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Syntheses of highly functionalized δ,γ-unsaturated-α-amino acids

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Abstract—The synthesis of several γ,δ-unsaturated-α-amino acid derivatives is described. The method features regioselective stannylation of propargylglycine derivatives followed by Stille coupling reactions.

1. Introduction

Non-proteinogenic α-amino acids are important nitrogenous building blocks that are useful for the synthesis of natural products and a multitude of biologically significant substances.[1] There has been a continuing interest in the development of new methods for the synthesis of enantiomerically pure amino acids with substituents strategically placed at side-chain positions including the capacity to install unsaturation. Many methods have been developed for the asymmetric synthesis of amino acids.[2,3] Despite the plethora of methodologies extant, many reactive functionalities remain incompatible with existing templates.[2]

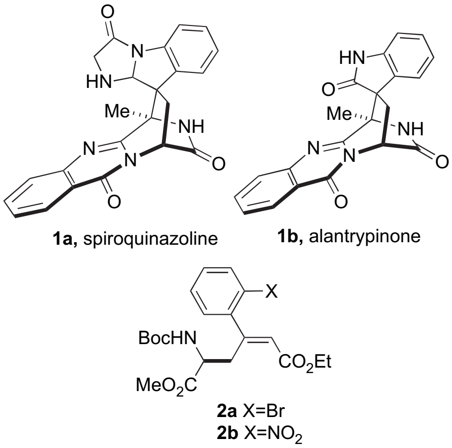

Figure 1. Structures of spiroquinazoline, alantrypinone, and γ,δ-unsaturated amino acid derivatives **2**.

As part of a strategy to synthesize the natural metabolites spiroquinazoline (**1a**)[4] and alantrypinone (**1b**),[5] we required access to γ-aryl-γ,δ-unsaturated-α-amino acids such as **2**. Several reported methods to prepare this type of amino acid were attempted but we were unsuccessful in constructing the target substances **2**.[6] Jackson et al. have reported the synthesis of enantiomerically pure unsaturated α-amino acids via coupling with readily available serine-derived β-iodoalanine derivatives using zinc/copper reagents.[7] We have adapted this approach to prepare a variety of γ-aryl-γ,δ-unsaturated-α-amino acids (Fig. 1).

2. Results and discussion

Our approach commenced with *N*-(*tert*-butoxycarbonyl)-L-iodoalanine methyl ester **3**, which is commercially available or can be prepared on a large scale by using the reported procedure with serine as the starting material.[8] Iodide **3** was converted into the corresponding Zn/Cu complex and then coupled with ethyl 3-bromopropiolate or *tert*-butyl 3-bromopropiolate.[7] The Zn/Cu complex **4** reacted with ethyl-3-bromopropiolate to produce the propargyl species **5a** and **5b** in 77 and 48% yields, respectively (Scheme 1).

Next, we examined the conjugate stannylation of organocopper(I) reagents to the γ,δ-alkynyl residue of **5**. The addition of compound **5a** to the solution of $Bu_3SnCu\cdot SMe_2$ or $[Bu_3SnCuCN]Li$[9,10] in THF resulted in no reaction. When **5a** was added to $Me_3SnCu\cdot SMe_2$ in THF, compound **6** was obtained in 23% yield with 40% recovery of **5a**. Piers et al. reported that (trimethylstannyl)copper(I)

Keywords: Syntheses; Amino acids.

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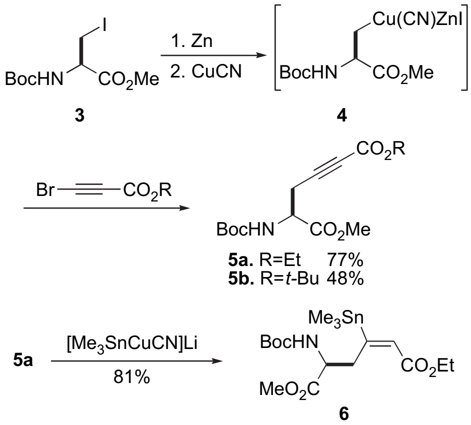


Scheme 1. Preparation of stannane **6**.

dimethylsulfide complex was relatively unreactive toward α,β-unsaturated carbonyl compounds.[9] When a more reactive species $[Me_3SnCuCN]Li$[10] was used in the place of $Me_3SnCu\cdot SMe_2$ for this reaction we observed that the yield was dramatically improved. When **5a** was added to $[Me_3SnCuCN]Li$ in dry THF at −78 °C, compound **6** and the corresponding *Z*-isomer were produced in a nearly 1:1 ratio with no recovery of the starting material. Separation of the two isomers by flash chromatography proved to be very difficult and synthetically intractable. When $[Me_3SnCuCN]Li$ was treated with EtOH prior to the addition of **5a**, the product obtained was exclusively the desired *E*-isomer. The geometric configuration of the product was determined by the coupling constant between the α-olefinic proton and the tin atom (^{117}Sn, ^{119}Sn) of the Me_3Sn group. It is well-known that when a trialkylstannyl group and a proton are vicinal on a C=C bond, the $^{3}J_{Sn-H}$ values are much larger when these moieties are trans- as opposed to cis-configuration.[11] The $^{3}J_{Sn-H}$ value in the present case of 69 Hz, falls into the expected range for the *E*-stereochemistry. The observation of a significant ^{1}H NOE between the vinyl proton and the Me_3Sn protons provided corroborating evidence to support the *E*-stereochemistry assigned for **6** (Fig. 2). The optical integrity of **6** was determined by ^{1}H NMR analysis of the derived Mosher's amide,[12] which revealed that **6** was obtained in at least 99.5:0.5 er. Compound **6** proved to be a stable substance and can be kept as an oil, exposed to air at ambient temperature for several weeks without detectable decomposition.

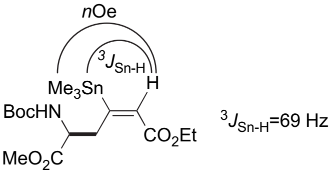
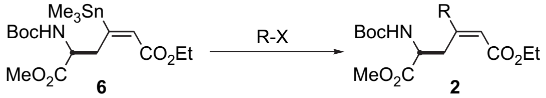
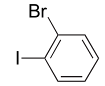
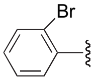
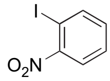
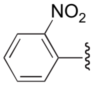
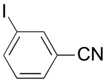
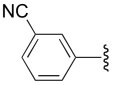
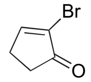
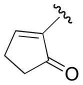
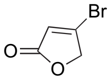
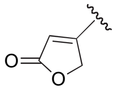
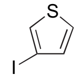
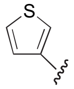
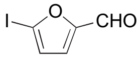
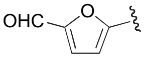
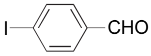
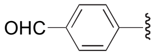


Figure 2. *E*-Stereochemical assignment for **6**.

