and Me_4Si (δ = 0.00) as internal standard. Infrared spectra were recorded on a Perkin-Elmer 397 or a Beckman FT 2100 spectrometer. Optical rotations were measured on a JASCO DIP-369 polarimeter using a 1-mL capacity cell. Melting points were taken in capillary tubes on a Thomas-Hoover Unimelt apparatus and are uncorrected. Elemental analyses were carried out by Desert Analytics, Tucson, AZ.

Osmium tetraoxide was purchased from Aldrich and used without further purification. Tetrahydrofuran (THF) was distilled under nitrogen from a deep blue solution of sodium/benzophenone ketyl. Acetone and methylene chloride were distilled from K_2CO_3 and CaH_2, respectively. Baker silica gel (60–200 mesh) was used for plugs and column chromatography. TLC was performed on Baker Si 250F (0.25 mm) TLC plates. All reactions were carried out under anhydrous conditions with an inert blanket of nitrogen or argon.

Preparation of 1(*R*)-Acetoxy-2,3(*R*,*R*),4(*S*)-trihydroxycyclopentane (4a). To a solution of 300 mg (2.11 mmol) of optically pure (>99% ee) **3**[7] in 3.5 mL of an 8:1 mixture of acetone/water was added 567 mg (4.8 mmol) of *N*-methylmorpholine *N*-oxide (NMO) followed by a small crystal of OsO_4 (approximately 15 mg, 0.06 mmol; reaction time is dependent upon the amount of OsO_4 present, however, under these conditions conversion is generally complete in 2–4 h). After complete consumption of the starting material (as deduced by TLC analysis), the solution was washed through a plug of silica gel (3 g) with 9:1 ethyl acetate/methanol. The filtrate was then concentrated under reduced pressure to give 638 mg of a crude brown oil. This residue was chromatographed over 36 g of silica gel to yield 350 mg (94%) of a clear oil; $[\alpha]^{25}_D$ −44.3° (*c* 1.30, MeOH), R_f 0.38 in 9:1 ethyl acetate/methanol. Due to the instability of this material it must be used immediately in the next step.

Preparation of Acetonide 4b. Triol **4a** (1.2 g, 6.8 mmol) and a small crystal of *p*-toluenesulfonic acid (*p*-TSA) were dissolved in 15.0 mL of dry acetone and 2 mL of 2,2-dimethoxypropane. The reaction was judged complete (as deduced by TLC) after being stirred overnight at room temperature. The mixture was passed through a plug of silica gel (5 g) with reagent grade acetone and concentrated in vacuo to give 1.49 g of a brown oil. This residue was chromatographed over 60 g of silica gel (1:1, hexane/ethyl acetate) to afford 1.168 g (79%) of the corresponding acetonide: $[\alpha]^{23}_D$ −10.3° (*c* 2.62, $CHCl_3$); ^1H NMR (60 MHz) δ 1.26 (s, 3 H, CCH_3), 1.40 (s, 3 H, CCH_3), 1.85 (dt, J = 1 Hz and 15 Hz, 1 H, β CH_2), 2.10 (s, 3 H, OAc), 2.30 (dt, J = 5 Hz and 15 Hz, 1 H, α CH_2), 2.7 (br s, 1 H, OH), 4.20 (br s, 1 H, HOCH), 4.60 (m, 2 H, COCH), 5.10 (d, J = 5 Hz, 1 H, AcOCH); IR (neat) 3295 (br, OH), 1730 (s, CO), 1370, 865 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O_5$: C, 55.50; H, 7.46; O, 36.99. Found: C, 55.53; H, 7.66.

