Efficient and General Synthesis of 5-(Alkoxycarbonyl)methylene-3-oxazolines by Palladium-Catalyzed Oxidative Carbonylation of Prop-2-ynylamides

Alessia Bacchi,[†] Mirco Costa,*[,‡] Bartolo Gabriele,[§] Giancarlo Pelizzi,[†] and Giuseppe Salerno[||]

Dipartimento di Chimica Generale, Analitica e Chimica Fisica, Università di Parma, Parco Area delle Scienze 17, 43100 Parma, Italy, Dipartimento di Chimica Organica e Industriale, Università di Parma, Parco Area delle Scienze 17, 43100 Parma, Italy, Dipartimento di Scienze Farmaceutiche, Università della Calabria, 87036 Arcavacata di Rende, Cosenza, Italy, and Dipartimento di Chimica, Università della Calabria, 87036 Arcavacata di Rende, Cosenza, Italy

mirco.costa@unipr.it

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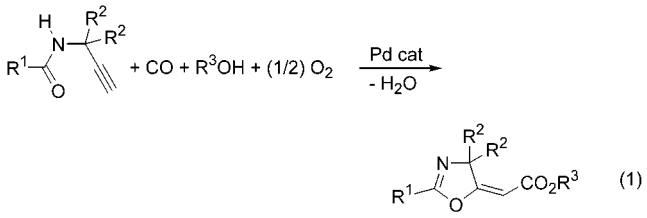
A variety of prop-2-ynylamides have been carbonylated under oxidative conditions to give oxazolines, oxazolines with chelating groups, and bisoxazolines bearing an (alkoxycarbonyl)methylene chain at the 5 position in good yields. The cyclization−alkoxycarbonylation process was carried out in alcoholic media at 50−70 °C and under 24 bar pressure of 3:1 carbon monoxide/air in the presence of catalytic amounts of 10% Pd/C or PdI_2 in conjunction with KI. Cyclization occurred by anti attack of an oxygen function on the palladium-coordinated triple bond, followed by stereospecific alkoxycarbonylation, strictly resulting in *E*-stereochemistry. The structures of representative oxazolines and bisoxazolines have been determined by X-ray diffraction analysis.

Introduction

The usefulness and peculiar activity of the PdI_2−KI (or Pd/C−KI) catalytic system in the oxidative carbonylation of alkynes was reported by us some years ago.[1] Oxidative PdI_2−KI- or Pd/C−KI-catalyzed cyclocarbonylation−alkoxycarbonylation or cyclization−alkoxycarbonylation of acetylenic compounds bearing a suitably placed nucleophilic group has allowed the direct synthesis of new heterocyclic derivatives such as functionalized β- and γ-lactones,[2] β- and γ-lactams,[3] nitrogen heterocycles,[4] pyrrole-3,4-diacetic acid and esters,[5] furans,[6] thiophenes,[7] and tetrahydrofurans[8] starting from readily available substrates. Formation of oxazolines by oxidative carbonylation of 2-ynylamides has only been disclosed in a preliminary communication.[3]

We now give a full account of the PdI_2- or Pd/C−KI-catalyzed oxidative cyclization−alkoxycarbonylation of 2-ynylamides to obtain 5-[(alkoxycarbonyl)methylene]-oxazolines in good yields according to eq 1. Oxazolines are a very interesting class of heterocyclic compounds with many important applications in the field of metal complex-catalyzed organic syntheses[9] and polymers.[10] Moreover, a variety of molecules containing the oxazoline ring display a wide range of biological activities.[11]



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Results and Discussion

We shall consider the synthesis of oxazolines, oxazolines with chelating groups, and bisoxazolines.

[†] Dipartimento di Chimica Generale, Analitica e Chimica Fisica, Università di Parma.

[‡] Dipartimento di Chimica Organica e Industriale, Università di Parma.

[§] Dipartimento di Scienze Farmaceutiche, Università della Calabria.

[||] Dipartimento di Chimica, Università della Calabria.

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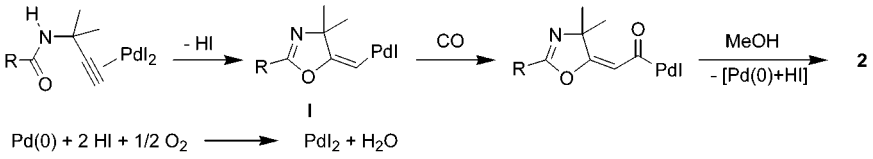
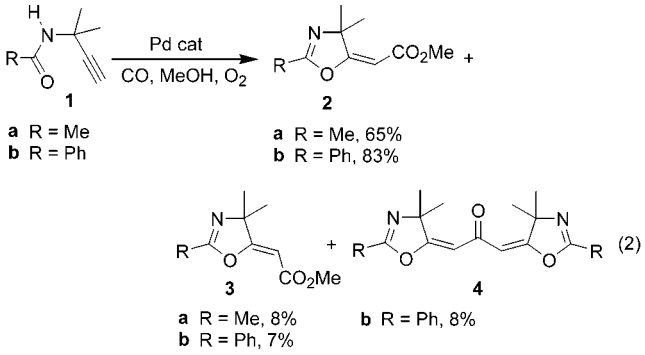
Scheme 1



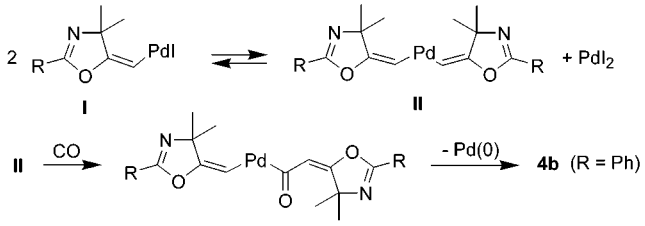
Synthesis of Oxazolines. *N*-(1,1-Dimethylprop-2-ynyl)amides **1** (**1a**, R = Me; **1b**, R = Ph; 3.0 mequiv) were caused to react at 55−60 °C under a 3:1 CO/air initial pressure of 24 bar in the presence of 10% Pd/C or PdI_2 (0.03 mequiv) and KI (0.45 mequiv) in MeOH (20 mL) for 30 h. (*E*)-5-[(Methoxycarbonyl)methylene]oxazolines **2** were formed as the main products through a cyclization−methoxycarbonylation process (65 and 83% GLC yield, respectively, eq 2).



The (*E*) configuration of the (methoxycarbonyl)methylene moiety in **2b** was supported by its X-ray structure (Figure S1, Supporting Information). The (*E*) configuration for **2a** was assigned by comparison of the chemical shift of the olefinic proton in **2a** with that of the same proton in **2b**.

Small amounts of (*Z*)-5-[(methoxycarbonyl)methylene]-oxazolines **3** (7−8%) were also detected in the reaction mixtures. Their formation was due to a subsequent isomerization of **2** as checked through low conversion reactions. Moreover, an 8% yield of (*E*,*E*)-1,3-bis(4,4-dimethyl-2-phenyl-4*H*-oxazol-5-ylidene)propan-2-one **4b**, whose structure was proved by X-ray analysis (Figure S2, Supporting Information), was obtained in the case of **1b**. The yield of product **4b** could be increased by carrying out the reaction in more concentrated solutions. For example, when 5 mL of MeOH instead of 20 mL was used under the above-mentioned conditions, **4b** was obtained as the main product (43%), together with its *E*,*Z* isomer **5b (**7% yield) and **2b** (30% yield).

Scheme 2



The molecule **4b**, shown in Figure S2 (Supporting Information), is symmetric with respect to the C1−O1 carbonyl group, which belongs to a crystallographic 2-fold axis; the two ligand arms are reciprocally syn in relation to the carbonyl group. Each of the two molecular arms is completely planar, and the carbonylic substituent is in a position anti to the heterocyclic oxygen relative to the C2−C3 double bond (O2−C3−C2−C1 = 178.6(1)°). However, the overall molecular planarity is slightly perturbed by the mutual repulsion between the two syn C−H groups adjacent to the carbonyl. The two molecular arms are planar, but the molecule is folded by 23° around the C1−C2 single bond due to H···H intramolecular repulsion. The molecular structure of **2b** (Figure S1, Supporting Information) corresponds to a single arm of compound **4b**, with a methoxy terminal group at C1. Similarly to compound **4b**, the molecular skeleton is remarkably planar. The carboxy substituent at C1 is in an anti position relative to O2 (O2−C3−C2−C1 = 178.5-(2)°); the bond distances and angles show a perfect agreement with those observed for the oxazoline ring of **4b**, as reported in Table S1 (Supporting Information). These are the first examples in the crystallographic literature[12] of an oxazolinic system containing an exocyclic double bond at C3.

The *E* configuration in compounds **2** is in agreement with an anti 5-*exo-dig* attack of oxygen on the triple bond coordinated to Pd(II) with formation of an (*E*)-vinylpalladium intermediate **I**, followed by stereospecific methoxycarbonylation to give **2** and Pd(0). Reoxidation of the latter according to the usual mechanism regenerates the catalytically active Pd(II) species[1] (Scheme 1, anionic iodide ligands are omitted for clarity).

