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Reaction of N-Haloamide. XXVII.[1] Reaction of N,N-Dihaloamides with Dienes[2]

Akemi Yamasaki, Hiromi Terauchi, and Shoji Takemura

Faculty of Pharmaceutical Sciences, Kinki University[3]

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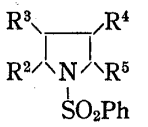
The reaction of N,N-dibromo-, and dichlorobenzenesulfonamides (DBBS and DCBS) and N,N-dichlorourethan (DCU) with dienes were examined.

Reactions of DBBS or DCBS with 1,5-hexadiene, 1,4-pentadiene, and 1,4-diphenyl-1,3-butadiene caused cyclic additions to give pyrrolidine derivatives in some extent accompanying with open-chain adducts whereas DCU gave no cyclic adduct but only mixtures of open chain-adducts. The reactions of N,N-dihaloamides with 1,4-cyclohexadiene also gave acyclic adducts.

In the previous papers, we have reported the additions of N-haloamides, especially of N,N-dibromobenzenesulfonamide (DBBS) to alkenes.[4–6] This work presents a set of reactions of N,N-dihaloamides with some dienes in which cyclic adducts may be produced.

Table I. Pyrrolidine Derivatives obtained by the Reactions of N,N-Dihaloamides with Dienes



Dihaloamide	Diene	Product	mp (Yield %)	Reduced product
$PhSO_2NBr_2$ (DBBS)	$CH_2=CH(CH_2)_2CH=CH_2$	$R^2=R^5$: CH_2Br, $R^3=R^4$: H (*cis*) **1a**	121—124° (28)	$R^2=R^5$: CH_3, $R^3=R^4$: H (*cis*) **1b**
$PhSO_2NCl_2$ (DCBS)	$CH_2=CH(CH_2)_2CH=CH_2$	$R^2=R^5$: CH_2Cl, $R^3=R^4$: H (*cis*) **2a**	85—87° (4.8)	**1b**
EtO_2CNCl_2 (DCU)	$CH_2=CH(CH_2)_2CH=CH_2$	—		
$PhSO_2NBr_2$ (DBBS)	$CH_2=CHCH_2CH=CH_2$	R^2: CH_2Br R^4: Br, $R^3=R^5$: H **3a**	92—95° (19)	R^2: CH_3, $R^3=R^4=R^5$: H **3b**
$PhSO_2NCl_2$ (DCBS)	$CH_2=CHCH_2CH=CH_2$	R^2: CH_2Cl, R^4: Cl, $R^3=R^5$: H **4a**	61—65° (1.3)	R^2: CH_3, R^4: Cl, $R^3=R^5$: H **4b** and **3b**
$PhSO_2NBr_2$ (DBBS)	PhCH=CHCH=CHPh	$R^2=R^5$: Ph, $R^3=R^4$: Br **5**	189—190° (9.2)	—
$PhSO_2NBr_2$		—		

1) Part XXVI: T. Adachi and K. Otsuki, *Chem. Pharm. Bull.* (Tokyo), **24**, 2803 (1976).
2) The work has been presented in brief at the 24th Meeting of the Kinki Branch of the Pharmaceutical Society of Japan, Osaka, 1974.
3) Location: *Kowakae, Higashi-osaka.*
4) Y. Ueno, S. Takemura, Y. Ando, and H. Terauchi, *Chem. Pharm. Bull.* (Tokyo), **13**, 1369 (1965).
5) S. Takemura, H. Terauchi, Y. Ando, and Y. Ueno, *Chem. Pharm. Bull.* (Tokyo), **15**, 1328 (1967).
6) H. Terauchi, A. Yamasaki, and S. Takemura, *Chem. Pharm. Bull.* (Tokyo), **23**, 3162 (1975).

Such cyclic addition has been reported on the reaction of *cis,cis*-1,5-cyclooctadiene with N,N-dibromo-*p*-toluenesulfonamide which gave an azabicyclic compound.[7] More recently, Okamoto, *et al.*[8] reported the addition of N,N-dihalosulfonamide to alicyclic conjugated dienes and the cyclization of the adducts with base.

In view of the above facts, N,N-dihaloamides, namely N,N-dibromobenzenesulfonamide (DBBS), N,N-dichlorobenzenesulfonamide (DCBS), and N,N-dichlorourethan (DCU) were allowed to react with 1,5-hexadiene, 1,4-pentadiene, 1,4-diphenyl-1,3-butadiene, and 1,4-cyclohexadiene, respectively. The desired ring closures occurred to some extent in the reactions of DBBS or DCBS with certain open-chain dienes whereas no cyclized product was obtained in the reaction of DCU. The reaction of DBBS with 1,4-cyclohexadiene gave no azabicyclo-compound but simple 1:1 and 1:2 molar adducts. It is interesting that all cyclized products isolated had five-membered pyrrolidine rings (Table I). DBBS was superior to DCBS in regard to the yields of such cyclic adducts. A general reaction procedure was adopted to compare the results of each reaction.

