A Novel Synthesis of 1,2,3,4-Tetrahydroquinolines *via* Pummerer-Type Reaction of *N*-Aryl-*N*-[(phenylsulfinyl)propyl]formamide

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A synthesis of 1,2,3,4-tetrahydroquinolines (TQs) 13 with two and three methoxyl groups on the benzene ring, was achieved *via* intramolecular cyclization of *N*-aryl-*N*-[(phenylsulfinyl)propyl]formamides 7 utilizing the Pummerer reaction as a key step. The reaction was carried out by using trifluoroacetic anhydride (TFAA) (method A) or TFAA–$BF_3 \cdot Et_2O$ (method B). The cyclization to 4-PhSTQs 8 proceeded effectively when the reaction center at the benzene ring was electronically activated by a methoxyl group. In the reaction of sulfoxide 7e having two OMe groups in the *ortho*- and *para*-positions, a different cyclization reaction leading to 1,5-benzothiazepine derivative 9 was observed, indicating that the high nucleophilicity of the benzene ring caused the unexpected reaction prior to cyclization to 4-PhSTQs 8. This route starting from methoxyanilines provides an efficient and convenient method of TQ synthesis.

Key words synthesis; 1,2,3,4-tetrahydroquinoline; Pummerer reaction; trifluoroacetic anhydride; sulfoxide

1,2,3,4-Tetrahydroquinolines (TQs) derivatives are synthetic intermediates for pharmaceuticals.[1] However, there are no general methods for constructing the TQ ring system,[2] except by selective hydrogenation of the nitrogen containing ring of quinolines,[3,4] whose preparation has been extensively explored.[5] Recently, we discovered a highly efficient and convenient method for synthesizing tetrahydroisoquinolines (TIQs) utilizing sulfoxide-mediated electrophilic intramolecular cyclization (Pummerer reaction) as a key step. Various substituted TIQs were obtained starting from aromatic aldehydes,[6] aromatic ketones,[7] and arylmethylamines[8] in excellent overall yields as depicted by Eq. 1. In this paper we describe a new synthesis of TQs *via* cyclization using Pummerer reaction as shown by Eq. 2.

Results and Discussion

N-Formylaniline sulfoxides **7**, substrates for the Pummerer reaction, were prepared from anilines **1** in three steps. 3-Chloropropyl phenyl sulfide (**4**), the required part of the side chain, was prepared from 3-chloropropanol (**2**) by the known method.[9] A solution of **1** and **4** in dioxane was heated under reflux in the presence of sodium iodide and a charge transfer catalyst (tetraethylammonium bromide : TEAB) for 6 days to give *N*-(3-phenylthiopropyl)anilines **5** in moderate yields. This reaction, even though it was very slow, resulted in monoalkylation selectively. The alkyl anilines **5** without purification were then formylated to give *N*-formyl anilines **6**. Oxidation of **6** with sodium metaperiodate in aqueous methanol gave the sulfoxides **7** in excellent yields. The products **6** and **7** were well characterized by MS, IR, and ^{1}H- and ^{13}C-NMR spectral data (see Experimental).

Pummerer Reaction (Method A) Pummerer reaction of **7** was carried out as follows. A solution of **7** in benzene was treated with trifluoroacetic anhydride (TFAA) at room temperature for appropriate times under an argon atmosphere to give *N*-formyl-4-PhSTQ **8** (method A). Reactions at higher temperature (for example; under reflux in benzene) caused extensive decomposition to give no characterizable products. **8** were isolated in a pure form and fully characterized by analytical and spectral data. The results are summarized in Table 1.

Sulfoxides **7a** and **7b** having at least one OMe group *para* to the reaction center, which electronically facilitates the intramolecular cyclization, gave the 4-PhSTQs **8a** and **8b** in 86% and 81% yields, respectively. Cyclization of the sulfoxide **7c** with an *ortho*- and *meta*-OMe groups also occurred, though very slowly (220 h), to give the 4-PhSTQ **8c** in moderate yield (50%). The sulfoxide **7d** with two *meta*-OMe groups which can not electronically activate the reaction center, did not give the 4-PhSTQ **8d** to any extent.

The sulfoxide **7e** bearing *ortho*- and *para*-OMe substituents gave the 4-PhSTQ **8e** in only 11% yield. The yield of **8e**, although it was a little improved (34%) when tetrahydrofuran (THF) instead of benzene was used as a solvent, was less than anticipated since both OMe groups increase the electron density of the reaction center and therefore should facilitate

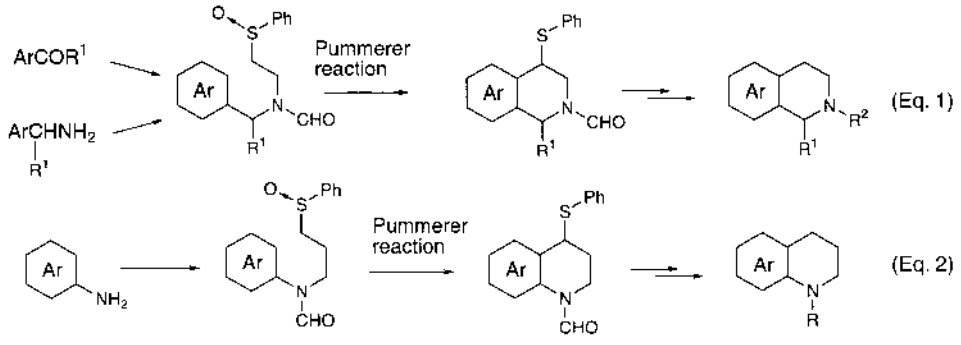

Chart 1

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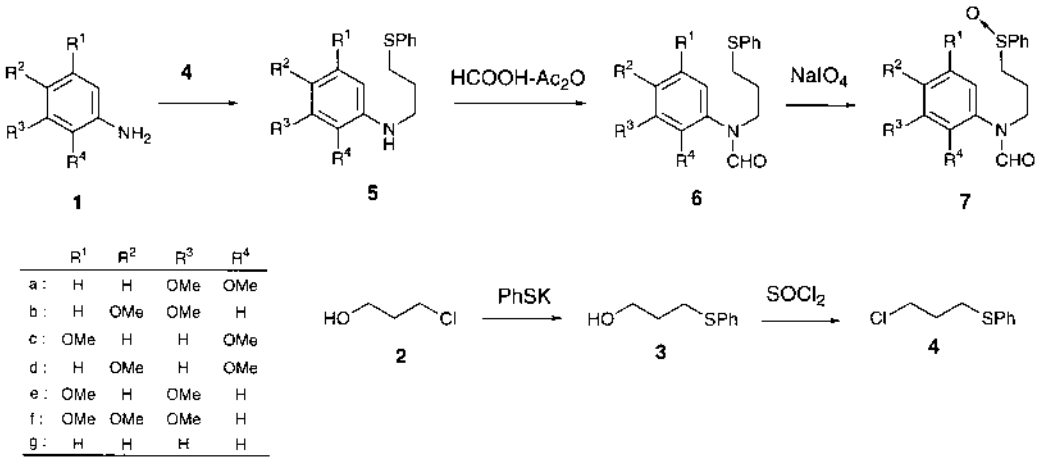
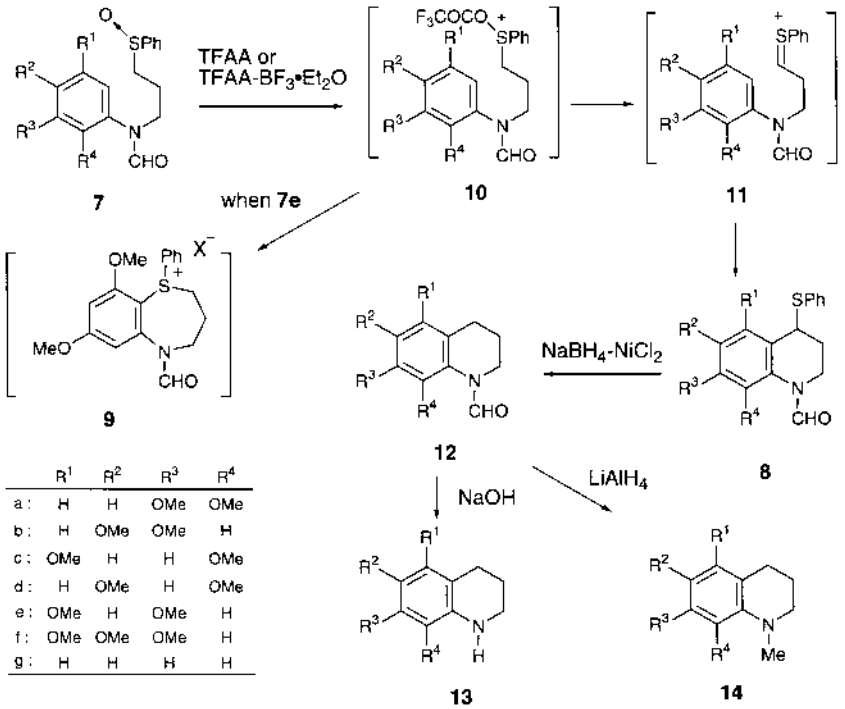


	R1	R2	R3	R4
a:	H	H	OMe	OMe
b:	H	OMe	OMe	H
c:	OMe	H	H	OMe
d:	H	OMe	H	OMe
e:	OMe	H	OMe	H
f:	OMe	OMe	OMe	H
g:	H	H	H	H

Chart 2



	R1	R2	R3	R4
a:	H	H	OMe	OMe
b:	H	OMe	OMe	H
c:	OMe	H	H	OMe
d:	H	OMe	H	OMe
e:	OMe	H	OMe	H
f:	OMe	OMe	OMe	H
g:	H	H	H	H

Chart 3

the cyclization. The reason of this observed low yield was shown to be attributable to the formation of the benzothiazepine salt **9**, although it could not be obtained as a pure form. The evidence for the formation of **9** will be described later.

