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SYNTHESIS OF 2,3,4,5-TETRAHYDRO-1*H*-2-BENZAZEPINES *VIA* PUMMERER-TYPE CYCLIZATION OF *N*-ARYLMETHYL-*N*-(3-PHENYLSULFINYLPROPYL)FORMAMIDES

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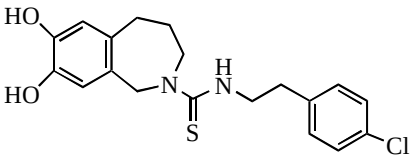
Abstract A construction of 1*H*-benzazepine ring system was achieved *via* a modified Pummerer reaction of *N*-arylmethyl-*N*-(3-phenylsulfinylpropyl)-formamides (**5**) using trifluoroacetic acid and borontrifluoride etherate. This method provides an effective synthesis of 7,8-dimethoxy-2,3,4,5-tetrahydro-1*H*-2-benzazepine (**10a**), the synthetic intermediate of capsazepine (**1**), an antagonist of capsaicin and resinferatoxin.

It is well known that the *in situ* formed thionium ion generated under the acidic conditions from a sulfinyl precursor (Pummerer reaction) is a powerfull 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] 2-quinolones,[7] and 2,3,4,5-tetrahydro-1*H*-3-benzazepines.[8]

In these studies we have found that the cyclization under a usual Pummerer condition using trifluoroacetic anhydride (TFAA) as a sole reagent highly effectively proceeds at room temperature when the aromatic ring is sufficiently electron-rich (method A).[3,4] On the other hand in the substrates lacking an electron donating substituent on the aromatic ring the method A does not induce the cyclization unless boron trifluoride diethyl etherate (BF_3•Et_2O) is used as an additive reagent.[3a-c,4] This method using TFAA and BF_3•Et_2O (method B) seems to be effective for the cyclization of a weak nucleophilic aromatic π-bond.

In this paper we described the synthesis of 2,3,4,5-tetrahydro-1*H*-2-benzazepine *via* cyclization using Pummerer reaction and an application to the synthesis of capsazepine (**1**), an antagonist of the sensory neuron excitants capsaicin and resinferatoxin.[9]



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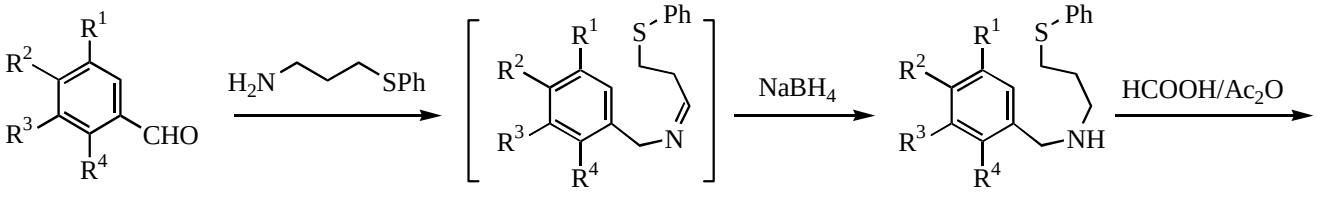
Preparation of Sulfoxides

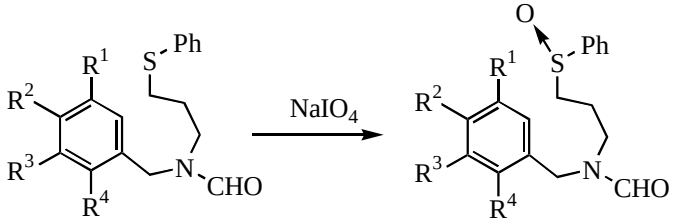
The sulfoxides **(5)**, substrates of Pummerer reaction, were prepared from aromatic aldehydes (**2)** and 3-phenylsulfanylpropylamine[4] as follows. Condensation of **2** with the amine in EtOH in the presence of



2 **3**

For compounds (**2-5**)

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



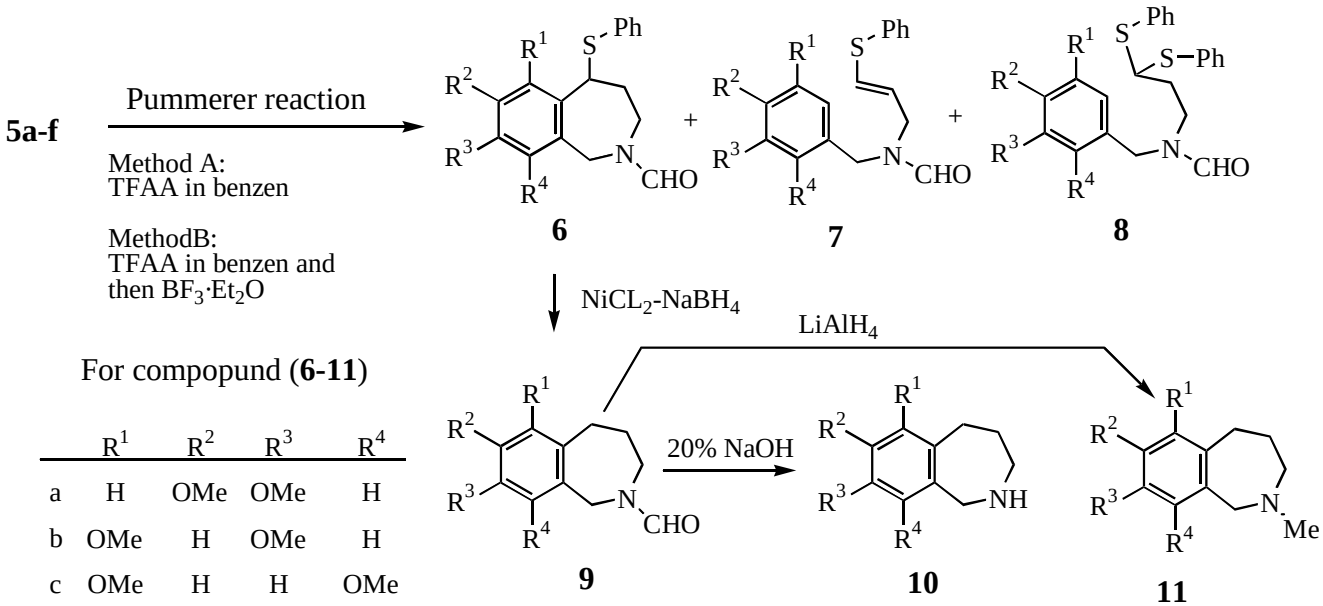
4 **5**

Scheme 2

acetic acid followed by $NaBH_4$ reduction of the resulting imine afforded *N*-arylmethyl-3-phenylsulfanylpropylamines (**4)** in good yields. The amines **(3)** were protected by formylation and the resulting formamides **(4)** were oxidized with sodium metaperiodate ($NaIO_4$) in aqueous methanol to produce **5** in excellent overall yields. The products **(3)**, **(4)**, and **(5)** were well characterized by MS, IR, and ^{1}H- and ^{13}C-NMR spectral data (See Experimental).