Preparation of Enone 5. To a stirred suspension of 2.4 g of diatomaceous earth and 1.75 g (8.2 mmol) of pyridinium chlorochromate in 20 mL of dry CH_2Cl_2 was added dropwise over 3 min a solution of 1.065 g (4.93 mmol) of **4b** in 4 mL of CH_2Cl_2. The reaction was complete after stirring 48 h at room temperature as indicated by TLC analysis. The suspension was filtered through an 8-g plug of silica gel with 150 mL of CH_2Cl_2 and the resulting filtrate was washed sequentially with saturated $NaHCO_3$ and brine, and dried over $MgSO_4$. The clear solution was concentrated at atmospheric pressure by boiling off the solvent through a 15-cm Vigreux column to afford 0.610 g (80%) of a colorless crystalline solid, mp 65–67 °C: $[\alpha]^{25}_D$ +68.0° (*c* 0.93, $CHCl_3$). Recrystallization from pentane/ether (8:1) provided pure crystals of **5**, mp 68–69 °C: $[\alpha]^{26}_D$ +70.0° (*c* 0.92, $CHCl_3$); R_f 0.50 (1:1, hexane/ethyl acetate); ^1H NMR (200 MHz) δ 1.39 (br s, 6 H, 2 CH_3), 4.43 (d, J = 5.5 Hz, 1 H, OCH), 5.24 (dd, J = 2.2 Hz and 5.5 Hz, 1 H, OCH), 6.19 (d, J = 5.9 Hz, 1 H, α HC=C), 7.58 (dd, J = 2.2 Hz and 5.9 Hz, 1 H, β C=CH); IR ($CHCl_3$) 2937, 1729 (s, CO), 1097 cm^{-1}.

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Registry No. 1, 72877-50-0; 3, 60410-16-4; 4a, 114739-33-2; 4b, 113565-13-2; 5, 104010-72-2.

Application of Episelenonium Ion Chemistry to Heterocyclic Ring Closure

Françoise Chrétien and Yves Chapleur*

Laboratoire de Chimie Organique 3, Unité Associée CNRS 486, Université de Nancy I, B.P. 239, F-54506 Vandoeuvre-les-Nancy, France

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Organoselenium derivatives have found numerous applications in organic synthesis,[1] and their use in either hetero- or carbocyclic ring formation is well documented.[2] Subsequent functional transformations through oxidative or reductive removal of the introduced seleno group have reinforced the interest of this approach. Furthermore, a number of easy to handle reagents such as *N*-(phenylseleno)phthalimide (NPSP) or -succinimide (NPSS) have been recently introduced.[3]

In connection with a synthetic program, we were interested in the formation of tetrahydroisoquinoline type ring systems. Several recent reports of Edstrom and Livinghouse[4] on the successful synthesis of tetrahydronaphthalenes prompted us to investigate the possibility of a selenium-mediated olefin–arene intramolecular bond formation according to Scheme I (path a).

Our investigation began with unsaturated amides **1–4**, which were of interest in our planned synthesis of alkaloids. Under the conditions described by Livinghouse[4] (see Table I, method A), amide **1** was transformed into **8** in 65% yield. Spectroscopic data of compound **8** did not support the expected tetrahydroisoquinoline structure. Disappearance of the amide absorption in IR spectroscopy led to the conclusion that **1** was cyclized into an oxazoline ring. Structural proof was obtained by reductive cleavage of the phenylseleno group with tributyltin hydride[5] and comparison of the resulting oxazoline **17** with an authentic sample prepared by standard procedures. Several amides were transformed into oxazolines under the same conditions.

The stoichiometry of the Lewis acid in analogous reactions seems to be of crucial importance as demonstrated by Ley et al.[5] Thus we varied reaction conditions in order to circumvent this undesired cyclization without success. Oxazoline formation[6] obviously proceeds via episelenonium ion opening by the amide oxygen atom. A related formation of imino lactones from unsaturated amides in the

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(2) Nicolaou, K. C. *Tetrahedron* **1981**, *37*, 4097.
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(5) Ley, S. V.; Lygo, B.; Molines, H.; Morton, J. A. *J. Chem. Soc., Chem. Commun.* **1982**, 1251.
(6) For the acid-catalyzed cyclization of *N*-allylbenzamides into oxazolines, see: McManus, S. P.; Carroll, J. T.; Pittman, C. U. *J. Org. Chem.* **1970**, *35*, 3768.

