A novel synthesis of polysubstituted phenols using the S_nAr reaction of 2,5-dinitrofuran

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Dedicated to Prof. Alfred Hassner on the occasion of his 70th birthday

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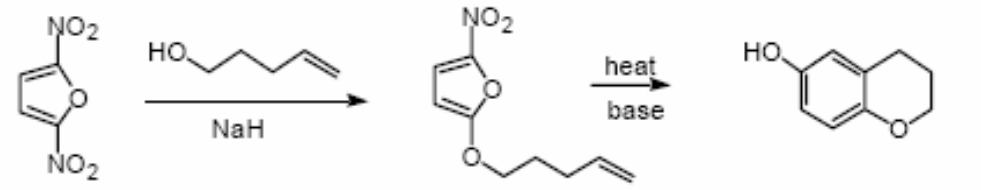
Abstract

2,5-Dinitrofuran is readily available from 2-nitrofuran by treatment with concentrated nitric acid. The reaction of this compound with various nucleophilic reagents proceeds by an addition/elimination sequence (S_NAr) to furnish substituted 5-nitrofurans in good yield. Diels—Alder cycloaddition of the resulting activated furans with various π-systems affords transient [4+2]-cycloadducts that undergo nitro group elimination and subsequent aromatization to produce polysubstituted phenols.

Keywords: SnAr, nitro, dinitro, furan, nucleophilic, substitution, Diels-Alder, phenol

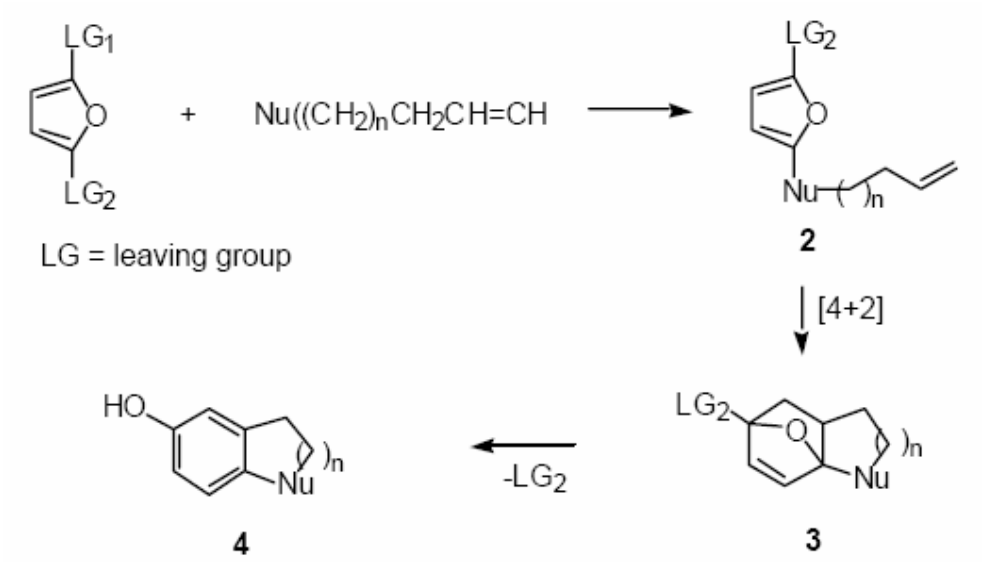
Introduction



Nucleophilic substitutions using benzenoid aromatics have been proposed to proceed through an addition-elimination mechanism (S_NAr). This proposal is consistent with the available kinetic data.[1,2] Molecular orbital calculations have been performed on the suspected intermediate Meisenheimer complex,[3] theories have been advanced to explain attack-site preferences,[4] and some theoretical work using bond energies have been carried out.[5] In contrast to this situation, nucleophilic aromatic substitution on the furan ring has been little studied. Monographs dealing with the chemistry of furans either ignore the subject entirely or sometimes present just a few

instances of this reaction.[6] One of the reasons for this state of affairs is no doubt the fact that furan derivatives with substituents suitable for nucleophilic displacement are not that easily available. A substrate of some interest to our research program is 2,5-dinitrofuran **1** which is readily available from 2-nitrofuran by treatment with concentrated nitric acid.[7] A survey of the literature revealed a limited number of examples where this diactivated furan underwent nucleophilic substitution.[8]

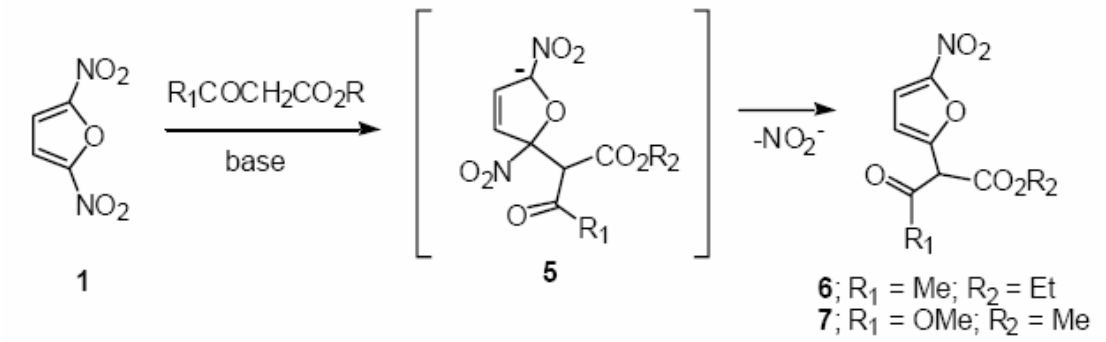
For the past several years, our laboratory has been interested in the Diels—Alder reaction of 2-substituted furans[9] as a method for preparing polyaromatic ring systems since these compounds are of interest as pharmaceutical agents.[10] Our long-range goal in this area involves the use of 2-nitro substituted furans such as **2** that contain both a suitable leaving group (*i.e.*, SPh, OMe, NO_2, *etc*.) and an olefinic tether which allows for an intramolecular Diels—Alder reaction (Scheme 1). The resultant cycloadduct **3** was expected to readily undergo ring opening and ejection of the leaving group to give phenols of type **4**. With this goal in mind, model studies were undertaken to determine the facility with which 2,5-dinitrofuran **1** would undergo substitution with various nucleophiles. Our intention was to use the resulting products as substrates for Diels— Alder cycloadditions. The present paper documents the results of these studies.



