov, B.A., Kalikhman, I.D., Shakhgel'diyev, M.A., Kuliyev, A.M., Voronkov, M.G.: Application of NMR spectroscopy to the study of coupling effects. 4.^{1}H,^{13}C, and ^{19}F NMR spectra of alkylthio-p-fluorobenzenes. Bull. Acad. Sci. USSR, chem. sci. **25**, 1882–1884 (1976)

[45] Bazhenov, B.N., Baranskii, V.A., Aliyev, I.A. The combined effect of structural, environmental and temperature factors on the alkaline hydrolysis of S-(aryl) thioacetates in water-ethanol mixtures. Comparison with the oxygen analogues. Zh. Org. Khim. **21**, 2348–2354 (1985)

[46] Bazhenov, B.N., Zasukhina, E.Yu., Baransky, V.A., Aliyev, I.A.: Alkaline hydrolysis of S-(aryl)thioacetates in mixtures of water with dioxane and acetonitrile. Zh. Org. Khim. **21**, 2354–2359 (1985)

[47] Bzhezovskii, V.M., Shcherbakov, V.V., Aliyev, I.A., Dolenko, G.N., Trofimov, B.A.: ^{13}C NMR and x-ray fluorescence spectra of a series of benzyl sulfides. Bull. Acad. Sci. USSR, chem. sci. **34**, 1281–1283 (1985)

[48] Gasanov, B.R., Stradyn, Ya.P., Azhdarova, Kh.A., Aliyev, I.A.: Anodic voltammetry of organosulfur compounds. I. Structural effects in the electrochemical oxidation of substituted thiophenols. Izv. AN Latv. SSR. Ser. Khim. 290–295 (1987)

[49] Gasanov, B.R., Stradyn, Ya.P., Shahgelidiyev, M.A., Aliyev, I.A., Azhdarova, Kh.A.: Anodic voltammetry of organosulfur compounds. II. The effects of substituents on the electrooxidation of substituted thioanisols. Izv. AN Latv. SSR. Ser. Khim. 296–301 (1987)

[50] Bzhezovskii, V.M., Valeev, R.B., Kalabin, G.A., Aliyev, I.A., Trofimov, B.A.: Study of conjugation effects. Communication 26.^{13}C,^{17}O, and ^{33}S NMR spectra of p-chlorophenyl alkyl sulfides and sulfones. Bull. Acad. Sci. USSR, chem. sci. **36**, 1819–1824 (1987)

[51] Krivdin, L.B., Shcherbakov, V.V., Aliyev, I.A., Kalabin, G.A.: ^{13}C-^{13}C spin-spin coupling constants in structural studies. III. Additivity of substitution effects on the values of direct carbon-carbon constants in the benzene ring of aromatic ethers and sulfides. Zh. Org. Khim. **23**, 569–576 (1987)

[52] Bzhezovsky, V.M., Valeev, R.B., Kalabin, G.A., Aliyev, I.A.: ^{13}C, ^{17}O and ^{33}S NMR spectra of alkyl phenyl sulfones $C_6H_5SO_2Alк$. Zh. Org. Khim. **23**, 147–150 (1987)

[53] Bzhezovskii, V.M., Valeev, R.B., Kalabin, G.A., Aliyev, I.A., Trofimov, B.A.: Study of conjugation effects. Communication 25.^{13}C,^{17}O, and ^{33}S NMR spectra of methyl aryl sulfones. Bull. Acad. Sci. USSR, chem. sci. **36**, 933–936 (1987)

[54] Gasanov, B.R., Stradin, Ya.P., Aliev, I.A., Azhdarova, Kh.A.: Study of conjugation effects. 25. ^{13}C, ^{17}O and ^{33}S NMR spectra of methyl aryl sulfones. Izv. AN Latv. SSR. Ser. Khim. 297–301 (1988)

[55] Dolenko, G.N., Bzhezovskii, V.M., Aliyev, I.A.: Conjugation effects. 27. Analysis of the ^{13}C NMR spectra and SK_β X-ray fluorescence spectra of 1-alkylthio-2,4,6-trimethylbenzenes. Bull. Acad. Sci. USSR, chem. sci. **37**, 900–904 (1988)

[56] Dolenko, G.N., Voronkov, M.G., Alyiev, I.A., Mirskova, A.N., Rakhlin, V.I., Seredkina, S. G.: X-ray spectral analysis of rotational isomerism of aryl-, vinyl-, ethynylalkyl sulfides. Zh. Obshch. Khim. **58**, 81–88 (1988)

[57] Trofimov, B.A., Krivdin, L.B., Shcherbakov, V.V., Aliev, I.A.: Effects of conjugation and the conformational structure of aromatic selenides. Bull. Acad. Sci. USSR, chem. sci. **38**, 54–58 (1989)

[58] *Comprehensive Organic Name Reactions and Reagents.* Wiley&Sons, 3824 p (2009)

[59] *Name Reactions in Heterocyclic Chemistry II.* Wiley, p. 704 (2011)

[60] Stradyn, Y.P.: Name reactions in the chemistry of heterocyclic compounds. Khim. Geterocycl. Soed. **15**, 1262–1266 (1979)

[61] Mashkina, A.V.: *Heterogeneous catalysis in the chemistry of organosulfur compounds.* Novosibirsk: Science, p. 342 (1977)

