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Studies on the Syntheses of Indoline Derivatives from N-Sulfonamides

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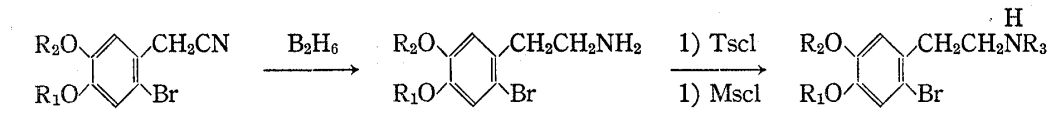
Several sulfonamides (IIIa—c and IVa—c) were synthesized for the investigation of benzyne reaction. The benzyne reaction of IIIa—c and IVa—c with sodium dimethylsulfinyl carbanion in dimethyl sulfoxide resulted in the formation of the corresponding indolines (Va—c and VIa—c) besides thioether phenol compounds (VIIa—c and VIIIa—c). These structures were respectively established from infrared and nuclear magnetic resonance spectra.

On the other hand, the same reaction of phenethylamines (IIa, IIb and IIc) with sodium dimethylsulfinyl carbanion afforded XIIa, XIIb and XIIIc, respectively.

Keywords——syntheses of indolines; benzyne reaction; reactivity of N-sulfonamides; intramolecular cyclization; dimethylsulfinyl carbanion in dimethyl sulfoxide

In the course of study on sulfonamides from phenethylamines, we became to take an interest in the reactivity of amino group of these sulfonamides, because the proton attached to nitrogen is considerably acidic in the molecule. Sulfonamides from primary amines are generally known[2] as very stable substances which are proved to be difficult to hydrolyze by acid or alkali. Furthermore, Klamann, *et al.*[3] and Neemann and coworkers[4] have revealed that N-alkylation of these sulfonamides with a variety of alkylating reagents takes place rapidly under mild basic conditions. On the other hand, it is known[5] that the reactions of various halogeno-phenethylamines with phenyllithium afford indolines *via* an intramolecular cyclization of the resulting benzyne, but the drastic conditions employed in these reactions tend to decrease yield of oxygenated indoline derivatives. From these facts, it might be expected that the amino group of these sulfonamides could be easily react with benzyne.

In this papers, we now report that the intramolecular benzyne reactions of bromosulfonamides (III and IV) with methylsulfinyl carbanion[6] in dimethyl sulfoxide give the corresponding indolines (V and VI) besides thioether phenol compounds (VII and VIII).



Ia: $R_1+R_2=CH_2$
Ib: $R_1=R_2=CH_3$
Ic: $R_1=CH_3$, $R_2=C_6H_5CH_2$

II

III: R_3=Ts
IV: R_3=Ms

Chart 1

1) Location: *Yagoto, Tenpaku-ku, Nagoya.*
2) R.A. Boissonnas, "Advances in Organic Chemistry: Methods and Results," Vol. 3, ed. by R.A. Raphael, E.C. Taylor, and H. Wynberg, Intersciences Publishers, Inc., New York and London, 1963, p. 175; J.F.W. McOmie, *ibid.*, Vol. 3, p. 214; J.F.W. McOmie, "Protective Groups in Organic Chemistry," ed. by J.W. Barton, Plenum Press, London and New York, 1973, p. 73.
3) D. Klamann, G. Hofbauer, and F. Drahowzal, *Monatsh. Chem.*, **83**, 870 (1952).
4) M. Neemann and A. Modiano, *J. Org. Chem.*, **21**, 667 (1956).
5) R. Huisgen and H. König, *Chem. Ber.*, **92**, 203 (1959); M. Julia and H.G. Breton, *Bull. Soc. Chim. France*, **1966**, 1335.
6) E.J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1345 (1965).

The starting materials (III and IV) were prepared according to the following method (Chart 1).

