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Nucleophilic Reactivities of Thiophenolates

Patrick M. Jüstel, Cedric D. Pignot, and Armin R. Ofial*

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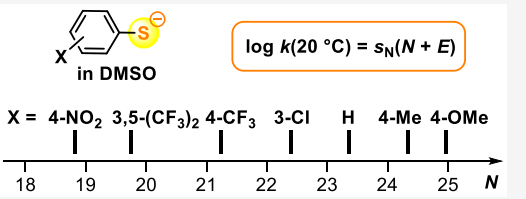
ABSTRACT: The nucleophilic reactivities of substituted thiophenolates were determined by following the kinetics of their reactions with a series of quinone methides (reference electrophiles) in DMSO at 20 °C. The experimentally determined second-order rate constants were analyzed according to the Mayr−Patz equation $\log k = s_N(N + E)$ to derive the nucleophile-specific reactivity parameters N and s_N for ten thiophenolate ions.



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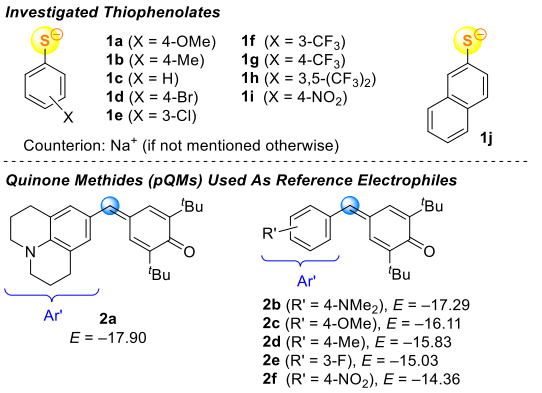
Sulfur nucleophiles are considered to be among the most reactive nucleophilic species. Importantly, the thiol moieties of cysteine (Cys) in proteins or in glutathione (GSH) are the reactive sites to trap xenobiotic Michael acceptors in cells.[1,2] Also the concept for the use of targeted covalent inhibitor drugs relies on the high reactivity of SH groups in peptides.[3−5] The nucleophilic reactivities of some aliphatic thiolates,[6] including Cys[7] and GSH[8] in aqueous solution, have recently been characterized utilizing Mayr's benzhydrylium methodology.[9]

It is common knowledge that also *aromatic* thiolates, that is, thiophenolates (ArS^-), are potent nucleophiles given that several Michael addition reactions to weak electrophiles have been reported.[10−14] Depletion kinetics of *p*-nitrothiophenolate (NBT) by electrophilic allergens were suggested as models to replace skin sensitization tests that use animals.[14] In addition, numerous kinetic studies of S_N2 reactions of ArS^- with C(sp^3)-centered electrophiles have been carried out to assess, for example, the effect of β-halogen atoms on the S_N2 reactivity of alkyl bromides,[15] the change in charge density at the electrophilic reaction center of substituted benzyl bromides,[16] and the susceptibility of the transition state structure on changes in the leaving group.[17] To characterize substituent effects on ArS^- reactivity, Bordwell and Hughes determined the rate constants for the reactions of several thiophenolates with *n*-butyl chloride in DMSO.[18] The influence of ion pairing on the reactivity of alkali metal thiophenolates toward *n*-butyl chloride in aq diglyme solutions was investigated by Fang and Westaway.[19]

Despite the fact that such quantitative data on the nucleophilic reactivity of ArS^- are at hand, the comparison of ArS^- with other types of nucleophiles, even with analogously substituted phenolates (ArO^-),[20] is hampered by a lack of kinetic data about ArS^- reactivity toward common reference electrophiles.

As we planned to use the UV-active thiophenolates ArS^- to investigate the reactivity of colorless electrophiles in future studies, we set out to calibrate their reactivity within the framework of Mayr's reactivity scales for polar reactions. The aryl-substituted *p*-quinone methides (*p*QMs) have repeatedly been used as reference electrophiles for reactions with anionic nucleophiles in DMSO,[21] a polar, non hydrogen bond donor solvent.[18b] We intended, therefore, to follow the kinetics of the 1,6-additions[22,23] of the X-substituted ArS^- **1a−j** (in DMSO) to the *p*QMs **2a−f** whose Mayr electrophilicity parameters E are known (Chart 1).[24]

Chart 1. Structures of Thiophenolates and *p*QMs Used in This Work



In a first step, we investigated the outcome of selected conjugate additions of ArS^- **1** to *p*QMs **2** (Scheme 1) in DMSO-d_6 by NMR spectroscopy and HRMS. Exclusive carbon−sulfur bond-formation was observed for the reactions of **1a−j** with the *p*QM **2d** to yield the adducts **4a−j**, and analogous thioethers **4k−o** resulted from the reactions of **1b**

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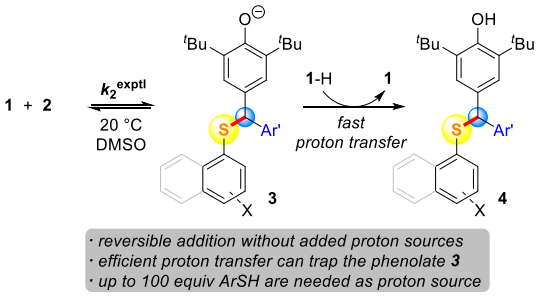
Scheme 1. Reactions of Thiophenolates 1 with *p*QMs 2



with a series of *p*QMs **2**. The reaction of **1b** with **2c** was performed at a 1 mmol scale and furnished **4m** in 88% yield after purification by column chromatography.

Analyzing the kinetics for the adduct formation with the Mayr–Patz eq 1 should allow one to assign the nucleophile-specific reactivity parameters N and s_N for the ArS^- ions **1** in DMSO solution.

$$\log k_2(20°C) = s_N(N + E) \quad (1)$$

Accordingly, the conjugate additions of the ArS^- **1** to the *p*QMs **2** were followed by using stopped-flow photometry to detect the absorption changes at or close to the *p*QMs' absorption maxima (λ_{max}) in DMSO at 20 °C.[25] Initial kinetic experiments indicated that the reactions did not go to completion but soon reached an equilibrium owing to reversible formation of the phenolate species **3** in the first step of the reaction (Scheme 1).

The relative Brønsted acidities of 2,6-di-*tert*-butylphenol (pK_a 17.3 in DMSO)[26] and thiophenols (pK_a 11.2 for the least acidic **1a**-H)[18] show that thiophenols **1**-H are capable to efficiently protonate the emerging phenolates **3**. In this way, **3** is removed from the equilibrium with the starting materials **1** and **2** and generates the phenols **4** in a fast, thermodynamically favorable step.

