Formation of *meta*-Arylsulfanyl- and *meta*-(Alkylsulfanyl)phenols from Cyclohexane-1,3-diones

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ABSTRACT: Reaction of cyclohexane-1,3-diones with TsCl/Et_3N and treatment of the resulting 3-(tosyloxy)cyclohex-2-en-1-ones with aryl- or alkyl thiols and K_2CO_3 in MeCN gives 3-(arylsulfanyl)cyclohex-2-en-1-ones or (alkylsulfanyl)cyclohex-2-en-1-ones, respectively. These compounds are easily brominated at C-2 by using NBS in MeCN; exposure to DBU in MeCN at room temperature then causes aromatization to afford *meta*-arylsulfanyl- and *meta*-(alkylsulfanyl)phenols.

Keywords:
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sulfides

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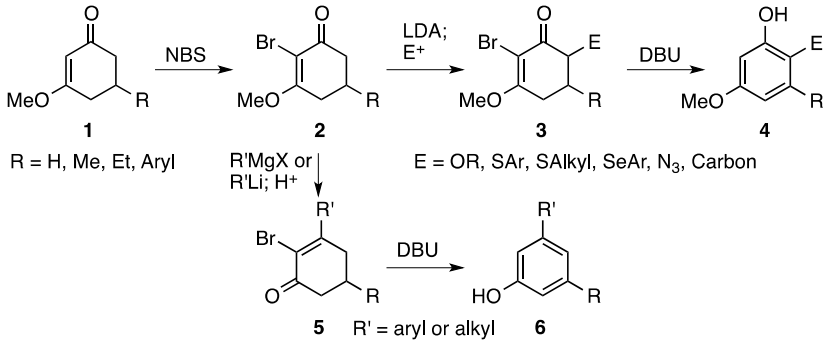
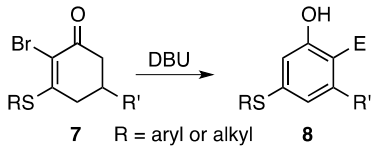
1. Introduction

Three recent publications from this laboratory have described (Scheme 1) the conversion of 2-bromocyclohex-2-en-1-one systems **2** into phenols[1, 2] (**2**→**3**→**4**) as well as the introduction of an alkyl or aryl substituent *meta* to the eventual phenolic hydroxyl (**2**→**5**→**6**).[3] We have now extended the aromatization of bromocyclohexenones to the preparation of *meta*-(arylsulfanyl)-



Scheme 1. Our previous routes to phenols from bromocyclohexenones

and *meta*-(alkylsulfanyl)phenols. The process involves preparation of a 2-bromo-3-(arylsulfanyl)cyclohex-2-en-1-one **7** or the corresponding alkylsulfanyl compound, and then aromatization (**7**→**8**) by treatment with DBU (Scheme 2). Some phenols of this type are mentioned in pharmaceutical patents[4] and a few publications explicitly disclose the level of biological activity of the compounds.[5]

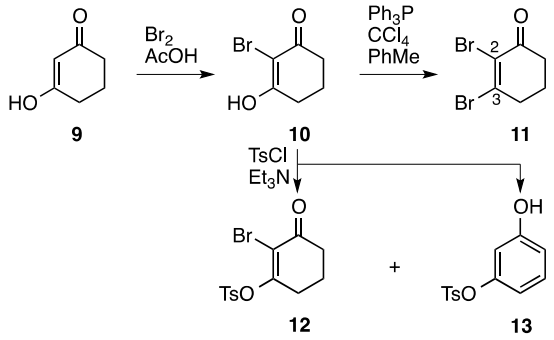


Scheme 2. Extension of the aromatization method to 3-arylsulfanyl and 3-(alkylsulfanyl)phenols

2. Results and discussion

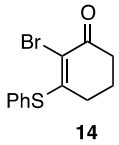
Development of a route to compounds of type **7**, required some exploration in order to identify the best of several alternative approaches. In principle, the bromine can be introduced either before or after the sulfur unit, and both possibilities were investigated.

Cyclohexane-1,3-dione (**9**) was easily brominated in near quantitative yield[6] (**9**→**10**), but conversion to the dibromide **11**,[7] with the intention of replacing the C-3 halogen by a sulfur unit, was unsatisfactory as the dibromide seemed to be unstable. Therefore, we treated **10** with TsCl and Et_3N in order to prepare the bromo tosylate **12**. However, the yield was poor (ca 40%) and the product was accompanied by the known tosyloxy phenol[8] **13**.

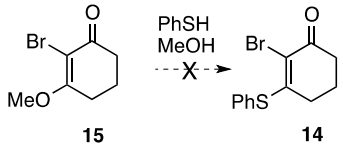


Scheme 3. Formation of 3-bromo- and 3-(tosyloxy)enones

Several attempts were then made to introduce the sulfur unit directly using the monobromide **10**. To that end, treatment of **10** with PhSH, Ph_3P and DEAD gave the desired product (**14**), but only in ca 20% yield. Use of other coupling reagents such as DCC/DMAP[9]

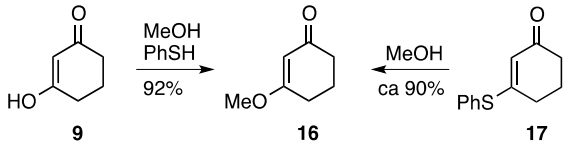


or MeOCOCl/HOBT[10] was equally unsatisfactory. We also treated cyclohexan-1,3-dione (**9**) with PhSSPh and Ph_3P, but again, the yield of the expected 3-(phenylsulfanyl)cyclohexenone was very low (8%). All of these initial experiments were done with CH_2Cl_2 as solvent, except for the experiment with PhSSPh, which was carried out in MeCN. We then examined the use of MeOH and found that in this solvent simple treatment of the bromocyclohexanedione **10** with 1 equiv of PhSH for 24 h afforded **14** in 60% yield; however, attempts to raise the yield by varying the number of equiv of PhSH or the nature of the solvent (MeOH, MeCN, CF_3CH_2OH, EtOH, DMF, DMSO) were unsuccessful. We wondered if the observed formation of **14** was the result of replacement of OH by OMe, followed by displacement of the methoxy group. To test this possibility we added PhSH to a methanol solution of **15** (Scheme 4). However, overnight storage of **15** in MeOH in the presence of PhSH did not provide any of the sulfide **14**, as judged by TLC analysis.



Scheme 4. Attempted displacement of OMe by SPh

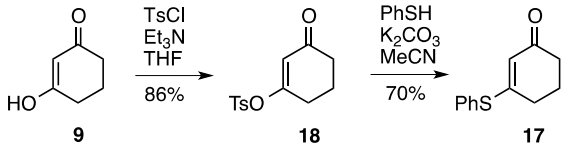
In related experiments (Scheme 5) cyclohexane-1,3-dione (**9**) was stored in MeOH for 1 week but very little ester **16** was formed (ca 10%). However, when PhSH (1 equiv) was added the ester **16** was formed in ca 90% yield after an overnight reaction period. When the keto sulfide **17** was kept overnight in MeOH, ester **16** was again produced (ca 90%). This observation cause us to store the brominated compound **14** in MeOH to see if incursion of PhS/MeO exchange was responsible for the modest yield of **14**, but in the event, **14** was found to be stable to MeOH.



