Synthesis of 2-Aryl-2,3-dihydro-3-sulfanyl-1*H*-isoindol-1-ones by *Pummerer*-Type Cyclization of *N*-Aryl-2-(sulfinylmethyl)benzamides

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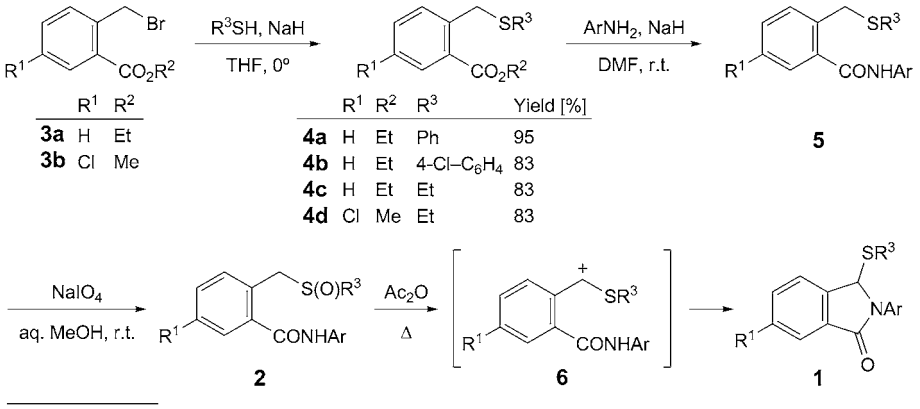
An efficient method for the synthesis of 2-aryl-2,3-dihydro-3-sulfanyl-1*H*-isoindol-1-ones **1** *via* *Pummerer*-type cyclization of *N*-aryl-2-(sulfinylmethyl)benzamides **2** is described. Thus, treatment of these sulfinyl-benzamides **2**, easily prepared from 2-(bromomethyl)benzoates **3** in three steps, with Ac_2O at *ca.* 100° resulted in the formation of the desired isoindolones **1** in generally good yields.

Introduction. – The dihydro-isoindol-1-one skeleton is commonly found in several biologically important compounds [1]. Therefore, our [2] and other research groups [3] have recently reported new and efficient methods for the preparation of dihydro-isoindol-1-ones. Some 3-sulfanylated dihydro-isoindol-1-ones have also been reported to display biological activities, *e.g.*, DNA gyrase inhibitory activity [4]. They have been utilized as key building blocks in the synthesis of biologically active compounds with more complex structures [5a][5b]. The most common route to access 3-sulfanylated dihydro-isoindol-1-ones involves reduction of phthalimide derivatives, followed by *Lewis* acid-mediated replacement of the OH group of the resulting hydroxy lactam intermediates with thiols [5]. Therefore, we were interested in investigating a more efficient approach for the preparation of this class of dihydro-isoindol-1-ones. We report here an efficient synthesis of 2-aryl-2,3-dihydro-3-sulfanyl-1*H*-isoindol-1-ones **1** *via* *Pummerer*-type cyclization of *N*-aryl-2-(sulfinylmethyl)benzamides **2**.

Results and Discussion. – The preparation of **1** was conducted as illustrated in the *Scheme*. Compounds **2** were prepared from 2-(bromomethyl)benzoates **3** in a three-step sequence. Thus, compounds **3** were treated with the respective thiolates, generated from thiols and NaH, in THF, to afford 2-(sulfanylmethyl)benzoates **4**. These esters were allowed to react with aromatic amines in DMF in the presence of NaH to afford *N*-aryl-2-(sulfanylmethyl)benzamides **5**. Oxidation of **5** was carried out with $NaIO_4$ in aqueous MeOH to provide **2**. Each of the steps could be carried out at 0° or room temperature and in relatively good yields as compiled in *Table 1*. Attempts to convert **4** into the corresponding amides using aliphatic amines under the same conditions failed; the reaction afforded rather intractable mixtures of products.

Having synthesized the precursor **2**, the conversion of these compounds to the desired products **1** *via* the *Pummerer*-type intermediate **6** was then carried out. The reactions were conveniently performed by simply heating solutions of **2** in Ac_2O at the

Scheme[a])



[a]) For R^1, R^3, and Ar, see *Tables 1* and *2*.

Table 1. *Preparation of 2-(Sulfinylmethyl)benzamides* **2**

Entry	**4**	Ar	**5**	Yield[a]) [%]	**2**	Yield[a]) [%]
1	**4a**	Ph	**5a**	70	**2a**	77
2	**4a**	4-Me–C_6H_4	**5b**	67	**2b**	78
3	**4a**	4-MeO–C_6H_4	**5c**	70	**2c**	79
4	**4b**	Ph	**5d**	66	**2d**	79
5	**4b**	4-Cl–C_6H_4	**5e**	42	**2e**	83
6	**4c**	Ph	**5f**	66	**2f**	78
7	**4c**	3,5-Me_2–C_6H_3	**5g**	68	**2g**	83
8	**4c**	3-MeO–C_6H_4	**5h**	72	**2h**	67
9	**4d**	Ph	**5i**	69	**2i**	82
10	**4d**	3,5-Me_2–C_6H_3	**5j**	62	**2j**	78
11	**4d**	3-MeO–C_6H_4	**5k**	66	**2k**	78

[a]) Yields of isolated products.

temperature (*ca.* 100°) and for the time indicated in *Table 2*. Removal of excess Ac_2O and AcOH, formed in the reaction, and subsequent purification of the residue by column chromatography on SiO_2 provided **1** in generally good yields as collected in *Table 2*. However, when (4-chlorophenyl)sulfinyl substrates **2d** and **2e** were used, somewhat higher temperatures and rather longer reaction times were required to complete the reactions, and rather lower yields compared to those from other substrates were obtained for **1d** and **1e**, respectively (*Entries 4* and *5*). Presumably, substitution with the electron-withdrawing Cl group renders the cationic intermediates **6** unstable. The progress of the reactions using ethylsulfinyl substrates **2f**–**2k** (*Entries 6–11*) was faster than that of using phenylsulfinyl substrates **2a**–**2c** (*Entries 1–3*). Introduction of a Cl substituent at C(5) of 2-(ethylsulfinyl)benzamides (*i.e.* **2i**–**2k**) tended to make the progress of the reaction smoothly (*Entries 9–11*). It