Pummerer Reaction (method A)

A solution of **5** in benzene was treated with TFAA at room temperature for appropriates times under an argon atmosphere (method A condition). Sulfoxide **(5a)** yielded 5-phenylsulfanylbenzazepine **(6a)** in moderate yield (56%) accompanied with vinyl sulfide **(7a)** as an uncyclized product (31%). The sulfoxide **(5b)** produced the corresponding benzazepine **(6b)** in yield of only 13%, although the aromatic ring is electronically activated by two OMe groups positioned at *para* and *ortho*. In this case no other products were characterized. The reaction of **5c** having two OMe groups at *ortho*- and *meta*-positions yielded no cyclized product. Furthermore, the sulfoxide **(5d)** having a *para* OMe group afforded the corresponding benzazepine **(6d)** in 13% yield. Other monomethoxy sulfoxides (**5e-5f)** having a *meta* OMe group and



For compopund (**6-11**)

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

Scheme 3

sulfoxide **(5g)** with no OMe group, when treated with TFAA, merely yielded complex mixtures. No benzazepines could be obtained in any extent.

Pummerer Reaction (method B)

The cyclization of sulfoxides **(5)** was examined under the method B conditions. A solution of **5a** in benzene was treated with TFAA for 45 min at room temperature, then BF_3•Et_2O was added and the mixture was allowed to react for further 45 min, giving the benzazepine **(6a)** in 66% yield and **4a** in 5% yield. Thus, the yield of **6a** was comparable to that achieved by method A. In the cases of **5b**, **5c**, and **5d** use of BF_3•Et_2O as an additive improved the ring closure reaction to give **6b**, **6c**, and **6d** in moderate yields as shown in the Table. However, the reactions of **5e-g** on the similar treatment under method B conditions did not caused the desired cyclization in any extent. The sulfoxides (**5e)** and **(5f)** only gave the bis-phenylsulfanyl derivative **(8e)** and **(8f)** respectively.

Table Pummere Reaction of Sulfoxides **(5)**

	Conditions[a)]			Yield (%)			
sulfoxide (**5**)	Reagent	Additive	Time	PheS-bebzazepine		Others	
5a	TFAA	non	4	**(6a)**	56	**(7a)**	31
5a	TFAA	BF_3·Et_2O	1.5	**(6a)**	66	**(4a)**	5
5b	TFAA	non	2	**(6b)**	13		
5b	TFAA	BF_3·Et_2O	1	**(6b)**	61		
5c	TFAA	non	12	**(6c)**	b)		
5c	TFAA	BF_3·Et_2O	4	**(6c)**	45		
5d	TFAA	non	18	**(6d)**	13		
5d	TFAA	BF_3·Et_2O	3	**(6d)**	78		
5e	TFAA	BF_3·Et_2O	4			**(8e)**	21
5f	TFAA	BF_3·Et_2O	3			**(8f)**	33
5g	TFAA	BF_3·Et_2O	24		b)		

a) In benzene at room temperature, b) No characterizable products

The results summarized in the Table indicated that the formation of benzazepine ring by Pummerer

reaction of **5** occurred under method B conditions if the nucleophilic center of the aromatic ring is activated by electron donating group such as OMe group, although this cyclization leading to benzazepine ring, particularly under method A conditions, was much less effective when compared with that of *N*-aryl-*N*-arylmethyl-*N*- (3-phenylsulfinylethyl)formamide leading to 1,2,3,4-tetrahydroisoquinoline ring.[4]

Preparation of Benzazepines

Reductive removal of the phenylsulfanyl group readily proceeded on treatment with $NiCl_2$-$NaBH_4$ in MeOH-THF to give *N*-formyl-benzazepines **(9)** in good yields. Deprotection of the *N*-formyl group was achieved by conventional methods. Alkaline hydrolysis gave the benzazepines **(10)**. Reduction of **9** with $LiAlH_4$ gave *N*-methylbenzazepines **(11)**.

The synthesis using this route provides 7,8-dimethoxy- (**10a**), 6,8-dimethoxy- (**10b**), 6,9-dimethoxy- (**10c**), 8-methoxy-2,3,4,5-tetrahydro-1*H*-2-benzazepine (**10d**), and their *N*-methyl derivatives (**11**) in moderate overall yields. 7,8-Dimethoxy derivative (**10a**) is the synthetic precursor of capsazepine (**1**).[9,10]

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-AL 300 (^{1}H-NMR, 300 MHz; ^{13}C-NMR, 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. 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. Elemental analyses were recorded on a Yanaco-CHN-corder MT-3. 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 *N*-(3,4-Dimethoxyphenyl)methyl-(3-phenylsulfanyl)propylamine (3a). Typical Procedure. A solution of 3,4-dimethoxybenzaldehyde (**2a**) (1.19 g, 7.2 mmol), 3-phenylsulfanylpropylamine (1.2 g, 7.2 mmol)[4] and acetic acid (5.184 g, 8.64 mmol) in EtOH (250 mL) was refluxed for 23 h. $NaBH_4$ (272 mg, 7.2 mmol) was added slowly to a reaction mixture at 0°C and stirred for 30 min at rt. Water was added to the reaction mixture. After removal of the solvent *in vacuo*, the residue was extracted with $CHCl_3$. The residual oil was purified by column chromatography with ethyl acetate to give **3a** (1.40g, 74%) as a yellow oil. IR (film): 3316, 1590. ^{1}H-NMR: 1.9-2.2 (2H, m, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.7-3.1 (4H, m, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh and -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.83 (3H, s, OMe), 3.90 (2H, s, -NHC$\underline{H}_2$Ar), 3.92 (3H, s, OMe), 6.7-7.0 (3H, m, ArH), 7.1-7.4 (5H, m, SPh). ^{13}C-NMR: 25.6 (t), 31.0 (t), 44.7 (t), 50.8 (t), 55.8 (q), 56.2 (q), 110.9 (d), 112.8 (d), 122.6 (d), 123.4 (s), 126.3 (d), 129.0 (dx2), 129.6 (dx2), 135.3 (s), 149.3 (s), 149.5 (s). LRMS *m/z*: 317 (M^+).

