

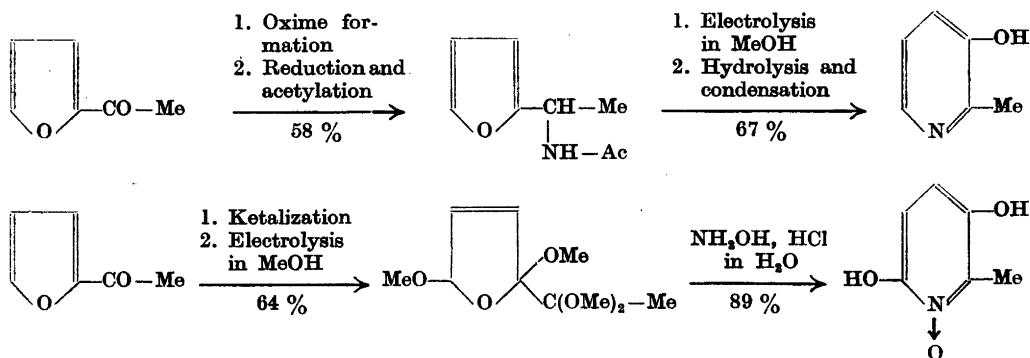
New Methods for the Transformation of Furans into Pyridines

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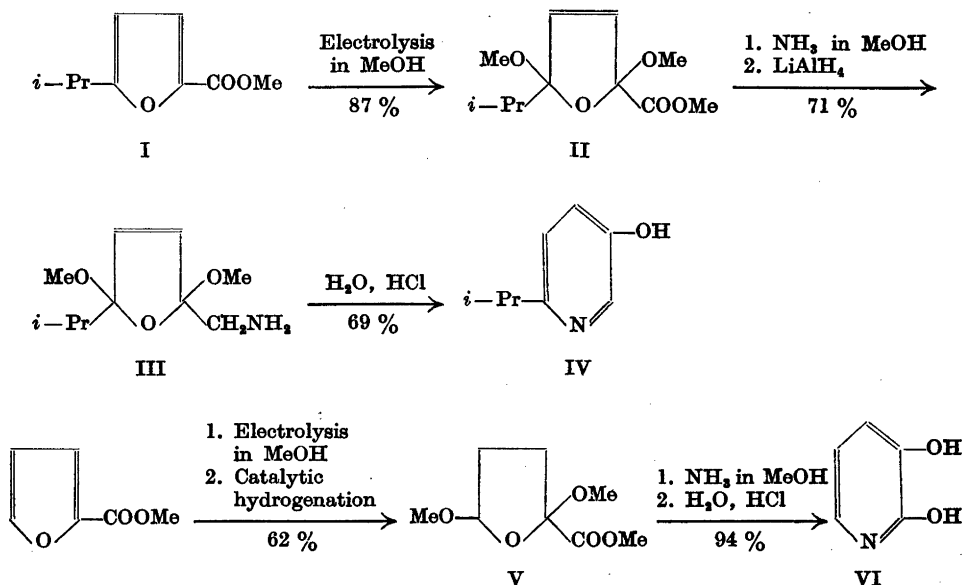
The preparation of 6-isopropyl-3-pyridinol (IV) and of 2,3-pyridinediol (VI) from 2-carbomethoxy-5-isopropylfuran (I) and methyl furoate, respectively, is described.

Two routes from furan-2-carboxaldehydes or furan-2-ketones to pyridines have recently been reported^{1,2}. These may be exemplified by the transformation of 2-acetylfuran into 2-methyl-3-pyridinol and 2-methyl-3,6-pyridinediol-1-oxide, respectively.



Two routes from furan-2-carboxylic acid esters, many of which are easily accessible, to 3-pyridinols and 2,3-pyridinediols, respectively, are described here. The first route is exemplified by the transformation of 2-carbomethoxy-5-isopropylfuran (I) into 6-isopropyl-3-pyridinol (IV), the second by the transformation of methyl furoate into 2,3-pyridinediol (VI).