To define conditions under which protonation of **3** proceeds faster than the backward reaction to the educts **1** and **2**, we kept the ArS^-/*p*QM ratio in reactions of **1a** or **1c** with **2c** constant and varied the concentrations of the thiophenol additives **1**-H. Fitting the exponential decay function $A = A_0 \cdot \exp(-k_{obs}t) + C$ to the decrease of the absorbance of **2** furnished the first-order rate constants k_{obs} (s^{-1}). The rate constants k_{obs} steadily increased with increasing concentration of ArSH (**1**-H) and reached a plateau (within experimental error) when more than 100 equiv of **1a**-H or 40 equiv of **1c**-H were added to the reaction mixture (Supporting Information, Tables S2 and S3). This suggests that the first step in Scheme 1 becomes rate determining when >100 equiv of **1**-H are added to the reaction mixtures.

Trapping the phenolates **3** by a sufficient amount of **1**-H allowed us, therefore, to reliably determine the rate for the 1,6-conjugate addition of thiophenolate ions **1** to *p*QMs **2** (Figure 1a). By utilizing this procedure, the second-order rate constants k_2^{exptl} (M^{-1} s^{-1}) were obtained as the slopes of the linear correlations of k_{obs} with [**1**] (Figure 1b). The k_2^{exptl} values are gathered in Table 1 for all investigated reactions of **1** with the reference electrophiles **2**.

Changing the counterion for ArS^- from sodium to potassium or the addition of crown ethers affected the reactivity of ArS^- only insignificantly (Table 2 and Tables S36 and S37, Supporting Information,). We, therefore, used

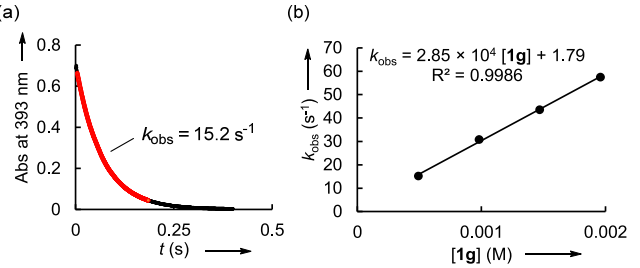


Figure 1. (a) Monoexponential decay of the absorbance A (at 393 nm) during the reaction of **1g** (c = 0.49 mM, counterion: K^+) with **2c** (c = 0.050 mM) in DMSO at 20 °C ([**1g**-H]$_0$ = 5.0 mM). (b) Linear dependence of the first-order rate constant k_{obs} on [**1g**].

kinetic data originating from Na-**1** and K-**1** side by side in the following analysis.

Figure 2 illustrates that the rate constants log k_2^{exptl} for the reactions of the thiophenolates **1** with the *p*QMs **2** correlate linearly with the known electrophilicities E of **2**. As a consequence, the nucleophile-specific reactivity parameters N (and s_N) were determined for the thiophenolates **1** and listed in the second column of Table 1.

Reported kinetic and thermodynamic data on substituted thiophenolates are compiled in Table S1 (Supporting Information) and used for further correlations as depicted in Figures 3 and 4.

In Figure 3a, the nucleophilicities N for the entire set of investigated thiophenolates **1a**-**1j** are shown to correlate linearly with Hammett σ constants,[27] which allows for a straightforward prediction of nucleophilicities of further substituted ArS^- ions. Though on a somewhat smaller data basis, the Brønsted-type correlation of N parameters for **1** with the corresponding basicities pK_{aH}[18a] (Figure 3b) spans almost 6 pK_{aH} units and is of similar quality as the Hammett-type correlation depicted in Figure 3a.

Figure 4a reflects that the relative reactivities of ArS^- determined toward the sp^2-hybridized carbon-centers of the *p*QMs **2** can also beneficially be used to predict the reactivity ordering of ArS^- toward sp^3-hybridized electrophiles, such as *n*-butyl chloride, in S_N2 reactions.[18a]

When a common reference electrophile is chosen, for example the *p*QM **2c**, the reactivities of *p*-substituted ArS^- and analogous phenolates (ArO^-)[20] in DMSO at 20 °C can be compared (Figure 4b). The slope >1 indicates, however, that phenolates are more sensitive toward substituent effects than their sulfur analogues.

To define the scope of the reactivity parameters for ArS^- determined in this work, we extended our kinetic studies to further classes of neutral electrophiles. Given that the Mayr reactivity scales for polar reactions currently span over 40 magnitudes of reactivity, a precision within 2 orders of magnitude is usually observed when eq 1 is used for predictions.[9b,c,24] We calculated the rate constants k_2^{eq1} for reactions of **1a**, **1c**, and **1g** with the structurally diverse carbon-centered electrophiles **E1**–**E3** (Table 3)[28] and studied the corresponding kinetics experimentally.

Experimentally determined k_2^{exptl} and the predicted k_2^{eq1} agreed within a factor <15 indicating that the N/s_N parameters for ArS^-, which were calibrated against the *p*QMs **2** as the reference electrophiles, also allow one to estimate the reactivity of ArS^- ions toward further classes of neutral electrophiles, including the Michael acceptor **E1**[29] as well as the

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Table 1. Second-Order Rate Constants k_2^{exptl} for the Reactions of Thiophenolates 1 with the Reference Electrophiles 2 (in DMSO, at 20 °C)[a]

		k_2^{exptl} (M^{-1} s^{-1})					
ArS^-	N/s_N	**2a**	**2b**	**2c**	**2d**	**2e**	**2f**
1a	24.97/0.68	6.60×10^4	1.36×10^5	7.59×10^5	1.86×10^6	n.d.	n.d.
1b	24.35/0.69	3.31×10^4	6.67×10^4	4.96×10^5	8.65×10^5	n.d.	n.d.
1c	23.36/0.74	1.33×10^4	2.75×10^4	2.25×10^5	4.61×10^5	n.d.	n.d.
1j	22.55/0.83	n.d.	2.61×10^4	1.97×10^5	3.48×10^5	2.05×10^6	n.d.
1d	22.80/0.78	8.06×10^3	1.84×10^4	1.49×10^5	2.83×10^5	1.39×10^6	n.d.
1e	22.50/0.78	4.38×10^3	1.00×10^4	9.19×10^4	1.14×10^5	7.94×10^5	n.d.
1f	21.75/0.86	2.33×10^3	5.65×10^3	5.63×10^4	n.d.	6.41×10^5	n.d.
1g	21.30/0.86	8.16×10^2	2.63×10^3	2.75×10^4 [b]	5.46×10^4	2.78×10^5	7.76×10^5
1h	19.71/0.86	n.d.	n.d.	1.18×10^3	2.34×10^3	1.27×10^4	3.80×10^4
1i	18.92/0.87	n.d.	n.d.	2.52×10^2	5.15×10^2	2.66×10^3	8.50×10^3

[a]Kinetics determined in the presence of 5.0 mM of the corresponding thiol **1**-H (≙100 equiv of **1**-H relative to [**2**]); the experimental error in k_2 is assumed to be ±10%. [b]With Na^+ as the counterion of **1g**, the analogous kinetics with K-**1g** gave $k_2^{exptl} = 2.85 \times 10^4$ M^{-1} s^{-1} (Figure 1).