[62] Voronkov, M.G., Vyazankin, N.S., Deryagina, E.N., Nakhmanovich, A.S., Usov, V.A.: *Reactions of sulfur with organic compounds.* New York-London, p. 342 (1987)

[63] Trofimov, B.A., Amosova, S.V.: *Divinyl sulfide and its derivatives*. Nauka, Novosibirsk, p. 119 (1983)

[64] *Chemistry of organosulfur compounds. General problems* (ed. L.I. Belen'kii). New York: Ellis Horwood, p. 378 (1990)

[65] Trofimov, B.A., Shainyan, B.A.: In: *The chemistry of sulfur-containing functional groups.* (Eds. S. Patai and Z. Rappoport). New York: Wiley, pp. 659–797 (1993)

[66] *Organic chemistry of sulfur* (Ed. S. Oae). Plenum, New York, 713 p (1977)

[67] Jocelyn, P.C.: *Biochemistry of the SH group.* London: Academic Press, p. 404 (1972)

[68] Huxtable, R.J.: *Biochemistry of Sulfur.* Plenum, New York, p. 445 (1986)

[69] Karchmer, J.H.: *The analytical chemistry of sulfur and its compounds.* Wiley-Interscience, New York, p. 534 (1972)

[70] Prilezhaeva, E.N.: *Study in the field of thiylation of multiple bonds and the chemistry of unsaturated sulfur-containing compounds.* Diss. Dr. Sc. Moscow, (1963)

[71] Prilezhaeva, E.N.: *Chemistry of sulfoxides and sulfones*. In: *Synthesis and properties of organosulfur compounds* (Ed. L.I. Belenky), M.: Khimiya, p. 560 (1998)

[72] Mangini, A.A.: Ken veguertekallapota ketertekii szerves vegyü leteuben. Këm. közl. **41**, 41–45 (1974)

[73] Mangini, A.A.: The conjugative ability of divalent sulfur groupings. Atti Accad. Naz. Lincei. **14**, 31–117 (1977)

[74] Chmutova, G.A.: *Investigation of spatial and electronic structure of aryl aliphatic compounds of VI A group elements.* Diss. Dr. Chem. Sci. Kazan, p. 475 (1979)

[75] Trofimov, B.A.: New reactions and chemicals based on sulfur and acetylene. Sulfur Rep. **3**, 83–118 (1983)

[76] Romm, I.P., Guryanova, E.N.: p-π-Conjugation in aromatic compounds of elements of V and VI groups. Usp. Khim. **55**, 225–250 (1986)

[77] Kalabin, G.A.: *NMR spectroscopy and the study of unsaturated chalcogenides.* Diss. Dr. Sc. Irkutsk, p. 490 (1982)

[78] *Organic sulfur chemistry: theoretical and experimental advances* (Eds. F. Bernardi, I. Csizmadia, A. Mangini). Amsterdam: Elsevier, p. 740 (1985)

[79] Dittami, J.P., Nie, X.Y.: Temperature dependent addition reactions during photolysis of aryl vinyl sulfides and aryl vinyl ethers. Design and construction of a variable temperature photoreactor. Synth. Commun. **20**, 541–547 (1990)

[80] Dittami, J.P., Nie, X.Y., Nie, H., Ramanathan, H., Buntel, C., Rigatti, S., Bordner, J., Decosta, D.L., Williard, P.: Tandem photocyclization-intramolecular addition reactions of aryl vinyl sulfides. Observation of a novel [2 + 2] cycloaddition-allylic sulfide rearrangement. J. Org. Chem. **57**, 1151–1158 (1992)

[81] Tsuchida, E., Yamamoto, K., Shouji, E.: Electrophilic reaction of phenyl bis(phenylthio) sulfonium cation as an active species for the oxidative polymerization of diphenyl disulfide. J. Macromol. Sci. A. **31**, 1579–1589 (1994)

[82] Dittami, J.P., Luo, Y., Moss, D., McGimpsey, W.G.: Photochemistry of aryl vinyl sulfides and aryl vinyl ethers: Evidence for the formation of thiocarbonyl and carbonyl ylides. J. Org. Chem. **61**, 6256–6260 (1996)

[83] Crucianelli, M., Bravo, P., Arnone, A., Corradi, E., Meille, S.V., Zanda, M.: The “non-oxidative” Pummerer reaction: Conclusive evidence for S_N2-type stereoselectivity, mechanistic insight, and synthesis of enantiopure l-α-trifluoromethylthreoninate and d-α-trifluoromethyl-allo-threoninate. J. Org. Chem. **65**, 2965–2971 (2000)

[84] Beletskaya, I.P., Ananikov, V.P.: Unusual Influence of the structures of transition metal complexes on catalytic C–S and C–Se bond formation under homogeneous and heterogeneous conditions. Eur. J. Org. Chem. **2007**, 3431–3444 (2007)

[85] Eichman, C.C., Stambuli, J.P.: Zinc-mediated palladium-catalyzed formation of carbon −sulfur bonds. J. Org. Chem. **74**, 4005–4008 (2009)

[86] Ananikov, V.P., Orlov, N.V., Zalesskiy, S.S., Beletskaya, I.P., Khrustalev, V.N., Morokuma, K., Musaev, D.G.: Catalytic adaptive recognition of thiol (SH) and selenol (SeH) groups toward synthesis of functionalized vinyl monomers. J. Am. Chem. Soc. **134**, 6637–6649 (2012)

