

## Short Communications

## A Convenient Synthesis of Pyrrole-2,5-dicarboxaldehyde

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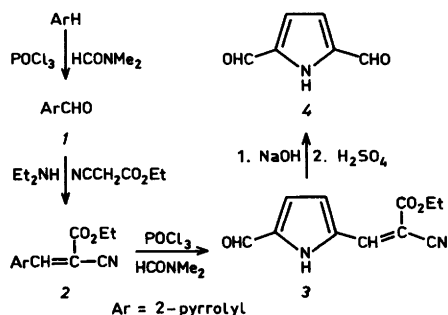
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The title compound (4) was needed as starting material for the synthesis of pyrroles formed in the Maillard reaction.<sup>1</sup> Several methods for preparing 4 from pyrrole have been described. Their most important characteristics are:

No. of steps	1	2	2	3	4	6
LC required	+	+	+	+	–	–
Yield, %	0.5	38	21	12	<11	<40
Ref.	2	3	4	2	5	5

Unfortunately, the most promising of these methods<sup>3</sup> in our hands gave <10% yield of 4, as shown by GC analysis of the crude reaction mixture. We now report the synthesis of 4 in 38% yield by the four-step sequence shown in Scheme 1.

The base-catalyzed reaction with ethyl cyanoacetate is a well-known method for protecting pyrrolecarboxaldehydes,<sup>6</sup> and the sequence 1→2→3 was described recently.<sup>7</sup> Since there is no need for chromatography or for purification of the intermediates 1–3, the present synthesis of 4 is simple and may be performed on a large scale.



Scheme 1.

*Experimental.* Compounds 1,<sup>8</sup> 2 and 3<sup>7</sup> were prepared according to the literature (2 and 3 are probably the *E* isomers<sup>9</sup>). However, 1 was neither distilled nor crystallized but converted directly to 2 (154 g, 81% calc. on pyrrole) after evaporation of the solvents. A more detailed procedure for the preparation of 3 is given below (*cf.* also Ref. 8).

*Ethyl α-cyano-5-formyl-2-pyrroleacrylate (3).* Phosphoryl chloride (150 g, 90 ml, 0.98 mol) was added over 20 min to *N,N*-dimethylformamide (72 g, 76 ml, 0.98 mol), stirred and kept at 10–20 °C by cooling with an ice-salt bath. After stirring for another 15 min without cooling, 1,2-dichloroethane (450 ml) was added. The stirring and cooling were continued while a suspension of ethyl α-cyano-2-pyrroleacrylate (2, 154 g, 0.81 mol) in 1,2-dichloroethane (675 ml) was added over 30 min at ca. 5 °C. The mixture was then refluxed for 15 min (HCl evolution!). Aqueous 4.0 M sodium acetate (1.25 l) was added over ca. 5 min at 25–30 °C to the vigorously stirred mixture, which was then refluxed for another 15 min. Crystallization overnight yielded 3 (141 g, 80%).

*Pyrrole-2,5-dicarboxaldehyde (4).* Aqueous 3 M sodium hydroxide (600 ml) was refluxed for 2 h with 3 (32.7 g, 0.150 mol), which dissolved within a few minutes. The solution was acidified below 20 °C with 2 M sulfuric acid to pH 4.5 and then extracted with ethyl acetate (500 + 100 ml). Rotary evaporation of the extract and crystallization of the residue from water (100 ml) yielded nearly pure but discoloured 4 (9.8 g), m.p. 117–121 °C. Processing of the mother liquor raised the yield to 10.9 g (59%; 38% calc. on pyrrole). Sublimation *in vacuo* or recrystallization from water or toluene in the presence of charcoal yielded pure 4, m.p. 123–124 °C (sealed tube, lit.<sup>5</sup> 122–123 °C). The mass, IR and <sup>1</sup>H NMR spectral data agreed with those reported.<sup>2,4,5</sup> At half neutralization of 4 with aqueous 0.1 M sodium hydroxide, pH 10.0 was observed, indicating that p*K*<sub>a</sub> is close to 10.

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