Scheme 1

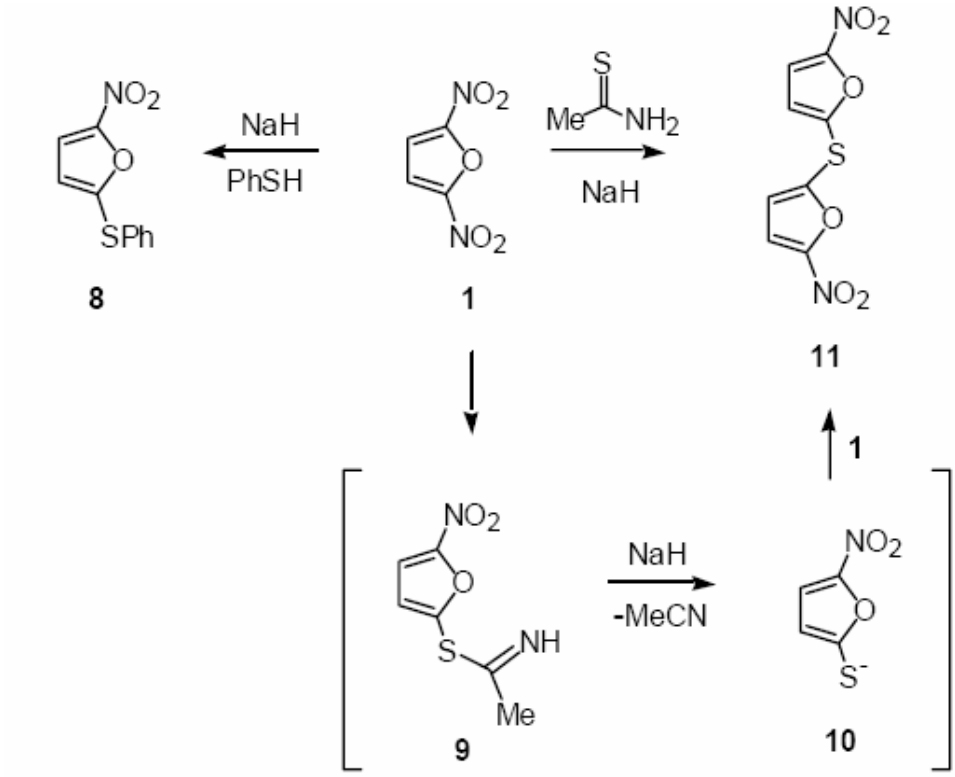
Results and Discussion

Our initial endeavors focused on the reaction of 2,5-dinitrofuran **1** with soft carbon nucleophiles such as the anions derived from ethyl acetoacetate or dimethyl malonate. Indeed, this reaction proceeded smoothly and afforded the substituted nitrofurans **6** and **7** in 90% and 97% yield, respectively. These substitutions presumably proceed by the addition/elimination mechanism *via* the Meisenheimer intermediate **5** as shown in Scheme 2.



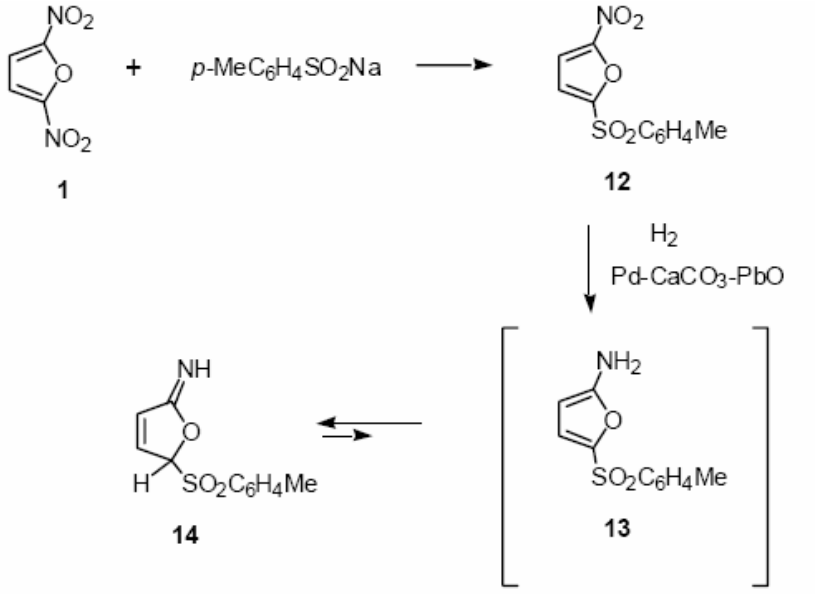
Scheme 2

To further illustrate the scope and synthetic utility of this S_NAr substitution reaction, we set out to expand the process using other nucleophilic agents. We found that treating dinitrofuran **1** with thiophenol in the presence of sodium hydride afforded 2-nitro-5-(phenylsulfanyl)furan **8** in 91% yield. Interestingly, the reaction of thioacetamide with furan **1** in the presence of NaH produced *bis*-(5-nitrofuranyl)-sulfide **11** as the exclusive product in 85% isolated yield (Scheme 3). The formation of **11** most probably proceeds through a sequence initiated by an addition-elimination of thioacetamide on the more nucleophilic sulfur atom to first produce **9** as a transient intermediate. Further reaction of **9** with NaH results in the loss of acetonitrile and the generation of thiolate **10** which reacts further with excess dinitrofuran to eventually produce sulfide **11**.



