



One Pot Synthesis of Formyl Phenyl Terpyridine: A Simplified Synthesis

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ABSTRACT

Formyl phenylterpyridine was synthesized from methyl phenylterpyridine using SeO_2 as the oxidizing agent. SeO_2 conventionally has been used to oxidize allylic and aliphatic methyl groups. The simple conversion of methyl group attached to aromatic ring appended to heterocycle in a clean one pot synthesis paves way for synthesis of similar aldehydes extendable to other classes of compound as well.

Keywords: Methyl phenylterpyridine (4-methyl-phenyl-2,2':6',2''-terpyridine), Formylphenylterpyridine(4-formyl-phenyl-2,2':6',2''-terpyridine)", Oxidation, Selenium dioxide.

INTRODUCTION

Aldehydes are the versatile reagents in the organic synthesis and especially aromatic aldehydes has been extensively used as a starting reagent for various products through various types of reactions¹⁻⁴. Synthesis of Oximes which are known for their biological activity from aldehydes has been reported in the literature⁵. Recently the synthesis of aryl amines from aldehydes which has pharmaceutical importance has been reported using $\text{Zn}(\text{BH}_4)_2/\text{MgBr}_2$ ⁶. Varieties of oxidizing agents are available for oxidation of aliphatic as well as aromatic alkyl groups which gets converted to carboxylic group in majority

of the reactions⁷. Mild oxidizing agents has been used to oxidize methyl group to alcohol. Variety of reagents convert methyl group to aldehyde. Methods like Etard reaction, chromyl chloride oxidation and oxidation with PCC involve multistep reactions for conversion⁸⁻¹¹. Cerium and Iridium catalyzed reaction can oxidize methyl group attached to aromatic group like benzene¹²⁻¹⁵ but is not successful in oxidizing methyl groups attached to heterocyclic rings. Selenium dioxide is a versatile reagent for oxidizing methyl groups directly attached to heterocyclic ring like 3-methylbipyridine, 4-methylphenanthroline, 2,5-dimethylpyridine¹⁶. Heterocyclic aldehydes are best known for their versatility in the synthesis of

biologically active molecules. But the problem arises when there is a aromatic ring like phenyl ring present in between heterocycle and the methyl group. Almost all the reported methods failed to oxidise such methyl groups. Schubert *et al.* reported the oxidation of such methyl group to aldehyde in a multistep process^{17,18}. SeO_2 was found to be unsuccessful in oxidation of methyl group of nitro toluene and even that of 2,4,6-trinitrotoluene, however on conversion to phenyl bromides conversion to aldehyde was found to be feasible¹⁹. Here we report the simplified synthesis of aldehyde (FPT) in one pot using SeO_2 in 1,4-dioxane paving the way for simplified oxidation of such class of compounds to aldehydes.

EXPERIMENTAL

Methyl phenyl terpyridine [1] (MPT)

was prepared using Krohnke methodology by condensation of 2-acetyl pyridine and p-tolualdehyde in 60% yield. 1.65 g (41 mmol) of crushed NaOH was added to the 30ml of Polyethylene Glycol (PEG-300) with constant stirring at room temperature. 5 g (41.6mmol) of 2-acetyl pyridine was added and after 10 minutes 2.472 g (20.6 mmol) of p- tolualdehyde was added with continuous stirring. The colorless solution turned to light yellow. After two hours the color changed to orange and then to pink. 25 ml of liquid NH_3 (18N) was added. The white precipitate formed was washed with water and recrystallized from ethanol.

Yield %- 60%, HNMR-(CDCl_3 , 400 MHz, ppm) 2.4 (s, 3 H) δ 7.49 (m,2 H), 8.01 (m, 2 H), 8.15 (m, 4H), 8.72 (d,2 H), 8.80 (d, 2 H), 8.98 (s, 2 H),.5, UV-Vis- 281 nm

Formyl phenylterpyridine[2] (FPT)

1 g (9.0 mmol) of SeO_2 and 0.1 ml (5.55 mmol) of H_2O was added to 700 (2.16mmol) mg of MPT in 10 ml of 1,4-dioxane. The mixture was heated at 200°C in autoclave for 2 hours. The steel bomb was taken out and cooled to room temperature. Additional 1 g of SeO_2 and 0.5 ml of H_2O was added and the steel bomb was heated in autoclave for 6 hrs. The steel bomb was cooled to room temperature and the pale yellow colored product formed was dried on water bath. The product was purified by column chromatography using CHCl_3 and 9:1 CHCl_3 :MeOH mixture as the eluent.

Yield - 20%, ¹HNMR (CDCl_3 , 400 MHz, ppm) δ 7.39 (m,2 H), 7.91 (m, 2 H), 8.05 (m, 4H), 8.69 (d, 2 H), 8.75 (d, 2 H), 8.78 (s, 2 H), 10.12 (s, 1 H).5, UV-Vis, 283 nm.