Table 2. Counterion Dependence of the Kinetics for the Reactions of the *p*QM 2c with Na/K-1a in DMSO[a] (20 °C)

reaction	crown ether	k_{obs} (s^{-1})
Na-**1a** + **2c**	none	$(1.06 \pm 0.01) \times 10^3$
Na-**1a** + **2c**	15-crown-5 (1.0 mM)	$(9.46 \pm 0.06) \times 10^2$
K-**1a** + **2c**	none	$(1.00 \pm 0.01) \times 10^3$
K-**1a** + **2c**	18-crown-6 (1.0 mM)	$(9.83 \pm 0.02) \times 10^2$

[a]Solutions of Na-**1a** and K-**1a** in DMSO were generated by deprotonation of **1a**-H with NaH and KO*t*Bu, respectively. Initial reactant concentrations were $[\mathbf{1a}]_0 = 1.0$ mM, $[\mathbf{1a}\text{-H}]_0 = 5.0$ mM, and $[\mathbf{2c}]_0 = 0.050$ mM. The kinetics were followed at 393 nm.

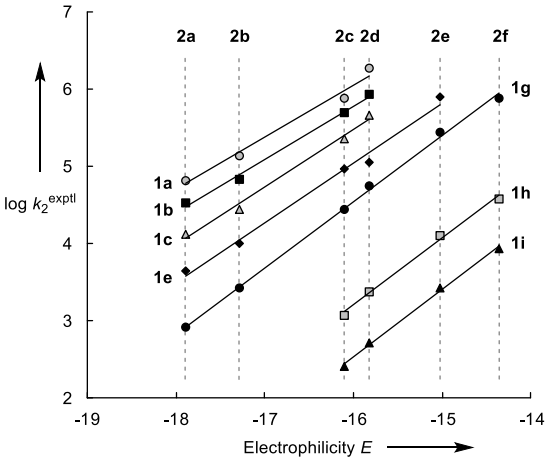


Figure 2. Determination of N/s_N for ArS^- (**1**) from the linear correlations of log k_2^{exptl} with the electrophilicities E of **2a–f**.

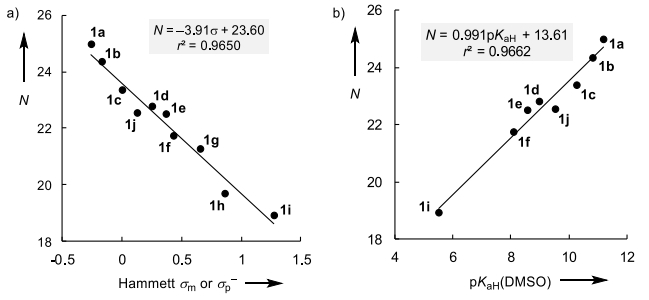


Figure 3. Linear relationships of $N(ArS^-)$ with (a) Hammett σ_m or σ_p^- substituent constants and (b) pK_{aH} (in DMSO).

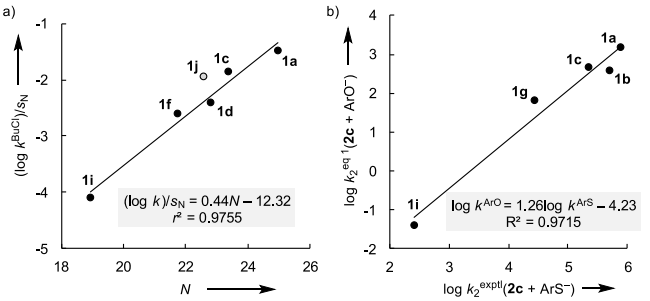
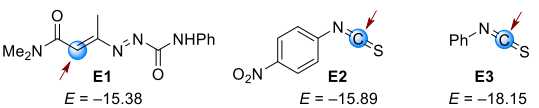


Figure 4. (a) Plot of $(\log k^{BuCl})/s_N$ for the reactions of **1** with *n*-butyl chloride (in DMSO, at 25 °C) vs the Mayr reactivities N; data for **1j** excluded when calculating the correlation line. (b) Linear correlation of the second-order rate constants for the reactions of phenolates (ArO^-) and thiophenolates (ArS^-) with the *p*QM **2c** in DMSO.

Table 3. Predicted and Experimentally Determined k_2 for Reactions of ArS^- (1) with E1–E3 (DMSO, 20 °C)



electrophile	ArS^-	k_2^{eq1} (M^{-1} s^{-1})	k_2^{exptl} (M^{-1} s^{-1})	k_2^{exptl}/k_2^{eq1}
E1	**1c**	8.0×10^5	7.19×10^5	1/1.1
E1	**1g**	1.2×10^5	8.78×10^4	1/1.4
E2	**1g**	4.5×10^4	5.69×10^5	13
E3	**1a**	4.3×10^4	4.75×10^4	1.1
E3	**1c**	7.2×10^3	4.90×10^3	1/1.5

heteroallenes **E2** and **E3** with C(sp)-hybridized electrophilic centers.[30]

In conclusion, we have used a set of *p*-quinone methides as reference electrophiles to characterize the Mayr nucleophilicity parameters N/s_N for meta- and para-substituted thiophenolates ArS^- in DMSO. Hammett- and Brønsted-type correlations of the nucleophilicities N make it possible to straightforwardly predict the reactivity of further thiophenolates. In addition, we have shown that applying the determined N/s_N values in eq 1 also holds for reactions of ArS^- with further types of neutral carbon-centered electrophiles.

In reactions of phenolate ions (ArO^-) with reference electrophiles, second-order rate constants in DMSO, acetonitrile, and DMF differed by less than 1 order of magnitude if the reference electrophile was kept constant.[20] We, therefore,

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expect that the ArS^- reactivities in DMSO determined herein will be of value to predict reaction rates in other aprotic, polar solvents, such as MeCN. Thus, the comparison of thiophenolate reactivities with those of other S-nucleophiles, such as phenylsulfinate,[31] dithiocarbamates,[32] and dithiocarbonates[32] has now become possible within the framework of Mayr's reactivity scales (Figure 5).[24] The parent PhS^- (**1c**) is only slightly less reactive than the piperidine-1-carbodithioate (N = 23.8 in MeCN), the most reactive S-nucleophile characterized by N/s_N so far.[24] The donor-substituted thiophenolates **1b** and **1a** exceed the S-nucleophilicity of this dithiocarbamate.

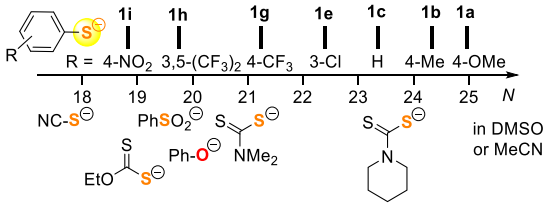

Figure 5. Nucleophilicity scale for sulfur-centered nucleophiles (and the parent phenolate ion) in aprotic polar solvents.