0022-3263/88/1953-3615$01.50/0

Scheme I

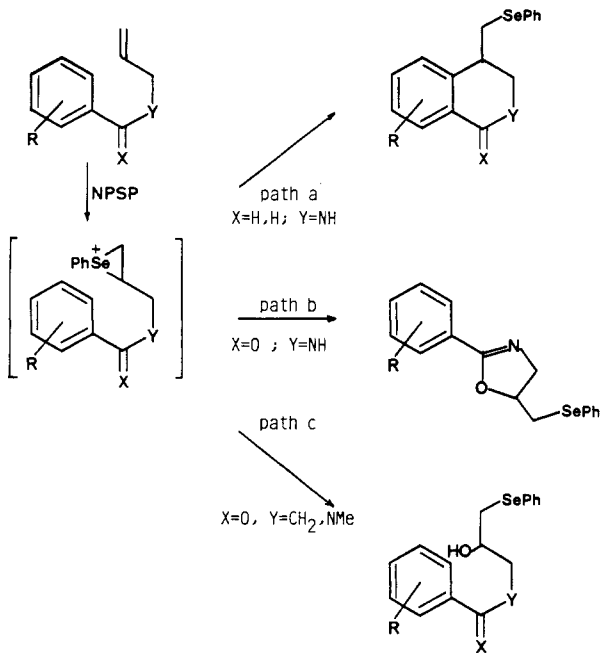


Table I. Selenium-Promoted Cyclization of *N*-Allylbenzamides

entry	substrate	product	method[a]	yield,[b] %
1	1	8	A	65
2	1	8	B	55
3	1	8	C	65
4	1	8	D	63
5	1	8	E	73
6	1	8	F	61
7	2	9	A	70
8	3	10	A	90
9	4	11	A	60
10	4	11	F	23
11	5	13	A	75
12	5	13	F	19
13	6	15	A	80
14	7	16	A	74

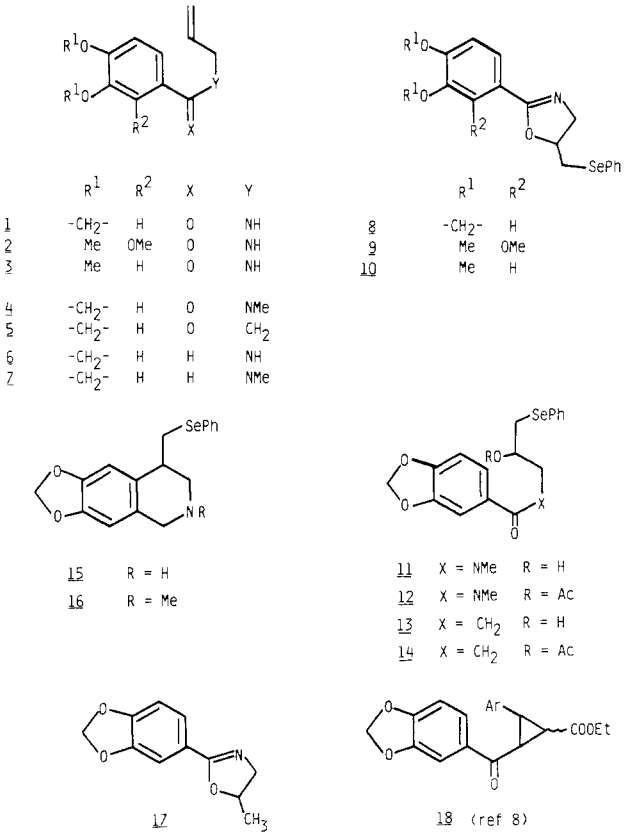
[a] Method A, NPSP (1.05 equiv), $SnCl_4$ (1.1 equiv), CH_2Cl_2, 1 h at −78 °C and then 3 h at room temperature; method B, NPSP (1.05 equiv), $SnCl_4$ (0.01 equiv), 72 h at room temperature; method C, NPSP (1.05 equiv), TMSOTf (1.1 equiv), 1 h at −78 °C and then 3 h at room temperature; method D, NPSP (1.05 equiv), TMSOTf, (0.01 equiv), 48 h at room temperature; method E, NPSP (1.05 equiv), BF_3/CH_3NO_2 (2 equiv), CH_2Cl_2, 1 h at −78 °C and then 3 h at room temperature; Method F, NPSP (1.05 equiv), BF_3 (2 equiv), CH_3NO_2, 15 days at room temperature. [b] Yields refer to pure isolated products.

presence of phenylselenyl chloride has been reported recently by Toshimitsu et al.[7] Tertiary amide **4** under the same conditions did not produce the expected oxazoline; hydrolysis of the episelenonium (Scheme I, path c) was observed, giving alcohol **11**, characterized as its acetate **12**. Finally, when ketone **5** was treated as above, only hydroxyselenylation of the double bond occurred, yielding alcohol **13**, which was acetylated into compound **14**.

