[Contribution from the Chemical Laboratory of the Academy of Commerce in Vienna]

BROMINATION OF *o*-ACETANISIDIDE, *o*-ANISIDINE, AND A MOLECULAR REARRANGEMENT IN THE BROMINATION OF 4,5-DIBROMO-*o*-ANISIDINE

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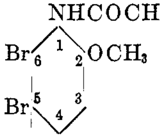
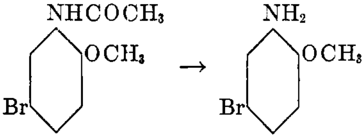
In the bromination of *o*-acetanisidide with 2 moles of bromine in glacial acetic acid Bureš and Souček (1) prepared a dibromo-*o*-acetanisidide (m.p. 146°) which they declared to be 5,6-dibromo-*o*-acetanisidide (I). Later on Madesani (2) repeated these experiments and he also assigns to this compound the structure I. However, Madesani found, that by cautious bromination with one mole of bromine a monobromo-*o*-acetanisidide can be obtained which is 5-bromo-*o*-acetanisidide (II), because upon saponification it yields 5-bromo-*o*-anisidine (III). Therefore it had to be expected with greatest probability that according to the rules of substitution the second bromine atom would enter the position 4 forming 4,5-dibromo-*o*-acetanisidide (IV). Less probable seemed the formation of I and improbable the formation of V. In order to make a decision among these three possibilities (I, IV, V) the dibromo-*o*-acetanisidide was saponified to the corresponding dibromo-*o*-anisidine and the latter was diazotized and the diazo-group replaced by bromine by the Sandmeyer reaction. The tribromoanisole (m.p. 102–104°) formed in this way was nitrated to the tribromonitroanisole (m.p. 71–72°). I should yield in this sequence of reactions 2,3,4-tribromoanisole (m.p. 106°) (3) (VI) and 2,3,4-tribromo-6-nitroanisole (m.p. 109–110°) (4) (VII); IV should yield 2,4,5-tribromoanisole (m.p. 105°) (5) (VIII) and 3,4,6-tribromo-2-nitroanisole (m.p. 70–72°) (6) (IX); and V should yield 2,4,6-tribromoanisole (m.p. 87°) (7) (X) and 2,4,6-tribromo-3-nitroanisole (m.p. 80–82°) (8) (XI). These data lead to the unquestionable conclusion that the dibromo-*o*-acetanisidide is IV.

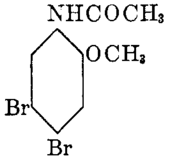


I



II

III



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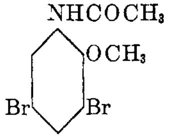

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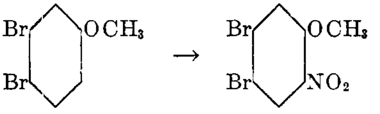

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VII

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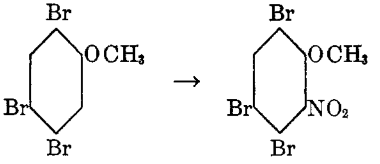
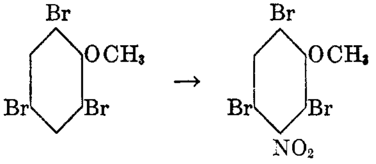


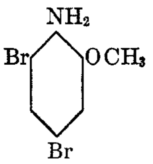
VIII IX



X XI

In the bromination of *o*-anisidine Fuchs (9) obtained 4,6-dibromo-*o*-anisidine (XII). However, Madesani (2) found that by cautious bromination a monobromo-*o*-anisidine can be prepared which can be either 4-bromo-*o*-anisidine (XIII) or 6-bromo-*o*-anisidine (XIV). According to the rules of substitution XIII was more probable than XIV. However, Madesani (2) concluded that his substance is 6-bromo-*o*-anisidine (XIV), because the corresponding bromo-*o*-acetanisidide by bromination with another mole of bromine was transformed into the dibromo-*o*-acetanisidide (m.p. 146°), to which both Bureš and Souček (1) and Madesani (2) erroneously assigned the structure I. Since this investigation showed that the bibromo-*o*-acetanisidide is IV it is selfevident that Madesani's monobromo-*o*-anisidine is XIII.

When the hydrobromide of 4,5-dibromo-*o*-anisidine (XV) is brominated with one mole of bromine 4,5,6-tribromo-*o*-anisidine (XVI) is not formed as expected. A molecular rearrangement occurs with migration of the bromine atom from the 5-position to the 3-position to give 3,4,6-tribromo-*o*-anisidine (XVII) This substance is identical with the substance prepared by M. Kohn and H Karlin (10) by the bromination of *o*-anisidine and the same molecular rearrangement was observed by M. Kohn and H. Karlin (11) in the bromination of 5-bromo-*o*-anisidine (III).



