Synthesis of 3-Chloropyrroles from 1-Chlorocyclopropanecarbaldehydes

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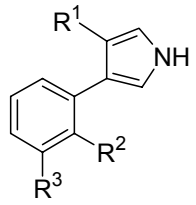
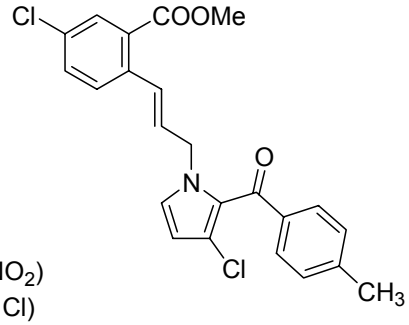
In the unabated search for new physiologically active compounds, the study of substituted pyrroles still remains a subject of considerable importance. Halogenated pyrroles isolated from nature are associated with diverse physiological activities and have served as lead structures to synthesize pyrroles with current use in agrochemistry (e.g. the antifungal pyrrolnitrin and derivatives **1**) and medicine (e.g. 3-chloropyrrole **2**, fibrosis inhibitor).



1a Pyrrolnitrin ($R^1 = R^3 = Cl$; $R^2 = NO_2$)
1b Fenpiclonil ($R^1 = CN$; $R^2 = R^3 = Cl$)
1c Fludioxonil ($R^1 = CN$; R^2, $R^3 = OCF_2O$)



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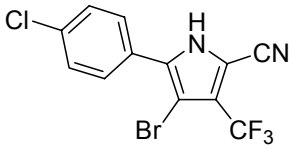

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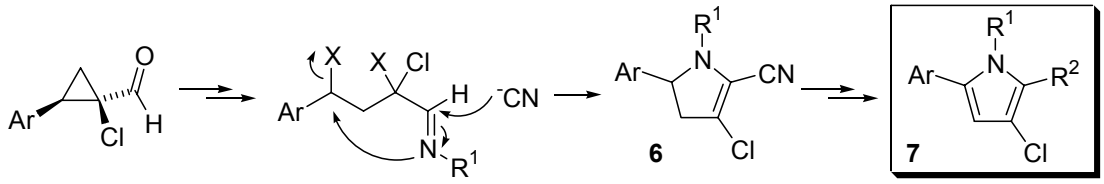
Of interest is the synthesis of 3-halogenated pyrroles bearing electron withdrawing groups (e.g. COOR, CN or CF_3). SAR-studies revealed that 2-arylpyrrole **3** showed remarkable insecticidal activities, resulting in a recent patent of various 2-arylpyrroles for use in the protection of wood from termites.

With respect to these interesting activities, an efficient synthetic route was developed towards pyrroles **7** via ring opening of cyclopropanecarbaldehydes **4**. A nucleophile-induced ring closure after imination of halogenated butanals resulted in 2-pyrrolines **6**, which could be aromatized to polyfunctionalized pyrroles **7**.



4 **5** **6** **7**

R^1 = alkyl, R^2 = H, CN, CHO, $COCH_3$, $COOCH_3$