

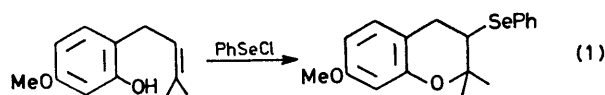
## Cyclofunctionalisation of Olefinic Urethanes with Benzeneselenenyl Reagents: a New General Synthesis of Nitrogen Heterocycles

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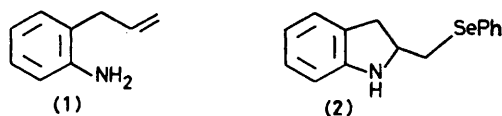
**Summary** Urethanes derived from *ortho*-alkenyl-anilines and from related compounds having a 5-amino-pentene or 6-amino-hexene system undergo cyclofunctionalisation with benzeneselenenyl halides to afford derivatives of 2,3-dihydroindole, pyrrolidine, or 1,2,3,4-tetrahydroisoquinoline (depending on the structure of the urethane).

CYCLOFUNCTIONALISATION<sup>1</sup> of olefinic acids,<sup>2</sup> alcohols,<sup>3</sup> and phenols<sup>1</sup> with PhSeCl is an efficient and mild procedure for synthesis of heterocycles, *e.g.*, equation (1). The technique

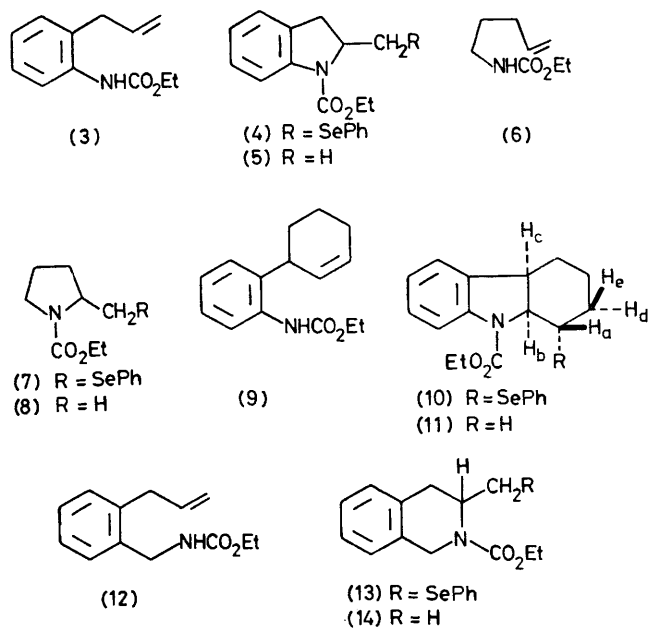


is valuable because the PhSe-group incorporated by the process permits a variety of modifications to be made to the product.<sup>4</sup> It was desirable to extend this method of cyclofunctionalisation to unsaturated amines because of the widely recognised importance of alkaloid synthesis.<sup>5</sup>

Simple anilines undergo substitution either in the *para*-position or on nitrogen, when treated<sup>6</sup> with areneselenenyl halides. The few aliphatic amines that have been studied<sup>6,7</sup> are acylated on nitrogen. We treated *o*-allyl-aniline (**1**) with PhSeCl, but were unable to observe clean transformation of (**1**) into (**2**) under a variety of conditions, including

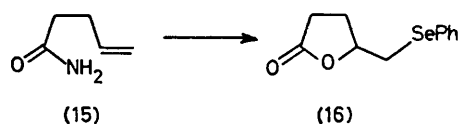


those that work well for the corresponding phenol.<sup>1</sup> Our observations suggested the need (in both the aniline and aliphatic series) to mask, temporarily, one of the N-H bonds and/or to lower the nucleophilicity of the N atom. We have discovered that olefinic urethanes (see Table), easily prepared<sup>8</sup> by the Schotten-Baumann method from the corresponding amines, do undergo the required transformation [*e.g.*, (**3**) → (**4**)].



In a typical procedure, a dry  $\text{CH}_2\text{Cl}_2$  solution of  $\text{PhSeCl}$  (1.1 equiv.) is added dropwise to a solution ( $\text{CH}_2\text{Cl}_2$ ) of the urethane, usually at  $-60$  or  $0^\circ\text{C}$ . The mixture is brought to room temperature and, after a suitable period, the product can be isolated with the results shown. In the case of (9) and (12) it appears advantageous to add the reagent to a mixture of urethane and a slight excess of  $\text{CF}_3\text{CO}_2\text{Ag}$ .<sup>9</sup> In these two examples  $\text{PhSeBr}$  was also tried and found to be suitable.

Although applicable to urethanes, the present reaction does not work for all types of amide. Compound (15), for example, gives the lactone (16)<sup>2a</sup> after treatment with  $\text{PhSeCl}$  and adventitious exposure to water.<sup>10</sup>



† The stereochemical course of the reduction has not been determined. The spectral data for (10) do not provide rigorous proof for the orientation of the  $\text{PhSe}$ -group.

