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A Benzannulation Protocol To Prepare Substituted Aryl Amines Using a Michael-Aldol Reaction of β-Keto Sulfones

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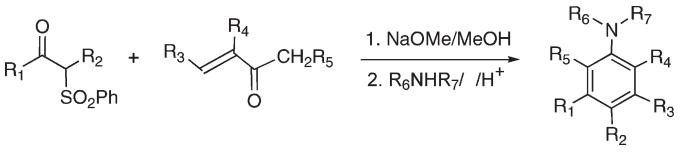

A practical benzannulation method to prepare variously substituted aryl amines and sulfides was developed. The approach involves a Michael-aldol reaction of β-keto sulfones with enones followed by a subsequent condensation of the initial adduct with various amines. The base-induced Michael-aldol cascade proceeds smoothly with a number of different β-keto sulfones, affording the adducts as single diastereomers. Heating the resulting Michael-aldol product with an amine in toluene at 120 °C results in the formation of a transient enamine, which then undergoes loss of phenyl sulfenic acid to furnish the aromatized amine in good yield. A related reaction also occurred when the Michael-aldol product was heated with thiols or alcohols, giving rise to aryl-substituted sulfides or ethers.

Introduction

Aromatic amines are useful intermediates in the preparation of dyes, pharmaceuticals, and agricultural chemicals.[1] Therefore, the development of efficient methods to synthesize these compounds continues to be a topic of immense importance. A wide variety of procedures to prepare aniline derivatives are available and many involve the use of a metal.[2] Over the years an assortment of metals have been used for the reduction of aromatic nitro compounds to aryl amines, with the most traditional methods employing zinc, tin, or iron in the presence of an acid.[3] However, selective metal reduction of a nitro group in the presence of other reducible functionalities in a molecule is often a challenging task. In addition, metal reduction of aromatic nitro compounds frequently stops at an intermediate stage, producing hydroxylamines, hydrazines, and azoarenes as side products.[4] More recently, the metal-catalyzed C−N bond-forming cross-coupling reaction of aryl halides has emerged as a powerful protocol for preparing aryl amines.[5−7] Amination reactions employing nucleophiles as diverse as primary and secondary aryl amines, carbamates, and hydrazones are all known.[8] Although great progress has been made in

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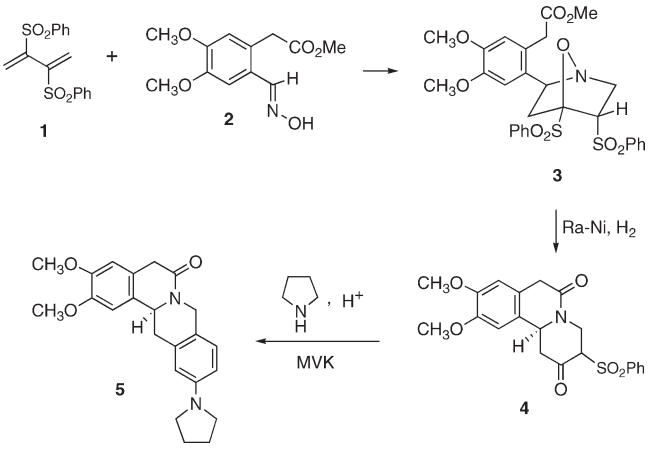
SCHEME 1



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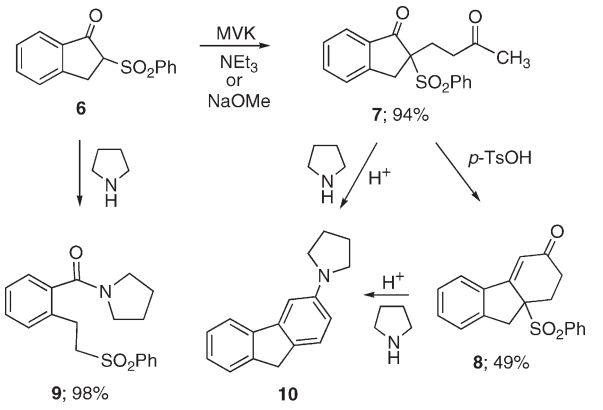

metal-catalyzed Ullmann-type *N*-arylation reactions, the efficiency of the coupling is highly dependent on the involvement of suitable ligands.[9] Also, the need to address specific mechanistic issues and in some cases the high cost of the ligand detracts somewhat from the overall utility of the amination reaction. Even though the aforementioned methods are broadly used, there remains a need for alternative strategies for the synthesis of highly functionalized arylamines as well as aryl thioethers.

In our laboratory, there has been an ongoing interest in domino and multicomponent processes to prepare azapolycyclic ring systems. As part of this program, we discovered some years ago a conjugate addition-dipolar cycloaddition cascade of 2,3-bis(phenylsulfonyl)-1,3-butadiene (**1**) with various oximes as an approach for constructing functionalized piperidone ring systems.[10] The first step in the cascade sequence was shown to involve conjugate addition of the oxime with diene **1**, and this was followed by proton transfer to create a transient nitrone that undergoes a subsequent 1,3-dipolar cycloaddition with the tethered vinyl sulfone.[11] The resulting cycloadduct can be cleaved reductively to provide an azapolycyclic scaffold with a strategically placed phenylsulfonyl functionality for further synthetic manipulation.[12] During our earlier studies, we found that treatment of the resulting phenylsulfonyl-substituted piperidone **4** derived from the reduction of cycloadduct **3** with MVK in the presence of pyrrolidine and acetic acid gave the unexpected benzo-isoquinolinone **5** in high yield (Scheme 1).[13] As a consequence of this observation, we became interested in making further use of this operation for the synthesis of various aryl amines. In this paper we describe the systematic optimization of this benzoannulation reaction and the applicability of the method for the preparation of variously substituted aryl amines and aryl thioethers.[14] It should be noted that a related Robinson annelation of β-keto sulfoxides with vinyl ketones had been reported by Boger and Mullican as a method to prepare highly substituted phenols.[15]

Results and Discussion

The 1,4-conjugate addition of stabilized anions to enones is one of the most fundamental and efficient methods to form C−C bonds.[16] Although the Michael addition of α-thioesters,[17] α-thioacetonitriles,[18] sulfinyl or sulfonyl carbanions[19] to activated π-bonds is well documented, the related conjugated addition of β-keto sulfones with Michael acceptors has been much less studied.[20−22] As a starting point for our investigation, we first tested which base and solvent system would work best for the Michael addition of 2-(phenylsulfonyl)-2,3-dihydro-1*H*-indene-1-one (**6**)[23] with methyl vinyl ketone (MVK). The reaction worked exceptionally well using either NaOMe or NEt_3 as the base to give the desired Michael addition product **7** in 94% yield (Scheme 2). We next examined the reaction of dione **7** with pyrrolidine (4.0 equiv) employing toluene as the solvent together with a trace amount of *p*-TsOH at 110 °C. Under these conditions, a 1:1 mixture of amide **9** and fluorenyl pyrrolidine **10** was obtained in 84% yield. The distribution of products was found to be markedly dependent on the concentration of pyrrolidine present in the solution. By using a

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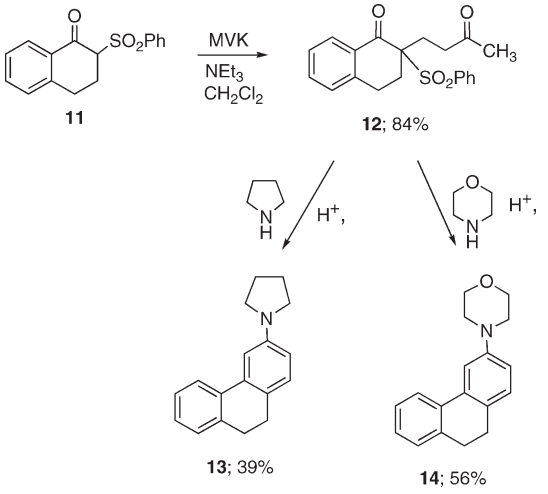
SCHEME 3