***N*-(3,5-Dimethoxyphenyl)methyl-(3-phenylsulfanyl)propylamine (3b):** From 3,5-dimethoxy-benzaldehyde (**2b**) (1.19 g, 7.2 mmol) and 3-phenylsulfanylamine (1.2g, 7.2 mmol);column chromatography with ethyl acetate gave **3b** (1.50 g, 79%) as a pale yellow oil. IR (film): 3311, 1596. ^{1}H-NMR: 1.82 (2H, quintet, *J*=7 Hz, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.75 (2H, t, *J*=7 Hz, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 2.99 (2H, t, *J*=7 Hz, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh) 3.71 (2H, s, -NHC$\underline{H}_2$Ar), 3.78 (6H, s, OMex2), 6.3-6.5 (3H, m, ArH), 7.1-7.4 (5H, m, SPh). ^{13}C-NMR: 29.4 (t), 31.4 (t), 47.9 (t), 53.9 (t), 55.2 (qx2), 98.9 (d), 105.8 (d), 125.7 (dx2), 128.8 (dx2), 129.0 (dx2), 136.5 (s), 142.8 (s), 160.8 (s). 160.9 (s). LRMS *m/z*: 317 (M^+).

***N*-(2,5-Dimethoxyphenyl)methyl-(3-phenylsulfanyl)propylamine (3c):** From 2,5-dimethoxy-benzaldehyde (**2c**) (1.19 g, 7.2 mmol) and 3-phenylsulfanylamine (1.2g, 7.2 mmol); column chromatography with ethyl acetate gave **3c** (1.90 g, 92%) as a yellow oil. IR (film): 3320, 1586.

^{1}H-NMR: 1.83 (2H, quintet, *J*=7 Hz, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.72 (2H, t, *J*=7 Hz, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 2.99 (2H, t, *J*=7 Hz, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh) 3.74 (2H, s, -NHC$\underline{H}_2$Ar), 3.76 (3H, s, OMe), 3.77 (3H, s, OMe), 6.7-7.4 (8H, m, ArH and SPh), ^{13}C-NMR: 29.4 (t), 31.3 (t), 47.7 (t), 49.0 (t), 55.5 (q), 55.6 (q), 111.0 (d), 112.0 (d), 115.8 (d), 125.6 (d), 128.7 (dx2), 128.9 (dx2), 129.5 (s), 136.6 (s), 151.7 (s). 153.3 (s). LRMS *m/z*: 317 (M^+).

***N*-(3-Methoxyphenyl)methyl-(3-phenylsulfanyl)propylamine (3d):** From 3-methoxybenzaldehyde (**2d**) (0.980 g, 7.2 mmol) and 3-phenylsulfanylamine (1.2g, 7.2 mmol); column chromatography with $CHCl_3$ gave **3d** (1.736 g, 84%) as yellow oil. IR (film): 1585. ^{1}H-NMR: 1.83 (2H, quintet, *J*=7 Hz, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.75 (2H, t, *J*=7 Hz, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 2.99 (2H, t, *J*=7 Hz, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh) 3.75 (2H, s, -NHC$\underline{H}_2$Ar), 3.80 (3H, s, OMe), 6.7-7.4 (9H, m, ArH and SPh), ^{13}C-NMR: 29.5 (t), 31.5 (t), 48.0 (t), 53.8 (t), 55.1 (q), 112.4 (d), 113.5 (d), 120.3 (d), 125.9 (d), 128.8 (dx2), 129.1 (dx2), 129.3 (d), 136.6 (s), 141.9 (s). 159.7 (s). LRMS *m/z*: 287 (M^+).

***N*-(4-Methoxyphenyl)methyl-(3-phenylsulfanyl)propylamine (3e):** From 4-methoxybenzaldehyde (**2e)** (0.980 g, 7.2 mmol) and 3-phenylsulfanylamine (1.2g, 7.2 mmol); column chromatography with $CHCl_3$ gave **3e** (1.488 g, 72%) as a yellow oil. IR (film): 1587. ^{1}H-NMR: 1.82 (2H, quintet, *J*=7 Hz, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.74 (2H, t, *J*=7 Hz, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 2.99 (2H, t, *J*=7 Hz, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh) 3.70 (2H, s, -NHC$\underline{H}_2$Ar), 3.79 (3H, s, OMe), 7.1-7.4 (9H, m, ArH and SPh), ^{13}C-NMR: 29.4 (t), 31.5 (t), 47.8 (t), 53.2 (t), 55.2 (q), 113.7 (dx2), 125.8 (d), 128.8 (dx2), 129.1 (dx2), 129.2 (dx2), 132.3 (s), 136.6 (s), 158.6 (s). LRMS *m/z*: 287 (M^+)

***N*-(2-Methoxyphenyl)methyl-(3-phenylsulfanyl)propylamine (3f):** From 2-methoxybenzaldehyde (**2f**) (0.980 g, 7.2 mmol) and 3-phenylsulfanylamine (1.2g, 7.2 mmol); column chromatography with $CHCl_3$ gave **4f** (1.570 g, 76%) as a yellow oil. IR (film): 1610. ^{1}H-NMR: 1.83 (2H, quintet, *J*=7 Hz, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.72 (2H, t, *J*=7 Hz, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 2.98 (2H, t, *J*=7 Hz, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh) 3.77 (2H, s, -NHC$\underline{H}_2$Ar), 3.82 (3H, s, OMe), 6.8-7.0 (2H, m, ArH), 7.1-7.4 (7H, m,

ArH and SPh), ^{13}C-NMR: 29.5 (t), 31.5 (t), 47.9 (t), 49.1 (t), 55.2 (q), 110.2 (d), 120.3 (d), 125.7 (d), 128.1 (d), 128.3 (d), 128.7 (dx2), 129.0 (dx2), 129.7 (d), 136.7 (s), 157.6 (s). LRMS *m/z*: 287 (M^+).

***N*-(3-phenylsulfanyl)propylbenzylamine (3g):** From benzaldehyde (**2g**) (0.763 g, 7.2 mmol) and 3-phenylsulfanylamine (1.2g, 7.2 mmol); column chromatography with $CHCl_3$ gave **3g** (1.091 g, 59 %) as a yellow oil. IR (film): 1583, 1481. ^{1}H-NMR: 1.84 (2H, quintet, *J*=7 Hz, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.76 (2H, t, *J*=7 Hz, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.00 (2H, t, *J*=7 Hz, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh) 3.77 (2H, s, -NHC$\underline{H}_2$Ar), 7.0-7.5 (10H, m, Ph and SPh), ^{13}C-NMR: 29.4 (t), 31.4(t), 47.9 (t), 53.8 (t), 125.7 (d), 126.8 (d), 128.0 (dx2), 128.3 (dx2), 128.7 (dx2), 129.0 (dx2), 136.6 (s), 140.2 (s). LRMS *m/z*: 257 (M^+).

