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ELECTROCHEMICAL REDUCTION OF HETEROCYCLIC ENAMMONIUM SALTS[1]

P. E. IVERSEN* and J. Ø. MADSEN†
Department of Organic Chemistry, University of Aarhus DK-8000 Aarhus C, Denmark

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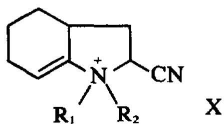
Abstract—Four N,N-disubstituted 2-cyano-Δ^7-hexahydroindolium salts, **1**, have been reduced at a mercury cathode in aqueous buffered solutions at intermediate pH-values. From the catholyte the following products were isolated and identified: 2-(β-cyanoethyl)-cyclohexanone, **5**, a secondary amine, **4**, and a mixture of *cis-trans* isomeric tertiary 2-(β-cyanoethyl) cyclohexylamines, **6**. A reaction path via the protonated enamine **3** is proposed based on the pH-dependence of the composition of the product mixture and a few reductions in DMF solution.

In a previous work[2] some N,N-disubstituted 2-cyano-Δ^7-hexahydroindolium salts of structure **1** were prepared from cyclohexanone enamines and α-chloroacrylonitrile. As part of a study of the properties of such heterocyclic enammonium salts it was decided to investigate their electrolytic reduction, and the results are reported below.

Unsaturated ammonium compounds do not seem to have been reduced electrochemically before, except in the form of immonium salts,[3] but saturated ammonium salts have been studied rather extensively giving mainly products from cleavage reactions on a mercury cathode.[4]

RESULTS AND DISCUSSION



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1a: $R_1 = R_2 = CH_3$; $X = Cl$
1b: $R_1,R_2 = -(CH_2)_4-$; $X = ClO_4$
1c: $R_1,R_2 = -(CH_2)_5-$; $X = Cl$
1d: $R_1,R_2 = -(CH_2)_2-O-(CH_2)_2-$; $X = Cl$

Polarography. Polarograms of 4 salts derived from dimethylamine **1a**, pyrrolidine **1b**, piperidine **1c**, and morpholine **1d** have been recorded in aqueous buffered solutions, and the pH-dependence of the halfwave potentials is depicted in Fig 1. The compounds generally gave only one polarographic wave (for **1b** two waves were just distinguishable in the pH-region 5–8), but the waves were mostly badly developed (drawn out) with maxima in the weakly alkaline region thus making the determination of $E_{1/2}$ values somewhat uncertain and the measurement of limiting currents unreliable. At pH < 4 the waves were partly masked by the hydrogen wave except for the morpholine derivative **1d** which could be distinguished down to pH 2. Around pH 10 the maxima became more pronounced, and the waveheight started decreasing due to the hydrolysis of the salts in alkaline medium. It is seen from Fig 1 that the halfwave potentials are rather insensitive to changes in pH of the medium, especially for compounds **1c** and **1d**, the discontinuities around pH 7 probably being related to a change in buffer system from phosphate to borate. The results point to a highly irreversible electrode process without participation of hydrogen ions in the rate determining step. The adsorption properties of the compounds have not been studied, and polarography or

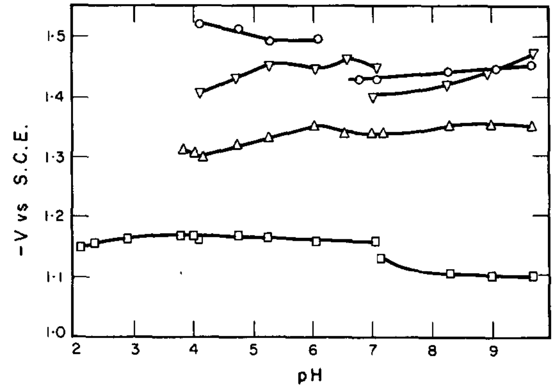

Fig 1. pH-Dependence of $E_{1/2}$ for some 2 - cyano - Δ^7 - hexahydroindolium salts (conc 80 mg/l, room temperature, ▽ **1a**, ○ **1b**, △ **1c**, □ **1d**).