Scheme 5. Studies on MeO/PhS exchange

The outcome of these exploratory experiments forced us to turn to the alternative approach in which the bromine is introduced *after* the sulfur unit.

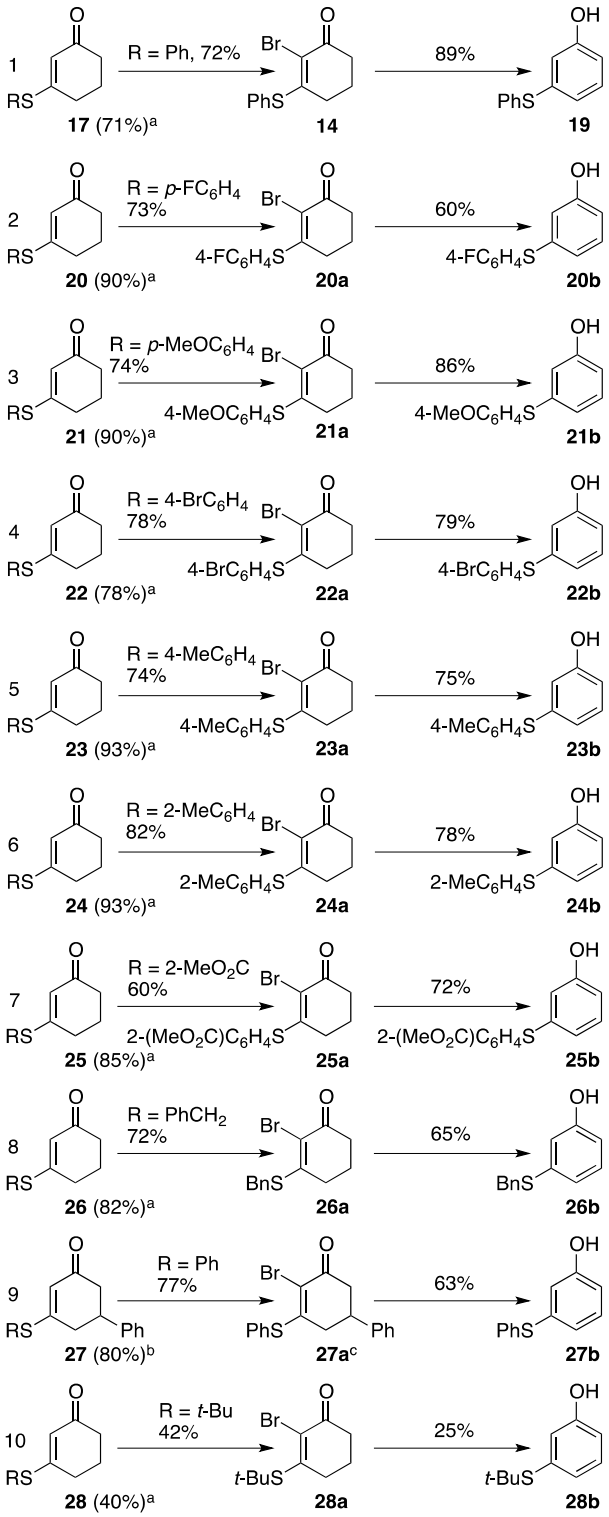
The reaction between PhSH and cyclohexane-1,3-dione (**9**) in the presence of $FeCl_3$, but without solvent, afforded **17** in 72% yield,[11] but this method is unsuitable for solid thiols as use of a solvent is reported[11] to greatly diminishes the yield. At this point we decided to evaluate the tosylate[12] **18**. This compound is easily made in almost 90% yield, but it should be stored in a freezer and used within a week. The best conditions for replacement of the tosyloxy group by



Scheme 6. Displacement of tosyloxy group by PhS

PhS involve use of MeCN as solvent with K_2CO_3 (5 equiv) as base and 1 equiv of PhSH. Under these conditions, which are similar to those reported for the corresponding mesylate,[13, 14] **17** was isolated in 71% yield. We have applied these conditions to a number of thiols (see Table 1) and prefer it to the use of NaH in DMF, a procedure that also afforded **17** in similar yield.

Table 1. Formation of *meta*-(arylsulfanyl)- and *meta*-(alkylsulfanyl)phenols



[a]Yield from tosylate **18**. [b]Yield from 3-oxo-5-phenylcyclohex-1-en-1-yl 4-methylbenzene-1-sulfonate. [c]The material contains slight impurities.

We next dealt with introduction of the bromine. In the case of the simplest example (**17**) bromination with NBS in CCl_4 had been reported,[15, 16] but we were uncertain of the generality of the method because of the potential for reaction at the sulfur atom[17] or at the benzene ring.[18] In our hands the action of NBS in MeCN on 3-(arylsulfanyl)cyclohex-2-enones was usually satisfactory irrespective of whether an electron-donating or an electron-withdrawing group is present in the arylsulfanyl unit. In the few examples where we made a comparison, use of CCl_4 for the NBS bromination gave a lower yield than use of MeCN as the solvent. The thiol addition and bromination steps worked equally well in the presence of an *ortho* methyl group (Table 1, entry 6) or an *ortho* ester group (Table 1, entry 7), but in the case of a *t*-butylsulfanyl group the yields were low (entry 10). The bromination was slow and so it was convenient to run the reaction for an arbitrary period of 24 h. Our results are given in Table 1.

Finally, we studied the aromatization with DBU. This step proceeded smoothly but took several hours; however, it was always complete after an overnight reaction period at room temperature. The effect of changing the solvent for the aromatization was also examined; MeCN generally gives a better result than THF, PhMe or CH_2Cl_2, and the reactions are best run at room temperature; raising the temperature (50 °C), with the one example we studied (compound **14**), resulted in a significantly decreased yield (by 20%) in two successive runs. With the exception of entry 10, the yields are in the range 63-90% with an average yield of 74%.

3. Other approaches

Other methods that have been used to prepare *inter alia meta*-(arylsulfanyl)- or *meta*-(alkylsulfanyl)phenols include a number of procedures based on transition metals and often run at an elevated temperature: Treatment of 3-(arylsulfanyl)cyclohexanones or the corresponding cyclohex-2-enones with Pd/C in the presence of K_2CO_3 and H_2 at 150 °C in $MeC(O)NMe_2$ effects dehydrogenation to the phenol.[19] Aryl thiols can be coupled with aryl iodides at modest temperature (80 °C) in a process catalyzed by CuI.[20] Similarly, both alkyl and aryl thiols undergo palladium-mediated coupling with aryl iodides and bromides at 90–110 °C in the presence of a base.[21] Aryl and alkyl thiols have been coupled with arylboronic acids under the influence of ultrasound in the presence of $Cu(OAc)_2$.[22] Deprotonation of 3-bromophenol, halogen/metal exchange and reaction with sulfur generates a thiolate that can be alkylated by an alkyl halide.[23] Aryl thiolates made by other methods can, of course, be alkylated with alkyl halides.[24] Aryl halides can be converted into thiolates by copper(II)-catalyzed reaction at 120 °C

with 1,2-ethanedithiol in the presence of KOH and, without isolation, the thiolates can be arylated on sulfur by addition of an aryl iodide in DMF and heating at 120 °C.[25]

4. Conclusion

3-(Tosyloxy)cyclohex-2-en-1-ones, readily made from cyclohexan-1,3-diones, are convertible into 3-(arylsulfanyl)- or 3-(alkylsulfanyl)cyclohex-2-en-1-ones by reaction at room temperature with thiols in the presence of K_2CO_3. The products can be brominated at C-2 with NBS in MeCN, and treatment with DBU in MeCN affords the corresponding 3-(arylsulfanyl)- or 3-(alkylsulfanyl)phenols. The reaction sequence occurs under mild conditions and avoids the use of heavy metals.

