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Esterification by Redox Dehydration using Diselenides as Catalytic Organooxidants

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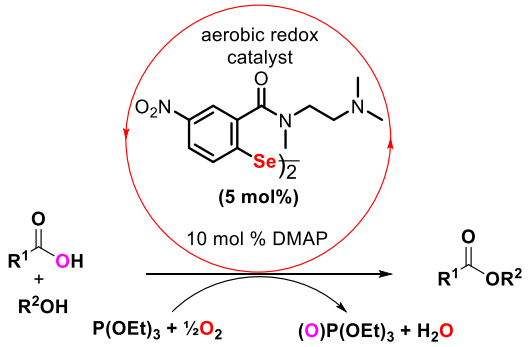
Supporting Information Placeholder

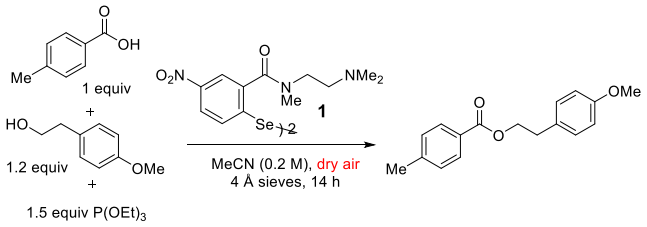


ABSTRACT: Ortho functionalized aryl diselenides are catalytic (5.0 mol %) oxidants for the construction of esters from carboxylic acids and alcohols in the presence of stoichiometric triethylphosphite and dioxygen in air as the terminal redox reagents (redox dehydration conditions). The reaction proceeds through the intermediacy of the anhydride and requires the presence of 10% DMAP to drive the esterification.

Introduction. Redox dehydration, which removes H_2O from two reaction partners through the action of an oxidant to accept [2H] and a reductant to accept [O],[1-5] has been used to carry out both alkylative [2-4] and acylative[1, 6-7] bond formation. Recent efforts have focused on developing catalytic versions of both alkylative[8-12] and acylative[13-14] redox dehydration reactions. For the latter, we have described the use of benzoisothiazolones[15] and ortho functionalized diselenides[16] as catalytic oxidants linked to O_2 in air for efficient and economical amidation and peptidation reactions. In these reactions triethylphosphite serves as an inexpensive terminal reductant. Herein we disclose a follow-up study where ortho functionalized aryl diselenides are used as oxidation organocatalysts for O-esterification reactions[17] proceeding through a redox dehydration mechanism. Taniguchi published a related aerobic, iron-catalyzed production of acyloxytriphenylphosphonium intermediates that that effectively esterify alcohols.[18]

Results and Discussion. Treatment of 1 equiv of *p*-toluic acid and 1.2 equiv of 4-methoxyphenethyl alcohol under the conditions previously established for effective amidation and peptidation[16] (2.5 mol % diaryldiselenide **1**, 1.5 equiv triethylphosphite, dry air, freshly dried and activated 4Å mol sieves, room temp in MeCN) over 14 h generated predominantly *p*-toluic anhydride (50%) along with 31% of the desired ester product, traces of recovered *p*-toluic acid, and 10% of ethyl -*p*-toluate (Table 1). Inclusion of 10 mol % of the acyl transfer catalyst DMAP[19] within the reaction mixture avoided buildup of the anhydride; the desired ester was formed in 65% yield along with quantities of unreacted *p*-toluic acid (16%) and ethyl *p*-toluate (11%). Raising the reaction temperature to 50 °C improved the conversion to ester (80%) leaving similar quantities of ethyl *p*-toluate (10%) and only minor traces of unreacted *p*-toluic acid.

Table 1. Optimization of Aerobic, Diselenide-Catalyzed Esterification Conditions



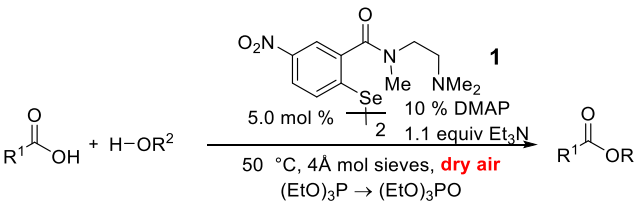
% **1**	°C	additives	% ester	other*
2.5	25	---	31	10, 50, trace
2.5	25	10% DMAP	65	11, 0, 16
2.5	50	10% DMAP	80	10, 0, trace
2.5	50	10% DMAP, 1.1 equiv Et_3N	74	trace, 0, 14
5.0	50	10% DMAP, 1.1 equiv Et_3N	84	trace, 0, trace

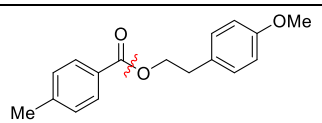
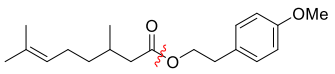
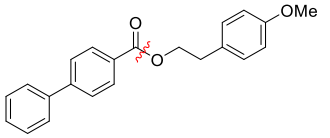
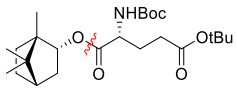
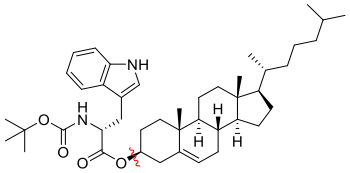
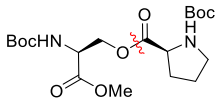
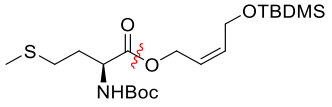
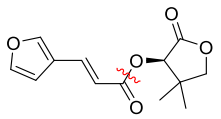
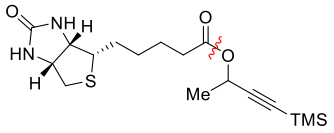
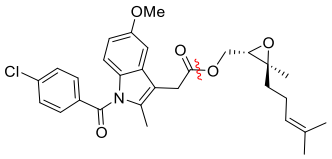
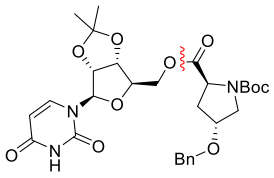
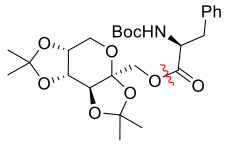
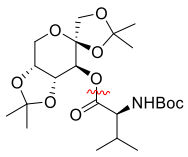
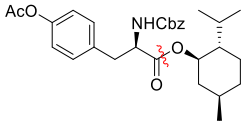
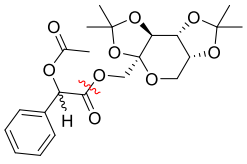
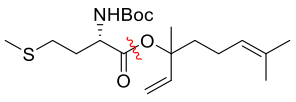
*yields of ethyl ester, *p*-toluic anhydride, recovered *p*-toluic acid, respectively