The obtainment of the ketonic derivative **4b** can be interpreted as involving a bis-vinylpalladium intermediate **II**, formed by disproportionation of complex **I**,[13] which undergoes carbon monoxide insertion, followed by reductive elimination to give **4b** and Pd(0), according to Scheme 2.

It is noteworthy that, as we already reported,[4] under the above-mentioned conditions *N*-(1,1-dimethylprop-2-

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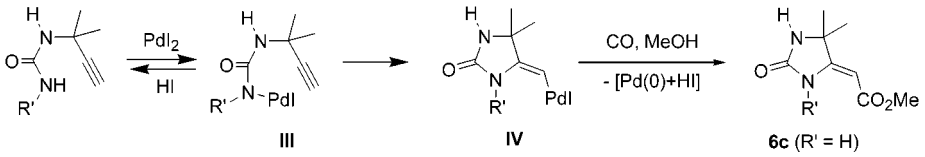
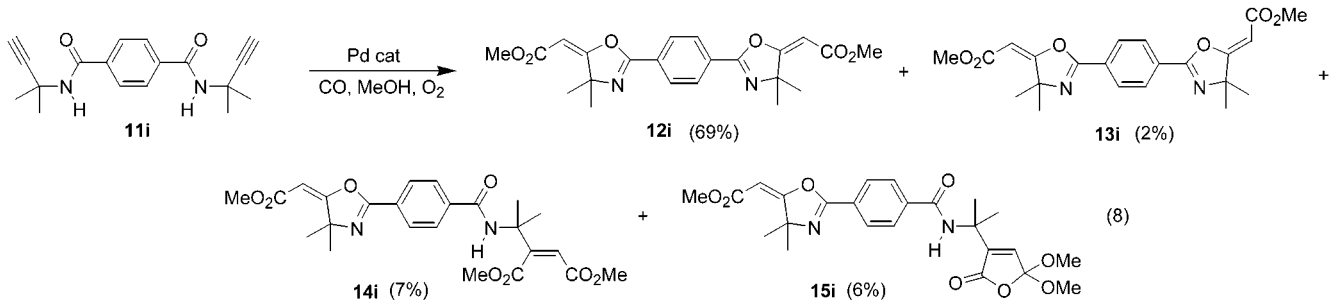
Scheme 3



Scheme 4

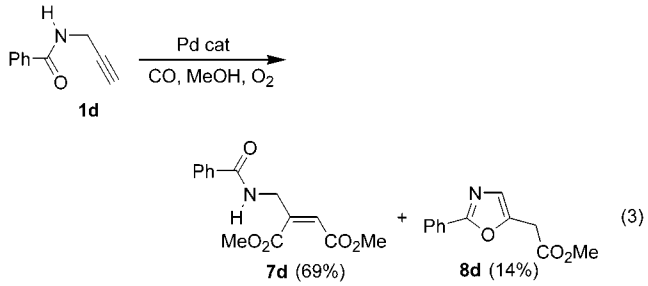


ynyl)ureas afforded two types of products simultaneously: oxazoline derivatives **2** and cyclic ureas **6** containing *E*- or *Z*-(methoxycarbonyl)methylene chains, respectively, depending on whether the cyclization was initiated by oxygen or nitrogen attack on the triple bond. The obtainment of **6** can be interpreted as involving the formation of an intermediate **III** resulting from the reaction between PdI_2 and the −NHR′ moiety of the urea. Intermediate **III** then inserts the triple bond through a syn 5-*exo*-*dig*-type attack, which leads to a (*Z*)-vinylpalladium intermediate **IV**. Methoxycarbonylation of the latter affords **6** (Scheme 3). In agreement with the mechanism shown in Scheme 3, bulky and electron-withdrawing groups in N-bonded R′ substituent favored the formation of product **2** with respect to **6**.[4]

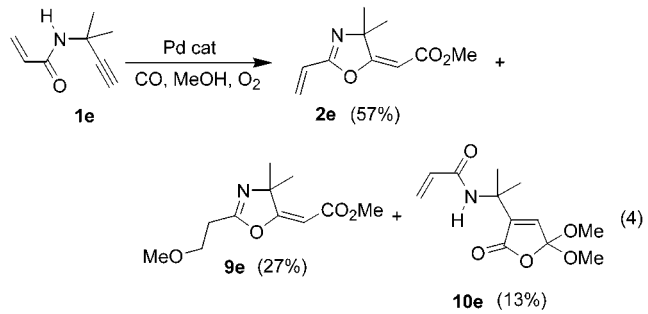
The X-ray structure of cyclic urea **6c** (R′ = H) supports the assigned stereochemistry for the (methoxycarbonyl)-methylene chain (Figure S3, Supporting Information).

The molecule has a rigid molecular structure, with torsion angles planar within 5°, apart from those involving methyl groups C6 and C7. The configuration of the methoxycarbonyl group around the C2−C3 double bond is opposite to the one observed for all the oxazoline compounds, being syn relative to N2, which takes the place of O2 in the heterocyclic system (N2−C3−C2−C1 = 0(1)°). The analysis of the bonding geometry within the ring (Table S1, Supporting Information) shows that the structural asymmetry of the ring is reflected in a different distribution of the bond strength among similar bonds, evidenced in particular by the remarkably diverse behavior of the two N atoms.

The presence of geminal alkyl groups α to the triple bond is a necessary requisite for directing the catalytic process toward the formation of cyclization products, as shown by the results obtained in the case of an α-unsubstituted substrate such as *N*-(prop-2-ynyl)benzamide **1d**. Carbonylation of this compound under the usual conditions afforded maleic diester **7d** (deriving from oxidative dialkoxycarbonylation of the triple bond)[1] as the main product (69% yield) and only modest amounts (14%) of oxazole **8d** (apparently deriving from isomerization of the initially formed 5-(methoxycarbonyl)methyleneoxazoline derivative) (eq 3). The *gem*-dialkyl effect[14] thus plays a fundamental role for the success of the reaction.



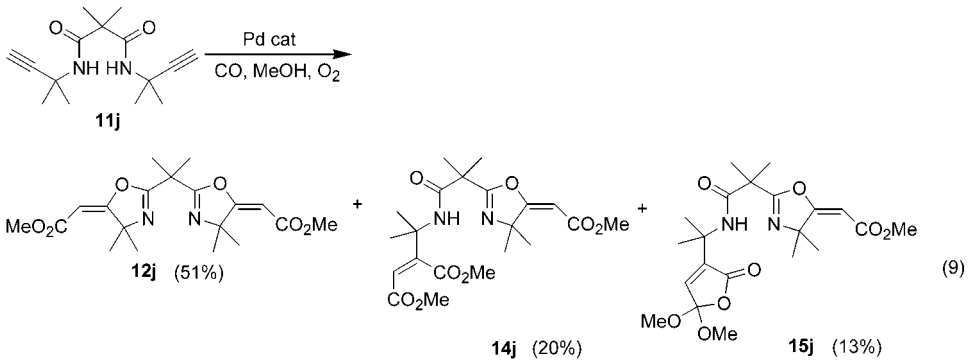
The presence of different functional groups is compatible with the cyclization−alkoxycarbonylation reaction. Thus, carbonylation of *N*-(1,1-dimethylprop-2-ynyl)acrylamide **1e** (2.5 mmol) under the above-mentioned conditions of CO/air pressure in the presence of 10% Pd−C (0.05 mmol) and KI (0.75 mmol) in MeOH (15 mL) at 50 °C for 24 h gave the expected product **2e** in 57% yield together with a 27% of oxazoline **9e**, clearly deriving from methanol addition to the vinyl group of **2e**. Small amounts of the dimethoxyfuranone derivative **10e** (13%), corresponding to oxidative dimethoxycarbonylation of the triple bond,[1] were also detected in the reaction mixture (eq 4).



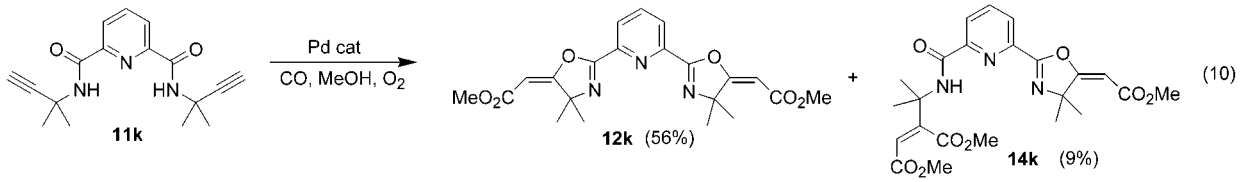
Analogously, ethyl 3-(1,1-dimethylprop-2-ynylcarbamoyl)acrylate **1f** reacted under the usual conditions (in ethanol instead of methanol) to give oxazoline **2f** in good

(14) Sammes, P. G.; Weller, D. J. *Synthesis* **1995**, 1205−1222 and references therein.

