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Reactions of Nitroxides, Part 7: Synthesis of Novel Nitroxide Selenoureas

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ABSTRACT: *The reactions of 4-isoselenocyanato-2,2,6,6-tetramethylpiperidine-1-oxyl with selected amines and lower alcohols give the corresponding novel selenoureas and selenocarbamates, all bearing the nitroxyl moiety. Some of the synthesized selenoureas and selenocarbamates show moderate-to-good activity against pathogenic fungi.* © 2008 Wiley Periodicals, Inc. Heteroatom Chem 19:549–556, 2008; Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/hc.20454

INTRODUCTION

Selenium plays an important role in living organisms. Its overexposure results in numerous diseases (from depression to some types of cancer). On the other hand, selenium is an important trace element (a human organism contains about 6 mg of selenium). Traces of selenium are important in oxygen metabolism. Selenium-containing compounds (the most popular is ebselen (2-phenyl-1,2-benzisoselenazol-3(2*H*)-one [1,2])) are considered to be inhibitors of free radicals, as well as anti-inflammatory and antioxidant agents. Recently, selenoureas have been recognized as effective superoxide radical scavengers [3]. Role and importance of selenium in living organisms have been recently reviewed [4]. Relationship between selenium and cancer was described [5]. Heterocyclic compounds containing selenium atom may restrain some cancer cell growth [6].

The basic method of the synthesis of selenoureas involves two steps. Direct selenation of either alkyl or aryl isocyanides with metallic selenium in a suitable solvent leads to the corresponding isoselenocyanates [7–21]. Their reaction with primary and secondary amines affords selenoureas [7,10,21–26]. Isoselenocynate may also be generated in situ from aryl nitrile oxide and a selenoamide, and, without purification, converted into a selenourea derivative [27]. Carbodiimides [3,28], or dichloromethylenedimethyliminium chloride (synthesized via *N*,*N*-dimethylselenocarbamoyl chloride) [29] are converted into selenoureas using a new selenating reagent (LiAlHSeH) obtained by treating lithium aluminum hydride with selenium [30,31]. There are also some specific methods of selenourea synthesis. A reaction of secondary amines, triethyl orthoformate, and elemental selenium [32] or a reaction of chloroform or sodium trichloroacetate with a secondary amine, sodium hydride, and elemental selenium [33,34] affords selenoureas.

There are only a few examples of nitroxyl radicals containing selenium known [35,36]. Here, as a continuation of our previous studies on urea and thiourea nitroxides [37], we report the synthesis of novel selenoureas bearing the nitroxyl moiety.

Following parts have published earlier: Part 4 (*Heteroatom Chem* 2006, 17(5), 393–401), Part 5 (*Org Prep Proc Int* 2003, 35(4), 387–390), and Part 6 (*Org Lett* 2004, 6(5), 695–697).

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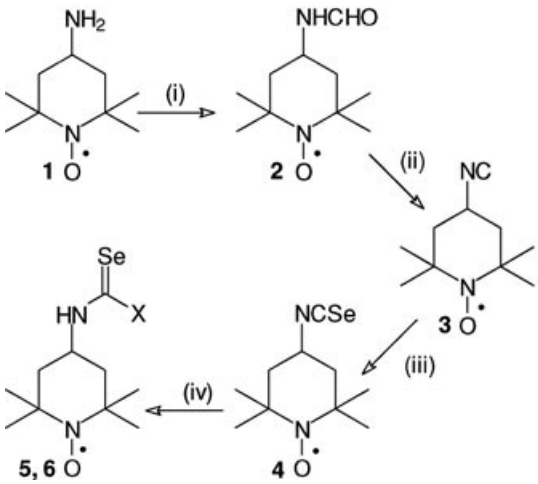
RESULTS AND DISCUSSION

4-Amino-2,2,6,6-tetramethylpiperidine-1-oxyl (**1**) was converted into 4-formylamino-2,2,6,6-tetramethylpiperidine-1-oxyl (**2**) by treatment with excess of ethyl formate [38]. The dehydration of **2** with gaseous phosgene [38] or diphosgene leads to 4-isocyano-2,2,6,6-tetramethylpiperidine-1-oxyl (**3**), which was selenated with metallic selenium to give 4-isoselenocyanato-2,2,6,6-tetramethylpiperidine-1-oxyl (**4**) [39].