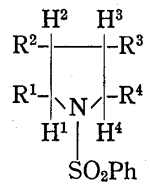
Table II. Open-chain Adducts obtained by the Reactions of N,N-Dihaloamides with Dienes

Dihaloamide	Diene	Product	mp (Yield %)	Reduced product
$PhSO_2NBr_2$ (DBBS)	$CH_2=CH(CH_2)_2CH=CH_2$	1:2 adduct: $R^1=R^4$: $NHSO_2Ph$, $R^2=R^3$: Br **6**	146—150° (3.7)	—
		1:1 adducts: a mixture of R^1: $NHSO_2Ph$, R^2: Br **7** and R^1: Br, R^2: $NHSO_2Ph$ **8**	oil (21)	R^1: $NHSO_2Ph$, R^2: H **21**; R^1: H, R^2: $NHSO_2Ph$ **22**
$PhSO_2NCl_2$ (DCBS)	$CH_2=CH(CH_2)_2CH=CH_2$	1:2 adduct: $R^1=R^4$: $NHSO_2Ph$, $R^2=R^3$: Cl **9**	160—162° (21.3)	—
		1:1 adducts: a mixture of R^1: $NHSO_2Ph$, R^2: Cl **10** and R^1: Cl, R^2: $NHSO_2Ph$ **11**	oil (16—21)	**21**; **22**
EtO_2CNCl_2 (DCU)	$CH_2=CH(CH_2)_2CH=CH_2$	a mixture of 1:2 adducts $C_{12}H_{22}O_4N_2Cl_2$ **12**	126—127° (18)	—
		a mixture of N,C-dichloro adducts $C_9H_{15}O_2NCl_2$ **13**	bp_3 102—105° (0.5)	—
		a mixture of 1:1 adducts $C_9H_{16}O_2NCl$ **14**	bp_2 80—82° (27.5)	—

7) H. Stetter and K. Heckel, *Chem. Ber.*, **106**, 339 (1973).
8) T. Okamoto, *et al.*, The 95th Meeting of the Pharmaceutical Society of Japan, Nishinomiya, 1975, Abstracts II, p. 19.

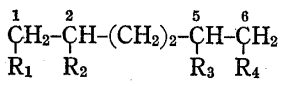
TABLE III. NMR Shifts and Assignments of the Products

Pyrrolidine derivatives



Compound	Substituents				Chemical shifts (60 Mc) ($CDCl_3$) ppm							
	R^1	R^2	R^3	R^4	H^2	H^3	H^1	H^4	R^2	R^1	R^4	R^3
1a	$BrCH_2$	H	H	$BrCH_2$	$2H_X$:4.2, m		4H:2.1, br. m		—	$BrCH_AH_B$, $2H_A$:3.2 t J_{AB}=10Hz J_{AX}=10Hz $2H_B$:3.8, 2 d J_{BA}=10Hz J_{BX}= 3Hz		—
1b	CH_3	H	H	CH_3	2H:4.05, m		2H:1.5m, 2H:2.1m		—	6H:1.25 d J=7Hz		—
2a	$ClCH_2$	H	H	$ClCH_2$	$2H_X$:4.1, m		4H:2.0, br. m		—	$ClCH_AH_B$, $2H_A$:3.45 q J_{AB}=8Hz J_{AX}=10Hz $2H_B$:3.95 q J_{BA}=8Hz J_{BX}=4Hz		—
3a	$BrCH_2$	H	Br	H	4H:3.7—4.2m[a]		2H: 2.45m		—	$BrCH_2$ 2H:3.7—4.2m[a]	—	—
3b	CH_3	H	H	H	3H:3.0—4.0m[a]		4H:1.6m		—	CH_3 3H:1.4 d J=8Hz		
4a	$ClCH_2$	H	Cl	H	4H:3.5—4.4m[a]		2H: 2.3 br, m		—	$ClCH_2$ 2H:3.5—4.4m[a]	—	—
4b	CH_3	H	Cl	H	3H:3.4—4.1[a]		1H:4.3m, 2H:2.0m		—	CH_3 3H:1.45 d J=7Hz	—	—
5	C_6H_5	Br	Br	C_6H_5	2H:5.4m		2H:4.55m		—	arom. 10H:7.3 s		

Open-chain 1:2 adducts



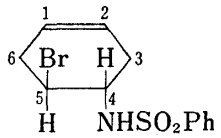
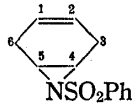
Compound	Substituents				Chemical shifts (60 Mc) ppm				
	R^1	R^4	R^2	R^3	H^1	H^6	H^2	H^5	NH
6	$NHSO_2Ph$		Br		4H:3.3 t J=7Hz D_2O: d J=7Hz		2H:4.1m		2H:6.9 t J=7Hz

Open-chain 1:2 adducts $\overset{1}{C}H_2\text{-}\overset{2}{C}H\text{-}(CH_2)_2\text{-}\overset{5}{C}H\text{-}\overset{6}{C}H_2$ (R^1, R^2, R^3, R^4)

Compound	Substituents				Chemical shifts (60 Mc) ppm				
	R^1	R^4	R^2	R^3	H^1	H^6	H^2	H^5	NH
9	$NHSO_2Ph$		Cl		4H:3.05 t J=6Hz D_2O: d J=6Hz		2H:4.0m		2H:8.0 t J=6Hz
12 (mixture)	$2NHCO_2Et$, 2Cl				2H:3.45 d J=6Hz and 2H:3.4 q J_1=11Hz J_2=5Hz		2H:4.0m		2H:5.3br

