文章编号: 1001-3555(2012)02-0099-06

N-溴代丁二酰亚胺水相氧化醇类化合物反应研究

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摘　要: 以水为反应介质、NBS 为氧化剂, 在水相无催化剂条件下实现了醇的氧化. 芳香醇、脂肪醇都可以达到 95% 以上的醛(或酮)产率, 但该体系对一些含供电子取代基的醇的反应活性不高, 选用 salen-Co(III)配合物作为催化剂, 可拓宽反应的底物适用范围.

关　键　词: N-溴代丁二酰亚胺; 氧化; 醇; 水; salen-Co(III)配合物
中图分类号: O643.32　　**文献标识码:** A

醇的氧化是有机合成的重要步骤之一, 醇氧化生成的醛、酮或羧酸在精细化工、生物和医药化工领域应用非常广泛, 因此醇氧化反应一直备受学术界和工业界的关注. 但是, 传统的醇氧化反应主要使用 MnO_2[1]、Cr(Ⅵ)[2]、高价碘[3]、活化的二甲亚砜[4]等氧化剂, 具有很多局限性如价格昂贵、毒性大、污染严重并且具有危险性等. 近年来, 由于 N-溴代丁二酰亚胺(NBS)廉价易得, 被广泛的应用于醇氧化反应之中. 2004 年 Krishnaveni 等人报道了 NBS 在环糊精催化下的水相中醇的氧化反应, 其反应条件温和, 且产率高[5]. 2005 年 Sharma 等人报道了以 $Co(acac)_2$为催化剂和 NBS 作为氧化剂的二级醇的氧化体系, 该体系以乙腈作为反应介质, 但对伯醇不太适用[6]. 同年 Lee 等人报道了以离子液体为介质的醇氧化反应, 该体系以 2,6-二甲基吡啶作碱, 在[bmim]BF_4离子液体中用 NBS 将苄醇氧化为相应的醛[7]. 2006 年 Bir Sain 等人报道了无金属的 NBS 氧化体系, NBS -NH_4Cl 在乙腈与水混合溶剂中 80 °C 加热可以将伯醇仲醇转化为相应的羰基化合物[8]. 2008 年 Shang 等人报道了以聚乙二醇为反应介质用 NBS 氧化醇类化合物的反应体系[9]. 最近, 我们课题组发现 NBS 可替代 $PhI(OAc)_2$, 可在 Salen-Mn(III)配合物催化仲醇的氧化动力学拆分反应中用作氧化剂[10]. 最近我们系统研究了 NBS 在水相中醇类化合物的氧化反应体系, 发现以水为溶剂, NBS 可在无催化剂条件下实现醇类化合物的氧化.

1 实验部分

1.1 仪器和试剂

Agilent-GC/MS(7890A/5975C)进行定性分析, 毛细管色谱柱为: HP-5MS (30 m × 0.25 mm × 0.25 μm), TCD 检测器. 用 Agilent-6820 气相色谱进行定量分析, 毛细管色谱柱为: SE-54 (50 m × 0.25 mm × 0.33 μm), FID 检测器, 程序升温.

1.2 醇的氧化反应

以苯乙醇为例, 取苯乙醇 0.5 mmol, 加入 1 mL H_2O, 1.0 当量的 NBS, 室温搅拌 10 h. 反应结束后用二氯甲烷萃取, TLC (Thin Layer Chromatography)、GC-MS 检测得到产物苯乙酮并计算其产率.

2 结果与讨论

2.1 反应底物的拓展

考察了 NBS-H_2O 体系对不同类型醇的氧化反应, 结果列在表 1 中. 芳香类的仲醇如苯乙醇、1-苯基 1-丙醇、1-苯基 2-丙醇、吡啶乙醇等在选定的实验条件下都能转化为相应的酮, 且产率大于 95% (Entry 1-5); 对简单的脂肪类仲醇, 如 4-壬醇也取得了很好的结果(Entry 6); 但对于环己基醇, 其相应的酮的产率为 63%, 反应活性明显下降(Entry 7-9). 另外, 对 1-环己基 1-丙醇和甲基环己醇则几乎没有氧化反应发生, 而对于 3,3-二甲基 2-丁醇的氧

收稿日期: 2012-03-15; **修回日期:** 2012-04-06.
基金项目: 国家自然科学基金青年科学基金资助项目(21103207).
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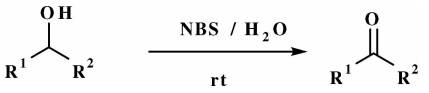
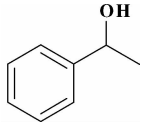
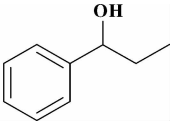
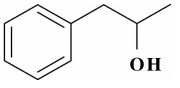
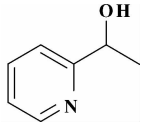
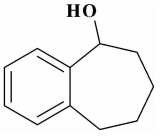
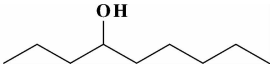
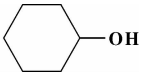
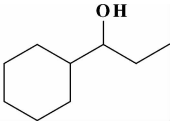
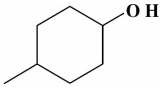
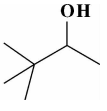
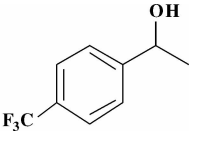
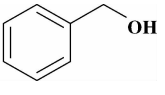
表1 无催化剂条件下在 NBS-H_2O 体系中的醇的氧化反应

