Synthesis of 2,3-dihydrobenzofuran-2-ones and 2,3-dihydrobenzothiophen-2- and 3-ones by rearrangements of 3-hydroxy analogs

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Dedicated to Professor Otto Gottlieb

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Abstract

Reactions of 2-hydroxybenzophenones **7a–c** and 2-sulfanylbenzophenones **13a–c** with 1-(1-chloroalkyl)benzotriazoles **8a–c** gave 2-(1-benzotriazolylalkoxy)- and 2-(1-benzotriazolylalkylsulfanyl)-benzophenones **9a–h** and **14a–h**, respectively. Treatment of **9a–h** and **14a–h** with lithium diisopropylamide (LDA) formed 2-(benzotriazol-1-yl)-3-substituted-2,3-dihydrobenzofuran-3-ols **10a–h** and -2,3-dihydrobenzothiophen-3-ols **15a–h**. Rearrangement of derivatives **10a–h** by $ZnBr_2$ afforded 3-alkyl-3-aryl-2,3-dihydrobenzofuran-2-ones **11a–h**. Rearrangement of derivatives **15a–h** gave 2-alkyl-2-aryl-2,3-dihydrobenzothiophen-3-ones **16a–g**, 3-alkyl-3-aryl-2,3-dihydrobenzothiophen-2-ones **17b,c,g**, and benzothiophenes **18g,h** depending on reaction conditions and substituents.

Keywords: Rearrangement, 2,3-dihydrobenzofuran-2-ones, 2,3-dihydrobenzothiophen-2-ones, 2,3-dihydrobenzothiophen-3-ones, benzotriazole

Introduction

The homologation of aldehydes and ketones by the insertion of a carbon atom next to the carbonyl group is an important transformation in synthetic organic chemistry, and one which has been extensively investigated. Available methods for the insertions of a single carbon carrying

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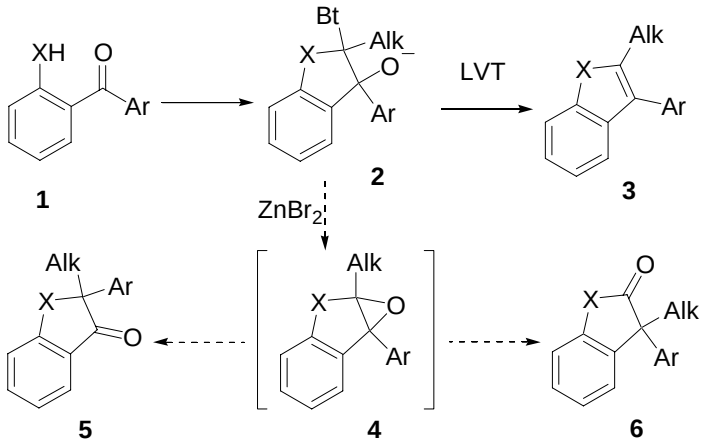
substituents next to a carbonyl have been summarized in several reviews[1] and in our own recent publications.[2]

The reported benzotriazole–mediated one-carbon insertion – functionalizations of ketones and aldehydes involve intermolecular reaction of a carbonyl group with a benzotriazole-activated nucleophile prior to rearrangement. Recently, we reported the preparation of 2,3-disubstituted benzofurans[3] and benzothiophenes[4] of common structure **3** (X = O and S respectively) starting from 2-hydroxy- and 2-sulfanyl-benzophenones **1** (X = O and S) via intermediate 2,3-dihydro-benzofurans and -benzothiophenes **2** (X = O and S). According to our previous work on the homologation of ketones and aldehydes,[2a,c,d] the Lewis Acid promoted rearrangement of intermediates **2** should provide ketones of structure **5** via oxiran **4** formation followed by the oxiran ring opening and migration of the 3-aryl group into the 2-position.[2a,c,d] However, previous literature work shows that 2-alkyl-3-aryl-2,3-dihydrobenzofuran epoxides of the structure **4** (X = O) can undergo tetraethylammonium bromide catalyzed rearrangement into 3-alkyl-3-aryl-2,3-dihydrobenzofuran-2-ones **6** (X = O) via the shift of a 2-alkyl group into the 3-position.[5] No information on possible formation of benzothiophene epoxides **4** (X = S) or their involvement in similar transformations has been previously reported.



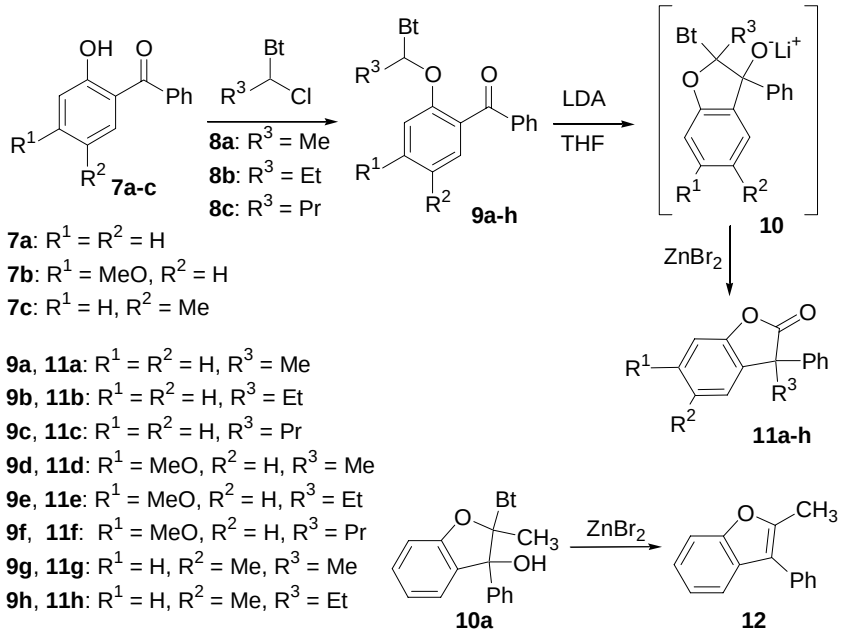
X = O, S; Bt = benzotriazol-1-yl; Alk = alkyl; LVT: low-valent titanium.

Scheme 1

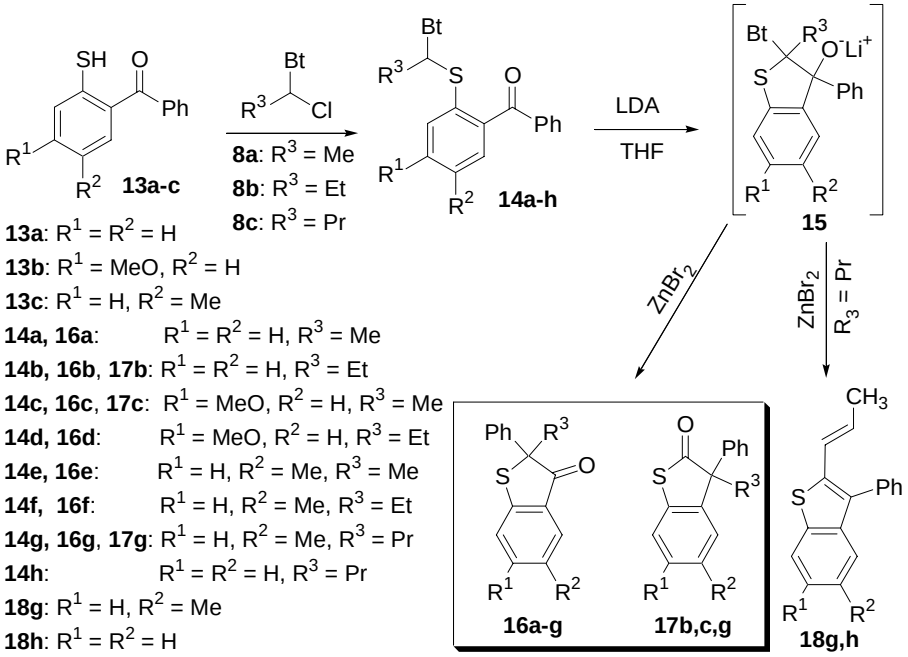
We now report type **4** → **6** Lewis Acid promoted rearrangements of 2,3-dihydrobenzofuran-3-ols **10a–h**, which provide a new approach to 3-alkyl-3-aryl-substituted 2,3-dihydrobenzofuran-2-ones **11a–h** starting from the appropriate 2-hydroxybenzophenones **7a–c** and 1-(1-chloroalkyl)benzotriazoles **8a–c** (Scheme 2). We also report the synthesis of both 2-alkyl-2-aryl-substituted 2,3-dihydrobenzothiophen-3-ones **16a–g** and 3-alkyl-3-aryl-substituted 2,3-dihydrobenzothiophen-2-ones **17b,c,g** (Scheme 3) via type **4** → **5** and type **4** → **6** rearrangements, respectively, of the corresponding intermediates **15**.