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†Present address: Department of Organic Chemistry, Technical University of Denmark, DK-2800 Lyngby, Denmark.

cyclic voltametry in non-aqueous media have not been included in the present investigation.

Preparative electrolyses. On the basis of the polarographic findings it was decided to try cathodic reductions at controlled potential in weakly acidic, nearly neutral, and weakly alkaline medium. The same working potential was used for all 4 compounds: – 1·45 V (*vs* Ag/AgCl) in an acetate buffer of (initial) pH 4·3, –1·55 V in a phosphate buffer of pH 6·7, and – 1·65 V in a borate buffer of pH 9·4. Due to insufficient buffer capacity the pH of the catholyte had usually increased by 0·5–1 at the end of the electrolyses. As the chosen working electrode potentials were rather near to the decomposition potential of the media, some hydrogen evolution occurred making measurements of the electricity consumption uncertain, but the tendency was clear: usually somewhat more than 4F/mole were consumed in the acetate buffer and about 3F/mole in borate. After electrolysis the catholyte was worked up by continuous extraction with ether, first from acidic and then from alkaline solution. The oily residues from evaporation of the ethereal solutions were analyzed by GLC, and the results are given in Table 1.

The acidic extraction residues were shown to consist only of 2-(β-cyanoethyl)cyclohexanone, **5**, identified by comparison with an authentic sample. The alkaline extraction residues contained varying amounts of a secondary amine, **4**, corresponding to the enamine moiety of **1** (quantitative estimation of the compounds **4** were not carried out because of their varying volatility and high solubility in the aqueous phase), and a mixture of two isomeric tertiary amines, **6**, derived from the corresponding 2-(β-cyanoethyl)cyclohexanone enamines, **2**, (Scheme 1). The amines **6** were not known, and their identity and stereochemistry were declared by comparison with the products from formic acid reduction of the enamines **2** (see the following paper).[5] The isomers of **6** were separated by analytical GLC only, and the first eluated (lower boiling) component has been assigned the *trans* structure (see ref 5 for details).

Besides the work in aqueous solution described above a few experiments have been performed in DMF solution with the salt **1b**, the enamine **2b**, and its protonated form **3b** (as the immonium perchlorate) in order to study the products without complications from hydrolysis of possible intermediates during the electrolysis.