The preparation of pyrocatechol from 2-acetylfuran reported in the foregoing article² represents a sequence of reactions similar to the reactions described here. The main feature of these transformations of furans into other



compounds with aromatic character is an intramolecular condensation of a straight chain of atoms including a 1,4-dicarbonyl C_4 -unit, the latter coming into existence by oxidation of a furan compound. We believe that many other heterocyclic or homocyclic aromatic compounds can be prepared by the same type of reactions by employing suitable 2-substituted furans.

EXPERIMENTAL

Microanalyses by E. Boss and K. Glens

2,5-Dimethoxy-2-aminomethyl-5-isopropyl-2,5-dihydrofuran (III). II* (3.45 g, 0.015 mole) was mixed at -50° with a solution of ammonia (2.2 ml, measured at -80°) and water (0.3 ml) in methanol (6 ml) and the resulting solution left standing (7 days) at room temperature and then evaporated in a vacuum from a water-bath (60°). The residue was dissolved in anhydrous ether and evaporated once more to dryness, at last under 0.1 mm, in order to remove traces of water and methanol. The residue was dissolved in ether (90 ml) and the ethereal solution added with stirring to a suspension of lithium aluminum hydride (0.97 g, 0.026 mole) in ether (60 ml). After stirring at room temperature for 20 hr the mixture was cooled to -20° , and water (20 ml) and then sodium hydroxide solution (20%, 25 ml) were added dropwise. The cloudy reaction mixture was continuously extracted with ether, the ethereal solution dried with magnesium sulfate and distilled. The yield was 2.13 g (71%) of III (colorless liquid, b. p.₁₃₋₁₂ $121-126^\circ$, n_D^{25} 1.4625).

$C_8H_{13}ON(OCH_3)_2$ (201.3)	Calc.	C 59.7	H 9.5	N 7.0	OCH_3 30.8
	Found	» 60.0	» 9.5	» 7.0	» 30.5

6-Isopropyl-3-pyridinol (IV). III (1.50 g, 0.0075 mole) and hydrochloric acid (N, 17 ml) were heated under reflux (15 min). The solution was evaporated to dryness in a vacuum and the residual dark-brown oil dissolved in water (10 ml). Potassium carbonate (1.0 g) was added and the solution continuously extracted with ether. A crust of yel-

lowish-white crystals was removed by decantation, washed with ether and dried. The yield was 0.65 g of IV (slightly yellow crystals, m. p. 155–157° (Hershberg apparatus, corr.)).

$C_8H_{11}ON$ (137.2)	Calc.	C	70.0	H	8.1	N	10.2
	Found	»	70.1	»	7.9	»	10.5

The product gave a wine-red ferric chloride reaction. Sublimation (0.06 mm, 135–140°) gave a perfectly white product in an almost quantitative yield (m. p. 156°).

From the ethereal solution another 0.06 g of IV was isolated by sublimation (white crystals, m. p. 154–156°), the total yield of IV thus being 0.71 g (69 %).

2,3-Pyridinediol (VI). V^4 (4.75 g, 0.025 mole) was mixed at -50° with a solution of ammonia (3.5 ml, measured at -80°) and water (0.5 ml) in methanol (10 ml) and the resulting solution left standing (4 days) at room temperature and then evaporated in a vacuum from a water-bath. The almost colorless viscous residue was dissolved in a mixture of water (10 ml) and methanol (3 ml). Sulfuric acid (0.1 *N*, 10.0 ml) was added and the solution heated under reflux (20 min). To the hot solution barium hydroxide (0.1 *N*, 10.0 ml) was added, the light yellow suspension evaporated to dryness in a vacuum and the solid residue sublimed (0.07 mm, 145–155°). The yield was 2.60 g (94 %) of VI (m. p. in an evacuated tube 250–52 (dec.)). The product gave the expected strong blue ferric chloride reaction.

$C_8H_5O_2N$ (111.1)	Calc.	C	54.1	H	4.5	N	12.6
	Found	»	54.3	»	4.4	»	12.8

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