Given the UV−vis absorption of the thiophenolates,[25] we are currently investigating their capacity as reference nucleophiles in kinetic studies with colorless electrophiles.

EXPERIMENTAL SECTION

Chemicals. The thiophenols 4-methoxybenzenethiol (97%), 4-methylbenzenethiol (98%), benzenethiol (97%), and naphthalene-2-thiol (99%) were purchased from Sigma-Aldrich, 4-bromobenzenethiol (97%), 3-chlorobenzenethiol (>97%), and 3-(trifluoromethyl)-benzenethiol (>95%) from TCI, 4-(trifluoromethyl)benzenethiol (97%), 4-nitrobenzenethiol (96%), and 3,5-bis(trifluoromethyl)-benzenethiol (97%) from ABCR. The thiophenols were used without further purification. All thiophenols, KO*t*Bu (>98%, Acros Organics) and NaH (95%, Sigma-Aldrich) were stored in a glovebox under argon. Thiophenols were deprotonated with either KO*t*Bu or NaH prior to each use to give the potassium or sodium thiophenolates K-**1** and Na-**1**, respectively. The quinone methides **2** were prepared as described before.[21] **E1** was donated by the Attanasi group (Univ Urbino, Italy).[28a] 4-Nitrophenyl isothiocyanate (**E2**, >99.0%) was purchased from TCI. Phenyl isothiocyanate (**E3**) was purchased and purified by vacuum distillation prior to use. Silica gel plates with a F-254 fluorescence indicator were obtained from Merck and used for thin-layer chromatography. Flash column chromatography was performed with Merck silica gel 60 (0.040−0.063 mm) and distilled solvents.

Analytics. Nuclear magnetic resonance (NMR) spectra were recorded on 400 and 600 MHz spectrometers. Deuterated solvents were purchased from EurIsotop. The following abbreviations and their combinations are used in the analysis of NMR spectra: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s = broad singlet. The ^{13}C NMR spectra were recorded under broad-band proton-decoupling. NMR signals were assigned based on information from additional 2D NMR experiments (COSY, gHSQC, gHMBC). Chemical shifts are given in ppm. Internal reference was set to the residual solvent signals (δ_H = 2.50 ppm, δ_C = 39.52 ppm for DMSO-d_6 and δ_H = 7.26 ppm, δ_C = 77.16 ppm for $CDCl_3$).[33]

Infrared (IR) spectra of neat samples were recorded on a PerkinElmer Spectrum BX-59343 instrument with a Smiths Detection DuraSamplIR II Diamond ATR sensor for detection in the range from 4500 to 600 cm^{-1}.

High-resolution mass spectra (HRMS) were acquired on a Thermo Finnigan LTQ FT Ultra Fourier transform ion cyclotron resonance, a Q-Exactive GC Orbitrap, a Finnigan MAT 95 or a Finnigan MAT 90 GC/MS. Samples were ionized either by electron impact (EI) or electron spray ionization (ESI).

UV−vis measurements were carried out using a J&M TIDAS diode array spectrophotometer, which was controlled by TIDASDAQ3 (v3) software and connected to a Hellma 661.502-QX quartz Suprasil immersion probe (light path d = 5 mm) via fiber optic cables and standard SMA connectors.

A DMSO solution of the thiophenol **1**-H was deprotonated (by NaH or KO*t*Bu) and added in multiple steps to a flask filled with DMSO. The increasing absorption of the solution was followed. The molar absorption coefficient ε was determined from the slope of the linear relationship of the absorbance (at λ_{max}) with [**1**], in accord with the Lambert−Beer law. All spectra were then normalized relative to the extinction coefficient at λ_{max} and are depicted in the Supporting Information.

Product Studies. *General Procedure.* A solution of the benzenethiol **1**-H (0.0408 mmol, in 0.1 mL DMSO-d_6) was partially (5%) deprotonated by adding an equal volume of a sodium dimsyl solution (19.5 mM in DMSO-d_6). The resulting **1**-H/Na-**1** mixture (0.2 mL) was mixed with a DMSO-d_6 solution of the *p*QM **2** (0.0389 mmol, in 1 mL). The color of the reaction mixture faded within seconds. Subsequently, the reaction mixture was analyzed by NMR spectroscopy and HRMS without further workup (see Supporting Information for atom labeling). NMR spectra of products **4** were usually found to be spectroscopically clean, indicating quantitative conversions (except for **4a** and **4i**, which show additional resonances caused by traces of starting materials).

*2,6-Di-tert-butyl-4-(((4-methoxyphenyl)thio)(p-tolyl)methyl)-phenol (**4a**).* According to the General Procedure, the thiophenol **1a**-H (5.7 mg, 0.041 mmol) and the *p*QM **2d** (12.0 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^1H NMR (600 MHz, DMSO-d_6) δ 7.32 (d, J = 8.1 Hz, 2 H, 9-H), 7.20 (d, J = 8.9 Hz, 2 H, 14-H), 7.10 (s, 2 H, 5-H), 7.09 (d, J = 7.9 Hz, 2 H, 10-H), 6.87 (s, 1 H, 1-OH), 6.77 (d, J = 8.9 Hz, 2 H, 15-H), 5.52 (s, 1 H, 7-H), 3.67 (s, 3 H, 17-H), 2.23 (s, 3 H, 12-H), 1.31 (s, 18 H, 4-H). $^{13}C\{^1H\}$ NMR (151 MHz, DMSO-d_6) δ 158.6 (C_q, C-16), 152.7 (C_q, C-1), 138.94 (C_q, C-8), 138.92 (C_q, C-2), 135.9 (C_q, C-11), 133.7 (CH, C-14), 132.1 (C_q, C-6), 128.9 (CH, C-10), 127.9 (CH, C-9), 125.7 (C_q, C-13), 124.2 (CH, C-5), 114.3 (CH, C-15), 57.1 (CH, C-7), 55.1 (CH, C-17), 34.5 (C_q, C-3), 30.3 (CH_3, C-4), 20.6 (CH_3, C-12) (additional resonances in the NMR spectra are caused by a slight excess of **1a**-H). HRMS (ESI) calcd m/z for $[C_{29}H_{35}O_2S^+]$ $[M - H^-]$ 447.2352, found 447.2360.

