Synthesis of Methoxy-2-quinolones *via* Pummerer-type Cyclization of *N*-Aryl-*N*-methyl-3-(phenylsulfinyl)propionamides

Jun TODA, Michiya SAKAGAMI, Yoko GOAN, Mina SIMAKATA, Toshiaki SAITOH, Yoshie HORIGUCHI, and Takehiro SANO*

Showa Pharmaceutical University, 3–3165, Higashi-tamagawagakuen, Machida, Tokyo 194–8543, Japan.
Received April 27, 2000; accepted August 6, 2000

The thionium ions 10 generated by Pummerer reaction of *N*-aryl-*N*-methyl-3-(phenylsulfinyl)propionamides 4 caused not only an electrophilic cyclization reaction producing 2-quinolones 8, but also the formation of the vinyl sulfides 5 and 6 in favor of the latter reaction. On the other hand, the treatment of the vinyl sulfides 5 and 6 with *p*-toluenesulfonic acid induced cyclization to afford the 2-quinolones 8 in excellent to moderate yields, depending on the electronic properties of the aromatic ring, thus providing a convenient method for the synthesis of methoxy-2-quinolones.

Key word Pummerer reaction; 2-quinolone; synthesis; trifluoroacetic anhydride; *p*-toluenesulfonic acid

It is well known that the thionium ion formed *in situ*, generated under acidic conditions from a sulfinyl precursor (Pummerer reaction), is a powerful electrophilic group reacting efficiently with nucleophilic carbon species such as alkenes, aromatics and enol ethers.[1)] This reaction was successfully applied for the synthesis of various carbocycles and heterocycles.[2)] Recently, we explored the reaction and used it as the key strategy for the syntheses of 1,2,3,4-tetrahydroisoquinolines,[3)] 1,2,3,4-tetrahydroquinolines,[4)] erythrinan,[5)] isopavine and pavine alkakoids.[6)] In these investigations we found that boron trifluoride diethyl etherate ($BF_3 \cdot Et_2O$), when used as an additive, facilitated the cationic cyclization. This efficiency was embodied particularly in the cyclization for a weak nucleophilic aromatic π-bond, which, without the additive, produced no cyclized product.[3a—c,4)] In this paper we describe the Pummerer reaction of *N*-aryl-*N*-methyl-3-(phenylsulfinyl)propionamides **4**, leading to the development of a convenient method for the synthesis of methoxy-2-quinolones.

Results and Discussion

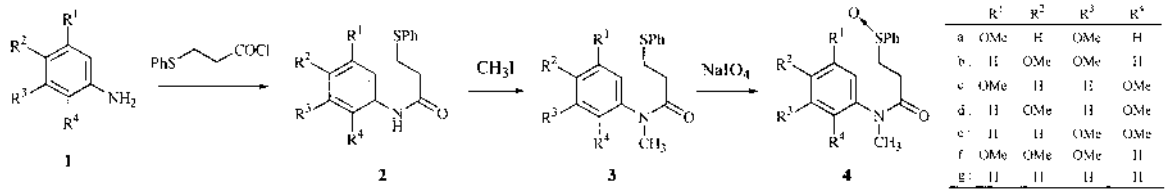
The sulfoxides **4**, the precursors of the Pummerer reaction, were prepared from anilines **1** in three steps. Acylation of **1** with 3-(phenylsulfanyl)propionyl chloride yielded the corresponding anilides **2**, which on methylation with methyl iodide in the presence of a phase transfer catalyst afforded the *N*-methyl derivatives **3**. Oxidation of **3** with sodium metaperiodate ($NaIO_4$) in aqueous methanol gave **4** in excellent overall yields. Products **3** and **4** were well characterized by MS, IR, and ^{1}H- and ^{13}C-NMR spectral data (See Experimental).

Pummerer Reaction A solution of **4** in benzene was treated with trifluoroacetic anhydride (TFAA) at room temperature for 20—72 h under an argon atmosphere. The reaction yielded three products: **5**, **6**, and **8**. The vinyl sulfides **5** and **6** were obtained as major ones in all cases (Table 1). Sulfoxides **4a**, **b**, **e**, and **f**, although the nucleophilic aromatic ring is electronically activated by the OMe group positioned at *ortho* and/or *para*, produced methoxy-2-quinolones **8a**, **b**, **e**, and **f** in yields of only 17—39%. The reaction of **4c** with an *ortho*- and *meta*-OMe group gave 5,8-dimethoxy-2-quinolone **8c** in only 7% yield (run 5).

The results were different with those of the Pummerer-type reaction of *N*-aryl-*N*-(3-phenylsulfinylpropyl)formamides **13**, which exclusively induced intramolecular cyclization to afford the *N*-formyl-1,2,3,4-tetrahydroquinolines **14** as sole products, though there is an exception of **13d**.[4)] Sulfoxides **4d** with two OMe groups *meta* to the reaction center, and **4g** lacking an OMe group on the benzene ring, as anticipated, produced no cyclized product to any extent. Instead, the *cis*-(**5d**, **g**) and *trans*-isomers (**6d**, **g**) of the vinyl sulfides were quantitatively produced (runs 7, 13).

The addition of $BF_3 \cdot Et_2O$ to the reaction mixture accelerates the reaction and in some cases dramatically improves the intramolecular cyclization reaction.[3a—b,4)] A solution of **4** in benzene was treated with TFAA for 30 min at room temperature, then 3 molar equivalents of $BF_3 \cdot Et_2O$ were added, and the mixture was allowed to react for another 5—24 h, giving rise to four products: **5**, **6**, **7**, and **8**. The product ratios varied depending on the electrophilic properties of the aromatic ring. The results are also summarized in Table 1.

The addition of $BF_3 \cdot Et_2O$ considerably improved the ring closure reaction. However, the vinyl sulfides **5** and **6** always accompanied the reaction product in significant amounts. For example, the reactions of **4c** and **4g**, which, without the additive, gave poor results in the cyclization as described above,



	R^1	R^2	R^3	R^4
a	OMe	H	OMe	H
b	H	OMe	OMe	H
c	OMe	H	H	OMe
d	H	OMe	H	OMe
e	H	H	OMe	OMe
f	OMe	OMe	OMe	H
g	H	H	H	H

Chart 1

* To whom correspondence should be addressed. e-mail: t-sano@ac.shoyaku.ac.jp

Table 1. Pummerer Reaction of *N*-Aryl-*N*-methyl-3-phenylsulfinylpropionamides (**4**)

Run	Substrates	Conditions[a]		Yield (%)							
		Reagent[b]	Time (h)	Vinyl sulfides (**5**, **6**)				4-SPh-Q (**7**)		2-Quinolones (**8**)	
1	**4a**	A	20	(**5a**)	30	(**6a**)	18			(**8a**)	32
2	**4a**	B	5	(**5a**)	10	(**6a**)	26			(**8a**)	51
3	**4b**	A	72	(**5b**)	32	(**6b**)	44			(**8b**)	17
4	**4b**	B	24	(**5b**)	13	(**6b**)	18	(**7b**)	15	(**8b**)	42
5	**4c**	A	72	(**5c**)	36	(**6c**)	53			(**8c**)	7
6	**4c**	B	24	(**5c**)	9	(**6c**)	20	(**7c**)	46	(**8c**)	22
7	**4d**	A	24	(**5d**)	36	(**6d**)	63				
8	**4d**	B	24	(**5d**)	45	(**6d**)	52				
9	**4e**	A	24	(**5e**)	39	(**6e**)	34			(**8e**)	21
10	**4e**	B	24	(**5e**)	17	(**6e**)	43			(**8e**)	40
11	**4f**	A	24	(**5f**)	32	(**6f**)	27			(**8f**)	39
12	**4f**	B	24	(**5f**)	21	(**6f**)	26			(**8f**)	51
13	**4g**	A	48	(**5g**)	41	(**6g**)	54				
14	**4g**	B	24	(**5g**)	13	(**6g**)	17	(**7g**)	43	(**8g**)	12

a) In benzene at room temperature. *b*) A: TFAA, B: TFAA–$BF_3 \cdot Et_2O$.

Table 2. Synthesis of 2-Quinolones (**8**, **17**) by Acid Catalyzed Cyclization of Vinyl Sulfides (**5**, **6, 15**)

Run	Substrate	Conditions[a]			Yield (%)[b]						
		Acid	Temp	Time (h)	2-Quinolones				Bis-sulfides		Recovered
1	**5a**	$BF_3 \cdot Et_2O$	150	140	(**8a**)	98					
2	**6a**	$BF_3 \cdot Et_2O$	150	140	(**8a**)	67					5
3	**5a**	*p*-TsOH	Reflux	5	(**8a**)	96					
4	**6a**	*p*-TsOH	Reflux	5	(**8a**)	90					
5	**5b**	*p*-TsOH	Reflux	2	(**8b**)	72					
6	**6b**	*p*-TsOH	Reflux	2	(**8b**)	68					12
7	**5c**	*p*-TsOH	Reflux	20	(**8c**)	55					16
8	**6c**	*p*-TsOH	Reflux	20	(**8c**)	52					10
9	**5d**	*p*-TsOH	Reflux	5							56
10	**6d**	*p*-TsOH	Reflux	4							95
11	**5g**	*p*-TsOH	Reflux	19	(**8g**)	67					17
12	**6g**	*p*-TsOH	Reflux	20	(**8g**)	58					34
13	**5h**	*p*-TsOH	Reflux	14	(**8h**)	55			(**16h**)	9	
14	**6h**	*p*-TsOH	Reflux	14	(**8h**)	54			(**16h**)	8	
15	**5i**	*p*-TsOH	Reflux	4	(**8i**)	75	(**8j**)	24			
16	**6i**	*p*-TsOH	Reflux	4	(**8i**)	73	(**8j**)	20			
17	**5k**	*p*-TsOH	Reflux	21	(**8k**)	2			(**16k**)	21	61
18	**6k**	*p*-TsOH	Reflux	21	(**8k**)	20			(**16k**)	24	31
19	**15a**	*p*-TsOH	Reflux	72	(**17a**)	68					
20	**15h**	*p*-TsOH	Reflux	14	(**17h**)	16					
21	**15i**	*p*-TsOH	Reflux	4	(**17i**)	40	(**17j**)	10			

a) Toluene was used as the solvent. *b*) A mixture of **5** and **6**.

afforded the 2-quinolones in considerable yields (runs 6, 14). However, in the case of **4d** with two *meta*-OMe groups, addition of the acid did not improve the cyclization reaction to any extent (run 8).

Acid-Induced Cyclization of the Vinyl Sulfides 5 and 6 As described above, $BF_3 \cdot Et_2O$ considerably improved the formation of the quinolones **7** and **8**. In order to examine whether $BF_3 \cdot Et_2O$ induces the cyclization of the vinyl sulfides **5** and **6**, we carried out the reactions under several conditions. For example, the vinyl sulfide **5a**, when treated with 5 molar equivalents of $BF_3 \cdot Et_2O$ in benzene at room temperature for 24 h, did not induce the cyclization to any extent. The cyclization to quinolones, however, was achieved on heating at an elevated temperature (150 °C) for a long time (7 d) in a sealed tube. Thus, **5a** and **6a** afforded the 2-quinolone **8a** in 98% and 67% yields, respectively (Table 2, runs 1, 2). *para*-Toluenesulfonic acid (*p*-TsOH) was found to be a more effective reagent for the cyclization. Thus, **5a** and **6a** on the reaction using 3 molar equivalents of *p*-TsOH under refluxing toluene for 5 h produced the 2-quinolone **8a** in excellent yields (runs 3, 4).

The results strongly indicated that the formation of 2-quinolone *via* the Pummerer reaction occurred *via* the *in situ* formed thionium ion **10** and not *via* the vinyl sulfides **5** and **6**. The protonation to **5** or **6** at the amide carbonyl group did not generate the thionium ion **10** but the other thionium, **11**, and/or the immonium ion **12**, which was probably converted into the 2-quinolone **8** as shown in Chart 2.