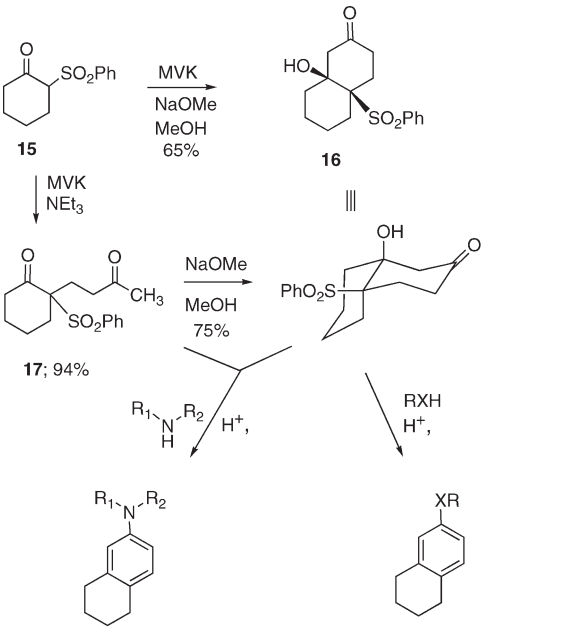


16-fold excess of pyrrolidine, the ratio of products **9**:**10** changed from 1:1 to 9:1. We assume that in the presence of a large excess of base, a retro-Michael reaction occurred to first regenerate β-keto sulfone **6**, which then underwent further reaction with pyrrolidine to give amide **9**. A single-crystal X-ray analysis of **9** unequivocally confirmed its structure assignment. In support of the above mechanistic suggestion, a control experiment showed that when β-keto sulfone **6** was heated for short periods of time in toluene with pyrrolidine, amide **9** was formed in 98% yield. We also found that heating Michael adduct **7** with a trace of *p*-TsOH in toluene furnished the Robinson annulated enone **8** in 49% yield. Further heating of **8** with pyrrolidine in the presence of a trace amount of acid gave fluorenyl pyrrolidine **10** in 95% yield. More than likely this reaction proceeds by formation of a transient enamine, which then undergoes loss of phenyl sulfenic acid to afford the aromatic pyrrolidine **10**.

The generality of the benzannulation reaction was further investigated using several different β-ketone sulfones. We next observed that 2-(phenylsulfonyl)-3,4-dihydronaphthalene-1(2*H*)-one (**11**) smoothly underwent 1,4-conjugate addition with MVK to give the corresponding Michael adduct **12** in 84% yield. Further reaction of **12** with pyrrolidine or morpholine furnished the corresponding aromatic amines **13** and **14** in 40−60% yield. With this system the byproduct that was also formed corresponded to β-keto sulfone **11**, and we believe that it is derived by a competitive retro-Michael reaction from dione **12** (Scheme 3).

We then turned our attention to the simpler β-keto sulfonyl cyclohexanone system **15**. The reaction of **15** with MVK using NaOMe as the base in methanol gave rise to the domino Michael-aldol reaction product **16**. Only a single diastereomer was obtained and from related results in the literature was assigned as the *cis*-stereoisomer.[24] On the other hand, when the reaction of **15** was carried out with MVK using the weaker NEt_3 as the base in CH_2Cl_2, only the Michael addition product **17** was obtained in 94% yield. Treatment of **17** with NaOMe in MeOH afforded the internal aldol product **16** in 75% yield. Heating a sample of **16** (or **17**) with either a primary or secondary amine in toluene furnished the aromatic tetrahydronaphthalene derivatives **18**−**22** in high yield. The entire reaction sequence proceeded rapidly, affording the aromatized system directly without isolation or detection of any reaction intermediates. A related aromatization reaction also occurred upon heating **16** (or **17**) with benzyl alcohol, methanol, or thiophenol, producing the aromatized compounds **23**−**25** in comparable yield (Scheme 4).

SCHEME 4

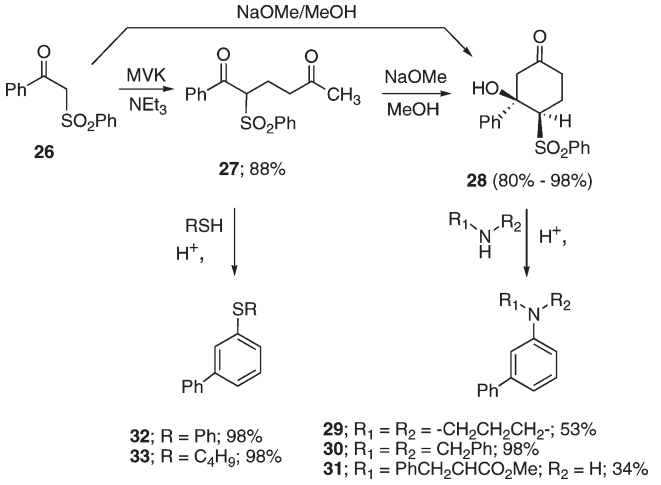


18; $R_1 = R_2 = -CH_2CH_2CH_2-$; 80%
19; $R_1 = CH_2Ph$; $R_2 = H$; 74%
20; $R_1 = R_2 = CH_2Ph$; 89%
21; $R_1 = Ph$; $R_2 = H$; 30%
22; $R_1 = PhCH_2CHCO_2Me$; $R_2 = H$; 70%
23; X = O; R = CH_2Ph; 72%
24; X = O; R = CH_3; 35%
25; X = S; R = Ph; 98%

The Michael-aldol reaction also proceeded well with acyclic β-keto sulfones such as 2-(phenylsulfonyl)acetophenone (**26**). As indicated by the results described in Scheme 5, the Michael reaction of **26** with MVK occurred smoothly in CH_2Cl_2 with NEt_3 as the base, affording dione **27** in 88% yield. Further treatment of **27** with NaOMe in MeOH gave the cyclized aldol product **28** as a single diastereomer in 98% yield. The same product was also obtained from the reaction of **26** with MVK in MeOH with NaOMe as the base in 80% yield. The intramolecular aldol reaction product **28** has the large substituent groups in the equatorial position, thereby resulting in the most stable diastereomer. Condensation of pyrrolidine with either **27** or **28** followed by loss of water and phenylsulfenic acid provided the aromatic substituted amine **29** (Scheme 5). The generality of this aromatic annulation protocol was further studied using several secondary amines as well as thiols. The isolated yields of the aromatized products are based on the starting ketone and ranged from 34% to 98%.

(24) The domino Michael-aldol reaction encountered with this system is related to the well-known proline-catalyzed Robinson annulation; see: (a) Eder, U.; Sauer, G.; Wiechert, R. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 496. (b) Hajos, Z. G.; Parrish, D. R. *J. Org. Chem.* **1974**, *39*, 1615. (c) Arai, T.; Sasai, H.; Aoe, K.-I.; Okamura, K.; Date, T.; Shibasaki, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 104. (d) Bui, T.; Barbas, C. F. III *Tetrahedron Lett.* **2000**, *41*, 6951. (e) Dieckmann, W.; von Fischer, K. *Ber. Dtsch. Chem. Ges.* **1911**, *44*, 966. (f) Christoffers, J. *J. Chem. Soc. Perkin Trans. 1* **1997**, 3141. (g) Tanaka, F.; Thayumanavan, R.; Barbas, C. F. III *J. Am. Chem. Soc.* **2003**, *125*, 8523.