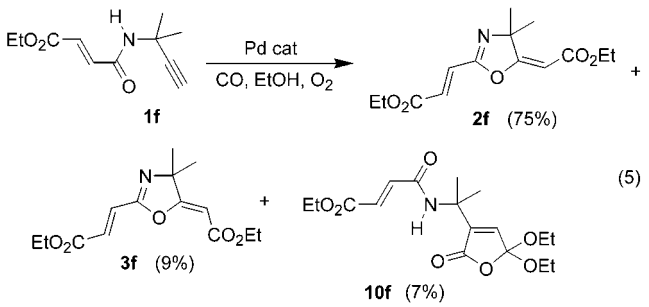
Scheme 5



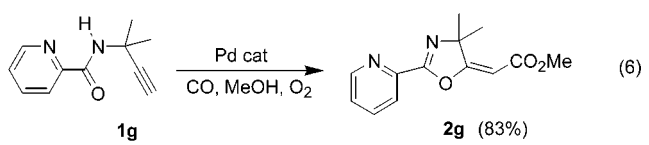
Scheme 6



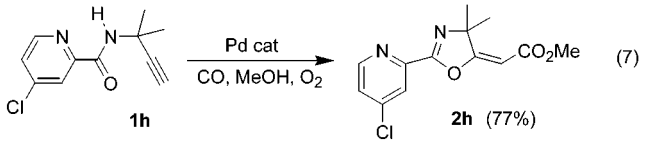
yield (75%), as well as small amounts of its *Z* isomer **3f** (9%) and dimethoxyfuranone **10f** (7%, eq 5). No ethanol addition to the vinyl group was observed in this case.



Synthesis of Oxazolines with Chelating Groups. To exploit the synthetic potentiality of our methodology, we also prepared some (1,1-dimethylprop-2-ynyl)amides of organic acids bearing a suitably placed coordinating atom and (1,1-dimethylprop-2-ynyl)amides of bibasic organic acids. Oxidative carbonylation of such substrates could in fact afford new chelating monooxazoline or bisoxazoline ligands by a very simple approach. Accordingly, carbonylation of the pyridine-2-carboxylic acid (1,1-dimethylprop-2-ynyl)amide **1g** (3.0 mmol) carried out under CO (21 atm) and air (7 atm) in MeOH in the presence of 10% Pd/C (0.06 mmol) and KI (0.9 mmol) at 70 °C for 30 h led to (*E*)-(4,4-dimethyl-2-pyridin-2-yl-4*H*-oxazol-5-ylidene)acetic acid methyl ester **2g** in 83% yield (eq 6).



Carbonylation of the 4-chloropyridine-2-carboxylic acid (1,1-dimethylprop-2-ynyl)amide **1h** led to the correspond ing *E* oxazoline **2h** in 77% yield (eq 7).



The X-ray analysis of a single crystal confirmed the *E* structure of the oxazoline-bonded methoxycarbonylmethylene group (Figure S4, Supporting Information).

The introduction of a *p*-chloropyridin-2-yl group in place of the phenyl at C5 (Figure S4, Supporting Information) does not result in any significant change in the molecular structure of oxazoline **2h** (anti, O2−C3−C2−C1 = −178.2(2)°) with respect to compounds **4b** and **2b**, as shown by the comparison of bonding geometry in Table S1 (Supporting Information). The presence of substituents on the terminal pyridinyl causes a perturbation of the molecular planarity, obtained by rotation of the aromatic ring around the C5−C6 bond (O2−C5−C6−N2 = 13.6(3)°).

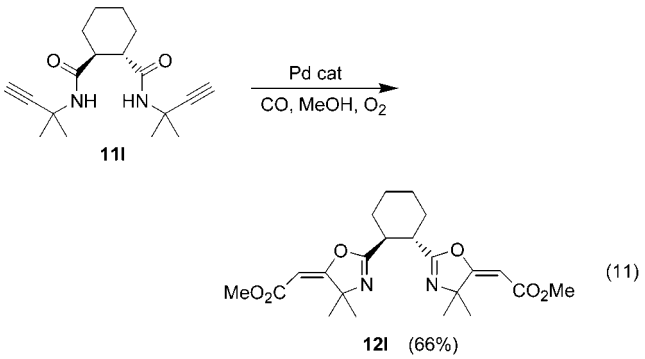
Synthesis of Bisoxazolines. The oxidative cyclization−alkoxycarbonylation reaction was also extended to the synthesis of bisoxazolines from several acetylenic diamides. Thus, *N*,*N*′-bis(1,1-dimethylprop-2-ynyl)terephthalamide **11i** (1.79 mmol) was reacted in MeOH (10 mL) with CO/air (18/6 bar) in the presence of 10% Pd−C (0.06 mmol) and KI (0.09 mmol) at 55 °C for 30 h: (*E*,*E*)-bisoxazoline **12i** was formed as the main product (69%) together with its (*E*,*Z*)-isomer **13i** (2%). Two byproducts **14i** and **15i**, both deriving from cyclization−methoxycarbonylation of one of the two propynyl groups and dimethoxycarbonylation of the other one, were formed in small yield (7% and 6% respectively) (eq 8, Scheme 4). Compound **15i** is the ring chain tautomer of **14i**.[1]

Analogously, bisoxazoline **12j** was obtained as the main product (51%) starting from 2,2-dimethylmalonic acid (1,1-dimethylprop-2-ynyl) amide **11j** (eq 9, Scheme 5). Two additional carbonylation products **14j** and **15j**, both deriving from cyclization−methoxycarbonylation of one of the two propynyl groups and dimethoxycarbonylation

of the other one, were also formed in moderate yields (20% and 13%, respectively). Compound **15j** is the ring chain tautomer of **14j**.[1]

Carbonylation of pyridine-2,6-dicarboxylic acid (1,1-dimethylprop-2-ynyl)amide **11k** carried out under the same conditions led to the formation of bisoxazoline **12k** (56% yield) and maleic diester derivative **14k** (9%) as shown in eq 10 (Scheme 6).

A cyclohexane ring was also chosen as a linkage between the two oxazoline rings. Oxidative carbonylation of *trans*-cyclohexane-1,2-dicarboxylic acid (1,1-dimethylprop-2-ynyl)amide **11l** led to the expected bisoxazoline derivative **12l** in 66% yield (eq 11), whose structure was confirmed by X-ray analysis (Figure S5, Supporting Information).



(11)

In compound **12l** (Figure S5, Supporting Information), the terminal aromatic at C5 is replaced by a cyclohexyl moiety, which in turn carries a second oxazoline arm. The two oxazoline rings are anti and axial (C5−C6−C7−C19 = −162(1)°). The two molecular halves are rotated in a trans arrangement, with a pseudo-2-fold axis bisecting the C9−C10 and C6−C7 bonds. The double bonds C2−C3 and C16−C17 both have a trans geometry with respect to the methoxycarbonyl substituent and endocyclic oxygen, as reported for the above derivatives. To get information on the effect of replacing the 5-aryl substituent with an aliphatic group on the molecular geometry of the heterocyclic system, the structures of the 5-aryl derivatives **4b**, **2b**, **2h**, and **6c** have been compared with that of **12l** (Table S1, Supporting Information). Even if a thorough comparison is biased by the high standard deviations associated to bonding parameters for **12l**, it can be seen that the removal of the aromatic substituent at C5 causes the elongation of the C−N and the shortening of the C−O bond, with a concomitant significant strengthening of the exocyxlic C=C bond and a weakening of the C−Me single bond. This is in agreement with electron density delocalization in the oxazoline system.

In conclusion, we have developed a new synthetic route to oxazoline and bisoxazoline derivatives containing the (alkoxycarbonyl)methylene moiety by oxidative cyclization-alkoxycarbonylation of readily available 2-ynylamides. The compounds reported here are not readily obtainable by other methods and offer a wide range of potential applications.

Experimental Section

Materials and General Methods. Solvents and chemicals were reagent grade and were used without further purifications except for 1,1-dimethylprop-2-ynylamine and prop-2-ynylamine, which were distilled from K_2CO_3 and stored over K_2CO_3. MeOH and EtOH were dried over 4A molecular sieves. Reactions were analytically monitored by GLC with an instrument equipped with a flame ionization detector and a electronic peak area integrator. A 5% methylsilicone (30 m × 0.25 mm) capillary column was used with helium as the carrier gas. All yields were determined gas chromatographically using the internal standard method unless otherwise specified. Thin-layer chromatography (TLC) was performed on silica gel coated aluminum plates. Gravity-flow liquid chromatography was carried out on silica gel (0.063−0.200 mm); solvent mixtures were prepared by volume. Melting points are uncorrected. Elemental analyses were performed at our analytical laboratory. IR spectra were obtained with a FT-IR spectrometer. Mass spectra (*m*/*z* relative intensity) were taken at 70 eV ionizing voltage. ^{1}H NMR and ^{13}C NMR spectra were taken in $CDCl_3$ at room temperature and recorded at 300 and 75 MHz, respectively. Chemical shifts and coupling constants (*J*) are given in ppm (δ) and in Hz, respectively.