Formylation of 3. Typical Procedure. The mixture of formic acid (13.8 g, 0.3 mol) and acetic anhydride (10.2 g, 0.1 mol) was added at rt to **3a** (3.17 g, 10 mmol) and the mixture was heated at 70 °C for 1 h. The reaction mixture was concentrated *in vacuo* and the residue was extracted with $CHCl_3$. After removal of the solvent, the residue was chromatographed with hexane-ethyl acetate (1:2) to give **4a** (3.45 g, quant.) as a yellow gum.

***N*-(3,4-Dimethoxyphenyl)methyl-*N*-[(3-phenylsulfany)propyl]fromamide (4a)** IR (film): 1669, 1593. ^{1}H-NMR: 1.7-1.9 (total 2H, m, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.8-3.0 (total 2H, m, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.2-3.4 (total 2H, m, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.84, 3.85, 3.86, 3.88 (total 6H, each s, OMe), 4.30, 4.44 (total 2H, each s, -NHC$\underline{H}_2$Ar), 6.7-6.8 (total 3H, m, ArH), 7.2-7.4 (total 5H, m, SPh), 8.19, 8.28 (total 1H, each s, CHO). LRMS *m/z*: 345 (M^+). HRMS *m/z* (M^+): Calcd for $C_{19}H_{23}NO_3S$: 345.1398. Found: 345.1398

***N*-(3,5-Dimethoxyphenyl)methyl-*N*-[(3-phenylsulfany)propyl]fromamide (4b)** From **3b** (3.17 g, 10 mmol); column chromatography with hexane-ethyl acetate (2:1) gave **4b** (3.45g, quant.) as a yellow gum. IR (film): 1671, 1599. ^{1}H-NMR: 1.7-1.9 (total 2H, m, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.8-2.9 (total 2H, m, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh) 3.2-3.5 (total 2H, m, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.76, 3.77, 3.79, 3.84 (total 6H, each s, OMe), 4.28, 4.43 (total 2H, each s, -NHC$\underline{H}_2$Ar), 6.3-6.4 (total 3H, m, ArH), 7.2-7.4 (total 5H, m, SPh), 8.19, 8.25 (total 1H, each s, CHO). LRMS *m/z*: 345 (M^+). HRMS *m/z* (M^+): Calcd for $C_{19}H_{23}NO_3S$:

345.1399. Found:345.1423.

***N*-(2,5-Dimethoxyphenyl)methyl-*N*-[(3-phenylsulfanyl)propyl]formamide (4c)** From **3c** (3.17 g, 10 mmol); column chromatography with hexane-ethyl acetate (2:1) gave **4c** (3.04g, 88%) as a yellow gum. IR (film): 1671, 1590. ^{1}H-NMR: 1.8-1.9 (total 2H, m, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.85 (2H, t, *J*=7 Hz, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.2-3.4 (total 2H, m, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.73, 3.76 (total 6H, each s, OMe), 4.32, 4.53 (total 2H, each s, -NHC$\underline{H}_2$Ar), 6.7-6.8 (total 3H, m, ArH), 7.2-7.3 (total 5H, m, SPh), 8.18, 8.26 (total 1H, each s, CHO). LRMS *m/z*: 345 (M$^+$). HRMS *m/z* (M$^+$): Calcd for $C_{19}H_{23}NO_3S$: 345.1399. Found:345.1434.

***N*-(3-Methoxyphenyl)methyl-*N*-[(3-phenylsulfanyl)propyl]formamide (4d)** From **3d** (2.87 g, 10 mmol); column chromatography with hexane-ethyl acetate (2:1) gave **4d** (2.96g, 94%) as a yellow gum. IR (film): 1678, 1601. ^{1}H-NMR: 1.80 (2H, quintet, *J*=7 Hz, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.83, 2.86 (total 2H, each t, *J*=7 Hz, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.28, 3.36 (total 2H, each t, *J*=7 Hz, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.78, 3.79 (total 3H, each s, OMe), 4.32, 4.47 (total 2H, each s, -NHC$\underline{H}_2$Ar), 6.7-7.4 (total 9H, m, ArH and SPh), 8.20, 8.27 (total 1H, each s, CHO). LRMS *m/z*: 315 (M$^+$). HRMS *m/z* (M$^+$): Calcd for $C_{18}H_{21}NO_2S$: 315.1290. Found: 315.1288.

***N*-(4-Methoxyphenyl)methyl-*N*-[(3-phenylsulfanyl)propyl]formamide (4e)** From **3e** (2.87 g, 10 mmol); column chromatography with hexane-ethyl acetate (2:1) gave **4e** (2.80 g, 89%) as colorless plates recrystallized from $CHCl_3$-Et_2O, mp 175-178°C. IR: 1672. ^{1}H-NMR: 1.79 (2H, quintet, *J*=7 Hz, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.85, 2.85 (total 2H, each t, *J*=7 Hz, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.27, 3.34 (total 2H, each t, *J*=7 Hz, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.79, 3.80 (total 3H, each s, OMe), 4.29, 4.43 (total 2H, each s, -NHC$\underline{H}_2$Ar), 6.8-7.4 (total 9H, m, ArH and SPh), 8.18, 8.27 (total 1H, each s, CHO). LRMS *m/z*: 315 (M$^+$). *Anal.* Calcd for $C_{18}H_{21}NO_2S$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.53; H, 6.76; N, 4.25.

***N*-(2-Methoxyphenyl)methyl-*N*-[(3-phenylsulfanyl)propyl]formamide (4f)** From **3f** (2.87 g, 10 mmol); column chromatography with hexane-ethyl acetate (2:1) gave **4f** (2.94g, 90%) as a yellow gum.

IR (film): 1670. ^{1}H-NMR: 1.7-2.0 (2H, m, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.85 (2H, t, *J*=7 Hz, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.29, 3.34 (total 2H, each t, *J*=7 Hz, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.80 (3H, each s, OMe), 4.35, 4.56 (total 2H, each s, -NHC$\underline{H}_2$Ar), 6.8-7.5 (total 9H, m, ArH and SPh), 8.18, 8.27 (total 1H, each s, CHO). LRMS *m/z*: 315 (M$^+$). HRMS *m/z* (M$^+$): Calcd for $C_{18}H_{21}NO_2S$: 315.1290. Found: 315.1279.