The sulfoxide **7f** with three OMe groups at the *ortho*-, *meta*-, and *para*-positions to the reaction center, in turn, smoothly cyclized to give 4-PhSTQ **8f** in 95% yield. The role of the *ortho*- and *para*-OMe groups which facilitate the cyclization, was clearly demonstrated by the fact that the sulfoxide **7g** lacking an OMe group in the benzene ring, did not undergo the cyclization to give characterizable products.

Pummerer Reaction (Method B) In our investigations of TIQ synthesis by utilizing the Pummerer reaction we found that the addition of boron trifluoride etherate ($BF_3 \cdot Et_2O$) to the reaction mixture accelerates the reaction and in some cases dramatically increases TIQ formation.[6—8] This reaction (method B) was applied to the sulfoxides **7**. A solution of **7** in benzene was treated with TFAA for 1 h at room temperature, then $BF_3 \cdot Et_2O$ was added and the mixture was allowed to react for a further 1—2 h, giving rise *N*-formyl-4-PhSTQ derivatives **8**. The results are also summarized in Table 1.

Addition of $BF_3 \cdot Et_2O$ enormously accelerated the reaction. The sulfoxides **7a**, **b**, **d**, **e**, and **f** gave comparable results to those under the method A conditions. Thus, the 4-PhSTQs **8a**, **b**, and **f** were obtained in excellent yields, and **8d** was not formed, and the sulfoxide **7e** gave the 4-PhSTQ **8e** in 24% yield, together with the benzthiazepine salt **9**. In the case of **7c** and **7g**, the yields of the 4-PhSTQs were significantly improved (A: 50% and B: 91% for **8c**, and A: 0% and B: 60% for **8g**).

Reductive removal of the phenylthio group of **8** readily proceeded on treatment with $NaBH_4$–$NiCl_2$ in MeOH–THF

to give *N*-formyl-TQs **12** in excellent yields. Deprotection of the *N*-formyl group was readily achieved by conventional methods. Alkaline hydrolysis of **12** gave TQs **13**. Reduction of **12** with $LiAlH_4$ gave *N*-methylTQs **14** in good yields.

Chemical Evidences for the 1,5-Benzothiazepine Sulfonium Salt 9 as a Pummerer Product The Pummerer reaction of **7e** by either method A or B yielded the 1,5-benzothiazepine sulfonium salt **9** together with the 4-PhSTQ **8e**. Compound **9** obtained by SiO_2 column chromatography of the reaction mixture, though it was impure, showed high polarity by TLC. This highly polar material, when allowed to stand two days at room temperature, gradually changed into a less polar compound which was identified as **15**. The formation of **15** bearing a SPh group in the benzene ring suggested that the sulfonium salt **9** is formed as a Pummerer product, since **15** could result from nucleophilic attack of water on the thiazepine ring.

Table 1. Pummerer Reaction of Sulfoxides **7**

Run	Sulfoxide **7**	Conditions[a]			Yield (%) of 4-PhSTQ **8**
		Reagent[b]	Solvent	Time (h)	
1	**7a**	A	Benzene	24	86 (**8a**)
2	**7a**	B	Benzene	1	89 (**8a**)
3	**7b**	A	Benzene	24	81 (**8b**)
4	**7b**	B	Benzene	1	84 (**8b**)
5	**7c**	A	Benzene	220	50 (**8c**)
6	**7c**	B	Benzene	1	97 (**8c**)
7	**7d**	A	Benzene	120	—[c]
8	**7d**	B	Benzene	2	—[c]
9	**7e**	A	Benzene	88	11 (**8e**)[d]
10	**7e**	A	THF	2	34 (**8e**)[d]
11	**7e**	B	Benzene	1	24 (**8e**)[d]
12	**7f**	A	Benzene	24	95 (**8f**)
13	**7f**	B	Benzene	1	97 (**8f**)
14	**7g**	A	Benzene	336	—[c]
15	**7g**	B	Benzene	2	60 (**8g**)

a) At room temperature. *b*) A: TFAA, B: TFAA–$BF_3 \cdot Et_2O$. *c*) No characterizable products were obtained. *d*) Compound **9** was isolated as a major product.

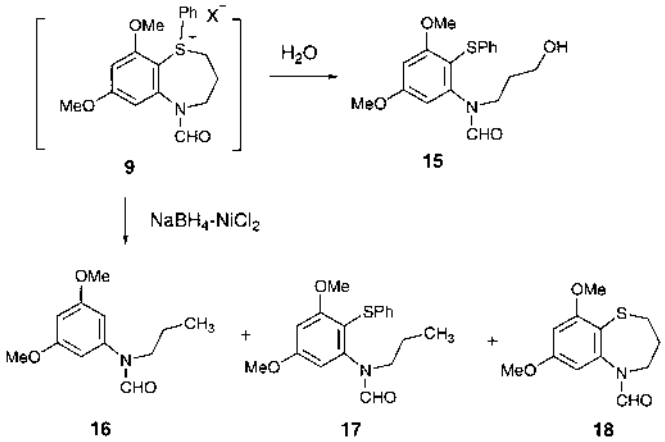


Chart 4

Confirmative evidence for the formation of **9** was obtained by the following chemical transformation. The reaction mixture obtained from **7e** by method A was reduced with $NaBH_4$–$NiCl_2$ in MeOH to give five products, **16** (22%), **17** (11%), and **18** (18%), together with *N*-formyl-TQ **12e** (17%) and TQ **13e** (trace). The similar reduction of the mixture obtained by method B gave the same five products **12e** (24%), **13e** (3%), **16** (33%), **17** (10%), and **18** (25%). The structures of products **16**, **17**, and **18** were deduced by analytical and spectral data. All derivatives **16**, **17**, and **18** can be produced from **9** by reduction of the thiazepine ring. In particular the formation of the 1,5-benzothiazepine **18** clearly demonstrated that Pummerer reaction of **7e** produced the 1,5-benzothiazepine sulfonium salt **9**.

Apparently, the benzothiazepine salt **9** can be formed *via* intramolecular cyclization of the initially formed Pummerer intermediate **10** by nucleophilic attack of the benzene ring on the sulfur atom, as shown in Chart 3. This cyclization was observed only in the reaction of **7e**. The benzene ring of the sulfoxide **7e** should be the most nucleophilic among the other sulfoxides **7a**—**g** since it has two electron-donating OMe groups *ortho* and *para* to the reaction center. This high nucleophilicity probably causes rapid C–S bond formation leading to the benzothiazepine prior to cyclization of sulfenium cation **11** to afford the TQ. The reaction of sulfoxide **7f** with three OMe groups exclusively produced the 4-PhSTQ **8f**. This result can be rationalized as follows; the *meta*-OMe present between the *ortho*- and *para*-OMe decreases the nucleophilicity at the reaction site, which, as a result of retardation of C–S bonding at **10**, favors C–C bond formation, leading to **8**.

The competition between C–S and C–C bond formation was also observed in the Pummerer reaction of the sulfoxide **19**, which afforded the 1,4-benzothiazepine **21** together with the 4-PhSTIQ **20**.[6b] C–S bond formation occurred only when

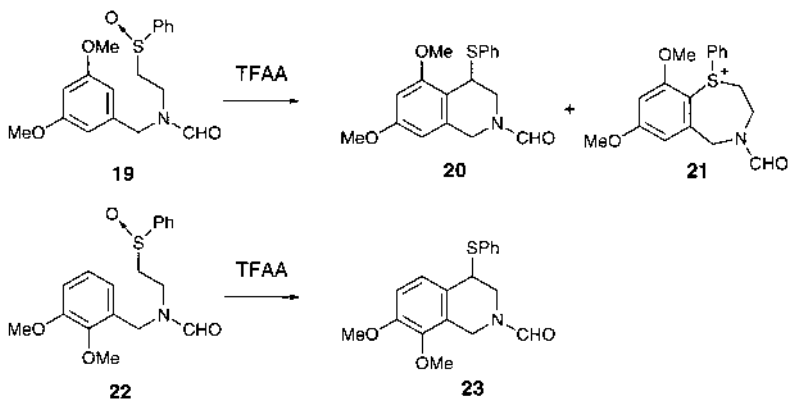


Chart 5

the reaction center is activated by two electron-donating OMe groups, otherwise C–C bond formation exclusively occurred, as shown by the reaction of **22** to give 4-PhSTIQ **23**. Thus, in the sulfoxide mediated cyclization to an aromatic ring, C–S bond formation reaction seems to be not unusual if the benzene ring is sufficiently electron-rich.