*2,6-Di-tert-butyl-4-(p-tolyl(p-tolylthio)methyl)phenol (**4b**).*[23a] According to the General Procedure, the thiophenol **1b**-H (5.1 mg, 0.041 mmol) and the *p*QM **2d** (12.0 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^1H NMR (600 MHz, DMSO-d_6) δ 7.35 (d, J = 8.1 Hz, 2 H, 9-H), 7.16 (d, J = 8.1 Hz, 2 H, 14-H), 7.14 (s, 2 H, 5-H), 7.08 (d, J = 7.9 Hz, 2 H, 10-H), 7.00 (d, J = 8.8 Hz, 2 H, 15-H), 6.89 (s, 1 H, 1-OH), 5.66 (s, 1 H, 7-H), 2.22 (s, 3 H, 12-H), 2.19 (s, 3 H, 17-H), 1.31 (s, 18 H, 4-H). $^{13}C\{^1H\}$ NMR (151 MHz, DMSO-d_6) δ 152.7 (C_q, C-1), 139.0 (C_q, C-2), 138.9 (C_q, C-8), 135.90 (C_q, C-11), 135.86 (C_q, C-16), 132.2 (C_q, C-13), 132.1 (C_q, C-6), 130.5 (CH, C-14), 129.4 (CH, C-15), 128.9 (CH, C-10), 127.8 (CH, C-9), 124.2 (CH, C-5), 55.6 (CH, C-7), 34.5 (C_q, C-3), 30.3 (CH_3, C-4), 20.6 (CH_3, C-12), 20.5 (CH_3, C-17). HRMS (ESI) calcd m/z for $[C_{29}H_{35}OS^+]$ $[M - H^-]$ 431.2403, found 431.2411.

*2,6-Di-tert-butyl-4-((phenylthio)(p-tolyl)methyl)phenol (**4c**).*[23b] According to the General Procedure, the thiophenol **1c**-H (4.5 mg, 0.041 mmol) and the *p*QM **2d** (12.0 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^1H NMR (600 MHz, DMSO-d_6) δ 7.38 (d, J = 8.1 Hz, 2 H, 9-H), 7.26 (dd, J = 8.4, 1.2 Hz, 2 H, 14-H), 7.19 (t, J = 7.6 Hz, 2 H, 15-H), 7.16 (s, 2 H, 5-H), 7.11 (dt, J = 8.0, 1.6 Hz, 1 H, 16-H), 7.09 (d, J = 7.9 Hz, 2 H, 10-H), 6.90 (s, 1 H, 1-OH), 5.75 (s, 1 H, 7-H), 2.23 (s, 3 H, 12-H), 1.32 (s, 18 H, 4-H). $^{13}C\{^1H\}$ NMR (151 MHz, DMSO-d_6) δ 152.8 (C_q, C-1), 139.1 (C_q, C-2), 138.8 (C_q, C-8), 136.03 (C_q, C-13), 135.99 (C_q, C-11), 131.9 (C_q, C-

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6), 129.6 (CH, C-14), 129.0 (CH, C-10), 128.7 (CH, C-15), 127.8 (CH, C-9), 126.1 (CH, C-16), 124.2 (CH, C-5), 54.9 (CH, C-7), 34.5 (C_q, C-3), 30.3 (CH_3, C-4), 20.6 (CH_3, C-12). HRMS (ESI) calcd m/z for $[C_{28}H_{33}OS^+]$ $[M - H^-]$ 417.2247, found 417.2251.

*4-(((4-Bromophenyl)thio)(p-tolyl)methyl)-2,6-di-tert-butylphenol (**4d**).* According to the General Procedure, the thiophenol **1d**-H (7.7 mg, 0.041 mmol) and the *p*QM **2d** (12.0 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.37 (d, J = 8.6 Hz, 4 H, 9-H and 14/15-H), 7.21 (d, J = 8.6 Hz, 2 H, 14/15-H), 7.14 (s, 2 H, 5-H), 7.10 (d, J = 7.9 Hz, 2 H, 10-H), 6.92 (s, 1 H, 1-OH), 5.79 (s, 1 H, 7-H), 2.23 (s, 3 H, 12-H), 1.31 (s, 18 H, 4-H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 152.9 (C_q, C-1), 139.1 (C_q, C-2), 138.3 (C_q, C-8), 136.2 (C_q, C-11), 135.6 (C_q, C-13), 131.6 (CH, C-14 or C-15), 131.54 (C_q, C-6), 131.48 (CH, C-14 or C-15), 129.0 (CH, C-10), 127.8 (CH, C-9), 124.3 (CH, C-5), 119.2 (C_q, C-16), 54.9 (CH, C-7), 34.5 (C_q, C-3), 30.3 (CH_3, C-4), 20.6 (CH_3, C-12). HRMS (ESI) calcd m/z for $[C_{28}H_{32}{}^{79}BrOS^+]$ $[M - H^-]$ 495.1352, found 495.1357; calcd m/z for $[C_{28}H_{32}{}^{81}BrOS^+]$ $[M - H^-]$ 497.1331, found 497.1337.

*2,6-Di-tert-butyl-4-(((3-chlorophenyl)thio)(p-tolyl)methyl)phenol (**4e**).* According to the General Procedure, the thiophenol **1e**-H (5.9 mg, 0.041 mmol) and the *p*QM **2d** (12.0 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.40 (d, J = 8.1 Hz, 2 H, 9-H), 7.30 (s, 1 H, 18-H), 7.24−7.19 (m, 2 H, 14-H and 15-H), 7.18 (s, 2 H, 5-H), 7.16−7.14 (m, 1 H, 16-H), 7.12 (d, J = 8.0 Hz, 2 H, 10-H), 6.92 (s, 1 H, 1-OH), 5.88 (s, 1 H, 7-H), 2.24 (s, 3 H, 12-H), 1.32 (s, 18 H, 4-H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 152.9 (C_q, C-1), 139.1 (C_q, C-2), 138.6 (C_q, C-13), 138.3 (C_q, C-8), 136.2 (C_q, C-11), 133.2 (C_q, C-17), 131.5 (C_q, C-6), 130.2 (CH, C-15), 129.1 (CH, C-10), 128.5 (CH, C-18), 127.82 (CH, C-14), 127.78 (CH, C-9), 125.9 (CH, C-16), 124.4 (CH, C-5), 54.4 (CH, C-7), 34.6 (C_q, C-3), 30.3 (CH_3, C-4), 20.6 (CH_3, C-12). HRMS (ESI) calcd m/z for $[C_{28}H_{32}{}^{35}ClOS^+]$ $[M - H^-]$ 451.1857, found 451.1861; calcd m/z for $[C_{28}H_{32}{}^{37}ClOS^+]$ $[M - H^-]$ 453.1827, found 453.1831.

*2,6-Di-tert-butyl-4-(p-tolyl((3-(trifluoromethyl)phenyl)thio)-methyl)phenol (**4f**).* According to the General Procedure, the thiophenol **1f**-H (7.3 mg, 0.041 mmol) and the *p*QM **2d** (12.0 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.56 (d, J = 7.5 Hz, 1 H, 14-H), 7.51 (s, 1 H, 18-H), 7.44−7.41 (m, 2 H, 15-H, 16-H), 7.40 (d, J = 8.2 Hz, 2 H, 9-H), 7.20 (s, 2 H, 5-H), 7.12 (d, J = 7.9 Hz, 2 H, 10-H), 6.91 (s, 1 H, 1-OH), 5.94 (s, 1 H, 7-H), 2.23 (s, 3 H, 12-H), 1.31 (s, 18 H, 4-H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 152.9 (C_q, C-1), 139.1 (C_q, C-2), 138.1 (C_q, C-8), 137.9 (C_q, C-13), 136.3 (C_q, C-11), 133.3 (br, CH, C-14), 131.2 (C_q, C-6), 129.5 (CH, C-15), 129.4 (q, $J_{C,F}$ = 38 Hz, C_q, C-17), 129.1 (CH, C-10), 127.8 (CH, C-9), 125.6 (q, $J_{C,F}$ = 3.9 Hz, CH, C-18), 124.4 (CH, C-5), 123.8 (q, $J_{C,F}$ = 273 Hz, CF_3, C-19), 122.6 (q, $J_{C,F}$ = 3.7 Hz, CH, C-16), 54.5 (CH, C-7), 34.5 (C_q, C-3), 30.2 (CH_3, C-4), 20.6 (CH_3, C-12). HRMS (ESI) calcd m/z for $[C_{29}H_{32}F_3OS^+]$ $[M - H^-]$ 485.2120, found 485.2125.

