Highly stereocontrolled syntheses of 2,3-disubstituted 1,4-butyrolactones using ionic and free radical reactions

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Received April 12, 1993

STEPHEN HANESSIAN, BENOIT VANASSE, HUA YANG, and MARCO ALPEGIANI. Can. J. Chem. **71**, 1407 (1993).

N-Substituted 3-amino-1,4-butyrolactones undergo highly stereocontrolled substitution reactions via anionic and free radical processes.

STEPHEN HANESSIAN, BENOIT VANASSE, HUA YANG et MARCO ALPEGIANI. Can. J. Chem. **71**, 1407 (1993).

Les dérivés des 3-amino-1,4-butyrolactones *N*-substitués réagissent de façon hautement stéréocontrollée dans de réactions de type anioniques et radicalaires.

The past decade has seen a resurgence in asymmetric processes in virtually all facets of preparative organic chemistry where chirality is an issue (1). Efforts in the area of amino acid chemistry (2) have focused on the synthesis of natural and unnatural analogs in connection with natural product synthesis (for some recent examples, see ref. 3), and a continuing interest in the design of enzyme inhibitors and peptidomimetics (ref. 4 for recent reviews). Thus, the search for enantiomerically pure "small" molecules as mimics and surrogates of proteinogenic amino acids has become an important area of research activity.

In the preceding paper (5), we described methods for the stereocontrolled hydroxylation of enolates derived from *N*-substituted dialkyl aspartates and glutamates, as well as from 3-*N*-substituted butyrolactones. It was shown that by utilizing steric control, influenced by resident functionality, hydroxylation of enolates took place from a side opposite to a bulky substituent. On the other hand, using a reagent capable of coordinating with the *N*-substituent, hydroxylation could be directed to produce significant amounts of the other diastereomer.

We now report on the utilization of (*S*)-3-benzyloxycarbonylamino butyrolactones, **1** and **2**, readily available from *L*-aspartic acid (6), as chiral templates for site-selective and stereocontrolled functionalizations at C-2 via the corresponding enolates and radicals. In this context, the 2-azido and 2-bromo products would constitute versatile 4-carbon chirons with preparatively useful applications (see, for example, ref. 7), as shown in Scheme 1.

Previous studies (6) with the same lactone showed that treatment of the dianion with methyl iodide led to the expected *anti* product (X = Me) as the preponderant isomer (88:12 *anti*:*syn*). More recently, this work was extended by Ohno and co-workers (8) to the corresponding ethyl (55%) and 2-propyl (15%) products, with high selectivity. Such 2-alkyl butyrolactones were subsequently transformed into monocyclic β-lactams (9).

We first addressed the problem of electrophilic bromination of the dianion **3** generated in the presence of LiHMDS. Using *N*-bromosuccinimide and bromine as the brominating reagents produced a single crystalline product **4**, in yields of 45% and 51%, respectively, with recovery of starting material. The stereochemical outcome of the reaction was proved by detailed NMR studies. Changing the base to LDA or KHMDS, among others, did not affect the reaction or the stereochemistry. Surprisingly, when bromodimethylsulfonium bromide (10) was used as the brominating reagent, a crystalline 2,2-dibromo lactone **5** was formed in 55% yield. Once again, starting material could be recovered from the reaction mixture.

Attempts to displace the bromine atom in **4** with azide ion, under different conditions (solvent, temperature), led to decomposition, presumably due to participation of the *N*-benzyloxycarbonyl group followed by subsequent reactions of the resulting 2-benzyloxy-1,3-oxazolinium ion.

We next investigated electrophilic amination of the dianion of **1**, as well as of the corresponding *N*-*tert*-butoxycarbonyl analog **2**. Since we sought to have two functional groups that could be chemically manipulated independently of one another, we looked into the prospects of electrophilic azidation reactions. Enolate anions of simple 2-azetidinones have been transformed into the 3-azido derivatives by treatment with arylsulfonyl azides in 30–76% yield (11). Evans and Britton (12) showed that treatment of the potassium enolate of anions bearing a chiral oxazolidone auxiliary with triisopropylbenzenesulfonyl azide produces the corresponding 2-azido derivatives in good yields and high selectivity. While our work was in progress, Nitta et al. (9) reported the azidation of the dianion **3** (R = *t*-Bu) with tosyl azide in the presence of trimethylsilyl chloride, to give the corresponding azido derivative **7** in 58% yield (Scheme 2).