The various phenethylamines (II) were synthesized by reduction of the corresponding benzylcyanides (I) with sodium borohydride and boron trifluoride in tetrahydrofuran. Yields are in the 71—85% range and several properties of the reduced compounds (II) are summarized in Table I.

Table I

Compd. No.	Yield (%)	mp (°C) ( ): cryst. solvt.	Appearance (colorless)	Formula	Analysis (%) Calcd. (Found) C	H	N
IIa[a]	73	214—216(decomp.)[b] (MeOH)	needles	$C_9H_{10}O_2NBr \cdot C_2H_2O_4$	39.54 (39.53)	3.62 (3.66)	4.19 (4.17)
IIb[c]	85	195—197[d] (MeOH)	needles	$C_{10}H_{14}O_2NBr \cdot 1/2C_2H_2O_4$	43.30 (43.07)	4.95 (4.93)	4.59 (4.29)
IIc	71	182—184[e] (EtOH-acetone)	needles	$C_{16}H_{18}O_2NBr \cdot HCl$	51.56 (51.63)	5.14 (4.98)	3.76 (3.46)

a) the hydrochloride, mp 205—207° (decomp.). lit.[7] mp 208—210°
b) isolated as oxalate
c) lit.[8] oil, $bp_{0.5}$ 141—145°
d) solated as the hemioxalate
e) isolated as hydrochloride. lit.[9] mp 181—182°

The reaction of IIa—c with *p*-toluenesulfonyl (tosyl) chloride proceeded readily in pyridine to give the corresponding N-tosylates (III) in high yield. In a similar manner the reaction of II with methanesulfonyl (mesyl) chloride in the presence of pyridine gave the N-mesylates (IV) in good yield.

Table II

Compd. No.	Yield (%)	mp (°C) ( ): cryst. solvt.	Appearance (colorless)	Formura	Analysis (%) Calcd. (Found) C	H	N	IR $\nu_{max}^{CHCl_3}$ cm^{-1} NH	SO_2	NMR τ ($CDCl_3$) NH (triplet) J in Hz
IIIa	84	112 (benzene)	needles	$C_{16}H_{16}O_4NBrS$	48.25 (48.26)	4.05 (3.90)	3.52 (3.52)	3380	1330 1160	5.32 (1H, t) J=7
IIIb	82	127—128 (benzene)	needles	$C_{17}H_{20}O_4NBrS$	49.28 (49.26)	4.87 (4.75)	3.38 (3.11)	3400	1350 1160	5.13 (1H, t) J=7
IIIc	74	136—137 (benzene)	needles	$C_{23}H_{24}O_4NBrS$	56.33 (56.59)	4.93 (4.92)	2.86 (2.98)	3380	1340 1160	5.14 (1H, t) J=7
IVa	80	104 (benzene)	needles	$C_{10}H_{12}O_4NBrS$	37.28 (37.31)	3.75 (3.70)	4.35 (4.11)	3390	1330 1150	5.56 (1H, t) J=7
IVb	69	165—166 (MeOH)	prisms	$C_{11}H_{16}O_4NBrS$	39.06 (39.07)	4.77 (4.74)	4.14 (3.86)	3400	1340 1160	5.28 (1H, t) J=7
IVc	79	163—164 (EtOH)	needles	$C_{17}H_{20}O_4NBrS$	49.28 (49.25)	4.87 (4.93)	3.38 (3.17)	3400	1340 1160	5.54 (1H, t) J=7

7) T. Stevens, *J. Chem. Soc.*, **1927**, 183.
8) C. Viel, *Ann. Chem.*, **8**, 515 (1963).
9) A.R. Battersby, R. Southgate, J. Staunton, and M. Hirst, *J. Chem. Soc.*, (*C*), **1966**, 1052.

The structures of III and IV are confirmed on the basis of elemental analysis, infrared (IR) spectra[10] and nuclear magnetic resonance (NMR) spectra.[11] All of the compounds in IR spectra exhibited the peaks at 3380—3400, 1330—1350 and 1150—1160 cm^{-1} which are typical for primary sulfonamides. In the NMR spectra, the signals of NH protons of these compounds appeared as broad triplets. III and IV thus prepared are listed in Table II.

