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ULTRASONIC FORMATION AND REACTIONS OF SODIUM PHENYLSELENIDE

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Abstract: Treatment of diphenyldiselenide with sodium metal in tetrahydrofuran under ultrasonic conditions conveniently gave a suspension of sodium phenylselenide which could be transferred by syringe or cannula and reacted with sulphonates, halides and epoxides.

The impact that organoselenium chemistry has had on modern organic synthesis is undisputed. While there are many methods for the introduction of the seleno-substituent, the use of phenylselenide anions is especially common. Several methods for the preparations of the requisite selenide anions have been recommended, the more important of which include the use of diphenyldiselenide with sodium borohydride in THF/EtOH[1] or using resin bound borohydride,[2] reduction of the diselenide with sodium in ammonia[3] or in boiling THF followed by solvation in HMPA.[4] Alternatively sodium phenylselenide may be obtained from the selenol using sodium hydride in THF[4] or even by treatment with aqueous sodium hydroxide under certain conditions.[5] The use of diphenyldiselenide and lithium aluminium hydride has also recently been reported[6] to give the selenide anion. Grignard reagents react with selenium to give selenide anions,[7] although aggregates formed in these reactions can react with variable results.

Despite these extensive studies the clean and efficient generation of selenide salts continues to cause practical problems owing to the odiferous nature of certain reagents, the use of toxic or incompatible solvents and the lack of reactivity of some of these salts. Here we report a method which solves these problems and provides an extremely mild and convenient process for the preparation of sodium phenylselenide. †

The method is based upon the observation that low intensity ultrasonication[§] dramatically improves the rate of reaction between diphenyldiselenide and metallic sodium in tetrahydrofuran.

$$PhSeSePh + 2Na \longrightarrow 2\ PhSe^{\ominus}Na^{\oplus}$$

The role of ultrasound in systems such as these has not been fully established but its rate enhancing effects would appear to stem from a combination of cavitational effects and increased mass transport from the bulk of the liquid to the surface of the metal as a result of acoustic streaming. Collapse of the cavitation bubbles at the interface momentarily produces huge increases in local pressures and temperatures. It also causes erosion of the surface which can be construed to augment the number of initiation sites available for reaction. Furthermore it generates high intensity shock waves, thought to be of the magnitude of 10^4 atmosphere, that is strong enough to produce plastic deformation in malleable metals.[8]

In our system the dependence of the rate of reaction on the total surface area of metal available is illustrated by the 3-fold decrease in reaction time observed when a commercial dispersion was used in place of the solid metal (Table 1).

In common with Luche *et al*[9] we have noted the tendency of sodium to aggregate in THF and found that the reaction time could be halved by using xylene in its place. However, from a practical point of view, the high boiling point of xylene makes its removal difficult and its use would limit the method to preparation of involatile and thermally stable selenides.

The greatest enhancement in rate of reaction was observed when a catalytic amount of benzophenone was added to the reaction mixture as an electron carrier. This modification had the added advantage that the reaction became self indicating as a result of the presence of the characteristically dark blue colour of sodium benzophenoneketyl. Dropwise addition of a solution of diphenyldiselenide appeared to result in virtually instantaneous formation of the cream coloured sodium phenylselenide and reaction was complete when the last mauve tinges of sodium benzophenoneketyl had disappeared.

The homogeneous colloidal suspension can then be transferred by syringe or cannula to the reaction vessel. The suspension is stable in the absence of oxygen and could be stored in a sealed flask for up to one week without any notable decrease in reactivity.

We have also briefly studied the reactivity of this ultrasonically generated salt towards nucleophilic reaction with halides, sulphonates, and epoxides (Table 2). It is noteworthy that the yields of selenide products are excellent even in cases where difficulties arose using conventional methods. For example the preparation of diethylphenylselenomethylphosphonate proceeded in 92% yield whereas the literature routes[10] were much less convenient and gave lower yields of product. It should also be noted that the allylic bromide (entry 5) was displaced by a clean S_N2 process and no products arising from a competitive S_N2' reaction could be detected. The substitution reactions, entries 4 and 7 are also interesting since the β-oxygen atom in such systems can cause problems arising from attenuation of substrate electrophilicity in some examples. Entry 3 in the table also illustrates the high nucleophilicity of $PhSe^{\ominus}$ rather than the alternative basic properties which would afford only a β-eliminated acrylate product. The sodium phenylselenide generated in this way was also shown to react with some simple terminal epoxides; (entries 8 and 9) however, reaction with secondary epoxides and lactone opening or ester cleavage failed under these conditions. Furthermore, the examples chosen in the table show that other functional groups such as THP ethers, ketones and dioxanes remain intact.