Treatment of the dilithium dianion of **1** with tosyl azide produced a single crystalline azido derivative **6** in 55% yield with recovery of starting material. The same reaction with the *N*-Boc derivative also produced the expected 2-azido derivative **7** in agreement with the published results (9). Several attempts to improve the yield, including changes in the nature of the base (e.g., KHMDS) and the use of tripsyl azide, were not successful. The lower reactivity of such dianions toward weak electrophiles is not uncommon (9, 11).

The lactones **6** and **7** offer the flexibility of differentiating the two vicinal amino groups with different protective groups. Thus, the azido group can be transformed to *N*-Cbz or *N*-Boc groups simply by reduction in the presence of the appropriate carbamoylating agent, as shown in Scheme 2.

With the availability of the 2-bromo derivative **4**, we became interested in their utilization in a free-radical *C*-allylation reaction (ref. 13, and, for a recent application to carbohydrate lactones, ref. 14), with a particular emphasis on the stereochemical outcome as compared to the analogous anionic reaction (6, 7). As a parallel study, we also

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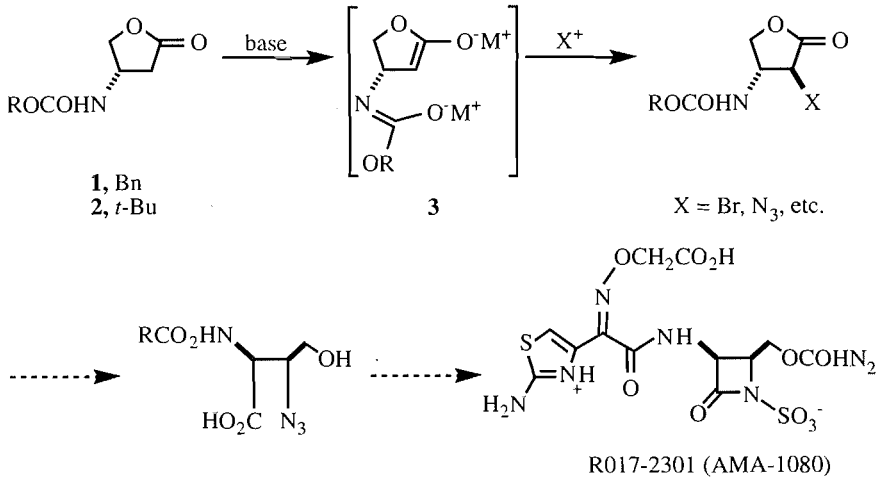
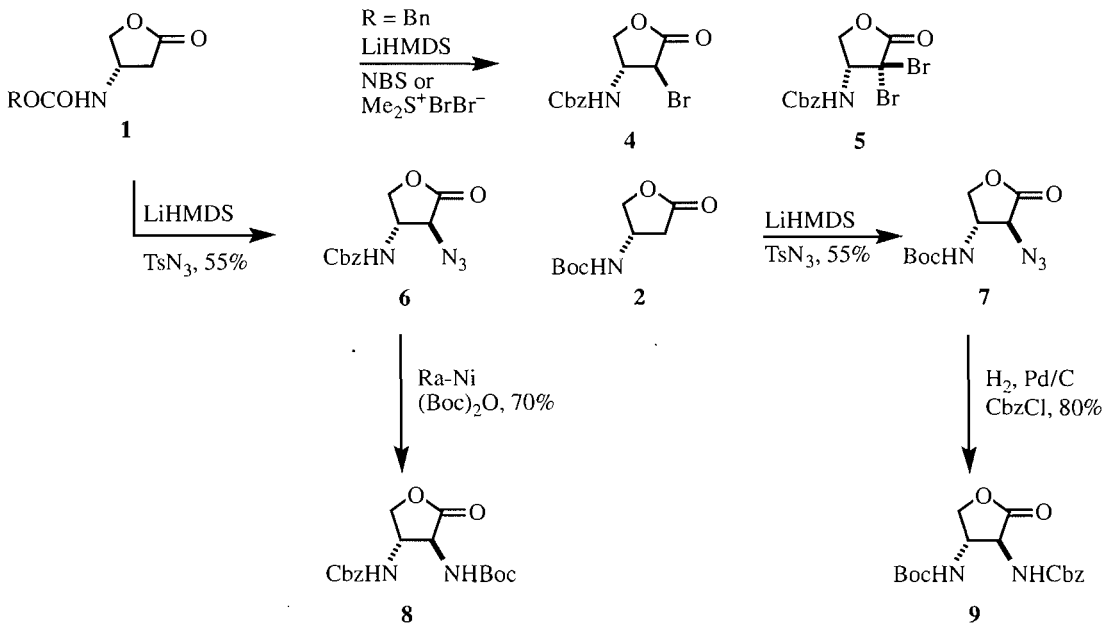


