

**ELECTROLYTIC REDUCTION OF ISATIN  
AND ITS DERIVATIVES. II.  
REDUCTION OF N-METHYL-ISATIN\***

By

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The electrolytic reduction of isatin and its derivatives provides a couple of highly engaging themes for investigation, namely, (1) Which of the two carbonyls in  $\alpha$ - and  $\beta$ - position is more easily subject to reduction as against its imide radical? and (2) Is the complete reduction of the two carbonyls possible? As for the first theme, the previous experiment, in which isatin<sup>(1)</sup> was reduced to oxyindol mainly through dioxyindol, has already affirmed that the carbonyl in  $\beta$ - position can be reduced more readily than the other, which also can be reduced to indoxyl, though it is quantitatively small. As for the second, the possibility was ascertained by conducting electrolysis with zinc amalgam cathode in sulphuric acid solution and thus a complete reduction, which could not be accomplished by purely chemical method, was successfully achieved by electrolysis.

In the present experiment the author tried to see how N-methyl derivatives of isatin would behave toward reduction as compared with the behaviour of isatin itself. N-methyl-isatin, quite different from isatin in that the former is liable to dissolve in alkaline solution, cannot possibly be subjected to electrolytic reduction in weak alkaline solution; so that it is considered impossible to apply to it the parallel reduction under the same conditions as isatin. However, as it turned out, this was found to be applicable by arranging favourable conditions such as follows:

The subject suspended in a mixture of 20% sulphuric acid solution and alcohol with lead-plate cathode was subjected to electrolysis so as to give a pretty satisfactory yield of N-methyldioxyindol.

For the purpose of obtaining N-methyloxyindol, neutral solution is absolutely necessary as in the case of isatin, because acidic solution is quite unfavourable, but in this case it is preferable to employ 10% sodium

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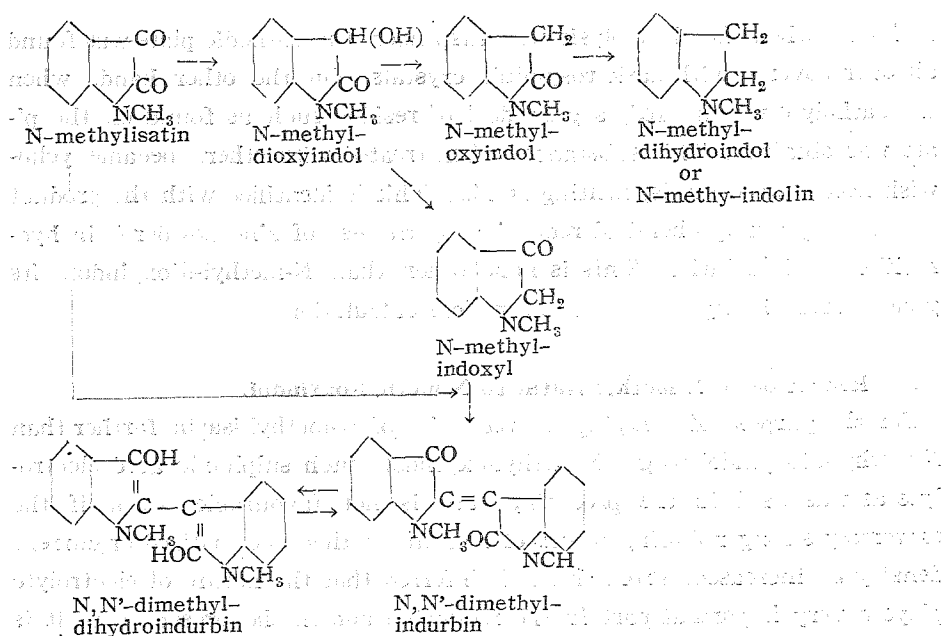
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sulphate containing alcohol with mercury cathode. It is extremely difficult to carry out electrolysis in the neutral condition by keeping apart the catholyte from the anolyte and this might be said to be one of the defects of electrolysis. This difficulty rises from the fact that, as the electrolysis advances, either alkali or acid constantly generates. When sodium sulphate is used for catholyte, it should be kept from becoming alkaline by neutralization. When electrolysis is conducted by maintaining the *PH* value of the solution between 7.2 and 7.4 by means of brom-thymol-blue paper by dripping sulphuric acid, *N*-methoxyindol is procured. At the same time a small amount of *N*-methylindoxyl is produced through the reduction of the carbonyl in  $\alpha$ - position. This is to be explained by the fact that the moment it is produced; its instability causes it to combine at once with the original material to make *N,N'*-dimethylindurbin. But, in case mercury cathode is used instead, it is as often as not difficult to decide whether the reduction is purely electrolytic or purely chemical one. The reason is that the sodium produced in the course of the electrolysis has no small probability of partaking in the reduction even after it has been absorbed in mercury, and the similar phenomenon was actually observed in the present experiment. Moreover, in the same experiment some unknown substance could be isolated, which was assumed to be *N,N'*-dimethyl-isatyd corresponding to isatyd which is an intermediate reduction product of isatin. But, after all, what was this substance was not confirmed for lack of any sufficient literature to refer to within the author's reach.