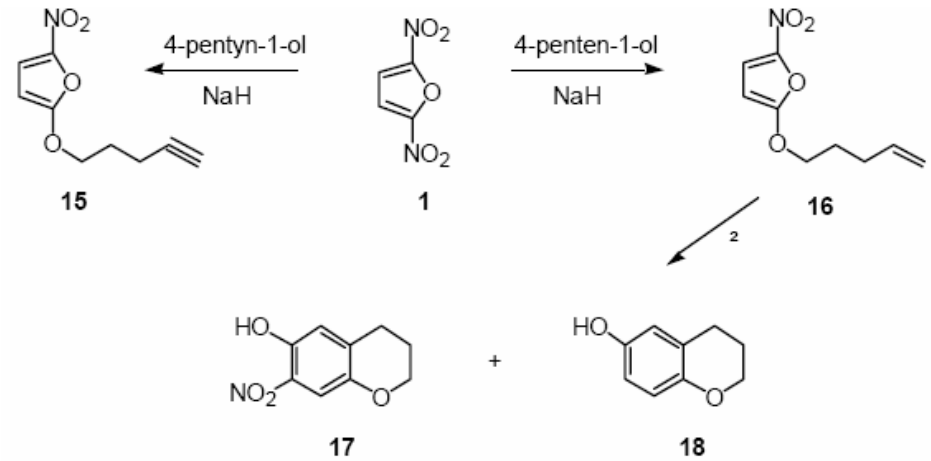
Scheme 3

We also examined the S_NAr reaction of dinitrofuran with sodium *p*toluenesulfinate. Displacement of one of the nitro groups with the sulfinate salt proceeded uneventfully to furnish sulfone **12** in 75% yield (Scheme 4). Exposure of **12** to hydrogen in the presence of Lindlar's catalyst did not produce the expected 2-amino substituted furan **13**, but rather gave the imine tautomer **14** in 91% yield. This transformation is not at all unreasonable given the fact that the related 2-hydroxy-furan system is known to exist preferentially in the butenolide tautomeric form.[6]



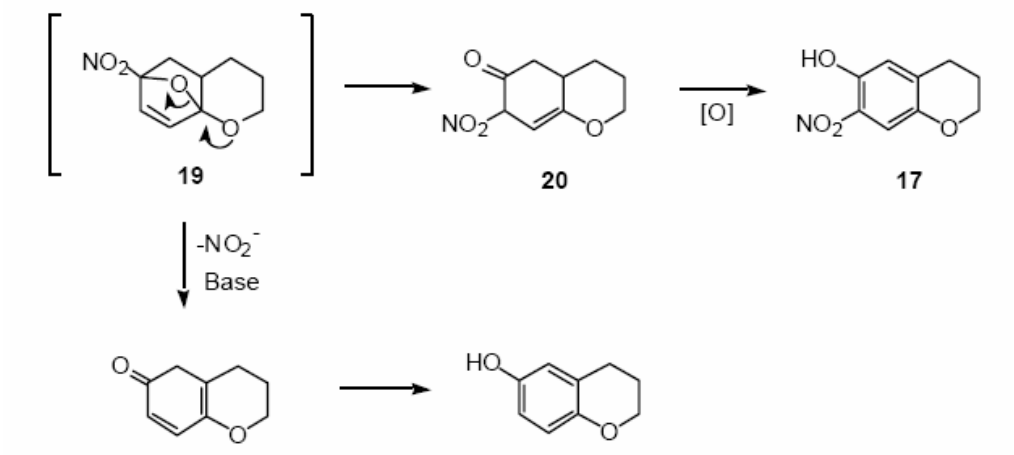
Scheme 4

Our attention was next directed toward the reaction of 2,5-dinitrofuran **1** with various oxygen and nitrogen nucleophiles. Treatment of a sample of **1** with both 4-pentyn-1-ol and 4-penten-1-ol in the presence of NaH furnished the expected 2-alkoxy-5-nitro substituted furans **15** and **16** in 53% and 61% yield, respectively (Scheme 5). Thermolysis of **15** at 120 °C failed to produce any characterizable products and only recovered starting material was obtained.



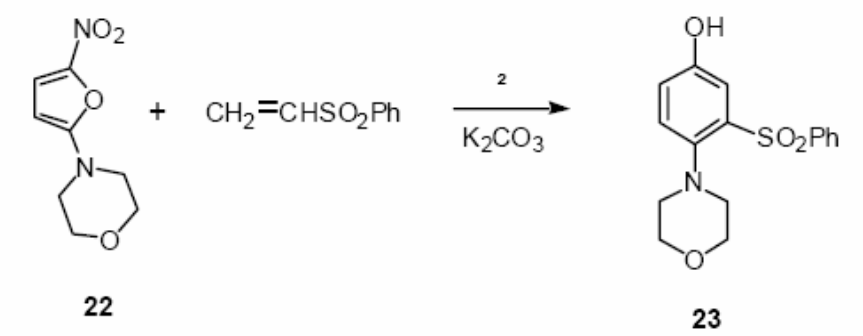
Scheme 5

On the other hand, heating a sample of **16** at 120 °C afforded a 2:1-mixture of chromanols **17** and **18** in 50% overall yield. The major chromanol (*i.e.*, **17**) produced in this reaction can be attributed to the formation of a Diels—Alder adduct (*i.e.*, **19**) derived from cycloaddition of the dienic system of the furan across the tethered π-bond. Opening of the oxabridge is assisted by the lone pair of electrons on the neighboring oxygen atom. 1,2-Migration of the nitro group to the adjacent double bond of the incipient oxonium ion then takes place to give enone **20** (Scheme 6). This transient intermediate is converted to nitro-chromanol **17** by subsequent tautomerization and air oxidation. Formation of the minor product **18** may be rationalized by invoking a competitive sequence involving loss of HNO_2 to give dienone **21** followed by a 1,3-sigmatropic hydrogen shift to ultimately produce chromanol **18**. After some experimentation, we eventually found a set of conditions that suppressed nitro group migration. The best conditions for minimizing formation of nitrochromanol **17** consisted of performing the thermolysis of **16** in *t*-butanol at 120 °C in the presence of potassium carbonate. These conditions resulted in the isolation of chromanol **18** as the exclusive product in 54% yield.



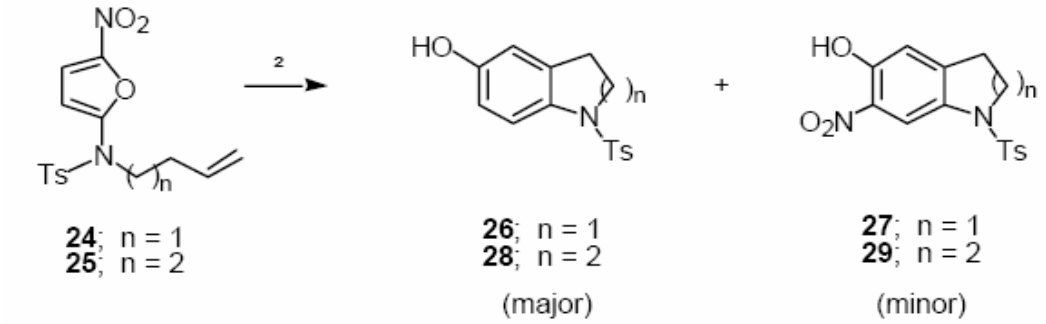
Scheme 6

The reaction of 2,5-dinitrofuran **1** with a typical secondary amine such as morpholine in ether at 35 °C afforded the morphilino-substituted nitrofuran **22** in 97% yield. Heating a sample of **22** with phenyl vinyl sulfone (120 °C, 12 h) in the presence of K_2CO_3 gave phenol **23** in 40% yield which is seemingly derived from a [4+2]-cycloaddition followed by nitro group ejection and subsequent aromatization.