SCHEME 1



SCHEME 2

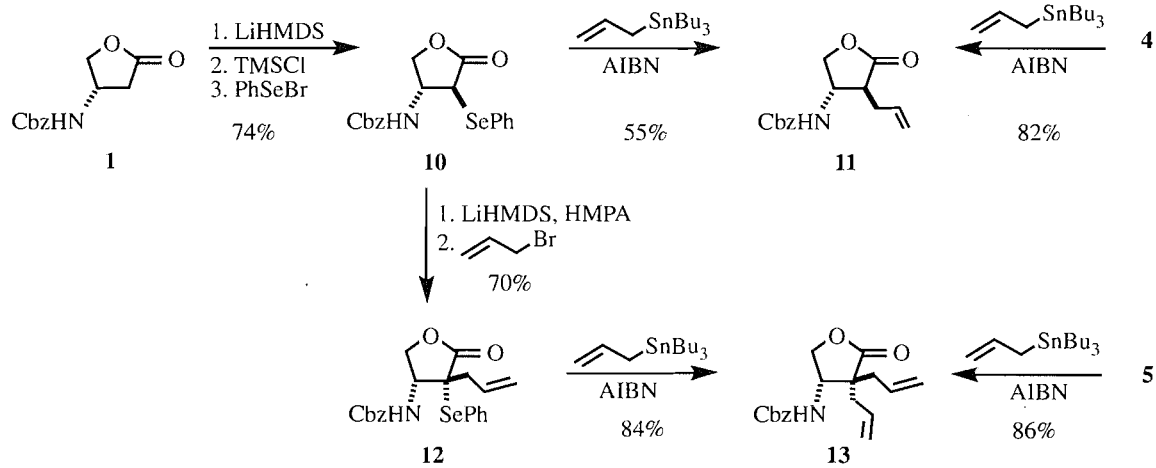
prepared the 2-phenylseleno lactone **10** for a series of reactions shown in Scheme 3.

Thus, treatment of either the 2-bromo or the 2-phenylseleno lactones **4** or **10** with allyltributylstannane, in refluxing benzene and in the presence of a radical initiator, led to the formation of the *C*-allyl derivative **11** in yields of 82% and 55%, respectively. It is of interest that the allylation of the dianion of **1** gave an 88:12 (*anti*:*syn*) mixture of *C*-allyl derivatives (6, 8). In spite of the more modest yield obtained with the phenylseleno derivative, the method is more practical since the bromination is sometimes accompanied by the dibromo compound **5**. When subjected to the same radical-induced *C*-allylation, **5** afforded the *gem* di-*C*-allyl product **13** accompanied by the monoallyl derivative. The two-step sequence proceeding through the phenylseleno derivative **12** gave an excellent and reproducible yield of **13**. Thus the lactone motifs **1** and **2** can be readily functionalized with a high degree of stereocontrol to provide chirons useful in a number of synthetic endeavors related to natural and unatural products.

