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Acyliminium Ions Derived from the Rearrangement of Bischler-Napieralski Cyclisation Products

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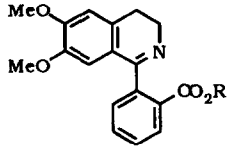
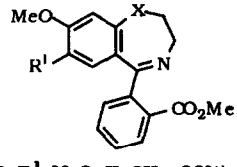
Abstract: *Reactions of pyrophosphoryl chloride with amides derived from arylethylamines and related compounds with 2-methoxycarbonylbenzoyl chloride give the expected Bischler-Napieralski products in good yields which then isomerise readily to afford N-acylaminol ethers under base catalysis; acyliminium ions are then generated using trimethylsilyl triflate and captured, for example with allyltrimethylsilane.*

Current interest in new methods for the generation of acyliminium ions and their use in synthesis,[1] together with our interest in this area[2] and also cyclisation reactions leading to reduced heterocycles[3] led us to investigate reactions of amides derived from 2-methoxycarbonylbenzoyl chloride and arylalkylamines. Surprisingly, Bischler-Napieralski reactions of such derivatives appear not to have been studied previously.[4] Such reactions were of potential interest because the location of the ester group in the initial products suggested that intramolecular rearrangement reactions should be possible. The related reactions involving amides derived from homophthalic acid derivatives were studied a considerable time ago, but in those cases the formation of a six-membered ring allowed stabilisation of the acyliminium ion by deprotonation.[5] Reactions of the appropriate half ester-half amides with pyrophosphoryl chloride[6] gave the isoquinoline derivatives (**1**) and (**2**) and the related compounds (**3**) and (**4**) in the yields shown.[7]



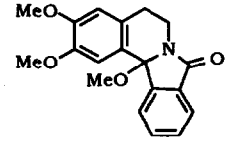
(1, R=Me; 100%)

(2, R=Et; 86%)



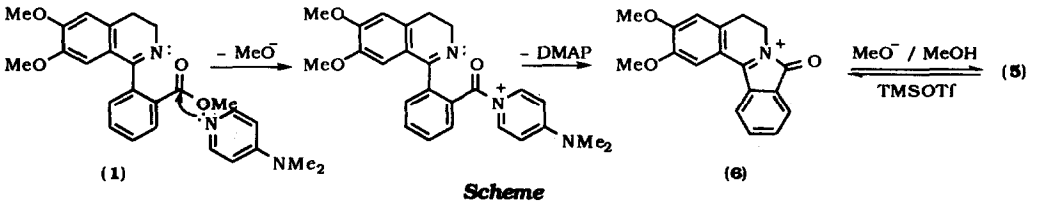
(3, R^1=MeO; X=CH_2; 86%)

(4, R^1=H; X=O; 57%)



(5)

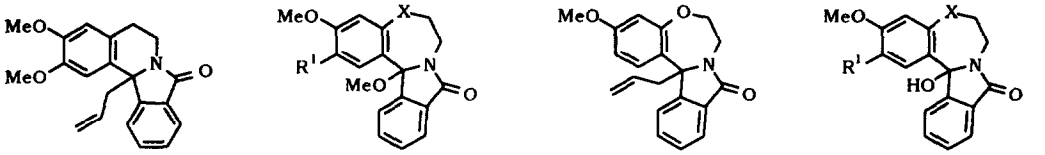
Our initial experiments have been centred on the isoquinoline derivative (**1**). Although the compound (**1**) did not cyclise spontaneously it did rearrange quantitatively to the related acyl aminol ether (**5**) when heated in methanol in the presence of a catalytic quantity of DMAP. A similar reaction of the compound (**4**) also gave the rearranged product (**9**) in a quantitative yield. In order to establish the nature of the rearrangement reaction we heated the compound (**1**) in anhydrous ethanol together with DMAP and again isolated the methoxy derivative (**5**). However, when the related ethyl ester (**2**) was heated in methanol in the presence of DMAP we isolated the methoxy derivative (**5**). These results suggest the mechanism indicated in the ***Scheme***. We presume that the size of ethanol makes its capture by the intermediate iminium ion difficult. The capture by water of acyliminium ions derived from (**3**) and (**4**) and (**8**) and (**9**) also illustrates this point.



(1) (6) (5)

Scheme

The methoxy derivative (**5**) also functions as a precursor to the acyliminium ion (**6**). A solution of the compound (**5**) in dichloromethane reacted slowly with allyltrimethylsilane in the presence of a catalytic amount of trimethylsilyl triflate and gave the allyl derivative (**7**) in a 78% yield. The methoxy derivative (**9**) also gave a related allyl derivative (**10**) and the compound (**12**) in 22% and 57% yields respectively in a similar reaction. We assume the low yield of the compond (**10**) relates to a slow reaction between allyltrimethylsilane and the acyliminium ion which is captured by water on work-up. The benzazepine derivative (**8**) was found to be very unstable and was largely converted into the hydroxy analogue (**11**) during flash chromatography on silica gel.



(7) (8. R^1 = MeO; X = CH_2) (9. R^1 = H; X = O) (10) (11. R^1 = MeO; X = CH_2) (12. R^1 = H; X = O)

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7. The compounds reported in this letter have been fully characterised, including elemental analyses and accurate mass measurements on molecular ions. The structures assigned to the rearrangement products are fully supported by high field nmr data, including nOe experiments.

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