Open-chain 1:1 adducts and derivatives $\overset{1}{C}H_2\text{-}\overset{2}{C}H\text{-}(CH_2)_2\text{-}\overset{5}{C}H\text{=}\overset{6}{C}H_2$ (R^1, R^2)

Compound	Substituents		Chemical shifts (60 Mc) ppm				
	R^1	R^2	H^1	H^2	H^5	H^6	NH
7 and	$NHSO_2Ph$ and	Br	2H:3.25 q J_1=7Hz J_2=3Hz	1H:4.0m	1H:5.5m	1H:4.85m 1H:5.1m	1H:5.4 m, br
8 (mixture)	Br	$NHSO_2Ph$	2H:3.5 d J=8Hz				
10 and	$NHSO_2Ph$ and	Cl	2H:3.2 q J_1=7Hz J_2=2Hz	1H:4.0m	1H:5.7m	1H:5.0m 1H:5.3m	1H:5.5 m, br
11	Cl	$NHSO_2Ph$	2H:3.25 d J=8Hz				
13 (mixture)	Cl, $ClNHCO_2Et$		2H:3.85 d J=4Hz and 2H:3.9 q J_1=9Hz J_2=8Hz	1H:4.2m	1H:5.7m	1H:5.1 q J_1= 2Hz J_2=13Hz 1H:5.0 q J_1= 2Hz J_2=11Hz	—
14 (mixture)	Cl, $NHCO_2Et$		2H:3.5 t J=7Hz 2H:3.4 q J_1=10Hz J_2= 6Hz	1H:4.0m	1H:5.7m	1H:4.9m 1H:5.2m	1H:5.3 m, br
21	$NHSO_2Ph$	H	2H:3.3 t J=7Hz	2H:2.0m	1H:5.4m	1H:4.8m 1H:5.1	1H:5.4 d, br J=7Hz
22	H	$NHSO_2Ph$	3H:1.8 d J=7Hz	1H:3.4m	1H:5.5m	1H:4.9m 1H:5.1m	1H:5.4 d, br J=6Hz
18	NSO_2Ph		2H:2.7m	1H:3.8br	1H:5.7m	1Ha:4.95 d Jac=15Hz Jab= 0Hz 1Hb:5.0 d Jbc=13Hz Jba= 0Hz	

		C^4-H	C^5-H	C^3-H	C^6-H	C^1-H	C^2-H
15		1H:3.6m	1H:4.2m	4H:1.6—3.0m		2H:5.6 t	
19		2H:3.15 q J_1=2Hz J_2=1Hz		4H:2.35br		2H:5.45br	

a) The signals were overlapped each other.

In the reaction of equimolar DBBS with 1,5-hexadiene, cyclized product (**1a**), mp 121—124°, benzenesulfonamide, and a mixture of open-chain adducts were obtained. The cyclic product, **1a**, was identified with authentic *cis*-2,5-bis(bromomethyl)-1-benzenesulfonylpyrrolidine which was synthesized from 2,5-pyrrolidine dicarboxylic acid *via* 2,5-bis(hydroxymethyl)-1-benzenesulfonylpyrrolidine (**20**) by a modified method of the preparation of toluenesulfonyl analogue of **1a**.[9] The residual mixture separated from crystalline **1a** was chromatographed to isolate additional **1a**, and a mixture of open-chain adducts from which a crystalline compound, **6**, was obtained. The analytical data showed that **6** is a 1:2 molar adduct. Its nuclear magnetic resonance (NMR) spectrum suggested a symmetric structure having benzenesulfonamido groups at terminal carbons (Table III). Thus the structure of 1,6-bis(benzenesulfonamido)-2,5-dibromohexane was given for 6. After the isolation of **6**, residual oil could not be recognized to be still a mixture or not neither by thin-layer chromatography (TLC) nor column chromatography, however the NMR spectrum (Table III) and the elemental analysis suggested that the oil was still a mixture of 1:1 molar adducts. The mixture was therefore reduced with lithium aluminum hydride to obtain a mixture of debrominated compounds which was separated to its components of almost equal amounts by preparative TLC. Structures, **21** and **22**, were given for them, respectively, on the basis of the NMR data (Table III). Thus the said mixture of 1:1 molar adducts may be composed of two isomers, **7** and **8**.

The reaction of DCBS with 1,5-hexadiene gave **2a**, **9**, and a mixture of **10** and **11**. The yield of **2a** was less than that of **1a**. The cyclic adduct, **2a**, was identified with authentic *cis*-2,5-bis(chloromethyl)-1-benzenesulfonylpyrrolidine which was synthesized by a similar manner as the preparation of **1a**. Both **1a** and **2a** were reduced to the same bis-methyl compound **1b** (Table I). The mixture of 1:1 and 1:2 molar adducts was separated chromatographycally to obtain **9** and the mixture of **10** and **11**. The structure of **9** was presumed to be 1,6-bis(benzenesulfonamido)-2,5-dichlorohexane from the NMR spectrum (Table III). The mixture of 1:1 molar adducts was reduced by the similar way as the bromo analogue and the resulted mixture was separated by TLC to its components of almost equal amounts. The spectral data and the *Rf* values of TLC of them were identical with those of **21** and **22**, respectively. Both mixtures of **7** and **8**, and **10** and **11** were converted to the same aziridine derivative, **18**, by the treatment with base, respectively.