Table 2. *Preparation of 3-(Arylsulfanyl)-2,3-dihydro-1*H*-isoindolin-1-ones* **1**

Entry	**2**	Temp. [°]	Time [h]	**1**	R^1	R^3	Ar	Yield[a]) [%]
1	**2a**	90	18	**1a**	H	Ph	Ph	73
2	**2b**	90	15	**1b**	H	Ph	4-Me–C_6H_4	86
3	**2c**	100	12	**1c**	H	Ph	4-MeO–C_6H_4	72
4	**2d**	110	19	**1d**	H	4-Cl–C_6H_4	Ph	48
5	**2e**	100	34	**1e**	H	4-Cl–C_6H_4	4-Cl–C_6H_4	44
6	**2f**	90	7	**1f**	H	Et	Ph	75
7	**2g**	100	5	**1g**	H	Et	3,5-Me_2–C_6H_3	82
8	**2h**	100	5	**1h**	H	Et	3-MeO–C_6H_4	72
9	**2i**	90	6	**1i**	Cl	Et	Ph	82
10	**2j**	90	9	**1j**	Cl	Et	3,5-Me_2–C_6H_3	81
11	**2k**	100	4	**1k**	Cl	Et	3-MeO–C_6H_4	76

[a]) Yields of isolated products.

was also found that the reaction was tolerant of the substituents on the *N*-aryl groups. They did not affect the yields of the products and the reaction times so much.

In conclusion, we have developed a simple and efficient method for the synthesis of dihydro-3-sulfanylisoindol-1-ones **1** by a four-step procedure from 2-(bromomethyl)-benzoates **3**, which involves *Pummerer*-type cyclization as the key and last step. Advantages of this method over the previous procedures [5] include simple and convenient reaction conditions, ready availability of the starting materials, and the avoidance of hazardous or precious metal catalyst.

Experimental Part

General. All of the org. solvents used in this study were dried over appropriate drying agents and distilled prior to use. TLC: *Merck* silica gel *60 PF_{254}*. Column chromatography (CC): *Wako Gel* C-200E. M.p.: *Laboratory Devices MEL-TEMP II* melting point apparatus; uncorrected. IR Spectra: *Shimadzu FTIR-8300* spectrophotometer. ^{1}H- and ^{13}C-NMR spectra: in $CDCl_3$ with TMS as an internal reference, with a *JEOL ECP500* FT NMR spectrometer, ^{1}H: 500 and ^{13}C: 125 MHz. LR-MS (EI, 70 eV): *JEOL JMS AX505 HA* spectrometer.

Ethyl 2-(bromomethyl)benzoate (**3a**) [6] and *methyl 2-(bromomethyl)-5-chlorobenzoate* (**3b**) [7] were prepared according to the methods reported in the literature. All other chemicals used in this study were commercially available.

2-[(Aryl- or alkylsulfanyl)methyl]benzoates **4**. These compounds were prepared by treating **3** (10 mmol) with sodium thiolates generated from the respective thiols (10 mmol) and NaH (60% in mineral oil; 0.40 g, 10 mmol) in THF (30 ml) at 0°.

Ethyl 2-[(Phenylsulfanyl)methyl]benzoate (**4a**) [8]. Colorless oil. R_f (Et_2O/hexane 1:3) 0.41. IR (neat): 1717. ^{1}H-NMR: 1.39 (*t*, *J* = 7.3, 3 H); 4.36 (*q*, *J* = 7.3, 2 H); 4.51 (*s*, 2 H); 7.17–7.26 (*m*, 4 H); 7.28–7.30 (*m*, 3 H); 7.35 (*t*, *J* = 7.3, 1 H); 7.92 (*dd*, *J* = 7.8, 0.9, 1 H).

Ethyl 2-{[(4-Chlorophenyl)sulfanyl]methyl}benzoate (**4b**) [8]. Colorless oil. R_f (Et_2O/hexane 1:19) 0.38. IR (neat): 1717. ^{1}H-NMR: 1.39 (*t*, *J* = 7.3, 3 H); 4.35 (*q*, *J* = 7.3, 2 H); 4.48 (*s*, 2 H); 7.16 (*d*, *J* = 7.8, 1 H); 7.20 (*s*, 4 H); 7.30 (*dd*, *J* = 7.8, 7.3, 1 H); 7.36 (*ddd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.93 (*d*, *J* = 7.8, 1 H).

Ethyl 2-[(Ethylsulfanyl)methyl]benzoate (**4c**). Colorless liquid. R_f (Et_2O/hexane 1:19) 0.50. IR (neat): 1717. ^{1}H-NMR: 1.22 (*t*, *J* = 7.3, 3 H); 1.40 (*t*, *J* = 7.3, 3 H); 2.44 (*q*, *J* = 7.3, 2 H); 4.13 (*s*, 2 H); 4.38 (*q*, *J* = 7.3, 2 H); 7.31 (*dd*, *J* = 7.8, 7.3, 1 H); 7.33 (*d*, *J* = 7.8, 1 H); 7.43 (*dd*, *J* = 7.8, 7.3, 1 H); 7.90 (*d*, *J* = 7.8, 1 H). Anal. calc. for $C_{12}H_{16}O_2S$ (224.32): C 64.25, H 7.19; found: C 70.17, H 7.27.

Methyl 5-Chloro-2-[(ethylsulfanyl)methyl]benzoate (**4d**). Colorless liquid. R_f (Et_2O/hexane 1:19) 0.43. IR (neat): 1726. ^{1}H-NMR: 1.21 (*t*, *J* = 7.3, 3 H); 2.44 (*q*, *J* = 7.3, 2 H); 3.92 (*s*, 3 H); 4.08 (*s*, 2 H); 7.29 (*d*, *J* = 8.2, 1 H); 7.40 (*dd*, *J* = 8.2, 2.3, 1 H); 7.89 (*d*, *J* = 2.3, 1 H). Anal. calc. for $C_{11}H_{13}ClO_2S$ (244.74): C 53.98, H 5.35; found: C 53.96, H 5.37.