Experimental

General data

Tetrahydrofuran was distilled over benzophenone and sodium prior to use. Analytical thin-layer chromatography (TLC) was carried out on Merck Kieselgel silica gel 60 F_{254} glass plates. Flash chromatography was performed according to the procedure of Still et al. (15) with Merck silica gel, 230–400 mesh. Infrared (IR) spectra were recorded in chloroform on a Perkin–Elmer 781 spectrometer. The wavenumbers reported are referenced to the polystyrene 1601 cm^{-1} absorption. Nuclear magnetic resonance spectra were obtained on a Bruker WH-400 (^1H 400 MHz) spectrometer with chloroform-*d* as solvent and tetramethylsilane as an internal standard, unless otherwise indicated. ^1H NMR multiplicities are recorded by use of the following abbreviations: s, singlet; d, doublet; dd, doublet doublet; t, triplet; q, quartet; m, multiplet; b, broad; *J*, coupling constant (hertz). High-resolution FAB mass spectra were



SCHEME 3

obtained by means of Kratos MS5OTCTA and AEI-MS 902 spectrometers at the Université de Montréal. Melting points were measured on a Büchi apparatus and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 polarimeter at 25°C.

(2S,3S)-3-Benzyloxycarbonylamino-2-bromo-1,4-butyrolactone (4)

Method A

A solution of butyllithium in hexanes (1.52 M, 1.3 mL, 2 mmol) was added dropwise to a solution of hexamethyldisilazane (0.422 mL, 2 mmol) in THF (4 mL) at 0°C. After 15 min, the solution was cooled down to −78°C, a solution of the lactone **1** (235 mg, 1 mmol) in THF (5 mL) was added, and the mixture was stirred at that temperature for 30 min. The reaction flask was covered with aluminum foil and a solution of *N*-bromosuccinimide (267 mg, 1.5 mmol), in THF (3 mL) was then added to the resulting dianion mixture at −78°C. After 3 min, trimethylsilyl chloride (0.33 mL, 2.6 mmol) was added to quench the reaction. The mixture was diluted with ether and washed successively with 10% aqueous HCl, 5% aqueous $NaHCO_3$, and brine and dried over $MgSO_4$. Concentration and flash column chromatography (EtOAc–hexanes 3:7) furnished the title compound **4** (160 mg, 51%) as a white solid, and the starting material (35 mg, 15%). Recrystallization from a mixture of ethyl acetate and hexanes gave colorless crystals, mp 97–99°C; $[\alpha]_D$ −32 (*c* 1, THF); IR ν_{max} (film): 3400 (NHCbz), 1800 (γ-lactone), 1740 (carbamate) cm^{-1}; ^1H NMR (400 MHz) δ: 4.28–4.31 (1H, d, $J_{2,3}$ = 9 Hz, H-2), 4.42–4.48 (2H, m, H-3 and H-4a), 4.70–4.74 (1H, m, H-4b), 5.13 (2H, CH_2Ph), 5.28 (1H, NH), 7.3–7.45 (5H, Ph); MS, *m/z*: 315 (MH^+). Anal. calcd. for $C_{12}H_{12}NO_4Br$: C 45.87, H 3.82, N 4.46; found: C 45,81, H 3.79, N 4.42.

Method B

The dianion was generated as described in Method A. Then a solution of bromine (0.077 mL, 1.5 mmol) in THF (3 mL) was added dropwise, in the dark at −78°C. After 3 min, the reaction was quenched with trimethylsilyl chloride (0.33 mL, 2.6 mmol) and worked up as described above to afford the title compound **4** (141 mg, 45%), as a white solid, and the starting material (35 mg, 15%).

(3S)-3-Benzyloxycarbonylamino-2,2-dibromo-1,4-butyrolactone (5)