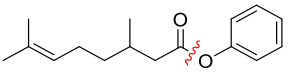
The undesired ethyl ester can be formed in one of two ways: either by carboxylate reacting in an S_N2 reaction with active Arbuzov-like intermediates that are generated during the reaction process when triethylphosphite cleaves the diselenide (i.e. $ArSeP^+(OEt)_3$), or by liberation of free ethanol during the reaction through the very rapid, acid-catalyzed hydrolysis[20] (or transesterification) of triethylphosphite. Addressing the latter possibility, 1.1 equiv of Et_3N was added to buffer the carboxylate acidity. While this tactic slightly slowed the rate of overall reaction, it effectively mitigated formation of the undesired ethyl ester pointing to acid-catalyzed hydrolysis/alcoholysis of triethylphosphite as the problematic side reaction. Thus, after 14 h the desired ester was formed in 74% yield with 14% of *p*-toluic acid remaining. Optimum conditions were achieved by raising the diselenide loading to 5 mol %. Thus, at 5 mol % diselenide, 10 mol % DMAP and 1.1 equiv of Et_3N amine at 50 °C in 14 h, the ester was generated in 84% yield. Only very minor traces of the ethyl ester and *p*-toluic acid were evident. For comparison, the same reactants generated the ester in 78% yield when treated under the Steglich conditions[21-22] with 1.5 equiv of EDCI (N-(3-Dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride), 1.5 equiv of Et_3N and catalytic DMAP in CH_2Cl_2 at room temperature for 3 hr. The Taniguchi procedure mentioned above[18] provided the ester in only 48% yield.

Having identified the optimal conditions for the esterification of toluic acid and *p*-methoxyphenethyl alcohol, the scope of the reaction was investigated (Table 2). Citronellic acid (entry 2, triethylamine not required) and biphenyl-4-carboxylic acid (entry 3) reacted smoothly with *p*-methoxyphenethyl alcohol to provide the desired esters in 92% and 84% yield, respectively

Table 2. Esterifications using Aerobic, Diselenide Catalyzed Redox Dehydration



entry	product	solv, time isol. yield
1		MeCN, 12 h, 83%
2		MeCN, 10 h, 86%[a]
3		MeCN, 12 h, 84%
4		MeCN, 14 h, 85%
5		EtOAc, 10 h, 75%
6		EtOAc, 10 h, 82%
7		MeCN, 12 h, 74%
8		MeCN, 12 h, 79%
9		DMF, 14 h, 88%
10		MeCN, 11 h, 86%
11		MeCN, 12 h, 72%
12		EtOAc, 10 h, 79%
13		EtOAc, 10 h, 82%
14		EtOAc, 10 h, 77%
15		EtOAc, 10 h, 83%[b]
16		MeCN, 12 h, 0%

17		MeCN, 8 h, 41%[a]

Reaction conditions: 1.0 equiv of carboxylic acid, 1.1 equiv of alcohol, 1.5 equiv of $P(OEt)_3$, 10 mol % DMAP, 1.1 equiv Et_3N, 5.0 mol % catalyst, solvent, dry air balloon and 4 Å mol sieves (1.0 x wt % of acid). Solvent, temperature and reaction time are given in the Table entries. [a] Reaction in the absence of triethylamine. [b] Mixture of diastereomers (1:0.6 dr).

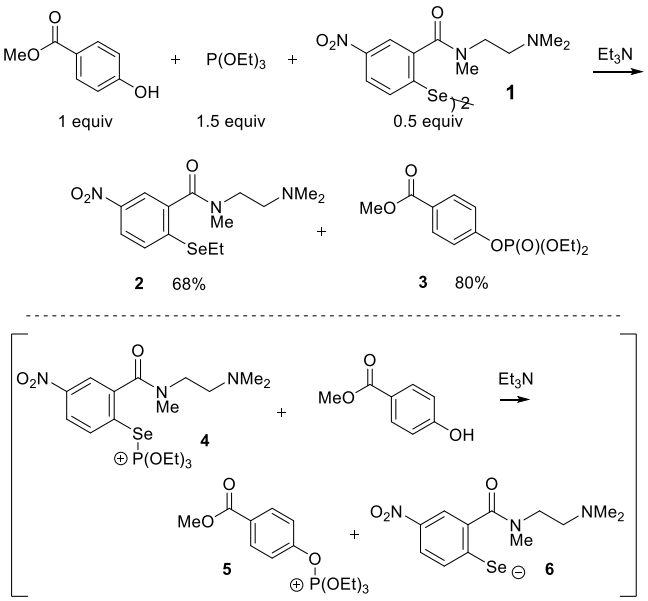
Attempted esterification of cholesterol with N-Boc-tryptophan was unsuccessful in MeCN, owing to the poor solubility of cholesterol in this solvent. Fortunately, a switch to EtOAc as solvent gave the anticipated ester in 75% yield (entry 5). An attempted coupling of N-Boc-serine methyl ester with N-Boc-proline in MeCN was seriously compromised by competitive dehydration of serine to dehydroalanine. Again, switching from MeCN to the less polar EtOAc as solvent was beneficial and delivered the desired product in 82% yield (entry 6) with no trace of the dehydroalanine byproduct. The esterification of biotin was challenging because of its poor solubility in MeCN. Switching to DMF provided product in 88% yield (entry 9).

Entries 12, 14, and 15 of Table 2 were first attempted in MeCN, but in each case the ester products were partially epimerized. Changing the solvent from MeCN to EtOAc completely suppressed the epimerization in entries 12 and 14, resulting in the formation of single diastereomers, although partial epimerization was unavoidable in entry 15. Attempts to engage a tertiary alcohol in esterification (entry 16) was unsuccessful.

The esterification of phenols was briefly investigated. Attempts to esterify phenol or methyl-4-hydroxybenzoate with citronellic acid resulted in substantial disappearance of the phenol, full consumption of triethylphosphite, and destruction of the diselenide catalyst, but none of the desired ester was generated. To determine how the diselenide and phenol were decaying, a control experiment was conducted with 1.0 equivalent of methyl-4-hydroxybenzoate, 0.5 equivalents of diselenide, 10 mol % DMAP, 1.1 equivalents of triethylamine, and 1.5 equivalents of triethylphosphite (Scheme 1).

The reaction was monitored by ^{31}P for changes in triethylphosphite concentration and then concentrated after 8 hr. After chromatographic separation of the reaction constituents, selenoether **2** was obtained in 68 % yield along with methyl-4-((ethoxy(ethoxymethyl)phosphoryl)oxy)benzoate (**3**) in 80% yield. It appears that the selenophosphonium intermediate **4**, generated from triethylphosphite and the diselenide, undergoes exchange with the phenol under basic reaction conditions to generate aryloxyphosphonium intermediate **5** and arylselenide **6**. Together these react to generate the observed products **2** and **3**.

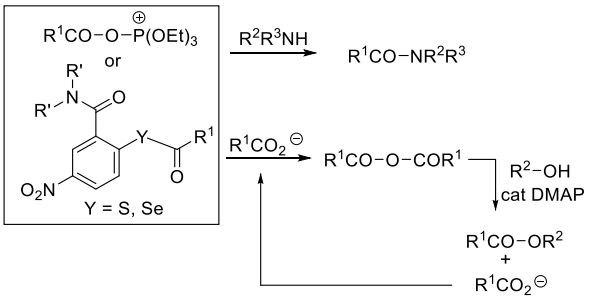
Scheme 1. Phenol Reaction Pathway



In the absence of triethylamine, transesterification of the phenol with selenophosphonium species does not occur and the diselenide does not undergo ethylation. Therefore, the esterification of phenol and citronellic acid was carried out in the absence of triethylamine, providing 41% yield of the phenolic ester after 8 hr (Table 2, entry 17). No attempt was made to optimize this reaction.