Synthesis of Methoxy-2-quinolones The preparation of **5** and **6** was readily achieved by acylation of the anilines **1** with *cis*-3-(phenylsulfanyl)acryloyl chloride, followed by methylation of the resulting anilides **15** (*cis* and *trans*-geo-

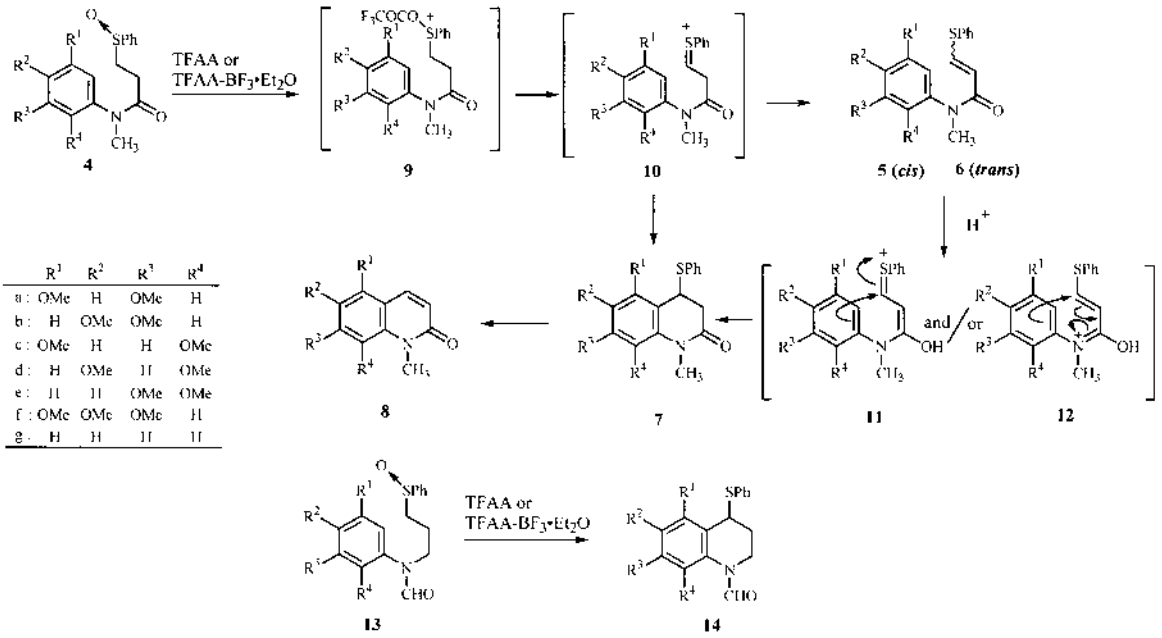


Chart 2

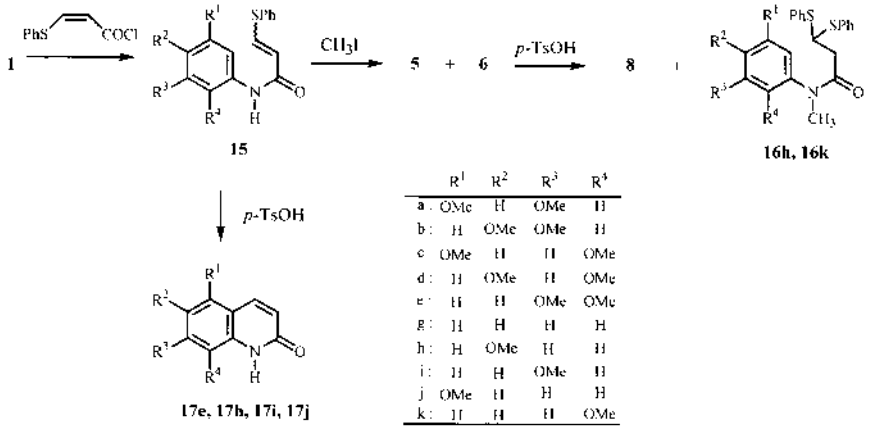


Chart 3

metric mixture) with methyl iodide in the presence of a phase transfer catalyst. During the reactions the geometrical isomerization of the SPh group occurred concomitantly. For example, **1a** afforded **5a** and **6a** in yields of 61% and 29%, respectively. The *cis*-**5** and *trans*-isomer **6** were readily separated by column chromatography (Chart 3).

Treatment involving vinyl sulfides **5** which had at least one OMe group at *para* or *ortho* to the reaction center with *p*-TsOH produced the corresponding 2-quinolones **8** in good to moderate yield, although 3,3-di(phenylsulfanyl)propionamides 1**6**, a Michael adduct of SPh to the double bond of the vinyl sulfides **5** or **6**, were formed in some cases (Table 2). The Michael addition reaction inhibited the cyclization to 2-quinolone. The cyclization of **5i** competitively occurred at the *para* and *ortho* positions to give 7-methoxy- **8i** and 8-methoxy-2-quinolone **8j** in yields of 75% and 24%, respectively (run 15). Even the reaction of the vinyl sulfide **5g**, which had no OMe group at the nucleophilic aromatic ring, caused the cyclization reaction to produce the 2-quinolone **8g** in good yield (run 11). The vinyl sulfide **5k**, having a *meta*-OMe group, gave poor results, as anticipated as shown in Table 2 (run 17).

The *trans*-isomers **6** also caused cyclization under conditions similar to those used for the corresponding *cis*-isomers **5**, thus giving rise to the corresponding 2-quinolones **8** in comparative yield. These facts demonstrated that the synthesis of 2-quinolone *via* the acid-induced cyclization of the vinyl sulfides is achieved without separation of the geometric isomers.

The 2-quinolones **17**, NH derivatives of **8**, were also prepared by the acid-induced cyclization of the corresponding vinyl sulfides **15**, although the reaction was less effective than that of the NMe analogs (**5**, **6**), as shown in Table 2 (runs 19, 20, 21).

In summary, the thionium ion **10** generated by Pummerer reaction of *N*-aryl-*N*-methyl-3-(phenylsulfinyl)propionamides **4** caused two reactions: the formation of vinyl sulfides **5** and **6**, and intramolecular cyclization which produced 2-quinolones **8**, in favor of the former reaction. The treatment of vinyl sulfides **5** and **6** under the Pummerer conditions did not induce intramolecular cyclization. In this sense, the Pummerer reaction of **4** is not a suitable method for con-

structing a 2-quinolone ring system. However, the proton-induced cyclization of the vinyl sulfides **5**, **6** and **15** produced the 2-quinolones **8** and **17** in excellent-to-moderate yields. Thus, this reaction provides a convenient method for the synthesis of 2-quinolones, since the vinyl sulfides can be readily prepared in short steps from commercially available compounds.

Experimental

General Notes Unless otherwise noted, the following procedures were adopted. Melting points were taken on a Yanagimoto SP-M1 hot-stage melting point apparatus and are uncorrected. IR spectra were obtained as films for oils and gums, and as KBr disks for solids, using a JASCO FT/IR-5000 spectrometer, and are given in cm^{-1}. UV spectra were recorded on a Hitachi U-3200 spectrophotometer in methanol, and values are given in λ_{max} nm (ε). NMR spectra were measured on a JEOL JNM-AL 300 (^1H, 300 MHz; ^{13}C, 75 MHz) NMR spectrometer in $CDCl_3$, with tetramethylsilane as an internal standard, at room temperature, and the chemical shifts are given in δ values. Low-resolution (LR)-MS were taken on JMS-AM20, and high resolution MS (HR-MS) on a JEOL JMS-D300 spectrometer at 70 eV [electron ionization MS (EI-MS)] or at 270 eV [chemical ionization (CI)-MS], reactant gas: isobutane) using direct or GC/MS inlet systems. Elemental analyses were recorded on a Yanaco-CHN-corder MT-3. Thin layer chromatography (TLC) was performed on Merck pre-coated Silica gel 60 F_{254} plates (Merck). Column chromatography was carried out with silica gel (Wakogel C-200). The organic extract from each reaction mixture was washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo* to dryness.

Preparation of 3-(Phenylsulfanyl)propionic Acid A solution of 3-bromopropionic acid (34.5 g, 226 mmol) in EtOH (150 ml) was slowly added to a solution of KOH (34.3 g, 520 mmol) and benzenethiol (25 g, 226 mmol) in EtOH (300 ml) at r.t. under an argon atmosphere, and the mixture was refluxed for 2 h. After removal of inorganic precipitates by filtration, the filtrate was concentrated *in vacuo*, and the residue was diluted with water and extracted with $CHCl_3$. Flash chromatograpy with benzene and recrystallization of the eluate with ether–hexane gave 3-(phenylsulfanyl)propionic acid (37.3 g, 91%) as colorless prisms from hexane, mp 55—59 °C (lit.[7] mp 56—56.5 °C). IR: 1696, 1584. ^1H-NMR: 2.5—2.8 (2H, m, $PhSC\underline{H}_2CH_2$–), 3.1—3.4 (2H, m, $PhSCH_2C\underline{H}_2$–), 7.1—7.6 (5H, m, S$\underline{Ph}$), 8.82 (1H, br s, OH). ^{13}C-NMR: 28.8 (t), 34.2 (t), 126.8 (d), 129.1 (d×2), 130.4 (d×2), 134.9 (s), 177.7 (s). LR-MS *m/z*: 182 (M^+, base peak).

Preparation of *N*-(3,5-Dimethoxyphenyl)-3-(phenylsulfanyl)propionamide (2a). Typical Procedure A solution of 3-(phenylsulfanyl)propionic acid (3.0 g, 16.5 mmol) and oxalyl chloride (6.3 g, 49.6 mmol) was stirred at r.t. for 2 h. Removal of excess oxalyl chloride by repeated evaporation under reduced pressure gave an oily material. To a solution of this acid chloride in benzene (30 ml) was slowly added a solution of 3,4-dimethoxyaniline (**1a**) (2.1 g, 13.7 mmol) and triethylamine (1.7 g, 16.8 mmol) in benzene (100 ml) at r.t., and the mixture was stirred for 17 h. The residual oil was chromatographed, eluted with ethyl acetate–hexane (1 : 3) to give **2a** (3.69 g, 71%) as colorless needles, mp 104—106 °C from Et_2O–hexane. IR: 3364, 1707, 1624, 1605, 1551. ^1H-NMR: 2.63 (2H, t, J=7 Hz, $PhSC\underline{H}_2CH_2$–), 3.28 (2H, t, J=7 Hz, $PhSCH_2C\underline{H}_2$–), 3.77 (6H, s, OCH_3×2), 6.24 (1H, t, J=2 Hz, ArH), 6.73 (2H, d, J=2 Hz, ArH), 7.2—7.4 (5H, m, S$\underline{Ph}$). ^{13}C-NMR: 29.2 (t), 37.1 (t), 55.3 (q×2), 96.9 (d), 98.2 (d×2), 126.5 (d), 129.1 (d×2), 129.7 (d×2), 135.2 (s), 139.4 (s), 161.0 (s×2), 169.3 (s). LR-MS *m/z*: 317 (M^+, base peak). HR-MS *m/z* (M^+): Calcd for $C_{17}H_{19}NO_3S$: 317.1083. Found: 317.1075. *Anal*. Calcd for $C_{17}H_{19}NO_3S$: C, 64.33; H, 6.03; N, 4.41. Found: C, 64.18; H, 6.01; N, 4.58.

N-(3,4-Dimethoxyphenyl)-3-(phenylsulfanyl)propionamide (**2b**): (3.68 g, 89%) was obtained from **1b** (2.0 g, 13.0 mmol) as colorless needles from ethyl acetate–hexane, mp 103—106 °C. IR: 3259, 1655, 1603, 1516. ^1H-NMR: 2.63 (2H, t, J=7 Hz, $PhSC\underline{H}_2CH_2$–), 3.30 (2H, t, J=7 Hz, $PhSCH_2C\underline{H}_2$–), 3.85, 3.87 (each 3H, s, OCH_3×2), 6.79, 6.81 (each 1H, s, ArH), 7.1—7.4 (6H, m, ArH and S$\underline{Ph}$), 7.85 (1H, br s, NH). ^{13}C-NMR: 29.3 (t), 37.0 (t), 55.8 (q), 56.1 (q), 105.1 (d), 111.4 (d), 112.0 (d), 126.4 (d), 129.0 (d×2), 129.6 (d×2), 131.3 (s), 135.3 (s), 145.9 (s), 149.0 (s), 169.0 (s). LR-MS *m/z*: 317 (M^+, base peak). HR-MS *m/z* (M^+): Calcd for $C_{17}H_{19}NO_3S$: 317.1086. Found: 317.1099. *Anal*. Calcd for $C_{17}H_{19}NO_3S$: C, 64.33; H, 6.03; N, 4.41. Found: C, 64.09; H, 6.05; N, 4.19.

