# LXIX.—*The Action of Alcoholic Potassium Hydroxide upon Chloronitrobenzene.*

By Donald Henry Richardson.

Heumann (*Ber.*, 1872, **5**, 910) obtained *pp*′-dichloroazoxybenzene by boiling *p*-chloronitrobenzene with alcoholic potash. Willgerodt (*Ber.*, 1879, **12**, 767) showed that *p*-nitrophenetole and *p*-nitrophenol also are products of the reaction, and later (*Ber.*, 1882, **15**, 1002) found that dilution of the alcohol with water diminishes the formation of dichloroazoxybenzene. Blom (*Helv. Chim. Acta*, 1921, **4**, 297) studied the kinetics of the reaction and found that by using aqueous alcohol at 70° no dichloroazoxybenzene is formed.

In an investigation with the object of discovering the conditions under which the maximum yield of nitrophenetole free from chloronitrobenzene could be most easily obtained, it was found that the formation of dichloroazoxybenzene could be avoided without dilution of the alcohol if the temperature was reduced to 60°, and the alkali strength to 0·2 normal. Excellent results having been obtained on the small scale, some large-scale trials were made in which 362 lb. of chloronitrobenzene were heated at 60° with 145 gallons of 0·2*N*-95% alcoholic soda, the alkali strength being maintained by the addition of the estimated amount of the powdered solid at frequent intervals. At the first attempt, in spite of considerable accidental loss, the yield amounted to 277 lb. of nitrophenetole, free from chloronitrobenzene, and containing only 3·4% of dichloroazoxybenzene, but in all subsequent experiments at least 17% of the theoretical amount of azoxy-compound was formed. It was not realised at the time that the alcohol used in the first experiment had been specially purified for pharmaceutical purposes, and the systematic investigation to be described was undertaken to discover the cause of the failure of the process.

The conclusions are as follows:

1. The presence of as much as 0·1% of acetaldehyde in the alcohol causes considerable reduction of the chloronitrobenzene, and the larger the percentage of acetaldehyde, the greater is the yield of dichloroazoxybenzene.
2. The formation of dichloroazoxybenzene may be avoided without dilution of the alcohol with water if chloronitrobenzene is heated for 140 hours at 60° in a 0·5*N*-solution of caustic potash in 95% ethyl alcohol free from acetaldehyde.
3. Under these conditions, 92% of the theoretical yield of pure *p*-nitrophenetole, 90% of *o*-nitrophenetole, and 96% of *p*-nitroanisole (using methyl alcohol) may be obtained, nitrophenol being the only by-product.
4. As the temperature or alkali concentration is raised, dichloroazoxybenzene is formed in rapidly increasing amount, even if the alcohol is free from acetaldehyde.
5. Under conditions resulting in the formation of a considerable amount of dichloroazoxybenzene, *p*-chloroaniline is also formed in appreciable quantity.
6. Although the reducing action of alcoholic alkali is decreased by dilution of the alcohol with water (Willgerodt, *loc. cit.*), this diminishes the rate of conversion of chloronitrobenzene into nitrophenetole.

7. Nitrophenol is always a by-product when chloronitrobenzene is heated with alcoholic alkali solution, and the yield is increased as the temperature and the strength of alkali are raised, but is not greatly affected by dilution of the alcohol with water.

## EXPERIMENTAL.

Five series of experiments were carried out, in each of which only one factor was subjected to variation. Pure chloronitrobenzene was heated at a constant temperature in a large excess of a standard solution of potash in alcohol of known strength. After a noted time, the solution was nearly neutralised with sulphuric acid, the alcohol distilled off, and the nitrophenetole isolated by blowing steam through the residue. Its weight and melting point were determined after filtering off and drying over calcium chloride in a vacuum desiccator. Nitrophenetole was appreciably volatile in alcohol vapour, and was estimated in the alcohol recovered by evaporating a known volume in a vacuum desiccator at laboratory temperature, and weighing the residue. Ether extraction of the filtered steam distillate showed that nitrophenetole was soluble in water at 15° to the extent of 0·11 g. per litre. The insoluble dichloroazoxybenzene was filtered off from the residual liquors, washed, dried, and weighed without further purification. After evaporation to smaller bulk, the filtrate and washings were acidified with sulphuric acid and the *p*-nitrophenol was extracted with ether.