The mechanism of the aerobic, diselenide catalyzed O-esterification of carboxylic acids and alcohols differs from the previously described amidation/peptidation protocols (Scheme 2).[15-16, 23] In the latter, both 1° and 2° amines are sufficiently nucleophilic to react with the in situ acyl electrophiles (activated thio/selenoester or an acyloxyphosphonium salt), to rapidly produce amides/peptides. In the former, where the rates of electrophile trapping by the neutral alcohol are much slower, the carboxylate preferentially attacks the implicit acyl electrophile producing the carboxylic acid anhydride, preferentially. Thus, the O-esterification reaction requires DMAP to catalyze the reaction of the anhydride with the reactant alcohol.

Scheme 2. Amidation vs Esterification. Mechanism Change



Conclusions. We have demonstrated an aerobic, diselenide-catalyzed redox dehydrative generation of O-esters from carboxylic acids and 1° and 2° alcohols; 3° alcohols do not react. The terminal redox reagents are triethylphosphite as reductant and O_2 in air as oxidant.

EXPERIMENTAL SECTION

General information. All solvents were purchased from Fisher Scientific and dried over 4Å mol sieves. Mol sieves were activated via heating in a microwave oven for three minutes and dried under reduced pressure for five minutes. Unless otherwise noted, all commercially available reagents and substrates were used directly as received. Compressed dry air was obtained from Nexair and used as received. Thin layer chromatography was performed on Merck silica gel plates and visualized by UV light/$KMnO_4$. ^1H, $^{13}C\{1H\}$, and ^{31}P NMR spectra were recorded on Brucker 600, Varian INOVA 600, INOVA 500, INOVA 400, and Mercury 300 spectrometers. In the spectra, the residual solvent absorbances were treated as internal reference signals ($CDCl_3$: ^1H- 7.26 ppm and ^{13}C- 77.16 ppm). Abbreviations for ^1H NMR coupling is as follows: singlet = s, doublet = d, triplet = t, quartet = q, pentet = p. IR spectra were recorded on a Nicolet iS10 FT-IR spectrometer and the absorption peaks were reported in cm^{-1}. A Thomas capillary melting point apparatus was used to determine the melting points (uncorrected). High resolution mass spectra were obtained with a Thermo LTQ-FTMS instrument equipped with tandem ion trap - ICR mass analyzers at the Emory University Mass Spec Facility Inc. 8-(4-Chlorophenylsulfonamido)-4-(3-(pyridin-3-yl)propyl)octanoic acid was obtained from Novartis (as a gift to the Emory University Center for C-H Functionalization).

General Experimental Procedure for Ester Bond Formation. A 12 mL test tube was charged with 4 Å molecular sieves (100 mg) previously activated in a microwave oven for three minutes and dried under reduced pressure for five minutes. Then the carboxylic acid (0.21 mmol), diselenide **1** (0.011 mmol), and 4-dimethylaminopyridine (2.6 mg, 0.021 mmol) were added followed by dry CH_3CN, EtOAc, or DMF (1.0 mL, 0.2M, moisture content <25 ppm). The alcohol (0.23 mmol), 4-dimethylaminopyridine (0.021 mmol), triethylamine, (0.23 mmol) and triethylphosphite (0.32 mmol) were added sequentially. The reaction mixture was stirred for 10 – 18 h at 50 °C (temperature controlled with an aluminum block on a hot plate) under a dry air atmosphere (balloon). Upon complete conversion of carboxylic acid as monitored by TLC, the reaction mixture was filtered, and the molecular sieves thoroughly washed with CH_2Cl_2 (DCM). The combined filtrate was concentrated under reduced pressure and the crude product was purified by flash column chromatography using the eluents mentioned below to obtain the ester product.

Experimental Procedure for Reactions Reported in Scheme 1. A 12 mL test tube was charged with 4 Å molecular sieves (100 mg) previously activated in a microwave oven for three minutes and dried under reduced pressure for five minutes. Then toluic acid (29 mg, 0.21 mmol) and diselenide **1** (3.6 mg, 0.0055 mmol or 7.2 mg, 0.011 mmol) were added. For the reactions in which 4-dimethylaminopyridine (2.6 mg, 0.021 mmol) was employed, it was added followed by dry CH_3CN (1.0 mL, 0.2M, moisture content <25 ppm) and *p*-methoxy-phenethyl alcohol (35 mg, 0.23 mmol). If triethylamine (33 µL, 0.23 mmol) was employed, it was added followed by triethylphosphite (0.32 mmol). Lastly, 1,3,5-trimethoxybenzene was added and used as an internal standard. The reaction was stirred at either 25 or 50 °C (temperature controlled with an aluminum block on a hot plate) under a dry air atmosphere (balloon) and stopped after 14 h, at which time the reaction mixtures were concentrated under reduced pressure and analyzed by ^1H NMR. Reported yields are based on NMR integration of product peaks versus the internal standard.

4-Methoxyphenethyl 4-methylbenzoate - (Table 2, entry 1). A mixture of *p*-toluic acid (29 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry CH_3CN (1 mL, 0.2M) was treated with *p*-methoxy-phenethyl alcohol (35 mg, 0.231 mmol), triethylamine (33 µL, 0.231 mmol), and $P(OEt)_3$ (54 µL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 10 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 7% EtOAc in hexanes to give the pure ester as a colorless oil (47 mg, 83% yield). ^1H NMR (400 MHz, chloroform-*d*) δ 7.95 – 7.87 (m, 2H), 7.25 – 7.22 (m, 2H), 7.22 – 7.18 (m, 2H), 6.88 – 6.84 (m, 2H), 4.47 (t, J = 7.0 Hz, 2H), 3.80 (s, 3H), 3.01 (t, J = 7.0 Hz, 2H), 2.41 (s, 3H). $^{13}C\{1H\}$ NMR (150 MHz, chloroform-*d*) δ 166.7, 158.5, 143.7, 130.2, 130.1, 129.7, 129.2, 127.8, 114.1, 65.7, 55.4, 34.5, 21.8. IR (neat, cm^{-1}): 1710. HRMS (ESI) Calcd for $C_{17}H_{19}O_3$ $[M+H]^+$: 271.1329. Found: 271.1328.

O-Esterification Comparison Results.

Steglich Conditions.[21-22] To a test tube under N_2 containing a magnetic stir bar and *p*-toluic acid (29 mg, 0.21 mmol), *p*-methoxyphenethyl alcohol (0.231, 0.231 mmol), and DMAP (2.5 mg, 0.021 mmol) in dichloromethane (1 mL, 0.2 M), Et_3N (44 uL, 0.315 mmol) was added N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (60 mg, 0.315 mmol) under a stream of nitrogen. The reaction was stirred at room temperature for 3 h and determined to be complete by TLC (7% EtOAc in hexanes). The crude reaction mixture was filtered over silica and the silica washed with dichloromethane to furnish the pure ester as a colorless oil (44 mg, 78% yield).

