[Chem. Pharm. Bull. 17(3) 523—527 (1969)]

UDC 547.541-117.11-114.04

Reaction of N-Haloamide. VIII.[1] Reactions of N-Bromobenzenesulfonamides or Bromine with Benzylamines[2]

Shoji Takemura, Hiromi Terauchi, Yoshiko Kamiya, and Yoshio Ueno

Faculty of Pharmacy, Kinki University[3]

(Received August 5, 1968)

Reaction of N-bromo-N-benzylbenzenesulfonamide (**2**), N,N-dibromobenzenesulfonamide, and bromine with benzylamines were studied.

Tertiary benzylamine degraded to secondary benzylamine hydrobromide and benzaldehyde, secondary benzylamine to primary benzylamine hydrobromide and benzaldehyde, and primary benzylamine to ammonia, benzaldehyde, and primary benzylamine hydrobromide in moist benzene.

When the reaction was carried out in dried medium, several intermediates such as salts of benzalbenzylamine (**8**,**9**) and benzalbenzenesulfonamide were identified. The structure of an intermediate, benzalbenzylamine hydrobromide perbromide (**9**) was established.

Results of the previous study of a cleavage reaction of ethers with N-halosulfonamide[4] have led us to the further investigation of the reaction of N-halosulfonamide with amines, and the present paper relates to the degradation of tertiary, secondary, and primary benzylamines with bromine, and with N-bromobenzenesulfonamides, and also to the intermediates of these reactions.

Concerning the reaction of tertiary benzylamine with bromine, Böhme and Krause[5] studied on the formation of bromine-addition compound and thermal decomposition of it, and they found that this addition compound was readily hydrolyzed to secondary benzylamine hydrobromide and benzaldehyde.

Henbest and Dunstan,[6] and Horner, Winkelmann, Knapp, and Ludwig[7] independently reported on the reaction of tertiary benzylamine with N-bromosuccinimide (NBS). They pointed out that secondary benzylamine hydrobromide and benzaldehyde were formed *via* a heat-labile oily complex or a reddish yellow intermediate. Horner, *et al.*[7] gave to this intermediate a structure of α-monobromotribenzylamine although no positive evidence for the structure was presented by them.

Reaction of N-bromo-N-benzylbenzenesulfonamide (2) with Benzylamines

By heating in moist benzene, N-bromo-N-benzylbenzenesulfonamide (**2**) decomposed tertiary benzylamine to secondary benzylamine hydrobromide and benzaldehyde, secondary benzylamine to primary benzylamine hydrobromide and benzaldehyde, and primary benzylamine to ammonia, benzaldehyde, and benzylamine hydrobromide.

1) Part VII: Y. Kamiya (née Ando), S. Takemura, and Y. Ueno, *Chem. Pharm. Bull.* (Tokyo), **17**, 520 (1969).
2) Presented in brief at the 16th Meeting of Kinki Branch of the Pharmaceutical Society of Japan, Osaka, November, 1966.
3) Location: *Kowakae, Higashi-Osaka, Osaka.*
4) S. Takemura, Y. Ando, H. Terauchi, and Y. Ueno, *Chem. Pharm. Bull.* (Tokyo), **15**, 1331 (1967).
5) H. Böhme and W. Krause, *Chem. Ber.*, **84**, 170 (1951).
6) S. Dunstan and H.B. Henbest, *J. Chem. Soc.*, **1957**, 4905.
7) L. Horner, E. Winkelmann, K.H. Knapp, and W. Ludwig, *Chem. Ber.*, **92**, 288 (1959).

