Electroörganic Preparations

XV. Reduction of Some Oximes to Ketimines

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Controlled potential reduction of oximes has previously been investigated.[1] The results were found to be best explained by assuming that the four-electron reduction of oximes generally found in acid solution passed through the ketimine rather than through the hydroxylamine, the nitrogen-oxygen single bond thus being cleaved in preference to the carbon-nitrogen double bond, but in no instances was the ketimine isolated. In a few cases, *e.g.* testosteronepropionate oxime, two two-electron reductions were found, but the ketimine presumably formed in the first two-electron reduction was unstable, and only the hydrolyzed ketimine, *i.e.* testosteronepropionate, was isolated.

In the present investigation an oxime and an oxime anhydride, both of which yield two two-electron polarographic waves in acid solution, are reduced at a potential controlled at a value corresponding to the first wave. The purpose was to find whether ketimines could be isolated from these reductions and thus yield further evidence for the reduction route previously postulated.[1] The compounds reduced were 2,4-dihydroxybenzophenone oxime and 4-(4'-methoxyphenyl)-2,3-benzoxazin-1-one.

2,4-Dihydroxybenzophenone oxime. This compound seems not to have been prepared before. The results from a polarographic investigation of 2,4-dihydroxybenzophenone oxime and 2,4-dihydroxybenzophenone imine in acid solution is found in Table 1. A few results from alkaline solutions are included in Table 1, but a detailed investigation seemed not warranted by the scope of this paper. The compounds contain three acidic groups and the polarographic behaviour of the imine is dependent on the buffer composition.

The oxime is reduced in two steps at pH < 4, and the half-wave potentials of the second wave are the same as the half-wave potentials of the imine. The half-wave potentials of 2,4-dihydroxybenzophenone are about 0.2 V more negative than those of the ketimine. At pH > 4 the polarographic behaviour of the oxime

Table 1. Limiting currents (μA) and half-wave potentials (*vs* S.C.E.) of 2,4-dihydroxybenzophenone oxime and 2,4-dihydroxybenzophenone imine hydrochloride. Concentration 40 mg/l.

		oxime				ketimine	
		1. wave		2. wave			
Buffer	pH	i_l	$-E_{½}$	i_l	$-E_{½}$	i_l	$-E_{½}$
Hydrochloric acid	0.15	1.05	0.57	1.05	0.72	1.00	0.71_5
,,	0.55	1.05	0.57_5	1.05	0.72_5	1.00	0.72
,,	0.85	1.05	0.59_5	1.05	0.73_5	1.00	0.73_5
,,	1.40	1.05	0.60_5	1.05	0.74_5	1.05	0.74_5
Glycine	2.20	1.05	0.64	1.10	0.76	/1.05	0.77
Citrate	2.60	1.00	0.68_5	1.10	0.78	1.00	0.79
,,	3.05	1.00	0.72	1.05	0.80	1.00	0.79_5
Acetate	4.40	2.10	0.84			1.05	0.85
,,	4.90	2.05	0.88			1.05	0.88
Succinate	5.10	2.10	0.90			1.05	0.90
Phosphate	6.20	1.90	0.97			1.00	0.95_5
,,	6.65	1.75	1.01			0.95	0.99_5
,,	7.20	1.55	1.05			1.00	1.03_5
Borate	8.30	1.5	1.57			0.90	1.53
,,	9.10	1.5	1.69			0.95	1.57
Glycine	9.10					0.90	1.25
Borate	9.70	1.4	1.75			0.90	1.60
Phosphate	11.2					0.95	1.50
,,	11.7					0.95	1.51_5
Potassium hydroxide	13					0.90	1.57

resembles that of benzophenone oxime, and at pH > 11 the oxime yields no polarographic wave. The ketimine is reducible in the whole pH-region, and at pH > 6 the imine is reduced at less negative potentials than is the oxime.