Table 1 Catalyst-free oxidation of various alcohols by NBS in water



Entry	Alcohols	Conv. (%)[e]	Yield(%)[e]
1		98	96
2		99	98
3		>99	>99
4		95	95
5[b]		>99	>99
6		>99	>99
7[b]		63	63
8		14	14
9		NR[d]	NR[d]
10		50	–[e]
11[b]		98	97
12		>99	66

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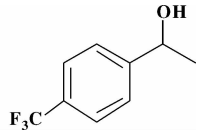
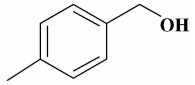
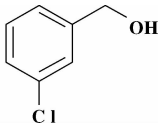
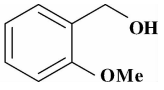
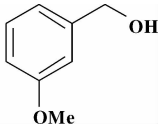
(续表 1)

Entry	Alcohols	Conv. (%)[e]	Yield(%)[e]
13[b]		>99	90
14[b]		>99	81
15		>99	44
16		>99	–[c]
17		>99	–[c]

[a]Reaction conditions: alcohol: 0.5 mmol, NBS: 1equiv., H_2O: 1.0 mL, reaction time: 10 h. [b] 0.5 mL CH_2Cl_2 was added as co-solvent. [c]No desired product was detected. [d]No reaction. [e] based on GC, *n*-nonane as internal standard.

化反应仅得到酮的 α-溴代物，没有相应的酮生成(Entry 10).

考察了苯环上取代基对芳香类仲醇氧化反应的影响. 结果发现对位三氟甲基取代的苯乙醇可以在 NBS-H_2O 体系中很好的转化为酮(Entry 11)；但对于邻甲氧基苯乙醇和 3-氟、3-甲基、4-甲基、4-氯及 2,6-二甲基取代的苯乙醇，反应均比较复杂，没有相应的酮生成.

在同样的条件下考察了苄醇在 NBS-H_2O 体系中的反应. 对于苄醇，苯甲醛的产率为 66%(Entry 12). 对于含有不同取代基的苄醇，反应中有不同程度的过度氧化产物羧酸或溴代物生成，以 4-三氟甲基苄醇和 4-甲基苄醇的氧化结果较好，分别可得到产率为 90% 和 81% 的醛(Entry 13-14)；但对 3-氯苯甲醛的产率为 44%(Entry 12). 另外，对于甲氧基取代的苄醇仅得到相应苯甲醛的溴代物(Entry 16-17).

在 NBS-H_2O 体系中加入 1% 的 Salen-Co(III)配合物(图 1)，并加入 0.5 mL CH_2Cl_2 作混合溶剂，以期达到更好的底物适用性，结果列在表 2 中. 由表 2 可见，甲基环己醇在 NBS-H_2O 体系中不反应，但是在 NBS-H_2O-Salen-Co(III)-CH_2Cl_2 体系中甲基环己醇几乎完全转化为相应的酮(Entry1). 对于 3,3-二甲基-2-丁醇在此体系中，得到 3,3-二甲基-2-丁酮(Entry2)，且无溴代物生成. 一些取代基的苯乙醇在 NBS-H_2O 体系中反应产物较为复杂，但是在 NBS-H_2O-Salen-Co(III)-CH_2Cl_2 体系中，均可以转化为相应的酮(Entry 3-6). 但对于含有邻位取代基的底物 7、8 仍然不能得到相应的酮.

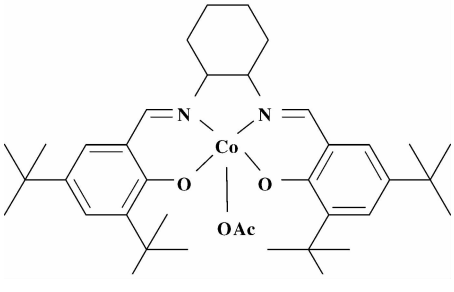
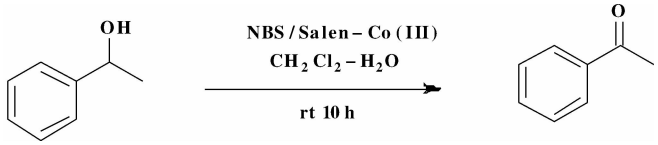


