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A novel system for the synthesis of nitriles from carboxylic acids

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Abstract—A simple, mild and high yielding method for the conversion of various carboxylic acids to nitriles has been developed using diphosphorus tetraiodide in combination with ammonium carbonate at room temperature.

A number of methods are known for the conversion of carboxylic acids into nitriles. In most cases, the conversion consists of two or more steps, which requires isolation of intermediates. Although, most of these methods are satisfactory, the use of more complex reagents, often tedious work-ups and applicability to a limited number of carboxylic acids[1–5] means that there is still scope for alternative reagent systems for the preparation of nitriles from carboxylic acids.

Iodine and iodine reagent systems have found widespread application in organic synthesis because of their selectivity and simplicity of use. Our group has been working extensively on the development of novel methodologies under mild reaction conditions using various iodine reagents.[6]

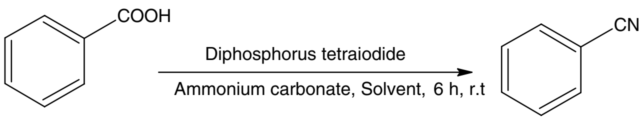
Diphosphorus tetraiodide is an orange crystalline solid, and is commercially available. This reagent exhibits high affinity for oxygen and acts as a unique reagent promoting substitution in the case of alcohols to form alkyl iodides,[7] dehydration in the case of aldoximes to give nitriles,[8] and reduction in the case of glycols or epoxides to form the corresponding alkenes.[9]

We observed that this reagent could be used in combination with ammonium carbonate at room temperature for the direct conversion of carboxylic acids to the corresponding nitriles. For our initial studies, benzoic acid was chosen as a model substrate. A mixture of benzoic acid (1.0 mmol), diphosphorus tetraiodide and ammonium carbonate (1.1 mmol) in anhydrous carbon disulfide was stirred at room temperature. The starting material was consumed within 6 h as indicated by TLC analysis. After work-up and purification by silica gel column chromatography (hexane:EtOAc, 9:1), benzonitrile was isolated in 90% yield. The reactions were also carried out in the presence of various anhydrous solvents and the results are presented in Table 1.

It was interesting to note that the reaction did not take place in the presence of acetonitrile, while in chloroform and dichloromethane, the reaction rate was slow.

Encouraged by these results we subjected various aromatic and aliphatic carboxylic acids to the reaction and the results are presented in Table 2. The results clearly indicate that acetyl, ether and ester groups are stable to the reaction conditions (Table 2, entries 4–7). Similarly, the heterocyclic aromatic carboxylic acid,

Table 1. Conversion of benzoic acid into benzonitrile using diphosphorus tetraiodide and ammonium carbonate in various solvents[a]



Entry	Solvent	Yield[a] (%)
1	CCl_4	75
2	CH_2Cl_2	60
3	$CHCl_3$	40
4	CH_3CN	NR[b]
5	CS_2	90

[a] Reaction conditions: substrate (1.0 equiv), diphosphorus tetraiodide (1.1 equiv), ammonium carbonate (1.1 equiv), 6 h.
[b] No reaction was observed.

Keywords: Diphosphorus tetraiodide; Ammonium carbonate; Carboxylic acid; Nitriles.

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Table 2. Nitriles from carboxylic acids using diphosphorus tetraiodide and ammonium carbonate[a]

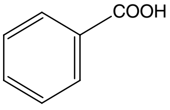
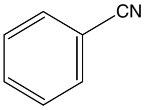
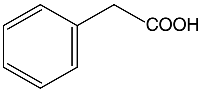
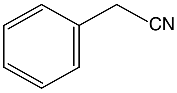
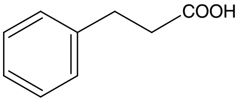
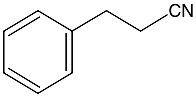
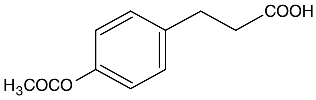
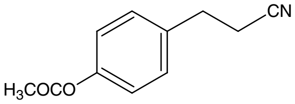
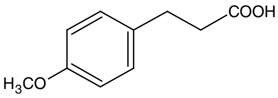
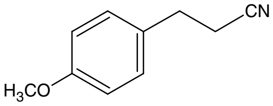
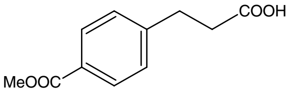
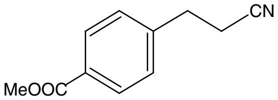
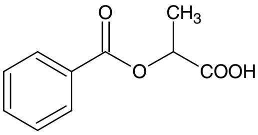
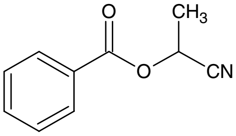
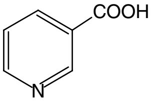
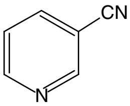
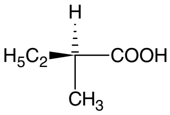
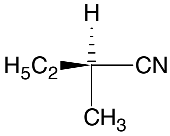
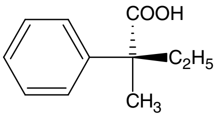
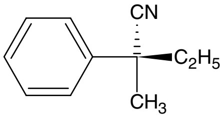
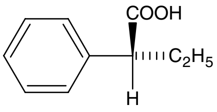
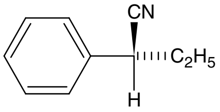
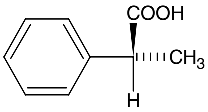
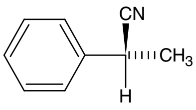
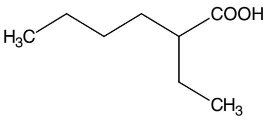
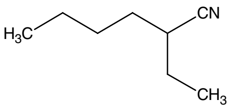
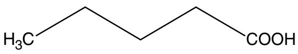
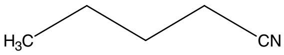
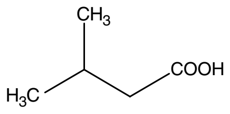
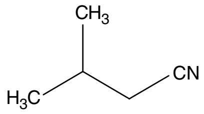
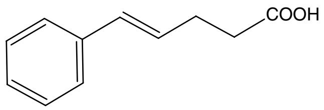
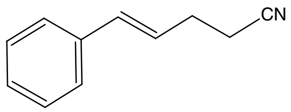
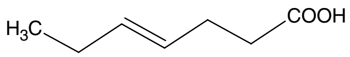
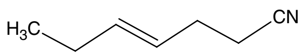
Entry	Substrate[b]	Product	Time (h)	Yield[c] (%)
1			6	90
2			6	92
3			6	90
4			7	80
5			7	85
6			7	80
7			8	88
8			5	90
9			9	85
10			7	85
11			7	90
12			7	90
13			9	92
14			9	85