As the methylsulfinyl carbanion is strongly basic, this reagent could be expected to react rapidly with halogeno-benzene derivatives to produce the aryn intermediates (IX), followed by intramolecular cyclization to give the indoline derivatives (V and VI), as illustrated in Chart 2. Thus, benzyne reactions of III and IV with sodium methylsulfinyl

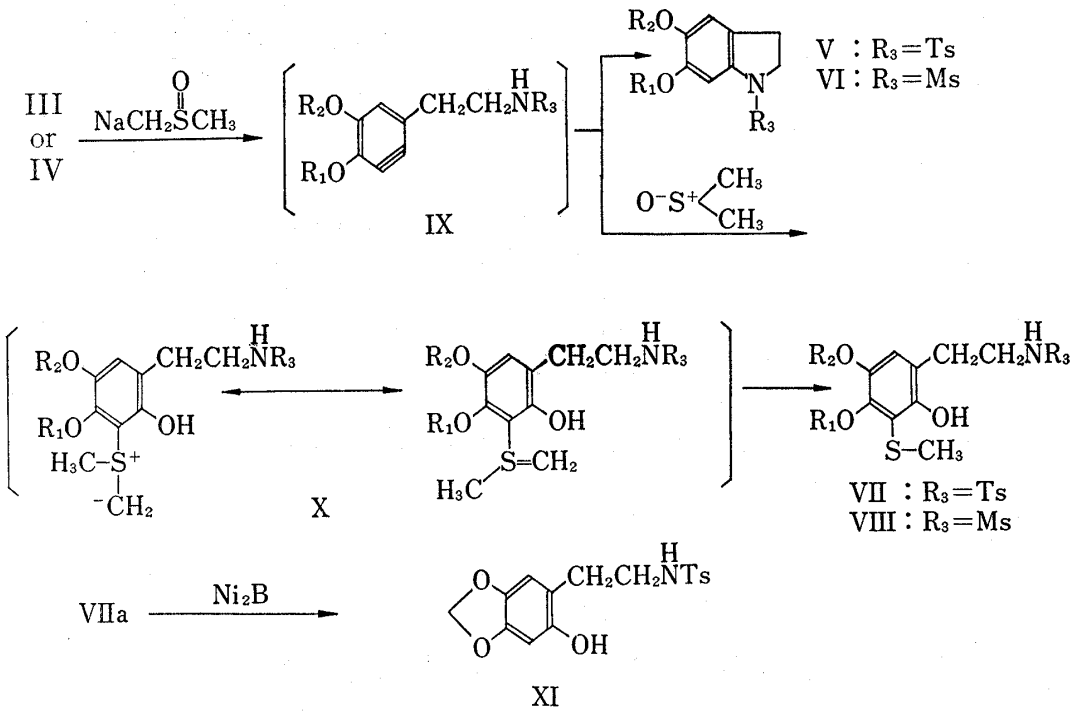


Chart 2

carbanion, which is formed sodium hydride and dimethyl sulfoxide, under a nitrogen atmosphere at room temperature were continued until spots due to the starting materials on thin-layer chromatography (TLC)[12] disappeared. After completion of the reaction, TLC showed 2 spots and the reaction mixture was subjected to chlromatographical separation on silica gel, affording indoline derivatives (V and VI) and the unexpected thioether phenol compounds (VII and VIII). All of Va—c and VIa—c have large *Rf* values than those of VIIa—c and VIIIa—c, respectively. The substances (V and VI), which were eluted primarily on column chromatography, were obtained as major products (36—49%). The structures of Va—c and VIa—c were ascertained on the basis of spectroscopic evidence together with elemental analysis, as listed in Table III.