Results and Discussion

Intermediates **9a–h** were prepared by the reaction of 2-hydroxybenzophenones **7a–c** with compounds **8a–c** (available from aldehydes, benzotriazole and thionyl chloride in 87-96% yields[6]) similar to published procedure,[3,7] but in the presence of anhydrous potassium carbonate as a base instead of sodium hydroxide in DMF solution at 20–25 °C.



Scheme 2



Scheme 3

Intermediates **9a–h** were treated with an equimolar amount of LDA in THF at temperatures ranging from –78 °C to 0 °C to give the corresponding lithium salts of 2-(benzotriazolyl)-2,3-dihydrobenzofuran-3-ols **10a–h**[3] (mixtures of diastereoisomers according to TLC analysis; for **9a**, a single isomer was observed), which were treated without isolation with 2–3 equivalents of zinc bromide in 1,1,2,2-tetrachloroethane under reflux for 24 h to give new products. The ^{1}H NMR spectra of these products show no signals corresponding to those assigned to the *N*-substituted benzotriazole groups of intermediates **9a–h** (7.2–8.1 ppm). The ^{13}C NMR spectra of these compounds also no longer show signals for a *N*-substituted benzotriazole group (in this particular case our assignments were based on signals with chemical shifts around 120 ppm and 146 ppm) and carbonyl carbon (in the range 195–196 ppm) of **9a–h**.

The product carbonyl signals appear at 178–180 ppm rather than at 190–200 ppm as would be expected for compounds of type **5**.[8] This suggests that zinc bromide promoted rearrangement of **10a–h** results in the migration of an alkyl group to give 3-alkyl-3-aryl-substituted 2,3-dihydrobenzofuran-2-ones **11a–h** rather than 2,3-dihydrobenzofuran-3-ones **5** (X = O). Compounds **11a–h** were obtained in 41–70 % yields. Intermediate lithium salts of 2-(benzotriazolyl)-2,3-dihydrobenzofuran-3-ols **10a,c** were treated without isolation with 2–3 equivalents of zinc bromide in THF at 150–155 °C for 1–2 h in a sealed tube to give **11a,c** in 95% and 42% yields, respectively. The initiation of the rearrangement usually can be observed by the formation of a suspension (benzotriazole / zinc bromide complex). Unexpectedly, the treatment of 2-benzotriazolyl-2-methyl-3-phenyl-2,3-dihydrobenzofuran-3-ol **10a** with zinc bromide (2.5 equivalents) in THF solution at 150–155 °C for 1 h in a sealed tube gave exclusively 2-methyl-3-phenylbenzofuran (**12**)[3] in 65% yield. The ^{1}H and ^{13}C NMR data for **12** are identical with those reported in the literature.[3] The mechanism of transformation **10a** → **12** is unclear and may involve the reduction of **10a** by bromide anion.

We isolated intermediate **10a** (82%, single isomer) to support the proposed reaction pathway (Scheme 2). The structure of **10a** was deduced from its ^{1}H NMR, ^{13}C NMR spectra (see experimental section). The ^{1}H NMR spectrum of **10a** shows no signals assigned to ethoxy group protons of **9a** (doublet at 1.8 ppm and multiplet in the range 6.92–7.08 ppm), but shows a singlet at 1.77 ppm assigned to the 2-methyl group and a singlet at 3.03 ppm assigned to the 3-hydroxy group of **10a**. The ^{13}C NMR spectrum shows no carbonyl carbon signal, while two new signals at 106.0 ppm and 86.7 ppm were assigned to C-2 and C-3 carbons of the 2,3-dihydrobenzofuran ring.

Following our previous work,[4] intermediates **14a–h** were prepared from 2-sulfanylbenzophenones **13a–c** and compounds **8a–c** in the presence of anhydrous potassium carbonate in DMF at 20–25 °C under a nitrogen atmosphere. On treatment with an equimolar amount of LDA in THF at temperatures ranging from -78 °C to 0 °C, **14a–h** give the corresponding 2,3-dihydrobenzothiophen-3-ols **15a–h**[4] as mixtures of diastereoisomers (for **14d**, the single isomer **15d** was isolated).

We isolated and characterized intermediates **15c** (two diastereoisomers, (2*R**,3*R**) **15c'** and (2*R**/3*S**) **15c''**, were isolated with approx. ratio 56:44) and **15d** (single isomer) to support the

reaction route described. The structures of **15c'**, **15c''** and **15d** were deduced from their ^{1}H and ^{13}C NMR spectra (see experimental section). For both isomers of **15c**, the ^{1}H NMR spectra no longer show the doublet at 2.06 ppm corresponding to methyl protons of *S*-ethyl group in **14c**, while new signals, singlets at 2.58 ppm (**15c'**) and 2.04 ppm (**15c''**), were assigned to 2-methyl groups in **15c**. The disappearance of the singlet signals at 3.05 ppm (**15c'**) and 4.21 ppm (**15c''**) in the spectra of diastereoisomers **15c** after the addition of D_2O suggested the presence of hydroxy groups. In the ^{13}C NMR spectra of diastereoisomers **15c**, the signal at 195.8 ppm corresponding to the carbonyl group in **14c**, as well as a signal at 62.4 ppm assigned to the carbon between benzotriazolyl group and sulfur in **14c** are no longer present. The new signals at 90.2 ppm, 87.5 ppm in ^{13}C NMR spectrum of the major diastereoisomer **15c'**, as well as at 90.3 ppm, 86.3 ppm in the spectrum of the minor isomer **15c''**, were assigned to the C-2 and C-3 carbons of the 2,3-dihydrobenzothiophene ring in **15c**.

Compounds **15a–h** were treated without separation or further purification with 2–3 equivalents of anhydrous zinc bromide in 1,1,2,2-tetrachloroethane at 100–110 °C for 0.3–2 h to give the corresponding 2,3-dihydrobenzothiophen-3-ones **16a–f** admixed in two cases with the benzothiophenes **18g,h**.

The structures **16a–f** were deduced from their ^{1}H and ^{13}C NMR spectra (see experimental section). The ^{1}H NMR spectra of **16a–f** show no signals at 7.2-8.0 ppm characteristic for the *N*-substituted benzotriazolyl groups in intermediates **14a–f** and **15c,d**. In the ^{13}C NMR spectra of **16a–f**, the signals assigned to the *N*-substituted benzotriazolyl groups of **14a–f** around 110 ppm, 120 ppm, 132 ppm, and 146 ppm are no longer present, while the new signals at 200.6–203.2 ppm were assigned to the carbonyl groups of **16a–f**.

For intermediates **15g,h**, concurrent processes of dehydration – benzotriazole elimination occur to form 2-(1-propenyl)benzothiophenes **18g,h**. Structures **18g,h** were deduced from their ^{1}H and ^{13}C NMR. The ^{1}H NMR spectra of **18g,h** show no characteristic signals of a *N*-substituted benzotriazolyl group as found for intermediates **14g,h** at 7.2-8.0 ppm, and no propyl group signals. The doublet of doublets around 1.83 ppm, multiplet at 6.13–6.28 ppm, and doublet of quartets at 6.52–6.54 ppm with J = 15.5 Hz were assigned to *trans*-propenyl groups in **18g,h**. The ^{13}C NMR spectra of **18g,h** show no carbonyl carbon signals and no characteristic benzotriazolyl signals; the only single signals in the aliphatic region at 18.6–18.7 ppm were assigned to the methyl carbon of the propenyl groups in **18g,h**.