22 23

Using the S_NAr reaction of 2,5-dinitrofuran, we were also able to synthesize *N*tosylamino furans **24** and **25** in 77% and 84% yields, respectively. Heating a sample of **24** in toluene at reflux resulted in a mixture of phenols **26** (50%) and **27** (14%). Similar results were obtained when the dienophile tether was lengthened by one methylene unit as illustrated in Scheme 7 for the conversion of nitrofuran **25** into **28** (55%) and **29** (7%). From these results it is evident that nitro-substituted aminofurans display some interesting cycloaddition chemistry.



24; n = 1
25; n = 2

26; n = 1
28; n = 2
(major)

27; n = 1
29; n = 2
(minor)

Scheme 7

Two distinct reaction pathways are observed: (1) cycloaddition followed by loss of the nitro group to give phenols (*i.e.*, **26** and **28**) and (2) cycloaddition followed by 1,2-nitro migration to eventually afford the corresponding *o*-nitrophenols **27** and **29**. Similar 1,2-shifts have been reported in cycloadditions involving silyl-substituted furans,[11] thereby providing good precedence for this rearrangement pathway.

In conclusion, this paper describes a versatile new approach to phenols with various substitution patterns. The synthetic procedure described here involves a S_NAr substitution reaction of 2,5-dinitrofuran with different nucleophilic reagents as a method for producing 5-nitro substituted furans. A subsequent Diels—Alder cycloaddition of the activated furan with several alkenyl π-bonds furnishes transient [4+2]-cycloadducts that are readily converted to polysubstituted phenols. Further application of the method and its utilization for alkaloid synthesis are in progress and will be reported in due course.

Experimental Section

General Procedures. Melting points are uncorrected. Mass spectra were determined at an ionizing voltage of 70eV. Unless otherwise noted, all reactions were performed in flame dried glassware under an atmosphere of dry argon. Solutions were evaporated under reduced pressure with a rotary evaporator and the residue was chromatographed on a silica gel column using an ethyl acetate/hexane mixture as the eluent unless specified otherwise. All solids were recrystallized from ethyl acetate/hexane for analytical data.

2,5-Dinitrofuran (1). To 50 mL (0.5 mol) of acetic anhydride at –30 ^{o}C was added 22 mL (0.5 mol) of fuming nitric acid, while maintaining the temperature below –10 °C. The acetyl nitrate solution was cooled to –30 °C and a solution containing 40 mL (0.3 mol) of furan in 20 mL of acetic anhydride was slowly added, while maintaining the temperature below –30 °C. When the addition was complete, the reaction was allowed to stir for an additional 15 min, poured into ice water, and neutralized to pH 6 by the slow addition of a 50% NaOH solution while maintaining the temperature at 0 °C. The mixture was extracted with ether, dried over $MgSO_4$, and concentrated under reduced pressure. The red liquid was taken up in 20 mL of dry THF and the mixture was slowly added to a solution of 40 mL of pyridine in 20 mL of THF. The rate of addition was controlled so as to maintain a temperature of 50 °C. Once the addition was complete, the reaction mixture was cooled to rt and concentrated by distillation under aspirator vacuum. The resulting residue was passed through a silica gel plug eluting with CH_2Cl_2. The yellow filtrate was concentrated under reduced pressure and the resulting oil was sublimed at 30 °C (2 mm) to give 16.5 g (53%) of 2-nitrofuran as bright yellow crystals: mp 27–28 °C (lit.[12] mp 28–29 °C).

A solution containing 3.0 g (26 mmol) of the above compound in 50 mL of 70% nitric acid was heated at 60 °C for 4 h. After cooling to rt, the solution was poured into ice water, neutralized by the careful addition of sodium carbonate, and extracted with CH_2Cl_2. The combined organic extracts were washed with water, brine, dried over Na_2SO_4, and concentrated under reduced pressure. Recrystallization of the residue from ethanol afforded 2.1 g (51%) of 2,5-dinitrofuran **1** as a pale yellow solid: mp: 99-101 °C (lit.[7] mp: 100–101 °C).

3-Hydroxy-2-(5-nitrofuran-2-yl)but-2-enoic acid ethyl ester (6). To a solution containing 0.4 mL (3 mmol) of ethyl acetoacetate in 25 mL of THF at 0 °C was added 0.1 g (3 mmol) of 60 % NaH in mineral oil. The reaction mixture was allowed to stir at 0 °C for 15 min and a solution containing 0.3 g (2 mmol) of 2,5-dinitrofuran in 10 mL of THF was added. The solution was allowed to warm to rt, stirred for 2 h, and quenched by the addition of water. The mixture was extracted with CH2Cl2 and the combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography to give 0.4 g (90 %) of **6** as a yellow oil: IR (neat) 3132, 1647, and 1352 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) d 1.28 (t, 3H, *J* = 7.2 Hz), 2.16 (s, 3H), 4.27 (q, 2H, *J* = 7.2 Hz), 6.50 (d, 1H, *J* = 3.6 Hz), 7.33 (d, 1H, *J* = 7.2 Hz), and 13.50 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) d 14.0, 15.0, 60.1,

107.3, 113.2, 115.6, 155.1, 155.6, 158.4, and 173.4; Anal. Calcd. for $C_{10}H_{11}NO_6$: C, 49.78; H, 4.60; N, 5.81. Found: C, 49.73; H, 4.55; N, 5.63.