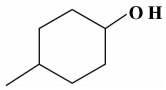
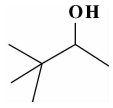
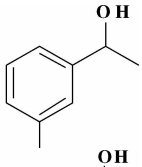
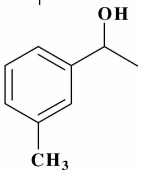
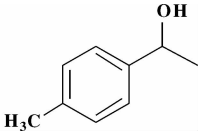
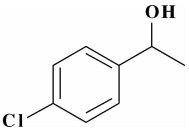
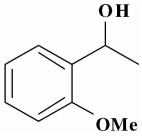
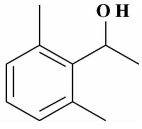
图 1 Salen-Co(III) 配合物

Fig. 1 Salen-Co(III) complex

表 2 Salen-Co(III)催化的醇的氧化

Table 2 Oxidation of alcohols with salen-Co(III) complex as a catalyst



Entry	Alcohols	Conv. (%)[c]	Yield(%)[c] of ketones or aldehydes
1		>99	>99
2		>99	>99
3		>99	>99
4		>99	>99
5		>99	>99
6		96	94
7		>99	–[b]
8		>99	–[b]

[a]Reaction conditions: alcohol: 0.5 mmol, catalyst: 1 mol%, NBS: 1equiv., H_2O: 1.0 mL, CH_2Cl_2: 0.5 mL, reaction time: 10 h. [b]No desired product was detected. [c] based on GC, *n*-nonane as internal standard.

2.2 反应机理

据文献报道，NBS 对醇的氧化的反应机理如图 2 所示[11,12]：NBS 产生的活性卤素物种对醇进行进攻(进攻的位置有以下两种争议)，然后脱除 HX 生成相应的酮. 虽然存在以上争议，但普遍认为在极性溶剂中活性卤素物种显电正性，电正性的溴容易

取代羰基 α 位的活泼氢及苯环上的氢——这恰好可以解释 NBS-H_2O 体系中副反应的发生；对不同取代基的苯甲醇，强拉电子的三氟甲基使苯环上电子云密度降低，不容易被电正性的溴取代；而供电子的甲氧基则使得苯环易于亲电取代而得不到相应的醛. 同样的对于各种取代基的苯乙醇，三氟甲基的强拉电子效应，使得羰基碳的电正性降低，α 位的活泼氢的活性降低，不容易被亲电取代；而供电子基使得羰基 α-H 更活泼，容易发生溴代. 4-三氟甲基苯乙醇没有发现溴代产物，而弱的拉电子基-F、-Cl 及弱供电子基-CH_3取代的苯乙醇主要产物均为相应酮的 α-H 卤代物. 在 Salen-Co(Ⅲ)配合物存在下，活泼溴可能先把催化剂氧化为高价 Co 中间体，高价钴再将醇氧化，从而在一定程度上抑制溴代物的生成使反应更好的向生成酮的方向进行.

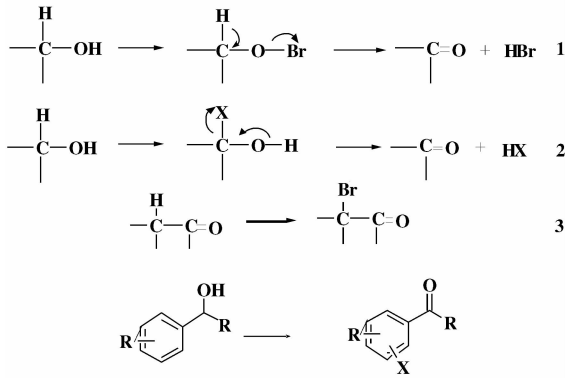


图 2 可能的反应机理

Fig. 2 Proposed mechanism

3 结　　论

我们报道的 NBS-H_2O 体系以最清洁环境友好的水作为溶剂，能在无催化剂条件下实现醇的氧化，对芳香族、脂肪族仲醇及伯醇都取得了很好的效果. 这是迄今为止报道的最为简单有效的方法，具有优异的环境友好性及原子经济性. 但取代基的电子效应对 NBS-H_2O 体系中醇的氧化反应影响非常明显，具有强吸电子基的底物可以很好地反应得到酮或醛，而具有供电子基的底物则反应较差甚至得不到醛或酮. 在 NBS-H_2O 体系中加入催化剂 Salen-Co(Ⅲ)配合物和 CH_2Cl_2可以在一定程度上拓宽底物的适用范围.

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Oxidation of Alcohols by N-bromosuccinimide in Water

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Abstract: The oxidation of alcohols by N-bromosuccinimide with water as the reaction medium was developed. A series of alcohols including benzylic and aliphatic alcohols were converted into the corresponding ketones or aldehydes in high yields under catalyst-free conditions in water, except for some alcohols bearing donating substituents. However, the oxidation of less active alcohols could be carried out smoothly with Salen-Co(III) complex as a catalyst in a medium of water and CH_2Cl_2 mixture.

Key words: N-bromosuccinimide; oxidation; alcohols; water; Salen-Co(III) complex