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Rate Enhancements in the Acetylation and Benzoylation of Certain Aromatic Compounds with Vilsmeier-Haack Reagents Using Acetamide, Benzamide and Oxychlorides under Non-Conventional Conditions

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Abstract

Acetylation and benzoylation reactions of certain aromatic aldehydes, ketones with Vilsmeier-Haack Reagents using Acetamide and Oxychloride ($SOCl_2$ or $POCl_3$) under conventional (thermal) and non conventional [microwave irradiated (MIR), ultrasonic assisted and solvent free mortar pestle (grinding)] conditions. Reactions afforded good to excellent yields of products with both the VH reagents, reaction times were fairly less in the case of [amide/$POCl_3$] than those of [amide/$SOCl_2$] reagent. Reactions are dramatically accelerated in under sonicated and microwave irradiations with a trend: MIR (few seconds) >> Sonication (minutes) > Grinding (min) >> thermal (several hrs).

Keywords: Acetylation, Benzoylation, Vilsmeier-Haack Reagent (VHR), Acetamide, Benzamide, Micro Wave Irradiation, Grinding, Sonication

1. Introduction

Acetylation (or ethanoylation in IUPAC nomenclature) describes a reaction that introduces an acetyl functional group into a chemical compound, while benzoylation introduces a benzoyl group into an organic compound. These reactions are included in the category of the most important transformations in Organic Synthesis [1-3]. A reaction involving the replacement of the hydrogen atom of a hydroxyl group with an acetyl group (CH_3 CO) yields a specific ester, the acetate. Acetylation is one of the principal metabolic pathways of the sulfonamides. It is also one of the important synthetic bio-transformations which operate in the metabolism of drugs in which metabolites are produced that are more readily excreted than the parent drug. However, dogs are exceptional amongst the domesticated species in that acetylation does not occur in their tissues. Acetylation of the *N*-terminal alpha-amine of proteins is a widespread modification in eukaryotes. Forty to fifty percent of yeast proteins and between 80% to 90% of human proteins are modified in this manner. The pattern of modification is found to be the same throughout evolution.

Among the various protecting groups used for the hydroxyl group, acetyl is one of the most common groups, being stable in the acid reaction conditions and also eases of removal by mild alkaline hydrolysis [1,2]. The most commonly used reagent combination for this reaction uses acid anhydride in the presence of acid or base catalysts [3]. Various metal salts [4-16] such as $CoCl_2$, $TiCl_4$-$AgClO_4$, $TaCl_5$, $TaCl_5$-SiO_2, Ce(III) triflate, Sn(IV) porphyrine and some metal triflates [17-21] such as Sc $(OTf)_3$, MeSiOTf, $In(OTf)_3$, $Cu(OTf)_2$ and $Bi(OTf)_3$, bis(cyclopentadienyl) zirconium dichloride [22], I_2 [23], 1,3-dibromo-5,5-dimethylhydentoin or trichloroisocyanuric acid [24] have been investigated to meet the demand for more efficient and selective methods.

Benzoylation reaction is generally carried out using benzoyl chloride with a Lewis acid as the benzoylating agent. In addition to benzoyl chloride [1-2], a number of reagents [25-29] such as, benzoic anhydride, benzoyltetrazole, 2-benzoyl-1-methylpyridinium chloride, S-benzoic-O,O-diethylphosphoro-dithoic anhydride, benzoyl cyanide, can be used for carrying out this reaction. Though benzoyl chloride may be a health hazard due to its toxicity, nevertheless it is widely used because of its ready

availability and low cost. The reaction is usually catalyzed by bases like pyridine, triethylamine and sodium hydroxide [30-31]. Recently Satya Paul *et al.* [32] developed a rapid, economic and environmentally friendly method for benzoylation of -NH_2, -OH and -SH groups using PhCOCl-Py/basic alumina. The developed reagent system was found to a good alternative to classical method since the benzoylation underwent expeditiously with high yields under solvent-free conditions.