A solution of the lactone **1** (235 mg, 1 mmol) in THF (5 mL) was added dropwise to a solution of lithium hexamethyldisilazide (2 mmol) in THF (4 mL) at −78°C. The mixture was stirred at −78°C for 30 min, then the flask was covered with aluminum foil, and a solution of bromodimethylsulfonium bromide (333 mg, 1.5 mmol) in THF (3 mL) was added dropwise. After stirring for 15 min at −78°C, the reaction was quenched with trimethylsilyl chloride (0.33 mL, 2.6 mmol). After allowing to warm up to room temperature, the resulting mixture was diluted with ether and washed successively with 10% aqueous HCl, 5% aqueous $NaHCO_3$, and brine and dried over $MgSO_4$. Evaporation of the solvent and flash column chromatography (ethyl acetate – hexanes 3:7) yielded starting material (35 mg, 15%), and the title compound **5** (200 mg, 51%) as a white solid. Recrystallization from a mixture of ethyl acetate and hexanes gave colorless crystals, mp 87–88°C; $[\alpha]_D$ +18.0° (*c* 1, THF); IR ν_{max} (film): 3400–3100 (NHCbz), 1800 (γ-lactone), 1740 (carbamate) cm^{-1}; ^1H NMR (400 MHz) δ: 4.42–4.48 (2H, m, H-3 and H-4a), 4.70–4.74 (1H, m, H-4b), 5.13 (2H, s, CH_2Ph), 5.28 (2H, NH), 7.3–7.45 (5H, Ph); MS, *m/z*: 394 (MH^+). Anal. calcd. for $C_{12}H_{11}NO_4Br_2$: C 36.66, H 2.80, N 3.56; found: C 36.34, H 2.76, N 3.49.

(2S,3S)-2-Azido-3-benzyloxycarbonylamino-1,4-butyrolactone (6)

A solution of the lactone **1** (1.0 g, 4.25 mmol) in THF (20 mL) was added dropwise to a solution of lithium hexamethyldisilazide (9.5 mmol) in THF (20 mL) at −78°C. The mixture was stirred at −78°C for 30 min, and a solution of *p*-toluenesulfonyl azide (1.0 g, 5.08 mmol) in THF (10 mL) was added rapidly, at −78°C. After stirring for 5 min, the reaction was quenched with trimethylsilyl chloride (1.6 mL, 12.75 mmol). The resulting mixture was diluted with ether and washed successively with 10% aqueous HCl, 5% aqueous $NaHCO_3$, and brine and dried over $MgSO_4$. Concentration and flash column chromatography (ethyl acetate – hexanes 3:7) gave the title compound **6** (0.65 g, 55%) as an oil that solidified upon standing. A small quantity of starting material (0.1 g, 10%) was also isolated. The product was recrystallized from a solvent mixture of ethyl acetate – hexanes, mp 86–87°C; $[\alpha]_D$ −99 (*c* 1, THF); IR ν_{max} (film): 2130 (azide), 1785 (γ-lactone), 1700 (carbamate) cm^{-1}; ^1H NMR (400 MHz) δ: 4.1–4.2 (1H, d, $J_{2,3}$ = 8 Hz), 4.42–4.48 (2H, m, H-3 and H-4a), 4.70–4.74 (1H, m, H-4b), 5.13 (2H, s, CH_2Ph), 5.28 (1H, NH), 7.3–7.45 (5H, Ph); MS, *m/z*: 277 (MH^+), 91 (100%, C_7H_7). Anal. calcd. for $C_{12}H_{12}N_4O_4$: C 52.17, H 4.35, N 20.29; found: C 51.92, H 4.31, N 20.04.

*(2S,3S)-3-Benzyloxycarbonylamino-2-*tert*-butoxycarbonylamino-1,4-butyrolactone (8)*

Raney nickel (0.5 g) and di-*tert*-butyl dicarbonate (1.09 g, 5.0 mmol) were added successively to a solution of the lactone **6** (1.03 g, 3.73 mmol) in THF (20 mL). Filtration of the suspension through Celite and concentration of the filtrate furnished a crude sample, which was purified through flash column chromatography (ethyl acetate – hexanes 45%) to give the title compound **8** (0.887 g, 70%) as a white solid, mp 150–152°C; $[\alpha]_D$ +25.3

(*c* 1, $CHCl_3$); IR ν_{max} (film): 3300 (NHBoc, NHCbz), 1780 (γ-lactone), 1720 (carbamate) cm^{-1}; ^1H NMR (60 MHz) δ: 1.47 (9H, s, *tert*-butoxy), 3.8–4.35 (3H, m, H-2, H-3, and H-4a), 4.70–4.74 (1H, m, 4-Hb), 5.03 (2H, s, CH_2Ph), 5.28 (1H, m, NH), 6.3 (1H, m, NH), 7.3–7.45 (5H, Ph); MS, *m/z*: 351 (80%, MH^+).