We believe that this extremely mild and convenient method supersedes other routes and is highly recommended for the simple preparation of sodium phenylselenide. In a recent example this procedure was used to introduce a phenylseleno substituent by mesylate displacement [††] during the synthesis of a fragment of the ionophore antibiotic M 139603.[11]

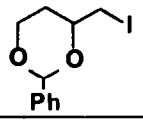
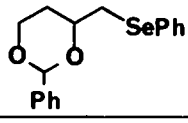
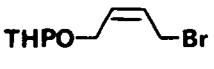
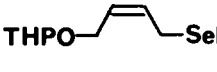
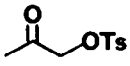
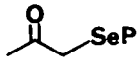
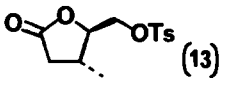
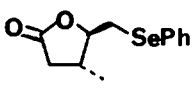
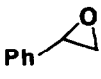
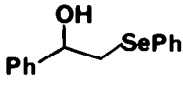
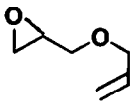
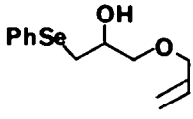
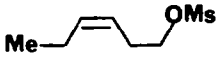
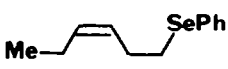
In principle the ultrasonic technique described above should be applicable, not only to a wide range of diselenides, but also to sulphides[Δ] and tellurides in a similar fashion.

Table 1

	Conditions	Reaction Time/h
1.	Solid Na cut into small lumps/THF	72
2.	Solid Na cut into small lumps/xylene	31
3.	Commercial Na dispersion[a]/THF	21
4.	Commercial Na dispersion[a]/THF/ benzophenone	1

a = 50% dispersion in paraffin from Aldrich

TABLE 2

Entry	Substrate	Product	Yield
1	$(EtO)_2P(O)CH_2I$ (1)	$(EtO)_2P(O)CH_2SePh$ (2)	92
2	$THPO(CH_2)_2CH_2I$ (3)	$THPO(CH_2)_2CH_2SePh$ (4)	86
3	$MeOOCCH_2CH_2I$ (5)	$MeOOCCH_2CH_2SePh$ (6)	88
4	 (7)	 (8)	84
5	 (9)	 (10)	94
6	 (11)	 (12)	93
7	 (13)	 (14)	83
8	 (15)	 (16)	78
9	 (17)	 (18)	86
10	$CH_3(CH_2)_6CH_2I$ (19)	$CH_3(CH_2)_6CH_2SePh$ (20)	92
11	$THPO(CH_2)_9CH_2Br$ (21)	$THPO(CH_2)_9CH_2SePh$ (22)	100
12	 (23)	 (24)	97

Experimental

^{1}H NMR spectra were obtained on Bruker WH-250 and Varian EM-360A spectrometers in deuteriochloroform solutions with tetramethylsilane as internal standard. IR spectra were recorded on a Perkin-Elmer 983 G spectrophotometer as liquid films or chloroform solutions. Mass spectra were obtained on a VG Micromass 7070B instrument. Melting points were determined using a Kofler hot-stage apparatus and are uncorrected. Column chromatography was performed on MN-silica gel 60 230-400 mesh, under pressure. Light petroleum refers to the fraction boiling in the range 40°-60°C and ether to diethyl ether. Solutions were dried over anhydrous sodium sulphate, and solvents by standard methods.

General procedure for the preparation of sodium phenylselenide

A 50% dispersion of sodium in paraffin (433 mg, 9.4 mmols) in THF (2 ml) was sonicated with a small portion of benzophenone in a sealed flask under argon for a few seconds until a deep blue colour had developed. Diphenyldiselenide (1.4 g, 4.7 mmols) was dissolved in the minimum volume of THF and the orange solution added dropwise to the reaction mixture. After 15 mins the reaction mixture had turned pale mauve and sonication was continued until all traces of colour had disappeared.