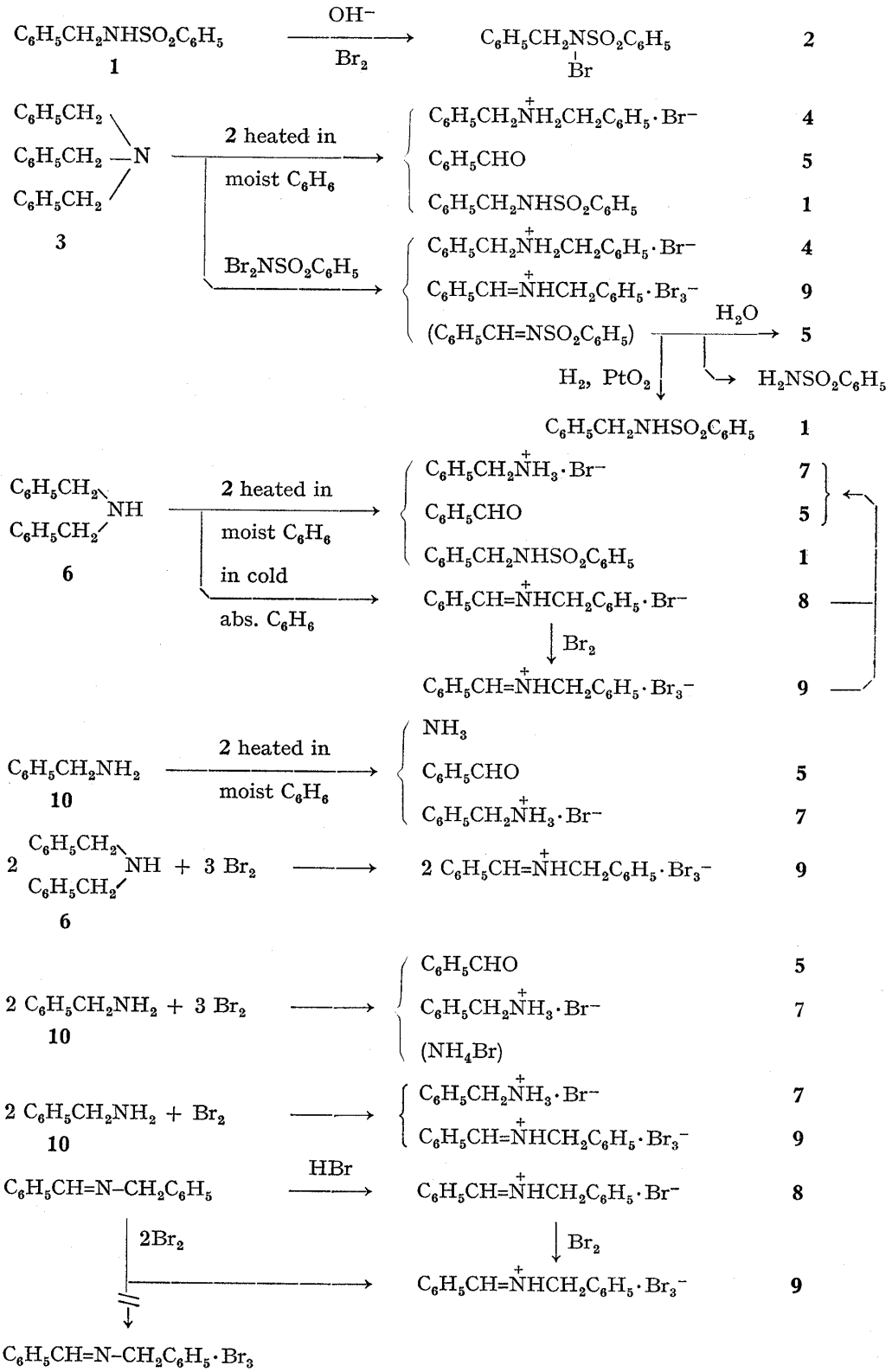


Chart 1

In case absolute benzene instead of moist benzene was used as a solvent, intermediates could be isolated. Namely, the reaction of secondary benzylamine with equimolar **2** gave benzalbenzylamine (**8**) as a labile oil which was readily hydrolyzed with water even at room temperature to benzaldehyde and primary benzylamine hydrobromide. **8** was further converted to perbromide (**9**) by the treatment with bromine.

Reaction of N,N-Dibromobenzenesulfonamide with Tertiary Benzylamine

Reaction between equimolar amounts of N,N-dibromobenzenesulfonamide and tertiary benzylamine in benzene afforded secondary benzylamine hydrobromide and benzalbenzylamine hydrobromide perbromide (**9**) in each one half molar amount. Then, after the removal of these products, the mother liquor was hydrolyzed to give benzenesulfonamide and benzaldehyde quantitatively. In another run, the said mother liquor was evaporated to dryness and the residue was catalytically hydrogenated over platinum oxide and N-benzylbenzenesulfonamide (**1**) was obtained. This fact suggests the presence of benzalbenzenesulfonamide in the raeaction mixture.

Structure of 9

Since the compound **9**, $C_{14}H_{14}NBr_3$, showed typical absorptions of ammonium group ($-CH=\overset{+}{N}-$) at 1670 cm^{-1} and ammonium group ($-CH_2-\overset{+}{N}=$) at 1420 cm^{-1}, and was easily converted from benzalbenzylamine hydrobromide (**8**) with bromine, the structure of this compound was presumed to be perbromide of **8** or a benzalbenzylammonium tribromide.