SCHEME 5



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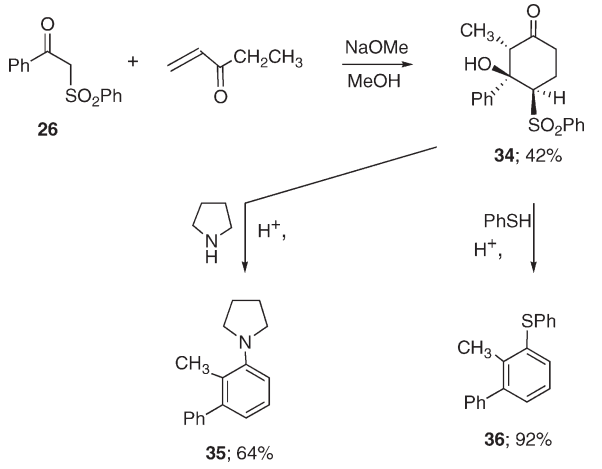
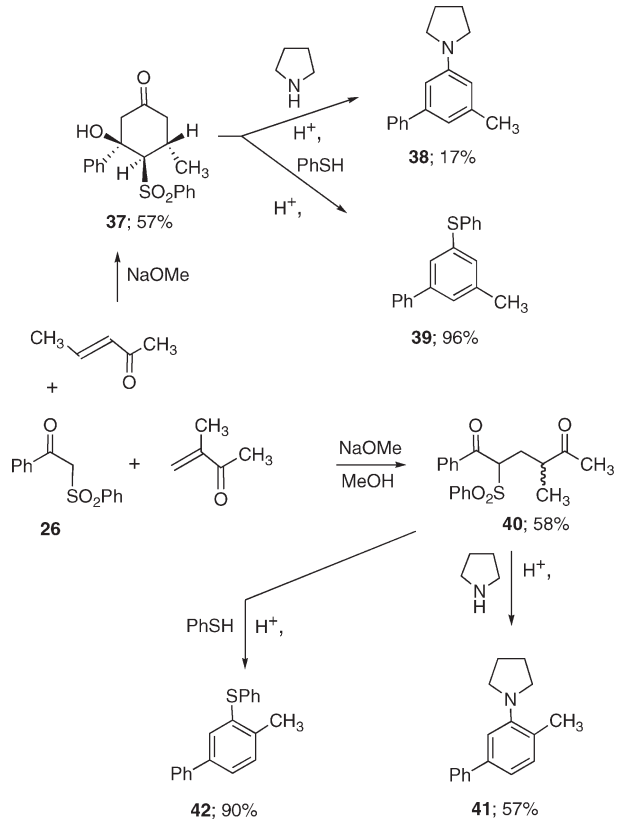


Continuing with our systematic analysis of the structure–reactivity relationship of the method, we next investigated the reaction of β-keto sulfone **26** with ethyl vinyl ketone. As before, this reaction occurred in the presence of NaOMe, producing the Michael-aldol product **34** in 42% yield as a single diastereomer together with the expected Michael adduct formed in 28% yield. We assume that the stereochemistry of **34** has all the large substituent groups in the equatorial position as is typically found with related systems.[25] Thermolysis of **34** with pyrrolidine gave aryl amine **35** in 64% yield, whereas heating **34** with thiophenol afforded the aromatized sulfide **36** in 92% yield (Scheme 6).

Condensation of β-keto sulfone **26** with other α,β-unsaturated carbonyl compounds provides a convenient method for accessing a variety of trisubstituted aryl amines. Several different enones varying in structure were used to generate the corresponding aromatic derivatives. For example, we observed that **26** smoothly underwent the Michael-aldol reaction with 3-penten-2-one to give the expected cyclized product **37** as a single diastereomer. As was the case with the earlier systems, the stereochemistry of **37** is assumed to have

SCHEME 7



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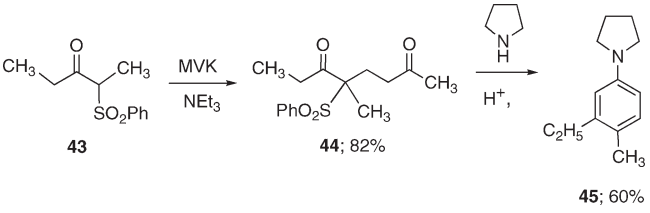

all of the large substituents located in the equatorial position. Heating **37** with either pyrrolidine or thiophenol produced the 1,3,5-trisubstituted aromatized amine **38** and the related sulfide **39**. Attempts to improve the yield of **38** were unsuccessful. Higher temperatures and longer reaction times did not upgrade the yield, nor did the use of an excess amount of pyrrolidine. Interestingly, we observed only the formation of the Michael addition product **40** as a 1:1 mixture of diastereomers when **26** was allowed to react with 3-methylbut-3-en-2-one using NaOMe as the base. Heating **40** with pyrrolidine in the presence of catalytic *p*-TsOH gave the 1,2,5-trisubstituted aryl amine **41** in 57% yield. Similarly, thermolysis of **40** with thiophenol afforded the related aromatic sulfide **42** in 90% yield (Scheme 7).

When an aliphatic β-keto sulfone such as 2-(phenylsulfonyl)-pentan-3-one (**43**) was used, the corresponding Michael addition product **44** was obtained as the exclusive product upon treatment of β-keto sulfone **43** with MVK and NEt_3. The resulting dione **44** was then converted into the corresponding 1,4,5-trisubstituted aryl amine **45** in 60% yield by heating with pyrrolidine in the presence of a trace of *p*-TsOH (Scheme 8).

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In conclusion, we have found a useful benzoannulation method that affords variously substituted aryl amines and sulfides. The key steps consist of a Michael-aldol reaction of β-keto sulfones with enones followed by a subsequent condensation of the initial adduct with an amine or thiol. The Michael-aldol cascade proceeds with a number of β-keto sulfones and enones, affording adducts as single diastereomers. This remarkably simple and environmentally benign method offers a practical route to substitued aryl amines and sulfides.

Experimental Section

2-(3-Oxobutyl)-2-(phenylsulfonyl)-2,3-dihydro-1*H*-inden-1-one (7). A sample of 2-(phenylsulfonyl)-2,3-dihydro-1*H*-inden-1-one (**6**)[23] (1.19 g, 4.4 mmol) was dissolved in 30 mL of CH_2Cl_2 and was treated with NEt_3 (0.67 mL, 4.8 mmol). After 20 min of stirring at room temperature, methyl vinyl ketone (0.39 mL, 4.8 mmol) was added to the solution. Stirring was continued for 14 h, and the mixture was quenched with a saturated aqueous NH_4Cl solution. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to furnish 1.49 g (94%) of the titled compound **7** as a white solid: mp 143−145 °C; IR (thin film) 3064, 2934, 1720, 1607, 1589 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.05 (s, 3H), 2.27−2.47 (m, 1H), 3.20 (d, 1H, J = 18.4 Hz), 4.05 (d, 1H, J = 18.4 Hz), 7.38 (t, 1H, J = 8.0 Hz), 7.45−7.53 (m, 3H), 7.60−7.64 (m, 2H), 7.70 (d, 1H, J = 8.0 Hz), and 7.82 (dd, 2H, J = 8.0 and 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.1, 30.2, 33.7, 37.8, 75.0, 125.0, 126.3, 128.5, 128.9, 130.9, 134.5, 135.0, 136.0, 136.3, 151.7, 198.4, and 206.2.

9*a*-(Phenylsulfonyl)-9,9*a*-dihydro-1*H*-fluoren-3(2*H*)-one (8). A solution containing sulfone **7** (1.03 g, 3.0 mmol) in toluene (20 mL) was treated with a catalytic amount of *p*-TsOH and was heated at reflux for 24 h. After cooling to room temperature, the reaction mixture was concentrated under reduced pressure, and the residue was purified by silica gel chromatography to furnish 0.48 g (49%) of the titled compound **8** as a yellow solid: mp 138−139 °C; IR (thin film) 3064, 2924, 1660, 1632, 1604, and 1141 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.31−2.41 (m, 1H), 2.51−2.58 (m, 1H), 3.04 (d, 1H, J = 18 Hz), 3.22−3.29 (m, 2H), 3.62 (d, 1H, J = 18 Hz), 6.58 (s, 1H), 6.83−6.86 (m, 1H), 7.10−7.13 (m, 2H), 7.19−7.23 (m, 2H), 7.34−7.41 (m, 2H), and 7.59 (dd, 2H, J = 8.0 and 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.8, 34.0, 41.8, 72.9, 122.5, 122.8, 124.9, 128.0, 128.5, 130.0, 132.0, 134.0, 135.7, 138.0, 144.4, 157.8, and 197.7. HRMS calcd for $[(C_{19}H_{16}O_3S) + H]^+$: 325.0898. Found: 325.0894.