Single-crystal X-ray diffraction analyses were carried out at room temperature by Siemens AED (**4b**, **2b**, **2h**, **12l**) and Enraf-Nonius CAD4 (**6c**) diffractometers. Graphite-monochromated Cu Kα (λ = 1.541 78 Å) radiation was used for all compounds apart from **2h**, which was analyzed using Mo Kα radiation (λ = 0.710 69 Å). Relevant details concerning data collection and structure refinements are listed in Table S2 (Supporting Information). Crystals were stable during data collection. The intensity data were processed with a peak profile analysis procedure and corrected for Lorentz and polarization effects. The phase problem was solved by direct methods using SIR97.[15] Full-matrix least-squares refinements were carried out by SHELXL97[16] on F^2, using all measured merged data.

Anisotropic thermal displacement parameters were refined for all non-hydrogen atoms. Hydrogen atoms were partly located on difference Fourier maps, and partly introduced in idealized positions, riding on their carrier atoms. Where appropriate, extinction was accounted for as implemented in the refinement program. Programs PARST97[17] and ZORTEP[18] were used for analyzing and drawing the molecular structures. Use was made of the packages of the Cambridge Structural Database (release October 2000). All the calculations were performed on a Digital Alpha 255 workstation at the Centro di Studio per la Strutturistica Diffrattometrica del C.N.R. in Parma.

Table S1 (Supporting Information) lists the main geometric features obtained by the diffraction analysis. Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 185162−185166. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44(0)-1223-336033; e-mail: deposit@ccdc.cam.ac.uk].

N-(1,1-Dimethylprop-2-ynyl)acetamide **1a** was prepared from acetic anhydride and acetylenic amine.[19] Benzamides **1b** and **1d**, acrylamide **1e**, picolinamides **1g** and **1h**, terephthalic diamide **11i**, 2,2-dimethylmalonamide **11j**, and pyridine-2,6-dicarboxylic acid (1,1-dimethylprop-2-ynyl) amide **11k** were prepared causing the respective acid chloride to react with acetylenic amines according to the procedures reported in the literature.[20] Ethyl 3-(1,1-dimethylprop-2-ynlyncarbamoyl)acry-

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late **1f** and bis(1,1-dimethylprop-2-ynyl)-1,2-cyclohexyldicarboxamide **11l** were obtained by transforming the corresponding carboxylic group into amide through reaction with *N*-hydroxysuccinimide and subsequently with acetylenic amine according to a procedure reported in the literature.[21] The pure amides were recovered by crystallization from suitable solvents. ^{1}H and ^{13}C NMR, IR, and mass spectra confirmed the assigned structures.

***N*-(1,1-Dimethylprop-2-ynyl)benzamide (1b):** white solid; mp 152−153 °C; IR (KBr) ν cm^{-1} 3335 (s), 3266 (s), 2116 (w), 1642 (s), 1544 (s); ^{1}H NMR ($CDCl_3$) δ 1.76 (s, 6 H, 2 CH_3), 2.36 (s, 1 H, ≡CH), 6.23 (s, 1 H, NH), 7.38−7.48 (m, 3 H aromatic), 7.72−7.77 (m, 2 H aromatic); MS *m*/*z* 187 (M^+, 20), 186 (22), 105 (100), 77 (28). Anal. Calcd for $C_{12}H_{13}NO$: C, 76.98; H, 7.00; N, 7.48. Found: C, 76.97; H, 6.99; N, 7.46.

***N*-(Prop-2-ynyl)benzamide (1d):** white solid; mp 111−112 °C; IR (KBr) ν cm^{-1} 3325 (s), 3270 (s), 2110 (w), 1645 (s), 1541 (s); ^{1}H NMR ($CDCl_3$) δ 2.22 (t, J = 2.5, 1 H, ≡CH), 4.18 (dd, J = 5.3, 2.5, 2 H, NCH_2), 7.12 (bs, 1 H, NH), 7.34−7.47 (m, 3 H aromatic), 7.74−7.83 (m, 2 H aromatic); MS *m*/*z* 159 (M^+, 27), 158 (47), 105 (100), 77 (28). Anal. Calcd for $C_{10}H_9NO$: C, 75.45; H, 5.70; N, 8.80. Found: C, 75.43; H, 5.71; N, 8.78.

***N*-(1,1-Dimethylprop-2-ynyl)acrylamide (1e):** white solid; mp 65−67 °C; IR (KBr) ν cm^{-1} 3328 (s), 3267 (s), 2111 (w), 1640 (s), 1610 (m); ^{1}H NMR ($CDCl_3$) δ 1.69 (s, 6 H, 2 CH_3), 2.35 (s, 1 H, ≡CH), 5.62 (dd, J = 10.2, 1.4, 1 H, =C*H*H), 5.70 (bs, 1 H, NH), 6.04 (dd, J = 16.9, 10.2, 1 H, =CH(CO)), 6.29 (dd, J = 16.9, 1.4, 1 H, =CH*H*); MS *m*/*z* 137 (M^+, 8), 136 (47), 122 (22), 68 (100). Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 70.01; H, 8.07; N, 10.19.

Ethyl 3-(1,1-dimethylprop-2-ynylcarbamoyl)acrylate (1f): white solid; mp 64−65 °C; IR (KBr) ν cm^{-1} 3308 (s), 3180 (s), 2111 (w), 1652 (s), 1601 (m); ^{1}H NMR ($CDCl_3$) δ 1.28 (t, J = 7.1, 3 H, $CO_2CH_2CH_3$), 1.67 (s, 6 H, $(CH_3)_2CN$), 2.35 (s, 1 H, ≡CH), 4.21 (q, J = 7.1, 2 H, $CO_2CH_2CH_3$), 6.32 (bs, 1 H, NH), 6.78 (d, J = 15.4, 1 H, =CH), 6.90 (d, J = 15.4, 1 H, =CH); ^{13}C NMR ($CDCl_3$) δ 14.0, 28.7, 47.9, 61.1, 69.6, 86.4, 130.4, 136.6, 162.5, 165.6; MS *m*/*z* 209 (M^+, 13), 194 (15), 127 (100), 68 (70). Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.11; H, 7.21; N, 6.67.

Pyridine-2-carboxylic acid (1,1-dimethylprop-2-ynyl)-amide (1g): white solid; mp 56−57 °C; IR (KBr) ν cm^{-1} 3324 (s), 3238 (s), 2128 (w), 1675 (s), 1558 (s); ^{1}H NMR ($CDCl_3$) δ 1.74 (s, 6 H, 2 CH_3), 2.37 (s, 1 H, ≡CH), 7.31−7.47 (m, 1 H aromatic at C-5), 7.82 (td, J = 7.8, 1.7, 1 H aromatic at C-4), 8.13 (s, 1 H, NH), 8.18 (ddd, J = 7.8, 1.2, 0.9, 1 H aromatic at C-3), 8.50 (ddd, J = 4.7, 1.7, 0.9, 1 H aromatic at C-6); MS *m*/*z* 188 (M^+, 30), 173 (100), 106 (80), 78 (65). Anal. Calcd for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.17; H, 6.44; N, 14.87.

4-Chloropyridine-2-carboxylic acid (1,1-dimethylprop-2-ynyl)amide (1h): pink solid from *n*-hexane; mp 101−102 °C; IR (KBr) ν cm^{-1} 3376 (s), 3276 (s), 2129 (w), 1685 (s), 1579 (s); ^{1}H NMR ($CDCl_3$) δ 1.75 (s, 6 H, 2 CH_3), 2.37 (s, 1 H, ≡CH), 7.40 (dd, J = 5.2, 2.1, 1 H aromatic at C-5), 8.11 (s, 1 H, NH), 8.18 (dd, J = 2.1, 0.6, 1 H aromatic at C-3), 8.40 (dd, J = 5.2, 0.6, 1 H aromatic at C-6); MS *m*/*z* 222 (M^+, 20), 207 (70), 112 (100). Anal. Calcd for $C_{11}H_{11}N_2ClO$: C, 59.33; H, 4.98; N, 12.58. Found: C, 59.31; H, 4.98; N, 12.59.

***N*,*N*′-Bis(1,1-dimethylprop-2-ynyl)terephthalamide (11i):** white solid; mp 248−251 °C; IR (KBr) ν cm^{-1} 3318 (s), 3287 (s), 2120 (w), 1645 (s), 1541 (s); ^{1}H NMR (DMSO-d_6) δ 1.62 (s, 12 H, 4 CH_3), 3.10 (s, 2 H, 2 ≡CH), 7.88 (s, 4 H aromatic), 8.33 (s, 2 H, 2 NH); MS *m*/*z* (CI) 298 [$(M + 2)^+$, 90], 296 (M^+, 100). Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80; N, 9.45. Found: C, 72.92; H, 6.80; N, 9.44.

***N*,*N*′-Bis(1,1-dimethylprop-2-ynyl)-2,2-dimethylmalonamide (11j):** pale yellow solid; mp 131−132 °C; IR (KBr) ν cm^{-1} 3417 (s), 3276 (s), 2104 (w), 1673 (s), 1545 (s); ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 6 H, $(CH_3)_2C(CO)$), 1.58 (s, 12 H, 2 $(CH_3)_2CN$), 2.29 (s, 2 H, 2 ≡CH), 6.48 (bs, 2 H, 2 NH); MS *m*/*z* 262 (M^+, 1), 138(100). Anal. Calcd for $C_{15}H_{22}N_2O_2$: C, 68.67; H, 8.45; N, 10.68. Found: C, 68.63; H, 8.44; N, 10.67.

