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A Synthesis of Dibenz[*b*,*f*]azecines from 1-Halogenobenzyl-1*H*-2-benzazepines[1]

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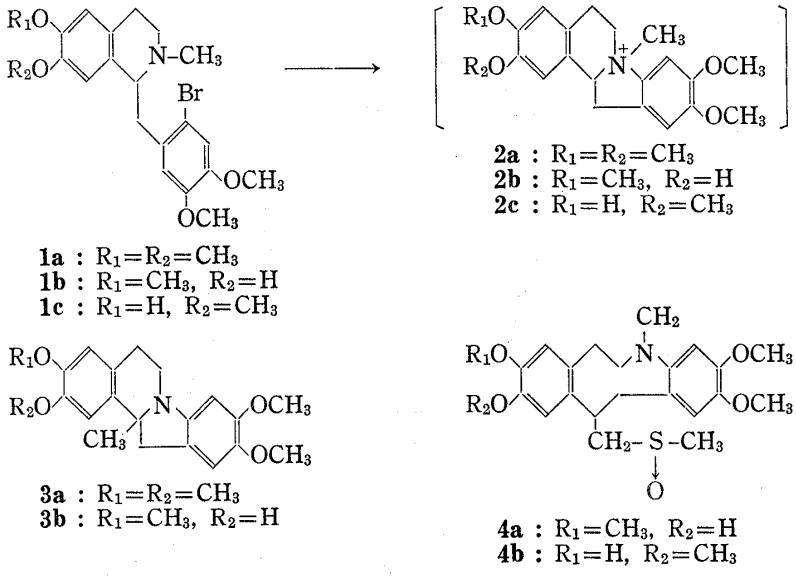
The reaction of 1-(2-bromo-4,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-7,8-dimethoxy-2-methyl-1*H*-2-benzazepine (**17**) with dimsylsodium afforded 13,14-*cis*-5,6,7,8-tetrahydro-2,3,10,11-tetramethoxy-5-methyldibenz[*b*,*f*]azecine (**28**) and 5,6,7,8,13,14-hexahydro-2,3,-10,11-tetramethoxy-5-methyl-13-(methylsulfinyl)methyldibenz[*b*,*f*]azecine (**29**). Similar reaction using 1-(2-bromo-4,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-7-hydroxy-8-methoxy-2-methyl-1*H*-2-benzazepine (**18**) gave the 13,14-*trans*-isomer (**39**) accompanying with the formation of 13-(methylsulfinyl)methyl derivative (**40**). The reaction of the 2,3,4,5-tetrahydro-8-hydroxy-1*H*-2-benzazepine (**19**) with dimsylsodium was also examined to give the 5,6,7,8-tetrahydrodibenz[*b*,*f*]azecines (**42**) and (**43**), and the 5,6,7,8,13,14-hexahydro-13-(methylsulfinyl)methyl derivative (**44**).

Keywords——benzyne reaction; 2-benzazepine; ring expansion; dibenz[*b*,*f*]azecine; *cis*-elimination

Previously we investigated the benzyne reaction of a series of 1-halogenobenzylisoquinolines using dimsylsodium.[3] The reaction of the isoquinoline (**1a**) with dimsylsodium gave the 12a-methylindolo[2,1-*a*]isoquinoline (**3a**)[4] through migration of a methyl group at the 7-position in the intermediate (**2a**) to the 12a-position. On the other hand, the 7-hydroxyisoquinoline (**1b**) afforded the 12-(methylsulfinyl)methyldibenz[*b*,*f*]azonine (**4a**) accompanying with formation of 12a-methylindolo[2,1-*a*]isoquinoline (**3b**) under similar conditions.[5] The



1a : $R_1=R_2=CH_3$
1b : $R_1=CH_3$, $R_2=H$
1c : $R_1=H$, $R_2=CH_3$

2a : $R_1=R_2=CH_3$
2b : $R_1=CH_3$, $R_2=H$
2c : $R_1=H$, $R_2=CH_3$

3a : $R_1=R_2=CH_3$
3b : $R_1=CH_3$, $R_2=H$

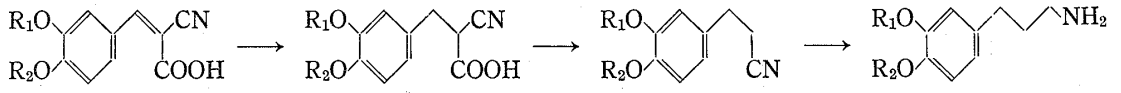
4a : $R_1=CH_3$, $R_2=H$
4b : $R_1=H$, $R_2=CH_3$

Chart 1

1) Communication of this paper appeared in *Heterocycles*, **4**, 933 (1976).
2) Location: *1432-1 Horinouchi, Hachioji, Tokyo.*
3) E.J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1345 (1965).
4) S. Kano, T. Yokomatsu, N. Yamada, K. Matsumoto, S. Tokita, and S. Shibuya, *Chem. Pharm. Bull.* (Tokyo), **22**, 1607 (1974).
5) S. Kano, E. Komiyama, K. Nawa, and S. Shibuya, *Chem. Pharm. Bull.* (Tokyo), **24**, 310 (1976).

similar results were also observed in the case of the reaction between the isoquinoline (**1c**) and dimsylsodium to yield **4b**.[6] In connection with these results, we successively investigated the reaction between a series of 1-halogenobenzyl-1*H*-2-benzazepines and dimsylsodium and found a formation of 5,6,7,8-tetrahydrodibenz[*b*,*f*]azecines possessing a *cis* and *trans* double bond at the 13,14-positions through the indolo[2,1-*a*][2]benzazepinium salts as intermediate.[1] We wish to report these results in this paper.

