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An Enantioselective Synthesis of Insecticidal 4-Alkynyloxazolines

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Abstract—2-(2,6-Difluorophenyl)-4-phenylalkynyl oxazolines are potent insect growth regulators. An efficient and enantioselective synthesis to these compounds has been developed which relies on a (−)-sparteine mediated hydroxymethylation of the lithium dianion of propargylic amides.

Introduction

2,4-Diaryl oxazolines such as **1** (Fig. 1) were recently found to be very potent growth regulators on species of acari and lepidoptera.[1] These compounds act by inhibiting the synthesis of chitin which is required for the development of the insect or aracnid exoskeleton. As compounds that inhibit a molecular pathway that is specific to arthropods, they represent a selective method of insect control.

The acetylene spaced analogues such as **5** (Scheme 1) were discovered at DuPont and found to possess excellent activity on the above species.[2] The compounds were originally synthesized through an electrochemical oxidation of urethane **2** to give **3** followed by reaction with an alkynyl aluminum to give the urethane **4**. Hydrolysis, acylation and then cyclization with Burgess' reagent yielded the desired oxazoline **5**. In addition to the generally low overall yield obtained in this synthesis, the route is not amenable to efficient analogueing around the aryl alkyne group since this is introduced early in the synthesis with an aluminum species that requires synthesis.

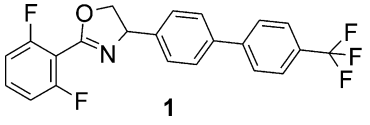
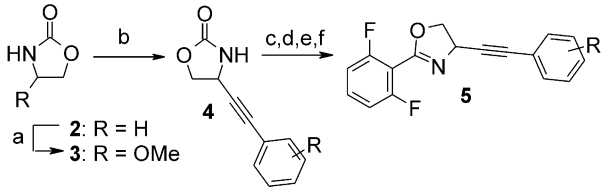


Figure 1. Arthropodicidal oxazolines.

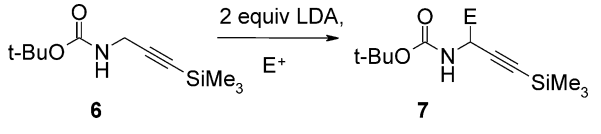
Results and Discussion

We therefore desired a more efficient approach and became interested in the work of Metcalf et al. who had described a bis-metalation of *N*-Boc protected propargylamines[3] (Scheme 2).

We suspected that this could be extended to the metalation of *N*-propargyl 2,6-difluorobenzamide systems such as **8**, thus obviating the need for protection of the amine function, followed by oxazoline formation and finally a divergent introduction of aryl groups via a Sonogashira coupling reaction.[4]



Scheme 1. Prior synthesis of acetylenic oxazolines **5**:[2] (a) MeOH, HOAc, n-Bu_4NBF_4, e-, 80%; (b) $Al(CCPh\text{-}X)_3$, toluene, 22 °C, 31% for R = H; (c) KOH, EtOH, H_2O, 78 °C, 70%; (d) 2,6-difluorobenzoyl chloride, NEt_3, CH_2Cl_2; (e) $LiBH_4$, THF, 66 °C, 62% for two steps; (f) $MeO_2CN^-SO_2NEt_3^+$, THF, 66 C, 70%.



Scheme 2. Metalation of *N*-Boc propargylamines according to Metcalf et al.[3]