N-*Aryl-2-[(aryl- or alkylsulfanyl)methyl]benzamides* **5**. These compounds were prepared by treating **4** (3.0 mmol) with aryl(or alkyl)amines (3.0 mmol) in the presence of NaH (60% in mineral oil; 0.12 g, 3.0 mmol) in THF (10 ml) at r.t.

N-*Phenyl-2-[(phenylsulfanyl)methyl]benzamide* (**5a**). Pale-yellow solid. M.p. 132–134° (hexane/THF). IR (KBr): 3231, 1645. ^{1}H-NMR: 4.36 (*s*, 2 H); 7.15 (*t*, *J* = 7.3, 1 H); 7.19–7.28 (*m*, 4 H); 7.30–7.38 (*m*, 6 H); 7.59–7.62 (*m*, 3 H); 8.10 (br. *s*, 1 H). Anal. calc. for $C_{20}H_{17}NOS$ (319.42): C 75.20, H 5.36, N 4.39; found: C 75.28, H 5.46, N 4.27.

N-*(4-Methylphenyl)-2-[(phenylsulfanyl)methyl]benzamide* (**5b**). Pale-yellow solid. M.p. 145–148° (hexane/THF). IR (KBr): 3231, 1642. ^{1}H-NMR: 2.34 (*s*, 3 H); 4.36 (*s*, 2 H); 7.15 (*d*, *J* = 8.2, 2 H); 7.19–7.28 (*m*, 4 H); 7.30–7.37 (*m*, 4 H); 7.49 (*d*, *J* = 8.2, 2 H); 7.59 (*d*, *J* = 7.8, 1 H); 8.03 (br. *s*, 1 H). Anal. calc. for $C_{21}H_{19}NOS$ (333.45): C 75.64, H 5.74, N 4.20; found: C 75.56, H 5.88, N 4.35.

N-*(4-Methoxyphenyl)-2-[(phenylsulfanyl)methyl]benzamide* (**5c**). White solid. M.p. 113–116° (hexane/THF). IR (KBr): 3310, 1645, 1601. ^{1}H-NMR: 3.81 (*s*, 3 H); 4.36 (*s*, 2 H); 6.88 (*d*, *J* = 9.2, 2 H); 7.19–7.28 (*m*, 4 H); 7.30–7.37 (*m*, 4 H); 7.51 (*d*, *J* = 9.2, 2 H); 7.59 (*dd*, *J* = 7.8, 2.7, 1 H); 7.99 (br. *s*, 1 H). Anal. calc. for $C_{21}H_{19}NO_2S$ (349.45): C 72.18, H 5.48, N 4.01; found: C 71.04, H 5.53, N 3.74.

2-{[(4-Chlorophenyl)sulfanyl]methyl}-N-*phenylbenzamide* (**5d**). White solid. M.p. 128–131° (hexane/THF). IR (KBr): 3277, 1651. ^{1}H-NMR: 4.36 (*s*, 2 H); 7.16 (*t*, *J* = 7.3, 1 H); 7.18 (*d*, *J* = 8.7, 2 H); 7.23 (*d*, *J* = 8.7, 2 H); 7.27 (*dd*, *J* = 7.8, 1.8, 1 H); 7.33–7.40 (*m*, 4 H); 7.57 (*d*, *J* = 7.3, 1 H); 7.60 (*d*, *J* = 7.8, 2 H); 7.89 (br. *s*, 1 H). Anal. calc. for $C_{20}H_{16}ClNOS$ (353.87): C 67.88, H 4.56, N 3.96; found: C 67.83, H 4.50, N 3.81.

N-*(4-Chlorophenyl)-2-{[(4-chlorophenyl)sulfanyl]methyl}benzamide* (**5e**). White solid. M.p. 120–122° (hexane/Et_2O). IR (KBr): 3275, 1645. ^{1}H NMR: 4.33 (*s*, 2 H); 7.19 (*d*, *J* = 8.7, 2 H); 7.22 (*d*, *J* = 8.7, 2 H); 7.26 (*dd*, *J* = 7.3, 1.4, 1 H); 7.32 (*d*, *J* = 9.2, 2 H); 7.36 (*d*, *J* = 7.3, 1 H); 7.39 (*td*, *J* = 7.3, 1.4, 1 H); 7.55–7.57 (*m*, 3 H); 7.92 (br. *s*, 1 H). Anal. calc. for $C_{20}H_{15}Cl_2NOS$ (388.31): C 61.86, H 3.89, N 3.61; found: C 61.87, H 3.81, N 3.41.

2-[(Ethylsulfanyl)methyl]-N-*phenylbenzamide* (**5f**). White solid. M.p. 96–98° (hexane/Et_2O). IR (KBr): 3310, 1651. ^{1}H-NMR: 1.28 (*t*, *J* = 7.3, 3 H); 2.59 (*q*, *J* = 7.3, 2 H); 3.96 (*s*, 2 H); 7.15 (*t*, *J* = 7.3, 1 H); 7.32 (*dd*, *J* = 7.3, 0.9, 1 H); 7.35–7.43 (*m*, 4 H); 7.66 (*d*, *J* = 7.3, 1 H); 7.70 (*d*, *J* = 7.8, 2 H); 8.65 (br. *s*, 1 H). Anal. calc. for $C_{16}H_{17}NOS$ (271.38): C 70.81, H 6.31, N 5.16; found: C 70.51, H 6.21, N 5.19.

N-*(3,5-Dimethylphenyl)-2-[(ethylsulfanyl)methyl]benzamide* (**5g**). White solid. M.p. 96–98° (hexane/Et_2O). IR (KBr): 3285, 1647, 1614. ^{1}H-NMR: 1.28 (*t*, *J* = 7.3, 3 H); 2.22 (*s*, 6 H); 2.59 (*q*, *J* = 7.3, 2 H); 3.94 (*s*, 2 H); 6.80 (*s*, 1 H); 7.30–7.34 (*m*, 3 H); 7.36 (*d*, *J* = 7.3, 1 H); 7.40 (*td*, *J* = 7.3, 1.4, 1 H); 7.64 (*d*, *J* = 7.3, 1 H); 8.51 (br. *s*, 1 H). Anal. calc. for $C_{18}H_{21}NOS$ (299.43): C 72.20, H 7.07, N 4.68; found: C 72.09, H 7.34, N 4.58.

