

PREPARATION OF 2,2,6,6-TETRAMETHYL-4-AMINOPIPERIDINE AND ITS SUBSTITUTED COMPOUNDS BY ELECTROREDUCTION OF AZOMETHINES OF 2,2,6,6-TETRAMETHYL-4-OXOPIPERIDINE (TRIACETONAMINE)

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Five methods have been developed for electrosynthesis of 2,2,6,6-tetramethyl-4-aminopiperidine in 95–98% yield *via* the lead-cathode reduction of 2,2,6,6-tetramethyl-4-oxiimino-piperidine, a mixture of triacetoneamine with inorganic salts of hydroxylamine, and a mixture of triacetoneamine with nitric acid in a solution of sulphuric acid, *via* the reduction of azine triacetoneamine and of a mixture of triacetoneamine with inorganic salts of hydrazine in a neutral solution. The corresponding saturated derivatives of 2,2,6,6-tetramethyl-4-aminopiperidine have been obtained in 60–80% yield by electroreduction of phenylimine and ethylene diimine.

2,2,6,6-Tetramethyl-4-aminopiperidine (*I*) finds application in the synthesis of highly effective polymer stabilizers¹ and pharmaceuticals^{2,3}. The known methods of producing *I* employ the reduction of 2,2,6,6-tetramethyl-4-oxiiminopiperidine (*II*) with metallic sodium in hot pentyl alcohol^{4,5} and with zinc in hydrochloric acid⁶. The yield of the final product is mentioned only in⁵ and amounts to 60%.

We have investigated the prospects of producing *I* and its substituted compounds from azomethines of 2,2,6,6-tetramethyl-4-oxopiperidine (*III*) by an electrochemical process. A scheme of electrochemical transformations of azomethines of *III* to *I* and its substituted compounds is given below.

EXPERIMENTAL

Conditions for electroreduction and analysis of *III* were selected on the basis of a polarographic study⁷. Electroreduction was performed in a cell with a ceramic or cation-exchange diaphragm separating the cathode and anode compartments. The concentration of the initial compounds and final products during the electrolysis was controlled polarographically^{8,9} and with the aid of thin-layer and gas-liquid chromatography. The yield of *I* was calculated from the results of polarographic analysis, the yield of the separated product was 80–85% of the product obtained under the laboratory conditions and 90% on a pilot plant.

RESULTS AND DISCUSSION

It is seen from Table I that the rate of conversion of the starting *II* (Scheme 1, 1(b)) is influenced by the material of the cathode both in hydrochloric- and sulphuric-acid solutions. The lowest current efficiency was observed on platinum and nickel, *i.e.* on electrodes with the lowest hydrogen overvoltage. Low yields of the final product on tin and electrodeposited Sn–Pb alloy electrodes are attributed to the dissolution of electrodes and to changes in their surface state during electrolysis.

Further investigations were conducted with lead as the cathode material.

The concentration of the acid affects greatly electroreduction of *II* and yield of *I*. The earlier data⁷ indicate that reduction of *II* takes place only in a strongly acid solution.