[87] Wang, L., He, W., Yu, Z.: Transition-metal mediated carbon-sulfur bond activation and transformations. Chem. Soc. Rev. **42**, 599–621 (2013)

[88] Zhang, C., McClure, J., Chou, C.J.: Silver-catalyzed direct thiolation of quinones by activation of aryl disulfides to synthesize quinonyl aryl thioethers. J. Org. Chem. **80**, 4919–4927 (2015)

[89] Kondo, T., Mitsudo, T.: Metal-catalyzed carbon−sulfur bond formation. Chem. Rev. **100**, 3205–3220 (2000)

[90] Ogawa, A.: Activation and reactivity of Group 16 inter-element linkage - transition-metal-catalyzed reactions of thiols and selenols. J. Organomet. Chem. **611**, 463–474 (2000)

[91] Ley, S.V., Thomas, A.W.: Modern synthetic methods for copper-mediated C(aryl)O, C(aryl) N, and C(aryl)S bond formation. Angew. Chem. Int. Ed. **42**, 5400–5449 (2003)

[92] Sizov, A.Y., Kovregin, A.N., Ermolov, A.F.: Fluorine-containing alkyl(aryl) vinyl sulfides. Russ. Chem. Rev. **72**, 357–374 (2003)

[93] Bichler, P., Love, J.A.: In: *Organometallic Approaches to Carbon–Sulfur Bond Formation*, (Ed. A. Vigalok), Berlin, Heidelberg: Springer, 39–64 (2010)

[94] Eichman, C.C., Stambuli, J.P.: Transition-metal-catalyzed synthesis of aryl sulfides. Molecules. **16**, 590 (2011)

[95] Beletskaya, I.P., Ananikov, V.P. Transition-metal-catalyzed C–S, C–Se, and C–Te bond formation via cross-coupling and atom-economic addition reactions. Chem. Rev. **111**, 1596–1636 (2011)

[96] Ananikov, V.P., Zalesskiy, S.S., Beletskaya, I.P.: Catalytic (Ni, Pd, Pt, Rh and Au) and non-catalytic reactions for atom- economic carbon-sulfur, carbon-selenium and carbon-tellurium bonds formation. Curr. Org. Synth. **8**, 2–52 (2011)

[97] Ogawa, A.: In: *Transition-Metal-Catalyzed S–H and Se–H Bonds Addition to Unsaturated Molecules* (Eds. V.P. Ananikov and M. Tanaka), Berlin, Heidelberg: Springer, 325–360 (2013)

[98] Shen, C., Zhang, P., Sun, Q., Bai, S., Hor, T.S.A., Liu, X.: Recent advances in C-S bond formation via C-H bond functionalization and decarboxylation. Chem. Soc. Rev. **44**, 291–314 (2015)

[99] Kazemi, M., Shiri, L. Thioesters synthesis: recent adventures in the esterification of thiols. J. Sulfur Chem. **36**, 613–623 (2015)

Contents

1 Synthesis of Aromatic Thiols 1
1.1 Reactions of Aromatic Compounds with Elemental Sulfur and its Inorganic Compounds 1
1.2 Reactions with Other Sulfur-containing Nucleophiles 4
1.3 Reactions with Sulfur-containing Electrophiles 10
1.4 Reduction of Diaryl Disulfides 14
1.5 Examples of Syntheses 15
1.5.1 Synthesis of 2- and 3-substituted Aryl Thiols from Diazonium Chlorides and Potassium Ethylxanthogenate 15
1.5.2 Synthesis of 4-substituted Aryl Thiols via Reduction of Aromatic Sulfonyl Chlorides 15
1.5.3 Synthesis of Aryl Thiols via Reduction of Diaryl Disulfides 16
References 16

2 Aromatic Sulfides 21
2.1 General Approaches to the Synthesis of Aryl Sulfides 21
2.2 Transition Metal-Catalyzed Methods of the C–S Bond Formation 32
2.3 Directed Synthesis of Substituted Aromatic Sulfides 48
2.3.1 Alkyl Aryl Sulfides 58
2.3.2 *tert*-Alkyl Aryl Sulfides 60
2.3.3 Diaryl Sulfides 61
2.3.4 Vinyl Sulfides 62
2.3.5 Benzyl Thiols and Benzyl Sulfides 65
2.3.6 Dialkyl Sulfides 70
2.4 Examples of Syntheses 72
2.4.1 Reactions of Thiols with Primary and Secondary Alkyl Halides 72
2.4.2 Reactions of Thiols with Tertiary Alkyl Halides and Alcohols 74
2.4.3 Reactions of Thiols with Alkenes 75

2.4.4 Reactions of Thiols with Acetylenes 76
2.4.5 Diaryl Sulfides 77
2.4.6 Functionally Substituted Alkyl Aryl Sulfides 77
References 78

3 Aromatic Disulfides, Sulfoxides, Sulfones, and Other Derivatives of Aromatic Thiols 89
3.1 Aromatic Disulfides 89
3.2 Aromatic Sulfoxides 102
3.3 Aromatic Sulfones 112
3.4 *S*-Alkyl, *S*-Aryl, *S*-Benzylthioacylates, and Organylthiobenzoates 119
3.5 2-(Arylthio)ethyl acylates 127
3.6 Dithiocarboxylic Acid Dibenzyl Esters 128
3.7 Derivatives of Aromatic Selenols 129
3.8 Examples of Syntheses 133
3.8.1 Aromatic Sulfoxides 133
3.8.2 Alkyl Aryl Sulfones 134
3.8.3 Alkyl-, Aryl- and Benzylthioacylates 134
3.8.4 Dithiocarboxylic Acid Dibenzyl Esters 135
3.8.5 Derivatives of Aromatic Selenols 135
References 137