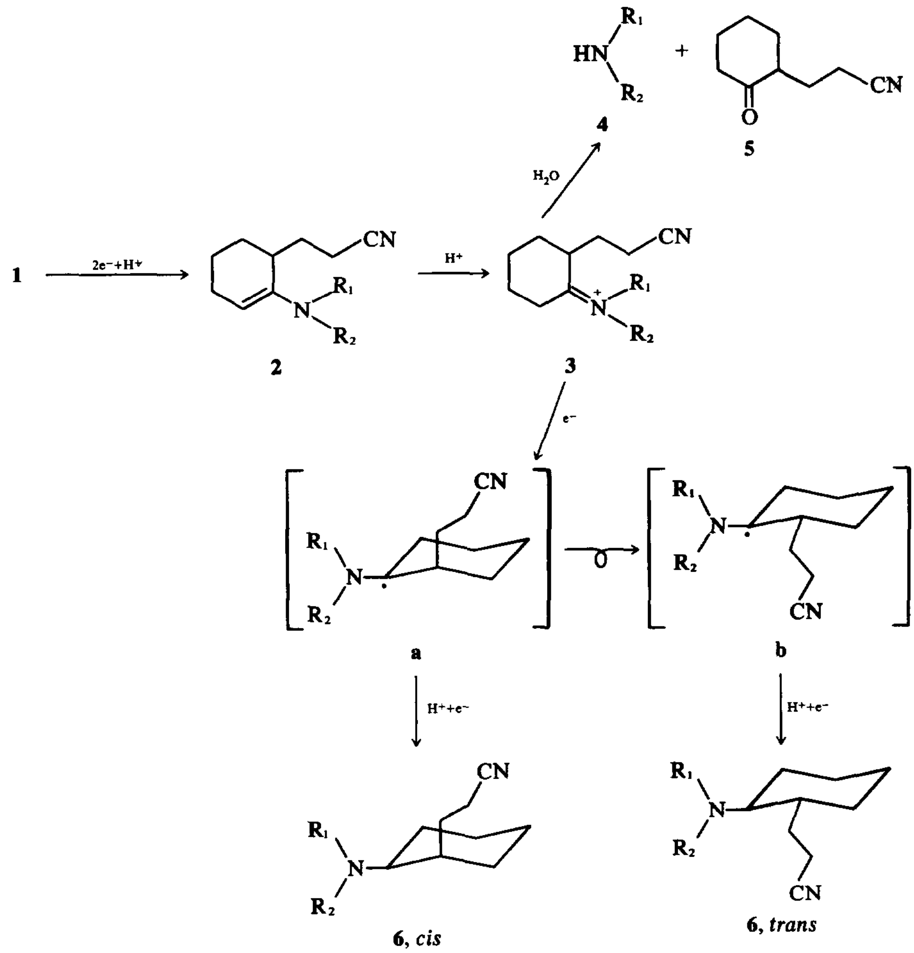
Compounds **1b** and **2b** were reduced in DMF containing about 1 M HCl, and after electrolysis water was added to the catholyte which was extracted as above. From the reduction of **1b** no ketone **5** was detected, but 50% of **6b** with a *trans* : *cis* ratio of 19:81 was produced. Reduction of **2b** gave 26% of **5** (probably from hydrolysis of unreduced **2b**) and 64% of **6b** with a *trans* : *cis* ratio of 15:85. Electrolysis of **3b** in the absence of added proton donor consumed nearly 1F/mole, and 52% of **5**, 16% of **6b** with a *trans* : *cis* ratio of 17:83. The isomer ratios were thus very close to that found in the aqueous (acetate buffer) electrolytic reduction of **1b** (Table 1) and not far from that of 12:88, found for the product from formic acid reduction[5] of **2b**.

The experimental findings can be rationalized in the following reaction scheme:

Thus the enammonium salt **1** is reduced in a 2-electron step to the enamine **2** with cleavage of the presumably weakest bond in α-position to the electronegative cyano group. A similar electrolytic cleavage has been reported for α-hydroxyacyl arylacetonitriles.[6] As the hydrolysis of enamines is subject to general acid and base catalysis,[7,8] generation of **2** in an aqueous buffer system must result in the formation of **4** and **5** during a preparative electrolysis, and these products have been observed. If, however, **2** is present in its protonated form **3** at the cathode surface in a protic medium, it is expected to undergo further reduction to the corresponding saturated amine **6** which was found to be present as a mixture of isomers. The experiment with such a salt (**3b**) in aprotic medium (described above) indicates, that the enamine **2b** (at the potential applied) is only reducible in its protonated form **3b**, and as a proton is needed for the formation of **6b** only half of the amount of **3b** is reduced in a 2-electron process giving (as found) an overall 1F/mole coulometry. The other half of **3b** then acts as a proton donor for the reduction of the first half of **3b** and is converted into **2b** which gives **5** upon hydrolysis during work-up. The rather low yield of **6b** can be explained by an unefficient

Table 1. Yields of products and isomer ratios from preparative electrolytic reduction of N,N-disubstituted 2-cyano-Δ^7-hexahydroindolium salts (**1**) in aqueous buffer systems

Starting material	Acetate			Phosphate			Borate		
	%**5**	%**6**	*trans* : *cis*	%**5**	%**6**	*trans* : *cis*	%**5**	%**6**	*trans* : *cis*
Ea	14	60	24:76	37	50	31:69		3	83:17
Ib	6	82	19:81	12	76	28:72	82	10	77:23
Ic	60	38	9:91	71	18	17:83	91	2	76:24
Id	42	50	60:34	93	0	—	88	0	—



SCHEME 1

alkaline extraction in this particular experiment. If an excess of a strong proton donor was used a yield of more than 50% of **6b** could easily be achieved (as described above).

