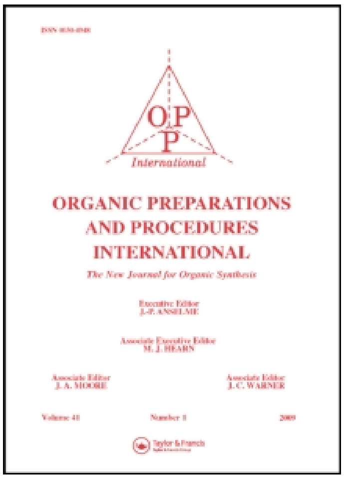

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AN EFFICIENT ONE-POT SYNTHESIS OF α-PHENYLSELENO-α,β-UNSATURATED NITRILES *via* ARSONIUM SALTS

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AN EFFICIENT ONE-POT SYNTHESIS OF α-PHENYLSELENO-α,β-UNSATURATED NITRILES *via* ARSONIUM SALTS

Submitted by
(06/02/99)

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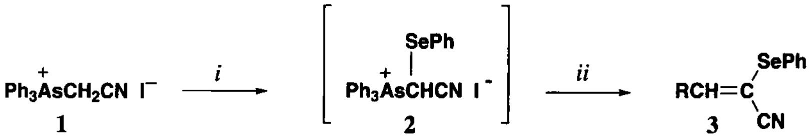
Functionalized vinyl selenides bearing α-electron-withdrawing groups such as the cyano group, have been found to be particularly useful radical acceptors, leading generally to fumaronitriles by treatment with a radical initiator, followed by dimerization and elimination of dialkyl diselenide.[1] Vinyl selenides and ethylenes bearing electron-withdrawing groups, undergo [2+2]-cycloaddition to afford selenocyclobutanes.[2] The selenyl group may readily be replaced by various groups to afford substituted unsaturated compounds.[3,4]

α-Phenylseleno-α,β-unsaturated nitriles have only been prepared by the addition of phenylselenenyl chloride, bromide or amide to the respective α,β-unsaturated nitriles, followed by elimination of hydrogen halide albeit in low overall yields.[5] This has greatly stimulated our interest in exploring an efficient one-pot synthesis of α-phenylseleno-α,β-unsaturated nitriles *via* the readily available arsonium salt **1** under mild condition in good yields. The arsonium iodide **1** reacted with phenylselenenyl iodide in the presence of anhydrous potassium carbonate at room temperature to produce the α-selenoarsonium iodide **2** which, without isolation, was treated with aromatic aldehydes to produce α-phenylseleno-α,β-unsaturated nitriles **3** in good yields; however, the yields were low with aliphatic aldehydes. The results are compiled in Table 1.



i) PhSeI, K_2CO_3, CH_3CN, RT *ii*) K_2CO_3, RCHO, RT or 60°

a) R= p-MeC_6H_4 b) R= p-$O_2NC_6H_4$ c) R= o-$O_2NC_6H_4$ d) R= m-$O_2NC_6H_4$
e) R= p-ClC_6H_4 f) R= p-BrC_6H_4 g) R= 2,4-$Cl_2C_6H_3$ h) R = $CH_3(CH_2)_2$
i) R = $CH_3(CH_2)_3$

The arsonium salt **1** was synthesized from triphenylarsine and chloroacetonitrile in the presence of potassium iodide under reflux. Triphenylcyanomethylenearsonium salts have been prepared generally from triphenylarsine and the more expensive bromoacetonitrile.[6] The modified method is less expensive and gave better yields. However, triphenylcyanomethylenearsonium iodide is more sensitive than triphenylcyanomethylene arsonium bromide to light and heat, and must be stored under dry conditions and protected from light.

TABLE 1. Yields, mps, Elemental Analysis and Spectral Data of Compounds **3**

Cmpd	Yield (%)	mp.^{a} (°C)	Time^{b,c} (hrs)	IR (cm^{-1}) (CN)	^{1}H NMR (δ)	Elemental Analysis (Found)			MS m/z (M$^+$)
						C	H	N	
3a	70	80-82	26	2220	7.69(d, 2H, J = 9Hz); 7.55-7.22(m, 6H)	61.17 (61.15)	4.17 (4.23)	4.46 (4.39)	314
3b	85	196-198^d	24^e	2210	8.21(d, 2H, J = 9Hz); 7.78(d, 2H, J = 9Hz); 7.62-7.19(m, 6H)	54.74 (54.61)	3.06 (3.02)	8.51 (8.68)	329
3c	86	62-64	14	2210	8.41-8.21(m, 2H); 7.79-7.35(m, 8H)	54.74 (54.99)	3.06 (3.19)	8.51 (8.43)	329
3d	80	65-67	26	2210	8.34-8.15(m, 2H); 7.74-7.38(m, 8H)	54.74 (54.96)	3.06 (3.02)	8.51 (8.79)	329
3e	78	57-60	24^e	2200	7.72-7.52(m, 4H); 7.38-7.27(m, 6H)	56.55 (56.44)	3.16 (3.18)	4.40 (4.53)	318
3f	70	49-51	21	2210	7.71-7.54(m, 4H); 7.45-7.28(m, 6H)	49.62 (49.54)	2.78 (2.90)	3.86 (3.96)	362
3g	75	52-53	22	2210	8.06-7.91(m, 1H); 7.67-7.21(m, 8H)	51.03 (51.17)	2.57 (2.65)	3.97 (3.83)	352
3h	34	oil	60	2220	7.52-7.12(m, 5H); 6.57(t, 1H, J = 8Hz); 2.33(q, 2H, J = 7Hz); 1.75-1.19(m, 2H); 0.89(t, 3H, J = 7Hz)	57.61 (57.69)	5.24 (5.37)	5.60 (5.51)	250
3i	35	oil	60	2220	7.46-7.03(m, 5H); 6.53(t, 0.95H, J = 8Hz); 6.18(t, 0.05H, J = 7Hz); 2.63-1.94(m, 2H); 1.73-1.10(m, 4H); 0.85 (t, 3H, J = 7Hz)	59.09 (58.81)	5.72 (5.81)	5.30 (5.25)	264

