

A convenient synthesis of Ricinine and its analogues

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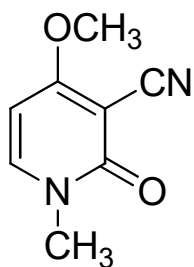
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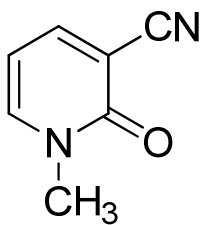
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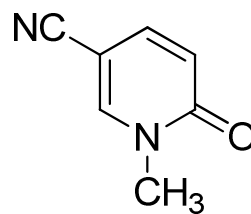
Ricine (1,2-Dihydro-4-methoxy-1-methyl-2-oxo-3-pyridinecarbonitrile) is a simple pyridinone alkaloid isolated by Tuson in 1864 from castor-oil seed (*Ricinus communis*)



Ricine



Rcinidine

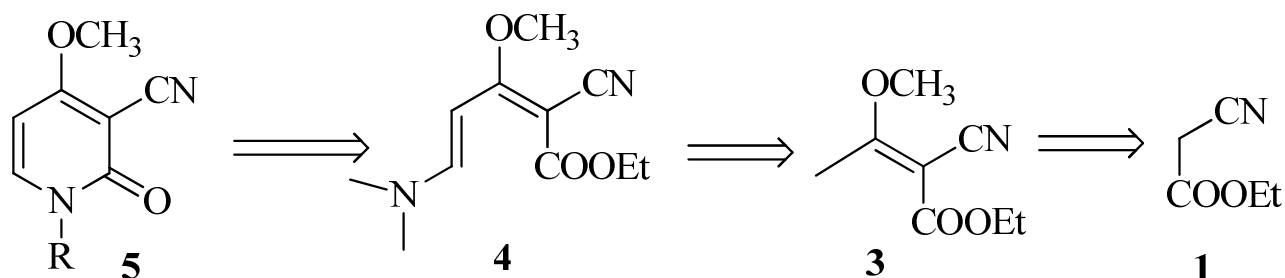


Nudiflorine

- Figure 1: Structure of **Ricine** and two natural cyanopyridines, **Rcinidine** and **Nudiflorine**.

Tuson, R.V., *J. Chem. Soc.*, 1864, 17, 195

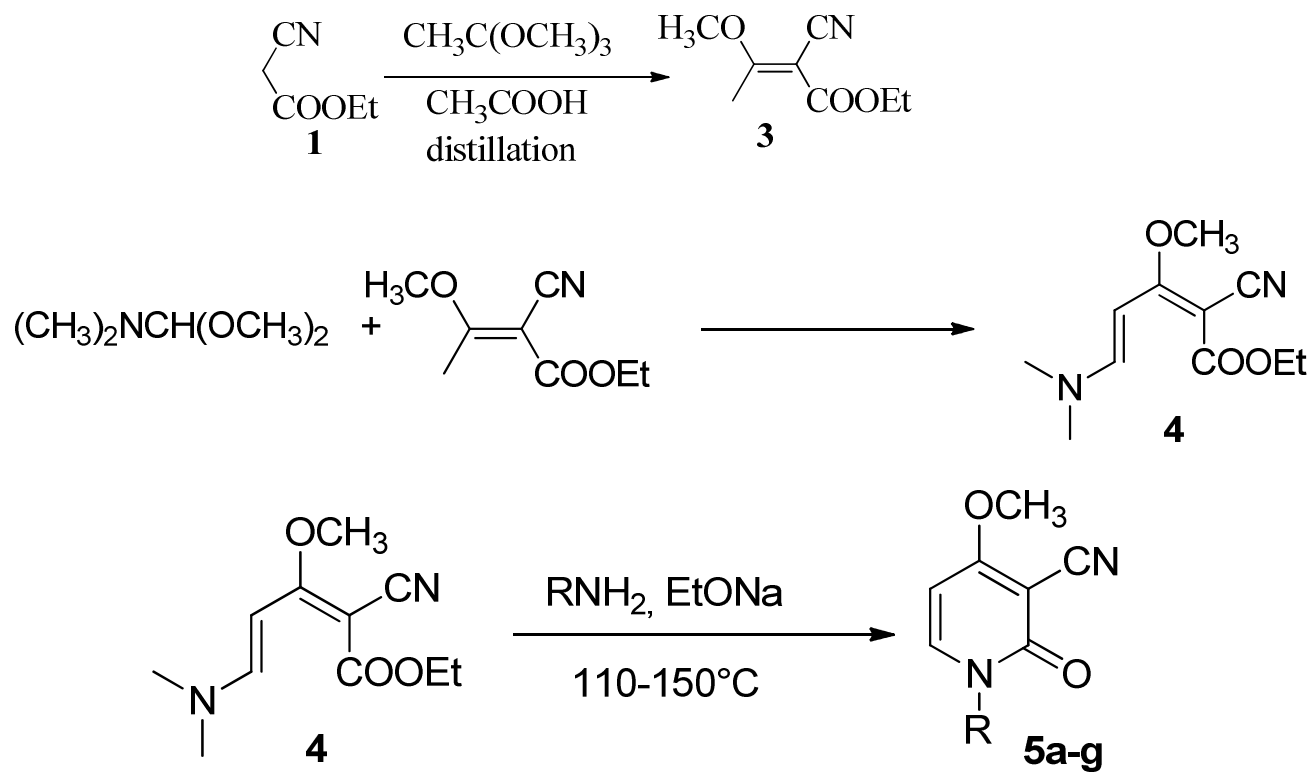
- We propose herein the synthesis of **Ricinine** and N-derivatives according to the retrosynthetic Scheme 1.