To optimize the procedure, compounds **14b,c,g** were treated with LDA (1 equivalent) in THF at temperatures ranging from -78 °C to 0 °C followed by addition of anhydrous zinc bromide (2–3 equivalents) to lithium salts of **15b,c,g** formed and rearrangement at 90–100 °C for 0.5–2 h in a sealed tube. These rearrangements, unlike the previous in tetrachloroethane, gave three pairs of products. For compounds **14b,c**, one of the products was identical to **16b,c** according to NMR data. The ^{1}H and ^{13}C NMR spectra of one product for **14g** show peaks similar to the **16a–f** pattern of signals (carbonyl group signal at 202.7 ppm). The ^{1}H and ^{13}C NMR spectra of the second products for **14b,c,g** showed sets of signals that are also in agreement with the expected structures **16b,c,g**, with the only difference being in the appearance of carbonyl signals at 207.2–

208.0 ppm. The formation of pairs of two carbonyl compounds suggested simultaneous **4** → **5** type and **4** → **6** type transformations of **14b,c,g**. The IR spectra of these products showed absorption bands in the range 1696–1701 cm^{-1} for products with carbonyl group signals in the range 201–203 ppm and in the range 1712–1707 cm^{-1} for products with carbonyl group signals in the range 207.4–208.0 ppm. These data suggest 2,3-dihydrobenzothiophen-3-ones structures **16b,c,g** for products with signals of the carbonyl group in ^{13}C NMR spectra at 201–203 ppm (IR absorption bands at 1696–1701 cm^{-1}) and structures **17b,c,g** for products with carbonyl group signals at 207.4–208.0 ppm (IR 1712–1707 cm^{-1}). A single crystal X-ray structure determination for the product from **14c** with carbonyl group signal at 207.4 ppm (IR 1707 cm^{-1}) unambiguously confirmed the thiolactone structure **17c** (Figure 1).

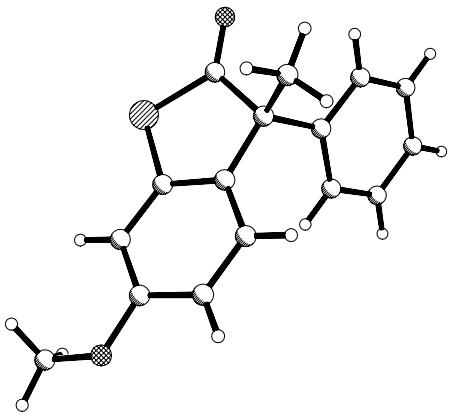
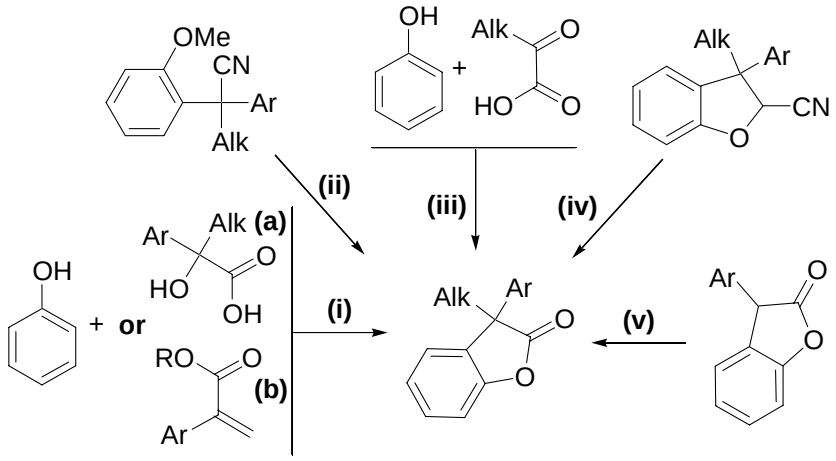


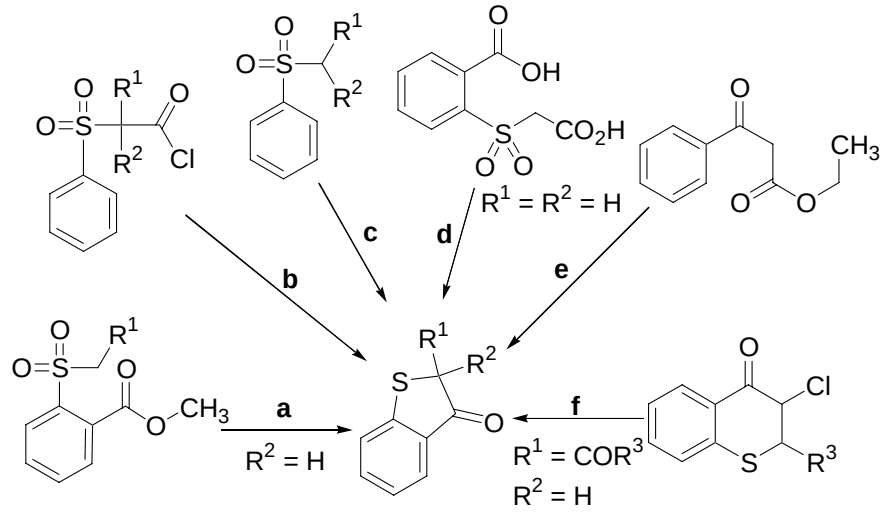
Figure 1. X-Ray crystal structure of **17c**.

3-Alkyl-3-aryl-2,3-dihydrobenzofuran-2-ones are important intermediates for the synthesis of the anti-cancer compound diazonamide A,[9] analgesics[10] and antidepressants.[10] 3-Alkyl-3-aryl-2,3-dihydrobenzofuran-2-one derivatives also possess antispasmodic,[11] antihypoxic,[12] and nootropic activity.[12] Previously reported synthetic routes to 2,2-disubstituted 2,3-dihydrobenzofuran-3-ones include (Scheme 4): (i) condensation of phenols with (a) 2-hydroxycarboxylic acids[13] or (b) acrylic esters;[14] (ii) hydrolysis – cyclization of 2-methoxyphenylacetonitriles in the presence of hydrobromic acid;[10] (iii) acid-catalyzed condensation of phenols with 2-oxo-carboxylic acids;[15] (iv) oxidative decyanation;[9a] e) alkylation of 3-aryl-2,3-dihydrobenzofuran-2-ones.[11–13,16]



Scheme 4

2,3-Dihydrobenzothiophen-3-ones are useful intermediates for the preparation of tetrahydro-1,2-benzothiazepin-5-ones and 3-vinyl-1,2-benzoisothiazoles.[17] Typical ring syntheses of 2,3-dihydrobenzothiophen-3-ones (Scheme 5) involve two steps: cyclization to a 2,3-dihydrobenzothiophen-3-one-1,1-dioxide followed by reduction of the sulfonyl group.[17b] These ring closures include (Scheme 5): a) the cyclization of *o*-methoxycarbonylphenyl methyl sulfones by base;[18] b) the cyclization of *α*-chlorocarbonyl sulfones under Lewis acid catalysis;[19] c) the cyclization of lithiated aryl alkyl sulfones with phosgene;[19] d) the cyclization of *o*-carboxyphenylsulfonylacetic acid with acetic anhydride in the presence of potassium acetate;[20] e) the cyclization of a benzoylacetic ester in oleum.[21] 2,3-Dihydrobenzothiophen-3-ones have also been obtained by ring transformation of 2-substituted 3-chlorothiochromen-4-ones (Scheme 2, route **f**).[22]



Scheme 5

No preparation of 3-alkyl-3-aryl-2,3-dihydrobenzothiophen-2-ones has been previously reported.

In summary, an efficient and simple route to 2,3-dihydrobenzofuran-2-ones **11** and 2,3-dihydrobenzothiophen-3-ones **16** has been developed from 1-(1-chloroalkyl)benzotriazoles and appropriate 2-hydroxybenzophenones and 2-sulfanylbenzophenones *via* the rearrangement of intermediates **10** and **15**.

Experimental Section

General Procedures. Melting points were determined on a hot-stage apparatus and are uncorrected. NMR spectra were recorded on a Varian Gemini 300 spectrometer in $CDCl_3$ with TMS as the internal standard for ^1H (300 MHz) or a solvent as the internal standard for ^{13}C (75 MHz). The elemental analyses were performed on a Carlo Erba EA–1108 instrument. DMF was dried over molecular sieves. THF was dried over sodium / benzophenone and used freshly distilled. LDA was used freshly prepared from *n*-butyllithium and di-*iso*-propylamine. Di-*iso*-propylamine was dried over calcium hydride. Column chromatography was conducted with silica gel 200-425 mesh.

X-Ray crystallography. Data were collected with a Siemens SMART CCD area detector, using graphite monochromatized MoKα radiation (λ = 0.71073 Å). The intensities were corrected for Lorentz and polarization effects and for absorption.[23] The structure was solved by direct methods using SHELXS[24] and refined on F^2, using all data, by full-matrix least-squares procedures using SHELXTL.[25] All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were included in calculated positions, with isotropic displacement parameters 1.2 times the isotropic equivalent of their carrier carbons. The crystal data and refinement details are listed along with the other data for the compound.

Phenyl(2-sulfanylphenyl)methanones (13a,c). were prepared according to the previously published procedure:[4] phenyl(2-sulfanylphenyl)methanone **13a**, white microcrystals from hexane, mp 50–52 °C (lit.[4] 51–52 °C) and (5-methyl-2-sulfanylphenyl)(phenyl)methanone **13c**, yellow prisms from benzene / hexane, mp 72–74 °C (lit.[4] 73–74 °C).

