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Solid supports in the synthesis of few vinyl quinolones

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ABSTRACT

The present investigation involves use of microwave technology aided by solid supports-alumina, montmorillonite clay, bentonite, silica gel , dowex and amberlite for the synthesis of few 4-substituted-3-vinyl quinolines and 4-substituted-3-vinyl quinoline-2(1H)-thiones, The results of the microwave reactions aided by solid supports indicate significant increase in the yield of product and reduction in the time of synthesis compared to classic conditions and in microwave reactions without solid supports. Neutral alumina and K10 clay were found to be more efficient in the synthesis of chloro -4- alkyl -3-vinyl quinolines and 4- alkyl -3-vinyl quinoline-2(1H)-thiones. The used solid-supports can be easily separated from the reaction mixture and recycled.

Keywords: microwave, quinolines, silica, Amberlite, K10 clay, Bentonite, Dowex.

INTRODUCTION

Organic reactions on solid supports [1-5] and those assisted by microwaves [6-9] especially under solvent –free condition have attracted ease of manipulation. Since only the polar reactants adsorbed on the surface of the solid support absorb microwaves, a variety of reagents supported on such surfaces can be utilized for the enhancement of organic reactions using an unmodified microwave oven. During microwave induction of reactions under dry conditions, the reactants adsorbed on the surface of alumina, silica gel, clay and others absorb the microwaves whereas the support does not, nor does it restrict the transmission of microwaves. Consequently, such supported reagents efficiently induce reactions under safe and simple conditions with domestic microwave ovens instead of specialized expensive commercial microwave systems.

The strategy of microwave activated synthesis on solid inorganic supports [10-11] seems to be the most efficient technology. Acidic and basic solid mineral oxides such as silica gel, alumina etc., act both as catalysts and supports [12].

The present investigation was thus undertaken with the confident expectation that microwave technology aided by solid supports-alumina, montmorillonite clay, bentonite, silica gel , dowex and amberlite could be conveniently exploited for the production of 2-chloro-4-methyl-3-vinyl quinolines,2-chloro-4- phenyl-3-vinyl quinolines, 2,6-dichloro-4-phenyl -3-vinyl quinolines, 6-nitro-2-chloro-4-phenyl-3-vinyl quinolines,4-methyl-3-vinyl quinoline-2(1H)-thiones, 6-chloro-4- phenyl -3-vinyl quinoline-2(1H)-thiones and 4- phenyl -3-vinyl quinoline-2(1H)-thiones.

EXPERIMENTAL SECTION

General

Melting points were determined in open-end capillaries using a Joshibha Model melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer Spectrometer model 599 and the absorption frequencies are quoted in cm^{-1}. The progress of the reaction and purity of all prepared compounds were followed by TLC with developing solvents- chloroform, benzene/ ethyl acetate and benzene / petroleum ether and visualizing spots under UV lamp and in iodine vapour. Thin layer chromatography was performed using glass plates (20x5cm) coated with SD Fine silica gel – G (incorporating calcium sulphate (13%) as binder). Purification of crude products was carried out using chromatographic columns packed with SD Fine aluminium oxide (neutral). All microwave reactions were carried out in domestic microwave ovens - IFB model 179 MIS of output power 750W

Preparation of 4-alkyl -3- vinyl quinoline-2(1H) ones

The ortho amino carbonyl compounds prepared were:

(i) 2- Aminoacetophenone **[13-14]**
(ii) 2-Aminobenzophenone **[15]**
(iii) 2-Amino-5-chlorobenzophenone **[16]**
(iv) 2-Amino-5-nitrobenzophenone was purchased from Messrs.Aldrich and used as such

The above compounds were utilized for the preparation of the corresponding 3- vinyl quinoline-2(1H) ones [17].