5. Experimental section

5.1 *General procedures.*

Solvents used for chromatography were distilled before use. Commercial thin layer chromatography plates (silica gel, Merck 60F-254) were used. Silica gel for flash chromatography was Merck type 60 (230−400 mesh). Dry solvents were prepared under an inert atmosphere (N_2) and transferred by syringe or cannula. The symbols s, d, t, and q used for ^{13}C NMR spectra indicate zero, one, two, or three attached hydrogens, respectively, the assignments being made from APT spectra. Solutions were evaporated under water pump vacuum, and the residue was then kept under oil pump vacuum. High resolution electrospray mass spectrometric analyses were done with an orthogonal time-of-flight analyzer, and electron ionization mass spectra were measured with a double-focusing sector mass spectrometer. Gradient flash chromatography was done by stepwise small increases in the proportion of the more polar solvent, as described for the individual experiments. NBS was recrystallized from water.[26]

*5.1.1. 3-(Phenylsulfanyl)cyclohex-2-en-1-one (**17**)*[11]

PhSH (0.055 mL, 0.50 mmol) was added to a stirred mixture of tosylate **18** (133 mg, 0.50 mmol), K_2CO_3 (413 mg, 2.50 mmol) and dry MeCN (1 mL) and stirring was continued overnight (N_2 atmosphere). Water (10 mL) was added and stirring was continued for 15 min. The mixture was extracted with EtOAc (3 × 15 mL) and the combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1 × 25 cm), using 4:1 hexane-EtOAc, gave **17** (72 mg, 71%) as an oil: ^1H NMR ($CDCl_3$, 400 MHz) δ 2.01–2.07 (m, 2 H), 2.34–2.38 (m, 2 H), 2.52 (td, *J* = 6.0, 0.8 Hz, 2 H), 5.47 (t, *J* = 1.2 Hz, 1

H), 7.40–7.48 (m, 5 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.9, 30.2, 37.2, 120.9, 128.0, 129.8, 130.1, 135.5, 166.8, 196.0.

*5.1.2. 2-Bromo-3-(phenylsulfanyl)cyclohex-2-en-1-one (**14**)*[15]

Thio enone **17** (102 mg, 0.50 mmol) and then freshly crystallized NBS (98 mg, 0.55 mmol) were placed in a round-bottomed flask containing a magnetic stirrer. Dry MeCN (1.0 mL) was added and the mixture was stirred for 24 h (N_2 atmosphere) with protection from light (flask wrapped in aluminum foil). EtOAc (15 mL) was added and the mixture was washed successively with aqueous $Na_2S_2O_3$ (1 M), saturated aqueous $NaHCO_3$, and brine. The organic extract was dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **14** (102 mg, 72%) as a solid: mp 112–113 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.93–1.97 (m, 2 H), 2.20 (t, J = 6.5 Hz, 2 H), 2.56 (t, J = 6.0 Hz, 2 H), 7.43–7.58 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.5, 32.2, 37.1, 116.8, 129.1, 129.7, 130.4, 136.0, 164.3, 187.7.

*5.1.3. 3-(Phenylsulfanyl)phenol (**19**)*[21]

DBU (0.032 mL, 0.212 mmol) was injected into a stirred solution of **14** (30 mg, 0.11 mmol) in dry MeCN (1.0 mL) and stirring was continued overnight (N_2 atmosphere). The mixture was diluted with hydrochloric acid (5%, 10 mL) and stirring was continued for 15 min. The mixture was extracted with EtOAc (3 × 15 mL) and the combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated. Flash chromatography of the residue over silica gel (1 × 15 cm), using successively hexane (ca 20 mL), 5% EtOAc-hexane (ca 50 mL), 10% EtOAc-hexane (ca 100 mL), gave **19** (19 mg, 89%) as an oil: ^{1}H NMR ($CDCl_3$, 400 MHz) δ 4.98 (br s, 1 H), 6.70–6.80 (m, 1 H), 6.85–6.86 (m, 1 H), 6.98–7.00 (m, 1 H), 7.26 (t, J = 8.0 Hz, 1 H), 7.36–7.39 (m, 1 H), 7.41–7.44 (m, 2 H), 7.48–7.51 (m, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 113.9, 116.9, 122.7, 127.5, 129.3, 130.2, 131.9, 134.8, 137.89, 156.0.

*5.1.4. 3-[(4-Fluorophenyl)sulfanyl]cyclohex-2-en-1-one (**20**)*[27]

The procedure for making **17** was followed exactly, using 4-fluorobenzene-1-thiol (0.042 mL, 0.50 mmol), tosylate **18** (133 mg, 0.50 mmol), K_2CO_3 (413 mg, 2.50 mmol) and dry MeCN (1 mL). Water (10 mL) was added and stirring was continued for 15 min. Flash chromatography of the crude product over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **20** (100 mg, 90%) as an oil: FTIR ($CDCl_3$, cast) 2949, 1659, 1589, 1491, 1324, 1227, 1187 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.03–2.06 (m, 2 H), 2.37 (t, J = 6.5 Hz, 2 H), 2.50–2.52 (m, 2 H), 5.41 (s, 1 H), 7.10–7.13 (m, 2 H), 7.44–7.47 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 23.0 (t), 30.2 (t), 37.3 (t), 117.2 (d, $^2J_{CF}$ = 22.2 Hz), 120.9 (d, $^4J_{CF}$ = 3.6 Hz), 123.4 (d), 137.7 (d, $^3J_{CF}$

= 8.5 Hz), 164.0 (d, $^{1}J_{CF}$ = 252.0 Hz), 165.0 (s), 166.7 (s), 196.0 (s); exact mass (EI) *m*/*z* calcd for $C_{12}H_{14}FOS$ (M^{+}) 222.0515, found 222.0515.

