微波关环合成取代吖啶酮*

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摘 要: 以 2, 5-二甲氧基苯胺和邻氯苯甲酸为原料, 通过 Ullmann 反应、PPA 关环合成了 2 种取代吖啶酮, 并提供一种新颖的选择性脱甲基的方法。

关键词: 取代吖啶酮; 多聚磷酸; 合成
中图分类号: O614.241 文献标识码: A 文章编号: 0529-6579 (2004) 04-0126-02

吖啶及吖啶酮类化合物具有抗炎、抗菌、抗疟, 特别是某些吖啶酮类化合物具有显著的抗癌活性[1,2]。为了寻找新的吖啶类药物, 采用 Cu 催化的 Ullman[3] 反应及微波催化的 PPA 关环[4] 合成了取代吖啶酮衍生物 **2**, **3**。合成路线如下:

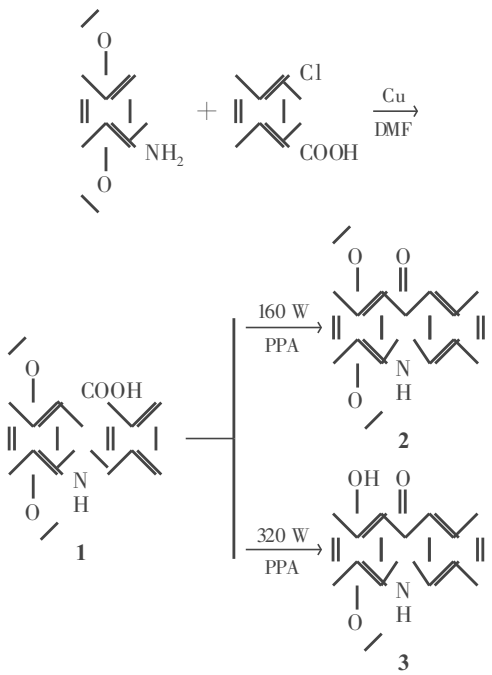

图 1 化合物 **2**, **3** 的合成路线

Fig 1 The synthesis of compounds **2**, **3**

2—苯氨基—3, 6—二甲氧基苯甲酸 **1** 的合成: 将 0.12 mol 2, 5—二甲氧基苯胺, 0.18 mol 邻氯苯甲酸溶于 150 mL DMF 中, 再加入 12 g 无水碳酸钾, 0.8 g Cu, 回流搅拌 2 h, 加入体积比为 1∶1 的盐酸 300 mL, 冷却, 过滤, 固体在沸水中煮 10 min, 冷却过滤得粗产物, 用乙醇重结晶得到浅黄色 **1**。

1, 4-二甲氧基吖啶酮 **2** 的合成: 将 0.01 mol 2-苯氨基 3, 6-二甲氧基苯甲酸与 20 g 多聚磷酸混合, 升温到 120 ℃维持温度恒定加热搅拌 2 h, 冷却后倒入到 100 mL 热至 80 ℃的水中, 煮沸, 然后冷却到室温, 过滤收集固体, 用稀乙醇重结晶, 得到黄色固体 **2**, 产率 85%, FABMS *m*/*s* 256[M+1]; ^{1}H NMR(500 MHz, $CDCl_3$, TMS) δ: 8.12~8.14 (dd, *J*=8 Hz, *J*=1.5 Hz, 1H), 7.85~7.87 (d, 8 Hz, 1H), 7.61~7.64 (m, 1H), 7.18~7.23 (m, 2H), 6.60~6.62(d, *J*=4 Hz, 1H), 3.97(s, 3H), 3.80(s, 1H)。

1—羟基—4—甲氧基吖啶酮 **3** 的合成: 同上 **2** 的合成, 加热温度高于 160 ℃(不超过 180 ℃), 浅黄色固体 **3**, 产率 52%, FABMS *m*/*s* 241[M+1]; ^{1}H NMR(500 MHz, $CDCl^3$, TMS) δ: 8.38~8.40(dd, *J*=8.5 Hz, *J*=1.5 Hz, 1H), 7.67~7.60(m, 1H), 7.36~7.37(d, *J*=3 Hz), 7.29~7.31(t, 1H), 7.06~7.07(d, *J*=4 Hz, 1H), 6.54~6.56(m, 1H), 3.98(s, 3H)。

以 2, 5-二甲氧基苯胺和邻氯苯甲酸为原料经 2 步反应合成了 2 种取代吖啶酮, 其中 **3** 的合成在 PPA 作用经历了一个关环、脱甲基的过程, 为我们提供一种新的选择性脱甲基的方法。

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* 收稿日期: 2004—03—12
基金项目: 国家自然科学基金资助项目 (20032021, 20272085)
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Microwave-assisted Synthesis of Substituted Acridones

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Abstract: Two substituted acridones were synthesized through Ullman reaction and microwave-assisted PPA cyclozation. And a novel demethylation method was found.

Key words: substituted acridones; PPA; synthesis

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Determination of Residual Solvent in Cefpiramide Sodium by Headspace GC

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Abstract: A method for the determination of residual solvent DMF in cefpiramide sodium by headspace gas chromatography was established. The analysis was performed on a HP-INNOWax capillary column (30 m×0.25 mm×0.25 μm) and a flame-ionization detector. Nitrogen was used as carrier gas. Oven temperature was programmed as following: initially at 60 ℃, raised up to 100 ℃ at 20 ℃/min and held for 2 min, and then to 120 ℃ at 10 ℃/min and raised up again to 200 ℃ at 40 ℃/min. The total run time was approximately 8 min. The temperatures set for injector and FID detector were 220 ℃ and 250 ℃ respectively. Injection volume was 1 mL in split mode (1∶20 ratio). The assay of residual solvent was calculated according to the external standard method. DMF was not found in the sample of cefpiramide sodium. There was a good linear relationship for DMF (r=0.997 2) within the range from 0.005 to 0.1 g/L. The detection limit of DMF was 0.004 g/L. The average recovery was 102%. The relative standard deviation of the residue was 5.4%.

Key words: gas chromatography; headspace injection; residual solvent; cefpiramide sodium