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

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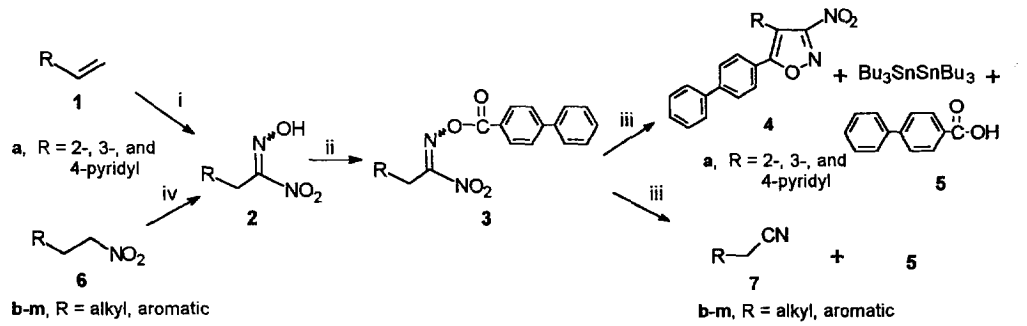
Abstract: *The reactions of alkane- and arylalkanenitrolic acids esters with Bu_3SnH in the presence of a catalytic amount of AIBN in refluxing benzene afforded the corresponding nitriles in excellent yields.* Copyright © 1996 Elsevier Science Ltd

Alkanenitriles are an important class of organic compounds and have been synthesized by a variety of methods. Among them, direct conversion of nitro coupounds into nitriles has been achieved by the reaction of alkali salts of nitromethyl compounds with diethylphosphorochloridite[1] or by subjecting primary nitro compounds to Vilsmeir-Haack formylation conditions at temperature above 100 °C.[2] Treatment of primary nitro compounds with either diphosphorous tetraiodide[3] or phosphorous iodide[4] in the presence of trimethylamine in CH_2Cl_2 at room temperature gave nitriles. Triethylamine - sulfur dioxide complex,[5] hexamethylphosphorous triamide,[5] or iodotrimethylsilane[6] 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.



Reagents and conditions: i, $NOBF_4$, CH_3CN, r.t.; ii, 4-biphenylcarbonyl chloride, Et_3N, CH_2Cl_2, r.t.; iii, Bu_3SnH, AIBN, PhH, Δ; iv, $NaNO_2$, NaOH, MeOH, 0 °C.

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 ($NOBF_4$) in CH_3CN at room temperature. From these reactions were isolated the corresponding pyridylacetonitrolic acids (**2a**).[9] Compounds **2a** were readily converted to the corresponding crystalline nitrolic acids esters **3a** by the reactions with 4-biphenylcarbonyl chloride in the presence of Et_3N at room temperature.

Since secondary and tertiary nitro compounds were reported to be readily denitrated by Bu_3SnH 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 Bu_3SnH under the conditions mentioned above. Treatment of compound **3a** (R = 2-pyridyl) with Bu_3SnH in the presence of a catalytic amount of AIBN in refluxing benzene gave 5-(4-biphenylyl)-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 nitrolic acids esters under the same conditions.

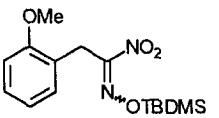
Table 1. Yields of nitrolic acids **2**,[14] nitrolic acids esters **3**,[15] 4-biphenylcarboxylic acid **5**,[13] and nitriles **7**[13]

		Yields[a](%)			
Entry	R	**2**	**3**	**5**	7
b	C_6H_5	84	59	94	100
c	2-MeC_6H_4	88	70	96	94
d	4-MeC_6H_4	80	43	93	93
e	2-$MeOC_6H_4$	81	93	95	100
f	4-$MeOC_6H_4$	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	$C_6H_5COCH_2$	74	70	96	96
l		88	93	96	93
m		91	92	97	75

[a]Isolated yield. [b]Yield obtained in the absence of Et_3N. Only small amount of a fluorescent unknown compound was isolated in the presence of Et_3N under the same conditions. [c]Compounds **3i** and **3j** were directly treated with Bu_3SnH 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 Bu_3SnH 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 Bu_3SnH. 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 Bu_3SnH or tin radicals.



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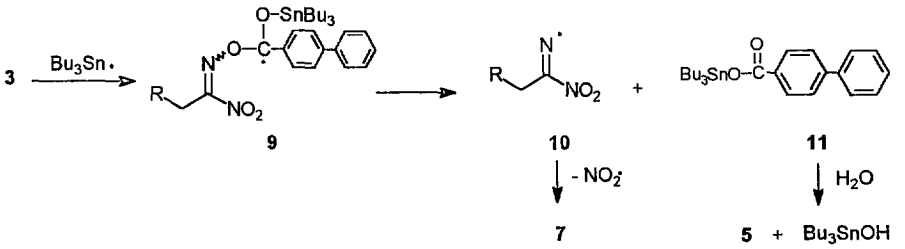
The formation of nitriles from compounds **3** might be explained by trapping of the tin radical by compounds **3** to give a new radical intermediates **9**, which undergo a bond cleavage between nitrogen and oxygen atoms leading to imino radicals **10** and 4-biphenylcarboxylate **11**. Since fragmentation of imino radicals to nitriles has been well established,[11,17] the imino radicals **10** are expected to lose $\cdot NO_2$ 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 (CCl_4); MS m/z 343; ^1H NMR (80MHz, $CDCl_3$) δ 8.74 - 7.40 (m, 13H); IR (KBr, pellet) 2920, 1598, 1517, 1477, 1366, 995 cm^{-1}; Anal Calcd for $C_{20}H_{13}N_3O_3$: 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 Bu_3SnH (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 hexabutylditin 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, $CDCl_3$) 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, $CDCl_3$) 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 $C_9H_{10}N_2O_3$: 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, $CDCl_3$) 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 $C_{22}H_{18}N_2O_4$: 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, $CDCl_3$) 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 $C_{15}H_{24}N_2O_4Si$: C, 55.53; H, 7.46; N, 8.63 ; Found: C, 55.70; H, 7.55; N, 8.47.
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