(4-Methoxy-2-sulfanylphenyl)(phenyl)methanone (13b). was prepared from 2-hydroxy-4-methoxy-benzophenone via Newman-Kwart[26] rearrangement of the corresponding dialkylthiocarbamate similarly to a published procedure[27] as yellow microcrystals, mp 72–74 °C (lit.[27] 74–76 °C).

General procedure for the preparation of *ortho*-substituted benzophenones 9a–h

To a stirred solution of 2-hydroxybenzophenone **7a–c** (4.0 mmol) and 1-(1-chloroalkyl)benzotriazole **8a–c** (5.0 mmol) in DMF (20 mL), K_2CO_3 (0.83 g, 6.0 mmol) was

added at room temperature and the reaction mixture was stirred for 4 h. The reaction mixture was poured into iced water and extracted with ethyl acetate. The extract was dried over magnesium sulfate and solvent was evaporated under vacuum. The residue was purified by column chromatography to give pure **9a–h**.

{2-[1-(1*H*-Benzotriazol-1-yl)ethoxy]phenyl}(phenyl)methanone (9a). White microcrystals from ethylacetate / hexanes (65%), mp 79–80 °C (lit.[3] 65–66 °C); ^{1}H NMR δ 8.02–7.98 (m, 1H), 7.74–7.71 (m, 2H), 7.61-7.56 (m, 1H), 7.44-7.39 (m, 3H), 7.33-7.26 (m, 4H), 7.08-6.92 (m, 3H), 1.80 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR δ 195.8, 153.6, 146.6, 137.7, 133.1, 131.9, 130.8, 130.2, 129.7, 129.6, 128.3, 127.7, 124.3, 122.8, 119.9, 115.4, 111.1, 85.2, 20.5.

{2-[1-(1*H*-Benzotriazol-1-yl)propoxy]phenyl}(phenyl)methanone (9b). White plates from ethyl acetate / hexanes (60%), mp 94–95 °C; ^{1}H NMR δ 8.02-7.98 (m, 1H), 7.74 (d, *J* = 7.3 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.45–7.27 (m, 7H), 7.08-6.97 (m, 2H), 6.73 (t, *J* = 6.9 Hz, 1H), 2.27-2.06 (m, 2H), 0.78 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR δ 195.8, 153.7, 146.6, 137.7, 133.1, 131.8, 130.9, 130.1, 129.7, 129.5, 128.4, 127.7, 124.3, 122.6, 119.9, 114.8, 111.2, 89.5, 27.6, 8.8. Anal. Calcd for $C_{22}H_{19}N_3O_2$: C, 73.93; H, 5.36; N, 11.76. Found: C, 73.71; H, 5.48; N, 11.82.

{2-[1-(1*H*-Benzotriazol-1-yl)butoxy]phenyl}(phenyl)methanone (9c). White solid from ethyl acetate / hexanes (70%), mp 85–87 °C (lit.[3] 85–87 °C); ^{1}H NMR δ 8.02-7.98 (m, 1H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.59 (t, *J* = 7.0 Hz, 1H), 7.45-7.26 (m, 7H), 7.07-6.97 (m, 2H), 6.81 (t, *J* = 6.8 Hz, 1H), 2.22-2.00 (m, 2H), 1.33-1.18 (m, 1H), 1.14-1.00 (m, 1H), 0.83 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR δ 195.9, 153.7, 146.6, 137.8, 133.1, 131.9, 130.9, 130.2, 129.7, 129.5, 128.4, 127.7, 124.3, 122.6, 119.9, 114.7, 111.3, 88.2, 36.1, 17.7, 13.2.

{2-[1-(1*H*-Benzotriazol-1-yl)ethoxy]-4-methoxyphenyl}(phenyl)methanone (9d). White plates from ethyl acetate / hexanes (75%), mp 138–140 °C (lit.[3] 138–140 °C); ^{1}H NMR δ 8.01 (d, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.50–7.28 (m, 6H), 6.95 (q, *J* = 6.2 Hz, 1H), 6.55 (d, *J* = 8.7 Hz, 1H), 6.40 (s, 1H), 3.65 (s, 3H), 1.80 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR δ 195.1, 162.9, 155.8, 146.6, 138.8, 132.5, 132.1, 131.0, 129.5, 128.2, 127.7, 124.3, 122.5, 119.9, 111.1, 108.4, 102.1, 85.3, 55.4, 20.4.

{2-[1-(1*H*-Benzotriazol-1-yl)propoxy]-4-methoxyphenyl}(phenyl)methanone (9e). White plates from ethyl acetate / hexanes (56%), mp 93–94 °C; ^{1}H NMR δ 8.02–7.98 (m, 1H), 7.74–7.71 (m, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.46–7.27 (m, 6H), 6.71 (t, *J* = 6.9 Hz, 1H), 6.54 (dd, *J* = 2.1 Hz, *J* = 8.5 Hz, 1H), 6.48 (d, *J* = 2.1 Hz, 1H), 3.68 (s, 3H), 2.25–2.07 (m, 2H), 0.78 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR δ 195.2, 162.9, 155.8, 146.6, 138.8, 132.6, 132.0, 131.0, 129.6, 128.2, 127.8, 124.4, 122.3, 120.0, 111.2, 108.1, 101.3, 89.6, 55.5, 27.5, 8.8. Anal. Calcd for $C_{23}H_{21}N_3O_3$: C, 71.30; H, 5.46; N, 10.85. Found: C, 71.41; H, 5.77; N, 11.17.

{2-[1-(1*H*-Benzotriazol-1-yl)butoxy]-4-methoxyphenyl}(phenyl)methanone (9f). Colorless prisms from methanol (72%), mp 76–77 °C; ^{1}H NMR δ 8.01 (d, *J* = 7.3 Hz, 1H), 7.73 (d, *J* = 7.3 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.48–7.29 (m, 6H), 6.80 (t, *J* = 6.9 Hz, 1H), 6.58–6.48 (m, 2H), 3.67 (s, 3H), 2.20–2.01 (m, 2H), 1.32–1.20 (m, 1H), 1.12–1.01 (m, 1H), 0.83 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR δ 195.1, 162.8, 155.7, 146.5, 138.8, 132.4, 131.9, 130.9, 129.4, 128.1, 127.7, 124.3,

122.2, 119.8, 111.2, 108.0, 101.2, 88.1, 55.3, 35.8, 17.6, 13.2. Anal. Calcd for $C_{24}H_{23}N_3O_3$: C, 71.80; H, 5.77; N, 10.47. Found: C, 72.04; H, 5.79; N, 10.73.

{2-[1-(1*H*-Benzotriazol-1-yl)ethoxy]-5-methylphenyl}(phenyl)methanone (9g). White solid from ethyl acetate / hexanes (77%), mp 80–81 °C (lit.[3] 80–81 °C); ^{1}H NMR δ 8.01–7.95 (m, 1H), 7.75–7.71 (m, 2H), 7.57 (t, *J* = 7.3 Hz, 1H), 7.44–7.26 (m, 5H), 7.11 (s, 1H), 7.08–7.02 (m, 1H), 6.92 (q, *J* = 6.2 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 2.23 (s, 3H), 1.78 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR δ 195.9, 151.4, 146.5, 137.6, 133.0, 132.5, 132.3, 130.8, 130.1, 130.0, 129.6, 128.2, 127.6, 124.2, 119.8, 115.7, 111.1, 85.5, 20.4, 20.3.

{2-[1-(1*H*-Benzotriazol-1-yl)propoxy]-5-methylphenyl}(phenyl)methanone (9h). White plates from ethyl acetate / hexanes (73%), mp 99–100 °C; ^{1}H NMR δ 8.01–7.97 (m, 1H), 7.74 (d, *J* = 7.3 Hz, 2H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.45–7.37 (m, 3H), 7.32–7.27 (m, 2H), 7.10–7.05 (m, 2H), 6.82 (d, *J* = 8.2 Hz, 1H), 6.67 (t, *J* = 6.9 Hz, 1H), 2.23–2.04 (m, 5H), 0.76 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR δ 196.0, 151.5, 146.6, 137.8, 133.1, 132.4, 132.3, 131.9, 130.0, 129.9, 129.7, 128.3, 127.6, 124.3, 120.0, 115.0, 111.2, 90.0, 27.6, 20.3, 8.8. Anal. Calcd for $C_{23}H_{21}N_3O_2$: C, 74.37; H, 5.70; N, 11.31. Found: C, 73.93; H, 5.84; N, 11.31.

