OXIDATIVE DEGRADATION OF ARYLFURO-1,2-OXAZOLES TO ARYLNITRILES BY POTASSIUM PERMANGANATE

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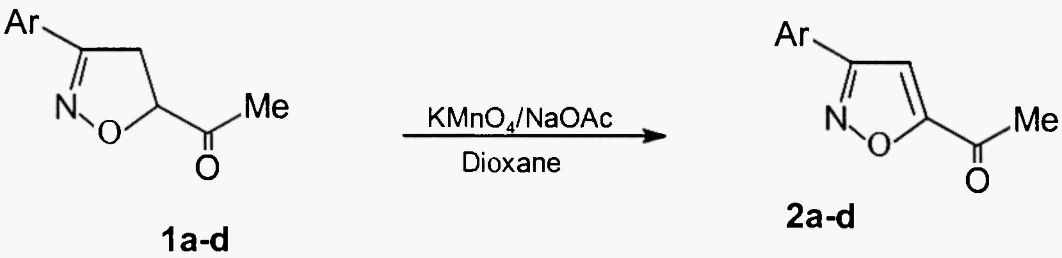
Abstract: Arylfuroisoxazolines are oxidatively degraded to arylnitriles by treatment with a mixture of potassium permanganate and sodium acetate in dry dioxane.

The ease of isoxazoline preparation through 1,3-dipolar cycloaddition reactions and the lability of the N-O bond have made this heterocyclic system a versatile intermediate in organic synthesis.[1] The isoxazolines are reductively cleaved to β-hydroxy ketones[2] or to aminoalcohols.[2,3] The latter methodology has been successfully applied to the synthesis of natural products.[3,4] β-Hydroxy ketones have also been prepared by peracid oxidation of 2-isoxazolines,[5] whereas oxidation of 4-isoxazolines leads to α,β-unsaturated carbonyl compounds.[6] Isoxazoles may be prepared from 2-isoxazolines under oxidative conditions.[7-9] However, few examples of dehydrogenation by $KMnO_4$ have been reported.[9]

Imidazolines can be dehydrogenated to imidazoles by treatment with $KMnO_4$ and NaOAc in dry dioxane.[10] By analogy, it was thought that isoxazoles could be obtained from isoxazolines. Accordingly, 5-acetylisoxazolines **1a-d** were dissolved in dry dioxane and treated with $KMnO_4$ (6 molar equivalents) and NaOAc (3 molar equivalents). The mixtures were stirred at 90 °C for 24 hours to give isoxazoles **2a-d** albeit in low yields.[11]

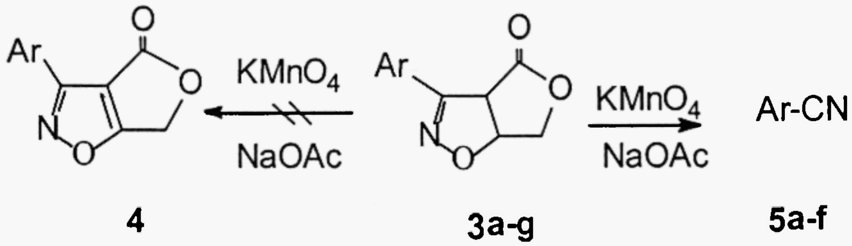


Ar: a, C_6H_5; b, 4-MeC_6H_4; c, 3,4-diMeOC_6H_3; d, 4-$NO_2C_6H_4$

By contrast, under similar experimental conditions the arylfuro derivatives **3a-g** were oxidized to the corresponding nitriles **5,** and the expected isoxazoles **4** were not obtained. The following procedure for 2-chloro-3,4-dimethoxybenzonitrile **5c** is representative.

