JOC*Article*

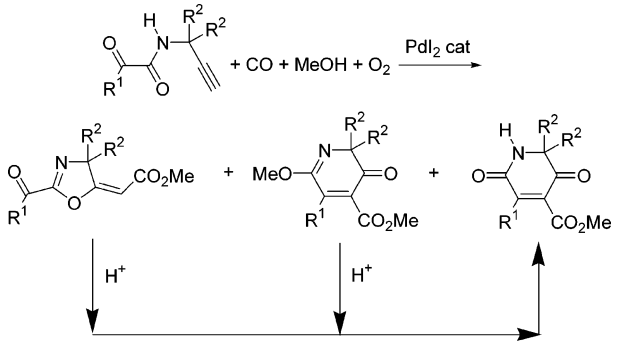
Heterocyclic Derivative Syntheses by Palladium-Catalyzed Oxidative Cyclization−Alkoxycarbonylation of Substituted γ-Oxoalkynes

Alessia Bacchi,[†] Mirco Costa,*[,‡] Nicola Della Cà,[‡] Bartolo Gabriele,[§] Giuseppe Salerno,[∥] and Silvia Cassoni[‡]

Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica e Chimica Fisica, Università di Parma, Parco Area delle Scienze 17/A, 43100 Parma, Italy, Dipartimento di Chimica Organica e Industriale, Università di Parma, Parco Area delle Scienze 17/A, 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

Received January 25, 2005



4-Yn-1-ones containing different substituents, prop-2-ynyl α-ketoesters, and prop-2-ynyl α-ketoamides have been caused to react catalytically under oxidative carbonylation conditions to give tetrahydrofuran, dioxolane and oxazoline, dihydropyridinone, and tetrahydropyridinedione derivatives in satisfactory yields. Reactions were carried out in MeOH or MeCN/MeOH mixtures at 65−100 °C in the presence of catalytic amounts of PdI_2 in conjunction with KI under 32 bar (at 25 °C) of a 3:1 mixture of CO and air. Anti and syn 5-*exo-dig* cyclization modes account for the formation of different products. It has been found that cyclopentenone, dihydropyridinone, and tetrahydropyridinedione derivatives, formed when the reaction is carried out at higher temperature and for a longer time, can also be selectively obtained through an acid treatment of tetrahydrofuran and oxazoline derivatives involving an unusual rearrangement. The structures of 6-methoxy-2,2-dimethyl-3-oxo-5-phenyl-2,3-dihydropyridine-4-carboxylic acid methyl ester and 2,2,5-trimethyl-3,6-dioxo-1,2,3,6-tetrahydropyridine-4-carboxylic acid methyl ester have been confirmed by X-ray diffraction analysis.

Introduction

Transition-metal-catalyzed annulation reactions represent an effective and straightforward methodology for the synthesis of heterocyclic compounds, which has brought significant results during the past years.[1] Palladium catalysis, in particular, has proven to be very useful to promote heterocyclization reactions with high selectivity under mild conditions.[2] An especially important application of Pd-catalysis concerns the synthesis of heterocyclic carbonyl compounds through heterocyclocarbonylation or heterocyclization−alkoxycarbonylation of unsaturated substrates bearing a nucleophilic function

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

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

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

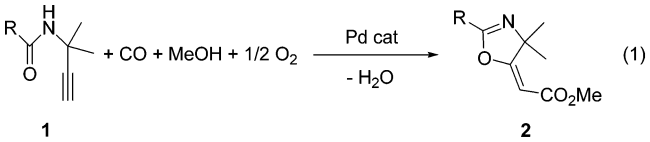
[∥] Dipartimento di Chimica, Università della Calabria.

(1) For a recent review, see: Nakamura, I.; Yamamoto, Y. *Chem. Rev.* **2004**, *104*, 2127−2198.

(2) (a) Li, J. J.; Gribble, G. W. *Palladium in Heterocyclic Chemistry*; Pergamon: Oxford, 2000. (b) Zeni, G.; Larock, R. C. *Chem. Rev.* **2004**, *104*, 2285−2309. For a recent account on PdI_2-catalyzed synthesis of heterocycles, see: (c) Gabriele, B.; Salerno, G.; Costa, M. *Synlett* **2004**, 2468−2483.

10.1021/jo050155v CCC: $30.25
Published on Web 05/19/2005

in appropriate position.[3] The catalytic system based on PdI_2 or 10% Pd−C in conjunction with an excess of KI has proven to be particularly effective to promote this kind of reaction in the presence of oxygen as an oxidant.[3a,4] In particular, some time ago we described the synthesis of (*E*)-5-(alkoxycarbonyl)methylene-3-oxazolines from prop-2-ynylamides promoted by the above-mentioned palladium catalytic system (PdI_2 + KI or Pd/C + KI)[5] (eq 1).