*2,6-Di-tert-butyl-4-(p-tolyl((4-(trifluoromethyl)phenyl)thio)-methyl)phenol (**4g**).* According to the General Procedure, the thiophenol **1g**-H (7.3 mg, 0.041 mmol) and the *p*QM **2d** (12.0 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.53 (d, J = 8.3 Hz, 2 H, 15-H), 7.44−7.41 (m, 4 H, 9-H and 14-H), 7.17 (s, 2 H, 5-H), 7.12 (d, J = 7.9 Hz, 2 H, 10-H), 6.95 (s, 1 H, 1-OH), 5.97 (s, 1 H, 7-H), 2.23 (s, 3 H, 12-H), 1.31 (s, 18 H, 4-H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 153.0 (C_q, C-1), 142.4 (C_q, C-13), 139.2 (C_q, C-2), 138.1 (C_q, C-8), 136.3 (C_q, C-11), 131.3 (C_q, C-6), 129.1 (CH, C-10), 128.4 (CH, C-14), 127.7 (CH, C-9), 125.8 (q, $J_{C,F}$ = 32.0 Hz, C_q, C-16), 125.4 (q, $J_{C,F}$ = 3.7 Hz, CH, C-15), 124.3 (CH, C-5), 124.2 (q, $J_{C,F}$ = 272 Hz, C_q, C-17), 53.7 (CH, C-7), 34.6 (C_q, C-3), 30.3 (CH_3, C-4), 20.6 (CH_3, C-12). HRMS (ESI) calcd m/z for $[C_{29}H_{32}F_3OS^+]$ $[M - H^-]$ 485.2120, found 485.2124.

*4-(((3,5-Bis(trifluoromethyl)phenyl)thio)(p-tolyl)methyl)-2,6-di-tert-butylphenol (**4h**).* According to the General Procedure, the thiophenol **1h**-H (10.0 mg, 0.0408 mmol) and the *p*QM **2d** (12.0 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.86 (s, 2 H, 14-H), 7.76 (br s, 1 H, 16-H), 7.43−7.41 (m, 2 H, 9-H), 7.22 (s, 2 H, 5-H), 7.14 (d, J = 7.9 Hz, 2 H, 10-H), 6.91 (s, 1 H, 1-OH), 6.14 (s, 1 H, 7-H), 2.24 (s, 18 H, 4-H), 1.30 (s, 3 H, 12-H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 153.0 (C_q, C-1), 140.4 (C_q, C-13), 139.2 (C_q, C-2), 137.4 (C_q, C-8), 136.6 (C_q, C-11), 130.5 (C_q, C-6), 130.3 (q, $J_{C,F}$ = 32.9 Hz, C_q, C-15), 129.5 (br, CH, C-14), 129.2 (CH, C-10), 127.8 (CH, C-9), 124.5 (CH, C-5), 123.0 (q, $J_{C,F}$ = 273 Hz, C_q, C-17), 119.1 (br, CH, C-16), 54.2 (CH, C-7), 34.5 (C_q, C-3), 30.1 (CH_3, C-4), 20.6 (CH_3, C-12). HRMS (ESI) calcd m/z for $[C_{30}H_{31}F_6OS^+]$ $[M - H^-]$ 553.1994, found 553.2000.

*2,6-Di-tert-butyl-4-(((4-nitrophenyl)thio)(p-tolyl)methyl)phenol (**4i**).* According to the General Procedure, the thiophenol **1i**-H (6.3 mg, 0.041 mmol) and the *p*QM **2d** (12.0 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.03 (d, J = 9.0 Hz, 2 H, 15-H), 7.47−7.42 (m, 4 H, 9-H and 14-H), 7.20 (s, 2 H, 5-H), 7.13 (d, J = 7.9 Hz, 2 H, 10-H), 6.97 (s, 1 H, 1-OH), 6.09 (s, 1 H, 7-H), 2.24 (s, 3 H, 12-H), 1.32 (s, 18 H, 4-H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 153.1 (C_q, C-1), 147.0 (C_q, C-13), 144.6 (C_q, C-16), 139.3 (C_q, C-2), 137.7 (C_q, C-8), 136.4 (C_q, C-11), 130.9 (C_q, C-6), 129.2 (CH, C-10), 127.7 (CH, C-9), 127.4 (CH, C-14), 124.3 (CH, C-5), 123.6 (CH, C-15), 53.3 (CH, C-7), 34.5 (C_q, C-3), 30.2 (CH_3, C-4), 20.6 (CH_3, C-12) (additional resonances are caused by a slight excess of the *p*QM **2d**). HRMS (ESI) calcd m/z for $[C_{28}H_{32}NO_3S^+]$ $[M - H^-]$ 462.2097, found 462.2101.

*2,6-Di-tert-butyl-4-((naphthalen-2-ylthio)(p-tolyl)methyl)phenol (**4j**).* According to the General Procedure, the thiophenol **1j**-H (6.5 mg, 0.041 mmol) and the *p*QM **2d** (12.0 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.80 (d, J = 8.0 Hz, 1 H, 17-H), 7.79−7.78 (m, 1 H, 22-H), 7.74 (d, J = 8.7 Hz, 1 H, 15-H), 7.69 (d, J = 8.2, 1 H, 20-H), 7.47−7.40 (m, 5 H, 9-H, 14-H, 18-H, 19-H), 7.22 (s, 2 H, 5-H), 7.09 (d, J = 8.0 Hz, 2 H, 10-H), 6.90 (s, 1 H, 1-OH), 5.93 (s, 1 H, 7-H), 2.21 (s, 3 H, 12-H), 1.31 (s, 18 H, 4-H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 152.8 (C_q, C-1), 139.1 (C_q, C-2), 138.7 (C_q, C-8), 136.1 (C_q, C-11), 133.6 (C_q, C-13), 133.1 (C_q, C-21), 131.9 (C_q, C-6), 131.3 (C_q, C-16), 129.0 (CH, C-10), 128.0 (CH, C-15), 127.9 (CH, C-9), 127.8 (C_q, C-22), 127.7 (CH, C-18), 127.5 (CH, C-17), 126.9 (CH, C-20), 126.5 (CH, C-19), 125.8 (CH, C-14), 124.3 (CH, C-5), 54.8 (CH, C-7), 34.5 (C_q, C-3), 30.3 (CH_3, C-4), 20.6 (CH_3, C-12). HRMS (ESI) calcd m/z for $[C_{32}H_{35}OS^+]$ $[M - H^-]$ 467.2403, found 467.2409.