*(3S)-3-*tert*-Butoxycarbonylamino-1,4-butyrolactone (2)*

10% Palladium-on-charcoal (0.4 g) and di-*tert*-butyl dicarbonate (4.09 g, 18.7 mmol) were added successively to a solution of the lactone **1** (4.0 g, 17.0 mmol) in THF (10 mL). The resulting mixture was vigorously stirred overnight under an atmosphere of hydrogen. Filtration of the suspension through Celite and concentration of the filtrate yielded a crude sample, which was purified through flash column chromatography (ether) to give the title compound **2** (3.2 g, 85%) as a white solid, mp 113–114°C; $[\alpha]_D$ −54.3 (*c* 1.15, $CHCl_3$) (lit. (8) mp 106–108°C; $[\alpha]_D^{25}$ −61 (*c* 1.0, EtOH); IR ν_{max} (film): 1780 (γ-lactone), 1700 (carbamate) cm^{-1}; ^1H NMR (400 MHz) δ: 1.45 (9H, s, *tert*-butyl), 2.45 (1H, dd, $J_{2,3}$ = 3.9 Hz and J_{gem} = 17.9 Hz, H-2a), 2.85 (1H, dd, $J_{2,3}$ = 7.7 Hz and J_{gem} = 17.9 Hz, H-2b), 4.2 (1H, m, H-4b), 4.5–4.8 (2H, m, H-3 and H-4a), 5.09 (2H, s, CH_2Ph), 5.5 (1H, NH), 7.3–7.40 (5H, Ph); MS, *m/z*: 202 (MH^+), 146 (*tert*-butyl).

*(2S,3S)-2-Azido-3-*tert*-butoxycarbonylamino-1,4-butyrolactone (7)*

A solution of the lactone **2** (0.854 g, 4.25 mmol) in THF (20 mL) was added dropwise to a solution of lithium hexamethyldisilazide (9.5 mmol) in THF (20 mL) at −78°C. The mixture was stirred at −78°C for 30 min. A solution of *p*-toluenesulfonyl azide (1.0 g, 5.08 mmol) in THF (10 mL) was then added rapidly to the resulting dianion suspension at −78°C. After stirring for 5 min, the reaction was quenched with trimethylsilyl chloride (1.6 mL, 12.75 mmol). After warming up to room temperature, the resulting mixture was diluted with ether and washed successively with 10% aqueous HCl, 5% aqueous $NaHCO_3$, and brine and dried over $MgSO_4$. Concentration and flash column chromatography (ethyl acetate – hexanes 3:7) furnished the title compound **7** (0.57 g, 55%) as an oil that solidified upon standing. Starting material (0.1 g, 11.7%) was also recovered. Compound **7** was recrystallized from a mixture of ethyl acetate and hexanes, mp 107–109°C; $[\alpha]_D$ −70 (*c* 1.0, EtOH) (lit. (9) mp 110–111°C; $[\alpha]_D$ −69 (*c* 1.0, EtOH)); IR ν_{max} (film): 2130 (azido), 1800 (γ-lactone), 1735 (carbamate) cm^{-1}; ^1H NMR (400 MHz) δ: 1.45 (9H, s, *tert*-butyl), 4.1–4.2 (1H, d, $J_{2,3}$ = 8 Hz, H-2), 4.42–4.48 (2H, m, H-3 and H-4a), 4.70–4.74 (1H, m, H-4b), 5.28 (1H, m, NH). Anal. calcd. for $C_9H_{14}N_4O_4$: C 44.63, H 5.79, N 23.14; found: C 44.59, H 5.71, N 23.11.