The conditions in each series of experiments are described below, and the yields given in tabular form.

*Series* 1.—*Variation in strength of alkali.* A solution of caustic potash in 95% alcohol was standardised and diluted with the calculated volume of alcohol so that 250 c.c. each of a 0·1, 0·2, 0·3, 0·4, and 0·5 *N*-solution of potash were obtained. Exactly 4 g. of pure chloronitrobenzene were dissolved in each solution, and all were heated together in a thermostat at 60°. After 187 hours' heating, 5 c.c. of each solution were titrated with *N*/10-sulphuric acid to determine the final concentration of the potash, and the reaction products analysed as previously described. The results are tabulated below :

| Experiment. | 1. | 2. | 3. | 4. | 5. |
|---|---|---|---|---|---|
| Strength of KOH (*N*) : initial ... | 0·1 | 0·2 | 0·3 | 0·4 | 0·5 |
| ,, ,, ,, final ... | 0·013 | 0·064 | 0·165 | 0·226 | 0·405 |
| Wt. of nitrophenetole (g.) ......... | 3·19 | 3·61 | 3·24 | 2·86 | 1·91 |
| M. p. of nitrophenetole ........... | 46° | 57° | 57° | 57° | 57° |
| Wt. of dichloroazoxybenzene (g.) | 0·02 | 0·10 | 0·37 | 0·70 | 0·92 |
| Wt. of *p*-nitrophenol (g.) ......... | 0·04 | 0·09 | 0·13 | 0·28 | 0·50 |
| % Theoretical yield : | | | | | |
| Nitrophenetole.................. | 75·3 | 85·1 | 76·4 | 67·5 | 44·8 |
| Dichloroazoxybenzene ...... | 0·6 | 2·9 | 10·9 | 20·6 | 27·1 |
| Nitrophenol ...................... | 1·1 | 2·6 | 3·7 | 7·9 | 14·2 |
| Total ........................ | 77·0 | 90·6 | 91·0 | 96·0 | 86·1 |

The low melting point of the nitrophenetole obtained in experiment 1 showed that some unchanged chloronitrobenzene remained, as would be expected in view of the small final concentration of the potash in this case. A considerable amount of tarry matter was noted during the extraction of the nitrophenol in experiment 5, and a smaller amount in experiment 4. It was not found possible to account for the remainder of the yield at this point.

The results indicated that an increase in the concentration of alkali causes a greater production of both dichloroazoxybenzene and nitrophenol, this being most marked in the case of the azoxy-compound.

*Series* 2.—*Variation in strength of alcohol.* Five 0·5*N*-potash solutions were prepared, one in absolute alcohol, and the other four in 95% alcohol diluted with noted volumes of water to a total of 250 c.c. each. The five solutions were heated in a constant-temperature water-bath at 60° for 24 hours, after which 4 g. of chloronitrobenzene were dissolved in each and the heating was continued for 187 hours.

The products were analysed with the following results:

| Experiment. | 6. | 7. | 8. | 9. | 10. |
|---|---|---|---|---|---|
| Strength of alcohol (%) | 100 | 87 | 80 | 70 | 60 |
| Wt. of nitrophenetole (g.) | 3·834 | 3·497 | 3·453 | 3·348 | 3·019 |
| M. p. of nitrophenetole | 57° | 57° | 57° | 56° | 56° |
| Wt. of dichloroazoxybenzene (g.) | 0·025 | 0·129 | 0·157 | 0·071 | 0·106 |
| Wt. of nitrophenol (g.) | Lost by accident. | 0·484 | 0·488 | 0·469 | 0·455 |
| % Theoretical yield: | | | | | |
| Nitrophenetole | 90·4 | 82·5 | 81·4 | 78·9 | 71·2 |
| Dichloroazoxybenzene | 0·7 | 3·8 | 4·6 | 2·1 | 3·1 |
| Nitrophenol | ? | 13·7 | 13·8 | 13·3 | 12·9 |
| Total | (91·1) | 100·0 | 99·8 | 94·3 | 87·2 |

