Summary

Several kinds of 1,5-substituted *s*-triazolidino〔1,2-*a*〕-*s*-triazolidine-3,7-dithiones and 1,5-substituted 3,7-bisalkylthio-*s*-triazolino〔1,2-*a*〕-*s*-triazolines (see Tables I and II) were synthesized and their chemical structure was determined from their chemical and spectroscopic properties.

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15. Makoto Yokoo : Application of Azotometry. XVI.* Quantitative Determination of Secondary Amines.

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There are found many reports on the qualitative determination of secondary amines, but methods for their quantitative determination are very few, such as the polarographic[1] or colorimetric[2] method.

Since Alekseev[3] previously announced that secondary amines can be converted into hydrazine derivatives via nitrosamines and since hydrazines can be readily determined by Iwasaki's azotometry[4] the author attempted utilization of this reaotion for the quantitative determination of secondary amines and succeeded in establishing a new method. The method was carried out after the following scheme.

$$\rangle NH + HNO_2 \longrightarrow \rangle N{\cdot}NO \xrightarrow{Zn + HCl} \rangle N{\cdot}NH_2 \xrightarrow[AZM]{K_3Fe(CN)_6} N_2\uparrow$$

Amines determined by this method were various kinds of secondary amines such as dimethylamine, diethylamine, dibenzylamine, diphenylamine, proline, and kainic acid. Of these amines, dimethylamine, diethylamine, and dibenzylamine were used as their hydrochlorides and the others as such after purification by recrystallization.

It was also found that coexistence of a primary and a tertiary amine dose not affect the value.

Method

1) **Reagents :**
   - i) Potassium nitrite solution : ca. 600 mg./cc.
   - ii) Sulfaminic acid solution : 200 mg./cc.
   - iii) Zinc powder
   - iv) Devarda's alloy : Al 45%, Cu 50%, Zn 5%.
   - v) Potassium ferricyanide solution : $K_3Fe(CN)_6$ 5 g, $NaNO_2$ 70 g, H_2O 100 cc.

2) **Procedure :**
   About 0.2 or 0.1 m.mole of a sample is weighed exactly and dissolved in a flask or

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1) A.A. Smales : J. Soc. Chem. Ind. (London), **67**, 210(1948).
2) S.J. Clark : Mikrochim. Acta, **1956**, 967.
3) N.F. Alekseev : C.A., **50**, 4722(1956).
4) K. Iwasaki : Seikagaku, **23**, 207(1951).

test tube by addition of 1 cc. of water and 0.5 cc. of glacial AcOH, 0.5 cc. of the KNO_2 solution is added, the vessel is stoppered, and left standing at 30° for 30 mins. After lapse of the time, the sulfaminic acid solution is added to decompose the excess HNO_2. In this case it is necessary to restrict the amount of the sulfaminic acid solution to a little excess, and for the purpose ca. 1~1.5 cc. of the solution is generally required. Addition of the solution is made under cooling because heat evolves strongly. Next, 2 g. of Zn powder is added gradually with cooling and shaking. After the warming slows down, 2 cc. of conc. HCl is added and the mixture is shaken vigorously for 10 mins. The same operation is repeated twice more but using 1 cc. of HCl each time. Thus, after reduction for 30 mins. in total, 0.5~1 g. of Devarda's alloy powder is added and the mixture is allowed to stand for 30 mins. with occasional shaking. The reaction mixture is then filtered through a sintered glass filter, the residue is washed with water, the filtrate is combined with the washing, and diluted exactly to 50 cc. to make a test solution.

A 1-cc. portion of the test solution is placed in the Iwasaki's azotometer,[4] the air in the meter is completely replaced by CO_2 gas and 1 cc. each of the $K_3Fe(CN)_6$ solution and 30% NaOH solution are introduced into the meter to conduct the ferricyanide-azotometry, whereupon the CO_2 gas is absorbed in the NaOH solution and the sample is oxidized by the $K_3Fe(CN)_6$ to give off N_2 gas.