N-(2,5-Dimethoxyphenyl)-3-(phenylsulfanyl)propionamide (**2c**): (6.16 g, 99%) was obtained from **1c** (3.0 g, 19.6 mmol) as a reddish orange gum. IR: 3410, 1685, 1601, 1533. ^1H-NMR: 2.68 (2H, t, J=7 Hz, $PhSC\underline{H}_2CH_2$–), 3.30 (2H, t, J=7 Hz, $PhSCH_2C\underline{H}_2$–), 3.77, 3.82 (each 3H, s, OCH_3×2), 6.3—6.9 (3H, m, ArH), 7.2—7.5 (5H, m, S$\underline{Ph}$), 7.85 (1H, br s, NH). ^{13}C-NMR: 29.3 (t), 37.4 (t), 55.7 (q), 56.2 (q), 106.0 (d), 108.8 (d), 110.8 (d), 126.4 (d), 128.1 (s), 129.0 (d×2), 129.9 (d×2), 135.3 (s), 142.0 (s), 153.9 (s), 168.9 (s). LR-MS *m/z*: 317 (M^+), 138 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{17}H_{19}NO_3S$: 317.1083. Found: 317.1072.

N-(2,4-Dimethoxyphenyl)-3-(phenylsulfanyl)propionamide (**2d**): (5.92 g, 95%) was obtained from **1d** (3.0 g, 19.6 mmol) as colorless needles from ethyl acetate–hexane, mp 92—95 °C. IR: 3400, 1674, 1614, 1533. ^1H-NMR: 2.65 (2H, t, J=7 Hz, $PhSC\underline{H}_2CH_2$–), 3.30 (2H, t, J=7 Hz, $PhSCH_2C\underline{H}_2$–), 3.79, 3.83 (each 3H, s, OCH_3×2), 6.4—6.6 (2H, m, ArH), 7.2—7.5 (5H, m, SPh), 7.60 (1H, br s, NH), 8.21 (1H, d, J=9 Hz, ArH). ^{13}C-NMR: 29.3 (t), 37.2 (t), 55.4 (q), 55.5 (q), 98.5 (d), 103.7 (d), 120.7 (d), 121.0 (s), 126.3 (d), 128.9 (d×2), 129.7 (d×2), 135.4 (s), 149.1 (s), 156.4 (s), 168.4 (s). LR-MS *m/z*: 317 (M^+), 153 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{17}H_{19}NO_3S$: 317.1083. Found: 317.1077. *Anal*. Calcd for $C_{17}H_{19}NO_3S$: C, 64.33; H, 6.03; N, 4.41. Found: C, 64.31 H, 6.04; N, 4.29.

N-(2,3-Dimethoxyphenyl)-3-(phenylsulfanyl)propionamide (**2e**): (6.20 g, 100%) was obtained from **1e** (3.0 g, 19.6 mmol) as a yellowish gum. IR: 3329, 1685, 1604, 1529. ^1H-NMR: 2.69 (2H, t, J=7 Hz, $PhSC\underline{H}_2CH_2$–), 3.30 (2H, t, J=7 Hz, $PhSCH_2C\underline{H}_2$–), 3.86 (6H, s, OCH_3×2), 6.66 (1H, dd, J=8, 1 Hz, ArH), 7.02 (1H, t, J=8 Hz, ArH), 7.2—7.5 (5H, m, S$\underline{Ph}$), 7.93 (1H, dd, J=8, 1 Hz, ArH). ^{13}C-NMR: 29.5 (t), 37.4 (t), 55.8 (q), 60.7 (q), 107.8 (d), 112.7 (d), 124.1 (d), 126.5 (d), 129.1 (d×2), 129.9 (d×2), 131.9 (s), 135.2 (s), 137.5 (s), 151.9 (s), 169.1 (s). LR-MS *m/z*: 317 (M^+), 153 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{17}H_{19}NO_3S$: 317.1085. Found: 317.1120.

N-(3,4,5-Trimethoxyphenyl)-3-(phenylsulfanyl)propionamide (**2f**): (5.47 g, 96%) was obtained from **1f** (3.0 g, mmol) as an orange gum. IR: 3338, 1689, 1664, 1610, 1547, 1508. ^1H-NMR: 2.64 (2H, t, J=7 Hz, $PhSC\underline{H}_2CH_2$–), 3.29 (2H, t, J=7 Hz, $PhSCH_2C\underline{H}_2$–), 3.80 (3H, s, OCH_3), 3.82 (6H, s, OCH_3×2), 6.80 (2H, s, ArH), 7.2—7.4 (5H, m, S$\underline{Ph}$), 7.85 (1H, br s, NH). ^{13}C-NMR: 29.1 (t), 36.9 (t), 55.9 (q×2), 60.8 (q), 97.6 (d×2), 126.3 (d), 129.0 (d×2), 129.4 (d×2), 134.0 (s), 134.4 (s), 135.3 (s), 153.1 (sx2), 169.3 (s). LR-MS *m/z*: 347 (M^+), 56 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{21}NO_4S$: 347.1188. Found: 347.1166.

N-Phenyl-3-(phenylsulfanyl)propionamide (**2g**): (13.4 g, 97%) was obtained from **1g** (5.0 g, 53.7 mmol) as colorless prisms from ethyl acetate–hexane, mp 78—82 °C. IR: 3319, 1668, 1597, 1523. ^1H-NMR: 2.61 (2H, t, J=7 Hz, $PhSC\underline{H}_2CH_2$–), 3.25 (2H, t, J=7 Hz, $PhSCH_2C\underline{H}_2$–), 7.0—7.7 (10H, m, ArH, SPh). ^{13}C-NMR: 29.4 (t), 37.1 (t), 120.0 (d×2), 124.5 (d), 126.5 (d), 129.0 (d×2), 129.1 (d×2), 129.8 (d×2), 135.2 (s), 137.6 (s), 169.3 (s). LR-MS *m/z*: 257 (M^+), 93 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{15}H_{15}NOS$: 257.0875. Found: 257.0896. *Anal*. Calcd for $C_{15}H_{15}NOS$: C, 70.01; H, 5.87; N, 5.44. Found: C, 70.01; H, 5.92; N, 5.28.

Preparation of *N*-(3,5-dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)-propionamide (3a). Typical Procedure A solution of **2a** (500 mg, 1.56 mmol), methyl iodide (2.24 g, 15.6 mmol), KOH (1.04 g, 15.8 mmol), and tetrabutylammonium bromide (255 mg, 0.79 mmol) in THF (40 ml) was stirred at r.t. for 5.5 h. After removal of inorganic precipitates by filtration, the filtrate was concentrated *in vacuo*, and the residue was diluted with water and extracted with $CHCl_3$. The residual oil was chromatographed, eluted with ethyl acetate–hexane (1 : 2) to give **3a** (522 mg, 100%) as a pale yellow oil. IR: 1657, 1605. ^1H-NMR: 2.48 (2H, t, J=7 Hz, $PhSC\underline{H}_2CH_2$–), 3.1—3.3 (2H, m, $PhSCH_2C\underline{H}_2$–), 3.23 (3H, s, $>NCH_3$), 3.75 (6H, s, OCH_3×2), 6.27 (2H, d, J=2 Hz, ArH), 6.41 (1H, t, J=2 Hz, ArH), 7.1—7.3 (5H, m, S$\underline{Ph}$). ^{13}C-NMR: 29.1 (t), 33.6 (t), 36.9 (q), 55.2 (q×2), 99.6 (d), 105.3 (d×2), 125.6 (d), 128.6 (d×2), 128.7 (d×2), 135.9 (s), 145.0 (s), 161.3 (s×2), 170.5 (s). LR-MS *m/z*: 331 (M^+), 221 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{21}NO_3S$: 331.1240. Found: 331.1215.

N-(3,4-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)propionamide (**3b**): (2.61 g, 93%) was obtained from **2b** (2.7 g, 8.2 mmol) as a pale yellow gum. IR: 1655, 1595, 1510. ^1H-NMR: 2.42 (2H, t, J=7 Hz, $PhSC\underline{H}_2CH_2$–), 3.18 (2H, t, J=7 Hz, $PhSCH_2C\underline{H}_2$–), 3.24 (3H, s, $>NCH_3$), 3.81, 3.89 (each 3H, s, OCH_3×2), 6.6—6.8 (3H, m, ArH), 7.1—7.3 (5H, m, S$\underline{Ph}$). ^{13}C-NMR: 29.2 (t), 33.7 (t), 37.4 (q), 55.9 (q×2), 110.4 (d), 111.5 (d), 119.3 (d), 125.8 (d), 128.7 (d×2), 128.8 (d×2), 136.0 (s), 136.5 (s), 148.6 (s), 149.6 (s), 171.1 (s). LR-MS *m/z*: 331 (M^+), 152 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{21}NO_3S$: 331.1240. Found: 331.1279.

N-(2,5-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)propionamide (**3c**): (5.74 g, 100%) was obtained from **2c** (5.5 g, 17.4 mmol) as a pale yellow gum. IR: 1655, 1610, 1585, 1508. ^1H-NMR: 2.35 (2H, t, J=7 Hz, $PhSC\underline{H}_2CH_2$–), 3.17 (2H, t, J=7 Hz, $PhSCH_2C\underline{H}_2$–), 3.17 (3H, s, $>NCH_3$), 3.72, 3.74 (each 3H, s, OCH_3×2), 6.68 (1H, t, J=2 Hz, ArH), 6.84 (2H, d,

J=2 Hz, ArH), 7.1—7.3 (5H, m, SPh). ^{13}C-NMR: 29.0 (t), 33.3 (t), 35.9 (q), 55.6 (q), 55.7 (q), 112.7 (d), 113.9 (d), 114.9 (d), 125.6 (d), 128.7 (d×2), 128.7 (d×2), 132.3 (s), 136.1 (s), 149.0 (s), 153.7 (s), 171.5 (s). LR-MS *m/z*: 331 (M^+), 152 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{21}NO_3S$: 331.1239. Found: 331.1222.

N-(2,4-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)propionamide (**3d**): (4.18 g, 100%) was obtained from **2d** (4.0 g, 12.6 mmol) as a pale yellow gum. IR: 1655, 1585, 1512. ^{1}H-NMR: 2.2—2.5 (2H, m, PhSC$\underline{H}_2$CH$_2$–), 3.0—3.3 (2H, m, PhSCH$_2$C$\underline{H}_2$–), 3.14 (3H, s, >NCH$_3$), 3.73, 3.82 (each 3H, s, OCH$_3$×2), 6.3—6.5 (2H, m, ArH), 6.9—7.2 (6H, m, ArH and SPh). ^{13}C-NMR: 29.1 (t), 33.4 (t), 36.2 (q), 55.4 (q), 55.5 (q), 99.6 (d), 104.6 (d), 125.2 (s), 125.7 (d), 128.7 (d×4), 129.3 (d), 136.3 (s), 155.8 (s), 160.5 (s), 172.0 (s). LR-MS *m/z*: 331 (M^+), 151 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{21}NO_3S$: 331.1240. Found: 331.1225.

N-(2,3-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)propionamide (**3e**): (5.88 g, 99%) was obtained from **2e** (5.7 g, 18.0 mmol) as a yellowish gum. IR: 1660, 1618, 1589. ^{1}H-NMR: 2.40 (2H, t, J=7 Hz, PhSC$\underline{H}_2$CH$_2$–), 3.19 (2H, t, J=7 Hz, PhSCH$_2$C$\underline{H}_2$–), 3.23 (3H, s, >NCH$_3$), 3.79, 3.88 (each 3H, s, OCH$_3$×2), 6.6—7.3 (8H, m, ArH and SPh). ^{13}C-NMR: 29.1 (t), 35.5 (t), 36.8 (q), 56.0 (q), 60.9 (q), 112.2 (d), 120.4 (d), 124.2 (d), 125.7 (d), 128.8 (d×4), 135.2 (s), 137.1 (s), 145.2 (s), 153.8 (s), 171.5 (s). LR-MS *m/z*: 331 (M^+), 152 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{21}NO_3S$: 331.1240. Found: 331.1195.