The reaction of **4** with a series of amines and lower alcohols such as methanol or ethanol leads to selenoureas **5a–h** and selenocarbamates **6a,b**, respectively (Scheme 1 and Table 1). When the starting radical **1** was applied as an amine, the biradical selenourea derivative **5h** was obtained.

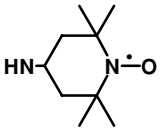
To investigate the possibility of direct selenation of 2,2,6,6-piperidine derivatives, a selenating reagent 2,4-diphenyl-1,3-diselena-2,4-diphosphetane-2,4-diselenide (**9**), ($[PhP(Se)(\mu\text{-}Se)]_2$) was synthesized and used. The reagent is able to selenate amides and formamides by substitution of the oxygen atom [40,41]. The condensation of dichlorphenylphosphine (**7**) with magnesium in THF [42–46] yields pentaphenylpentaphospholane ($[(PhP)_5$, (**8**)]



5,6	X
5a	$N(CH_3)_2$
5b	$N(C_2H_5)_2$
5c	$N(n\text{-}C_3H_7)_2$
5d	$N(iso\text{-}C_3H_7)_2$
5e	$N(n\text{-}C_4H_9)_2$
5f	
5g	
5h	
6a	OCH_3
6b	OC_2H_5

SCHEME 1 (i) HCOOEt [38] (ii) $COCl_2$ [38] or $ClCOOCCl_3$ (diphosgene) (iii) Se, $CHCl_3$ [39] (iv) (**5a–h**) HX, benzene (**6a,b**) HX/NaX.

TABLE 1 Synthesized Selenoureas (**5a–h**), and Selenocarbamates **6a,b**

X	*Compound*	*Purification Method*[a]	*Yield (%)*	*mp(°C) (dec)*	*R_f(BM9)*
$N(CH_3)_2$	**5a**	Cryst.(B)	35.7	164.5–167.5	0.18
$N(C_2H_5)_2$	**5b**	Cryst.(B)	49.2	171–175	0.2
$N(n\text{-}C_2H_7)_2$	**5c**	Cryst.(B)	42.2	144–152	0.28
$N(i\text{-}C_2H_7)_2$	**5d**	Cryst.(B)	47.8	187–190	0.38
$N(n\text{-}C_4H_9)_2$	**5e**	C (BM9)	37.2	119–123	0.33
	**5f**	Cryst.(B)	54.3	177.5–179	0.13
	**5g**	Cryst.(B)	19.1	168	0.18
	**5h**	C (BM9)	63.4	159	0.09
OCH_3	**6a**	C (BM9)	40.0	Oil	0.36
OC_2H_5	**6b**	C (BE9)	86.5	108–116.5	0.44[b]

[a]Cryst.(B): crystallization (benzene), C: column chromatography; BM9 = benzene:methanol 9:1; BE9 = benzene:ethanol 9:1; BA95 = benzene:ethyl acetate 95:5.
[b]BE9.

(62% yield). Surprisingly, contrary to [42], when diethyl ether instead of THF had been used as a solvent, no product **8** was obtained. The parent peak (*m/z* 540) in mass spectrum of **8** clearly indicates the five-membered ring [42,45,47]. The reaction of $(PhP)_5$ with metallic selenium affords compound **9** (89% yield) [48–50].

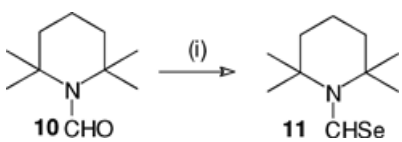
2,2,6,6-Tetramethylpiperidin-1-oxyl (TEMPO), 2,2,6,6-tetramethylpiperidinol-4-oxyl-1 (TEMPO-4-OL), 2,2,6,6-tetramethylpiperidinone-4-oxyl-1 (TEMPO-4-ONE), 2,2,6,6-tetramethylpiperidinone-4 (TAA), and 1-formyl-2,2,6,6-tetramethylpiperidine (**10**) were treated with **9**. The attempted selenation of TEMPO resulted in decomposition of the radical, whereas the selenation of TEMPO-4-OL, TEMPO-4-ONE, and TAA yielded products containing selenium (UV irradiation of TLC spots). Unfortunately, attempts to isolate detected products were unsuccessful. The products decompose during column chromatography with formation of red selenium.

