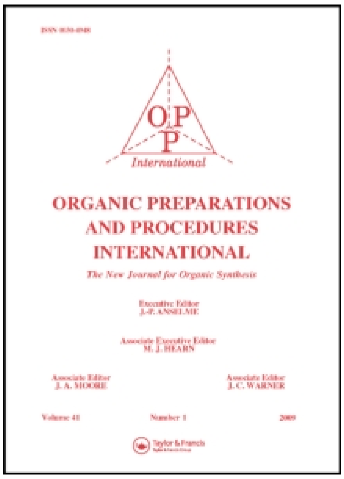

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A DETAILED PROCEDURE FOR SYNTHESIS OF 2,3-DIHYDROXYBENZALDEHYDE

Charles F. Hoyng[a]
[a] Department of Chemistry, Texas A & M University, College Station, Texas

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mp. 224-224.7° with slight decomposition; MS: m/e 184 (base peak, M^+), 169 (50%). This material showed no melting point depression on mixing with an authentic specimen.[1]

Anal. Calcd. for $C_8H_8O_5$: C, 52.18; H, 4.38.

Found: C, 52.08; H, 4.21.

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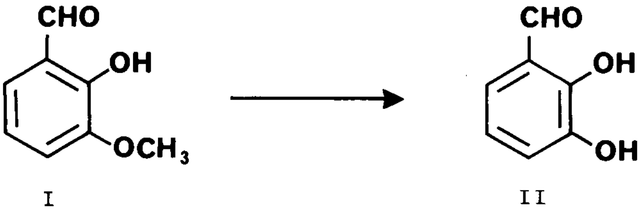
A DETAILED PROCEDURE FOR SYNTHESIS OF 2,3-DIHYDROXYBENZALDEHYDE

Submitted by Charles F. Hoyng
(7/7/80)

Department of Chemistry
Texas A & M University
College Station, Texas 77843

2,3-Dihydroxybenzaldehyde (II) has been used as an intermediate in organic synthesis[1,2] and as a reagent for enzyme modification.[3] Although II is commercially available, the high cost limits its use. The demethylation of o-vanillin (I) provides an inexpensive, direct route to 2,3-dihydroxybenzaldehyde (II). This approach has been reported by Merz and Fink using aluminum tribromide (29%) of hydrobromic acid/glacial acetic acid (45%).[4] Kemp et al., recently reported the demethylation of I with hydrobromic acid/glacial acetic acid in 49%.[2] We have found that in this procedure, the presence of even trace amounts of reaction acid during the distillation of the crude product greatly reduced the yield and the quality of the product. The procedure herein avoids this problem and describes in detail the conversion of o-vanillin (I) into 2,3-dihydroxybenzaldehyde (II) in 57% yield. We have not been successful in demethylating o-vanillin using trimethylsilyl iodide[5] or its equivalent.[6]



EXPERIMENTAL

Infrared spectra were determined on a Perkin-Elmer Model 297 spectrometer, and ^{1}H NMR spectra were recorded with a Varian Model T-60 spectrometer. Chemical shifts are reported on solutions as δ values relative to tetramethylsilane (TMS) as an internal standard. Gas chromatography was performed with a Hewlett-Packard Model 5712A and 10% UCW on Gas Chrom Q 80/100 mesh columns. The melting point is uncorrected.

2,3-Dihydroxybenzaldehyde (II).- A solution of 100 g (0.66 mol) of o-vanillin (I) in 400 ml of glacial acetic acid and 120 ml of commercial 48% hydrobromic acid was placed in a 1000 ml round bottom flask equipped with a glass covered magnetic stir bar. The mixture was degassed for 30 min. by vigorous bubbling from a nitrogen gas inlet tube positioned at the bottom of the reaction flask. The gas inlet tube was removed and the flask was fitted with a Graham, spiral, water cooled condenser. The solution was stirred and heated to reflux under a nitrogen atmosphere for 9 hrs at an oil bath temperature of 135°. The coal-black mixture was cooled under a nitrogen atmosphere. The reflux condenser was removed and replaced by a simple distillation head with thermometer, West condenser and vacuum take-off adapter, and 1000 ml receiving flask. The bulk of the solvent was removed under aspirator vacuum and oil bath heating. The distillation head temperature at the end of this phase of solvent removal was 110-115°. The apparatus was cooled under a nitrogen atmosphere. The distillation was resumed at 0.5 mm pressure. Solvent removal was complete when condensation in the West condenser ceased, and when the distillation head was plugged with yellow, crystalline product. The apparatus was cooled and the crystalline material in the distillation head was returned to the reaction flask. The reaction flask was fitted with a 75° angle tube with a 24/40 ground glass, inner joint at each end leading to a 500 ml 3-neck flask equipped with a straight path vacuum lead-off tube[7] and a stopper. The distillation flask was surrounded by a spherical heating mantle and the distillation tube was wrapped with heating tape and then glass wool. The receiver was chilled in ice water. The product was distilled at 0.5 mm pressure, using a flameless heat gun to move condensed product from the mouth of the receiver whenever necessary. Distillation was continued until yellow product was no longer observed in the distillation tube or at the mouth of the reaction pot. A black, charcoal-like residue remained. The yellow, solid distillate was extracted into three portions of hot benzene. Each extract volume (250 ml, 150 ml, and 100 ml) was warmed on a steam bath. When the solvent reached the boiling point, the yellow solution was decanted from a small amount of black, oily residue and filtered directly into a round bottom flask. The combined benzene extract was concentrated under reduced pressure to a volume of approximately 150 ml. The solid material present was redissolved by mild heating at the steam bath. The solution was transferred to a 1000 ml Erlenmeyer flask and diluted with carbon tetrachloride until crystallization began. The material was collected and air dried (49.5 g). The mother liquor was concentrated under reduced pressure to approximately 100 ml, seeded with material obtained above, and cooled to 0-5°. The crystals were collected and air dried (2.0 g). The combined yield was 51.5 g (57%) of 2,3-dihydroxybenzaldehyde (II) as yellow crystals, mp. 105-107°, lit.[4] 105°. IR (mull): 3320, 1655, 1615, 1585, 1260 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.78 (bs, 1H, -OH), 6.83-7.40 (m, 3H, aryl), 10.00 (s, 1H, -CHO), 11.20 (s, 1H, -OH).

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