The actual quantities of the reagents and solvent employed are:

Reagents **Product**	**4-Methyl -3- vinyl quinoline-2(1H) one**	**4- Phenyl -3- vinyl quinoline-2(1H) one**	**6-Chloro -4- phenyl -3- vinyl quinoline-2(1H) one**	**6-Nitro -4- phenyl -3- vinyl quinoline-2(1H) one**
	2-Amino acetophenone: 12g	2-Amino benzophenone:4g	2-Amino-5-chloro benzophenone:4.1g	2-Amino-5-nitro benzophenone:3.5g
3-Butenoyl chloride (g)	9.2	2.3	1.9	2.1
Pyridine (g)	10	1.8	1.5	2
Benzene (ml)	250	60	75	60
Chloroform (ml)	50	50	50	50
KOH(g)	10	1	4	3
Ethanol (ml)	100	40	40	30

Microwave Reactions Aided by Solid Support

Solid support aided preparation of 2-chloro-3-vinyl quinolines

The vinyl quinolone was microwaved at 350W after impregnating it onto the solid support. To it phosphorous oxychloride was added just to wet the reaction mixture. The completion of reaction was monitored by thin layer chromatography after which the reaction mixture was cooled, added ice and macerated to get a solid. The solid was then extracted with chloroform and solvent dried to get the product 2-chloro-3-vinyl quinoline which was then recrystallized from benzene-petroleum ether. The recovered solid support can be reused after purification and activation.

Reagent/product	**2-Chloro-4-methyl-3-vinyl quinoline**	**2-Chloro-4-phenyl -3-vinyl quinoline**	**2,6-dichloro-4- phenyl-3-vinyl quinoline**	**6-Nitro-2-chloro-4-phenyl-3-vinyl quinoline**
4-substituted-3-vinyl quinoline-2(1H)-one(mg)	100	100	100	100
$POCl_3$ (ml)	0.3	0.4	0.5	0.5
*Solid support (mg)	10			

Solid support aided preparation of 3-vinyl quinoline-2(1H)-thiones

A mixture of chloroquinoline (0.005mole), thiourea (0.007mole) and anhydrous ethanol (just to wet the reaction mixture) was microwaved after impregnating it on to the solid support. The completion of reaction was monitored by thin layer chromatography after which the reaction mixture was cooled, added ice and macerated to get a solid. The thiouronium salt that precipitated was collected and washed with little ethanol and then digested with 10% aqueous sodium hydroxide on a steam bath for 30min.The thione was recovered from the alkaline extract by acidification, as yellow powder. The actual quantities of the reagent and the solvent employed are:

Reagent/product	**4- Methyl -3-vinyl quinoline-2(1H)-thiones**	**4- Phenyl-3-vinyl quinoline-2(1H)-thiones**	**6-Chloro-4-phenyl -3-vinyl quinoline-2(1H)-thiones**	**6-Nitro-4-phenyl-3-vinyl quinoline-2(1H)-thiones**
Corresponding vinly quinolines (mg)	100	130	100	100
Thiourea (mg)	50	60	60	65
Absolute ethanol(ml)	0.7	0.7	0.8	1
*Solid support (mg)	10			

Characterization of the compounds

The synthesized compounds were identified by thin layer chromatographic technique, comparison with authentic samples, literature melting points and by recording IR spectra.

RESULTS AND DISCUSSION

More accessible, convenient and efficient inorganic solid supports – silica gel, bentonite, neutral alumina, dowex, amberlite and montmorillonite were chosen. The organic compounds that are adsorbed on the surface of inorganic oxides do not absorb or restrict the transmission of microwaves. The results of the microwave reactions aided by solid supports are given in **tables 1 and 2**.

