CCCXCI.—*The Isomerism of the Oximes. Part XXXII. Sulphates.*

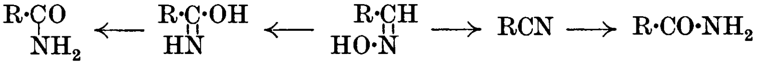
By Oscar L. Brady and Alan D. Whitehead.

Luxmoore (J., 1896, **69**, 180) showed that α-benzaldoxime could be converted into the β-isomeride by means of concentrated sulphuric acid and isolated both the α- and the β-benzaldoxime sulphate, $C_6H_5\cdot CH:NOH,H_2SO_4$. The α-oximesulphate regenerated the α-oxime on decomposition with aqueous ammonia at 0°, and on keeping rapidly changed to the β-oxime sulphate; this gave the β-oxime on treatment with alkalis. A number of other aromatic aldoxime sulphates have now been prepared and Luxmoore's method of converting the α- into the β-oxime has been investigated in the hope that it would prove more convenient than the usual procedure through the hydrochloride. Further, it was thought that it might be possible, through the sulphate, to bring about isomeric change in those oximes which do not form hydrochlorides (Brady and Dunn, J., 1915, **107**, 1862; Brady and Manjunath, J., 1924, **125**, 1068).

When α- *o*-, *m*-, or *p*-nitro- or α-*p*-methoxy-benzaldoxime is dissolved in concentrated sulphuric acid, the sulphate of the α-oxime is first formed, and the solution on neutralisation with sodium carbonate regenerates the α-oxime; if the solution be kept for some time or heated to 100°, or if the temperature rises too much during the dissolution owing to the heat of reaction, the sulphate of the β-oxime is produced, and the solution on neutralisation gives the β-oxime. Provided that the temperature is kept low, the dry sulphates of these oximes, isolated by various means from the freshly prepared solutions, consist mainly of the α-form, differing in this respect from the hydrochlorides, since, although the α-hydrochloride of *p*-methoxybenzaldoxime can be obtained at — 10°, those of *m*- and *p*-nitrobenzaldoxime are stable only at very low temperatures (Brady and Dunn, J., 1916, **109**, 680; 1923, **123**, 1798). The solid sulphate from benzaldoxime consisted of the β-form (compare Luxmoore, *loc. cit.*). In the case of α-*o*-methoxybenzaldoxime, which cannot be converted into the β-isomeride through the hydrochloride, sulphate formation likewise failed to bring about the change; α-*o*-chlorobenzaldoxime, which yields the β-form only with difficulty through the hydrochloride, gave only an α-sulphate; 3 : 4-methylenedioxybenzaldoxime gave an α-sulphate which could not be converted into the β-form owing to decomposition of the methylene group on heating or keeping. α-6-Nitro-3 : 4-methylenedioxybenzaldoxime and α-6-bromo-3 : 4-dimethoxybenzaldoxime, which do not form hydrochlorides, gave α-sulphates, but these compounds did not change to the β-forms.

When solutions of α-benzaldoxime, *o*-, *m*-, and *p*-nitro-, and *p*-methoxy-benzaldoximes in concentrated sulphuric acid were heated for a short time at 100°, cooled, and poured into a large excess of sodium carbonate solution, products were obtained which on crystallisation gave fairly satisfactory yields of the β-oximes. This method is probably the quickest way of preparing small amounts of the β-oximes, but does not work well with quantities much above 2 grams; it seems that owing to the longer time required for neutralisation when larger quantities are used, as in the case of the hydrochlorides, partial reversion of the β- to the α-oxime takes place.

Prolonged heating of aldoximes with concentrated sulphuric acid results in the formation of the corresponding amides. It is impossible to decide at present whether this is a Beckmann change (I) or dehydration to nitrile followed by addition of water in another way (II), since the nitrile on similar treatment yields the amide.



$$\underset{NH_2}{R\cdot CO} \longleftarrow \underset{HN}{R\cdot C\cdot OH} \longleftarrow \underset{HO\cdot N}{R\cdot CH} \longrightarrow RCN \longrightarrow R\cdot CO\cdot NH_2$$

(I.) (II.)

o-Nitro-, *o*-methoxy-, 3 : 4-methylenedioxy-, and 6-nitro-3 : 4-methylenedioxy-benzaldoxime undergo extensive charring on heating with sulphuric acid and could not be investigated under such conditions.