4 Reactivity of Aromatic Thiols and Their Derivatives 149
4.1 Electrochemical Oxidation of Aryl Thiols and Their Derivatives 149
4.1.1 Aryl Thiols 149
4.1.2 Aromatic Sulfides 157
4.2 Bromination of Alkyl Aryl and Alkyl Benzyl Sulfides 168
4.3 Acylation of Alkyl Aryl Sulfides 171
4.4 Hydrolysis of *S*-Aryl Thioacylates 175
4.4.1 The Effect of Leaving Group (Arylthioanion) on Kinetics of Alkaline Hydrolysis of *S*-Aryl Thioacylates 175
4.4.2 The Effect of Acyl Group on Alkaline Hydrolysis of *S*-Aryl Thioacylates 176
4.4.3 The Combined Effects of Structure, Medium and Temperature on Alkaline Hydrolysis of *S*-aryl Thioacylates in Aqueous-Ethanol Mixtures 178
4.4.4 Alkaline Hydrolysis of Aryl Thioacylates in Aqueous–Organic Solvents 184

4.5 Other Reactions Involving Aromatic Thiols and Their Derivatives 189
  4.5.1 Free Radical Reactions 189
  4.5.2 Ionic Reactions 195
  4.5.3 Transition Metal-Catalyzed Reactions 197
References 201

5 Acylated Aromatic Sulfides in Organic Synthesis 209
5.1 Synthesis of Oximes of Acylated Aromatic Sulfides 209
5.2 Alkylthioaryl Pyrroles 210
  5.2.1 Synthesis from (Alkylthio)aryl Alkyl Ketoximes and Acetylene 211
  5.2.2 Synthesis from (Alkylthio)aryl Alkyl Ketoximes and Vinyl Chloride 211
  5.2.3 Synthesis from (Alkylthio)aryl Alkyl Ketoximes and Dihaloalkanes 214
  5.2.4 Structure and Physical–chemical Characteristics of 2-(4-(Alkylthio)phenyl)pyrroles 218
  5.2.5 Addition of Aryl Thiols to *N*-vinylpyrroles 225
5.3 Examples of Syntheses 226
  5.3.1 (Alkylthio)aryl Ketoximes 226
  5.3.2 Pyrroles and *N*-vinyl Pyrroles 226
  5.3.3 Addition of Thiophenols to *N*-vinylpyrroles [52] 230
References 231

6 Electronic and Conformational Structure of Aromatic Thiols and Their Derivatives 235
6.1 ^{1}H, ^{13}C, ^{17}O, ^{19}F, ^{33}S NMR Spectra 235
  6.1.1 ^{1}H and ^{33}S NMR Spectra of Aromatic Thiols 235
  6.1.2 ^{13}C NMR Spectra of Aromatic Sulfides 238
  6.1.3 Direct Spin-Spin Coupling Constants ^{13}C–^{13}C of Alkyl Aryl Sulfides 251
  6.1.4 ^{1}H, ^{13}C, ^{19}F NMR Spectra of Organyl 4-Fluorophenyl Sulfides 253
  6.1.5 NMR Spectra of Alkyl Aryl Sulfoxides 262
  6.1.6 ^{13}C, ^{17}O and ^{33}S NMR Spectra of Alkyl Aryl Sulfones 263
  6.1.7 Conjugation Effects and Conformational Structure in Aromatic Selenides 271
  6.1.8 ^{13}C NMR Spectra of Thiobenzoates and Alkyl Benzyl Sulfides 277
6.2 Effects of Conjugation of the Sulfur Atom 280
  6.2.1 Alkyl Aryl Sulfides 280
  6.2.2 Alkyl Aryl Sulfoxides and Sulfones 288

6.3 Relative Basicity of Alkyl Aryl Sulfides and Some of Their Analogs 290
  6.3.1 Alkyl Phenyl Sulfides 290
  6.3.2 Alkyl Aryl Sulfides 293
  6.3.3 Oxygen and Selenium Analogs of Aromatic Sulfides 296
6.4 Electronic Effects in *S*-Aryl Thioacylates and 2-(Arylthio)ethyl Acylates 299
6.5 ^{35}Cl NQR Spectra 303
  6.5.1 Alkyl 4-Chlorophenyl Sulfides 303
  6.5.2 Alkyl 4-Chlorophenyl Sulfoxides and Sulfones 307
6.6 $^{79/81}$Br NQR Spectra of Alkyl 4-Bromophenyl Sulfides 309
6.7 X-Ray Fluorescent Spectra of Aromatic Thiols and Sulfides 312
6.8 Theoretical Studies of the Structure and Electronic Properties of Aromatic Thiols and Their Derivatives 319
References 323

7 Some Areas of Application of Aromatic Thiols and Their Derivatives 335
7.1 Versatile Reagents 335
7.2 Advanced Polymers 339
7.3 Bioorganic and Medical Chemistry 342
7.4 Optoelectronic Devices 348
7.5 Additives to Oil Products 352
  7.5.1 Antimicrobial Additives 352
  7.5.2 Anti-wear and Extreme Pressure Additives to Lubricating Oils 355
7.6 2-(4-Ethylthiophenyl)Pyrrole as a Reagent for Palladium Determination 357
References 360