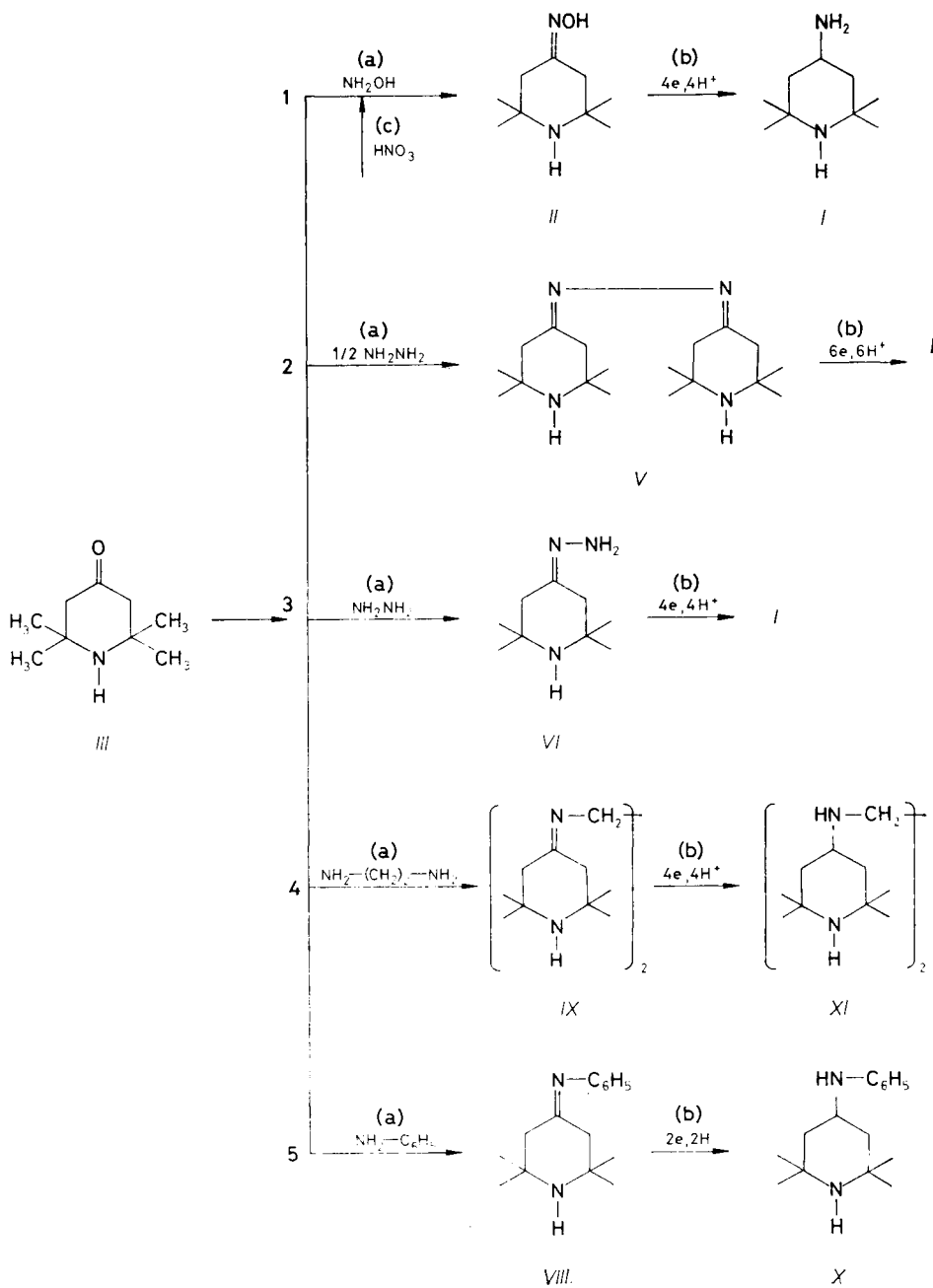
It is formed in the reaction between 2,2,6,6-tetramethyl-4-oxopiperidine *III* and inorganic salts of hydroxylamine (*IV*), the yield of the separated product being 85% (ref.⁴). Some of the product is lost due to the hydrolytic decomposition of *II* which takes place during electrolysis in a strongly acid solution. To increase the yield and eliminate the stage of separation of *II*, the possibility of electrosynthesis of *I* from a mixture of *III* with inorganic salts of hydroxylamine has been investigated.

As it is seen from scheme, *I* forms in two stages: *III* is oximized by hydroxylamine to give *II* (1a) which is then electrochemically reduced to *I* (1b). Since the electrochemical reduction of *II* takes place only in an acid medium, the effect of the experimental conditions on the rate of the interaction of *III* with the inorganic salts of

TABLE I

Yields of 2,2,6,6-tetramethyl-4-aminopiperidine — effect of the electrode material. *a*: Conc. of *II* 0.03 mol l⁻¹ in 0.55M HCl; current density $i_c = 300 \text{ A m}^{-2}$. *b*: Conc. of *II* 0.235 mol l⁻¹ in 0.51M H₂SO₄; $i_c = 700 \text{ A cm}^{-2}$