The volume (V_t mm^3) of the N_2 generated is converted to that (V_0) of dry N_2 at 0°C, 760 mm. by the equation (a).

$$V_0 = fVt, \quad f = \frac{P_0 - P_w}{(1+\alpha t)\times 760} \qquad (a)$$

where P_0 = pressure (mm. Hg)
P_w = maximum vapor pressure of water at $t°$
α = average coefficient of expansion of N_2(0.00367)
t = temperature

Since 10^{-6} mole of a $>N-NH_2$ compound generates 11.2 mm^3 of N_2 gas, the quantity of the sample is calculated by the equation (b).

$$\text{Quantity of sample (mg.)} = \frac{V_0\times M\times 50}{11.2\times 1000} = \frac{V_0\times M\times 5}{1120} \qquad (b)$$

M=Molecular weight of the sample

Result

1) Results of determination with dimethylamine, diethylamine, dibenzylamine, and diphenylamine are shown in Table I.

2) Results of determination with proline and kainic acid are shown in Table II.

Table I.

Sample	Weighed (mg.)	N_2 V_0 measured (mm^3)					Sample detd. (mg.)	Recovery (%)
		1	2	3	4	mean		
Dimethylamine-HCl	8.20	22.8	22.3	22.5	22.3	22.4	8.15	99.4
〃	17.80	48.6	48.5	48.4	48.6	48.5	17.65	99.2
Diethylamine-HCl	11.60	23.8	23.9	23.7	24.0	23.9	11.70	100.8
〃	21.90	44.4	44.7	44.4	44.3	44.5	21.75	99.3
Dibenzylamine-HCl	28.30	27.0	26.9	27.2	27.0	27.0	28.15	99.4
Diphenylamine	20.80	27.7	27.9	27.6	27.9	27.8	21.00	100.9

Table II.

Sample	Weighed (mg.)	N_2 V_0 measured (mm^3)					Sample detd. (mg.)	Recovery (%)
		1	2	3	4	mean		
Proline	23.10	45.5	45.5	45.1	45.2	45.3	23.30	100.8
Kainic acid	40.70	42.8	42.5	42.2	42.7	42.5	40.45	99.4

Discussion

1) Nitrosation

As already studied extensively, nitrosation of secondary amines gives different results depending on various conditions such as quantity and concentration of the nitrous acid used and reaction temperature. In the present work the nitrosation was naturally conducted bearing this point in mind. About 30~50 moles of nitrous acid to 1 mole of the amine was sufficient and a concentration of 2~3*M* of the acid was suitable. After various studies it was found convenient to conduct the nitrosation at 30° for 30 minutes because a higher temperature volatilizes the nitrous acid and a lower temperature prolongs the reaction.

2) Reduction

The reduction is effected first with zinc powder and hydrochloric acid and then with Devarda's alloy. For, though a majority of excess nitrous acid is decomposed by sulfaminic acid after nitrosation, a part of it decomposes into nitric acid during the reaction as shown below :

$$3\,HNO_2 \longrightarrow HNO_3 + 2NO + H_2O$$

The nitric acid and other nitrogen compounds thus produced are converted by subsequent reduction into hydroxylamine and the like which generate nitrogen gas by the ferricyanide-azotometry. It is necessary, therefore, to reduce the nitric acid and the other nitrogen compounds with Devarda's alloy into ammonia which is harmless in Iwasaki's azotometry.

It may appear better to conduct the reduction with Devarda's alloy from the beginning, but nitrosamines, when reduced with a metal other than zinc and a mineral acid, is partly reverted to the original amines by the following reaction, while some nitrosamines are hardly reduced by such a method.

$$\rangle N\text{-}NO + H_2O \longrightarrow \rangle NH + HNO_2$$

After all, the above-mentioned method was found to be the best.

3) Azotometry of $>N\text{-}NH_2$ Compounds

$>N\text{-}NH_2$ Compounds may be determined by Iwasaki's ferricyanide-azotometry as well as by nitrite-azotometry.[5] The first method was adopted because in the latter method the sulfaminic acid used for decomposition of the excess nitrous acid hampers the generation of nitrogen gas from nitrous acid and makes the procedure complicated.

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Summary

Some secondary amines were reacted with nitrous acid to produce the corresponding nitrosamines, which were further led to N-amino compounds by reduction with zinc powder and hydrochloric acid and the products were determined quantitatively by Iwasaki's ferricyanide-azotometry, which comprises of oxidizing the amino compounds with potassium ferricyanide to generate nitrogen gas quantitatively.

By this method 0.1~0.2 mole each of dimethylamine, diethylamine, dibenzylamine, diphenylamine, proline, and kainic acid were determined with an accuracy of ±1%.

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5) M. Yamagishi, M. Yokoo : Yakugaku Zasshi, **74**, 278(1954).