General procedure for the preparation of 11a–h

To a stirred solution of the intermediate **9a–h** (1.0 mmol) in THF (10 mL), a solution of LDA (0.6 mL, 1.2 mmol, 2M) was added at –78 °C and the reaction mixture was stirred for 12 h at temperatures ranging from –78 °C to 0 °C. (In the case of **9a**, saturated aqueous ammonium chloride (20 mL) was added and the product **10a** was extracted with ethyl acetate; the extract was washed with water, dried and concentrated in vacuum. Intermediate **10a** was isolated using column chromatography on silica gel). Then a solution of anhydrous zinc bromide in THF (2.0–3.0 mL, 1M) was added followed by the addition of anhydrous 1,1,2,2-tetrachloroethane (30 mL) and THF was distilled off at normal pressure followed by reflux for 12–24 h (under nitrogen atmosphere). The reaction progress was monitored by TLC analysis. Upon completion, chloroform (20 mL) was added to the reaction mixture and it was washed with dilute hydrochloric acid and then with water. The organic layer was dried over magnesium sulfate and evaporated under vacuum. The product was purified by column chromatography to give **11a–h**.

2-(1*H*-Benzotriazol-1-yl)-2-methyl-3-phenyl-2,3-dihydro-1-benzofuran-3-ol (10a). White plates from ethyl acetate (82%), mp 179–181 °C; ^{1}H NMR δ 7.98 (d, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.50-7.44 (m, 1H), 7.39-7.28 (m, 8H), 7.18-7.11 (m, 2H), 3.03 (s, 1H), 1.77 (s, 3H); ^{13}C NMR δ 157.2, 145.9, 139.2, 134.1, 131.5, 130.5, 128.6, 128.3, 127.7, 127.6, 126.2, 123.9, 122.9, 119.7, 113.4, 111.1, 106.0, 86.7, 25.4. Anal. Calcd for $C_{21}H_{17}N_3O_2$: C, 73.45; H, 4.99; N, 12.24. Found: C, 73.53; H, 5.11; N, 12.31.

3-Methyl-3-phenyl-1-benzofuran-2(3*H*)-one (11a). Colorless oil[5b,28] (70%); ^{1}H NMR δ 7.30–7.19 (m, 6H), 7.16–7.09 (m, 3H), 1.81 (s, 3H); ^{13}C NMR δ 178.6, 152.7, 139.4, 132.6, 129.0, 128.7, 127.8, 126.4, 124.5, 124.5, 110.9, 50.8, 24.7.

3-Ethyl-3-phenyl-1-benzofuran-2(3*H*)-one (11b). Yellow oil (50%); ^{1}H NMR δ 7.42–7.15 (m, 9H), 2.56–2.44 (m, 1H), 2.35–2.21 (m, 1H), 0.79 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR δ 178.1, 153.4,

138.8, 130.0, 129.0, 128.8, 127.8, 126.7, 125.1, 124.3, 110.9, 56.4, 32.0, 9.3. HRMS Calcd for $C_{16}H_{14}O_2$ [M]: 238.0994; Found: 238.0995.

3-Phenyl-3-propyl-1-benzofuran-2(3*H*)-one (11c). Yellow oil (41%); ^{1}H NMR δ 7.41–7.16 (m, 9H), 2.47–2.37 (m, 1H), 2.26–2.15 (m, 1H), 1.35–1.16 (m, 1H), 1.08–0.90 (m, 1H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR δ 178.3, 153.3, 139.0, 130.4, 129.0, 128.8, 127.8, 126.7, 125.1, 124.4, 111.0, 55.9, 41.1, 18.3, 14.0. HRMS Calcd for $C_{17}H_{16}O_2$ [M]: 252.1150; Found: 252.1151.

6-Methoxy-3-methyl-3-phenyl-1-benzofuran-2(3*H*)-one (11d). Yellow oil (41%); ^{1}H NMR δ 7.36–7.26 (m, 5H), 7.12 (d, *J* = 8.2 Hz, 1H), 6.77–6.72 (m, 2H), 3.84 (s, 3H), 1.88 (s, 3H); ^{13}C NMR δ 25.1, 50.6, 55.7, 97.6, 110.3, 124.2, 125.0, 126.5, 127.7, 128.7, 139.9, 153.7, 160.5, 179.0. HRMS Calcd for $C_{16}H_{14}O_3$ [M]: 254.0942; Found: 254.0929.

3-Ethyl-6-methoxy-3-phenyl-1-benzofuran-2(3*H*)-one (11e). White plates from ethyl acetate / hexanes (43%), mp 88–89 °C; ^{1}H NMR δ 7.41–7.25 (m, 5H), 7.15 (d, *J* = 9.1 Hz, 1H), 6.80–6.76 (m, 2H), 3.85 (s, 3H), 2.50–2.40 (m, 1H), 2.30–2.17 (m, 1H), 0.79 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR δ 178.5, 160.5, 154.3, 139.1, 128.7, 127.7, 126.8, 125.6, 121.4, 110.2, 97.4, 56.2, 55.6, 32.1, 9.3. Anal. Calcd for $C_{17}H_{16}O_3$: C, 76.10; H, 6.01; Found: C, 76.03; H, 6.19.

6-Methoxy-3-phenyl-3-propyl-1-benzofuran-2(3*H*)-one (11f). White plates from ethyl acetate / hexanes (41%), mp 86–87 °C; ^{1}H NMR δ 7.41–7.25 (m, 5H), 7.16 (d, *J* = 8.9 Hz, 1H), 6.79–6.75 (m, 2H), 3.84 (s, 3H), 2.44–2.33 (m, 1H), 2.21–2.11 (m, 1H), 1.28–1.16 (m, 1H), 1.10–0.97 (m, 1H), 0.88 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR δ 178.6, 160.5, 154.2, 139.3, 128.7, 127.7, 126.7, 125.6, 121.7, 110.2, 97.4, 55.7, 55.5, 41.2, 18.3, 14.0. Anal. Calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43; Found: C, 76.44; H, 6.70.

3,5-Dimethyl-3-phenyl-1-benzofuran-2(3*H*)-one (11g). Yellow oil (41%); ^{1}H NMR δ 7.34–7.28 (m, 5H), 7.17–7.11 (m, 1H), 7.07 (d, *J* = 8.2 Hz, 1H), 7.01 (br s, 1H), 2.35 (s, 3H), 1.89 (s, 3H); ^{13}C NMR δ 179.1, 150.6, 139.6, 134.2, 132.6, 129.4, 128.8, 127.8, 126.5, 124.9, 110.6, 51.0, 24.7, 21.2. HRMS Calcd for $C_{16}H_{14}O_2$ [M]: 238.0994; Found: 238.0991.

3-Ethyl-5-methyl-3-phenyl-1-benzofuran-2(3*H*)-one (11h). Yellow oil (43%); ^{1}H NMR δ 7.41–7.25 (m, 5H), 7.15 (d, *J* = 8.1 Hz, 1H), 7.06 (d, *J* = 8.2 Hz, 2H), 2.55–2.18 (m, 5H), 0.79 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR δ 178.5, 151.3, 139.0, 134.0, 129.9, 129.4, 128.7, 127.7, 126.7, 125.4, 110.5, 56.6, 31.8, 21.2, 9.3. HRMS Calcd for $C_{17}H_{16}O_2$ $[M]^+$: 252.1150; Found: 252.1151.

The rearrangement of zinc reagent of 10a in THF using a sealed tube. A solution of butyllithium in hexanes (0.7 mL, 1.12 mmol, 1.6 M) was added to a stirred solution of **10a** (0.34 g, 1 mmol) in THF (10 mL) at –78 °C followed by the addition of a solution of anhydrous zinc bromide in THF (2.5 mL, 2.5 mmol, 1M) under a nitrogen atmosphere. The reaction mixture (slurry) was allowed to warm to 20–25 °C and was transferred to a sealed tube. The reaction mixture was stirred at 150–155 °C for 1 h. Then, the mixture was cooled down to 20–25 °C and filtered. The filtrate was concentrated in vacuum and the residue was purified by gradient column chromatography on silica gel using ethyl acetate / hexanes (1/20) to give **11a** (0.21 g, 93 %) as a colorless oil.[5b,28]

The preparation of 2-methyl-3-phenylbenzofuran (12). A mixture of 2-benzotriazolyl-2-methyl-3-phenyl-2,3-dihydrobenzofuran-3-ol **10a** (0.34 g, 1 mmol) with anhydrous zinc bromide (0.9 g, 4 mmol; additionally dried by heating at 220–225 °C for 1 h in vacuum) in THF (10 mL) was stirred at 150–155 °C for 30 min (the formation of a slurry was observed at 155 °C). Then, the reaction mixture was cooled down to 20–25 °C, filtered and concentrated in vacuum. The residue was purified by column chromatography on silica gel using hexanes to give **12** (135 mg, 65 %) as a colorless oil.[29] ^{1}H NMR δ 7.59–7.55 (m, 1H), 7.52–7.43 (m, 5H), 7.38–7.32 (m, 1H), 7.28–7.18 (m, 2H), 2.53 (s, 3H); ^{13}C NMR δ 154.0, 151.2, 132.8, 128.9, 128.7, 126.9, 123.5, 122.6, 119.3, 116.9, 110.7, 12.8.

