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Synthesis of *N*,*N*-disubstituted selenoamides by O/Se-exchange with selenium–Lawesson's reagent

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Abstract—The selenium analogue of Lawesson's reagent, $[PhP(Se)(\mu\text{-}Se)]_2$ is an effective reagent for synthesizing *N*,*N*-disubstituted selenoamides. The reaction is carried out under mild conditions (room temperature) and affords the selenoamide in higher yield than using other selenation reagents.

Selenoamides are well known in preparative organic chemistry. Publications on this topic reach back to the beginning of the last century and many different reagents for the introduction of selenium were used.[1] In contrast to the homologous thioamides, however, the synthesis of selenoamides is still a challenge, due to the lack of suitable, readily obtainable, and easy to handle selenating reagents. Here we report a general and highly effecient synthesis of *N*,*N*-disubstituted selenoamides using the novel selenating reagent 1,3-diselena-2,4-diphosphetane-2,4-diselenide (**2**, Fig. 1).[2,3]

Compound **2** represents a selenium analogue of the well-known sulfur transfer reagent **1** (Lawesson's reagent) and is easily prepared by reaction of $(PhP)_5$ with 10 equiv. of grey selenium.[4] Its ability to act as a selenium transfer reagent by means of an O/Se-exchange was initially reported by one of us,[5] and the group of J. D. Woollins.[6]

Reaction of the formamides **3**–**7** with the selenide **2** in a 4:1 molar ratio in benzene at ambient temperature results in an O/Se-exchange at the carbonyl carbon atom with formation of the selenoformamides **17**–**21** (Scheme 1). The reaction proceeds smoothly and is complete within a maximum of 20 h. The selenoformamides **17**–**21** are isolated in yields up to 85% (Table 1). This method is of general applicability and can be extended to the synthesis of various *N*,*N*-dialkylsubstituted selenoamides (**22**–**28**) having an alkyl or aryl substituent at the selenocarbonyl group. As expected, the reactivity of the amides decreases with increasing chain length and bulkiness of the substituents at nitro-

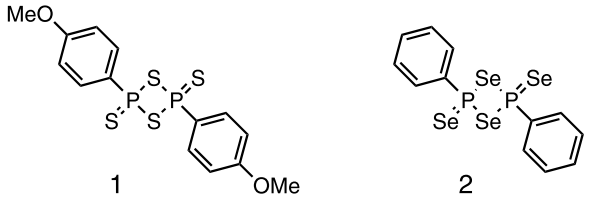
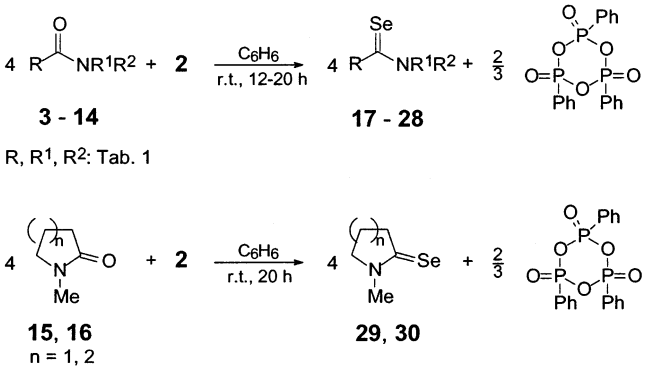


Figure 1. Lawesson's reagent **1** and the selenium analogue **2**.



Scheme 1. Syntheses of selenoamides using **2**.