The variation of the yields of **2a**, **9**, **10**+**11**, and benzenesulfonamide in regard to the reaction condition was briefly examined changing the molar ratio of the reactants and the temperature (Table IV). It is conclusive that the reaction in a 1:1 molar ratio at 0° gives the highest yield of the cyclic product, **2a**, and the yield is strongly influenced by the temperature. The cyclization to **1a** or **2a** is likely occurred before the treatment of the reaction mixture with sodium bisulfite because the cyclic adducts were also obtained without the treatments.

The reaction of DCU with 1,5-hexadiene gave no cyclized product contrary to the above two cases but open chain adducts which were fractionated to **12**, **13**, and **14**. The elemental

9) G. Cignarella, G.G. Gallo, and E. Testa, *J. Am. Chem. Soc.*, **83**, 4999 (1961).

Table IV. The Variation of the Yields of **2a**, **9**, **10**+**11**, and Benzene sulfonamide (BSA) in regard to the Reaction Condition

Temperature °C	Molar ratio of DCBS *vs.* 1,5-hexadiene	Yield (%)			
		2a	**9**	**10**+**11**	BSA
−50	1:1	2.5	21.3	1.2	42.1
0	1:1	5.1	20.0	2.3	29.4
0	2:1	4.8	20.2	4.5	31.4
15	1:1	0	0	2.1	39.3
15	2:1	0.9	16.9	4.7	15.4

analysis of them showed that **12** is 1: 2, and **13** and **14** are 1: 1 molar adducts, respectively. The NMR spectra of these products exhibited overlapped signals of quartets and doublets in the regions of 3.2—4.0 ppm (Table III). These facts suggested that the products were still mixtures however no further studies on the structures of them were performed. The mixture, **13**, still retained active chloride. The mixture, **14** was obtained by the reduction of **13** with aqueous sodium bisulfite for a long period of time.

Reaction of 1,4-pentadiene with DBBS and DCBS gave cyclic adducts, **3a** and **4a**, respectively. Both of the products were reduced to give same product, **3b**. This compound was identified with authentic 2-methyl-1-benzenesulfonylpyrrolidine which was synthesized by the route of Schmitz and Murawski.[10] The structures, **3a** and **4a** (Table I) were presumed on the basis of the NMR spectra of them (Table III), respectively. The yields of them appeared to be less than those of the cyclic adducts from 1,5-hexadiene.

The reaction of 1,4-diphenyl-1,3-butadiene with DBBS also gave a pyrrolidine derivative, **5**, and 1,2,3,4-tetrabromo-1,4-diphenylbutane, **17**,[11] in low yields.

The reaction of 1,4-cyclohexadiene with DBBS gave no cyclic adduct contrary to that of 1,5-cyclohexadiene[7] and the isolated products were *trans*-4-benzenesulfonamido-5-bromo-1-cyclohexene, **15**, and *trans*-4,5-dibromo-1-cyclohexane, **16**.[12] The structure of **15** was presumed from the NMR spectra of it and its aziridine derivative (Table III).

On the basis of above results, it was concluded that N,N-dihalobenzenesulfonamides reacted with 1,5- and 1,4-dienes to give pyrrolidine derivatives whereas 1,4-cyclohexadiene produced no cyclic adduct, and the reactions of N,N-dichlorocarbamate gave no cyclic adduct.

Experimental

General Procedure——N,N-Dihaloamide (0.1 mole) in CH_2Cl_2 (200 ml) was dropwise added to a stirred solution of diene (0.1 mole) in CH_2Cl_2 (200 ml) in a period of 5 hr keeping the temperature at −50°. The reaction mixture was stirred for additional 1 hr at −50° and the mixture was allowed to stand overnight at room temperature. After the solution was refluxed for 4 hr, the mixture was stirred with 20% aq. $NaHSO_3$ (100 ml) at 20—30° until KI-starch test was negative. The organic layer was then washed with three 100 ml portions of H_2O, and dried over Na_2SO_4. The solvent was removed under reduced pressure to leave crude reaction mixture.

Reaction of N,N-Dibromobenzenesulfonamide (DBBS) with 1,5-Hexadiene——By an addition of CCl_4 to the crude product obtained by the general procedure, a solid was precipitated. This was recrystallized from hot CCl_4 to give colorless crystals of **1a**, mp 121—124°. *Anal.* Calcd. for $C_{12}H_{15}O_2NSBr_2$ C, 36.28; H, 3.81; N, 4.42. Found: C, 36.33; H, 4.26; N, 4.52. IR ν_{max}^{Nujol} cm^{-1}: 1330, 1150 (ν_{SO_2N}). NMR: Table III. The mother liquor, the filtrate of crude **1a**, was distilled to remove CCl_4 and the residue was chromatographed on a silica gel column. Elution with CCl_4 gave additional crystals of **1a** (total yield: 28%). Successive elution gave white crystals, mp 107—110°, whose yield was so poor that further purification was unsuccessful. The third fraction gave an oil (**7**+**8**) which showed one spot on TLC. This was purified by repeated chromatography.