***N*-Benzyl-*N*-[(3-phenylsulfanyl)propyl]formamide (4g)** From **3g** (2.57 g, 10 mmol); column chromatography with hexane-ethyl acetate (2:1) gave **4g** (2.565g, 90%) as a yellow gum. IR (film): 1672. ^{1}H-NMR: 1.79 (2H, quintet, *J*=7 Hz, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.83, 2.86 (total 2H, each t, *J*=7 Hz, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.29, 3.36 (total 2H, each t, *J*=7 Hz, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 4.35, 4.50 (total 2H, each s, -NHC$\underline{H}_2$Ar), 7.1-7.5 (10H, m, Ph and SPh), 8.20, 8.28 (total 1H, each s, CHO). LRMS *m/z*: 285 (M$^+$). HRMS *m/z* (M$^+$): Calcd for $C_{17}H_{19}NOS$: 285.1184. Found: 285.1177

Oxidation of 4a with $NaIO_4$. Typical Procedure. $NaIO_4$ (6.42g, 30 mmol) in H_2O (35 mL) was added to a solution of **4a** (6.9g, 20 mmol) in MeOH (70 mL) and stirred at rt for 5 h. After removal of inorganic precipitates by filtration, the filtrate was concentrated *in vacuo*. The residue was extracted with $CHCl_3$. The product was purified by column chromatography with ethyl acetate to give **5a** (6.137 g, 84%) as a yellow gum.

***N*-(3,4-Dimethoxyphenyl)methyl-*N*-[(3-phenylsulfinyl)propyl]formamide (5a)** IR (film): 1666, 1025. ^{1}H-NMR: 1.8-2.1 (total 2H, m, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.5-2.8 (total 2H, m, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.1-3.5 (total 2H, m, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.86, 3.87, 4.22 (total 6H, each s, OMe), 4.31, 4.41 (total 2H, each s, -NHC$\underline{H}_2$Ar), 6.6-6.9 (total 3H, m, ArH), 7.4-7.6 (total 5H, m, SPh), 8.14, 8.28 (total 1H, each s, CHO). LRMS *m/z*: 361 (M$^+$).

***N*-(3,5-Dimethoxyphenyl)methyl-*N*-[(3-phenylsulfinyl)propyl]formamide (5b)** From **4b** (3.45 g, 10 mmol); column chromatography with ethyl acetate gave **5b** (3.1g, 86%) as a yellow gum. IR (film): 1668, 1047. ^{1}H-NMR: 1.8-2.1 (total 2H, m, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.5-2.9 (total 2H, m, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.2-3.5 (total 2H, m, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.76, 3.78 (total 6H, each s, OMe), 4.2-4.5 (total 2H, m,

-NHC$\underline{H}_2$Ar), 6.2-6.4 (total 3H, m, ArH), 7.4-7.7 (total 5H, m, SPh), 8.15, 8.25 (total 1H, each s, CHO). LRMS *m/z*: 361 (M^+).

***N*-(2,5-Dimethoxyphenyl)methyl-*N*-[(3-phenylsulfinyl)propyl]fromamide (5c)** From **4c** (3.45 g, 10 mmol); column chromatography with ethyl acetate gave **5c** (3.45g, 95%) as a yellow gum. IR (film): 1669, 1048. ^{1}H-NMR: 1.8-2.0 (total 2H, m, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.6-2.8 (total 2H, m, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.2-3.5 (total 2H, m, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.73, 3.76 (total 6H, each s, OMe), 4.32, 4.50 (total 2H, each s, -NHC$\underline{H}_2$Ar), 6.7-6.8 (total 3H, m, ArH), 7.4-7.6 (total 5H, m, SPh), 8.11, 8.25 (total 1H, each s, CHO). LRMS *m/z*: 361 (M^+).

***N*-(3-Methoxyphenyl)methyl-*N*-[(3-phenylsulfinyl)propyl]fromamide (5d)** From **4d** (6.3 g, 20 mmol); column chromatography with ethyl acetate gave **5d** (4.965, 75%) as a yellow gum. IR (film): 1664, 1045. ^{1}H-NMR: 1.7-2.3 (2H, quintet, *J*=7 Hz, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.5-2.9 (total 2H, m, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.1-3.5 (total 2H, m, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.78, 3.80 (total 3H, each s, OMe), 4.2-4.6 (total 2H, m, -NHC$\underline{H}_2$Ar), 6.7-7.8 (total 9H, m, ArH and SPh), 8.15, 8.27 (total 1H, each s, CHO). LRMS *m/z*: 315 (M^+-16).

***N*-(4-Methoxyphenyl)methyl-*N*-[(3-phenylsulfinyl)propyl]fromamide (5e)** From **4e** (6.3 g, 20 mmol); column chromatography with ethyl acetate gave **5e** (5.43 g, 82%) as a colorless gum. IR: 1664, 1033. ^{1}H-NMR: 1.7-2.0 (total 2H, m, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.6-2.9 (total 2H, m, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.2-3.4 (total 2H, m, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.79, 3.81 (total 3H, each s, OMe), 4.2-4.6 (total 2H, m, -NHC$\underline{H}_2$Ar), 6.7-7.4 (total 9H, m, ArH and SPh), 8.13, 8.27 (total 1H, each s, CHO). LRMS *m/z*: 286 (M^+-45).

***N*-(2-Methoxyphenyl)methyl-*N*-[(3-phenylsulfinyl)propyl]fromamide (5f)** From **4f** (6.3 g, 20 mmol); column chromatography with ethyl acetate gave **5f** (4.90g, 74%) as a yellow gum. IR (film): 1664, 1045. ^{1}H-NMR: 1.7-2.1 (2H, m, -NHCH$_2$C$\underline{H}_2$CH$_2$SPh), 2.6-2.9 (2H, m, -NHCH$_2$CH$_2$C$\underline{H}_2$SPh), 3.0-3.5 (total 2H, m, -NHC$\underline{H}_2$CH$_2$CH$_2$SPh), 3.81 (3H, s, OMe), 4.35, 4.51 (total 2H, each s, -NHC$\underline{H}_2$Ar), 6.8-7.7

(total 9H, m, ArH and SPh), 8.12, 8.27 (total 1H. each s, CHO). LRMS *m/z*: 286 (M^+-45).

***N*-Benzyl-*N*-[(3-phenylsulfinyl)propyl]fromamide (5g)** From **4g** (7.5 g, 26.3 mmol); column chromatography with ethyl acetate gave **5g** (6.71g, 85%) as a colorless gum. IR (film): 1670, 1045. ^{1}H-NMR: 1.7-2.0 (total 2H, m, -NHCH$_2$C<u>H$_2$</u>CH$_2$SPh), 2.4-3.0 (total 2H, m, -NHCH$_2$CH$_2$C<u>H$_2$</u>SPh), 3.1-3.5 (total 2H, m, -NHC<u>H$_2$</u>CH$_2$CH$_2$SPh), 42-4.5 (total 2H, m, -NHC<u>H$_2$</u>Ar), 7.1-7.7 (total10H, m, Ph and SPh), 8.16, 8.28 (total 1H, each s, CHO). LRMS *m/z*: 256 (M^+-45).