Cathode material	<i>a</i>		<i>b</i>	
	Yield of <i>I</i> , %	Current efficiency, %	Yield of <i>I</i> , %	Current efficiency, %
Platinum	78	4	—	—
Nickel	78	12	89	8
Tin	74	11	90	3
Alloy Sn–Pb	—	—	98	4
Steel (Cr 18%, Ni 9%, Ti under 1.5%)	—	—	96	11
Copper	95	30	97	11
Lead	90	31	99	27
Amalgamated copper	90	28	95	39
Amalgamated lead	87	27	100	24



SCHEME 1

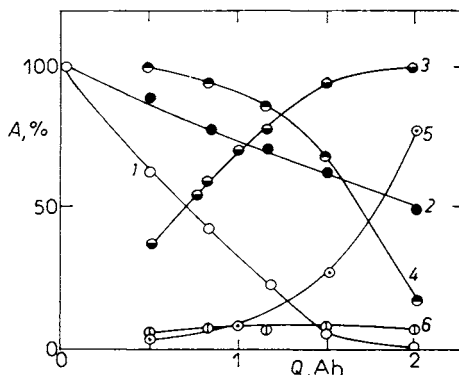
hydroxylamine and on the yield of *II* was studied under these conditions. An increase in the hydroxylamine concentration and a decrease in the acidity speed up the reaction and increase the yield of *II*. An increase in temperature also accelerates accumulation of *II*. A 90–95% yield of *II* is attained in 30–60 min of the reaction between *III* and hydroxylamine depending on the conditions.

At the cathode, along with the reduction of *II*, some of the surplus hydroxylamine required for a complete oximation of *III* is partially reduced to ammonia and hydrogen is evolved (Fig. 1). During electrolysis of the mixture of *III* with hydroxylamine the yield of *I* is not affected by the duration of the preliminary interaction between the starting components (Table II). Current efficiency, however, increases with an extension of this period due to a rise in concentration of *II* and redistribution of current consumption for reduction of *II* and hydrogen evolution.

An increase in the *IV* to *III* concentration ratio from 1 to 1.5 enhances the yield of *I* and current efficiency which then remains practically unaffected by a further increase in the concentration ratio (Table III). The product of reduction of *III*, 2,2,6,6-tetramethyl-4-hydroxypiperidine, has been detected in the products of electrolysis at 1 : 1 concentration ratio of the reagents which is a result of an incomplete oximation and is responsible for a lower yield of *I*.

From Fig. 2 we can see that the concentration of the acid in the electrolyte should correspond to that of *III*. If the amount of the acid is sufficient for a complete transformation of *II* into *I*, the yield of *I* does not depend on the concentration of the acid. The dependence of current efficiency on the acidity is of an extreme nature. A decrease in current efficiency with increasing concentration of sulphuric acid is attributed to a rise in the current consumption for the liberation of hydrogen. An increase in the current density from 100 to 1 000 A m⁻² does not affect the yield of *I* but reduces the current efficiency from 83% to 31% due to an increase in the current

FIG. 1
Effect of the quantity of electricity on: 1, 2 concentration of *II* and *IV*; 3 yield of *I*; 4 current efficiency; 5 current efficiency for liberating hydrogen and 6 ammonia during electrolysis of a mixture of *III* with *IV*. Conc., mol l⁻¹: *III* 0.26; *IV* 0.37; 0.5M H₂SO₄. Cathode: lead, 400 A m⁻², 20°C



consumption for hydrogen liberation. The optimum temperature for electrolysis of the mixture of *III* with *IV* is 15–20°C.

TABLE II

Effect of the duration of preliminary interaction between *III* and hydroxylamine on yield of *I* and current efficiency. Concentration, mol l⁻¹: *III* 0.25, *IV* 0.37, H₂SO₄ 0.5; Pb-cathode; *i*_c = 400 A m⁻²; 20°C

<i>t</i> , min	2	10	20	30	60
Yield of <i>I</i> , %	99	99	99	99	99
Current efficiency, %	49	57	60	67	68

TABLE III

Effect of the hydroxylamine-to-triacetonamine mole ratio on yield of *I* and current efficiency. Concentration, mol l⁻¹: *III* 0.25, H₂SO₄ 0.5; Pb-cathode; *i*_c = 400 A m⁻²; 20°C

Mole ratio	1 : 1	1.25 : 1	1.5 : 1	1.75 : 1	2 : 1
Yield of <i>I</i> , %	88	94	99	99	99
Current efficiency, %	46	59	68	68	69