2-(5-Nitrofuran-2-yl)malonic acid diethyl ester (7). To a solution containing 1.5 mL (13 mmol) of dimethyl malonate in 50 mL of THF at 0 °C was added 0.6 g (15 mmol) of 60 % NaH in mineral oil. The mixture was allowed to stir at 0 °C for 10 min and a solution containing 1.0 g (6 mmol) of 2,5-dinitrofuran in 5 mL of THF was added. The solution was allowed to warm to rt, stirred for 20 min, and quenched by the addition of water. The mixture was extracted with CH2Cl2 and the combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography to give 1.5 g (97 %) of **7** as a yellow oil: IR (neat) 3137, 1742, and 1589 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ3.84 (s, 6H), 4.91 (s, 1H), 6.73 (d, 1H, *J* = 3.6 Hz), and 7.28 (d, 1H, *J* = 3.6 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 51.6, 53.6, 112.3, 113.1, 149.1, and 164.9; HRMS Calcd. for $C_9H_9NO_7$: 243.0389. Found: 243.0391.

2-Nitro-5-(phenylsulfanyl)furan (8). To a solution containing 0.7 mL (6.0 mmol) of thiophenol in 25 mL of acetonitrile at 0 °C was added 0.3 g (9 mmol) of 60 % NaH in mineral oil. The reaction mixture was allowed to stir at 0 °C for 20 min and a solution containing 1.0 g (6.0 mmol) of 2,5-dinitrofuran in 10 mL of acetonitrile was added. The reaction mixture was heated at reflux for 2.5 h, cooled, and quenched by the addition of water. The mixture was extracted with CH_2Cl_2 and the combined extracts were washed with 10% aqueous NaOH and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography to give 1.2 g (91 %) of **8** as a pale yellow solid: mp 67–68 °C; IR ($CHCl_3$) 1641, 1544, and 1432 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.59 (d, 1H, *J* = 3.5 Hz), 7.38 (d, 1H, *J* = 3.5 Hz), 7.37 (m, 3H), and 7.47 (m, 2H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ115.3, 118.2, 122.4, 129.7, 129.9, 131.1, 133.5, and 154.2; Anal. Calcd. for $C_{10}H_7NO_3S$: C, 54.30; H, 3.19; N, 6.34. Found: C, 54.21; H, 3.04; N, 6.28.

***Bis*-(5-nitrofuranyl)sulfide (11).** To a solution containing 0.1 g (1.4 mmol) of thioacetamide in 40 mL of THF at 0 °C was added 0.08 mg (1.8 mmol) of 60% NaH in mineral oil. The mixture was stirred at 0 °C for 20 min and a solution containing 0.2 g (1.3 mmol) of 2,5-dinitrofuran was added. The solution was allowed to warm to rt, stirred for 1 h, and quenched by the addition of water. The mixture was extracted with CH_2Cl_2 and the combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography to give 0.14 g (85 %) of **11** as a white solid; mp 92-93 °C; IR ($CHCl_3$) 1647, 1548, and 1445 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.96 (d, 2H, *J* = 3.0 Hz), and 7.33 (d, 2H, *J* = 3.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ112.7, 120.7, 144.4, and 148.8; Anal. Calcd. for $C_8H_4N_2SO_6$: C, 37.51; H, 1.57; N, 10.93. Found: C, 37.56; H, 1.63; N, 10.83.

2-Nitro-5-(*p*-toluene-4-sulfonyl)furan (12). To a solution containing 2.4 g (15 mmol) of 2,5-dinitrofuran in 75 mL of methanol was added 2.7 g (15 mmol) of sodium *p*toluenesulfinate. The reaction mixture was heated at reflux for 24 h, cooled to rt, and the solvent was removed under reduced pressure. The residue was subjected to silica gel chromatography to give 3.0 g (75 %) of **12** as a white solid: mp 114-115 °C; IR ($CHCl_3$) 1592, 1526, and 1342 cm^{-1}; ^{1}H-NMR ($CDCl_3$,

300 MHz) δ 2.46 (s, 3H), 7.29 (d, 1H, *J* = 6.0 Hz), 7.30 (d, 1H, *J* = 6.0 Hz), 7.41 (d, 2H, *J* = 8.1 Hz), and 7.94 (d, 2H, *J* = 8.1 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 22.0, 111.3, 117.6, 117.7, 128.8, 130.7, 135.1, 146.7, and 151.8; Anal. Calcd. for $C_{11}H_9NO_5S$: C, 49.40; H, 3.39; N, 5.24. Found: C, 49.63; H, 3.54; N, 5.29.

5-(*p*-Toluene-4-sulfonyl)-5*H*-furan-2-ylideneamine (14). To a sample of 0.6 g (2.0 mmol) of furan **12** in 100 mL of MeOH was added 0.14 g of Lindlar's catalyst. The reaction mixture was hydrogenated at 40 psi for 3 h. At the end of this time, the mixture was filtered through a pad of Celite and the solvent was removed under reduced pressure. The residue was subjected to silica gel chromatography to give 0.46 g (91 %) of **14** as a white solid; mp 125-126 °C; IR ($CHCl_3$) 3423, 1669, and 1320 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.46 (s, 3H), 5.98 (s, 1H), 6.37 (dd, 1H, *J* = 6.0 and 2.0 Hz), 6.79 (dd, 1H, *J* = 6.0 and 2.0 Hz), 7.37 (d, 2H, *J* = 8.2 Hz), and 7.82 (d, 2H, *J* = 8.2 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 20.7, 98.9, 109.8, 127.1, 129.6, 129.7, 131.8, 132.4, 145.8, 148.6, and 158.4; Anal. Calcd. for $C_{11}H_{11}NO_3S$: C, 55.68; H, 4.67; N, 5.98. Found: C, 55.61; H, 4.64; N, 5.79.

2-Nitro-5-(pent-4-ynyloxy)furan (15). To a solution containing 0.11 g (1.3 mmol) of 4-pentyne-1-ol in 30 mL of THF was at 0 °C was added 0.06 g (1.5 mmol) of 60 % NaH in mineral oil. The reaction mixture was allowed to stir for 15 min at 0 °C and a solution containing 0.2 g (1 mmol) of 2,5-dinitrofuran in 7 mL of THF was added. The solution was allowed to warm to rt, stirred for 2.5 h, and quenched by the addition of water. The mixture was extracted with CH_2Cl_2 and the combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography to give 0.13 g (53 %) of **15** as a yellow solid: mp 51-53 °C; IR ($CHCl_3$) 3292, 1590, and 1484 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ1.98-2.05 (m, 2H); 2.35-2.40 (m, 2H); 4.35 (t, 2H, *J* = 6.0 Hz); 5.51 (d, 1H, *J* = 4.0 Hz); and 7.32 (d, 1H, *J* = 4.0 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ14.8, 27.5, 69.8, 70.4, 82.2, 86.7, 116.7, 143.7, and 161.1; Anal. Calcd. for $C_9H_9NO_4$: C, 55.37; H, 4.65; N, 7.18. Found: C, 55.24; H, 4.49; N, 7.01.