*5.1.5. 2-Bromo-3-[(4-fluorophenyl)sulfanyl]cyclohex-2-en-1-one (**20a**)*

The procedure for making **14** was followed exactly, using thio enone **20** (60 mg, 0.27 mmol), freshly crystallized NBS (53 mg, 0.30 mmol) and dry MeCN (1.0 mL). Flash chromatography of the crude product over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **20a** (60 mg, 73%) as a solid: mp 135–136 °C; FTIR ($CDCl_3$, cast) 3097, 3070, 2956, 2935, 1665, 1588, 1543, 1491, 1266, 1222, 1185 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.95 (quintet, *J* = 6.5 Hz, 2 H), 2.16–2.19 (m, 2 H), 2.55 (t, *J* = 6.5 Hz, 2 H), 7.12–7.15 (m, 2 H), 7.54–7.56 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.5 (t), 32.2 (t), 37.1 (t), 117.02 (d, $^{2}J_{CF}$ = 22.1 Hz), 117.03 (s), 124.6 (d, $^{4}J_{CF}$ = 3.6 Hz), 138.2 (d, $^{3}J_{CF}$ = 8.7 Hz), 163.8 (s), 164.1 (d, $^{1}J_{CF}$ = 252.6 Hz), 187.6 (s); exact mass (EI) *m*/*z* calcd for $C_{12}H_{10}{}^{81}BrFOS$ (M^{+}) 301.9599, found 301.9597.

*5.1.6. 3-[(4-Fluorophenyl)sulfanyl]phenol (**20b**)*

The procedure for making **19** was followed exactly, using DBU (0.088 mL, 0.590 mmol) and **20a** (88.4 mg, 0.294 mmol) in dry MeCN (1.0 mL). Flash chromatography of the crude product over silica gel (1 × 15 cm), using 3:7 hexane-CH_2Cl_2, gave **20b** (39 mg, 60%) as an oil: FTIR ($CDCl_3$, cast) 3380, 3092, 1589, 1489, 1474, 1439, 1225, 1156 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.81 (s, 1 H), 6.65–6.67 (m, 2 H), 6.80–6.82 (m, 1 H), 7.02–7.06 (m, 2 H), 7.14 (td, *J* = 8.0, 1.0 Hz, 1 H), 7.40–7.43 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 113.7 (d), 115.9 (d), 116.5 (d), 116.6 (d, $^{2}J_{CF}$ = 22.4 Hz), 121.7 (d), 129.3 (d, $^{4}J_{CF}$ = 3.4 Hz), 130.2 (d), 134.9 (d, $^{3}J_{CF}$ = 8.5 Hz), 138.7 (d), 156.0 (s), 162.7 (d, $^{1}J_{CF}$ = 248.5 Hz), ; exact mass (EI) *m*/*z* calcd for $C_{12}H_9OFS$ (M^{+}) 220.0358, found 220.0355.

*5.1.7. 3-[(4-Methoxyphenyl)sulfanyl]cyclohex-2-en-1-one (**21**)*[11]

The procedure for making **17** was followed exactly, using 4-methoxybenzene-1-thiol (0.12 mL, 1.00 mmol), tosylate **18** (266 mg, 1.00 mmol), K_2CO_3 (826 mg, 5.00 mmol) and dry MeCN (2 mL) Flash chromatography of the crude product over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **21** (210 mg, 90%) as an oil: FTIR ($CDCl_3$, cast) 3004, 2962, 1654, 1587, 1578, 1494, 1325, 1290, 1250 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.04 (quintet, *J* = 6.5 Hz, 2 H), 2.36 (t, *J* = 6.5 Hz, 2 H), 2.49–2.51 (m, 2 H), 3.82 (s, 3 H), 5.42 (s, 1 H), 6.90–6.93 (m, 2 H), 7.36–7.38 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.9 (t), 30.1 (t), 37.3 (t), 55.4 (q), 115.5 (d), 118.5 (s), 120.6 (d), 137.0 (d), 161.2 (s), 168.0 (s), 196.1 (s); exact mass (EI) *m*/*z* calcd for $C_{13}H_{14}O_2S$ (M^{+}) 234.0715, found 234.0718.

*5.1.8. 2-Bromo-3-[(4-methoxyphenyl)sulfanyl]cyclohex-2-en-1-one (**21a**)*

The procedure for making **14** was followed exactly, using thio enone **20** (86.2 mg, 0.353 mmol), freshly crystallized NBS (69.2 mg, 0.389 mmol) and dry MeCN (1.0 mL). Flash chromatography of the crude product over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **21a** (81.9 mg, 74%) as a solid: mp 115–117 °C; FTIR ($CDCl_3$, cast) 2971, 2947, 1662, 1590, 1454, 1438, 1253, 1187 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.93 (quintet, J = 6.4 Hz, 2 H), 2.18 (t, J = 6.4 Hz, 2 H), 2.53 (t, J = 6.4 Hz, 2 H), 3.84 (s, 3 H), 6.94 (d, J = 8.8 Hz, 2 H), 7.46 (d, J = 8.8 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 22.5 (d), 32.1 (d), 37.2 (d), 55.5 (q), 115.2 (d), 116.2 (s), 119.7 (s), 137.6 (d), 161.4 (s), 165.6 (s), 187.7 (s); exact mass (EI) *m*/*z* calcd for $C_{13}H_{13}{}^{81}BrO_2S$ (M^+) 313.9799, found 313.9796.

*5.1.9. 3-[(4-Methoxyphenyl)sulfanyl]phenol (**21b**)*

The procedure for making **19** was followed exactly, using DBU (0.035 mL, 0.240 mmol) and **21a** (37.5 mg, 0.120 mmol) in dry MeCN (1.0 mL). Flash chromatography of the crude product over silica gel (1 × 15 cm), using successively hexane (ca 20 mL), 5% EtOAc-hexane (ca 50 mL), 10% EtOAc-hexane (ca 100 mL), gave **21b** (24 mg, 86%) as an oil: FTIR ($CDCl_3$, cast) 3396, 1591, 1493, 1439, 1289, 1248, 1173 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.85 (s, 3 H), 4.92 (br s, 1 H), 6.57–6.60 (m, 2 H), 6.74 (ddd, J = 5.0, 1.5, 1.0 Hz, 1 H), 6.90 (dd, J = 9.0, 3.0 Hz, 2 H); 7.10 (t, J = 8.0 Hz, 1 H), 7.43 (dd, J = 9.0, 3.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 55.4 (q), 112.8 (d), 114.4 (d), 115.1 (d), 120.2 (d), 123.6 (s), 130.0 (d), 135.9 (d), 140.6 (s), 156.0 (s), 160.1 (s); exact mass (EI) *m*/*z* calcd for $C_{13}H_{12}O_2S$ (M^+) 232.0558, found 232.0561.

*5.1.10. 3-[(4-Bromophenyl)sulfanyl]cyclohex-2-en-1-one (**22**)*

The procedure for making **17** was followed exactly, using 4-bromobenzene-1-thiol (378 mg, 2.00 mmol), tosylate **18** (532 mg, 2.00 mmol), K_2CO_3 (1.652 g, 10 mmol) and dry MeCN (4 mL). Flash chromatography of the crude product over silica gel (2 × 25 cm), using 4:1 hexane-EtOAc, gave **22** (443 mg, 78%) as an oil: FTIR ($CDCl_3$, cast) 3076, 2950, 2889, 1649, 1579 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.03–2.08 (m, 2 H), 2.38 (dd, J = 7.5, 1.0 Hz, 2 H), 2.51 (ddd, J = 7.5, 6.0, 1.0 Hz, 2 H), 5.45 (apparent t, J = 1.5 Hz, 1 H), 7.33–7.35 (m, 2 H), 7.54–7.57 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.9 (t), 30.2 (t), 37.2 (t), 121.1 (d), 125.0 (s), 127.1 (s), 133.1 (d), 137.0 (d), 165.9 (s), 195.9 (s); exact mass (EI) *m*/*z* calcd for $C_{12}H_{11}{}^{81}BrOS$ (M^+) 283.9694, found 283.9691.