1-(9*H*-Fluoren-3-yl)pyrrolidine (10). A solution containing 0.05 g (0.18 mmol) of 2-(phenylsulfonyl)-2,3-dihydro-1*H*-inden-1-one (**6**) in toluene (2 mL), pyrrolidine (0.046 mL, 0.54 mmol), and methyl vinyl ketone (0.046 mL, 0.54 mmol) was treated with a catalytic amount of *p*-TsOH. The reaction mixture was heated at reflux for 7 h and then cooled to room temperature. The solution was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 11 mg (26%) of the titled compound **10** as a clear oil: IR (thin film) 3049, 3016, 2964, 1619, and 1567 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.04−2.08 (m, 4H), 3.37−3.41 (m, 4H), 3.82 (s, 2H), 6.59 (dd, 1H, J = 11.2 and 3.2 Hz), 7.00 (d, 1H, J = 3.2 Hz), 7.26−7.32 (m, 1H), 7.35−7.41 (m, 2H), 7.53 (d, 1H, J = 9.6 Hz), and 7.77 (d, 1H, J = 9.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.7, 36.2, 48.3, 102.9, 111.4, 119.8, 125.1, 125.5, 126.5, 126.6, 130.5, 1422.5, 142.7, 144.7, and 147.8. HRMS calcd for $[(C_{17}H_{17}N) + H]^+$: 236.1439. Found: 236.1432.

A solution of ketosulfone **7** (0.1 g, 0.29 mmol) in toluene (3 mL) was also treated with a catalytic amount of *p*-TsOH and pyrrolidine (0.097 mL 1.17 mmol). The reaction mixture was heated at reflux for 1 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 29 mg (42%) of **10** together with 43 mg (43%) of (2-(2-phenylsulfonyl)ethyl)phenyl)-(pyrrolidin-1-yl)methanone (**9**): mp 127−128 °C; IR (thin film) 3059, 2970, 1625, and 1448 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.76−1.90 (m, 4H), 2.95 (t, 2H, J = 8.4 Hz), 3.05 (t, 2H, J = 6.8 Hz), 3.42−3.47 (m, 4H), 7.12−7.28 (m, 4H), 7.53−7.63 (m, 2H), and 7.91−7.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 26.2, 27.0, 45.5, 48.8, 57.2, 126.3, 127.4, 128.3, 129.4, 129.6, 130.1, 133.8, 134.0, 138.0, 139.1, and 169.0.

2-(3-Oxobutyl)-2-(phenylsulfonyl)-3,4-dihydronaphthalen-1(2*H*)-one (12). A sample of 2-(phenylsulfonyl)-3,4-dihydronaphthalen-1(2*H*)-one[23] (**11**) (0.6 g, 2.1 mmol) was dissolved in 15 mL of CH_2Cl_2 and was treated with NEt_3 (0.32 mL, 2.3 mmol). After 20 min of stirring at room temperature, methyl vinyl ketone (0.19 mL, 2.3 mmol) was added to the mixture. Stirring was continued for 2 days, and then an additional quantity of NEt_3 (0.1 mL, 0.8 mmol) and methyl vinyl ketone (0.4 mL, 4.6 mmol) was added to the mixture. After stirring for another 2 days, the mixture was quenched with a saturated aqueous NH_4Cl solution. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to furnish 0.62 g (84%) of the titled compound **12** as a yellow solid: mp 100−102 °C; IR (thin film) 3066, 2936, 1716, 1675, and 1600 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.05−2.22 (m, 5H), 2.34−2.50 (m, 3H), 2.84 (dt, 1H, J = 14.8 and 4.8 Hz), 2.98 (dt, 1H, J = 16.8 and 4.8 Hz), 3.58−3.67 (m, 1H), 7.25 (d, 1H, J = 7.6 Hz), 7.32 (t, 1H, J = 7.6 Hz), 7.49−55 (m, 3H), 7.65 (t, 1H, J = 7.6 Hz), 7.78−7.81 (m, 2H), and 8.01 (d, 1H, J = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.9, 27.1, 27.6, 30.1, 38.1, 72.8, 127.2, 128.3, 128.9, 129.1, 130.9, 132.1, 134.4, 134.6, 136.3, 143.8, 192.0, and 206.6. HRMS calcd for $[(C_{20}H_{20}O_4S) + H]^+$: 357.1161. Found: 357.1156.

1-(9,10-Dihydrophenanthren-3-yl)pyrrolidine (13). A solution containing 76 mg (0.21 mmol) of ketosulfone **12** in toluene (2 mL) and pyrrolidine (0.09 mL, 1.1 mmol) was treated with a catalytic amount of *p*-TsOH. The reaction mixture was heated at reflux for 3 h and was then cooled to room temperature. The solution was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 17 mg (39%) of **13** as clear oil: IR (thin film) 3057, 3021, 2964, 1615, and 1561 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.02−2.05 (m, 4H), 2.76−2.87 (m, 4H), 3.34−3.38 (m, 4H), 6.52 (dd, 1H, J = 8.4 and 2.4 Hz), 7.10 (d, 1H, 2.4 Hz), 7.19−7.25 (m, 2H), 7.30 (dt, 1H, J = 6.0 and 2.4 Hz), and 7.77 (d, 1H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.7, 28.2, 29.9, 48.1, 107.2, 111.3, 123.8, 124.9, 126.8, 127.2, 128.3, 128.3, 135.0, 135.4, 138.2, and 147.5. HRMS calcd for $[(C_{18}H_{19}N) + H]^+$: 250.1596. Found: 250.1589.

4-(9,10-Dihydrophenanthren-3-yl)morpholine (14). A solution containing 0.05 g (0.13 mmol) of ketosulfone **12** in toluene (1 mL) and morpholine (0.6 mL, 0.068 mmol) was treated with a catalytic amount of *p*-TsOH. The reaction mixture was heated at reflux for 2 h and then cooled to room temperature. The solution was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 20 mg (56%) of the titled compound **14** as a colorless oil: IR (thin film) 3058, 3031, 2957, 1611, and 1562 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.78−2.88 (m, 4H), 3,21 (t, 4H, J = 4.8 Hz), 3.91 (t, 4H, J = 4.8 Hz), 6.84 (dd, 1H, J = 8.4 and 2.4 Hz), 7.16 (d, 1H, J = 8.4 Hz), 7.23−7.26 (m, 2H), 7.29−7.34 (m, 2H), and 7.74 (d, 1H, J = 7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 29.6, 50.2, 67.2, 111.8, 115.6, 123.7, 127.0, 127.5, 128.4, 128.9, 129.8, 13.9, 135.2, 137.9, and 150.8. HRMS calcd for $[(C_{18}H_{19}NO) + H]^+$: 266.1545. Found: 266.1541.

8*a*-Hydroxy-4*a*-(phenylsulfonyl)octahydronaphthalen-2(1*H*)-one (16). A sample of 2-(phenylsulfonyl)cyclohexanone (**15**)[23] (0.25 g, 1.0 mmol) was dissolved in 4 mL of MeOH and 8 mL of benzene and was treated with NaOMe (72 mg, 1.3 mmol). After 20 min of stirring at room temperature, methyl vinyl ketone (0.12 mL, 1.5 mmol) was added to the reaction mixture. Stirring was continued for 1 h, and then the solvent was removed under reduced pressure. The residue was dissolved in EtOAc and washed with a saturated aqueous NH_4Cl solution. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to provide 0.21 g (65%) of the titled compound **16** as a white solid: mp 144−146 °C; IR (thin film) 3481, 3066, 2933, 1715, and 1446 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.13−1.39 (m, 4H), 1.51−1.75 (m, 3H), 1.92−1.99 (m, 1H), 2.03−2.13 (m, 1H), 2.20−2.32 (m, 2H), 2.40 (dd, 1H, J = 14.4 and 1.6 Hz), 3.10−3.19 (m, 1H), 3.65 (d, 1H, J = 14.4 Hz), 4.18 (d, 1H, J = 1.2 Hz), 7.48−7.52 (m, 2H), and 7.82 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 20.7, 25.5, 28.9, 37.0, 37.4, 54.4, 68.7, 74.9, 129.0, 130.5, 134.3, 136.2, and 208.3. HRMS calcd for $[(C_{16}H_{20}O_4S) + H - H_2O)]^+$: 291.1055. Found: 291.1053.