General procedure for the preparation of phenylselenols

Sodium phenylselenide (1.2 equivalents) was added to a stirred solution of the substrate in dry THF (10 ml) and the reaction followed by tlc. When the reaction had reached completion, the mixture was partitioned between water (20 ml) and diethylether (20 ml). The aqueous phase was then extracted with two further portions of ether and the combined organic phases dried over sodium sulphate. Removal of the solvent gave a yellow oil which was purified by column chromatography (silica gel; 40/60° petrol/diethyl ether gradient)

Preparation of Diethylphenylselenomethylphosphonate (2).- Treatment of iodide (1) (0.280g, 1.00mmol) with sodium phenylselenide (1.20 mmol) gave diethylphenylselenomethylphosphate (2) (0.283g, 92%) as a pale yellow oil, ν_{max} (film) 3467, 2982, 2938, 1635, 1477, 1440, 1389, 1249, 1163, 1097, 1024 and 968 cm^{-1}; δ_H (60 MHz; $CDCl_3$) 1.26 (6H, t, J = 7.0 Hz, Me), 2.90 (2H, d, J = 13.0 Hz, CH_2), 4.03 (4H, dq, J = 8.0, 7.0 Hz, CH_3CH_2), 7.10-7.30 (3H, m, aromatic), 7.40-7.70 (2H, m, aromatic); m/z = 308 (M^+).

Preparation of (+) 3-(Selenophenyl)-1-((tetrahydro-2H-pyran-2'-yl)oxy) propane (4).- Treatment of iodide (3) (0.270g, 1.00ml) with sodium phenylselenide (1.20mmol) gave 3-(selenophenyl) 1-((tetrahydro-2H-pyran-2-yl)oxy) propane (4) (0.258g, 86%) as a pale yellow oil, ν_{max} (film) 3055, 2939, 2867, 1576, 1476, 1352, 1259, 1200, 1134, 1075 and 870cm^{-1}; δ_H (250 MHz; $CDCl_3$) 1.45-1.90 (6H, m, H-3', H-4', H-5'), 1.98 (2H quintet J = 7.9 Hz, H-2), 3.00 (2H, t, J = 7.9 Hz, H-3), 3.49 (2H, m, H-1), 3.82 (2H, m, H-6'), 4.54 (1H, t, J = 3.6 Hz, H-2') 7.20-7.50 (5H, m, aromatic); m/z = 300 (MH^+) (Found: C, 55.98; H, 6.76%. $C_{14}H_{20}O_2Se$ requires C, 56.19; H, 6.74%).

Preparation of Methyl-3-(selenophenyl) propanate (6).- Treatment of iodide (5) (0.214g, 1.00mmol) with sodium phenylselenide (1.20mmol) gave methyl-3-(selenophenyl) propanoate (6) (0.214g, 88%) as a pale yellow oil, ν_{max} (film) 2949, 1736, 1476, 1434, 1347, 1223, 1165, 1022 and 738cm^{-1}; δ (250 MHz; $CDCl_3$) 2.72 (2H, t, J = 7.9Hz, H2), 3.10 (2H, t, J = 7.9 Hz, H-3), 3.68 (3H, s, CO_2Me), 7.27 (3H, m, aromatic), 7.52 (2H, m, aromatic); m/z = 243 (M^+).

Preparation of (+) 4-(Selenophenylmethyl)-2-phenyl-1,3-dioxane (8).- Treatment of iodide (7) (0.304g, 1.00mmol) with sodium phenylselenide (1.20mmol) gave 4-(selenophenylmethyl)-2-phenyl-1,3,-dioxane (8) (0.280g, 84%) as a pale yellow oil, ν_{max} (film) 3062, 2954, 2925, 2853, 1576, 1476, 1450, 1395, 1359, 1248, 1175, 1127, 1022, 983 and 738cm^{-1}; δ_H (250 MHz; $CDCl_3$) 1.80 (2H, m, H-5), 3.00 (1H, dd, J = 14.3, 7.2 Hz, $PhSeCH_2$), 3.23 (1H, dd, J = 14.3, 7.2 Hz $PhSeCH_2$), 3.86-4.10 (2H, m, H-6), 4.38 (1H, ddd, J = 14.6, 7.2, 2.7 Hz, H-4), 5.49 (1H, s, H-2), 7.20-7.58 (10H, m, aromatic); m/z = 334 (MH^+) (Found: C, 61.14; H, 5.60%. $C_{17}H_{18}O_2Se$ requires C, 61.26; H, 5.44%).