The melting point of the nitrophenetole obtained in experiments 9 and 10 showed that a small amount of chloronitrobenzene remained unchanged, indicating that dilution of the alcohol retards the rate of conversion of chloronitrobenzene into nitrophenetole. The most remarkable result was the very small yield of dichloroazoxybenzene in all five experiments, in spite of a concentration of potash equal to that in experiment 5, in which a 27% yield of the azoxy-compound was obtained.

The use of absolute alcohol having resulted in the smallest production of dichloroazoxybenzene, it seemed probable that some impurity in the alcohol was the cause of the formation of the azoxy-compound. Since the chloronitrobenzene is reduced to dichloroazoxybenzene, acetaldehyde would be the most likely impurity to cause this reduction. The preliminary 24 hours' heating of the alcoholic potash before the introduction of the chloronitrobenzene would have at least partly resinified the aldehyde, so accounting for the small yield of dichloroazoxybenzene in these five experiments. It was noted that a yellow colour developed in the alcoholic potash solutions during the preliminary heating, indicating the formation of aldehyde-resin.

*Series* 3.—*Effect of acetaldehyde upon the production of dichloroazoxybenzene.* To determine the effect of acetaldehyde upon chloronitrobenzene in alcoholic potash solution, a third series of five experiments was commenced, using 250 c.c. of 0·5 *N*-alkali in 95% alcohol. The chloronitrobenzene was added before heating in experiment 11, but after 66 hours' preliminary heating in experiment 12, while 25 c.c. of hydrogen peroxide solution were added in experiment 13. Methylated spirit known to contain acetaldehyde was used in experiment 14, and 10 c.c. of acetaldehyde were added to the alcohol in experiment 15, in both cases the chloronitrobenzene being added before heating was commenced. The five solutions were heated simultaneously for 235 hours at 60°, and gave the following yields on analysis :

| Experiment. | 11. | 12. | 13. | 14. | 15. |
|---|---|---|---|---|---|
| Wt. of nitrophenetole (g.) ......... | 3·69 | 3·77 | 3·58 | 2·13 | 0·82 |
| Wt. of dichloroazoxybenzene (g.) | 0·04 | 0·02 | 0·015 | 0·315 | 2·29* |
| Wt. of nitrophenol (g.) ............ | 0·43 | 0·41 | 0·52 | 0·68† | 0·67† |
| % Theoretical yield : | | | | | |
| Nitrophenetole.................. | 87·0 | 88·9 | 84·4 | 50·2 | 19·2 |
| Dichloroazoxybenzene ...... | 1·2 | 0·6 | 0·5 | 9·3 | 67·6* |
| Nitrophenol ..................... | 12·2 | 11·5 | 14·7 | 19·5† | 19·0† |
| Total ........................ | 100·4 | 101·0 | 99·6 | 79·0 | 105·8 |

* Includes aldehyde-resin. † Includes tar.

The very large yield of dichloroazoxybenzene in the presence of acetaldehyde left little cause for doubt that the latter plays an important part in the reduction of the chloronitrobenzene. It was resolved to test this conclusion by heating chloronitrobenzene with alcoholic potash containing known small quantities of acetaldehyde.

Acetaldehyde was eliminated from ethyl alcohol as completely as possible by refluxing with 0·2% of *m*-phenylenediamine hydrochloride for 12 hours, after which the alcohol was distilled off through a fractionating column, the first 100 c.c. of the distillate being rejected. The product gave no colour on standing with Schiff's reagent, and remained practically colourless after heating for 24 hours with 0·5*N*-potash at 60°.

A standard solution of acetaldehyde was prepared by dissolving about 10 c.c. of freshly distilled acetaldehyde (b. p. 21°) in 100 c.c. of aldehyde-free alcohol and estimating its strength by the sodium sulphite method.