Pummerer Reaction of 5a. Typical Procedure.

i) Method A. TFAA (1.586 g, 7.55 mmol) was added to a solution of **5a** (500 mg, 1.51 mmol) in benzene (50 mL) at rt, and the mixture was stirred for 4 h under an argon atmosphere. After removal of the solvent *in vacuo*, the product was purified by column chromatography with ethyl acetate-hexane (1:4) to give **6a** (260 mg, 56%) and **7a** (146 mg, 31%).

ii) Method B. TFAA (582 mg, 2.8 mmol) was added to a solution of **5a** (200 mg, 0.55 mmol) in benzene (20 mL) at rt, and the mixture was stirred for 30 min under an argon atmosphere. To this solution BF_3•Et_2O (394 mg, 2.8 mmol) was added, and the mixture was stirred at rt for 45 min. After removal of the solvent *in vacuo*, the residue was treated with 5% $NaHCO_3$ and extracted with $CHCl_3$. The residual oil was purified by column chromatography with ethyl acetate to give **6a** (125 mg, 66%) and **4a** (9 mg, 5%).

2-Formyl-7,8-dimethoxy-5-phenylsulfanyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine (6a) Colorless gum. IR(film): 1668. ^{1}H-NMR: 2.0-2.3 (total 2H, m, 4-H), 3.67, 3.88 (total 6H, each s, OMe), 3.4-5.1 (total 5H, m, 1-H, 3-H, 5-H), 6.41, 6.44, 6.69, 6.89 (total 2H, each s, ArH), 7.2-7.3 (total 5H, m, SPh), 8.05, 8.15 (total 1H, each s, CHO). LRMS *m/z*: 343 (M^+). HRMS *m/z* (M^+): Calcd for $C_{19}H_{21}NO_3S$: 343.1240. Found: 343.1227.

***N*-[(3,5-Dimethoxyphenyl)methyl]-*N*-[(3-phenylsulfanyl)-2-propenyl]formamide (7a)**: Yellow gum. IR (film): 1671. ^{1}H-NMR: 3.80, 3.83, 3.84, 3.86, 3.87 (total 6H, each s, OMe), 3.7-4.2 (total 2H, m, -C<u>H$_2$</u>CH=), 4.33, 4.41, 4.46 (total 2H, each s, -CH$_2$Ar), 5.4-5.8 (total 1H, m, -CH=CH-), 6.1-6.6 (total 1H,

m, -CH=CH=), 6.6-6.9 (total 3H, m, -ArH), 7.2-7.5 (total 5H, m, SPh), 8.20, 8.26, 8.30, 8.32 (total 1H. each s, CHO). LRMS *m/z*: 343 (M^+). HRMS *m/z* (M^+): Calcd for $C_{19}H_{21}NO_3S$: 343.1239. Found: 343.1223.

Pummerer Reaction of 5b.

i) Method A. **5b** (100 mg, 0.28 mmol) gave **6b** (12 mg, 13%).

ii) Method B. **5b** (1g, 2.8 mmol) gave **6b** (578 mg, 61%).

2-Formyl-6,8-dimethoxy-5-phenylsulfanyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine (6b) Pale yellow gum. IR(film): 1671, 1604. ^{1}H-NMR: 1.8-2.2 (total 2H, m, 4-H), 3.64, 3.80 (total 6H, each s, OMe), 3.8-5.1 (total 4H, m, 1-H, 3-H), 5.4-5.5 (total 1H, m, 5-H), 6.28, 63.1 (total 1H, each s, 7-H), 6.53-6.55 (total 1H, each s, 9-H), 7.2-7.5 (total 5H, m, SPh), 8.04, 8.13 (total 1H. each s, CHO). LRMS *m/z*: 343 (M^+).

Pummerer Reaction of 5c.

Method B. **5c** (500 mg, 1.4 mmol) gave **6c** (214mg, 45%).

2-Formyl-6,9-dimethoxy-5-phenylsulfanyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine (6c) Pale yellow gum. IR(film): 1668, 1593. ^{1}H-NMR: 3.5-4.3 (total 4H, m, 3-H, 4-H), 3.62, 3.64, 3.80, 3.86 (total 6H, each s, OMe), 4.53, 4.71 (toatal 1H, each s, 1-H), 5.10, 5.27 (total 1H, each bs, 1-H), 5.4-5. (total 1H, m, 5-H), 6.7-6.8 (total 2H, m, 7-H and 8-H), 7.2-7.5 (total 5H, m, SPh), 8.07, 8.11 (total 1H. each s, CHO). LRMS *m/z*: 343 (M^+). HRMS *m/z* (M^+): Calcd for $C_{19}H_{21}NO_3S$: 343.1242. Found: 343.1288.

Pummerer Reaction of 5d.

i) Method A. **5d** (125 mg, 0.38 mmol) gave **6d** (15 mg, 13%).

ii) Method B. **5d** (3 g, 9.06 mmol) gave **6d** (2.2 g, 78%).

2-Formyl-8-methoxy-5-phenylsulfanyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine (6d) Pale yellow gum. IR(film): 1670. ^{1}H-NMR: 2.0-2.3 (total 2H, m, 4-H), 3.5-3.9 (total 1H, m, 5-H), 3.78 (3H, s, OMe), 4.3-5.1 (total 4H, m, 1-H, 3-H), 6.5-6.9 (total 3H, m, ArH), 7.2-7.4 (total 5H, m, SPh), 8.04, 8.13 (total 1H. each s, CHO). LRMS *m/z*: 313 (M^+). HRMS *m/z* (M^+): Calcd for $C_{18}H_{19}NO_2S$: 313.1133. Found: 313.1101.

Pummerer Reaction of 5e.

Method B. **5e** (500 mg, 1.51 mmol) gave **8e** (68 mg, 21%).

***N*-(4-Methoxyphenyl)methyl-*N*-[3,3-di(phenylsulfanyl)propyl]formamide (8e)** Yellow gum. IR (film): 1670, 1512. ^{1}H-NMR: 1.97 (2H, brq, *J*=7 Hz, -NHCH$_2$C<u>H$_2$</u>CH(SPh)$_2$), 3.2-3.6 (total 2H, m, -NHC<u>H$_2$</u>CH$_2$CH(SPh)$_2$), 3.79, 3.80 (total 3H, each s, OMe), 4.1-4.4 (total 3H, m, -NHC<u>H$_2$</u>Ar and –C<u>H</u>(SPh)$_2$), 6.7-7.6 (total 14H, m, ArH and SPhx2), 8.16, 8.23 (total 1H. each s, CHO). LRMS *m/z*: 423 (M^+).

Pummerer Reaction of 5f.

Method B. **5f** (500 mg, 1.51 mmol) gave **8f** (107 mg, 33%).