2-[(Ethylsulfanyl)methyl]-N-*(3-methoxyphenyl)benzamide* (**5h**). Pale-yellow oil. R_f (AcOEt/hexane 1:5) 0.32. IR (neat): 3295, 1659, 1609. ^{1}H-NMR: 1.28 (*t*, *J* = 7.3, 3 H); 2.59 (*q*, *J* = 7.3, 2 H); 3.84 (*s*, 3 H); 3.95 (*s*, 2 H); 6.71 (*dd*, *J* = 8.2, 2.3, 1 H); 7.16 (*d*, *J* = 7.8, 1 H); 7.26 (*dd*, *J* = 8.2, 7.8, 1 H); 7.31 (*dd*, *J* = 7.3, 0.9, 1 H); 7.36 (*t*, *J* = 7.3, 1 H); 7.41 (*td*, *J* = 7.3, 1.4, 1 H); 7.48 (*s*, 1 H); 7.66 (*d*, *J* = 7.3, 1 H); 8.68 (br. *s*, 1 H). Anal. calc. for $C_{17}H_{19}NO_2S$ (301.40): C 67.74, H 6.35, N 4.65; found: C 67.69, H 6.40, N 4.63.

5-Chloro-2-[(ethylsulfanyl)methyl]-N-*phenylbenzamide* (**5i**). White solid. M.p. 122–124° (hexane/Et_2O). IR (KBr): 3281, 1649. ^{1}H-NMR: 1.27 (*t*, *J* = 7.3, 3 H); 2.58 (*q*, *J* = 7.3, 2 H); 3.91 (*s*, 2 H); 7.17 (*t*, *J* = 7.3, 1 H); 7.26 (*d*, *J* = 8.2, 1 H); 7.37–7.40 (*m*, 3 H); 7.65–7.69 (*m*, 3 H); 8.64 (br. *s*, 1 H). Anal calc. for $C_{16}H_{16}ClNOS$ (305.82): C 62.84, H 5.27, N 4.58; found: C 62.63, H 5.39, N 4.48.

5-Chloro-N-*(3,5-dimethylphenyl)-2-[(ethylsulfanyl)methyl]benzamide* (**5j**). White solid. M.p. 94–96° (hexane/CH_2Cl_2). IR (KBr): 3260, 1651, 1616. ^{1}H-NMR: 1.28 (*t*, *J* = 7.3, 3 H); 2.24 (*s*, 6 H); 2.58 (*q*, *J* = 7.3, 2 H); 3.90 (*s*, 2 H); 6.82 (*s*, 1 H); 7.25 (*d*, *J* = 8.2, 1 H); 7.30 (*s*, 2 H); 7.37 (*dd*, *J* = 8.2, 2.3, 1 H); 7.62 (*s*, *J* = 2.3, 1 H); 8.49 (br. *s*, 1 H). Anal. calc. for $C_{18}H_{20}ClNOS$ (333.88): C 64.75, H 6.04, N 4.20; found: C 64.92, H 6.13, N 4.02.

5-Chloro-2-[(ethylsulfanyl)methyl]-N-*(3-methoxyphenyl)benzamide* (**5k**). White solid. M.p. 79–81° (hexane/CH_2Cl_2). IR (KBr): 3293, 1651, 1609. ^{1}H-NMR: 1.28 (*t*, *J* = 7.3, 3 H); 2.58 (*q*, *J* = 7.3, 2 H); 3.84 (*s*, 3 H); 3.90 (*s*, 2 H); 6.72 (*dd*, *J* = 7.8, 1.8, 1 H); 7.14 (*dd*, *J* = 7.8, 0.9, 1 H); 7.25–7.29 (*m*, 2 H); 7.38 (*dd*, *J* = 8.2, 2.3, 1 H); 7.44 (*t*, *J* = 1.8, 1 H); 7.64 (*d*, *J* = 2.3, 1 H); 8.65 (br. *s*, 1 H). Anal. calc. for $C_{17}H_{18}ClNO_2S$ (335.85): C 60.80, H 5.40, N 4.17; found: C 60.52, H 5.45, N 3.93.

N-*Aryl-2-[(aryl- or alkylsulfinyl)methyl]benzamides* **2**. These compounds were prepared by treating **5** (2.0 mmol) with $NaIO_4$ (0.43 g, 2.0 mmol) in MeOH/H_2O 9:1 (10 ml; *v*/*v*) at r.t.

N-*Phenyl-2-[(phenylsulfinyl)methyl]benzamide* (**2a**). White solid. M.p. 164–168° (hexane/CH_2Cl_2). IR (KBr): 3235, 1660, 1031. ^{1}H-NMR: 4.30 (*d*, *J* = 13.3, 1 H); 4.35 (*d*, *J* = 13.3, 1 H); 7.01 (*d*, *J* = 7.3, 1 H); 7.17 (*t*, *J* = 7.3, 1 H); 7.36–7.41 (*m*, 3 H); 7.44 (*ddd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.48–7.53 (*m*, 3 H); 7.58 (*dd*, *J* = 7.8, 1.8, 2 H); 7.73 (*dd*, *J* = 7.8, 0.9, 1 H); 7.87 (*d*, *J* = 8.2, 2 H); 9.98 (br. *s*, 1 H). Anal. calc. for $C_{20}H_{17}NO_2S$ (335.42): C 71.62, H 5.11, N 4.18; found: C 71.50, H 5.26, N 4.04.

N-*(4-Methylphenyl)-2-[(phenylsulfinyl)methyl]benzamide* (**2b**). White solid. M.p. 171–173° (hexane). IR (KBr): 3235, 1667, 1030. ^{1}H-NMR: 2.36 (*s*, 3 H); 4.28 (*d*, *J* = 12.8, 1 H); 4.34 (*d*, *J* = 12.8, 1 H); 7.00 (*d*, *J* = 7.3, 1 H); 7.19 (*d*, *J* = 8.2, 2 H); 7.37 (*ddd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.43 (*ddd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.48–7.54 (*m*, 3 H); 7.57 (*dd*, *J* = 7.8, 1.4, 2 H); 7.72 (*dd*, *J* = 7.8, 1.4, 1 H); 7.74 (*d*, *J* = 8.2, 2 H); 9.84 (br. *s*, 1 H). Anal. calc. for $C_{21}H_{19}NO_2S$ (349.45): C 72.18, H 5.48, N 4.01; found: C 72.17, H 5.67, N 3.94.