2-Nitro-5-(pent-4-enyloxy)furan (16). To a solution containing 0.3 mL (3.2 mmol) of 4-penten-1-ol and 25 mL of THF at 0 °C was added 0.2 g (4.5 mmol) of 60 % NaH in mineral oil. The mixture was stirred at 0 °C for 30 min and a solution containing 0.5 g (3 mmol) of 2,5-dinitrofuran in 5 mL of THF was added. The solution was allowed to warm to rt, stirred for 3 h, and quenched by the addition of water. The mixture was extracted with CH_2Cl_2 and the combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography to give 0.37 g (60 %) of **16** as a white solid; mp 55-56 °C; IR ($CHCl_3$) 1590, 1485, and 1420 cm^{-1}; ^{1}H- NMR ($CDCl_3$, 300 MHz) d 1.90 (quint, 2H, *J* = 6.8 Hz), 2.21 (q, 2H, *J* = 6.8 H), 4.23 (t, 2H, *J* = 6.8 Hz), 5.00-5.09 (m, 2H), 5.64 (d, 1H, *J* = 3.5 Hz), 5.75-5.85 (m, 1H), and 7.38 (d, 1H, *J* = 3.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) d 15.0, 27.5, 30.5, 87.5 105.0, 114.8, 117.3, 144.0, and 166.8; Anal. Calcd. for $C_9H_{11}NO_4$: C, 54.80; H, 5.63; N, 7.11. Found: C, 54.70; H, 5.51; N, 7.05.

7-Nitrochroman-6-ol (17). A solution containing 0.3 g (2 mmol) of furan **16** and 30 mL of toluene was heated at reflux for 12 h. The solvent was removed under reduced pressure and the

residue was subjected to silica gel chromatography. The first fraction to elute from the column contained 0.12 g (34 %) of a yellow solid that was identified as 7-nitrochroman-6-ol **17**; mp 120-121 °C; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.00– 2.05 (m, 2H), 2.83 (t, 2H, *J* = 7.2 Hz), 4.16 (t, 2H, *J* = 7.2 Hz), 6.81 (s, 1H), 7.44 (s, 1H), and 10.10 (s, 1H); Anal. Calcd. for $C_9H_9NO_4$: C, 55.37; H, 4.65; N, 7.18. Found: C, 55.24; H, 4.39; N, 7.27. The minor product eluted from the column contained 0.04 g (16 %) of a white solid that was identified as chroman-6-ol (**18**): mp 98-100 °C (lit.[13] mp 99-100 °C); ^{1}H-NMR ($CDCl_3$, 300 MHz) d 1.95-2.00 (m, 2H), 2.70 (t, 2H, *J* = 7.5 Hz), 4.20 (t, 2H, *J* = 7.5 Hz), 4.77 (brs, 1H), 6.50-6.60 (m, 2H), and 6.84 (d, 1H, *J* = 8.0 Hz).

4-(5-Nitro-furan-2-yl)morpholine (22). To a solution containing 0.33 g (2.1 mmol) of 2,5-dinitrofuran in 25 mL of ether was added 0.3 g (5 mmol) of morpholine. The solution was stirred at 35 °C for 2.5 h and was concentrated under reduced pressure. The residue was subjected to silica gel chromatography to give 0.4 g (97%) of **22** as a yellow solid: mp 114–115 °C; IR ($CHCl_3$) 3119, 2913, 1610, 1517, and 1391 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.46 (m, 4H), 3.81 (m, 4H), 5.38 (d, 1H, *J* = 4.2 Hz), and 7.47 (d, 1H, *J* = 4.2 Hz); ^{13}C-NMR (75 MHz, $CDCl_3$) δ 45.8, 65.8, 87.8, 120.0, 139.6, and 159.7; HRMS Calcd. for $C_8H_{10}N_2O_4$: 198.0640. Found 198.0641.

3-Benzenesulfonyl-4-(morpholin-4-yl)phenol (23). A mixture containing 0.1 g (0.5 mmol) of furan **22**, 0.2 g (1.2 mmol) of phenyl vinyl sulfone, 0.07 g (0.5 mmol) of K_2CO_3, and 15 mL of chloroform was heated at reflux for 12 h, cooled to rt, and then 10 ml of a saturated aqueous solution of ammonium chloride was added. The mixture was extracted with CH2Cl2 and the combined extracts were dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was subjected to silica gel chromatography to give 0.06 g (40 %) of **23** as a white solid: mp 120-122 °C; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.61-2.75 (m, 4H), 3.52-3.70 (m, 4H), 6.80 (brs, 1H), 7.14-7.19 (m, 1H), 7.22-7.30 (m, 1H), 7.45-7.60 (m, 3H), and 7.89-8.00 (m, 3H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 48.6, 66.6, 111.9, 112.0, 117.7, 123.5, 125.0, 128.1, 131.1, 133.2, 136.8, and 150.9; Anal. Calcd. for $C_{16}H_{17}NO_4S$: C, 60.17; H, 5.37; N, 4.39. Found: C, 60.03; H, 5.28; N, 4.19.

***N*-But-3-enyl-4-methyl-*N*-(5-nitrofuran-2-yl)benzenesulfonamide (24).** To a stirred solution containing 4.7 g (17 mmol) of freshly prepared *N*-(*tert*-butyl-carbamate)sulfonamide[14] in 20 mL of THF was added 9.1 g (35 mmol) of triphenylphosphine, followed by the addition of 0.8 g (12 mmol) of 3-buten-1-ol. The mixture was cooled to 0 °C and 5 mL (30 mmol) of dimethyl acetylenedicarboxylate was added dropwise. The mixture was allowed to stir at rt for 3 h, and the solvent was removed under reduced pressure. The resulting oil was subjected to silica gel chromatography to give 3.5 g (93%) of *N*-(*tert*-butylcarbamate)-*N*-but-3-enyl-4-methylbenzenesulfonamide as a colorless oil: IR (neat) 2978, 1729, 1642, and 1595 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ1.52 (s, 9H), 2.33 (s, 3H), 2.42 (q, 2H, *J* = 7.5 Hz), 3.80 (t, 2H, *J* = 7.5 Hz), 5.00-5.20 (m, 2H), 5.70-5.80 (m, 1H), 7.21 (d, 2H, *J* = 8.1 Hz), and 7.71 (d, 2H, *J* = 8.1 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 21.5, 27.8, 34.5, 46.3, 84.0, 117.3, 127.8, 129.2, 134.4, 137.4, 144.1, and 150.8; HRMS Calcd. for $C_{16}H_{23}NO_4S$: 325.1348. Found: 325.1354.