*Series* 4.—*Effect of variation in concentration of aldehyde.* Three solutions were prepared containing measured volumes of the standard acetaldehyde solution diluted to 250 c.c. with aldehyde-free alcohol in which was dissolved sufficient potash to give 250 c.c. of a 0·5*N*-solution. Four g. of chloronitrobenzene were dissolved in each, and all were heated simultaneously with a blank experiment, using the same aldehyde-free alcohol, for 160 hours at 60°. The following table gives the yields in the four experiments :

| Experiment. | 16. | 17. | 18. | 19. |
|---|---|---|---|---|
| Strength of acetaldehyde (%) | 0·0 | 0·14 | 0·2 | 0·67 |
| Wt. of nitrophenetole (g.) | 3·902 | 3·434 | 2·685 | 1·121 |
| Wt. of dichloroazoxybenzene (g.) | Nil | 0·317 | 0·536 | 2·178† |
| Wt. of nitrophenol (g.) | 0·276 | 0·210 | 0·405* | 0·468* |
| % Theoretical yield : | | | | |
| Nitrophenetole | 92·0 | 81·0 | 63·3 | 26·4 |
| Dichloroazoxybenzene | 0·0 | 9·3 | 15·8 | 64·2† |
| Nitrophenol | 7·8 | 5·9 | 11·5* | 13·3* |
| Total | 99·8 | 96·2 | 90·6 | 103·9 |

* Includes tar. † Contained aldehyde-resin.

From these results, it is evident that the complete elimination of acetaldehyde from the reaction mixture prevents the formation of dichloroazoxybenzene, under the conditions obtaining in these experiments. As little as 0·1% of acetaldehyde appears to be capable of causing a considerable amount of reduction of the chloronitrobenzene, and an increase in the concentration of the aldehyde, within the limits investigated, causes a corresponding increase in the formation of dichloroazoxybenzene.

Experiments were now made to determine whether, with the use of aldehyde-free alcohol, the temperature and the alkali concentration could be increased without the formation of dichloroazoxybenzene. It had been noted that whenever the latter appeared in the reaction product in any quantity, the total yields of nitrophenetole, dichloroazoxybenzene, and nitrophenol did not account for the whole of the chloronitrobenzene employed. It was thought possible that a small amount of the latter might have become completely reduced to *p*-chloroaniline.

To investigate this possibility, the solutions obtained in the following series of experiments were acidified with dilute sulphuric acid before distilling off the alcohol. After steam distillation of the nitrophenetole and filtration of the dichloroazoxybenzene, the acid filtrate was made alkaline and distilled to a small volume. The distillate was extracted with ether, and the residue after its evaporation weighed.

The residue melted at 66°, was soluble in dilute acids and reprecipitated by alkali, and could be diazotised and coupled with β-naphthol to give a red dye. It was acetylated with acetyl chloride, and the product melted at 171—173°. After recrystallisation from dilute alcohol, it melted sharply at 177°. These facts indicated that the residue was *p*-chloroaniline.

*Series 5.—Effect of higher temperature, and greater concentration of alkali, on the reaction of chloronitrobenzene with aldehyde-free alcoholic potash.* Five solutions of potash in 250 c.c. of aldehyde-free alcohol were prepared so that two contained 0·5*N*-alkali, and the other three 1·0, 1·5, and 2·0 *N*-alkali, respectively. In each were dissolved 4 g. of chloronitrobenzene, and, whilst one of the 0·5 *N*-solutions was refluxed for 24 hours, the other four were heated for 140 hours at 60°.