Taniguchi Conditions. Following the procedure reported by Taniguchi and coworkers,[18] a mixture of p-toluic acid (29 mg, 0.21 mmol), *p*-methoxyphenethyl alcohol (0.231, 0.231 mmol), triphenylphosphine (110 mg, 0.42 mmol), iron(II) phthalocyanine (6.2 mg, 0.011 mmol), and 4-methoxypyridine N-oxide (2.6 mg, 0.021 mmol) in MeCN (0.5 mL, 0.5 M) was heated at reflux with an aluminum block on hot plate under dry air (balloon) for 24 h. The mixture was filtered, and the solvent was removed under reduced pressure. The residue was purified by filtration over silica gel, eluting with dichloromethane to give the pure ester as a colorless oil (27 mg, 48% yield).

4-Methoxyphenethyl 3,7-dimethyloct-6-enoate - (Table 2, entry 2). A mixture of racemic citronellic acid (36 mg, 0.21 mmol, 94% pure), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry CH_3CN (1 mL, 0.2M) was treated with *p*-methoxyphenethyl alcohol (35 mg, 0.231 mmol), triethylamine (33 µL, 0.23 mmol), and $P(OEt)_3$ (54 µL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 10 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 5% EtOAc in hexanes to give the pure ester as a colorless oil (55 mg, 86% yield). ^1H NMR (600 MHz, chloroform-*d*) δ 7.14 (AA' of AA'XX', 2H), 6.84 (XX' of AA'XX', 2H), 5.08 (tp, J = 7.1, 1.4 Hz, 1H), 4.25 (t, J = 7.1 Hz, 2H), 3.79 (s, 3H), 2.88 (t, J = 7.1 Hz,

2H), 2.30 (dd, *J* = 14.7, 5.9 Hz, 1H), 2.10 (dd, *J* = 14.7, 8.2 Hz, 1H), 2.04 – 1.89 (m, 3H), 1.68 (q, *J* = 1.3 Hz, 3H), 1.60 (d, *J* = 1.3 Hz, 3H), 1.36 – 1.29 (m, 1H), 1.20 (dddd, *J* = 13.6, 9.4, 7.8, 5.9 Hz, 1H), 0.91 (d, *J* = 6.7 Hz, 3H). ^{13}C{1H} NMR (150 MHz, chloroform-*d*) δ 173.4,158.4, 131.7, 130.04, 129.98, 124.4, 114.1, 65.0, 55.4, 42.0, 36.9, 34.4, 30.2, 25.9, 25.6, 19.7, 17.8. IR ($CDCl_3$, cm^{-1}): 1733. HRMS (ESI) Calcd for $C_{19}H_{32}NO_3$ $[M+NH_4]^+$: 322.2377. Found: 322.2379.

4-methoxyphenethyl [1,1'-biphenyl]-4-carboxylate - (Table 2, entry 3). A mixture of biphenyl-4-carboxylic acid (42 mg, 0.21 mmol, 95% pure), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry CH_3CN (1 mL, 0.2M) was treated with *p*-methoxyphenethyl alcohol (35 mg, 0.231 mmol), triethylamine (33 µL, 0.23 mmol), and $P(OEt)_3$ (54 µL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 12 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 7% EtOAc in hexanes to give the pure ester as a crystalline white solid (56 mg, 84% yield). ^{1}H NMR (600 MHz, chloroform-*d*) δ 8.10 – 8.07 (m, 2H), 7.68 – 7.64 (m, 2H), 7.64 – 7.61 (m, 2H), 7.50 – 7.45 (m, 2H), 7.40 (ddt, *J* = 8.1, 6.7, 1.3 Hz, 1H), 7.25 – 7.20 (m, 2H), 6.90 – 6.86 (m, 2H), 4.52 (t, *J* = 7.0 Hz, 2H), 3.80 (s, 3H), 3.04 (t, *J* = 7.0 Hz, 2H). ^{13}C{1H} NMR (150 MHz, chloroform-*d*) δ 166.6, 158.5, 145.8, 140.2, 130.2, 130.1, 129.2, 129.1, 128.3, 127.4, 127.2, 114.1, 65.9, 55.4, 34.6. IR ($CDCl_3$, cm^{-1}): 1711. HRMS (ESI) Calcd for $C_{22}H_{21}O_3$ $[M+H]^+$: 333.1485. Found: 333.1490. Melting point: 127-128 °C (recrystallized from EtOAc/hexanes).

5-(*tert*-Butyl) 1-((1*S*,2*R*,4*S*)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-yl) (*tert*-butoxycarbonyl)-*D*-glutamate - (Table 2, entry 4). A mixture of Boc-L-glutamic acid 1-tert-butyl ester (64 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry CH_3CN (1 mL, 0.2M) was treated with (1S,2R,4S)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-ol (36 mg, 0.23 mmol), triethylamine (33 µL, 0.23 mmol), and $P(OEt)_3$ (54 µL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 14 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 10% EtOAc in hexanes to give the pure ester as a colorless oil (78 mg, 85% yield). ^{1}H NMR (600 MHz, chloroform-*d*) δ 5.09 (d, *J* = 8.4 Hz, 1H), 4.94 (ddd, *J* = 10.0, 3.5, 2.2 Hz, 1H), 4.38 – 4.28 (m, 1H), 2.35 (ddd, *J* = 16.3, 8.6, 6.7 Hz, 2H), 2.27 (ddd, *J* = 16.3, 8.6, 6.3 Hz, 1H), 2.18 – 2.10 (m, 1H), 1.97 – 1.88 (m, 2H), 1.75 (ddq, *J* = 12.2, 8.1, 4.0 Hz, 1H), 1.69 (t, *J* = 4.6 Hz, 1H), 1.45 (s, 9H), 1.44 (s, 9H), 1.34 – 1.23 (m, 2H), 1.02 (dd, *J* = 13.8, 3.4 Hz, 1H), 0.90 (s, 3H), 0.88 (s, 3H), 0.83 (s, 3H). ^{13}C{1H} NMR (150 MHz, chloroform-*d*) δ 172.8, 172.2, 155.5, 81.4, 80.8, 80.0, 53.5, 49.1, 48.1, 45.0, 36.7, 31.8, 28.5, 28.2, 28.13, 28.11, 27.3, 19.8, 19.0, 13.7.IR ($CDCl_3$, cm^{-1}): 3361, 1734, 1717, 1700. HRMS (ESI) Calcd for $C_{24}H_{42}NO_6$ $[M+H]^+$: 440.3007. Found: 440.3013.

