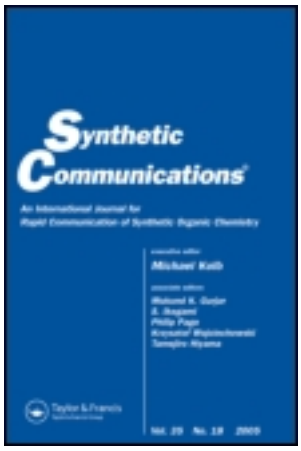

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MICROWAVE ASSISTED McFADYEN-STEVENS AND HUANG-MINLON REACTIONS

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ABSTRACT

Microwave irradiation has been employed in McFadyen–Stevens reaction to convert *p*-toluenesulfonyl hydrazides **1** to the aldehydes **2**. Also, microwave has been applied in Huang–Minlon reduction of carbonyl compounds **3** to the corresponding hydrocarbons **4**.

Key Words: Microwave; Reduction; McFadyen-Stevens; Huang-Minlon; Nauclefidine

Microwave heating has been employed as a frequent resource for improvement of classical reactions, and sometimes it led to discover new reactions. In the last few years there has been a growing interest in the use of microwave heating in organic synthesis. The use of such non-conventional

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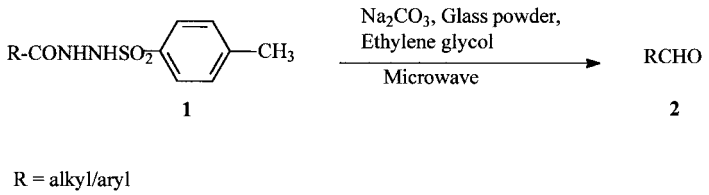


Scheme 1.

reaction conditions reveals several features like: a short reaction time compared to conventional heating, ease of work-up after a reaction, reduction in the usual thermal degradation and better selectivity.[1]

McFadyen–Stevens[2] aldehyde synthesis is a well-known reaction used for the reduction of carboxylic acids to the corresponding aldehydes via their arylsulfonhydrazides. Earlier, in the course of synthesizing the alkaloid nauclefidine, McFadyen–Stevens reaction was used by us.[3] Now we had applied this reaction but under microwave condition to successfully synthesize the same alkaloid **2d** in excellent yield from the corresponding tosylhydrazide (**1d**). The microwave conditions for the McFadyen–Stevens reaction (Scheme 1) have been generalized and the results are summarized in Table 1.

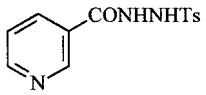
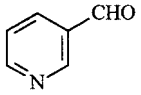
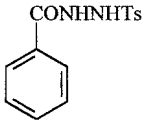
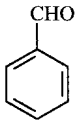
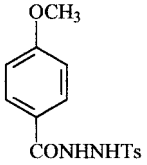
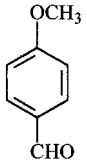
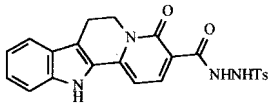
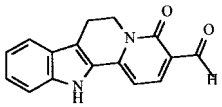
Although, Sandu et al.[4] have employed the well-known Wolff–Kishner[5] reduction under microwave conditions but then it is a two step process. Earlier, we had employed Huang–Minlon reduction, a modification of Wolff–Kishner reduction for converting the compound **3a** to **4a**, which is an important intermediate in the synthesis of the alkaloid flavopereirine, a cancer cell inhibiting alkaloid.[6]

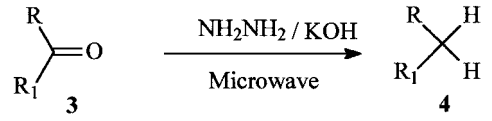
We have now obtained the same intermediate **4a** from **3a** with Huang–Minlon reduction but under microwave conditions (Scheme 2) with excellent yield. The procedure has been generalized and the results are summarized in Table 2.