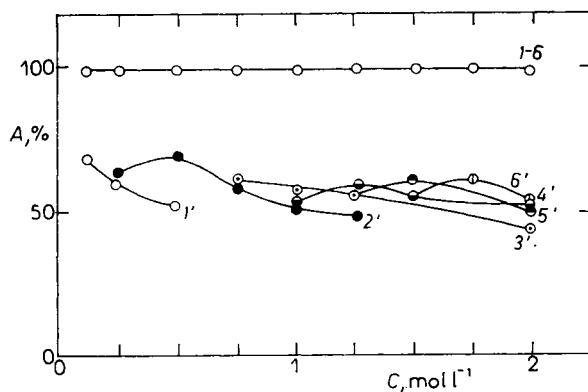


FIG. 2

Effect of the sulphuric acid concentration on the yield of *I* (1–6) and current efficiency (1'–6') for various concentrations of *III*, mol l⁻¹: 1 0.129; 2 0.258; 3 0.516; 4 0.774; 5 0.032; 6 1.290. *IV* to *III* concentration ratio 1.5 : 1. Cathode: lead. 400 A m⁻², 20°C

Hydroxylamine can be obtained by electrochemical reduction of nitric acid in an acid solution¹⁰. Therefore, attention has been focused on the production of *I* by the electrolysis of a mixture of *III* and nitric acid under the conditions providing for an efficient electrosynthesis of *I* from a mixture of *III* and *IV*. It has turned out that electroreduction of nitric acid (1c) on amalgamated electrodes at a current density within the range of 100–1 000 A m⁻², proceeds at a high rate and ensures, if the quantity of electricity is theoretical, a hydroxylamine content needed for a complete oximation of *III* present in an amount of 0.2 and 0.5 mol l⁻¹ in solutions with a nitric acid content of 0.7 and 1.4 mol l⁻¹, respectively. The dependence of the hydroxylamine yield on the electric charge applied passes through a maximum which is related to its further reduction to ammonia ion (Fig. 3).

Table IV illustrates the results of the preliminary studies of electrosynthesis of *I* from *III* and nitric acid (Scheme 1, 1c, a, b).

Electrosynthesis of *I* was carried out in two versions: (i) introduction of nitric acid simultaneously with *III* and (ii) preliminary reduction of nitric acid to a point when the hydroxylamine concentration reaches maximum for given concentrations of nitric and sulphuric acids with subsequent addition of *III*.

Since the electrosynthesis of *I* from *III* and nitric acid involves two stages, the current efficiency was calculated for a total process comprising the reduction of nitric acid to hydroxylamine (6F per mole of NH₂OH) and reduction of *II* to *I* (4F per mole of *I*), i.e. 10F per mole of *I*.

From Table IV it is seen that the yield of *I* obtained on amalgamated electrodes is 97–99%. A somewhat lower yield is obtained on a mercury electrode, and 2,2,6,6-tetramethyl-4-hydroxypiperidine (product of the reduction of *III*), is identified in the reaction mixture in this case. Simultaneous and successive introduction of *III* and nitric acid has little effect on the yield and current efficiency. Lower values of current density, higher *III* content and the corresponding increase in the concentrations of nitric and sulphuric acids enhance current efficiency for *I*.

To find optimum conditions for the electrosynthesis of *I*, the method of mathematical planning of the experiment was used. The optimum conditions of electrolysis of a mixture of *III* and nitric acid which gives 99% of *I* and a current efficiency of 64% are as follows: concentration of *III* 0.65 mol l⁻¹; nitric acid concentration 1.15 mol l⁻¹; sulphuric acid concentration 1.75 mol l⁻¹; current density 300 A m⁻².

A polarographic study of the behaviour of azine of 2,2,6,6-tetramethyl-4-oxopiperidine (*V*) and hydrazone of 2,2,6,6-tetramethyl-4-oxopiperidine (*VI*) (2b and 3b) and the results of electrolysis with a controlled potential have revealed that both compounds are stable over the range of pH-values between 4 and 7, and are reduced to *I* (ref.⁸).