The IR spectra of V and VI showed the absorption due to sulfonamide at 1360—1370 and 1160—1170 cm^{-1}. In the NMR spectra, the methylene protons showed signal pattern of A_2X_2, the higher field signals (6.92—7.34) of which corresponded to the methylene proton signals at C-3 and the signals in the lower field (5.96—6.14) were ascribed to two protons at

10) IR spectra were measured on a Nippon Bunko Model IRA-I spectrometer.
11) NMR spectra were determined on a Nippon Denshi PS-100 Spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard and chemical shift were given in τ-value.
12) TLC were carried out with silica gel HF_{254} Merck, Type 60 and detected by Dragendorff's reagent.

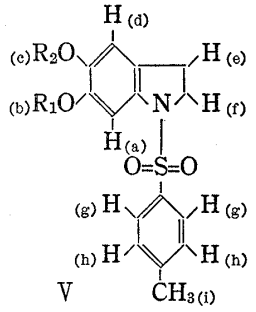
Table III

Compd. No.	Yield (%)	Silica gel *Rf* ($CHCl_3$)	mp (°C) ( ): cryst. solvt.	Appearance (colorless)	Formula	Analysis (%) Calcd. (Found) C	H	N	IR $\nu_{max}^{CHCl_3}$ cm^{-1} SO_2
Va	37	0.71	165—166 (benzene)	prisms	$C_{16}H_{15}O_4NS$	60.55 (60.71)	4.76 (4.68)	4.41 (4.29)	1360 1170
Vb	36	0.77	140[a] (benzene)	prisms	$C_{17}H_{19}O_4NS$	61.24 (61.09)	5.74 (5.90)	4.20 (4.37)	1360 1170
Vc	36	0.79	101—102 (ligloin)	needles	$C_{23}H_{23}O_4NS$	67.46 (67.63)	5.66 (5.67)	3.42 (3.27)	1370 1170
VIa	38	0.69	132—133 (benzene)	needles	$C_{10}H_{11}O_4NS$	49.78 (49.80)	4.60 (4.47)	5.81 (5.59)	1370 1160
VIb	49	0.64	125—126 (benzene)	needles	$C_{11}H_{15}O_4NS$	51.35 (51.38)	5.88 (5.91)	5.44 (5.23)	1370 1170
VIc	47	0.52	187—189 (benzene)	needles	$C_{17}H_{19}O_4NS$	61.24 (61.04)	5.74 (5.74)	4.20 (3.91)	1360 1160

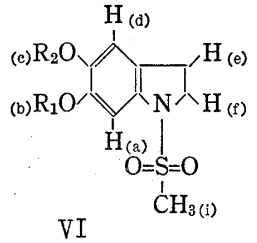
a) lit.[13] mp 142°

C–2. In the aromatic proton region, these compounds exhibited the presence of two singlet protons: (2.72—3.05 (C_7-H)) and (3.20—3.54 (C_4-H)). The extraordinary low τ-value of signal (2.72—3.05) in the lower field for the aromatic proton-region suggests that anisotropic effect of SO_2 group in these compounds has influence upon the chemical shift of aromatic proton at C–7, as shown in Table IV.

Table IV. The NMR[a] Spectra of V and VI (τ, J=Hz)