Conclusion 369

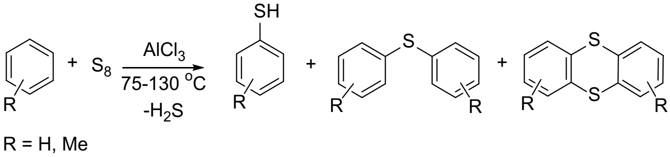
Synthesis of Aromatic Thiols

1

1.1 Reactions of Aromatic Compounds with Elemental Sulfur and its Inorganic Compounds

Synthesis of aromatic thiols and their derivatives is a rather poorly explored area of organosulfur chemistry. Meanwhile, with the rapid progress in industrial organic synthesis, aromatic thiols and their derivatives attract an ever-increasing attention from wide circles of chemical community.

Classical methods for the introduction of the SH-groups into various aromatic compounds are based on the interaction of arenes with sulfur or its inorganic derivatives and are described in the fundamental monograph of Houben-Weyl [1]. It is shown [2] that thiophenol can be obtained using elemental sulfur and anhydrous aluminum chloride, which react with benzene at 75–80 °C. The reaction of toluene with S_8 (115–130 °C) in the presence of $AlCl_3$ affords thiocresols [3]. However, these methods for the synthesis of aromatic thiols are not widely spread, since, along with thiols, which are the major products of the reaction, diarylsulfides and thianthrenes are also formed. The yields of the products depend on the reactants ratio and catalyst amount.

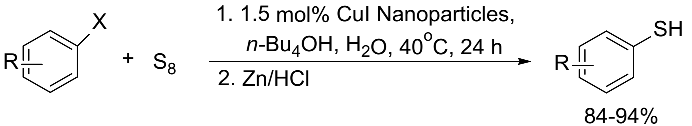


Aryl thiols are also synthesized by the interaction of aryl magnesium halides with elemental sulfur followed by decomposition of the resulting halothiolates with diluted acids or water [4–6]

$$ArMgX \xrightarrow{S_8} ArSMgX \xrightarrow{H^+/H_2O} ArSH$$

I. A. Aliyev et al., *Aromatic Thiols and Their Derivatives*,
https://doi.org/10.1007/978-3-030-69621-4_1

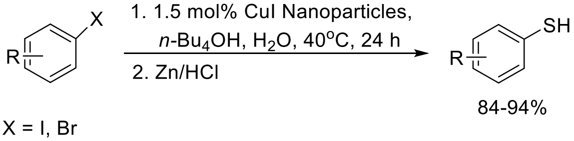
Various bases and Lewis acids are employed to activate elemental sulfur. For instance, aryl iodides upon heating (90 °C) in the presence of K_2CO_3 undergo a CuI-catalyzed cross-coupling reaction with elemental sulfur to deliver, after subsequent treatment with $NaBH_4$ or triphenylphosphine, aromatic thiols with a high yield [7]. A wide range of functional groups including methoxy, hydroxy, acyl, carboxy, amide, bromo, and trifluoromethyl were tolerated in this process.



X = I, Br

R = Me, MeO, CO_2H, NH_2, Cl

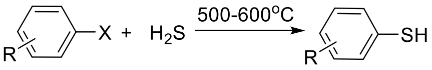
Aryl thiols were also synthesized by the coupling of aryl halides and sulfur powder in the presence of CuI-nanoparticles followed by the reduction with Zn/HCl [8]. The reaction is implemented in water and *n*-Bu_4NOH that makes the process green. Both aryl iodides and activated aryl bromides are formed in moderate to excellent yields.



X = I, Br

R = Me, MeO, CO_2H, NH_2, Cl

Academician M.G. Voronkov et al. have developed promising methods for the synthesis of aryl thiols via high-temperature reactions of halogenated aromatic hydrocarbons with hydrogen sulfide [9–12].



X = Cl, Br; R = H, OH, Cl, Me, CF_3

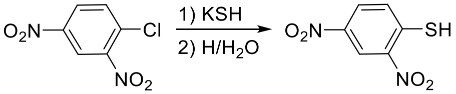
The methods of high-temperature synthesis are also suitable for the preparation of heteroaromatic thiols [10, 12].

Direct nucleophilic substitution of a halogen atom in organohalogen compounds by hydrosulfide anion has become a paradigmatic case in the synthesis of organic thiols [13, 14]. In order to avoid the formation of sulfides due to the equilibrium characteristic of hydrosulfides.

$$2NaSH \overset{H_2O}{\rightleftharpoons} Na_2S + H_2S$$

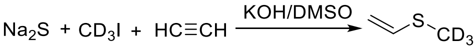
the reaction is carried out in an anhydrous solvent or in an excess of hydrogen sulfide, which limits its scope. Under these conditions, the yields of organic thiols range 36–74% [15].

This method is often used for the synthesis of *ortho*- and *para*-nitro and amino-substituted aryl thiols from the corresponding nitrohaloaromatic compounds [16].