Selenation of 1-formyl-2,2,6,6-tetramethylpiperidine **10** with **9** gave 1-selenoformyl-2,2,6,6-tetramethylpiperidine **11** in 83% yield (Scheme 2). Selenation of **10** with Se/P gives **11** in only 17% yield.

Structures of the synthesized selenoureas **5a–h** and selenocarbamates **6a,b** were confirmed by EI MS, IR (Table 2), and for **11** additionally by ^1H, ^{13}C NMR spectra.

The molecular ions in the EI mass spectra of the synthesized selenoureas **5** are abundant only for **5a** and **5g**. The base peaks belong to *m/z* 124 (except for **5d** (97%) and **5g** (26%)). The peak *m/z* 124 is attributed to C_9H_{16}, which is formed via elimination of the substituent at C(4) and a hydrogen atom at C(3) of the substituted TEMPO (*m/z* 154) followed by the NO loss [51,52].

Pesticidal activity of the synthesized selenoureas **5a–h** and selenocarbamates **6a,b** was tested using preliminary screening tests. The derivatives **5a–h** and **6a,b** were tested for acaricidal, herbicidal, insecticidal, and fungicidal activity. No activity was found for weeds, insects, and mites. The preliminary studies indicated that most of the compounds showed potential fungicidal activity against phytopathogenic fungi at the concentration of 200 ppm. Selenoureas **5a–c, e–h** and selenocabamate **6b** showed moderate-to-good activity against *Botrytis cinerea* (most of these compounds inhibited >90% growth of the fungi), and moderate activity against *Fusarium culmorum*. Ebselen (2-phenyl-1,2-benzisoselenazol-3(2*H*)-one) and fenuron (*N*-phenyl-*N*′,*N*′-dimethylurea) were used as reference compounds (Table 3). The fungicidal activity of the synthesized selenoureas is significantly better than the fungicidal activity of ureas and thioureas bearing a nitroxyl moiety, which has been tested previously [37].



SCHEME 2 (i) **9**, toluene, r.t., 18 h, 83%.

CONCLUSIONS

Nitroxide selenoureas **5a–h**, and selenocarbamates **6a,b**—new nitroxyl radicals containing selenium atom—were synthesized. Some of them show moderate-to-good activity against pathogenic fungi.

EXPERIMENTAL

General

4-Amino-2,2,6,6-tetramethylpiperidine-1-oxyl (**1**) [53], 4-formylamino-2,2,6,6-tetramethylpiperidine-1-oxyl (**2**) [38], 4-isocyano-2,2,6,6-tetramethylpiperidine-1-oxyl (**3**) (using gaseous phosgene as a reagent) [38], 4-isoselenocyanato-2,2,6,6-tetramethylpiperidine-1-oxyl **4** [39], and 1-formyl-2,2,6,6-tetramethylpiperidine (**10**) [37] were synthesized as described previously. A protocol for a synthesis of 4-isocyano-2,2,6,6-tetramethylpiperidine-1-oxyl (**3**) using diphosgene as a reagent is presented below. 2,4-Diphenyl-1,3-diselena-2,4-diphosphetane-2,4-diselenide (**9**) was obtained following the method described in [49,50]. Yield: 61.7%, mp 202–204°C (192–204°C [48]); MS (EI, 70 eV, *m/z*, int. [%]): 536 (M^+, 1), 534 (1), 456 (7), 454 (8), 452 (6), 268 (96), 266 (86), 188 (19), 157 (11), 111 (99), 109 (45), 107 (100), 77 (30), 51 (33). IR (ν, cm^{-1}, KBr): 3432, 1621, 1437, 1119, 911, 744, 720, 689, 514. Other reagents are commercially available and were used as received without further purification. All experiments were performed in a multinecked round-bottomed flask equipped with a magnetic bar, a thermometer, a reflux condenser protected against humidity, and a dropping funnel. The formation of products was monitored by means of TLC. TLC control and column chromatography were carried out on a silica gel Merck Alurolle 5562, Alufolien 5554, and Merck 1.09385.1000 (0.040–0.063 mm, 230–400 mesh), respectively. For the abbreviations for mobile phases used throughout