N-(3,4,5-Trimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)propionamide (**3f**): (5.20 g, 100%) was obtained from **2f** (5.0 g, 14.4 mmol) as a yellow gum. IR: 1655, 1593, 1502. ^{1}H-NMR: 2.47 (2H, t, J=7 Hz, PhSC$\underline{H}_2$CH$_2$–), 3.20 (2H, t, J=7 Hz, PhSCH$_2$C$\underline{H}_2$–), 3.24 (3H, s, >NCH$_3$), 3.78 (6H, s, OCH$_3$×2), 3.85 (3H, s, OCH$_3$), 6.34 (2H, s, ArH), 7.1—7.3 (5H, m, SPh), 7.85 (1H, br s, >N–H). ^{13}C-NMR: 29.4 (t), 33.7 (t), 37.3 (q), 56.2 (q×2), 60.9 (q), 104.6 (d×2), 126.0 (d), 128.8 (d×2), 129.0 (d×2), 136.0 (s), 137.7 (s), 139.2 (s), 153.8 (s×2), 170.9 (s). LR-MS *m/z*: 361 (M^+), 182 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{19}H_{23}NO_4S$: 361.1348. Found: 361.1360.

N-Methyll-*N*-phenyl-3-(phenylsulfanyl)propionamide (**3g**): (10.54 g, 100%) was obtained from **2g** (10.0 g, 38.9 mmol) as a yellow gum. IR: 1657, 1595. ^{1}H-NMR: 2.40 (2H, t, J=7 Hz, PhSC$\underline{H}_2$CH$_2$–), 3.18 (2H, t, J=7 Hz, PhSCH$_2$C$\underline{H}_2$–), 3.27 (3H, s, >NCH$_3$), 7.0—7.4 (10H, m, ArH, SPh). ^{13}C-NMR: 29.2 (t), 33.9 (t), 37.3 (q), 125.8 (d), 127.1 (d×2), 127.8 (d), 128.8 (d×2), 128.9 (d×2), 129.7 (d×2), 136.0 (s), 143.6 (s), 170.9 (s). LR-MS *m/z*: 271 (M^+), 51 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{16}H_{17}NOS$: 271.1028. Found: 271.1010.

Preparation of *N*-(3,5-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfinyl) propionamide (4a). Typical Procedure To a solution of **3a** (1.0 g, 3.02 mmol) in MeOH (100 ml) was added a solution of $NaIO_4$ (0.97 g, 4.54 mmol) in H_2O (20 ml), and the mixture was stirred at r.t. for 6 h. After removal of inorganic precipitates by filtration, the filtrate was concentrated *in vacuo*. The residue was extracted with $CHCl_3$. The product was chromatographed, eluted with ethyl acetate to give **4a** (1.05 g, 100%) as a pale yellow oil. IR: 1657, 1605, 1046. ^{1}H-NMR: 2.4—3.2 (4H, m), 3.22 (3H, s, >NCH$_3$), 3.80 (6H, s, OCH$_3$×2), 6.29 (2H, d, J=2 Hz, ArH), 6.44 (1H, t, J=2 Hz, ArH), 7.4—7.7 (5H, m, SPh). ^{13}C-NMR: 26.9 (t), 37.2 (q), 52.8 (t), 55.5 (q×2), 100.0 (d), 105.4 (d×2), 123.9 (d), 129.1 (d×2), 130.9 (d×2), 143.7 (s), 144.8 (s), 161.6 (s×2), 169.9 (s). LR-MS *m/z*: 347 (M^+), 222 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{21}NO_4S$: 347.1369. Found: 347.1406.

N-(3,4-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfinyl)propionamide (**4b**): (2.49 g, 95%) was obtained from **3b** (2.5 g, 7.5 mmol) as a yellow gum. IR: 1655, 1595, 1512, 1026. ^{1}H-NMR: 2.2—3.4 (4H, m), 3.23 (3H, s, >NCH$_3$), 3.87, 3.91 (each 3H, s, OCH$_3$×2), 6.6—7.0 (3H, m, ArH), 7.3—7.7 (5H, m, SPh). ^{13}C-NMR: 26.9 (t), 37.5 (q), 52.8 (t), 56.0 (q×2), 110.4 (d), 111.7 (d), 119.4 (d), 123.9 (d×2), 129.0 (d×2), 130.8 (d), 136.1 (s), 143.8 (s), 148.9 (s), 149.8 (s), 170.3 (s). LR-MS *m/z*: 347 (M^+), 56 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{21}NO_4S$: 347.1192. Found: 347.1203.

N-(2,5-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfinyl)propionamide (**4c**): (5.38 g, 99%) was obtained from **3c** (5.2 g, 15.6 mmol) as a yellow gum. IR: 1655, 1610, 1508, 1043. ^{1}H-NMR: 2.2—3.4 (4H, m), 3.15, 3.16 (total 3H, s, >NCH$_3$), 3.70, 3.76, 3.79, 3.81 (total 6H, s, OCH$_3$×2), 6.6—6.9 (3H, m, ArH), 7.4—7.7 (5H, m, SPh). ^{13}C-NMR: 26.2, 26.3 (each t), 36.1 (q), 52.8 (t×2), 55.7 (q), 55.8 (q), 112.7, 112.8 (each d), 114.0, 114.2 (each d), 114.8 (d), 123.8 (d×2), 128.9 (d×2), 130.7 (d), 131.8 (s), 143.7 (s), 148.8, 148.9 (s), 153.7, 153.8 (s), 170.6 (s). LR-MS *m/z*: 347 (M^+), 56 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{21}NO_4S$: 347.1190. Found: 347.1195.

N-(2,4-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfinyl)propionamide (**4d**): (5.63 g, 98%) was obtained from **3d** (5.5 g, 16.5 mmol) as a pale yellow gum. IR: 1655, 1512, 1039. ^{1}H-NMR: 2.2—3.4 (4H, m), 3.13 (3H, s, >NCH$_3$), 3.72, 3.84 (each 3H, s, OCH$_3$×2), 6.4—6.6 (2H, m, ArH), 6.9—7.2 (1H, m, ArH), 7.4—7.7 (5H, m, SPh). ^{13}C-NMR: 26.1, 26.2 (each t), 36.2 (q), 52.8, 52.9 (each t), 55.2 (q), 55.4 (q), 99.5 (d), 104.7 (d), 123.7 (d×2), 124.5 (s), 128.9 (d×2), 129.2 (d), 130.6 (d), 143.7 (s), 155.5, 155.6 (s), 160.5 (s), 170.9 (s). CI-MS *m/z*: 348 (MH^+), 141 (base peak).

N-(2,3-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfinyl)propionamide (**4e**): (3.10 g, 98%) was obtained from **3e** (3.0 g, 9.0 mmol) as a pale yellow gum. IR: 1658, 1589, 1045. ^{1}H-NMR: 2.3—3.2 (4H, m), 3.20, 3.23 (total 3H, s, >NCH$_3$), 3.76, 3.86, 3.89, 3.90 (total 6H, s, OCH$_3$×2), 6.6—7.2 (3H, m, ArH), 7.4—7.7 (5H, m, SPh). ^{13}C-NMR: 26.5, 26.8 (each t), 36.8, 36.8 (each q), 52.9, 53.1 (each t), 56.0 (q), 60.9 (q), 112.5 (d), 120.1, 120.3 (each d), 123.9 (d×2), 124.2, 124.4 (each d), 129.0 (d×2), 130.8 (d), 136.6 (s), 143.8, 144.0 (s), 145.0 (s), 153.6, 153.7 (s), 170.4, 170.6 (s). LR-MS *m/z*: 347 (M^+), 190 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{21}NO_4S$: 347.1189. Found: 347.1184.

N-(3,4,5-Trimethoxyphenyl)-*N*-methyl-3-(phenylsulfinyl)propionamide (**4f**): (4.89 g, 98%) was obtained from **3f** (4.8 g, 13.2 mmol) as a yellow gum. IR: 1655, 1593, 1508, 1047. ^{1}H-NMR: 2.2—3.4 (4H, m), 3.24 (3H, s, >NCH$_3$), 3.85 (6H, s, OCH$_3$×2), 3.88 (3H, s, OCH$_3$), 6.37 (2H, s, ArH), 7.4—7.7 (5H, m, SPh). ^{13}C-NMR: 25.9 (t), 36.6 (q), 51.9 (t), 55.5 (q×2), 60.1 (q), 104.0 (d×2), 123.2 (d×2), 127.6 (d×2), 130.2 (d), 137.2 (s), 138.2 (s), 143.0 (s), 153.2 (s×2), 169.3 (s). LR-MS *m/z*: 377 (M^+), 56 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{19}H_{23}NO_5S$: 377.1297. Found: 377.1300.

N-Methyll-*N*-phenyl-3-(phenylsulfinyl)propionamide (**4g**): (10.51 g, 99%) was obtained from **3g** (10.0 g, 30.0 mmol) as a yellow gum. IR: 1657, 1595, 1043. ^{1}H-NMR: 2.2—3.2 (4H, m), 3.25 (3H, s, >NCH$_3$), 7.1—7.6 (10H, m, ArH and SPh). ^{13}C-NMR: 26.9 (t), 37.2 (q), 52.6 (t), 123.7 (d×2), 127.0 (d), 127.9 (d), 128.9 (d×2), 129.8 (d×2), 130.7 (d×2), 143.0 (s), 143.6 (s), 169.8 (s). LR-MS *m/z*: 287 (M^+), 106 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{16}H_{17}NO_2S$: 287.0978. Found: 287.0963.

Pummerer Reaction of 4a. Typical Procedure i) Method A. TFAA (303 mg, 1.44 mmol) was added to a solution of **4a** (100 mg, 0.29 mmol) in benzene (50 ml) at r.t., and the mixture was stirred for 20 h under argon atmosphere. After removal of the solvent *in vacuo*, the product was chromatographed with ethyl acetate–hexane (1 : 3) to give **5a** (28 mg, 30%), **6a** (17 mg, 18%), and **8a** (20 mg, 32%).

ii) Method B. TFAA (913 mg, 4.35 mmol) was added to a solution of **4a** (300 mg, 0.87 mmol) in benzene (50 ml) at r.t., and the mixture was stirred for 30 min under argon atmosphere. To this solution, $BF_3 \cdot Et_2O$ (370 mg, 2.61 mmol) was added, and the mixture was stirred at r.t. for 3 h. After removal of the solvent *in vacuo*, the residue was treated with 5% $NaHCO_3$ and extracted with $CHCl_3$. The residual oil was chromatographed, eluted with ethyl acetate–hexane (1 : 3) to give **5a** (29 mg, 10%), **6a** (74 mg, 26%), and **8a** (97 mg, 51%).

cis-*N*-(3,5-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)acrylamide (**5a**): Colorless prisms from Et_2O–hexane, mp 114—118 °C. IR: 1638, 1593. ^{1}H-NMR: 3.34 (3H, s, >NCH$_3$), 3.79 (6H, s, OCH$_3$×2), 5.89 (1H, d, J=10 Hz, PhSCH=C$\underline{H}$–), 6.3—6.5 (3H, m, ArH), 7.01 (1H, d, J=10 Hz, PhSC$\underline{H}$=CH–), 7.2—7.5 (5H, m, SPh). ^{13}C-NMR: 36.8 (q), 55.5 (q×2), 99.6 (d), 105.6 (d×2), 113.6 (d), 127.7 (d), 129.1 (d×2), 130.9 (d×2), 137.6 (s), 145.4 (s), 146.5 (d), 161.4 (s×2), 166.3 (s). CI-MS *m/z*: 330 (MH^+), 57 (base peak). *Anal*. Calcd for $C_{18}H_{19}NO_3S$: C, 65.63; H, 5.81; N, 4.25. Found: C, 65.41; H, 5.88; N, 4.17.

trans-*N*-(3,5-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)acrylamide (**6a**): Yellow gum. IR: 1644, 1593. ^{1}H-NMR: 3.28 (3H, s, >NCH$_3$), 3.78 (6H, s, OCH$_3$×2), 5.78 (1H, d, J=15 Hz, PhSCH=C$\underline{H}$–), 6.25 (1H, d, J=1 Hz, ArH), 6.28 (1H, d, J=1 Hz, ArH), 6.3—6.4 (1H, m, ArH), 7.2—7.4 (5H, m, SPh), 7.70 (1H, d, J=15 Hz, PhSC$\underline{H}$=CH–). ^{13}C-NMR: 37.0 (q), 55.4 (q×2), 99.5 (d), 105.7 (d×2), 117.0 (d), 128.3 (d), 129.2 (d×2), 131.8 (d×2), 132.0 (s), 142.8 (d), 145.0 (s), 161.2 (s×2), 164.4 (s). LR-MS *m/z*: 329 (M^+), 206 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{19}NO_3S$: 329.1082. Found: 329.1074.