For the purpose of obtaining the complete reduction product of *N*-methyl-dihydroindol, the author, considering this substance to be strongly basic and therefore it should be expelled outside the reaction field in the form of salt, carried out the electrolysis by employing in sulphuric acid solution the zinc amalgam<sup>(2)</sup> cathode which the author is accustomed to use, acknowledging its remarkable reducing power. Thus he has succeeded in opening the way to the production of *N*-methylindoxyl by direct reduction method.

It has now been made known that in the case of *N*-methyl-isatin the reduction takes place in nearly the same manner as isatin, though the condition is not necessarily the same.

The synopsis of the reduction process is formulated as follows:



## Experimental

### (1) Reduction of N-methyl-isatin to N-methyl-dioxyindol.

As was already communicated, the best way of reducing isatin to dioxyindol was by electrolysis with lead cathode in weak alkaline solution, but this was found unsuitable for obtaining N-methyl-dioxyindol from its derivative, N-methyl-isatin, because the latter, different from isatin, is disposed to be decomposed by alkali. The most satisfactory result, therefore, was obtained by the use of lead cathode in acidic solution, namely, sulphuric acid electrolyte. From a series of electrolyses done by changing the density of catholyte, 20% sulphuric acid solution was confirmed to be most favourable for the purpose. The electrolysis was conducted under such conditions as follows:

Cathode: lead plate, 100 cm<sup>2</sup>.; Cathodic solution: 5g of N-methyl-isatin suspended in a mixture of 50 c.c. of 20% sulphuric acid and 50 c.c. of alcohol; Anode: lead; Anodic solution: 20% sulphuric acid; Current density: 2.5 amp/sq. dm; Temperature: 18°C; Time of electrolysis: 14 hours; Current quantity: 38.39 F/mol.

The electrolysis was carried out by cooling the electrolytic bath in cold water and vigorously stirring the cathodic solution therein. As the electrolysis advanced, the solution changed its colour from red to rosy-pink. After

14 hours, when the electrolysis was suspended, the cathodic plate was found all over covered with dark rosy-pink crystals. On the other hand, when the catholyte was filtered, a good deal of residue such as found on the plate was obtained. This substance, when treated with ether, became yellowish needlelike crystals, melting at 149°. This is identified with the product obtained by purely chemical reduction by the use of zinc powder<sup>3)</sup> in hydrochloric acid solution. This is none other than N-methyl-dioxyindol, its yield corresponding to 40% of theoretical calculation.

(2) Reduction of N-methyl-isatin to N-methyl-oxyindol.

For the purpose of carrying the reduction of N-methyl-isatin farther than N-methyl-dioxyindol to get N-methyl-oxyindol, such sulphuric acid electrolyte as was used in the preceding case is not favourable, even if the extremely strong reducing power of mercury cathode be utilized or current density be increased. From this it is inferred that the nature of electrolyte plays a very important part in the reduction and in the present case it is required imperatively to be neutral. Consequently the electrolysis was conducted by using sodium sulphate catholyte and mercury cathode and, as the electrolysis advanced, neutralizing with acid the ever-generating alkali, and thereby was obtained N-methyl-oxyindol. The most favourable conditions for this were as follows:

Cathode: mercury, 15.8 sq. cm.; Cathodic solution: 5g of N-methyl-isatin suspended in a mixture of 90 c.c. of 10% sodium sulphate solution and 10c.c. of alcohol; PH value of catholyte: between 7.2 and 7.4; Anodic solution: 10% sodium sulphate solution; Current density: 12.7 amp/sq. cm; Temperature: 25°C; Time: 5 hours; Current quantity: 60.07 F/mol.

The electrolysis was carried out by cooling the electrolyte with ice from outside and, at the same time, stirring the solution to prevent the rising of temperature by passing cold water incessantly through a spiral lead tube inserted into the catholyte; on the other hand, the alkali produced during the electrolysis was continually neutralized by dripping 10% sulphuric acid from a burette, thereby maintaining the hydrogen-ion density of the electrolyte at PH-value between 7.2 and 7.4 by means of brom-thymol-blue test paper. The colour of the catholyte was red at the start, but gradually faded to yellow and then finally to colourless. In spite of the constancy of current density, the quantity of the sulphuric acid which was required for neutralization per unit hours was comparatively small at an early stage, but gradually increased till at last it remained nearly constant. As for the mercury