TABLE 2 Spectral Data of Selenoureas (**5a–h**) and Selenocarbamates **6a,b**

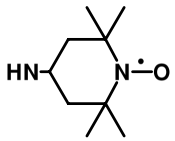
X	*Compound*	*HRMS*	*MS (EI, 70 eV, m/z, int. (%))*	*IR (ν, cm^{-1}, KBr)*
$N(CH_3)_2$	**5a**	Found: 306.1079, Calcd: 306.1085 for $C_{12}H_{24}N_3OSe$, M^+ (EI).	306 (28, M^+), 233 (34), 154 (39), 138 (96), 124 (100), 109 (32), 97 (85), 82 (25), 71 (80), 55 (47), 41 (96).	3335, 2984, 2940, 1554, 1338.
$N(C_2H_5)_2$	**5b**	Found: 334.1388, Calcd: 334.1398 for $C_{14}H_{28}N_3OSe$, M^+ (EI).	334 (4, M^+), 182 (20), 166 (30), 124 (100), 98 (25.5), 58 (49), 41 (46).	3342, 2971, 2940, 1538.
$N(n\text{-}C_3H_7)_2$	**5c**	Found: 362.1704, Calcd: 362.1711 for $C_{16}H_{32}N_3OSe$, M^+ (EI).	362 (M^+, 2), 210 (18), 194 (42), 124 (100), 58 (30), 41 (50).	3345, 2964, 1536, 1344, 1242.
$N(i\text{-}C_3H_7)_2$	**5d**	Found: 362.1699, Calcd: 362.1711 for $C_{16}H_{32}N_3OSe$, M^+ (EI).	362 (M^+, 2), 167 (17), 140 (24), 124 (97), 98 (46), 69 (100), 55 (40), 41 (80).	3418, 2966, 1534, 1325.
$N(n\text{-}C_4H_9)_2$	**5e**	Found: 413.1903, Calcd: 413.1916 for $C_{18}H_{36}N_3OseNa$, $[M^+Na]^+$ (ESI).	390 (1, M^+), 238 (17), 222 (24), 124 (100), 86 (24), 57 (28), 41 (50).	3272, 2960, 2940, 1540.
	**5f**	Found: 348.1204, Calcd: 348.1190 for $C_{14}H_{26}N_3O_2Se$, M^+ (EI).	348 (2, M^+), 254 (12), 236 (14), 196 (41), 180 (55), 139 (56), 124 (100), 58 (32), 41 (49).	3316, 2970, 1541, 1332.
	**5g**	Found: 346.1408, Calcd: 346.1398 for $C_{15}H_{28}N_3OSe$, M^+ (EI).	346 (67, M^+), 273 (100), 217 (24), 193 (25), 176 (37), 154 (11), 140 (32), 124 (26), 111 (40), 84 (54), 69 (71), 55 (24), 41 (51).	3323, 2992, 2975, 2932, 2853, 1549, 1335, 1238.
	**5h**	Found: 431.1919, Calcd: 431.1920 for $C_{19}H_{35}N_4O_2Se$ $[M - H]^-$ (ESI).	432 (1, M^+), 182 (32), 140 (46), 124 (100), 98 (24), 74 (34), 58 (61), 41 (45).	3462, 3300, 2975, 2950, 1653, 1558.
OCH_3	**6a**	Found:.293.0773, Calcd: 293.0768 for $C_{11}H_{21}N_2O_2Se$, M^+ (EI).	294 (2.5), 293 (2, M^+), 181 (19), 167 (34), 154 (15), 140 (35), 124 (51), 109 (36), 94 (70), 81 (27), 67 (54), 56 (37), 41 (100).	3222, 2970, 2928, 1534.
OC_2H_5	**6b**	Found: 306.0831, Calcd: 306.0841 for $C_{12}H_{22}N_2O_2Se$, $[M–H]^-$ (ESI).	308 (7), 307 (5, M^+), 183 (28), 167 (31), 154 (31), 140 (84), 124 (82), 109 (42), 94 (29), 84 (21), 83 (14.5), 82 (28), 69 (39), 55 (53), 41 (100).	3206, 2974, 2930, 1541.