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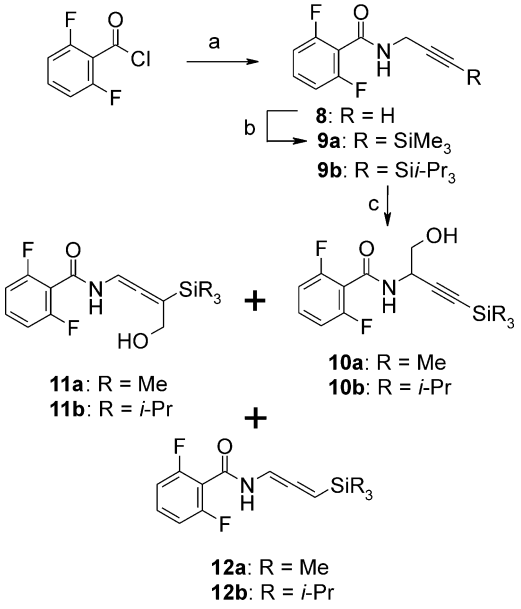
The TIPS protected alkyne **9a** was readily available in two steps from propargyl amine and 2,6-difluorobenzoyl chloride. Treatment of this alkyne with LDA in the presence of TMEDA in THF at −78 °C followed by the introduction of formaldehyde gas gave the desired hydroxymethyl compound **10a** along with the allene **11a** in a 4:3 ratio. It was thought that by increasing the size of the alkyne protecting group it might be possible to increase the amount of **10** relative to **11**. Thus, applying the same procedure to **9b** gave alkyne **10b** which was contaminated with only trace (ca. 5%) amounts of allene **11b** (Scheme 3).

The use of formaldehyde in this reaction presented a few technical difficulties due to its rapid repolymerization at −78 °C. It was best introduced through a thick cannula well above the surface of the liquid and rely on vigorous vortexing of the mixture for its absorption (see Experimental). The moderate yield obtained in this reaction was suspected to be due to the formation of formic acid via a Cannizzaro reaction of formaldehyde. This led to the recovery of a mixture of starting material and allene **12** in a 1:1 ratio and was later addressed by the controlled heating of paraformaldehyde at 130 °C.

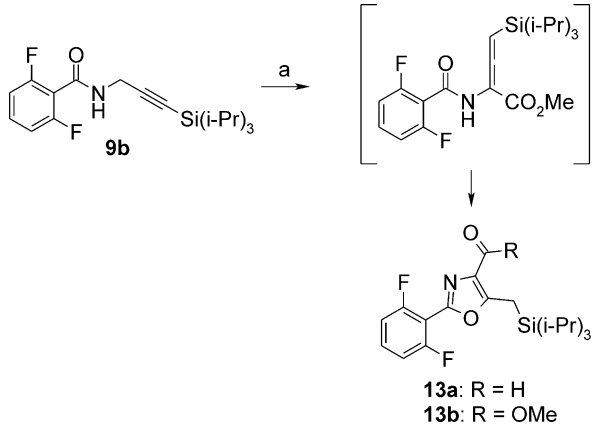
Dimethylformamide and methyl chloroformate were also examined as alternative electrophiles that might provide a more convenient access to the desired alcohol **10** and might also be of utility in preparing analogues of the antibiotic ethynyl glycine.[5] However, upon quenching the dianion of **9** with either of the above, compounds **13a** and **13b** were isolated, apparently resulting from a 1,4-addition of the amide oxygen into an α,β,γ unsaturated carbonyl group followed by tautomerisation (Scheme 4).



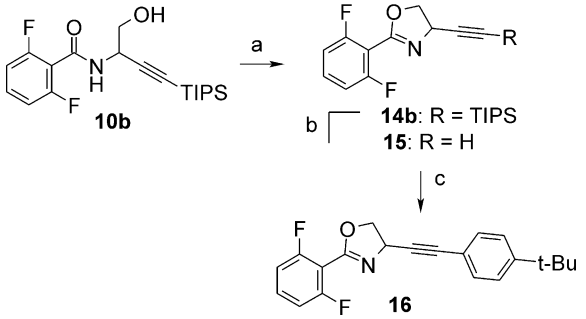
Scheme 3. Reagents and conditions: (a) 1.05 equiv propargylamine, 1.25 equiv NEt_3, 0.01 equiv DMAP, CH_2Cl_2, 0–20 °C, 6 h, 97%: (b) 2.1 equiv *n*-BuLi, 2.2 equiv diisopropylamine, THF, −78 °C, then 1.1 equiv R_3SiCl, −78 to 20 °C, 14 h, 85% for **9b**; (c) 2.05 equiv *n*-BuLi, 2.1 equiv diisopropylamine, 2.1 equiv TMEDA, THF, −78 °C, then excess CH_2O(g), 0.5 h, 45% of **10b**.