Vilsmeier-Haack reagent (VH) is one of the most efficient synthetic organic reagents for formylation and acetylation reactions. VH reagents could be prepared form equimolar mixture of formamide or *N*, *N*'-dialkyl formamides such as *N*, *N*'-dimethyl formamide (DMF), *N*, *N*'-diethyl formamide (DEF), along with oxy halides such as $POCl_3$ and $SOCl_2$ at freezing temperatures. Recent reports on Vilsmeier-Haack (VH) reactions revealed that organic compounds in general and hydrocarbons with excess pi-electrons in particular undergo formylation very easily on synthetic scale [33-49]. However, these reactions are known to afford acetyl derivatives when *N*, *N*'-dialkyl formamides are replaced by acetamide or *N*, *N*'-dialkyl acetamides such as *N*, *N*'-dimethyl acetamide (DMA) and *N*, *N*'-diethyl acetamide (DEA) in VH reagent. However, not many systematic reports are published in this direction. In view of this the author has embarked on a systematic synthetic study of certain VH acetylation and benzoylation reactions using (Acetamide + $SOCl_2$)/(Acetamide + $POCl_3$) or (Benzamide + $SOCl_2$)/(Benzamide + $POCl_3$) as VH regents. A set of organic compounds such as aldehydes and ketones are used in these studies, which have been found their importance in a number of industrially important and biologically important reactions.

2. Experinental Details

2.1. General Procedure for Preparation of Vilsmeier-Haack Reagent

The Vilsmeier Haack (VH) adduct is prepared afresh before use from $SOCl_2$ and acetamide (ACTAM). To a chilled (at –50˚C) actamide (ACTAM) in dichloro ethane (DCE) or acetonitrile (ACN), calculated amount of $POCl_3$ was slowly added drop wise to get VH reagent and stored under cold conditions. Similar procedure is adopted for the preparation of VH reagent with Benzamide (BNZAM).

2.2. General Procedure for Vilsmeier-Haack Synthesis in Reflux Condition

A centimolar (0.01 mol) organic substrate (aromatic aldehydes, ketones), about 0.015 moles of VH reagent and solvent DCE were taken in a cleaned in a Round bottom flask and refluxed till the reaction is completed. After completion of the reaction, as confirmed by TLC, the reaction mixture is treated with 5% sodium thio sulphate solution, followed by the addition of pet ether. The organic layer was separated, dried over Na_2SO_4 and evaporated under vacuum, purified with column chromatography using DCE: n-hexane (8:2) as eluent to get pure product. This methodology has also been successfully used for ACN mediated reactions. This methodology has been successfully is adopted for CAN mediated reactions. The yields of major products are compiled in **Tables 1** to **4**.

2.3. General Procedure for Vilsmeier-Haack Synthesis under Solvent Free Conditions by Grinding in Mortar with Pestle

A centimolar (0.01mol) organic substrate (aldehydes, ketones or acetophenone), and about 0.015 moles of VH reagent were taken in a previously cleaned mortar and grounded till the reaction is completed. After completion of the reaction, as checked by TLC, the reaction mixture is treated with 5% sodium thio sulphate solution, followed by the addition of pet ether. The organic layer was separated, dried over Na_2SO_4 and evaporated under vacuum, purified with column chromatography using DCE: n-hexane (8:2) as eluent to get pure product. The yields of major products are given in **Tables 1** to **4**.

2.4. General Procedure for Sonicated Vilsmeier-Haack Synthesis

A centimolar (0.01mol) organic substrate (aldehydes, ketones or acetophenone), about 0.015 moles of VH reagent and solvent DCE were taken in a cleaned in a Round bottom flask and clamped in a sonicator and progress of the reaction is monitored by TLC. After completion of the reaction, as ascertained by TLC, the reaction mixture is treated with 5% sodium thio sulphate solution, followed by a the same work-up procedure as mentioned the above section to get the final product. This methodology has also been successfully for ACN mediated reactions. The yields of major products are shown in **Tables 1** to **4**.