*(2S,3S)-2-Benzyloxycarbonylamino-3-*tert*-butoxycarbonylamino-1,4-butyrolactone (9)*

10% Palladium-on-charcoal (50 mg) was added to a solution of the lactone **7** (0.25 g, 1.03 mmol) in THF (5 mL). The resulting mixture was stirred under an atmosphere of hydrogen for 40 min, and the suspension was filtrated through Celite. Triethylamine (0.153 mL, 1.1 mmol) and benzyl chloroformate (0.142 mL, 1 mmol) were then added successively to the filtrate, which was precooled down to 0°C. After allowing the mixture to stir overnight, water was added, and the solution extracted several times with ether. The combined organic phases were dried ($MgSO_4$) and concentrated to give a crude sample as an oil, which was purified through flash column chromatography (ethyl acetate – hexanes, 1:1) to give the title compound **9** (0.28 g, 80%) as a white crystalline solid, mp 118–120°C; $[\alpha]_D$ −33.2 (*c* 1, $CHCl_3$); IR ν_{max} (film): 3300 (NHBoc + NHCbz), 1780 (γ-lactone), 1720 (carbamate) cm^{-1}; ^1H NMR (60 MHz); δ: 1.47 (9H, s, *tert*-butoxy), 3.8–4.35 (3H, m, H-2, H-3 and H-4a), 4.70–4.74 (1H, m, H-4b), 5.03 (2H, s, CH_2Ph), 5.28 (1H, m, NH), 6.3 (1H, m, NH), 7.3–7.45 (5H, Ph); MS, *m/z*: 351 (10%, MH^+).

(2S,3S)-3-Benzyloxycarbonylamino-2-phenylselenyl-1,4-butyrolactone (10)

A solution of the lactone **1** (1.0 g, 4.25 mmol) in 10 mL THF was added dropwise to a solution of LiHMDS (9.00 mmol) in 25 mL THF at −78°C under an argon atmosphere with stirring. After 1 h at that temperature, trimethylsilyl chloride (1.8 mL, 14.18 mmol) was added, and the resulting mixture was stirred at 0°C for 2 h. It was then recooled down to −78°C, followed by addition of *N*-(phenylseleno)phthalimide (1.28 g, 4.24 mmol) in THF (15 mL) at −78°C through a canal. After 30 min stirring at −78°C, the mixture was poured into a mixed solution of 200 mL 5% aqueous HCl, 100 mL ether, and 100 mL pentane. The organic phase was separated and washed successively with water, 10% aqueous $NaHCO_3$, and brine and dried over sodium sulfate. Concentration and flash column chromatography (ethyl acetate – hexanes 3:7) afforded the title compound as an off-white solid (1.22 g, 74%). IR ν_{max} (film): 1780 (lactone), 1710 (carbamate) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 3.83 (1H, d, *J* = 4 Hz, H-2), 4.10 (1H, dd, J_{gem} = 10 Hz and $J_{4,3}$ = 3 Hz, H-4), 4.25 (1H, dd, J_{gem} = 10 Hz and $J_{4,3}$ = 4 Hz, H-4), 4.35 (1H, m, H-3), 5.10 (2H, s, CH_2Ph), 5.60 (1H, bd, NH), 7.50–7.25 (8H, m, Ph and SePh), 7.70 (2H, m, SePh); MS (EI), *m/z*: 391 (M), 300 (M − Bn), 284 (M − BnO); HRMS calcd. for $C_{18}H_{17}NO_4Se$: 391.0322; found: 391.0348.

(2S,3S)-2-C-Allyl-3-benzyloxycarbonylamino-1,4-butyrolactone (11)

A solution of **10** (320 mg, 0.82 mmol), allyl tributyltin (0.31 mL, 0.99 mmol), and AIBN (15 mg, 0.0914 mmol) in benzene (3.7 mL) was degassed and brought to reflux under an argon atmosphere for 16 h. The volume of the mixture was reduced and the residue was purified through flash column chromatography (ethyl acetate – hexanes 0:1–3:7) to yield the title compound as a colorless thick oil (125 mg, 55%); $[\alpha]_D$ −34 (*c* 1.0, $CHCl_3$); IR ν_{max} (film): 1780 (lactone), 1720 (carbamate) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.70–2.35 (3H, m, H-2, CH_2 CH=CH_2), 4.01 (1H, dd, J_{gem} = 8 Hz and $J_{4,3}$ = 7 Hz, H-4), 4.28 (1H, m, H-3), 4.52 (1 H, dd, J_{gem} = 8 Hz and $J_{4,3}$ = 7 Hz, H-4), 4.98 (1H, bs, NH), 5.11 (2H, s, CH_2Ph), 5.15 (1H, bd, *J* = 11.5 Hz, CH=CH_2-*cis*), 5.20 (1H, bd, *J* = 18 Hz, CH=CH_2-*anti*), 5.90–5.70 (1H, m, CH=CH_2), 7.43–7.31 (5H, m, Ph); MS (EI), *m/z*: 275 (M), 184 (M − Bn), 167 (M − HOBn), 140 (M − O=C − OBn); HRMS calcd. for $C_{15}H_{17}NO_4$: 275.1157; found: 275.1174.

