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Michele C. Jetter^a, Robert E. Boyd^a & Allen B. Reitz^a

^a Drug Discovery Division, The R. W. Johnson Pharmaceutical Research Institute, Spring House, PA, 19477

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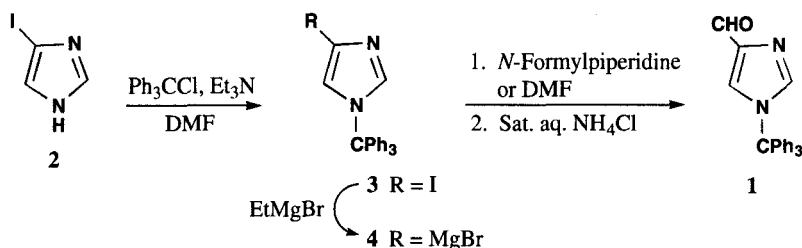
EXPEDIENT SYNTHESIS OF *N*¹-TRITYLIMIDAZOLE-4-CARBOXALDEHYDE

Submitted by
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Michele C. Jetter*, Robert E. Boyd, and Allen B. Reitz

Drug Discovery Division
The R. W. Johnson Pharmaceutical Research Institute
Spring House, PA 19477

*N*¹-Tritylimidazole-4-carboxaldehyde (**1**) is an important reagent for the synthesis of various 4-substituted imidazoles, and two routes to this compound have been reported.¹ It can be prepared *via* tritylation of 4(5)-(hydroxymethyl)imidazole and subsequent oxidation.^{1a} However, this procedure requires synthesis of the 4(5)-(hydroxymethyl)imidazole either from fructose or from 1,3-dihydroxy-2-propanone.^{2,3} An alternate route for the synthesis of **1** involves tritylation of 4(5)-iodoimidazole (**2**) to give *N*¹-trityl-4-iodoimidazole (**3**), followed by lithiation and formylation with dimethylformamide.^{1b} However, mixtures of the 2- and 4-carboxaldehydes are produced, which are difficult to separate.^{1b} Alternatively, a synthesis of *N*¹-sulfamoyl-4-imidazolecarboxaldehyde has been recently published,⁴ but our own work required trityl protection on the imidazole ring. Lindell and Turner have shown that imidazo-4(5)-yl anions can be generated by reaction of **3** with EtMgBr to give



Grignard reagent **4**.⁵ We now report that reaction of C-4(5) anion **4** with either dimethylformamide⁶ or *N*-formylpiperidine⁷ affords **1** in >75% yield. The details for the reaction employing *N*-formylpiperidine are given in the experimental section (81% yield). A similar result was obtained when dimethylformamide was used as the formylating reagent under identical reaction conditions and scale (77% yield), with the exception that 1.2 mol-equiv. of dimethylformamide was employed. In addition to high yield, these reactions are fairly rapid and easy to perform with no reaction time greater than 1 hr, and purification is readily achieved *via* flash chromatography. Because of these advantages, we believe that this procedure is the best means of obtaining **1** that has been reported to date.

EXPERIMENTAL SECTION

Melting points are uncorrected. The ¹H NMR spectra were obtained in solutions of deuteriochloroform using a Bruker AC-300 instrument (300 MHz) using TMS as internal standard. *N*¹-Trityl-4-iodoimidazole (**3**) was readily obtained from 4(5)-iodoimidazole by a published procedure.^{1b} Flash column chromatography was conducted according to the standard literature method.⁸ Solvents were used as

commercially obtained without any further purification or drying. Elemental analysis was determined by Robertson Microlit Laboratories.

***N*¹-Tritylimidazole-4-carboxaldehyde (1).**- To a solution of *N*¹-trityl-4-iodoimidazole (3, 2.18 g, 0.005 mol) in 50 mL of dry THF was added 2.0 mL (0.006 mol) of a 3.0 M solution of EtMgBr in diethyl ether. The reaction mixture was stirred at room temperature for 30 min, after which time TLC analysis (7:3 hexane:ethyl acetate) showed complete consumption of the starting material. *N*-Formylpiperidine (0.57 g, 0.56 mL, 0.005 mol) was added to the solution *via* syringe, and the reaction mixture was stirred for 1 hr. Saturated aqueous NH₄Cl (50 mL) was then added and the aqueous phase was extracted with CH₂Cl₂ (2 x 50 mL). The combined organic extracts were dried (Na₂SO₄) and evaporated. The residue was purified by flash chromatography on silica gel, eluting with a 7:3 mixture of hexane/ethyl acetate. The product was obtained as 1.37 g (81%) of a white solid, mp 198-199°, lit.^{1a} mp 197-199°. ¹H NMR (CDCl₃): δ 9.85 (s, 1H, HC=O), 7.61 (s, 1H, ImH), 7.54 (s, 1H, ImH), 7.1-7.38 (m 15H, ArH).

Anal. Calcd for C₂₃H₁₈N₂O: C, 81.63; H, 5.36; N, 8.28. Found: C, 81.82; H, 5.40; N, 8.17

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