(3*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-10,13-Dimethyl-17-((*R*)-6-methylheptan-2-yl)-2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1*H*-cyclopenta[*a*]phenanthren-3-yl (*tert*-butoxycarbonyl)-*D*-tryptophanate - (Table 2, entry 5). A mixture of N-α-Boc-D-tryptophan (64 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry EtOAc (1 mL, 0.2M) was treated with cholesterol (89 mg, 0.23 mmol), triethylamine (33 µL, 0.23 mmol), and $P(OEt)_3$ (54 µL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 14 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 3% EtOAc in DCM to give the pure ester as a white foam (106 mg, 75% yield). ^{1}H NMR (600 MHz, chloroform-d) δ 8.05 (s, 1H), 7.59 (d, J = 6.9 Hz, 1H), 7.35 (d, J = 8.2 Hz, 1H), 7.19 (ddd, J = 8.1, 7.0, 1.1 Hz, 1H), 7.12 (t, J = 7.5 Hz, 1H), 7.02 (d, J = 2.4 Hz, 1H), 5.33 (d, J = 5.7 Hz, 1H), 5.07 (d, J = 8.3 Hz, 1H), 4.67 – 4.49 (m, 2H), 3.38 – 3.18 (m, 2H), 2.20 (d, J = 10.1 Hz, 2H), 2.00 (dt, J = 12.6, 3.5 Hz, 1H), 1.99 – 1.93 (m, 1H), 1.82 (dtd, J = 13.2, 6.3, 3.5 Hz, 2H), 1.75 – 1.67 (m, 1H), 1.61 – 1.23 (m, 21H), 1.19 – 0.89 (m, 16H), 0.87 (d, J = 2.8 Hz, 3H), 0.86 (d, J = 2.7 Hz, 3H), 0.67 (s, 3H). ^{13}C{1H} NMR (150 MHz, chloroform-*d*) δ 171.8, 155.4, 139.6, 136.2, 128.1, 122.9, 122.8, 122.3, 119.7, 119.2, 111.2, 110.7, 79.8, 75.2, 56.8, 56.3, 54.6, 50.1, 42.5, 39.9, 39.7, 38.0, 37.1, 36.7, 36.3, 35.9, 32.04, 31.99, 28.5, 28.4, 28.2, 27.7, 24.4, 24.0, 23.0, 22.7, 21.2, 19.4, 18.9, 12.0. IR ($CDCl_3$, cm^{-1}): 3415, 3349, 1696. HRMS (ESI) Calcd for $C_{43}H_{63}N_2O_4$ $[M-H]^-$: 671.4793. Found: 671.4799. Melting point: 87-89 °C (recrystallized from ether/hexanes).

2-((S)-2-((tert-Butoxycarbonyl)amino)-3-methoxy-3-oxopropyl) 1-(tert-butyl) (S)-pyrrolidine-1,2-dicarboxylate - (Table 2, entry 6). A mixture of N-Boc-L-proline (45 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry EtOAc (1 mL, 0.2M) was treated with N-Boc-L-serine methyl ester (51 mg, 0.23 mmol), triethylamine (33 µL, 0.23 mmol), and $P(OEt)_3$ (54 µL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 10 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 30% EtOAc in hexanes to give the pure ester as a colorless oil (70 mg, 82% yield). ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.60, 5.24 (d, *J* = 8.6 Hz, 1H, rotamers), 4.63 – 4.50 (m, 2H), 4.41 (dtd, *J* = 33.9, 11.2, 3.8 Hz, 2H), 4.29, 4.21 (dd, *J* = 8.6, 4.0 Hz, 1H, rotamers), 3.75 (s, 3H), 3.60 – 3.31 (m, 2H), 2.20 (ddq, *J* = 16.0, 12.4, 8.2 Hz, 1H), 2.05 – 1.81 (m, 3H), 1.48, 1.40 (s, 9H rotamers), 1.44 (s, 9H). ^{13}C{1H} NMR (150 MHz, chloroform-*d*) δ 172.8, 172.5, 170.4, 170.2, 155.5, 155.2, 154.7, 153.7, 80.5, 80.2, 80.1, 64.9, 64.8, 59.2, 59.0, 53.05, 53.02, 52.8, 52.7, 46.7, 46.4, 31.0, 30.1, 28.6, 28.42, 28.38, 24.5, 23.6.

IR ($CDCl_3$, cm^{-1}): 3347, 1755, 1737, 1712, 1693. HRMS (ESI) Calcd for $C_{19}H_{36}N_3O_8$ $[M+NH_4]^+$: 434.2497. Found: 434.2492.

(*Z*)-4-((*tert*-Butyldimethylsilyl)oxy)but-2-en-1-yl (*tert*-butoxycarbonyl)-*L*-methioninate - (Table 2, entry 7). A mixture of N-Boc-L-methionine (52 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry CH_3CN (1 mL, 0.2M) was treated with (*Z*)-4-((*tert*-butyldimethylsilyl)oxy)but-2-en-1-ol (47 mg, 0.23 mmol), triethylamine (33 uL, 0.231 mmol), and $P(OEt)_3$ (54 µL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 12 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 15% EtOAc in hexanes to give the pure ester as a

colorless oil (68 mg, 74% yield). ^{1}H NMR (600 MHz, chloroform-*d*) δ 5.75 (dtt, *J* = 11.5, 5.8, 1.5 Hz, 1H), 5.56 (dtt, *J* = 11.3, 6.8, 1.8 Hz, 1H), 5.11 (d, *J* = 8.2 Hz, 1H), 4.78 – 4.70 (m, 2H), 4.44 – 4.38 (m, 1H), 4.28 (ddt, *J* = 5.8, 1.8, 0.9 Hz, 2H), 2.57 – 2.50 (m, 2H), 2.17 – 2.10 (m, 1H), 2.09 (s, 3H), 1.92 (dq, *J* = 14.6, 7.6 Hz, 1H), 1.44 (s, 9H), 0.90 (s, 9H), 0.08 (s, 6H). ^{13}C{1H} NMR (150 MHz, chloroform-*d*) δ 172.2, 155.4, 134.7, 123.6, 80.2, 61.5, 59.7, 52.3, 32.4, 30.1, 28.5, 26.1, 18.5, 15.7, -5.1. IR (neat, cm^{-1}): 3351, 1714. HRMS (ESI) Calcd for $C_{20}H_{40}NO_5SSi$ $[M+H]^+$: 434.2391. Found: 434.2389.

(*R*)-4,4-dimethyl-2-oxotetrahydrofuran-3-yl (*E*)-3-(furan-3-yl)acrylate - (Table 2, entry 8). A mixture of (*E*)-3-(furan-3-yl)acrylic acid (29 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry CH_3CN (1 mL, 0.2M) was treated with (*R*)-3-hydroxy-4,4-dimethyldihydrofuran-2(3*H*)-one (30 mg, 0.23 mmol), triethylamine (33 µL, 0.23 mmol), and $P(OEt)_3$ (54 µL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 12 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 30% EtOAc in hexanes to give the pure ester as a colorless oil (40 mg, 79% yield). ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.76 – 7.62 (m, 2H), 7.45 (ddd, *J* = 2.1, 1.5, 0.8 Hz, 1H), 6.61 (dt, *J* = 1.9, 0.7 Hz, 1H), 6.25 (dd, *J* = 15.8, 0.5 Hz, 1H), 5.49 (s, 1H), 4.09 (d, *J* = 9.0 Hz, 1H), 4.06 (d, *J* = 9.3 Hz, 2H), 1.24 (s, 3H), 1.16 (s, 3H). ^{13}C{1H} NMR (150 MHz, chloroform-*d*) δ 172.7, 165.8, 145.3, 144.8, 137.0, 122.6, 116.2, 107.5, 76.4, 75.2, 40.6, 23.3, 20.1. IR ($CDCl_3$, cm^{-1}): 1781, 1716, 1684. HRMS (ESI) Calcd for $C_{13}H_{15}O_5$ $[M+H]^+$: 251.0914. Found: 251.0913.