V



VI

Compd. No.	Ha	Hb	Hc		Hd	He	Hf	Hg	Hh	Hi
Va	2.80 (1H, s)	4.09 (2H, s)			3.53 (1H, s)	7.34 (2H, t, J=7)	6.10 (2H, t, J=7)	2.43 (2H, d, J=8)	2.88 (2H, d, J=8)	7.82 (3H, s)
Vb	2.84 (1H, s)	6.14 (3H, s)	6.28 (3H, s)		3.54 (1H, s)	7.36 (2H, t, J=8)	6.16 (2H, t, J=8)	2.56 (2H, d, J=8)	2.96 (2H, d, J=8)	7.68 (3H, s)
Vc	2.72 (1H, s)	6.09 (3H, s)	2.64 (5H, m)	4.96 (2H, s)	3.36 (1H, s)	7.36 (2H, t, J=7)	6.14 (2H, t, J=7)	2.38 (2H, d, J=8)	2.80 (2H, d, J=8)	7.64 (3H, s)
VIa	2.92 (1H, s)	4.01 (2H, s)			3.28 (1H, s)	6.92 (2H, t, J=7)	5.96 (2H, t, J=7)			7.13 (3H, s)
VIb	3.05 (1H, s)	6.18 (3H, s)	6.21 (3H, s)		3.34 (1H, s)	6.96 (2H, t, J=7)	6.07 (2H, t, J=7)			7.23 (3H, s)
VIc	2.88 (1H, s)	6.12 (3H, s)	2.40—2.72 (5H, m)	4.90 (2H, s)	3.20 (1H, s)	6.96 (2H, t, J=8)	6.02 (2H, t, J=8)			7.16 (3H, s)

a) The following abbreviations are used: s=singlet; d=doublet; t=triplet; m=multiplet

13) S.N. Mishra and G.A. Swan, *J. Chem. Soc.* (*C*), **1967**, 1424.

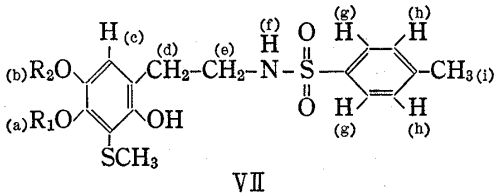
IR spectra of VII and VIII showed the sulfonamide bands at 3380—3400, 1340 and 1160—1170 cm^{-1} and the hydroxyl band at 3580—3600 cm^{-1} (Table V). The NMR spectra of these compounds strongly support their structures. Namely, NMR spectra contained a singlet corresponding to S-CH_3 group at 7.68—7.76. A sharp signal at 5.20—5.58 was assigned to hydroxyl proton since it disappeared upon addition of D_2O. In the aromatic proton region, singlet due to one proton was observed. Furthermore, in these compounds,

Table V

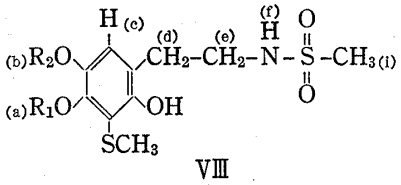
Compd. No.	Yield (%)	Silica gel *Rf* ($CHCl_3$)	mp (°C) ( ): cryst. solvt.	Appearance (colorless)	Formula	Analysis (%) Calcd. (Found) C	H	N	IR $\nu_{max}^{CHCl_3}$ cm^{-1} OH	NH	SO_2
VIIa	13	0.29	—	oil[a]	$C_{17}H_{19}O_5NS_2$	—	—	—	3600	3400	1340, 1170
VIIb	12	0.38	—	oil[b]	$C_{18}H_{23}O_5NS_2$	—	—	—	3580	3360	1340, 1170
VIIc	20	0.43	132 (benzene)	needles	$C_{24}H_{27}O_5NS_2$	60.87 (60.97)	5.75 (5.78)	2.96 (2.88)	3600	3380	1340, 1160
VIIIa	23	0.31	167—168 (MeOH)	prisms	$C_{11}H_{15}O_5NS_2$	43.27 (43.03)	4.95 (4.91)	4.59 (4.43)	3590	3400	1340, 1160
VIIIb	30	0.16	—	oil[c]	$C_{12}H_{19}O_5NS_2$	—	—	—	3600	3400	1340, 1150
VIIIc	28	0.24	108—109 (benzene)	needles	$C_{18}H_{23}O_5NS_2$	54.39 (54.31)	5.83 (5.87)	3.52 (3.52)	3600	3380	1340, 1150

a) Mass Spectrum[14] *m/e*: 381 (M^+), 210, 198, 197 (base peak), 155, 151, 91
b) Mass Spectrum *m/e*: 397 (M^+), 226, 213 (base peak), 198, 155, 91
c) Mass Spectrum *m/e*: 321 (M^+), 226, 213 (base peak), 199, 185, 170, 151

