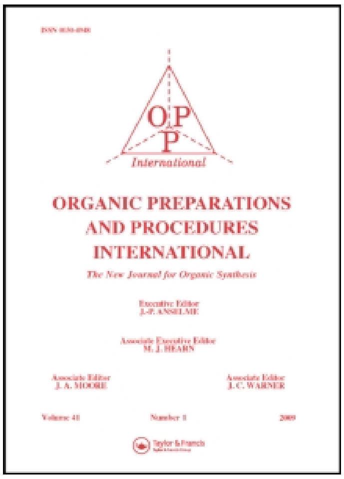


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

A SIMPLE 'ONE-POT' CONVERSION OF CARBOXYLIC ACIDS INTO NITRILES

A. D. Dunn[a]; M. J. Mills[a]; W. Henry[a]
[a] Dundee College of Technology, Dundee, SCOTLAND

To cite this Article Dunn, A. D. , Mills, M. J. and Henry, W.(1982) 'A SIMPLE 'ONE-POT' CONVERSION OF CARBOXYLIC ACIDS INTO NITRILES', Organic Preparations and Procedures International, 14: 6, 396 — 399
To link to this Article: DOI: 10.1080/00304948209354940
URL: http://dx.doi.org/10.1080/00304948209354940

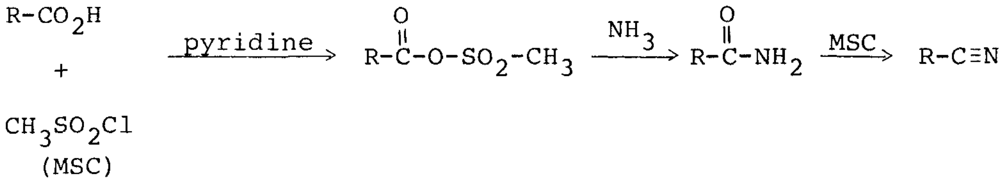
A SIMPLE 'ONE-POT' CONVERSION OF CARBOXYLIC ACIDS INTO NITRILES

Submitted by A. D. Dunn*, M. J. Mills and W. Henry
(5/4/82)

Dundee College of Technology
Bell Street
Dundee, DD1 1HG
SCOTLAND

Although several routes have been reported[1-3] for the direct conversion of carboxylic acids into nitriles, there are few general methods for this useful synthetic transformation. Relatively expensive chlorosulphonylisocyanate (CSI) is one reagent capable of converting $-CO_2H$ to $-C{\equiv}N$.[4-6] Other methods are in some cases[7] not applicable to carboxylic acids with sensitive functional groups (e.g. esters), or fail to give consistently high yields with a range of carboxylic acids of various structural types.[8] We now report a general method for the transformation of carboxylic acids into nitriles in high yields; this method is not, however, applicable to acids containing $-NH_2$, $-NHR$, $-OH$ or $-SH$ groups.

The carboxylic acid is initially converted into its mixed sulphonic anhydride with one equivalent of methanesulphonyl chloride (MSC) in dry pyridine at 0°.[9] Treatment of the mixed anhydride with ammonia gas at 0° followed by removal of the excess ammonia (rotary evaporator) yields an intermediate[10] which on recooling to 0° can be dehydrated by the addition of



$$\begin{matrix} R\text{-}CO_2H \\ + \\ CH_3SO_2Cl \\ (MSC) \end{matrix} \xrightarrow{\text{pyridine}} R\text{-}\overset{\overset{O}{\|}}{C}\text{-}O\text{-}SO_2\text{-}CH_3 \xrightarrow{NH_3} R\text{-}\overset{\overset{O}{\|}}{C}\text{-}NH_2 \xrightarrow{MSC} R\text{-}C{\equiv}N$$

further MSC.[11] The products are isolated after 24 hrs by either pouring the reaction mixture into dilute acid followed by extraction with ethyl acetate or in the case of substrates 6 and 7 (see Table), by removing the solvent *in vacuo* to give a residue which was partitioned between saturated $NaHCO_3$ and ethyl acetate. For example, 4-methoxybenzoic acid (2.55 g) and dry pyridine (85 ml) were stirred at 0° and MSC (1.92 g) added dropwise. After 1 hr. dry ammonia gas was passed into the reaction mixture for two minutes and the excess ammonia removed by placing the reaction vessel on the rotary evaporator for five minutes. The mixture was recooled to 0°, MSC (16 g) added and the mixture stirred at 20° for 24 hrs. The mixture was poured into dilute acid, the pH adjusted to 7, and the mixture extracted with ethyl acetate (2 x 100 ml). Concentration of the combined dried extracts gave 2.16 g. of crude 4-methoxybenzonitrile. Recrystallization from light petroleum gave 1.83 g (82%) of pure nitrile, mp. 58-59°. In several instances a colouration is produced in the initial reaction, e.g. red in the case of substrate 6 (see Table) and purple in the case of substrate 7. This fortuitous colouration greatly simplifies the procedure since it allows the anhydride to be titrated (if desired) with the ammonia gas (end point = yellow/orange). The results from a range of substrates are shown in the Table.