In summary, Pummerer reaction of the sulfoxides **7** of *N*-aryl-*N*-(3-phenylthiopropyl)formamide **6** resulted in intramolecular carbon–carbon bond formation under very mild conditions to produce *N*-formyl-4-PhSTQs **8**. This route produced non-substituted TQ **13g**, 7,8-dimethoxy- **13a**, 6,7-dimethoxy-**13b**, 5,8-dimethoxy-**13c**, and 5,6,7-trimethoxy-TQ **13f** in good overall yields. In particular, it was shown that Pummerer reaction under method B conditions using TFAA and $BF_3 \cdot Et_2O$ is applicable to the synthesis of TQ derivatives which lack electron-donating groups in the benzene ring. Thus, this route leading to TQs using Pummerer reaction provides an efficient and convenient method of TQ synthesis.

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 KBr disks for solids with a JASCO FT/IR-5000 spectrometer, and are given in cm^{-1}. NMR spectra were measured on a JEOL JNM-EX 90 (^1H, 90 MHz; ^{13}C, 22.5 MHz) or a JEOL JNM-A 300 (^1H, 300 MHz; ^{13}C, 75 MHz) spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard at room temperature and the chemical shifts are given in δ values. 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: iso butane) using direct or GC/MS inlet systems. Thin-layer chromatography (TLC) was performed on Merck precoated 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-Phenylthiopropanol (3) A solution of 85% KOH (36.8 g, 557 mmol) and thiophenol (26.8 g, 242 mmol) in EtOH (300 ml) was stirred under Ar atmosphere at room temperature for 10 min. To this solution of PhSK, 3-chloropropanol (**2**) (22.9 g, 242 mmol) in EtOH (150 ml) was slowly added at room temperature and the whole was then refluxed for 3.5 h. After removal of precipitates by filtration, the filtrate was concentrated *in vacuo*. The residue was diluted with water, and extracted with ether. The product was purified by distillation under reduced pressure to give **3** (35.5 g, 87%) as a colorless oil (bp 143 °C (5 mmHg)). IR: 3330, 1584. ^1H-NMR: 1.89 (2H, quintet, J=7 Hz, $=CH_2C\underline{H}_2CH_2-$), 3.05 (2H, t, J=7 Hz, $PhSC\underline{H}_2-$), 3.77 (2H, t, J=7 Hz, $-C\underline{H}_2OH$), 7.1—7.4 (5H, m, PhH). ^{13}C-NMR: 29.9 (t), 31.5 (t), 60.9 (t), 125.8 (d), 128.7 (d×2), 128.9 (d×2), 136.1 (s). LR-MS *m/z*: 168 (M^+), 110 (base peak).

Preparation of 3-Chloropropyl Phenyl Sulfide (4) To a solution of **3** (20.0 g, 119 mmol) in pyridine (10.4 g, 131 mmol) thionyl chloride (18.4 g, 155 mmol) was added dropwise at 0 °C and the mixture then heated at 110 °C for 10 h. The reaction mixture was diluted with water, and extracted with ether. The product was purified by distillation under reduced pressure to give **4** (18.5 g, 83%) as a pale yellow oil (bp 117 °C (5 mmHg)). IR: 1584. ^1H-NMR: 2.07 (2H, quintet, J=7 Hz, $-CH_2C\underline{H}_2CH_2-$), 3.08 (2H, t, J=7 Hz, $PhSC\underline{H}_2-$), 3.66 (2H, t, J=7 Hz, $-CH_2Cl$), 7.2—7.5 (5H, m, PhH). ^{13}C-NMR: 30.8 (t), 31.8 (t), 43.3 (t), 126.3 (d), 129.0 (d×2), 129.6 (d×2), 135.7 (s). LR-MS *m/z*: 186, 188 (M^+), 123 (base peak).

Preparation of *N*-Aryl-*N*-(3-phenylthiopropyl)formamide (6) (General Procedure) A solution of aromatic amine **1** (1 mol eq), **4** (1 mol eq), NaI (1 mol eq), Na_2CO_3 (1.5 mol eq), and TEAB (0.5 mol eq) in dioxane was heated under reflux for 6 d under Ar atmosphere. After removal of precipitates by filtration, the filtrate was concentrated *in vacuo*. The residue was diluted with water and extracted with $CHCl_3$. After evaporation of the solvent, to this residue a mixed solution of formic acid (30 mol eq) and acetic anhydride (10 mol eq) was slowly added at room temperature, and the whole was heated at 60 °C for 1 h. After removal of the solvent by evaporation *in vacuo*, the residue was diluted with water, basified with 5% NaOH and then extracted with $CHCl_3$. Chromatography of the product with hexane–AcOEt (4 : 1) gave **6**.

N-(2,3-Dimethoxyphenyl)-*N*-(3-phenylthiopropyl)formamide (**6a**): Yield: 64% (3.42 g from 2.46 g of **1a**). A yellow gum. IR: 1684, 1591. ^1H-NMR: 1.83 (2H, quintet, J=7 Hz, $-CH_2C\underline{H}_2CH_2-$), 2.91 (2H, t, J=7 Hz, $PhSC\underline{H}_2-$), 3.7—4.0 (2H, m, $>NC\underline{H}_2-$), 3.79, 3.89 (each 3H, s, OCH_3×2), 6.6—7.1 (3H, m, ArH), 7.1—7.4 (5H, m, PhH), 8.20 (1H, s, CHO). ^{13}C-NMR: 27.4 (t), 31.2 (t), 44.2 (t), 55.9 (q), 60.9 (q), 111.9 (d), 119.7 (d), 123.9 (d), 125.9 (d), 128.7 (d×2), 129.5 (d×2), 134.0 (s), 136.0 (s), 145.1 (s), 153.6 (s), 163.1 (d). LR-MS *m/z*: 331 (M^+), 222 (base peak). HR-MS *m/z*: Calcd for $C_{18}H_{21}NO_3S$ (M^+): 331.1243. Found: 331.1265.

N-(3,4-Dimethoxyphenyl)-*N*-(3-phenylthiopropyl)formamide (**6b**): Yield: 67% (3.54 g from 2.46 g of **1b**). A reddish yellow gum. IR: 1678, 1597, 1518. ^1H-NMR: 1.88 (2H, quintet, J=7 Hz, $-CH_2C\underline{H}_2CH_2-$), 2.91 (2H, t, J=7 Hz, $PhSC\underline{H}_2-$), 3.85, 3.89 (each 3H, s, OCH_3×2), 3.89 (2H, t, J=7 Hz, $>NCH_2-$), 6.6—6.9 (3H, m, ArH), 7.1—7.4 (5H, m, PhH), 8.30 (1H, s, CHO). ^{13}C-NMR: 27.1 (t), 31.0 (t), 44.1 (t), 55.8 (q×2), 108.5 (d), 111.4 (d), 117.1 (d), 125.9 (d), 128.6 (d×2), 129.3 (d×2), 133.6 (s), 135.7 (s), 148.1 (s), 149.5 (s), 162.2 (d). LR-MS *m/z*: 331 (M^+, base peak). HR-MS *m/z*: Calcd for $C_{18}H_{21}NO_3S$ (M^+): 331.1243. Found: 331.1191.

N-(2,5-Dimethoxyphenyl)-*N*-(3-phenylthiopropyl)formamide (**6c**): Yield : 67% (3.55 g from 2.46 g of **1c**). A yellow gum. IR: 1680, 1613, 1591, 1510. 1H-NMR: 1.82 (2H, quintet, J=7 Hz, $-CH_2C\underline{H}_2CH_2-$), 2.92 (2H, t, J=7 Hz, $PhSC\underline{H}_2-$), 3.74, 3.75 (each 3H, s, OCH_3×2), 3.84 (2H, t, J=7 Hz, $>NCH_2-$), 6.67 (1H, dd, J=1, 2 Hz, ArH), 6.86 (1H, d, J=2 Hz, ArH), 6.86 (1H, d, J=1 Hz, ArH), 7.1—7.4 (5H, m, PhH), 8.13 (1H, s, CHO). ^{13}C-NMR: 27.4 (t), 31.2 (t), 44.1 (t), 55.8 (q), 56.0 (q), 112.9 (d), 113.4 (d), 114.8 (d), 125.9 (d), 128.8 (d×2), 129.4 (d×2), 129.7 (s), 136.2 (s), 149.4 (s), 153.7 (s), 163.5 (d). LR-MS *m/z*: 331 (M^+, base peak). HR-MS *m/z*: Calcd for $C_{18}H_{21}NO_3S$ (M^+): 331.1243. Found: 331.1314.

N-(2,4-Dimethoxyphenyl)-*N*-(3-phenylthiopropyl)formamide (**6d**): Yield: 69% (3.66 g from 2.46 g of **1d**). A yellow gum. IR: 1678, 1611, 1586, 1514. ^1H-NMR: 1.80 (2H, quintet, J=7 Hz, $-CH_2C\underline{H}_2CH_2-$), 2.92 (2H, t, J=7 Hz, $PhSC\underline{H}_2-$), 3.77 (2H, t, J=7 Hz, $>NCH_2-$), 3.77, 3.82 (each 3H, s, OCH_3×2), 6.4—6.6 (2H, m, ArH), 6.9—7.1 (1H, m, ArH), 7.1—7.4 (5H, m, PhH), 8.06 (1H, s, CHO). ^{13}C-NMR: 27.4 (t), 31.3 (t), 44.3 (t), 55.5 (q×2), 99.5 (d), 104.4 (d), 122.2 (s), 126.0 (d), 128.8 (d×2), 129.5 (d×2), 129.6 (d), 136.3 (s), 156.5 (s), 160.5 (s), 163.8 (d). LR-MS *m/z*: 331 (M^+, base peak). HR-MS *m/z*: Calcd for $C_{18}H_{21}NO_3S$ (M^+): 331.1243. Found: 331.1232.