*2,6-Di-tert-butyl-4-((julolidin-9-yl)(p-tolylthio)methyl)phenol (**4k**).* According to the General Procedure, the thiophenol **1b**-H (6.3 mg, 0.041 mmol) and the *p*QM **2a** (15.2 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.14−7.11 (m, 4 H, 5-H and 16-H), 7.00 (d, J = 8.0 Hz, 2 H, 17-H), 6.82 (s, 1 H, 1-OH), 6.79 (s, 2 H, 9-H), 5.38 (s, 1 H, 7-H), 3.05−3.03 (m, 4 H, 14-H), 2.61 (t, J = 6.4 Hz, 4 H, 12-H), 2.20 (s, 3 H, 19-H), 1.82 (pent, J = 6.4 Hz, 4 H, 13-H), 1.31 (s, 18 H, 4-H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 152.4 (C_q, C-1), 141.6 (C_q, C-11), 138.8 (C_q, C-2), 135.6 (C_q, C-18), 132.8 (C_q, C-15), 132.7 (C_q, C-6), 130.5 (CH, C-16), 129.3 (CH, C-17), 128.2 (C_q, C-8), 126.2 (CH, C-9), 124.2 (CH, C-5), 120.6 (C_q, C-10), 56.0 (CH, C-7), 49.2 (CH_2, C-14), 34.5 (C_q, C-3), 30.3 (CH_3, C-4), 27.2 (CH_2, C-12), 21.6 (CH_2, C-13), 20.5 (CH_3, C-19). HRMS (ESI) calcd m/z for $[C_{34}H_{44}NOS^+]$ $[M + H^+]$ 514.3138, found 514.3139.

*2,6-Di-tert-butyl-4-((4-(dimethylamino)phenyl)(p-tolylthio)-methyl)phenol (**4l**).* According to the General Procedure, the thiophenol **1b**-H (6.3 mg, 0.041 mmol) and the *p*QM **2b** (13.1 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-

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d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.26 (d, J = 8.7 Hz, 2 H, 9-H), 7.16−7.14 (m, 4 H, 5-H, 14-H), 7.00 (d, J = 8.0 Hz, 2 H, 15-H), 6.87 (s, 1 H, 1-OH), 6.62 (d, J = 8.8 Hz, 2 H, 10-H), 5.57 (s, 1 H, 7-H), 2.83 (s, 6 H, 12-H), 2.19 (s, 3 H, 17-H), 1.32 (s, 18 H, 4-H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6) δ 152.5 (C_q, C-1), 149.2 (C_q, C-11), 138.9 (C_q, C-2), 135.6 (C_q, C-16), 132.7 (C_q, C-6), 132.6 (C_q, C-13), 130.4 (CH, C-14), 129.3 (CH, C-15), 129.1 (C_q, C-8), 128.5 (CH, C-9), 124.1 (CH, C-5), 112.1 (CH, C-10), 55.6 (CH, C-7), 40.1 (CH_3, C-12), 34.5 (C_q, C-3), 30.3 (CH_3, C-4), 20.5 (CH_3, C-17). HRMS (ESI) calcd m/z for $[C_{30}H_{40}NOS^+]$ $[M + H^+]$ 462.2825, found 462.2827.

*2,6-Di-tert-butyl-4-((4-methoxyphenyl)(p-tolylthio)methyl)-phenol (**4m**).*[23a] A solution of the thiol **1b**-H (128 mg, 1.03 mmol) in acetonitrile (1 mL) was mixed with a suspension of sodium hydride in DMSO (0.72 mg, 0.03 mmol in 1 mL). After gas formation had ceased, a DMSO solution of the *p*QM **2c** (324.5 mg, 1.00 mmol in 23 mL) was added to the reaction mixture. The color of the solution changed from yellow to green within a few seconds. After another 5 min of stirring, the solution was acidified by addition of two drops of aq HCl (2 M) to produce a solution of yellow color. Evaporation of the volatiles (in the vacuum) furnished a crude material, which was purified by column chromatography (silica gel, eluent: ethyl acetate/*n*-pentane = 5/95) to yield **4m** (393 mg, 88%) as a yellow solid. R_f 0.55 (ethyl acetate/*n*-pentane = 5/95). mp 112−114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.7 Hz, 2 H, 9-H), 7.13−7.11 (m, 4 H, 5-H and 14-H), 6.98 (d, J = 8.3 Hz, 2 H, 15-H), 6.84 (d, J = 8.6 Hz, 2 H, 10-H), 5.36 (s, 1 H, 7-H), 5.11 (s, 1 H, 1-OH), 3.79 (s, 3 H, 12-H), 2.27 (s, 3 H, 17-H), 1.39 (s, 18 H, 4-H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 158.6 (C_q, C-11), 152.9 (C_q, C-1), 136.8 (C_q, C-16), 135.7 (C_q, C-2), 134.0 (C_q, C-8), 132.8 (C_q, C-13), 132.1 (CH, C-14), 132.0 (C_q, C-6), 129.6 (CH, C-9), 129.5 (CH, C-15), 125.2 (CH, C-5), 113.8 (CH, C-10), 58.0 (CH, C-7), 55.4 (CH_3, C-12), 34.5 (C_q, C-3), 30.4 (CH_3, C-4), 21.2 (CH_3, C-17). IR (ATR probe, neat) $\tilde{\nu}$ 3592, 2952, 1721, 1609, 1512, 1485, 1431, 1234, 1207, 1175, 1132, 1118, 1111, 1026, 891, 841, 809, 792, 778, 739 cm^{-1}. HRMS (ESI) calcd m/z for $[C_{29}H_{35}O_2S^+]$ $[M - H^-]$ 447.2352, found 447.2357. Anal. Calcd for $C_{29}H_{36}O_2S$: C, 77.63; H, 8.09; S, 7.15. Found: C, 77.67; H, 8.15; S, 6.97.