10) E. Schmitz and D. Murawski, *Chem. Ber.*, **99**, 1493 (1966).
11) C.F.H. Allen, A. Bell, and J.W. Gates, Jr., *J. Org. Chem.*, **8**, 373 (1943).
12) E.E. Van Tammelen, J. Am. Chem. Soc., **77**, 1704 (1958).

Anal. Calcd. for $C_{12}H_{16}O_2NSBr$: C, 45.29; H, 5.07; N, 4.40. Found: C, 45.20; H, 5.22; N, 4.55. IR ν_{max}^{Nujol} cm^{-1}: 3250 (ν_{NH}), 1320, 1160 (ν_{SO_2N}). NMR: Table III. From the fourth fraction of the elution, an oil was obtained which was recrystallized from ether to give crystals of **6** in 3.7% yield, mp 146—150°. *Anal.* Calcd. for $C_{18}H_{22}O_4N_2S_2Br_2$: C, 41.08; H, 4.21; N, 5.32. Found: C, 40.98; H, 4.13; N, 5.34. IR ν_{max}^{Nujol} cm^{-1}: 3300 (ν_{NH}), 1320, 1150 (ν_{SO_2N}). NMR Table III.

***cis*-2,5-Bis(bromomethyl)-1-benzenesulfonylpyrrolidine (1a)**——A solution of benzenesulfonyl chloride (17 g) in dry C_5H_5N (70 ml) was dropwise added to stirred *cis*-2,5-dicarbethoxypyrrolidine[13] in dry C_5H_5N (50 ml) at 0° during 1 hr. The reaction mixture was warmed at 40° for 3 hr and kept at room temperature overnight. The separated solid was filtered off and the filtrate was condensed at 40° under reduced pressure. The residue was mixed with 50 ml of H_2O and acidified to pH 3 with conc. HCl. The crude crystals were filtered and washed with H_2O. The filtrate was extracted with C_6H_6 (25 ml × 2) and the extract was combined with the crystals. The mixture was dried over Na_2SO_4, concentrated to about 25 ml and *n*-hexane (50 ml) was added. The precipitate was filtered and recrystallized from *n*-hexane to obtain *cis*-1-benzenesulfonyl-2,5-dicarbethoxypyrrolidine, mp 72—73°. Yield 13 g. *Anal.* Calcd. for $C_{16}H_{21}O_6NS$: C, 54.07; H, 5.96; N, 3.94. Found: C, 54.13; H, 6.02; N, 3.90. IR ν_{max}^{Nujol} cm^{-1}: 1730 ($\nu_{C=O}$), 1350, 1157 (ν_{SO_2N}). To a suspension of $LiAlH_4$ (4.0 g) in dry tetrahydrofurane (THF) (100 ml), *cis*-1-benzenesulfonyl-2,5-dicarbethoxypyrrolidine (12 g) in dry THF (120 ml) was added under stirring at 0° during 1 hr. The mixture was refluxed for 1 hr and decomposed with H_2O (15 ml). The precipitate was filtered off and the filtrate was condensed under reduced pressure. The residue was stirred with H_2O (20 ml) and filtered to collect crude *cis*-2,5-bis(hydroxymethyl)-1-benzenesulfonylpyrrolidine (**20**) (7 g). mp 125—127°. A part of the crude product was purified from AcOEt to give crystals of mp 132—134°. *Anal.* Calcd. for $C_{12}H_{17}O_4NS$: C, 53.12; H, 6.32; N, 5.16. Found: C, 53.33; H, 6.40; N, 5.21. IR ν_{max}^{Nujol} cm^{-1}: 3300 (ν_{OH}), 1350, 1155 (ν_{SO_2N}). The crude bishydroxymethyl compound (**20**) (2 g) was added to a stirred PBr_3 (3 ml) at −10°. After stirring for 5 hr at 0°, the mixture was allowed to stand overnight. It was poured on ice and extracted with $CHCl_3$. The $CHCl_3$–layer was washed with H_2O, dried over Na_2SO_4, and the solvent was removed by distillation. The remaining solid was recrystallized from CCl_4 to give crystals of mp 121—123° (0.5 g). This compound was identified with **1a** by mixed melting point determination and comparison of infrared (IR) spectra.

Reduction of 1a with Lithium Aluminum Hydride——The crystals of **1a** (5 g) were dissolved in abs. THF (100 ml). Into the solution, $LiAlH_4$ (5 g) was added in portions under cooling. The mixture was refluxed for 3 hr and excess reagent was decomposed by addition of THF–H_2O mixture. The precipitate formed was dissolved by addition of 10% HCl, and the mixture was extracted with ether. The ether layer was washed with sat. NaCl, dried over Na_2SO_4, and the solvent was removed. The residue was chromatographed on a silica gel column to collect a fraction which showed single spot on a TLC. An oil thus obtained was purified by repeated chromatography to give **1b**, mp 90—91° (3.1 g). *Anal.* Calcd. for $C_{12}H_{17}O_2NS$: C, 60.22; H, 7.16; N, 5.85. Found: C, 60.01; H, 7.66; N, 5.45. IR ν_{max}^{Nujol} cm^{-1}: 3200 (ν_{NH}), 1320, 1160 (ν_{SO_2N}). NMR: Table III.