2-(3-Oxobutyl)-2-(phenylsulfonyl)cyclohexanone (17). A sample of 2-(phenylsulfonyl)cyclohexanone (**15**) (0.5 g, 2.1 mmol) was dissolved in 15 mL of CH_2Cl_2 and was treated with NEt_3 (0.32 mL, 2.3 mmol). After 20 min of stirring at room temperature, methyl vinyl ketone (0.19 mL, 2.3 mmol) was added to the mixture. Stirring was continued for 2 days, and then an additional amount of NEt_3 (0.1 mL, 0.8 mmol) and methyl vinyl ketone (0.4 mL, 4.6 mmol) was added to the mixture. After stirring for an additional 2 days, the reaction mixture was quenched with a saturated aqueous NH_4Cl solution. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to furnish 0.61 g (94%) of the titled compound **17** as a colorless oil: IR (thin film) 3065, 2948, 1712, 1584, and 1446 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.65−1.90 (m, 4H), 1.98−2.03 (m, 5H), 2.24−2.54 (m, 4H), 2.62−2.69 (m, 1H), 2.91−2.99 (m, 1H), 7.51 (t, 1H, J = 8.0 Hz), 7.62−7.66 (m, 1H), and 7.72 (dd, 1H, J = 8.0 and 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 25.4, 26.7, 30.1, 30.8, 38.0, 41.5, 129.0, 130.4, 134.4, 135.4, 205.3, and 206.8.

Treatment of a sample of **17** with NaOMe in a benzene/methanol mixture at 25 °C for 1 h afforded 8*a*-hydroxy-4*a*-(phenylsulfonyl)octahydronaphthalen-2(1*H*)-one (**16**) in 75% yield.

1-(5,6,7,8-Tetrahydronaphthalen-2-yl)pyrrolidine (18). A 54 mg (0.17 mmol) sample of ketosulfone **17** (or the cyclized cyclohexanone derivative **16**) in toluene (2 mL) was treated with a catalytic amount of *p*-TsOH and pyrrolidine (0.03 mL, 0.35 mmol). The reaction mixture was heated at reflux for 1 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 27 mg (80%) of the titled compound **18** as a colorless oil: IR (thin film) 3051, 2925, 1616, ad 1513 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.76−1.79 (m, 4H), 1.97−2.00 (m, 4H), 2.65−2.79 (m, 4H), 3.23−3.27 (m, 4H), 6.30 (d, 1H, J = 2.8 Hz), 6.41 (dd, 1H, J = 8.0 and 2.8 Hz), and 6.94 (d, 1H, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.7, 24.0, 25.6, 28.6, 30.1, 48.0, 110.2, 112.0, 124.4, 129.9, 137.8, and 146.4. HRMS calcd for $[(C_{14}H_{19}N) + H]^+$: 202.1596. Found: 202.1588.

***N*-Benzyl-5,6,7,8-tetrahydronaphthalen-2-amine (19).** A 45 mg (0.13 mmol) sample of ketosulfone **17** (or the cyclized cyclohexanone derivative **16**) and benzylamine (0.03 mL, 0.29 mmol) in toluene (1.5 mL) was treated with a catalytic amount of *p*-TsOH. The reaction mixture was heated at reflux for 20 min and then was cooled to room temperature. The solution was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 28 mg (74%) of the titled compound **19** as a colorless oil: IR (thin film) 3411, 3027, 2925, 1615, and 1509 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.77−1.80 (m, 4H), 2.67−2.74 (m, 4H), 3.85 (brs, 1H), 4.32 s, 2H), 6.40 (d, 1H, J = 2.4 Hz), 6.47 (dd, 1H, J = 8.4 and 2.4 Hz), 6.92 (d, 1H, J = 8.4 Hz), and 7.27−7.42 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.6, 23.8, 28.7, 29.9, 48.8, 111.3, 113.1, 126.6, 127.3, 127.7, 128.8, 130.0, 138.0, 140.0, and 146.2.

***N*,*N*-Dibenzyl-5,6,7,8-tetrahydronaphthalen-2-amine (20).** A 40 mg (0.13 mmol) sample of ketosulfone **17** (or the cyclized cyclohexanone derivative **16**) and dibenzylamine (0.05 mL, 0.26 mmol) in toluene (1.5 mL) was treated with a catalytic amount of *p*-TsOH. The reaction mixture was heated at reflux for 3 h and then was cooled to room temperature. The solution was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 38 mg (89%) of the titled compound **20** as a colorless oil: IR (thin film) 3061, 3026, 2925, 1613, and 1510 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.73−1.80 (m, 4H), 2.25−2.71 (m, 4H), 4.64 (s, 4H), 6.52 (d, 1H, J = 2.8 Hz), 6.57 (dd, 1H, J = 8.4 and 2.8 Hz), 6.91 (d, 1H, J = 8.4 Hz), and 7.24−7.37 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.6, 23.8, 28.6, 30.1, 54.2, 110.8, 112.7, 125.7, 126.9, 128.8, 130.0, 138.0, 139.2, and 147.5.

***N*-Phenyl-5,6,7,8-tetrahydronaphthalen-2-amine (21).** A solution containing 47 mg (0.15 mmol) of ketosulfone **17** (or the cyclized cyclohexanone derivative **16**) in toluene (1.5 mL) and aniline (0.022 mL, 0.23 mmol) was treated with a catalytic amount of *p*-TsOH. The reaction mixture was heated at reflux for 4 h and then was cooled to room temperature. The solution was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 10 mg (30%) of the titled compound **21** as a colorless oil: IR (thin film) 3393, 3051, 3030, 2926, 1598, and 1497 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.76−1.81 (m, 4H), 2.70−2.77 (m, 4H), 6.82−6.91 (m, 3H), 6.98−7.05 (m, 3H), and 7.23−7.27 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.4, 23.6, 28.9, 29.8, 116.7, 117.1, 119.2, 120.4, 129.5, 130.0, 130.6, 138.3, and 140.4.

(*S*)-Methyl 2-(5,6,7,8-tetrahydronaphthalen-2-ylamino)-3-phenylpropanoate (22). A 32 mg (0.10 mmol) sample of ketosulfone **17** (or the cyclized cyclohexanone derivative **16**), NEt_3 (0.018 mL, 0.135 mmol), and L-phenylalanine methyl ester hydrochloride (29 mg, 0.14 mmol) in toluene (1 mL) was treated with a catalytic amount of *p*-TsOH. The reaction mixture was heated at reflux for 4 h and then was cooled to room temperature. The solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 23 mg (70%) of the titled compound **22** as a colorless oil: IR (thin film) 3391, 3027, 2926, 1739, 1616, 1509 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.73−1.77 (m, 4H), 2.65−2.68 (m, 4H), 3.06−3.17 (m, 2H), 3.66 (s, 3H), 4.00 (brs, 1H), 3.66 (s, 3H), 4.33 (t, 1H), 6.33 (d, 1H, J = 2.4 Hz), 6.40 (dd, 1H, J = 2.4, 8.0 Hz), 6.89 (d, 1H, J = 8.0 Hz), 7.17−7.32 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.5, 23.7, 28.7, 29.8, 39.0, 52.2, 58.2, 111.9, 114.0, 127.1, 127.5, 128.7, 129.4, 130.1, 136.7, 138.1, 144.3, 174.1.

6-(Benzyloxy)-1,2,3,4-tetrahydronaphthalene (23). A 55 mg (0.18 mmol) sample of ketosulfone **17** (or the cyclized cyclohexanone derivative **16**) and benzyl alcohol (0.04 mL, 0.36 mmol) in toluene (2 mL) was treated with a catalytic amount of *p*-TsOH. The reaction mixture was heated at reflux for 3 h and then was cooled to room temperature. The solution was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 38 mg (72%) of the titled compound **23**: IR (thin film) 3063, 3031, 2927, 1610, and 1501 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.78−1.82 (m, 4H), 2.70−80 (m, 4H), 5.05 (s, 2H), 6.73 (d, 1H, J = 2.8 Hz), 6.77 (dd, 1H, J = 8.4 and 2.8 Hz), 7.00 (d, 1H, J = 8.4 Hz), and 7.32−7.47 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.4, 23.6, 28.8, 29.9,

70.2, 112.7, 115.0, 127.7, 128.0, 128.7, 129.8, 130.1, 137.6, 138.4, and 156.8. HRMS calcd for $[(C_{17}H_{18}O) + H]^+$: 239.1436. Found: 239.1432.