2.5. General Procedure for MW Irradiated Vilsmeier-Haack Synthesis

Methodology adopted for MW assisted VH synthesis is almost similar to that used in the above section. A centimolar (0.01 mol) organic substrate (aldehydes, ketones or acetophenone), about 0.015 moles of VH reagent and

Table 1. VH acetylation reactions with (Acetamide + $SOCl_2$) and carbonyl compounds.

Entry	Substrate	Thermal (Room temp)		Grinding (Solvent free)		Sonication		Microwave (300 watt)	
		RT (hrs)	Yield (%)	RT (min)	Yield (%)	RT (min)	Yield (%)	RT (sec)	Yield (%)
1	Benzaldehyde	13	68	120	70	90	65	200	70
2	Salicyl adehyde	13	70	140	75	90	78	200	75
3	4-OH benzaldehyde	11	80	110	83	90	79	180	80
4	4-OMe benzaldehyde	12	64	110	63	90	67	200	68
5	4-Cl benzaldehyde	11	67	100	63	90	67	200	65
6	4-Br benzaldehyde	12	7	110	69	90	63	200	77
7	4-NO_2 benzaldehyde	11	78	110	80	90	78	190	82
8	Cinamaldehyde	13	69	130	70	90	69	200	73
9	Acetophenone	12	76	110	73	90	80	190	77
10	2-OH acetophenone	11	78	110	80	90	76	190	81
11	4-OH acetophenone	11	69	110	74	90	71	200	68
12	4-Me acetophenone	10	64	140	61	90	66	200	65
13	3-OH acetophenone	11	69	110	73	90	71	200	71
14	4-Br acetophenone	13	65	110	69	90	66	200	64
15	4-NO_2 acetophenone	12	85	100	80	90	79	180	81

Table 2. VH acetylation reactions with (Acetamide + $POCl_3$) and carbonyl compounds.

Entry	Substrate	Thermal (Room temp)		Grinding (Solvent free)		Sonication		Microwave (300 watt)	
		RT (hrs)	Yield (%)	RT (min)	Yield (%)	RT (min)	Yield (%)	RT (sec)	Yield (%)
1	Benzaldehyde	11	69	120	70	90	65	200	70
2	Salicyladehyde	12	70	140	75	90	78	200	75
3	4-OH benzaldehyde	11	83	110	80	90	80	180	79
4	4-OMe benzaldehyde	12	67	110	68	90	67	200	68
5	4-Cl benzaldehyde	11	70	100	69	90	70	200	67
6	4-Br benzaldehyde	12	72	110	66	90	63	200	77
7	4-NO_2 benzaldehyde	11	79	110	82	90	78	190	82
8	Cinamaldehyde	13	70	130	71	90	73	200	68
9	Acetophenone	12	77	110	74	90	77	190	80
10	2-OH acetophenone	11	76	110	80	90	69	190	81
11	4-OH acetophenone	11	74	110	75	90	71	200	80
12	4-Me acetophenone	12	66	140	65	90	66	200	69
13	3-OH acetophenone	11	68	110	73	90	77	200	71
14	4-Br acetophenone	13	64	110	69	90	68	200	64
15	4-NO_2 acetophenone	12	80	100	84	90	79	180	85

Table 3. VH benzoylation reactions with (Benzamide + $SOCl_2$) and carbonyl compounds.