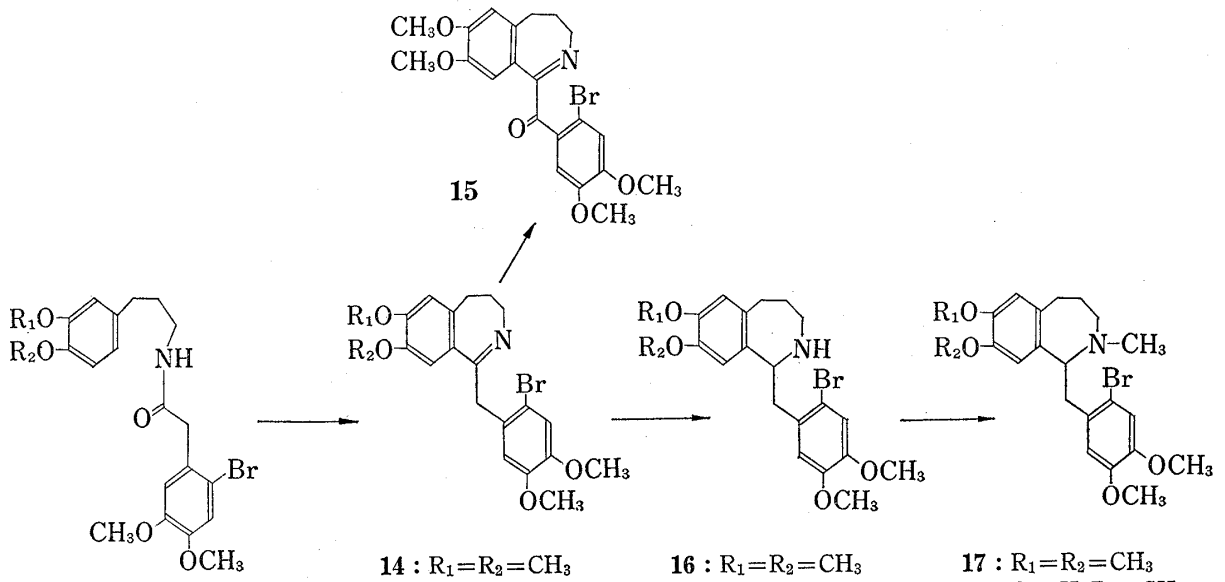
Firstly, we synthesized a series of 1-halogenobenzyl-2,3,4,5-tetrahydro-2-methyl-1*H*-2-benzazepines. Reduction of α-cyanocinnamic acid (**5**), prepared by condensation of 3-benzyloxy-4-methoxybenzaldehyde with cyanoacetic acid, afforded the α-cyanophenylpropionic acid (**6**), whose decarboxylation, followed by reduction of phenylpropionitrile (**7**) gave the amine (**8**). 4-Benzyloxy-3-methoxyphenylpropylamine (**9**) was also prepared by the same method as in formation of **8** (**10**→**11**→**12**→**9**).



5: $R_1=C_7H_7$, $R_2=CH_3$ **6**: $R_1=C_7H_7$, $R_2=CH_3$ **7**: $R_1=C_7H_7$, $R_2=CH_3$ **8**: $R_1=C_7H_7$, $R_2=CH_3$
10: $R_1=CH_3$, $R_2=C_7H_7$ **11**: $R_1=CH_3$, $R_2=C_7H_7$ **12**: $R_1=CH_3$, $R_2=C_7H_7$ **9**: $R_1=CH_3$, $R_2=C_7H_7$

Chart 2

The Bischler-Napieralski type cyclization of the amide (**13**), prepared from 3,4-dimethoxyphenylpropylamine[7] and 2-bromo-4,5-dimethoxyphenylacetic acid, with phosphoryl chloride in acetonitrile afforded the 4,5-dihydro-3*H*-2-benzazepine (**14**), which was easily oxidized to 1-(2-bromo-4,5-dimethoxybenzoyl)-4,5-dihydro-7,8-dimethoxy-3*H*-2-benzazepine (**15**) during purification, as in the case of some 1-benzyl-3,4-dihydroisoquinolines.[8] Reduction of **14**



13 : $R_1=R_2=CH_3$
22 : $R_1=C_7H_7$, $R_2=CH_3$
25 : $R_1=CH_3$, $R_2=C_7H_7$

14 : $R_1=R_2=CH_3$
23 : $R_1=C_7H_7$, $R_2=CH_3$
26 : $R_1=CH_3$, $R_2=C_7H_7$

16 : $R_1=R_2=CH_3$
24 : $R_1=C_7H_7$, $R_2=CH_3$
27 : $R_1=CH_3$, $R_2=C_7H_7$

17 : $R_1=R_2=CH_3$
18 : $R_1=H$, $R_2=CH_3$
19 : $R_1=CH_3$, $R_2=H$
20 : $R_1=C_7H_7$, $R_2=CH_3$
21 : $R_1=CH_3$, $R_2=C_7H_7$

Chart 3

6) S. Kano, E. Komiyama, T. Ogawa, Y. Takahagi, T. Yokomatsu, and S. Shibuya, *Chem. Pharm. Bull.* (Tokyo), **23**, 2058 (1975).
7) I. Jirkovsky and M. Protiva, *Collect, Czech. Chem. Commun.*, **32**, 1197 (1967).
8) T. Kametani and K. Fukumoto, *Yakugaku Zasshi*, **83**, 1031 (1963).

with sodium borohydride, followed by reductive methylation of the 2,3,4,5-tetrahydro-1*H*-2-benzazepine (**16**) with 37% formalin and sodium borohydride gave 1-(2-bromo-4,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-7,8-dimethoxy-2-methyl-1*H*-2-benzazepine (**17**). Similarly, 1-(2-bromo-4,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-7-hydroxy-8-methoxy-2-methyl-1*H*-2-benzazepine (**18**) and 1-(2-bromo-4,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-8-hydroxy-7-methoxy-2-methyl-1*H*-2-benzazepine (**19**) were obtained by debenzylation of the O-benzyl derivatives (**20**) and (**21**), prepared from the corresponding amide (**22**) and (**25**), respectively, through the same manner as in formation of **17** (**22**→**23**→**24**→**20**; **25**→**26**→**27**→**21**) as shown in Chart 3 and described in the experimental section.

Treatment of the 1*H*-2-benzazepine (**17**), thus obtained, with dimsylsodium in tetrahydrofuran[9] gave two products (**28**) and (**29**), which were separated by column chromatography on silica gel. The structure of the first product was determined as the 5,6,7,8-tetrahydro-2,3,10,11-tetramethoxy-5-methyldibenz[*b*,*f*]azecine (**28**) as follows. Its microanalysis and mass spectrum revealed the molecular formula as $C_{22}H_{27}NO_4$, and its nuclear magnetic resonance (NMR) spectrum showed a singlet due to NCH_3 at 2.19 ppm. Two olefinic protons