By analogy with *II*, the use of *VI* for synthesis of *I* is impractical, since its yield after separation is only 65%. *VI* is unstable and disproportionates into *V* and hydra-

zine. Therefore, VI has been prepared prior to electrolysis by mixing solutions of III and hydrazine sulfate (VII) with a ratio of the reagents 1 : 1.5 (3a).

TABLE IV
Yield of I and current efficiency on different electrodes; 22°C

Electrode material	Conditions of electrolysis				Yield of I, %	Current efficiency, %	
	Concentration, HNO ₃	H ₂ SO ₄	mol l ⁻¹ III	i_c A m ⁻²			Other
Cu-Hg	0.7	2	0.235	1 000	<i>a</i>	98	27
Cu-Hg	0.7	2	0.235	1 000	<i>b</i>	98	27
Cu-Hg	0.7	0.5	0.235	500	<i>b</i>	99	46
Cu-Hg	1.4	2	0.7	500	<i>b</i>	99	58
Pb-Hg	0.7	2	0.235	1 000	<i>b</i>	98	33
Pb-Hg	0.7	2	0.235	500	<i>b</i>	98	41
Pb-Hg	0.7	2	0.235	500	<i>a</i>	99	39
Hg	0.7	2	0.235	1 000	<i>a</i>	92	29

^a Simultaneous load of III and HNO₃; ^b consequent load of III and HNO₃.

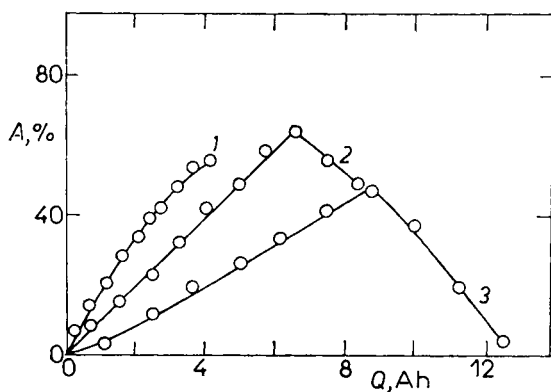


FIG. 3

Effect of the quantity of electricity on the hydroxylamine yield in 1M H₂SO₄ for various concentrations of nitric acid, mol l⁻¹: 1 0.7; 2 1.4; 3 2.1. 500 A m⁻², 20°C

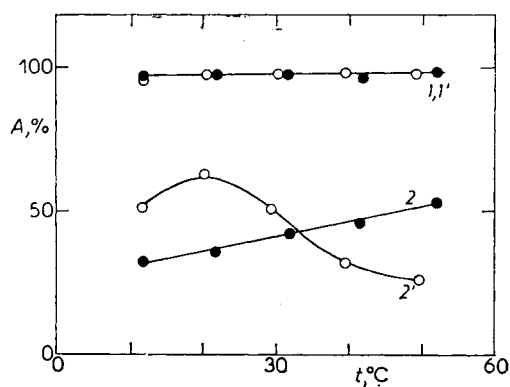


FIG. 4

Effect of the temperature on the yield of I (1, 1') and current efficiency (2, 2') in electrolysis of: 1, 2 V, pH 5.1 and 1', 2' a mixture of VII and III, pH 5.8. VII to III concentration ratio 1.5 : 1. Conc., mol l⁻¹: 1' 0.13; III 0.26. Cathode: lead. 400 A m⁻²

The results of studying electrolysis of *V* and a mixture of *III* and *VII* in buffer phosphoric acid solutions having various pH-values are given in Table V. The pH-values of background electrolyte has no effect on the yield of *I*. Higher pH-values diminish current efficiency which agrees with the data of polarographic studies. Thus, buffer solutions of phosphoric acid with pH-values 4–6 and 5–7 can be recommended for preparative electrosynthesis of *I* from *V* and a mixture of *III* with *VII*, respectively.

It is evident from Table VI that the yield of *I* in electrolysis of *V* and a mixture of *III* and *VII* on different cathodes is close to quantitative. The current efficiency obtained on amalgamated electrodes, lead, and mercury is higher than that on the rest of electrodes. The high yields of *I* on mercury cathode may be due to the formation of sodium amalgam (close to the reduction potentials of the starting materials). The low current efficiency on cadmium, tin, aluminium, and zinc result, apparently, from the instability of their surface during electrolysis.