Cyclization was assumed to be impeded by the presence of a carbonyl group in compounds **1–5**. This was confirmed by the following experiments. Amines **6** and **7** were prepared and submitted to episelenonium formation. In these cases, regiospecific ring closure occurred, resulting in tetrahydroquinolines **15** and **16**, respectively, as a single product. No ring closure at the ortho position of the

(7) Toshimitsu, A.; Terao, K.; Uemura, S. *J. Org. Chem.* **1987**, *52*, 2018.

Chart I



aromatic ring was observed. Electrophilic substitution of piperonyl derivatives such as **18** via Lewis acid catalyzed opening of cyclopropanes is known. This electrophilic ring closure occurred only in nitromethane but was rather sluggish (15 days).[8] We used such conditions with compounds **1**, **4**, and **5**. Cyclization of **1** into oxazoline was observed (entry 6); nevertheless, tertiary amide **4** and ketone **5** were transformed into **11** and **13** and several decomposition products because of the long reaction time.

These observations can be rationalized in terms of deactivation of the ortho positions of **1–5** to electrophilic substitution by the carbonyl group. One may assume that episelenonium ion is not electrophilic enough to react at the ortho position of the keto or amide group. In contrast, carbocations are electrophilic enough to ensure carbocyclization of compound **18**.[9] A possible explanation for such a difference is the presence of an oxygen atom in a suitable position which can interact with the intermediate episelenonium ion by formation of a six-membered ring "chelate". This type of interaction, already postulated in the literature,[10] will lower the electrophilic character of the episelenonium ion, which will be opened only by nucleophiles such a water (entries 9–12) or the oxygen atom itself (entries 1–8). In the case of amines **6** and **7** as well as in the examples described by Edstrom and Livinghouse,[4] the reactivity of episelenonium ion toward the ortho position of the aromatic ring is sufficient to ensure carbo- and heterocyclization.

(8) Murphy, S. W.; Wattanasin, S. *J. Chem. Soc., Chem. Commun.* **1980**, 262.

(9) Nevertheless a benzylic carbocation is expected to be more electrophilic than an episelenonium ion. We thank one of the referees for drawing our attention to this fact.

(10) Toshimitsu, A.; Terao, K.; Uemura, S. *J. Chem. Soc., Perkin Trans. 1* **1987**, 1059. Liotta, D.; Zima, G.; Saindane, M. *J. Org. Chem.* **1982**, *47*, 1258. Shimizu, M.; Takeda, R.; Kuwajima, I. *Tetrahedron Lett.* **1979**, 3461.

Experimental Section

^1H and ^{13}C NMR spectra were recorded on a Bruker Aspect 3000 spectrometer operating at 400 and 100.5 MHz, respectively, using deuteriochloroform as solvent. Assignments were confirmed by double irradiation. Chemical shifts are reported relative to internal $SiMe_4$. Infrared spectra were recorded on a Perkin-Elmer PE 580 spectrometer. TLC was performed on silica gel (Merck 60 F_{254}). Column chromatography was conducted on silica gel (Merck 60, 70-230 mesh). Elemental analyses were performed by the Service Central de Microanalyse du CNRS at Vernaison (France).