5,7-Dimethoxy-1-methyl-2-quinolone (**8a**): Yellow needles from ethyl acetate, mp 117—120 °C. IR: 1684, 1642, 1622, 1582, 1501. UV: 213 (14800), 238 (11400), 257 (4600), 306 (4700), 324 (4200), 338 (2900). ^{1}H-NMR: 3.67 (3H, s, >NCH$_3$), 3.91 (6H, s, OCH$_3$×2), 6.29, 6.37 (each 1H, d, J=2 Hz, 6-H, 8-H), 6.51, 8.02 (each 1H, d, J=10 Hz, 3-H, 4-H). ^{13}C-NMR: 29.6 (q), 55.4 (q), 55.6 (q), 90.2 (d), 92.5 (d), 105.9 (s), 116.1 (d), 133.1 (d), 142.2 (s), 157.4 (s), 162.6 (s), 163.0 (s). LR-MS *m/z*: 219 (M^+, base peak). *Anal*. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.90; H, 5.95; N, 6.44.

Pummerer Reaction of 4b i) Method A. **4b** (1.0 g, 2.88 mmol) gave **5b**

(305 mg, 32%), **6b** (416 mg, 44%), and **8b** (108 mg, 17%).

ii) Method B. **4b** (1.0 g, 2.88 mmol) gave **5b** (123 mg, 13%), **6b** (166 mg, 18%), **7b** (139 mg, 15%), and **8b** (268 mg, 42%).

cis-N-(3,4-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)acrylamide (**5b**): Pale yellow prisms from Et_2O–hexane, mp 102—104 °C. IR: 1633, 1595, 1566. UV: 296 (24100). ^{1}H-NMR: 3.34 (3H, s, >NCH_3), 3.87, 3.90 (each 3H, s, OCH_3×2), 5.80 (1H, d, J=10 Hz, PhSCH=C<u>H</u>–), 6.7—6.9 (3H, m, ArH), 6.99 (1H, d, J=10 Hz, PhSC<u>H</u>=CH–), 7.2—7.6 (5H, m, S<u>Ph</u>). ^{13}C-NMR: 37.1 (q), 56.0 (q×2), 110.7 (d), 111.5 (d), 113.6 (d), 119.5 (d), 127.7 (d), 129.1 (d×2), 130.8 (d×2), 136.7 (s), 137.7 (s), 146.2 (d), 148.5 (s), 149.6 (s), 166.5 (s). LR-MS *m/z*: 329 (M^+), 167 (base peak). *Anal*. Calcd for $C_{18}H_{19}NO_3S$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.70; H, 5.87; N, 4.11.

trans-N-(3,4-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)acrylamide (**6b**): Pale yellow prisms from Et_2O–hexane, mp 99—101 °C. IR: 1633, 1570, 1512. UV: 284 (15500). ^{1}H-NMR: 3.28 (3H, s, >NCH_3), 3.85, 3.91 (each 3H, s, OCH_3×2), 5.70 (1H, d, J=15 Hz, PhSCH=C<u>H</u>–), 6.6—6.9 (3H, m, ArH), 7.2—7.5 (5H, m, S<u>Ph</u>), 7.69 (1H, d, J=15 Hz, PhSC<u>H</u>=CH–). ^{13}C-NMR: 37.2 (q), 55.93 (q), 55.98 (q), 110.7 (d), 111.3 (d), 116.9 (d), 119.5 (d), 128.2 (d), 129.2 (d×2), 131.8 (d×2), 131.9 (s), 136.3 (s), 142.5 (d), 148.4 (s), 149.4 (s), 164.7 (s). LR-MS *m/z*: 329 (M^+), 167 (base peak). *Anal*. Calcd for $C_{18}H_{19}NO_3S$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.55; H, 5.87; N, 4.11.

6,7-Dimethoxy-1-methyl-4-phenylsulfanyl-3,4-dihydro-2-quinolone (**7b**): Colorless needles from ethyl acetate–hexane, mp 147—151 °C. IR: 1666, 1612, 1520. ^{1}H-NMR: 2.90 (2H, d, J=4 Hz, 3-H), 3.30 (3H, s, >NCH_3), 3.76, 3.90 (each 3H, s, OCH_3×2), 4.34 (1H, t, J=4 Hz, 4-H), 6.54, 6.59 (each 1H, s, 5-H, 8-H), 7.2—7.5 (5H, m, S<u>Ph</u>). ^{13}C-NMR: 29.5 (q), 37.5 (t), 44.9 (d), 56.3 (q×2), 100.5 (d), 112.0 (d), 116.3 (s), 128.4 (d), 128.9 (d×2), 132.7 (s), 134.0 (s), 135.0 (d×2), 144.4 (s), 149.3 (s), 167.1 (s). LR-MS *m/z*: 329 (M^+), 220 (base peak). *Anal*. Calcd for $C_{18}H_{19}NO_3S$: C, 65.63; H, 5.81; N, 4.25. Found: C, 65.43; H, 5.82; N, 4.09.

6,7-Dimethoxy-1-methyl-2-quinolone (**8b**): Yellow prisms from Et_2O–hexane, mp 148—152 °C. IR: 1649, 1583, 1562, 1520. UV: 236 (20300), 276 (2600), 286 (2700), 348 (6100), 366 (4300). ^{1}H-NMR: 3.72 (3H, s, >NCH_3), 3.93, 4.01 (each 3H, s, OCH_3×2), 6.59, 7.56 (each 1H, d, J=9 Hz, 3-H, 4-H), 6.77, 6.95 (each 1H, s, 5-H, 8-H). ^{13}C-NMR: 29.6 (q), 56.1 (q), 56.2 (q), 97.2 (d), 109.5 (d), 113.9 (s), 119.0 (d), 135.7 (s), 138.1 (d), 145.0 (s), 152.1 (s), 162.2 (s). LR-MS *m/z*: 219 (M^+, base peak). HR-MS *m/z* (M^+): Calcd for $C_{12}H_{13}NO_3$: 219.0893. Found: 219.0795. *Anal*. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.58; H, 6.08; N, 6.34.

Pummerer Reaction of 4c i) Method A. **4c** (1.0 g, 2.88 mmol) gave **5c** (343 mg, 36%), **6c** (498 mg, 53%), and **32c** (44 mg, 7%).

ii) Method B. **4c** (1.0 g, 2.88 mmol) gave **5c** (84 mg, 9%), **6c** (185 mg, 20%), **7c** (434 mg, 46%), and **8c** (137 mg, 22%).

cis-N-(2,5-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)acrylamide (**5c**): Colorless prisms from Et_2O–hexane, mp 128—130 °C. IR: 1635, 1568, 1508. UV: 298 (19500). ^{1}H-NMR: 3.27 (3H, s, >NCH_3), 3.76, 3.77 (each 3H, s, OCH_3×2), 5.73 (1H, d, J=10 Hz, PhSCH=C<u>H</u>–), 6.7—6.9 (3H, m, ArH), 6.95 (1H, d, J=10 Hz, PhSC<u>H</u>=CH–), 7.2—7.6 (5H, m, S<u>Ph</u>). ^{13}C-NMR: 35.5 (q), 55.7 (q), 56.0 (q), 112.9 (d), 113.4 (d), 113.7 (d), 115.2 (d), 127.5 (d), 129.0 (d×2), 130.7 (d×2), 132.4 (s), 137.7 (s), 145.7 (d), 149.4 (s), 153.5 (s), 166.6 (s). LR-MS *m/z*: 329 (M^+), 167 (base peak). *Anal*. Calcd for $C_{18}H_{19}NO_3S$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.55; H, 5.92; N, 4.09.

trans-N-(2,5-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)acrylamide (**6c**): Colorless prisms from Et_2O–hexane, mp 91—95 °C. IR: 1631, 1583, 1560. UV: 283 (20300). ^{1}H-NMR: 3.21 (3H, s, >NCH_3), 3.73, 3.76 (each 3H, s, OCH_3×2), 5.67 (1H, d, J=15 Hz, PhSCH=C<u>H</u>–), 6.65 (1H, t, J=2 Hz, ArH), 6.83 (2H, d, J=2 Hz, ArH), 7.2—7.3 (5H, m, S<u>Ph</u>), 7.69 (1H, d, J=15 Hz, PhSC<u>H</u>=CH–). ^{13}C-NMR: 35.8 (q), 55.7 (q), 56.0 (q), 112.8 (d), 113.7 (d), 115.1 (d), 116.9 (d), 128.0 (d), 129.1 (d×2), 131.6 (d×2), 132.0 (s), 142.2 (d), 149.3 (s), 153.4 (s), 164.8 (s). LR-MS *m/z*: 329 (M^+), 167 (base peak). *Anal*. Calcd for $C_{18}H_{19}NO_3S$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.64; H, 5.92; N, 4.06.

5,8-Dimethoxy-1-methyl-4-phenylsulfanyl-3,4-dihydro-2-quinolone (**7c**): Colorless prisms from Et_2O–hexane, mp 137—141 °C. IR: 1666, 1597. ^{1}H-NMR: 2.76 (2H, d, J=3 Hz, 3-H), 3.34 (3H, s, >NCH_3), 3.79, 3.79 (each 3H, s, OCH_3×2), 4.80 (1H, t, J=3 Hz, 4-H), 6.60, 6.86 (each 1H, d, J=9 Hz, 6-H, 7-H), 7.2—7.6 (5H, m, S<u>Ph</u>). ^{13}C-NMR: 34.4 (q), 37.6 (t), 38.6 (d), 56.1 (q), 56.7 (q), 106.8 (d), 113.8 (d), 117.8 (s), 128.1 (d), 128.7 (d×2), 132.0 (s), 133.1 (s), 134.6 (d×2), 144.3 (s), 150.0 (s), 169.3 (s). LR-MS *m/z*: 329 (M^+), 220 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{18}H_{19}NO_3S$: 329.1086. Found: 329.1122. *Anal*. Calcd for $C_{18}H_{19}NO_3S$: C, 65.63; H, 5.81; N, 4.25. Found: C, 65.47; H, 5.85; N, 4.15.

5,8-Dimethoxy-1-methyl-2-quinolone (**8c**): Yellow needles from Et_2O–hexane, mp 70—74 °C. IR: 1657, 1597. UV: 213 (25700), 241 (20100), 263 (13100), 302 (8100), 314 (6800), 340 (2300). ^{1}H-NMR: 3.83 (3H, s, >NCH_3), 3.88, 3.94 (each 3H, s, OCH_3×2), 6.59, 7.00 (each 1H, d, J=9 Hz, 6-H, 7-H), 6.64, 8.09 (each 1H, d, J=10 Hz, 3-H, 4-H). ^{13}C-NMR: 34.8 (q), 55.9 (q), 57.7 (q), 102.7 (d), 113.4 (s), 115.5 (d), 120.3 (d), 132.6 (s), 133.1 (d), 142.7 (s), 150.5 (s), 163.6 (s). LR-MS *m/z*: 219 (M^+, base peak). HR-MS *m/z* (M^+): Calcd for $C_{12}H_{13}NO_3$: 219.0895. Found: 219.0915.