cathode, it began losing its liquidity by degrees and in the end hardened into a semi-solid body. This seems to have been caused by the formation of amalgam owing to the dissolution of the sodium produced in the catholyte into the mercury before its participation in the reaction process. This is why the quantity expended for neutralization of the alkali was small at first, and its becoming constant later on shows that the product quantity and the expenditure quantity of the sodium reached the stage of equilibrium. It follows, therefore, that it is quite doubtful whether the reduction by means of mercury cathode be an electrolytic or a purely chemical one. The catholyte taken out after the suspension of the electrolysis was colourless at first, but when left alone exposed to the air, it slowly began to assume colour, changing from pinky-red to dark red. This was extracted with ether in its neutral state and then the remaining catholyte was re-extracted with ether in the condition made alkaline with caustic soda, but in both cases there remained the same red-brown resin-like substance after the evaporation of the ether. When the remaining catholyte was subjected to ether extraction in its acidic condition, brown crystals were obtained. What was obtained by purifying these crystals through recrystallization in ether solvent was N-methyl-oxyindol, <sup>(4)</sup> melting at 90°. Again, the resin-like substance procured from neutral and alkaline catholytes also became N-methyl-oxyindol, melting at 90°, when it was subjected to ether refinement. The yield of N-methyl-oxyindol in the above three cases put together corresponds to 16%. The remaining catholyte before and after acidic extraction, when left alone as it was, yielded yellow spheric or red-brown crystals. They melt at 170°-180°, but they are not yet identified.

The moment it was taken out, the electrolyte was colourless, but when it was left stand exposed to the air, after separated from mercury, gradually assumed reddish colour and then finally red colour. The cause of this phenomenon remains a problem for further investigation. But the supposition, so far, is that, as in the case of isatin-electrolysis, N,N'-dimethyl-indurbin produced by electrolysis was reduced by sodium amalgam to N,N'-dimethyl-dihydro-indurbin, which, though colourless at first, assumed red colour by becoming N,N'-dimethyl-indurbin through oxydization while left alone in the air after it had been separated from mercury cathode. This was confirmed by the fact that the above-mentioned red-brown resin-like substance became colourless sodium amalgam was added into its alcoholic solution and became red when it was kept swinging to and fro in the air after separation from sodium amalgam. It is, therefore, clear that in the course of electrolysis

in neutral electrolyte a small quantity of N, N'-dimethyl-indurbin is produced in addition to N-methyl-oxyindol.

### (3) Reduction of N-methyl-oxyindol to N-methyl-indolin.

For this purpose a cathode of strong reducing power is necessarily to be employed. According to the author's experience, zinc amalgam is considered as most suitable. On the other hand, acidic solution is regarded as the most effective electrolyte, from the fact that N-methyl-indolin is a strong basic substance. Thus by the use of zinc amalgam cathode in acidic solution, the reduction of N-methyl-oxyindol to N-methyl-indolin, which had been attempted to no effect by purely chemical method, was successfully achieved by electrolysis, under comparatively favourable conditions such as follows:

Cathode: 15.8 sq. cm. of zinc amalgam; Catholyte: 3.4g of N-methyl-oxyindol suspended in a mixture of 80c. c. of 50% sulphuric acid and 20c. c. of alcohol; Anode: lead plate; Anolyte: 50% sulphuric acid; Current density: 63.5amp/sq. cm; Temperature: 28°C.; Time of electrolysis: 9 hours; Current quantity: 348.3 F/mol.

The electrolysis was carried out, as in the previous case, by cooling the catholyte with ice from outside and passing cold water through a spiral lead tube inserted into the catholyte, which was kept vigorously stirring all the time. The catholyte, red at first, gradually grew lighter in colour and in 4.5 hours the material had completely dissolved. The electrolysis was still continued nearly as long and then stopped. The electrolyte was taken out, made strong alkaline with caustic soda, and then subjected to steam distillation. The distillate was collected as long as it reacted alkaline. The ether extract of the distillate was treated with picric acid, producing needle-like yellow crystals, melting at 149°. This product was picrate of N-methyl-indolin<sup>5</sup> and its yield was calculated to correspond to 8%.

### Literature

- (1) Sakurai: Bull. Chem. Soc. Jap., 17, 269(1942)
- (2) Sakurai: Bull. Chem. Soc. Jap., 7, 155(1932)
- (3) Colman: Ann. 248, 121(1888)
- (4) Hinsberg, Rosenzweig: Ber. 27, 3257(1894) Colman: Ann. 248, 120(1888)
- (5) Wenzig: Ann. 239, 246(1887)

### Abstract

N-methyl-isatin can be reduced by the same process as in the case of isatin only by controlling the conditions as follows:

- (1) It is reduced to N-methyl-dioxyindol with lead cathode suspended in 20% dilute sulphuric acid solution.
- (2) It is reduced to N-methyl-oxyindol with mercury cathode in sodium sulphate solution.
- (3) N-methyl-oxyindol is further reduced to N-methyl-dihydro-indol with zinc amalgam cathode in 50% sulphuric acid solution.