(1)

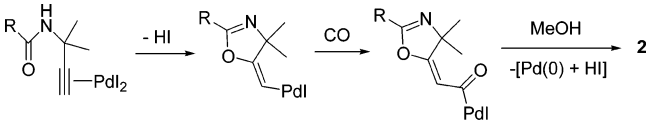
1 **2**

R= Alkyl, aryl

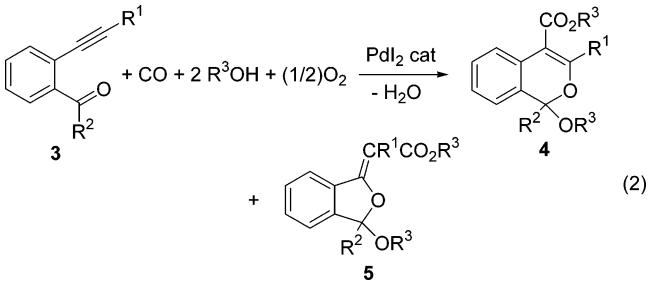
Pd cat= 10% Pd-C or PdI_2 and KI

In this case, intramolecular *anti* nucleophilic attack of oxygen to the triple bond coordinated to Pd(II) was followed by alkoxycarbonylation, so the overall process corresponded to 5-*exo-dig* cyclization−alkoxycarbonylation (Scheme 1; in this and in the following schemes anionic iodide ligands are omitted for clarity).

SCHEME 1



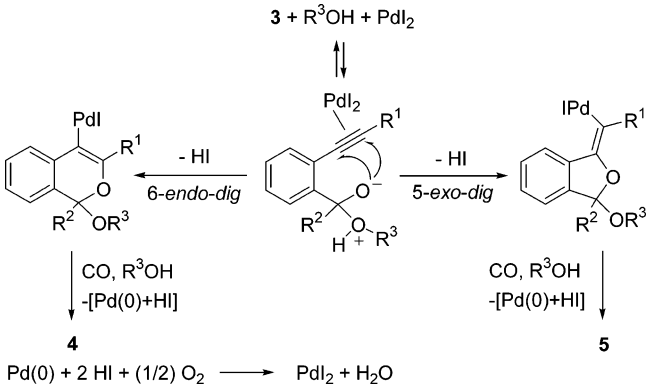
The presence of geminal groups α to the triple bond was a necessary requisite for directing the catalytic process toward the formation of cyclization products. More recently we reported the direct synthesis of benzo[*c*]pyran derivatives **4** and 1,3-dihydroisobenzofuran derivatives **5** by Pd-catalyzed oxidative cyclization−alkoxycarbonylation of 2-alkynylbenzaldehydes or 2-alkynylphenyl ketones **3** (eq 2).[6]



(2)

The reaction proceeded through 6-*endo-dig* or 5-*exo-dig* intramolecular attack on the triple bond coordinated to Pd(II) by the nucleophilic oxygen atom generated in situ by R^3OH attack on the carbonyl group of **3**, followed by alkoxycarbonylation (Scheme 2). The presence of substituents on the triple bond (R^1) and at the carbonyl group (R^2) played a key role in the selectivity of the process toward the formation of a five- or six-membered ring.

SCHEME 2

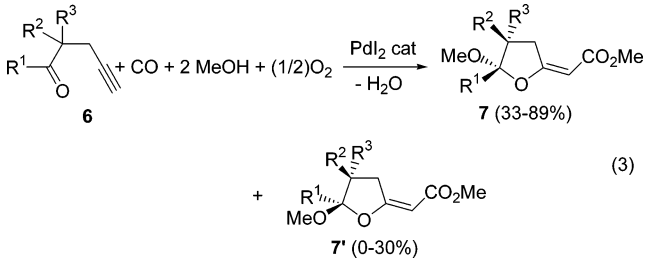


We have now extended our investigations on heterocyclic ring formation by means of PdI_2-catalyzed oxidative cyclization−alkoxycarbonylation reactions to aliphatic acetylenic ketones. The Pd-catalyzed oxidative carbonylation of 4-yn-1-ones, to give 2-methoxy-5-[(methoxycarbonyl)methylene]tetrahydrofurans as the main products, using $(MeCN)_2PdCl_2$ as catalyst and 1,4-benzoquinone as oxidant has been reported recently.[7] Under the applied mild conditions, the reactions of 4-yn-1-ones afforded cyclic ketals either as single diastereomers, sometimes together with a methoxyacrylate derivative, or as a diastereomeric mixture.

