SYNLETT
# 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

Mrs. Tasneem received her Bachelor Degree from Osmania University, Hyderabad, India and a Masters degree from the University of Hyderabad. After completion of her MSc, she joined Prof. K. C. Rajanna (Osmania University) to pursue her research work leading to a PhD. She has been assigned to carry out micellar-mediated kinetic studies of organic substitution reactions such as formylation, acetylation and nitration. At present, she is actively engaged in the field of kinetic and mechanistic studies of Vilsmeier–Haack reactions under various conditions.

E-mail: tasneems@rediffmail.com

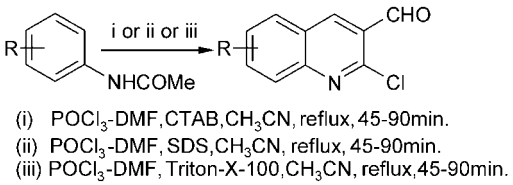
## Introduction

The Vilsmeier–Haack reagent (halomethyleneiminium salt) formed from the interaction of dialkyl formamides such as DMF with $POCl_3$ has attracted the attention of synthetic organic chemists since its discovery in 1927.[1] It is one of the most commonly used reagents for the introduction of an aldehydic (CHO) group into aromatic and heteroaromatic compounds.[2]

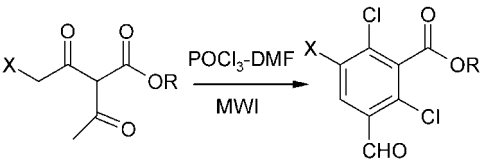
Some interesting cyclisation reactions have also been reported under Vilsmeier conditions.[3] In addition, certain striking applications eg halogenation, alkylation (methylation) and haloalkylation have been recently reported.[4]

## Abstract

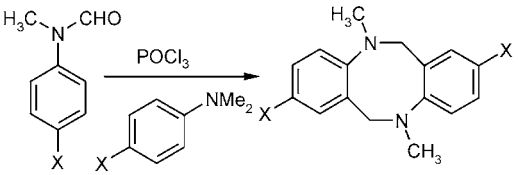
(A) Rajanna et al reported that acetanilides, particularly deactivated acetanilides, undergo Vilsmeier–Haack cyclisation in micellar media to afford the corresponding 2-chloro-3-formyl quinoline derivatives in good yields. This procedure works efficiently in the presence of micelles i.e. CTAB (cetyltrimethylammonium 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.[5]
Under ultrasonic irradiation, the reaction times were even more reduced with dramatic enhancement in the yield of reaction products.[6]




(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.[7]



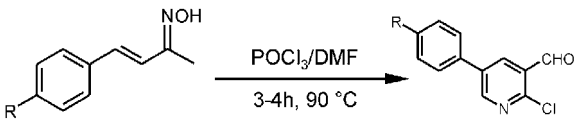

(C) Cheng et al. reported the formation of unexpected products from the formylation of *N*,*N*-dimethylanilines with 2-formamidopyridine in $POCl_3$ under Vilsmeier–Haack reaction conditions. 2-Formamidopyridine in $POCl_3$ solution reacts with *N*,*N*-dimethylaniline to give tris(4-dimethylaminophenyl)methane in 80% yield, whereas with 4-*N*,*N*-dimethylaniline it gives 2-dimethylamino-5-phenyl(2-*N*-methylformamido-5X-Phenyl)(2-pyridyloamino)methane.[8]



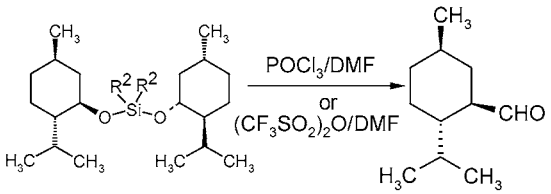

Synlett 2003, No. 1, Print: 30 12 2002.
Art Id.1437-2096,E;2003,1,01,0138,0139,ftx,en;V05702ST.pdf.

ISSN 0936-5214

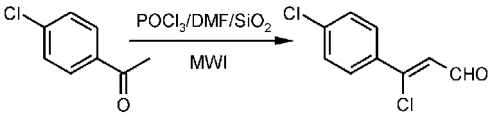
(D) 2-Chloro-3-pyridine carboxaldehydes were synthesised for the first time by Vilsmeier–Haack reaction of 4-aryl-3-buten-2-one oxime. The reaction proceeds via the formation of *N*-(2-arylethenyl) acetamides as intermediates.[9]




(E) Lellouche et al reported that the two electrophilic Vilsmeier–Haack complexes formed from $POCl_3$–DMF or $(CF_3SO_2)_2O$–DMF react with $C_2$-symmetrical dialkoxysilanes $R^1O–Si(R^2)_2–OR^1$ affording the corresponding formates $R^1CHO$ in low/medium to high yields depending on conditions and substrates.[10]




(F) $POCl_3$–DMF over silica gel has been used for the synthesis of β-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.
(2) (a) Massa, C. M. *Tetrahedron* **1992**, *48*, 3659. (b) Jutz, C. In *Advances in Organic Chemistry*, 9; Taylor, E. C., Ed.; Wiley: New York, **1976**, 225. (c) Seshadri, S. *J. Sci. Ind. Res.* **1973**, *32*, 128.
(3) (a) Meth-Cohn, O.; Tarnowshi, B. *Adv. Heterocycl. Chem.* **1982**, *31*, 207. (b) Meth-Cohn, O.; Taylor, D. L. *J. Chem. Soc., Chem Commun.* **1995**, 1463. (c) Jackson, A.; Meth-Cohn, O. *J. Chem. Soc., Chem Commun* **1995**, 1319.
(4) (a) Selvi, S.; Perumal, P. T. *Org. Prep. Proced. Int.* **2001**, *33*, 194. (b) Dinakaran, K.; Perumal, P. T. *Ind. J. Chem., Sect. B.* **2000**, *39*, 135. (c) Krapivin, G. D.; Kozhina, N. D.; Chernousenko, L. A. Zavodnik. V. E. *Chem. Heterocycl. Compd.* **1999**, *35*, 23.
(5) Ali, M. M.; Tasneem; Rajanna, K. C.; Saiprakash, P. K. *Synlett* **2001**, 251.
(6) Ali, M. M.; Sana, Sariah.; Tasneem; Rajanna, K. C.; Saiprakash, P. K. *Synth. Commun.* **2002**, *32*, 1351.
(7) Selvi, S.; Perumal, P. T. *Synth. Commun.* **2000**, *30*, 3925.
(8) Cheng, Y.; Jiao, P.; Williams, D. J.; Meth-Cohn, O. *J. Chem. Soc., Perkin Trans. 1* **2001**, 44.
(9) Perumal, P. T.; Amaresh, R. R. *Synth. Commun.* **2000**, *30*, 2269.
(10) Cohen, Y.; Kotlyar, V.; Koeller, S.; Lellouche, J. P. *Sylett* **2001**, 1543.
(11) Paul, S.; Gupta, M.; Gupta, R. *Synlett* **2000**, 1115.