Entry	Substrate	Thermal (Room temp)		Grinding (Solvent free)		Sonication		Microwave (300 watt)	
		RT (hrs)	Yield (%)	RT (min)	(Yield) (%)	RT (min)	Yield (%)	RT (sec)	Yield (%)
1	Benzaldehyde	12	65	120	67	90	62	200	69
2	Salicyladehyde	12	70	110	75	90	76	200	72
3	4-OH benzaldehyde	11	80	110	81	90	79	190	76
4	4-OMe benzaldehyde	13	67	130	63	90	66	200	68
5	4-Cl benzaldehyde	13	63	130	67	90	65	220	62
6	4-Br benzaldehyde	12	70	130	68	90	63	200	72
7	4-NO_2 benzaldehyde	11	81	100	80	90	75	180	82
8	Cinamaldehyde	13	62	110	70	90	67	200	71
9	Acetophenone	12	74	110	76	90	80	190	79
10	2-OH acetophenone	12	80	110	78	90	81	190	76
11	4-OH acetophenone	12	71	110	74	90	69	200	72
12	4-Me acetophenone	11	64	140	61	90	66	200	65
13	3-OH acetophenone	11	69	110	73	90	71	200	68
14	4-Br acetophenone	11	68	110	65	90	63	200	64
15	4-NO_2 acetophenone	10	85	100	80	90	79	180	81

Table 4. VH benzoylation reactions with (Benzamide + $POCl_3$) and carbonyl compounds.

Entry	Substrate	Thermal (Room temp)		Grinding (Solvent free)		Sonication		Microwave (300 watt)	
		RT (hrs)	Yield (%)	RT (min)	(Yield) (%)	RT (min)	Yield (%)	RT (sec)	Yield (%)
1	Benzaldehyde	11	69	120	70	90	65	200	70
2	Salicyladehyde	12	70	140	75	90	78	200	75
3	4-OH benzaldehyde	11	83	110	80	90	80	180	79
4	4-OMe benzaldehyde	12	67	110	68	90	67	200	68
5	4-Cl benzaldehyde	11	75	100	69	90	76	200	74
6	4-Br benzaldehyde	12	76	110	67	90	65	200	77
7	4-NO_2 benzaldehyde	11	79	110	82	90	80	190	82
8	Cinamaldehyde	13	73	130	71	90	73	200	75
9	Acetophenone	12	77	110	79	90	77	190	80
10	2-OH acetophenone	11	76	110	80	90	69	190	81
11	4-OH acetophenone	11	75	110	77	90	73	200	80
12	4-Me acetophenone	12	67	140	65	90	68	200	69
13	3-OH acetophenone	11	70	110	74	90	77	200	73
14	4-Br acetophenone	13	69	110	70	90	68	200	67
15	4-NO_2 acetophenone	12	81	100	84	90	79	180	84

solvent DCE were taken in a cleaned in a Round bottom flask and clamped in a laboratory MW oven. Progress of the reaction, under micro wave irradiated conditions, is followed by TLC. After completion of the reaction, as ascertained by TLC, the reaction mixture is treated with 5% sodium thio sulphate solution, followed by a the same work-up procedure as mentioned the above section to get the final product. This methodology has also been successfully extended for ACN mediated reactions. The yields of major products are presented in **Tables 1** to **4**.

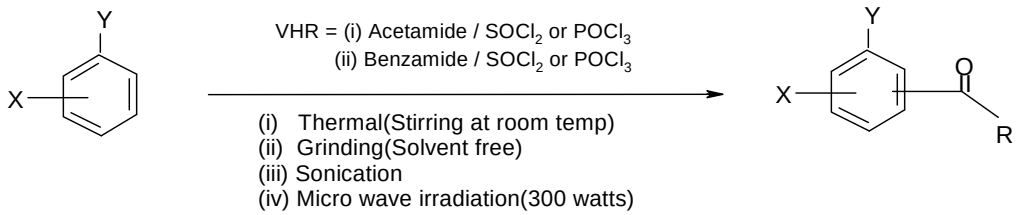
2.6. Product Analysis

TLC pure products were characterized by spectroscopic methods. The melting points were determined on Mettler FP 51 (Neo Pharma Instrument Corp.) and are not corrected. We have recorded H NMR spectra on a Jeol FX-90A instrument in chloroform-d using TMS as internal standard. The mass spectra were recorded on a VG micromass 70-70H spectrometer. The IR was recorded on a Nicolet 740 FT-IR spectrometer. The UV was recorded on Shimadzu-240 UV-Visible spectrophotometer. Spectroscopic data for certain representative isolated products compiled **Tables 5** and **6**.