*5.1.11. 2-Bromo-3-[(4-bromophenyl)sulfanyl]cyclohex-2-en-1-one (**22a**)*

The procedure for making **14** was followed exactly, using thio enone **22** (200 mg, 0.710 mmol), freshly crystallized NBS (151 mg, 0.840 mmol) and dry MeCN (1.5 mL). Flash chromatography of the crude product over silica gel (1.2 × 25 cm), using 4:1 hexane-EtOAc, gave **22b** (100 mg, 78%) as a solid: mp 118–120 °C; FTIR ($CDCl_3$, cast) 3079, 3060, 2957, 2931, 1666, 1538 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.94–1.99 (m, 2 H), 2.20 (dd, *J* = 6.0, 6.0 Hz, 2 H), 2.55–2.58 (m, 2 H), 7.41–7.44 (m, 2 H), 7.57–7.60 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.5 (t), 32.3 (t), 37.1 (t), 117.4 (s), 125.4 (s), 128.2 (s), 132.9 (d), 137.4 (d), 163.0 (s), 187.6 (s); exact mass (EI) *m*/*z* calcd for $C_{12}H_{10}{}^{79}BrOS$ $(M + H)^+$ 360.8892, found 360.8894.

*5.1.12. 3-[(4-Bromophenyl)sulfanyl]phenol (**22b**)*

The procedure for making **19** was followed exactly, using DBU (0.08 mL, 0.53 mmol) and **22a** (97 mg, 0.26 mmol) in dry MeCN (1.5 mL). Flash chromatography of the crude product over silica gel (1 × 30 cm), using successively hexane (ca 20 mL), 5% EtOAc-hexane (ca 50 mL), 10% EtOAc-hexane (ca 100 mL), gave **22b** (60 mg, 79%) as an oil: FTIR ($CDCl_3$, cast) 3375, 3059, 2954, 2925, 1583, 1472 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.84 (br s, 1 H), 6.72 (ddd, *J* = 8.0, 2.5, 0.5 Hz, 1 H), 6.77 (m, 1 H), 6.90 (ddd, *J* = 8.0, 1.5, 0.5 Hz, 1 H), 7.16–7.26 (m, 3 H), 7.43 (dt, *J* = 9.0, 2.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 114.5 (d), 117.4 (d), 121.4 (s), 123.2 (d), 130.4 (d), 132.4 (d), 132.9 (d), 134.5 (s), 136.8 (s), 156.0 (s); exact mass (EI) *m*/*z* calcd for $C_{12}H_8{}^{79}BrOS$ $(M - H)^-$ 278.9485, found 278.9477.

*5.1.13. 3-[(4-Methylphenyl)sulfanyl]cyclohex-2-en-1-one (**23**)*[11]

The procedure for making **17** was followed exactly, using 4-methylbenzene-1-thiol (248 mg, 2.00 mmol), tosylate **18** (532 mg, 2.00 mmol), K_2CO_3 (1.652 g, 10.00 mmol) and dry MeCN (4 mL). Flash chromatography of the crude product over silica gel (2 × 25 cm), using 4:1 hexane-EtOAc, gave **23** (401 mg, 93%) as a solid: mp 45–48 °C; FTIR ($CDCl_3$, cast) 3023, 2948, 2866, 1659, 1578 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.02–2.07 (apparent dt, *J* = 13.0, 6.0 Hz, 2 H), 2.35–2.38 (m, 2 H), 2.38 (s, 3 H), 2.52 (ddd, *J* = 6.0, 6.0, 1.0 Hz, 2 H), 5.46 (apparent t, *J* = 1.0 Hz, 1 H), 7.21–7.23 (m, 2 H), 7.35 (dt, *J* = 8.0, 2.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.3 (q), 23.0 (t), 30.2 (t), 37.3 (t), 120.7 (d), 124.4 (s), 130.7 (d), 135.4 (d), 140.6 (s), 167.5 (s), 196.1 (s); exact mass (EI) *m*/*z* calcd for $C_{13}H_{14}OS$ (M^+) 218.0765, found 218.0766.

*5.1.14. 2-Bromo-3-[(4-methylphenyl)sulfanyl]cyclohex-2-en-1-one (**23a**)*

The procedure for making **14** was followed exactly, using thio enone **23** (209 mg, 1.00 mmol), freshly crystallized NBS (195 mg, 1.10 mmol) and dry MeCN (1.5 mL). Flash chromatography of the crude product over silica gel (1.2 × 25 cm), using 4:1 hexane-EtOAc,

gave **23a** (210 mg, 74%) as a solid: mp 128–130 °C; FTIR ($CDCl_3$, cast) 3052, 3033, 2956, 2931, 1662, 1542 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.91–2.0 (m, 2 H), 2.20 (dd, *J* = 6.0, 6.0 Hz, 2 H), 2.41 (s, 3 H), 2.55 (dd, *J* = 7.0, 7.0 Hz, 2 H), 7.23–7.25 (m, 2 H), 7.42–7.44 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.4 (q), 22.5 (t), 32.1 (t), 37.2 (t), 116.5 (s), 125.6 (s), 130.4 (d), 135.9 (d), 140.9 (s), 164.9 (s), 187.7 (s); exact mass (EI) *m*/*z* calcd for $C_{13}H_{13}{}^{81}BrOS$ (M^+) 297.9850, found 297.9851.

*5.1.15. 3-[(4-Methylphenyl)sulfanyl]phenol (**23b**)*[19]

The procedure for making **19** was followed exactly, using DBU (0.10 mL, 0.67 mmol) and **23a** (102 mg, 0.33 mmol) in dry MeCN (1.5 mL). Flash chromatography of the crude product over silica gel (1 × 30 cm), using successively hexane (ca 20 mL), 5% EtOAc-hexane (ca 50 mL), 10% EtOAc-hexane (ca 100 mL), gave **23b** (56 mg, 75%) as an oil: FTIR ($CDCl_3$, cast) 3383, 3022, 2920, 2862, 1584, 1474 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.37 (s, 3 H), 4.90 (br s, 1 H), 6.63–6.68 (m, 2 H), 6.82–6.85 (m, 1 H), 7.11–7.17 (m, 3 H), 7.35 (dd, *J* = 6.5, 2.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.2 (q), 113.4 (d), 115.7 (d), 121.6 (d), 130.1 (d), 130.2 (d), 130.3 (s), 133.1 (d), 138.1 (s), 139.2 (s), 155.9 (s); exact mass (electrospray) *m*/*z* calcd for $C_{13}H_{11}OS$ $(M - H)^-$ 215.0536, found 215.0534.