To a stirred solution containing 3.5 g (11 mmol) of the above sulfonamide in 50 mL of CH_2Cl_2 was added 2.5 mL (0.3 mol) trifluoroacetic acid. The solution was allowed to stir at rt for 12 h and was quenched with an aqueous K2CO3 solution. The organic layer was separated, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Silica gel chromatography of the residue afforded 2.1 g (88%) of *N*-but-3-enyl-4-methylbenzenesulfonamide[15] as a colorless oil: IR (neat) 3278, 2934, 1641, 1430, and 1325 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.20 (q, 2H, *J* = 6.9 Hz), 2.42 (s, 3H), 2.99 (q, 2H, *J* = 6.9 Hz), 5.00-5.10 (m, 2H), 5.17 (brs, 1H), 5.6-5.75 (m, 1H), 7.30 (d, 2H, *J* = 8.2 Hz), and 7.77 (d, 2H, *J* = 8.2 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 21.5, 33.6, 42.3, 117.8, 127.1, 129.7, 134.3, 136.9, and 143.4; HRMS Calcd. for $C_{11}H_{15}NO_2S$: 225.0823. Found: 225.0825.

To a stirred solution containing 1.4 g (6 mmol) of the above sulfonamide in 30 mL of THF at 0 °C was added 0.3 g (9 mmol) of 60% NaH in mineral oil. The mixture was stirred for 30 min at rt, and cooled to 0 °C, then a solution of 1.0 g (6.3 mmol) of 2,5-dinitrofuran in 5 mL of THF was added. The mixture was allowed to warm to rt, stirred at this temperature for 3.5 h, and quenched with water. The solvent was removed under reduced pressure and the residue was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Silica gel chromatography afforded 2.0 g (94%) of **24** as a clear oil: IR (neat) 3133, 2920, 1600, 1493, and 1347 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.35 (q, 2H, *J* = 7.2 Hz), 2.43 (s, 3H), 3.72 (t, 2H, *J* = 7.2 Hz), 5.06 (m, 2H), 5.71 (m, 1H), 6.49 (d, 1H, *J* = 3.6 Hz), 7.32 (d, 3H, *J* = 7.2 Hz), and 7.57 (d, 2H, *J* = 7.8 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 21.6, 33.1, 48.8, 107.2, 113.8, 117.9, 127.4, 130.1, 133.4, 134.9, 145.1, and 148.1; HRMS Calcd. for $C_{15}H_{16}N_2O_5S$: 336.0780. Found: 336.0774.

1-(*p*-Toluene-4-sulfonyl)-2,3-dihydro-1*H*-indol-5-ol (26). A solution containing 1.0 g (3.1 mmol) of furan **24** in 30 mL of toluene was heated at reflux for 12 h. The solution was allowed to cool to rt and 10 mL of a saturated NH_4Cl solution was added. The mixture was extracted with CH_2Cl_2, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was subjected to silica gel chromatography. The major fraction contained 0.46 g (50%) of **26** as a white solid; mp 196–197 °C; IR (neat) 3369, 2909, 1606, 1459, and 1150 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.37 (s, 3H), 2.71 (t, 2H, *J* = 8.2 Hz), 3.90 (t, 2H, *J* = 8.2 Hz), 4.60 (s, 1H), 6.57 (d, 1H, *J* = 2.0 Hz), 6.68 (dd, 1H, *J* = 8.6 and 2.3 Hz), 7.21 (d, 2H, *J* = 8.0 Hz), 7.51 (d, 1H, *J* = 8.6 Hz), and 7.60 (d, 2H, *J* = 8.2 Hz); ^{13}C–NMR ($CDCl_3$, 75 MHz) δ 21.8, 28.5, 50.6, 112.4, 114.5, 177.1, 127.6, 129.8, 134.1, 134.5, 135.8, 144.1, 152.8, and 152.8; Anal. Calcd. for $C_{15}H_{15}NO_3S$: C, 62.26; H, 5.23; N, 4.84. Found: C, 62.24; H, 5.27; N, 4.79.

The minor fraction contained 0.14 g (14%) of a white solid that was identified as 6-nitro-1-(*p*-toluene-4-sulfonyl)-2,3-dihydro-1H-indol-5-ol (**27**); mp 219–221 °C; IR ($CHCl_3$) 3324, 2919, 1736, 1642, and 1593 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 2.40 (s, 3H), 2.94 (t, 2H, *J* = 8.3 Hz) , 3.96 (t, 2H, *J* = 8.3 Hz), 6.88 (s, 1H), 7.28 (d, 2H, *J* = 8.2 Hz), 7.69 (d, 2H, *J* = 8.2 Hz), 8.24 (s, 1H), and 10.69 (s, 1H); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 21.8, 28.5, 50.1, 109.4, 116.3, 127.6, 130.2, 133.5, 135.5, 144.1, 145.0, 153.0, and 158.6; Anal. Calcd. for $C_{15}H_{14}N_2O_5S$: C, 53.89; H, 4.22; N, 8.38. Found: C, 53.95; H, 4.28; N, 8.32.