General procedure for the preparation of *ortho*-substituted benzophenones 14a–h

To a stirred solution of **13a–c** (4.0 mmol) and 1-(1-chloroalkyl)benzotriazole **8a–c** (5.0 mmol) in DMF (20 mL) under a nitrogen atmosphere, K_2CO_3 (0.83 g, 6.0 mmol) was added at room temperature and the reaction mixture was stirred for 4 h. After starting material **13** had disappeared, iced water was added slowly and a product was extracted with ethyl acetate. The extract was dried over magnesium sulfate and evaporated under vacuum. The residue was purified by column chromatography using ethyl acetate / hexanes mixture to give pure **14a–h**.

(2-{[1-(1*H*-Benzotriazol-1-yl)ethyl]sulfanyl}phenyl)(phenyl)methanone (14a). White microcrystals from ethyl acetate / hexanes (93%), mp 125–126 °C (lit.[4] 135–136 °C); ^{1}H NMR δ 8.00–7.94 (m, 1H), 7.64–7.54 (m, 3H), 7.52–7.46 (m, 1H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.26–7.20 (m, 4H), 7.14–7.04 (m, 1H), 7.00–6.97 (m, 1H), 6.46 (q, *J* = 7.0 Hz, 1H), 2.03 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR δ 196.6, 146.0, 143.5, 136.7, 135.3, 133.4, 131.8, 130.3, 130.1, 130.0, 129.8, 128.4, 128.3, 127.0, 123.8, 119.8, 110.7, 62.9, 20.5.

(2-{[1-(1*H*-Benzotriazol-1-yl)propyl]sulfanyl}phenyl)(phenyl)methanone (14b). White microcrystals from methanol (95%), mp 114–115 °C; ^{1}H NMR δ 7.99-7.95 (m, 1H), 7.62-7.51 (m, 4H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.28-7.23 (m, 4H), 7.14-7.08 (m, 1H), 7.00 (d, *J* = 7.5 Hz, 1H), 6.22-6.16 (m, 1H), 2.50-2.25 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR δ 196.5, 146.1, 143.3, 136.8, 134.9, 133.3, 131.7, 130.3, 129.9, 129.8, 128.4, 128.3, 128.1, 127.0, 123.9, 119.8, 110.8, 69.1, 27.7, 11.1. Anal. Calcd for $C_{22}H_{19}N_3OS$: C, 70.75; H, 5.13; N, 11.25. Found: C, 70.83; H, 5.01; N, 11.24.

(2-{[1-(1*H*-Benzotriazol-1-yl)ethyl]sulfanyl}-4-methoxyphenyl)(phenyl)methanone (14c). White prisms from ethyl acetate / hexanes (98%), mp 118-119 °C; ^{1}H NMR δ 7.99-7.97 (m, 1H), 7.62-7.52 (m, 4H), 7.42-7.37 (m, 2H), 7.28-7.22 (m, 3H), 6.68-6.59 (m, 3H), 3.57 (s, 3H), 2.06 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR δ 195.8, 161.0, 146.3, 137.6, 134.5, 133.4, 132.8, 131.6, 130.0, 128.3, 127.1, 124.0, 119.8, 117.5, 114.0, 111.1, 100.2, 62.4, 55.4, 20.6. Anal. Calcd for $C_{22}H_{19}N_3O_2S$: C, 67.84; H, 4.92; N, 10.79. Found: C, 68.07; H, 4.82; N, 10.92.

(2-{[1-(1*H*-Benzotriazol-1-yl)propyl]sulfanyl}-4-methoxyphenyl)(phenyl)methanone (14d). White microcrystals from ethyl acetate / hexanes (89%), mp 114-115 °C; ^{1}H NMR δ 8.00-7.97 (m, 1H), 7.67-7.52 (m, 4H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.29-7.23 (m, 3H), 6.67-6.65 (m, 2H), 6.36 (dd, *J* = 8.6 , 6.6 Hz, 1H), 3.60 (s, 3H), 2.45-2.35 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR δ

195.8, 161.1, 146.4, 137.7, 135.0, 133.0, 132.7, 131.8, 131.6, 130.0, 128.3, 127.1, 124.0, 119.8, 116.9, 113.7, 111.2, 68.4, 55.4, 27.8, 11.2. Anal. Calcd for $C_{23}H_{21}N_3O_2S$: C, 68.46; H, 5.25; N, 10.41. Found: C, 68.49; H, 5.22; N, 10.49.

(2-{[1-(1*H*-Benzotriazol-1-yl)ethyl]sulfanyl}-5-methylphenyl)(phenyl)methanone (14e). White prisms from ethyl acetate / hexanes (43%), mp 112-113 °C (lit.[4] 109-111 °C); ^{1}H NMR δ 8.00-7.95 (m, 1H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.60-7.49 (m, 2H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.25 (d, *J* = 7.7 Hz, 2H), 7.05 (s, 1H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.37 (q, *J* = 7.0, 1H), 2.25 (s, 3H), 2.00 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR δ 196.5, 145.8, 143.8, 138.8, 136.6, 135.5, 133.2, 131.5, 130.8, 129.7, 128.5, 128.2, 126.7, 125.6, 123.6, 119.5, 110.6, 62.9, 20.8, 20.2.

(2-{[1-(1*H*-Benzotriazol-1-yl)propyl]sulfanyl}-5-methylphenyl)(phenyl)methanone (14f). Brown microcrystals from ethyl acetate / hexanes (76%), mp 107-108 °C; ^{1}H NMR δ 7.99-7.96 (m, 1H), 7.63-7.51 (m, 4H), 7.42-7.36 (m, 2H), 7.29-7.22 (m, 2H), 7.04 (s, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 6.13-6.07 (m, 1H), 2.44-2.20 (m, 2H), 2.24 (s, 3H), 0.86 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR δ 196.7, 146.2, 143.8, 138.8, 136.9, 135.4, 133.3, 131.8, 131.0, 129.9, 128.8, 128.4, 126.9, 125.9, 123.8, 119.8, 110.9, 69.5, 27.6, 20.9, 11.1. Anal. Calcd for $C_{23}H_{21}N_3OS$: C, 71.29; H, 5.46; N, 10.84. Found: C, 71.47; H, 5.43; N, 11.22.

(2-{[1-(1*H*-Benzotriazol-1-yl)butyl]sulfanyl}phenyl)(phenyl)methanone (14g). Colorless prisms from ethyl acetate / hexanes (62%), mp 97-98 °C; ^{1}H NMR δ 7.99-7.95 (m, 1H), 7.63-7.59 (m, 2H), 7.56-5.50 (m, 2H), 7.42-7.37 (m, 2H), 7.28-7.19 (m, 4H), 7.12-7.06 (m, 1H), 6.98 (d, *J* = 7.7 Hz, 1H), 6.29 (dd, *J* = 9.1, 6.3 Hz, 1H), 2.45-2.17 (m, 2H), 1.36-1.14 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR δ 196.5, 146.1, 143.3, 136.8, 134.9, 133.3, 131.8, 130.2, 130.0, 129.8, 128.4, 128.3, 128.1, 127.0, 123.8, 119.8, 110.8, 67.4, 36.1, 19.7, 13.1. Anal. Calcd for $C_{23}H_{21}N_3OS$: C, 71.29; H, 5.46; N, 10.84. Found: C, 70.97; H, 5.35; N, 10.85.