4-(Trimethylsilyl)but-3-yn-2-yl 5-((3aS,4S,6aR)-2-oxohexahydro-1H-thieno[3,4-d]imidazol-4-yl)pentanoate - (Table 2, entry 9). A mixture of biotin (51 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry DMF (1 mL, 0.2M) was treated with racemic 4-(trimethylsilyl)but-3-yn-2-ol (33 mg, 0.23 mmol), triethylamine (33 µL, 0.23 mmol), and $P(OEt)_3$ (54 µL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 14 h under dry air at 50 °C and purified by triturating the crude mixture with H_2O to remove triethylphosphate, followed by flash column chromatography using SiO_2 and 7% MeOH in DCM to give the ester as white gummy semi-solid (68 mg, 88% yield, 1:1 mixture of diastereomers). ^{1}H NMR (400 MHz, chloroform-*d*) δ 5.95 (s, 1H), 5.46 (q, *J* = 6.7 Hz, 1H), 5.36 (s, 1H), 4.58 – 4.44 (m, 1H), 4.30 (ddd, *J* = 7.9, 4.6, 1.5 Hz, 1H), 3.15 (ddd, *J* = 8.2, 6.3, 4.5 Hz, 1H), 2.90 (dd, *J* = 12.8, 4.9 Hz, 1H), 2.75 (d, *J* = 12.8 Hz, 1H), 2.35 (td, *J* = 7.5, 2.2 Hz, 2H), 1.80 – 1.57 (m, 4H), 1.51– 1.39 (m, 5H), 0.16 (s, 9H). ^{13}C{1H} NMR (100 MHz, chloroform-*d*) δ 172.6, 163.7, 103.7, 89.6, 62.1, 60.7, 60.2, 55.6, 40.7, 34.0, 28.40, 28.38, 28.35, 28.33, 24.8, 24.8, 21.7. IR ($CDCl_3$, cm^{-1}): 3206, 1737, 1695. HRMS (ESI) Calcd for $C_{17}H_{29}N_2O_3SSi$ $[M+H]^+$: 369.1663. Found: 369.1660.

((2*S*,3*S*)-3-Methyl-3-(4-methylpent-3-en-1-yl)oxiran-2-yl)methyl 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetate - (Table 2, entry 10). A mixture of 2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetic acid (75 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry CH_3CN (1 mL, 0.2M) was treated with ((2*S*,3*S*)-3-methyl-3-(4-methylpent-3-en-1-yl)oxiran-2-yl)methanol (39 mg, 0.23 mmol), triethylamine (33 µL, 0.23 mmol), and $P(OEt)_3$ (54 µL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 11 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 15% EtOAc in hexanes to give the pure ester as a pale yellow oil (93 mg, 86% yield). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 7.69 – 7.63 (m, 2H), 7.50 – 7.43 (m, 2H), 6.97 (d, *J* = 2.5 Hz, 1H), 6.87 (dd, *J* = 9.0, 0.5 Hz, 1H), 6.67 (dd, *J* = 9.0, 2.5 Hz, 1H), 5.06 (ddq, *J* = 8.6, 5.7, 1.5 Hz, 1H), 4.36 (dd, *J* = 12.1, 4.0 Hz, 1H), 4.07 (dd, *J* = 12.1, 7.1 Hz, 1H), 3.84 (s, 3H), 3.72 (s, 2H), 2.98 (dd, *J* = 7.1, 4.0 Hz, 1H), 2.39 (s, 3H), 2.11 – 1.96 (m, 2H), 1.68 (d, *J* = 1.3 Hz, 3H), 1.67 – 1.61 (m, 1H), 1.59 (d, *J* = 1.2 Hz, 3H), 1.45 (ddd, *J* = 13.8, 9.7, 6.8 Hz, 1H), 1.28 (s, 3H). ^{13}C{1H} NMR (150 MHz, Chloroform-*d*) δ 170.8, 168.4, 156.2, 139.4, 136.2, 134.0, 132.4, 131.3, 131.0, 130.7, 129.3, 123.3, 115.1, 112.4, 111.9, 101.4, 64.2, 60.7, 59.7, 55.9, 38.4, 30.3, 25.8, 23.7, 17.8, 17.0, 13.5. IR (neat, cm^{-1}): 1737, 1681. HRMS (ESI) Calcd for $C_{29}H_{33}ClNO_5$ $[M+H]^+$: 510.2042. Found: 510.2048.

1-(*tert*-Butyl) 2-(((3a*R*,4*R*,6*R*,6a*R*)-6-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methyl) (2*S*,4*R*)-4-(benzyloxy)pyrrolidine-1,2-dicarboxylate - (Table 2, entry 11). A mixture of (2*S*,4*R*)-4-(benzyloxy)-1-(*tert*-butoxycarbonyl)pyrrolidine-2-carboxylic acid (68 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry CH_3CN (1 mL, 0.2M) was treated with 1-((3a*R*,4*R*,6*R*,6a*R*)-6-(hydroxymethyl)-2,2-dimethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)pyrimidine-2,4(1*H*,3*H*)-dione (66 mg, 0.23 mmol), triethylamine (33 µL, 0.23 mmol), and $P(OEt)_3$ (54 µL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 12 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 70% EtOAc in hexanes to give the pure ester as a white foam (89 mg, 72% yield). ^{1}H NMR (600 MHz, chloroform-*d*) δ 8.17, 8.14 (s, 1H, rotamers), 7.38 – 7.27, 7.21– 7.18 (m, 6H rotamers), 5.76 – 5.71, 5.59 – 5.57 (m, 2H rotamers), 5.01, 4.86 (dd, *J* = 6.4, 1.8 Hz, and dd, *J* = 6.4, 2.6 Hz, 1H rotamers), 4.79 (dt, *J* = 6.6, 3.7 Hz, 1H), 4.55 – 4.26 (m, 6H), 4.20 – 4.13 (m, 1H), 3.74 – 3.70, 3.61 – 3.54 (m, 2H), 2.47 – 2.33 (m, 1H), 2.11 – 2.02 (m, 1H), 1.56 (s, 3H), 1.45, 1.40 (s, 9H, rotamers), 1.35 (s, 3H). ^{13}C{1H} NMR (150 MHz, chloroform-*d*) δ 172.8, 172.6, 162.7, 162.5, 154.6, 153.9, 149.9, 149.7, 142.6, 141.7, 137.8, 137.9, 128.70, 128.67, 128.1, 128.0, 127.8, 127.7, 114.9, 114.9, 103.0, 102.8, 95.4, 93.5, 85.5, 84.6, 84.5, 84.4, 81.3, 80.7, 80.6, 76.1, 71.4, 71.3, 64.8, 64.5, 58.2, 57.8, 52.1, 51.5, 37.0, 35.9, 28.6, 28.4, 27.4, 27.3, 25.54, 25.48. IR (neat, cm^{-1}): 3194, 1746, 1687. HRMS (ESI) Calcd for $C_{29}H_{36}N_3O_{10}$ $[M-H]^-$: 586.2406. Found: 586.2415. Melting point: 74-78 °C (recrystallized from EtOAc/hexanes).