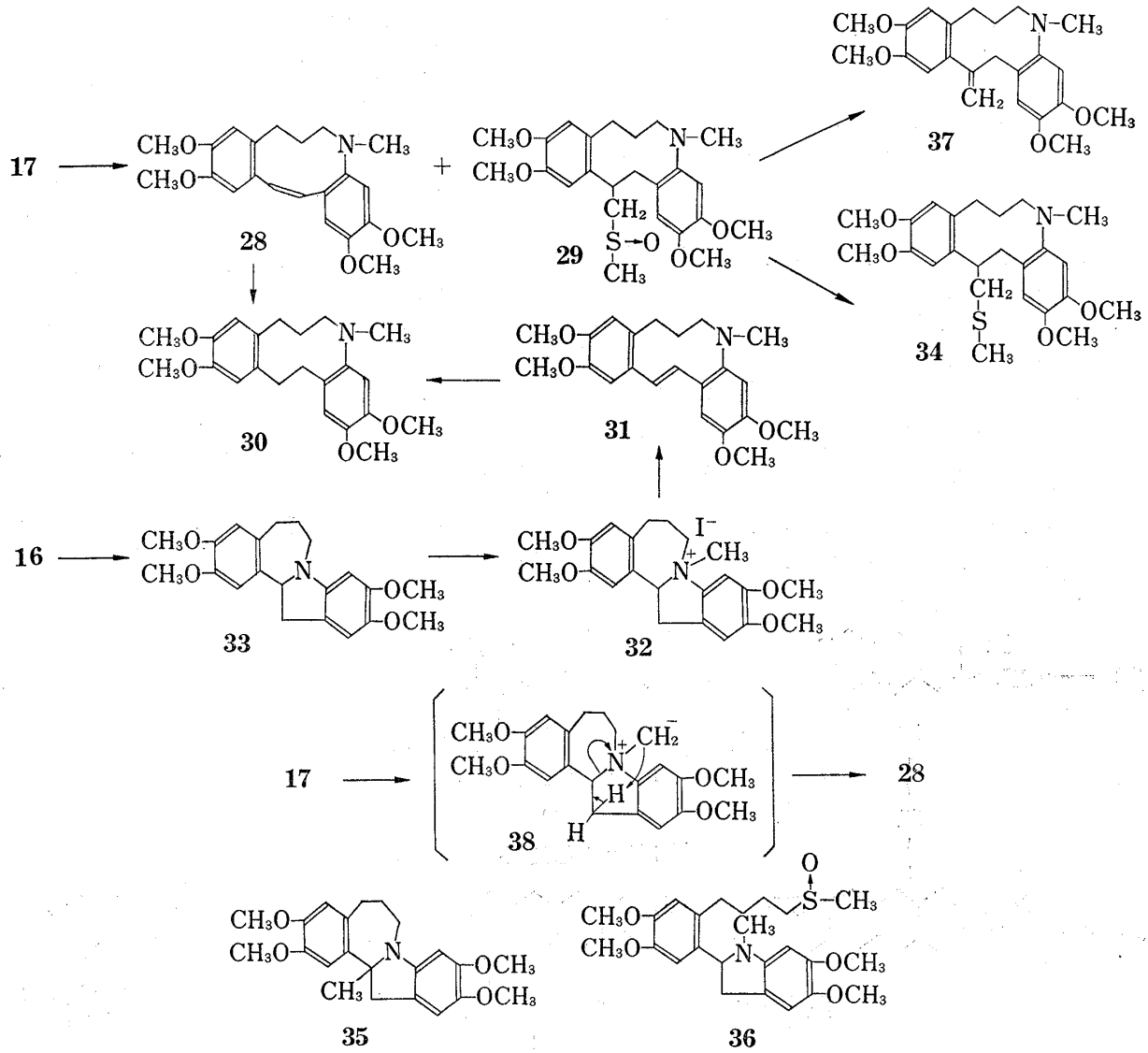


Chart 4

9) In the preminary communication,[1] this reaction was carried out in dimethylsulfoxide (DMSO). This way was improved by using THF.

resonated at 6.58 ppm as a singlet and four aromatic proton signals were observed at 6.22, 6.31, 6.63 and 6.68 ppm as singlets, respectively. Catalytic hydrogenation of **28** over Adams catalyst afforded the 5,6,7,8,13,14-hexahydrodibenz[*b*,*f*]azecine (**30**), which was identical with the authentic specimen obtained by hydrogenation of the 13,14-*trans*-5,6,7,8-tetrahydrodibenz[*b*,*f*]azecine (**31**). The *trans*-isomer (**31**) was prepared by the Hofmann degradation of the indolo[2,1-*a*][2]benzazepinium salt (**32**), obtained through cyclization of the 2,3,4,5-tetrahydro-1*H*-2-benzazepine (**16**), followed by methylation of **33** with methyl iodide. The NMR spectrum of **31** was significantly different from that of the *cis*-isomer (**28**) and two olefinic protons resonated at 6.28 and 7.64 ppm as doublet (J=17 Hz) and NCH_3 signal was observed at 2.77 ppm as a singlet. These facts indicated that **28** was a geometric isomer of **31**. Thus, the geometry of the double bond located at the 13,14-positions in **28** was confirmed as *cis*.

Deoxygenation of the second product (**29**) with zinc amalgam afforded the 13-(methylthio)methyldibenz[*b*,*f*]azecine (**34**). The signals due to SCH_3 and NCH_3 were observed at 1.98 and 2.47 ppm in its NMR spectrum. These two products (**28**) and (**29**) were also obtained by the reaction of **32** with dimsylsodium. Formation of the other expected products, 13a-methylindolo[2,1-*a*][2]benzazepine (**35**) and 1-methyl-2-phenylindoline derivative (**36**) was not observed in this reaction. The sulfoxide (**29**) was heated in xylene to yield the dibenz[*b*,*f*]azecine (**37**) possessing an exo double bond at at the 13-position.

It is of interest that the 5,6,7,8-tetrahydrodibenz[*b*,*f*]azecine possessing a *cis* double bond at the 13,14-positions was formed from the non-phenolic 1-halogenobenzyl-2,3,4,5-tetrahydro-1*H*-2-benzazepine. The *cis* double bond at the 13,14-positions would be introduced by a spontaneous *cis*-elimination of the corresponding intermediate (**38**). On the other hand, the similar reaction between the 7-hydroxy-1*H*-2-benzazepine (**18**) with dimsysylsodium afforded the 13,14-*trans*-5,6,7,8-tetrahydrodibenz[*b*,*f*]azecine (**39**) and 13-(methylsulfinyl)methyl-5,6,7,8,13,14-hexahydro derivative (**40**). The NMR spectrum of **39** showed a pair of doublet (J=17 Hz) at 6.24 and 7.63 ppm attributable to the *trans* –CH=CH– at the 13,14-positions and four aromatic proton signals appeared at 6.60, 6.70, 6.75 and 6.84 ppm as singlets, respectively. O-Methylation of **39** with diazomethane yielded **31**. Thus the geometry of the double bond at the 13,14-positions in **39** was determined as *trans*. Deoxygenation of **40** by the same manner as in formation of **34** gave the 13-(methylthio)methyl derivative (**41**), the NMR spectrum of which exhibited two singlets due to SCH_3 and NCH_3 at 2.02 and 2.50 ppm, respectively. O-Methylation of **41** afforded the tetramethoxy derivative (**34**), which was identical with the authentic specimen obtained from **29**.