Table 1. Stille coupling reactions of stannane **6**



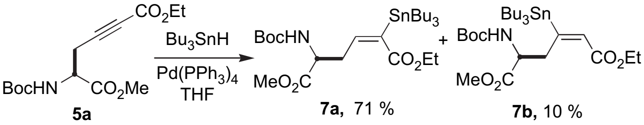
Entry	R-X	Conditions	Yield (%)	R
a		Pd_2dba_3, CuI, $AsPh_3$, DMF	68	
b		$Pd_2Cl_2(CH_3CN)_2$, Bu_3SnH	79 (brsm)	
c		Pd_2dba_3, CuI, $AsPh_3$, DMF	71	
d		Pd_2dba_3, CuI, $AsPh_3$, DMF	77	
e		Pd_2dba_3, CuI, $AsPh_3$, DMF	57	
f		Pd_2dba_3, CuI, $AsPh_3$, DMF	80	
g		Pd_2dba_3, CuI, $AsPh_3$, DMF	84	
h		$Pd_2Cl_2(CH_3CN)_2$, Bu_3SnH, 45 °C	67	

Compound **6** was then coupled with a variety of aryl and heterocyclic halides under Stille cross-coupling conditions (Table 1).[13] Our initial efforts examined $Pd(PPh_3)_4$ as the catalyst in the presence of CuI[14] at room temperature. But under these conditions either no product or trace amount of product was obtained. Higher temperature only led to the decomposition of compound **6**. Amino acid **2a** was successfully prepared by coupling *o*-bromoiodobenzene with compound **6** by using Pd_2dba_3 in the presence of $AsPh_3$ and CuI.[15] Only the bromide product **2a** was observed as evidenced by ^{13}C NMR and MS; the corresponding iodide was not observed. The 3-cyanophenyl moiety can be introduced under similar conditions (entry c). Heterocyclic species such as 2-bromocyclopent-2-enone and 4-bromofuran-2(5*H*)-one were also successfully coupled with compound **6** to yield **2d** and **2e** in 77 and 57% yields, respectively (entries d and e). The coupling of **6** with 3-iodothiophene or 5-iodofuran-2-carboxaldehyde also provided the cross-coupling products in useful yields (entries f and g).

In all cases, the reaction was complete in just 2 h and no loss of optical integrity was observed by chiral HPLC analysis.[16] *o*-Iodonitrobenzene coupled with compound **6** to deliver **2b**, however in very poor yield. When $PdCl_2(CH_3CN)_2$ was used as the catalyst, incomplete reaction was observed. We found that the yields could be improved by increasing the catalyst loading, but this also caused more homocoupling. Eventually, it was found that treatment of $PdCl_2(CH_3CN)_2$ with tri-*n*-butyltin hydride followed by the addition of compound **6** and *o*-iodonitrobenzene portionwise resulted in a 79% yield of **2b** (based on a small amount of unreacted starting material).

It proved unnecessary to employ dry, deoxygenated solvent (DMF) and the reaction can be manipulated in air at ambient temperature. It should be noted that no reaction occurred when commercially available Pd-black was used. This system also proved effective for the coupling of *p*-iodobenzaldehyde with compound **6** (entry h). In this case the catalyst could be added in one portion and heating to 45 °C was required. It is known that for aryl iodide substrates, the oxidative addition of Pd(0) in the Stille reaction cycle is accelerated by electron-withdrawing substituents.[17] Strong electron-withdrawing groups, such as the aldehyde or nitro group consequently accelerates the oxidative addition step so that no ligand is needed (entries b and h). For the other halides examined, which were devoid of strong electron-withdrawing substituents, the ligand has to be added to facilitate the oxidative addition.[18]

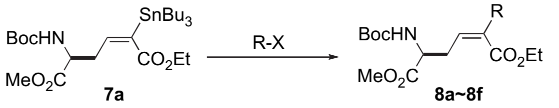
In contrast to the copper(I) chemistry described above, compound **5a** underwent a Pd-catalyzed hydrostannylation reaction[19] with tri-*n*-butyltin hydride providing **7a** as the major product in 71% yield along with regioisomer **7b** (10%) as shown in Scheme 2.

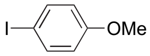
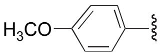
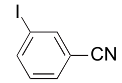
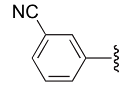
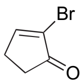
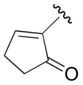
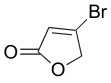
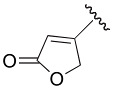
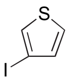
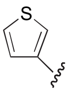
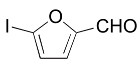
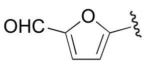


Scheme 2.

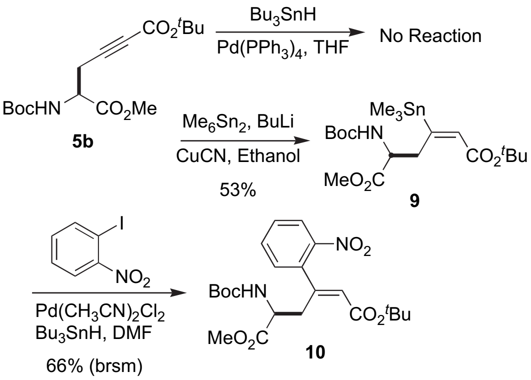
The two regioisomers **7a** and **7b** can be separated by flash chromatography and may be stored by exposing to air for weeks without significant decomposition. The major isomer **7a** can couple with a variety of halides to give the amino acids listed in Table 2. The catalytic system Pd_2dba_3/CuI/$AsPh_3$ works quite well for the Stille coupling reactions of **7a** and the halides that are listed in Table 2. It does not appear to matter whether the substituent on the phenyl group is an electron-withdrawing group such as cyano or an electron-donating group such as methoxy. 2-Bromocyclopent-2-enone and 4-bromofuran-2(5*H*)-one can couple with compound **7a** to yield **8c** and **8d**, respectively. The coupling of **7a** with 3-iodothiophene or 5-iodofuran-2-carboxaldehyde delivered **8e** and **8f**, respectively, in good yields.