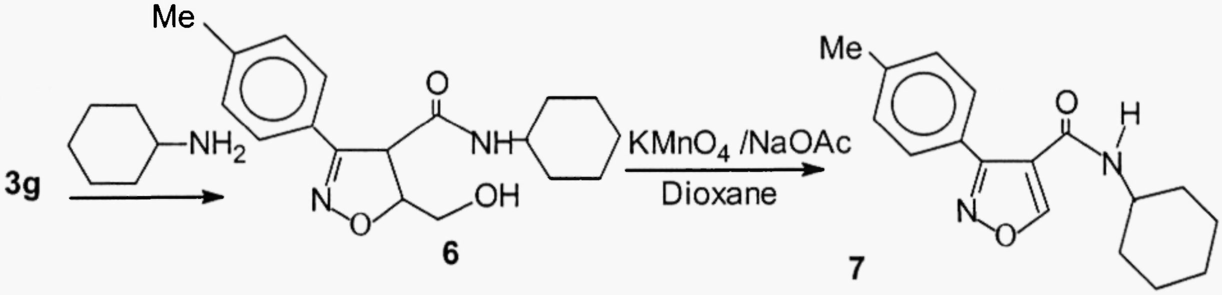
A solution of **3c** (1.0 g, 3.4 mmol) in anhydrous dioxane (12 mL) was treated with sodium acetate (2.0 g, 24.5 mmol). The suspension was heated to 60 °C, treated portionwise with powdered $KMnO_4$ (4.6 g, 29 mmol), and then heated under reflux for 24 h under a nitrogen atmosphere. The mixture was allowed to cool to room temperature, filtered through Celite and concentrated under a reduced pressure. Ethyl acetate (25 mL) was added to the residue and the solution was washed with water (3 x 15 mL), dried (anh. Na_2SO_4), and concentrated. Product **5c** was obtained by chromatography on silica gel eluting with ethyl acetate/hexane (1:9, v/v). The remaining compounds **5a, b, d-f** were obtained in a similar way.[14]

It is interesting to note that no reaction took place on the cycloadduct **3g** even after prolonged heating. Oxidation of substrates **3a-c** was also carried out with barium manganate [Mn(VI)] in dioxane to give the corresponding nitriles in similar yields. In both cases isoxazoles **4** were not detected.



3a-d, 5a-d	Ar	3e-g, 5e-f	Ar
a	3,4-dimethoxyphenyl	e	2-chloro-4,5-methylenedioxyphenyl
b	2-bromo-4,5-dimethoxyphenyl	f	2,6-dichlorophenyl
c	2-chloro-4,5-dimethoxyphenyl	g	4-tolyl
d	2-chloro-4-methoxyphenyl		

In another attempt to obtain the isoxazole ring the amide **6** derived from **3g**[17] was treated with potassium permanganate and sodium acetate. This reaction gave the 3,4-disustituted isoxazole **7** by oxidation of the hydroxymethyl group followed by decarboxylation.[18] Formation of the corresponding nitrile was not observed.



Arylnitriles have been prepared from 5-acylated-2-isoxazolines by base[19] or acid[20] treatment, but formation of arylnitriles from isoxazolines under oxidative conditions has not been previously reported. The overall result is the conversion of arylaldehydes into nitriles because furoisoxazolines behave like cyclic oximes.[21]

REFERENCES AND NOTES

1 (a) K.G.B. Torssell, Nitrile Oxides, Nitrones and Nitronates in Organic Synthesis, Novel Strategies in Synthesis, VCH Publishers, Inc. New York, 1988; (b) Ch. J. Easton, C.M. Hughes, G.P. Savage and G. W. Simpson, in Adv. Heterocycl.Chem. **60**, 261 (1994)

2 A. P. Kozikowski, Acc. Chem. Res. **17**, 410 (1984)

3 V. Jäger, R. Muller, T. Leibold, M. Hein, M. Schwarz, M. Fengler, L. Jaroskova, M. Pätzel, and

P-I. Leroy, Bull. Soc. Chim. Belg. **103**, 491 (1994)

4 (a) V. Jäger, H. Grund, V. Buβ, W. Schwäb, I. Muller, R. Schohe, R. Franz, and R. Ehrler, Bull. Soc. Chim. Belg. **92**, 1039 (1983); (b) P. G. Baraldi, A. Barco, S. Benetti, G. P. Pollini, D. Simoni., Synthesis, 857 (1987)