((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-Tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)methyl (*tert*-butoxycarbonyl)-*D*-phenylalaninate - (Table 2, entry 12). A mixture of N-Boc-*D*-phenylalanine (58 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular

sieves (100 mg) in dry EtOAc (1 mL, 0.2M) was treated with ((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)methanol (60 mg, 0.23 mmol), triethylamine (33 μL, 0.23 mmol), and $P(OEt)_3$ (54 μL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 10 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 20% EtOAc in hexanes to give the pure ester a colorless oil (84 mg, 79% yield). ^{1}H NMR (600 MHz, chloroform-*d*) δ 7.31 (t, *J* = 7.3 Hz, 2H), 7.26 (t, *J* = 7.4 Hz, 1H), 7.15 (d, *J* = 6.9 Hz, 2H), 5.02 (d, *J* = 8.4 Hz, 1H), 4.69 (dt, *J* = 8.6, 5.6 Hz, 1H), 4.63 (dd, *J* = 7.9, 2.7 Hz, 1H), 4.29 (d, *J* = 11.7 Hz, 1H), 4.28 – 4.24 (m, 2H), 4.20 (d, *J* = 11.6 Hz, 1H), 3.95 (dd, *J* = 13.0, 1.9 Hz, 1H), 3.80 (d, *J* = 13.0 Hz, 1H), 3.22 – 3.08 (m, 2H), 1.57 (s, 3H), 1.43 (s, 9H), 1.42 (s, 3H), 1.37 (s, 3H). ^{13}C{1H} NMR (150 MHz, chloroform-*d*) δ 171.3, 155.1, 135.9, 129.6, 128.8, 127.2, 109.4, 109.1, 101.3, 80.1, 70.9, 70.5, 70.1, 66.3, 61.5, 54.5, 38.4, 28.5, 26.7, 26.1, 25.5, 24.2. IR ($CDCl_3$, cm^{-1}): 3355, 1746, 1711. HRMS (ESI) Calcd for $C_{26}H_{38}NO_9$ $[M+H]^+$: 508.2541. Found: 508.2543.

(3a'*R*,4*S*,7'*S*,7a'*R*)-2,2,2',2'-Tetramethyltetrahydrospiro[[1,3]dioxolane-4,6'-[1,3]dioxolo[4,5-*c*]pyran]-7'-yl (*tert*-butoxycarbonyl)-*L*-valinate - (Table 2, entry 13). A mixture of N-Boc-*L*-valine (46 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry EtOAc (1 mL, 0.2M) was treated with (3a'*R*,4*S*,7'*S*,7a'*S*)-2,2,2',2'-tetramethyltetrahydrospiro[[1,3]dioxolane-4,6'-[1,3]dioxolo[4,5-*c*]pyran]-7'-ol (60 mg, 0.23 mmol), triethylamine (33 μL, 0.23 mmol), and $P(OEt)_3$ (54 μL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 10 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 20% EtOAc in hexanes to give the pure ester as a white solid (79 mg, 82% yield). ^{1}H NMR (500 MHz, chloroform-*d*) δ 5.15 (d, *J* = 7.7 Hz, 1H), 5.04 (d, *J* = 9.2 Hz, 1H), 4.34 (dd, *J* = 9.2, 4.4 Hz, 1H), 4.29 (dd, *J* = 7.8, 5.4 Hz, 1H), 4.25 – 4.21 (m, 1H), 4.13 (dd, *J* = 13.5, 2.5 Hz, 1H), 4.07 (d, *J* = 13.4 Hz, 1H), 3.96 (d, *J* = 9.3 Hz, 1H), 3.82 (d, *J* = 9.3 Hz, 1H), 2.21 (pd, *J* = 6.9, 4.6 Hz, 1H), 1.54 (s, 3H), 1.47 (s, 3H), 1.44 (s, 9H), 1.41 (s, 3H), 1.35 (s, 3H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H). ^{13}C{1H} NMR (100 MHz, chloroform-*d*) δ 171.7, 155.5, 112.1, 109.8, 103.6, 79.9, 74.8, 73.8, 72.2, 71.3, 60.8, 58.9, 31.6, 28.4, 27.8, 26.48, 26.46, 26.2, 19.4, 17.3. IR (neat, cm^{-1}): 3393, 1746, 1688. HRMS (ESI) Calcd for $C_{22}H_{38}NO_9$ $[M+H]^+$: 460.2541. Found: 460.2542. Melting point: 106 – 108 °C (recrystallized from ether/hexanes).

(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl (*S*)-3-(4-acetoxyphenyl)-2-(((benzyloxy)carbonyl)amino)propanoate - (Table 2, entry 14). A mixture of (*S*)-3-(4-acetoxyphenyl)-2-(((benzyloxy)carbonyl)amino)propanoic acid (75 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry EtOAc (1 mL, 0.2M) was treated (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexan-1-ol (36 mg, 0.23 mmol), triethylamine (33 μL, 0.23 mmol), and $P(OEt)_3$ (54 μL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 10 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 20% EtOAc in hexanes to give the pure ester as a colorless oil (80 mg, 77% yield). ^{1}H NMR (600 MHz, chloroform-*d*) δ 7.39 – 7.28 (m, 5H), 7.16 – 7.11 (m, 2H), 7.01 – 6.96 (m, 2H), 5.26 (d, *J* = 8.1 Hz, 1H), 5.10 (s, 2H), 4.70 (td, *J* = 10.9, 4.4 Hz, 1H), 4.61 (dt, *J* = 8.1, 5.9 Hz, 1H), 3.13 (dd, *J* = 14.0, 6.0 Hz, 1H), 3.07 (dd, *J* = 14.0, 5.8 Hz, 1H), 2.28 (s, 3H), 1.94 – 1.83 (m, 1H), 1.73 (pd, *J* = 6.9, 2.2 Hz, 1H), 1.69 – 1.63 (m, 2H), 1.51 – 1.41 (m, 1H), 1.34 (ddt, *J* = 14.4, 11.2, 3.2 Hz, 1H), 1.02 (qd, *J* = 13.4, 12.7, 3.7 Hz, 1H), 0.96 – 0.80 (m, 8H), 0.71 (d, *J* = 6.9 Hz, 3H). ^{13}C{1H} NMR (75 MHz, $CDCl_3$) δ 171.0, 169.5, 155.7, 149.8, 136.4, 133.5, 130.6, 128.6, 128.3, 128.3, 121.7, 76.0, 67.1, 54.8, 46.9, 40.8, 37.7, 34.1, 31.5, 26.2, 23.4, 22.1, 21.3, 20.8, 16.3. IR ($CDCl_3$, cm^{-1}): 3362, 1751, 1721, 1688. HRMS (ESI) Calcd for $C_{29}H_{38}NO_6$ $[M+H]^+$: 496.2694. Found: 496.2687.