Preparation of z-4-(Selenophenyl)-1-((tetrahydro-2H-pyran-2-yl)oxy)but-2-ene (10).- Treatment of allylic bromide (9) (0.234g, 1.00mmol) with sodium phenylselenide (1.20mmol) gave z-4-(selenophenyl)-1-(tetrahydro-2H-pyran-2-yloxy)but-2-ene (10) (0.292g, 94%) as a pale yellow oil, ν_{max} (film) 3022, 2940, 2868, 1576, 1474, 1436, 1321, 1201, 1118, 1075, 1024 and 739cm^{-1}; δH (250 MHz; $CDCl_3$) 1.40-1.92 (6H, m, H-3', H-4', H-5'), 3.40-3.55 (2H, m, H-6'), 3.58 (1H, dd, J 8.2, 1.8 Hz, H-4), 3.73-3.93 (2H, m, H-1, H-4), 4.04 (1H, ddd, J = 16.1, 5.4, 1.0 Hz, H-1), 4.62 (1H, dd, J 3.6 and 4.3 Hz, H-1'), 5.57 (1H, m, H-3), 5.78 (1H, m, H-2), 7.24 (3H, m, aromatic), 7.51 (2H, m, aromatic); m/z = 312 (M^+) (Found: C, 58.07; H, 6.58%. $C_{15}H_{20}O_2Se$ requires C, 57.88; H, 6.48%).

Preparation of 1-(Selenophenyl)propan-2-one (12).- Treatment of tosylate (11) (0.23g, 1.00mmol) with sodium phenylselenide (1.20mmol) gave 1-(selenophenyl)propan-2-one (12) (0.198g, 93%) as a pale yellow oil, ν_{max} (film) 3055, 2998, 2923, 1699, 1576, 1477, 1436, 1356, 1229, 1139, 1022 and 738cm^{-1}; δ_H (60MHz; $CDCl_3$) 2.30 (3H, s, COMe), 3.65 (2H, s, CH_2), 7.20-7.75 (5H, m, aromatic); m/z = 214 (MH^+) (Found: C, 50.67; H, 4.94%. $C_9H_{10}OSe$ requires C, 50.72; H, 4.73%).

Preparation of (+) 3α-Methyl-4β(selenophenylmethyl)-γ-butyrolactone (14).- Treatment of tosylate (13) (0.256g, 1.00mmol) with sodium phenylselenide (1.20mmol) gave (+) 3α-Methyl-4β-(selenophenylmethyl)-γ-butyrolactone (14) (0.223g, 83%) as a pale yellow oil, ν_{max} (film) 3055, 2871, 2961, 1930, 2871, 1774, 1476, 1418, 1293, 1192, 1150, 1022, 939 and 739cm^{-1}; δ_H (250 MHz; $CDCl_3$) 1.15 (3H, d, J = 7.1 Hz, Me), 2.19 (1H, dd, J = 17.8, 8.5Hz, H-2α), 2.42 (1H, m, H-3), 2.74 (1H, dd, J = 17.8, 8.2 Hz, H-2β), 3.10 (1H, dd, J = 12.8, 5.7 Hz, CH_2SePh), 3.28 (1H, dd, J = 12.8, 5.7 Hz, CH_2SePh), 4.23 (1H, dd, J = 12.8, 5.7 Hz, H-4), 7.24-7.31 (3H, m, aromatic), 7.50-7.60 (2H, m, aromatic); m/z = 270 (MH^+) (Found: C, 53.65; H, 5.44%. $C_{12}H_{14}O_2Se$ requires C, 53.54; H, 5.34%).

Preparation of 1-Phenyl-2-(selenophenyl)ethan-1-ol (16).- Treatment of styrene oxide (15) (0.120g, 1.00mmol) with sodium phenylselenide (1.20mmol) gave 1-phenyl-2-(selenophenyl)ethan-1-ol (16) (0.216g, 78%) as a pale yellow oil, ν_{max} (film) 3403, 3058, 2929, 1576, 1475, 1435, 1300, 1054, 1022, 973 and 737cm^{-1}; δ_H (250 MHz; $CDCl_3$) 2.83 (1H, br, OH), 3.12 (1H, dd, J = 12.5, 9.0 Hz, H-2), 3.30 (1H, dd, J = 12.5, 3.7 Hz, H-2), 4.73 (1H, dd, J = 9.0, 3.7 Hz, H-1), 7.20-7.35 (8H, m, aromatic), 7.50-7.60 (2H, m, aromatic); m/z = 278 (MH^+) (Found: C, 60.39; H, 5.12%. $C_{14}H_{14}Se$ requires C, 60.65; H, 5.09%).