TABLE 3 The Effect of Selenoureas **5a–h** and Selenocarbamates **6a,b** on Mycelial Growth of Phytopathogenic Fungi (In Vitro test, 200 ppm)

	% of Growth Reduction[a]	
Compound No.	*Botrytis cinerea*	*Fusarium culmorum*
5a	3	2
5b	2	2
5c	3	2
5d	0	0
5e	3	2
5f	2	2
5g	3	Not tested
5h	3	2
6a	0	0
6b	3	2
Ebselen	1	0
Fenuron	0	0
Control	0	0

[a]Score index:
0 = 0%–20% growth reduction–no effect.
1 = 20.1%–50% growth reduction–weak activity.
2 = 50.1%–90% growth reduction–moderate activity.
3 = 90.1%–100% growth reduction–good activity.

the text, see Table 1's footnote a. HRMS and MS (EI, 70 eV, *m/z*, int. (%)) data were recorded using an AMD 604 mass spectrometer. HRMS (ESI) (for **5e,5h,6b**) were recorded using a Mariner apparatus. IR (ν, cm^{-1}, KBr) data were recorded using a FT/IR Jasco 420 spectrophotometer. ^1H NMR (δ (ppm), J (Hz), $CDCl_3$, TMS) and ^{13}C NMR (δ (ppm), $CDCl_3$, TMS) (for nonradical compound **11**) data were recorded using a Varian UNITYplus 200 (200 MHz for ^1H) apparatus. EPR data (for **3** and **4**) were obtained with a Bruker ESP 300E (X band) spectrometer. Conditions of fungicidal bioassay in vitro are identical with those described previously in [37].

*4-Isocyano-2,2,6,6-tetramethylpiperidine-1-oxyl (**3**) (using Diphosgene [$ClCOOCCl_3$] as a Reagent)*

To a magnetically stirred solution of **2** (2.985 g, 15 mmol), triethylamine (3.825 g, 38 mmol, ~5.3 mL), and methylene chloride (15 mL) was cooled in an ice bath, diphosgene (1.5 mL = 500 μL + 4 × 250 μL) was added dropwise with a syringe at the temperature below 10°C. The formation of **3** was monitored using TLC (BM9, R_f of **3** ~0.6 to 0.7). The reaction mixture was transferred into a pear-shaped flask, and methylene chloride was evaporated under the reduced pressure. Benzene (30 mL) was then added. The resulting suspension was vigorously stirred, then the precipitate of triethyl hydrochloride was filtered off. The precipitate was thoroughly washed twice with benzene. The benzene filtrate was concentrated under the reduced pressure, and the solid, red residue (4.4 g) was subjected to column chromatography (BM95) to give 2.1233 g (78.2%) of **3**, mp 142–144°C (hexane) [38]; (133–134°C [54,55], 143.5–144.5°C [56]); MS (70 eV, *m/z*, int. (%)): 181 (31, M^+), 167 (18), 166 (11), 151 (10), 140 (8), 136 (10), 126 (9), 124 (24), 109 (35), 94 (100), 81 (36), 69 (40), 68 (74), 67 (67), 57 (23), 56 (38), 55 (52), 53 (33), 41 (98), 39 (40); IR (KBr, ν, cm^{-1}): 2143; EPR (a_N [G]): 15.49 (toluene), 15.77 (dichloromethane), 15.83 (DMSO); $g = 2.0060$.