We have observed that in the case of aromatic aldehydes and ketones the reaction is influenced by the substituents in the ortho, para or meta position of the carbonyl functionality. 3-Acetyl pyrrole on Huang–Minlon reduction under microwave irradiation undergoes deacetylation to afford pyrrole, a phenomenon earlier reported by us for similar systems under microwave free conditions.[7]

All the products in both the reactions have been identified by comparison with authentic samples. Both McFadyen–Stevens and Huang–Minlon reactions require high temperature. We have utilised these reactions under microwave conditions in the synthesis of the alkaloids nauclefidine and flavopereirine respectively. In summary, we have achieved a simple and efficient procedure for the above two important reactions.

Table 1.

Starting Material (**1**)	Reaction Time (Watt)	Product (**2**) (Yield)
a 	3 × 1/2 min (650 W)	 (82%)
b 	2 × 1 min (250 W) 3 × 1/2 min (350 W)	 (78%)
c 	5 × 1 min (350 W)	 (68%)
d 	6 × 1 min (450 w)	 (90%)



R = H or alkyl/aryl
R_1 = alkyl or aryl

R = H or alkyl/aryl
R_1 = alkyl or aryl

Scheme 2.

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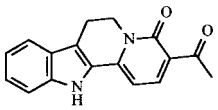
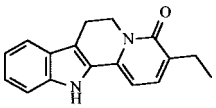
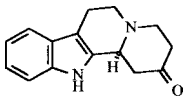
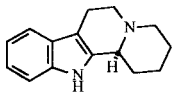
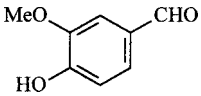
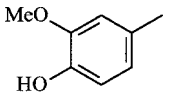
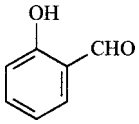
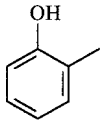
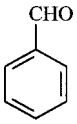
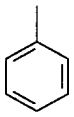
Table 2.

Starting Material (**3**)	Reaction Time	Product (**4**) (Yield)
a 	2 × 1 min 2 × 1 min	 (85%)
b 	2 × 1 min 3 × 1 min (1 × 1 min at 450 W)	 (80%)
c 	2 × 1 min 3 × 1 min	 (83%)
d 	2 × 1 min 2 × 1 min	 (80%)
e 	2 × 1 min 2 × 1 min	 (78%)

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. NMR spectra were measured on a Bruker 300 MHz spectrometer using TMS as internal standard. Compounds **1** were prepared following the reported[3] procedure. The reactions were performed in a commercial microwave oven of 1000 W capacity. For oils and low melting solids the irradiation has to be done at a lower wattage (150 W) to begin with and then, it is further irradiated at higher wattage (250–350 W) in the same reaction flask.

General Procedure for McFadyen–Stevens Aldehyde Synthesis: A mixture of the *p*-toluenesulfonyl acid hydrazide **1** (2 mmol), Na_2CO_3 (2.2 mmol), and powdered glass (500 mg) in ethylene glycol (5 mL) was taken in an Erlenmeyer flask. The reaction flask was placed in a commercial microwave oven of 1000 W capacity. The reaction mixture was initially irradiated at 150 W for a couple of minutes and then at 250–650 W for 1–6 min (monitored by tlc). The reaction mixture was cooled to room temperature, neutralised and then extracted with chloroform. The extract was dried over Na_2SO_4, evaporated, and then column chromatography over silica gel afforded the corresponding aldehydes in reasonable yield.

General Procedure for Huang–Minlon Reduction: In a typical example, a mixture of the ketone/aldehyde **3** (2 mmol) hydrazine hydrate (4 mmol, 200 mg) and powdered KOH (5 pellets) was taken in an Erlenmeyer flask. The reaction flask was placed in a commercial microwave oven of 1000 W capacity. The reaction mixture was initially irradiated at 150 W for a couple of minutes and then at 250–350 W for 1–5 min (monitoring by tlc). The reaction mixture was cooled to room temperature, neutralised and then extracted with chloroform. The extract was dried over Na_2SO_4, evaporated, and then column chromatography over silica gel afforded the corresponding hydrocarbon in reasonable yield.

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