N-(3,5-dimethoxyphenyl)-*N*-(3-phenylthiopropyl)formamide (**6e**): Yield: 66% (1.18 g from 0.82 g of **1e**). A reddish yellow gum. IR: 1680, 1599. ^1H-NMR: 1.89 (2H, quintet, J=7 Hz, $-CH_2C\underline{H}_2CH_2-$), 2.91 (2H, t, J=7 Hz, $PhSC\underline{H}_2-$), 3.78 (6H, s, OCH_3×2), 3.92 (2H, t, J=7 Hz, $>NCH_2-$), 6.28 (2H, d, J=2 Hz, ArH), 6.38 (1H, t, J=2 Hz, ArH), 7.1—7.4 (5H, m, PhH), 8.41 (1H, s, CHO). ^{13}C-NMR: 27.4 (t), 31.2 (t), 43.8 (t), 55.5 (q×2), 98.5 (d), 102.5 (d×2), 126.1 (d), 128.9 (d×2), 129.5 (d×2), 136.0 (s), 142.5 (s), 161.6 (s×2), 162.3 (d). LR-MS *m/z*: 331 (M^+), 222 (base peak). HR-MS *m/z*: Calcd for $C_{18}H_{21}NO_3S$ (M^+): 331.1243. Found: 331.1258.

N-(3,4,5-Trimethoxyphenyl)-*N*-(3-phenylthiopropyl)formamide (**6f**): Yield: 77% (4.97 g from 3.30 g of **1f**). A yellow gum. IR: 1676, 1593, 1508. ^1H-NMR: 1.90 (2H, quintet, J=7 Hz, $-CH_2C\underline{H}_2CH_2-$), 2.92 (2H, t, J=7 Hz, $PhSC\underline{H}_2-$), 3.83 (6H, s, OCH_3×2), 3.85 (3H, s, OCH_3), 3.91 (2H, t, J=7 Hz, $>NCH_2-$), 6.34 (2H, s, ArH), 7.1—7.4 (5H, m, PhH), 8.35 (1H, s, CHO). ^{13}C-NMR: 27.3 (t), 31.2 (t), 44.3 (t), 56.3 (q×2), 60.9 (q), 102.4 (d×2), 126.2 (d), 128.9 (d×2), 129.5 (d×2), 135.9 (s), 136.6 (s), 137.3 (s), 153.8 (s×2), 162.3 (d). LR-MS *m/z*: 361 (M^+, base peak). HR-MS *m/z*: Calcd for $C_{19}H_{23}NO_4S$ (M^+): 361.1348. Found: 361.1358.

N-Phenyl-*N*-(3-phenylthiopropyl)formamide (**6g**): Yield: 68% (9.84 g from 5.0 g of **1g**). A reddish yellow gum. IR: 1676, 1595. ^1H-NMR: 1.88 (2H, quintet, J=7 Hz, $-CH_2C\underline{H}_2CH_2-$), 2.90 (2H, t, J=7 Hz, $PhSC\underline{H}_2-$), 3.95 (2H, t, J=7 Hz, $>NCH_2-$), 7.0—7.5 (10H, m, PhH×2), 8.38 (1H, s, CHO). ^{13}C-NMR: 27.2 (t), 31.2 (t), 43.8 (t), 123.9 (d×2), 126.1 (d), 126.8 (d), 128.8 (d×2), 129.6 (d×2), 129.6 (d×2), 135.8 (s), 140.7 (s×2), 162.3 (d). LR-MS *m/z*: 271 (M^+), 77 (base peak). HR-MS *m/z*: Calcd for $C_{16}H_{17}NOS$ (M^+): 271.1031. Found: 271.1032.

Preparation of *N*-Aryl-*N*-(3-phenylsulfinylpropyl)formamide (7) by $NaIO_4$ Oxidation of 6 (General Procedure) An aqueous solution of $NaIO_4$ (1.5 mol eq) was added to a solution of **6** (1 mol eq) in MeOH, and the mixture was stirred at room temperature for 6 h. After removal of inorganic materials by filtration, the filtrate was concentrated *in vacuo* to dryness. The residue was purified by chromatography with AcOEt to give **7**.

N-(2,3-Dimethoxyphenyl)-*N*-(3-phenylsulfinylpropyl)formamide (**7a**): Yield: 92% (3.18 g from 3.30 g of **6a**). A reddish gum. IR: 1673, 1593, 1050. ^1H-NMR: 1.94 (2H, quintet, J=7 Hz, $-CH_2C\underline{H}_2CH_2-$), 2.7—3.0 (2H,

m, PhSC$\underline{H}_2$–), 3.7—4.0 (2H, m, >NCH_2–), 3.79, 3.90 (each 3H, s, OCH_3×2), 6.6—7.2 (3H, m, ArH), 7.4—7.7 (5H, m, PhH), 8.17 (1H, s, CHO). ^{13}C-NMR: 20.8 (t), 43.9 (t), 54.5 (t), 56.0 (q), 61.1 (q), 112.3 (d), 119.9 (d), 123.9 (d×2), 124.1 (d), 129.2 (d×2), 130.9 (d), 133.7 (s), 143.7 (s), 145.2 (s), 153.7 (s), 163.4 (d). LR-MS *m/z*: 347 (M^+), 222 (base peak). HR-MS *m/z*: Calcd for $C_{18}H_{21}NO_4S$ (M^+): 347.1189. Found: 347.1189.

N-(3,4-Dimethoxyphenyl)-*N*-(3-phenylsulfinylpropyl)formamide (**7b**): Yield: 96% (3.51 g from 3.50 g of **6b**). Colorless needles from AcOEt, mp 95—99 °C. IR: 1671, 1599, 1518, 1027. ^{1}H-NMR: 2.00 (2H, quintet, *J*=7 Hz, –$CH_2C\underline{H}_2CH_2$–), 2.7—3.0 (2H, m, PhSC$\underline{H}_2$–), 3.79, 3.90 (each 3H, s, OCH_3×2), 3.87 (2H, t, *J*=7 Hz, >NCH_2–), 6.6—7.0 (3H, m, ArH), 7.4—7.7 (5H, m, PhH), 8.28 (1H, s, CHO). ^{13}C-NMR: 20.7 (t), 44.2 (t), 54.2 (t), 56.1 (q×2), 109.1 (d), 111.6 (d), 117.7 (d), 123.9 (d×2), 129.2 (d×2), 130.9 (d), 133.4 (s), 143.6 (s), 148.6 (s), 149.8 (s), 162.6 (d). LR-MS *m/z*: 347 (M^+), 331 (base peak). *Anal*. Calcd for $C_{18}H_{21}NO_4S$: C, 62.23; H, 6.09; N, 4.03. Found: C, 62.13; H, 6.09; N, 4.00.

N-(2,5-Dimethoxyphenyl)-*N*-(3-phenylsulfinylpropyl)formamide (**7c**): Yield: 95% (3.29 g from 3.30 g of **6c**). A reddish yellow gum. IR: 1680, 1613, 1510, 1044. ^{1}H-NMR: 1.93 (2H, quintet, *J*=7 Hz, –$CH_2C\underline{H}_2CH_2$–), 2.7—3.0 (2H, m, PhSC$\underline{H}_2$–), 3.76, 3.78 (each 3H, s, OCH_3×2), 3.7—4.0 (2H, m, >NCH_2–), 6.67 (1H, dd, *J*=1, 2 Hz, ArH), 6.87 (1H, d, *J*=2 Hz, ArH), 6.88 (1H, d, *J*=1 Hz, ArH), 7.4—7.7 (5H, m, PhH), 8.10 (1H, s, CHO). ^{13}C-NMR: 20.7 (t), 43.8 (t), 54.5 (t), 55.8 (q), 56.0 (q), 112.8 (d), 113.7 (d), 114.9 (d), 123.9 (d×2), 129.1 (d×2), 129.2 (s), 130.8 (d), 143.7 (s), 149.4 (s), 153.7 (s), 163.6 (d). LR-MS *m/z*: 347 (M^+), 222 (base peak). HR-MS *m/z*: Calcd for $C_{18}H_{21}NO_4S$ (M^+): 347.1189. Found: 347.1178.

N-(2,4-Dimethoxyphenyl)-*N*-(3-phenylsulfinylpropyl)formamide (**7d**): Yield: 93% (3.22 g from 3.30 g of **6d**). A reddish yellow gum. IR: 1673, 1609, 1586, 1514, 1033. ^{1}H-NMR: 1.91 (2H, quintet, *J*=7 Hz, –$CH_2C\underline{H}_2$-CH_2–), 2.7—3.0 (2H, m, PhSC$\underline{H}_2$–), 3.6—3.9 (2H, m, >NCH_2–), 3.77, 3.83 (each 3H, s, OCH_3×2), 6.4—6.6 (2H, m, ArH), 6.9—7.1 (1H, m, ArH), 7.4—7.7 (5H, m, PhH), 8.03 (1H, s, CHO). ^{13}C-NMR: 20.6 (t), 43.9 (t), 54.5 (t), 55.5 (q×2), 99.6 (d), 104.5 (d), 121.8 (s), 123.9 (d×2), 129.1 (d×2), 129.7 (d), 130.8 (d), 143.8 (s), 156.4 (s), 160.7 (s), 164.0 (d). LR-MS *m/z*: 347 (M^+), 222 (base peak). HR-MS *m/z*: Calcd for $C_{18}H_{21}NO_4S$ (M^+): 347.1189. Found: 347.1180.