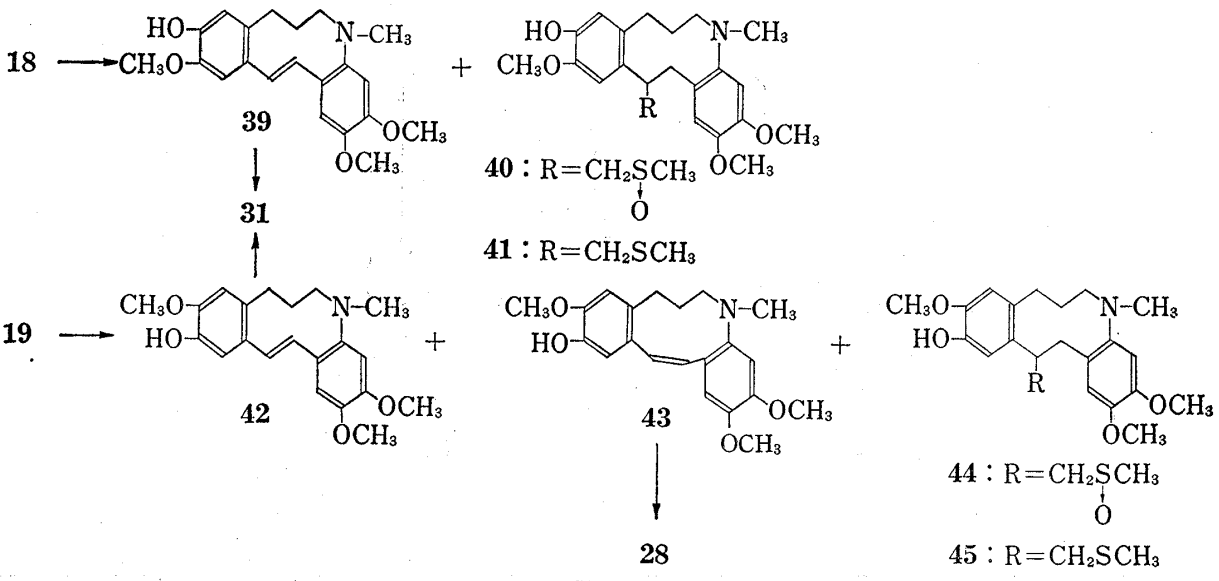


Chart 5

Finally, the 8-hydroxy-1*H*-2-benzazepine (**19**) was also treated with dimsylsodium to give two geometric isomer of 5,6,7,8-tetrahydrodibenz[*b*,*f*]azecines (**42**) and (**43**) accompanying with formation of the 5,6,7,8,13,14-hexahydro-13-(methylsulfinyl)methyldibenz[*b*,*f*]azecine (**44**). These were separated by column chromatography on silica gel. Elution with benzene–chloroform (2:3) gave the 13,14-*trans*-5,6,7,8-tetrahydrodibenz[*b*,*f*]azecine (**42**). Its NMR spectrum was very similar to that of **31** and showed a pair of doublet (J=17 Hz) at 6.21 and 7.61 ppm, which were characteristic of *trans* –CH=CH– at the 13,14-positions. Further elucidation with the same solvent gave the *cis*-isomer (**43**), whose olefinic protons resonated at 6.52 ppm in its NMR spectrum. O-Methylation of both products (**42**) and (**43**) with diazomethane yielded the corresponding 2,3,10,11-tetramethoxy derivatives (**31**) and (**28**), respectively. Deoxygenation of **44**, obtained from 2% methanol-chloroform fraction, afforded the 13-(methylthio)methyl derivative (**45**). The signals due to SCH_3 and NCH_3 were observed at 2.03 and 2.50 ppm, respectively.

Apparently, these dibenz[*b*,*f*]azecines were derived from the corresponding 8-methylindolo[2,1-*a*][2]benzazepinium salts (**46a,b,c**) as an intermediate and the 13,14-*trans*-5,6,7,8-tetrahydrodibenz[*b*,*f*]azecines (**39**) and (**42**) would be formed through the intermediates (**47**) and (**48**), respectively.

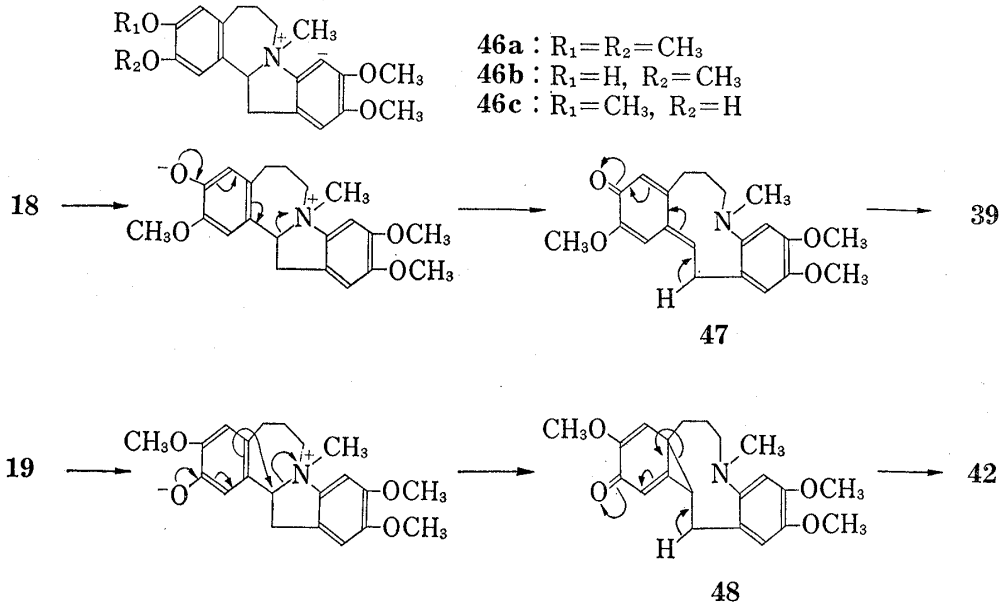


Chart 6

Experimental[10]

α-Cyano-3-benzyloxy-4-methoxycinnamic Acid (**5**)——A mixture of 54 g of 3-benzyloxy-4-methoxybenzaldehyde, 21 g of cyanoacetic acid, 1 g of $AcONH_4$, 240 ml of benzene and 45 ml of pyridine was refluxed using Dean-Stark apparatus for 24 hr. After removal of the solvent, the remaining residue was made acidic with conc. HCl and the precipitate was collected to give 63 g of **5** as yellowish needles, mp 186—188° (MeOH–benzene). *Anal.* Calcd. for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53. Found: C, 69.89; H, 4.79; N, 4.28.

