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Short Communication

Microwave-induced acetylation of 2-methyl-5-hydroxy-1,4-naphthoquinone (plumbagin)

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Abstract: A rapid route for acetylation of 2-methyl-5-hydroxy-1,4-naphthoquinone (plumbagin) using acetic anhydride and iodine under irradiation in a modified commercial domestic microwave is reported. The acetate was obtained in high yield after a short reaction time compared to conventional method and ultrasonic method.

Key words: microwave reaction, plumbagin, acetylation, plumbagin acetate

Introduction

Quinones, notably anthraquinones and naphthoquinones, occur widely in natural products and are of considerable interest due to their varied biological properties, e.g. as an antimalarial [1-2], anticancer [3-6] and antimicrobial [2,7]. Moreover, they are also useful as dyes and pigments [8].

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Plumbagin (2-Methyl-5-hydroxy-1,4-naphthoquinone) is well distributed among the *Plumbago* spp. This compound has been described in the literature and is known to possess various pharmaceutical activities [7, 9-11].

The protection of the phenols as their acetates is a commonly-used transformation in organic synthesis as the acetate group is easily installed and removed [12]. Acetylation of the hydroxyl group of plumbagin is usually required for its synthetic utility. It has been shown that iodine is an effective catalyst in the activation of acetic anhydride for promoting the acetylation reaction [13]. Recently, acetylation of deactivated and hindered phenols using microwave irradiation coupled with the use of iodine as catalyst was reported by Deak et al. [14]. The resulting substantial reduction of reaction time and appreciably increased yields obtained by these researchers prompted us to investigate the acetylation of plumbagin by a similar method using our modified domestic microwave oven, in comparison with conventional and ultrasonic-bath methods.

Materials and Methods

Chemicals

Plumbagin was procured from natural source by a method adapted from that of Chairungsi et al. [15]. Briefly, fresh roots of *Plumbago rosea* Linn. were washed, cut, and repeatedly macerated in 50% aqueous ethanol at room temperature for 24 h to obtain a combined aqueous alcoholic extract, the major part of which was then distilled. The yellow distillate obtained was partitioned with dichloromethane:water (4:1). The organic layer was separated and dried over Na_2SO_4. After evaporation of the solvent it gave 0.4 % yield of pure plumbagin. The identity of the compound was confirmed by m.p., TLC, IR and GC-MS. All other chemicals and solvents used were of AR grade.

Acetylation of plumbagin

For microwave-induced acetylation, a mixture of plumbagin (0.5 g), iodine (0.0067 g) and acetic anhydride (5 mL) was heated in our modified domestic microwave oven [16-17] at 62-65 °C (450 W) for 4 min. For conventional acetylation, a mixture of plumbagin (0.5 g), acetic anhydride (5 mL) and iodine (0.0067 g) or pyridine (5 mL) was stirred at room temperature overnight. For ultrasonic bath acetylation, a mixture of plumbagin (0.5 g), acetic anhydride (5 mL) and iodine (0.0067 g) or pyridine (5 mL) was sonicated in an ultrasonic bath (Decon, FS300B) at 27-28^o C for 4 min [18]. Each acetylated mixture was then worked up by addition of dichloromethane. The resulting mixture was successively washed with water, saturated $NaHCO_3$ and water. The organic extract was dried over Na_2SO_4 and the solvent removed by evaporation under reduced pressure. The crude product was purified by crystallisation in hexane and characterised by m.p. determination and spectroscopic methods (IR, NMR, GC-MS).

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Results and Discussion

The acetylation of plumbagin (Figure 1) was carried out by three methods in order to compare the respective yields and reaction times. The results are shown in Table 1. Acetylation using the adapted microwave oven at 450 W and a temperature of 62-65^{o} C for 4 min gave a high yield (98%) of the acetate, while acetylation using conventional method with acetic anhydride-iodine or acetic anhydride-pyridine mixture gave moderate yields (70% and 66% respectively). Acetylation by ultrasonic bath method for 4 min with acetic anhydride-iodine or acetic anhydride-pyridine mixture gave the acetate in 38% and 83% yields respectively. Increasing the sonication time to 8 and 12 min decreased the yield to 35% and 30% respectively for iodine-catalysed reaction, and to 67% and 50% respectively for pyridine-catalysed reaction. Thus, the acetylation of plumbagin, an important natural product used as starting material for the synthesis of many plumbagin-based compounds, employing a microwave irradiation in the presence of iodine as catalyst seems to be a more efficient and enviromentally friendly method compared to the conventional or ultrasonic acetylation.

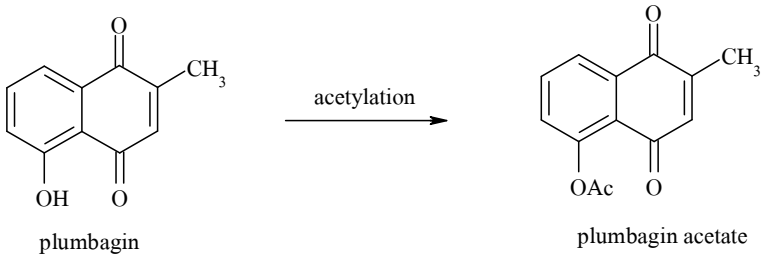

Figure 1. Acetylation of plumbagin

Table 1. Comparison of different methods of acetylation of plumbagin

Method	Reaction time	Reaction temperature (°C)	% Yield of plumbagin acetate (catalyst: I_2)	% Yield of plumbagin acetate (catalyst: pyridine)
Microwave	4 min	62-65	98	-
Conventional	24 h	room	70	66
Ultrasonic bath	4 min	27-28	38	83
	8 min		35	67
	12 min		30	50

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