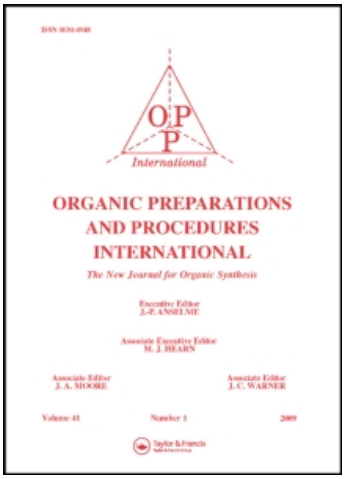

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THE SYNTHESIS OF KNORR'S PYRROLE BY INVERSE ADDITION

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THE SYNTHESIS OF KNORR'S PYRROLE BY INVERSE ADDITION

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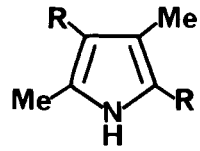
In the course of our efforts to assess the role of pyrroles in synfuel storage instability, we required a convenient, high yield route to 2,4-dimethylpyrrole.[1] The key precursor is diethyl 2,4-dimethylpyrrole-3,5-dicarboxylate (I), which is available in approximately 50% yield (after purification by a classic in situ Knorr synthesis.[2,3] An inverse addition scheme, wherein the pre-formed nitroso compound of ethyl acetoacetate is added to the zinc reduction mixture, has been claimed to afford up to a 75% yield of I; however, the actual conditions used, as well as the purity of the product which results, have not been defined.[2,4] We now report that the inverse addition route to Knorr's pyrrole is superior to the Fischer procedure[2] in yield and purity of product obtained. Furthermore, the synthesis of 2,4-dimethylpyrrole in 60-70% overall yield from ethyl acetoacetate has been achieved.[5] This was made possible by a convenient and nearly quantitative conversion of I to II in a heated stainless steel pressure vessel.[6,7] Thus, the early reports of Corwin et al. have been confirmed.[4,6]



I, R = CO_2Et
II, R = H

EXPERIMENTAL

Diethyl 2,4-dimethylpyrrole-3,5-dicarboxylate (I).- To a stirred mixture of 25 ml glacial acetic acid and 97.5 g (0.75 mol) of ethyl acetoacetate

cooled in an ice-salt bath to 5° was added slowly (in 5 ml portions and over a 1 hr period) a cooled solution of 53.4 g (0.75 mol) of 97% sodium nitrite in 75 ml of water. Throughout the addition, the temperature of the reaction mixture was maintained at 5°. After the addition was complete, the yellow solution of nitroso compound was stirred for an additional hour at 5°, the ice bath removed, and the reaction mixture allowed to warm to room temperature over a 2 hrs period.

Into a 2 liter three neck flask fitted with an additional funnel, a condenser, and a mechanical stirrer was placed 225 ml glacial acetic acid, 15 g (0.18 mol) of sodium acetate, 98 g (1.5 mol) of fresh zinc dust, and 97.5 g (0.75 mol) of ethyl acetoacetate. The solution of nitroso compound was placed in the addition funnel and was added in small portions (over a 1.5 hr period) to the stirred zinc reduction mixture at such a rate that the acetic acid refluxed moderately. After an additional hour of reflux, the still-hot reaction mixture was decanted from the zinc residue and was added to 5 liters of water with vigorous stirring. The zinc residue was washed with two 50 ml portions of hot acetic acid, which were added to the aqueous mixture. A large quantity of light yellow, fine crystalline precipitate formed almost immediately. Stirring was continued for 0.5 hr, then the beaker was wrapped in aluminum foil (to exclude light) and allowed to stand overnight. The product was collected, washed with 150 ml cold aqueous acetic acid (50:50 v/v) to lighten the color,[8] washed with large quantities of cold water, and allowed to dry thoroughly in a vacuum oven overnight to afford 113.6 g (63.3%) of light yellow crystals,[9] mp 134-135° (corr.), lit.[2] mp 136-137°.

2,4-Dimethylpyrrole (II).- Compound I (69.7 g, 0.291 mol) and 106.4 g (1.90 mol) of 85% potassium hydroxide were mixed thoroughly by grinding together, stirred into a paste with 56 ml water, and pressed into a stain-

less steel pressure vessel of 220 ml capacity. The vessel was sealed, evacuated, and placed into a 160° fluidized sand bath for 6.5 hrs. When cooled to room temperature, the pressure vessel contained an amber liquid phase, a small amount of a green aqueous phase and a good quantity of crystalline potassium carbonate. The liquid phases were decanted into a round bottom flask, the pressure vessel rinsed with ether (2 x 100 ml), and the ether and liquids combined. The ether was removed under water aspiration, and the ether-free liquid was steam distilled and 300 ml of distillate was collected. The distillate was extracted with ether (2 x 150 ml) and the combined organic layers were dried over $MgSO_4$. Removal of the solvent by rotary evaporation (under nitrogen) afforded the crude pyrrole which upon distillation in vacuo under nitrogen gave 26.5 g (96%) of purified II as a clear liquid, bp. 78-80°/26.5 mm, lit.[6,7] bp. 72°/25 mm and 56°/10 mm).[10] The product autoxidizes very rapidly and should be stored in a brown bottle under nitrogen.

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8. If the crude product is not washed with aqueous acetic acid, the yield is 126.5 g (70%) and the mp is 130.7-133° (corr.). Some product loss occurs with this step as I is partially soluble in acetic acid.
9. The purity of the product is greater than 99% (pure by nmr and ir). The product darkens upon exposure to light.
10. Identified by nmr and ir spectra and by comparison with an authentic sample kindly provided by D. R. Latham of the Laramie Energy Technology Center (DOE).