(2-{[1-(1*H*-Benzotriazol-1-yl)butyl]sulfanyl}-5-methylphenyl)(phenyl)methanone (14h). White microcrystals from petroleum ether / ethyl acetate (86%), mp 71-71 °C; ^{1}H NMR δ 7.99-7.96 (m, 1H), 7.63 (d, *J* = 7.42 Hz, 2H), 7.59-7.51 (m, 2H), 7.40 (t, *J* = 7.7 Hz, 2H), 7.28-7.22 (m, 2H), 7.04 (s, 1H), 6.87 (d, *J* = 8.0, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.20 (dd, *J* = 9.1 Hz, 6.2 Hz, 1H), 2.39-2.30 (m, 1H), 2.26-2.16 (m, 1H), 2.23 (s, 3H), 1.36-1.10 (m, 2H), 0.85 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR δ 196.7, 146.1, 143.8, 138.8, 136.9, 135.4, 133.3, 131.8, 131.0, 129.9, 128.7, 128.4, 126.9, 125.9, 123.8, 119.8, 110.9, 67.7, 36.0, 20.9, 19.7, 13.1. Anal. Calcd for $C_{24}H_{23}N_3OS$: C, 71.79; H, 5.77; N, 10.46. Found: C, 71.55; H, 5.74; N, 10.45.

General procedure for the preparation of 16a–f

To a stirred solution of the intermediate **14a–f** (1.0 mmol) in THF (10 mL), LDA (0.6 mL, 1.2 mmol, 2M) was added at -78 °C and the reaction mixture was stirred for 12 h at temperatures ranging from -78 °C to 0 °C (under a nitrogen atmosphere). Then, saturated aqueous ammonium chloride was added and **15a–f** was extracted with ethyl acetate. The extract was washed with water, dried over magnesium sulfate and evaporated under vacuum to dryness (in the case of **14d**, the intermediate **15c,d** was purified by column chromatography on silica gel and characterized). The mixture of crude **15a–f** with anhydrous zinc bromide (0.68 g, 3.0 mmol) in

1,1,2,2-tetrachloroethane (30 mL) was heated up to 100–110 °C for 0.3-2 h. The reaction was monitored by TLC and upon disappearance of starting material was cooled down to 20–25 °C. Chloroform (20 mL) was added to the reaction mixture. The mixture was washed with dilute hydrochloric acid (5%, 30 mL), and then with water. The organic layer was dried over magnesium sulfate and evaporated under vacuum. The residue was purified by column chromatography using mixture of hexanes / ethyl acetate as an eluent to give the corresponding **16a–f**.

(2*R,3*R**)-2-(1*H*-Benzotriazol-1-yl)-6-methoxy-2-methyl-3-phenyl-2,3-dihydro-1-benzothiophen-3-ol (15c').** Yellow microcrystals from ethyl acetate / hexanes (35%), mp 192-193 °C; ^{1}H NMR δ 7.80–7.77 (m, 1H), 7.29–7.26 (m, 1H), 7.15–7.12 (m, 2H), 6.99–6.95 (m, 3H), 6.86–6.79 (m, 4H), 6.68 (dd, *J* = 8.5, 2.3 Hz, 1H), 3.87 (s, 3H), 3.05 (s, 1H), 2.58 (s, 3H); 13C NMR δ 161.6, 146.2, 141.8, 137.7, 134.5, 132.9, 128.2, 127.7, 127.4, 126.8, 126.5, 123.1, 119.6, 112.8, 111.9, 107.6, 90.2, 87.5, 55.6, 23.5. Anal. Calcd for $C_{22}H_{19}N_3O_2S$: C, 67.84; H, 4.92; N, 10.79. Found: C, 67.60; H, 4.88; N, 10.79.

(2*R,3*S**)-2-(1*H*-Benzotriazol-1-yl)-6-methoxy-2-methyl-3-phenyl-2,3-dihydro-1-benzothiophen-3-ol (15c").** White microcrystals from ethyl acetate / hexanes (28%), mp 160-161 °C; ^{1}H NMR δ 8.01 (d, *J* = 7.8 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.43–7.18 (m, 8H), 6.82 (d, *J* = 1.8 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 4.21 (s, 1H), 3.81 (s, 3H), 2.04 (s, 3H); ^{13}C NMR δ 161.1, 146.1, 139.4, 138.5, 134.6, 133.8, 128.4, 128.1, 127.8, 127.3, 127.0, 123.9, 120.0, 114.5, 112.1, 108.3, 90.3, 86.3, 55.5, 26.1. Anal. Calcd for $C_{22}H_{19}N_3O_2S$: C, 67.84; H, 4.92; N, 10.79. Found: C, 68.07; H, 4.89; N, 10.84.

2-(1*H*-Benzotriazol-1-yl)-6-methoxy-2-ethyl-3-phenyl-2,3-dihydro-1-benzothiophen-3-ol (15d). White microcrystals from ethyl acetate / hexanes (74%), mp 152-153 °C; ^{1}H NMR δ 7.81-7.78 (m, 1H), 7.48-7.45 (m, 1H), 7.20-7.15 (m, 2H), 6.98-6.92 (m, 3H), 6.83-6.82 (m, 4H), 6.65 (dd, *J* = 8.5, 2.3 Hz, 1H), 3.86 (s, 3H), 3.40-3.30 (m, 1H), 3.24 (s, 1H), 2.75-2.67 (m, 1H), 0.91 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR δ 161.4, 146.2, 140.7, 138.3, 135.1, 133.2, 128.0, 127.3, 127.2, 126.9, 126.4, 123.1, 119.5, 112.8, 111.8, 107.7, 93.2, 90.5, 55.6, 27.5, 10.1. Anal. Calcd for $C_{23}H_{21}N_3O_2S$: C, 68.46; H, 5.25; N, 10.41. Found: C, 68.23; H, 5.21; N, 10.45.

2-Methyl-2-phenyl-1-benzothiophen-3(2*H*)-one (16a). Yellow microcrystals from ethyl acetate / hexanes (44%), mp 84–85 °C (lit.[17b] 95–97 °C); ^{1}H NMR δ 7.80 (d, *J* = 7.7 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 7.5 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.33–7.20 (m, 4H), 2.00 (s, 3H); ^{13}C NMR δ 203.2, 151.8, 140.2, 136.1, 128.9, 128.6, 127.8, 127.7, 126.6, 124.9, 123.8, 63.7, 25.5. Anal. Calcd for $C_{15}H_{12}OS$: C, 74.97; H, 5.03. Found: C, 75.30; H, 4.92.

2-Ethyl-2-phenyl-1-benzothiophen-3(2*H*)-one (16b). Yellow oil (75%); ^{1}H NMR δ 7.75 (d, *J* = 7.7 Hz, 1H), 7.59-7.52 (m, 3H), 7.41 (d, *J* = 7.9 Hz, 1H), 7.33-7.17 (m, 4H), 2.50-2.29 (m, 2H), 0.97 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR δ 202.7, 151.9, 139.1, 135.9, 130.1, 128.5, 127.7, 127.3, 127.1, 124.8, 123.8, 70.5, 32.4, 9.8; ν_{max}(KBr) 1701 cm^{-1} (C=O); Anal. Calcd for $C_{16}H_{14}OS$: C, 75.56; H, 5.55. Found: C, 75.49; H, 5.55.

6-Methoxy-2-methyl-2-phenyl-1-benzothiophen-3(2*H*)-one (16c). Yellow oil (43%); ^{1}H NMR δ 7.73 (d, *J* = 8.7 Hz, 1H), 7.45-7.42 (m, 2H), 7.33-7.25 (m, 3H), 6.84 (d, *J* = 2.0 Hz, 1H), 6.77

(dd, *J* = 2.0 Hz, *J* = 8.7 Hz, 1H),3.88 (s, 3H), 2.00 (s, 3H); ^{13}C NMR δ 201.2, 166.4, 154.7, 140.5, 129.1, 128.6, 127.7, 126.6, 122.1, 113.6, 106.7, 64.1, 55.8, 25.5; ν_{max}(KBr) 1694 cm^{-1} (C=O). Anal. Calcd for $C_{16}H_{14}O_2S$: C, 71.08; H, 5.22; Found: C, 70.81; H, 5.25.

2-Ethyl-6-methoxy-2-phenyl-1-benzothiophen-3(2*H*)-one (16d). Green oil (37%); ^{1}H NMR δ 7.68 (d, *J* = 8.6 Hz, 1H), 7.57-7.81 (m, 1H), 7.33-7.22 (m, 3H), 6.86 (d, *J* = 2.0 Hz, 1H), 6.74 (dd, *J* = 8.6, 2.0 Hz, 1H), 3.87 (s, 3H), 2.45-2.31 (m, 2H), 0.97 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR δ 200.6, 166.2, 154.9, 139.6, 128.8, 128.5, 127.6, 127.1, 123.5, 113.4, 106.7, 70.9, 55.8, 32.2, 9.8. Anal. Calcd for $C_{17}H_{16}O_2S$: C, 71.80; H, 5.67; Found: C, 72.01; H, 5.75.