Pummerer Reaction of 4d i) Method A. **4d** (1.0 g, 2.88 mmol) gave **5d** (340 mg, 36%) and **6d** (598 mg, 63%).

ii) Method B. **4d** (1.0 g, 2.88 mmol) gave **5d** (427 mg, 45%) and **6d** (493 mg, 52%).

cis-N-(2,4-Dimethoxyphenyl)-*N*-methyl-3-phenylsulfanylacrylamide (**5d**): Pale yellow prisms from Et_2O–hexane, mp 73—75 °C. IR: 1639, 1577, 1512. UV: 290 (20400). ^{1}H-NMR: 3.23 (3H, s, >NCH_3), 3.79, 3.82 (each 3H, s, OCH_3×2), 5.70 (1H, d, J=10 Hz, PhSCH=C<u>H</u>–), 6.47 (1H dd, J=8, 3 Hz, 5′-H), 6.52 (1H, d, J=3 Hz, 3′-H), 6.93 (1H, d, J=10 Hz, PhSC<u>H</u>=CH–), 7.07 (1H, d, J=8 Ha, 6′-H), 7.2—7.5 (5H, m, S<u>Ph</u>). ^{13}C-NMR: 35.8 (q), 55.49 (q), 55.55 (q), 99.6 (d), 104.4 (d), 113.6 (d), 125.3 (s), 127.5 (d), 129.0 (d×2), 129.7 (d), 130.8 (d×2), 145.3(d), 156.2 (s), 160.4 (s), 167.1 (s). LR-MS *m/z*: 329 (M^+), 109 (base peak). *Anal*. Calcd for $C_{18}H_{19}NO_3S$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.62; H, 5.92; N, 4.11.

trans-N-(2,4-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)acrylamide (**6d**): Pale yellow prisms from ether–hexane, mp 100—102 °C. IR: 1637, 1608, 1570. UV: 285 (17400). ^{1}H-NMR: 3.18 (3H, s, >NCH_3), 3.76, 3.84 (each 3H, s, OCH_3×2), 5.69 (1H, d, J=15 Hz, PhSCH=C<u>H</u>–), 6.43 (1H, dd, J=8, 3 Hz, 5′-H), 9.46 (1H, d, J=3 Hz, 3′-H), 6.97 (1H, d, J=8 Hz, 6′-H), 7.2—7.4 (5H, m, S<u>Ph</u>), 7.67 (1H, d, J=15 Hz, PhSC<u>H</u>=CH–). ^{13}C-NMR: 36.0 (q), 55.5 (q×2), 99.5 (d), 104.4 (d), 117.2 (d), 124.9 (s), 127.9 (d), 129.1 (d×2), 129.6 (d), 131.5 (d×2), 132.3 (s), 141.8 (d), 156.0 (s), 160.4 (s), 165.3 (s). LR-MS *m/z*: 329 (M^+), 167 (base peak). *Anal*. Calcd for $C_{18}H_{19}NO_3S$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.61; H, 5.92; N, 4.07

Pummerer Reaction of 4e i) Method A. **4e** (1.0 g, 2.88 mmol) gave **5e** (374 mg, 39%), **6e** (321 mg, 34%), and **8e** (127 mg, 21%).

ii) Method B. **4e** (1.0 g, 2.88 mmol) gave **5e** (156 mg, 17%), **6e** (409 mg, 43%), and **8e** (252 mg, 40%).

cis-N-(2,3-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)acrylamide (**5e**): Yellow gum. IR: 1635, 1585, 1566. ^{1}H-NMR: 3.32 (3H, s, >NCH_3), 3.81, 3.89 (each 3H, s, OCH_3×2), 5.77 (1H, d, J=10 Hz, PhSCH=C<u>H</u>–), 6.7—7.1 (3H, m, ArH), 6.98 (1H, d, J=10 Hz, PhSC<u>H</u>=CH–), 7.2—7.6 (5H, m, S<u>Ph</u>). ^{13}C-NMR: 36.2 (q), 56.0 (q), 60.9 (q), 112.1 (d), 113.4 (d), 121.0 (d), 124.0 (d), 127.7 (d), 129.1 (d×2), 130.9 (d×2), 137.3 (s), 137.8 (s), 145.5 (s), 146.3 (d), 153.8 (s), 166.6 (s). LR-MS *m/z*: 329 (M^+), 57 (base peak).

trans-N-(2,3-Dimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)acrylamide (**6e**): Yellow gum. IR: 1643, 1585. ^{1}H-NMR: 3.26 (3H, s, >NCH_3), 3.76, 3.90 (each 3H, s, OCH_3×2), 5.72 (1H, d, J=15 Hz, PhSCH=C<u>H</u>–), 6.6—7.1 (3H, m, ArH), 7.2—7.5 (5H, m, S<u>Ph</u>), 7.72 (1H, d, J=15 Hz, PhSC<u>H</u>=CH–). ^{13}C-NMR: 36.3 (q), 56.0 (q), 60.8 (q), 112.1 (d), 116.8 (d), 121.0 (d), 123.9 (d), 128.1 (d), 129.2 (d×2), 131.7 (d×2), 132.1 (s), 136.9 (s), 142.7 (d), 145.4 (s), 153.6 (s), 164.7 (s). LR-MS *m/z*: 329 (M^+), 153 (base peak).

7,8-Dimethoxy-1-methyl-2-quinolone (**8e**): Yellow prisms from Et_2O–hexane, mp 92—94 °C. IR: 1653, 1589, 1558, 1502. UV: 240 (36200), 262 (8800), 294 (8800), 328 (6200). ^{1}H-NMR: 3.81 (3H, s, >NCH_3), 3.96 (6H, s, OCH_3×2), 6.53, 7.52 (each 1H, d, J=9 Hz, 3-H, 4-H), 6.87, 7.24 (each 1H, d, J=9 Hz, 5-H, 6-H). ^{13}C-NMR: 33.6 (q), 56.3 (q), 61.7 (q), 107.6 (d), 117.1 (s), 119.0 (d), 124.7 (d), 135.0 (s), 137.0 (s), 139.0 (d), 155.3 (s), 163.9 (s). LR-MS *m/z*: 219 (M^+) 64 (base peak). HR-MS *m/z* (M^+): Calcd for $C_{12}H_{13}NO_3$: 219.0895. Found: 219.0928. *Anal*. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39. Found: C, 65.66; H, 6.01; N, 6.25.

Pummerer Reaction of 4f i) Method A. **4f** (2.0 g, 5.31 mmol) gave **5f** (609 mg, 32%), **6f** (504 mg, 27%), and **8f** (515 mg, 39%).

ii) Method B. **4f** (2.0 g, 5.31 mmol) gave **5f** (404 mg, 21%), **6f** (485 mg, 26%), and **8f** (677 mg, 51%).

cis-N-(3,4,5-Trimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)acrylamide (**5f**): Colorless plates from ethyl acetate, mp 159—163 °C. IR: 1643, 1591, 1502. ^{1}H-NMR: 3.35 (3H, s, >NCH_3), 3.85 (6H, s, OCH_3×2), 3.87 (3H, s, OCH_3), 5.85 (1H, d, J=10 Hz, PhSCH=C<u>H</u>–), 6.44 (2H, s, 2′-H, 6′-H), 7.03 (1H, d, J=10 Hz, PhSC<u>H</u>=CH–), 7.2—7.6 (5H, m, S<u>Ph</u>). ^{13}C-NMR: 36.8 (q), 56.1 (q×2), 60.7 (q), 104.6 (d×2), 113.4 (d), 127.6 (d), 129.0 (d×2), 130.6 (d×2), 137.3 (s), 137.5 (s), 139.2 (s), 146.2 (d), 153.6 (s×2), 166.1 (s). LR-MS *m/z*: 359 (M^+), 163 (base peak). *Anal*. Calcd for $C_{19}H_{21}NO_4S$:

C, 63.49; H, 5.89; N, 3.90. Found: C, 63.35; H, 5.91; N, 3.74.

trans-*N*-(3,4,5-Trimethoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)acrylamide (**6f**): Colorless prisms from Et_2O–hexane, mp 85—90 °C. IR: 1641, 1593, 1504. ^{1}H-NMR: 3.28 (3H, s, >NCH_3), 3.82 (6H, s, OCH_3×2), 3.87 (3H, s, OCH_3), 5.68 (1H, d, *J*=15 Hz, PhSCH=C<u>H</u>–), 6.31 (2H, s, 2′-H, 6′-H), 7.2—7.4 (5H, m, S<u>Ph</u>), 7.71 (1H, d, *J*=15 Hz, PhSC<u>H</u>=CH–). ^{13}C-NMR: 37.1 (q), 56.2 (q×2), 60.9 (q), 104.8 (d×2), 116.7 (d), 128.5 (d), 129.3 (d×2), 131.6 (s), 132.1 (d×2), 137.5 (s), 139.0 (s), 142.9 (d), 153.6 (s×2), 164.5 (s). *Anal*. Calcd for $C_{19}H_{21}NO_4S$: C, 63.49; H, 5.89; N, 3.90. Found: C, 63.22; H, 5.95; N, 3.79.

5,6,7-Trimethoxy-1-methyl-2-quinolone (**8f**): Reddish orange gum. IR: 1653, 1589, 1560, 1504. UV: 239 (30000), 294 (6700), 337 (7900), 352 (5900). ^{1}H-NMR: 3.68 (3H, s, >NCH_3), 3.89, 4.00, 4.03 (each 3H, s, OCH_3×3), 6.54, 7.93 (each 1H, d, *J*=10 Hz, 3-H, 4-H), 6.54 (1H, s, 8-H). ^{13}C-NMR: 29.5 (q), 56.0 (q), 60.9 (q), 61.5 (q), 92.6 (d), 109.2 (s), 117.9 (d), 133.0 (d), 136.8 (s), 137.4 (s), 149.5 (s), 156.1 (s), 162.4 (s). LR-MS *m*/*z*: 249 (M^+, base peak). HR-MS *m*/*z* (M^+): Calcd for $C_{13}H_{15}NO_4$: 249.0999. Found: 249.0996.

Pummerer Reaction of 4g i) Method A. **4g** (2.0 g, 6.97 mmol) gave **5g** (769 mg, 41%) and **6g** (1.02 g, 54%).

ii) Method B. **4g** (2.0 g, 6.97 mmol) gave **5g** (243 mg, 13%), **6g** (315 mg, 17%), **7g** (744 mg, 43%), and **8g** (127 mg, 12%).

cis-*N*-Methyl-*N*-phenyl-3-(phenylsulfanyl)acrylamide (**5g**): Colorless needles from Et_2O–hexane, mp 84—86 °C. IR: 1635, 1585, 1558. UV: 259 (7500), 297 (8100). ^{1}H-NMR: 3.37 (3H, s, >NCH_3), 5.79 (1H, d, *J*=10 Hz, PhSCH=C<u>H</u>–), 6.99 (1H, d, *J*=10 Hz, PhSC<u>H</u>=CH–), 7.2—7.6 (10H, m, ArH, S<u>Ph</u>). ^{13}C-NMR: 37.0 (q), 113.6 (d), 127.3 (d×2), 127.5 (d), 127.7 (d), 129.2 (d×2), 129.6 (d×2), 130.9 (d×2), 137.7 (s), 146.5 (d), 166.3 (s). LR-MS *m*/*z*: 269 (M^+), 107 (base peak). *Anal*. Calcd for $C_{16}H_{15}NOS$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.28; H, 5.78; N, 5.01

trans-*N*-Methyl-*N*-phenyl-3-(phenylsulfanyl)acrylamide (**6g**): Yellow gum. IR: 1637, 1595, 1570. UV: 262 (12700), 291 (16200). ^{1}H-NMR: 3.34 (3H, s, >NCH_3), 5.73 (1H, d, *J*=15 Hz, PhSCH=C<u>H</u>–), 7.0—7.5 (10H, m, ArH, S<u>Ph</u>), 7.75 (1H, d, *J*=15 Hz, PhSC<u>H</u>=CH–). ^{13}C-NMR: 37.1 (q), 116.8 (d), 127.1 (d×2), 127.3 (d), 128.1 (d), 129.2 (d×2), 129.3 (d×2), 131.7 (d×2), 131.8 (s), 142.8 (d), 143.3 (s), 164.4 (s). LR-MS *m*/*z*: 269 (M^+), 163 (base peak).

