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Microwave-Assisted Synthesis of Phthalein Dyes

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Abstract

Some phthalein dyes have been synthesized by the condensation of phthalic anhydride with various phenols through a novel route of microwave irradiation technique under solvent free condition in high yields within minutes. The inexpensive, solvent free and fast reaction conditions are the important features of this procedure.

Introduction

Phthaleins are an important class of organic compounds which have many applications, such as analytical reagents viz. pH indicators in chemistry and colorants i.e. dye dilution methods to determine kidney or liver function. A large number of phenolphthalein derivatives exhibit cathartic activity and some have been used in pharmaceutical preparations[1]. Many methods are described in literature for the synthesis of phthaleins or xanthenes dyes. Simple fusion of both components[2] and sometimes combined with azeotropic removal of water[3] or fusion in the presence of catalysts[4] such as $POCl_3$, PPA, $POCl_3$-$HClO_4$, $ZnCl_2$ and methane sulphonic acid. The inherent drawbacks of all described synthetic methods are long heating time (upto 10-15hrs) and at defined temperature in the presence of acidic catalyst necessary for high yield reactions. However, the synthesis of these phthaleins through conventional method are facilitated by long heating in the presence of solvent with low yield has received special attention[5] to develop more facile and rapid procedure for the synthesis of phthaleins of various phenols.

In recent years microwave heating has gained popularity in organic synthesis. Microwave irradiation is a non-conventional energy source which generates rapid intense heating of polar substances with consequent significant reductions in reaction time from hours to minutes, and give cleaner reactions that are easier to work up, and in many cases increases the yields than those from conventional heating methods[6]. Here we describe the application of solvent- free microwave methodology to the synthesis of phthaleins of various phenols.

Results and Discussion:

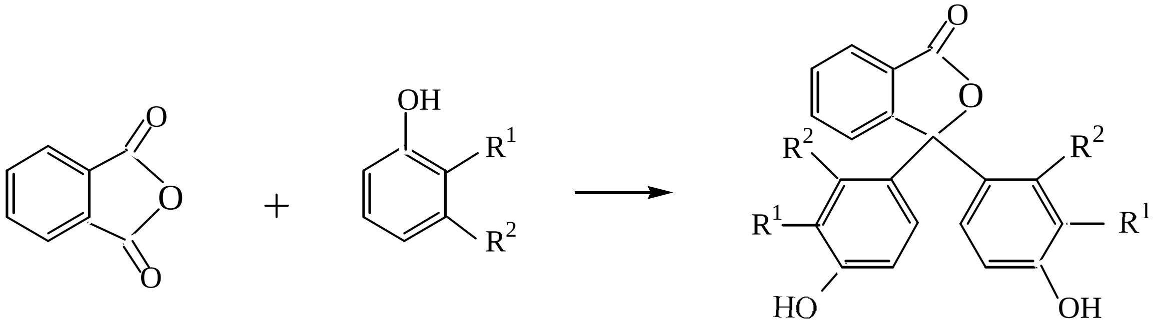
A mixture of phthalic anhydride (1) and phenols (2) with conc. H_2SO_4 catalyst was irradiated in microwave oven for a specific time (Scheme 1). After usual work up it offered the pure compound (3). Synthesis of phthalein dyes using conc. H_2SO_4 catalysts under microwave irradiations is rapid. The reaction takes place in a single step. In this step condensation reaction takes place which results the formation of the product. Phthaleins themselves are believed to prefer the lactone form. Accordingly, the high conversion is attainable only if the free acid formed during the reaction is immediately transformed to the starting phthalic anhydride and water. This reaction takes place only at temperature above 120^0C, which is too high for less stable dyes. Most of the reaction was completed within 2-4 minutes giving 60-85% yield of products (Table 1). The suggested method is more suitable due to the shorter reaction time with better yield and easy work up too. The best result was obtained with 1-2 drop of conc. H_2SO_4 catalysts. High amount of the catalyst does not improve the yield of products. Conc. H_2SO_4 exhibited superior catalytic activity as compare to the other catalysts such as anhy. $AlCl_3$, anhy. $ZnCl_2$ in terms of better yield and easy disposal. Furthermore, the anhy. $ZnCl_2$ catalyst is least preferred by the industry because of environmental pollution, safety and corrosion problems. However, the reaction did not proceed in the absence of any catalyst. The reactants phthalic anhydride and phenol (1:2), the ratio is stiochiometric due to this the purification of the reaction mixture is simple as the separation of excess phenol by time-consuming steam distillation can be avoided.

Some of the known compounds (1a-f) have been reported by conventional method. Here we have repeated their preparation under microwave irradiation. The results obtained are summarised in Table 1.

Table 1: Yield and time of compounds 3a-f

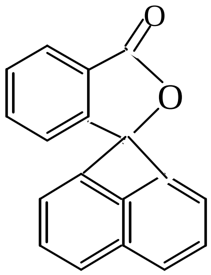
Compound	%Yield			Time	M.P.	Colour of Dye in NaOH Solution
	Catalyst			(Min.)	(^{0}C)	
	Conc. H_2SO_4	Anhy. $ZnCl_2$	Anhy. $AlCl_3$			
3a	84	65	62	2	256-258	Pink
3b	72	60	52	2	223-225	Red
3c	67	57	49	4	198-200	Bluish purple
3d	80	61	57	4	210-212	Blue (alizarin)
3e	74	60	48	2	238-240	Prussian blue
3f	81	66	54	3	196-197	Faint green

*IR[7]: 3200-3450(ν OH), 1740-1780 (ν C=O), 1590, 1500, 1470



1 2 3

3a.. $R^1 = R^2 = H$
3b.. $R^1 = CH_3$, $R^2 = H$
3c. $R^1 = H$, $R^2 = CH_3$
3d.. $R^1 = OH$, $R^2 = H$
3e. R^1, R^2 = Benzo



3f ; 2g = β-Naphthol

Scheme 1: Synthesis of phthalein dyes in Microwave

Conclusion:

It may be concluded that microwave synthesis of the phthalein dyes is the method of choice, especially for thermostable compounds. This reaction condition provides an efficient method for the rapid access of medicinally important class of organic compounds and can be used as an alternative to the existing procedure.

Experimental

IR spectra were recorded as neat samples on a Perkin-Elmer Spectrum 100 FT-IR spectrophotometer. The microwave irradiated reactions (MWI) were made in a domestic microwave oven (LG, 900W at 2450 MHz). Analytical thin layer chromatography was performed using E. Merck silica gel G. Visualization was accomplished with UV light as well as iodine vapour.

Synthesis of phthalein dyes (3a-f) of various phenols:

Phthalic anhydride was intimately mixed with various phenols in (1:2) molar proportion. The reaction mixture was irradiated in a microwave oven at 360W for 2-4 minutes in the presence of various catalyst mainly, conc. H_2SO_4, anhy. $AlCl_3$, anhy. $ZnCl_2$. The completion of the reaction was monitored by TLC on silica gel using toluene-ethyl acetate as a solvent system. The reaction mixture was allowed to attain room temperature. The product thus obtained was washed thoroughly with water to remove excess of the phenols. The condensation product was then dissolved in (10%) aq. NaOH and filtered. Phthalein dyes (3a-f) were precipitated from the filtrate by gradual addition of dilute HCl with stirring. Pure phthaleins were obtained by recrystallisation from ethanol.

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