Eco-friendly and highly efficient synthesis, including multigram synthesis, of aldehyde isonicotinoyl hydrazones using sonochemistry.

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Abstract

Synthesis utilizing ultrasonic irradiation multigram/ smaller scales of a series arylaldehyde isoniazid *N*-acylhydrazones.

Introdução

The drug, isoniazid, has been a key compound in first-line tuberculosis treatment, usually in combination with other drugs.[1] Following on from the use of isoniazid itself, various derivatives of isoniazid have also been investigated as anti-TB agents.[2] The potential of isoniazid and its derivatives in combating other diseases have attracted much recent attention.[3] The importance and utility of **2**, has led us to work on environmentally friendly, multigram scale and highly efficient synthesis, utilizing ultrasonic irradiation to be an excellent energy source for its formation. Additionally, we have been interested in establishing a general, smaller-scale, ultrasonic driven synthesis of arylaldehyde isoniazid *N*-acylhydrazones.

Resultados e Discussão

The syntheses of acylhydazones generally involve a condensation reaction between an aldehyde or ketone and an acylhydrazine, with elimination of water. The compound **2** was obtained from **1** and **3** in an water:ethanol solvent system using ultrasonic irradiation, **Scheme 1**. In addition to the procedure using ultrasonic irradiation, we also carried out a 4 mole scale reaction in aqueous ethanol at room temperature (30 °C) and 2 mole scale reaction at heating (80 °C), both without ultrasonic irradiation but with vigorous magnetic stirring. The reactions involved solvent removal, washing with small quantities of water and drying in air. Ultrasonic procedure, reduced reaction times to 30 min and slightly higher purity as measured by HPLC 99.43%.

A group of isoniazid *N*-acylhydrazones, possessing good anti-TB and/or anticancer activities,[3] have also been synthesised from isoniazid and the appropriate substituted benzaldehyde using ultrasonic irradiation (**Tabela 1**).

Scheme 1. Synthesis of salicylaldehyde isonicotinoyl hydrazone and a series arylaldehyde isoniazid *N*-acylhydrazones.

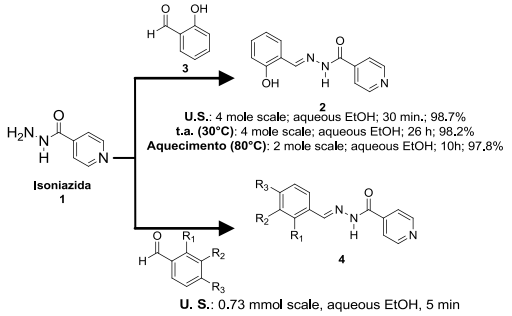

Tabela 1. Room and ultrasonic methods for the preparation of the isoniazid *N*-acylhydrazone, **4**.

Compound, **4**			**Ultrasonic reaction**[a]	**Classical reaction**
R1	R2	R3	Yield% /Reaction time: min	Yield% /Reaction time: h
MeO	H	H	90/5	91/3
H	EtO	H	86/5	88/2
H	Cl	H	99/5	91/1
H	H	Cl	99/5	91/2
H	H	F	80/5	83/2
Cl	Cl	H	99/5	81/7
Cl	H	Cl	91/5	79/7
HO	H	H	85/5	85/6
HO	HO	H	90/5	88/12
HO	MeO	H	85/5	89/6
MeO	H	H	90/5	91/3

[a]The frequency was 20 kHz, the amplitude was 20% of the maximum power output, there was no pulse.

Conclusões

In this study, we report the high yielding ultrasonic synthesis of pure **2** on a 4 mole scale. In addition, a series of ten isoniazid *N*-acylhydrazone derivatives **4** were synthesized. U.S. procedures are simple, safe, with short reaction times, and produce high yields.

Agradecimentos

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