Table 1 Microwave synthesis aided by solid supports

Entry	**Product formed**	**Solid support**	**Yield (%)**	**Time of reaction (min) for product**	
				formation	**completion**
I	2-chloro-4- methyl -3-vinyl quinoline	Silica gel	90	1	3
		Bentonite	91	1	3
		Neutral alumina	95	1	3
		Dowex	85	1	5
		Amberlite	87	1/2	5
		Montmorillonite (K 10 clay)	81	1	4

II	2-chloro-4- phenyl -3-vinyl quinoline	Silica gel	83	9	15
		Bentonite	89	5	9
		Neutral alumina	91	2	10
		Dowex	89	5	11
		Amberlite	90	4	41/2
		Montmorillonite (K 10 clay)	90	2	8
III	2,6- dichloro -4- phenyl -3-vinyl quinoline	Silica gel	91	2	5
		Bentonite	92	2	5
		Neutral alumina	95	1	41/2
		Dowex	93	2	5
		Amberlite	94	1	5
		Montmorillonite (K 10 clay)	95	1	41/2
IV	6- nitro -2-chloro -4- phenyl -3-vinyl quinoline	Silica gel	84	5	9
		Bentonite	85	5	8
		Neutral alumina	88	3	8
		Dowex	83	5	8
		Amberlite	84	5	8
		Montmorillonite (K 10 clay)	84	3	9

Table 2 Microwave synthesis aided by solid supports

Entry	**Product formed**	**Solid support**	**Yield (%)**	**Time of the reaction (min) for product**	
				formation	**completion**
I	4- methyl -3-vinyl quinoline-2(1H)-thione	Silica gel	88	1 1/2	4
		Bentonite	88	2	4
		Neutral alumina	90	2	41/2
		Dowex	89	2	4
		Amberlite	89	2	5
		Montmorillonite (K 10 clay)	90	2	5
II	4- phenyl -3-vinyl quinoline-2(1H)-thione	Silica gel	85	2	5
		Bentonite	85	2	4
		Neutral alumina	88	1	4
		Dowex	86	2	5
		Amberlite	85	1	5
		Montmorillonite (K 10 clay)	86	1	4
III	6-chloro-4- phenyl -3-vinyl quinoline-2(1H)-thione	Silica gel	95	3	5
		Bentonite	95	3	5
		Neutral alumina	97	2	4
		Dowex	95	3	5
		Amberlite	96	2	5
		Montmorillonite (K 10 clay)	96	2	4
IV	6-nitro-4- phenyl -3-vinyl quinoline-2(1H)-thione	Silica gel	87		8
		Bentonite	87		8
		Neutral alumina	90		7
		Dowex	88		7
		Amberlite	89		7
		Montmorillonite (K 10 clay)	89		6

The melting point and IR spectral values of the synthesized compounds are given in **tables 3 and 4** respectively.

Table 3: Melting points of compounds

Entry	Product	Melting point (°C)
1	4-methyl -3- vinyl quinoline-2(1H) one	204-205
2	4- phenyl -3- vinyl quinoline-2(1H) one	230
3	6-chloro-4- phenyl-3-vinyl quinoline-2(1H) one	237-240
4	6-nitro -4- phenyl -3- vinyl quinoline-2(1H) one	195
5	2-chloro-4- methyl -3-vinyl quinolines	68-69
6	2–chloro– 4 –phenyl-3 vinyl quinoline	78 – 79
7	2,6 -dichloro-4- phenyl -3-vinyl quinoline	116-117
8	6-nitro-2-chloro-4-phenyl -3-vinyl quinoline	180-185
9	4- methyl -3-vinyl quinoline-2(1H)-thione	168-172
10	4–phenyl–3 vinyl quinoline–2(IH)–thione	189 – 190
11	6-chloro-4- phenyl -3-vinyl quinoline-2(1H)-thione	150-151
12	6-nitro-4- phenyl -3-vinyl quinoline-2(1H)-thione	190-196