The observed pH-dependence of the ketone/amine product ratio is in good accordance with the assumption of **3** being the intermediate reducible species leading to more of the amine **6** with increasing acidity of the medium. This is also consistent with the fact that **1d** derived from the less basic morpholine did only give **6d** in the most acidic buffer. The variation of the *trans* : *cis* ratios with pH, the relative amount of the *trans* isomer increasing with decreasing acidity, may be explained if it is assumed that electron transfer to the immonium ion **3** stereoselectively leads to the neutral radical **a** (Scheme 1) of *cis* geometry (in the same way as hydride ion transfer to **3** in formic acid reductions predominantly produces the *cis* amine).[5] At lower pH protonation at nitrogen and transfer of the second electron followed by proton shift from N to C take place so rapidly that stereomutation of the radical **a** is limited except for the less basic morpholine derivative. At higher pH the lifetime of the intermediate radical **a** is sufficiently increased to permit isomerization to the thermodynamically more stable radical **b** of *trans* geometry.

The formation of a saturated tertiary amine of type **6** is different from the findings of Andrieux and Saveant[3] who observed dimer amine products from electrolytic reduction of immonium salts derived from acyclic carbonyl compounds in acetonitrile or benzonitrile solutions. We have not found any dimeric products, but cannot exclude their presence in trace amounts. However, in view of the high steric requirements for dimerization of cyclohexyl radicals like **a** or **b** the different course of the reduction of our substrates is understandable, and these may also very well be more efficient proton donors in the more basic solvent DMF.

EXPERIMENTAL

Apparatus. The reductions in aqueous media were performed in a conventional 3-electrode H-type cell[9] (160–180 ml catholyte volume, about 40 cm^2 electrode area) surrounded by an ice bath, using a Juul Electronic 100 V/3A or 100 V/10A potentiostat. The reductions in DMF were run in a similar cell with closed cathode compartment and a Ag/AgCl/0·5 M LiCl reference electrode. The polarograph was a Radiometer PO4fg using a capillary with m = 1·75 mg Hg/sec and t = 4·80 sec (water, open circuit). Analytical GLC was done on a FM 810 gaschromatograph, details are given in ref 5. A Radiometer PHM22r instrument was used for measurements of pH.

Materials. The preparation of the salts **1b**, **1c**, and **1d** has been described earlier.[2] The salt **1a** was prepared by a similar procedure.[10] 2-(β-Cyanoethyl)cyclohexanone **5** was prepared by hydrolysis of the corresponding pyrrolidine enamine[5] **2b**.

2 - (β - Cyanoethyl)cyclohexylidenepyrrolidinium perchlorate, **3b**. Compound **2b** (5·0 ml = 5·15 g = 0·0262 mole) was dissolved in dry ether and precipitated as a partly oily hydrochloride (very hygroscopic) by bubbling excess dry HCl through the soln during 5 min. The solvent was evaporated leaving 6·65 g of oily residue which was dissolved in acetonitrile (50 ml, dried over type 4A molecular sieves), and the soln was added to a soln of sodium perchlorate (3·09 g = 0·0262 mole) in acetonitrile (50 ml). The NaCl ppt was filtered off, washed with acetonitrile (20 ml + 10 ml) and dried, giving 1·43 g (97·5%). To the acetonitrile soln was added dry ether (400 ml), the ppt filtered off and dried, giving 5·85 g (72%) of crude, nonhygroscopic **3b**, m.p. 125–6° (uncorr.). Recrystallization from abs EtOH (100 ml) gave 3·55 g of analytically pure **3b**, m.p. 126–7°. (Found: C, 51·09; H, 6·80; N, 9·30; Cl, 11·68. $C_{13}H_{21}N_2ClO_4$ requires: C, 51·19; H, 6·95; N, 9·20; Cl, 11·64%).