*2,6-Di-tert-butyl-4-((3-fluorophenyl)(p-tolylthio)methyl)phenol (**4n**).* According to the General Procedure, the thiophenol **1b**-H (6.3 mg, 0.041 mmol) and the *p*QM **2e** (12.2 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (600 MHz, DMSO-d_6) δ 7.33−7.31 (m, 2 H, 12-H and 13-H), 7.28−7.27 (m, 1 H, 9-H), 7.19 (d, J = 8.1 Hz, 2 H, 15-H), 7.16 (s, 2 H, 5-H), 7.02 (d, J = 8.0 Hz, 2 H, 16-H), 7.01−6.99 (m, 1 H, 11-H), 6.96 (s, 1 H, 1-OH), 5.77 (s, 1 H, 7-H), 2.19 (s, 3 H, 18-H), 1.33 (s, 18 H, 4-H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 162.0 (d, $J_{C,F}$ = 244 Hz, C_q, C-10), 153.0 (C_q, C-1), 144.9 (d, $J_{C,F}$ = 6.9 Hz, C_q, C-8), 139.2 (C_q, C-2), 136.2 (C_q, C-17), 131.6 (C_q, C-14), 131.2 (C_q, C-6), 130.7 (CH, C-15), 130.3 (d, $J_{C,F}$ = 8.3 Hz, CH, C-12), 129.4 (CH, C-16), 124.3 (CH, C-5), 124.1 (CH, C-13), 114.6 (d, $J_{C,F}$ = 21.9 Hz, CH, C-9), 113.7 (d, $J_{C,F}$ = 20.9 Hz, CH, C-11), 55.2 (CH, C-7), 34.6 (C_q, C-3), 30.3 (CH_3, C-4), 20.5 (CH_3, C-18). HRMS (ESI) calcd m/z for $[C_{28}H_{32}FOS^+]$ $[M - H^-]$ 435.2152, found 435.2154; calcd m/z for $[C_{28}H_{32}FOS^-]$ $[M - H^+]$ 435.2163, found 435.2163.

*2,6-Di-tert-butyl-4-((4-nitrophenyl)(p-tolylthio)methyl)phenol (**4o**).*[23a] According to the General Procedure, the thiophenol **1b**-H (6.3 mg, 0.041 mmol) and the *p*QM **2f** (13.2 mg, 0.0389 mmol) were mixed. The reaction mixture (in 1.2 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.14 (d, J = 8.6 Hz, 2 H, 10-H), 7.75 (d, J = 8.6 Hz, 2 H, 9-H), 7.22 (d, J = 7.9 Hz, 2 H, 13-H), 7.19 (s, 2 H, 5-H), 7.02 (d, J = 8.2 Hz, 2 H, 14-H), 5.95 (s, 1 H, 7-H), 2.19 (s, 3 H, 16-H), 1.33 (s, 18 H, 4-H). ^{13}C{^{1}H} NMR (151 MHz, DMSO-d_6) δ 153.2 (C_q, C-1), 149.9 (C_q, C-8), 146.2 (C_q, C-11), 139.4 (C_q, C-2), 136.5 (C_q, C-15), 131.1 (C_q, C-12), 130.9 (CH, C-13), 130.6 (C_q, C-6), 129.6 (CH, C-14), 129.2 (CH, C-9), 124.3 (CH, C-5), 123.6 (CH, C-10), 55.0 (CH, C-7), 34.6 (C_q, C-3), 30.2 (CH_3, C-4), 20.5 (CH_3, C-16). HRMS (ESI) calcd m/z for $[C_{28}H_{32}NO_3S^-]$ $[M - H^+]$ 462.2108, found 462.2110.

*(E)-2-(4-(Dimethylamino)-4-oxo-3-(phenylthio)butan-2-ylidene)-N-phenylhydrazine-1-carboxamide (**5**).* In analogy to the General Procedure, the thiophenol **1c**-H (7.6 mg, 0.069 mmol) and the electrophile **E1** (17.0 mg, 0.0653 mmol) were mixed. The reaction mixture (in 0.6 mL DMSO-d_6) was analyzed by NMR spectroscopy and HRMS. ^{1}H NMR (400 MHz, DMSO-d_6, + 20 °C) δ 9.73 (br s, 1 H, 8-H), 8.55 (s, 1 H, 10-H), 7.50−7.48 (m, 4 H, 12-H and 16-H), 7.31−7.27 (m, 4 H, 13-H and 17-H), 7.19 (t, J = 7.4 Hz, 1 H, 14-H), 7.01 (t, J = 7.3 Hz, 1 H, 18-H), 5.35 (s, 1 H, 4-H), 3.11 and 2.87 (2 s, 2 × 3 H, 1-H and 2-H), 1.92 (s, 3 H, 6-H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d_6, at +80 °C) δ 166.3 (C_q, C-3), 152.6 (C_q, C-9), 144.9 (C_q, C-5), 138.5 (C_q, C-15), 133.3 (C_q, C-11), 131.3 (CH, C-12), 128.4 (CH, C-13), 128.2 (CH, C-17), 126.9 (CH, C-14), 122.1 (CH, C-18), 118.9 (CH, C-16), 57.2 (CH, C-4), 36.9 and 35.3 (2 × CH_3, C-1 or C-2), 12.5 (CH_3, C-6). HRMS (EI) calcd m/z for $[C_{19}H_{22}N_4O_2S^{\bullet+}]$ $[M^{\bullet+}]$ 370.1458, found 370.1452.

Kinetics. Kinetic measurements were performed on Applied Photophysics SX.20 stopped-flow UV−vis photometric systems. The temperature (20.0 ± 0.2 °C) was maintained constant by using circulating bath cryostats. All solutions were freshly prepared under an atmosphere of dry argon by using dry DMSO (over molecular sieves, Acros Organics).

To achieve pseudo-first-order kinetics, the ArS^- concentrations were kept constant through thiophenolate regeneration from thiophenols or chosen at least ten times higher than the electrophile concentrations. The rates of the consumption of the *p*QMs (λ_{max} = 354−520 nm)[25] were followed photometrically at or close to their absorption maxima. Due to an overlap of the absorption bands with the thiophenolates,[25] the absorbances did not reach zero in all reactions investigated. Rate constants were obtained from the kinetics by least-squares fitting of the absorbance A with the equation $A_t = A_0 e^{-k_{obs}t} + C$.

The kinetics of the reactions of K-**1g** with **E2** gave rise to formation of a colored product whose increasing absorption was followed at 440 nm. The rates of product formation were also detected in the kinetics of reactions of K-**1a** and K-**1c** with **E3** (at λ = 320−326 nm), respectively, which were performed with excess concentrations of **E3** (>10 equiv). Least-squares fitting of the function $A_t = A_0 \cdot (1 - e^{-k_{obs}t}) + C$ to the increasing absorptions of the solutions furnished k_{obs}.

Plots of k_{obs} versus $[ArS^-]$ (or [**E3**]) gave k_2 as the slopes of the linear correlations.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c00025.

Additional data used for correlations, details on kinetic measurements, and copies of NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

Armin R. Ofial − *Department Chemie, Ludwig-Maximilians-Universität München, 81377 München, Germany;* orcid.org/0000-0002-9600-2793; Email: ofial@lmu.de

Authors

Patrick M. Jüstel − *Department Chemie, Ludwig-Maximilians-Universität München, 81377 München, Germany*

Cedric D. Pignot − *Department Chemie, Ludwig-Maximilians-Universität München, 81377 München, Germany*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.joc.1c00025

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Notes

The authors declare no competing financial interest.

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