***N*-Pent-4-enyl-4-methyl-*N*-(5-nitrofuran-2-yl)benzenesulfonamide (25).** To a stirred solution containing 4.2 g (16 mmol) of freshly prepared *N*-(*tert*-butylcarbamate)sulfonamide[14] in 20 mL of THF was added 8 g (23 mmol) of triphenylphosphine followed by 0.9 g (10 mmol) of 4-penten-1-ol. The mixture was cooled to 0 °C and 5 mL (30 mmol) of dimethyl acetylenedicarboxylate was added dropwise. The reaction mixture was allowed to stir at rt for 3 h. The solvent was removed under reduced pressure and the resulting oil was subjected to silica gel chromatography to give 3.4 g (95%) of *N*-(*tert*-butylcarbamate)-*N*-pent-4-enyl-4-methylbenzenesulfonamide as a colorless oil: IR (neat) 3073, 2973, 1727, 1347, and 1154 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ1.33 (s, 9H), 1.87 (m, 2H), 2.13 (q, 2H, *J* = 7.8 Hz), 2.44 (s, 3H), 3.83 (t, 2H, *J* = 7.8 Hz), 5.85 (m, 1H), 5.10 (m, 2H), 7.32 (d, 2H, *J* = 10.5 Hz), and 7.79 (d, 2H, *J* = 10.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 21.6, 27.9, 29.2, 30.9, 32.9, 46.8, 115.2, 127.8, 128.5, 129.2, 133.8, 137.5, and 150.9; HRMS Calcd. for $C_{17}H_{25}NO_4S$: 339.1504. Found: 339.1508.

To a stirred solution containing 3.4 g (9.9 mmol) of the above sulfonamide in 50 mL of CH_2Cl_2 was added 3 mL (0.3 mol) of trifluoroacetic acid. The solution was allowed to stir at rt for 12 h and was quenched with an aqueous K_2CO_3 solution. The organic layer was separated, washed with brine, dried over Na2SO4, and concentrated under reduced pressure. Silica gel chromatography afforded 2.3 g (96%) of *N*-pent-4-enyl-4-methyl-benzenesulfonamide[15] as a colorless oil: IR (neat) 3289, 2930, 1636, 1330, and 1150 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ1.49 (m, 2H), 1.97 (q, 2H, *J* = 7.0 Hz), 2.35 (s, 3H), 2.86 (q, 2H, *J* = 6.5 Hz), 4.88 (m, 2H), 5.30 (s, 1H), 5.63 (m, 1H), 7.24 (d, 2H, *J* = 8.1 Hz), and 7.72 (d, 2H, *J* = 8.1 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ21.5, 28.7, 30.6, 42.6, 115.5, 127.1, 129.7, 137.0, 137.2, and 143.4; HRMS Calcd. for $C_{12}H_{17}NO_2S$: 239.0979. Found; 239.0976.

To a stirred solution containing 1.5 g (6.3 mmol) of the above sulfonamide in 30 mL of THF at 0 °C was added 0.3 g (9 mmol) of 60% NaH in mineral oil. The ice bath was removed and the mixture was stirred for 30 min at rt. The solution was cooled to 0 °C and 1.0 g (6 mmol) of 2,5-dinitrofuran in 5 mL THF was added. The mixture was allowed to warm to rt, stirred at rt for 3.5 h, and quenched with water. The solvent was removed under reduced pressure and the residue was extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. Silica gel chromatography of the residue afforded 2.0 g (92%) of **25** as a clear oil: IR (neat) 3136, 2923, 1636, 1489, and 1343 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ1.71 (q, 2H, *J* = 7.2 Hz), 2.10 (q, 2H, *J* = 7.2 Hz), 2.43 (s, 3H), 3.66 (t, 2H, *J* = 7.2 Hz), 5.00 (m, 2H), 5.75 (m, 1H), 6.51 (d, 1H, *J* = 3.9 Hz), 7.32 (m, 3H), and 7.64 (d, 2H, *J* = 8.4 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 21.6, 27.8, 30.3, 48.9, 106.9, 113.8, 115.7, 127.4, 130.1, 134.8, 136.8, 145.1, 148.1, and 148.3; HRMS Calcd. for $C_{16}H_{18}N_2O_5S$: 350.0936. Found: 350.0941.

1-(*p*-Toluene-4-sulfonyl)-1,2,3,4-tetrahydroquinolin-6-ol (28). A solution containing 1.1 g (3 mmol) of furan **25** in 30 mL of toluene was heated at reflux for 12 h. The solution was allowed to cool to rt and 10 mL of a saturated NH_4Cl solution was added. The mixture was extracted with CH_2Cl_2, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was subjected to silica gel chromatography. The major fraction contained 0.5 g (55%) of **28** as a

white solid; mp 155-156 °C; IR ($CHCl_3$) 3414, 2919, 1611, 1504, and 1155 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) d 1.54 (m, 2H), 2.28 (t, 2H, *J* = 6.7 Hz), 2.38 (s, 3H), 3.74 (t, 2H, *J* = 6.7 Hz), 5.29 (s, 1H), 6.49 (d, 1H, *J* = 2.8 Hz), 6.68 (dd, 1H, *J* = 8.8 and 2.8 Hz), 7.18 (d, 2H, *J* = 8.1 Hz), 7.43 (d, 2H, *J* = 8.1 Hz), and 7.62 (d, 1H, *J* = 8.8 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) d 21.2, 21.5, 26.3, 46.4, 113.7, 115.1, 127.1, 127.2, 129.5, 129.7, 133.0, 136.5, 143.5, and 153.2; Anal. Calcd. for $C_{16}H_{17}NO_3S$: C, 63.35; H, 5.65; N, 4.62. Found: C, 63.28; H, 5.65; N, 4.54.

The minor fraction contained 0.08 g (7%) of a white solid that was identified as 6-nitro-1-(*p*-toluene-4-sulfonyl)-1,2,3,4-tetrahydroquinolin-6-ol **29**; mp 174–175 °C; IR ($CHCl_3$) 3419, 3119, 1632, 1592, and 1535 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ1.66 (m, 2H), 2.40 (s, 3H), 2.46 (t, 2H, *J* = 6.5 Hz), 3.79 (t, 2H, *J* = 6.5 Hz), 6.81 (s, 1H), 7.24 (d, 2H, *J* = 8.2 Hz), 7.52 (d, 2H, *J* = 8.2 Hz), 8.52 (s, 1H), and 10.41 (s, 1H); ^{13}CNMR ($CDCl_3$, 75 MHz) δ 21.3, 21.8, 27.4, 46.1, 119.2, 120.9, 127.4, 130.1, 130.1, 132.1, 136.2, 142.8, 144.4, and 151.8; Anal. Calcd. for $C_{16}H_{16}N_2O_5S$: C, 55.16; H, 4.63; N, 8.05. Found: C, 55.22; H, 4.70; N, 8.08.

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