Keywords: selenoamides; O/Se-exchange; selenium–Lawesson's reagent; selenium-NMR.
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Table 1. Selenoamides prepared by O/Se-exchange with reagent **2**[19]

Carboxamide	Selenoamide	R	R^1	R^2	Yield (%)	Mp (°C, uncorr.)	δ ^{77}Se[20]
3	**17**[10]	H	Me	Me	82		609.5[a]
4	**18**[11]	H	Et	Et	77		568.8[a]
5	**19**[10]	H	*i*Pr	*i*Pr	75		586.3[a]
6	**20**[12]	H	Me	Ph	85		768.8[a]
7	**21**[12]	H	Ph	Ph	59		879.4[a]
8	**22**[13]	Me	Me	Me	66	87–88	627.4[b]
9	**23**[14]	Me	Et	Et	29	–	592.9[c]
10	**24**	Me	*i*Pr	*i*Pr	21	105	597.9[c]
11	**25**	Me	Me	Ph	48	70	659.3[c]
12	**26**[13]	Et	Me	Me	57	–	578.2[c]
13	**27**[15]	Ph	Et	Et	72		771.0[a]
14	**28**[16]	4-$MeOC_6H_4$	Me	Me	66		718.4[a]
15	**29**[17]	$n=1$	Me	–	74	30	376.4[b]
16	**30**[18]	$n=2$	Me	–	61	45	538.9[c]

[a] Measured in C_6D_6.
[b] Measured in CD_2Cl_2.
[c] Measured in $CDCl_3$.

gen, which results in longer reaction times and somewhat lower yields. Cyclic selenoamides, e.g. **29** and **30**, can be prepared starting from the corresponding lactams **15** and **16** by the same procedure.

In all investigated reactions, all four selenium atoms of the diselenide **2** are transferred to the organic compound. Thus, in its selenium-transfer ability **2** is more effective than Lawesson's reagent in its sulfur-transfer ability, where only half of the sulfur atoms are used to generate the thioamide. The main phosphorus containing by-product (> 80%) is the 2,4,6-triphenyl-1,3,5,2,4,6-trioxatriphosphinane-2,4,6-trioxide, which is readily identified by its ^{31}P NMR spectrum (A_2B type spectrum, $\delta_A = 1.6$, $\delta_B = 3.5$, $^2J_{AB} = 39.9$ Hz).

The isolated selenoamides are identified and characterized by ^{1}H, ^{13}C, ^{77}Se NMR spectroscopy, IR spectroscopy, and mass spectrometry. Characteristic is the low field chemical shift of the selenocarbonyl carbon atom ($\delta = 188.6$–194.1 for the formamides, and 200.8–209.7 for other carboxamides) in the ^{13}C NMR spectrum and the large value of $^1J_{SeC}$ (210.4–219.2 Hz).[7,8] In the ^{77}Se NMR spectrum, the signal of the one-coordinated selenium atom appears at low field ($\delta = 539$–880) in a range typical for δ ^{77}Se of selenoamides.[8,9] It is worth noting the well resolved ^{77}Se-satellites observed for the signal of the formamide proton ($\delta = 10.3$–11.7) in the ^{1}H NMR spectrum with $^2J_{SeH}$ in the range of 7–10 Hz. The α-CH-protons of the higher selenoamides synthesized appear between 2.4 and 3.1 ppm.

In conclusion, the selenation of amides using a selenium analogue of Lawesson's reagent, the 1,3-diselena-2,4-diphosphetane-2,4-diselenide **2**, provides a general and straightforward route to *N*,*N*-disubstituted selenoformamides and selenoamides. The easy availability of selenoamides by this route stimulates a systematic study of their chemical properties. Further chemistry of **2** and of other analogues of Lawesson's reagent is under current investigation.