5 P. Park and A.P. Kozikowski, Tetrahedron Lett. **29,** 6703 (1988)

6 A. Padwa, D.N. Kline, and J. Perumattam, Tetrahedron Lett.**28**, 913 (1987)

7 (a) C. J. Easton, C.M. Hughes, and E.R.T. Tiekink, Tetrahedron Lett. **35**, 3589 (1994); (b) P. Grünanger and P.Vita - Finzi, Isoxazoles John Wiley & Sons, Inc., New York, 1991

8 A. Barco, S. Benetti, G.P.. Pollini, and P. G. Baraldi, Synthesis, 837 (1977)

9 W. R., Vaughan and J.L. Spenser, J. Org. Chem. **25**, 1160 (1960)

10 M. E. Campos, R. Jiménez, F. Martínez, and H. Salgado Zamora, Heterocycles **40**, 841 (1995)

11 Compound **2a:** yield 32 %, mp 103-103.5 ° C, reported[12] mp 102-103 ° C; **2b:** yield 27 %, mp 91-92 ° C, reported[13] mp 92-93 ° C; **2c:** yield 30 %, mp140-141 ° C, reported[13] mp 140-142 ° C; **2d:** yield 35 %, mp 158-159 ° C, reported[13] mp 157-159 ° C.

12 G. Bianchi and P. Grünanger, Tetrahedron **21,** 817 (1965)

13 R. Jimenez, L.Pérez, J, Tamariz, H. Salgado, Heterocycles **35**, 591 (1993)

14 The starting materials **3a-g** have been reported previously: (a) L. Fisera P. Oravec, L. Stibrányi, N.D. Kozina, and A. Badovskaja, Synthesis, 565 (1986); (b) R.Metelli and G. F.Bettinetti, Synthesis, 365 (1970). Product **5a:** yield 70 %, mp 69-70 ° C, reported[15] mp 66-68 ° C; **5b:** yield 51 %, mp 113-115 ° C; **5c:** yield 59 %, mp 90-92 ° C; **5d:** yield 40 %, mp 73-74 ° C, reported[16] mp 70-73 ° C; **5e:** yield 52 %, mp 128-121 ° C; **5f:** yield 50 %, mp 141-142 ° C, reported[16] mp 143-144 ° C. All compounds **5a-f** show IR absorption at ν 2200-2230 cm^{-1} for CN. The new products **5b, 5c** and **5e** gave satisfactory results of microanalysis (C, ± 0.4; H, ± 0.2; N, ± 0.5). Additional spectral data for **5c:** ^{1}HNMR ($CDCl_3$, 300MHz) δ7.05 (2s, 2H), 3.90 (s, 6H); MS m/z 243 (M^+).

15 C. S. Rao, M. Rambabu, and P.S. Srinivasan, Synth. Commun· **19**, 1431 (1989)

16 M. B. Sommer, M. Begtrup, and K. P. Bogeso, J. Org. Chem. **55**, 4817 (1990)

17 L. Fisera, P. Oravec, L. Stibrányi, N.D. Kozina, and L. A. Badovskaja, Czech, Cs. Pat. 250565 (Chem. Abstr., **110**, 95210v 1989)

18 Compound **7** was obtained a 30 % yield as a white solid, mp 62-63 ^{0} C, and gave the following spectroscopic data: IR (ν, cm^{-1}) 3248, 1638, 1590; ^{1}HNMR ($CDCl_3$) δ, 0.9-2.9 (m, 11 H), 2.4 (s, 3 H), 7.3 (d, 2 H), 7.4 (d, 2 H), 8.9 (s, 1 H); MS m/z 284 (M^+), 186 (100 %). Anal. Calcd for $C_{17}H_{20}N_2O_2$: C, 71.8; H,7.0; N, 9.8. Found: C, 71.4; H, 7.2; N, 9.3.

19 G. Bianchi, A. Gamba Invernizzi, and R. Gandolfi, J. Chem. Soc., Perkin I, 1757 (1974)

20 Z. K. Mukerji, K.K. Sharma, and K.B.G. Torssell, Tetrahedron, **39**, 223 (1983)

21 A. P. Kozikowski and M. Adamczyk, Tetrahedron Lett. **23**, 3123 (1982)

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