

Tetrabutylammonium Peroxydisulfate in Organic Synthesis. Part 8.¹ An Efficient and Convenient Nickel-catalyzed Oxidation of Primary Amines to Nitriles with Tetrabutylammonium Peroxydisulfate[†]

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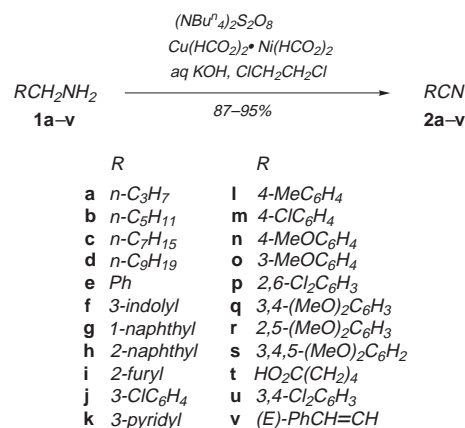
Fen-Er Chen,* Zuo-Zhong Peng, Han Fu, Ji-Dong Liu and Lan-Ying Shao

Department of Chemistry, Fudan University Shanghai, 200433, P.R. China

A series of primary amines are oxidized to the corresponding nitriles in excellent yields with tetrabutylammonium peroxydisulfate catalyzed by nickel copper formate under basic aqueous conditions.

The oxidation of primary amines to nitriles is an important process in the field of synthetic organic chemistry. A number of methods have been developed for this transformation. The modes of oxidation of primary amines to nitriles are classified into two categories: chemical² and electrochemical oxidation.³ However, these methods have not been entirely satisfactory, particularly for large scale preparations, owing to factors such as low yields, tedious reaction procedures, long reaction times and the necessity of handling explosive and/or other hazardous chemicals. Consequently, there is continued interest in developing new and convenient methods for this conversion under mild reaction conditions.

Tetrabutylammonium peroxydisulfate (NBuⁿ₄)₂S₂O₈ has been extensively used as an efficient oxidant for a variety of functional group transformations in organic synthesis.⁴ In continuation of our study on the oxidizing ability of (NBuⁿ₄)₂S₂O₈, we report on the oxidation of primary amines by (NBuⁿ₄)₂S₂O₈ catalyzed by nickel copper formate under basic aqueous conditions, providing an efficient and convenient route for the preparation of nitriles (Scheme 1).



Scheme 1

A variety of aliphatic, and aromatic/heterocyclic primary amines **1a–v** were converted into the corresponding nitriles **2a–v**, when reacted with (NBuⁿ₄)₂S₂O₈ as oxidant and

Table 1 Oxidation of primary amines **1a–v** with (NBuⁿ₄)₂S₂O₈ catalyzed by nickel copper formate^a

Entry	Solvent	Product	<i>t</i> /h	Yield ^b (%)	Mp (°C) or bp (°C)/Torr	
					Found	Reported
1	ClCH ₂ CH ₂ Cl	2a	10	92	116–117	115 ^{2e}
2	ClCH ₂ CH ₂ Cl	2b	12	93	164–165	162 ^{3e}
3	CH ₂ Cl ₂	2c	12	92	90–92/20	90/20 ^{3e}
4	CH ₂ Cl ₂	2d	12	90	120–122/20	120/19 ^{3e}
5	ClCH ₂ CH ₂ Cl	2e	10	95	190–191	190–190 ⁵
6	CH ₂ Cl ₂	2f	13	94	180–182	182–183 ^{2m}
7	ClCH ₂ CH ₂ Cl	2g	12	90	36–38	35–36 ⁶
8	CH ₂ Cl ₂	2h	13	92	64–66	62.5–64 ⁶
9	CH ₂ Cl ₂	2i	10	95	146–148	146–148 ⁷
10	CH ₂ Cl ₂	2j	10	87	42–44	45–46 ⁸
11	CH ₂ Cl ₂	2k	12	90	50–52	52 ^{2m}
12	CH ₂ Cl ₂	2l	11	94	216–218	216–217 ⁷
13	ClCH ₂ CH ₂ Cl	2m	13	95	92–94	91–93 ⁷
14	CH ₂ Cl ₂	2n	10	90	60–62	61–62 ⁷
15	CH ₂ Cl ₂	2o	10	90	85–87	87 ^{2m}
16	CH ₂ Cl ₂	2p	13	92	144–146	142–145 ⁹
17	CH ₂ Cl ₂	2q	13	93	65–67	67 ^{2m}
18	CH ₂ Cl ₂	2r	12	95	81–83	81 ^{2m}
19	CH ₂ Cl ₂	2s	11.5	90	92–95	93–94 ⁸
20	CH ₂ Cl ₂	2t	10	93	163–165/2	162/1 ^{2g}
21	ClCH ₂ CH ₂ Cl	2u	13	90	70–72	70 ¹⁰
22	CH ₂ Cl ₂	2v	10	91	254–256	254–255 ⁵

