The Conversion of Carboxylic Acids into Isonitriles *via* Selenium-Phenyl Selenocarbamates

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Carboxylic acids are converted into isonitriles *via* Schmidt rearrangement of the derived acyl azides, addition of phenylselenol to the resultant isocyanate, tributylstannane reduction and dehydration.

Recently, during work on isonitrile antibiotics,[1] we had need to convert an α,β-unsaturated carboxylic acid into vinyl isonitrile under mild non-polar conditions. In principle, such a transformation should be possible *via* conversion of the acid into a vinyl isocyanate,[2] reduction[2,3] and dehydration of the resultant vinyl formamide.[2,4] Alternatively, there is the possibility of directly deoxygenating the isocyanate to reveal the isonitrile.[5] However, neither of these methods are appropriate for delicate vinyl isonitriles. Since Baldwin showed, with his studies on isonitrin B,[6] that delicate vinyl formamides may be dehydrated to the corresponding isonitriles in high yields, we sought a radical method to convert vinyl isocyanates into vinyl formamides. Herein, we report our first observations on this process.

Octanoyl chloride **1** was converted into the corresponding *Se*-phenyl selenocarbamate **3**†[7] (65%) by reaction with sodium azide in *N,N′*-dimethylformamide (DMF), rearrangement of the resultant acyl azide **2** by heating in toluene and addition of benzeneselenol[8] to the intermediate heptyl isocyanate (Scheme 1). The selenol addition was catalysed using potassium *tert*-butoxide. Heating the selenocarbamate **3** with tributylstannane in benzene under reflux in the presence of azoisobutyronitrile (AIBN) gave *N*-heptyl formamide **4**[9] (94%). Clearly, this reaction proceeds *via* homolysis of the weak carbon–selenium bond[10] and subsequent hydrogen atom transfer to the carbamyl radical. Finally, dehydration of formamide **4** using toluene-4-sulfonyl chloride in pyridine[2] gave heptyl isonitrile **5**[1] (88%).

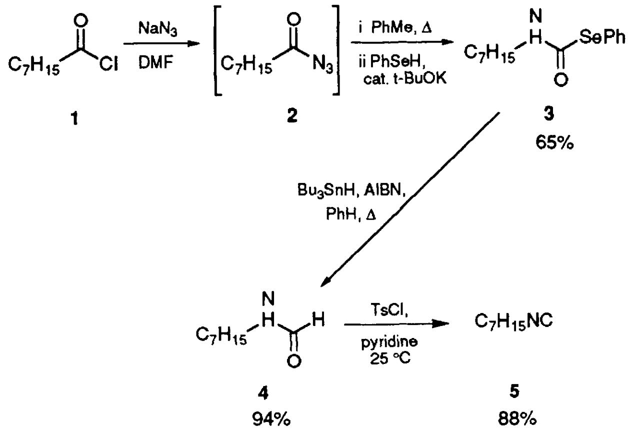


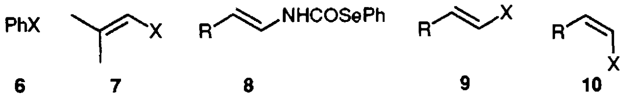
Table 1 Conversion of acyl chlorides into isonitriles

	Selenocarbamate (%)	Formamide (%)	Isonitrile (% Method[a])
1	**3** (65)	**4** (94)	**5** (88, i)
2	**6a** (82)	**6b** (88)	[b]
3	**7a** (63)	**7b** (73)	[c]
4	**8a** (78)	**9a** (65)	**9c** (65, ii)
		10a (7)	—
5	[d]	**9b** (39)	**9d** (52, ii)
		10b (15)	**10d** (58, ii)

[a] i TsCl, pyridine, 25 °C; ii Tf_2O, Pr^i_2NEt, CH_2Cl_2, −78 °C; [b] See reference 3. [c] Volatile unstable product not isolated. [d] Selenocarbamate **8b** routinely not isolated but reduced directly.

The methodology was extended to a range of carboxylic acids including α,β-unsaturated systems (Table 1).‡ Several acyl chlorides were converted into the corresponding isocyanates in the standard way and without purification, were allowed to react with benzeneselenol catalysed by potassium *tert*-butoxide to provide the corresponding selenocarbamates. In entry 5, the selenocarbamate was found to decompose extensively on attempted purification and it was converted directly into the corresponding vinyl formamides **9b** and **10b**. Indeed all of the selenocarbamates were sensitive and the lower yields in entries 1 and 3 reflect chromatographic losses rather than inefficiency of reaction. It is interesting to note that (*E*)-cinnamoyl chloride (entry 4) was converted into the corresponding (*E*)-selenocarbamate **8a** with retention of geometry.

Radical cleavage of the selenocarbamates gave the corresponding formamides. Both alkenyl formamides were obtained as mixtures of *E*- and *Z*-isomers (**9a**:**10a** 9:1; **9b**:**10b** 39:15). Chromatography gave samples of geometrically pure (*E*)-non-1-enylformamide (**9b**, 39%) and (*Z*)-non-1-enylformamide (**10b**, 15%). Finally, dehydration of the formamides **9a**, **9b** and **10b** using trifluoromethanesulfonic anhydride and ethyl(diisopropyl)amine in dichloromethane at −78 °C[6] gave the corresponding isonitriles **9c**, **9d** and **10d**. Dehydration of formanilide **6b** is reported elsewhere.[3] Attempts to isolate the vinyl isonitrile from formamide **7b** were complicated by its volatility and instability.



a X = NHCOSePh
b X = NHCHO

a R = Ph
b R = C_7H_{15}

a R = Ph, X = NHCHO
b R = C_7H_{15}, X = NHCHO
c R = Ph, X = NC
d R = C_7H_{15}, X = NC

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† New compounds were fully characterised by spectroscopic data and microanalyses and/or MS with the following exceptions: the unstable isonitriles **9c**, **9d** and **10d** were characterised by IR, ^1H NMR and ^{13}C NMR spectroscopy only.

‡ The following procedures for the preparation of selenocarbamate **3**, formamide **4** and isonitrile **5** are representative: octanoyl chloride (0.51 ml) was added with stirring to NaN_3 (0.23 g) in DMF (5 ml). After 2 h, the mixture was diluted with Et_2O and washed with H_2O. The organic layer was dried ($MgSO_4$), evaporated, dissolved in toluene (5 ml) and heated at 100 °C for 6 h (Ar). The solution was then cooled to 0 °C and PhSeH (0.32 ml) and Bu^tOK in THF (1 mol dm^{-3}; 0.3 ml) added sequentially. The reaction mixture, containing a yellow precipitate, was allowed to warm to room temp., stirred for 30 min, diluted with Et_2O, washed with H_2O, dried ($MgSO_4$) and evaporated. Chromatography on silica (hexane : ethyl acetate 10 : 1) gave **3** (0.579 g, 65%). Bu_3SnH (0.11 ml) and AIBN (10 mg) were added to **3** (80 mg) in benzene (5 ml). After heating under reflux for 8 h, the mixture was cooled to room temp. and evaporated. Chromatography on silica (ethyl acetate) gave **4**[9] (36 mg, 94%). Dehydration of **4** (0.258 g) using TsCl and pyridine[2] gave **5**[11] (0.219 g, 88%).

It is clear from these results that radical-mediated deselenylation of selenocarbamates represents a useful method for the synthesis of delicate formamides and isonitriles.

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