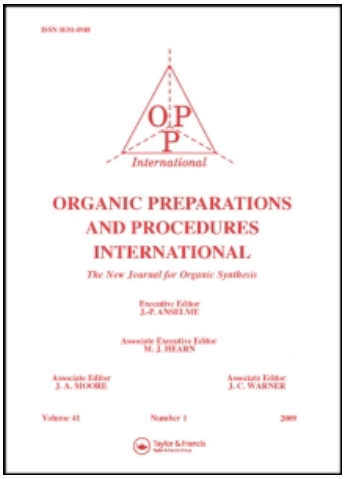


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# A CONVENIENT SYNTHESIS OF PYRROLE-3-CARBOXALDEHYDE

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3. Biological results on the radiosensitizing effects of these compounds will be reported elsewhere.



## A CONVENIENT SYNTHESIS OF PYRROLE-3-CARBOXALDEHYDE

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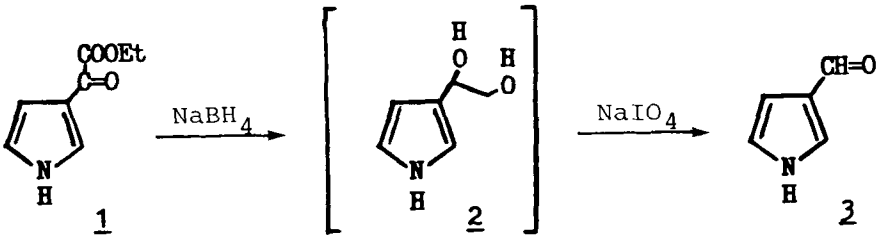
Pyrrole-3-carboxaldehyde (3) may become an important synthon[1] in the design of complex compounds derived from 3-substituted pyrroles.[2,3] Yet there exists no efficient synthesis of 3 on a reasonable scale. It has been obtained in low yields from 4-formylpyrrole-2-carboxylic acid[4] and S-ethyl 4-formylpyrrole-2-thiocarboxylate[5] by decarboxylation and catalytic

decarbonylation respectively. A higher yield route to this aldehyde has been developed recently, starting from N-(triisopropylsilyl)pyrrole;[3] a major disadvantage of this latter approach is the expense of the reagents used. It was speculated that ethyl pyrrole-3-glyoxylate (1), prepared[2] in 64% yield from pyrrole in a two-step sequence, might be a suitable precursor to the title aldehyde. It was found that this transformation




could be done in a one-pot 63% overall yield reaction. Thus, ethyl pyrrole-3-glyoxylate (1) was first reduced with sodium borohydride[6-8] to 1,2-pyrrol-3-ylethanediol (2) followed by in situ oxidative cleavage with sodium metaperiodate[9] to pyrrole-3-carboxaldehyde (3). Although 1,2-pyrrol-3-ylethanediol (2) was not isolated, its formation is supported by the ease of reaction with sodium metaperiodate.

## EXPERIMENTAL SECTION

Mps were determined on a Büchi 510 apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 597 spectrophotometer. $^1$H NMR spectra were obtained on a Varian A-60A instrument using TMS as an internal standard. Elemental analyses were performed on a Perkin-Elmer 240 automated analyzer.

Pyrrole-3-carboxaldehyde (3).- Methanol (12 ml) was added dropwise over a period of 2 hrs to a stirred mixture of 1[2] (3.34 g, 20 mmol) and sodium borohydride (1.89 g, 50 mmol) in tetrahydrofuran (80 ml) at room temperature under nitrogen; stirring was continued at room temperature for 30 min. The mixture was cooled in an ice bath and acetone (10 ml), water (80 ml) and diethyl ether (160 ml) were added. Stirring was continued at

the same temperature for 15 min. A solution of sodium metaperiodate (4.5 g, 21 mmol) in water (40 ml) was then added dropwise over a period of 15 min; stirring was continued at the same temperature for 1 hr and at room temperature for 20 min. Saturated aqueous sodium chloride (50 ml) was added, the two layers were separated and the aqueous layer extracted with diethyl ether (2 x 50 ml). The aqueous layer was then neutralized with dilute aqueous hydrogen chloride and extracted again with diethyl ether (2 x 50 ml). The combined extracts and organic layer were washed with saturated aqueous sodium chloride (1 x 100 ml) and dried over anhydrous sodium sulfate. The solvents were evaporated under reduced pressure and the residue purified by TLC mesh column chromatography[10] on silica gel (Merck, 7747) with diethyl ether–hexane (2:1) as the eluent to afford 1.19 g (63%) of pyrrole-3-carboxaldehyde, mp. 62-63°. An analytical sample was prepared by recrystallization from diethyl ether–hexane, mp. 63.5°, lit.,[4,5,3] mp. 64°, 63-63.5°, 63°.



Anal. Calcd for $C_5H_5NO$: C, 63.14; H, 5.30; N, 14.73

Found: C, 63.05; H, 5.34; N, 14.62

$^1H$ NMR($CDCl_3$): δ 6.60 (m, 1H), 6.79 (m, 1 H), 7.47 (m, 1 H), 9.80 (s, 1 H); 10.50 (broad s, 1 H); IR (Nujol): 1650, 3200 $cm^{-1}$.

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## DIRECT PREPARATION OF 1,3,5-TRIAZA-1,3,5-TRINITROCYCLOHEXANE FROM HEXAMETHYLENETETRAMINE

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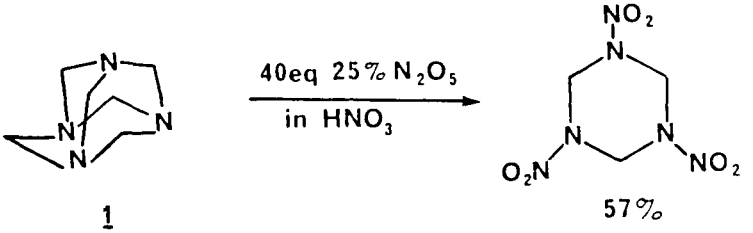
Recent synthetic efforts in our laboratory have involved the development of new methods for the preparation of nitramines,[1] which are usually obtained by nitrolysis of a protected amine precursor.[2] We have reported[1] the facile nitrolysis of a number of cyclic nitrosamines to the corresponding nitramines employing dinitrogen pentoxide in 100% $HNO_3$[3] and now describe the extension of the method to the preparation of 1,3,5-triaza-1,3,5-trinitrocyclohexane (RDX, 2), an important energetic material.

Pure RDX had previously been prepared by nitrolysis of 1,3,5-triaza-1,3,5-trinitrosocyclohexane (R-salt) with excess 100% nitric acid.[4]

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