A New Method for the Preparation of Substituted 5,6,7,8-Tetrahydro-4H-/-benzopyran and 4H -Pyrans by Vilsmeier -Haack Reagent.

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<u>Abstract</u>: Substituted 5,6,7,8-tetrahydro-4H-1-benzopyran and 4H-pyran derivatives were synthesized from their corresponding substituted 1,5-diketones with vilsmeier-haack reagent in moderate yields.

Vilsmeier-Haack reagent has been used for different synthetic reactions.¹ It undergoes different courses namely formylation², acylhalo addition ³, cyclization ⁴ and ring annulation ⁵. 2-Chloro-3-substituted quinolines are prepared effeciently by using Vilsmeier Haack reagent ⁶.Vilsmeier reagent has been used to provide exclusively β -halo- α , β -unsaturated ketones⁷. Recently, Vilsmeier-Haack reagent has been used to prepare 2,6-dichloro-1,4-dihydropyridine-3,5-dicarboxylic aldehydes from glutarimides by Guzman et al⁸. The same type of reaction is also reported in the literature which uses excess of Vilsmeier-Haack reagent in the conversion of N-substituted succinimides to 2,5-dichloropyrrole-3,4-dicarboxylic aldehydes⁹. The reaction of tetrahydro-4H-pyran-4-one, tetrahydro-4H-thiopyran-4-one, chroman-4-one and thiochroman-4-one with Vilsmeier reagent affords the corresponding β -chlorovinylaldehydes. However, with excess of reagent at 100°C ,chromanone-4-one gives (chloromethyl)chromone, and thiochromanone affords 3-formylthiochromone ¹⁰.

Recently, we reported the conversion on a variety of substituted chalcones to the corresponding chloroindenes with the excess of phosphorus oxychloride and dimethylformamide in 22-31% yields¹¹. In continuation of our studies on carbonyl compounds with the Vilsmeier reagent, we became interested in the study of substituted 1,5-diketones. In this communication, we wish to report the synthesis of substituted 5,6,7,8-tetrahydro-4H-1-benzopyran and 4H-pyrans from the corresponding substituted 1,5-diketones by using Vilsmeier reagent. The reactions are carried out at 80° C for 5 h with 5.4 equiv. POCl₃ in DMF. Table 1 summarizes the preparation of the various penta substituted 4H-pyrans from the corresponding 1,5-

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SI. No.	Substrate	Product ^a	m.p. (°C)	yield (%) b
1	Ph o O Ph Ph	Ph OF Ph CHO	190	52
2	Ph o Ph	Ph Ph Ph OHC CHO	160	45
3	Ph O O Ph Me	Ph OHC Me	142	53
4	Ph O O Ph	Ph OF Ph OHC CHO	198	55
5	Ph Ph	CHO Ph CHO	152	45

Table 1 : Reaction products of 1,5-diketones with Phosphorus oxychloride and DMF

(a) The products were characterised by Proton and Carbon-13 NMR spectra, IR and Mass. All the new compounds gave statisfactory C & H analysis.
(b) The yields reported here are after separation from column chromatography.

_ _ diketones. Our method will be the first one to report such a kind of cyclization by the use of Vilsmeier reagent. The literature reveals that the reaction of 1,5-diketones with either acid or base gives different type of products ¹². Various diketones were synthesized by base catalysed condensation reaction of chalcone with the corresponding ketones ¹³.

Scheme 1.



While it would be premature to discuss the detailed mechanism, at this stage. The general pattern of the reaction can be recognized. Phosphorus oxychloride reacts with DMF to give a complex (I), which in turn undergoes electrophilic substitution reaction with the one of the carbonyl moiety in the 1,5-diketone (II) to provide the chloromethyleminium species (III). The chloromethyleminium species (III), then reacts with the other carbonyl group in the 1,5-diketone to afford the cyclized dimethylamino compound (IV). Elimination of the chloride ion from the compound (IV) gives a stable species (V), which then reacts with the reagent complex (I) to provide the dieminium

species (VI). The compound (VI) then undergoes to the stable dieminium species(VI). Hydrolysis of the dieminium compound (VII) with aqueous sodium acetate affords the 2,4,6-triphenyl-4H-Pyran-3,5-dicarboxylic aldehyde (Scheme 1).

<u>Typical procedure</u>: Preparation of 2,4,6-triphenyl-4H-Pyran-3,5-dicarboxylic aldehyde: 1,3,5-triphenyl-1,5-pentanedione 3.3g (10 mmol) was dissolved in 8 ml of DMF was cooled to 0° C and 5 ml of POCl₃ was added dropwise over 40 minutes and stirred for

1 h at room temperature and for 5 h at 80°C. The reaction mixture was then poured under the stirring onto a mixture of crushed ice (100 g) containing sodium acetate (5 g) and water (30 ml). The product was extracted with chloroform (3 x 50 ml) and dried over anhydrous sodium sulfate. After removal of the solvent, the crude product was chromatographed through a short column of silica gel using 1.9 ratio of chloroform and petroleum ether as eluent to provide the 2,4,6-triphenyl-*4H*-pyran-3,5-dicarboxylic aldehydes (a white solid m.p. 190 °C).(1.90g, 52% yield). ¹H NMR ; δ 5.17 (s,1H), 7.55 (m,15 H),9.6 (s,2 H); ¹³ C NMR ; δ 32.88, 118.97, 126.96, 128.22, 128.52, 128.74, 130.17, 137.47, 143.56, 164.66, 189.6 ; MS;M/Z (%) 366 (25), 338 (55), 289 (15), 202 (10), 105 (70), 77 (100).

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