***N*-(2-Methoxyphenyl)methyl-*N*-[3,3-di(phenylsulfany)propyl]fromamide (8f)** IR (film): 1670. ^{1}H-NMR: 1.6-2.2 (2H, m, -NHCH$_2$C<u>H$_2$</u>CH(SPh)$_2$), 3.44 (2H, brq, *J*=7 Hz, -NHC<u>H$_2$</u>CH$_2$CH(SPh)$_2$), 3.76, 3.79 (total 3H, each s, OMe), 4.1-4.7 (total 3H, m, -NHC<u>H$_2$</u>Ar and –C<u>H</u>(SPh)$_2$), 6.8-7.6 (total 14H, m, ArH and SPhx2), 8.16, 8.24 (total 1H. each s, CHO). LRMS *m/z*: 423 (M^+).

Reductive Desulfulization of 6. Typical Procedure. To a stirred suspension of **6a** (1.81 g, 5.3 mmol) and NiCl$_2$•6H$_2$O (4.40g, 18.5 mmol) in MeOH-THF (3:1, 80 mL) was added NaBH$_4$ (2.11 g, 55.5mmol) by portions at 0°C. After the addition completed, stirring was continued for 20 min. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The products were purified by column chromatography with ethyl acetate-hexane (1:1) and recrystallized from ethyl acetate-Et$_2$O to give **9a** (998 mg, 80%) as colorless prisms, mp 130-132 °C.

2-Formyl-7,8-dimethoxy-2,3,4,5-tetrahydro-1*H*-2-benzazepine (9a). IR: 1666, 1604. ^{1}H-NMR: 1.7-1.9 (total 2H, m, 4-H), 2.8-3.0 (total 2H, m, 5-H), 3.5-3.8 (total 2H, m, 3-H), 3.83, 3.84 (total 6H, each s, OMe), 4.36, 4.46 (total 2H, each s, 1-H), 6.66, 6.89 (total 2H, each s, ArH), 7.98, 8.12 (total 1H, each s, CHO), LRMS *m/z*: 235 (M^+). HRMS *m/z* (M^+): Calcd for $C_{13}H_{17}NO_3$: 235.1209. Found: 235.1208.

2-Formyl-6,8-dimethoxy-2,3,4,5-tetrahydro-1*H*-2-benzazepine (9b). From **6b** (578 mg, 1.7 mmol); column chromatography with ethyl acetate-hexane (1:1) gave **9b** (297 mg, 75%) as colorless prisms

recrystallized from ethyl acetate-Et_2O, mp 83-85 °C. IR: 1664. ^{1}H-NMR: 1.6-1.9 (total 2H, m, 4-H), 2.9-3.2 (total 2H, m, 5-H), 3.5-3.7 (total 2H, m, 3-H), 3.77, 3.78, 3.80 (total 6H, each s, OMe), 4.38, 4.50 (total 2H, each s, 1-H), 6.3-6.6 (total 2H, m, ArH), 8.00, 8.13 (total 1H, each s, CHO), LRMS *m/z*: 235 (M^+).

2-Formyl-6,9-dimethoxy-2,3,4,5-tetrahydro-1*H*-2-benzazepine (9c). From **6c** (963 mg, 2.8 mmol); column chromatography with ethyl acetate-hexane (1:1) gave **9c** (338 mg, 53%) as pale yellow prisms recrystallized from ethyl acetate-Et_2O, mp 83-88 °C. IR: 1670, 1596. ^{1}H-NMR: 1.7-1.9 (total 2H, m, 4-H), 2.9-3.1 (total 2H, m, 5-H), 3.4-3.63 (total 2H, m, 3-H), 3.76, 3.80, 3.84 (total 6H, each s, OMe), 4.59, 4.73 (total 2H, each s, 1-H), 6.7 (total 2H, m, ArH), 8.02, 8.12 (total 1H, each s, CHO), LRMS *m/z*: 235 (M^+). HRMS *m/z* (M^+): Calcd for $C_{13}H_{17}NO_3$: 235.1206. Found: 235.1298.

2-Formyl-8-methoxy-2,3,4,5-tetrahydro-1*H*-2-benzazepine (9d). From **6d** (2 g, 6.39 mmol); column chromatography with ethyl acetate-hexane (1:1) gave **9d** (935 mg, 71%) as a pale yellow gum. IR (film): 1670. ^{1}H-NMR: 1.6-2.0 (2H, m, 4-H), 2.92 (2H, t, *J*=6 Hz, 5-H), 3.5-4.0 (total 2H, m, 3-H), 3.78 (3H, s, OMe), 4.59, 4.73 (total 2H, each s, 1-H), 6.7 (3H, m, ArH), 8.02, 8.12 (total 1H, each s, CHO), LRMS *m/z*: 205 (M^+). HRMS *m/z* (M^+): Calcd for $C_{12}H_{15}NO_2$: 205.1103. Found: 205.1121.

Hydrolysis of 9a. Typical Procedure. A solution of **9a** (300 mg, 1.3 mmol) in EtOH (5 mL) and 10% NaOH (5 mL) was refluxed for 1 h. The reaction mixture was concentrated *in vacuo* and the residue was extracted with $CHCl_3$. The product was purified by column chromatography with ethyl acetate to give **10a** (259 mg, 98%) as a pale yellow gum.[11]

7,8-Dimethoxy-2,3,4,5-tetrahydro-1*H*-2-benzazepine (10a).[9,10] IR (film): 1606. ^{1}H-NMR: 1.6-1.9 (2H, m, 4-H), 2.8-3.0 (2H, m, 5-H), 3.1-3.3 (2H, m, 3-H), 3.85 (3H, s, OMe), 3.86 (3H, s, OMe), 3.88 (2H, s, 1-H), 6.68 (1H, s, ArH), 6.70 (1H, s, ArH). ^{13}C-NMR: 30.3 (t), 34.9 (t), 52.8 (t), 53.9 (t), 55.1 (qx2), 111.9 (d), 112.7 (d), 134.3 (s), 134.5 (s), 145.7 (s), 146.4 (s). LRMS *m/z*: 207 (M). HRMS *m/z* (M^+): Calcd for $C_{12}H_{17}NO_2$: 207.1260. Found: 207.1290.

6,8-Dimethoxy-2,3,4,5-tetrahydro-1*H*-2-benzazepine (10b). From **9b** (297 mg, 1.3 mmol); column

chromatography with ethyl acetate gave **10b** (169 mg, 65%) as colorless prisms recrystallized from ethyl acetate-hexane, mp 68-70 °C. IR: 1587. ^{1}H-NMR: 1.5-1.8 (2H, m, 4-H), 2.8-3.0 (2H, m, 5-H), 3.1-3.2 (2H, m, 3-H), 3.78 (6H, s, OMe), 3.88 (2H, s, 1-H), 6.31 (1H, d, *J*=2 Hz, ArH), 6.36(1H, d, *J*=2 Hz, ArH). ^{13}C-NMR: 24.5 (t), 30.4 (t), 53.6 (t), 55.2 (t), 55.3 (q), 55.8 (q), 97.2 (d), 105.3 (d), 123.3 (s), 145.1 (s), 157.6 (s), 158.1 (s). LRMS *m/z*: 207 (M^+). HRMS *m/z* (M^+): Calcd for $C_{12}H_{17}NO_2$: 207.1256. Found: 207.1238.