Table 2. Stille coupling reactions of stannane **7a**



Entry	R-X	Conditions	Yield (%)	R
a		Pd_2dba_3, CuI, $AsPh_3$, DMF	74	
b		Pd_2dba_3, CuI, $AsPh_3$, DMF	79	
c		Pd_2dba_3, CuI, $AsPh_3$, DMF	72	
d		Pd_2dba_3, CuI, $AsPh_3$, DMF	69	
e		Pd_2dba_3, CuI, $AsPh_3$, DMF	84	
f		Pd_2dba_3, CuI, $AsPh_3$, DMF	76	

Compound **5a** underwent hydrostannylation with good regioselectivity favoring the δ-stannane **7a**. We also examined the reaction conditions by using a hindered *tert*-butyl ester that would favor the γ-stannane-type regioisomer **7b**. Compound **5b** underwent conjugate addition with $[Me_3SnCuCN]Li$ to yield the γ-substituted stannane **9** in 53% yield (Scheme 3). As a preliminary demonstration of the utility of this species, compound **9** underwent Stille cross-coupling with *o*-iodonitrobenzene to produce the γ-aryl-γ,δ-unsaturated amino acid derivative **10** in which the two ester groups are differentiated. This amino acid and related derivatives are currently being examined for their utility in an intramolecular S_N2'-type strategy to access the core ring systems of spiroquinazoline and alantrypinone.



Scheme 3. Synthesis of **10** via **9**.

3. Conclusion

In summary, we have developed an efficient strategy to synthesize two types of γ,δ-unsaturated-α-amino acids bearing substitution at either γ- or δ-position. Further applications of this methodology toward the total synthesis of spiroquinazoline and other nitrogen-rich substances are currently underway and will be reported on in due course.

4. Experimental

4.1. General

All anhydrous reactions were conducted under an inert argon atmosphere. Dry solvents were obtained from a glass contour solvent purification system. Flash column chromatography was carried out using silica gel 60. All chemical shifts (*δ*) are reported in parts per million. Ethyl 3-bromopropiolate and *tert*-butyl 3-bromopropiolate were prepared by Leory's method.[20] 2-Bromocyclopent-2-enone[21] and 4-bromofuran-2(5*H*)-one[22] were prepared by literature procedures.

4.1.1. (*S*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)hex-2-ynedioate (5a).[7] A suspension of zinc (9.83 g, 150.4 mmol) in 11.2 mL dry THF and 1,2-dibromoethane

(0.65 mL, 7.53 mmol) was heated under Ar to 60 °C for 3 min. After cooling the mixture to 35 °C, trimethylsilyl chloride (0.194 mL, 1.53 mmol) was added and the mixture was vigorously stirred for 30 min. At this point the reaction vessel was warmed to 35 °C, compound **3** (8.25 g, 25.1 mmol) in 50 mL dry THF was slowly added, and the mixture was stirred for 15–40 min until no starting material remained. The solution of zinc reagent was then converted to the zinc/copper reagent **4** by the following procedure. The solution of zinc reagent was cooled to −10 °C, and a solution prepared from CuCN (2.27 g, 25.1 mmol) and LiCl (2.15 g, 50.2 mmol) in 50 mL dry THF was added. The mixture was stirred at 0 °C for 10 min and then cooled to −55 °C. A solution of ethyl 3-bromoprop-2-ynoate (5.91 g, 33.4 mmol) in 67 mL dry THF was introduced followed by stirring at this temperature for 20 h. After quenching with saturated aqueous NH_4Cl, the mixture was extracted with ethyl acetate (3×400 mL), the combined organic layers were washed with 400 mL water, dried ($MgSO_4$), and concentrated in vacuo. The residue was separated by silica gel flash chromatography (eluted with 20% ethyl acetate/hexane) to give 6.2 g of **5a** as a yellow oil (yield 77%). $[\alpha]_D^{20}$ +55.7 (*c* 0.670, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6): δ 0.79 (3H, t, J=7.2 Hz), 1.38 (9H, s), 2.39 (1H, dd, J=17.4, 5.4 Hz), 2.54 (1H, dd, J=17.4, 5.1 Hz), 3.18 (3H, s), 3.81 (2H, q, J=7.2 Hz), 4.34 (1H, ddd, J=7.8, 5.4, 5.1 Hz), 5.29 (1H, d, J=7.8 Hz). ^{13}C NMR (75 MHz, C_6D_6): δ 14.3, 23.3, 28.7, 52.5, 52.6, 62.1, 76.6, 80.3, 83.6, 153.5, 155.4, 170.7. IR (NaCl, neat) 3366, 2980, 2240, 1748, 1712, 1507. HRMS (FAB+) calcd mass for $C_{14}H_{22}NO_6$ 300.1447 (M+1), found: 300.1453. R_f 0.33 (eluted with 20% ethyl acetate/hexane).

4.1.2. (*S*)-1-*tert*-Butyl 6-methyl 5-(*tert*-butoxycarbonylamino)hex-2-ynedioate (5b). A procedure similar to the one described above for the preparation of **5a** was used for the synthesis of **5b** starting from 2.1 g (6.38 mmol) of compound **3** and 1.44 g (7.02 mmol) of *tert*-butyl 3-bromoprop-2-ynoate. Yield: 1.0 g (48%). $[\alpha]_D^{20}$ +52.5 (*c* 1.46, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6): δ 1.24 (9H, s), 1.37 (9H, s), 2.39 (1H, dd, J=17.1, 5.4 Hz), 2.53 (1H, dd, J=17.1, 5.1 Hz), 3.15 (3H, s), 4.34 (1H, ddd, J=7.8, 5.4, 5.1 Hz), 5.26 (1H, d, J=7.8 Hz). ^{13}C NMR (75 MHz, C_6D_6): δ 23.1, 28.1, 28.6, 52.3, 52.5, 77.8, 80.2, 81.3, 83.0, 152.7, 155.4, 170.8. IR (NaCl, neat) 3366, 2980, 2244, 1750, 1709, 1505. HRMS (FAB+) calcd mass for $C_{16}H_{26}NO_6$ 328.1760 (M+1), found 328.1746. R_f 0.33 (eluted with 20% ethyl acetate/hexane).

