**SYNLETT Spotlight**

**Spotlight 55**

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research.

**Vilsmeier–Haack Reagent**

(Halomethyleneiminium Salt)

Compiled by Tasneem

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**Introduction**

The Vilsmeier–Haack reagent (halomethyleneiminium salt) formed from the interaction of dialkyl formamides such as DMF with POCl₃ has attracted the attention of synthetic organic chemists since its discovery in 1927. It is one of the most commonly used reagents for the introduction of an aldehydic (CHO) group into aromatic and heteroaromatic compounds.

Some interesting cyclisation reactions have also been reported under Vilsmeier conditions. In addition, certain striking applications eg halogenation, alkylation (methylation) and haloalkylation have been recently reported.

**Abstract**

(A) Rajanna et al reported that acetanilides, particularly deactivated acetanilides, undergo Vilsmeier–Haack cyclisation in micellar media to afford the corresponding 2-chloro-3-formyl quinoline derivatives in good yields. This procedure works efficiently in the presence of micelles i.e. CTAB (cetyltrimethylammonium bromide), SDS (sodium dodecylsulfate) and TX (Triton-X-100) under reflux conditions. Surprisingly, the reaction time was reduced up to 10-fold in the present method. Under ultrasonic irradiation, the reaction times were even more reduced with dramatic enhancement in the yield of reaction products.

(B) Alkyl diacylacetalates are efficiently converted into 2,6-dichloro-3-formyl benzoates using the Vilsmeier–Haack reagent under microwave irradiation. The reaction time has been decreased from hours to seconds.

(C) Cheng et al. reported the formation of unexpected products from the formylation of N,N-dimethylanilines with 2-formamidopyridine in POCl₃ under Vilsmeier–Haack reaction conditions. 2-Formamidopyridine in POCl₃ solution reacts with N,N-dimethylaniline to give tris(4-dimethylaminophenyl)methane in 80% yield, whereas with 4,N,N-dimethylaniline it gives 2-dimethylamino-5-phenyl(2-N-methylformamido-5X-Phenyl)(2-pyridyloamino)methane.
(D) 2-Chloro-3-pyridine carboxaldehydes were synthesised for the first time by Vilsmeier–Haack reaction of 4-aryl-3-buten-2-one oxime. The reaction proceeds via the formation of $\text{N-(2-arylethenyl) acetamides}$ as intermediates.\(^9\)

(E) Lellouche et al reported that the two electrophilic Vilsmeier–Haack complexes formed from $\text{POCl}_3$–DMF or ($\text{CF}_3$SO$_2$)$_2$O–DMF react with $\text{C}_2$-symmetrical dialkoxy silanes $\text{R'O-Si(R'')_2-OR''}$ affording the corresponding formates $\text{R'}\text{CHO}$ in low/medium to high yields depending on conditions and substrates.\(^10\)

(F) $\text{POCl}_3$–DMF over silica gel has been used for the synthesis of $\beta$-chlorovinylaldehydes, 2-aryl-3-formylindoles, 2-chloro-3-formylquinolines and other aromatic aldehydes using solvent-free conditions and microwave irradiation. The Vilsmeier–Haack reaction was performed in 1.5–2.5 minutes under microwave irradiation in solvent-free conditions with good yields. Furthermore, the present method is rapid and efficient and avoids the use of the reagent as solvent and thus is environmentally friendly.\(^11\)

References

(1) Vilsmeier, A.; Haack, A. Berichte 1927, 60, 119.