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AMINOSELENENYLATION OF OLEFINS. SYNTHESES OF β-PHENYLSELENO CARBAMATES

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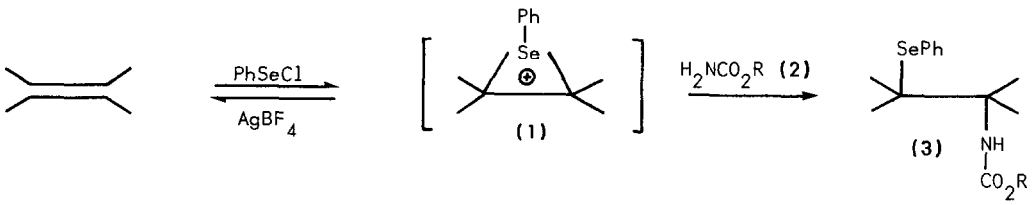
Summary: β-Phenylseleno carbamates have been synthesized by reaction of olefins with phenylselenenyl chloride and carbamates in presence of silver tetrafluoroborate. This reaction constitutes a good method for the conversion of olefins to β-functionalized protected amines.

The alkene amination reaction is of current interest in organic synthesis due to the important role of nitrogen functional groups in biologically active compounds. Those methods which involve the introduction of a phenylseleno group (aminoselenenylation of olefins) are particularly interesting owing to the versatility and easy manipulation of organoselenium compounds.

Although several methods to accomplish this reaction have been reported, e.g. those leading to the synthesis of β-phenylseleno- carboxamides,[1] sulfonamides,[2] azides,[3] and isothiocyanates,[4] most of them do not allow an easy preparation of primary amines.

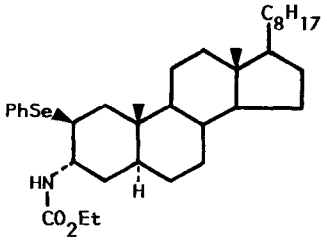
We report here that olefins react with phenylselenenyl chloride and carbamates (2) in presence of silver tetrafluoroborate to afford β-phenylseleno carbamates (3) as shown in the Scheme.



When $AgBF_4$ was omitted or substituted by acids (e.g. CF_3SO_3H, HBF_4, p-TsOH, etc.) no carbamate was detected (Table, entry 1), and only the expected products arising from the addition of PhSeCl to the double bond and the starting olefin could be observed.

As shown in the Table, the reaction proceeded well with mono- and 1,2-disubstituted olefins, and with ethyl, cyclohexyl and benzyl carbamates. Nevertheless, β-phenylseleno tert-butyl carbamates are produced in low yields even with longer reaction times (entry 6), and several tentatives to improve the reaction yield, under different conditions, were unsuccessful.

Initial attempts to extend this reaction to 1,1-disubstituted and trisubstituted olefins are indicated in entries 9 and 10. Methylenecyclohexane partially isomerizes under the stronger conditions needed to accomplish the addition to the olefin affording the seleno



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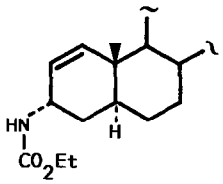

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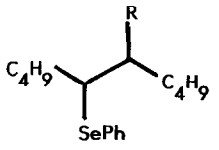
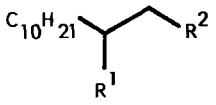
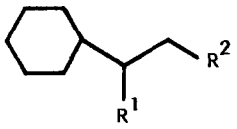


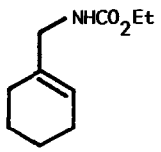
(6) R = $NHCO_2Et$
(7) R = $NHCO_2C_6H_{11}$
(8) R = $NHCO_2CH_2Ph$
(9) R = $NHCO_2$-t-C_4H_9
(10) R = OH