4.1.3. (*S*,*E*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-3-(trimethylstannyl)hex-2-enedioate (6).[9] To a cold (−20 °C), stirred solution of 5.2 g of hexamethylditin (15.87 mmol) in 150 mL dry THF was added a solution of 10.7 mL (17.12 mmol) of a 1.6 M solution of methyl lithium in ether. The mixture was stirred at −20 °C for 15 min to afford a pale yellow solution of Me_3SnLi. This solution was then cooled to −78 °C and 1.66 g (18.52 mmol) of solid CuCN was added in one portion. The mixture was stirred at −78 °C for 5 min and at −48 °C for 15 min to afford a bright orange solution. This solution was then cooled to −78 °C and 0.95 mL (16.0 mmol) of dry ethanol was added. After 5 min, a solution of compound **5a** in 50 mL dry THF was added dropwise and the mixture was stirred at −78 °C for 4 h. NH_4Cl–NH_4OH buffer (200 mL, consisting of a 9:1 ratio of saturated aqueous NH_4Cl/28–30% NH_4OH, pH=8) was added, the mixture was opened to the atmosphere, allowed to warm to room temperature, and stirred vigorously until the aqueous phase became a deep blue color. The organic phase was separated and the aqueous phase was extracted thoroughly with ether. The combined organic extracts were washed with brine, dried over Na_2SO_4, and concentrated. The residue was purified by silica gel flash column chromatography (eluted with 15% ethyl acetate/hexane) to give 5.0 g of compound **6** as a yellow oil (81% yield). $[\alpha]_D^{20}$ +60.8 (*c* 2.65, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6): δ 0.18 (9H, s), 0.95 (3H, t, J=7.2 Hz), 1.36 (9H, s, $^{2}J_{Sn-H}$=54.3 Hz), 2.89 (1H, dd, J=12.0, 3.9 Hz), 3.28 (3H, s), 3.90 (1H, t, J=12.0 Hz), 3.95 (2H, q, J=7.2 Hz), 4.68 (1H, J=12.0, 8.1, 3.9 Hz), 6.09 (1H, d, J=8.1 Hz), 6.22 (1H, s, $^{3}J_{Sn-H}$=69.0 Hz). ^{13}C NMR (75 MHz, C_6D_6): δ −8.7, 28.7, 28.9, 37.2, 52.3, 54.5, 79.5, 81.0, 133.4, 156.2, 164.9, 165.5, 172.8. IR (NaCl, neat) 3371, 2977, 1751, 1717, 1598, 1507, 1446 cm^{-1}. HRMS (FAB+) calcd mass for $C_{19}H_{36}NO_6Sn$: 494.1565 (M+1), found: 494.1557. R_f 0.33 (eluted with 15% ethyl acetate/hexane).

4.1.4. (*S*,*E*)-1-Ethyl 6-methyl 3-(2-bromophenyl)-5-(*tert*-butoxycarbonylamino)hex-2-enedioate (2a). A solution of *o*-iodobromobenzene (41.2 mg, 0.146 mmol), CuI (6.67 mg, 35 μmol), $AsPh_3$ (10.7 mg, 35 μmol), and Pd_2dba_3 (9.45 mg, 8.74 μmol) in 1.2 mL dry DMF under Ar was treated with compound **6** (61.3 mg, 0.132 mmol). The reaction mixture was then stirred for 2 h. The solution was then diluted with EtOAc (5 mL) and washed with water. The combined aqueous layers were back-extracted with EtOAc (2×5 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and evaporated to dryness. The resulting oil was purified by silica gel chromatography (eluted with 25% EtOAc in hexanes) to yield 41.0 mg of **2a** as a yellow oil (yield 68%). $[\alpha]_D^{20}$ +53.2 (*c* 1.17, CH_2Cl_2). ^{1}H NMR (400 MHz, C_6D_6): δ 0.91 (3H, t, J=7.2 Hz), 1.41 (9H, s), 3.13 (3H, s), 3.33 (1H, dd, J=12.4, 4.0 Hz), 3.88 (2H, q, J=7.2 Hz), 4.02 (1H, t, J=12.4 Hz), 4.70 (1H, ddd, J=12.4, 6.6, 4.0 Hz), 5.89 (1H, s), 5.96 (1H, d, J=6.6 Hz), 6.58–7.25 (4H, m). ^{13}C NMR (75 MHz, C_6D_6): δ 14.4, 28.7, 35.4, 52.1, 53.3, 60.9, 79.6, 121.8, 124.6, 127.9, 128.9, 130.1, 130.9, 133.6, 142.5, 156.2, 167.0, 172.5. IR (NaCl, neat) 3382, 2978, 1748, 1717, 1645, 1507, 1436 cm^{-1}. HRMS (FAB+) calcd mass for $C_{20}H_{27}NO_6Br$: 456.1021 (M+1, ^{80}Br), found: 456.1005. R_f 0.30 (eluted with 25% ethyl acetate/hexane).

4.1.5. (*S*,*E*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-3-(2-nitrophenyl)hex-2-enedioate (2b). A 25 mL flask, equipped with a magnetic stir bar was charged with 80 mg (0.308 mmol) of $PdCl_2(CH_3CN)_2$ and 10 mL of DMF. Tri-*n*-butyltin hydride (182 μL, 0.339 mmol) was added dropwise and a black precipitate was formed immediately. The mixture was stirred for 10 min and then added to a solution of compound **6** (1.98 g, 4.27 mmol) and 1.12 g (4.49 mmol) of *o*-iodonitrobenzene in DMF (50 mL) in three portions (one portion every 5 h). The mixture was stirred overnight. The reaction was then quenched with water and the mixture was extracted with ether (3×100 mL). The combined organic extracts were washed with 300 mL water, dried over Na_2SO_4, and concentrated in vacuo. The residue was separated by silica gel flash column chromatography (eluted with 25% ethyl acetate/hexane) to give 850 mg (47% conversion and 79% yield based on recovered **6**) of **2b** as a yellow oil along with 800 mg of unreacted **6**. $[\alpha]_D^{20}$ +17.8 (*c* 0.835, CH_2Cl_2). ^1H NMR (300 MHz, C_6D_6): δ 0.89 (3H, t, *J*=7.2 Hz), 1.42 (9H, s), 3.11 (3H, s), 3.16 (1H, dd, *J*=12.9, 3.6 Hz), 3.85 (2H, q, *J*=7.2 Hz), 4.03 (1H, t, *J*=12.9 Hz), 4.64 (1H, ddd, *J*=12.9, 9.0, 3.6 Hz), 5.75 (1H, s), 5.9 (1H, d, *J*=9.0 Hz), 6.5–7.6 (4H, m). ^{13}C NMR (75 MHz, C_6D_6): δ 14.8, 28.4, 35.6, 52.1, 53.3, 79.6, 81.4, 124.2, 125.3, 128.9, 131.7, 133.6, 137.3, 147.4, 153.4, 156.3, 166.3, 172.4. IR (NaCl, neat) 3389, 2979, 1747, 1716, 1640, 1608, 1528, 1367, 1347 cm^{-1}. HRMS (FAB+) calcd mass for $C_{22}H_{31}N_2O_8$: 451.2080 (M+1), found: 451.2086. R_f 0.30 (eluted with 25% ethyl acetate/hexane).