Pyridine-2,6-dicarboxylic acid (1,1-dimethylprop-2-ynyl)amide (11k): white solid; mp 130−132 °C; IR (KBr) ν cm^{-1} 3306 (s), 3270 (s), 2115 (w), 1654 (s), 1544 (s); ^{1}H NMR ($CDCl_3$) δ 1.81 (s, 12 H, 4 CH_3), 2.41 (s, 2 H, 2 ≡CH), 7.81 (s, 2 H, 2 NH), 8.02 (t, J = 2.6, 1 H aromatic at C-4), 8.34 (d, J = 2.6, 2 H aromatic at C-3 and C-5); MS *m*/*z* 297 (M^+, 10), 282 (20), 216 (100), 149 (70), 121 (65). Anal. Calcd for $C_{17}H_{19}N_3O_2$: C, 68.67; H, 6.44; N, 14.13. Found: C, 68.64; H, 6.44; N, 14.11.

***trans*-Cyclohexane-1,2-dicarboxylic acid (1,1-dimethylprop-2-ynyl)amide (11l):** white solid; mp 195−197 °C; IR (KBr) ν cm^{-1} 3386 (s), 3288 (s), 2115 (w), 1652 (s), 1540 (s); ^{1}H NMR ($CDCl_3$) δ 1.11−1.37 (m, 4 H, 4 CH), 1.58 (s, 6 H, 2 CH_3), 1.59 (s, 6 H, 2 CH_3), 1.71−1.95 (m, 4 H, 4 CH), 2.24−2.28 (m, 2 H, 2 CH(CO)) 2.70 (s, 2 H, 2 ≡CH), 5.81 (bs, 2 H, 2 NH); ^{13}C NMR ($CDCl_3$) δ 24.8, 28.7, 28.9, 29.0, 47.2, 47.3, 69.0, 87.1, 174.0; MS *m*/*z* 302 M^+, 1), 154 (100), 67 (80). Anal. Calcd for $C_{18}H_{26}N_2O_2$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.46; H, 8.66; N, 9.24.

General Procedure for the Oxidative Cyclization−Alkoxycarbonylation Reactions of *N*-Prop-2-ynylamides. All reactions were carried out in a 125 mL stainless steel autoclave with a magnetic stirring. In a typical experiment, the autoclave was charged under air with 1,1-dimethylprop-2-ynylbenzamide (0.561 g, 3 mmol), 10% Pd−C (0.032 g, 0.03 mmol), and KI (0.075 g, 0.45 mmol) in methanol (20 mL**)**. The autoclave was pressurized with air (6 atm) and CO (up to 24 atm) and heated under stirring for the required time. Different conditions are indicated in the text. At the end of the reaction, the alcohol was eliminated under vacuum, the residue was recovered with CH_2Cl_2 and filtered to remove KI, and the solid catalyst and the solution was checked by GC/MSD (if necessary an internal standard was added).

(*E*)-2,4,4-Trimethyl-4*H*-oxazol-5-ylideneacetic Acid Methyl Ester (2a). The reaction was carried out as described in the general procedure starting from **1a** (0.375 g, 3.0 mmol) at 55 °C for 30 h. Chromatography with *n*-hexane/EtOAc (8/2) gave **2a** (0.326 g, 59%) as colorless oil: IR (neat) ν cm^{-1} 1720 (s), 1691 (m), 1449 (m), 1264 (s), 1166 (s); ^{1}H NMR ($CDCl_3$) δ 1.61 (s, 6 H, $(CH_3)_2CN$), 2.09 (s, 3 H, CH_3C=), 3.69 (s, 3 H, CO_2CH_3), 5.61 (s, 1 H, =CH); MS *m*/*z* 183 (M^+, 9), 168 (6), 69 (100), 59 (12). Anal. Calcd for $C_9H_{13}NO_3$: C, 59.00; H, 7.15; N, 7.65. Found: C, 58.97; H, 7.18; N, 7.62.

(*Z*)-2,4,4-Trimethyl-4*H*-oxazol-5-ylideneacetic Acid Methyl Ester (3a). Chromatography with *n*-hexane/EtOAc (8/2) gave **3a** (0.032 g, 5%) as colorless oil: IR (neat) ν cm^{-1} 1720 (s), 1690 (m), 1265 (s), 1165 (s); ^{1}H NMR ($CDCl_3$) δ 1.48 (s, 6 H, $(CH_3)_2CN$), 1.99 (s, 3 H, CH_3C=), 3.73 (s, 3 H, CO_2CH_3), 5.09 (s, 1 H, =CH); MS *m*/*z* 183 (M^+, 17), 141 (48), 69 (100), 59 (12). Anal. Calcd for $C_9H_{13}NO_3$: C, 59.00; H, 7.15; N, 7.65. Found: C, 58.95; H, 7.18; N, 7.61.

(*E*)-4,4-Dimethyl-2-phenyl-4*H*-oxazol-5-ylideneacetic Acid Methyl Ester (2b). The reaction was carried out as described above for the synthesis of compounds **2a** and **3a**. Chromatography with *n*-hexane/EtOAc (8/2) gave **2b** (0.566 g, 77%) as a white solid: mp 85−86 °C; IR (KBr) ν cm^{-1} 1720 (s), 1673 (s), 1661 (s), 1648 (s), 1075 (s); ^{1}H NMR ($CDCl_3$) δ 1.74 (s, 6 H, 2 CH_3), 3.70 (s, 3 H, CO_2CH_3), 5.79 (s, 1 H, =CH), 7.44−7.54 (m, 3 H aromatic), 7.96−8.00 (m, 2 H aromatic); ^{13}C NMR ($CDCl_3$) δ 24.6, 50.9, 72.8, 93.8, 125.8, 128.0, 128.6, 131.8, 157.7, 166.4, 178.0; MS *m*/*z* 245 (M^+, 10), 230 (15), 217 (40), 69 (100), 59 (16). Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.53; H, 6.15; N, 5.67.

(*Z*)-4,4-Dimethyl-2-phenyl-4*H*-oxazol-5-ylideneacetic Acid Methyl Ester (3b). Chromatography with *n*-hexane/EtOAc (8/2) gave **3b** (0.032 g, 5%) as a white solid: mp 77−78 °C; IR (KBr) ν cm^{-1} 1720 (s), 1673 (s), 1661 (s), 1648 (s); ^{1}H NMR ($CDCl_3$) δ 1.77 (s, 6 H, 2 CH_3), 3.77 (s, 3 H, CO_2CH_3), 5.19 (s, 1 H, =CH), 7.43−7.53 (m, 3 H aromatic), 8.05−8.08 (m, 2 H aromatic); MS *m*/*z* 245 (M^+, 9), 230 (21), 145 (67), 104 (100), 77 (32), 69 (95), 59 (12). Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.52; H, 6.14; N, 5.66.

(*E*,*E*)-1,3-Bis-(4,4-dimethyl-2-phenyl-4*H*-oxazol-5-ylidene)propan-2-one (4b). The reaction was carried out as

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described above for the synthesis of compound **2a**, except in a more concentrated methanol solution (5 mL instead of 20 mL). Chromatography with *n*-hexane/EtOAc (7/3) gave **4b** (0.228 g, 38%) as a white solid: mp 241−244 °C; IR (KBr) ν cm^{-1} 1685 (m), 1580 (s), 1449 (s); ^{1}H NMR ($CDCl_3$) δ 1.78 (s, 12 H, 4 CH_3), 6.22 (s, 2 H, 2 =CH), 7.43−7.56 (m, 6 H aromatic),7.97−8.00 (m, 4 H aromatic); ^{13}C NMR ($CDCl_3$) δ 24.2, 73.2, 104.3, 126.0, 127.1, 128.4, 131.8, 157.9, 177.2, 183.5; MS *m*/*z* 400 (M^+, 2), 145 (100), 104 (39), 77 (10), 69 (23). Anal. Calcd for $C_{25}H_{24}N_2O_3$: C, 74.98; H, 6.04; N, 7.00. Found: C, 74.95; H, 6.05; N, 6.96.

(*E*,*Z*)-1,3-Bis(4,4-dimethyl-2-phenyl-4*H*-oxazol-5-ylidene)propan-2-one (5b): The reaction was carried out as described above for the synthesis of compound **4b**. Chromatography with *n*-hexane/EtOAc (7/3) gave **5b** (0.030 g, 5%) as a white solid: mp 221−223 °C; IR (KBr) ν cm^{-1} 1685 (m), 1645 (s), 1583 (s); ^{1}H NMR ($CDCl_3$) δ 1.52 (s, 6 H, 2 CH_3), 1.81 (s, 6 H, 2 CH_3), 5.49 (s, 1 H, =CH), 6.68 (s, 1 H, =CH), 7.45−7.57 (m, 6 H aromatic), 7.99−8.12 (m, 4 H aromatic); ^{13}C NMR ($CDCl_3$) δ 24.2, 28.7, 72.4, 73.2, 102.3, 102.7, 125.8, 126.1, 128.0, 128.4, 128.5, 128.6, 131.9, 132.2, 159.5, 159.7, 171.5, 172.0, 185.8; MS *m*/*z* 400 (M^+, absent), 145 (100), 104 (45), 77 (24), 69 (16). Anal. Calcd for $C_{25}H_{24}N_2O_3$: C, 74.98; H, 6.04; N, 7.00. Found: C, 74.93; H, 6.05; N, 6.94.