α-Cyano-4-benzyloxy-3-methoxycinnamic Acid (**10**)——A mixture of 54 g of 4-benzyloxy-3-methoxybenzaldehyde, 21 g of cyanoacetic acid, 1 g of $AcONH_4$, 240 ml of benzene and 45 ml of pyridine was refluxed and worked up as above to give 60 g of **10** as yellowish needles, mp 203—204° (MeOH–$(C_2H_5)_2O$). *Anal.* Calcd. for $C_{18}H_{15}NO_4$: C, 69.89; H, 4.89; N, 4.53. Found: C, 69.60; H, 4.89; N, 4.36.

3-(3-Benzyloxy-4-methoxyphenyl)propionitrile (**7**)——To a solution of 20 g of **5** in a mixture of 180 ml of 5% $NaHCO_3$ and 220 ml of MeOH was added 10 g of $NaBH_4$ under stirring at room temperature. After

10) All melting points were uncorrected. NMR spectra were taken with a Varian T-60 spectrometer in $CDCl_3$ using tetramethylsilane (TMS) as an internal standard.

the stirring had been continued for 5 hr, the solvent was evaporated. The remaining residue was made acidic with conc. HCl and extracted with $(C_2H_5)_2O$. The extract was washed with H_2O, dried (Na_2SO_4) and evaporated to give 15 g of the nitrile (**6**), mp 123—125°, which was heated in 40 ml of dimethylformamide (DMF) at 180° for 2 hr. After removal of DMF *in vacuo*, the remaining residue was extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4 and evaporated to leave 12 g of **7** as colorless needles, mp 79—80° (MeOH–$(C_2H_5)_2O$). *Anal.* Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.42; H, 6.45; N, 5.46.

3-(4-Benzyloxy-3-methoxyphenyl)propionitrile (12)——To a solution of 20 g of **10** in a mixture of 180 ml of 5% $NaHCO_3$ and 220 ml of MeOH was added 10 g of $NaBH_4$ under stirring at room temperature. After the stirring had been continued for 5 hr, the mixture was refluxed for 0.5 hr and the solvent was evaporated. The resulting residue was made acidic with conc. HCl and extracted with $(C_2H_5)_2O$. The extract was washed with H_2O, dried (Na_2SO_4) and evaporated to leave 15 g of the nitrile (**11**), mp 124—125°, which was heated in 40 ml of DMF at 180° for 2 hr. The mixture was worked up as above to give 11 g of **12** as colorless needles, mp 75—76° (MeOH–$(C_2H_5)_2O$). *Anal.* Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.38; H, 6.27; N, 4.93.

3-(3-Benzyloxy-4-methoxyphenyl)propylamine (8)——A mixture of 20 g of **7**, 200 ml of MeOH and 4 ml of Ni catalyst was shaken in the presence of H_2 until uptake of H_2 ceased. After removal of catalyst, the solvent was evaporated to give 17 g of **8** as a colorless oil, hydrochloride, mp 168—170° (MeOH–$(C_2H_5)_2O$). *Anal.* Calcd. for $C_{17}H_{22}ClNO_2$: C, 66.33; H, 7.20; N, 4.55. Found: C, 66.24; H, 7.35; N, 4.17.

3-(4-Benzyloxy-3-methoxyphenyl)propylamine (9)——A mixture of 20 g of **12**, 200 ml of MeOH and 3 ml of Ni catalyst was shaken in the presence of H_2 until uptake of H_2 ceased. The mixture was worked up as above to give 17 g of **9** as a colorless oil, hydrochloride, mp 159—160° (MeOH–$(C_2H_5)_2O$). *Anal.* Calcd. for $C_{17}H_{22}ClNO_2$: C, 66.33; H, 7.20; N, 4.55. Found: C, 66.20; H, 7.29; N, 4.37.

N-(3,4-Dimethoxyphenylpropyl)-2-bromo-4,5-dimethoxyphenylacetamide (13)——A mixture of 7 g of 3,4-dimethoxyphenylpropylamine[7] and 8 g of 2-bromo-4,5-dimethoxyphenylacetic acid was heated at 180° for 1.5 hr. After cooling, the mixture was recrystallized from benzene–$(C_2H_5)_2O$ to give 9 g of **13**, mp 128—130°. *Anal.* Calcd. for $C_{21}H_{26}BrNO_5$: C, 55.76; H, 5.79; N, 3.10. Found: C, 55.96; H, 5.51; N, 2.59.

1-(2-Bromo-4,5-dimethoxybenzoyl)-4,5-dihydro-7,8-dimethoxy-3*H*-2-benzazepine (15)——A mixture of 6 g of **13**, 150 ml of CH_3CN and 6 g of $POCl_3$ was refluxed for 4 hr. After removal of the solvent, the resulting residue was made basic with 28% NH_4OH and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4 and evaporated. The remaining residue was chromatographed on 20 g of silica gel using $CHCl_3$ as an eluant. Removal of the solvent (150 ml) yielded 3 g of **15** as colorless needles, mp 169—170° (MeOH), MS *m/e*: 447 (M^+), 449 (M^++2), NMR ($CDCl_3$) δ: 3.85 (3H, singlet, OCH_3), 3.87 (3H, singlet, OCH_3), 3.91 (6H, singlet, 2×OCH_3), 6.73, 6.98, 7.02, 7.03 (4H, each singlet, 4×Ar–H). *Anal.* Calcd. for $C_{21}H_{22}BrNO_5$: C, 56.26; H, 4.95; N, 3.13. Found: C, 56.20; H, 4.93; N, 2.80.

1-(2-Bromo-4,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-7,8-dimethoxy-1*H*-2-benzazepine (16)——A mixture of 6 g of the amide (**13**), 150 ml of CH_3CN and 6 g of $POCl_3$ was refluxed for 4 hr. The solvent was evaporated and the remaining residue was washed with excess hexane. To a stirred solution of the residue in 150 ml of MeOH was added 4 g of $NaBH_4$ under ice-cooling. After the stirring had been continued for 0.5 hr, the solvent was evaporated. The mixture was worked up as usual to give 4 g of **16** as an oil, picrate, mp 180—182° (MeOH). *Anal.* Calcd. for $C_{27}H_{29}BrN_4O_{11}$: C, 48.73; H, 4.39; N, 8.42. Found: C, 48.71; H, 4.47; N, 8.41.

1-(2-Bromo-4,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-7,8-dimethoxy-2-methyl-1*H*-2-benzazepine (17)——A solution of 4 g of **16** in 200 ml of MeOH containing 12 ml of 37% HCHO was stirred for 0.5 hr at room temperature and then 10 g of $NaBH_4$ was added to this solution under ice-cooling. After the mixture was refluxed for 0.5 hr, the solvent was evaporated. The resulting residue was suspended in 150 ml of H_2O and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4 and evaporated to leave 3 g of **17** as an oil, which was used for the following reaction because of difficulty of crystallization. NMR ($CDCl_3$) δ: 2.35 (3H, singlet, NCH_3), 3.64 (6H, singlet, 2×OCH_3), 3.84 (6H, singlet, 2×OCH_3), 6.23, 6.37, 6.63, 6.93 (4H, each singlet, 4×Ar–H).