Composition of buffer systems. Acetate: 1·0 M acetic acid/0·5 M potassium acetate; phosphate: 1·0 M potassium dihydrogenphosphate/1·0 M potassium monohydrogenphosphate; borate: 0·5 M boric acid/0·5 M potassium borate.

General electrolytic procedures

Aqueous solution. **1** (5·0 g) was dissolved in the appropriate buffer system in the cathode compartment of the cell and reduced overnight at the specified potential (− 1·45 V, − 1·55 V, or − 1·65 V *vs* Ag/AgCl/sat. KCl). During the electrolysis some oil separated, and the cell and the mercury were washed with ether (25 ml) after separation of the catholyte at the end of the electrolysis. 2N HCl (70 ml) was added to the catholyte which was then extracted continuously overnight by ether which was dried over $MgSO_4$. After the first extraction the catholyte was neutralized by addition of Na_2CO_3, made alkaline by addition of 100 ml of 2N NaOH, and again extracted continuously overnight by ether which was dried over K_2CO_3. The oily residues from the ethereal extracts were analyzed by means of GLC.

The crude residues were worked up by distillation *in vacuo* to give the pure products **5** or **6** which were identified by their b.ps, elemental analysis, and comparison of their NMR and IR spectra and GLC retention times with those of authentic specimens. The efficiency of the extraction was found to be of the order 95% by checking the procedure with 2·0 ml samples of **5** and **6b**. The yields given in Table 1, however, have not been corrected for these losses, but are the actual isolated yields measured by GLC and based on determinations from several experiments.

Non-aquous solution. **1b** (5·0 g) was reduced at −0·9 V in DMF (dried over type 4A molecular sieves) containing 1·1 M HCl and 0·5 M LiCl. **2b** (5·0 ml) was reduced at − 1·2 V in 0·75 M HCl/DMF. In both cases some gas evolution was observed during the electrolysis which was stopped at an arbitrary point next day, because the current did not cease totally. **3b** (4·7 g) was reduced at − 1·6 V in 0·5 M LiCl/DMF with the consumption of nearly 1F/mole, and only a very small current was flowing through the cell when the electrolysis was stopped. To the catholytes was added water (200-300 mg), followed by continuous extraction with ether from acidic and alkaline soln as above. The ethereal solutions were washed a couple of times with water to remove DMF before drying and analysis as above.

REFERENCES

[1] Presented (in part) at the Journées d'Electrochimie Organique, Clermont-Ferrand, May 28–29 (1970)

[2] J. Ø. Madsen and S.-O. Lawesson, *Tetrahedron* **24**, 3369 (1968)

[3] C. P. Andrieux and J. M. Saveant, *J. Electroanal. Chem.* **26**, 223 (1970)

[4] L. Horner, *Organic Electrochemistry—An Introduction and a Guide* (Edited by M. M. Baizer) p. 731. Marcel Dekker, New York (1973), and refs cited

[5] J. Ø. Madsen and P. E. Iversen, *Tetrahedron* **30**, 3493 (1974)

[6] S. Wawzonek and J. D. Fredrickson, *J. Electrochem. Soc.* **106**, 325 (1959)

[7] E. J. Stamhuis and W. Maas, *J. Org. Chem.* **30**, 2156 (1965)

[8] W. Maas, M. J. Janssen, E. J. Stamhuis, and H. Wynberg, *Ibid.* **32**, 1111 (1967)

[9] P. E. Iversen, *J. Chem. Ed.* **48**, 136 (1971)

[10] J. Ø. Madsen and S.-O. Lawesson, forthcoming paper