6,9-Dimethoxy-2,3,4,5-tetrahydro-1*H*-2-benzazepine (10c). From **9c** (100 mg, 0.43 mmol); column chromatography with ethyl acetate gave **10c** (82 mg, 85%) as colorless prisms recrystallized from ethyl acetate-hexane, mp 58-60 °C. IR: 1594. ^{1}H-NMR: 1.6-1.7 (2H, m, 4-H), 3.0 (2H, m, 5-H), 3.2 (2H, m, 3-H), 3.75 (6H, s, OMe), 4.07 (2H, s, 1-H), 6.66 (1H, d, *J*=9 Hz, ArH), 6.70 (1H, d, *J*=9 Hz, ArH). ^{13}C-NMR: 25.3 (t), 29.3 (t), 44.6 (t), 53.4 (t), 56.3 (q), 56.6 (q), 109.2 (d), 110.6 (d), 132.2 (s), 133.5 (s), 150.7 (s), 150.9 (s). LRMS *m/z*: 207 (M^+). HRMS *m/z* (M^+): Calcd for $C_{12}H_{17}NO_2$: 207.1258. Found: 207.1253

8-Methoxy-2,3,4,5-tetrahydro-1*H*-2-benzazepine (10d). From **9d** (300 mg, 1.46 mmol); column chromatography with ethyl acetate gave **10d** (240 mg, 93%) as colorless needles recrystallized from ethyl acetate-hexane, mp 39-41 °C. IR: 1610. ^{1}H-NMR: 1.68 (2H, m, 4-H), 2.89 (2H, t, *J*=5 Hz, 5-H), 3.19 (2H, t, *J*=5 Hz, 3-H), 3.77 (3H, s, OMe), 3.88 (2H, s, 1-H), 6.5-7.2 (3H, m, ArH). ^{13}C-NMR: 31.1 (t), 35.1 (t), 53.4 (t), 55.1 (t), 55.1 (q), 111.2 (d), 114.4 (d), 130.0 (d), 134.8 (s), 143.8 (s), 157.7 (s). LRMS *m/z*: 178 (M^+).

Reduction of 9a with $LiAlH_4$. Typical Procedure. $LiAlH_4$ (97 mg, 2.6 mmol) was added to the solution of **9a** (300 mg, 1.3 mmol) in dry THF (15 mL) 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 filtrate was concentrated *in vacuo* and the residue was extracted with $CHCl_3$. The product was purified by column chromatography with ethyl acetate to give **11a** (258 mg, 91%) as a pale yellow gum.

7,8-Dimethoxy-2-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine (11a). IR(film): 1606. ^{1}H-NMR:

1.6-1.9 (2H, m, 4-H), 2.32 (3H, s, NMe), 2.7-3.0 (4H, m, 5-H and 3-H), 3.49 (2H, s, 1-H), 3.83 (6H, s, OMe), 6.67 (1H, s, ArH), 6.68 (1H, s, ArH). ^{13}C-NMR: 25.7 (t), 34.7 (t), 43.2 (q), 55.3 (q), 55.4 (q), 60.8 (t), 61.4 (t), 112.4 (d), 113.4 (d), 130.7 (s), 134.6 (s), 146.0 (s), 146.9 (s). LRMS *m/z*: 221 (M^+). HRMS *m/z* (M^+): Calcd for $C_{13}H_{19}NO_2$: 221.1414. Found: 221.1399.

6,8-Dimethoxy-2-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine (11b). From **9b** (256 mg, 1.3 mmol); column chromatography with ethyl acetate gave **11b** (240 mg, 99%) as a colorless gum. IR(film): 1606. ^{1}H-NMR: 1.6-1.8 (2H, m, 4-H), 2.31 (3H, s, NMe), 2.8-3.0 (4H, m, 3-H and 5-H), 3.75 (2H, s, 1-H), 3.777 (3H, s, OMe), 3.782 (3H, s, OMe), 6.33 (1H, d, *J*=2 Hz, ArH), 6.36 (1H, d, *J*=2 Hz, ArH). ^{13}C-NMR: 24.3 (t), 25.5 (t), 43.5 (q), 55.3 (q), 55.8 (q), 61.4 (t), 62.3 (t), 97.4 (d), 106.7 (d), 123.4 (s), 141.6 (s), 157.2 (s), 158.1 (s). LRMS *m/z*: 221 (M^+). HRMS *m/z* (M^+): Calcd for $C_{13}H_{19}NO_2$: 221.1416. Found: 221.1454.

6,8-Dimethoxy-2-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine (11c). From **9c** (500 mg, 2.1 mmol); column chromatography with ethyl acetate gave **11c** (435 mg, 93%) as a colorless gum. IR(film): 1594. ^{1}H-NMR: 1.6-1.7 (2H, m, 4-H), 2.27 (3H, s, NMe), 2.8-2.9 (4H, m, 3-H and 5-H), 3.657 (3H, s, OMe), 3.664 (3H, s, OMe), 3.79 (2H, s, 1-H), 6.54 (1H, d, *J*=9 Hz, ArH), 6.66 (1H, d, *J*=9 Hz, ArH). ^{13}C-NMR: 24.8 (t), 25.9 (t), 44.9 (q), 52.0 (t), 56.1 (q), 56.5 (q), 61.9 (t), 108.8 (d), 110.5 (d), 129.2 (s), 133.5 (s), 150.5 (s), 151.4 (s). LRMS *m/z*: 221 (M^+).

8-Methoxy-2-methyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine (11d). From **9d** (100 mg, 0.49 mmol); column chromatography with ethyl acetate gave **11d** (87 mg, 94%) as a colorless gum. IR (film): 1608. ^{1}H-NMR: 1.5-1.8 (2H, m, 4-H), 2.21 (3H, s, NMe), 2.72 (2H, t, *J*=6 Hz, 5-H),.2.90 (2H, t, *J*=6 Hz, 3-H), 3.65 (2H, s, 1-H), 3.67 (3H, s, OMe), 6.4-7.0 (3H, m, ArH). ^{13}C-NMR: 25.8 (t), 34.7 (t), 43.0 (q), 55.1 (q), 61.1 (t), 62.1 (t), 111.5 (d), 115.8 (d), 129.5 (d), 134.8 (s), 140.1 (s), 157.7 (s). LRMS *m/z*: 191 (M^+).

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