((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-Tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)methyl 2-acetoxy-2-phenylacetate - (Table 2, entry 15). A mixture of (S)-(+)-O-acetylmandelic acid (40 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry EtOAc (1 mL, 0.2M) was treated with ((3a*S*,5a*R*,8a*R*,8b*S*)-2,2,7,7-tetramethyltetrahydro-3a*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-3a-yl)methanol (60 mg, 0.23 mmol), triethylamine (33 μL, 0.23 mmol), and $P(OEt)_3$ (54 μL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 10 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 25% EtOAc in hexanes to give the pure ester as a colorless oil (76 mg, 83% yield, 1:0.6 mixture of diastereomers based on integration of ^{1}H NMR spectrum). ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.51 – 7.34 (m, 5H), 6.04, 5.96 (s, 1H, mixture of diastereomers), 4.59, 4.53 (dd, *J* = 7.9, 2.7 Hz, 1H, mixture of diastereomers), 4.46 – 4.02 (m, 4H), 3.89, 3.86 (d, *J* = 1.9 Hz, 1H, diastereomers), 3.73, 3.70 (dd, *J* = 4.6, 0.8 Hz, 1H mixture of diastereomers), 2.18, 2.17 (s, 3H, mixture of disatereomers), 1.50, 1.46 (s, 3H, mixture of disatereomers), 1.45 (s, 3H,), 1.33, 1.31 (s, 3H, mixture of diastereomers), 1.26, 1.05 (s, 3H, mixture of diastereomers). ^{13}C{1H} NMR (100 MHz, chloroform-*d*) δ 196.4, 170.4, 170.1, 168.3, 168.3, 133.9, 133.5, 129.56, 129.55, 129.03, 128.98, 128.21, 128.15, 109.30, 109.25, 109.1, 109.0, 101.23, 101.16, 74.6, 74.4, 70.9, 70.8, 70.3, 70.12, 70.09, 70.05, 65.61, 65.56, 61.42, 61.38, 26.60, 26.57, 26.01, 26.00, 25.2, 25.0, 24.19, 24.17, 20.9. IR ($CDCl_3$, cm^{-1}): 1743. HRMS (ESI) Calcd for $C_{22}H_{27}O_9$ $[M-H]^-$: 435.1661. Found: 435.1660.

Phenyl 3,7-dimethyloct-6-enoate - (Table 2, entry 17). A mixture of racemic citronellic acid (36 mg, 0.21 mmol), diselenide **1** (7.2 mg, 0.011 mmol), 4-dimethylaminopyridine (2.6 mg, 0.021 mmol), and 4 Å molecular sieves (100 mg) in dry CH_3CN (1 mL, 0.2M) was treated with phenol (22 mg, 0.23 mmol) and $P(OEt)_3$ (54 μL, 0.32 mmol) according to the general procedure. The coupling reaction was stirred for 9 h under dry air at 50 °C and purified by flash column chromatography using SiO_2 and 10% EtOAc in hexanes to give the pure ester as a colorless oil (21 mg, 41% yield). ^{1}H NMR (400 MHz, chloroform-*d*) δ 7.42 – 7.34 (m, 2H), 7.25 – 7.19 (m, 1H), 7.11 – 7.05 (m, 2H), 5.13 (tp, *J* = 10.7, 2.2 Hz, 1H), 2.57 (dd, *J* = 14.7, 6.0 Hz, 1H), 2.37 (dd, *J* = 14.8, 8.2 Hz, 1H), 2.16 – 1.99 (m, 3H), 1.70 (q, *J* = 1.3 Hz, 3H), 1.62 (d, *J* = 1.2 Hz, 3H), 1.46 (dddd, *J* = 13.5, 9.2, 6.7, 5.7 Hz, 1H), 1.32 (dddd, *J* = 13.6,

9.1, 7.8, 6.2 Hz, 1H), 1.06 (d, J = 6.7 Hz, 3H). $^{13}C\{1H\}$ NMR (100 MHz, chloroform-*d*) δ 171.8, 150.9, 131.9, 129.5, 125.9, 124.3, 121.8, 77.5, 77.2, 76.8, 41.9, 36.9, 30.3, 25.9, 25.6, 19.8, 17.8. IR (neat, cm^{-1}): 1755. HRMS (ESI) Calcd for $C_{16}H_{22}O_2$ $[M+H]^+$: 247.1693. Found: 247.1691.

Experimental details for reaction described in Scheme 1. A mixture of methyl-4-hydroxybenzoate (15 mg, 0.099 mmol), diselenide **1** (32 mg, 0.049 mmol), 4-dimethylaminopyridine (1.0 mg, 0.001 mmol), and 4 Å molecular sieves (100 mg) in dry CH_3CN (1 mL, 0.2M) was treated with triethylamine (15 µL, 0.11 mmol) and $P(OEt)_3$ (26 µL, 0.15 mmol) according to the general procedure. The coupling reaction was stirred for 12h under dry air at 50 °C and the components separated by SiO_2 and 30% EtOAc in hexanes (phosphate ester, colorless oil, 24 mg, 84% yield) followed by 10% MeOH in DCM (ethyl selenoether, yellow gummy solid, 24 mg, 68% yield).

***N*-(2-(Dimethylamino)ethyl)-2-(ethylselanyl)-*N*-methyl-5-nitrobenzamide. – (2)** ^1H NMR (300 MHz, chloroform-*d*) δ 8.16 – 7.99 (m, 2H), 7.54 (d, J = 8.7 Hz, 1H), 3.67 (t, J = 6.9 Hz, 1H), 3.20 (t, J = 6.8 Hz, 1H), 3.14, 2.91 (s, 3H, rotamers), 3.05 (q, J = 7.5 Hz, 2H), 2.63 (t, J = 6.9 Hz, 1H), 2.42 (d, J = 7.0 Hz, 1H), 2.33 (s, 3H), 2.06 (s, 3H), 1.49 (t, J = 7.5 Hz, 3H). $^{13}C\{1H\}$ NMR (150 MHz, chloroform-*d*) δ 168.6, 168.0, 146.0, 145.8, 140.3, 139.8, 139.5, 139.1, 130.5, 130.2, 123.7, 122.4, 121.7, 57.5, 56.5, 49.2, 45.8, 45.6, 37.4, 33.2, 29.8, 21.3, 21.1, 20.9, 14.8. IR ($CDCl_3$, cm^{-1}): 1639, 1632. HRMS (ESI) Calcd for $C_{14}H_{22}O_3N_3Se$ $[M+H]^+$: 360.0821. Found: 360.0818.

Methyl 4-((diethoxyphosphoryl)oxy)benzoate. – (3) ^1H NMR (400 MHz, chloroform-*d*) δ 8.03 (AA' of AA'XX', 2H), 7.27 (XX' of AA'XX', 2H), 4.22 (dqd, J = 8.2, 7.1, 2.0 Hz, 4H), 3.90 (s, 3H), 1.35 (td, J = 7.1, 1.1 Hz, 6H). $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$) δ 166.4, 154.53, 154.49, 131.7, 127.0, 119.9, 119.9, 77.4, 77.2, 77.0, 65.01, 64.97, 52.3, 16.23, 16.19. ^{31}P NMR (121 MHz, chloroform-*d*) δ -6.89. IR ($CDCl_3$, cm^{-1}): 1721. HRMS (ESI) Calcd for $C_{12}H_{18}O_6P$ $[M+H]^+$: 289.0836. Found: 289.0832.

ASSOCIATED CONTENT

Supporting Information

^1H and $^{13}C\{^1H\}$ spectra are provided (pdf file) free of charge via the Internet at http://pubs.acs.org.

The Supporting Information is available free of charge on the ACS Publications website.

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The manuscript was written through contributions of all authors. / All authors have given approval to the final version of the manuscript. /

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