6-Methoxy-1,2,3,4-tetrahydronaphthalene (24). A solution containing 47 mg (0.15 mmol) of ketosulfone **17** (or the cyclized cyclohexanone derivative **16**) in toluene (1.5 mL) and methanol (1.0 mL) was treated with a catalytic amount of *p*-TsOH. The reaction mixture was heated at reflux for 1 h and then was cooled to room temperature. The solution was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 9 mg (35%) of the titled compound **24** as a colorless oil: IR (thin film) 3059, 2927, 1610, 1501, and 1253 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.76−1.80 (m, 4H), 2.68−2.78 (m, 4H), 3.75 (s, 3H), 6.61 (d, 1H, $J = 2.8$ Hz), 6.68 (dd, 1H, $J = 8.4$ and 2.8 Hz), and 6.98 (d, 1H, $J = 8.4$ Hz).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.3, 23.6, 28.7, 29.9, 55.4, 111.9, 113.8, 129.4, 130.1, 138.3, and 157.5.

Phenyl-(5,6,7,8-tetrahydronaphthalen-2-yl)sulfane (25). A solution containing 24 mg (0.1 mmol) of **17** (or the cyclized cyclohexanone derivative **16**) in toluene (1 mL) and thiophenol (0.1 mL, 1 mmol) was treated with a catalytic amount of *p*-TsOH. The reaction mixture was heated at reflux for 2 h and then was cooled to room temperature. The solution was concentrated under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 18 mg (98%) of the titled compound **25** as a colorless oil: IR (thin film) 3058, 3008, 2928, 1582, and 1477 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.77−1.80 (m, 4H), 2.70−2.77 (m, 4H), 7.02 (d, 1H, $J = 8.0$ Hz), and 7.11−7.14 (m, 2H), 7.16−7.20 (m, 1H), and 7.24−7.29 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.1, 23.2, 29.3, 29.4, 126.4, 129.2, 129.7, 129.8, 130.3, 131.0, 133.2, 137.2, 137.5, and 138.5.

1-Phenyl-2-(phenylsulfonyl)hexane-1,5-dione (27). A sample of 2-(phenylsulfonyl)acetophenone (**26**)[23] (0.5 g, 1.9 mmol) was dissolved in 15 mL of CH_2Cl_2 and was treated with NEt_3 (0.32 mL, 2.3 mmol). After 20 min of stirring at room temperature, methyl vinyl ketone (0.21 mL, 2.5 mmol) was added to the reaction mixture. Stirring was continued for 4 days, and the mixture was quenched with a saturated aqueous NH_4Cl solution. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to furnish 0.56 g (88%) of the titled compound **27** as a white solid: mp 105−106 °C; IR (thin film) 3065, 2934, 1714, 1679, and 1596 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.08 (s, 3H), 2.22−2.32 (m, 1H), 2.35−2.48 (m, 2H), 2.65−2.73 (m, 1H), 5.35−5.38 (m, 1H), 7.45−7.53 (m, 4H), 7.59−7.66 (m, 2H), 7.80 (dd, 2H, $J = 8.4$ and 1.2 Hz), 7.94 (dd, 2H, $J = 8.4$ and 1.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.3, 30.1, 39.6, 68.3, 129.0, 129.2, 129.8, 134.4, 134.5, 136.7, 136.9, 192.6, and 207.4.

3-Hydroxy-3-phenyl-4-(phenylsulfonyl)cyclohexanone (28). A sample of 2-(phenylsulfonyl)acetophenone (**26**) (0.5 g, 1.9 mmol) was dissolved in 3 mL of MeOH and 12 mL of benzene and was treated with NaOMe (0.12 g, 2.1 mmol). After 20 min of stirring at room temperature, methyl vinyl ketone (0.2 mL, 2.5 mmol) was added to the reaction mixture. Stirring was continued for 16 h, and the solvent was removed under reduced pressure. The residue was dissolved in EtOAc and was washed with a saturated aqueous NH_4Cl solution. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to provide 0.51 g (80%) of the titled compound **28** as a white solid: mp 176−178 °C; IR (thin film) 3466, 3053, 2958, 1715, and 1445 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.49−2.77 (m, 6H), 4.12 (dd, 1H, $J = 10.4$ and 2.8 Hz), 4.64 (d, 1H, $J = 2.8$ Hz), 6.99−7.12 (m, 5H), 7.19−7.28 (m, 4H), and 7.40−7.44 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.8, 39.4, 55.6, 67.0, 125.0, 127.6, 127.8, 128.4, 129.1, 133.2, 140.0, 142.1, and 205.6. HRMS calcd for $[(C_{18}H_{18}O_4S) + H]^+$: 331.1004. Found: 331.1003. The same compound **28** was prepared by treating a sample of **27** under the above conditions.

1-(Biphenyl-3-yl)pyrrolidine (29). A solution containing dione **27** (or **28**) (45 mg, 0.13 mmol) in toluene (1.3 mL) was treated with a catalytic amount of *p*-TsOH and pyrrolidine (0.022 mL, 0.27 mmol). The reaction mixture was heated at reflux for 2 h and was cooled to room temperature. The solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 16 mg (53%) of **29** as a colorless oil: IR (thin film) 3055, 3030, 2963, 1597, 1568, 1484 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.02−2.05 (m, 4H), 3.34−3.37 (m, 4H), 6.58 (dd, 1H, $J = 2.4$, 8.4 Hz), 6.77 (s, 1H), 7.29−7.36 (m, 2H), 7.42−7.46 (m, 2H), 7.62−7.63 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.7, 47.9, 110.7, 110.9, 114.8, 127.2, 127.5, 128.7, 129.6, 142.5, and 148.4. HRMS calcd for $[(C_{16}H_{17}N) + H]^+$: 224.1439. Found: 224.1432.

***N,N*-Dibenzylbiphenyl-3-amine (30).** A solution containing dione **27** (or **28**) (35 mg, 0.11 mmol) in toluene (1 mL) was treated with a catalytic amount of *p*-TsOH and dibenzylamine (0.04 mL, 0.21 mmol). The reaction mixture was heated at reflux for 5 h and was cooled to room temperature. The solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 36 mg (98%) of the titled compound **30** as a colorless oil: IR (thin film) 3060, 3028, 2924, 1597, 1569 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.71 (s, 4H), 6.74 (dd, 1H, $J = 2.4$, 8.0 Hz), 6.93−6.98 (m, 2H), 7.22−7.39 (m, 14H), and 7.46−7.48 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 54.4, 111.5, 111.7, 116.2, 126.9, 127.2, 127.3, 127.5, 128.8, 128.9, 129.8, 138.7, 142.2, 142.5, and 149.8.

(*S*)-Methyl-2-(biphenyl-3-ylamino)-3-phenylpropanoate (31). A solution containing dione **27** (or **28**) (35 mg, 0.11 mmol) in toluene (1 mL) was treated with a catalytic amount of *p*-TsOH, NEt_3 (0.019 mL, 0.138 mmol) and L-phenylalanine methyl ester hydrochloride (30 mg, 0.14 mmol). The mixture was heated at reflux for 7 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 12 mg (34%) of the titled compound **31** as a colorless oil: IR (thin film) 3396, 3028, 2924, 1738, 1604, 1567 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.11−3.23 (m, 2H), 3.69 (s, 3H), 4.27 (brs, 1H), 4.44 (t, 1H, $J = 6.0$ Hz), 6.60 (dd, 1H, $J = 8.4$ and 2.4 Hz), 6.81 (s, 1H), 6.98 (d, 1H, $J = 8.0$ Hz), 7.18−7.35 (m, 7H), 7.42 (t, 2H, $J = 8.0$ Hz), and 7.54 (d, 2H, $J = 8.4$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.9, 38.9, 52.4, 59.0, 112.6, 117.8, 127.2, 127.3, 127.4, 128.8, 128.8, 129.5, 129.5, 129.9, 136.4, 141.6, 142.7, 146.9, and 173.8.