a) Recrystallized from diethyl ether, unless otherwise noted. b) The phenylselenenylation of arsonium iodide **1** was complete after 8 h. c) At 60°, unless otherwise noted. d) Recrystallized from CCl_4. e) Reaction temperature: r.t.

EXPERIMENTAL SECTION

^{1}H NMR spectra were determined in CCl_4 solution using hexamethyldisilane (HMDS) as the internal standard at 60MHz on a Varian PMX60SI. IR spectra were recorded on a PE683 instrument. Mass spectra were obtained with electron ionization (EI) on a HP 5989A mass spectrometer. Melting points are uncorrected. Benzeneselenenyl iodide was synthesized *in situ* from equimolar amount of diphenyl diselenide and iodine at room temperature according to the literature.[7] Acetonitrile was dried with P_2O_5 under 2 h reflux and redistilled before use.

Synthesis of Triphenylcyanomethylenearsonium Iodide (1).- A mixture of triphenylarsine (3.06 g, 10 mmol), chloroacetonitrile (0.755 g, 10 mmol) and potassium iodide (1.66 g, 10 mmol) in dry acetonitrile (10 mL) was stirred under 4 h reflux in the absence of light. After cooling at room temperature, the mixture was filtered to remove inorganic salts. The solvent was removed at 60° (oil-bath) under reduced pressure; then 5 mL of acetone was added to the residue (~2 mL) to precipitate a yellowish white solid. The solid was washed with small amount of acetone to give a pure white solid which was recrystallized from ethanol-diethyl ether, mp. 155-156°. Yield: 3.55g (81%). ^{1}H NMR (60MHz, $CDCl_3$, TMS): δ 7.85-7.66 (m, 15H), 5.82 (s, 2H). IR (KBr) cm^{-1}: 2250(m), 1495(s), 1395(s), 1180(m), 1085(s), 1000(s), 840(m), 735(s), 685(s).

Anal. Calcd for $C_{20}H_{17}AsIN$: C, 50.77; H, 3.62; N, 2.96; I, 26.07
Found: C, 50.52; H, 3.71; N, 2.82; I, 26.32

Preparation of 3-(4-Methoxyphenyl)-2-phenylselenoacrylonitrile (3a). Typical Procedure.- A mixture of triphenylcyanomethylenearsonium iodide **1** (0.473 g, 1.0 mmol), potassium carbonate (0.138 g, 1.0 mmol) and phenylselenenyl iodide (1.0 mmol) in acetonitrile (4 mL) was stirred at room temperature under nitrogen. After 8 h, the color of phenylselenenyl iodide had almost disappeared, indicating that the reaction was completed. *p*-Methoxybenzaldehyde (0.11 g, 0.9 mmol), potassium carbonate (0.138 g, 1 mmol) and a trace water (10 mL) were added into the above mixture. After stirring at 60° (oil-bath) for 26 h, the reaction was completed (monitored by TLC). After cooling, diethyl ether (10 mL) was added to the reaction mixture which was then filtered to remove triphenylarsine oxide and inorganic salts. The filtrate was concentrated and separated by flash chromatography on a preparative TLC (light petroleum-diethyl ether 7:3 as eluent) to afford **3a**. The yields, mps, elemental analyses and spectral data of compounds (**3a-3i**) are given in Table 1.

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AN IMPROVED SYNTHESIS OF N^{α}-BENZYLOXYCARBONYL-L-LYSINE

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(05/27/99)

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Lysine contains two amino groups and thus may form peptides (α-peptides) and isopeptides (ε-peptides). The former (α-peptides) occur universally and their synthesis[1] and the production of the suitable derivatives for them[2] has been elaborated. Those latter occur first of all in fungi and bacteria.[3,4] Since ε-peptides containing lysine are less common, it is anticipated that future studies will be focused on these isopeptides.

Z-Lys[5] belongs to the type of derivatives useful in ε-peptide synthesis.[6] The compound is produced on a large scale in a two-step process *via* blocking with the N^{ε}-benzylidene group; N^{ε}-benzylidene-L-lysine is isolated and subjected to the action of benzyl chlorocarbonate followed by treatment with hydrochloric acid to remove the N^{ε}-benzylidene protection.[7] This sequence gives only 66% yield of Z-Lys, based on lysine. Moreover, the process has severe inconveniences resulting from the great instability of the benzylidene derivative. Introduction of the benzylidene group must be performed under nitrogen and argon. All reactions and operations during the preparation of N^{ε}-benzylidene-L-lysine and N^{α}-benzyloxycarbonyl-N^{ε}-benzylidene-L-lysine require low temperatures. Its maintenance is troublesome, particularly during benzyloxycarbonylation, an exothermic process accompanied by local overheating. In our hands, the synthesis of N^{ε}-benzylidene-L-lysine failed.