NOTES

BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 271—272 (1971)

Studies of the *N*-Oxides of *N,N*-Dialkylamino Acids. IV. The Decarboxylation of *N,N*-Dimethylamino Acid *N*-Oxides with *p*-Toluenesulfonyl Chloride in Pyridine

Yoshikazu Ikutani
Department of Chemistry, Osaka Kyoiku University, Tennoji-ku, Osaka

(Received December 30, 1969)

Though many investigations have been made of the reactions between heteroaromatic tertiary amine *N*-oxides and acylating reagents, little attention has been paid to the similar reactions of aliphatic tertiary amine *N*-oxides especially *N,N*-dialkylamino acid *N*-oxides.

In the previous papers of this series, the preparations of *N*-oxides of *N,N*-dimethyl neutral amino acids,[1] *N,N*-dialkylglycine,[2] and *N,N*-dimethyl acidic amino acids[3] were investigated. In the present study, the decarboxylations of *N,N*-dimethylamino acid *N*-oxides with *p*-toluenesulfonyl chloride in pyridine and the hydrolysis of the reaction products have been investigated.

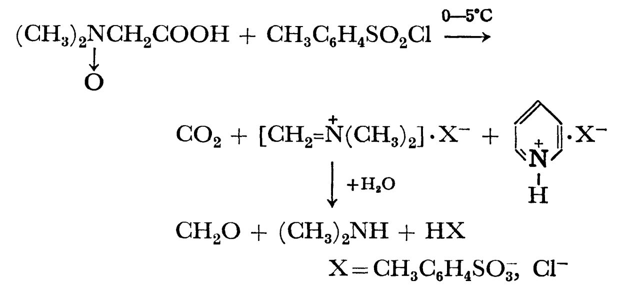
The evolution of carbon dioxide was observed immediately when *N,N*-dimethylamino acid *N*-oxide was treated with an equivalent amount of *p*-toluenesulfonyl chloride in pyridine at 5°C or below. The mixture, when allowed to stand for about a half an hour with shaking, turned a light red-brown. The carbon dioxide generated was collected as barium carbonate and weighed. The results thus obtained are shown in Table 1.

Table 1. The decarboxylation of *N,N*-dimethylamino acid *N*-oxide with *p*-toluenesulfonyl chloride in pyridine

Parent amino acid	Yields of carbon dioxide (%)
Gly	80
DL-Ala	33
DL-Val	16
L-Glu	57
L-Phe	74

In the reaction of *N,N*-dimethylglycine *N*-oxide with *p*-toluenesulfonyl chloride, the reaction mixture was concentrated to remove the excess pyridine; the residue was then treated with hot acetone to remove the pyridine hydrochloride and the pyridine hydro-*p*-toluenesulfonate. All attempts to obtain any crystalline product from the dark red-brownish sticky residue failed, but the following experiments confirmed the syrup to be a mixture of *N,N*-dimethyl-methyleneimmonium chloride and *p*-toluenesulfonate. The acid hydrolysis of the syrup gave formaldehyde and dimethylamine.

Further experiments with ion-exchange resin were performed in order to confirm the structure of the reaction product. The decarboxylation was performed much as has been described above, and the residue was dissolved in water. A half of the resulting solution was deposited on an ion-exchange column (Amberlite IRA-410, OH-form); it was then eluted with water. The eluate was hydrolysed much as has been described above. Formaldehyde as 2,4-dinitrophenylhydrazone and dimethylamine as *p*-toluenesulfonamide were obtained in almost quantitative yields. Another half of the resulting solution was deposited on an ion-exchange column (Amberlite IR-120, H-form), and subsequently eluted with water. The eluate included *p*-toluenesulfonic acid and hydrochloric acid. A part of the effluent was titrated directly, and another part was dried up in order to remove the hydrochloric acid, dissolved in water, and titrated. The value of the former was 2.02 equivalents of the corresponding *N*-oxide, while the value of the latter was 0.98. These results indicate that the formation of the immonium salts and the reaction mechanism shown in Fig. 1 may be postulated.