In conclusion we have described a general method for the conversion of carboxylic acids into nitriles in high yield, which should be of great synthetic use. Further studies on the use of mixed sulphonic-carboxylic anhydrides are continuing in this laboratory.

TABLE. Nitriles from Carboxylic Acids[1]

	Acid	Nitrile	Yield (%) (isolated)	mp. (bp.) (°C)
1.	3-nitrobenzoic	3-nitrobenzonitrile	70	118-119[2]
2.	4-methoxybenzoic	4-methoxybenzonitrile	82	58-59[2]
3.	4-chlorobenzoic	4-chlorobenzonitrile	72	93-94[2]
4.	cinnamic	cinnamonitrile	70	(249)[2]
5.	stearic	stearonitrile	78	39[2e]
6.	2-carbomethoxy nicotinic	2-carbomethoxynicotinonitrile	73	150-152[3]
7.	4-carbomethoxy nicotinic	4-carbomethoxynicotinonitrile	63	84.5-85.5[4]

---

[1] All mp's and bp's are uncorrected and all compounds had satisfactory analyses (C,H,N) and IR and pmr spectra are consistent with the proposed structure.

[2] Dictionary of Organic Compounds, Fourth Edition, Eyre and Spottiswoode (London) (1965), a) 117-118°, b) 61-62°, c) 94-96°, d) 255-256°), e) 42.5-43.5°.

[3] S. Fallab and M. Erlenmeyer, Helv. Chim. Acta., 34, 488, (1951), mp. 150-151°.

[4] E. Wenkert, E. B. Spitzner and R. L. Webb, Aust. J. Chem., 25, 433 (1972), mp. 82.5-83.5°.

REFERENCES

1. "The Chemistry of the Cyano Group", Z. Rappoport, Ed. Interscience Publishers, New York, N.Y. (1970).

2. "Compendium of Organic Synthetic Methods", Volume I, I. T. Harrison and S. Harrison, Interscience Publishers, New York, N.Y. (1971); Volume II, I. T. Harrison and S. Harrison, Interscience Publishers, New York, N.Y. (1974), Volume III, L. S. Hegedus and L. G. Wade, Jr., Interscience Publishers, New York, N.Y. (1977).

3. D. T. Mowry, Chem. Rev., 42, 189 (1948).

4. G. Lohaus, Chem. Ber., 100, 2719 (1967); Org. Synth., 50, 52 (1970).

5. R. Graf, Angew. Chem., 80, 183 (1968).

6. J. Bretschneider and K. Wallenfels, Tetrahedron, 24, 1078 (1968).

7. M. S. Newman, A. Arkell and T. Fukunaga, J. Am. Chem. Soc., 82, 2498 (1960).

8. P. Oxley, M. W. Patridge, T. D. Robson and W. F. Short, J. Chem. Soc., 763 (1946).

9. J. H. Brewster and C. J. Ciotti, Jr., J. Am. Chem. Soc., 77, 6214 (1955).

10. C. G. Overberger and E. Sarlo, ibid., 85, 2446 (1963).

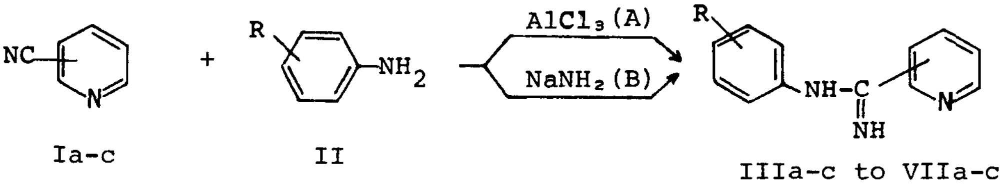
11. L. A. Carpino, ibid., 84, 2197 (1962).

AN EFFICIENT SYNTHESIS OF N'-(o-ALKOXYPHENYL)-PYRIDINECARBOXAMIDINE DERIVATIVES

Submitted by (2/25/82) Takuzo Hisano*, Masanobu Tasaki, Toshikazu Matsuoka and Masataka Ichikawa

Faculty of Pharmaceutical Sciences
Kumamoto University
5-1 Oe-honmachi, Kumamoto 862
JAPAN

N'-Aryl-pyridinecarboxamidines (III) are of current interest because of their useful biological properties,[1] and because they can serve as precursors of the corresponding benzimidazoles.[2] While the aluminum chloride-catalyzed condensation of



Ia-c II IIIa-c to VIIa-c

R = CH_3, C_2H_5 a) 2-pyridyl; b) 3-pyridyl; c) 4-pyridyl