N-*(4-Methoxyphenyl)-2-[(phenylsulfinyl)methyl]benzamide* (**2c**). White solid. M.p. 131–133° (hexane/CH_2Cl_2); IR (KBr) 3258, 1649, 1609, 1028. ^{1}H-NMR: 3.84 (*s*, 3 H); 4.29 (*d*, *J* = 13.3, 1 H); 4.34 (*d*, *J* = 13.3, 1 H); 6.93 (*d*, *J* = 9.2, 2 H); 7.01 (*d*, *J* = 7.8, 1 H); 7.37 (*dd*, *J* = 7.8, 7.3, 1 H); 7.43 (*dd*, *J* = 7.8, 7.3, 1 H); 7.49–7.53 (*m*, 3 H); 7.56 (*d*, *J* = 7.8, 2 H); 7.72 (*d*, *J* = 7.8, 1 H); 7.78 (*d*, *J* = 9.2, 2 H); 9.85 (br. *s*, 1 H). Anal. calc. for $C_{21}H_{19}NO_3S$ (365.45): C 69.02, H 5.24, N 3.83; found: C 68.83, H 5.28, N 3.68.

2-{[(4-Chlorophenyl)sulfinyl]methyl}-N-*phenylbenzamide* (**2d**). White solid. M.p. 133–135° (hexane/CH_2Cl_2). IR (KBr): 3281, 3248, 1662, 1030. ^{1}H-NMR: 4.27 (*d*, *J* = 13.3, 1 H); 4.39 (*d*, *J* = 13.3, 1 H); 7.03 (*d*, *J* = 7.3, 1 H); 7.17 (*dd*, *J* = 7.8, 7.3, 1 H); 7.38–7.50 (*m*, 8 H); 7.71 (*dd*, *J* = 7.8, 1.4, 1 H); 7.81 (*d*, *J* = 8.2, 2 H); 9.60 (br. *s*, 1 H). Anal. calc. for $C_{20}H_{16}ClNO_2S$ (369.86): C 64.95, H 4.36, N 3.79; found: C 65.05, H 4.45, N 3.61.

N-*(4-Chlorophenyl)-2-{[(4-chlorophenyl)sulfinyl]methyl}benzamide* (**2e**). White solid. M.p. 183–184° (hexane/CH_2Cl_2). IR (KBr): 3271, 3242, 1661, 1030. ^{1}H-NMR: 4.25 (*d*, *J* = 13.3, 1 H); 4.36 (*d*, *J* = 13.3, 1 H); 6.99 (*d*, *J* = 7.8, 1 H); 7.26 (*dd*, *J* = 7.8, 7.3, 1 H); 7.35 (*d*, *J* = 8.7, 2 H); 7.40 (*ddd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.44–7.50 (*m*, 4 H); 7.71 (*d*, *J* = 7.8, 1 H); 7.79 (*d*, *J* = 8.7, 2 H); 9.89 (br. *s*, 1 H). Anal. calc. for $C_{20}H_{15}Cl_2NO_2S$ (404.31): C 59.41, H 3.74, N 3.46; found: C 59.39, H 3.77, N 3.30.

2-[(Ethylsulfinyl)methyl]-N-*phenylbenzamide* (**2f**). White solid. M.p. 122–124° (hexane/CH_2Cl_2). IR (KBr): 3271, 3235, 1667, 1015. ^{1}H-NMR: 1.40 (*t*, *J* = 7.3, 3 H); 2.85–2.97 (*m*, 2 H); 4.03 (*d*, *J* = 12.8, 1 H); 4.35 (*d*, *J* = 12.8, 1 H); 7.12 (*tt*, *J* = 7.3, 0.9, 1 H); 7.34–7.38 (*m*, 3 H); 7.45 (*t*, *J* = 7.3, 1 H); 7.50 (*t*, *J* = 7.3, 1 H); 7.74 (*d*, *J* = 7.3, 1 H); 7.81 (*d*, *J* = 8.2, 2 H); 10.07 (br. *s*, 1 H). Anal. calc. for $C_{16}H_{17}NO_2S$ (287.38): C 66.87, H 5.96, N 4.87; found: C 66.85, H 6.16, N 4.74.

N-*(3,5-Dimethylphenyl)-2-[(ethylsulfinyl)methyl]benzamide* (**2g**). White solid. M.p. 173–175° (hexane/CH_2Cl_2). IR (KBr): 3235, 1665, 1009. ^{1}H-NMR: 1.40 (*t*, *J* = 7.3, 3 H); 2.32 (*s*, 6 H); 2.83–2.98 (*m*, 2 H); 4.04 (*d*, *J* = 12.8, 1 H); 4.33 (*d*, *J* = 12.8, 1 H); 6.78 (*s*, 1 H); 7.37 (*dd*, *J* = 7.3, 1.4, 1 H); 7.43–7.46 (*m*, 3 H); 7.49 (*td*, *J* = 7.3, 1.4, 1 H); 7.72 (*dd*, *J* = 7.3, 1 H); 9.85 (br. *s*, 1 H). Anal. calc. for $C_{18}H_{21}NO_2S$ (315.43): C 68.54, H 6.71, N 4.44; found: C 68.61, H 6.90, N 4.36.