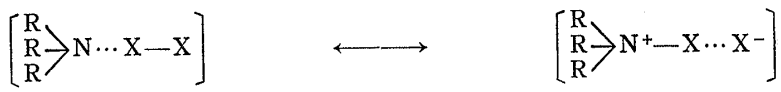
Franzen, Wegrzyn, and Kritschewsky[8] reported that benzalbenzylamine reacts with two molar bromine in cold chloroform affording a compound of mp 147° and they gave to it a structure of benzalbenzylamine tribromide, $C_{14}H_{13}NBr_3$. However, our compound **9** was found to be identical with Franzen's tribromide in view of their infrared spectra and by the mixed melting point determination. We give the structure, **9** to this compound on the following supplementary evidences. Thus, the yield of the compound by the reaction of the hydrobromide of benzalbenzylamine with bromine was quantitative while Franzen's method gave only 50% yield of it, the analitical results were more agreeable with $C_{14}H_{14}NBr_3$ than with $C_{14}H_{13}NBr_3$, and the existence of immonium and ammonium absorptions in the infrared region suggests the presence of the partial structure, $-CH=\overset{+}{N}H-CH_2-$.

Degradation of Benzylamines with Bromine

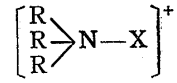
Secondary benzylamine and bromine were allowed to react in 2:3 molar ratio in benzene and benzalbenzylamine hydrobromide perbromide (**9**) was obtained in good yield.

In the case of reacting two molar primary benzylamine with one molar bromine, benzaldehyde and primary benzylamine hydrobromide were isolated, and when three molar bromine was allowed to react with two molar primary benzylamine, the isolated products were primary benzylamine hydrobromide and **9**.

It is known that, since amines are strong electron donors, they form charge transfer complexes with halogens



and, on the other hand, it also afford complexes which have a character of salt with halogens.[9]

Böhme and Krause[5] described on the formation of the latter complex  of tribenzylamine which was pointed out by Hantzsch.[10]

In our experiments, these types of complexes could not be isolated but a stable charge transfer complex was obtained by the action of N,N-dibromobenzenesulfonamide with pyridine,

8) H. Franzen, H. Wegrzyn, and W. Kritschewsky, *J. Prakt. Chem.*, **95**, 389 (1917).
9) D.L. Glusker and A. Miller, *J. Chem. Phys.*, **26**, 231 (1957); O. Hassel and H. Hope, *Acta Chem. Scand.*, **14**, 391 (1960); **15**, 407 (1961).
10) A. Hantzsch, *Ber.*, **38**, 2161 (1905).

and in the reaction of bromine or N-bromosulfonamide with ether, some evidences of the formation of complex in the initial stage were obtained.[11]

Experimental

N-Bromo-N-benzylbenzenesulfonamide (2)——Bromine (16 g) was dropwise added to a mixture of a solution of N-benzylbenzenesulfonamide[12] (24.7 g) in $CHCl_3$ (60 ml) and aqueous 4% NaOH (100 ml) with vigorous stirring and cooling. The $CHCl_3$ layer was separated and dried over Na_2SO_4. Addition of *n*-hexane (100 ml) and allowing the solution to stand for 1 hr with cooling afforded pale yellow crystals. The crystals were filtered and recrystallized from $CHCl_3$–*n*-hexane to give crystals of mp 95—98°. *Anal.* Calcd. for $C_{13}H_{12}O_2NBrS$: C, 47.84; H, 3.71; N, 4.30. Found: C, 47.91; H, 3.66; N, 4.21. IR ν_{max}^{KBr} cm^{-1}: 1360, 1170 (ν_{RSO_2N}).

Reaction of N-Bromo-N-benzylbenzenesulfonamide with Tribenzylamine——Tribenzylamine (1.5 g) in C_6H_6 (5 ml) was added in small portions to a solution of N-bromo-N-benzylbenzenesulfonamide (1.6 g) in C_6H_6 (10 ml). The colorless crystals separated out and the reaction mixture was refluxed on a water bath for 20 min. After cooling, the crystals were filtered and recrystallized from 95% EtOH to give colorless needles (1 g), mp 264—266°, which were identified with authentic dibenzylamine hydrobromide (4) by mixed melting point test and the comparison of IR spectra.