N-(3,5-Dimethoxyphenyl)-*N*-(3-phenylsulfinylpropyl)formamide (**7e**): Yield: 94% (1.96 g from 2.20 g of **6e**). Colorless needles from AcOEt–hexane, mp 73—76 °C. IR: 1680, 1599, 1048. ^{1}H-NMR: 1.7—2.2 (2H, m, –$CH_2C\underline{H}_2CH_2$–), 2.7—2.9 (2H, m, PhSC$\underline{H}_2$–), 3.80 (6H, s, OCH_3×2), 3.7—4.0 (2H, m, >NCH_2–), 6.27 (2H, d, *J*=2 Hz, ArH), 6.39 (1H, t, *J*=2 Hz, ArH), 7.4—7.7 (5H, m, PhH), 8.37 (1H, s, CHO). ^{13}C-NMR: 20.6 (t), 43.3 (t), 54.1 (t), 55.3 (q×2), 98.5 (d), 102.5 (d×2), 123.7 (d×2), 129.0 (d×2), 130.8 (d), 141.9 (s), 143.4 (s), 161.4 (s×2), 162.2 (d). LR-MS *m/z*: 347 (M^+), 222 (base peak). *Anal*. Calcd for $C_{18}H_{21}NO_4S$: C, 62.23; H, 6.09; N, 4.03. Found: C, 62.45; H, 6.07; N, 4.10.

N-(3,4,5-Trimethoxyphenyl)-*N*-(3-phenylsulfinylpropyl)formamide (**7f**): Yield: 95% (4.46 g from 4.50 g of **6f**). Colorless plates from AcOEt–hexane, mp 119—122 °C. IR: 1672, 1595, 1506, 1045. ^{1}H-NMR: 2.04 (2H, quintet, *J*=7 Hz, –$CH_2C\underline{H}_2CH_2$–), 2.7—3.0 (2H, m, PhSC$\underline{H}_2$–), 3.8—4.1 (2H, m, >NCH_2–), 3.86 (9H, s, OCH_3×3), 6.36 (2H, s, ArH), 7.4—7.6 (5H, m, PhH), 8.32 (1H, s, CHO). ^{13}C-NMR: 20.8 (t), 44.1 (t), 54.2 (t), 56.3 (q×2), 60.9 (q), 102.8 (d×2), 123.8 (d×2), 129.2 (d×2), 131.0 (d), 136.1 (s), 137.6 (s), 143.5 (s), 153.9 (s×2), 162.5 (d). LR-MS *m/z*: 377 (M^+, base peak). *Anal*. Calcd for $C_{19}H_{23}NO_5S$: C, 60.46; H, 6.14; N, 3.71. Found: C, 60.28; H, 6.11; N, 3.52.

N-Phenyl-*N*-(3-phenylsulfinylpropyl)formamide (**7g**): Yield: 98% (9.67 g from 9.30 g of **6g**). A reddish orange gum. IR: 1672, 1595, 1039. ^{1}H-NMR: 1.93 (2H, quintet, *J*=7 Hz, –$CH_2C\underline{H}_2CH_2$–), 2.7—3.0 (2H, m, PhSC$\underline{H}_2$–), 3.94 (2H, t, *J*=7 Hz, >NCH_2–), 7.0-7.6 (10H, m, PhH×2), 8.35 (1H, s, CHO). ^{13}C-NMR: 20.7 (t), 43.7 (t), 54.2 (t), 123.9 (d×2), 124.3 (d×2), 127.2 (d), 129.2 (d×2), 129.8 (d×2), 130.9 (d), 140.3 (s), 143.5 (s), 162.5 (d). CI-MS *m/z*: 288 (MH^+), 57 (base peak). HR-MS *m/z*: Calcd for $C_{16}H_{17}NO_2S$ (M^+): 287.0981. Found: 287.1008.

Pummerer Reaction of Sulfoxides 7 (General Procedure) Method A TFAA (5 mol eq) was added to a solution of a sulfoxide **7** in dry benzene at room temperature, and the mixture was stirred for an appropriate time as described in Table 1. The reaction mixture was concentrated *in vacuo*, and the product was purified by column chromatography with (hexane–AcOEt= 1 : 1) to give **8** as a sole product, except for the reactions of **7d**, **e**, and **g**. The yields were given in Table 1.

Method B TFAA (5 mol eq) was added to a solution of a sulfoxide **7** (1 mol eq) in dry benzene at room temperature. After the mixture was stirred for 1 h, $BF_3\cdot Et_2O$ (3 mol eq) was added, and the reaction mixture was further stirred at the same temperature for an appropriate time as described in Table 1. The reaction mixture was washed with 5% NaOH, and the organic extract was purified by column chromatography to give **8** as a sole product except the reactions of **7d** and **7e**. In the case of **7e** alcohol **15** was obtained in 10% yield when the crude products was allowed to stand 2 d at room temperature and was purified with chromatography eluting with hexane–AcOEt (3 : 1). The results are given in Table 1.

1-Formyl-1,2,3,4-tetrahydro-7,8-dimethoxy-4-phenylthioquinoline (**8a**): A reddish orange gum. IR: 1669, 1601. ^{1}H-NMR: 2.0—2.2 (2H, m, C_3-H), 3.73, 3.89 (each 3H, s, OCH_3×2), 3.8—4.2 (2H, m, C_2-H), 4.50 (1H, t, *J*=4 Hz, C_4-H), 6.72, 7.15 (each 1H, d, *J*=9 Hz, $C_{5,6}$-H), 7.2—7.5 (5H, m, PhH), 8.76 (1H, s, CHO). ^{13}C-NMR: 28.5 (t), 36.5 (t), 45.1 (d), 55.9 (q), 60.4 (q), 108.6 (d), 122.4 (s), 125.2 (d), 127.6 (d), 129.0 (d×2), 131.2 (s), 132.6 (d×2), 134.1 (s), 140.6 (s), 152.9 (s), 164.1 (d). LR-MS *m/z*: 329 (M^+), 220 (base peak). HR-MS *m/z*: Calcd for $C_{18}H_{19}NO_3S$ (M^+): 329.1083. Found: 329.1063.

1-Formyl-1,2,3,4-tetrahydro-6,7-dimethoxy-4-phenylthioquinoline (**8b**): Colorless prisms from AcOEt, mp 105—109 °C. IR: 1659, 1522. ^{1}H-NMR: 2.0—2.3 (2H, m, C_3-H), 3.6—4.4 (2H, m, C_2-H), 3.82, 3.90 (each 3H, s, OCH_3×2), 4.50 (1H, t, *J*=4 Hz, C_4-H), 6.65, 6.87 (each 1H, s, $C_{5,8}$-H), 7.2—7.6 (5H, m, PhH), 8.74 (1H, s, CHO). ^{13}C-NMR: 27.9 (t), 36.1 (t), 45.0 (d), 56.1 (q×2), 101.0 (d), 113.3 (d), 118.4 (s), 127.7 (d), 129.2 (d×2), 130.5 (s), 132.7 (d×2), 134.2 (s), 146.3 (s), 149.3 (s), 160.4 (d). 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, 65.63; H, 5.86; N, 4.06.

1-Formyl-1,2,3,4-tetrahydro-5,8-dimethoxy-4-phenylthioquinoline (**8c**): A yellow gum. IR: 1673, 1597. ^{1}H-NMR: 1.8—2.4 (2H, m, C_3-H), 3.78, 3.80 (each 3H, s, OCH_3×2), 3.9—4.1 (2H, m, C_2-H), 4.86 (1H, t, *J*=3 Hz, C_4-H), 6.62, 6.89 (each 1H, d, *J*=9 Hz, $C_{6,7}$-H), 7.2—7.6 (5H, m, PhH), 8.72 (1H, s, CHO). ^{13}C-NMR: 27.5 (t), 36.6 (t), 40.2 (d), 56.0 (q), 56.4 (q), 106.7 (d), 112.4 (d), 120.3 (s), 127.4 (d), 127.7 (s), 128.7 (d×2), 133.0 (d×2), 134.7 (s), 145.3 (s), 150.8 (s), 164.4 (d). LR-MS *m/z*: 329 (M^+), 220 (base peak). HR-MS *m/z*: Calcd for $C_{18}H_{19}NO_3S$ (M^+): 329.1083. Found: 329.0972.

1-Formyl-1,2,3,4-tetrahydro-5,7-dimethoxy-4-phenylthioquinoline (**8e**): A yellow gum. IR: 1669, 1609, 1586, 1502. ^{1}H-NMR: 1.6—2.3 (2H, m, C_3-H), 3.6—4.5 (2H, m, C_2-H), 3.81, 3.85 (each 3H, s, OCH_3×2), 4.7—4.9 (1H, m, C_4-H), 6.28, 6.33 (1H, d, *J*=2 Hz, $C_{6,8}$-H), 7.0—7.6 (5H, m, PhH), 8.84 (1H, s, CHO). ^{13}C-NMR: 26.7 (t), 36.4 (t), 40.3 (d), 55.5 (q), 55.9 (q), 94.0 (d), 94.5 (d), 108.2 (s), 127.4 (d), 128.9 (d×2), 132.8 (d×2), 135.3 (s), 138.5 (s), 158.5 (s), 160.7 (s), 161.2 (d). LR-MS *m/z*: 329 (M^+), 108 (base peak). HR-MS *m/z*: Calcd for $C_{18}H_{19}NO_3S$ (M^+): 329.1083. Found: 329.1088.