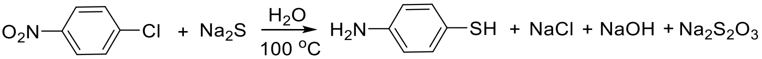
A kinetic study of the reaction between phenylacetylene and sodium hydrosulfide in aqueous DMSO [17] has shown that NaSH is quite stable in DMSO, i.e. the above equilibrium is actually shifted to the left. It turns out [18] that due to the ability of DMSO of extracting sodium hydrosulfide from hydrated Na_2S, it is possible to easily and simply prepare a stable solution of NaSH in DMSO. In the case of $Na_2S•4H_2O$, up to 90% of sodium hydrosulfide is transferred to a solution of DMSO [19]. The purity of NaSH solution in DMSO thus obtained reaches 98%. According to the data [17], such a solution is stable and does not undergo hydrolysis, as it occurs with aqueous or alcohol solutions of NaSH, the hydrosulfide being almost completely dissociated [20]. Upon slow addition of an organic halide to a solution of NaSH in DMSO at room temperature, the corresponding thiols are formed in almost quantitative yields [14]. The method has been implemented using a series of aliphatic bromides (C_2-C_{12}).

It is shown that in the system M_2S/organic halide (M = Na, K), acetylene behaves as an efficient trap of the organic thioanion, which leads to the formation of vinyl organosulfides. Using this new highly effective carrier of hydrosulfide anion, namely a solution of NaSH in DMSO, the deuterated vinyl methyl sulfide has been synthesized with a yield of 95% from CD_3I, Na_2S, and acetylene in DMSO in one preparative stage under very mild conditions (room temperature and atmospheric pressure) [19].

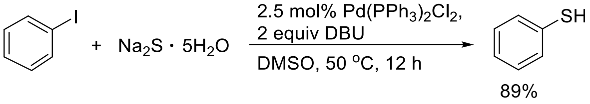


Despite the obvious efficiency, simplicity, and availability of the system Na_2S/H_2O/DMSO, which allows introducing the thiol function into organic compounds via the nucleophilic substitution of the halogen by the SH-group, this reagent is underestimated by organic chemists. In particular, the potential of this reagent for obtaining aromatic thiols from aromatic halides is still obscure. It can be predicted with a high probability that this system will also be very effective for the above purpose. Eventually, the preparative significance of the existing methods for the synthesis of aromatic thiols will be revisited.

The heating of *para*-nitrochlorobenzene with an excess of Na_2S in an aqueous solution is accompanied by the reduction of the nitro group to furnish *para*-aminothiophenol [21, 22].



Formation of thiophenol (89% yield) was observed in $Pd(PPh_3)Cl_2$/dppb-catalyzed coupling reaction of iodobenzene and $Na_2S{\cdot}5H_2O$ in the presence of DBU [23].



1.2 Reactions with Other Sulfur-containing Nucleophiles

The direct nucleophilic substitution of aryl halides with sodium alkylthiolates was considered a simple strategy for the synthesis of aryl thiols. Non-activated aryl halides (chlorides and bromides), as a rule, hardly participate in nucleophilic substitution reactions. The employment of polar non-hydroxyl solvents has significantly expanded the scope of this method. For instance, aryl thiols can be obtained by the reaction of aryl halides with a 2–threefold excess of primary or secondary sodium alkylthiolates in HMPA [24–26], DMF [27], and N-methylpyrrolidone [28]. The one-pot synthesis involves two consecutive stages: the formation of alkyl aryl sulfide via nucleophilic aromatic substitution of the halogen atom by an alkylthiolate anion and the subsequent cleavage of the sulfide across the S − Alkyl bond (dealkylation) to give aromatic thiols [24–28].

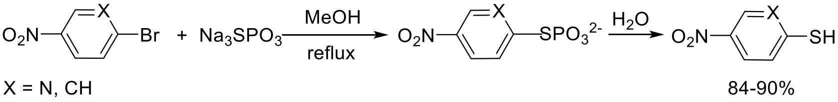
$$\mathrm{ArX} + \mathrm{RSNa} \xrightarrow[\mathrm{-NaX}]{} \left[\mathrm{ArSR}\right] \xrightarrow[\mathrm{-RSR}]{} \mathrm{ArSNa} \xrightarrow{\mathrm{H^+/H_2O}} \mathrm{ArSH}$$

Usually, the reaction proceeds at 100–160 °C. In addition, the dealkylation of sulfides can be executed under the action of alkali metal alkoxides and amides as well as using metal sodium in DMF [27].

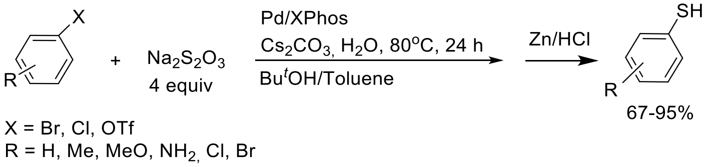
This approach is also suitable for the synthesis of hetaryl thiols such as 2-mercaptothiophene [24], mercaptopyridines [27], and thioquinolines [24, 27].

The methods based on the usage of such *S*-nucleophiles as thiourea, dithiocarbamates, xanthogenates, as well as thioamides and thiophosphates, appear to be more expedient for the preparation of aryl thiols. These one-pot two-step syntheses permit to avoid side processes, which often accompany the direct reactions.

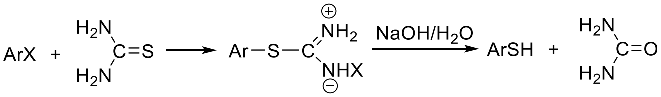
The interaction of activated electron-withdrawing groups of aryl halides with two equivalents of sodium thiophosphate upon boiling in methanol affords arylthiophosphate, which, after treatment with water, is converted into the corresponding thiol in a high yield [29].