(11) R^1= $NHCO_2$ Et ; R^2= SePh
(12) R^1= SePh ; R^2= $NHCO_2Et$



(13) R^1= $NHCO_2Et$; R^2= SePh
(14) R^1= SePh ; R^2= $NHCO_2Et$



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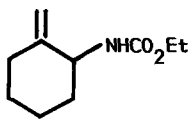

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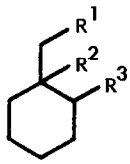


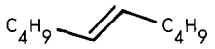
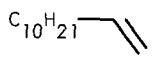
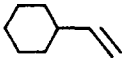
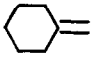
(17) R^1= SePh ; R^2= $NHCO_2Et$; R^3= H
(18) R^1= H ; R^2= SePh ; R^3= $NHCO_2Et$
(19) R^1= H ; R^2= $NHCO_2Et$; R^3= SePh

carbamates (17), (18), and (19) and the allylic urethanes (15) and (16) (produced by acid catalyzed elimination of the phenylseleno group) in 46% overall yield. Cholesteryl acetate did not undergo the aminoselenenylation reaction.[12]

As illustrated below, the regiochemistry of the aminoselenenylation reaction seems to be highly dependent on steric factors. The Markovnikov adduct is predominantly formed from 1-dodecene (entry 7), but when the steric hindrance is slightly increased, as in vinylcyclohexane (entry 8), the regiochemistry is reversed, the anti-Markovnikov product predominating. Also, in the reaction of 5α-cholest-2-ene (entry 2) only one regioisomer (4) is obtained[13] because the nucleophilic attack produced by the carbamate takes place by the less hindered α-face of the unfavourable 2β,3β-episelenonium intermediate.

Taking into account the versatility of organoselenium chemistry and since effective methods for carbamate deprotection are known (noteworthy Me_3SiCl/NaI for benzyl carbamates),[14] this aminoselenenylation reaction can be formally considered as a synthesis of β-functionalized amines from olefins.[15] A representative experimental procedure follows.

TABLE. Aminoselenenylation of representative olefins.[a]

Entry	Olefin	Carbamate	Temp, °C; Time, h	Adduct(s) (Yield %)
1	5α-Cholest-2-ene	**2** (R=Ethyl)	25;24	--[b]
2		**2** (R=Ethyl)	25;1	**4** (83)[5]
3		**2** (R=Ethyl)	25;5	**6** (95)[c,6]
4		**2** (R=Cyclohexyl)	25;6	**7** (74)[c,7]
5		**2** (R=Benzyl)	25;6	**8** (76)[c]
6		**2** (R=tert-Butyl)	25;19	**9** (20)[c]; **10** (17)[c,8]
7		**2** (R=Ethyl)	25;7	**11** (58); **12** (25)[9]
8		**2** (R=Ethyl)	25;6	**13** (24); **14** (56)[10]
9		**2** (R=Ethyl)	40-45;16	**15**; **16**; **17** **18**; **19** (46)[d,11]
10	Cholesteryl ac.	**2** (R=Ethyl)	25;20	--

[a] Olefin(1 mmol), PhSeCl(1.2 mmol), $AgBF_4$(1.3 mmol), **2**(20-30 mmol), CH_2Cl_2(30 ml). [b] $AgBF_4$ was omitted. [c] Since the product is a single stereoisomer it is assumed to be the erythro isomer, formed by antiperiplanar opening by the carbamate of the episelenonium ion (**1**). [d] The ratio of **15**/ **16**/ **17**/ **18**/ **19** is 19.5 : 6.5 : 12.4 : 4.6 : 3.