1-Formyl-1,2,3,4-tetrahydro-5,6,7-trimethoxy-4-phenylthioquinoline (**8f**): A colorless gum. IR: 1676, 1601, 1581. ^{1}H-NMR: 1.7—2.2 (2H, m, C_3-H), 3.7—4.0 (2H, m, C_2-H), 3.85, 3.88, 4.08 (each 3H, s, OCH_3×3), 4.78 (1H, br s, C_4-H), 6.47 (1H, s, C_8-H), 7.2—7.6 (5H, m, PhH), 8.77 (1H, s, CHO). ^{13}C-NMR: 26.6 (t), 36.2 (t), 40.6 (d), 56.1 (q), 60.8 (q), 61.5 (q), 96.4 (d), 113.3 (s), 127.5 (d), 129.0 (d×2), 132.5 (d×2), 133.1 (s), 134.9 (s), 139.2 (s), 151.9 (s), 153.8 (s), 160.9 (d). LR-MS *m/z*: 359 (M^+), 250 (base peak). HR-MS *m/z*: Calcd for $C_{19}H_{21}NO_4S$ (M^+): 359.1191. Found: 359.1198.

1-Formyl-1,2,3,4-tetrahydro-4-phenylthioquinoline (**8g**): A yellow gum. IR: 1676, 1581. ^{1}H-NMR: 2.0—2.3 (2H, m, C_3-H), 3.6—4.4 (2H, m, C_2-H), 4.54 (1H, t, *J*=4 Hz, C_4-H), 6.9—7.6 (9H, m, ArH, PhH), 8.81 (1H, s, CHO). LR-MS *m/z*: 269 (M^+), 160 (base peak). HR-MS *m/z*: Calcd for $C_{16}H_{15}NOS$ (M^+): 269.0875. Found: 269.0887.

N-(3,5-Dimethoxy-2-phenylthiophenyl)-(3-hydroxypropyl)formamide (**15**): Yield: 10% (50 mg from 500 mg of **8e**). A yellow gum. IR: 3437, 1685, 1597. ^{1}H-NMR: 1.4—1.7 (2H, m, –$CH_2C\underline{H}_2CH_2$–), 3.4—4.0 (4H, m, –$C\underline{H}_2CH_2C\underline{H}_2$–), 3.81, 3.86 (each 3H, s, –OCH_3×2), 6.45, 6.58 (each 1H, d, *J*=2 Hz, ArH), 6.9—7.2 (5H, m, PhH), 7.94 (1H, s, CHO). ^{13}C-NMR: 26.1 (t), 39.0 (t), 51.6 (q), 52.3 (q), 54.6 (t), 95.0 (d), 102.1 (d), 106.5 (s), 121.3 (d), 121.9 (d×2), 124.7 (d×2), 133.3 (s), 141.7 (s), 158.2 (s), 158.5 (s), 160.1 (d). LR-MS *m/z*: 347 (M^+), 256 (base peak).

Reductive Desulfurylation of 1-Formyl-4-phenylthioTQs 8 (General Procedure) $NaBH_4$ (10.5 mol eq) was added in small portions to a stirred solution of **8** (1 mol eq) and $NiCl_2\cdot 6H_2O$ (3.5 mol eq) in MeOH–THF (3 : 1) under ice-cooling. The mixture was stirred at room temperature for a further 1.5 h, then filtered and the filtrate was concentrated *in vacuo*. The residue was suspended in water, and the suspension acidified with 5% HCl, and extracted with $CHCl_3$. The product was purified by column chromatography, eluting with hexane–AcOEt (2 : 1) to give 1-formyl TQ **12**.

1-Formyl-1,2,3,4-tetrahydro-7,8-dimethoxyquinoline (**12a**): Yield: 94% (1.26 g from 2.0 g of **8a**). A colorless gum. IR: 1671, 1607. ^{1}H-NMR: 1.92 (2H, quintet, *J*=7 Hz, C_3-H), 2.70 (2H, t, *J*=7 Hz, C_4-H), 3.7—3.9 (2H, m, C_2-H), 3.73, 3.88 (each 3H, s, OCH_3×2), 6.69, 6.86 (each 1H, d, *J*=9 Hz,

$C_{5,6}$-H), 8.75 (1H, s, CHO). ^{13}C-NMR: 22.4 (t), 25.6 (t), 39.1 (t), 55.1 (q), 59.5 (q), 108.2 (d), 122.7 (d), 124.0 (s), 130.2 (s), 140.3 (s), 151.1 (s), 163.1 (d). LR-MS *m/z*: 221 (M^+), 178 (base peak). HR-MS *m/z*: Calcd for $C_{12}H_{15}NO_3$ (M^+): 221.1050. Found: 221.1044.

1-Formyl-1,2,3,4-tetrahydro-6,7-dimethoxyquinoline (**12b**): Yield: 91% (1.10 g from 1.8 g of **8b**). Colorless prisms from AcOEt, mp 89—93 °C. IR: 1671, 1599. ^{1}H-NMR: 1.94 (2H, quintet, J=7 Hz, C_3-H), 2.76 (2H, t, J=7 Hz, C_4-H), 3.79 (2H, t, J=7 Hz, C_2-H), 3.86, 3.88 (each 3H, s, OCH_3×2), 6.66 (2H, s, $C_{5,8}$-H), 8.73 (1H, s, CHO). ^{13}C-NMR: 22.5 (t), 26.5 (t), 40.0 (t), 56.2 (q×2), 102.0 (d), 112.6 (d), 120.5 (s), 130.2 (s), 146.5 (s), 148.0 (s), 160.6 (d). LR-MS *m/z*: 221 (M^+, base peak). *Anal*. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.00; H, 6.78; N, 6.14.

1-Formyl-1,2,3,4-tetrahydro-5,8-dimethoxyquinoline (**12c**): Yield: 94% (756 mg from 1.2 g of **8c**). A yellow gum. IR: 1671, 1599. ^{1}H-NMR: 1.90 (2H, quintet, J=7 Hz, C_3-H), 2.71 (2H, t, J=7 Hz, C_4-H), 3.77, 3.80 (each 3H, s, OCH_3×2), 3.77 (2H, t, J=7 Hz, C_2-H), 6.59, 6.80 (each 1H, d, J=9 Hz, $C_{6,7}$-H), 8.72 (1H, s, CHO). ^{13}C-NMR: 21.1 (t), 22.5 (t), 39.3 (t), 55.7 (q), 56.4 (q), 105.9 (d), 110.1 (d), 121.0 (s), 128.8 (s), 145.4 (s), 151.5 (s), 164.2 (d). LR-MS *m/z*: 221 (M^+), 178 (base peak). HR-MS *m/z*: Calcd for $C_{12}H_{15}NO_3$ (M^+): 221.1050. Found: 221.1038.

1-Formyl-1,2,3,4-tetrahydro-5,7-dimethoxyquinoline (**12e**): Yield: 77% (50 mg from 100 mg of **8e**). Colorless plates from hexane–AcOEt, mp 99—104 °C. IR: 1665, 1618, 1591, 1510. ^{1}H-NMR: 1.89 (2H, quintet, J=7 Hz, C_3-H), 2.65 (2H, t, J=7 Hz, C_4-H), 3.78 (2H, t, J=7 Hz, C_2-H), 3.81, 3.82 (each 3H, s, OCH_3×2), 6.29 (2H, s, ArH), 8.79 (1H, s, CHO). ^{13}C-NMR: 20.5 (t), 22.0 (t), 39.7 (t), 55.5 (q), 55.5 (q), 94.4 (d), 94.4 (d), 109.6 (s), 138.5 (s), 158.6 (s), 159.2 (s), 161.0 (d). LR-MS *m/z*: 221 (M^+), 176 (base peak). *Anal*. Calcd for $C_{12}H_{15}NO_3$: C, 65.14; H, 6.83; N, 6.33. Found: C, 65.11; H, 6.77; N, 6.31.

1-Formyl-1,2,3,4-tetrahydro-5,6,7-trimethoxyquinoline (**12f**): Yield: 91% (1.28 g from 2.0 g of **8f**). Colorless needles from AcOEt–hexane, mp 92—98 °C. IR: 1668, 1603, 1577, 1502. ^{1}H-NMR: 1.90 (2H, quintet, J=6 Hz, C_3-H), 2.71 (2H, t, J=6 Hz, C_4-H), 3.77 (2H, t, J=6 Hz, C_2-H), 3.85, 3.86, 3.89 (each 3H, s, OCH_3×3), 6.45 (1H, s, C_8-H), 8.73 (1H, s, CHO). ^{13}C-NMR: 20.8 (t), 22.0 (t), 39.8 (t), 56.2 (q), 60.5 (q), 60.9 (q), 97.5 (d), 115.0 (s), 133.1 (s), 139.4 (s), 151.7 (s), 152.2 (s), 160.8 (d). LR-MS *m/z*: 251 (M^+, base peak). *Anal*. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 61.93; H, 6.78; N, 5.39.