2-(Benzoylaminomethyl)maleic Acid Dimethyl Ester (7d). The reaction was carried out as described above for the synthesis of compound **2a**. Chromatography with *n*-hexane/EtOAc (7/3) gave **7d** (0.498 g, 60%) as a colorless oil: IR (neat) ν cm^{-1} 3325 (s), 1721 (s), 1640 (s), 1552 (s); ^{1}H NMR ($CDCl_3$) δ 3.72 (s, 3 H, CO_2CH_3), 3.81 (s, 3 H, CO_2CH_3), 4.32 (dd, J = 6.0, 1.5, 2 H, CH_2), 6.12 (t, J = 1.5, 1 H, =CH), 6.75 (bt, 1 H, NH), 7.38−7.50 (m, 3 H aromatic), 7.73−7.78 (m, 2 H aromatic); MS *m*/*z* 277 (M^+, 2), 105 (100), 77 (28), 59 (6). Anal. Calcd for $C_{14}H_{15}NO_5$: C, 60.65; H, 5.45; N, 5.05. Found: C, 60.60; H, 5.40; N, 4.99.

(2-Phenyloxazol-5-yl)acetic Acid Methyl Ester (8d). Chromatography with *n*-hexane/EtOAc (7/3) gave **8d** (0.061 g, 9%) as a white solid: mp 56−57 °C; IR (film) ν cm^{-1} 1740 (s), 1645 (s), 1167 (s); ^{1}H NMR ($CDCl_3$) δ 3.74 (s, 3 H, CO_2CH_3), 3.79 (s, 2 H, CH_2), 7.06 (s, 1 H on oxazole ring), 7.40−7.43 (m, 3 H on phenyl ring), 7.97−8.01 (m, 2 H on phenyl ring); MS *m*/*z* 217 (M^+, 21), 158 (100), 104 (18), 77 (15), 59 (8). Anal. Calcd for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.31; H, 5.06; N, 6.41.

(*E*)-(4,4-Dimethyl-2-vinyl-4*H*-oxazol-5-ylidene)acetic Acid Methyl Ester (2e). The reaction was carried out as described in the general procedure starting from **1e** (0.343 g, 2.5 mmol), 10% Pd−C (0.053 g, 0.05 mmol), and KI (0.125 g, 0.75 mmol) at 50 °C for 24 h. Chromatography with *n*-hexane/EtOAc (8/2) gave **2e** (0.244 g, 50%) as a white solid: mp 46−47 °C; IR (neat) ν cm^{-1} 1718 (s), 1651 (m), 1264 (s); ^{1}H NMR ($CDCl_3$) δ 1.65 (s, 6 H, $(CH_3)_2CN$), 3.68 (s, 3 H, CO_2CH_3), 5.68 (s, 1 H, =CH), 5.81 (d, J = 11.0, 1 H, =C*H*H), 6.14 (d, J = 17.3, 1 H, =CH*H*), 6.29 (dd, J = 11.0, 17.3, 1 H, C*H*=CH_2); MS *m*/*z* 195 (M^+, 17), 180 (14), 167 (18), 69 (100), 59 (8). Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.17. Found: C, 61.49; H, 6.70; N, 7.13.

(*E*)-[2-(2-Methoxyethyl)-4,4-dimethyl-4*H*-oxazol-5-ylidene]acetic Acid Methyl Ester (9e). Chromatography with *n*-hexane/EtOAc (8/2) gave **9e** (0.108 g, 19%) as colorless oil: IR (neat) ν cm^{-1} 1719 (s), 1655 (s), 1245 (s); ^{1}H NMR ($CDCl_3$) δ 1.62 (s, 6 H, $(CH_3)_2CN$), 2.67 (t, J = 6.8, 2 H, C$H_2$$CH_2OCH_3$), 3.35 (s, 3 H, OCH_3), 3.68 (s, 3 H, CO_2CH_3), 3.69 (t, J = 6.8, 2 H, C$H_2$$OCH_3$), 5.62 (s, 1 H, =CH); MS *m*/*z* 227 (M^+, 3), 212 (5), 141 (64), 69 (100), 59 (12). Anal. Calcd for $C_{11}H_{17}NO_4$: C, 58.14; H, 7.54; N, 6.16. Found: C, 58.10; H, 7.51; N, 6.12.

***N*-[1-(5,5-Dimethoxy-2-oxo-2,5-dihydrofuran-3-yl)-1-methylethyl]acrylamide (10e).** Chromatography with *n*-hexane/EtOAc (8/2) gave **10e** (0.051 g, 8%) as colorless oil: IR (neat) ν cm^{-1} 3351 (s), 1750 (s), 1645 (s); ^{1}H NMR ($CDCl_3$) δ 1.64 (s, 6 H, $(CH_3)_2CN$), 3.45 (s, 6 H, 2 OCH_3), 5.60 (dd, J = 10.2, 1.2, 1 H, =C*H*H), 5.84 (bs, 1 H, NH), 6.05 (dd, J = 16.9, 1.2, 1 H, =CH*H*), 6.19 (dd, J = 16.9, 10.2, 1 H, C*H*=CH_2) 6.68 (s, 1 H, =C*H*C$(OMe)_2$); MS *m*/*z* 255 (M^+, 1), 224 (17), 196 (100), 170 (46), 55 (49). Anal. Calcd for $C_{12}H_{17}NO_5$: C, 56.46; H, 6.71; N, 5.49. Found: C, 56.41; H, 6.69; N, 5.45.

(*E*)-3-[(*E*)-(5-Ethoxycarbonyl)methylene-4,4-dimethyl-4,5-dihydrooxazol-2-yl]acrylic Acid Ethyl Ester (2f). The reaction was carried out as described above for the synthesis of compound **2a**. Chromatography with *n*-hexane/EtOAc (8/2) gave **2f** (0.548 g, 61%) as a white solid: mp 81−82 °C; IR (KBr) ν cm^{-1} 1724 (s), 1662 (m), 1045 (s); ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.1, 3 H, $CO_2CH_2CH_3$), 1.30 (t, J = 7.1, 3 H, $CO_2CH_2CH_3$), 1.66 (s, 6 H, $(CH_3)_2CN$), 4.15 (q, J = 7.1, 2 H, $CO_2CH_2CH_3$), 4.25 (q, J = 7.1, 2 H, $CO_2CH_2CH_3$), 5.68 (s, 1 H, EtO_2CCH=CO), 6.65 (d, J = 15.9, 1 H, CH=C*H*CO_2Et), 7.08 (d, J = 15.9, 1 H, C*H*=$CHCO_2Et$); ^{13}C NMR ($CDCl_3$) δ 14.0, 14.1, 24.5, 59.9, 61.2, 73.0, 95.1, 128.6, 130.7, 156.0, 164.8, 165.8, 176.5; MS *m*/*z* 281 (M^+, 10), 266 (30), 180 (100), 69 (35), 59 (28). Anal. Calcd for $C_{14}H_{19}NO_5$: C, 59,78; H, 6.81; N, 4.98. Found: C, 59.74; H, 6.80; N, 4.93.

(*Z*)-3-[(*E*)-(5-Ethoxycarbonyl)methylene-4,4-dimethyl-4,5-dihydrooxazol-2-yl]acrylic Acid Ethyl Ester (3f). Chromatography with *n*-hexane/EtOAc (8/2) gave **3f** (0.042 g, 5%) as a pale yellow deliquescent solid: IR (neat) ν cm^{-1} 1724 (s), 1688 (s), 1161 (s); ^{1}H NMR ($CDCl_3$) δ 1.31 (t, J = 7.1, 6 H, 2 $CO_2CH_2CH_3$), 1.43 (s, 6 H, $(CH_3)_2CN$), 4.21 (q, J = 7.1, 2 H, $CO_2CH_2CH_3$), 4.26 (q, J = 7.1, 2 H, $CO_2CH_2CH_3$), 5.15 (s, 1 H, EtO_2CCH=CO), 6.87 (d, J = 15.8, 1 H, CH=C*H*CO_2Et), 7.15 (d, J = 15.8, 1 H, C*H*=$CHCO_2Et$); MS *m*/*z* 281 (M^+, 10), 266 (25), 180 (100), 69 (95), 59 (45). Anal. Calcd for $C_{14}H_{19}NO_5$: C, 59,78; H, 6.81; N, 4.98. Found: C, 59.72; H, 6.78; N, 4.93.