Biphenyl-3-yl(phenyl)sulfane (32). A solution containing dione **27** (or **28**) (40 mg, 0.12 mmol) in toluene (1.2 mL) was treated with a catalytic amount of *p*-TsOH and thiophenol (0.12 mL, 1.2 mmol). The reaction mixture was heated at reflux for 5 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 32 mg (98%) of the titled compound **32** as a colorless oil: IR (thin film) 3057, 2924, 1586, 1562, 1466 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26−7.29 (m,1H), 7.31−7.50 (m, 10H), 7.54−7.58 (m, 2H), and 7.62 (t, 1H, $J = 1.6$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 126.1, 127.3, 127.8, 129.0, 129.5, 129.80, 129.83, 129.9, 131.3, 135.8, 136.6, 140.5, and 142.4.

Biphenyl-3-yl(butyl)sulfane (33). A solution containing dione **27** (or **28**) (36 mg, 0.11 mmol) in toluene (1 mL) was treated with a catalytic amount of *p*-TsOH and *n*-butylthiol (0.12 mL, 1.1 mmol). The reaction mixture was heated at reflux for 2 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and resulting residue was purified by silica gel chromatography to provide 26 mg (98%) of the titled compound **33** as a colorless oil: IR (thin film) 3058, 3030, 2957, 1588, 1563, and 1465 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.94

(t, 3H, $J = 7.2$ Hz), 1.49 (sextet, 2H, $J = 7.2$ Hz), 1.68 (p, 2H, $J = 7.2$ Hz), 3.00 (t, 2H, $J = 7.2$ Hz), 7.29−7.41 (m, 4H), 7.43−7.48 (m, 2H), and 7.55−7.60 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.2, 31.4, 33.4, 124.8, 127.3, 127.6, 129.0, 129.3, 137.8, 140.9, and 142.1.

3-Hydroxy-2-methyl-3-phenyl-4-(phenylsulfonyl)cyclohexanone (34). A sample of 2-(phenylsulfonyl)acetophenone (**26**) (0.4 g, 1.5 mmol) dissolved in 2 mL of MeOH and 8 mL of benzene was treated with NaOMe (0.1 g, 1.8 mmol). After 20 min of stirring at room temperature, ethyl vinyl ketone (0.24 mL, 2.3 mmol) was added to the reaction mixture. Stirring was continued for 3 h, and then the solution was concentrated under reduced pressure. The residue was dissolved in EtOAc and washed with a saturated aqueous NH_4Cl solution. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to provide 0.2 g (42%) of the titled compound **34** as white solid: mp 170−172 °C; IR (thin film) 3468, 3069, 2981, 1710, 1638, and 1446 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.61 (d, 3H, $J = 6.8$ Hz), 2.55−2.80 (m, 5H), 4.19 (dd, 1H, $J = 12.4$ and 4.0 Hz), 4.52 (brs, 1H), 6.92−7.16 (m, 4H), 7.18−7.26 (m, 5H), and 7.38−7.43 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.2, 22.1, 39.6, 55.0, 68.4, 80.1, 125.7, 127.5, 127.7, 128.3, 129.0, 133.0, 140.0, 140.8, and 207.1. HRMS calcd for $[(C_{19}H_{20}O_4S) - H_3O]^+$: 327.1055. Found: 327.1051.

In addition to compound **34**, 0.15 g (28%) of 1-phenyl-2-(phenylsulfonyl)-heptane-1,5-dione was obtained as a white solid: mp 120−122 °C; IR (thin film) 3067, 2977, 1713, 1678, and 1596 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.96 (t, 3H, $J = 7.2$ Hz), 2.21−2.42 (m, 5H), 2.59−2.67 (m, 1H), 5.34−5.38 (m, 1H), 7.42−7.50 (m, 4H), 7.56−7.63 (m, 2H), 7.76−7.78 (m, 2H), and 7.90−7.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.8, 22.4, 36.1, 38.2, 68.3, 129.0, 129.1, 129.2, 129.8, 134.41, 134.48, 136.7, 136.9, 192.7, and 210.2. HRMS calcd for $[(C_{19}H_{20}O_4S) + H]^+$: 345.1161. Found: 345.1162.

1-(2-Methylbiphenyl-3-yl)pyrrolidine (35). A solution containing 50 mg (0.145 mmol) of **34** in toluene (1.5 mL) was treated with a catalytic amount of *p*-TsOH and pyrrolidine (0.024 mL, 0.290 mmol). The reaction mixture was subjected to microwave irradiation at 120 °C (150 W) with a maximum internal pressure of 100 psi for 10 min. After the reaction mixture cooled to rt, the solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 22 mg (64%) of the titled compound **35** as a clear oil: IR (thin film) 3056, 3027, 2963, 1600, 1561 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.95−1.98 (m, 4H), 2.38 (s, 2H), 3.24−3.30 (m, 4H), 7.06−7.11 (m, 2H), 7.20 (d, 1H, $J = 8.0$ Hz), 7.29−7.45 (m, 3H), and 7.57−7.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 25.2, 51.2, 114.8, 119.1, 127.0, 127.3, 127.8, 128.8, 132.3, 139.6, 142.0, and 149.8. HRMS calcd for $[(C_{17}H_{19}N) + H]^+$: 238.1596. Found: 238.1591.

(2-Methylbiphenyl-3-yl)(phenyl)sulfane (36). A solution containing 31 mg (0.09 mmol) of **34** in toluene (1 mL) was treated with a catalytic amount of *p*-TsOH and thiophenol (0.09 mL, 0.9 mmol). The mixture was heated at reflux for 2 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 23 mg (92%) of the titled compound **36** as a colorless oil: IR (thin film) 3057, 3027, 2923, 1582, and 1562 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3H), 7.17−7.19 (m, 2H), 7.24−7.28 (m, 2H), 7.30−7.38 (m, 7H), and 7.41−7.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 126.3, 126.9, 127.2, 128.3, 129.4, 130.7, 131.3, 135.6, 135.9, 136.8, 142.0, and 143.5.

3-Hydroxy-5-methyl-3-phenyl-4-(phenylsulfonyl)cyclohexanone (37). A sample of 2-(phenylsulfonyl)acetophenone (**26**) (0.25 g, 0.96 mmol) was dissolved in 1.5 mL of MeOH and 6 mL of benzene and was treated with NaOMe (0.07 g, 1.2 mmol). After 20 min of stirring at room temperature, 3-penten-2-one (0.22 mL, 1.44 mmol) was added to the reaction mixture. Stirring was continued for 2 days, and then the solvent was removed under reduced pressure. The residue was dissolved in EtOAc and washed with a saturated aqueous NH_4Cl solution. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to provide 0.19 g (57%) of the titled compound **37** as a white solid: mp 186−187 °C; IR (thin film) 3346, 3066, 1712, 1445, and 1146 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (d, 3H, ($J = 7.2$ Hz), 2.29−2.36 (m, 1H), 2.45−2.58 (m, 2H), 3.32−3.41 (m, 2H), 3.70 (d, 1H, $J = 6.0$ Hz), 5.02 (d, 1H, $J = 2.8$ Hz), 7.00−7.10 (m, 5H), 7.19−7.26 (m, 4H), and 7.38−7.43 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.5, 27.4, 45.6, 54.0, 73.2, 76.5, 125.1, 127.5, 127.6, 128.4, 129.0, 133.1, 140.4, 142.8, and 207.7.