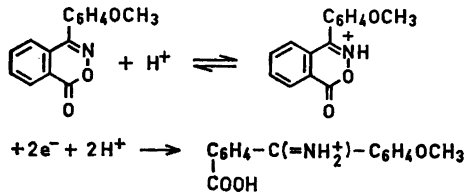
A preparative reduction of 2,4-dihydroxybenzophenone oxime in N hydrochloric acid containing 5 % alcohol at a potential corresponding to the first polarographic wave yielded the ketimine, which was isolated as the hydrochloride. At higher alcohol concentrations (40 %) the separation of the two waves was less satisfactory for a preparative reduction. The electrode reaction corresponding to the first wave of the oxime can be formulated as:

$$RR'C{=}N{-}OH + H^+ \rightleftharpoons RR'C{=}NH^+{-}OH$$
$$+ 2\ e^- + 2\ H^+ \rightarrow RR'C{=}NH_2^+ + H_2O$$

At a more negative potential the ketimine is reduced to the amine.

4-(4'-Methoxyphenyl)-2,3-benzoxazin-1-one. The polarographic behaviour of this compound, which is the anhydride of 2-(4'-methoxybenzoyl)benzoic acid oxime, has been described previously.[2] The half-wave potentials of 2-(4'-methoxybenzoyl)benzoic acid ketimine are the same as those of the second wave of the oxime anhydride. At high pH the benzoxazinone ring is opened thus forming the oxime, which is not reducible at high pH. The ketimine is reducible at all pH's at a potential about 0.2 V less negative than that of the ketone, but in neutral and alkaline solution the imine is hydrolyzed to the ketone at a pH-dependent rate. The imine has its highest stability in mineral acid solution, and the lowest stability in neutral solution. At pH 13 it seems more stable than in an acetate buffer pH 5.

The oxime anhydride was reduced in 0.5 N hydrochloric acid containing 60 % alcohol at the potential of the first wave. The reduction consumed two electrons per molecule. From the reduced solution could be isolated a hydrochloride which was shown to be the ketimine hydrochloride of 2-(4'methoxybenzoyl)benzoic acid by the analysis and its hydrolysis to the ketone. The electrode reaction thus is:



The isolation of the ketimines from the reduction of these two oximes substantiates the reduction route previously postulated for the reduction of oximes in acid solution: The primary reduction of the protonated oxime is the reductive cleavage of the nitrogen-oxygen bond and this is followed by the reduction of the azomethine compound thus formed. A similar reduction route is believed to operate in the four-electron reduction of phenylhydrazones in acid solution. In some hydrazone derivatives, *e.g.* 4-phenylphthalazin-1-one, a two-electron reduction is found,[2] and in this case a reduction of the carbon-nitrogen double bond occurs.

Experimental. The apparatus was the same as that used previously.[3] The capillary delivered 3.14 mg of mercury per second at a corrected mercury column height of 48.5 cm. The drop time was 3.82 sec. (H_2O, open circuit).

Materials. 2,4-Dihydroxybenzophenone imine was prepared according to Hoesch.[4] The oxime was prepared by heating the ketimine with an excess of hydroxylamine in an acetate buffer containing 25 % alcohol to 100° in a closed vessel for 48 h. On evaporation of the alcohol and cooling, the compound forms a viscous oil which crystallizes slowly. It can be recrystallized from dilute alcohol or benzene, but is best purified by sublimation *in vacuo*. M. p. 178°–180°. (Found: C 68.28; H 4.79; N 6.31. Calc. for $C_{13}H_{11}NO_3$: C 68.11; H 4.84; N 6.11). The compound can also be made from the ketone, but more resinous material is formed.

Reduction of 2,4-dihydroxybenzophenone oxime. This compound (0.5 g) was dissolved in alcohol (8 ml) and added to 160 ml of a prereduced aqueous N hydrochloric acid. Owing to its low rate of crystallization most of it remained in solution and the rest formed an emulsion. The compound was reduced at the potential of the crest of the first wave. The reduction consumed two electrons per molecule. The reduction completed, the solution was evaporated *in vacuo* at a bath temperature not exceeding 50°C. The residue was extracted with absolute alcohol and dry ether was added to the extract. The precipitate formed was identified as 2,4-dihydroxybenzophenone imine hydrochloride from the I.R. spectrum and polarographic data. It was dissolved in water and on addition of bicarbonate the yellow imine was precipitated m.p. 225°.