N-(3-Benzyloxy-4-methoxyphenylpropyl)-2-bromo-4,5-dimethoxyphenylacetamide (22)——A mixture of 7 g of **8** and 7 g of 2-bromo-4,5-dimethoxyphenylacetic acid was heated at 180° for 1.5 hr. After cooling, the mixture was recrystallized from MeOH–$(C_2H_5)_2O$ to give 10 g of **22** as colorless needles, mp 124—126°. *Anal.* Calcd. for $C_{27}H_{30}BrNO_5$: C, 61.36; H, 5.72; N, 2.65. Found: C, 61.53; H, 5.75; N, 2.33.

N-(4-Benzyloxy-3-methoxyphenylpropyl)-2-bromo-4,5-dimethoxyphenylacetamide (25)——A mixture of 7 g of **9** and 7 g of 2-bromo-4,5-dimethoxyphenylacetic acid was heated at 180° for 1.5 hr and the mixture was worked up as above to give 10.5 g of **25** as colorless needles, mp 124—125° (MeOH–$(C_2H_5)_2O$). *Anal.* Calcd. for $C_{27}H_{30}BrNO_5$: C, 61.36; H, 5.72; N, 2.65. Found: C, 61.59; H, 5.80; N, 2.54.

7-Benzyloxy-1-(2-bromo-4,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-8-methoxy-1*H*-2-benzazepine (24)——A mixture of 6 g of **22**, 150 ml of CH_3CN and 6 g of $POCl_3$ was refluxed for 4 hr. The solvent was evaporated and the resulting residue was washed with excess hexane to give the hydrochloride of **23**. To a stirred solution of this crude **23** in 200 ml of MeOH was added 4 g of $NaBH_4$ under ice-cooling. After the stirring had been continued for 1 hr, the solvent was evaporated and the remaining residue was worked up as usual to

give 4.1 g of **24** as an oil. Since any attempts to crystallize were not successful, this was used for the following reaction.

1-(2-Bromo-4,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-7-hydroxy-8-methoxy-2-methyl-1*H*-2-benzazepine (**18**)——A mixture of 4 g of **24**, 200 ml of MeOH and 12 ml of 37% HCHO was stirred for 0.5 hr at room temperature and then to this solution was added 10 g of $NaBH_4$ under ice-cooling. The mixture was worked up as in formation of **17** to give 3.1 g of **20** as an oil, NMR ($CDCl_3$) δ: 2.31 (3H, singlet, NCH_3), 3.58 (3H, singlet, OCH_3), 3.75 (6H, singlet, $2\times OCH_3$), 5.02 (2H, singlet, $PhCH_2O$), 6.17, 6.28, 6.60, 6.85 (4H, each singlet, $4\times$Ar–H); this was subjected to the following reaction because of difficulty of crystallization. A solution of 2 g of above **20** in 80 ml of EtOH–conc. HCl (1: 1) was refluxed for 1.5 hr. The solvent was evaporated and the resulting residue was made basic with 28% NH_4OH and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4 to give 1.5 g of **18** as colorless needles, mp 168—169° (MeOH–$(C_2H_5)_2O$), NMR ($CDCl_3$) δ: 2.35 (3H, singlet, NCH_3), 3.63 (6H, singlet, $2\times OCH_3$), 3.82 (3H, singlet, OCH_3), 6.13, 6.27, 6.66, 6.92 (4H, each singlet, $4\times$Ar–H). *Anal.* Calcd. for $C_{21}H_{26}BrNO_4$: C, 57.80; H, 6.01; N, 3.21. Found: C, 58.08; H, 6.06; N, 2.99.

8-Benzyloxy-1-(2-bromo-4,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-7-methoxy-1*H*-2-benzazepine (**27**)—— A mixture of 6 g of **25**, 150 ml of CH_3CN and 6 g of $POCl_3$ was refluxed for 4 hr and the mixture was worked up as in the case of **23**. To a stirred solution of **26**, thus obtained, in 200 ml of MeOH was added 4 g of $NaBH_4$ under ice-cooling. The mixture was worked up as usual to give 4.1 g of **27** as a colorless oil; this was used for the following reaction, since any attempts to crystallize were unsucessful.

1-(2-Bromo-4,5-dimethoxybenzyl)-2,3,4,5-tetrahydro-8-hydroxy-7-methoxy-2-methyl-1*H*-2-benzazepine (**19**)——A mixture of 4 g of **27**, 200 ml of MeOH and 12 ml of 37% HCHO was stirred for 0.5 hr at room temperature and then to this solution was added 10 g of $NaBH_4$, in small portions, under ice-cooling within 0.5 hr. The mixture was worked up as usual to give 3.8 g of **21** as an oil, NMR ($CDCl_3$) δ: 2.25 (3H, singlet, NCH_3), 4.87 (2H, singlet, $PhCH_2O$), 6.33, 6.38, 6.65, 6.92 (4H, each singlet, $4\times$Ar–H); this was used for the following reaction because of difficulty of crystallization. A solution of 3.5 g of **21** in 70 ml of EtOH–conc. HCl (1: 1) was refluxed for 1.5 hr. The solvent was evaporated and the resulting residue was made basic with 28% NH_4OH and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4 and evaporated to leave 2.8 g of **19** as colorless needles, mp 127—129° (MeOH–$(C_2H_5)_2O$), NMR ($CDCl_3$) δ: 2.25 (3H, singlet, NCH_3), 3.68, 3.80, 3.83 (9H, each singlet, $3\times OCH_3$), 6.42, 6.48, 6.60, 6.91 (4H, each singlet, $4\times$Ar–H). *Anal.* Calcd. for $C_{21}H_{26}BrNO_4$: C, 57.80; H, 6.01; N, 3.21. Found: C, 57.88; H, 6.12; N, 3.03.