4.1.6. (*S*,*E*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-3-(3-cyanophenyl)hex-2-enedioate (2c). A procedure similar to the one described above for the preparation of **2a** was used for the synthesis of **2c** starting from 19.5 mg (0.0421 mmol) of compound **6** and 10.6 mg (0.0464 mmol) of 3-iodobenzonitrile. Yield: 12.0 mg (71%). $[\alpha]_D^{20}$ +46.7 (*c* 0.405, CH_2Cl_2). ^1H NMR (400 MHz, C_6D_6): δ 0.99 (3H, t, *J*=7.0 Hz), 1.36 (9H, s), 3.16 (3H, s), 3.20 (1H, dd, *J*=13.4, 10.0 Hz), 3.59 (1H, dd, *J*=13.4, 9.6 Hz), 3.96 (2H, q, *J*=7.0 Hz), 4.46 (1H, ddd, *J*=10.0, 9.6, 8.4 Hz), 5.71 (1H, d, *J*=8.4 Hz), 5.81 (1H, s), 6.40–7.20 (3H, m), 7.21 (1H, s). ^{13}C NMR (100 MHz, C_6D_6): δ 14.5, 28.6, 33.4, 52.1, 53.5, 60.9, 79.8, 113.9, 118.7, 122.8, 129.7, 130.9, 131.1, 132.6, 141.5, 153.0, 155.9, 166.7, 172.2. IR (NaCl, neat) 3371, 2878, 2231, 1744, 1713, 1632, 1510 cm^{-1}. HRMS (FAB+) calcd mass for $C_{21}H_{27}N_2O_6$ 403.1869 (M+1), found 403.1869. R_f 0.30 (eluted with 25% ethyl acetate/hexane).

4.1.7. (*S*,*E*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-3-(5-oxocyclopent-1-enyl)hex-2-enedioate (2d). A procedure similar to the one described above for the preparation of **2a** was used for the synthesis of **2d** starting from 21.0 mg (0.0454 mmol) of compound **6** and 8.05 mg (0.05 mmol) of 4-bromocyclopent-2-enone. Yield: 13.3 mg (77%). $[\alpha]_D^{20}$ +46.5 (*c* 0.550, CH_2Cl_2). ^1H NMR (300 MHz, C_6D_6): δ 0.91 (3H, t, *J*=6.9 Hz), 1.39 (9H, s), 1.58 (2H, m), 1.78 (2H, t, *J*=4.5 Hz), 3.07 (1H, dd, *J*=13.5, 5.1 Hz), 3.33 (3H, s), 3.74 (1H, *J*=13.5, 10.8 Hz), 3.91 (2H, q, *J*=6.9 Hz), 4.70 (1H, ddd, *J*=10.8, 8.1, 6.9 Hz), 6.37 (1H, d, *J*=8.1 Hz), 7.41 (1H, t, *J*=3.0 Hz), 7.66 (1H, s). ^{13}C NMR (100 MHz, C_6D_6): δ 14.7, 26.3, 28.9, 32.6, 36.2, 52.4, 54.5, 61.0, 79.8, 122.5, 140.5, 144.0, 156.4, 163.0, 168.4, 172.8, 205.7. IR (NaCl, neat) 3371, 2978, 1746, 1708, 1625, 1510, 1367 cm^{-1}. HRMS (FAB+) calcd mass for $C_{19}H_{28}NO_7$ 382.1866 (M+1), found 382.1873. R_f 0.30 (eluted with 50% ethyl acetate/hexane).

4.1.8. (*S*,*E*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-3-(5-oxo-2,5-dihydrofuran-3-yl)hex-2-enedioate (2e). A procedure similar to the one described above for the preparation of **2a** was used for the synthesis of **2e** starting from 45.0 mg (0.097 mmol) of compound **6** and 17.4 mg (0.107 mmol) of 4-bromofuran-2(5*H*)-one. Yield: 21.1 mg (57%). $[\alpha]_D^{20}$ +36.0 (*c* 2.19, CH_2Cl_2). ^1H NMR (300 MHz, C_6D_6): δ 0.93 (3H, t, *J*=7.2 Hz), 1.35 (9H, s), 2.90 (1H, dd, *J*=13.2, 4.8 Hz), 3.21 (1H, dd, *J*=13.2, 9.6 Hz), 3.24 (3H, s), 3.87 (2H, q, *J*=7.2 Hz), 3.96 (2H, s), 4.69 (1H, ddd, *J*=9.6, 8.1, 4.8 Hz), 5.34 (1H, s), 5.62 (1H, d, *J*=8.1 Hz), 6.15 (1H, s). ^{13}C NMR (75 MHz, C_6D_6): δ 14.4, 28.6, 32.3, 52.4, 53.9, 61.3, 70.0, 80.0, 120.3, 123.2, 143.9, 155.9, 162.1, 166.0, 171.9, 172.2. IR (NaCl, neat) 3376, 2979, 1789, 1752, 1714, 1630, 1599, 1507 cm^{-1}. HRMS (FAB+) calcd mass for $C_{18}H_{26}NO_8$ 384.1658 (M+1), found 384.1673. R_f 0.30 (eluted with 50% ethyl acetate/hexane).

4.1.9. (*S*,*E*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-3-(thiophen-3-yl)hex-2-enedioate (2f). A procedure similar to the one described above for the preparation of **2a** was used for the synthesis of **2f** starting from 19.6 mg (0.0423 mmol) of compound **6** and 9.8 mg (0.0466 mmol) of 3-iodothiophene. Yield: 13.0 mg (80%). $[\alpha]_D^{20}$ +46.1 (*c* 0.460, CH_2Cl_2). ^1H NMR (300 MHz, C_6D_6): δ 0.99 (3H, t, *J*=7.1 Hz), 1.38 (9H, s), 3.27 (1H, dd, *J*=12.9, 5.1 Hz), 3.28 (3H, s), 3.76 (1H, dd, *J*=12.9, 9.9 Hz), 3.96 (2H, q, *J*=6.9 Hz), 4.77 (1H, ddd, *J*=7.8, 6.9, 5.1 Hz), 6.22 (1H, d, *J*=7.8 Hz), 6.26 (1H, s), 6.65 (1H, dd, *J*=5.1, 3.0 Hz), 6.88 (1H, dd, *J*=5.1, 1.5 Hz), 7.35 (1H, dd, *J*=3.0, 1.5 Hz). ^{13}C NMR (100 MHz, C_6D_6): δ 14.8, 28.9, 33.4, 52.3, 54.9, 60.8, 79.7, 118.5, 125.8, 125.9, 126.9, 141.3, 148.7, 156.1, 167.8, 172.6. IR (NaCl, neat) 3366, 2978, 1745, 1711, 1698, 1619, 1503, 1450 cm^{-1}. HRMS (FAB+) calcd mass for $C_{18}H_{26}NO_6S$ 384.1481 (M+1), found 384.1489. R_f 0.40 (eluted with 20% ethyl acetate/hexane).

