

The Synthesis of Amino Naphthol Compounds Catalyzed by Brønsted Acidic Ionic Liquids [DC₂O₂IM][HSO₄]

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Abstract

A series of amino naphthol compounds were synthesized via three component condensations of aromatic aldehyde, β -naphthol and amide employing Brønsted acid ionic liquid [DC₂O₂IM][HSO₄] as a catalyst at 90°C for 10 minutes under solvent-free conditions. The method has the advantages of simple operation and short reaction time.

Keywords

Ionic Liquid, Catalysis, Solvent-Free, Amino Naphthol

Brønsted酸性离子液体[DC₂O₂IM][HSO₄]催化合成氨基萘酚化合物

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摘 要

Brønsted酸性离子液体1,3-二羧甲基咪唑硫酸氢盐[DC₂O₂IM][HSO₄]催化芳香醛、 β -萘酚和酰胺在无溶剂条件下合成氨基萘酚化合物。该方法具有操作简单、反应时间短等优点。
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剂条件下90°C反应10 min合成了一系列氨基萘酚化合物。该方法有操作简单、反应时间短等特点。

关键词

离子液体, 催化, 无溶剂, 氨基萘酚

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1. 引言

利用多组分反应构建复杂分子结构对于有机合成领域意义重大[1], 常见的反应有 Bigenilli 反应[2], Ugi 反应[3], Passerini 反应[4]和 Mannich 反应[5]等。含氨基和羟基官能团的化合物广泛存在于天然产物和药物分子中, 如核苷抗生素和 HIV 蛋白酶抑制剂[6]。1-氨基烷基-2-萘酚衍生物对于心跳过慢和高血压等心血管疾病有重要的作用[7]。

氨基萘酚类化合物通常是由醛、 β -萘酚和酰胺发生三组分反应而成, 碘[8]、蒙脱石[9]、 $\text{HClO}_4 \cdot \text{SiO}_2$ [10]、十二钨钴酸钾[11]、 $\text{FeCl}_3 \cdot \text{SiO}_2$ [12]、氨基磺酸[13]和离子液体 $[(\text{CH}_2)_4\text{SO}_3\text{HMIM}][\text{HSO}_4]$ [14]等作为催化剂已被应用于该反应。离子液体(ILs)因具有低蒸气压、稳定性高、易回收利用和对环境友好等特点被广泛应用于有机合成中, 基于我们课题组在酸性离子液体方面的研究基础[15], 本文发展了一种 Brønsted 酸性离子液体 $[\text{DC}_2\text{O}_2\text{IM}][\text{HSO}_4]$ 催化反应合成氨基萘酚的方法。考察了催化剂的种类和用量、反应时间和温度等因素对产物产率的影响, 并对反应底物的普适性进行了探究。

2. 实验部分

2.1. 仪器与试剂

Varian inova-400 型核磁共振仪(400 MHz, TMS); 美国 HP 1100 液相色谱质谱仪; 瑞士 Büchi B-560 型熔点仪等。

所有药品及试剂均为市售分析纯, 用前未经处理。离子液体 1-乙基-3-丁基咪唑硫酸氢盐 $[\text{BEIM}][\text{HSO}_4]$ 的合成参考文献[16]、1,3-二羧甲基咪唑硫酸氢盐 $[\text{DC}_2\text{O}_2\text{IM}][\text{HSO}_4]$ 的合成参考文献[17]和 1,3-二羧甲基咪唑对甲苯磺酸盐 $[\text{DC}_2\text{O}_2\text{IM}][p\text{-CH}_3\text{PhSO}_3]$ 的合成参考文献[18], 离子液体 1-乙基-3-羧甲基咪唑氯盐 $[\text{C}_2\text{O}_2\text{EIM}][\text{Cl}]$ 的合成参考文献[19]、1,3-二羧甲基咪唑氯盐 $[\text{DC}_2\text{O}_2\text{IM}][\text{Cl}]$ 的合成参考文献[20]。

2.2. 离子液体 $[\text{C}_2\text{O}_2\text{EIM}][\text{HSO}_4]$ 和 $[\text{DC}_2\text{O}_2\text{IM}][\text{CF}_3\text{COO}]$ 的合成

离子液体 1-乙基-3-羧甲基咪唑硫酸氢盐 $[\text{C}_2\text{O}_2\text{EIM}][\text{HSO}_4]$ 和 1,3-二羧甲基咪唑三氟乙酸盐 $[\text{DC}_2\text{O}_2\text{IM}][\text{CF}_3\text{COO}]$ 的合成如式 1 所示: 将 0.05 mol 咪唑氯盐和 0.05 mol 的酸在 90°C 反应 72 h。冷却, 用乙醚洗涤反应混合物, 旋除乙醚, 残余物在 90°C 真空干燥至恒重即得离子液体 $[\text{C}_2\text{O}_2\text{EIM}][\text{HSO}_4]$ 和 $[\text{DC}_2\text{O}_2\text{IM}][\text{CF}_3\text{COO}]$ 。