*4-Isoselenocyanato-2,2,6,6-tetramethylpiperidine-1-oxyl (**4**)*

According to [39], metallic selenium and **3** (about 2:1 mol:mol) and chloroform (about 1.5 mL/1 mmol of **3**) were stirred at a gentle reflux for 70 h. Unreacted selenium was filtered off, then the filtrate was evaporated. Crude product was subjected to column chromatography (BM95) to give **4** (38%, mp 156–158°C, R_f 0.75 /BM9/); HRMS Found: 261.0514, Calcd: 261.0506 for $C_{10}H_{17}N_2O^{80}Se$, M^+ (EI); MS (70 eV, *m/z*, int. (%)): 264 (1), 263 (6), 262 (7), 261 (35, M), 260 (3), 259 (17), 258 (6), 257 (6), 247 (7), 175 (14), 174 (11), 173 (8), 172 (7), 160 (13), 154 (42), 140 (19), 124 (26), 109 (24), 98 (15), 95 (18), 94 (29), 83 (10), 82 (11), 81 (20), 74 (9), 69 (100), 68 (17), 67 (25), 56 (24), 55 (41), 53 (15.5), 43 (13), 42 (12), 41 (75), 39 (21); IR (KBr, ν, cm^{-1}:) 2161; EPR (a_N [G]): 15.46 (toluene), 15.73 (dichloromethane), 15.80 (DMSO); (g): 2.0061 (toluene), 2.0060 (dichloromethane), 2.0059 (DMSO).

Selenoureas **5a–h***: General Procedure*

The appropriate amine was added at 10–15°C to 4-isoselenocyanate-2,2,6,6-tetramethylpiperidin-1-oxyl (**4**) (0.26 g, 1 mmol) and anhydrous benzene (about 4 mL). In the case of **5b–g**, appropriate liquid amine (1.15 mmol) was added with a syringe. In the case of **5a**, the excess of chilled dimethylamine dissolved in a small amount of benzene was added in one portion from a dropping funnel. In the case of **5h**, 4-amine-2,2,6,6-tetramethylpiperidine-1-oxyl **1** (1 mmol) was added dropwise as a solution in a small amount of benzene. The reaction mixture was partially concentrated. The pink, fine crystalline precipitate (**5a–d,f,g**) was collected, washed with a small portion of chilled benzene or hexane, and air dried. In the case of selenoureas **5e** and **5h**, the benzene solution is evaporated to dryness under reduced pressure. The residues were subjected to column chromatography (mobile phase BM9) to give **5e** and **5h** as solidifying oils. Melting points, TLC properties, and spectral data (HRMS, MS, IR) of the synthesized nitroxide thioureas **5a–h** are presented in Tables 1 and 2, respectively.

Selenocarbamates **6a,b***: General Procedure*

The solution of sodium alkoxide (1 mmol/1 mL) was prepared by dissolving elemental natrium (0.23 g, 0.01 g atom) in the appropriate anhydrous alcohol and diluting the resulting solution with the same alcohol up to the 10 mL volume. The starting 4-isoselenocyanate-2,2,6,6-tetramethylpiperidin-1-oxyl (**4**) (0.260 g, 1 mmol) was dissolved in the appropriate anhydrous alcohol (methanol, ethanol, 6 mL). The alcohol solution of the appropriate sodium alkoxide (1.2 mL, 1.2 mmol) was added to the suspension of **4** with a pipette or a syringe in three approximately equal portions at 20°C. The reaction mixture was stirred for 10 min at ambient temperature. The appropriate alcohol was evaporated under reduced pressure. Diethyl ether (about 10 mL) was added to the residue. The white precipitate was dissolved and then formed again. The precipitate was filtered off and washed with diethyl ether. The filtrate was dried over anhydrous magnesium sulfate overnight. Drying agent was filtered off, then ether was evaporated under reduced pressure. The crude selenocarbamates **6a** or carbamates **6b** were subjected to column chromatography (mobile phase benzene:appropriate alcohol 9:1, i.e. BM9 and BE9, respectively) to give selenocarbamates **6a,b**. Melting points, TLC properties, and spectral data (HRMS, MS, IR) of the synthesized nitroxide selenocarbamates **6a,b** are presented in Tables 1 and 2, respectively.