Preparation of 1-(Prop-2'-eneoxy)-3-(selenophenyl)propan-2-ol (18).- Treatment of epoxide (17) (0.113g, 1.00mmol) with sodium phenylselenide give 1-(prop-2'-eneoxy)-3-(selenophenyl) propan-2-ol (18) (0.233g,, 86%) as a pale yellow oil, ν_{max} (film) 3429, 3068, 2857, 1642, 1475, 1266, 1108, 1020, 929 and 737cm^{-1}; δ_H (250 MHz; $CDCl_3$) 2.79 (1H, d, J = 4.6Hz, OH), 3.03 (1H, dd, J = 14.3, 6.4 Hz H-3), 3.12 (1H, dd, J = 14.3, 6.4 Hz, H-3), 3.52 (2H, m, H-1), 3.86-4.01 (3H, m, H-2, H-1'), 5.20 (1H, dd, J = 11.4, 2.0 Hz, H-3' anti), 5.27 (1H, dd, J = 17.8, 2.0 Hz, H-3' syn), 5.88 (1H, m, H-1'), 7.20-7.32 (3H, m, aromatic), 7.50-7.61 (2H, m, aromatic); m/z = 272 (MH^+) (Found: C, 53.34; H, 6.03%. $C_{12}H_{16}O_2Se$ requires C, 53.14; H, 5.95%).

Preparation of 1-Selenophenyloctane (20).- Treatment of octyl iodide (19) (0.240 g, 1.00 mmol) with sodium phenylselenide (1.2 mmol) gave 1-selenophenyloctane (20) (0.247 g, 92%) as a pale yellow oil, ν_{max} (film) 3017, 2922, 2857, 1576, 1454, 1377, 1219, 1119, 1041, 1022, 795, 735 cm^{-1}; δH (60 MHz; $CDCl_3$) 0.80 (3H, t, J = 8Hz, H-8), 1.1-2.0 (12H, m, H-2 to H-7), 2.8-3.3 (2H, m, H-1), 7.2-7.7 (5H, m, aromatic); m/z = 270 (MH^+).

Preparation of 10-(selenophenyl)-1-((tetrahydro-2H-pyran-2'-yl)oxy)decane (22).- Treatment of 1-bromo-10-tetrahydropyranyl decane (21) (0.100 g, 0.33 mmol) with sodium phenylselenide (0.39 mmols) gave 10-(selenophenyl)-1-((tetrahydro-2H-pyran-2'-yl)oxy)decane (0.33 mmol, 100%) as a pale yellow oil, ν_{max} (film) 2926, 2852, 1559, 1576, 1475, 1276, 1119, 1076, 1033, 904, 869, 735 cm^{-1}; δH (250 MHz; $CDCl_3$) 1.28-1.86 (24H, m, H-3', H-4', H-5', H-3 to H-9), 2.91 (2H, t, J 7.6 Hz, H-10), 3.37 (1H, m, H-1), 3.49 (1H, m, H-1), 3.73 (1H, m, H-2), 3.87 (1H, m, H-2), 4.57 (1H, t, J 3.8 Hz), H-6'), 7.20-7.50 (5H, m, aromatic); m/z = 398 (M^+).

Preparation of 1-Selenophenylhex-3-ene (24).- Treatment of methanesulphonyloxyhex-3-en-1-ol (23) (0.178 g, 1.00 mmol) with sodium phenylselenide (1.20 mmols) gave 1-selenophenylhex-3-ene (24) as a pale yellow oil ν_{max} (film) 3004, 2961, 2927, 1576, 1474, 1434, 1298, 1258, 1190, 1072, 1022, 733, 689 cm^{-1}; δH (250 MHz; $CDCl_3$) 0.98 (3H, t, J = 8 Hz, H-6), 2.00 (2H, dt, J 16, 8 Hz, H-5), 2.43 (2H, dd, J 15, 8 Hz, H-2), 2.93 (2H, t, J 8 Hz, H-1), 5.41 (2H, m, H-3, H-4), 7.26 (3H, m, aromatic), 7.50 (2H, m, aromatic); m/z = 240 (MH^+) (Found: C, 60.54; H, 6.77% $C_{12}H_{16}Se$ requires C, 60.25; H, 6.74%).

Acknowledgements

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Footnotes

† The anions Se^{2-}_2 and Se^{2-} have also been prepared by the ultrasonically promoted electrochemical reduction of selenium. Reaction with alkyl halides gave the dialkyl mono- and diselenides.
B. Gautheron, G. Tainturier and C. Degrand, J. Am. Chem. Soc., 1985, 107, 5579.

†† Other literature routes to introduce the phenyseleno group in this example or to directly reduce the mesylate group rather than proceed through the selenide failed.

Δ Dimethyldisulphide may be converted to sodium methane thiolate using this method E.M. Naylor and W.B. Motherwell personal communication.

§ All reactions were carried out using a Semat 80W, 50 kHz ultrasonic cleaning bath.

References

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