Alcohol **10b** could now be cyclized to the desired oxazoline **14b** using Tf_2O in pyridine[6] and the TIPS group was readily removed using TBAF/HOAc to give the terminal alkyne **15**. This compound was stable for 1–2 days at ambient temperature if kept in solution but it appears to polymerize when stored neat. The overall yield of the sequence was around 30% and multigram amounts are readily obtainable. Finally, as anticipated, alkyne **15** was readily coupled to aryl iodides at ambient temperature and, albeit in lower yield, to aryl bromides at elevated temperature (80–90 °C) (Scheme 5).

The 4-*t*-butylphenyl analogue **16** was a representative example. This compound completely controlled larval two spotted spider mites (*Tetranychus urticae*) on kidney bean at 0.1 ppm and larval Fall Army Worm (*Spodoptera frugiperda*) on lima bean at 1.0 ppm. Smaller substituents on the alkynyl phenyl group resulted in a sharp loss in lepidopteran activity. Naphthalene alkynes were somewhat more active but the most potent compounds were substituted biphenyl alkynes such as **21**. Methyl substitution around the oxazoline ring had a detrimental effect on activity (Tables 1 and 2).



Scheme 4. Reagents and conditions: (a) 2.1 equiv *n*-BuLi, 2.2 equiv diisopropylamine, THF, −78 °C, then 1.1 equiv HCO_2Et or ClC(O)OMe, 2 h, 50%.



Scheme 5. Reagents and conditions: (a) 1.05 equiv Tf_2O, pyridine, 15–20 °C, 0.5 h, 64%; (b) 1.2 equiv TBAF, 1.2 equiv HOAc, THF, 20 °C, 3 h, 88%; (c) 0.05 equiv $Pd(PPh_3)_4$, 0.1 equiv CuI, 3.5 equiv NEt_3, 2 equiv 4-*t*-butyliodobenzene, DMF, 20 °C, 14 h, 98%.

Given the successful preparation of the target compounds, we now examined a modification of the route to provide an enantiomeric synthesis. To the best of our knowledge, a sparteine mediated enantioselective deprotonation/alkylation[7] of proparglic amide systems has not been reported. Treatment of propargyl amide **9b** with LDA in ethyl ether in the presence of one equivalent of (−)-sparteine followed by introduction of gaseous formaldehyde gave optically active alcohol **10b**. Mosher ester analysis of this material showed a 5:2 ratio of diastereomers. This ratio was not affected by the use of 2 equivalents of (−)-sparteine. The reaction did not proceed well in toluene. Conversion of this optically active alcohol to the 4-bromobiphenyl analogue **21** gave a solid with α_D +2.5°. This could be crystallized from chlorobutane to give material with α_D of +7.8°. Recrystallization did not increase the optical rotation of the material. The absolute configuration was determined by X-ray crystallographic analysis (Fig. 2). Unfortunately, this enantiomer proved not to be the biologically relevant material.

Table 1. Insecticidal and acaricidal activity of substituted phenyl alkynes

Compd	X	Y	Z	R	Fall army worm (LC_{80}, ppm)	Two spotted spider mite (LC_{80}, ppm)
16	H	H	H	*t*-Bu	0.1	0.01
17	H	H	H	O-*t*-Bu	10	
18	H	H	H	H	>10	
19	H	H	H	CF_3	>10	
20	H	H	H	4-OTf-Ph	<0.1	
21	H	H	H	4-Br-Ph	<0.1	0.01
22	H	H	H	4-F-Ph	<0.1	0.01
23	H	H	H	Ph	<0.1	
24	Me	H	H	4-*t*-Bu	0.3	
25	H	Me	H	4-*t*-Bu	0.5	
26	H	H	Me	4-*t*-Bu	10	

IC_{50}'s are accurate to approximately ±50%.