4.1.10. (*S*,*E*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-3-(5-formylfuran-2-yl)hex-2-enedioate (2g). A procedure similar to the one described above for the preparation of **2a** was used for the synthesis of **2g** starting from 53.5 mg (0.116 mmol) of compound **6** and 28.2 mg (0.127 mmol) of 5-iodofuran-2-carbaldehyde. Yield: 38.4 mg (84%). $[\alpha]_D^{20}$ +27.2 (*c* 1.13, CH_2Cl_2). ^1H NMR (300 MHz, C_6D_6): δ 0.94 (3H, t, *J*=7.1 Hz), 1.36 (9H, s), 3.17 (1H, dd, *J*=13.2, 5.7 Hz), 3.29 (3H, s), 3.50 (1H, dd, *J*=13.2, 9.9 Hz), 3.90 (2H, q, *J*=7.1 Hz), 4.69 (1H, ddd, *J*=9.9, 8.1, 5.7 Hz), 6.02 (1H, d, *J*=8.1 Hz), 6.37 (1H, d, *J*=4.2 Hz), 6.55 (1H, d, *J*=4.2 Hz), 6.67 (1H, s), 9.13 (1H, s). ^{13}C NMR (75 MHz, C_6D_6): δ 14.4, 28.6, 31.1, 52.3, 54.7, 61.0, 79.9, 113.9, 119.6, 121.1, 140.6, 153.4, 156.2, 156.7, 167.2, 172.2, 177.7. IR (NaCl, neat) 3366, 2978, 1746, 1713, 1683, 1623, 1500, 1447 cm^{-1}. HRMS (FAB+) calcd mass for $C_{19}H_{26}NO_8$ 396.1658 (M+1), found 396.1649. R_f 0.25 (eluted with 25% ethyl acetate/hexane).

4.1.11. (*S*,*E*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-3-(4-formylphenyl)hex-2-enedioate (2h). A procedure similar to the one described above for the preparation of **2b** was used for the synthesis of **2h** starting from 45.0 mg (0.0972 mmol) of compound **6** and 21.6 mg (0.117 mmol) of 4-iodobenzaldehyde. Yield: 26.4 mg (67%). $[\alpha]_D^{20}$ +66.8 (*c* 0.467, CH_2Cl_2). ^1H NMR (300 MHz, C_6D_6): δ 0.99 (3H, t, *J*=6.9 Hz), 1.37 (9H, s), 3.19 (3H, s), 3.28 (1H, dd, *J*=13.2, 5.1 Hz), 3.75 (1H, dd, *J*=13.2, 9.9 Hz), 3.87 (2H, q, *J*=6.9 Hz), 4.55 (1H, ddd, *J*=9.9, 8.4, 5.1 Hz), 5.80 (1H, d, *J*=8.4 Hz), 6.03 (1H, s), 7.12 (2H, d, *J*=4.8 Hz), 7.39 (2H, d, *J*=4.8 Hz), 9.59 (1H, s). ^{13}C NMR (400 MHz,

C_6D_6): δ 14.5, 28.7, 33.4, 52.1, 53.7, 60.9, 79.7, 122.7, 130.0, 130.2, 137.4, 145.7, 154.2, 155.9, 166.9, 172.4, 191.0. IR (NaCl, neat) 3371, 2979, 1745, 1704, 1604, 1511 cm^{-1}. HRMS (FAB+) calcd mass for $C_{21}H_{28}NO_7$ 406.1866 (M+1), found 406.1874. R_f 0.30 (eluted with 33% ethyl acetate/hexane).

4.1.12. (*S*,*E*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-2-(tri-*n*-butylstannyl)hex-2-enedioate (7a) and (*S*,*E*)-1-ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-3-(tri-*n*-butylstannyl)hex-2-enedioate (7b).[18] A solution of compound **5a** (347.8 mg, 022 mmol) and $Pd(PPh_3)_4$ (5 mg, 4.3 mmol) in dry THF (10 mL) under Ar was treated with tri-*n*-butyltin hydride (343 mmol, 0.24 mmol). The reaction mixture was then stirred for 2 h and the solvent was evaporated to dryness. The resulting oil was purified by silica gel chromatography (eluted with 5% ethyl acetate, 95% hexane). The fast eluting compound was **7b** (66 mg, 10%) and the slower eluting substance was **7a** (487 mg, yield 71%). Data for **7a**: $[\alpha]_D^{20}$ +33.5 (c 1.10, CH_2Cl_2). ^{1}H NMR (400 MHz, C_6D_6): δ 0.96 (9H, t, J=7.6 Hz), 1.01 (3H, t, J=7.2 Hz), 1.02 (6H, t, J=8.8 Hz), 1.37 (6H, m), 1.42 (9H, s), 1.59 (6H, m), 2.90 (2H, m), 3.28 (3H, s), 3.95 (2H, q, J=7.2 Hz), 4.58 (1H, ddd, J=13.2, 7.2, 0.4 Hz), 5.76 (1H, d, J=7.2 Hz), 6.09 (1H, t, J=7.4 Hz, $^3J_{Sn-H}$=45.0 Hz). ^{13}C NMR (100 MHz, C_6D_6): δ 11.0, 14.3, 14.7, 28.0, 28.7, 29.6, 35.2, 52.1, 54.0, 60.8, 79.6, 141.1, 146.9, 156.1, 171.1, 172.8. IR (NaCl, neat) 3364, 2957, 2928, 2872, 2854, 1754, 1719, 1607, 1500 cm^{-1}. HRMS (FAB+) calcd mass for $C_{26}H_{50}NO_6Sn$: 591.2671 (M+1), found: 591.2647. R_f 0.33 (eluted with 10% ethyl acetate/hexane). Data for **7b**: $[\alpha]_D^{20}$ +54.3 (c 3.30, CH_2Cl_2). ^{1}H NMR (400 MHz, C_6D_6): δ 0.93 (9H, t, J=7.4 Hz), 0.94 (3H, t, J=7.0 Hz), 1.02 (6H, t, J=8.2 Hz), 1.36 (6H, m), 1.41 (9H, s), 1.58 (6H, m), 2.97 (1H, dd, J=12.4, 3.6 Hz), 3.31 (3H, s), 3.92 (2H, q, J=7.0 Hz), 4.02 (1H, t, J=12.4 Hz), 4.71 (1H, ddd, J=12.4, 12.4, 8.4 Hz), 6.23 (1H, d, J=8.4 Hz), 6.34 (1H, s, $^3J_{Sn-H}$=60.0 Hz). ^{13}C NMR (100 MHz, C_6D_6): δ 10.7, 14.2, 14.5, 28.1, 28.8, 29.7, 37.6, 52.2, 54.6, 60.6, 79.5, 132.1, 156.5, 165.3, 168.1, 173.0. IR (NaCl, neat) 3364, 2957, 2929, 2872, 2854, 1754, 1719, 1607, 1503 cm^{-1}. HRMS (FAB+) calcd mass for $C_{26}H_{50}NO_6Sn$: 591.2671 (M+1), found: 591.2671. R_f 0.30 (eluted with 15% ethyl acetate/hexanes).

