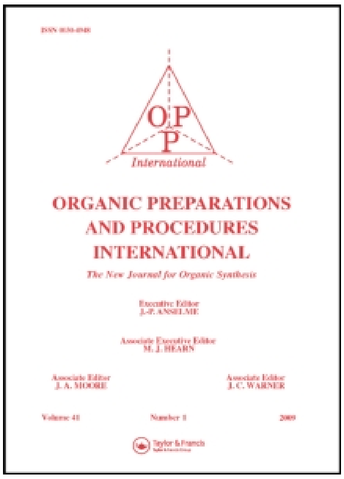

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REDUCTION OF 2-FUROIC ACID WITH METAL-AMMONIA SOLUTIONS

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REDUCTION OF 2-FUROIC ACID WITH METAL-AMMONIA SOLUTIONS

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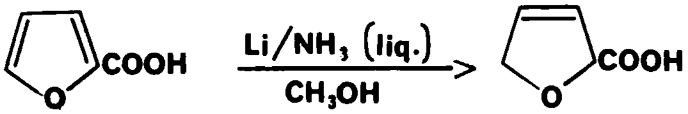
The synthesis of 2,5-dihydrofurans *via* the metal-alcohol-ammonia reduction of furan compounds[1-6] requires a furan ring activated by either carboxyl or phenyl groups. However, product yields in these reactions, are extremely sensitive to reactants and reaction conditions. We have found that addition of 3 equivalents of finely divided lithium to a solution of 2-furoic acid in methanol and dry liquid ammonia affords 2,5-dihydrofuran-2-carboxylic acid in 90% yield. 5-Methyl-2-furoic acid was also reduced under the same conditions to give a 1:1 mixture of *cis* and *trans* diastereoisomers, also in 90% yield.

In addition to the use of lithium in place of sodium, another factor



critical to high product yields is the purity and dryness of ammonia and of the proton source (methanol). The ammonia has to be purified and dried by distillation over sodium. The proton source must also be carefully dried and a mechanical stirrer provided with a glass blade should be used rather than a magnetic stirrer.[7]

EXPERIMENTAL

Purification of Ammonia.- A 250 ml three-necked round-bottomed flask equipped with a Dewar condenser was charged, under nitrogen, with 2 g of sodium and then cooled to -78°. Ammonia was condensed in the flask, producing a deep blue solution. Additional sodium was added as needed to preserve the blue color. When sufficient ammonia collected, the cooling bath was removed and the Dewar condenser was replaced with a distillation column, packed with potassium hydroxide pellets, leading to the reduction setup.

Purification of Methanol.- In a 500 ml round-bottomed flask with a condenser and drying tube, was placed 3 g of magnesium metal, 10 ml of methanol and a few crystals of iodine. An immediate reaction was observed. The solution was then heated at reflux until the brown iodine color was discharged. To the flask was next added 250 ml of reagent grade methanol. The resulting mixture was refluxed for one hour, whereupon the dried methanol was distilled and collected over activated molecular sieves.

Preparation of 2,5-Dihydro-2-furoic Acid.- The apparatus consisted of a 250 ml three-necked, round-bottomed flask equipped with a mechanical stirrer utilizing a glass blade, a gas inlet adapter and a Dewar condenser attached, *via* a drying tube filled with anhydrous potassium carbonate, to an oil bubbler. The flask was flame-dried under a flow of nitrogen, purged with nitrogen for ten minutes, and cooled to -78° with the aid of a dry ice-acetone bath. Dry ammonia (100 ml) was then condensed in the flask. To the flask was added 1.68 g (15 mmoles) of 2-furoic acid dissolved in 10 ml of dry methanol. The cooling bath was then removed and the ammonia brought to reflux (-33°). To this solution, under a flow of nitrogen, was added 312 mg (45 mmoles) of finely divided lithium over a period of fifteen minutes. During the initial stages of the addition, the reaction mixture remained colorless. At the end of the addition, the reaction mixture acquired a transient blue color. The ammonia was then allowed to evaporate at ambient temperature. Residual ammonia was removed under reduced pressure. The residue was dissolved in 40 ml of distilled water and acidified with 15 ml of 4 M hydrochloric acid to pH 2. The solution was then saturated with sodium chloride and extracted with 3x50 ml portions of ether. The combined extracts were dried over anhydrous magnesium sulfate, filtered and evaporated in vacuo to give 1.53 g (13.50 mmole) of product, 90% yield, bp 78-80°/2 mm, lit.[1] bp 84.5-85°/2 mm. IR (CCl_4) cm^{-1}: 3100-2860 (OH), 1738 (CO_2H); NMR ($CDCl_3$): δ 4.66-4.83 (m, 2H, $\underline{CH_2}$), 5.15-5.40 (m, 1H, $C\underline{H}CO_2H$), 5.80-6.20 (m, 2H, $C\underline{H}=C\underline{H}$), and 10.51 (s, 1H, $CO_2\underline{H}$).

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7. Magnetic stirring bars should not be used since small particles of iron attached to the surface of the stirring bar can catalyze the reaction of ammonia and lithium to form lithium amide.