Table 2. Insecticidal and acaricidal activity of substituted naphthyl alkynes

Compd	R =	Fall army worm (LC_{80}, ppm)
27	OTf	0.2
28	OCH_2CF_3	1
29	Br	5

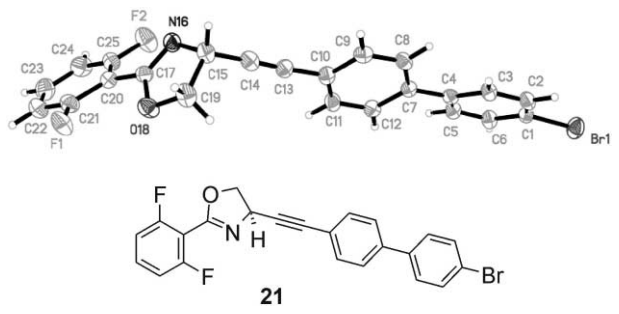


Figure 2. ORTEP representation of the X-ray crystal structure of compound **21**.

Conclusion

In conclusion, an efficient route to 2-aryl-4-alkynyl oxazolines has been developed which enables the divergent synthesis of compounds such as **16**. This route is also amenable to the synthesis of enantioenriched analogues via an enantioselective lithiation/alkylation mediated by (−)-sparteine.

Experimental

General

Reactions were carried out under an atmosphere of dry nitrogen using anhydrous solvents purchased from the Aldrich Chemical Company Inc. where appropriate. Amine bases were dried and stored over potassium hydroxide. Glassware was oven dried before use. Reactions were monitored by TLC on E. Merck silica gel plates (0.25 mm) and visualized under UV light (254 nm) and/or heating with phosphomolybdic acid ethanol solution. Reaction temperatures were measured internally. Solvents used for work up and chromatography were reagent grade from E. Merck or VWR Scientific. Flash chromatography was performed on E. Merck silica gel (60, particle size 0.040–0.063 mm). Yields refer to chromatographically and spectroscopically (^{1}H NMR) pure materials.

NMR spectra were recorded on a Varian 300 MHz instrument at 25 °C. Chemical shifts are reported relative to the residual solvent peak. Multiplicities are designated singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m) or broad singlet/multiplet (bs/bm). IR samples were prepared by evaporation of a solution of the compound from $CDCl_3$ onto a NaCl plate under a stream of nitrogen. IR spectra were recorded on a Perkin–Elmer 1600 series spectrometer. Mass spectra were recorded on a Micromass spectrometer under FAB conditions. Melting points were recorded on a Thomas Hoover Unimelt apparatus and are uncorrected. Microanalyses were performed at Quantitative Technologies Inc., Whitehouse, NJ, USA.

***N*-Propargyl 2,6-difluorobenzamide (8).** To a solution of propargylamine (17.67 g, 321 mmol), 4-dimethylaminopyridine (391 mg, 3.2 mmol) and triethylamine (54 mL, 388 mmol) in methylene chloride (320 mL) at 0 °C was added 2,6-difluorobenzoyl chloride (38.3 mL, 305 mmol) in a dropwise fashion. Upon complete addition, the cooling bath was removed and the mixture was stirred at ambient temperature for a further 6 h. The reaction mixture was then washed with normal HCl, dried (magnesium sulfate), concentrated and crystallized from toluene to give amide **8** (57.6 g, 97%) as a white solid. White solid, mp 89–90 °C. R_f 0.32 (silica gel, 3:2 ethyl ether/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.4 (m, 1H), 6.96 (t, 2H), 6.2 (bs, 1H), 4.27 (m, 2H), 2.29 (d, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.5, 158.5 (dt, J = 253, 6.9 Hz), 130.5 (t, J = 10.4 Hz), 111.9 (t, J = 19.5 Hz), 110.4 (m), 77.17, 70.6, 28.1; IR (film) ν_{max} 3296, 3072, 1650, 1536, 1463, 1235, 1004 cm^{-1}; MS ($M+H^+$)