After the removal of (4), the mother liquor was mixed with aqueous 40% $NaHSO_3$ (20 ml) and vigorously stirred for 30 min. The aqueous layer was separated, acidified with conc. HCl, extracted with C_6H_6, and the extract was dried over Na_2SO_4. The solution was condensed to 2 ml under reduced pressure at 40°. The condensate was mixed with MeOH (5 ml), conc. HCl (0.2 ml), and a slight excess of 2,4-dinitrophenylhydrazine and the mixture was warmed for a short time on a water bath. The separated yellow crystals were filtered and recrystallized from AcOEt to give yellow needles (0.3 g), mp 233—235°, which was identical with 2,4-dinitrophenylhydrazone of benzaldehyde. The C_6H_6 layer separated from aqueous $NaHSO_3$ was washed with H_2O, dried over Na_2SO_4, and the solvent was evaporated under reduced pressure. The residue was recrystallized from 70% EtOH to give colorless short prisms (1 g), mp 85—87°, which were identical with N-benzylbenzenesulfonamide.

Reaction of N-Bromo-N-benzylbenzenesulfonamide with Dibenzylamine——i) Reaction in moist benzene: A solution of dibenzylamine (1 g) in C_6H_6 (10 ml) was added to a mixture of N-bromo-N-benzylbenzenesulfonamide (1.6 g) and C_6H_6 (10 ml), and the reaction mixture was refluxed for 40 min on a water bath. Colorless crystals precipitated. The crystals were filtered, and purified by recrystallization from 95% EtOH to obtain colorless needles, mp 215—220° (0.8 g). These were identified with benzylamine hydrobromide by the comparison of IR spectra and by mixed fusion with authentic sample. After the removal of the crude hydrobromide crystals, the mother liquor was treated with $NaHSO_3$, the isolated benzaldehyde was converted to 2,4-dinitrophenylhydrazone (0.4 g). N-Benzylbenzenesulfonamide (1 g) was also obtained by the procedure described above.

ii) Reaction in cold absolute C_6H_6: Dibenzylamine (1 g) was dissolved in absolute C_6H_6 (10 ml), and the solution was added to a solution of N-bromo-N-benzylbenzenesulfonamide (1.6 g) in absolute C_6H_6 (10 ml) without heating. A slight excess of bromine was added to the mixture and reddish orange crystals appeared with heat evolution. These crystals were collected after cooling and recrystallized from absolute MeOH to give reddish orange plates, mp 147—149° (1.6 g), which were identical with a sample of benzalbenzylamine hydrobromide perbromide by mixed fusion and by the comparison of IR.

The mother liquor, after removal of the above perbromide, was evaporated to dryness, and the residue was extracted with ether (5 ml). The solvent was evaporated *in vacuo*, and the residue was chromatographed on a silica gel (10 g) column followed by the elution with $CHCl_3$–*n*-hexane (3:1) to obtain a small amount of a mixture of benzaldehyde and benzoic acid (detected by TLC). The subsequent elution with same solvent system gave N-benzylbenzenesulfonamide (1 g).

In another run, a mixture of N-bromo-N-benzylbenzenesulfonamide (0.8 g), dibenzylamine (0.5 g), and dried C_6H_6 (10 ml) was warmed for 5 min. A yellow oil precipitated was identified with authentic benzalbenzylamine hydrobromide by the comparison of IR. IR ν_{max}^{KBr} cm^{-1}: 1680 ($\nu_{C=N^+}$), 1420 ($\delta_{-CH_2-N^+}$), 1610, 750, 700 ($\delta_{C_6H_5-}$). This hydrobromide was unstable and easily decomposed into benzylamine hydrobromide and benzaldehyde even with moist air.

Reaction of N-Bromo-N-benzylbenzenesulfonamide with Benzylamine——A solution of N-bromo-N-benzylbenzenesulfonamide (1.6 g) in C_6H_6 (10 ml) was mixed with a mixture of benzylamine (1 g) and C_6H_6 (10 ml), and the whole mixture was refluxed for 10 min on a water bath. Colorless crystals separated out from the solution with a simultaneous evolution of ammonia. It was detected by Nessler's reagent. After

11) On the formation of the complexes between pyridine or ethers and bromine or N-bromosulfonamide will be reported in a later paper in detail.

12) O. Hinsberg, *Ann.*, 265, 183 (1891).

cooling, the crystals were collected and recrystallized from 95% EtOH to give crystals, mp 215—220° (0.8 g), which were identical with the authentic benzylamine hydrobromide. After the removal of the hydrobromide from the mother liquor, benzaldehyde and N-benzylbenzenesulfonamide in theoretical yields. The former was confirmed as its 2,4-dinitrophenylhydrazone.

