



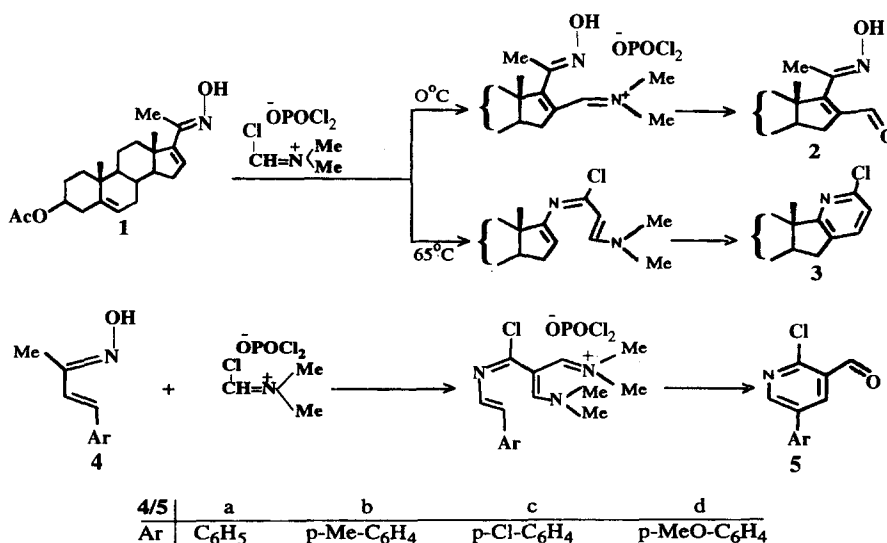
An Efficient Conversion of Conjugated Oximes into Substituted Pyridines under Vilsmeier Conditions

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Abstract : A facile synthesis of a pyrido fused steroidal D-ring and functionalised pyridine is described. Copyright © 1996 Published by Elsevier Science Ltd

Some pyridines constitute an important class of antitumor compounds and attract much attention.^{1,2} Azadienes have frequently been employed³ as precursors to functionalized pyridines and recently conjugated oximes have shown enhanced reactivity.⁴ The steroidal molecule 16-dehydropregnenolone acetate (16-DPA) is an important key intermediate for antitumor drugs^{5,6} and bears a conjugated enone group at the D-ring. However, the potential of the azadiene group in the steroidal D-ring received scant attention.^{5,7} Our interest in aza compounds^{8,9} has led us to report here an efficient and facile synthesis of functionalized pyridines from conjugated oximes employing a Vilsmeier reagent.



The reaction of **1** with a mixture of phosphorus oxychloride and dimethylformamide (1:10:10 eq) at 0°C for 3 h afforded the C_{16} -formyl compound **2** in 82% yield. However, the reaction at 65°C for 2 h resulted a fused pyrido-steroidal product **3** in 75% yield.

The formation of the compound **2** can be explained by the nucleophilic attack of the azadiene moiety on the chloromethyleneiminium salt triggered by electron donating -OH group at N₁-position. At an elevated temperature the oxime **1** undergoes preferentially a Beckmann rearrangement followed by the monoformylation of the side chain and cyclisation to afford **3** as the sole product.¹⁰ Under Vilsmeier conditions neither **3** could be isolated at 0°C nor **2** at 65°C.

The aromatic conjugated oximes **4a-d** under Vilsmeier conditions afforded formylated chloro pyridines **5a-d** in 71 - 82% yields.¹¹ The formation of **5** occurs by diformylation of the Beckmann rearranged product of **4**.

In conclusion, we have observed that the steroidal oxime **1** led to monoformylation; however, the aromatic conjugated oxime **4** underwent diformylation of the Beckmann rearranged product.¹² Further work on functionalized pyridines and fused pyrido steroidal compounds is in progress.

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10. All the new compounds gave satisfactory IR, ¹HNMR and mass/or elemental analysis. Selected physical and ¹HNMR data: **2**: mp 225°C (MeOH); 82% yield; ¹HNMR(CDCl₃): δ 9.15(1H,s), 5.18(1H,bs), 4.35(1H,m), 2.05(3H,s), 1.90(3H,s), 1.08(3H,s), 1.0(3H,s), 2.35-1.20(17H,m); **3**: m.p.200°C(EtOAc); 75% yield; ¹HNMR (CDCl₃): δ 7.11(1H,d,J= 8Hz), 6.76(1H,d, J=Hz), 5.20(1H,bs), 4.35(1H,m), 1.90(3H,s), 1.05(3H,s), 0.90(3H,s), 2.67-1.15 (17H,m).
11. **5a**: mp 92°C (EtOAc); yield, 75%; ¹HNMR(CDCl₃): δ 10.40(1H,s, -CHO), 8.52(1H,d,J = 2Hz), 8.15 (1H,d,J = 2Hz), 7.50-7.15(5H,m, aromatic protons).
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