General Procedure. Method A. A solution of 317 mg (1.05 mmol) of *N*-(phenylseleno)phthalimide (NPSP) dissolved in methylene chloride (2 mL) was cooled to -78 °C and treated with $SnCl_4$ (0.22 mL, 1.1 mmol). After 2 min of stirring, a methylene chloride solution (5 mL) of the unsaturated substrates (1 mmol) was added, and the mixture was stirred 1 h at -78 °C and then 3 h (48 h in the case of substrates **6** and **7**) at room temperature. The reaction mixture was diluted with methylene chloride (150 mL) and washed with a saturated $NaHCO_3$ solution and with water. In the case of compounds **6** and **7**, the precipitate was filtered off, diluted in aqueous 2 M sodium hydroxide (5 mL), and extracted with methylene chloride. The organic layer was dried over magnesium sulfate and concentrated under reduced pressure. Products were purified by column chromatography.

Method B. A solution of 317 mg (1.05 mmol) of NPSP dissolved in methylene chloride (2 mL) was treated with $SnCl_4$ (1 mL of a 10 mM methylene chloride solution). Amide **1** (205 mg, 1 mmol) dissolved in methylene chloride (5 mL) was added, and the reaction mixture was stirred 72 h at room temperature. The mixture was worked up as described in method A.

Method C. This method was like method A, but 0.2 mL of trimethylsilyl triflate (TMSOTf) was used instead of $SnCl_4$.

Method D. This method was like method B, but 1 mL of a 10 mM methylene chloride solution of TMSOTf was used instead of $SnCl_4$.

Method E. A solution of 317 mg (1.05 mmol) of NPSP dissolved in methylene chloride (2 mL) was cooled to -78 °C and treated with 2 mmol of BF_3 (as a stock solution of CH_3NO_2). After 2 min of stirring, **1** (205 mg, 1 mmol) was added and the mixture was then stirred for 1 h at room temperature. The mixture was worked up as described in method A.

Method F. A solution of 317 mg (1.05 mmol) of NPSP dissolved in nitromethane (2 mL) was treated with 4 mmol of BF_3 (as a stock solution in CH_3NO_2). The unsaturated derivative (1 mmol) was added and the mixture was stirred 15 days at room temperature under argon. The mixture was worked up as described in method A.

2-(3,4-(Methylenedioxy)phenyl)-4-((phenylseleno)methyl)-2-oxazoline (8): ^1H NMR ($CDCl_3$) δ 3.03 (1 H, dd, J = 12.5 Hz, J = 7.5 Hz, C*H*-Se-Ph), 3.26 (1 H, dd, J = 5.5 Hz, C*H*-Se-Ph), 3.79 (1 H, dd, $J_{5',5}$ = 15 Hz, $J_{4,5}$ = 7 Hz, H5), 4.12 (1 H, dd, $J_{5',4}$ = 9.5 Hz, H5'), 4.86 (1 H, m, H4), 6.00 (2 H, s, O-CH_2-O), 6.79 (1 H, d, J = 8 Hz), 7.27 (3 H, m, Se-Ph), 7.31 (1 H, d, J = 1.25 Hz), 7.39 (1 H, dd), 7.57 (2 H, m, Se-Ph); ^{13}C NMR ($CDCl_3$) δ 31.92 (*C*-Se-Ph), 60.13 (C5), 78.95 (C4), 101.50 (O-CH_2-O), 107.99, 108.32, 121.61, 123.17, 147.59, 150.23 (*C* arom, piperonyl), 123.38, 127.47, 128.97, 129.05, 133.35, 134.05 (Se-Ph), 163.27 (C2). Anal. Calcd for $C_{17}H_{15}NO_3Se$: C, 56.68; H, 4.20; N, 3.89; Se, 21.92. Found: C, 56.82; H, 4.28; N, 3.86; Se, 21.88.

2-(3,4-Dimethoxyphenyl)-4-((phenylseleno)methyl)-2-oxazoline (9): ^1H NMR ($CDCl_3$) δ 3.05 (1 H, dd, J = 12.5 Hz, J = 7.5 Hz, C*H*-Se-Ph), 3.29 (1 H, dd, J = 5 Hz, C*H*-Se-Ph), 3.82 (1 H, dd, $J_{5,5'}$ = 15 Hz, $J_{4,5}$ = 6.5 Hz, H5), 3.92 (6 H, s, 2OCH_3), 4.15 (1 H, dd, $J_{4,5'}$ = 9.5 Hz, H5'), 4.87 (1 H, m, H4), 6.85 (2 H, m), 7.22 (3 H, m), 7.44 (2 H, m), 7.56 (1 H, m). Anal. Calcd for $C_{18}H_{19}NO_3Se$: C, 57.45; H, 5.09; N, 3.72; Se, 20.98. Found: C, 57.82; H, 5.13; N, 3.63; Se, 21.04.