196.06. Anal. calcd for $C_{10}H_7NOF_2$: C, 61.54; H, 3.62; N, 7.18. Found: C, 61.40; H, 3.75; N, 7.09.

***N*-3-(Triisopropylsilyl)-2-propargyl 2,6-difluorobenzamide (9b).** To a solution of diisopropylamine (36.2 mL, 258 mmol) in tetrahydrofuran (240 mL) at −10 °C was added, dropwise with stirring, *n*-BuLi (99 mL, 2.5 M solution in hexane, 248 mmol). After 0.25 h at this temperature the mixture was added to a cooled solution of terminal alkyne **8** (22.93 g, 118 mmol) in tetrahydrofuran (240 mL) such that the temperature was maintained below −65 °C. After complete addition, the mixture was stirred for an additional 0.25 h before the addition of chlorotriisopropylsilane (26.4 mL, 123 mmol). The mixture was then stirred at −78 °C for an additional 3.5 h and at ambient temperature overnight. The reaction was quenched with a saturated solution of ammonium chloride and the mixture was twice extracted with ethyl ether. The ether extract was dried (magnesium sulfate), concentrated and crystallized from hexanes to give an off white solid. The solid was dissolved in methylene chloride and filtered through a pad of silica gel to give alkynyl silane **9b** (35.2 g, 85%) as a white solid upon concentration. White solid, mp 94–95 °C. R_f 0.24 (silica gel, 3:7 ethyl ether/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.5–7.3 (m, 1H), 6.96 (t, 2H), 6.1 (bs, 1H), 4.31 (d, 2H), 1.07 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6 (dt, J = 253, 6.8 Hz), 158.2, 130.4 (t, J = 10.4 Hz), 110.5 (m), 100.4, 83.9, 29.3, 17.0, 9.6; IR (film) ν_{max} 3251, 3069, 2942, 2866, 2183, 1643, 1468, 1007 cm^{-1}; MS (M + H$^+$) 352.14. Anal. calcd for $C_{19}H_{27}NOF_2Si$: C, 64.92; H, 7.74; N, 3.98; Si, 7.99. Found: C, 64.78; H, 7.81; N, 3.92; Si, 8.16.

***N*-(1-Hydroxy-4-triisopropylsilyl-3-butyn-2-yl) 2,6-difluorobenzamide (10b).** To a solution of diisopropylamine (24.0 mL, 171 mmol) in tetrahydrofuran (200 mL) at 0 °C was added, dropwise with stirring, *n*-BuLi (65.5 mL, 2.5 M solution in hexane, 164 mmol). After 0.5 h at this temperature the mixture was cooled in a dry ice/acetone bath and TMEDA (25.9 mL, 172 mmol) was added. Amide **9b** (27.35 g, 77.9 mmol) was added in dropwise fashion keeping the temperature below −65 °C. After an additional 1 h, with very rapid mechanical stirring, formaldehyde (generated by thermal decomposition of paraformaldehyde with a heat gun) was introduced near the top of the flask via a 15 cm long 12 gauge cannula. A stream of nitrogen is introduced into the flask containing paraformaldehyde to aid the transfer and is outlet from the reaction flask via a bubbler so that the system can be monitored for blockage. It is important to keep the cannula end as far from the cold solution as possible and employ an extremely vigorous mechanical stirring for efficient absorption of the gas.