Reaction of N,N-Dibromobenzenesulfonamide with Tribenzylamine——A solution of tribenzylamine (2.9 g) in absolute C_6H_6 (10 ml) was dropwise added to a solutioh of N,N-dibromobenzenesulfonamide (3.1 g) in absolute C_6H_6 (50 ml) with stirring at room temperature. After the addition was completed, the stirring was continued for 30 min, and the mixture was heated on a water bath for 10 min. The hot reaction mixture was filtered and the resulting crystals (1.4 g) were recrystallized from 95% EtOH to give crystals of mp 264—266°. These were identical with authentic dibenzylamine hydrobromide. After the removal of the hydrobromide, the hot mother liquor was cooled and reddish orange solid separated out (1.8 g) was recrystallized from absolute MeOH to give reddish orange plates, mp 147—149°. These were identified with a sample of benzalbenzylamine hydrobromide perbromide by a mixed melting point determination and the comparison of IR. After the removal of the perbromide, the mother liquor was allowed to stand for 48 hr and benzenesulfonamide (1.5 g) was obtained. The filtrate after removal of the above amide was concentrated to 5 ml, then MeOH (5 ml), conc. HCl (1 ml), and a slight excess of 2,4-dinitrophenylhydrazine were added, and the mixture was warmed for a short time on a water bath. The separated crystals, after recrystallization, were identified with a sample of 2,4-dinitrophenylhydrazone of benzaldehyde.

In another run, after the crystals of benzalbenzylamine hydrobromide perbromide were removed, the mother liquor was condensed *in vacuo* to leave an oily substance which have an odor of benzaldehyde. The residue was hydrogenated on platinum oxide (0.5 g) in MeOH (50 ml). After the uptake of hydrogen was subsided, the catalyst was removed, the filtrate was condensed *in vacuo*, and the residue was chromatographed on a silicagel column (1 × 10 cm). Elution of the column with $CHCl_3$ afforded N-benzylbenzenesulfonamide (0.2 g), and the subsequent elution with MeOH gave benzenesulfonamide (0.7 g).

Benzalbenzylamine Hydrobromide Perbromide (9)——A solution of benzalbenzylamine (0.54 g) in $CHCl_3$ (5 ml) was saturated with HBr, and bromine (0.5 g) in $CHCl_3$ (1 ml) was added to the solution. The mixture was allowed to stand for 2 hr and the separated reddish orange crystals were filtered. Recrystallization of them from absolute MeOH gave plates, mp 147—149°, which showed no melting point depression by admixing with Franzen's benzalbenzylamine tribromide[8] and IR of both samples were also completely identical. The yield of this compound by Franzen's method was below 50% of theory while our process gave quantitative yield. *Anal.* Calcd. for $C_{14}H_{14}NBr_3$: C, 38.54; H, 3.24; N, 3.21. Found: C, 38.86; H, 3.14; N, 3.08. IR ν_{max}^{KBr} cm^{-1}: 1670 ($\nu_{C=N^+}$), 1420 ($\delta_{-CH_2N^+}$), 1600, 750, 700 ($\delta_{C_6H_5-}$).

Reaction of Bromine with Dibenzylamine——A solution of bromine (12.4 g) in C_6H_6 (15 ml) was added to a mixture of dibenzylamine (2 g) and C_6H_6 (20 ml) at room temperature with vigorous stirring. A small amount of crystals appeared were identified with authentic benzylamine hydrobromide. The whole mixture was refluxed on a water bath for 15 min, meanwhile the crystals were dissolved. After allowing the mixture to stand at room temperature, the separated red crystals (3.3 g) were recrystallized from absolute MeOH, and identified as benzalbenzylamine hydrobromide perbromide (9).

Reaction of Bromine with Benzylamine——i) Reaction of 1 Molar Br_2 with 2 Molar Amine: Br_2 (0.4 g) in C_6H_6 (10 ml) with stirring at room temperature. White precipitate which was identified as benzylamine hydrobromide after purification was obtained. The mother liquor obtained by the filtration of the crude hydrobromide was treated with $NaHSO_3$ solution and 2,4-dinitrophenylhydrazine as described above, and the hydrazone of benzaldehyde was obtained (0.002 g).

ii) Reaction of 3 Molar Br_2 with 2 Molar Amine: A solution of Br_2 (1.2 g) in C_6H_6 (10 ml) was added to a mixture of benzylamine (0.5 g) and C_6H_6 (10 ml), meanwhile the reaction mixture colored red and a precipitate was obtained. The solid was recrystallized to give colorless crystals (0.4 g), which were identified with authentic benzylamine hydrobromide. After the removal of the hydrobromide, the filtrate was allowed to stand to obtain a small amount of red crystals, which were idenitical with the perbromide (9).