(3S)-2-C-Allyl-3-benzyloxycarbonylamino-2-phenylselenyl-1,4-butyrolactone (12)

A solution of compound **10** (208 mg, 0.53 mmol) in 3 mL THF was added dropwise to a solution of LiHMDS (1.20 mmol) in 3 mL THF at −78°C under an argon atmosphere. After being stirred at −78°C for 30 min, HMPA (2 mL) was then added, followed by addition of allyl bromide (0.23 mL, 2.66 mmol). The resulting mixture was allowed to stir at −78°C for 2 h, and then treated with 10% aqueous HCl. The mixture was extracted with ether several times and the combined organic phases were washed successively with water, $NaHCO_3$, and brine and dried over $MgSO_4$. The solvent was removed to give a crude sample, which was purified by flash column chromatography (ethyl acetate – hexanes 3:7) to furnish the title compound as a colorless viscous oil (160 mg, 70%). IR ν_{max} (film): 1770 (lactone), 1725 (carbamate) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ: 2.70–2.50 (2H, m, CH_2CH=CH_2), 4.15–4.05 (1H, m, H-4), 4.70–4.50 (2H, m, H-3, H-4), 5.11 (2H, s, CH_2Ph), 5.23–5.15 (2H, m, CH=CH_2), 5.28 (1H, b, NH), 6.00–5.85 (1H, m, CH=CH_2), 7.50–7.30 (8H, m, Ph and SePh), 7.65 (2H, m, SePh); MS, *m/z*: 431 (M); HRMS, calcd. for $C_{21}H_{21}NO_4Se$: 431.0635; found: 431.0700.

(3S)-2,2-Di-C-Allyl-3-benzyloxycarbonylamino-1,4-butyrolactone (13)

A solution of **12** (0.35) g, 0.814 mmol), allyl tributyltin (0.38 mL, 1.226 mmol), and a catalytic amount of AIBN in 3 mL benzene was degassed and brought to reflux under an atmosphere of argon for 1.45 h. The solvent was removed and the residue was subjected to flash column chromatography (ethyl acetate – hexanes 0:1–3:7) to give the title compound as a colorless thick oil (0.217 g, 84%); $[\alpha]_D$ +23 (*c* 2.1, $CHCl_3$). IR ν_{max} (film): 1770 (lactone), 1720 (carbamate) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ:

2.55–2.27 (4H, m, $CH_2CH{=}CH_2$), 3.80 (1H, t, J = 9 Hz, H-4), 4.47 (1H, t, J = 9 Hz, H-4), 4.71 (1H, q, J = 9 Hz, H-3), 5.03 (1H, bd, J = 9 Hz, NH), 5.11 (1H, d, J_{gem} = 12 Hz, *CH*Ph), 5.17 (1H, d, J_{gem} = 12 Hz, *CH*Ph), 5.35–5.18 (4H, m, $CH{=}CH_2$), 5.90–5.70 (2H, m, $CH{=}CH_2$), 7.38 (5H, m, Ph); MS (EI), m/z: 315 (M), 224 (M − Bn); HRMS, calcd. for $C_{18}H_{21}NO_4$: 315.1471; found: 315.1475.

Acknowledgments

We thank the Natural Sciences and Engineering Research Council of Canada (NSERCC) and the Fonds pour la formation de chercheurs et l'aide à la recherche (Québec) (FCAR) for financial assistance. We thank the Mass Spectrometry Laboratory, Université de Montréal, for services.

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