After the purple color was quenched, a saturated solution of ammonium chloride was added and the mixture was warmed to ambient temperature. The mixture was extracted with ethyl ether and the ether extract was washed with normal HCl. The aqueous washings were re-extracted with ethyl ether and the combined organic phase was washed with a saturated solution of sodium bicarbonate, dried (magnesium sulfate), concentrated and purified by flash column chromatography (silica gel, 2:3 ethyl ether/hexanes) to give the alcohol **10b** (13.5g, 45%) as a white solid. White solid. Mp 100–101 °C. R_f 0.32 (silica gel, 7:3 ethyl ether/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44–7.33 (m, 1H), 6.96 (t, 2H), 6.43 (bd, 1H), 5.17–5.09, (m, 1H), 3.88–3.80 (m, 2H), 2.22 (t, 1H), 1.07 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.6 (dt), 158.4, 130.6 (t, J = 10.6 Hz), 110.6 (m), 101.3, 85.2, 64.2, 43.9, 17.0, 9.5; IR (film) ν_{max} 3420, 3280, 2943, 2865, 2176, 1658, 1626, 1468, 1010 cm^{-1}; MS (M + H$^+$) 381.96. Anal. calcd for $C_{20}H_{29}NO_2F_2Si$: C, 62.96; H, 7.66; N, 3.67; Si, 7.36. Found: C, 63.05; H, 7.83; N, 3.57; Si, 7.34.

Enantioselective alkylation of 9b. To a solution of diisopropylamine (8.0 mL, 57.1 mmol) in ethyl ether (150 mL) at −10 °C was added, dropwise with stirring, *n*-BuLi (21.8 mL, 2.5 M solution in hexane, 54.5 mmol). After 0.5 h at this temperature the mixture was cooled in a dry ice/acetone bath and (−)-sparteine (11.9 mL, 51.8 mmol) was added. Amide **9b** (9.1 g, 25.9 mmol) in ethyl ether (50 mL) was added in dropwise fashion keeping the temperature below −60 °C. After an additional 2 h, formaldehyde was introduced as described above with the exception that the paraformaldehyde was held at 130 °C by means of an oil bath and not decomposed with a heat gun. After the purple color was quenched, a saturated solution of ammonium chloride was added and the mixture was warmed to ambient temperature. The mixture was extracted with ethyl ether and the ether extract was twice washed with normal HCl, dried (magnesium sulfate), concentrated and purified by flash column chromatography (silica gel, 2:3 ethyl ether/hexanes) to give the non-racemic alcohol **10b** (1.0 g, 10%) as a white solid. This material (ca. 40% ee by Mosher ester analysis) had an α_D of −0.7°.

2-(2,6-Difluorophenyl)-4-(2-triisopropylethynyl)-1,3-oxazoline (14b). To a solution of hydroxy amide **10b** (9.3 g, 24.4 mmol) in pyridine (50 mL) was added trifluoromethanesulfonic anhydride (4.5 mL, 25.2 mmol) such that the internal temperature was maintained below −15 °C. On complete addition, the mixture was allowed to warm to ambient temperature and stirred for an additional 0.3 h. The mixture was then diluted with ethyl ether and washed with a saturated solution of sodium bicarbonate, dried (magnesium sulfate), concentrated and purified by flash column chromatography (silica gel, 1:9 ethyl ether/hexanes) to give the oxazoline **14b** (5.65 g, 64%) as a colorless oil. R_f 0.33 (silica gel, 1:4 ethyl ether/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46–7.35 (m, 1H), 6.96 (t, 2H), 5.09, (t, 1H), 4.64 (dd, 1H), 4.40 (t, 1H), 1.08 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) 159.7 (dt, J = 256, 5.8 Hz), 156.6, 131.0 (t, J = 10.6 Hz), 110.3 (m), 105.3 (t, J = 16.6 Hz), 103.9, 84.2, 71.9, 56.8, 17.0, 9.6; IR (film) ν_{max} 2944, 2866, 2183, 1666, 1622, 1470, 133, 1291, 1240, 1084, 1014 cm^{-1}; MS (M + H$^+$) 364.13. Anal. calcd for $C_{20}H_{27}NOF_2Si$: C, 66.08; H, 7.49; N, 3.85; Si, 7.73. Found: C, 66.07; H, 7.56; N, 3.80; Si, 7.55.