2-(2,3,4-Trimethoxyphenyl)-4-((phenylseleno)methyl)-2-oxazoline (10): ^1H NMR ($CDCl_3$) δ 3.03 (1 H, dd, J = 12.5 Hz, J = 7.5 Hz, C*H*-Se-Ph), 3.29 (1 H, dd, J = 5.5 Hz, C*H*-Se-Ph), 3.83 (1 H, dd, $J_{5,5'}$ = 15 Hz, $J_{5,4}$ = 6.5 Hz, H5), 3.87 (3 H, s, OCH_3), 3.88 (3 H, s, OCH_3), 3.89 (3 H, s, OCH_3), 4.16 (1 H, dd, $J_{4,5'}$ = 9.5 Hz, H5'), 4.82 (1 H, m, H4), 6.66 (1 H, d, J = 9 Hz), 7.27 (s H, m, Se-Ph), 7.44 (1 H, d), 7.57 (2 H, m, Se-Ph). Anal. Calcd for $C_{19}H_{21}NO_4Se$: C, 56.16; H, 5.21; N, 3.45; Se, 19.43. Found: C, 55.83; H, 5.33; N, 3.30; Se, 19.47.

***N*-Methyl-*N*-(2-acetoxy-3-(phenylseleno)propyl)piperonylamide (12):** IR (film) cm^{-1} 1675 (C=O), 1735 (CH_3O-C=O); ^1H NMR ($CDCl_3$) δ 1.95 (3 H, s, CH_3), 2.99 (3 H, s, OAc), 3.09 (2 H, m), 3.60 (1 H, m), 3.90 (1 H, m), 5.34 (1 H, m), 6.00 (2 H, s, O-CH_2-O), 6.84 (3 H, m), 7.27 (3 H, m, Se-Ph), 7.53 (2 H, m, Se-Ph). Anal. Calcd for $C_{19}H_{19}NO_5Se$: C, 54.29; H, 4.56; N, 3.33; Se, 18.79. Found: C, 54.10; H, 4.53; N, 3.06; Se, 18.75.

3-Acetoxy-4-(phenylseleno)butyl 3,4-(Methylenedioxy)phenyl Ketone (14): IR (film) cm^{-1} 1635 (C=O), 1735 (CH_3O-C=O); ^1H NMR ($CDCl_3$) δ 1.92 (3 H, s, OAc), 2.08 (1 H, m, H2), 2.19 (1 H, m, H2'), 2.81 (2 H, t, J = 7.5 Hz, H1, H1'), 3.09 (1 H, dd, $J_{4,4'}$ = 12 Hz, $J_{3,4'}$ = 6 Hz, *H4'*), 3.14 (1 H, dd, $J_{3,4}$ = 6 Hz, H4), 5.10 (1 H, m, H3), 6.04 (2 H, s, O-C*H*$_2$-O), 6.84 (1 H, d, J = 8 Hz), 7.28 (3 H, m, Se-Ph), 7.40 (1 H, d, J = 1.25 Hz), 7.51 (1 H, dd), 7.55 (2 H, m, Se-Ph). Anal. Calcd for $C_{20}H_{20}O_5Se$: C, 57.29; H, 4.81; Se, 18.83. Found: C, 57.12; H, 4.87; Se, 18.75.

6,7-(Methylenedioxy)-4-((phenylseleno)methyl)-1,2,3,4-tetrahydroisoquinoline (15): ^1H NMR ($CDCl_3$) δ 2.39 (1 H, s, NH), 2.85 (1 H, m, H4), 3.06 (1 H, dd, J = 12.5 Hz, J = 4.5 Hz, C*H*-Se-Ph), 3.21 (2 H, m, H3, H3'), 3.34 (1 H, dd, J = 3 Hz, C*H*-Se-Ph), 3.85 (2 H, s, H1, H1'), 5.88 (2 H, s, O-C*H*$_2$-O), 6.47 (1 H, s), 6.55 (1 H, s), 7.26 (3 H, m, Se-Ph), 7.54 (2 H, m, Se-Ph). Anal. Calcd for $C_{17}H_{17}NO_2Se$: C, 58.96; H, 4.95; N, 4.04; Se,22.80. Found: C, 59.03; H, 4.83; N, 3.97; Se, 22.62.