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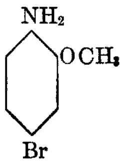

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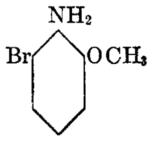
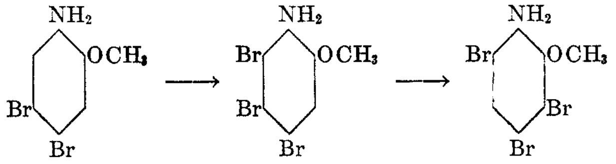


XIV



XV XVI XVII

EXPERIMENTAL

4,5-Dibromo-o-acetanisidide (IV) was prepared according to Bureš and Souček (1) (m.p. 140–143°). Bureš and Souček give the m.p. 146°.

Preparation of 4,5-dibromo-o-anisidine (XV) *hydrobromide:* 5 g. of IV, 75 ml. of hydrobromic acid (45%), and 50 ml. of water were boiled under reflux. After one hour a colorless clear solution was formed. By cooling 5.8 g. of the hydrobromide separated and was filtered. The filtrate which then also contained the acetic acid split off in the saponification could be used again for another saponification.

Preparation of 3,4,6-tribromo-2-nitroanisole (IX) *starting from the hydrobromide of 4,5-dibromo-o-anisidine* (XV). The hydrobromide (16 g.) was mixed with 700 ml. of ice-water and 8 ml. of hydrobromic acid (45%) and a solution of 3.5 g. of sodium nitrite in 200 ml. of H_2O drop by drop was added under continuous stirring until a potassium iodide starch paper gave a distinct blue coloration. The yellow solution was filtered to give a clear filtrate. Cuprous bromide was prepared from 13 g. of $CuSO_4 \cdot 5H_2O$, 14 g. of sodium bromide, and sodium sulfite. The cuprous bromide was dissolved in hydrobromic acid and a small quantity of copper powder was poured in. When this mixture was added to the diazonium solution a precipitation of the reaction product was produced immediately. The mixture began to foam and was shaken and finally heated to boiling. It was cooled down and the brown substance was filtered with suction, washed with water, and mixed with 3 ml. of 45% HBr, 100 cc. of water, and enough sodium bromide so that sodium bromide remained undissolved in the boiling mixture. The tribromoanisole was collected by a steam-distillation. The residue in the boiling flask was again mixed with water and again tribromoanisole was collected by a steam-distillation. The residue in the boiling flask contained a considerable quantity of a tarry resinous material. The crude tribromoanisole (3 g.) (VIII) was recrystallized from alcohol (m.p. 102–104°). The nitration carried out in the usual manner gave 3,4,6-tribromo-2-nitroanisole (m.p. 70–72°) (6) (IX).

Anal. Calc'd for $C_7H_4Br_3NO_3$: N, 3.59. Found: N, 3.70.

4-Bromo-o-anisidine (XIII) was prepared by bromination of *o*-anisidine. A solution of 9 ml. of bromine in glacial acetic acid was added slowly with cooling to 21 ml. of *o*-anisidine in 100 ml. of glacial acetic acid. The mixture was shaken and the hydrobromide was filtered in order to remove the brown mother liquor. The hydrobromide was decomposed by adding a small excess of potassium hydroxide with stirring. The solid precipitate was filtered, washed with water, and upon pressing with a glass stopper a brown oil was removed. The yield of the crude vacuum-dried product was 29 g. A sample of the substance, recrystallized from alcohol melted at 61°. Another recrystallization from ligroin and benzine raised the m.p. to 63°. *Madesani* (2) gives 65°. The bromination of the acetyl derivative (m.p. 164–167°) of this substance yielded an acetyl derivative which, recrystallized from alcohol, had m.p. 140–143°. The mixture m.p. of this acetyl derivative and the acetyl derivative prepared according to *Bureš* and *Souček* (1) was 140–143°.

Bromination of 4,5-dibromo-o-anisidine (XV). The hydrobromide of 4,5-dibromo-*o*-anisidine (6 g.) was dissolved in 40 ml. of glacial acetic acid and slightly more than 1 ml. of bromine in 10 ml. of glacial acetic acid was added. The substance was filtered (7 g.), recrystallized from alcohol, and again filtered. Upon heating with water to boiling a small quantity of hydrogen bromide was removed. The pure substance when heated with water should not give any acid reaction. It was recrystallized from alcohol, m.p. 99–101°.

Anal. Calc'd for $C_7H_6Br_3NO$: N, 3.89. Found: N, 3.90.

The mixture m.p. of this substance (XVII) and the substance prepared from *o*-anisidine according to M. Kohn and H. Karlin (10, 11) gives no depression.

SUMMARY

1. Dibromo-*o*-acetanisidide, prepared by the bromination of *o*-acetanisidide and the corresponding dibromo-*o*-anisidine are not 5,6-dibromo compounds as former investigators have concluded but instead are the 4,5-dibromo compounds.

2. Bromo-*o*-anisidine, prepared by the bromination of *o*-anisidine, is not 6-bromo-*o*-anisidine as is stated in the literature but is 4-bromo-*o*-anisidine.

3. In the bromination of 4,5-dibromo-*o*-anisidine hydrobromide a molecular rearrangement takes place whereby 3,4,6-tribromo-*o*-anisidine is formed.

VIENNA, AUSTRIA

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