3. Results and Discussion

Aromatic compounds such as Benzaldehyde and Acetophenone derivatives underwent acetylation under Vilsmeier-Haack conditions in fairly good to very good yields when treated with [Acetamide/$SOCl_2$] and [Acetamide/$POCl_3$] respectively under conventional and non-conventional conditions. However, to check the generality of the reaction an array of substituted aromatic aldehydes and ketones are used as substrates under present reaction conditions as shown in **Scheme 1**. The yields of major products are compiled in **Tables 1** to **4**. The products were characterized by ^{1}H-NMR, Mass spectra with authentic samples and found to be satisfactory. It is of interest to note that orthohydroxy acetophenone (OHAP) underwent cyclization followed by acetylation and afforded acetyl chromone as described in earlier workers. However, Meta (MHAP) and para hydroxy acetophenones (PHAP) did not undergo cyclization but afforded acetyl derivatives. The difference in the reactivity of OHAP from MHAP and PHAP could be attributed to the fact that the -OH group is away from the carbonyl (main) functional group which is favorable to form a stable ring through cyclization.

Data for VH synthesis of acetylation/benzoylation reactions are presented in tables 1 to 4 and **Figures 1** and **2**, which clearly indicate remarkable rate enhancements and increase in reaction yields from thermal reactions to microwave assisted reactions with an increasing trend: MIR >> Sonication >> Grinding (mortar-pestle) > thermal. Reactions are too sluggish under times in thermal conditions even at elevated temperatures. The reaction times are in the range of 10 to 12 hours. However, the reactions are completed only in 100 - 120 min under solvent free conditions suggesting that the present method could be employed for small scale. Progress of the reaction under solvent free conditions might be due to the heat energy generated from the mechanical energy when the reactionmixture is grounded in the mortar. The yields are highly superior over corresponding solution phase reactions. Since the reaction time of solvent free reaction is at least six times less than corresponding solution phase reaction and avoids the use of toxic solvents, this methodology could be considered as a green chemistry oriented synthesis of VH reactions. Rate enhancements in the case of grinding reactions could be probably attributed to the faster activation of molecules due to the direction friction followed by conversion of mechanical energy into heat energy. In the case of sonicated reactions reaction times are further reduced to 90 minutes. The rate accelerations under sonicated could be explained by the cavitation phenomenon. Activation of molecules is done by the *in situ* energy released due to the rupture of cavitation bubbles generated by ultrasonic waves. It is also of interest to note that the reactions times are reduced from several minutes to only few seconds under microwave irradiation (MIR). The extremely faster reaction rates in MIR system could be due to the bulk activation of molecules rather than random activation.



Where R = CH_3 when VHR = (Acetamide + $SOCl_2$) or (Acetamide + $POCl_3$); R = C_6H_5 when VHR = (Benzamide + $SOCl_2$) or (Benzamide + $POCl_3$); Y= CHO, $COCH_3$; X = electron donating or electron withdrawing groups.

Scheme 1. Acetylation and benzoylation of benzaldehydes and acetophenones under Vilsmeier Haack conditions.

Table 5. Spectroscopic data for VH acetylation of aromatic carbonyl compounds.

