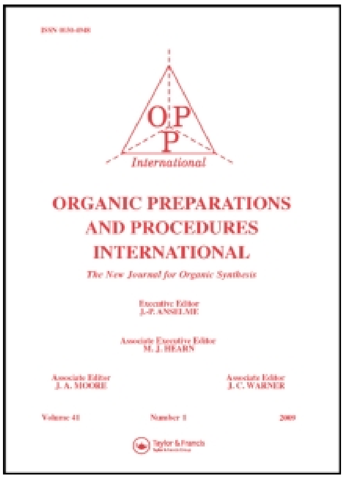

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AN IMPROVED SYNTHESIS OF WINTERS' PYRIDINE REISSERT ANALOG

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AN IMPROVED SYNTHESIS OF WINTERS' PYRIDINE REISSERT ANALOG

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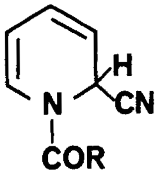
In 1974, Winters et al.[1] reported the synthesis of 1-carbethoxy-2-cyano-1,2-dihydropyridine (I). Although isolated in low (25%) yield, this compound represents the first and only known Reissert-like compound synthesized from pyridine. In contrast to quinoline, isoquinoline and related nitrogen heterocycles, pyridine has been notorious in its inability to form isolable species of structure II under conditions commonly used in



I R = OC_2H_5
II R = alkyl, aryl

Reissert compound synthesis.[2-4] Recent interest in the chemistry of dihydropyridines[5] and in the application of Reissert compounds to organic synthesis[2] has prompted the reinvestigation of synthetic routes to I and II. We now report that I is obtained in high purity in 92% yield by a convenient, phase-transfer catalyzed reaction of pyridine with ethyl chloroformate and potassium cyanide in aqueous methylene chloride.

EXPERIMENTAL SECTION

1-Carbethoxy-2-cyano-1,2-dihydropyridine (I).- To a vigorously stirred mixture of 6.33 g (80.0 mmol) pyridine, 100 ml methylene chloride, 40 ml water, 15.63 g (240 mmol) potassium cyanide and 0.37 g (2.0 mmol) benzyltrimethylammonium chloride, maintained under a nitrogen atmosphere, was added dropwise (over a 45 min. period) a solution of 17.36 g (160 mmol) ethyl chloroformate in 20 ml methylene chloride. Throughout the addition, the temperature of the reaction mixture was maintained at 25^{o} by periodic cooling. After the addition was complete, stirring was continued for 15 min, then the reaction mixture was poured into 100 ml cold water and the layers separated. The aqueous layer was extracted with methylene chloride (2 x 50 ml). The combined organic layers were washed with 0.2 N hydrochloric acid (2 x 100 ml), brine (100 ml), then dried over $MgSO_4$. Removal of solvent by rotary evaporation provided 13.16 g (92.4%) of I as a red-brown oil, with properties identical to those reported previously.[1,6] nmr ($CDCl_3$): δ 1.37 (t, 3H, J = 7 Hz), 4.33 (q, 2H, J = 7 Hz), 5.56 (m, 2H), 5.92 (d, 1H, J = 6.5 Hz), 6.25 (dd, 1H, J = 9 and 6 Hz), 6.88 (d, 1H, J = 8 Hz); ir (neat, NaCl): 2240 cm^{-1} (weak, CN).

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6. Purity 96-98% by nmr. Identified by nmr (90 MHz), ir, elemental analysis and ms. Product I is not entirely stable to typical gc injector temperatures and partially decomposes to give pyridine, 2-cyanopyridine and other unidentified products. The nmr shifts given differ only slightly from those in the literature.[1] The ir spectrum displayed a weak nitrile band. The compound did not decompose appreciably after two months of refrigerated storage at 4°.

ONE-STEP PREPARATIONS OF ISOMERIC (2,6-DIOXACYCLOHEXYL)PHENOLS†

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The utility of (2,6-dioxacyclohexyl)phenols as immediate precursors of insecticides[1] as well as synthetic intermediates of 1,2,3-trisubstituted aromatic compounds is well documents.[2] It has been long known that hydroxybenzaldehydes do not undergo acetalization under acid-catalyzed conditions in satisfactory yields.[3,4] Reasonable yields of acetal[4] are obtained when the phenolic group is blocked as an acetate. Acetalization followed by alkaline hydrolysis generates the phenolic acetal[2] in overall yields of 60%. This report describes a one-step procedure to transform