RESULT AND DISCUSSION

Several reactions were carried out using different amount of SeO_2 to obtain maximum conversion. As per the Table 1. large scale synthesis of aldehyde using higher concentration failed to yield any product even after keeping the reaction mixture

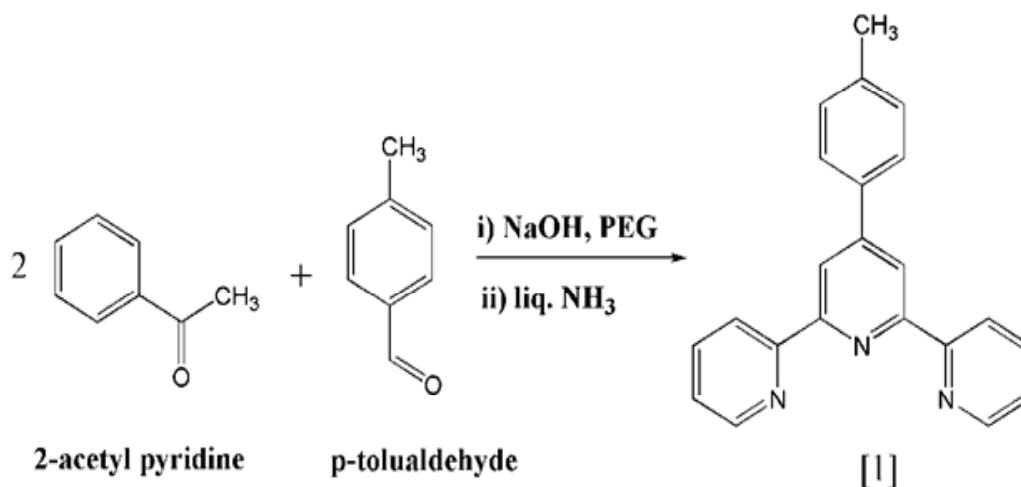


Fig.1: Synthesis of Methyl Phenyl Terpyridine following Krohnke Methodology

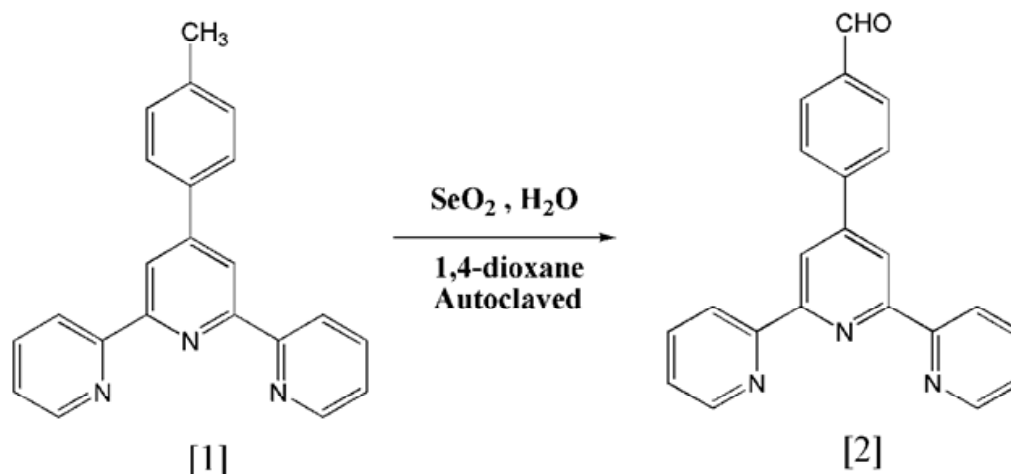


Fig. 2: Autoclave synthesis of FormylPhenylTerpyridine from Methyl PhenylTerpyridine using SeO_2 as oxidant

Table 1: Standardization of the synthesis of FormylPhenyl Terpyridine

MPT mmols	SeO_2 mmols	1,4-Dioxane ml	H_2O mmols	Temp. $^\circ\text{C}$	Time h	Yield %
6.31	9.00	35	11.1	120	12	0
0.30	1.15	10	5.55	125	12	0
0.30	1.15 +* 1.15	10	5.55+*5.55	125	2 +* 8	10
0.30	1.80 +*1.80	16	2.77+*2.77	150	2 +*10	9
2.16	4.50+*4.50	10	5.55+*5.55	200	2+*6	20

*Time after addition of additional amount of SeO_2 and H_2O .

at 120°C for 12 hours. Even in low concentration the reaction failed and no product was detected. Upon slight modification of the reaction condition i.e. changing from one time addition to two time addition of oxidizing agents after an interval resulted in formation of desired product. It can be inferred with ample support from literature that in the first step of reaction the methyl group gets converted to alcohol group which in next step gets converted to the desired formyl group. Molar ratio of SeO_2 :MPT: H_2O in proportion of 3/2:1 : 5 gave the best yield. Though small amount of unreacted MPT was detected it was reused for further reaction. The study also suggests that at the optimal temperature of 200°C , the yield is best and the reaction time required for second step of reaction could be reduced to 6 hours. The method opens up the new route for the oxidation of

tolyl group attached to heterocycle to aldehyde in one pot synthesis which otherwise is not possible in normal conditions. Though the conversion was standardized with only one heterocycle it can be easily extended to other heterocycles. 1,4-dioxane was chosen on the basis of solubility of the initial/ reactants.

The aldehyde prepared has been successfully used for the synthesis of porphyrin as revealed by UV-vis spectroscopy and detailed characterization of which is under progress.

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