Entry	Substrate	Product	Spectroscopic data	
			m/z	^{1}H NMR
1	Benzaldehyde	3-Acetyl Benzaldehyde	148	δ 2.65 (s 3H, CH_3); δ 7.66 (m 1H, Ar); δ 8.2 (d 2H, Ar) δ 8.5 (s 1H, Ar); δ 9.9 (s 1H, Ar-CHO)
2	Salicyladehyde	3-Acetyl Salicyladehyde	164	δ 2.65 (s 3H, CH_3);δ 7.2 (m 1H, Ar);δ 7.6 (d 1H, Ar) δ 7.9 (d 1H, Ar);δ 10.3 (s 1H, Ar-CHO);δ 11.05 (s 1H, Ar-OH)
3	4-OH benzaldehyde	3-Acetyl 4-OH benzaldehyde	164	δ 2.65 (s 3H, CH_3); δ 7.1 (d 1H, Ar); δ 7.95 (d 1H, Ar) δ 8.3 (s 1H, Ar); δ 9.5 (s 1H, Ar-CHO); δ 10.5 (s 1H, Ar-OH)
4	4-OMe benzaldehyde	3-Acetyl 4-OMe benzaldehyde	178	δ 2.65 (s 3H, CH_3); δ 3.93 (s 3H, Ar-OCH_3); δ 7.15 (d 1H, Ar) δ 8.0 (d 1H, Ar); δ 8.4 (s 1H, Ar); δ 10.05 (s 1H, Ar-CHO)
5	4-Cl benzaldehyde	3-Acetyl 4-Cl benzaldehyde	182	δ 2.65 (s 3H, CH_3); δ 7.65 (d 1H, Ar); δ 8.05 (d 1H, Ar) δ 8.4 (s 1H, Ar); δ 9.95 (s 1H, Ar-CHO)
6	4-Br benzaldehyde	3-Acetyl 4-Br benzaldehyde	226	δ 2.63 (s 3H, CH_3); δ 7.78 (d 1H, Ar); δ 7.95(d 1H, Ar) δ 8.5 (s 1H, Ar); δ 10.0 (s 1H, Ar-CHO)
7	4-NO_2 benzaldehyde	3-Acetyl 4-NO_2 benzaldehyde	193	δ 2.66 (s 3H, CH_3); δ 8.35 (d 1H, Ar); δ 8.55 (d 1H, Ar) δ 8.75 (s 1H, Ar); δ 9.95 (s 1H, Ar-CHO)
8	Cinnamaldehyde	3-Acetyl Cinnamaldehyde	174	δ 2.65 (s 3H, CH_3); δ 6.75 (d 1H, =CH); δ 7.0 (m 1H, Ar) δ 7.53 (d 1H, Ar); δ 7.68 (s 1H, Ar-CH=); δ 7.85 (d 1H, Ar) δ 8.05 (s 1H, Ar); δ 9.9 (s 1H, Ar-CHO)
9	Acetophenone	3-Acetyl Acetophenone	162	δ 2.8 (s 6H, CH_3); δ 6.7 (m 1H, Ar); δ 8.2 (d 2H, Ar) δ 8.6 (s 1H, Ar)
10	2- OH acetophenone	3-Acetyl Chromone	187	δ 2.6 (s 3H, CH_3); δ 6.65 (d 2H, Ar); δ 7.4 (m 2H, Ar) δ 8.2 (s 1H, Ar)
11	4-OH acetophenone	3-Acetyl 4-OH acetophenone	178	δ 2.8 (s 6H, CH_3); δ 7.0 (d 1H, Ar); δ 8.0 (d 1H, Ar) δ 8.6 (d 1H, Ar) ;δ 11.4 (d 1H, Ar-OH)
12	4-Me acetophenone	3-Acetyl 4-Me acetophenone	176	δ 2.8 (s 6H, CH_3); δ 5.3 (s 3H, Ar-CH_3); δ 7.05 (d 1H, Ar) δ 7.53 (d 1H, Ar); δ 7.75 (s 1H, Ar)
13	3-OH acetophenone	3-Acetyl 3-OH acetophenone	178	δ 2.8 (s 3H, CH_3); δ 7.45 (s 1H, Ar); δ 7.6 - 7.8 (m 5H, Ar) δ 7.95 (s 2H, Ar); δ 10.05 (s 1H, Ar)
14	4-Br acetophenone	3-Acetyl 4-Br acetophenone	240	δ 2.8 (s 6H, CH_3); δ 7.4 (d 1H, Ar); δ 8.05 (d 1H, Ar) δ 8.7 (d 1H, Ar)
15	4-NO_2 acetophenone	3-Acetyl 4-NO_2 acetophenone	207	δ 2.8 (s 6H, CH_3); δ 7.5 (d 1H, Ar); δ 8.1 (d 1H, Ar) δ 8.8 (d 1H, Ar)