Table VI. The NMR Spectra of VII and VIII



VII



VIII

Compd. No.	Ha	Hb	Hc	Hd	He	Hf	Hg	Hh	Hi	OH	SCH_3
VIIa	4.12 (2H, s)		3.63 (1H, s)	7.33 (2H, t, J=7)	6.82 (2H,q,[a] J=7)	5.41 (1H, t, J=7)	2.44 (2H, d, J=8)	2.80 (2H, d, J=8)	7.61 (3H, s)	3.70 (1H, s)	7.71 (3H, s)
VIIb	6.16 (3H, s)	6.31 (3H, s)	3.52 (1H, s)	7.31 (2H, t, J=7)	6.84 (2H, q, J=7)	5.20 (1H, t, J=7)	2.49 (2H, d, J=8)	2.92 (2H, d, J=8)	7.64 (3H, s)	3.49 (1H, s)	7.76 (3H, s)
VIIc	6.04 (3H, s)	2.56 (5H, br, s) 4.99 (2H, s)	3.28 (1H, s)	7.26 (2H, t, J=7)	6.76 (2H, q, J=7)	5.28 (1H, t, J=7)	2.30 (2H, d, J=8)	2.74 (1H, d, J=8)	7.58 (3H, s)	3.28 (1H, s)	7.68 (3H, s)
VIIIa	4.10 (2H, s)		3.46 (1H, s)	7.20 (2H, t, J=7)	6.66 (2H, q, J=7)	5.58 (1H, t, J=7)			7.16 (3H, s)	3.58 (1H, s)	7.70 (3H, s)
VIIIb	6.15 (3H, s)	6.24 (3H, s)	3.38 (1H.s)	7.16 (2H, t, J=7)	6.66 (2H, q, J=7)	5.32 (1H, t, J=7)			7.18 (3H, s)	3.38 (1H, s)	7.72 (3H, s)
VIIIc	6.08 (3H, s)	2.40—2.76 (5H, m) 4.96 (2H, s)	3.18 (1H, s)	7.16 (2H, t, J=7)	6.62 (2H, q, J=7)	5.30 (1H, t, J=7)			7.20 (3H, s)	3.18 (1H, s)	7.70 (3H, s)

a) abbreviation; q=quartet

14) Mass spectra were determined on the Hitachi RMU-6 mass spectrometer using a direct inlet system.

the same signal pattern in N-sulfonyl phenethylamide portion as that of the starting materials (III and IV) was indicated (Table VI).

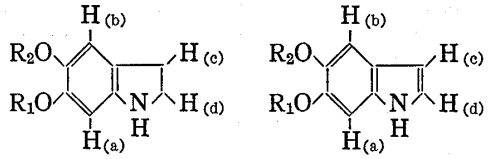
Recently, Oae and coworkers[15] reported the reaction of benzyne derivatives with dimethyl sulfoxide and they isolated similar addition products. An attractive mechanism for the direct production of VII from III and VIII from IV, respectively is as follows. The initial step of reaction is formation of an intermediate aryn (IX) by the attack of carbanion and 1,2-dipolar addition of the element of dimethyl sulfoxide to (IX) leads to the formation of the sulfonium salt (X), followed by elimination of methylene group from (X) to VII and VIII, as shown in Chart 2.

Further evidence for the structure VIIa was obtained by desulfurization of S-CH_3 with nickel boride[16] to give phenol compound. Its NMR spectrum revealed the presence of two aromatic protons as two singlets which was characteristic of *para* coupling. Consequently, the structure of this compound was found to be N-tosyl-3: 4-methyenedioxy-6-hydroxyphenethylamine (XI) and hence that of VIIa was ascertained.

From these data, the secondarily eluted products would be anticipated to be thioether phenol compounds (VIIa—c and VIIIa—c).