EXPERIMENTAL.

α-Benzaldoxime.—Formation of β-oxime. The method of converting the α- into the β-oxime by means of sulphuric acid has been investigated in order to find the best conditions. When benzaldoxime was dissolved in 96% sulphuric acid (5 g.) the temperature rose to 40—50° and after 4·5 g. of oxime had been added the solution became thick with crystals of benzaldoxime sulphate. If the solid sulphate was separated from the acid, pressed on a porous tile, and added to excess of 2*N*-sodium carbonate, fairly pure β-oxime was obtained, but when the whole semi-solid material was slowly stirred into a volume of 2*N*-sodium carbonate containing 4 mols. of carbonate for each mol. of acid used (this will subsequently be referred to as neutralisation), an oil separated consisting of a mixture of β- and unchanged α-oxime. With 5 g. of oxime and 10 g. of acid, complete solution was attained, but neutralisation gave a waxy product still containing much α-oxime. When a solution of 5 g. of oxime in 20 g. of acid was kept for a month in a closed flask, or when a solution of 1 g. of oxime in 5 g. of acid was heated on the water-bath for 30 minutes, the product obtained yielded on neutralisation a fairly pure β-oxime (m. p. 108—111°), one crystallisation from benzene giving the pure compound.

Formation of benzamide. A solution of α-benzaldoxime (5 g.) in concentrated sulphuric acid (15 g.) was heated on the water-bath for 12 hours, kept for 2 days, and neutralised, a white precipitate being obtained. The suspension was extracted with ether and then with chloroform. The ethereal solution contained impure β-benzaldoxime (identified by comparison with an authentic specimen and by conversion into the α-benzoyl derivative; the yield was 14% of the oxime taken), no aldehyde or nitrile, and 1·42 g. of benzamide; 1 g. of benzamide was obtained from the chloroform extract, the total yield being approximately 50% of the oxime taken. The aqueous solution, after being acidified with hydrochloric acid, yielded to ether 0·6 g. of benzoic acid, corresponding to 12% of the oxime employed. Of the 24% of the oxime unaccounted for, most was probably lost during manipulation, some possibly as sulphonate.

α-m-*Nitrobenzaldoxime.*—When the oxime (1 g.) was stirred into sulphuric acid (2 g.), the temperature rose to 35°. The almost colourless, viscous solution was cooled in a desiccator for 30 minutes and poured into dry ether. The precipitated α-m-*nitrobenzaldoxime sulphate* was collected, washed rapidly twice with dry ether, and kept for 12 hours in an evacuated desiccator. It consisted of a white, crystalline powder, m. p. 71—76°, and was analysed by decomposition of a weighed amount with water and titration of the sulphuric acid with *N*/10-sodium carbonate and methyl-orange (Found: H_2SO_4, 41·2. $C_7H_6O_3N_2,H_2SO_4$ requires H_2SO_4, 37·1%). The freshly prepared solid sulphate on decomposition with 2*N*-sodium carbonate regenerated the α-oxime.

When α-*m*-nitrobenzaldoxime (2 g.) was dissolved in sulphuric acid (10 g.), and the solution neutralised at once, a product, m. p. 107°, was obtained which was almost pure α-oxime. If the solution was kept for 24 hours before being neutralised, the recovered oxime melted at 75°, indicating that about 50% conversion had occurred; whilst if the solution was heated on the water-bath for 30 minutes and then neutralised, a fairly pure β-oxime was obtained which gave a good yield of pure β-*m*-nitrobenzaldoxime after one crystallisation from benzene.

α-*m*-Nitrobenzaldoxime (5 g.) was dissolved in sulphuric acid (15 g.) and heated for 7 hours on the water-bath. On neutralisation of the clear brown solution an oil separated which soon solidified.