$$(CH_3)_2\underset{\downarrow\atop O}{N}CH_2COOH + CH_3C_6H_4SO_2Cl \xrightarrow{0-5^\circ C}$$

$$CO_2 + [CH_2{=}\overset{+}{N}(CH_3)_2]\cdot X^- + \ldots$$

$$\downarrow{+H_2O}$$

$$CH_2O + (CH_3)_2NH + HX$$

$$X = CH_3C_6H_4SO_3^-,\ Cl^-$$

Fig. 1

Experimental

The Decarboxylation of N,N-*Dimethylglycine* N-*Oxide with* p-*Toluenesulfonyl Chloride in Pyridine.* In a flask, 3.5 g of *N,N*-dimethylglycine *N*-oxide were placed, the flask was cooled in an ice bath to 5°C or below, and then 5.7 g of *p*-toluenesulfonyl chloride in 20 m*l* of pyridine were added, drop by drop with shaking, over a period of approximately 15 min, after which the mixture was shaken for more than 15 min. At the end of the reaction, the evolution of carbon dioxide ceased. The carbon dioxide generated was led into

---

[1] Y. Ikutani, This Bulletin, **41**, 1679 (1968).

[2] Y. Ikutani, *ibid.*, **42**, 2330 (1969).

[3] Y. Ikutani, *ibid.*, **43**, 3602 (1970).

a solution of barium hydroxide with nitrogen gas; 4.7 g of barium carbonate were thus obtained. The reaction mixture was concentrated under reduced pressure to remove the excess pyridine. The residue was then extracted with three 20 m*l* portions of hot acetone. The combined extract was concentrated under reduced pressure and stored in a refrigerator overnight. Pyridinium *p*-toluenesulfonate (5.1 g) was thus obtained as a precipitate. The filtrate was then dried up under reduced pressure; 1.2 g of pyridine hydrochloride were obtained. The extracted remnant was washed with ether several times and dried under reduced pressure. It was then dissolved in 100 m*l* of water, controlled to pH 2 with hydrochloric acid. To a half of the resulting solution, a mixture of 3.0 g of 2,4-dinitrophenylhydrazine, 15 g of concentrated sulfuric acid, 20 m*l* of water, and 70 m*l* of ethanol was added; the solution was then allowed to stand at room temperature for a few days. The yield of 2,4-dinitrophenylhydrazone of formaldehyde thus obtained was 3.1 g. To the other half of the solution, 15 m*l* of 2N hydrochloric acid were added, and the mixture was allowed to stand at room temperature for 5 days. To the resulting solution 5.0 g of *p*-toluenesulfonyl chloride were added, and then 2N aqueous sodium hydroxide was added with vigorous stirring to keep the mixture in a weak alkaline condition overnight. The precipitates were then collected by filtration, washed with water, and dried under reduced pressure to yield 2.2 g of *N*,*N*-dimethyl-*p*-toluenesulfonamide.

In another experiment, the decarboxylation of 2.4 g of *N*,*N*-dimethylglycine *N*-oxide and 3.8 g of *p*-toluenesulfonyl chloride in 15 m*l* of pyridine was performed in a manner similarly to that described above. After the completion of the reaction, 30 m*l* of water were added. A half of the resulting solution was deposited on an ion-exchange column of Amberlite IRA-410 (OH-form), and then eluted with water. The eluate was collected until it became neutral. To a half of the effluent, 25 m*l* of 2N hydrochloric acid, and then a mixture of 2.0 g of 2,4-dinitrophenylhydrazine, 10 g of concentrated sulfuric acid, 15 m*l* of water, and 50 m*l* of ethanol, were added. The mixture was allowed to stand at room temperature, and then it was heated at 80°C for 6 hr. 2,4-Dinitrophenylhydrazone of formaldehyde (1.0 g) was thus obtained. To one half of the effluent, 25 m*l* of 2N hydrochloric acid were added. When the mixture was treated much as has been described above, 0.90 g of *N*,*N*-dimethyl-*p*-toluenesulfonamide was obtained. The other half of the resulting solution was deposited on a column of Amberlite IR-120 (H-form) and then eluted with water. The effluent was diluted to 250 m*l* with water. The titration of 25 m*l* of the resulting solution with 0.1N (f=1.14) aqueous sodium hydroxide, using phenolphthalein as an indicator, required 17.93 m*l*. Another 25 m*l* portion of the resulting solution was dried up under reduced pressure and dissolved in 20 m*l* of water. The titration required 8.50 m*l* of 0.1N (f=1.14) aqueous sodium hydroxide.

The author is indebted to Professor Eizo Matsumura for his constant guidance in the course of the work, and to Professor Yoshiharu Izumi of Osaka University for his valuable advice and encouragement.