2-[(Ethylsulfinyl)methyl]-N-*(3-methoxyphenyl)benzamide* (**2h**). White solid. M.p. 111–113° (hexane/CH_2Cl_2). IR (KBr): 3246, 1667, 1609, 1015. ^{1}H-NMR: 1.40 (*t*, *J* = 7.3, 3 H); 2.84–2.99 (*m*, 2 H); 3.83 (*s*, 3 H); 4.02 (*d*, *J* = 12.8, 1 H); 4.36 (*d*, *J* = 12.8, 1 H); 6.69 (*dd*, *J* = 8.2, 1.8, 1 H); 7.24 (*t*, *J* = 8.2, 1 H); 7.30 (*d*, *J* = 8.2, 1 H); 7.37 (*d*, *J* = 7.8, 1 H); 7.45 (*ddd*, *J* = 7.8, 7.3, 0.9, 1 H); 7.50 (*dd*, *J* = 7.8, 7.3, 1.4, 1 H); 7.59 (*s*, 1 H); 7.74 (*d*, *J* = 7.8, 1 H); 10.09 (br. *s*, 1 H). Anal. calc. for $C_{17}H_{19}NO_3S$ (317.40): C 64.33, H 6.03, N 4.41; found: C 64.17, H 5.95, N 4.35.

5-Chloro-2-[(ethylsulfinyl)methyl]-N-*phenylbenzamide* (**2i**). White solid. M.p. 130–132° (hexane/CH_2Cl_2). IR (KBr): 3235, 1661, 1005. ^{1}H-NMR: 1.41 (*t*, *J* = 7.3, 3 H); 2.84–2.99 (*m*, 2 H); 3.99 (*d*, *J* = 13.3, 1 H); 4.34 (*d*, *J* = 13.3, 1 H); 7.14 (*tt*, *J* = 7.3, 1.4, 1 H); 7.31 (*d*, *J* = 8.2, 1 H); 7.36 (*t*, *J* = 7.3, 2 H); 7.47 (*dd*, *J* = 8.2, 2.3, 1 H); 7.73 (*d*, *J* = 2.3, 1 H); 7.79 (*d*, *J* = 7.3, 2 H); 10.13 (br. *s*, 1 H). Anal. calc. for $C_{16}H_{16}ClNO_2S$ (321.82): C 59.71, H 5.01, N 4.35; found: C 59.55, H 5.19, N 4.47.

5-Chloro-N-*(3,5-dimethylphenyl)-2-[(ethylsulfinyl)methyl]benzamide* (**2j**). White solid. M.p. 155–158° (hexane/CH_2Cl_2). IR (KBr): 3236, 1659, 1620, 1009. ^{1}H-NMR: 1.40 (*t*, *J* = 7.3, 3 H); 2.32 (*s*, 6 H); 2.83–2.98 (*m*, 2 H); 3.99 (*d*, *J* = 13.3, 1 H); 4.30 (*d*, *J* = 13.3, 1 H); 6.79 (*s*, 1 H); 7.31 (*d*, *J* = 8.2, 1 H); 7.42 (*s*, 2 H); 7.46 (*dd*, *J* = 8.2, 2.3, 1 H); 7.71 (*d*, *J* = 2.3, 1 H); 9.93 (br. *s*, 1 H). Anal. calc. for $C_{18}H_{20}ClNO_2S$ (349.87): C 61.79, H 5.76, N 4.00; found: C 61.66, H 5.63, N 4.01.

5-Chloro-2-[(ethylsulfinyl)methyl]-N-*(3-methoxyphenyl)benzamide* (**2k**). Pale-yellow oil. R_f (AcOEt/hexane 3:1) 0.34. IR (neat): 3248, 1668, 1609, 1016. ^{1}H-NMR: 1.41 (*t*, *J* = 7.3, 3 H); 2.85–2.99 (*m*, 2 H); 3.83 (*s*, 3 H); 3.97 (*d*, *J* = 13.3, 1 H); 4.34 (*d*, *J* = 13.3, 1 H); 6.70 (*dt*, *J* = 7.8, 1.4, 1 H); 7.23–7.32 (*m*, 3 H); 7.47 (*dd*, *J* = 8.2, 2.3, 1 H); 7.55 (*dd*, *J* = 2.3, 1.4, 1 H); 7.73 (*d*, *J* = 2.3, 1 H); 10.17 (br. *s*, 1 H). Anal. calc. for $C_{17}H_{18}ClNO_3S$ (351.85): C 58.03, H 5.16, N 3.98; found: C 59.99, H 5.46, N 3.94.

2,3-Dihydro-3-sulfanylisoindol-1-ones **1**. *General Procedure.* A soln. of **2** (1.0 mmol) in Ac_2O (3 ml) was heated at the temp. and for the time indicted in *Table 2*. After removal of excess Ac_2O, the residue was purified by CC (SiO_2; AcOEt/hexane 1:10) to afford **1**.

*2,3-Dihydro-2-phenyl-3-(phenylsulfanyl)-1*H-*isoindol-1-one* (**1a**). White solid. M.p. 146–148° (hexane/CH_2Cl_2). IR (KBr): 1685. ^{1}H-NMR: 6.35 (*s*, 1 H); 6.89 (*d*, *J* = 7.3, 2 H); 7.02 (*t*, *J* = 7.8, 2 H); 7.16 (*t*, *J* = 7.3, 1 H); 7.28 (*t*, *J* = 7.3, 1 H); 7.41 (*t*, *J* = 7.3, 1 H); 7.49 (*t*, *J* = 7.8, 2 H); 7.60–7.67 (*m*, 4 H); 7.74 (*d*, *J* = 7.8, 1 H). ^{13}C-NMR: 66.87; 123.23; 123.34; 123.61; 123.75; 125.49; 128.45; 128.95; 128.97; 129.26; 131.77; 132.21; 135.89; 136.66; 142.36; 170.71. MS: 317 (0.4, M^+), 208 (100). Anal. calc. for $C_{20}H_{15}NOS$ (317.40): C 75.68, H 4.76, N 4.41; found: C 75.71, H 4.82, N 4.32.

*2,3-Dihydro-2-(4-methylphenyl)-3-(phenylsulfanyl)-1*H-*isoindol-1-one* (**1b**). White solid. M.p. 146–148° (hexane/CH_2Cl_2). IR (KBr): 1684, 1613. ^{1}H-NMR: 2.41 (*s*, 3 H); 6.30 (*s*, 1 H); 6.91 (*d*, *J* = 7.3, 2 H); 7.02 (*t*, *J* = 7.8, 2 H); 7.15 (*t*, *J* = 7.3, 1 H); 7.29 (*d*, *J* = 8.2, 2 H); 7.39 (*dd*, *J* = 7.8, 7.3, 1 H); 7.53 (*d*, *J* = 8.2, 2 H); 7.60 (*ddd*, *J* = 7.8, 7.3, 0.9, 1 H); 7.64 (*d*, *J* = 7.3, 1 H); 7.71 (*d*, *J* = 7.3, 1 H). ^{13}C-NMR: 21.03; 67.03; 123.37; 123.53; 123.71; 127.63; 128.41; 128.90; 129.19; 129.58; 131.86; 132.06; 134.02; 135.31; 135.87; 142.31; 166.25. MS: 331 (2.6, M^+), 222 (100). Anal. calc. for $C_{21}H_{17}NOS$ (331.43): C 76.10, H 5.17, N 4.23; found: C 75.86, H 5.37, N 4.04.