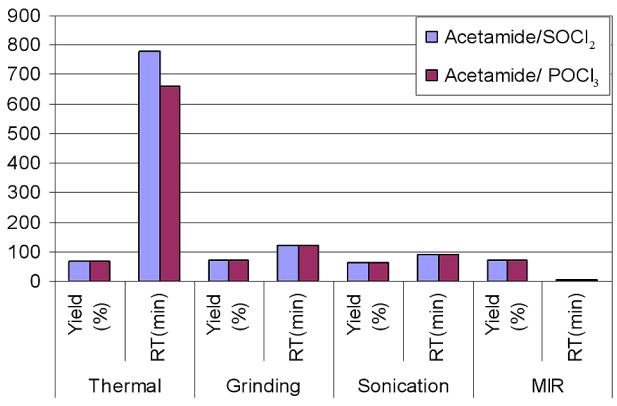


Figure 1. VH acetylation of benzaldehyde under thermal and non-conventional conditions.

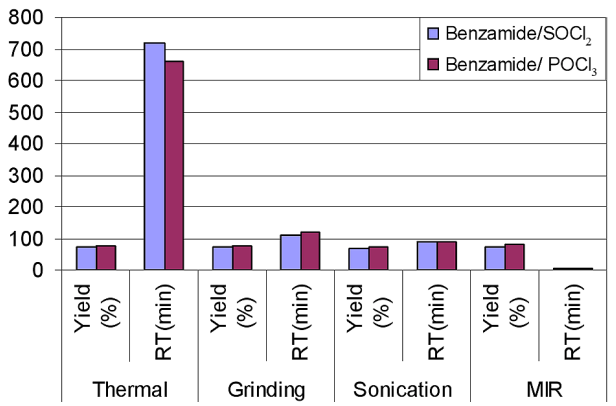


Figure 2. VH benzoylation of 4-OHAP under thermal and non-conventional conditions.

Table 6. Spectroscopic data for VH benzoylation of aromatic carbonyl compounds.