Table 2 (*continued*)

Entry	Substrate[b]	Product	Time (h)	Yield[c] (%)
15			9	85
16			9	87
17			9	86

[a] Reaction conditions: substrate (1.0 equiv), diphosphorus tetraiodide (1.1 equiv), ammonium carbonate (1.1 equiv), anhydrous CS_2, rt.

[b] Starting compounds were prepared by standard literature procedures.

[c] Isolated yields after column chromatography. Structures confirmed by comparison of the IR and ^1H NMR spectra with those of authentic materials.

pyridine-3-carboxylic acid, was converted into 3-cyanopyridine in good yield (Table 2, entry 8).

The optically active acids, *R*-(−)-2-methyl-butanoic acid, *R*-(−)-2-phenyl-2-methyl-2-butanoic acid, *S*-(+)-2-phenyl butanoic acid and *S*-(+)-2-phenyl propionic acid, were converted into the corresponding nitriles without inversion of configuration (Table 2, entries 9–12).

A slower reaction rate was observed in the cases of the aliphatic carboxylic acids: 2-ethyl-hexanoic acid (entry 13), valeric acid (entry 14) and isovaleric acid (entry 15) which were converted to the corresponding nitrile compounds in good yields. Double bonds were not affected under these reaction conditions (entries 16 and 17).

In conclusion, a novel method has been developed for direct conversion of carboxylic acids to the corresponding nitriles using diphosphorus tetraiodide in combination with ammonium carbonate in anhydrous carbon disulfide at room temperature.[10] The method is mild and gave good to excellent yields of nitriles with both aliphatic and aromatic substrates.

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References and notes

1. Tsuneo, I.; Tomoko, T.; Masataka, Y. *Synthesis* **1983**, 142–143.
2. Hulkenberg, A.; Troost, J. J. *Tetrahedron Lett.* **1982**, 1505–1508.
3. Vincent, J. H.; Richard, A. B. *Tetrahedron* **1998**, *54*, 9281–9288.
4. Klein, D. A. *J. Org. Chem.* **1971**, *36*, 3050–3051.
5. Guthrie, L.; Rabjohn, N. *Org. Synth. Coll.* **1963**, *Vol. IV*, 513–514.
6. Telvekar, V. N.; Arote, N. D.; Herlekar, O. P. *Synlett* **2005**, 2495–2497.
7. Lauwers, M.; Regnier, B.; Van Eenoo, M.; Denis, J. N.; Krief, A. *Tetrahedron Lett.* **1979**, 1801–1804.
8. Suzuki, H.; Fuchita, T.; Iwasa, A.; Mishina, T. *Synthesis* **1978**, 905–908.
9. Newkome, G. R.; Sauer, J. D.; Erbland, M. L. *Chem. Commun.* **1975**, 885–886.
10. *General experimental procedure:* To a stirred solution of diphosphorus tetraiodide (1.1 equiv) in anhydrous CS_2 (15 mL) was added carboxylic acid (1.0 equiv). The resultant mixture was stirred at rt for 2 min followed by the addition of ammonium carbonate (1.1 equiv) and stirring was continued at rt until the starting material had been completely consumed (TLC). The reaction mixture was diluted with CS_2 and washed successively with 10% aq sodium bisulfite solution (2 × 15 mL), 10% aq $NaHCO_3$ (2 × 15 mL) and H_2O (1 × 10 mL). The organic layer was dried over Na_2SO_4 and concentrated in vacuo. The residue obtained was purified by silica gel column chromatography (10% EtOAc–hexane) to afford pure nitriles.