Reduction of a Mixture of 7 and 8 to 21 and 22——A suspension of $LiAlH_4$ (0.7 g) in dry THF (30 ml) was added to a solution of the mixture of **7** and **8** (0.7 g) in dry THF (30 ml). The mixture was refluxed for 3 hr. After addition of H_2O (20 ml) and 10% HCl (10 ml), the solution was extracted with ether. The ether extract was washed with H_2O, dried over Na_2SO_4, and the solvent was distilled to leave an oil (0.2 g) which was separated to two components of *Rf* 0.32 and 0.45 on TLC (silica gel-$CaSO_4$ plates, $CHCl_3$: CH_2Cl_2 1: 1). The recoveries of them were 31 and 28% for **21** and **22**, respectively. **21**: IR ν_{max}^{liquid} cm^{-1}: 3280 (ν_{NH}), 1320, 1160 (ν_{SO_2N}). NMR:Table III. **22**: IR ν_{max}^{liquid} cm^{-1}: 3300 (ν_{NH}), 1320, 1160 (ν_{SO_2N}). NMR: Table III.

Reaction of the Mixture of Benzenesulfonamido-bromo-1-hexene (7+8) with KOH——The mixture of **7** and **8** (1 g) was dissolved in CH_2Cl_2 (30 ml) and added with 5% aq. KOH (30 ml). The mixture was stirred for 1 hr at room temperature, the organic layer separated was washed with H_2O, dried (Na_2SO_4), and the solvent was evaporated to leave an oil which was distilled, bp_2 135° (**18**), yield 0.4 g. *Anal.* Calcd. for $C_{12}H_{15}O_2NS$: C, 60.74; H, 6.37. Found: C, 60.41; H, 6.63. IR ν_{max}^{liquid} cm^{-1}: 1310, 1150 (ν_{SO_2N}). NMR: Table III.

Reaction of N,N-Dichlorobenzenesulfonamide (DCBS) with 1,5-Hexadiene——i) The mixture of the products obtained by the general procedure was chromatographed on a silica gel column. Elution with *n*-hexane–$CHCl_3$ gave **2a**, mp 85—87°, in 4.8% yield; **9**, mp 160—162°, in 21.3% yield; and a mixture of **10** and **11**, an oil, in 16—21% yield. Successive elution of the column with EtOH gave benzenesulfonamide in 42.1% yield. **2a**: IR ν_{max}^{Nujol} cm^{-1}: 1340, 1150 (ν_{SO_2N}). NMR: Table III. *Anal.* Calcd. for $C_{12}H_{15}O_2NSCl_2$: C, 46.76; H, 4.91; N, 4.54. Found: C, 46.56; H, 4.87; N, 4.63. **9**: IR ν_{max}^{Nujol} cm^{-1}: 3250 (ν_{NH}), 1320, 1150 (ν_{SO_2N}). NMR: Table III. *Anal.* Calcd. for $C_{18}H_{22}O_4N_2S_2Cl_2$: C, 46.45; H, 4.76; N, 6.01. Found: C, 46.12; H, 4.65; N, 6.08. The mixture of **10** and **11**: IR ν_{max}^{liquid} cm^{-1}: 3250 (ν_{NH}), 1320, 1150 (ν_{SO_2N}). NMR: Table III. *Anal.* Calcd. for $C_{12}H_{16}O_2NSCl$: C, 52.64; H, 5.89; N, 5.12. Found: C, 52.82; H, 5.97; N, 5.82.

Results obtained under other conditions: see Table IV.

***cis*-2,5-Bis(chloromethyl)-1-benzenesulfonylpyrrolidine (2a)**——To a solution of *cis*-2,5-bis(hydroxymethyl)-1-benzenesulfonylpyrrolidine (**20**) prepared in the synthesis of **1a** (2 g) in dry C_6H_6 (20 ml), $SOCl_2$ (2.5 g) was added under stirring at 0°. The mixture was stirred for 2 hr at room temperature and for 2 hr at

13) M.R. Bell and S. Archer, *J. Am. Chem. Soc.* **82**, 151 (1960).

40—50°. The solvent and excess $SOCl_2$ were eliminated *in vacuo*. The residual oil was recrystallized from CCl_4 two times to give crystals of mp 86—87°. This compound was identified with **2a** by comparison of IR spectra and mixed melting point determination.

Reduction of 2a with Lithium Aluminum Hydride——Compound **2a** (0.6 g) was dissolved in THF (10 ml) and $LiAlH_4$ (0.6 g) was added into the solution under ice-cooling. The mixture was refluxed for 2 hr. THF containing H_2O was added to the mixture which was acidified with 10% HCl and extracted with ether. The ether layer was dried (Na_2SO_4), and the solvent was eliminated to leave colorless crystals which were recrystallized from EtOH to give **1b**, mp 90—91°, yield 0.2 g. This was identified with authentic sample obtained by the reduction of **1a** in comparison of IR and NMR spectra.