(*E*)-3-[1-(5,5-Diethoxy-2-oxo-2,5-dihydrofuran-3-yl)-1-methylethylcarbamoyl]acrylic Acid Ethyl Ester (10f). Chromatography with *n*-hexane/EtOAc (8/2) gave **10f** (0.043 g, 4%) as a pale yellow oil: IR (neat) ν cm^{-1} 3350 (s), 1750 (s), 1720 (s), 1645 (s), 1541 (s); ^{1}H NMR ($CDCl_3$) δ 1.22 (t, J = 7.1, 6 H, 2 OCH_2CH_3), 1.29 (t, J = 7.1, 3 H, OCH_2CH_3), 1.64 (s, 6 H, $(CH_3)_2CN$), 3.70 (q, J = 7.1, 2 H, OCH_2), 3.73 (q, J = 7.1, 2 H, OCH_2), 4.21 (q, J = 7.1, 2 H, OCH_2), 6.37 (bs, 1 H, NH), 6.68 (d, J = 15.3, 1 H, CH=C*H*CO_2Et), 6.70 (s, 1 H, =C*H*C$(OEt)_2$), 6.88 (d, J = 15.3, 1 H, C*H*=$CHCO_2Et$); MS *m*/*z* 355 (M^+, absent), 282 (100), 186 (50). Anal. Calcd for $C_{17}H_{25}NO_7$: C, 57,46; H, 7.09; N, 3.94. Found: C, 57.42; H, 7.08; N, 3.88.

(*E*)-(4,4-Dimethyl-2-pyridin-2-yl-4*H*-oxazol-5-ylidene)-acetic Acid Methyl Ester (2g). The reaction was carried out as described above for the synthesis of compound **2a**. Chromatography with *n*-hexane/EtOAc (7/3) gave **2g** (0.539 g, 73%) as a white solid: mp 126−127 °C; IR (KBr) ν cm^{-1} 1720 (s), 1672 (m), 1439 (s); ^{1}H NMR ($CDCl_3$) δ 1.75 (s, 6 H, $(CH_3)_2$-CN), 3.72 (s, 3 H, CO_2CH_3), 5.87 (s, 1 H, =CH), 7.42−7.48 (m, 1 H aromatic at C-5), 7.83 (td, J = 5.9, 1.3, 1 H aromatic at C-4), 8.07 (d,t J = 5.9, 0.8, 1 H aromatic at C-3), 8.77 (ddd, J = 3.6, 1.3, 0.8, 1 H aromatic at C-6); MS *m*/*z* 246 (M^+, 10), 231 (15), 105 (100), 69 (75), 59 (15). Anal. Calcd for $C_{13}H_{14}N_2O_3$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.36; H, 5.69; N, 11.34.

(*E*)-[2-(4-Chloropyridin-2-yl)-4,4-dimethyl-4*H*-oxazol-5-ylidene]acetic Acid Methyl Ester (2h). The reaction was carried out as described above for the synthesis of compound **2a**. Chromatography with *n*-hexane/EtOAc (7/3) gave **2h** (0.588 g, 70%) as a white solid: mp 143−145 °C; IR (KBr) ν cm^{-1} 1719 (s), 1648 (s); ^{1}H NMR ($CDCl_3$) δ 1.75 (s, 6 H, $(CH_3)_2CN$), 3.71 (s, 3 H, CO_2CH_3), 5.87 (s, 1 H, =CH), 7.45 (dd, J = 6.0, 2.0, 1 H aromatic at C-5), 8.09 (dd, J = 2.0, 0.5, 1 H aromatic at C-3), 8.64 (dd, J = 6.0, 0.5, 1 H aromatic at C-6); MS *m*/*z* 280 (M^+, 5), 265 (10), 141 (95), 69 (100), 59 (20). Anal. Calcd for $C_{13}H_{13}ClN_2O_3$: C, 55.62; H, 4.67; N, 9.98. Found: C, 55.57; H, 4.66; N, 9.93.

(*E*,*E*)-1,4-Bis[(5-methoxycarbonylmethylene)-4,4-dimethyl-4,5-dihydrooxazol-2-yl]benzene (12i). The reaction was carried out as described above in the general procedure starting from **11i** (1.79 mmol) in the presence of 10% Pd−C (0.06 mmol) and KI (0.09 mmol) in MeOH (10 mL). Chromatography with *n*-hexane/EtOAc (7/3) gave **12i** (0.742 g, 60%) as a white solid: mp 192−194 °C; IR (KBr) ν cm^{-1} 1720 (s), 1678 (s), 1653 (s); ^{1}H NMR ($CDCl_3$) δ: 1.75 (s, 12 H, 2 $(CH_3)_2$-CN), 3.72 (s, 6 H, 2 CO_2CH_3), 5.80 (s, 2 H, 2 =CH), 8.05 (s, 4 H aromatic); ^{13}C NMR ($CDCl_3$) δ 24.7, 51.2, 73.1, 94.5, 128.3,

129.0, 157.2, 166.4, 177.7; MS *m*/*z* 412 (M^+, 11), 397 (56), 384 (100), 312 (76), 141 (62), 69 (96), 59 (17). Anal. Calcd for $C_{22}H_{24}N_2O_6$: C, 64.07; H, 5.87; N, 6.79. Found: C, 64.02; H, 5.85; N, 6.74.

(*E*,*Z*)-1,4-Bis[(5-methoxycarbonylmethylene-4,4-dimethyl-4,5-dihydrooxazol-2-yl]benzene (13i). Chromatography with *n*-hexane/EtOAc (7/3) gave **13i** (0.012 g, 1%) as a white solid: mp 180−182 °C; IR (KBr) ν cm^{-1} 1719 (s), 1706 (s), 1677 (s), 1653 (s); ^1H NMR ($CDCl_3$) δ 1.50 (s, 6 H, $(CH_3)_2$CN), 1.75 (s, 6 H, $(CH_3)_2$CN), 3.73 (s, 3 H, CO_2CH_3), 3.78 (s, 3 H, CO_2CH_3), 5.23 (s, 1 H, =CH), 5.81 (s, 1 H, =CH), 8.05−8.08 (m, 2 H, aromatic), 8.15−8.18 (m, 2 H aromatic); ^{13}C NMR ($CDCl_3$) δ 24.7, 28.6, 51.2, 51.3, 72.7, 73.1, 90.6, 94.5, 128.3, 128.6, 128.9, 129.3, 157.2, 158.9, 165.0, 166.5, 174.4, 177.7; MS *m*/*z* 412 (M^+, 4), 397 (14), 141 (59), 69 (100), 59 (16). Anal. Calcd for $C_{22}H_{24}N_2O_6$: C, 64.07; H, 5.87; N, 6.79. Found: C, 64.01; H, 5.85; N, 6.71.

(*Z*)-2-[1-[4-(*E*)-(5-Methoxycarbonylmethylene-4,4-dimethyl-4,5-dihydrooxazol-2-yl)benzoylamino]-1-methylethyl]-maleic Acid Dimethyl Ester (14i). Chromatography with *n*-hexane/EtOAc (7/3) gave **14i** (0.071 g, 5%) as a white solid: mp 93−95 °C; IR (KBr) ν cm^{-1} 1723 (s), 1653 (s), 1104 (s); ^1H NMR ($CDCl_3$) δ 1.72 (s, 6 H, $(CH_3)_2$CN), 1.73 (s, 6 H, $(CH_3)_2$CN), 3.71 (s, 3 H, CO_2CH_3), 3.72 (s, 3 H, CO_2CH_3), 3.77 (s, 3 H, CO_2CH_3), 5.79 (s, 1 H, =CH), 6.05 (s, 1 H, =CH), 6.45 (bs, 1 H, NH), 7.79 (d, J = 8.3, 2 H aromatic), 8.01 (d, J = 8.3, 2 H aromatic); ^{13}C NMR ($CDCl_3$) δ 24.7, 26.7, 51.2, 51.9, 51.5, 73.1, 94.5, 118.4, 127.0, 128.4, 128.7, 137.6, 154.2, 157.1, 165.1, 166.4, 168.4, 177.7; MS *m*/*z* 472 (M^+, 7), 413 (68), 272 (66), 130 (100), 69 (47), 59 (11). Anal. Calcd for $C_{24}H_{28}N_2O_8$: C, 61.01; H, 5.97; N, 5.93. Found: C, 60.98; H, 5.95; N, 5.87.