*5.1.16. 3-[(2-Methylphenyl)sulfanyl]cyclohex-2-en-1-one (**24**)*

The procedure for making **17** was followed exactly, using 2-methylbenzene-1-thiol (0.30 mL, 2.46 mmol), tosylate **18** (655 mg, 2.45 mmol), K_2CO_3 (1.70 g, 12.3 mmol) and dry MeCN (4 mL). Flash chromatography of the crude product over silica gel (2 × 25 cm), using 4:1 hexane-EtOAc, gave **24** (500 mg, 93%) as an oil: FTIR ($CDCl_3$, cast) 3059, 2949, 2866, 1656, 1578 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.06 (quintet, *J* = 6.5 Hz, 2 H), 2.37–2.39 (m, 5 H), 2.54 (td, *J* = 6.0, 1.0 Hz, 2 H), 5.32 (apparent t, *J* = 1.0 Hz, 1 H), 7.21–7.24 (m, 1 H), 7.30–7.37 (m, 2 H), 7.46 (ddd, *J* = 7.5, 1.0, 0.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.4 (q), 23.0 (t), 30.2 (t), 37.3 (t), 120.4 (d), 127.3 (s), 127.3 (d), 130.8 (d), 131.2 (d), 136.6 (d), 142.7 (s), 165.9 (s), 196.1 (s); exact mass (EI) *m*/*z* calcd for $C_{13}H_{14}OS$ (M^+) 218.0765, found 218.0765.

*5.1.17. 2-Bromo-3-[(2-methylphenyl)sulfanyl]cyclohex-2-en-1-one (**24a**)*

The procedure for making **14** was followed exactly, using thio enone **24** (224 mg, 1.03 mmol), freshly crystallized NBS (200 mg, 1.13 mmol) and dry MeCN (1.5 mL). Flash chromatography of the crude product over silica gel (1.2 × 25 cm), using 4:1 hexane-EtOAc, gave **24a** (250 mg, 82%) as a solid: mp 111–113 °C; FTIR ($CDCl_3$, cast) 3060, 3011, 2950, 2923, 1671, 1537 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.91–1.96 (m, 2 H), 2.1 (t, *J* = 6.0 Hz, 2 H), 2.45 (s, 3 H), 2.56 (dd, *J* = 7.5, 6.0 Hz, 2 H), 7.25–7.27 (m, 1 H), 7.33–7.37 (m, 1 H), 7.40

(ddd, J = 7.5, 1.5, 1.5 Hz, 1 H), 7.54 (dd, J = 7.5, 1.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.2 (q), 22.5 (t), 31.7 (t), 37.2 (t), 117.3 (s), 127.2 (d), 128.7 (s), 130.9 (d), 131.2 (d), 137.0 (d), 143.1 (s), 164.4 (s), 187.7 (s); exact mass (EI) m/z calcd for $C_{13}H_{13}{}^{79}BrOS$ (M^+) 295.9871, found 295.9872.

*5.1.18. 3-[(2-Methylphenyl)sulfanyl]phenol (**24b**)*

The procedure for making **19** was followed exactly, using DBU (0.10 mL, 0.67 mmol) and **24a** (95 mg, 0.32 mmol) in dry MeCN (1.5 mL). Flash chromatography of the crude product over silica gel (1 × 30 cm), using successively hexane (ca 20 mL), 5% EtOAc-hexane (ca 50 mL), and 10% EtOAc-hexane (ca 100 mL), gave **24b** (54 mg, 78%) as an oil: FTIR ($CDCl_3$, cast) 3376, 3060, 2961, 2923, 1584, 1473 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.41 (s, 3 H), 4.76 (br s, 1 H), 6.61–6.62 (m, 1 H), 6.66 (dd, J = 8.0, 1.0 Hz, 1 H), 6.80 (dd, J = 8.0, 1.0 Hz, 1 H), 7.15 (t, J = 8.0 Hz, 1 H), 7.18–7.21 (m, 1 H), 7.26–7.30 (m, 2 H), 7.41 (d, J = 8.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 20.7 (q), 113.3 (d), 115.5 (d), 121.4 (d), 126.8 (d), 128.5 (d), 130.2 (d), 130.8 (d), 132.8 (s), 134.0 (d), 138.3 (s), 140.8 (s), 156.0 (s); exact mass (electrospray) m/z calcd for $C_{13}H_{11}OS$ $(M - H)^-$ 215.0536, found 215.0538.

*5.1.19. Methyl 2-[(3-oxocyclohex-1-en-1-yl)sulfanyl]benzoate (**25**)*

The procedure for making **17** was followed exactly, using methyl 2-sulfanylbenzoate[28] (168 mg, 1.00 mmol), tosylate **18** (266 mg, 1.00 mmol), K_2CO_3 (826 mg, 5.00 mmol) and dry MeCN (2 mL). Flash chromatography of the crude product over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **25** (222.5 mg, 85%) as an oil: FTIR ($CDCl_3$, cast) 1731, 1656, 1578, 1467, 1293, 1271 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.05 (quintet, J = 6.5 Hz, 2 H), 2.38 (t, J = 6.5 Hz, 1 H), 2.52–2.54 (m, 2 H), 3.88 (s, 3 H), 5.57 (s, 1 H), 7.46–7.53 (m, 2 H), 7.56–7.58 (m, 1 H), 7.89 (dd, J = 6.0, 1.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.9 (t), 30.4 (t), 37.2 (t), 52.5 (q), 122.4 (d), 129.2 (d), 129.8 (s), 131.2 (d), 132.4 (d), 135.2 (s), 137.1 (d), 165.6 (s), 166.5 (s), 196.3 (s); exact mass (EI) m/z calcd for $C_{14}H_{14}O_3S$ (M^+) 262.0664, found 262.0663.

*5.1.20. Methyl 2-[(2-bromo-3-oxocyclohex-1-en-1-yl)sulfanyl]benzoate (**25a**)*

The procedure for making **14** was followed exactly, using thio enone **25** (204.4 mg, 0.780 mmol), freshly crystallized NBS (153.6 mg, 0.860 mmol) and dry MeCN (1 mL). Flash chromatography of the crude product over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **25a** (160 mg, 60%) as a solid: mp 117–120 °C; FTIR ($CDCl_3$, cast) 3089, 1726, 1668, 1569, 1351, 1136, 1118 cm^{-1}; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 1.95 (quintet, J = 6.0 Hz, 2 H), 2.26 (t, J = 6.0 Hz, 2 H), 2.57 (t, J = 6.5 Hz, 2 H), 3.90 (s, 3 H), 7.54–7.56 (m, 2 H), 7.64–7.66 (m, 1 H), 7.87–7.89 (m, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.6 (t), 32.3 (t), 37.3 (t), 52.8 (q), 117.5 (s),

129.2 (s), 130.5 (d), 130.8 (d), 132.1 (d), 136.7 (s), 137.8 (d), 164.4 (s), 166.9 (s), 188.0 (s); exact mass (EI) *m*/*z* calcd for $C_{14}H_{13}{}^{81}BrO_3S$ (M^+) 341.9748, found 341.9752.

