Chlorine directed formylation of chloroindanones under Vilsmeier-Haack reaction condition[†]

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Highly selective bisformylation of 4-chloroindanone derivatives on treatment with POCl₃ + DMF have been discovered.

β -Chloro- α,β -unsaturated acrolein derivatives have been found to be important starting material for the synthesis of various natural and non-natural products¹. One of the simplest method for the synthesis of β -chloro- α,β -unsaturated acrolein moiety is the reaction of compounds with ketomethylene groups and POCl₃ + DMF, popularly known as Vilsmeier-Haack reagent². In our^{3,4} and others⁵ earlier studies of this reagent with cyclic ketones revealed facile formation of β -chloro- α,β -unsaturated acrolein systems. However, when 4-chloro substituted indanones were treated with Vilsmeier-Haack reagent (VM), the only isolable product was bisformylated one. Reactions of VM reagent with other cyclic ketones viz. unsubstituted indanone, and suberone afforded only mono aldehydes. This is the first example of chlorine directed bisformylation of indanone system. This extra formyl group could be used in the synthesis of several heterocyclic systems. To verify the role of chlorine in bisformylation we took unsubstituted indanone (entry no. 1), methyl indanone (entry no. 2), then keeping the chlorine at the same position we increased the size of the ring of the cyclic ketone, i.e. 5-chloro-1-tetralone (entry no. 5) and 1-tetralone (entry no. 6), benzo suberone (entry no. 8) and the corresponding acyclic analogue, 3-chloropropane-2-one (entry no. 9) which needed TCE (trichloroethane) together with VM reagent for complete conversion in to the regular VM product.

Thus, bisformylation was only observed when there was a chlorine substitution at the 4-position of the indanone (viz. entry no. 3 and 4).

In literature⁵, only β -tetralone is reported to produce bisaldehyde in only 20% yield along with the normal β -chloro- α,β -unsaturated acrolein derivative in 70% yield (entry no. 7). The two aldehyde groups (enolisable) are found to take part in intramolecular H-bonding (confirmed by ¹H

Entry no.	Reactions	Products	Yield %
1			65
2			80
3			70
4			70
5			70
6			75
7			65
8			75
9			70

NMR). This type of bisformylation is not reported earlier, although the mechanism of the reaction is not fully elucidated, but present studies demonstrate that the chlorosubstituted indanone is a good chelating agent for Vilsmeier-Haack reagents which picked up the acidic proton in chloroindanone only and not in higher homologues, we presume, because of the 'proximity effect' in indanone derivatives and electronic effect are the causes.

[†]Dedicated to Professor S. M. Mukherji.

General procedure for the preparation of bischlorovinylaldehydes (entry no. 3 and 4) : To an ice cold (0–5°) and stirred solution of DMF (10 ml) and POCl₃ (1.5 eq.) under argon blanket, chloroindanone (1 eq.) in DMF (5 ml) was added dropwise. The mixture was stirred at (0–5°) for 2 h and decomposed with saturated ice cold sodium acetate solution, solvent extraction and stripping off the solvent produced dialdehyde (entry no. 3 and 4).

Spectral data of selected chlorovinylaldehydes :

1,4-Dichloro-indene-2,3-dialdehyde (3) : ¹H NMR δ (CDCl₃) 7.27–7.34 (1H, m, aromatic), 7.51 (1H, d, *J* 8.7 Hz, aromatic), 7.71 (1H, d, *J* 8.7 Hz, aromatic), 8.90 (1H, d, *J* 9.0 Hz, =CH), 10.05 (1H, s, CHO), 13.46 (1H, d, *J* 9.1 Hz, =CH-OH); D₂O exchange : ¹H NMR 7.27–7.34 (1H, m, aromatic), 7.51 (1H, d, *J* 8.7 Hz, aromatic), 8.90 (1H, s), 10.05 (1H, s, CHO); mass : (EI, *m/z*), 240 (M⁺).

1,4-Dichloro-7-methyl-indene-2,3-dialdehyde (4) : ¹H NMR δ (CDCl₃) 2.80 (3H, s, CH₃), 7.0 (1H, d, *J* 8.6 Hz, aromatic), 7.35 (1H, d, *J* 8.6 Hz, aromatic), 9.0 (1H, d, *J*

8.9 Hz, =CH-OH), 10.0 (1H, s, CHO), 13.6 (1H, d, *J* 9.2 Hz, =CH-OH); D₂O exchange : ¹H NMR 2.80 (3H, s, CH₃), 7.0 (1H, d, *J* 8.6 Hz, aromatic), 7.35 (1H, d, *J* 8.6 Hz, aromatic), 9.0 (1H, s), 10.0 (1H, s, CHO); ¹³C NMR 20, 121.5, 127.3, 128.5, 129, 131, 133, 133.5, 134, 143, 158, 190; mass : (EI, *m/z*), 254 (M⁺).

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