β-Phenylseleno benzyl carbamate (**8**). To a solution of trans-5-decene (1 mmol), benzyl carbamate (20 mmol), and silver tetrafluoroborate (1.3 mmol) in dry methylene chloride (30 ml) at 25 °C, in the dark, was added dropwise a solution of phenylselenenyl chloride (1.2 mmol) in dry methylene chloride (4 ml) under argon and over 2h. The mixture was then stirred at 25 °C for 4h, poured into aqueous potassium hydroxide and extracted with ethyl ether. The ether extract was filtered through celite 545 and washed with water. Silica gel column chromatography of the residue (eluant n-hexane:ethyl acetate 97:3) gave the β-phenylseleno carbamate (**8**) in 76% yield: oil; IR ν_{max} ($CHCl_3$) 3420, 1705, 1570, 1500 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.51, 7.19 (5H, m, $W_{1/2}$ 10 Hz, 10 Hz, C_6H_5Se), 7.32 (5H, m, $W_{1/2}$ 9 Hz, C_6H_5), 5.03 (1H, m, NH), 5.02 (2H, AB, J 14.5 Hz, H_2C-O), 3.84 (1H, m, $W_{1/2}$ 25 Hz, HC-N), 3.32 (1H, m, $W_{1/2}$ 19 Hz, HC-Se); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 156.0, 136.8, 134.1, 130.6, 129.1, 128.5, 128.0, 127.3, 66.6, 55.4, 54.8; MS m/z 447, 445 (M^+, 10%), 227 (100%).