4.1.13. (*S*,*Z*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-2-(4-methoxyphenyl)hex-2-enedioate (8a). A procedure similar to the one described above for the preparation of **2a** was used for the synthesis of **8a** starting from 40.0 mg (0.0678 mmol) of compound **7a** and 17.4 mg (0.0745 mmol) of 1-iodo-4-methoxybenzene. Yield: 20.4 mg (74%). $[\alpha]_D^{20}$ +20.9 (c 0.675, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6): δ 0.94 (3H, t, J=7.1 Hz), 1.42 (9H, s), 2.81 (2H, t, J=7.2 Hz), 3.25 (3H, s), 3.28 (3H, s), 4.01 (2H, q, J=7.1 Hz), 4.61 (1H, q, J=7.5 Hz), 5.71 (1H, d, J=7.5 Hz), 5.89 (1H, t, J=7.5 Hz), 6.72 (2H, d, J=8.7 Hz), 7.23 (2H, d, J=8.7 Hz). ^{13}C NMR (75 MHz, C_6D_6): δ 14.4, 28.7, 33.5, 52.1, 54.1, 55.1, 61.2, 79.8, 114.4, 129.3, 130.6, 131.6, 138.5, 156.1, 160.4, 168.6, 172.8. IR (NaCl, neat) 3371, 2978, 1745, 1715, 1608, 1513 cm^{-1}. HRMS (FAB+) calcd mass for $C_{21}H_{30}NO_7$ 408.2022 (M+1), found 408.2003. R_f 0.33 (eluted with 33% ethyl acetate/hexane).

4.1.14. (*S*,*Z*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-2-(3-cyanophenyl)hex-2-enedioate (8b). A procedure similar to the one described above for the preparation of **2a** was used for the synthesis of **8b** starting from 41.3 mg (0.070 mmol) of compound **7a** and 17.6 mg (0.077 mmol) of 3-iodobenzonitrile. Yield: 22.0 mg (79%). $[\alpha]_D^{20}$ +27.4 (c 0.625, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6): δ 0.84 (3H, t, J=6.9 Hz), 1.41 (9H, s), 2.82 (1H, t, J=7.5 Hz), 3.25 (3H, s), 3.88 (2H, q, J=6.9 Hz), 4.57 (1H, q, J=7.5 Hz), 5.53 (1H, d, J=7.2 Hz), 5.75 (1H, t, J=7.8 Hz), 6.61 (1H, t, J=7.5 Hz), 6.8–7.4 (4H, m). ^{13}C NMR (100 MHz, C_6D_6): δ 14.3, 28.7, 33.7, 52.3, 53.8, 61.5, 80.1, 113.5, 118.9, 129.2, 131.5, 131.8, 132.1, 136.1, 138.1, 139.5, 156.0, 166.8, 172.5. IR (NaCl, neat) 3373, 2979, 2231, 1745, 1716, 1511, 1438 cm^{-1}. HRMS (FAB+) calcd mass for $C_{21}H_{27}N_2O_6$ 403.1869 (M+1), found 403.1864. R_f 0.30 (eluted with 25% ethyl acetate/hexane).

4.1.15. (*S*,*Z*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-2-(5-oxocyclopent-1-enyl)hex-2-enedioate (8c). A procedure similar to the one described above for the preparation of **2a** was used for the synthesis of **8c** starting from 42.4 mg (0.0718 mmol) of compound **7a** and 12.7 mg (0.079 mmol) of 4-bromocyclopent-2-enone. Yield: 19.7 mg (72%). $[\alpha]_D^{20}$ +20.2 (c 0.130, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6): δ 1.01 (3H, t, J=7.2 Hz), 1.66 (9H, s), 1.68 (2H, m), 1.85 (2H, m), 2.83 (2H, m), 3.30 (3H, s), 4.05 (2H, q, J=7.2 Hz), 4.59 (1H, m), 5.64 (1H, d, J=6.9 Hz), 6.82 (1H, t, J=7.8 Hz), 6.96 (1H, t, J=2.9 Hz). ^{13}C NMR (75 MHz, C_6D_6): δ 14.5, 26.3, 28.7, 33.2, 35.3, 52.2, 53.9, 61.4, 79.7, 130.0, 135.6, 140.5, 156.0, 160.0, 167.0, 172.6, 205.6. IR (NaCl, neat) 3367, 2978, 1745, 1709, 1509, 1367 cm^{-1}. HRMS (FAB+) calcd mass for $C_{19}H_{28}NO_7$ 382.1866 (M+1), found 382.1874. R_f 0.33 (eluted with 50% ethyl acetate/hexane).

4.1.16. (*S*,*Z*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-2-(5-oxo-2,5-dihydrofuran-3-yl)hex-2-enedioate (8d). A procedure similar to the one described above for the preparation of **2a** was used for the synthesis of **8e** starting from 36.0 mg (0.061 mmol) of compound **7a** and 10.93 mg (0.0671 mmol) of 4-bromofuran-2(5*H*)-one. Yield: 16.0 mg (69%). $[\alpha]_D^{20}$ +20.8 (c 1.00, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6): δ 0.82 (3H, t, J=7.2 Hz), 1.37 (9H, s), 2.65 (1H, m), 2.66 (1H, t, J=8.1 Hz), 3.21 (3H, s), 3.81 (2H, q, J=7.2 Hz), 4.11 (2H, s), 4.40 (1H, dd, J=14.1, 8.1 Hz), 5.36 (1H, d, J=8.1 Hz), 5.54 (1H, t, J=7.8 Hz), 5.98 (1H, s). ^{13}C NMR (75 MHz, C_6D_6): δ 14.2, 28.6, 33.7, 52.4, 53.5, 61.8, 70.5, 80.3, 117.5, 129.5, 140.4, 155.9, 158.7, 164.9, 172.1, 172.9. IR (NaCl, neat) 3364, 2979, 1785, 1750, 1716, 1634, 1516 cm^{-1}. HRMS (FAB+) calcd mass for $C_{18}H_{26}NO_8$ 384.1658 (M+1), found 384.1649. R_f 0.30 (eluted with 50% ethyl acetate/hexane).