1-Methyl-4-phenylsulfanyl-3,4-dihydro-2-quinolone (**7g**): Colorless needles from Et_2O–hexane, mp 97—103 °C. IR: 1660, 1597. ^{1}H-NMR: 2.92 (2H, d, *J*=4 Hz, 3-H), 3.30 (3H, s, >NCH_3), 4.42 (1H, t, *J*=4 Hz, 4-H), 6.9—7.5 (9H, m, ArH, S<u>Ph</u>). ^{13}C-NMR: 29.4 (q), 37.3 (t), 44.8 (d), 115.1 (d), 122.8 (d), 124.7 (s), 128.5 (d×2), 129.0 (dx2), 132.4 (s), 134.9 (d×3), 140.1 (s), 167.3 (s). LR-MS *m*/*z*: 269 (M^+), 160 (base peak). *Anal*. Calcd for $C_{16}H_{15}NOS$: C, 71.34; H, 5.61; N, 5.20. Found: C, 71.22; H, 5.68; N, 4.96.

1-Methyl-2-quinolone (**8g**): Colorless needles from Et_2O–hexane, mp 68—73 °C. IR: 1647, 1585. UV: 231 (44200), 268 (5100), 277 (5600), 333 (5800), 350 (3700). ^{1}H-NMR: 3.72 (3H, s, >NCH_3), 6.70, 7.66 (each 1H, d, *J*=9 Hz, 3-H, 4-H), 7.1—7.7 (4H, m, ArH). ^{13}C-NMR: 29.4 (q), 114.1 (d), 120.7 (s), 121.8 (d), 122.0 (d), 128.7 (d), 130.6 (d), 138.9 (d), 140.1 (s), 162.3 (s). LR-MS *m*/*z*: 159 (M^+), 107 (base peak). HR-MS *m*/*z* (M^+): Calcd for $C_{10}H_9NO$: 159.0682. Found: 159.0656. *Anal*. Calcd for $C_{10}H_9NO$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.40; H, 5.81; N, 8.60.

Preparation of 5a and 6a by Acylation of 1a with *cis*-3-(Phenylsulfanyl)acrylic Acid. A Typical Procedure A solution of *cis*-3-(phenylsulfanyl)acrylic acid (1.44 g, 7.8 mmol) and oxalyl chloride (2.98 g, 23.5 mmol) was stirred at r.t. for 2 h. Removal of excess oxalyl chloride by repeated evaporation under reduced pressure gave an oily material. To a solution of this acid chloride in benzene (30 ml) was slowly added a solution of **1e** (1.0 g, 6.5 mmol) and triethylamine (0.79 g, 7.8 mmol) in benzene (100 ml) under ice-cooling, and the mixture was stirred at r.t. for 14 h. After removal of the precipitates by filtration, the filtrate was evaporated *in vacuo*. The residue was chromatographed, eluted with ethyl acetate–hexane (1 : 2) to give *N*-(3,5-dimethoxyphenyl)-3-(phenylsulfanyl)acrylamide (**15a**) as a mixture of *cis*- and trans-stereoisomers.

To a solution of **15a** (200 mg, 0.63 mmol) in tetrahydrofuran (THF) (25 ml), CH_3I (900 mg, 6.34 mmol), KOH (420 mg, 6.36 mmol), and tetrabutylammonium bromide (TBAB) (102 mg, 0.32 mmol) were added at r.t., and the mixture was stirred for 3 h. After removal of the precipitates by filtration, the filtrate was extracted with $CHCl_3$ and evaporated *in vacuo*. The residual oil was chromatographed with ethyl acetate–hexane (3 : 1) to give **5a** (128 mg, 61%) and **6a** (60 mg, 29%). The acrylamides (**5b**—**e**, **g**) and the *trans*-isomers (**6b**—**e**, **g**) were prepared from the corresponding vinyl sulfides (**15**) in similar yields.

Preparation of *cis*-*N*-(4-Methoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)-acrylamide (5h) and the *trans*-Isomer (6h) From **15h** (2.0 g, 6.99 mmol); column chromatography ($CHCl_3$) followed by medium pressure column chromatography (benzene–acetone 20 : 1) gave **5h** (0.66 g, 31%) and **6h** (0.95 g, 45%).

5h: Colorless needles from Et_2O–hexane, mp 89—91 °C. IR: 1635. UV: 299 (20600). ^{1}H-NMR: 3.33 (3H, s, NMe), 3.83 (3H, s, OMe), 5.77 (1H, d, *J*=10 Hz, olefinic H), 6.90 (2H, d, *J*=9 Hz, ArH), 7.14 (2H, d, *J*=9 Hz, ArH), 7.2—7.5 (6H, m, S<u>Ph</u> and olefinic H). ^{13}C-NMR: 36.9 (q), 55.3 (q), 113.5 (d), 114.6 (d×2), 127.5 (d), 128.2 (d×2), 129.0 (d×2), 130.6 (d×2), 136.4 (s), 137.6 (s), 145.9 (d), 158.6 (s), 166.4 (s). LR-MS *m*/*z*: 299 (M^+), 137 (base peak). HR-MS *m*/*z* (M^+): Calcd for $C_{17}H_{17}NO_2S$: 299.0980. Found: 299.0982.

6h: Yellow gum. IR (Film): 1635. UV: 289 (16200). ^{1}H-NMR: 3.26 (3H, s, NMe), 3.80 (3H, s, OMe), 5.69 (1H, d, *J*=15 Hz, olefinic H), 5.83 (2H, d, *J*=9 Hz, ArH), 7.02 (2H, d, *J*=9 Hz, ArH), 7.1—7.4 (5H, m, S<u>Ph</u>), 7.68 (1H, d, *J*=15 Hz, olefinic H). ^{13}C-NMR: 36.9 (q), 55.1 (q), 114.3 (d×2), 116.7 (d), 127.8 (d), 127.9 (d×2), 128.9 (d×2), 131.4 (d×2), 131.6 (s), 135.7 (s), 142.1 (d), 158.3 (s), 164.3 (s). LR-MS *m*/*z*: 299 (M^+), 137 (base peak). HR-MS *m*/*z* (M^+): Calcd for $C_{17}H_{17}NO_2S$: 299.0980. Found: 299.0997

Preparation of *cis*-*N*-(3-Methoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)-acrylamide (5i) and the *trans*-Isomer (6i) From **15i** (0.97 g, 3.4 mmol); column chromatography ($CHCl_3$) followed by medium pressure column chromatography (benzene–acetone 20 : 1) gave **5i** (0.66 g, 31%) and **6i** (0.95 g, 45%).

5i: Yellow gum. IR (film): 1641. UV: 298 (14900). ^{1}H-NMR: 3.36 (3H, s, NMe), 3.81 (3H, s, OMe), 5.84 (1H, d, *J*=10 Hz, olefinic H), 6.7—7.1 (3H, m, ArH), 7.2—7.5 (7H, m, ArH, S<u>Ph</u>). ^{13}C-NMR: 36.8 (q), 55.3 (q), 113.0 (d×2), 113.5 (d), 119.3 (d), 127.6 (d), 129.0 (d×2), 130.2 (d), 130.7 (d×2), 137.6 (s), 144.7 (s), 146.2 (d), 160.4 (s), 166.1 (s). LR-MS *m*/*z*: 299 (M^+), 163 (base peak). HR-MS *m*/*z* (M^+): Calcd for $C_{17}H_{17}NO_2S$: 299.0980. Found: 299.0983.

6i: Yellow gum. IR (film): 1633. UV: 380 (200), 280 (16500). ^{1}H-NMR: 3.29 (3H, s, NMe), 3.79 (3H, s, OMe), 5.74 (1H, d, *J*=15 Hz, olefinic H), 6.6—6.9 (3H, m, ArH), 7.1—7.4 (6H, m, ArH, S<u>Ph</u>), 7.71 (1H, d, *J*=15 Hz, olefinic H). ^{13}C-NMR: 36.5 (q), 54.8 (q), 112.5 (d×2), 116.5 (d), 118.9 (d), 127.8 (d), 128.8 (d×2), 129.6 (d), 131.3 (d×2), 142.1 (d), 144.0 (s×2), 159.9 (s), 163.8 (s). LR-MS *m*/*z*: 299 (M^+), 163 (base peak). HR-MS *m*/*z* (M^+): Calcd for $C_{17}H_{17}NO_2S$: 299.0977. Found: 299.0952.

Preparation of *cis*-*N*-(2-Methoxyphenyl)-*N*-methyl-3-(phenylsulfanyl)-acrylamide (5k) and the *trans*-Isomer (6k) From **15k** (10.0 g, 35.0 mmol); column chromatography ($CHCl_3$) followed by medium pressure column chromatography (benzene–acetone 20 : 1) gave **5k** (3.56 g, 34%), **6k** (3.56 g, 34%), and the mixture of **5k** and **6k** (2.4 g, 23%).

5k: Colorless prisms from Et_2O–hexane, mp 135—137 °C. IR: 1625. UV: 293 (19900). ^{1}H-NMR: 3.27 (3H, s, NMe), 3.82 (3H, s, OMe), 5.68 (1H, d, *J*=10 Hz, olefinic H), 6.8—7.5 (10H, m, ArH, S<u>Ph</u> and olefinic H). ^{13}C-NMR: 35.3 (q), 55.3 (q), 111.8 (d), 113.3 (d), 120.6 (d), 127.3 (d), 128.8 (d×2), 129.0 (d×2), 130.4 (d×2), 131.6 (s), 137.5 (s), 145.2 (d), 154.9 (s), 166.4 (s). LR-MS *m*/*z*: 299 (M^+), 137 (base peak). HR-MS *m*/*z* (M^+): Calcd for $C_{17}H_{17}NO_2S$: 299.0978. Found: 299.0967.

6k: Yellow gum. IR (film): 1631. UV: 283 (16400). ^{1}H-NMR: 3.21 (3H, s, NMe), 3.79 (3H, s, OMe), 5.66 (1H, d, *J*=15 Hz, olefiinic H), 6.8—7.4 (10H, m, ArH, S<u>Ph</u>), 7.69 (1H, d, *J*=15 Hz, olefinic H). ^{13}C-NMR: 35.5 (q), 55.1 (q), 111.6 (d), 116.5 (d), 120.5 (d), 127.7 (d), 128.8 (d×4), 131.1 (s), 131.2 (d×2), 131.6 (s), 141.7 (d), 154.6 (s), 164.5 (s). LR-MS *m*/*z*: 299 (M^+), 109 (base peak). HR-MS *m*/*z* (M^+): Calcd for $C_{17}H_{17}NO_2S$: 299.0979. Found: 299.0979.

Acid-Induced Cyclization of 5a and 6a. Typical Procedure i) With $BF_3 \cdot Et_2O$: A solution of **5a** or **6a** (each 30 mg, 0.09 mmol) and $BF_3 \cdot Et_2O$ (66 mg, 0.46 mmol) in toluene (5 ml) was heated at 150 °C in a sealed tube for 150 h. The mixture was extracted with $CHCl_3$, and the extract was washed with 5% NaOH and water. The product was chromatographed, eluted with ethyl acetate–hexane (2 : 1) to give **8a** (18 mg, 98% from **5a** and 12 mg, 67% from **6a**).

ii) With *p*-TsOH: A solution of **5a** or **6a** (each 450 mg, 0.09 mmol) and *p*-$TsOH \cdot H_2O$ (780 mg, 4.1 mmol) in toluene (80 ml) was refluxed using a Dean–Stark water separator for 5 h. The mixture was extracted with $CHCl_3$, and the extract was washed with 5% NaOH and water. The product was chromatographed, eluted with ethyl acetate–hexane (2 : 1) to give **8a** (288 mg, 96 % from **5a** and 275 mg, 90% from **6a**). Acid-induced cyclization reactions of **5** and **6** using *p*-TsOH were carried out in a similar way, and the results are summarized in Table 2.