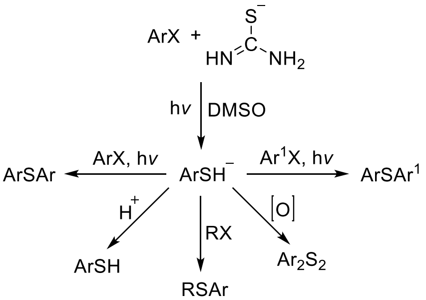
The development of transition-metal-catalyzed C−S coupling reactions has stimulated the emergence of new protocols for the synthesis of thiols. $Pd(OAc)_2$/X-Phos-catalyzed thiolation of aryl halides and trifluomethanesulfonates with sodium thiosulfate as a thiol source proceeds in *tert*-butanol/toluene in the presence of Cs_2CO_3 to give aryl thiosulfate, which is further reduced by Zn/HCl delivering aryl thiols [30]. Water in the system improves the solubility of the sodium thiosulfate.



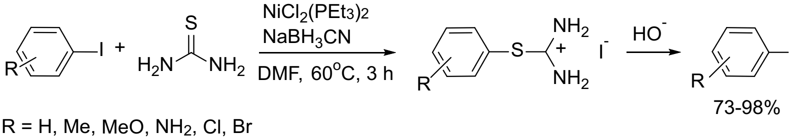
Aryl halides react with thiourea upon heating in alcohol to produce arylisothiuronium salts, the hydrolysis of which leads to the formation of the corresponding thiols [1].



This reaction easily proceeds with aryl halides activated for a nucleophilic attack. Aryl halides with donor substituents in the ring (amino-, alkoxy groups) are activated by UV irradiation [28]. In the photoinduced reactions with thiourea in DMSO (20 °C, 3 h), aryl(benzyl, naphthyl)- and hetaryl(pyridine, quinoline, pyrazine, pyrimidine) halides with OMe, SMe, CN, NO_2, PhCO-substituents successfully generate arylthiolate ions, which, without isolation, can undergo protonation, nucleophilic aliphatic substitution or oxidation to deliver aryl thiols, aryl methyl sulfides, diaryl sulfides or diaryl disulfides in 50–80% yields [31].

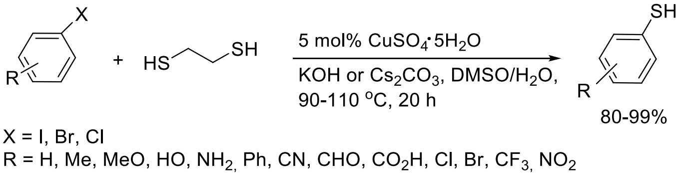


Transition metal catalysts are often exploited to facilitate aromatic nucleophilic substitution in aryl halides. In the presence of catalytic amounts of Ni(0), generated in situ from $[NiCl_2(PPh_3)_2]$, and BH_4CN as a reducing agent, aryl iodides react with thiourea (60 °C, 3–25 h) to give rise to, after the decomposition of isothiouronium iodide and acidification with hydrochloric acid, aryl thiols in quantitative yields [32].

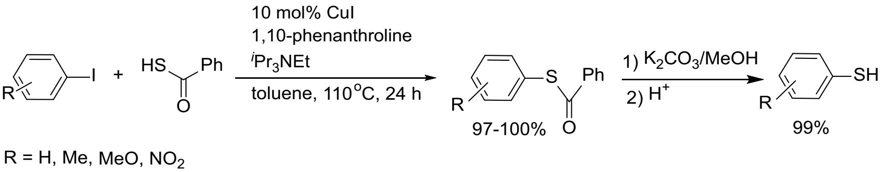


The reaction is successfully implemented in DMF, MeCN, acetone, and dioxane. Electron-donating substituents (amino and alkoxy groups) do not reduce the reactivity of aryl iodides. Under similar conditions, aryl bromides and chlorides do not react with thiourea. The CuI/L-proline-catalyzed coupling of aryl iodides and thiourea occurs in the presence of NaOBu^t in DMSO (90 °C, 24 h) [33].

A highly efficient transition metal-catalyzed one-step synthesis of aryl thiols from aryl halides has been developed [34]. The protocol employs $CuSO_4{\cdot}5H_2O$ as a catalyst and KOH or Cs_2CO_3 as bases, and allows converting aryl iodides, bromides, and chlorides bearing electron-withdrawing groups to the corresponding aryl thiols in good to excellent yields. During the reaction, neither disulfide nor sulfide is formed. It is shown that aryl halides are first coupled with 1, 2-ethanedithiol and the coupled product is transformed in situ to aryl thiols through the C−S bond cleavage via an intramolecular nucleophilic substitution. The protocol tolerates a broad range of functional groups such as amino, hydroxy, trifluoromethyl, ester, carboxy, and formyl.

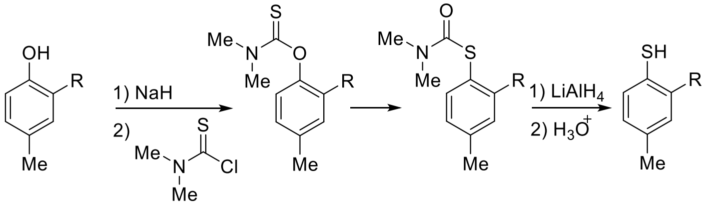


Also, aryl iodides react with thiobenzoic acid in the presence of a copper catalyst and 1,10-phenanthroline to furnish *S*-aryl thiocarboxylates in excellent yields [35]. The coupled product is converted to aryl thiols in quantitative yields upon treatment with K_2CO_3.