Entry	Substrate	Product	Spectral data	
			m/z	^{1}H NMR
1	Benzaldehyde	3-Benzoyl Benzaldehyde	210	δ 7.35 (m 4H, Ar); δ 7.65 (d 2H, Ar); δ 8.0 (d 2H, Ar) δ 8.37 (s 1H, Ar); δ 10.05 (s 1H, Ar-CHO)
2	Salicyladehyde	3-Benzoyl Salicyladehyde	258	δ 7.35-7.92 (m 8H, Ar); δ 10.1 (s 1H CHO); δ 10.7 (s 1H, Ar-OH)
3	4-OH benzaldehyde	3-Benzoyl 4-OH benzaldehyde	258	δ 7.3 (m 4H, Ar); δ 7.6 (d 1H, Ar); δ 8.0 (d 2H, Ar) δ 8.3 (s 1H, Ar); δ 9.95 (s 1H, Ar-CHO); δ 10.95 (s 2H, Ar-OH)
4	4-OMe benzaldehyde	3-Benzoyl 4-OMe benzaldehyde	240	δ 3.7 (s 3H, OCH_3); δ 7.4 (m 4H, , Ar); δ 7.75 (d 1H, Ar) δ 7.9 (d 2H, Ar); δ 7.75 (d 1H, Ar); δ 7.9 (d 2H, Ar) δ 8.2 (d 1H, Ar); δ 10.05 (s 1H, Ar-CHO)
5	4-Cl benzaldehyde	3-Benzoyl 4-Cl benzaldehyde	244	δ 7.4 (m 4H, Ar); δ 7.7 (d 1H, Ar); δ 8.3 (d 2H, Ar) δ 8.45 (s 1H, Ar); δ 10.0 (s 1H, Ar-CHO)
6	4-Br benzaldehyde	3-Benzoyl 4-Br benzaldehyde	288	δ 7.4 (m 4H, Ar); δ 7.7 (d 1H, Ar); δ 8.0 (d 2H, Ar) δ 8.2 (d 1H, Ar); δ 9.8 (s 1H, Ar-CHO)
7	4-NO_2 benzaldehyde	3-Benzoyl 4-NO_2 benzaldehyde	255	δ 7.35 (m, 4H Ar); δ 7.65 (d ,1H, Ar); δ 8.05 (d, 2H, Ar) δ 8.35 (s 1H, Ar); δ 9.95 (s 1H, Ar-CHO)
8	Cinnamaldehyde	3-Benzoyl Cinnamaldehyde	235	δ 6.75 (d ,1H, =CH); δ 7.4 (m, 1H, Ar); δ 7.45 (d 1H, Ar) δ 7.5-7.8 (m 7H, Ar); δ 8.05 (d 1H, =CH); δ 9.9 (s 1H, Ar)
9	Acetophenone	3-Benzoyl Acetophenone	224	δ 2.8 (s 3H, CH_3); δ 7.8 (m 5H, Ar); δ 7.6 (m 1H, Ar) δ 7.95 (d 2H, Ar); δ 8.45 (s 1H, Ar)
10	2-OH acetophenone	3-Benzoyl Chromone	250	δ 6.34 (s 1H, Ar); δ 7.4 (m 6H, Ar); δ 7.65 (d 2H, Ar) δ 7. 9 (d 1H, Ar)
11	4-OH acetophenone	3-Benzoyl 4-OH acetophenone	240	δ 2.9 (s 3H, CH_3); δ 7.3 (m 3H, Ar); δ 7.6 (d 2H, Ar) δ 8.45 (m 2H, Ar); δ 8.8 (s 1H, Ar);δ 10.9 (s 1H, Ar-OH)
12	4-Me acetophenone	3-Benzoyl 4-Me acetophenone	238	δ 2.45 (s 3H, CH_3); δ 2.85 (s 3H, CH_3-C=O); δ 7.5 (m 3H, Ar) δ 7.7 (d 2H, Ar); δ 8.5 (m 2H, Ar); δ 8.9 (s 1H, Ar)
13	3-OH acetophenone	3-Benzoyl 3-OH acetophenone	240	δ 2.8 (s 3H, CH_3); δ 7.45 (s 1H, Ar); δ 7.6 - 7.8 (m 5H, Ar) δ 7.95 (s 2H, Ar); δ 10.05 (s 1H, Ar)
14	4-Br acetophenone	3-Benzoyl 4-Br acetophenone	302	δ 2.65 (s 3H, CH_3); δ 7.4 (m 3H, Ar); δ 7.7 (d 2H, Ar) δ 8.5 (m 2H, Ar); δ 8.7 (s 1H, Ar)
15	4-NO_2 acetophenone	3-Benzoyl -NO_2 acetophenone	269	δ 2.9 (s 3H, CH_3); δ 7.3 (m 3H, Ar); δ 7.6 (d 2H, Ar) δ 8.45 (m 2H, Ar); δ 8.8 (s 1H, Ar)

4. Conclusions

In conclusion Vilsmeier-Haack Reagents [Acetamide and Oxychloride ($SOCl_2$ or $POCl_3$)] with aromatic aldehydes, ketones afforded acetyl derivatives under conventional (thermal) and non conventional [microwave irradiated (MIR), ultrasonic assisted and solvent free mortar pestle (grinding)] conditions with a trend: MIR (few seconds) >> Sonication (minutes) > Grinding (min) >> thermal (several hrs). Even though both the VH reagents afforded good to excellent yields of products reaction times were fairly less in the case of [Acetamide/$POCl_3$] than those of [Acetamide/$SOCl_2$] reagent.

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