6-Methoxy-1-methyl-2-quinolone (**8h**): Colorless needles from Et_2O–

hexane, mp 75—77 °C. IR: 1646. UV: 356 (6000), 279 (5200), 270 (5600), 232 (25900). ^{1}H-NMR: 3.70 (3H, s, NMe), 3.86 (3H, s, OMe), 6.70 (1H, d, J=9 Hz, 3-H), 6.99 (1H, br d, J=2 Hz, 5-H), 7.16 (1H, dd, J=9, 2 Hz, 7-H), 7.32 (1H, d, J=9 Hz, 8-H), 7.60 (1H, d, J=9 Hz, 4-H). ^{13}C-NMR: 29.1 (q), 55.3 (q), 110.1 (d), 115.0 (d), 118.8 (d), 120.9 (s), 121.8 (d), 134.2 (s), 138.0 (d), 154.3 (s), 161.4 (s). LR-MS m/z: 189 (M^+), 174 (base peak). HR-MS m/z (M^+): Calcd for $C_{11}H_{11}NO_2$: 189.0790. Found: 189.0805.

N-(4-Methoxyphenyl)-*N*-methyl-3,3-di(phenylsulfanyl)propionamide (**16h**): Yellow gum. IR (film): 1652. ^{1}H-NMR: 2.62 (2H, d, J=7 Hz, $COCH_2$), 3.25 (3H, s, NMe), 3.83 (3H, s, OMe), 5.03 (1H, t, J=7 Hz, $COCH_2$C<u>H</u>), 6.86 (2H, d, J=9 Hz, ArH), 7.05 (2H, d, J=9 Hz, ArH), 7.2—7.5 (10H, m, S<u>Ph</u>×2). ^{13}C-NMR: 37.6 (q), 40.1 (t), 53.8 (d), 55.5 (q), 114.9 (d×2), 127.6 (d×2), 128.5 (d×2), 128.9 (d×4), 132.3 (d×4), 134.0 (s×2), 136.1 (s), 159.0 (s), 169.4 (s). CI-MS m/z: 409 (MH^+), 190 (base peak). HR-MS m/z (M^+): Calcd for $C_{23}H_{23}NO_2S_2$: 409.1167. Found: 409.1150.

7-Methoxy-1-methyl-2-quinolone (**8i**): Colorless needles from acetone–hexane, mp 100—102 °C. IR: 1646. UV: 344 (8500), 329 (12300), 286 (6700), 257 (5800), 229 (39400), 223 (37400). ^{1}H-NMR: 3.68 (3H, s, NMe), 3.92 (3H, s, OMe), 6.54 (1H, d, J=10 Hz, 3-H), 6.7—6.9 (2H, m, 6-H, 8-H), 7.96 (1H, d, J=9 Hz, 5-H), 7.59 (1H, d, J=10 Hz, 4-H). ^{13}C-NMR: 29.1 (q), 55.3 (q), 98.4 (d), 109.3 (d), 114.6 (s), 118.1 (d), 129.8 (d), 138.4 (d), 141.4 (s), 161.6 (s), 162.4 (s). LR-MS m/z: 189 (M^+, base peak). HR-MS m/z (M^+): Calcd for $C_{11}H_{11}NO_2$: 189.0787. Found: 189.0776

5-Methoxy-1-methyl-2-quinolone (**8j**): Pale yellow needles from ethyl acetate–hexane, mp 131—133 °C (lit.[8] mp 129—130 °C). IR: 1652. ^{1}H-NMR: 3.70 (3H, s, NMe), 3.94 (3H, s, OMe), 6.64 (1H, d, J=9 Hz, 3-H), 6.68 (1H, d, J=8 Hz, 6-H), 6.94 (1H, d, J=8 Hz, 8-H), 7.48 (1H, t, J=8 Hz, 7-H), 8.13 (1H, d, J=9 Hz, 4-H). ^{13}C-NMR: 29.6 (q), 55.8 (q), 102.8 (d), 106.7 (d), 111.3 (s), 119.8 (d), 131.2 (d), 133.1 (d), 141.2 (s), 156.4 (s), 162.4 (s). LR-MS m/z: 189 (M^+), 146 (base peak).

8-Methoxy-1-methyl-2-quinolone (**8k**): Yellow needles from hexane, mp 81—83 °C (lit.[9] mp 80—81 °C). IR: 1646. UV: 341 (2900), 282 (5700), 257 (15300), 240 (28000), 217 (19600). ^{1}H-NMR: 3.84 (3H, s, NMe), 3.90 (3H, s, OMe), 6.64 (1H, d, J=9 Hz, 3-H), 6.9—7.2 (3H, m, 5-H, 6-H, 7-H), 7.52 (1H, d, J=9 Hz, 4-H). ^{13}C-NMR: 35.2 (q), 56.6 (q), 113.9 (d), 121.6 (d), 121.9 (d), 122.7 (d), 122.9 (s), 131.5 (s), 139.1 (d), 148.6 (s), 163.6 (s). LR-MS m/z: 189 (M^+), 174 (BP). HR-MS m/z (M^+): Calcd for $C_{11}H_{11}NO_2$: 189.0787. Found: 189.0777.

N-(2-Methoxyphenyl)-*N*-methyl-3,3-di(phenylsulfanyl)propionamide (**16k**): Yellow gum. IR (film): 1658. ^{1}H-NMR: 2.57 (2H, d, J=7 Hz, $COCH_2$), 3.20 (3H, s, NMe), 3.74 (3H, s, OMe), 5.04 (1H, t, J=7 Hz, $COCH_2$CH), 6.8—7.5 (14H, m, ArH, S<u>P</u>h×2). ^{13}C-NMR: 36.2 (q), 39.7 (t), 53.5 (d), 55.4 (q), 112.0 (d), 121.2 (d), 127.4 (d), 127.6 (d), 128.8 (d×4), 129.1 (d), 129.5 (d), 131.7 (s), 132.2 (d×2), 132.5 (d×2), 134.0 (s), 134.3 (s), 155.0 (s), 169.8 (s). LR-MS m/z: 409 (M^+), 164 (BP). HR-MS m/z (M^+): Calcd for $C_{23}H_{23}NO_2S_2$: 409.1170. Found: 409.1177.

Acid-Induced Cyclization of 15a. Typical Procedure i) With $BF_3\cdot Et_2O$: A solution of **15a** (130 mg, 0.40 mmol) and $BF_3\cdot Et_2O$ (293 mg, 2.06 mmol) in toluene (5 ml) was refluxed for 24 h. The mixture was extracted with $CHCl_3$, and the extract was washed with 5% NaOH and water. The product was chromatographed, eluted with ethyl acetate–hexane (2 : 1) to give **17a** (13 mg, 15%) and the recovered material (55 mg, 42%).

ii) with *p*-TsOH: A solution of **15a** (250 mg, 0.76 mmol) and *p*-TsOH·H_2O (226 mg, 1.19 mmol) in toluene (50 ml) was refluxed using a Dean–Stark water separator for 72 h. The mixture was extracted with $CHCl_3$, and the extract was washed with 5% NaOH and water. The product was chromatographed, eluted with ethyl acetate to give 5,7-dimethoxy-2-quinolone (**17a**) (110 mg, 68%) as yellow needles from MeOH, mp 275–278 °C. IR: 1651, 1632, 1562, 1510. UV: 213 (17900), 237 (15500), 256 (5400), 307 (7600), 322 (7400), 337 (5000). ^{1}H-NMR: 3.89 (3H, s, OCH_3), 3.90 (3H, s, OCH_3), 6.23, 6.29 (each 1H, d, J=2 Hz, 6-H and 8-H), 6.44, 8.06 (each 1H, d, J=10 Hz, 3-H, 4-H). ^{13}C-NMR: 55.7 (q), 55.8 (q), 90.3 (d), 93.8 (d), 105.8 (s), 116.4 (d), 135.7 (d), 141.0 (s), 157.2 (s), 162.9 (s), 164.6 (s). LR-MS m/z: 205 (M^+, base peak). *Anal*. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.14; H, 5.58; N, 6.71. Acid-induced cyclization reactions of **15h** and **15i** were carried out in a similar way and the results are summarized in Table 2.

6-Methoxy-2-quinolone (**17h**): Yellow needles from ethyl acetate–hexane, mp 218—223 °C (lit.[10] mp 207—208 °C). IR: 3138, 1672. UV: 353 (4300), 278 (4300), 269 (4900), 232 (33100). ^{1}H-NMR: 3.81 (3H, s, OMe), 6.71 (1H, d, J=10 Hz, 4-H), 7.04 (1H, d, J=3 Hz, 5-H), 7.14 (1H, dd, J=9, 3 Hz, 7-H), 7.38 (1H, d, J=9 Hz, 8-H), 7.75 (1H, d, J=10 Hz, 3-H). LR-MS m/z: 175 (M^+), 58 (base peak).

7-Methoxy-2-quinolone (**17i**): Pale yellow prisms from ethyl acetate–hexane, mp 179—182 °C (lit.[11] mp 201 °C). IR: 3400, 1600. UV: 342 (6000), 328 (8500), 285 (5200), 228 (26900), 220 (29800). ^{1}H-NMR: 3.90 (3H, s, OMe), 6.54 (1H, d, J=10 Hz, 3-H), 6.7—6.9 (2H, m, 6-H, 8-H), 7.48 (1H, d, J=9 Hz, 5-H), 7.73 (1H, d, J=10 Hz, 4-H). ^{13}C-NMR: 55.7 (q), 98.2 (d), 112.4 (d), 114.2 (s), 118.0 (d), 129.1 (d), 140.3 (s), 140.8 (d), 161.9 (s), 164.8 (s). LR-MS m/z: 175 (M^+, base peak).

5-Methoxy-2-quinolone (**17j**): Pale yellow prisms from ethyl acetate–hexane, mp 170—175 °C (lit.[8] mp 240 °C). ^{1}H-NMR: 4.03 (3H, s, OMe), 6.57 (1H, d, J=10 Hz), 6.67 (1H, dd, J=10, 9 Hz), 6.92 (1H, d, J=9 Hz), 7.58 (1H, d, J=10 Hz), 7.61 (1H, d, J=9 Hz), 8.12 (1H, d, J=10 Hz). LR-MS m/z: 175 (M^+, base peak).

Acknowledgments This work was supported by a Grant-in-Aid for Scientific Research (No 11672115) from the Ministry of Education, Science, Sports and Culture of Japan.

References and Notes

1) Kennedy M., McKervey M., "Comprehensive Organic Chemistry," Vol. 7, ed. by Trost B. M., Fleming I., Pergamon, Oxford, 1991, pp. 193—216.
2) Padwa A., Gunn D. E., Jr., Osterhout, H., *Synthesis*, **1997**, 1353—1377.
3) *a*) Shinohara T., Toda J., Sano T., *Chem. Pharm. Bull*., **45**, 813—819 (1997); *b*) Shinohara T., Takeda A., Toda J., Ueda Y., Kohno M., Sano T., *ibid*., **46**, 918—927 (1998); *c*) Shinohara T., Takeda A., Toda J., Terasawa N., Sano T., *Heterocycles*, **46**, 555—565 (1997); *d*) Shinohara T., Takeda A., Toda J., Sano T., *Chem. Pharm. Bull*., **46**, 430—433 (1998); *e*) Toda J., Matsumoto S., Saitoh T., Sano T., *ibid*., **48**, 91—98 (2000).
4) Toda J., Sakagami M., Sano T., *Chem. Pharm. Bull.*, **47**, 1269—1275 (1999).
5) Toda J., Niimura Y., Takeda K., Sano T., Tsuda Y., *Chem. Pharm. Bull*., **46**, 906—912 (1998); *Idem*, *Heterocycles*, **48**, 1599—1607 (1998).
6) Shinohara T., Takeda A., Toda J., Sano T., *Heterocycles*, **48**, 981—992 (1998).
7) Node M., Nishide K., Ochiai M., Fuji K., Fujita E., *J. Org. Chem*., **46**, 5163—5166 (1981).
8) Fernandez M., De la Cuesta E., Avendano C., *Heterocycles*, **38**, 2615—1620 (1994).
9) Gesto C., De la Cuesta E., Avendano C., *Synth. Commun*., **1990**, 35—39.
10) Moreno T., Fernandez M., De la Cuesta E., Avendano C., *Heterocycles*, **43**, 817—828 (1996).
11) Effenberger F., Hartmann W., *Chem. Ber*., **102**, 3260—3267 (1969).