Reaction of 17 with Dimsylsodium——To a stirred solution of dimsylsodium (prepared from 3.5 g of NaH and 30 ml of DMSO) in 50 ml of THF was added a solution of 2.5 g of **17** in 50 ml of tetrahydrofuran (THF) under ice-cooling. After the stirring had been continued for 4 hr at room temperature, the mixture was poured into ice-H_2O and extracted with $CHCl_3$. The extract was washed with H_2O, dried (Na_2SO_4) and evaporated. The resulting residue was chromatographed on 20 g of silica gel. Elution with $CHCl_3$ gave 0.9 g of **28** as colorless needles, mp 159—160° (MeOH), MS *m/e*: 369 (M^+), NMR ($CDCl_3$) δ: 2.19 (3H, singlet, NCH_3), 3.63, 3.76 (6H, each singlet, $2\times OCH_3$), 3.83 (6H, singlet, $2\times OCH_3$), 6.22 (1H, singlet, Ar–H), 6.31 (1H, singlet, Ar–H), 6.58 (2H, singlet, 13-H and 14-H), 6.63 (1H, singlet, Ar-H), 6.68 (1H, singlet, Ar-H). *Anal.* Calcd. for $C_{22}H_{27}NO_4$: C, 71.52; H, 7.37; N, 3.79. Found: C, 71.60; H, 7.23; N, 3.69. Successive elution with 2% MeOH–$CHCl_3$ (200 ml) afforded 0.7 g of **29** as colorless needles, mp 174—176° (MeOH–$(C_2H_5)_2O$), MS *m/e*: 423 (M^+). *Anal.* Calcd. for $C_{22}H_{23}NO_5S$: C, 64.41; H, 7.43; N, 3.13. Found: C, 64.21; H, 7.31; N, 2.98.

5,6,7,8,13,14-Hexahydro-2,3,10,11-tetramethoxy-5-methyldibenz[*b*,*f*]azecine (**30**)——a) A solution of 100 mg of **28** in 100 ml of EtOH was shaken in the presence of H_2 over 90 mg of Adams catalyst until uptake of H_2 ceased. After removal of catalyst, the solvent was evaporated to leave 70 mg of **30** as colorless oil, MS *m/e*: 371 (M^+), NMR ($CDCl_3$) δ: 2.48 (3H, singlet, NCH_3), 3.76 (12H, singlet, $4\times OCH_3$), 6.49 (3H, singlet, $3\times$Ar–H), 6.55 (1H, singlet, Ar–H). picrate, mp 154—156° (EtOH–$(C_2H_5)_2O$). *Anal.* Calcd. for $C_{28}H_{32}N_4O_{11}$: C, 55.99; H, 5.37; N, 9.33. Found: C, 55.68; H, 5.63; N, 8.84.

b) A solution of 100 mg of **31** in 100 ml of EtOH was shaken in the presence of H_2 over 100 mg of Adams catalyst and the mixture was worked up as above to give 75 mg of colorless oil, the spectroscopic data of which were identical with those of **30** obtained from **28** by the method a.

Indolo[2,1-*a*][2]benzazepine (**33**)——To a solution of dimsylsodium (prepared from 3.5 g of NaH and 30 ml of (DMSO) was added a solution of 2.5 g of **16** in 30 ml of DMSO at room temperature under stirring. After the stirring had been continued for 14 hr, the mixture was poured into H_2O and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4 and evaporated. The remaining residue was chromatographed on 15 g of silica gel using $CHCl_3$ as an eluant. Removal of the solvent (100 ml) yielded 1.5 g of **33** as colorless oil, NMR ($CDCl_3$) δ: 3.79, 3.82 (6H, each singlet, $2\times OCH_3$), 3.86 (6H, singlet, $2\times OCH_3$), 6.19, 6.61, 6.71, 6.83 (4H, each singlet, $4\times$Ar–H); this was characterized as the methiodide (**32**), mp 257—258° (dec.) (MeOH–$(C_2H_5)_2O$). *Anal.* Calcd. for $C_{22}H_{28}INO_4$: C, 53.12; H, 5.67; N, 2.82. Found: C, 52.89; H, 5.81; N, 2.78.

Hofmann Degradation of 32——A solution of 2 g of **32** in 60 ml of 10% ethanolic NaOH was refluxed for 7 hr. The solvent was evaporated and extraceted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4 and evaporated. The remaining solid was recrystallized from MeOH–$(C_2H_5)_2O$ to give

0.8 g of **31** as colorless needles, mp 150—152°, MS *m/e*: 369 (M^+), NMR ($CDCl_3$) δ: 2.77 (3H, singlet, NCH_3), 6.28 (1H, doublet, $J=17$ Hz, olefinic H), 6.61 (1H, singlet, Ar–H), 6.70 (2H, singlet, $2\times$Ar–H), 6.88 (1H, singlet, Ar–H), 7.64 (1H, doublet, $J=17$ Hz, olefinic H). *Anal.* Calcd. for $C_{22}H_{27}NO_4$: C, 71.52; H, 7.37; N, 3.79. Found: C, 71.31; H, 7.44; N, 3.65.

Reaction of 32 with Dimsylsodium——To a solution of dimsylsodium (prepared from 2 g of NaH and 30 ml of DMSO) was added a solution of 1.5 g of **32** in 40 ml of DMSO at room temperature under stirring. After the stirring had been continued for 9 hr, the mixture was poured into 300 ml of H_2O and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4 and evaporated. The resulting residue was chromatographed on 15 g of silica gel. Elution with $CHCl_3$ (100 ml) afforded 0.6 g of colorless needles, which was identical with **28**, obtained from **17**, in all respects. Elution with 2% MeOH–$CHCl_3$ (70 ml) gave 0.4 g of colorless needles, the spectroscopic data of which were identical with those of **29**, obtained from **17**.

5,6,7,8,13,14-Hexahydro-2,3,10,11-tetramethoxy-5-methyl-13-(methylthio)methyldibenz[*b*,*f*]azecine (**34**)——A mixture of 1.2 g of **29**, 50 ml of 50% AcOH–conc. HCl (1: 1) and Zn-Hg (prepared from 5 g of Zn and 0.5 g of $HgCl_2$) was heated on a water bath for 1 hr. After removal of inorganic substance the mixture was made basic with 28% NH_4OH and extracted with $CHCl_3$. The extract was washed with H_2O, dried (Na_2SO_4) and evaporated to give **34** as colorless needles, mp 134—136° (MeOH–$(C_2H_5)_2O$), MS *m/e*: 431 (M^+), NMR ($CDCl_3$) δ: 1.98 (3H, singlet, SCH_3), 2.49 (3H, singlet, NCH_3), 3.76 (12H, singlet, $4\times OCH_3$). *Anal.* Calcd. for $C_{24}H_{33}NO_4S$: C, 66.80; H, 7.71; N, 3.25. Found: C, 66.51; H, 7.82; N, 2.92.

Thermal Decomposition of 29——A solution of 1 g of **29** in 50 ml of xylene for 24 hr. The solvent was evaporated and the residual oil was chromatographed on 10 g of silica gel using $CHCl_3$ as an eluant. Removal of the solvent (30 ml) gave 0.5 g of **37** as colorless oil, MS *m/e*: 383 (M^+), NMR ($CDCl_3$) δ: 2.43 (3H, singlet, NCH_3), 3.69 (3H, singlet, OCH_3), 3.73 (3H, singlet, OCH_3), 3.78 (3H, singlet, OCH_3), 3.79 (3H, singlet, OCH_3), 4.84 (1H, multiplet with small spliting, olefinic H), 5.21 (1H, multiplet with small splitting, olefinic H), 6.42, 6.43, 6.53, 6.61 (4H, each singlet, $4\times$Ar–H).