离子液体的表征如下:

离子液体 1-乙基-3-羧甲基咪唑硫酸氢盐 $[\text{C}_2\text{O}_2\text{EIM}][\text{HSO}_4]$, 棕黄色液体; $^1\text{H NMR}$ (400 MHz, D_2O), δ : 1.41 (t, $J = 7.6$, 3H, CH_3), 4.14~4.20 (q, $J = 7.2$, 2H, CH_2), 5.03 (s, 2H, CH_2), 7.43 (d, 2H, ArH), 8.76 (s, 1H, ArH); ESI-MS: m/z (%) = 169.1 (100) $[\text{M}^+]$, 97.0 (100) $[\text{M}^-]$.

离子液体 1,3-二羧甲基咪唑三氟乙酸盐咪唑[DC₂O₂IM][CF₃COO], 淡黄色固体; m.p. 237°C~240°C, ¹H NMR (400 MHz, D₂O), δ: 5.13 (s, 4H, 2 × CH₂), 7.54 (d, 2H, ArH), 8.92 (s, 1H, ArH); ESI-MS: m/z (%) = 185.1 (100) [M⁺], 113.0 (100) [M⁻].

2.3. 目标化合物的合成

化合物 4a-4m 的合成反应如式 2 所示。将 1.0 mmol 芳香醛、1.0 mmol β-萘酚、1.2 mmol 酰胺和催化剂[DC₂O₂IM][HSO₄] (20 mol%)混合均匀后在无溶剂条件 90°C 下搅拌 10 min。反应结束后, 向反应体系中加入大量碎冰, 充分搅拌, 过滤, 大量冰水洗涤固体, 即得纯净的产物 4a-4m。不需要重结晶。

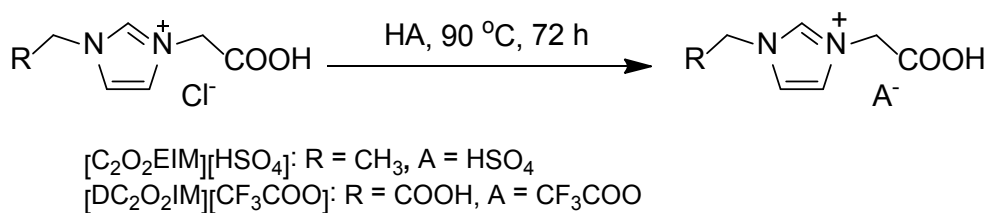
3. 结果与讨论

3.1. 反应条件优化

以苯甲醛、β-萘酚和苯甲酰胺三组分为模型反应, 考察了离子液体的种类及其用量、反应时间、反应温度等条件对反应的影响。首先, 考察了五种 Brønsted 酸性离子液体对反应的影响(表 1, entries 1~5), 从中看出, 1,3-二羧甲基咪唑硫酸氢盐离子液体([DC₂O₂IM][HSO₄])为最优催化剂, 产物产率为 89%。其次, 讨论了催化剂用量对反应的影响(表 1, entries 5~7), 从中可知当催化剂用量为 10 mol%和 30 mol%时产物产率均下降, 因此催化剂用量为 20 mol%时最佳。然后, 探究了反应温度对反应的影响(表 1, entries 5, 8~10), 当反应温度分别为 80°C, 90°C, 100°C, 130°C, 产物产率分别为 78%, 94%, 93%, 89%。最后, 研究了反应时间对反应的影响(表 1, entries 11~13), 发现反应时间为 10 min 时产率最高可达 96%, 随着时间的延长产物产率略有下降。综上, 该反应的最佳条件为: 催化剂离子液体 1,3-二羧甲基咪唑硫酸氢盐[DC₂O₂IM][HSO₄]的用量 20 mol%, 反应温度 90°C, 回流反应 10 min。