This method is applicable to both electron-deficient and electron-rich aryl iodides, and even to sterically hindered substrates.

Phenols can also be used as the starting compounds for the synthesis of aromatic thiols. The phenols are converted to *O*-arylthiocarbamates or thiocarboxylic acid esters and then subjected to thermal rearrangement and hydrolysis [36, 37]. The synthesis of 2,4-disubstituted thiophenols from the corresponding phenols has been described [37]. Deprotonation of the starting phenols followed by the treatment with dimethylcarbamoyl chloride (NaH, dimethoxyethane, boiling, 24 h) furnishes *O*-arylthiocarbamates, which undergo thermolysis (250–310 °C) and rearrangement into *S*-arylthiocarbamates. Reduction of the latter with $LiAlH_4$ in THF and acid hydrolysis give thiophenols in 55–68% yields.

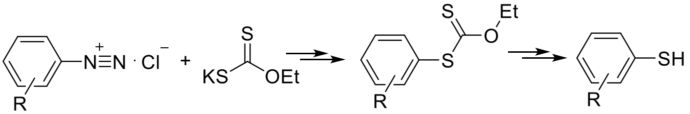


R = Me, *t*-Bu, Ad

A mild conversion of mono- and bicyclic phenols into aryl thiols by palladium-catalyzed coupling reaction of the corresponding triflate with sodium triisopropylsilanethiolate (NaSTIPS) (THF, reflux, 4 h) and subsequent deprotection of the silyl function with tetrabutylammonium fluoride has been published [38].

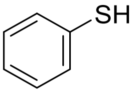
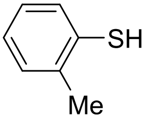
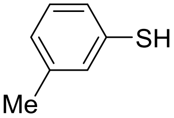
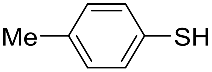
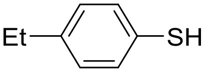
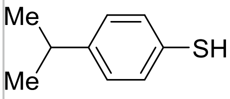
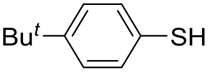
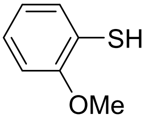
$$\mathrm{ArOH} \xrightarrow{\mathrm{Tf_2O}} \mathrm{ArOTf} \xrightarrow[\text{THF, reflux, 4 h}]{\text{NaSTIPS}} \underset{40\text{-}86\%}{\mathrm{ArS{-}SiPr}^i_3} \xrightarrow[0^\circ\mathrm{C}]{\mathrm{Bu_4NF}} \underset{43\text{-}72\%}{\mathrm{ArSH}}$$

Substitution of the amino group involving the formation of the C–S bond proceeds through diazonium salt, which is readily obtained from primary aromatic amines [13]. Thiourea [39], thiocarboxylates [40], and alkali metal xanthagentes can act as *S*-nucleophiles. Direct reaction with potassium hydrosulfide is not performed, since the latter is a strong reducing agent and under the process conditions is oxidized to molecular sulfur. The Leuckart method comprises the treatment of an aqueous solution of aryldiazonium salts with potassium ethylxanthagenate on moderate heating (40–45 °C). Subsequent alkaline hydrolysis (KOH/EtOH) of the formed *S*-aryl *O*-ethyl xantagenates gives the corresponding aryl thiols.



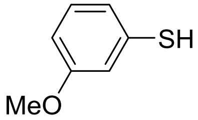
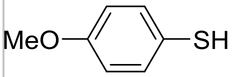
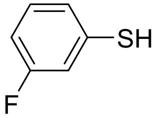
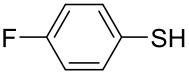
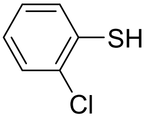
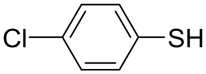
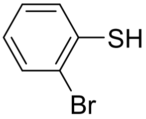
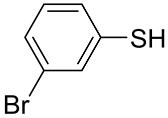
This approach has been used to synthesize a large series of 2- and 3-substituted aryl thiols (Table 1) [41].

Table 1 Aromatic thiols

No.	Structure	Yield, %	B.p., °C/torr (m.p., °C)	n_D^{20}	d_4^{20}
1	2	3	4	5	6
1		72	167–170	1.5870	1.0740
2		45	90–91/25	1.5733	1.0427
3		75	103–104/40	1.5715	1.0446
4		82	195 (43)		
5		65	94–95/16	1.5715	1.0365
6		75	112/20	1.5538	1.0085
7		66	110–111/12	1.5510	0.9888
8		67	100–101/8	1.5926	

(continued)

Table 1 (continued)

No.	Structure	Yield, %	B.p., °C/torr (m.p., °C)	n_D^{20}	d_4^{20}
9		62	87–88/4		
10		80	69–70/3	1.5812	1.1385
11		58	49/10	15466	1.1921
12		75	64-65/12 48/6	1.5522	1.1986
13		57	100/26	1.5985	1.2783
14		76	80–90/16 (53–54)		
15		55	99–100/11		
16		51	107–108/6	1.6330	

(continued)