TABLE<sup>a</sup>

Urethane	Conditions	Cyclic amine (% yield)	Reduction product (% yield)
(3) <sup>b</sup>	c	(4) (73)	(5) (80)
(6)	d	(7) (77)	(8) (88)
(9)	e	(10) <sup>f</sup> (59)	(11) <sup>g</sup> (72)
(12)	h	(13) <sup>i</sup> (52)	(14) (64)

<sup>a</sup> Yields refer to pure compounds that have been distilled or crystallised. The required amines were made by the published methods as follows (urethane, ref. to parent amine): (3), C. D. Hurd and W. W. Jenkins, *J. Org. Chem.*, 1957, **22**, 1418; cf. S. Jolidon and H.-J. Hansen, *Helv. Chim. Acta*, 1977, **60**, 978; (6), A. Kjær and R. B. Jensen, *Acta Chem. Scand.*, 1956, **10**, 1365; (9) and (12), L. S. Hegedus, G. F. Allen, and E. L. Waterman, *J. Amer. Chem. Soc.*, 1976, **98**, 2675. <sup>b</sup> M.p. 45–46 °C. <sup>c</sup>  $\text{PhSeCl}$  added at  $-65^\circ\text{C}$ , mixture kept 2 h at  $-65^\circ\text{C}$  and 1 h at room temp. <sup>d</sup>  $\text{PhSeCl}$  added at  $-60^\circ\text{C}$ , mixture kept 20 min at  $-60^\circ\text{C}$  and 1 h at room temp. <sup>e</sup>  $\text{PhSeBr}$  added at  $0^\circ\text{C}$  to mixture of (9) and  $\text{CF}_3\text{CO}_2\text{Ag}$ . Mixture then kept 2 h at room temp. <sup>f</sup> M.p. 99–101 °C;  $\delta$  ( $\text{CCl}_4$ , 100 MHz, 32 °C) 3.11,  $H_a$ , centre of t of d (broad signals),  $J_{ab} = ca. J_{ad} = ca. 10\text{ Hz}$ ,  $J_{ae} = ca. 4\text{ Hz}$ ; 3.54,  $H_c$ , centre of broad t,  $J = ca. 6\text{ Hz}$ ; 4.54,  $H_b$ , centre of q,  $J$  7.5 and 9 Hz. <sup>g</sup> Identical with an authentic specimen (M. A. Fletcher, M. W. Lakin, and S. G. P. Plant, *J. Chem. Soc.*, 1953, 3898). <sup>h</sup>  $\text{PhSeCl}$  added to mixture of (12) and  $\text{CF}_3\text{CO}_2\text{Ag}$  at room temp.; (13) isolated after 4 h. <sup>i</sup>  $\delta$  ( $\text{CDCl}_3$ , 100 MHz, 32 °C) 1.23, br t,  $J$  6.5 Hz; 2.55–3.24, 4H m; 3.95–4.9, 5H, comprising q ( $\text{OCH}_2\text{Me}$ ), m (NCH), q ( $\text{ArCH}_2\text{N}$ ).

The structures of the selenides reported are evident from n.m.r. measurements. However, the spectra are complicated and show temperature-dependent effects. Therefore, additional evidence was sought to confirm the spectral assignments. Each selenide was reduced with  $\text{Ph}_3\text{SnH}^{4b}$  in the yield indicated, and the resultant n.m.r. spectra were found to define the structures unambiguously.†

Satisfactory mass measurements and C, H, N combustion analytical data were obtained for all new compounds.

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<sup>1</sup> D. L. J. Clive, G. Chittattu, N. J. Curtis, W. A. Kiel, and C. K. Wong, *J.C.S. Chem. Comm.*, 1977, 725.

<sup>2</sup> (a) D. L. J. Clive and G. Chittattu, *J.C.S. Chem. Comm.*, 1977, 484; (b) K. C. Nicolaou and Z. Lysenko, *J. Amer. Chem. Soc.*, 1977, **99**, 3185.

<sup>3</sup> D. L. J. Clive, G. Chittattu, and C. K. Wong, *Canad. J. Chem.*, 1977, **55**, 3894; K. C. Nicolaou and Z. Lysenko, *Tetrahedron Letters*, 1977, 1257.

<sup>4</sup> (a) For a review of organoselenium chemistry, see D. L. J. Clive, *Tetrahedron Report*, in the press; (b) for replacement of  $\text{PhSe}$  by H or D see D. L. J. Clive, G. Chittattu, and C. K. Wong, *J.C.S. Chem. Comm.*, 1978, 41, and refs. therein.

<sup>5</sup> See, for example, 'The Alkaloids,' Senior Reporter, M. F. Grunton, Specialist Periodical Reports (The Chemical Society), 1976, Vol. 6.

<sup>6</sup> D. L. Klayman, in 'Organic Selenium Compounds: Their Chemistry and Biology,' Eds. D. L. Klayman and W. H. H. Günther, Wiley-Interscience, New York, 1973, p. 108.

<sup>7</sup> H. J. Reich and J. M. Renga, *J. Org. Chem.*, 1975, **40**, 3313.

<sup>8</sup> *Org. Synth.*, 1963, Coll. Vol. 4, 780.

<sup>9</sup> Cf. D. L. J. Clive, *J.C.S. Chem. Comm.*, 1974, 100; H. J. Reich, *J. Org. Chem.*, 1974, **39**, 428; K. B. Sharpless and R. F. Lauer, *ibid.*, p. 429.

<sup>10</sup> A  $\gamma$ -lactam is formed if  $\text{I}_2$  is used for cyclofunctionalisation: E. N. Rengevich, V. I. Staninets, and E. A. Shilov, *Proc. Acad. Sci. (U.S.S.R.)*, 1962, **146**, 787.