Table 4: IR spectral values

Product	Spectral values υ max (cm^{-1})
4-methyl-3-vinyl quinoline-2(1H)-one	1625, 935 and 920 (vinyl)
4-phenyl-3-vinyl quinoline-2(1H)-one	1620, 930 and 910 (vinyl)
6-chloro-4-phenyl-3-vinyl quinoline-2(1H)- one	1635, 995 and 930 (vinyl)
6-nitro-4-phenyl-3-vinyl quinoline-2(1H)- one	1650,1020 and 940 (vinyl)
2-chloro-4-methyl-3-vinyl quinoline	1620,1550, 990,920- (vinyl)
2-chloro-4-phenyl-3 vinyl quinoline	1540, 990, 935(vinyl)
2,6-dichloro-4- phenyl -3-vinyl quinoline	1610,1560, (thio carbonyl) 1030,940- (vinyl)
6-nitro-2-chloro-4-phenyl -3-vinyl quinoline	1640,1580, due to thio carbonyl absorption;1050,945(vinyl)
4-methyl-3-vinyl quinoline-2(1H)-thione	1180 thiocarbonyl,990,935-(vinyl)
4-phenyl-3 vinyl quinoline-2(IH)-thione	1190 cm^{-1} due to thio carbonyl absorption 985 and 930 cm^{-1} (vinyl)
6-chloro-4-phenyl-3-vinyl quinoline-2(1H)-thione	1180,1030,925- (vinyl)
6-nitro-4-phenyl-3-vinyl quinoline-2(1H)-thione	1190,1050,945- (vinyl)

The compounds were characterized from CO-IR with authentic samples. The results indicate the significant increase in the yield of product and reduction in the time of synthesis compared to classic conditions [18]and in microwave reactions without solid supports [15]. In the synthesis of chloro-4-alkyl-3-vinyl quinolines and 4-alkyl-3-vinyl quinoline-2(1H)-thiones, neutral alumina and K10 clay were found to be more efficient.

Alumina provides excellent properties as a support like ease of diffusion of reactant in the pore structure and a large available specific surface. The good reaction conditions with alumina may be attributed to the acidic nature of alumina. Montmorillonite K-10 is a K- catalyst derived from the aluminium hydro silicate mineral montmorillonite. The K- catalysts are acidic, lamellar materials which function as efficient and highly selective acid catalysts in various types of reactions, The enhanced yields and reduction in time with K10 clay may be due the bulky organic alkyl ammonium ion which carries out ion exchange reactions with inorganic exchangeable cations between the clay unit layers, leading to the increase of the distance between the clay layers[19]. Due to the interlayer microenvironment clays are effective heterogenous catalysts for a wide variety of organic reactions [20-21]. The microenvironment of montmorillonite K10 clay and its various cation-exchanged forms, would have promoted the formation of products in the present work.

In general we could suggest the explanations for the improvement achieved with microwave with and without solid supports, both on product yields and reduction in the time of synthesis. The more polar charged intermediate could have strong microwave absorption with a consequent rise of temperature which accelerates the formation of the products and also avoids the reversibility of the process. These observations demonstrate that our method is an expeditious, facile and environmentally benign one. The used solid-supports can be easily separated from the reaction mixture and recycled. Additionally the use of inexpensive clay and its recyclability renders this an economical and eco-friendly procedure.

Characterization of Compounds

The synthesized compounds were identified by thin layer chromatographic technique, comparison with authentic samples,literature melting point and by recording IR spectra. Fluorescence analysis of the compounds showed that 4-phenyl-3-vinylquinoline-2(1H)-one showed an intense blue fluorescence at the base, 2-chloro-4-phenyl-3-vinyl quinoline showed as a round spot near the solvent front and 4-phenyl-3-vinyl quinoline-2(1H)- thiones appeared as a visible yellow spot with pale orange fluorescence at medium R_f.

CONCLUSION

The results of the microwave reactions aided by solid supports indicate significant increase in the yield of product and reduction in the time of synthesis compared to classic conditions and in microwave reactions without solid supports. In the synthesis of chloro -4- alkyl -3-vinyl quinolines and 4- alkyl -3-vinyl quinoline-2(1H)-thiones neutral alumina and K10 clay were found to be more efficient. The used solid-supports can be easily separated from the reaction mixture and recycled. Additionally the use of inexpensive clay and the recyclability of the solid supports render this an economical and eco-friendly procedure.

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