*2,3-Dihydro-2-(4-methoxyphenyl)-3-(phenylsulfanyl)-1*H-*isoindol-1-one* (**1c**). White solid. M.p. 155–158° (hexane/CH_2Cl_2). IR (KBr): 1682, 1614. ^{1}H-NMR: 3.87 (*s*, 3 H); 6.26 (*s*, 1 H); 6.92 (*dd*, *J* = 7.8, 1.4, 2 H); 7.01 (*d*, *J* = 9.2, 2 H); 7.03 (*dd*, *J* = 7.8, 7.3, 2 H); 7.16 (*dd*, *J* = 7.8, 7.3, 1 H); 7.41 (*dd*, *J*0 = 7.8, 7.3, 1 H); 7.52 (*d*, *J* = 9.2, 2 H); 7.61 (*ddd*, *J* = 7.8, 7.3, 0.9, 1 H); 7.66 (*d*, *J* = 7.8, 1 H); 7.72 (*d*, *J* = 7.8, 1 H). ^{13}C-NMR: 55.49; 67.61; 114.27; 123.55; 123.74; 125.24; 127.95; 128.46; 128.96; 129.15; 129.54; 131.84; 132.05; 135.67; 142.33; 157.43; 166.29. MS: 347 (3.3, M^+), 238 (100). Anal. calc. for $C_{21}H_{17}NOS$ (347.43): C 72.60, H 4.93, N 4.03; found: C 72.53, H 5.07, N 3.88.

*3-[(4-Chlorophenyl)sulfanyl]-2,3-dihydro-2-phenyl-1*H-*isoindol-1-one* (**1d**). White solid. M.p. 150–152° (hexane/CH_2Cl_2). IR (KBr): 1688, 1601. ^{1}H-NMR: 6.33 (*s*, 1 H); 6.79 (*d*, *J* = 8.7, 2 H); 6.99 (*d*, *J* = 8.7, 2 H); 7.29 (*t*, *J* = 7.3, 1 H); 7.44 (*t*, *J* = 7.3, 1 H); 7.49 (*dd*, *J* = 7.8, 7.3, 2 H); 7.62–7.66 (*m*, 3 H); 7.69 (*d*, *J* = 7.3, 1 H); 7.73 (*d*, *J* = 7.3, 1 H). ^{13}C-NMR: 66.68; 123.19; 123.65; 123.80; 125.57; 125.86; 128.69; 129.03; 129.20; 131.72; 132.37; 135.90; 136.48; 137.12; 142.02; 166.21. MS: 351 (3.2, M^+), 208 (100). Anal. calc. for $C_{20}H_{14}ClNOS$ (351.85): C 68.27, H 4.01, N 3.98; found: C 68.27, H 4.03, N 3.85.

*2-(4-Chlorophenyl)-3-[(4-chlorophenyl)sulfanyl]-2,3-dihydro-1*H-*isoindol-1-one* (**1e**). White solid. M.p. 158–160° (hexane/CH_2Cl_2). IR (KBr): 1699. ^{1}H-NMR: 6.27 (*s*, 1 H); 6.75 (*d*, *J* = 8.2, 2 H); 6.99 (*d*, *J* = 8.2, 2 H); 7.43–7.47 (*m*, 3 H); 7.63 (*d*, *J* = 9.2, 2 H); 7.66–7.68 (*m*, 2 H); 7.74 (*d*, *J* = 7.3, 1 H). ^{13}C-NMR: 66.42; 123.66; 123.84; 124.05; 125.47; 128.77; 129.10; 129.32; 130.83; 131.43; 132.60; 135.10; 136.11; 137.10; 141.92; 166.16. MS: 385 (6.8, M^+), 242 (100). Anal. calc. for $C_{20}H_{13}Cl_2NOS$ (386.29): C 62.18, H 3.39, N 3.63; found: C 61.90, H 3.42, N 3.61.

*3-(Ethylsulfanyl)-2,3-dihydro-2-phenyl-1*H-*isoindol-1-one* (**1f**). White solid. M.p. 178–180° (hexane/CH_2Cl_2). IR (KBr): 1686. ^{1}H-NMR: 0.89 (*t*, *J* = 7.3, 3 H); 1.85–1.92 (*m*, 1 H); 2.01–2.08 (*m*, 1 H); 6.14 (*s*, 1 H); 7.29 (*tt*, *J* = 7.3, 0.9, 1 H); 7.48 (*dd*, *J* = 7.8, 7.3, 2 H); 7.54 (*t*, *J* = 7.3, 1 H); 7.60 (*dd*, *J* = 7.8, 0.9, 2 H); 7.67 (*td*, *J* = 7.3, 0.9, 1 H); 7.70 (*d*, *J* = 7.3, 1 H); 7.92 (*d*, *J* = 7.3, 1 H). ^{13}C-NMR: 13.94; 20.81; 64.78; 123.59; 123.85; 124.07; 125.94; 128.97; 129.14; 131.94; 132.64; 136.50; 142.99; 166.51. MS: 269 (1.0, M^+), 208 (100). Anal. calc. for $C_{16}H_{15}NOS$ (269.36): C 71.34, H 5.61, N 5.20; found: C 71.28, H 5.67, N 5.05.