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19. **General procedure**: To a suspension of reagent **2** (0.53 g, 1 mmol) in 3–5 ml benzene the corresponding carboxamide (4 mmol) is added. The resulting mixture is stirred for 12–20 h at room temperature, while **2** dissolves completely. From the resulting clear yellow–green solution the solvent is evaporated in vacuo and the residue is subjected to vacuum distillation [10^{-1} mbar and 90–150°C Kugelrohr apparatus temperature (Büchi)] or chromatographed on dried (!) silica gel with CH_2Cl_2.
20. *Spectral data for some typical selenoamides*:**17**: ^{1}H NMR (C_6D_6, 270.17 MHz): 10.32 (s, 1H, C*H*=Se), 2.73 (s, 3H, CH_3), 2.07 (s, 3H, CH_3) ppm. $^{13}C\{^1H\}$ NMR (C_6D_6, 67.94 MHz): 191.3 (*C*H=Se), 47.9 (CH_3), 40.9 (CH_3) ppm. ^{77}Se NMR (C_6D_6, 51.39 MHz): 609.5 ppm. **22**: ^{1}H NMR ($CDCl_3$, 300 MHz): 3.62 (s, 3H, CH_3), 3.26 (s, 3H, CH_3), 2.69 (s, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): 202.7 (C=Se), 48.7 (CH_3), 42.7 (CH_3), 37.2 (CH_3) ppm. ^{77}Se NMR (CD_2Cl_2, 95.4 MHz): 627.4 ppm. GC–MS (70 eV): *m*/*z* 151 ($M^{+\bullet}$, 100%), 107 (32%), MS (ESI): 151.99662. Anal. calcd for C_4H_9NSe (150.08): C, 32.01; H, 6.04; N, 9.33. Found: C, 31.98; H, 5.91; N, 8.93%. **24**: ^{1}H NMR ($CDCl_3$, 300 MHz): 6.35–6.16 (m, 1H), 4.24–4.04 (m, 1H), 2.89 (s, 3H, CH_3), 1.46 (d, J=6.6 Hz, 6H, CH_3), 1.27 (d, J=5.9 Hz, 6H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): 202.8 (C=Se), 60.4 (NCH), 50.1 (NCH), 37.4 (CH_3), 22.0 (CH_3), 19.1 (CH_3) ppm. ^{77}Se NMR ($CDCl_3$, 95.4 MHz): 597.9 ppm. GC–MS (70 eV): *m*/*z* 207 ($M^{+\bullet}$, 46%), 123 (43%), 58 (100%). MS (ESI): 208.05959; calcd: 208.0599. **25**: ^{1}H NMR ($CDCl_3$, 300 MHz): 7.51–7.37 (m, 3H, arom. H), 7.22–7.16 (m, 2H, arom. H), 3.85 (s, 3H, CH_3), 2.43 (s, 3H, CH_3) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): 205.1 (C=Se), 145.6 (C-*i*), 129.9 (C-*m*), 128.6 (C-*p*), 124.3 (C-*o*), 49.9 (NCH_3), 38.4 (CH_3) ppm. ^{77}Se NMR ($CDCl_3$, 95.4 MHz): 659.3 ppm. GC–MS (70 eV): *m*/*z* 213 ($M^{+\bullet}$, 31%), 91 (38%), 56 (100%). MS (ESI): 214.01217; calcd: 214.0129. **30**: ^{1}H NMR ($CDCl_3$, 300 MHz): 3.58 (s, 3H, NCH_3), 3.42 (t, J=6.2 Hz, 2H, NCH_2), 3.04 (t, J=6.2 Hz, 2H, CH_2), 1.96 (quint, J=6.2 Hz, 2H, CH_2), 1.70 (quint, J=6.2 Hz, 2H, CH_2) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): 202.4 (C=Se), 53.8 (NCH_2), 47.5 (NCH_3), 45.1 (CH_2), 22.9 (CH_2), 20.4 (CH_2) ppm. ^{77}Se NMR ($CDCl_3$, 95.4 MHz): 538.9 ppm. GC–MS (70 eV): *m*/*z* 177 ($M^{+\bullet}$, 91%), 68 (100%). MS (ESI): 178.01214. Anal. calcd for $C_6H_{11}NSe$ (176.12): C, 40.92; H, 6.30; N, 7.95. Found: C, 40.88; H, 6.21; N, 7.63%.