



FACILE SYNTHESIS OF NITRILES FROM PRIMARY NITRO COMPOUNDS VIA NITROLIC ACIDS AND THEIR ESTERS

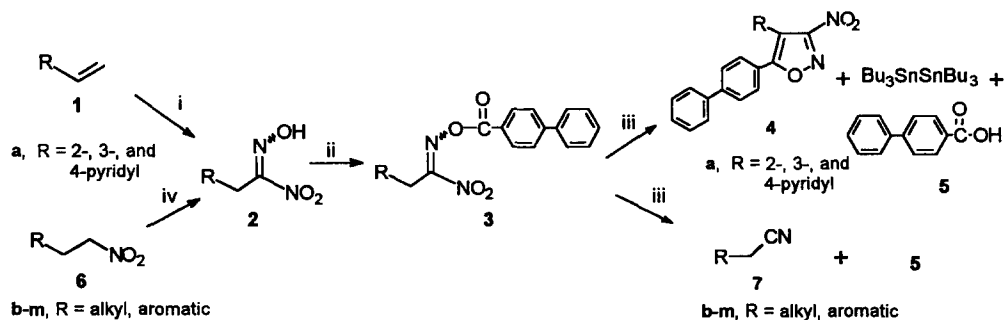
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Abstract: The reactions of alkane- and arylalkanenitrolic acids esters with Bu_3SnH in the presence of a catalytic amount of AIBN in refluxing benzene afforded the corresponding nitriles in excellent yields. Copyright © 1996 Elsevier Science Ltd

Alkanenitriles are an important class of organic compounds and have been synthesized by a variety of methods. Among them, direct conversion of nitro compounds into nitriles has been achieved by the reaction of alkali salts of nitromethyl compounds with diethylphosphorochloridite¹ or by subjecting primary nitro compounds to Vilsmeier-Haack formylation conditions at temperature above 100 °C.² Treatment of primary nitro compounds with either diphosphorous tetraiodide³ or phosphorous iodide⁴ in the presence of trimethylamine in CH_2Cl_2 at room temperature gave nitriles. Triethylamine - sulfur dioxide complex,⁵ hexamethylphosphorous triamide,⁵ or iodotrimethylsilane⁶ was reported to be good agents for conversion of primary nitro compounds into nitriles. Recently allylic nitro compounds were reported to give the corresponding nitriles by using CS_2 as the deoxygenating and dehydrating agent and tetrabutylammonium bromide or hydrogensulfate as the phase-transfer agent.⁷ Conversion of primary nitro compounds into thiohydroxamic acids in the dark by using $Me_3SiSSiMe_3$ under alkaline conditions, followed by decomposition in the light was reported to afford nitriles in good yields.⁸






One common feature of these reactions mentioned above is that the formation of nitriles from nitro compounds has been explained on the basis of ionic mechanisms.



In connection with our ongoing project for exploring the synthetic utility of nitrosonium ion with non-nucleophilic counter anion, 2-, 3-, and 4-vinylpyridines (**1**) were treated with nitrosonium tetrafluoroborate (NOBF₄) in CH₃CN at room temperature. From these reactions were isolated the corresponding pyridylacetonitric acids (**2a**).⁹ Compounds **2a** were readily converted to the corresponding crystalline nitric acids esters **3a** by the reactions with 4-biphenylcarbonyl chloride in the presence of Et₃N at room temperature.

Since secondary and tertiary nitro compounds were reported to be readily denitrated by Bu₃SnH in the presence of azobisisobutyronitrile (AIBN)¹⁰ and tin radicals were trapped by an ester carbonyl group,¹¹ it was of interest to see if compounds **3a** having an ester and a vinyl nitro functionalities react with Bu₃SnH under the conditions mentioned above. Treatment of compound **3a** (R = 2-pyridyl) with Bu₃SnH in the presence of a catalytic amount of AIBN in refluxing benzene gave 5-(4-biphenyl)-3-nitro-4-(2-pyridyl)oxazole (**4**)¹² (44%), hexabutylditin (85%), 4-biphenylcarboxylic acid (**5**) (31%), and unidentifiable complex mixtures along with unreacted compound **3a** (R = 2-pyridyl) (12%). The result prompted us to investigate the reactions of other nitric acids esters under the same conditions.

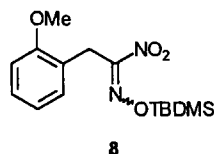
Table 1. Yields of nitric acids **2**,¹⁴ nitric acids esters **3**,¹⁵ 4-biphenylcarboxylic acid **5**,¹³ and nitriles **7**¹³

Entry	R	Yields ^a (%)			
		2	3	5	7
b	C ₆ H ₅	84	59	94	100
c	2-MeC ₆ H ₄	88	70	96	94
d	4-MeC ₆ H ₄	80	43	93	93
e	2-MeOC ₆ H ₄	81	93	95	100
f	4-MeOC ₆ H ₄	83	63	100	94
g	1-Naphthyl	93	62	95	98
h		92	15 ^b	94	94
i		78	^c	95	81
j		93	^c	97	86
k	C ₆ H ₅ COCH ₂	74	70	96	96
l		88	93	96	93
m		91	92	97	75

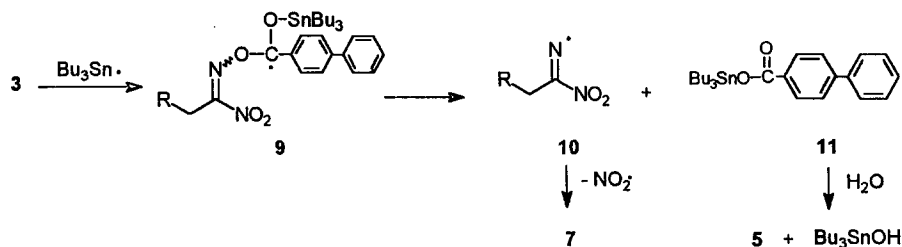
^aIsolated yield. ^bYield obtained in the absence of Et₃N. Only small amount of a fluorescent unknown compound was isolated in the presence of Et₃N under the same conditions. ^cCompounds **3i** and **3j** were directly treated with Bu₃SnH without isolation because of their instabilities.