1-Formyl-1,2,3,4-tetrahydroquinoline (**12g**): Yield: 98% (0.88 g from 1.5 g of **8g**). A colorless gum. IR: 1672, 1603, 1583. ^{1}H-NMR: 1.95 (2H, quintet, J=6 Hz, C_3-H), 2.81 (2H, t, J=6 Hz, C_4-H), 3.81 (2H, t, J=6 Hz, C_2-H), 6.9—7.3 (4H, m, ArH), 8.78 (1H, s, CHO). ^{13}C-NMR: 22.2 (t), 27.1 (t), 40.3 (t), 117.0 (d), 124.5 (d), 127.1 (d), 128.9 (s), 129.6 (d), 137.2 (s), 161.1 (d). LR-MS *m/z*: 161 (M^+), 160 (base peak). HR-MS *m/z*: Calcd for $C_{10}H_{11}NO$ (M^+): 161.0840. Found: 161.0870.

Hydrolysis of 1-Formyl TQ 12 (General Procedure) A solution of **12** (1 mol eq) in EtOH–10% NaOH (1 : 1) was refluxed for 6 h. The reaction mixture was diluted with water and extracted with $CHCl_3$. The product was purified by column chromatography eluting with hexane–AcOEt (2 : 1) to give TQ **13**.

1,2,3,4-Tetrahydro-7,8-dimethoxyquinoline (**13a**): Yield: 82% (216 mg from 300 mg of **12a**). A reddish yellow gum. IR: 3418, 1615. ^{1}H-NMR: 1.8—2.1 (2H, m, C_3-H), 2.71 (2H, t, J=6 Hz, C_4-H), 3.30 (2H, t, J=6 Hz, C_2-H), 3.79, 3.81 (each 3H, s, OCH_3×2), 6.19, 6.65 (each 1H, d, J=8 Hz, $C_{5,6}$-H). ^{13}C-NMR: 22.2 (t), 26.2 (t), 41.3 (t), 55.7 (q), 59.6 (q), 100.2 (d), 115.1 (s), 123.8 (d), 134.5 (s), 138.7 (s), 150.7 (s). LR-MS *m/z*: 193 (M^+), 178 (base peak). HR-MS *m/z*: Calcd for $C_{11}H_{15}NO_2$ (M^+): 193.1101. Found: 193.1061.

1,2,3,4-Tetrahydro-6,7-dimethoxyquinoline (**13b**): Yield: 87% (152 mg from 200 mg of **12b**). A reddish yellow gum (lit.[10] mp 45—45.5 °C). IR: 3390, 1622, 1520. ^{1}H-NMR: 1.91 (2H, quintet, J=6 Hz, C_3-H), 2.69 (2H, t, J=6 Hz, C_4-H), 3.25 (2H, t, J=6 Hz, C_2-H), 3.79 (6H, s, OCH_3×2), 6.11, 6.52 (each 1H, s, $C_{5,8}$-H). ^{13}C-NMR: 22.4 (t), 26.1 (t), 42.0 (t), 55.6 (q), 56.6 (q), 99.7 (d), 112.7 (s), 114.0 (d), 138.5 (s), 141.1 (s), 148.1 (s). LR-MS *m/z*: 193 (M^+), 178 (base peak). HR-MS *m/z*: Calcd for $C_{11}H_{15}NO_2$ (M^+): 193.1103. Found: 193.1115.

1,2,3,4-Tetrahydro-5,8-dimethoxyquinoline (**13c**): Yield: 83% (146 mg from 200 mg of **12c**). A yellow gum (lit.[11] bp 180 °C (3.5 mmHg)). IR: 3424, 1605, 1508. ^{1}H-NMR: 1.8—2.1 (2H, m, C_3-H), 2.67 (2H, t, J=7 Hz, C_4-H), 3.2—3.4 (2H, m, C_2-H), 3.75, 3.78 (each 3H, s, OCH_3×2), 6.09, 6.54 (each 1H, d, J=9 Hz, $C_{6,7}$-H). ^{13}C-NMR: 20.6 (t), 21.6 (t), 40.8 (t), 55.3 (q), 55.6 (q), 96.5 (d), 106.9 (d), 110.1 (s), 135.5 (s), 140.9 (s), 152.0 (s). LR-MS *m/z*: 193 (M^+), 178 (base peak). HR-MS *m/z*: Calcd for $C_{11}H_{15}NO_2$ (M^+): 193.1101. Found: 193.1086.

1,2,3,4-Tetrahydro-5,7-dimethoxyquinoline (**13e**): Yield: 95% (41 mg from 50 mg of **12e**). A yellow gum. IR: 3408, 1618, 1510. ^{1}H-NMR: 1.7—2.1 (2H, m, C_3-H), 2.58 (2H, t, J=6 Hz, C_4-H), 3.1—3.3 (2H, m, C_2-H), 3.73, 3.76 (each 3H, s, OCH_3×2), 5.71, 5.86 (each 1H, d, J=2 Hz, $C_{6,8}$-H). ^{13}C-NMR: 20.1 (t), 22.1 (t), 41.7 (t), 55.2 (q), 55.2 (q), 88.1 (d), 91.7 (d), 102.5 (s), 146.0 (s), 158.7 (s), 159.2 (s). LR-MS *m/z*: 193 (M^+), 192 (base peak). HR-MS *m/z*: Calcd for $C_{11}H_{15}NO_2$ (M^+): 193.1101. Found: 193.1071.

1,2,3,4-Tetrahydro-5,6,7-trimethoxyquinoline (**13f**): Yield: 97% (258 mg from 300 mg of **12f**). A yellow gum. IR: 3390, 1612, 1591. ^{1}H-NMR: 1.88 (2H, quintet, J=6 Hz, C_3-H), 2.65 (2H, t, J=6 Hz, C_4-H), 3.22 (2H, t, J=6 Hz, C_2-H), 3.77, 3.77, 3.85 (each 3H, s, OCH_3×3), 5.86 (1H, s, C_8-H). ^{13}C-NMR: 20.6 (t), 22.0 (t), 41.9 (t), 55.8 (q), 60.3 (q), 61.0 (q), 94.4 (d), 107.3 (s), 133.8 (s), 141.1 (s), 151.9 (s), 152.1 (s). LR-MS *m/z*: 223 (M^+), 208 (base peak). HR-MS *m/z*: Calcd for $C_{12}H_{17}NO_3$ (M^+): 223.1209. Found: 223.1210.

1,2,3,4-Tetrahydroquinoline (**13g**): Yield: 93% (231 mg from 300 mg of **12g**). A yellow gum (lit.[4b] oil (bp 126—127 °C (3 mmHg)). IR: 3408, 1606, 1583, 1504. ^{1}H-NMR: 1.7—2.1 (2H, m, C_3-H), 2.75 (2H, t, J=6 Hz, C_4-H), 3.28 (2H, t, J=6 Hz, C_2-H), 3.60 (1H, br s, NH), 6.3—7.2 (4H, m, ArH). ^{13}C-NMR: 22.2 (t), 27.0 (t), 42.0 (t), 114.2 (d), 116.9 (d), 121.4 (s), 126.7 (d), 129.5 (d), 144.8 (s). LR-MS *m/z*: 133 (M^+), 106 (base peak). HR-MS *m/z*: Calcd for $C_9H_{11}N$ (M^+): 133.0962. Found: 133.0933.

$LiAlH_4$ Reduction of 1-Formyl TQ 12 (General Procedure) $LiAlH_4$ (2 mol eq) was added to a solution of **12** (1 mol eq) in dry THF under ice-cooling, and the mixture was refluxed for 1 h. Et_2O, saturated with water, was added to the reaction mixture and insoluble material was filtered off. The product was purified by column chromatography eluting with hexane–AcOEt (3 : 1) to give 1-methylTQ **14**.

1,2,3,4-Tetrahydro-7,8-dimethoxy-1-methylquinoline (**14a**): Yield: 78% (218 mg from 300 mg of **12a**). A yellow gum. IR: 1605. ^{1}H-NMR: 1.7—2.0 (2H, m, C_3-H), 2.69 (2H, t, J=6 Hz, C_4-H), 2.98 (3H, s, >NCH_3), 3.10 (2H, t, J=6 Hz, C_2-H), 3.77, 3.82 (each 3H, s, OCH_3×2), 6.39, 6.69 (each 1H, d, J=8 Hz, $C_{5,6}$-H). ^{13}C-NMR: 19.9 (t), 27.8 (t), 42.2 (q), 52.8 (t), 55.8 (q), 59.0 (q), 103.7 (d), 121.2 (s), 123.5 (d), 139.9 (s), 141.8 (s), 151.7 (s). LR-MS *m/z*: 207 (M^+), 192 (base peak). HR-MS *m/z*: Calcd for $C_{12}H_{17}NO_2$ (M^+): 207.1257. Found: 207.1244.

1,2,3,4-Tetrahydro-6,7-dimethoxy-1-methylquinoline (**14b**): Yield: 79% (148 mg from 200 mg of **12b**). A yellow gum (lit.[10] bp 135—136 °C (1 mmHg)). IR: 1522. ^{1}H-NMR: 1.96 (2H, quintet, J=6 Hz, C_3-H), 2.71 (2H, t, J=7 Hz, C_4-H), 2.86 (3H, s, >NCH_3), 3.13 (2H, t, J=6 Hz, C_2-H), 3.79, 3.85 (each 3H, s, OCH_3×2), 6.28, 6.56 (each 1H, s, $C_{5,8}$-H). ^{13}C-NMR: 22.5 (t), 27.0 (t), 39.8 (q), 51.3 (t), 55.9 (q), 56.7 (q), 97.9 (d), 114.1 (d), 114.6 (s), 140.5 (s), 141.4 (s), 148.1 (s). LR-MS *m/z*: 207 (M^+), 192 (base peak). HR-MS *m/z*: Calcd for $C_{12}H_{17}NO_2$ (M^+): 207.1259. Found: 207.1280.

