Electrosynthesis of 5-Chloro- and 5-Azido-4-pyrazole Carboxylic Acid at the Nickel Hydroxide Electrode

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(Received December 16, 1993)

Pyrazole derivatives are valuable intermediates for drugs and agrochemicals.[1—5] The literature seems to be almost devoid of suitable methods, from environmental point of view for the preparation of simple pyrazole carboxylic acid derivatives which could be prepared from aldehydes with oxidizing agents such as $NaClO_4$.[6] These reagents are partially toxic and large scale conversions create waste disposal problems. A clean oxidation technique would be the indirect electrochemical oxidation at the nickel hydroxide anode. Until recently there have been few examples of oxidation of heterocyclic aldehydes to the corresponding acids.[7] We represent here an electrochemical method for oxidizing 5-chloro-4-pyrazole carbaldehyde (**1**) and 5-azido-4-pyrazole carbaldehyde (**2**) to their corresponding acids (**3** and **4**) at a nickel hydroxide anode in good yields (80—85%) (Scheme 1).

Experimental

5-Chloro-3-methyl-1*H*-pyrazole-4-carbaldehyde[8] **1** and 5-azido-3-methyl-1-phenyl-1*H*-pyrazole-4-carbaldehyde[9] **2** were prepared according to the reported procedures.

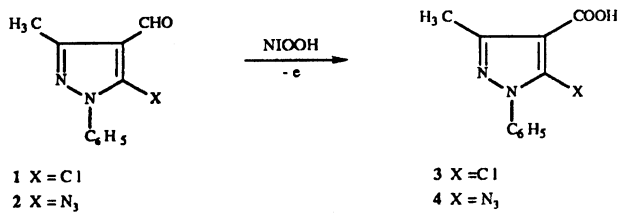
Constant current electrolysis was carried out using a stabilized current source model NTN 700 M 200 (FuG, Rosenheim). The electrolytic cell comprised a beaker (300 ml) equipped with nickel net anode and stainless steel plate cathode; the anode was converted to nickel hydroxide after the method reported by Kaulen and Schafer.[10]

Results and Discussion

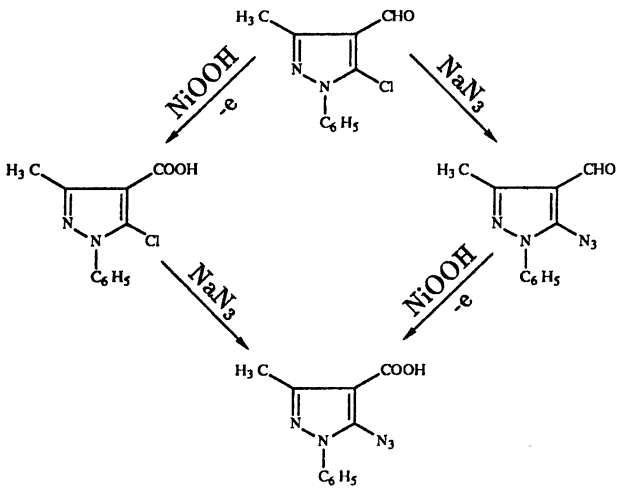
Preparation of Pyrazolecarboxylic Acid Derivatives: 5-Chloro-3-methyl-1-phenyl-1*H*-pyrazole-4-carboxylic acid **3** was obtained by the dissolution of the corresponding aldehyde **1**. The aldehyde (1 g, 4.5 mmol) was dissolved in 200 cm^3 *t*-butyl alcohol/water (1:1) containing 0.15 M sodium hydroxide (1 M=1 mol dm^{-3}), and the solution was electrolyzed at a constant current of 0.4 A in a 300 cm^3 beaker at 25 °C. The termination of electrolysis was detected by TLC (toluene/ethyl acetate/methanol 6:3:1). After electrolysis, the solution was acidified by HCl (pH 1.5) and the resulting precipitate was collected. On recrystallization from chloroform it gave 0.9 g (84%) of the acid **3** mp 217—219 °C. The spectroscopic data were: IR (KBr) 1690 (CO), 2750—3050 cm^{-1} (broad OH). The ^{1}H NMR (DMSO-d_6) δ=6.6 (1H, s, COOH), 7.38 (5H, m, ArH); ^{13}C NMR (DMSO-d_6) δ=14.15 (CH_3), 137.08 (C–C=N–N–), 130.32, 163.4 (C–COOH respectively), 124.98 (N–Ph), 127.86, 128.57, 125.14 (–Ph), 151 (C–Cl). M^+ *m/z* 236 (100%), 219 (M^+−OH, 38%), 192 (M^+-CO_2, 5%).

5-Azido-3-methyl-1-phenyl-1*H*-pyrazole-4-carboxylic acid **4** was obtained by a procedure as above applied to compound **3**. The resulting product was recrystallized from cyclohexanone (80% yield), mp 140 °C. The spectroscopic data were: IR (KBr) 2200 cm^{-1} (sharp N_3). The ^{1}H NMR (DMSO-d_6) δ=2.48(3H, s, CH_3), 7.45 (5H, m, ArH), 9.85 (1H, s, COOH); ^{13}C NMR (DMSO-d_6) δ=14.87 (CH_3), 152.29 (–C=N–N–), 128.55, 183.68 (C–COOH respectively), 168.29 (C–N_3), 128.4 (N–Ph), 124.27, 124.51, 129.03 (–Ph). M^+ *m/z* 243 (48%), 215 (M^+ −N_2, 19%), 199 (M^+-CO_2, 100%).

5-Azido-3-methyl-1-phenyl-1*H*-pyrazole-4-carboxylic acid **4** from compound **3** was accomplished thus: To a well-stirred solution of NaN_3 (7.8 g, 120 mmol) in 25 cm^3 of DMF 9.4 g (40 mmol) of compound **3** was added. The reaction mixture was refluxed for about 8 h. The reaction mixture was poured into 50 cm^3 of cold water. The aqeuous phase was extracted by ether and the organic layer was dried over anhydrous sodium sulfate and filtered. Evaporation till dryness yielded a crude material which was recrystallized from metahnol–water.



Scheme 1.



Scheme 2.

It should be pointed out that in the above preparations by anodic oxidation, different currents (0.1 to 1 A) were tested. The better yield was obtained at a current strength of 0.4 A. Also, different NaOH concentrations were tested, whereby the optimum results were obtained in 0.15 M NaOH.

The scheme used in the above experiments is shown in the following (Scheme 2):

Conclusion

The methodology described in this study may be conceived as a new route to prepare azidopyrazolecarboxylic acid which would be difficult to prepare by classical organic procedures due to the reactivity of the azido group. Anodic oxidation affords obtaining the acid in high yield, under relatively mild conditions without any waste hazard to environment.

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