4.1.17. (*S*,*Z*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-2-(thiophen-3-yl)hex-2-enedioate (8e). A procedure similar to the one described above for the preparation of **2a** was used for the synthesis of **8e** starting from 35.6 mg (0.0603 mmol) of compound **7a** and 13.9 mg (0.0633 mmol) of 3-iodothiophene. Yield: 19.4 mg (84%). $[\alpha]_D^{20}$ +17.0 (c 0.635, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6): δ 0.91 (3H, t, J=7.1 Hz), 1.40 (9H, s), 2.76 (2H, t,

J=7.5 Hz), 3.25 (3H, s), 3.96 (2H, q, J=7.1 Hz), 4.57 (1H, q, J=7.5 Hz), 5.64 (1H, d, J=7.5 Hz), 5.95 (1H, t, J=8.1 Hz), 6.77 (1H, dd, J=5.1, 3.3 Hz), 6.94 (1H, dd, J=5.1, 1.2 Hz), 7.08 (1H, dd, J=3.3, 1.2 Hz). ^{13}C NMR (75 MHz, C_6D_6): δ 14.6, 28.9, 33.5, 52.3, 54.2, 61.5, 79.9, 123.2, 125.9, 127.2, 132.3, 133.4, 138.6, 156.0, 168.5, 172.6. IR (NaCl, neat) 3372, 2978, 1743, 1717, 1506, 1436, 1366 cm^{-1}. HRMS (FAB+) calcd mass for $C_{18}H_{26}NO_6S$ 384.1481 (M+1), found 384.1486. R_f 0.30 (eluted with 25% ethyl acetate/hexane).

4.1.18. (*S*,*Z*)-1-Ethyl 6-methyl 5-(*tert*-butoxycarbonylamino)-2-(5-formylfuran-2-yl)hex-2-enedioate (8f). A procedure similar to the one described above for the preparation of **2a** was used for the synthesis of **8f** starting from 40.3 mg (0.0683 mmol) of compound **7a** and 16.7 mg (0.0751 mmol) of 5-iodofuran-2-carbaldehyde. Yield: 20.5 mg (76%). $[\alpha]_{\mathrm{D}}^{20}$ −1.3 (c 0.555, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6): δ 0.92 (3H, t, J=7.2 Hz), 1.39 (9H, s), 2.78 (2H, t, m), 3.23 (3H, s), 3.93 (2H, q, J=7.2 Hz), 4.50 (1H, m), 5.42 (1H, d, J=7.8 Hz), 6.36 (1H, d, J=3.6 Hz), 6.46 (1H, d, J=3.6 Hz), 6.66 (1H, t, J=7.95 Hz), 9.22 (1H, s). ^{13}C NMR (75 MHz, C_6D_6): δ 14.3, 28.6, 33.2, 52.2, 53.7, 61.8, 80.0, 111.8, 121.8, 127.0, 137.5, 152.8, 154.9, 155.9, 165.0, 172.4, 177.0. IR (NaCl, neat) 3365, 2979, 1742, 1716, 1678, 1500, 1439 cm^{-1}. HRMS (FAB+) calcd mass for $C_{19}H_{26}NO_8$ 396.1658 (M+1), found 396.1640. R_f 0.30 (eluted with 33% ethyl acetate/hexane).

4.1.19. (*S*,*E*)-1-*tert*-Butyl 6-methyl 5-(*tert*-butoxycarbonylamino)-3-(trimethylstannyl)hex-2-enedioate (9). A procedure similar to the one described above for the preparation of **6** was used for the synthesis of **9** starting from 0.91 mg (2.78 mmol) of compound **5b** and 1.09 g (3.34 mmol) of hexamethylditin. Yield: 729 mg (53%). $[\alpha]_{\mathrm{D}}^{20}$ +60.8 (c 2.65, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6): δ 0.13 (9H, s, $^{2}J_{\mathrm{Sn-H}}$=54.3 Hz), 1.36 (9H, s), 1.42 (9H, s), 2.89 (1H, dd, J=12.0, 3.9 Hz), 3.28 (3H, s), 3.95 (1H, t, J=12.0 Hz), 4.68 (1H, J=12.0, 8.1, 3.9 Hz), 6.09 (1H, d, J=8.1 Hz), 6.22 (1H, s, $^{3}J_{\mathrm{Sn-H}}$=69.0 Hz). ^{13}C NMR (75 MHz, C_6D_6): δ −8.7, 28.7, 28.9, 37.2, 52.3, 54.5, 79.5, 81.0, 133.4, 156.2, 164.9, 165.5, 172.8. IR (NaCl, neat) 3371, 2977, 1751, 1717, 1598, 1507, 1446 cm^{-1}. HRMS (FAB+) calcd mass for $C_{19}H_{36}NO_6Sn$ 494.1565 (M+1), found 494.1557. R_f 0.33 (eluted with 15% ethyl acetate/hexane).

4.1.20. (*S*,*E*)-1-*tert*-Butyl 6-methyl 5-(*tert*-butoxycarbonylamino)-3-(2-nitrophenyl)hex-2-enedioate (10). A procedure similar to the one described above for the preparation of **2b** was used for the synthesis of **10** starting from 404 mg (1.03 mmol) of compound **9** and 284 mg (1.14 mmol) of *o*-iodonitrobenzene. Product of 94.9 mg was obtained along with the recovery of 246 mg compound **9** (25% conversion and 66% yield based on recovered **9**). $[\alpha]_{\mathrm{D}}^{20}$ +17.8 (c 0.835, CH_2Cl_2). ^{1}H NMR (300 MHz, C_6D_6): δ 1.36 (9H, s), 1.42 (9H, s), 3.11 (3H, s), 3.16 (1H, dd, J=12.9, 3.6 Hz), 4.03 (1H, t, J=12.9 Hz), 4.64 (1H, ddd, J=12.9, 9.0, 3.6 Hz), 5.75 (1H, s), 6.02 (1H, d, J=9.0 Hz), 6.5–7.6 (4H, m). ^{13}C NMR (75 MHz, C_6D_6): δ 28.4, 28.8, 35.6, 52.1, 53.3, 79.6, 81.4, 124.2, 125.3, 128.9, 131.7, 133.6, 137.3, 147.4, 153.4, 156.3, 166.3, 172.4. IR (NaCl, neat) 3389, 2979, 1747, 1716, 1640, 1608, 1528, 1367, 1347 cm^{-1}. HRMS (FAB+) calcd mass for $C_{22}H_{31}N_2O_8$ 451.2080 (M+1), found 451.2086. R_f 0.30 (eluted with 25% ethyl acetate/hexane).

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