Change in concentration of *V* has no effect on the yield of *I*. Change in concentration of *III* during electrolysis of the mixture of *III* with *VII* does not affect the yield of *I*, either. However, an increase in the concentration of *III* above 0.4 mol l^{-1} lowers the current efficiency due to a poor solubility of *VI*.

Yield of *I* is not influenced by the changes in current density during either the reduction of *V* or electrolysis of the mixture of *III* and *VII*. However, an increase in current density lowers considerably the current efficiency, due to current consumption for hydrogen liberation.

Temperature does not influence the yield of *I* obtained by electrolysis of *V* or the mixture of *III* and *VII*. But a temperature rise causes an increase in the current efficiency during electroreduction of *V*, evidently because of the fact that the rate of reduction of *V* exceeds that of hydrogen liberation. Above 25°C the reduction of the mixture of *III* and *VII* slows down due to an increase in current consumption required for hydrogen liberation (Fig. 4).

The possibility was studied of electrosynthesis of *I* from *III* and ammonia salts. Electrolysis of *III* in the presence of ammonia sulphate lacks selectivity in an acid, neutral, or alkaline solution: *I* and 2,2,6,6-tetramethyl-4-hydroxypiperidine are formed. Evaluation of the product yielded in ammonia solutions is difficult due to the abundance of salts.

Polarographic study has revealed that imines of 2,2,6,6-tetramethyl-4-oxopiperidine: 2,2,6,6-tetramethyl-4-phenyliminopiperidine (*VIII*) and *N,N'*-bis(2,2,6,6-tetramethylpiperidine)ethylenediimine (*IX*) are reduced to saturated derivatives 2,2,6,6-tetramethyl-4-phenylaminopiperidine (*X*) and *N,N'*-bis(2,2,6,6-tetramethylpiperidine)ethylenediamine (*XI*).

VIII appears to be electrochemically active at pH 8–9 (*5b*) and *IX* is unstable in aqueous solutions (*4b*). Taking into account a poor solubility of *VIII* in aqueous solutions and instability of *IX* in water, the electroreduction of these compounds

was carried out in methanol or dioxane with lithium chloride or quaternary ammonium salts.

TABLE V

Effect of pH on the yield of *I* (*a*) and current efficiency (*b*) during electrolysis of *V* and mixture of *III* and *VII*. Concentration, mol l⁻¹: *V* 0.13, *III* 0.25, *VII* 0.38; Pb-cathode; *i*_c = 400 A m⁻²; 22°C

pH	<i>V</i>		<i>III</i> + <i>VII</i>	
	(<i>a</i>) %	(<i>b</i>) %	(<i>a</i>) %	(<i>b</i>) %
3.8	98	35	—	—
4.4	97	35	97	61
4.7	98	35	—	—
5.1	98	35	—	—
5.8	95	28	97	62
6.4	97	23	98	62
7.0	95	17	99	63
8.8	—	—	97	51

TABLE VI

Effect of the cathode material on yield of *I* (*a*) and current efficiency (*b*) during electrolysis of *V* and a mixture of *III* and *VII*. Concentration, mol l⁻¹: *V* 0.13, *III* 0.258, *VII* 0.38; *i*_c = 400 A . m⁻²; 22°C

Cathode material	<i>V</i> ^b		<i>III</i> + <i>VII</i> ^c	
	(<i>a</i>) %	(<i>b</i>) %	(<i>a</i>) %	(<i>b</i>) %
Mercury	98	88	98	96
Amalgamated copper	99	40	97	80
Amalgamated lead	98	39	98	73
Zinc	99	40	95	35
Lead	98	35	97	62
Cadmium ^a	93	12	96	18
Tin ^a	94	11	electrolysis is not completed	
Aluminium ^a	96	13	—	—
Copper	98	29	92	49

^a Calculated for the reacted product; ^b pH 5.1; ^c pH 5.8.

Electrolysis of VIII and IX on metals with a high hydrogen overvoltage yields X and XI. The product yield is 60–80% and the current efficiency 30–50%. X and XI were identical to compounds synthesized by chemical methods published in^{11,12}. Changes in the concentration of the starting materials, current density, or other experimental conditions have little effect on the yield of the final product and affects only the reaction rate.

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