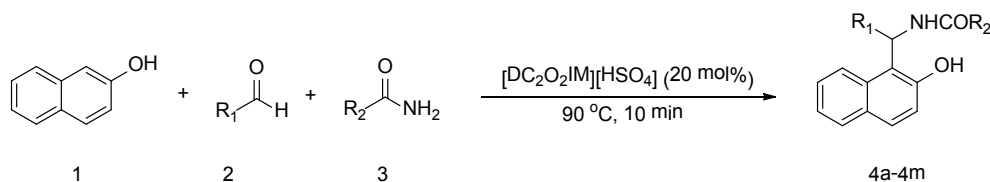
3.2. 底物普适性研究

在最佳反应条件下, 开展了底物的普适性研究。首先, 对于取代芳香醛的取代基进行拓展, 发现无论取代基连有吸电子基如 2-氯、2-溴、3-溴、4-氟、2-硝基、4-硝基还是给电子基如 4-甲基和 3-甲氧基都能以良好到优秀的产率得到氨基萘酚类化合物(表 2 entries 4a-4i)。然后, 我们将乙酰胺代替苯甲酰胺用于该反应也以优秀的产率得到氨基萘酚类衍生物(表 2 entries 4j-4m)。综上所述, 该反应具有较好的普适性。



Scheme 1. The synthesis of ionic liquid [C₂O₂EIM][HSO₄] and [DC₂O₂IM][CF₃COO]

式 1. 离子液体[C₂O₂EIM][HSO₄]和[DC₂O₂IM][CF₃COO]的合成



Scheme 2. Synthesis of amino naphthol

式 2. 氨基萘酚的合成

Table 1. Optimization of reaction conditions^a**表 1.** 反应条件的优化^a

Entry	Cat. (mol%)	T °C	Time (min)	Yields ^b (%)
1	[BEIM][HSO ₄] (20)	130	30	70
2	[CO ₂ EIM][HSO ₄] (20)	130	30	82
3	[DCO ₂ IM][CF ₃ COO] (20)	130	30	84
4	[DC ₂ O ₂ IM][<i>p</i> -CH ₃ Ph ₃ SO ₃] (20)	130	30	85
5	[DC ₂ O ₂ IM][HSO ₄] (20)	130	30	89
6	[DC ₂ O ₂ IM][HSO ₄] (10)	130	30	80
7	[DC ₂ O ₂ IM][HSO ₄] (30)	130	30	74
8	[DC ₂ O ₂ IM][HSO ₄] (20)	80	30	78
9	[DC ₂ O ₂ IM][HSO ₄] (20)	90	30	94
10	[DC ₂ O ₂ IM][HSO ₄] (20)	100	30	93
11	[DC₂O₂IM][HSO₄] (20)	90	10	96
12	[DC ₂ O ₂ IM][HSO ₄] (20)	90	20	94
13	[DC ₂ O ₂ IM][HSO ₄] (20)	90	40	82

^a 反应条件: β -萘酚(1.0 mmol), 苯甲醛(1.0 mmol), 苯甲酰胺(1.2 mmol), 催化剂, 温度, 时间, 无溶剂反应; ^b 分离产率。

Table 2. Research of substrate scope^a**表 2.** 底物的普适性研究^a

Entry	R ₁	R ₂	Yields ^b (%)	m.p. (°C)	
				Found	Reported [lit.]
4a	C ₆ H ₅	C ₆ H ₅	96	240~241	238~240 [21]
4b	2-Cl-C ₆ H ₄	C ₆ H ₅	94	283~285	284~285 [22]
4c	2-Br-C ₆ H ₄	C ₆ H ₅	91	227~229	228~230 [23]
4d	3-Br-C ₆ H ₄	C ₆ H ₅	89	229~231	230~231 [21]
4e	4-F-C ₆ H ₄	C ₆ H ₅	72	190~193	192~194 [24]
4f	2-NO ₂ -C ₆ H ₄	C ₆ H ₅	84	264~268	263~265 [25]
4g	4-NO ₂ -C ₆ H ₄	C ₆ H ₅	89	224~225	228~229 [22]
4h	4-Me-C ₆ H ₄	C ₆ H ₅	63	216~217	214~215 [22]
4i	3-MeO-C ₆ H ₄	C ₆ H ₅	89	216~219	214~216 [26]
4j	4-Me-C ₆ H ₄	CH ₃	73	211~214	214~216 [25]
4k	3-F-C ₆ H ₄	CH ₃	94	247~249	248~249 [27]
4l	3-Br-C ₆ H ₄	CH ₃	85	253~255	250~252 [28]
4m	3-NO ₂ -C ₆ H ₄	CH ₃	93	253~256	256~258 [28]

^a 反应条件: β -萘酚(1.0 mmol), 芳香醛(1.0 mmol), 酰胺(1.2 mmol), 催化剂([DC₂O₂IM][HSO₄]) 20 mol%, 无溶剂反应, 90°C, 10 min; ^b 分离产率。

4. 总结

本文成功地在无溶剂条件下用离子液体 1,3-二羧甲基咪唑硫酸氢盐[DC₂O₂IM][HSO₄]催化合成了一系列氨基萘酚类化合物。该反应具有操作简单、反应时间短、对环境友好的特点, 是离子液体催化合成氨基萘酚类化合物的重要补充。

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