Reduction of 4-(4'-methoxyphenyl)-2,3-benzoxazin-1-one. 1.00 g of the oxime anhydride was reduced in 0.5 N hydrochloric acid containing 60 % alcohol. The reduction consumed two

electrons per molecule. The solution was evaporated nearly to dryness *in vacuo* in a slow current of air at a bath temperature not exceeding 40°C. To the residue were added 200 ml of butanol; the butanol solution was concentrated *in vacuo* to 30 ml. A small precipitate of potassium chloride (from the agar bridge) was filtered off and dry ether added to the filtrate. A precipitate, 940 mg, was filtered off, dissolved in alcohol and reprecipitated with ether. (Found: C 61.60; H 5.52; N 4.54; Cl^- 11.12. Calc. for $C_{15}H_{14}NO_3Cl,1/2\ C_2H_5OH$: C 61.07; H 5.44; N 4.45; Cl^- 11.26). On heating in a closed capillary the compound turned yellow at about 100°, decomposed around 170° and was completely melted at 178°. The I.R.-spectrum contained a.o. bands at (cm^{-1}): 3300—2500, 1705 (s), 1640 (ms), and 1594 (ms).

1. Lund, H. *Acta Chem. Scand.* **13** (1959) 249.
2. Lund, H. *Acta Chem. Scand.* **14** (1960) 359.
3. Lund, H. *Acta Chem. Scand.* **17** (1963) 972.
4. Hoesch, K. *Ber.* **48** (1915) 1122.

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Studies on Sphingosines

3. C_{20}-Dihydrosphingosine, a hitherto Unknown Sphingosine *

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Three sphingosines have so far been reported, namely C_{18}-sphingosine,[3] C_{18}-dihydrosphingosine [4,5] and C_{20}-sphingosine.[6] A fourth sphingosine, C_{20}-dihydrosphingosine, is the subject of this communication.

The new compound has been isolated as a dinitrophenyl (DNP) derivative from a mixture of DNP-sphingosines, prepared as described earlier.[1] The DNP-sphingosines are freed from impurities and by-products from the acid hydrolysis [2] by chromatography on silicic acid using increasing proportions of diethyl ether in light petroleum (b.p. 60°—70°). The mixture of DNP-sphingosines is then fractionated on paper on a preparative scale. This procedure is a modification of an earlier described analytical method based on reversed phase chromatography.[1] The separated compounds are extracted from the paper with ethanol, rechromatographed and finally freed from solvent (tetralin) by-products on a silicic acid column. In this way five hitherto unknown sphingosines have been prepared in a pure form. Of these C_{20}-dihydrosphingosine is separated from the known sphingosines as shown in Fig. 1.

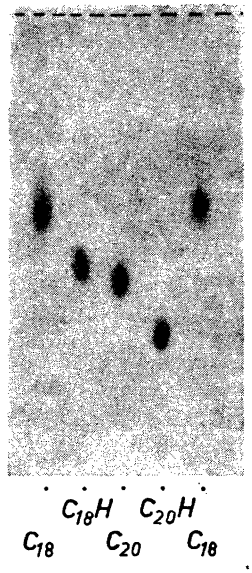

Fig. 1. Chromatogram showing from left to right pure dinitrophenyl derivatives of C_{18}-sphingosine, C_{18}-dihydrosphingosine, C_{20}-sphingosine, C_{20}-dihydrosphingosine and C_{18}-sphingosine. Solvent: Upper phase of methanol-tetralin-water 90—10—10 (v/v). Time for development: 6 h. For further details, see Ref.[1] The chromatogram was photographed with »Kodak, Photographic Plates, B 10». (C_{20}-sphingosine, which has not been isolated before, will be subject of a later communication by the author.)

The pure DNP-C_{20}-dihydrosphingosine (Found: C 61.38; H 8.77; N 8.42. Calc. for DNP-C_{20}-dihydrosphingosine,

* Communications 1 and 2 in this series are Refs. 1 and 2, respectively.