(*E*)-[2-[4-[1-(5,5-Dimethoxy-2-oxo-2,5-dihydrofuran-3-yl)-1-methylethylcarbamoyl]phenyl]-4,4-dimethyl-4*H*-oxazol-5-ylidene]acetic Acid Methyl Ester (15i). Chromatography with *n*-hexane/EtOAc (7/3) gave **15i** (0.089 g, 6%) as a white solid: mp 83−85 °C; IR (KBr) ν cm^{-1} 1773 (s), 1722 (s), 1301 (s), 1105 (s); ^1H NMR ($CDCl_3$) δ 1.71 (s, 6 H, $(CH_3)_2$CN), 1.72 (s, 6 H, $(CH_3)_2$CN), 3.44 (s, 6 H, $C(OCH_3)_2$), 3.70 (s, 3 H, CO_2CH_3), 5.78 (s, 1 H, =C*H*CO_2Me), 6.54 (bs, 1 H, NH), 6.73 (s, 1 H, =CHC$(OMe)_2$), 7.73−7.77 (m, 2 H aromatic), 7.95−7.98 (m, 2 H, aromatic); ^{13}C NMR ($CDCl_3$) δ: 24.7, 26.6, 51.1, 51.3, 51.9, 73.1, 94.4, 118.3, 127.1, 128.3, 137.9, 140.6, 142.1, 157.1, 158.9, 166.3, 166.4, 166.9, 177.7; MS *m*/*z* 472 (M^+, absent), 413 (47), 272 (51), 130 (100), 69 (48), 59 (9). Anal. Calcd for $C_{24}H_{28}N_2O_8$: C, 61.01; H, 5.97; N, 5.93. Found: C, 60.97; H, 5.95; N, 5.88.

(*E*,*E*)-[2-[1-(5-Methoxycarbonylmethylene-4,4-dimethyl-4,5-dihydrooxazol-2-yl)-1-methylethyl]-4,4-dimethyl-4*H*-oxazol-5-ylidene]acetic Acid Methyl Ester (12j). The reaction was carried out as described above for the synthesis of compound **2a**. Chromatography with *n*-hexane/EtOAc (7/3) gave **12j** (0.500 g, 45%) as a white solid: mp 89−90 °C; IR (KBr) ν cm^{-1} 1720 (s), 1689 (s), 1068 (s); ^1H NMR ($CDCl_3$) δ 1.56 (s, 6 H, $(CH_3)_2$C), 1.61 (s, 12 H, 2 $(CH_3)_2$CN), 3.67 (s, 6 H, 2 CO_2CH_3), 5.59 (s, 2 H, 2 =CH); ^{13}C NMR ($CDCl_3$) δ:23.3, 24.3, 37.9, 51.0, 72.6, 94.0, 162.0, 166.3, 177.9; MS *m*/*z* 378 (M^+, 1), 335 (15), 142 (100), 69 (75), 59 (12). Anal. Calcd for $C_{19}H_{26}N_2O_6$: C, 60.31; H, 6.92; N, 7.40. Found: C, 60.26; H, 6.90; N, 7.35.

(*Z*)-2-[1-[2-(*E*)-(5-Methoxycarbonylmethylene-4,4-dimethyl-4,5-dihydrooxazol-2-yl)-2-methylpropionylamino]-1-methylethyl]maleic Acid Dimethyl Ester (14j). Chromatography with *n*-hexane/EtOAc (7/3) gave **14j** (0.197 g, 15%) as a colorless oil: IR (neat) ν cm^{-1} 3378 (m), 1723 (s), 1671 (s), 1075 (s); ^1H NMR ($CDCl_3$) δ 1.46 (s, 6 H, $(CH_3)_2$C), 1.54 (s, 6 H, $(CH_3)_2$CN), 1.64 (s, 6 H, $(CH_3)_2$CN), 3.68 (s, 3 H, CO_2CH_3), 3.70 (s, 3 H, CO_2CH_3), 3.78 (s, 3 H, CO_2CH_3), 5.67 (s, H, =CH), 5.93 (s, 1 H, =CH), 7.23 (bs, 1 H, NH); MS *m*/*z* 438 (M^+, absent), 211 (100), 143 (80), 69 (25), 59 (9). Anal. Calcd for $C_{21}H_{30}N_2O_8$: C, 57.52; H, 6.90; N, 6.39. Found: C, 57.47; H, 6.88; N, 6.35.

(*E*)-[2-[1-[1-(5,5-Dimethoxy)-2-oxo-2,5-dihydrofuran-3-yl)-1-methylethylcarbamoyl]-1-methylethyl]-4,4-dimethyl-4*H*-oxazol-5-ylidene]acetic Acid Methyl Ester (15j). Chromatography with *n*-hexane/EtOAc (7/3) gave **15j** (0.118 g, 9%) as a white solid: mp 135−136 °C; IR (neat) ν cm^{-1} 3351 (s), 1750 (s), 1720 (s); ^1H NMR ($CDCl_3$) δ 1.42 (s, 6 H, $(CH_3)_2$C), 1.54 (s, 6 H, $(CH_3)_2$CN), 1.64 (s, 6 H, $(CH_3)_2$CN), 3.40 (s, 6 H, 2 OCH_3), 3.68 (s, 3 H, CO_2CH_3), 5.64 (s, H, =C*H*CO_2Me), 6.60 (s, 1 H, =C*H*C$(OMe)_2$), 7.19 (bs, 1 H, NH); MS *m*/*z* 438 (M^+, absent), 211 (100), 143 (80), 69 (27), 59 (7). Anal. Calcd for $C_{21}H_{30}N_2O_8$: C, 57.52; H, 6.90; N, 6.39. Found: C, 57.48; H, 6.87; N, 6.36.

(*E*)-[2-[6-(5-Methoxycarbonylmethylene-4,4-dimethyl-4,5-dihydrooxazol-2-yl)pyridin-2-yl]-4,4-dimethyl-4*H*-oxazol-5-ylidene]acetic Acid Methyl Ester (12k). The reaction was carried out as described above for the synthesis of compound **2a**. Chromatography with *n*-hexane/EtOAc (7/3) gave **12k** (0.595 g, 48%) as a white solid: mp 130−131 °C; IR (KBr) ν cm^{-1} 1728 (s), 1437 (s); ^1H NMR ($CDCl_3$) δ 1.76 (s, 12 H, 2 $(CH_3)_2$CN), 3.73 (s, 6 H, 2 CO_2CH_3), 5.92 (s, 2 H, 2 =CH), 7.98 (t, J = 7.8 Hz, 1 H aromatic at C-4), 8.28 (d, J = 7.8 Hz, 2 H aromatic at C-3 and C-5); MS *m*/*z* 413 (M^+, 38), 385 (40), 353 (100), 141 (50), 59 (8). Anal. Calcd for $C_{21}H_{23}N_3O_6$: C, 61.01; H, 5.61; N, 10.16. Found: C, 60.97; H, 5.58; N, 10.13.

(*Z*)-2-[1-[[6-(*E*)-(5-Methoxycarbonylmethylene-4,4-dimethyl-4,5-dihydrooxazol-2-yl)pyridine-2-carbonyl]amino]-1-methylethyl]maleic Acid Dimethyl Ester (14k). Chromatography with *n*-hexane/EtOAc (7/3) gave **14k** (0.071 g, 5%) as a white solid: mp 146−147 °C; IR (KBr) ν cm^{-1} 3391 (m), 1722 (s), 1683 (s); ^1H NMR ($CDCl_3$) δ: 1.71 (s, 6 H, $(CH_3)_2$CN), 1.75 (s, 6 H, $(CH_3)_2$CN), 3.67 (s, 3 H, CO_2CH_3), 3.71 (s, 3 H, CO_2CH_3), 3.76 (s, 3 H, CO_2CH_3), 5.84 (s, 1 H, =CH), 6.01 (s, 1 H, =CH), 7.96 (t, J = 7.9, aromatic at C-4), 8.18 (d, J = 7.9, 1 H aromatic at C-3 or C-5), 8.29 (d, J = 7.9, 1 H aromatic at C-5 or C-3), 8.33 (bs, 1H, NH); MS (CI): *m*/*z* 474 [$(M + 1)^+$, 100]. Anal. Calcd for $C_{23}H_{27}N_3O_8$: C, 58.35; H, 5.75; N, 8.87. Found: C, 58.33; H, 5.74; N, 8.84.

(*E*,*E*)-*trans*-[2-[2-(5-Methoxycarbonylmethylene-4,4-dimethyl-4,5-dihydrooxazol-2-yl)cyclohexyl]-4,4-dimethyl-4*H*-oxazol-5-ylidene]acetic Acid Methyl Ester (12l). The reaction was carried out as described above for the synthesis of compound **2a**. Chromatography with *n*-hexane/EtOAc (8/2) gave **12l** (0.740 g, 59%) as a white solid: mp 118−120 °C; IR (KBr) ν cm^{-1} 1722 (s), 1659 (m); ^1H NMR ($CDCl_3$) δ 1.28−1.36 (m, 4 H, 4 CH), 1.54 (s, 12 H, 2 $(CH_3)_2$CN), 1.49−1.56 (m, 4 H, 4 CH), 2.05−2.08 (m, 2 H, 2 CH), 3.67 (s, 6 H, 2 CO_2CH_3), 5.63 (s, 2 H, 2 =CH); MS *m*/*z* 418 (M^+, 1), 83 (30), 69 (100), 59 (13). Anal. Calcd for $C_{22}H_{30}N_2O_6$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.09; H, 7.19; N, 6.64.

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Supporting Information Available: X-ray structural information for **2b**, **4b**, **2h**, **12l**, and **6c** is collected in the Tables S1 and S2. The structures of **2b**, **4b**, **2h**, **12l**, and **6c** are shown in Figures S1−S5, respectively. This material is available free of charge via the Internet at http://pubs.acs.org.

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