Apart from the reaction with compound **3a** (R = 2-pyridyl), excellent yields of the corresponding nitriles were obtained from alkane- and arylalkanenitrolic acids esters of 4-biphenylcarboxylic acid **3** (R = alkyl, aromatic). The results are summarized in Table 1.¹³

The necessity of the ester functionality for the formation of nitriles was confirmed by the reaction of **2b** with Bu₃SnH under the same conditions. However, only **2b** was quantitatively recovered. This result indicates that the nitro groups of nitrolic acids **2** are unable to be reduced by Bu₃SnH. In addition, it might be reasonable to assume that tin radicals are trapped by ester carbonyl groups of **3** as an initial step. The fact that compound **8**¹⁷ having a protected oxime functionality by *tert*-butyldimethylsilyl moiety (TBDMS) was quantitatively recovered under the same reaction conditions supports further the inertness of vinyl nitro groups of compounds **2** to Bu₃SnH or tin radicals.



The formation of nitriles from compounds **3** might be explained by trapping of the tin radical by compounds **3** to give a new radical intermediates **9**, which undergo a bond cleavage between nitrogen and oxygen atoms leading to imino radicals **10** and 4-biphenylcarboxylate **11**. Since fragmentation of imino radicals to nitriles has been well established,^{11,17} the imino radicals **10** are expected to lose •NO₂ to give nitriles **7**. The formation of compound **5** can be explained by hydrolysis of **11** (Scheme 1).



Scheme 1

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12. The procedure leading to compound **4** is the same as that described in a typical procedure of ref. 13. Compound **4**: mp 165-166 °C (CCl₄); MS m/z 343; ¹H NMR (80MHz, CDCl₃) δ 8.74 - 7.40 (m, 13H); IR (KBr, pellet) 2920, 1598, 1517, 1477, 1366, 995 cm⁻¹; Anal Calcd for C₂₀H₁₃N₃O₃: C, 69.97; H, 3.82; N, 12.24; Found: C, 70.09; H, 4.16; N, 12.36.
13. Typical procedure: To a solution of **3f** (101 mg, 0.259 mmol) in benzene (20 mL) were added Bu₃SnH (87 mg, 0.297 mmol) and AIBN (10 mg). The mixture was heated for 3h at reflux and then cooled to room temperature. After removal of the solvent, the residue was chromatographed on a silica gel (70 - 230 mesh, ASTM, 1 x 15 cm) column. Elution with *n*-hexane (200 mL) gave a mixture of hexabutyliditin and other unidentified compounds (145 mg). Elution with a mixture of *n*-hexane and EtOAc (5:1, 70 mL) gave unknown mixtures (12 mg). Elution with the same solvent mixture (30 mL) gave 2-methoxyphenylacetonitrile (**7f**) (36 mg, 94 %): ¹H NMR (80 MHz, CDCl₃) δ 7.23 (d, *J* = 11.2 Hz, 2H), 6.88 (d, *J* = 11.2 Hz, 2H), 3.80 (s, 2H); IR (KBr, neat) 2960, 2256, 1612, 1587, 1514, 1466, 1306, 1181, 1034 cm⁻¹. Elution next with the same solvent mixture (2:1, 100 mL) gave **5** (52 mg, 100 %).
14. Synthesis of compounds **2** from compounds **6** was achieved by the literature methods: Hegarty A. F.; Egan C.; Clery M.; Welch A. J. *J. Chem. Soc., Perkin Trans. 2* **1991**, 249-256. Compound **2c**: mp 86-87 °C (*n*-Hexane); ¹H NMR (80MHz, CDCl₃) δ 12.70 (s, 1H), 7.10 (s, 4H), 4.21 (s, 2H), 2.33 (s, 3H); IR (KBr, pellet) 3280, 1549, 1494, 1418, 1338, 1030 cm⁻¹; Anal Calcd for C₉H₁₀N₂O₃: C, 55.66; H, 5.19; N, 14.43; Found: C, 55.52; H, 5.11; N, 14.17.
15. Compound **3c**: mp 122-124 °C (*n*-Hexane); ¹H NMR (80MHz, CDCl₃) δ 8.09-7.17 (m, 13H), 4.42 (s, 2H), 2.37 (s, 3H); IR (KBr, pellet) 1765, 1608, 1550, 1248, 1043 cm⁻¹; Anal Calcd for C₂₂H₁₈N₂O₄: C, 70.58; H, 4.85; N, 7.48 ; Found: C, 70.54; H, 4.87; N, 7.45.
16. Compound **8**: Colorless liquid; MS m/z 324; ¹H NMR (80MHz, CDCl₃) δ 7.29-6.73 (m, 4H), 4.18 (s, 2H), 3.73 (s, 3H), 0.84 (s, 9H), 0.26 (s, 6H); IR (KBr, neat) 2960, 1603, 1546, 1494, 1290, 1027 cm⁻¹; Anal Calcd for C₁₅H₂₄N₂O₄Si: C, 55.53; H, 7.46; N, 8.63 ; Found: C, 55.70; H, 7.55; N, 8.47.
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