1,2,3,4-Tetrahydro-5,8-dimethoxy-1-methylquinoline (**14c**): Yield: 76% (142 mg from 200 mg of **12c**). A yellow gum. IR: 1601. ^{1}H-NMR: 1.6—2.0 (2H, m, C_3-H), 2.63 (2H, t, J=7 Hz, C_4-H), 2.84 (3H, s, >NCH_3), 3.0—3.2 (2H, m, C_2-H), 3.76, 3.82 (each 3H, s, OCH_3×2), 6.38, 6.64 (each 1H, d, J=9 Hz, $C_{6,7}$-H). ^{13}C-NMR: 16.5 (t), 22.0 (t), 41.9 (q), 51.7 (t), 55.3 (q), 55.4 (q), 101.7 (d), 107.9 (d), 118.5 (s), 138.8 (s), 146.5 (s), 151.6 (s). LR-MS *m/z*: 207 (M+), 192 (base peak). HR-MS *m/z*: Calcd for $C_{12}H_{17}NO_2$ (M^+): 207.1260. Found: 207.1280.

1,2,3,4-Tetrahydro-5,7-dimethoxy-1-methylquinoline (**14e**): Yield: 83% (55 mg from 70 mg of **12e**). A pale yellow gum. IR: 1613, 1502. ^{1}H-NMR: 1.8—2.1 (2H, m, C_3-H), 2.60 (2H, t, J=6 Hz, C_4-H), 2.87 (3H, s, N-CH_3), 3.16 (2H, t, J=6 Hz, C_2-H), 3.77, 3.78 (each 3H, s, OCH_3×2), 5.89 (2H, s, ArH). ^{13}C-NMR: 20.6 (t), 22.1 (t), 39.7 (q), 51.2 (t), 55.2 (q), 55.4 (q), 87.0 (d), 90.5 (d), 103.5 (s), 148.2 (s), 158.0 (s), 159.3 (s). LR-MS *m/z*: 207 (M^+), 206 (base peak). HR-MS *m/z*: Calcd for $C_{12}H_{17}NO_2$ (M^+): 207.1257. Found: 207.1247.

1,2,3,4-Tetrahydro-5,6,7-trimethoxy-1-methylquinoline (**14f**): Yield: 79% (224 mg from 300 mg of **12f**). A reddish yellow gum. IR: 1608, 1577, 1504. ^{1}H-NMR: 1.93 (2H, quintet, J=6 Hz, C_3-H), 2.67 (2H, t, J=6 Hz, C_4-H), 2.86 (3H, s, >NCH_3), 3.14 (2H, t, J=6 Hz, C_2-H), 3.79 (3H, s, OCH_3), 3.84 (6H, s, OCH_3×2), 6.01 (1H, s, C_8-H). ^{13}C-NMR: 21.1 (t), 22.2 (t), 39.7 (q), 51.2 (t), 56.1 (q), 60.3 (q), 61.0 (q), 92.6 (d), 108.8 (s), 133.4 (s), 143.4 (s), 151.4 (s), 151.8 (s). LR-MS *m/z*: 237 (M^+), 222 (base peak). HR-MS *m/z*: Calcd for $C_{13}H_{19}NO_3$ (M^+): 237.1365. Found: 237.1372.

1,2,3,4-Tetrahydro-1-methylquinoline (**14g**): Yield: 80% (219 mg from 300 mg of **12g**). A yellow gum (lit.[4] bp 110 °C (15 mmHg)). IR: 1603, 1508. ^{1}H-NMR: 1.8—2.1 (2H, m, C_3-H), 2.76 (2H, t, J=6 Hz, C_4-H), 2.87 (3H, s, >NCH_3), 3.20 (2H, t, J=6 Hz, C_2-H), 6.5—7.2 (4H, m, ArH). ^{13}C-NMR: 22.5 (t), 27.8 (t), 39.1 (q), 51.3 (t), 111.0 (d), 116.2 (d), 122.9 (s), 127.0 (d), 128.8 (d), 146.8 (s). LR-MS *m/z*: 147 (M^+), 120 (base peak). HR-MS *m/z*:

Calcd for $C_{10}H_{13}N$ (M^+): 147.1046. Found: 147.0959.

Pummerer Cyclization of the Sulfoxide 7e Followed by Reductive Desulfurization i) TFAA (1.52 g, 7.24 mmol) was added to a solution of **7e** (500 mg, 1.44 mmol) in benzene (40 ml) under Ar atmosphere at room temperature for 21 h. The reaction mixture was concentrated *in vacuo* to dryness to give a crude Pummerer product. $NaBH_4$ (572 mg, 15.1 mmol) was added to the product and $NiCl_2 \cdot H_2O$ (1.2 g, 5.05 mmol) in MeOH–THF (3 : 1) (40 ml) in small portions under ice-cooling. The mixture was stirred at room temperature for 1.5 h. Chromatography of the products with hexane–AcOEt (3 : 1) gave **12e** (54 mg, 17%), **16** (71 mg, 22%), **17** (53 mg, 11%), and **18** (67 mg, 18%).

ii) TFAA (1.52 g, 7.24 mmol) was added to a solution of **7e** (500 mg, 1.44 mmol) in benzene (40 ml) under Ar atmosphere at room temperature. After the mixture was stirred at room temperature for 1 h, $BF_3 \cdot Et_2O$ (614 mg, 4.32 mmol) was added, and the whole was stirred for a further 2 h at the same temperature. The products and $NiCl_2 \cdot 6H_2O$ (1.2 g, 5.05 mmol) in MeOH–THF (3 : 1) (40 ml) was treated with $NaBH_4$ at room temperature for 1.5 h. Purification of the products as described above gave **12e** (76 mg, 24%), **13e** (7 mg, 3%), **16** (106 mg, 33%), **17** (48 mg, 10%), **18** (90 mg, 25%).

N-(3,5-Dimethoxyphenyl)-*N*-propylformamide (**16**): A yellow gum. IR: 1680, 1595, 1504. ^{1}H-NMR: 0.90 (3H, t, J=7 Hz, $-CH_3$), 1.4—1.7 (2H, m, $-CH_2C\underline{H}_2CH_3$), 3.75 (2H, t, J=7 Hz, $>NCH_2-$), 3.80 (6H, s, $OCH_3\times2$), 6.31 (2H, d, J=2 Hz, ArH), 6.39 (1H, t, J=2 Hz, ArH), 8.40 (1H, s, CHO). ^{13}C-NMR: 10.8 (q), 20.5 (t), 45.9 (t), 55.0 (q×2), 97.7 (d), 102.1 (d×2), 142.4 (s), 161.1 (s×2), 161.7 (d). LR-MS *m/z*: 223 (M^+), 138 (base peak). HR-MS *m/z*: Calcd for $C_{12}H_{17}NO_3$ (M^+): 223.1209. Found: 223.1219.

N-(3,5-Dimethoxy-2-phenylthiophenyl)-*N*-propylformamide (**17**): A yellow gum. IR: 1680, 1597, 1572. ^{1}H-NMR: 0.83 (3H, t, J=7 Hz, $-CH_3$), 1.2—1.6 (2H, m, $-CH_2C\underline{H}_2CH_3$), 3.5—3.9 (2H, m, $>NCH_2-$), 3.81, 3.87 (each 3H, s, $OCH_3\times2$), 6.45, 6.56 (each 1H, d, J=2 Hz, ArH), 6.9—7.2 (5H, m, PhH), 7.96 (1H, s, CHO). ^{13}C-NMR: 11.3 (q), 20.8 (t), 47.8 (t), 55.6 (q), 56.3 (q), 98.6 (d), 106.5 (d), 110.8 (s), 125.2 (d), 126.0 (d×2), 128.7 (d×2), 137.6 (s), 146.2 (s), 162.1 (s), 162.5 (s), 162.6 (d). LR-MS *m/z*: 331 (M^+), 222 (base peak). HR-MS *m/z*: Calcd for $C_{18}H_{21}NO_3S$ (M^+): 331.1243. Found: 331.1219.

5-Formyl-1,2,3,4-tetrahydro-7,9-dimethoxy-1,5-benzothiazepine (**18**): Colorless needles from hexane–AcOEt, mp 132—136 °C. IR: 1676, 1597, 1572. ^{1}H-NMR: 2.0—2.3 (2H, m, C_3-H), 2.7—2.9 (2H, m, C_2-H), 3.6—3.9 (2H, m, C_4-H), 3.82, 3.89 (each 3H, s, $OCH_3\times2$), 6.32, 6.47 (each 1H, d, J=2 Hz, $C_{6,8}$-H), 8.30 (1H, s, CHO). ^{13}C-NMR: 29.5 (t), 31.6 (t), 44.6 (t), 55.6 (q), 56.4 (q), 98.1 (d), 104.6 (d), 114.3 (s), 145.6 (s), 159.6 (s), 160.1 (s), 162.0 (d). LR-MS *m/z*: 253 (M^+, base peak). *Anal*. Calcd for $C_{12}H_{15}NO_3S$: C, 56.90; H, 5.97; N, 5.53. Found: C, 56.88; H, 5.94; N, 5.43.

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References and Notes

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