*Pentaphenylpentaphospholane (***8***)*

According to [43, 44] with some modifications, dichlorphenylphosphine **7** (2.5 g, 1.9 mL, 0.014 mol) in tetrahydrofuran (5 mL) was thoroughly added dropwise to anhydrous tetrahydrofuran (20 mL) and thoroughly dried magnesium turnings (0.3414 g, 0.014 mol) at temperature not exceeding 30°C (ice-water bath). After all magnesium had been dissolved (about 2 h), the reaction mixture was stirred for 3 h. Tetrahydrofuran was evaporated off. Water (about 10–20 mL) was added to the residue. The mixture was extracted with methylene chloride (about 10–20 mL). The organic solution was dried with anhydrous magnesium sulfate. The solvent was evaporated to give an oil (1.43 g), which was triturated with pentane and was allowed to crystallize in a refrigerator below 0°C. After approximately 1 month, dark red precipitate was filtered off and dried under reduced pressure (1.2816 g). The precipitate was thoroughly washed on a filter with a small amount of methanol to give fine, off-white crystalline precipitate of pentaphenylpentaphospholane (**8**) (according to [43,44] with some modifications): (0.9297 g, 61.7%); mp 150–151.5°C (148–152°C [42], 148–152°C [57], 149–150°C [44], 149–150°C [45], 149–152°C [58] 151–153°C [43]). MS (EI, 70 eV, m/z, int. (%)): 540 [57] (66, M^+), 370 (16), 355 (58), 324 (26), 293 (13), 262 (100), 185 (53), 183 (70). IR (ν, cm^{-1}, KBr): 3048, 1580, 1480, 1431, 1183, 1067, 1024, 998, 741, 693.

*1-Selenoformyl-2,2,6,6-Tetramethylpiperidine (***11***) (Selenation with* **9***)*

1-Formyl-2,2,6,6-tetramethylpiperidine (**10**) (0.169 g, 1 mmol), $[PhP(Se)(\mu\text{-}Se)]_2$ (**9**) (0.1325 g, 0.25 mmol), and toluene (about 1 mL) were stirred at ambient temperature for 18 h. The progress of the reaction was monitored by means of TLC (BM9). Compound **9** was dissolved, and yellow color of the toluene solution appeared. Some amount of the colloidal selenium was present in the reaction mixture. The reaction mixture was directly subjected to column chromatography (mobile phase BA95) to give the yellow-green zone of the 1-selenoformyl-2,2,6,6-tetramethylpiperidine (**11**): 0.1932 g, 83.3%, mp 113–115°C, $R_f = 0.6$ (BM9).

*1-Selenoformyl-2,2,6,6-tetramethylpiperidine (***11***) (Selenation with Se/P)*

Red phosphorus (0.124 g, 4 mmol), metallic selenium (0.790 g, 10 mmol), 1-formyl-2,2,6,

6-tetramethylpiperidine (**10**) (0.169 g, 1 mmol), and xylene (about 3 mL) were stirred at reflux for 5 h. The progress of the reaction was monitored by means of TLC (BM9). Reaction mixture was filtered through Cellite and washed with benzene until colorless filtrate was obtained. Benzene was evaporated. The residue was subjected to column chromatography (mobile phase BA95) to give the intensely colored yellow zone of the 1-selenoformyl-2,2,6,6-tetramethylpiperidine (**11**): 0.0392 g, 16.9%, mp 110–114°C, Rf = 0.57 (BM9); HRMS Found: 233.0675, Calcd: 233.0683 for $C_{10}H_{19}NSe$, M^+(EI); MS (EI, 70 eV, *m/z*, int. (%)): 233 (49, M^+), 231 (24), 152 (14), 109 (17), 69 (100), 55 (17), 41 (32); IR (ν, cm^{-1}, KBr): 3436, 2970, 2937, 1424, 1353, 1159, 1125, 990; ^1H NMR (200 MHz, $CDCl_3$): 1.45 (s, 6H), 1.7–1.9 (m, 6H), 1.98 (s, 6H), 11.28 (s, ^1H, CHSe); ^{13}C NMR (50 MHz, $CDCl_3$): 15.15 (CH_2 26.81 (CH_3), 31.93 (CH_3), 37.87 (CH_2), 40.76 (CH_2), 189.80 (CHSe).

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