

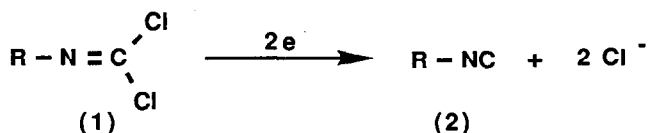
## ELECTROCHEMICAL REDUCTION OF CARBONIMIDOYL DICHLORIDES. A NEW METHOD FOR THE PREPARATION OF ISOCYANIDES

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**Abstract:** The cathodic reduction of carbonimidoyl dichlorides provides a new, mild and free-reagent method for the preparation of isocyanides in almost quantitative yields.

The synthesis of isocyanides was excellently reviewed some time ago<sup>1</sup>. Although a wide variety of reactions leading to isocyanides were reported those that appear to have the most general application in synthesis are fewer in number: reaction of alkyl halides with heavy metal cyanide salts, reaction of primary amines with dichlorocarbene and the elimination of water from N-monosubstituted formamides by treatment with either phosgene, arylsulfonyl chlorides, cyanuric chloride or phosphorus oxychloride. The phosgene method gives by far the best results generally, but it has the inconvenience of its high toxicity. In the subsequent literature numerous efforts devoted to improving the methods of synthesis of isocyanides, using alternatives reagents to phosgene are found<sup>2</sup>. Advances in this field are substantial because of the proved synthetic utility of isocyanides, especially in the synthesis of heterocyclic compounds, metal complexes, and polymers, as well as a recent attention to the isolation and synthesis of naturally occurring isocyanides<sup>3</sup>.



We herein report a new, efficient and simple method for the synthesis of isocyanides, via the cathodic reduction of carbonimidoyl dichlorides (1) which are easily available from isothiocyanates, isocyanates and N-monosubstituted formamides<sup>4,5</sup>. These reactions provide the corresponding isocyanides (2) in almost quantitative yields. While the electrochemical reductive dehalogenation processes of other gem-polyhalogenated compounds had been studied from different points of view<sup>6</sup>, the electrochemical reductions of carbonimidoyl dichlorides remained unknown.

In contrast with other methods this procedure shows valuable noteworthy advantages. Thus, the preparation of isocyanides is performed by a reagent-free reaction which is carried out under very mild conditions. Therefore, two serious obstacles in isocyanide synthesis can be suppressed: (i) loss of yield due to secondary processes and (ii) isolation and purification of the products from a complex reaction mixture. The application of the usual techniques of purification is frequently difficult because the exposure to isocyanide vapours, even at low levels, is "extremely distressing"<sup>1</sup>. However, by the present method any subsequent working up after the electrochemical reaction can be avoided since isocyanides are quantitatively generated in a dimethylformamide solution which additionally contains inorganic lithium perchlorate and lithium chloride salts, exclusively. This solution could be used for most synthetic purposes. The very pronounced mildness of the procedure is also a promising feature of the method in order to enable "in situ" synthesis by electrolysis of carbonimidoyl dichlorides in the presence of non-electroactive reagents. This would permit the capture of labile isocyanides and work with them at very low concentrations<sup>7</sup>. If isolated isocyanides are required in a pure state, these are easily obtained by addition of water and simple extraction with ether.

**Typical Experimental Procedure.** Electrolyses were carried out under a constant cathodic potential in a concentric cylindrical cell with two compartments separated by a circular glass frit (medium) diaphragm. A mercury pool (diameter 5 cm) was used as the cathode and a platinum plate as the anode. The catholyte was magnetically stirred. The temperature was kept at 15 °C by external cooling. The reductions were carried out<sup>8</sup> in DMF-LiClO<sub>4</sub>, 0.2 M. Approximately 50 mL and 20 mL of this solution were placed in the cathodic and the anodic compartments, respectively. To prevent accumulation of electrogenerated acid in the anode compartment, anhydrous sodium carbonate (3g) was placed in this compartment. Solutions of the carbonimidoyl dichlorides (1) (5 mmol) were electrolyzed under the appropriate cathodic potential. The electricity consumption was 2 F · mol<sup>-1</sup> for all cases. GC/MS analyses with capillary column of the catholyte solutions showed a single peak of the corresponding isocyanides. High purity products were

isolated dropping the catholyte solution onto cold brine (200 mL) and filtrating or extracting the mixture with ether, which was washed with cold water and dried (Na<sub>2</sub>SO<sub>4</sub>). The directly collected solid products and those obtained after removing ether under reduced pressure gave satisfactory IR, MS and high field <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra<sup>9</sup>. The results are summarized in Table 1. Entry numbers 3 and 4 correspond to new isocyanides<sup>10</sup>.

Table 1. Preparation of isocyanides (2) by cathodic reduction of carbonimidoyl dichlorides (1).

Entry	R	Cathode Potential	
		(V vs SCE)	Yield (%) <sup>a</sup>
1	Phenyl	- 1.90	91
2	4-Chlorophenyl	- 1.40	94
3	2-Chloro-4-Methylphenyl	- 1.45	82
4	2,4-Dichlorophenyl	- 1.25	95
5	Benzyl	- 1.75	96
6	Cyclohexyl	- 1.85	90

<sup>a</sup>yields in isolated products.

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3. See review: Edenborough, M.S.; Herbert, R.B. *Natural Product Reports*, 1988, 229.
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  5. The formation of isocyanides along with coupling products was observed when the reaction of phenyl and cyclohexyl carbonimidoyl dichlorides with Grignard reagents were carried out in the presence of palladium catalyst Ito, Y.; Inouye, M.; Murakami, M. *Tetrahedron Lett.* **1988**, 29, 5379.
  6. See for example: Peters, D.G. in *Organic Electrochemistry*; Lund, H.; Baizer, M.M. Eds.; Marcel Dekker, Inc.: New York, 1991; Chap. 8.
  7. Some of these reactions are now in progress in our laboratory.
  8. DMF was taken from a freshly opened bottle and dried with molecular sieve. LiClO<sub>4</sub> was anhydrous. Both were purchased from Fluka, and were used directly without purification.
  9. Products of reduction of phenyl and benzylcarbonimidoyl dichlorides were compared with authentic samples of phenyl and benzyl isocyanides respectively.
  10. Spectral data for 3: IR (nujol) 2126 cm<sup>-1</sup>; MS 70 eV m/z (rel. intensity) 153 (M<sup>+</sup> + 2, 8), 151 (M<sup>+</sup>, 26), 116 (100), 89 (31), 63 (17), 50 (11); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 2.36 (s, 3H), 7.08 (d, 1H, <sup>3</sup>J = 8.1 Hz) 7.27 (s, 1H), 7.29 (d, 2H, <sup>3</sup>J = 8.3 Hz), <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ: 21.04, 122.77, 127.44, 128.12, 130.19, 130.33, 141.07, 168.28.; spectral data for 4: IR (nujol) 2128 cm<sup>-1</sup>; MS 70 eV m/z (rel. intensity) 173 (M<sup>+</sup> + 2, 66), 171 (M<sup>+</sup>, 100), 136 (35), 100 (23); <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ: 7.30 (dd, 1H, <sup>3</sup>J = 8.5 Hz, <sup>4</sup>J = 1.8 Hz), 7.39 (d, 1H, <sup>3</sup>J = 8.5 Hz), 7.51 (d, 1H, <sup>4</sup>J = 1.8 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ: 124.02, 127.87, 128.49, 129.99, 131.66, 135.71, 170.67.

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