In the case of benzyne reaction carried out under the same condition as described above, phenethylamine derivatives (IIa—c) afforded indolines (XIIa and XIIb) and indole derivatives (XIIIc), respectively. However, the yields of desirable indolines were relatively poor and especially our attempts to preparation of XIIc from IIc were unsuccessful on account of ready oxidation to indole derivative (XIIIc). These compounds summarized in Table VII.

TABLE VII.



XIIa: $R_1+R_2=CH_2$ XIIb: $R_1=R_2=CH_3$ XIIIc: $R_1=CH_3$, $R_2=C_6H_5CH_2$

Compd. No.	Yield (%)	mp (°C) ( ): cryst. solvt.	Appearance (colorless)	Formula	Analysis (%) Calcd. (Found) C	H	N	NMR τ ($CDCl_3$) J=Hz Ha	Hb	Hc	Hd
XIIa	18	206—208 (decomp.)[a] (MeOH-acetone)	prisms	$C_9H_9O_2N\cdot HCl$	54.15 (54.00)	5.05 (4.95)	7.02 (6.81)	3.78 (1H, s)	3.42 (1H, s)	7.08 (2H, t, J=8)	6.48 (2H, t, J=8)
XIIb	28	105[b] (benzene)	prisms	$C_{10}H_{13}O_2N$	67.02 (67.02)	7.31 (7.34)	7.82 (7.53)	3.79 (1H, s)	3.38 (1H, s)	7.12 (2H, t, J=8)	6.57 (2H, t, J=8)
XIIIc	27	97[c] (benzene)	needles	$C_{16}H_{15}O_2N$	75.87 (75.59)	5.97 (5.91)	5.53 (5.38)	2.88 (1H, s)	3.36 (1H, s)	3.63 (1H, d, J=3)	3.04 (1H, d, J=3)

a) isolated as hydrochloride, *b*) lit.[18] mp 108.5°, *c*) lit.[17] mp 95—96°

As mentioned above, it has become apparent that the cyclization reaction using N-sulfonyl phenethylamines to indolines proceeds successfully and this procedure serves as a useful one for the preparation of oxygenated indolines.

15) M. Kise, T. Asari, N. Furukawa, and S. Oae, *Chem. Ind.* (London), **1967**, 276.
16) This reagent lacks desulfurization activity toward sulfones; W.E. Truce and F.M. Perry, *J. Org. Chem.*, **30**, 1316 (1965).
17) J.D. Benigni and R.L. Minnis, *J. Heterocyclic Chem.*, **1965**, 387.

Experimental[18]

6-Bromo-3,4-disubstituted Benzylcyanides——Ia,[19] Ib[20] and Ic[9] were synthesized according to the methods described in the literatures.

6-Bromo-3,4-disubstituted Phenethylamines (IIa—c) (Table I)——As a typical procedure, the preparation of 6-bromo-3,4-methylenedioxyphenethylamine (IIa) is described.

To a mixture of Ia (8.5 g) and $NaBH_4$ (2 g) in cold redistilled THF (60 ml) was added dropwise a solution of BF_3-etherate (2 ml). The reaction mixture was stirred at room temperature for 5 hr. Excess B_2H_6 was destroyed by slow addition of EtOH. A stream of hydrogen chloride was then passed through the mixture. The volatile materials were removed *in vacuo* and the residue was dissolved in water (40 ml). The resulting solution was neutralized with NH_4OH and extracted with ether. The ethereal layer was dried over Na_2SO_4 and evaporated. The residue was obtained as a colorless oil (6.4 g). This compound (IIa) was characterized as its oxalate.

N-Tosyl-6-bromo-3,4-disubstituted Phenethylamines (IIIa—c) (Table II)——As a typical procedure, the preparation of N-tosyl-6-bromo-3,4-methylenedioxyphenethylamine (IIIa) is described.