*5.1.21. Methyl 2-[(3-hydroxyphenyl)sulfanyl]benzoate (**25b**)*

The procedure for making **19** was followed exactly, using DBU (0.08 mL, 0.54 mmol) and **25a** (92 mg, 0.27 mmol) in dry MeCN (1 mL). Flash chromatography of the crude product over silica gel (3 × 20 cm), using successively hexane (ca 100 mL), 5% EtOAc-hexane (ca 100 mL), and 10% EtOAc-hexane (ca 100 mL) and 20% EtOAc-hexane (ca 100 mL), gave **25b** (50.5 mg, 72%) as an oil: FTIR ($CDCl_3$, cast) 3409, 1714, 1693, 1587, 1307, 1273, 1255 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 3.97 (s, 3 H), 5.24 (br s, 1 H), 6.89–6.92 (m, 2 H), 7.08–7.14 (m, 3 H), 7.24–7.31 (m, 2 H), 7.96 (dd, *J* = 6.5, 1.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 52.3 (q), 116.4 (d), 121.9 (d), 124.5 (d), 126.9 (s), 127.6 (d), 127.8 (d), 130.8 (d), 131.0 (d), 132.5 (d), 133.9 (s), 142.9 (s), 156.5 (s), 167.2 (s); exact mass (EI) *m*/*z* calcd for $C_{14}H_{12}O_3S$ (M^+) 260.0507, found 260.0508.

*5.1.22. 3-(Benzylsulfanyl)cyclohex-2-en-1-one (**26**)*[29]

The procedure for making **17** was followed exactly, using phenylmethanethiol (0.12 mL, 1.0 mmol), tosylate **18** (266 mg, 1.00 mmol), K_2CO_3 (826 mg, 5.00 mmol) and dry MeCN (2 mL). Flash chromatography of the crude product over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **26** (179 mg, 82%) as a solid: mp 75–77 °C; FTIR ($CDCl_3$, cast) 3054, 1654, 1573, 1452, 1295, 1264 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.03 (quintet, *J* = 6.0 Hz, 2 H), 2.40 (t, *J* = 6.0 Hz, 2 H), 2.45–2.47 (m, 2 H), 4.03 (s, 2 H), 5.95 (s 1 H), 7.26–7.34 (m, 5 H; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 23.0 (t), 30.7 (t), 35.9 (t), 37.4 (t), 120.0 (d), 127.8 (d), 128.9 (d), 134.7 (s), 165.2 (s), 195.8 (s); exact mass (EI) *m*/*z* calcd for $C_{13}H_{14}OS$ (M^+) 218.0765, found 218.0767.

*5.1.23. 3-(Benzylsulfanyl)-2-bromocyclohex-2-en-1-one (**26a**)*

The procedure for making **14** was followed exactly, using thio enone **26** (54.5 mg, 0.250 mmol), freshly crystallized NBS (49.2 mg, 0.275 mmol) and dry MeCN (1.0 mL). Flash chromatography of the crude product over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **26a** (54 mg, 72%) as a solid: mp 112-114 °C; FTIR ($CDCl_3$, cast) 2950, 2666, 1667, 1532, 1494, 1453, 1261, 1184 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.07 (quintet, *J* = 6.5 Hz, 2 H), 2.55–2.58 (m, 2 H), 2.70 (t, *J* = 6.0 Hz, 2 H), 4.15 (s, 2 H), 7.30–7.38 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.4 (t), 31.2 (t), 36.6 (t), 36.9 (t), 117.1 (s), 127.9 (d), 128.8 (d), 129.0 (d), 135.0 (s), 163.7 (s), 187.3 (s); exact mass (EI) *m*/*z* calcd for $C_{13}H_{13}{}^{81}BrOS$ (M^+) 297.9850, found 297.9856.

*5.1.24. 3-(Benzylsulfanyl)phenol (**26b**)*[24]

The procedure for making **19** was followed exactly, using DBU (0.050 mL, 0.318 mmol) and **26a** (31.5 mg, 0.106 mmol) in dry MeCN (1.0 mL). Flash chromatography of the crude product over silica gel (1 × 15 cm), using 3:7 hexane-CH_2Cl_2, gave **26b** (15 mg, 65%) as an oil: FTIR ($CDCl_3$, cast) 3386, 3084, 3061, 1581, 1493, 1475, 1247, 1216 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 4.12 (s, 2 H), 4.90 (br s, 1 H), 6.64 (dd, *J* = 8.0, 2.0 Hz, 1 H), 6.78 (t, *J* = 2.0 Hz, 1 H), 6.88 (d, *J* = 8.0 Hz, 1 H), 7.13 (t, *J* = 8.0 Hz, 1 H), 7.23–7.33 (m, 5 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 38.7 (t), 113.4 (d), 116.1 (d), 121.8 (d), 127.3 (d), 128.6 (d), 128.9 (d), 129.9 (d), 137.3 (s), 138.2 (s) 155.8 (s); exact mass (EI) *m*/*z* calcd for $C_{13}H_{12}OS$ (M^+) 216.0609, found 216.0605.

*5.1.25. 5-Phenyl-3-(phenylsulfanyl)cyclohex-2-en-1-one (**27**)*

(a) 3-Oxo-5-phenylcyclohex-1-en-1-yl 4-methylbenzene-1-sulfonate[30]

Et_3N (0.5 mL, 3.6 mmol) was added to a stirred solution of commercial 3-hydroxy-5-phenylcyclohex-2-en-1-one (565 mg, 3.00 mmol) and TsCl (573 mg, 3.00 mmol) in dry THF (10 mL), and stirring was continued overnight (N_2 atmosphere). Water (15 mL) was added and stirring was continued for 30 min. The mixture was extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$) and evaporated to afford 3-oxo-5-phenylcyclohex-1-en-1-yl 4-methylbenzene-1-sulfonate (946.5 mg, 92%) as a solid, which was used directly in the next step. The material had: mp 86–88 °C; FTIR ($CDCl_3$, cast) 3063, 1678, 1635, 1426, 1376, 1194, 1179 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.48 (s, 3 H), 2.56 (dd, *J* = 16.0, 13.0 Hz, 1 H), 2.65 (dd, *J* = 16.0, 4.0 Hz, 1 H), 2.74 (dd, *J* = 6.5, 1.5 Hz, 2 H), 3.31–3.38 (m, 1 H), 5.90 (s, 1 H), 7.17–7.20 (m, 2 H), 7.25–7.29 (m, 1 H), 7.32–7.35 (m, 2 H), 7.37–7.39 (m, 2 H), 7.81–7.84 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 21.8 (d), 36.4 (t), 39.2 (q), 43.6 (t), 116.6 (d), 126.6 (d), 127.4 (d), 128.3 (d), 129.0 (d), 130.2 (d), 132.5 (s), 141.6 (s), 146.3 (s), 167.3 (s), 197.8 (s); exact mass (EI) *m*/*z* calcd for $C_{19}H_{18}O_4S$ (M^+) 342.0926, found 342.0926.