2-(2,6-Difluorophenyl)-4-ethynyl)-1,3-oxazoline (15). To a solution of alkynyl silane **14** (5.65 g, 15.6 mmol) in

tetrahydrofuran (65 mL) was added acetic acid (1.08 mL, 18.9 mmol) followed by tetrabutylammonium fluoride (18.8 mL, 1.0 M in tetrahydrofuran). After stirring at ambient temperature for 3 h, the mixture was diluted with ethyl ether, washed with a saturated solution of sodium bicarbonate, dried (magnesium sulfate), concentrated and purified by flash column chromatography (silica gel, 1:4 then 2:3 ethyl ether/hexanes) to give the terminal alkyne **15** (2.83 g, 88%) as a colorless oil. The compound appears to polymerize when neat but may be stored in solution. R_f 0.32 (silica gel, 2:3 ethyl ether/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48–7.36 (m, 1H), 6.97 (t, 2H), 5.06, (ddd, 1H), 4.65 (dd, 1H), 4.42 (t, 1H), 2.47 (d, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 159.7 (dt, J=257, 5.7Hz), 157.2 (t, J=2.3Hz), 131.2 (t, J=10.4Hz), 110.4 (m), 105.0 (t, J=17.3Hz), 80.4, 71.4, 71.2, 55.7; IR (film) ν_{max} 3300, 2907, 1661, 1622, 1591, 1469, 1357, 1292, 1240, 1089, 1053, 1012 cm^{-1}; MS (M + H$^+$) 208.11. Anal. calcd for $C_{11}H_7NOF_2$: C, 63.77; H, 3.41; N, 6.76. Found: C, 62.33; H, 3.30; N, 6.67.

4-(4-*tert*-Butylphenyl)ethynyl-2-(2,6-difluorophenyl)-1,3-oxazoline (16). To a mixture of alkyne **15** (0.285 g, 1.38 mmol), copper(I) iodide (26 mg, 0.14 mmol), triethylamine (670 μL, 4.83 mmol) and 4-*t*-butyliodobenzene (716 mg, 2.75 mmol) in dimethylformamide (3 mL) was added palladium tetrakis(triphenylphosphine) (40 mg, 0.035 mmol). The mixture was stirred at ambient temperature for 14 h before being diluted with ethyl ether, twice washed with water, dried (magnesium sulfate), concentrated and purified by flash column chromatography (silica gel, 1:4 ethyl ether/hexanes) to give compound **16** (0.46 g, 98%) as a colorless oil. The compound turns brown on standing. R_f 0.40 (silica gel, 2:3 ethyl ether/hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46–7.28 (m, 5H), 6.97 (t, 2H), 5.30, (t, 1H), 4.71 (dd, 1H), 4.48 (t, 1H), 1.30 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.7 (dt, J=258, 5.8 Hz), 156.9 (t, J=2.3 Hz), 150.2, 131.2 (t, J=10.4 Hz), 130.0, 123.7, 117.9, 110.4 (m), 105.2 (t, J=17.3 Hz), 84.8, 83.3, 71.5, 56.7, 29.6; IR (film) ν_{max} 2963, 1659, 1622, 1469, 1354, 1291, 1239, 1087, 1052, 1011 cm^{-1}; MS (M + H$^+$) 340.12. Anal. calcd for $C_{21}H_{19}NOF_2$: C, 74.32; H, 5.64; N, 4.13. Found: C, 73.59; H, 5.61; N, 4.16.