To a stirred solution of IIa (0.74 g) dissolved in dry pyridine (20 ml), tosyl chloride (0.7 g) was added gradually. The mixture was stirred at room temperature for 2 hr. After cooling, water was added to this mixture, which was extracted with $CHCl_3$. The extract was washed with diluted HCl and water, dried over Na_2SO_4 and evaporated. The residue was recrystallized from benzene to give IIIa (1 g).

N-Mesyl-6-bromo-3,4-disubstituted Phenethylamines (IVa—c) (Table II)——IVa—c were prepared according to the procedure described above for IIIa—c. N-Mesylation was carried out using IIa—c (0.003 mol), pyridine (25 ml) and mesyl chloride (0.6 g) at room temperature. After recrystallization from benzene, MeOH and EtOH, products were obtained as almost colorless needles or prisms.

Benzyne Reaction of IIIa—c and IVa—c (Table III, IV, V and VI)——General Procedure: A solution containing sodium methylsulfinyl carbanion was prepared in a stream of nitrogen from sodium hydride (0.5 g) and dimethyl sulfoxide (30 ml) according to the Corey's method.[6] To this solution IIIa (1 g) in dry dimethyl sulfoxide (5 ml) was added with stirring at room temperature. The red-brownish mixture was stirred at room temperature for 30 min and then poured into cold water. The resulting mixture was extracted with $CHCl_3$. The $CHCl_3$ extract was washed with water, dried over Na_2SO_4 and evaporated to leave a brownish oil. This oil was chromatographed on a silica gel column and eluted with $CHCl_3$. The fraction eluted primarily with $CHCl_3$ was evaporated and the residue was recrystallized from benzene to give Va, which is shown in Table III. The fraction eluted secondarily with $CHCl_3$ was evaporated to give VIIa, which is shown in Table V.

All of the compounds included in Table III and V was prepared by a similar method and characterised by elemental analysis, and IR NMR spectra (Table III—VI).

Desulfurization of VIIa using Nickel Boride (Formation of XI)——VIIa (90 mg) and nickel chloride (1.2 g) in EtOH (30 ml) were stirred under a nitrogen gas and a solution of sodium borohydride (380 mg) in water (2 ml) was dropwise added. A black precipitate was formed immediately. The mixture was heated under refux for 5 hr. The resulting mixture was evaporated to small amounts and the concentrate was extracted with $CHCl_3$. The extract was washed with water and dried over Na_2SO_4, followed by evaporation. The residue was crystallized from benzene to give XI. Colorless prisms, mp 166—167° (40 mg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 3380 (NH), 1340, 1160 (SO_2). NMR ($CDCl_3$) τ: 7.58 (3H, s., CH_3), 7.32 (2H, t., J=7 Hz, $C\underline{H}_2CH_2NH$), 6.86 (2H, t., J=7 Hz, $CH_2C\underline{H}_2NH$), 5.16 (1H, t., J=7 Hz, $CH_2CH_2N\underline{H}$), 4.68 (1H, br.s., OH), 4.18 (2H, s., $-OCH_2O-$), 3.68, 3.64 (2H, 2×s., 2×arom. H), 2.78 (2H, d., J=8 Hz, 2×arom. H), 2.36 (2H, d., J=8 Hz, 2×arom. H). *Anal.* Calcd. for $C_{16}H_{17}O_5NS$: C, 57.30; H, 5.11; N, 4.18. Found: C, 57.52; H, 5.05; N, 4.06.

Benzyne Reaction of IIa—c (Table VII)——In a similar manner to the benzyne reaction for III and IV, a mixture of methylsulfinyl carbanion (0.02 mol) and IIa—c (0.003 mol) in dimethyl sulfoxide (30 ml) was treated. The resulting products were purified by silica gel column chromatography using $CHCl_3$ as an eluent. The products were recrystallized from benzene to give XIIb and XIIIc as colorless prisms and needles. XIIa obtained as an oil, was led to hydrochloride.

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18) All melting points are uncorrect. Column chromatography was carried out on silica gel (Kieselgel 60, Merck).

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