2,5-Dimethyl-2-phenyl-1-benzothiophen-3(2*H*)-one (16e). Yellow microcrystals from ethyl acetate / hexanes (40%), mp 82-83 ºC; ^{1}H NMR δ 7.60 (s, 1H), 7.44-7.37 (m, 3H), 7.31-7.22 (m, 4H), 2.34 (s, 3H), 1.98 (s, 3H); ^{13}C NMR δ 203.1, 148.6, 140.3, 137.4, 134.9, 128.9, 128.5, 127.7, 127.5, 126.5, 123.4, 63.9, 25.5, 20.6. Anal. Calcd for $C_{16}H_{14}OS$: C, 75.55; H, 5.55; Found: C, 75.93; H, 5.69.

2-Ethyl-2-phenyl-5-methyl-1-benzothiophen-3(2*H*)-one (16f). Yellow oil (58%); ^{1}H NMR δ 7.57-7.54 (m, 3H), 7.40-7.36 (m, 1H), 7.33-7.24 (m, 4H), 2.46-2.30 (m, 5H), 0.96 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR δ 202.7, 148.9, 139.4, 137.2, 134.8, 130.3, 128.5, 127.6, 127.2, 127.1, 123.5, 70.8, 32.3, 20.7, 9.8. Anal. Calcd for $C_{17}H_{16}OS$: C, 76.08; H, 6.01; Found: C, 76.32; H, 6.51.

General procedure for the preparation of benzothiophenes 18g,h

By following the same procedure described for **16a–f**, benzothiophenes **18g,h** were prepared from **14g,h** respectively.

5-Methyl-3-phenyl-2-(1-propenyl)-1-benzothiophene (18g). Yellow oil (20%); ^{1}H NMR δ 7.64 (d, *J* = 8.0 Hz, 1H), 7.53-7.47 (m, 2H), 7.43-7.38 (m, 3H), 7.27 (s, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 6.52 (dq, *J* = 15.5, 1.5 Hz, 1H), 6.20 (dq, *J* = 15.5, 6.7 Hz, 1H), 2.36 (m, 3H), 1.83 (dd, *J* = 6.7, 1.5 Hz, 3H); ^{13}C NMR δ 140.8, 138.9, 135.1, 134.7, 134.0, 133.2, 130.4, 128.7, 128.5, 127.4, 126.3, 124.1, 122.7, 121.7, 21.4, 18.6. HRMS Calcd for $C_{18}H_{16}S$ [M]: 264.0972; Found: 264.0969.

3-Phenyl-2-(1-propenyl)-1-benzothiophene (18h). Orange oil (43%); ^{1}H NMR δ 7.77-7.75 (m, 1H), 7.52-7.23 (m, 7H), 6.54 (dq, *J* = 15.5, 1.6 Hz, 1H), 6.21 (dq, *J* = 15.5, 6.6 Hz, 1H), 1.83 (dd, *J* = 6.6 Hz, *J* = 1.6 Hz, 3H); ^{13}C NMR δ 140.6, 138.7, 137.6, 135.0, 133.5, 130.4, 129.0, 128.5, 127.5, 124.6, 124.3, 124.0, 122.8, 122.0, 18.7. Anal. Calcd for $C_{17}H_{14}S$: C, 81.56; H, 5.64; Found: C, 81.28; H, 5.94.

General procedure for the preparation of 16b,c,g and 17b,c,g

To a stirred solution of the intermediate **14b,c,g** (1.0 mmol) in THF (10 mL), LDA (0.6 mL, 1.2 mmol, 2M) was added at -78 °C and the reaction mixture was stirred for 12 h at temperatures ranging from -78 °C to 0 °C (under nitrogen atmosphere). A solution of anhydrous zinc bromide in THF (1M, 3 mL, 3.0 mmol) was added to the reaction mixture. The reaction mixture was transferred to a sealed tube and stirred at 90–100 °C for 1-2 h (a suspension of benzotriazole / zinc bromide usually appears at 80 °C). The reaction mixture was cooled down to 20–25 °C and

filtered. The filtrate was concentrated in vacuum. The residue was subjected to column chromatography using a mixture of hexanes as an eluent to give corresponding **16b,c,g** and **17b,c,g**.

2-Ethyl-2-phenyl-1-benzothiophen-3(2*H*)-one (16b). Yellow oil (20%); identical with compound **16b** prepared following the procedure for **16a–f**.

3-Ethyl-3-phenyl-1-benzothiophen-2(3*H*)-one (17b). Yellow oil (20%); ^{1}H NMR δ 7.44 (d, *J* = 7.7 Hz, 1H), 7.36–7.22 (m, 7H), 7.05 (dd, *J* = 7.4, 1.0 Hz, 1H), 2.74–2.65 (m, 1H), 2.26–2.14 (m, 1H), 0.79 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR δ 207.4, 140.7, 140.6, 136.0, 128.6, 128.4, 127.6, 126.9, 126.5, 125.8, 123.0, 68.1, 31.5, 8.8; ν_{max}(KBr) 1712 cm^{-1} (C=O). Anal. Calcd for $C_{16}H_{14}OS$: C, 75.56; H, 5.55. Found: C, 75.35; H, 5.66.

6-Methoxy-2-methyl-2-phenyl-1-benzothiophen-3(2*H*)-one (16c). Yellow oil (20%); identical with compound **16c** prepared following the procedure for **16a–f**.

6-Methoxy-3-methyl-3-phenyl-1-benzothiophen-2(3*H*)-one (17c). Colorless needles from hexanes (30%), mp 87-88 °C; ^{1}H NMR δ 7.33–7.20 (m, 5H), 6.98 (t, *J* = 2.5 Hz, 1H), 6.95 (s, 1H), 6.78 (dd, *J* = 8.5, 2.5 Hz, 1H), 3.83 (s, 3H), 1.85 (s, 3H); ^{13}C NMR δ 207.4, 159.6, 141.1, 135.4, 134.9, 128.6, 127.6, 126.7, 126.2, 112.9, 108.3, 62.5, 55.5, 24.7; ν_{max}(KBr) 1707 cm^{-1} (C=O). Anal. Calcd for $C_{16}H_{14}O_2S$: C, 71.08; H, 5.22; Found: C, 71.03; H, 5.35.

Crystal data for 17c: $C_{16}H_{14}O_2S$, MW 270.33, triclinic, space group P-1, *a* = 8.3006(10), *b* = 8.5277(11), *c* = 11.2064(14) Å, α = 73.496(2), β = 70.336(2),γ = 62.764(2) °, V = 656.1(1) Å^3, F(000) = 284, Z = 2, T = -105 ºC, μ(MoKα) = 0.241 mm^{-1}, D_{calcd} = 1.368 g.cm^{-3}, $2\theta_{max}$ 53º (CCD area detector, MoKα radiation), GOF = 1.060, wR(F^2) = 0.0907 (all 2624 data), R = 0.0328 (2174 data with I > 2σI).

5-Methyl-2-phenyl-2-propyl-1-benzothiophen-3(2H)-one (16g). Orange oil (31%); ^{1}H NMR δ 7.64–7.55 (m, 3H), 7.39 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.33–7.24 (m, 4H), 2.44–2.22 (m, 4H), 1.53–1.43 (m, 1H), 1.32–1.21 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR δ 202.7, 148.9, 137.2, 134.8, 130.5, 130.2, 128.5, 127.6, 127.3, 127.1, 123.5, 70.1, 41.5, 20.7, 18.8, 14.1; ν_{max}(KBr) 1696 cm^{-1} (C=O). Anal. Calcd for $C_{18}H_{18}OS$: C, 76.55; H, 6.42; Found: C, 76.23; H, 6.72.

5-Methyl-3-phenyl-3-propyl-1-benzothiophen-2(3H)-one (17g). White microcrystals from ethyl acetate / hexanes (16%), mp 64-65 °C; ^{1}H NMR δ 7.33–7.20 (m, 6H), 7.15–7.13 (m, 1H), 6.86 (s, 1H), 2.65–2.55 (m, 1H), 2.32 (s, 3H), 2.17–2.07 (m, 1H), 1.35–1.22 (m, 1H), 1.07–0.94 (m, 1H), 0.89 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR δ 208.0, 141.1, 136.5, 132.3, 129.3, 128.6, 127.6, 126.9, 126.3, 122.7, 67.7, 40.6, 21.3, 17.7, 14.3; ν_{max}(KBr) 1711 cm^{-1} (C=O). Anal. Calcd for $C_{18}H_{18}OS$: C, 76.55; H, 6.42; Found: C, 76.43; H, 6.68.

Supplementary Information Available: Crystallographic data for compound **17c**. This material is available free of charge via the Internet at http://www.arkat-usa.org/. See Page 147

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