Reaction of 18 with Dimsylsodium——To a stirred solution of dimsylsodium (prepared from 3 g of NaH and 30 ml of DMSO) was added a solution of 4 g of **18** in 35 ml of DMSO at room temperature. After the stirring had been continued for 14 hr, the mixture was poured into H_2O containing excess NH_4Cl and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4 and evaporated. The remaining residue was chromatographed on 20 g of silica gel. Elution with $CHCl_3$ (60 ml) gave 0.2 g of **39** as colorless needles, mp 143—144° (MeOH), MS *m/e*: 355 (M^+), NMR ($CDCl_3$) δ: 2.78 (3H, singlet, NCH_3), 3.85, 3.90, 3.93 (9H, each singlet, $3\times OCH_3$), 6.24 (1H, doublet, $J=17$ Hz, olefinic H), 6.60, 6.70, 6.75, 6.84 (4H, each singlet, $4\times$Ar-H), 7.63 (1H, doublet, $J=17$ Hz, olefinic H). *Anal.* Calcd. for $C_{21}H_{25}NO_4$: C, 70.96; H, 7.09; N, 3.94. Found: C, 70.75; H, 7.25; N, 4.03. Successive elution with 2% MeOH–$CHCl_3$ afforded 1.0 g of **40** as an oil which was characterized as the deoxygenated product (**41**).

O-Methylation of 39——To a solution of 150 mg of **39** in 50 ml of MeOH was added a solution of excess CH_2N_2 in $(C_2H_5)_2O$ and the mixture was kept to stand for 10 hr. Removal of the solvent gave 150 mg of colorless needles the spectroscopic data of which were identical with those of **31**, obtained from **32**.

5,6,7,8,13,14-Hexahydro-10-hydroxy-2,3,11-trimethoxy-5-methyl-13-(methylthio)methyldibenz[*b*,*f*]azecine (**41**)——A mixture of 1 g of **40**, 50 ml of 50% AcOH–conc. HCl (1: 1) and Zn–Hg (prepared from 0.5 g of $HgCl_2$ and 5 g of Zn) was heated on a water bath for 1 hr. The mixture was worked up as in formation of **34** to give 0.7 g of **41** as colorless needles, mp 109—110° ($(C_2H_5)_2O$). NMR ($CDCl_3$) δ: 2.02 (3H, singlet, SCH_3), 2.50 (3H, singlet, NCH_3), 3.80 (9H, singlet, $3\times OCH_3$). *Anal.* Calcd. for $C_{23}H_{31}NO_4S$: C, 66.15; H, 7.48; N, 3.35. Found: C, 66.17: H, 7.48; N, 3.12.

O-Methylation of 41——A solution of 200 mg of **41** in 100 ml of MeOH was added a solution of excess CH_2N_2 in $(C_2H_5)_2O$ as in the case of **31** to give 200 mg of colorless needles, which was identical with **34**, obtained from **29**, in all respects.

Reaction of 19 with Dimsylsodium——To a solution of dimsylsodium (prepared from 3 g of NaH and 30 ml of DMSO) was added a solution of 2.5 g of **19** in 30 ml of DMSO under stirring at room temperature. After the stirring had been continued for 14 hr, the mixture was poured into 150 ml of H_2O containing excess NH_4Cl and extracted with $CHCl_3$. The extract was washed with H_2O, dried over Na_2SO_4 and evaporated. The remaining residue was chromatographed on 20 g of silica gel. Elution with 40% benzene–$CHCl_3$ (40 ml) afforded 0.1 g of **42** as an oil, MS *m/e*: 355 (M^+), NMR ($CDCl_3$) δ: 2.74 (3H, singlet, NCH_3), 3.82, 3.83, 3.86 (9H, each singlet, $3\times OCH_3$), 6.21 (1H, doublet, $J=17$ Hz, olefinic H), 6.58, 6.64, 6.67, 6.88 (4H, each singlet, $4\times$Ar–H), 7.61 (1H, doublet, $J=17$ Hz, olefinic H). Because of unstability, this was characterized as the tetramethoxy derivative (**31**) by O-methylation of 0.1 g of **42** with excess CH_2N_2 in 50 ml of MeOH as usual. Successive elution with the same solvent (60 ml) gave 0.2 g of **43** as an unstable oil, MS *m/e*: 355 (M^+), NMR ($CDCl_3$) δ: 2.18 (3H, singlet, NCH_3), 3.71, 3.74, 3.76 (9H, each singlet, $3\times OCH_3$), 6.31 (2H, singlet, $2\times$Ar–H), 6.52 (2H, singlet, olefinic H), 6.59, 6.62 (2H, each singlet, $2\times$Ar–H). This was characterized as the tetramethoxy derivative (**28**) by O-methylation of 150 mg of **43** with excess CH_2N_2 in 50 ml of MeOH as usual. Elution with 2% MeOH–$CHCl_3$ (120 ml) afforded 0.9 g of **44** as colorless needles, mp 216—220° (MeOH–$(C_2H_5)_2O$), MS *m/e*: 433 (M^+). *Anal.* Calcd. for $C_{23}H_{31}NO_5S$: C, 63.71; H, 7.21; N, 3.23. Found: C, 63.37; H, 7.22; N, 3.10.

5,6,7,8,13,14-Hexahydro-11-hydroxy-2,3,10-trimethoxy-5-methyl-13-(methylthio)methyldibenz[*b*,*f*]-

azecine (45)——A mixture of 1 g of **44**, 50 ml of 50% AcOH–conc. HCl (1: 1) and Zn–Hg (prepared from 5 g of Zn and 0.5 g of $HgCl_2$) was heated for 1 hr on a water bath. The mixture was worked up as usual to give 0.7 g of **45** as colorless needles, mp 122—123° (MeOH–$(C_2H_5)_2O$), MS *m/e*: 417 (M^+), NMR ($CDCl_3$) δ: 2.03 (3H, singlet, SCH_3), 2.50 (3H, singlet, NCH_3), 3.77 (9H, singlet, $3\times OCH_3$), 6.43 (1H, singlet, Ar–H), 6.50 (2H, singlet, $2\times$Ar–H), 6.63 (1H, singlet, Ar–H). *Anal.* Calcd. for $C_{23}H_{31}NO_4S$: C, 66.15; H, 7.48; N, 3.35. Found: C, 65.95; H, 7.65; N, 3.26.

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