^a All products gave satisfactory IR, ¹H NMR and elemental analysis. ^b Refers to isolated yield.

* To receive any correspondence (e-mail: rfchen@fudan.edu.cn).

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nickel copper formate as a catalyst in the presence of aqueous potassium hydroxide in dichloromethane or dichloroethane at room temperature. The progress of the reaction, was monitored by TLC and high conversion could

be achieved within 10–13 h of reaction. Products were isolated by usual work-up and purification was by distillation or recrystallization. Results on the transformations are summarized in Table 1.

Furthermore, the results suggest that this procedure shows considerable chemoselectivity for the oxidation of various primary amines. Other functionalities such as isolated double bond (**1v**) or ethers (**1n**, **o**, **1q–s**) are all compatible with the reaction conditions.

It is noteworthy that the presence of nickel copper formate was essential for the dehydrogenation of amines to nitriles, no nitriles were obtained in its absence and reactions did not go to completion when reduced amounts of nickel copper formate catalyst were used.

In conclusion, this new procedure has the following practical advantages compared with the previously reported preparation of nitriles from primary amines: (i) our procedure is quite simple with the reagents being simply mixed together at the beginning of reaction, (ii) the reaction conditions are mild enough to allow the preparation of rather unstable nitriles; (iii) the yields are excellent in all cases, (iv) there are virtually no side reactions which complicate isolation and purification of the products.

Experimental

Mps and bps are uncorrected. IR spectra were recorded on a Nicolet FI-IR 360 spectrophotometer; ^1H NMR spectra were measured on a JEOL FX-90Q instrument using CDCl_3 as solvent and TMS as internal standard; elemental analyses (C, H, N) were performed on a Carlo Erba 1106-type analyzer.

Nickel copper formate (non-hydrate) was purchased from Shanghai Chemical Reagent Company. All primary amines (**1a–v**) are commercially available. $(\text{NBu}_4)_2\text{S}_2\text{O}_8$ was prepared according to the known procedure.^{4a}

General Procedure for the Oxidation of Primary Amines (1a–v) to Nitriles (2a–v).—To a solution of nickel copper formate (1 mmol) in H_2O (10 ml) was added, dropwise, a primary amine **1a–v** (100 mol) in $\text{CH}_2\text{ClCH}_2\text{Cl}$ or CH_2Cl_2 (100 ml), $(\text{NBu}_4)_2\text{S}_2\text{O}_8$ (125 mmol) in $\text{CH}_2\text{ClCH}_2\text{Cl}$ or CH_2Cl_2 (275 ml) and KOH (125 mmol) in H_2O (300 ml). The mixture was stirred at room temperature for 10–13 h (Table 1). Insoluble compounds (NiO_2 and CuO) were then filtered off and the filtrate was poured into H_2O (100 ml) and extracted with $\text{CH}_2\text{ClCH}_2\text{Cl}$ or CH_2Cl_2 (2×75 ml). The combined extracts were washed with brine (3×100 ml), dried (Na_2SO_4) and evaporated under reduced pressure. The crude product was purified by distillation or recrystallization to give pure nitriles **2a–v** in 87–95% yield.

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