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4. A. Toshimitsu, S. Uemura, and M. Okano, **J. Org. Chem., 48**, 5246 (1983).
5. Compound (**4**): m.p. 168-172 °C (MeOH); IR ν_{max} ($CHCl_3$) 3440, 1705, 1575, 1500 cm^{-1}; ^1H NMR ($CDCl_3$, 50 °C) δ 7.62, 7.59 (5H, m, m, $W_{1/2}$ 10 Hz, 10 Hz, C_6H_5), 4.96 (1H, br d, J 7 Hz, NH), 4.05 (1H, m, 3β-H), 4.01 (2H, q, J 7 Hz), 3.59 (1H, m, $W_{1/2}$ 9 Hz, 2α-H), 1.14 (3H, t, J 7 Hz); ^{13}C NMR ($CDCl_3$, 50 °C) δ 155.7, 133.5, 132.2, 129.2, 127.3, 60.9, 56.8, 56.7; the spectra show temperature-dependent effects; measurements performed at lower temperatures display complicated patterns; MS m/z 613, 615 (M^+, 10%), 569.3175 (M^+-EtOH, $C_{34}H_{51}O^{80}SeN$: 569.3132), 370 (100%).
6. Compound (**6**): IR ν_{max} ($CHCl_3$) 3420, 1700, 1570, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53, 7.23 (5H, m, m, $W_{1/2}$ 10 Hz, 10 Hz, C_6H_5), 4.90 (1H, br d, J 9 Hz, NH), 4.02 (2H, q, J 7 Hz), 3.81 (1H, m, $W_{1/2}$ 24 Hz, HC-N), 3.32 (1H, m, $W_{1/2}$ 19 Hz, HC-Se), 1.18 (3H, t, J 7 Hz); ^{13}C NMR ($CDCl_3$) δ 156.2, 134.1, 130.6, 128.9, 127.2, 60.6, 55.2, 54.6; MS m/z 385, 383 (M^+, 4%), 158 (100%).
7. Compound (**7**): IR ν_{max} ($CHCl_3$) 3420, 1700, 1570, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54, 7.24 (5H, m, m, $W_{1/2}$ 10 Hz, 10 Hz, C_6H_5), 4.91 (1H, br d, J 9 Hz, NH), 4.58 (1H, m, $W_{1/2}$ 30 Hz, HC-O), 3.82 (1H, m, $W_{1/2}$ 26 Hz, HC-N), 3.30 (1H, m, $W_{1/2}$ 20 Hz, HC-Se); ^{13}C NMR ($CDCl_3$) δ 155.0, 133.3, 129.9, 128.2, 126.4, 72.0, 54.7, 53.7; MS m/z 439, 437 (M^+, 10%), 212 (100%).
8. Compound (**9**): m.p. 46-7 °C; IR ν_{max} ($CHCl_3$) 3420, 1695, 1570, 1495 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54, 7.24 (5H, m, m, $W_{1/2}$ 10 Hz, 10 Hz, C_6H_5), 4.80 (1H, br d, J 9 Hz, NH), 3.75 (1H, m, $W_{1/2}$ 26 Hz, HC-N), 3.30 (1H, m, $W_{1/2}$ 19 Hz, HC-Se), 1.39 (9H, s). MS m/z 413, 411 (M^+, 30%), 228 (100%).
9. Compound (**11**): IR ν_{max} ($CHCl_3$) 3420, 1700, 1570, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53, 7.24 (5H, m, m, $W_{1/2}$ 10 Hz, 10 Hz, C_6H_5), 4.71 (1H, br d, J 9 Hz, NH), 4.06 (2H, q, J 7 Hz), 3.85 (1H, m, $W_{1/2}$ 24 Hz, HC-N), 3.10 (2H, d, J 5 Hz, H_2C-Se), 1.20 (3H, t, J 7 Hz); ^{13}C NMR ($CDCl_3$) δ 155.2, 132.0, 129.5, 128.3, 126.2, 59.9, 50.3; MS m/z 413, 411 (M^+, 2%), 367 (100%). Compound (**12**): IR ν_{max} ($CHCl_3$) 3420, 1700, 1570, 1505 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53, 7.26 (5H, m, m, $W_{1/2}$ 12 Hz, 12 Hz, C_6H_5), 5.10 (1H, m, $W_{1/2}$ 18 Hz, NH), 4.09 (2H, q, J 7 Hz), 3.4-3.2 (2H, complex, H_2C-N), 3.25 (1H, m, HC-Se), 1.22 (3H, t, J 7 Hz); ^{13}C NMR ($CDCl_3$) δ 156.7, 135.3, 133.0, 129.3, 128.0, 61.0, 46.9, 45.1; MS m/z 413, 411 (M^+, 10%), 367 (100%).
10. Compound (**13**): IR ν_{max} ($CHCl_3$) 3420, 1700, 1570, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53, 7.24 (5H, m, m, $W_{1/2}$ 11 Hz, 11 Hz, C_6H_5), 4.71 (1H, br d, J 8 Hz, NH), 4.07 (2H, q, J 7 Hz), 3.70 (1H, m, $W_{1/2}$ 21 Hz, HC-N), 3.10 (2H, d, J 5 Hz, H_2C-Se), 1.21 (3H, t, J 7 Hz); MS m/z 355, 353 (M^+, 15%), 309 (100%). Compound (**14**): IR ν_{max} ($CHCl_3$) 3440, 1700, 1570, 1500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.54, 7.25 (5H, m, m, $W_{1/2}$ 11 Hz, 10 Hz, C_6H_5), 5.08 (1H, m, $W_{1/2}$ 20 Hz, NH), 3.5-3.2 (2H, complex, H_2C-N), 3.16 (1H, m, $W_{1/2}$ 19 Hz, HC-Se); MS m/z 355, 353 (M^+, 15%), 309 (100%).
11. The reaction products were separated into two unresolved mixtures comprised of (**15**) + (**16**) and (**17**) + (**18**) + (**19**). Nevertheless, their structures were unequivocally established by spectroscopic methods.
12. The only product observed was the 5α,6β-dihydroxy derivative in 29% yield.
13. The structure of (**4**) was confirmed by oxidative elimination of the phenylseleno group to give (**5**) which in turn was synthesized from 5α-cholest-1-en-3-one: P. Longevialle, **Tetrahedron, 25**, 3075 (1969).
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15. The intramolecular version of this reaction, leading to pyrrolidines and piperidines, has been reported: D.L.J. Clive, V. Farina, A. Singh, C.K. Wong, W.A. Kiel, and S.M. Menchen, **J. Org. Chem., 45**, 2120 (1980); R.R. Webb II and S. Danishefsky, **Tetrahedron Letters, 24**, 1357 (1983).

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