Scheme 1: Retrosynthesis of N-derivatives of Ricinine.

Synthesis of pyridinones: **A simple and Efficient Procedure for a 2-Pyridones Synthesis under Solvent-Free Conditions**

Kibou, Z., Cheikh, N., Villemin, D., Choukchou-Braham, N., Mostefa-Kara, B. and Benabdallah, M., *Int. J. Org. Chem.*, 2011, 1, 242-249; doi: [10.4236/ijoc.2011.14035](https://doi.org/10.4236/ijoc.2011.14035).

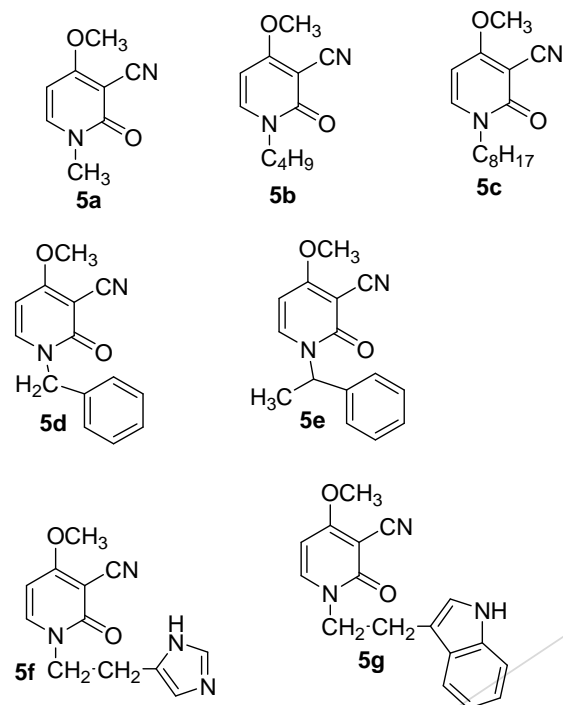


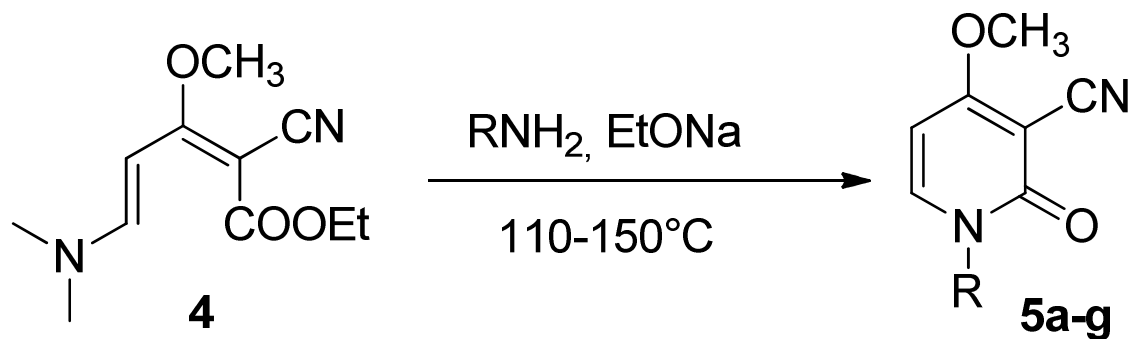
R= CH₃ (a), C₄H₉ (b), C₈H₁₇ (c), CH₂C₆H₅ (d), CH(CH₃)C₆H₅(e),
 CH₂CH₂C₃H₃N₂ (f), CH₂CH₂ C₈H₅N (g)

Scheme : Synthesis of Ricinine (5a) and N-analogues of Ricinine (5b-g)

Table 1 : Synthesis of Ricinine (5a) and N-analogues of Ricinine (5b-g)

Entry	Amine	Product	Yield (%)
a	methylamine	5a	61
b	n-butylamine	5b	92
c	n-octylamine	5c	95
d	benzylamine	5d	92
e	α -methylbenzylamine	5e	87
f	histamine	5f	60
g	tryptamine	5g	58





- ▶ In conclusion, the reaction of primary amines with the ethyl 2-cyano-1-methoxy-5-(dimethylamino)pentadienoate in the presence of sodium ethoxide conducts to N-derivative of **Ricinine**.
- ▶ This reaction allows a simple and easy synthesis of a variety of N-substituted Ricinine derivatives.
- ▶ The biological properties of these new compounds (**5b-5g**) are being tested.