The whole was extracted once with ether, the undissolved solid was collected and dissolved in hot chloroform, and the aqueous layer also was extracted with chloroform. The ethereal solution was extracted twice with 2*N*-sodium hydroxide, and then with a solution of hydroxylamine hydrochloride in excess of 2*N*-sodium hydroxide to remove aldehyde as the sodium salt of the oxime; the aqueous layer in the latter case was but faintly coloured, indicating that little aldehyde was present. The ether on evaporation yielded 0·8 g. of somewhat impure *m*-nitrobenzamide, one crystallisation from water giving the pure product. The sodium hydroxide extracts were saturated with carbon dioxide and the precipitated oxime was extracted with ether, 2·1 g. of a mixture of α- and β-oximes being obtained (the time of manipulation would account for some conversion of β- into α-oxime); crystallisation from water, containing a little hydrochloric acid to convert the β- into the α-oxime, yielded pure α-*m*-nitrobenzaldoxime. The combined chloroform solutions were extracted with 2*N*-sodium hydroxide and the faintly coloured alkaline solution was added to those obtained from the ethereal extract. The chloroform on evaporation gave 0·5 g. of *m*-nitrobenzamide.

m-Nitrobenzonitrile (2 g.) was heated with sulphuric acid (6 g.) for 7 hours; some charring occurred due probably to the presence of a little of the *o*-nitro-compound. On neutralisation a dark solid was precipitated which, after crystallisation from water (animal charcoal), gave more than 1 g. of pure *m*-nitrobenzamide.

m-Nitrobenzamide often crystallises with water of crystallisation and must be kept in a desiccator for 12 hours before its melting point is taken. A specimen, crystallised from hot water with rapid cooling and dried rapidly by pressing on several porous tiles, collapsed in a melting-point tube when this was put into a bath at 105°, but it did not melt until 141°. On being kept in a desiccator, it lost 12·4% of its weight (calc. for $1H_2O$, 9·8%); the high result is due to the difficulty of freeing the compound from extraneous moisture.

The following sulphates were prepared by analogous methods, and the products of their decomposition investigated as before. The results are described in the introduction. The compounds consist, unless otherwise stated, of white microcrystalline powders. α-o-*Methoxybenzaldoxime sulphate* (1 g. of oxime; 4 g. of acid), m. p. 143° (Found: H_2SO_4, 38·3. $C_8H_9O_2N,H_2SO_4$ requires H_2SO_4, 39·3%). α-o-*Chlorobenzaldoxime sulphate* (1 g. of oxime; 1 g. of acid) (Found: H_2SO_4, 36·9. C_7H_6ONCl,H_2SO_4 requires H_2SO_4, 38·6%). α-6-*Bromo*-3 : 4-*dimethoxybenzaldoxime sulphate* (1 g. of oxime; 2 g. of acid), a canary-yellow, granular solid, m. p. 105° (Found: H_2SO_4, 27·7. $C_9H_{10}O_3NBr,H_2SO_4$ requires H_2SO_4, 27·3%). α-6-*Nitro*-3 : 4-*methylenedioxybenzaldoxime sulphate* (1 g. of oxime; 1 g. of acid), a brown powder, m. p. 110—135°, readily dissociating into oxime and acid in the presence of ether or on exposure to moist air (Found: H_2SO_4, 31·1. $C_8H_6O_5N_2,H_2SO_4$ requires H_2SO_4, 31·8%). p-*Nitrobenzaldoxime sulphate*, a light fawn, granular solid too deliquescent for a melting point to be obtained (Found: H_2SO_4, 38·6. $C_7H_6O_3N_2,H_2SO_4$ requires H_2SO_4, 37·1%). This compound dissociates very easily and is difficult to obtain; it was prepared by adding the oxime (1·5 g.) to sulphuric acid (1 g.) until the mixture began to crystallise; the pasty mass was stirred into ether, rapidly collected, and washed once only with dry ether. No solid sulphate could be obtained from *o*-nitrobenzaldoxime, only a very small amount of oil being precipitated from the sulphuric acid solution by ether. α-3:4-*Methylenedioxybenzaldoxime sulphate* (Found: H_2SO_4, 37·6. $C_8H_7O_3N,H_2SO_4$ requires H_2SO_4, 37·2%) was obtained by stirring the oxime (2·5 g.) into acid (2 g.) warmed to 60°, cooling, collecting the solid which separated, and washing it with dry ether. α-p-*Methoxybenzaldoxime sulphate* (2 g. of oxime; 10 g. of acid), m. p. 79—80° (Found: H_2SO_4, 38·9. $C_8H_9O_2N,H_2SO_4$ requires H_2SO_4, 39·3%).

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