The yields of nitrophenetole, nitrophenol, dichloroazoxybenzene, and chloroaniline in each of the five experiments were estimated as described above, with the following results :

| Experiment. | 20. | 21. | 22. | 23. | 24. |
|---|---|---|---|---|---|
| Strength of potash (*N*) | 0·5 | 0·5 | 1·0 | 1·5 | 2·0 |
| Wt. of nitrophenetole (g.) | 1·241 | 3·800 | 2·134 | 0·778 | 0·328 |
| Wt. of nitrophenol (g.) | 0·553 | 0·279 | 0·434 | 0·364 | 0·304 |
| Wt. of dichloroazoxybenzene (g.) | 1·526 | Nil | 0·988 | 2·243 | 2·372 |
| Wt. of *p*-chloroaniline (g.) | 0·205 | Nil | 0·338 | 0·293 | 0·572 |
| % Theoretical yield : | | | | | |
| Nitrophenetole | 29·3 | 89·6 | 50·3 | 18·4 | 7·7 |
| Dichloroazoxybenzene | 45·0 | 0·0 | 29·1 | 66·2 | 70·0 |
| Chloroaniline | 6·3 | 0·0 | 10·4 | 9·1 | 17·7 |
| Nitrophenol | 15·7 | 7·9 | 12·3 | 10·3 | 8·6 |
| Total | 96·3 | 97·5 | 102·1 | 104·0 | 104·0 |
| | Refluxed. | | The dichloroazoxybenzene was very impure. | | |

These results proved conclusively that the absence of aldehyde from the alcohol does not preclude the formation of dichloroazoxybenzene under all conditions. They confirm the conclusion that higher temperature and higher concentration of alkali favour the reduction of the chloronitrobenzene, an appreciable quantity of which becomes completely reduced to *p*-chloroaniline whenever dichloroazoxybenzene is formed to any extent.

In order to determine the minimum time required for the conversion of chloronitrobenzene into nitrophenetole under the conditions giving the maximum yield, 63 g. of chloronitrobenzene in 2 litres of 0·5*N*-95% aldehyde-free alcoholic potash were heated at 60°, whilst 5 c.c. of the solution were titrated at intervals with *N*/10-acid, and the melting point of the precipitated chloronitrobenzene–nitrophenetole mixture was determined.

*Experiment* 25.

| Time (hours). | *N*/10-$H_2SO_4$ (c.c.) for 5 c.c. | Strength of KOH (*N*). | Equivs. of KOH neutralised. | M. p. of ppted. product. |
|---|---|---|---|---|
| 0 | 25 | 0·5 | 0·0 | 83° |
| 28½ | 18·45 | 0·369 | 0·655 | 49—51 |
| 50 | 16·85 | 0·337 | 0·815 | 54—55 |
| 78½ | 15·75 | 0·315 | 0·925 | 55—56 |
| 142 | 15·0 | 0·300 | 1·0 | 56—57 |

After 142 hours, the whole solution was neutralised with dilute sulphuric acid, and the alcohol distilled off on the water-bath. The residue of nitrophenetole was well washed with dilute caustic soda to remove nitrophenol, then with water, and dried over calcium chloride in a vacuum desiccator. The mother-liquors and washings were evaporated down, acidified, and extracted with ether.

| | | | |
|---|---|---|---|
| Yield : | 61·1 g. of nitrophenetole, m. p. 56·5° | = 91·5% | of theor. |
| | 3·3 g. of nitrophenol | = 6·0 | ,, ,, |
| | 20 c.c. of solution withdrawn for titration | = 1·0 | ,, ,, |
| | Total | = 98·5 | ,, ,, |

This experiment confirmed the conclusion that *p*-chloronitrobenzene can be converted into nitrophenetole by heating at 60° for approximately 140 hours in 0·5 *N*-95% alcoholic potash, without the formation of any dichloroazoxybenzene, if the alcohol is free from acetaldehyde.

Under similar conditions, 65 g. of *o*-chloronitrobenzene, dissolved in 1 litre of aldehyde-free ethyl alcohol, gave a yield of 62·2 g. of *o*-nitrophenetole (90·3% of the theoretical), whilst 4 g. of *p*-chloronitrobenzene in 250 c.c. of methyl alcohol gave 3·750 g. of *p*-nitroanisole (96·5% of the theoretical).

No dichloroazoxybenzene was formed in either case.

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