4-(4′-Bromobiphen-1-yl)ethynyl-2-(2,6-difluorophenyl)-1,3-oxazoline (21). To a solution of non-racemic alkyne **15** (0.36 g, 1.74 mmol), copper(I) iodide (33 mg, 0.17 mmol), triethylamine (850 μL, 6.09 mmol) and 4,4′-dibromobiphenyl (1.62 g, 5.22 mmol) in dimethylformamide (15 mL) was added palladium tetrakis(triphenylphosphine) (100 mg, 0.087 mmol). The mixture was heated at 90 °C for 1.3 h before being cooled, diluted with ethyl ether, twice washed with water, dried (magnesium sulfate), concentrated and purified by flash column chromatography (silica gel, 1:4 ethyl ether/hexanes) to give compound non racemic **21** (0.12 g, 16%) as a white solid. The compound was crystallized from chlorobutane. R_f 0.34 (silica gel, 2:3 ethyl ether/hexanes); α_D +7.8°; mp 132–134 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59–7.38 (m, 9H), 6.99 (t, 2H), 5.33, (dd, 1H), 4.74 (dd, 1H), 4.52 (t, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) 158.0, 138.4, 137.7, 131.3, 131.2, 131.0, 130.8, 130.4, 127.0, 125.2, 120.4, 120.3, 110.6, 110.4, 86.9, 82.5, 71.4, 56.6; IR (film) ν_{max} 2906, 1658, 1621, 1588, 1482, 1468, 1355, 1330, 1291, 1239, 1088, 1052, 1012 cm^{-1}; MS (M + H$^+$) 437.85, 440. Anal. calcd for $C_{23}H_{14}NOBrF_2$: C, 63.03; H, 3.22; N, 3.20; Br, 18.23. Found: C, 62.83; H, 3.25; N, 2.85; Br, 19.96.

Testing on Fall Armyworm (*Spodoptera frugiperda*)

Test units, each consisting of a HIS (high impact styrene) tray with 16 cells were prepared. Wet filter paper and approximately 8 cm^2 of lima bean leaf was placed into 12 of the cells. A 0.5-cm layer of wheat germ diet was placed into the four remaining cells. Fifteen to 20 third-instar larvae of fall armyworm (*Spodoptera frugiperda*) were placed into a 230-mL (8-ounce) plastic cup. Solutions of each of the test compounds in 75:25 acetone/distilled water solvent were sprayed into the tray and cup. Spraying was accomplished by passing the tray and cup on a conveyer belt directly beneath a flat fan hydraulic nozzle which discharged the spray at a rate of 0.138 kg of active ingredient per hectare (about 0.13 pounds per acre) at 207 kPa (30 psi). The insects were transferred from the 230-mL cup to the HIS tray (one insect per cell). The trays were covered and held at 27 °C and 50% relative humidity for 48 h, after which time readings were taken on the 12 cells with lima bean leaves. The four remaining cells were read at 6–8 days for delayed toxicity.

Testing of Two-spotted spider mite (*Tetranychus urticae*)

Pieces of kidney bean leaves, each approximately 6.5 cm^2 (1 square inch) in area, that had been infested on the undersides with 25 to 30 adult mites (*T. urticae*), were sprayed with their undersides facing up on a hydraulic sprayer with a solution of the test compound in 75:25 acetone-distilled water solvent. Spraying was accomplished by passing the leaves, on a conveyor belt, directly beneath a flat fan hydraulic nozzle which discharged the spray at a rate of 0.138 kg of active ingredient per hectare (about 0.13 pounds per acre) at 207 kPa (30 psi). The leaf squares were then placed underside-up on a square of wet cotton in a Petri dish and the perimeter of the leaf square was tamped down onto the cotton with forceps so that the mites could not escape onto the untreated leaf surface. The test units were held at 27 °C and 50% relative humidity for 48 h, after which time mortality readings were taken.

The same units were held an additional 5 days and read for larvicide/ovicide mortality and/or developmental effects.

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