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REACTIONS ON SOLID SUPPORTS PART I: NOVEL PREPARATION OF α-FORMYL PYRROLES FROM α-METHYLPYRROLES BY OXIDATION WITH THALLIUM (III) NITRATE ON CLAY

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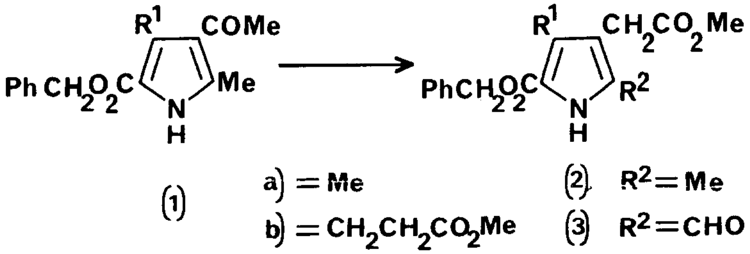
Summary: Treatment of α-methylpyrroles with thallium (III) nitrate/Montmorillonite clay affords the corresponding α-formylpyrroles in excellent yields.

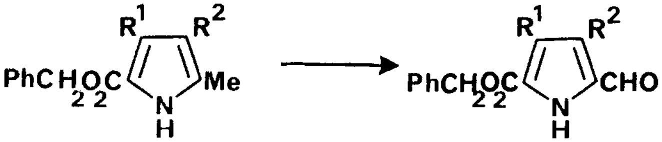
There has been a rapid surge of interest in recent years in the use of reagents supported on solid matrices in a variety of chemical and biological reactions, especially because the reactions often occur much more readily, and with greater specificity than in the absence of the support.[1] For these reasons we became interested in the use of Montmorillonite clay to catalyse the thallium (III) nitrate (TTN) oxidative rearrangements of β-methoxycarbonylmethylpyrroles,[2] as shown in the Scheme below. These reactions have been of considerable utility in preparation of pyrroles required for porphyrin synthesis,[3] but in some cases they take up to twentyfour hours or more to go to completion.



In a typical procedure a solution of the pyrrole (1a) (5.0 g.; 18 mmol.) in dichloromethane (200 ml.) was treated with the TTN/clay reagent (10 g.; 18 mmol.) prepared by McKillop's method,[4] and the slurry was stirred at 25° for 45 min. The orange-red mixture produced was filtered through a short column of alumina (20 g.; Brockmann Grade III) and the latter was washed with dichloromethane (50 ml.) containing methanol (0.5%). Evaporation of the filtrate afforded the α-formyl pyrrole (3a) in ca. 80% yield rather than the expected α-methyl pyrrole (2a) as shown very clearly by the n.m.r. spectrum (absence of an α-methyl resonance at δ7.7 and presence of a formyl resonance at δ10.1, in addition to all the other expected resonances). Similar results were obtained with the analogous pyrrole (1b), the product being the α-formyl pyrrole (3b) rather than the α-methyl pyrrole (2b).

In view of this unexpected enhancement of the reactivity of thallium III nitrate by the clay, we have also studied the oxidation of a range of other pyrroles not containing a β-acetyl substituent, and have found that TTN clay also oxidises each of them to the corresponding α-formyl pyrroles (representative examples are given in the Table below):

Table: Yields of α-formylpyrroles (5) obtained by TTN/clay oxidation of α-methylpyrroles (4).



(4) (5)

(4)	R^1	R^2	Yield of (5) (%)
a)	Me	Et	85
b)	CH_2CO_2Me	$CH_2CH_2CO_2Me$	80
c)	Me	$CH_2CH_2CO_2Me$	85
d)	$CH_2CH_2CO_2Me$	CH_2CO_2Me	80

The oxidation of the α-methyl groups by the TTN/clay reagent may involve radical intermediates, as has been proposed for halogenation and acetoxylation (by lead tetraacetate). However, exclusive formation of the aldehyde rather than formation of products at the alcohol or carboxylic acid level of oxidation points to a possible two electron process (in which the thallium is reduced from the (III) to the (I) state); on the other hand the reagent oxidises pyrromethanes to pyrromethenes rather than to pyrroketones. Further work on the mechanism and applications of this reagent is in progress.

Acknowledgement

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