*2-(3,5-Dimethylphenyl)-3-(ethylsulfanyl)-2,3-dihydro-1*H-*isoindol-1-one* (**1g**). Pale-yellow oil. R_f (AcOEt/hexane 1:10) 0.28. IR (neat): 1699. ^{1}H-NMR: 0.90 (*t*, *J* = 7.3, 3 H); 1.87–1.92 (*m*, 1 H);

2.04–2.09 (*m*, 1 H); 2.38 (*s*, 6 H); 6.10 (*s*, 1 H); 6.93 (*s*, 1 H); 7.17 (*s*, 2 H); 7.53 (*ddd*, *J* = 7.8, 7.3, 0.9, 1 H); 7.66 (*td*, *J* = 7.3, 1.4, 1 H); 7.69 (*d*, *J* = 7.8, 1 H); 7.91 (*d*, *J* = 7.3, 1 H). ^{13}C-NMR: 13.96; 20.86; 21.46; 65.07; 122.22; 123.54; 123.79; 128.06; 129.06; 132.06; 132.49; 136.21; 138.58; 143.04; 166.52. MS: 297 (1.9, M^+), 236 (100). Anal. calc. for $C_{18}H_{19}NOS$ (297.41): C 72.69, H 6.44, N 4.71; found: C 72.61, H 6.48, N 4.71.

*3-(Ethylsulfanyl)-2,3-dihydro-2-(3-methoxyphenyl)-1*H-*isoindol-1-one* (**1h**). White solid. M.p. 126–128° (hexane/CH_2Cl_2). IR (KBr): 1686. ^{1}H-NMR: 0.90 (*t*, *J* = 7.3, 3 H); 1.86–1.93 (*m*, 1 H); 2.02–2.09 (*m*, 1 H); 3.86 (*s*, 3 H); 6.11 (*s*, 1 H); 6.84 (*dd*, *J* = 8.2, 1.8, 1 H); 7.14 (*dd*, *J* = 7.8, 1.8, 1 H); 7.28 (*t*, *J* = 1.8, 1 H); 7.37 (*dd*, *J* = 8.2, 7.8, 1 H); 7.54 (*td*, *J* = 7.3, 1.4, 1 H); 7.67 (*td*, *J* = 7.3, 1.4, 1 H); 7.70 (*d*, *J* = 7.3, 1 H); 7.91 (*d*, *J* = 7.3, 1 H). ^{13}C-NMR: 13.96; 20.90; 55.37; 64.87; 110.07; 111.57; 116.12; 123.58; 123.82; 129.14; 129.58; 131.91; 132.69; 137.67; 142.97; 160.04; 166.52. MS: 299 (1.8, M^+), 238 (100). Anal. calc. for $C_{17}H_{17}NO_2S$ (299.39): C 68.20, H 5.72, N 4.68; found: C 67.95, H 5.65, N 4.66.

*6-Chloro-3-(ethylsulfanyl)-2,3-dihydro-2-phenyl-1*H-*isoindol-1-one* (**1i**). White solid. M.p. 203–205° (hexane/CH_2Cl_2). IR (KBr): 1686. ^{1}H-NMR: 0.91 (*t*, *J* = 7.3, 3 H); 1.86–1.93 (*m*, 1 H); 2.02–2.09 (*m*, 1 H); 6.11 (*s*, 1 H); 7.30 (*t*, *J* = 7.3, 1 H); 7.48 (*dd*, *J* = 7.8, 7.3, 2 H); 7.58 (*d*, *J* = 7.8, 2 H); 7.64 (*s*, 2 H); 7.89 (*s*, 1 H). ^{13}C-NMR: 13.90; 20.89; 64.54; 123.94; 124.07; 124.94; 126.25; 129.05; 132.89; 133.57; 135.44; 136.15; 141.19; 165.13. MS: 303 (1.6, M^+), 242 (100). Anal. calc. for $C_{16}H_{14}ClNOS$ (303.81): C 63.25, H 4.64, N 4.61; found: C 63.18, H 4.70, N 4.49.

*6-Chloro-2-(3,5-dimethylphenyl)-3-(ethylsulfanyl)-2,3-dihydro-1*H-*isoindol-1-one* (**1j**). White solid. M.p. 113–116° (hexane/CH_2Cl_2). IR (KBr) 1694. ^{1}H-NMR: 0.93 (*t*, *J* = 7.3, 3 H); 1.86–1.93 (*m*, 1 H); 2.04–2.11 (*m*, 1 H); 2.38 (*s*, 6 H); 6.07 (*s*, 1 H); 6.95 (*s*, 1 H); 7.14 (*s*, 2 H); 7.62 (*s*, 2 H); 7.88 (*s*, 1 H). ^{13}C-NMR: 13.93; 20.94; 21.46; 64.81; 122.19; 123.88; 124.88; 128.34; 132.73; 133.70; 135.35; 135.86; 138.71; 141.24; 165.13. MS: 331 (2.8, M^+), 270 (100). Anal. calc. for $C_{18}H_{18}ClNOS$ (331.86): C 65.15, H 5.47, N 4.22; found: C 64.96, H 5.54, N 4.25.

*6-Chloro-3-(ethylsulfanyl)-2,3-dihydro-2-(3-methoxyphenyl)-1*H-*isoindol-1-one* (**1k**). White solid. M.p. 116–119° (hexane/CH_2Cl_2). IR (KBr): 1690, 1604. ^{1}H-NMR: 0.92 (*t*, *J* = 7.3, 3 H); 1.87–1.94 (*m*, 1 H); 2.03–2.10 (*m*, 1 H); 3.85 (*s*, 3 H); 6.08 (*s*, 1 H); 6.85 (*dt*, *J* = 8.2, 1.4, 1 H); 7.12 (*dd*, *J* = 7.8, 1.8, 1 H); 7.23 (*t*, *J* = 2.3, 1 H); 7.38 (*t*, *J* = 8.2, 1 H); 7.63 (*s*, 2 H); 7.88 (*dd*, *J* = 1.4, 0.9, 1 H). ^{13}C-NMR: 13.94; 20.98; 55.40; 64.63; 110.16; 11.78; 116.15; 123.91; 124.93; 129.67; 132.93; 133.54; 135.43; 137.31; 141.17; 160.08; 165.13. MS: 333 (2.4, M^+), 272 (100). Anal. calc. for $C_{17}H_{16}ClNO_2S$ (333.83): C 61.16, H 4.83, N 4.20; found: C 61.18, H 4.59, N 4.21.

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