Reduction of a Mixture of 10 and 11 to 21 and 22——A suspension of $LiAlH_4$ (0.15 g) in dry THF (10 ml) was added to a cold solution of the mixture of **10** and **11** (0.15 g) in dry THF (10 ml) at 0°. The following procedure was carried out by the similar manner as the reduction of **7**+**8**. The recoveries of **21** and **22** from TLC plate were 25 and 22%, respectively. Each product was identified with corresponding authentic samples by TLC and IR spectral comparisons.

Reaction of the Mixture of 10 and 11 with KOH——A solution of the mixture of **10** and **11** (1.5 g) in CH_2Cl_2 (20 ml) was mixed with 10% aq. KOH and the mixture was stirred for 1 hr at room temperature. After removal of the aqueous phase, the CH_2Cl_2 layer was washed with H_2O, dried (Na_2SO_4), and condensed to give a syrup which was purified by column chromatography and distillation, bp_2 135° (0.6 g). This oil was identified with **18** by comparison of IR and NMR spectra.

Reaction of N,N-Dichlorourethan (DCU) with 1,5-Hexadiene——DCU and 1,5-hexadiene were made to react by the method described in the general procedure. The mixture of the products was chromatographed on a silica gel column. Elution with $CHCl_3$–*n*-hexane gave crystals of **12**, mp 126—127° in 18% yield; an oil, **13**, bp_3 102—105° in 0.5% yield; and an oil, **14**, bp_2 80—82° in 27.5% yield. **12**: *Anal.* Calcd. for $C_{12}H_{22}O_4N_2Cl_2$: C, 43.77; H, 6.73; N, 8.50. Found: C, 43.72; H, 6.72; N, 8.52. IR ν_{max}^{Nujol} cm^{-1}: 3250 (ν_{NH}), 1700 ($\nu_{C=O}$). NMR: Table III. **13**: *Anal.* Calcd. for $C_9H_{15}O_2NCl_2$: C, 45.19; H, 6.29; N, 5.86. Found: C, 45.17; H, 6.06; N, 5.88. IR ν_{max}^{liquid} cm^{-1}: 1700 ($\nu_{C=O}$). NMR: Table III. **14**: *Anal.* Calcd. for $C_9H_{16}O_2NCl$: C, 52.52; H, 7.84; N, 6.81. Found: C, 51.59; H, 7.68; N, 6.45. IR ν_{max}^{liquid} cm^{-1}: 3200 (ν_{NH}), 1700 ($\nu_{C=O}$). NMR: Table III.

Conversion of 13 to 14——A solution of **13** (0.5 g) in $CHCl_3$ (10 ml) was mixed with 10% aq. $NaHSO_3$ (10 ml). The mixture was stirred for 42 hr at room temperature. The $CHCl_3$ layer was washed with H_2O, dried (Na_2SO_4), and the solvent was evaporated. The residue was distilled to obtain an oil, bp_3 82—85° (0.2 g), which showed an identical IR spectrum with **14**.

Reaction of DBBS with 1,4-Pentadiene——A general procedure using DBBS and 1,4-pentadiene gave a mixture of products which was chromatographed on a silica gel column. Elution with CH_2Cl_2–*n*-hexane (4: 6) gave colorless needles of **3a**, mp 92—95° (from EtOH), in 19% yield. *Anal.* Calcd. for $C_{11}H_{13}O_2NSBr_2$: C, 34.49; H, 3.42; N, 3.66. Found: C, 34.50; H, 3.38; N, 3.70. IR ν_{max}^{Nujol} cm^{-1}: 1330, 1150 (ν_{SO_2N}). NMR: Table III.

Reduction of 3a to 3b with Lithium Aluminum Hydride——Compound **3a** (0.5 g) dissolved in dry THF (15 ml) was added with $LiAlH_4$ (0.5 g). The mixture was refluxed for 2 hr, mixed with THF containing H_2O under cooling, and acidified with 10% HCl. The mixture was then extracted with ether, and the extract was dried (Na_2SO_4). The solvent was removed by distillation and the residue was purified through a silica gel column. Elution with CCl_4–CH_2Cl_2 (7: 3) gave an oil, bp_3 165—167°, **3b** (52%). *Anal.* Calcd. for $C_{11}H_{15}O_2NS$: C, 58.64; H, 6.71; N, 6.22. Found: C, 58.38; H, 6.71; N, 6.21. IR ν_{max}^{liquid} cm^{-1}: 1335, 1150 (ν_{SO_2N}). NMR: Table III.

2-Methyl-1-benzenesulfonylpyrrolidine (3b)——A solution of 2-methylpyrrolidine (0.8 g) prepared from N-chloro-1-aminopentane[10] in dry C_6H_6 (4 ml) was added with benzenesulfonyl chloride (0.9 g). The mixture was warmed at 100° for 10 min. Precipitated pyrrolidine hydrochloride was filtered off and the filtrate was condensed *in vacuo* to leave an oil, bp_2 161—163° (0.8 g), which was identified with **3b** by the comparison of IR spectra.