*(b) 5-Phenyl-3-(phenylsulfanyl)cyclohex-2-en-1-one (**27**)*

The procedure for making **17** was followed exactly, using PhSH (0.105 mL, 1.00 mmol), 3-oxo-5-phenylcyclohex-1-en-1-yl 4-methylbenzene-1-sulfonate (342 mg, 1.00 mmol), K_2CO_3 (826 mg, 12.3 mmol) and dry MeCN (2 mL). Flash chromatography of the crude product over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **27** (234.2 mg, 80%) as a solid: mp 85–87 °C; FTIR ($CDCl_3$, cast) 3059, 3028, 1653, 1577, 1440, 1290, 1255, 1040 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.58–2.83 (m, 4 H), 3.37–3.44 (m, 1 H), 5.56 (d, *J* = 1.5 Hz, 1 H), 7.24–7.29 (m, 3 H), 7.34–7.37 (m, 2 H), 7.42–7.45 (m, 3 H), 7.49–7.51 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 37.8 (s), 41.0 (d), 44.2 (s), 120.7 (d), 126.8 (d), 127.2 (d), 127.9 (d), 128.9 (s), 130.0 (d), 130.3

(d), 135.5 (d), 142.6 (s), 166.0 (s), 195.5 (s); exact mass (EI) *m*/*z* calcd for $C_{18}H_{16}OS$ (M^+) 280.0922, found 280.0923.

*5.1.26. 3-Bromo-5-phenyl-3-(phenylsulfanyl)cyclohex-2-en-1-one (**27a**)*

The procedure for making **14** was followed exactly, using thio enone **27** (200 mg, 0.714 mmol), freshly crystallized NBS (140.6 mg, 0.786 mmol) and dry MeCN (1.0 mL). Flash chromatography of the crude product over silica gel (3 × 15 cm), using 9:1 hexane-EtOAc, gave **27a** (197 mg, 77%) as a solid: mp 128–132 °C; FTIR ($CDCl_3$, cast) 3059, 1671, 1538, 1453, 1440, 1264, 1242 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 2.39–2.48 (m, 2 H), 2.76 (dd, *J* = 16.0, 13.0 Hz, 1 H), 2.87 (ddd, *J* = 11.5, 4.0, 1.5 Hz, 1 H), 3.30–3.37 (m, 1 H), 7.06–7.08 (m, 2 H), 7.20–7.30 (m, 3 H), 7.38–7.46 (m, 3 H), 7.52–7.55 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 39.2 (t), 40.4 (d), 43.9 (t), 116.9 (d), 126.6 (d), 127.3 (d), 128.8 (d), 128.9 (s), 129.8 (d), 130.6 (d), 135.9 (d), 141.8 (s), 163.0 (s), 187.2 (s); exact mass (EI) *m*/*z* calcd for $C_{18}H_{15}{}^{81}BrOS$ (M^+) 360.0006, found 360.0002.

*5.1.27. 5-Phenyl-3-(phenylsulfanyl)phenol (**27b**)*

The procedure for making **19** was followed exactly, using DBU (0.025 mL, 0.17 mmol) and **27a** (30.6 mg, 0.085 mmol) in dry MeCN (1.0 mL). Flash chromatography of the crude product over silica gel (1 × 15 cm), using 3:7 hexane-CH_2Cl_2, gave **27b** (17 mg, 63%) as an oil: FTIR ($CDCl_3$, cast) 3391, 3059, 2953, 1586, 1570, 1476, 1449, 1196 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 4.83 (s, 1 H), 6.71 (dd, *J* = 2.0, 1.5 Hz, 1 H), 6.91 (dd, *J* = 2.0, 1.5 Hz, 1 H), 7.15 (t, *J* = 1.5 Hz, 1 H), 7.27–7.36 (m, 4 H), 7.40–7.45 (m, 4 H), 7.50–7.52 (m, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 112.9 (d), 115.7 (d), 121.6 (d), 127.1 (d), 127.6 (d), 127.8 (d), 128.8 (d), 129.4 (d), 132.0 (d), 134.7 (s), 138.4 (s), 140.1 (s), 143.7 (s), 156.3 (s); exact mass (EI) *m*/*z* calcd for $C_{18}H_{14}OS$ (M^+) 278.0765, found 279.0771.

*5.1.28. 3-(tert-Butylsulfanyl)cyclohex-2-en-1-one (**28**)*

The procedure for making **17** was followed exactly, using 2-methylpropane-2-thiol (0.11 mL, 1.00 mmol), tosylate **18** (266 mg, 1.00 mmol), K_2CO_3 (826 mg, 5.00 mmol) and dry MeCN (2 mL). Flash chromatography of the crude product over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **28** (73.4 mg, 40%) as an oil: FTIR ($CDCl_3$, cast) 2963, 1659, 1570, 1457, 1338 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.48 (s, 9 H), 1.99 (quintet *J* = 6.0 Hz, 2 H), 2.36–2.38 (m, 4 H), 6.11 (s, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.8 (t), 30.4 (q), 31.7 (t), 37.2 (t), 47.4 (s), 122.6 (d), 164.5 (s), 196.0 (s); exact mass (EI) *m*/*z* calcd for $C_{10}H_{16}OS$ (M^+) 184.0922, found 184.0922.

*5.1.29. 2-Bromo-3-(tert-butylsulfanyl)cyclohex-2-en-1-one (**28a**)*

The procedure for making **14** was followed exactly, using thio enone **28** (65 mg, 0.35 mmol), freshly crystallized NBS (63.2 mg, 0.350 mmol) and dry MeCN (0.5 mL). Flash chromatography of the crude product over silica gel (3 × 15 cm), using 4:1 hexane-EtOAc, gave **28a** (40 mg, 42%) as a solid: mp 102–103 °C; FTIR ($CDCl_3$, cast) 2965, 1661, 1517, 1472, 1262, 1248 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.56 (s, 9 H), 2.09 (quintet, *J* = 6.0 Hz, 2 H), 2.60 (t, *J* = 6.0 Hz, 2 H), 2.93 (t, *J* = 6.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.8 (t), 32.3 (q), 32.9 (t), 37.4 (t), 49.6 (s), 119.2 (s), 164.6 (s), 187.8 (s); exact mass (EI) *m*/*z* calcd for $C_{10}H_{15}{}^{81}BrOS$ (M^+) 264.0006, found 264.0004.

*5.1.30. 3-(tert-Butylsulfanyl)phenol (**28b**)*

The procedure for making **19** was followed exactly, using DBU (0.034 mL, 0.226 mmol) and **28a** (29.5 mg, 0.113 mmol) in dry MeCN (1 mL). Flash chromatography of the crude product over silica gel (1 × 15 cm), using 2:8 hexane-CH_2Cl_2, gave **28b** (5 mg, 25%) as an oil: FTIR ($CDCl_3$, cast) 3355, 2961, 1583, 1469, 1456, 1245, 1210, 1159 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.29 (s, 9 H), 4.76 (s, 1 H), 6.84 (dd, *J* = 8.0, 2.5 Hz, 1 H), 7.03 (t, *J* = 1.5 Hz, 1 H), 7.11 (d, *J* = 7.5 Hz, 1 H), 7.20 (t, *J* = 8.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 31.0 (q), 46.1 (s), 115.9 (d), 124.0 (d), 129.4 (d), 129.9 (d), 134.1 (s), 155.2 (s); exact mass (EI) *m*/*z* calcd for $C_{10}H_{14}OS$ (M^+) 182.0765, found 182.0764.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/

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