Tetrahedron Letters No. 33, pp 3023 - 3025. 0040-4039/78/0808-3023$02.00/0
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SYNTHESIS OF PYRROLIDINE OR PIPERIDINE DERIVATIVES BY ELECTROCHEMICAL REDUCTION OF SCHIFF BASES IN THE PRESENCE OF 1,ω-DIBROMOALKANES

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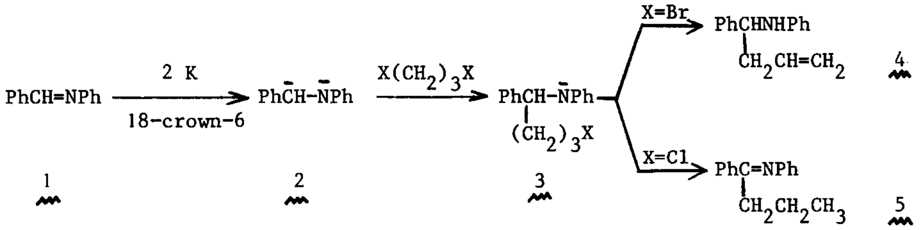
It has been recently shown[1] that attempts to utilize the monomeric dianion **2** of N-benzalaniline **1** in order to prepare pyrrolidine derivatives by alkylation with 1,3-dihalopropane did not succeed. Alkylation took place first at the carbon anionic site of **2** which was generated by chemical reduction of N-benzalaniline **1** with potassium in the presence of crown ether (scheme 1). The formation of the basic amine anion **3** favored a dehydrohalogenation and the formation of **4** and **5** (scheme 1). Previous attempts to use dihalides to synthesize aziridines and azetidines were unsuccessful too[2]. In the absence of crown ether, reduction of Schiff bases by alkali metals leads to dimeric dianions[3,4].

Scheme 1



Below is reported a convenient method of synthesis of pyrrolidine or piperidine derivatives by electrochemical reduction of Schiff bases in the presence of 1,ω-dibromoalkanes. The electrochemical reductions of N-benzalaniline **1** in the presence of 1,4-dibromobutane and of benzeneamine N-(2-pyridylmethylene) **6**[5] in the presence of 1,3-dibromopropane illustrate this method.

The electrolyses are run in DMF, at a mercury cathode, with tetrabutylammonium iodide 0.1 M as supporting electrolyte. In DMF, polarograms of Schiff bases usually exhibit two waves of unequal height[6-8]. The first wave may correspond to the formation of an anion radical ; its lifetime is of the order of one second in the case of N-benzalaniline **1**[8]. In table 1 are given the polarographic half-wave potentials $E_{1/2}$ (vs SCE) of the first wave of the substrate and of the corresponding dibromoalkane. The conditions for the electrolytic reductions are also given in table 1.

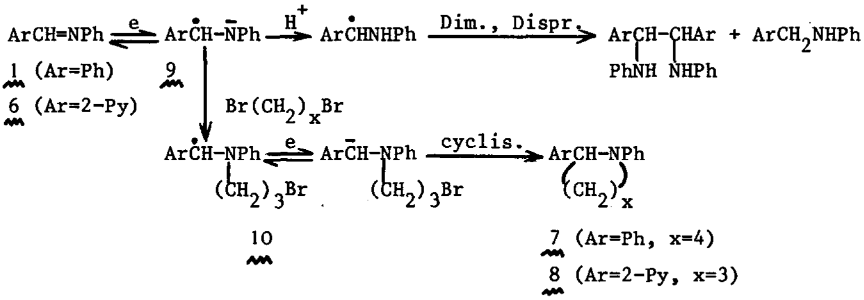
Table 1

Schiff base	$E_{1/2}$ (V)	Conc. (10^{-3}M)	$Br(CH_2)_xBr$	Conc. (10^{-3}M)	$E_{1/2}$ (V)	Applied Pot. (V)	F consumed	Isolated Cyclic Compounds	Yield (%)
1	- 1.83[8]	3.4	4	3.5	- 2.06	- 1.80	2.1	**7**	38
		3.4		35		- 1.80	3.1		59
6	- 1.54	11	3	110	- 2.02	- 1.56	8.3	**8**	23

After dilution of the catholyte with water, neutralization, extraction with ether and evaporation of the solvent in vacuo, the electrolysis compounds are separated from the excess of dibromoalkane by an acid extraction. The cyclic compounds **7**[9] and **8**[10] were isolated after purification by column chromatography on silica. Their yields are given in table 1. When dibromoalkane is added in a ten fold excess, the yield of cyclic compounds increases as well as the number of faraday consumed. This last phenomenon may be due to an indirect[11] or a direct reduction of dibromoalkane in excess. In this case, the electrolysis is stopped before a total depletion of the current.

The following mechanism of reductive cyclisation agrees with our experimental results and the known results on the electrochemical reduction of Schiff bases in the absence[6-8] or in the presence[12] of alkylhalides.

Scheme 2



The N-alkylation of the radical anion **9** competes with its protonation by residual water[8]. The formation then the reduction of the radical **10** into a cyclic compound is therefore favored by increasing the dibromoalkane concentration.

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9. 1,2-diphenyl-piperidine **7** is a known compound. A. Gaumeton and C. Glacet, Bull. Soc. Chim. France, 1501 (1959).
   Nmr ($CDCl_3$) 1.5-2.1 (m, 6H) ; 3.1-3.4 (m, 2H) ; 4.45 (t, 1H, 5Hz) ; 6.7-7.3 (m, 10H).
10. 1-phenyl-2-(2-pyridyl)-pyrrolidine **8**. White needles. m_p = 90°C (petrol ether).
   Nmr ($CDCl_3$) : 1.7-2.5 (m, 4H) ; 3.15-3.9 (m, 2H) ; 4.7-4.9 (q, 1H) ; 6.4-7.6 (m, 8H) ; 8.5-8.7 (m, 1H). Ir (KBr)cm^{-1} (intensity) : 3150-2700 (m), 1610 (s), 1600 (m), 1575 (m), 1510 (s), 1475 (m), 1440 (m), 1380 (s), 1190 (s), 1000 (m), 865 (m), 750 (s), 695 (s).
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(Received in France 16 April 1978; received in UK for publication 22 June 1978)