2-Methyl-6,7-(methylenedioxy)-4-((phenylseleno)methyl)-1,2,3,4-tetrahydroisoquinoline (16): ^1H NMR ($CDCl_3$) δ 2.33 (3 H, s, NCH_3), 2.45 (1 H, dd, $J_{3,3'}$ = 11.5 Hz, $J_{3',4}$ = 4 Hz, H3'), 2.89 (1 H, m, H4), 2.99 (1 H, dd, $J_{3,4}$ = 3 Hz, H3), 3.20 (1 H, d, $J_{1,1'}$ = 15 Hz, H1), 3.21 (1 H, dd, J = 12 Hz, J = 3 Hz, C*H*-Se-Ph), 3.29 (1 H, dd, J = 10.5 Hz, C*H*-Se-Ph), 3.63 (1 H, d, H1'), 5.89 (2 H, br s, O-CH_2-O), 6.48 (1 H, s, H5), 6.55 (1 H, s, H8), 7.28 (3 H, m, Se-Ph), 7.57 (2 H, m, Se-Ph). Anal. Calcd for $C_{18}H_{18}NO_2Se$: C, 60.17; H, 5.05; N, 3.90; Se, 21.98. Found: C, 59.91; H, 5.17; N, 3.83; Se, 22.04.

2-(3,4-(Methylenedioxy)phenyl)-4-methyl-2-oxazoline (17): ^1H NMR ($CDCl_3$) δ 1.41 (3 H, d, J = 6 Hz, CH_3), 3.57 (1 H, dd, $J_{5,5'}$ = 15 Hz, $J_{4,5}$ = 7 Hz, H5), 4.11 (1 H, dd, $J_{4,5'}$ = 9.5 Hz, H5'), 4.82 (1 H, m, H4), 6.00 (2 H, s, O-CH_2-O), 6.82 (1 H, d, J = 8 Hz, H arom), 7.40 (1 H, d, J = 1.5 Hz, H arom), 7.49 (1 H, dd, H arom); ^{13}C NMR ($CDCl_3$) δ 21.05 (CH_3), 61.52 (C5), 76.27 (C4), 101.45 (O-CH_2-O), 107.97, 108.31, 122.13, 123.02, 147.60, 150.09 (C arom), 163.42 (C2). Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.57; H, 5.22; N, 6.64.

Registry No. **1**, 64654-11-1; **2**, 114908-28-0; **3**, 73664-69-4; **4**, 114908-29-1; **5**, 114908-30-4; **6**, 68291-57-6; **7**, 114908-31-5; **8**, 114908-32-6; **9**, 114908-33-7; **10**, 114908-34-8; **11**, 114908-35-9; **12**, 114908-36-0; **13**, 114908-37-1; **14**, 114908-38-2; **15**, 114908-39-3; **16**, 114908-40-6; **17**, 114908-41-7; NPSP, 71098-88-9.

Organocuprate Conjugate Addition to 2,3-Dihydro-4*H*-pyran-4-ones[1]

Daniel L. Boring[†] and Robert D. Sindelar*[,†,‡]

Department of Medicinal Chemistry and The Research Institute of Pharmaceutical Sciences, The University of Mississippi, University, Mississippi 38677

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The scope and utility of organocopper-mediated conjugate addition methodologies have been amply illustrated during the past 15 years with numerous reviews[2-8] and at least one monograph[9] appearing on the subject. A variety of organocuprate reagents have been developed utilizing stoichiometric (Gilman),[10] mixed ligand (heterocuprate),[11] catalytic,[12] and "higher order" (copper(I) cyanide)[13] cuprate

[†] Department of Medicinal Chemistry.
[‡] The Research Institute of Pharmaceutical Sciences.

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