Reaction of DCBS with 1,4-Pentadiene——General procedure starting from DCBS and 1,4-pentadiene gave a mixture of products. Chromatography of this using silica gel column gave cyclized compound, **4a**, mp 61—65°, in 1.3% yield. *Anal.* Calcd. for $C_{11}H_{13}O_2NSCl_2$: C, 44.91; H, 4.45; N, 4.76. Found: C, 44.83; H, 4.45; N, 4.79. IR ν_{max}^{Nujol} cm^{-1}: 1330, 1150 (ν_{SO_2N}). NMR: Table III.

Reduction of 4a with Lithium Aluminum Hydride——Compound **4a** (0.8 g) was dissolved in dry THF (10 ml) and $LiAlH_4$ (0.8 g) was added into the solution under cooling. After reflux for 2 hr, the mixture was diluted with THF–H_2O mixture and extracted with ether. The ether layer was dried (Na_2SO_4), and the solvent was evaporated. The residue was purified by passing through a silica gel column to obtain colorless crystals, **4b**, mp 75—76° in 7% yield. *Anal.* Calcd. for $C_{11}H_{14}O_2NSCl$: C, 50.86; H, 5.43; N, 5.39. Found: C, 50.78; H, 5.33; N, 5.46. IR ν_{max}^{Nujol} cm^{-1}: 1320, 1150 (ν_{SO_2N}). NMR: Table III. From the other fraction of the chromatography, an oil, bp_2 160—165° (30%), was obtained which was identical with **3b** in the comparison of IR spectra.

Reaction of DBBS with 1,4-Diphenyl-1,3-butadiene——To a solution of 1,4-diphenyl-1,3-butadiene (4.1 g, 0.02 mole) in CH_2Cl_2 (100 ml), DBBS (6.3 g, 0.02 mole) in CH_2Cl_2 (50 ml) was dropwise added under stirring at room temperature during 40 min. The stirring was continued for 8 hr. Crystals separated were collected

and recrystallized from EtOH to give **17**, mp 249—251° (7.6%). *Anal.* Calcd. for $C_{16}H_{14}Br_4$: C, 36.58; H, 2.68. Found: C, 36.76; H, 2.70. This compound was identified with authentic sample[9] by mixed melting point determination. The filtrate of crystals of **17** was stirred with 10% aq. $NaHSO_3$ (30 ml) until KI-stach test showed negative. After washing with H_2O and drying with Na_2SO_4, the CH_2Cl_2 layer was condensed. The residue was fractionated by chromatography on a silica gel column. Elution with $CHCl_3$–hexane mixture gave crystals of crude **5**. Recrystallization from EtOH gave crystals, mp 189—190° (9.2%). *Anal.* Calcd. for $C_{22}H_{19}O_2NSBr_2$: C, 50.59; H, 3.67; N, 2.69. Found: C, 50.55; H, 3.71; N, 2.82. IR ν_{max}^{Nujol} cm^{-1}: 1330, 1150 (ν_{SO_2N}). NMR: Table III.

Reaction of DBBS with 1,4-Cyclohexadiene——To a solution of 1,4-cyclohexadiene (2.4 g, 0.03 mole) in CH_2Cl_2 (100 ml), DBBS (9.8 g, 0.03 mole) in CH_2Cl_2 (100 ml) was dropwise added with stirring at −50° during 4 hr. The stirring was continued for additional 2 hr at the same temperature. Active bromine remained in the mixture was reduced with 20% aq. $NaHSO_3$, and the organic layer was washed with H_2O, dried over Na_2SO_4, and condensed to leave crude product. It was chromatographed on a silica gel column eluting with hexane, hexane–$CHCl_3$, successively. From the first fraction, *trans*-4,5-dibromo-1-cyclohexene, **16**,[10] was obtained. mp 34—36° (from *n*-hexane) (1.7 g, 22.6%). *Anal.* Calcd. for $C_6H_8Br_2$: C, 30.03; H, 3.35; Found: C, 30.07; H, 3.26. NMR ($CDCl_3$) δ: 2.9 (4H, q, $2CH_2$), 4.5 (2H, br, BrCH), 5.65 (2H, br, -CH=CH-). The second fraction gave **15**, *trans*-5-bromo-4-benzenesulfonamidocyclohexene, as colorless crystals, mp 114—116° (from CCl_4) (5.9 g, 60%). *Anal.* Calcd. for $C_{12}H_{14}O_2NSBr$: C, 45.58; H, 4.46; N, 4.43. Found: C, 45.17; H, 4.37; N, 4.69. IR ν_{max}^{Nujol} cm^{-1}: 3200 (ν_{NH}), 1330, 1150 (ν_{SO_2N}). NMR: Table III.

Reaction of *trans*-5-Bromo-4-benzenesulfonamido-1-cyclohexene (15) with KOH——Aqueous 5% KOH (10 ml) was added to a stirred solution of **15** (1 g) in $CHCl_3$ (10 ml) under stirring during 2 hr. The organic layer was separated, washed (H_2O), dried (Na_2SO_4), and condensed. The residue was crystallized from CCl_4 to give crystals of mp 87°, **19**, in 53% yield. *Anal.* Calcd. for $C_{12}H_{13}O_2NS$: C, 61.25; H, 5.57; N, 5.95. Found: C, 61.05; H, 5.45; N, 5.95. IR ν_{max}^{Nujol} cm^{-1}: 1350, 1150 (ν_{SO_2N}). NMR: Table III.

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