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

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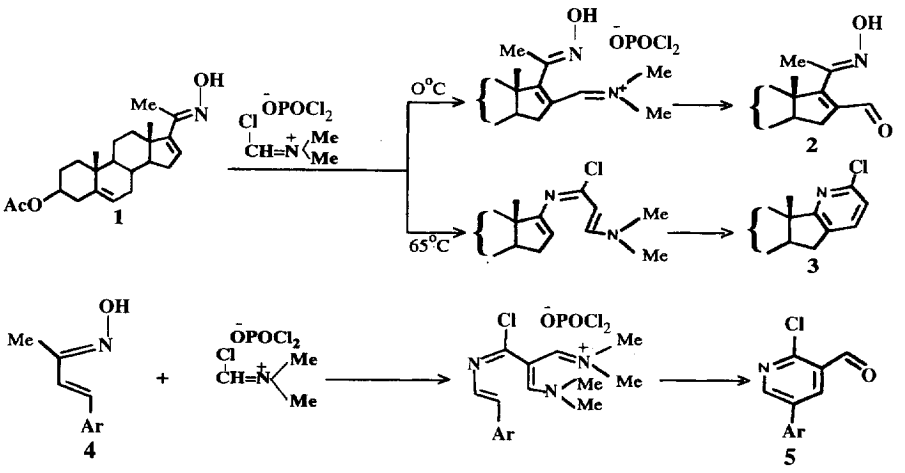
Abstract : A facile synthesis of a pyrido fused steroidal D-ring and functionalised pyridine is described.

Some pyridines constitute an important class of antitumor compounds and attract much attention.[1,2] Azadienes have frequently been employed[3] 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.



4/5	a	b	c	d
Ar	C_6H_5	p-Me-C_6H_4	p-Cl-C_6H_4	p-MeO-C_6H_4

The reaction of **1** with a mixture of phosphorus oxychloride and dimethylformamide (1:10:10 eq) at O°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 N_1-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 Vilsmeir conditions neither **3** could be isolated at O^0C nor **2** at 65^0C.

The aromatic conjugated oximes **4**a-d under Vilsmeier conditions afforded formylated chloro pyridines **5**a-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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REFERENCES AND NOTES

1. Boger, D.L.; Nakahara, S. *J. Org. Chem.*, **1991**, *56*, 880-884.
2. a) Boger, D.L.; Kasper, A.M. *J. Am. Chem. Soc.*, **1989**, *111*, 1517-1519.
   b) Zhang, T.Y.; Stout, J.R.; Keay, J.G.; Scriven, E.F.V.; Toomey, J.E.; Goe, G.L. *Tetrahedron*, **1995**, *51*, 13177 - 13184.
3. a) Cheng, Y.-S.; Lupo, A.T.; Fowler, F.W. *J. Am. Chem. Soc.*, **1983**, *105*, 7696-7703.
   b) Boger, D.L. *"Comprehensive Organic Synthesis"*, edit. Paquette, L. A.; Pergamon Press, **1991**, *Vol 5*, 451-512.
4. Behforouz, M.; Gu, Z.; Cai, W.; Horn, M.A.; Ahmedian, M. *J.Org. Chem.*, **1993**, *58*, 7089-7091.
5. Hong, C.I. *"Antitumor Steroids"* by Blickenstaff, R.T.; Academic Press, New York, **1992**, 155 -174.
6. Rasmusson, G.H.; Reynolds, G.F.; Steinberg, N.G.; Walton, E.; Patel, G.F.; Liang, T.; Cascieri, M.A.; Cheung, A.H.; Brooks, J.R.; Bermann, C. *J. Med. Chem.*,**1986**, *29*, 2298-2315.
7. a) Nguyen, X.C.; Nguyen, V.D.; *Tap. Chi. Duoc. Hoc.*, **1983**, *4*,12.(*Chem Abstr.*, **1984**, *100*, 103724b.).
   b) Bahamonde, J.L.; Sanchis, P.R.; Martin, M.M.; Chinchilla, A.J.J.Y.; Calvo, A.C.; Lopez, J.J.S. *Span. Spain.*, **1981**, 492225.(*Chem. Abstr.*, **1982**, *96*, 20371).
8. a) Konwar, D.; Boruah, R.C.; Sandhu, J.S. *Tetrahedron Lett.*, **1987**, *28*, 955-956.
   b) *ibid.*, **1990**, *31*, 1063-1064.
9. Boruah, R.C.; Skibo, E.B. *J. Org. Chem.*, **1995**, *60*, 2232-2243.
10. All the new compounds gave satisfactory IR, ^{1}HNMR and mass/or elemental analysis. Selected physical and ^{1}HNMR data: **2**: mp 225°C (MeOH); 82% yield; ^{1}HNMR($CDCl_3$): 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; ^{1}HNMR ($CDCl_3$): 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%; ^{1}HNMR($CDCl_3$): 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).
12. a) Meth-Cohn, O., Narine, B.; Tarnwski, B. *Tetrahedron Lett.*, **1979**, 3111- 3114.
    b) Meth-Cohn, O.; Stanforth, S. P. *Comprehensive Organic Synthesis*, Pergamon Press, **1991**, *Vol-2*, 777-794.

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