1-(5-Methylbiphenyl-3-yl)pyrrolidine (38). A solution of the above compound **37** (37 mg, 0.11 mmol) in toluene (1 mL) was treated with a catalytic amount of *p*-TsOH and pyrrolidine (0.018 mL, 0.21 mmol). The reaction mixture was heated at reflux for 4 h and was cooled to room temperature. The solvent was removed under reduced pressure and resulting residue was purified by silica gel chromatography to provide 4.4 mg (17%) of the titled compound **38** as a colorless oil: IR (thin film) 3057, 2959, 2924, 1598, and 1576 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99−2.02 (m, 4H), 2.37 (s, 3H), 3.32−3.35 (m, 4H), 6.40 (s, 1H), 6.57 (s, 1H), 6.71 (s, 1H), 7.30−7.34 (m, 1H), 7.36−7.43 (m, 2H), and 7.58−7.60 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.6, 29.9, 47.9, 108.1, 111.6, 115.9, 127.1, 127.5, 128.7, 139.3, 142.5, 142.6, and 148.5. HRMS calcd for [(C17H19N) + H]$^+$: 238.1596. Found: 238.1591.

(5-Methylbiphenyl-3-yl)(phenyl)sulfane (39). A solution containing **37** (30 mg, 0.087 mmol) in toluene (1 mL) was treated with a catalytic amount of *p*-TsOH and thiophenol (0.089 mL, 0.89 mmol). The reaction mixture was heated at reflux for 2 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 23 mg (96%) of the titled compound **39** as a colorless oil: IR (thin film) 3058, 3035, 2922, 1570, and 1477 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 7.16−7.19 (m, 1H), 7.23−7.27 (m, 1H), 7.30−7.42 (m, 9H), and 7.52−7.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 127.2, 127.3, 127.7 128.9, 129.4, 130.8, 131.0, 136.0, 136.1, 139.6, 140.7, and 142.4.

4-Methyl-1-phenyl-2-(phenylsulfonyl)hexane-1,5-dione (40). A sample of 2-(phenylsulfonyl)acetophenone (**26**) (0.3 g, 1.15 mmol) was dissolved in 1.5 mL of MeOH and 6 mL of benzene and was treated with NaOMe (0.08 g, 1.38 mmol). After 20 min of stirring at room temperature, 3-methylbut-3-en-2-one (0.15 g, 1.4 mmol) was added to the reaction mixture. Stirring was continued for 2 days, and the solvent was removed under reduced pressure. The residue was dissolved in EtOAc and washed with a saturated aqueous NH_4Cl solution. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to provide 0.23 g (58%) of a 1:1 mixture of diastereomers of dione **40** as a clear oil: IR (thin film) 3064, 2970, 2964, 1619, and 1567 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (d, 3H, $J = 6.8$ Hz), 1.11 (d, 3H, $J = 7.2$ Hz), 1.94 (s, 3H), 2.13−2.20 (m, 5H), 2.27−2.44 (m, 3H), 2.85−2.94 (m, 1H), 5.20 (t, 1H, $J = 7.2$ Hz), 5.26−5.29 (m, 1H), 7.41−7.63 (m, 12H), 7.73−7.79 (m, 4H), 7.84−7.93 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.0, 17.9, 28.1, 28.6, 29.9, 30.3, 30.5, 44.0, 44.2, 67.5, 67.7, 128.8, 129.0, 129.5, 129.7, 129.8, 134.3, 134.42, 134.48, 136.5, 136.8, 136.9, 137.1, 192.5, 192.6, 211.2, and 211.4.

1-(4-Methylbiphenyl-3-yl)pyrrolidine (41). A solution of dione **40** (60 mg, 0.17 mmol) in toluene (2 mL) was treated with a catalytic amount of *p*-TsOH and pyrrolidine (0.029 mL,

0.34 mmol). The reaction mixture was heated at reflux for 15 h and was cooled to room temperature. The solvent was removed under reduced pressure, and resulting residue was purified by silica gel chromatography to provide 23 mg (57%) of the titled compound **41** as a colorless oil: IR (thin film) 3057, 3028, 2963, 1600, 1561, and 1484 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.95−1.99 (m, 4H), 2.39 (s, 3H), 3.25−3.30 (m, 4H), 7.08 (dd, 1H, $J = 8.0$ and 1.6 Hz), 7.11 (d, 1H, $J = 1.6$ Hz), 7.20 (d, $J = 8.0$ Hz), 7.31−7.36 (m, 1H), 7.41−7.45 (m, 2H), 7.59−7.62 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 25.2, 51.2, 114.8, 119.1, 127.0, 127.3, 127.8, 128.8, 132.3, 139.6, 142.1, 149.8. HRMS calcd for $[(C_{17}H_{19}N) + H]^+$: 238.1596. Found: 238.1592.

(4-Methylbiphenyl-3-yl)(phenyl)sulfane (42). A solution of of dione **40** (58 mg, 0.17 mmol) in toluene (1 mL) was treated with a catalytic amount of *p*-TsOH and thiophenol (0.086 mL, 0.84 mmol). The mixture was heated at reflux for 2 h and was then cooled to room temperature. The reaction solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 41 mg (90%) of the titled compound **42** as a colorless oil: IR (thin film) 3058, 3026, 2920, 1581, and 1553 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.43 (s, 3H), 7.19−7.35 (m, 7H), 7.39−7.43 (m, 2H), 7.48 (dd, 1H, $J =$ 8.0 and 2.0 Hz), 7.51−7.54 (m, 2H), 7.60 (d, 1H, $J = 2.0$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 126.6, 126.8, 127.1, 127.5, 129.0, 129.4, 129.6, 131.2, 131.9, 134.3, 136.3, 139.3, 139.9, 140.4.

5-Methyl-5-(phenylsulfonyl)octane-2,6-dione (44). A sample of 2-(phenylsulfonyl)-pentan-3-one (**43**)[26] (0.4 g, 1.8 mmol) dissolved in 15 mL of CH_2Cl_2 was treated with NEt_3 (0.34 mL, 2.4 mmol). After 20 min of stirring at room temperature, methyl vinyl ketone (0.28 mL, 3.5 mmol) was added to the reaction mixture. Stirring was continued for an additional 8 days, and the mixture was then quenched with a saturated aqueous NH_4Cl solution. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by silica gel chromatography to furnish 0.41 g (82%) of the titled compound **44** as a colorless oil: IR (thin film) 3066, 2980, 1713, 1447, and 1303 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.05 (t, 3H, $J = 7.8$ Hz), 1.55 (s, 3H), 2.06−2.17 (m, 4H), 2.24−2.45 (m, 3H), 2.74−2.93 (m, 2H), 7.52−7.56 (m, 2H), 7.65−7.69 (m, 1H), and 7.72−7.75 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 8.1, 16.3, 26.8, 30.1, 34.0, 38.2, 75.7, 129.1, 130.4, 134.5, 135.0, 205.5, and 206.5.

1-(3-Ethyl-4-methylphenyl)pyrrolidine (45). A solution of the above compound **44** (34 mg, 0.12 mmol) in toluene (1 mL) was treated with a catalytic amount of *p*-TsOH and pyrrolidine (0.019 mL, 0.23 mmol). The mixture was heated at reflux for 4 h and was then cooled to room temperature. The solvent was removed under reduced pressure, and the resulting residue was purified by silica gel chromatography to provide 13 mg (60%) of the titled compound **45** as a colorless oil: IR (thin film) 2963, 2927, 1616, 1511, and 1366 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.21 (t, 3H, $J = 8.0$ Hz), 1.97−2.00 (m, 4H), 2.21 (s, 3H), 2.58 (q, 2H, $J = 8.0$ Hz), 3.25−3.28 (m, 4H), 6.37 (dd, 1H, $J = 8.0$ and 2.4 Hz), 6.42 (d, 1H, $J = 2.4$ Hz), and 7.00 (d, 1H, $J = 8.0$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.9, 18.2, 25.6, 27.0, 48.0, 109.5, 111.9, 122.7, 130.8, 143.2, and 146.9. HRMS calcd for $[(C_{13}H_{19}N) + H]^+$: 190.1596. Found: 190.1588.

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Supporting Information Available: ^1H and ^{13}C NMR data of various key compounds together with an ORTEP drawing for compound **9**, as well as the corresponding CIF file. Atomic coordinates for compound **9** will be deposited with the Cambridge Crystallographic Data Centre. This material is available free of charge via the Internet at http://pubs.acs.org.

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