We caused 4-yn-1-ones containing different substituents, prop-2-ynyl α-ketoesters, and prop-2-ynyl α-ketoamides to react catalytically under oxidative carbonylation conditions with our catalytic system, PdI_2−KI. Here we report the results of our investigations, which allowed us to compare the activity of our catalytic system with the one based on $(MeCN)_2PdCl_2$[7] and to discover rearrangement processes leading to different classes of heterocyclic derivatives.

Results and Discussion

Oxidative Carbonylation of 4-Yn-1-ones. The oxidative carbonylation reactions of 4-yn-1-ones **6** were carried out at 65−100 °C for 24−36 h in a mixture of MeOH/MeCN (0.4/5.0 v/v) and under a CO-air pressure of 24/8 bar measured at room temperature, in the presence of PdI_2 (3.3 mol %) and KI (KI/PdI_2 molar ratio = 10). The reaction led to the formation of 2-methoxy-5-[(methoxycarbonyl)methylene]tetrahydrofurans **7** and **7′** in moderate to good yields and fair diastereoselectivity



(3)

(3) For recent reviews, see: (a) Gabriele, B.; Salerno, G.; Costa, M.; Chiusoli, G. P. *Curr. Org. Chem.* **2004**, *8*, 919−946. (b) Alonso, F.; Beletskaya, I.; Yus, M. *Chem. Rev.* **2004**, *104*, 3079−3159. (c) Vizer, S. A.; Yerzhanov, K. B.; Al Quntar, A. A. A.; Vembitsky, V. M. *Tetrahedron* **2004**, *60*, 5499−5538.

(4) (a) Gabriele, B.; Costa, M.; Salerno, G.; Chiusoli, G. P. *J. Chem. Soc., Chem. Commun.* **1992**, 1007−1008. (b) Gabriele, B.; Costa, M.; Salerno, G.; Chiusoli, G. P. *J. Chem. Soc., Perkin Trans. 1* **1994**, 83−87.

(5) Bacchi, A.; Costa, M.; Gabriele, B.; Pelizzi, G.; Salerno, G. *J. Org. Chem.* **2002**, *67*, 4450−4457.

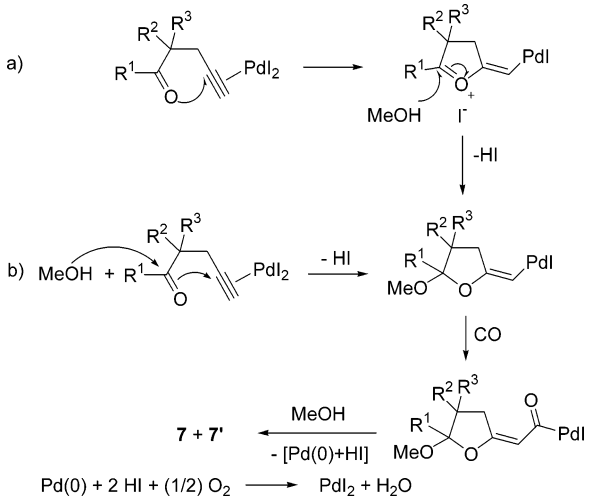
(6) Bacchi, A.; Costa, M.; Della Cà, N.; Fabbricatore, M.; Fazio, A.; Gabriele, B.; Nasi, C.; Salerno, G. *Eur. J. Org. Chem.* **2004**, 574−585.

TABLE 1. Synthesis of 2-Methoxy-5-[(methoxycarbonyl)methylene]tetrahydrofurans 7 and 7′ by Oxidative Carbonylation of 4-Yn-1-ones 6 (2.0 mmol)[a]

entry	6	R^1	R^2	R^3	*T* (°C)	*t* (h)	conv **6** (%)[b]	yield **7** (%)[c]	yield **7′** (%)[c]
1	**6a**	Me	H	CO_2Me	70	36	55	33	11
2	**6a**	Me	H	CO_2Me	100	36	97	55 (39)	27 (13)
3	**6b**	Me	Et	CO_2Me	65	36	72	65 (54)	3
4[d]	**6b**	Me	Et	CO_2Me	100	24	89	41 (30)	8
5	**6c**	Me	Bn	CO_2Et	100	36	90	74 (62)	6
6	**6d**	Me	Et	COMe	70	36	90	85 (73)	3
7	**6e**	$(CH_2)_4$		CO_2Me	70	36	96	89 (78)	0
8	**6f**	Ph	H	H	70	36	88	77 (65)	
9	**6g**	Ph	Me	CO_2Et	100	36	66	39	21
10[e]	**6g**	Ph	Me	CO_2Et	100	36	98	61 (46)	30 (14)

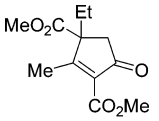
[a] In MeCN/MeOH (5.0/0.4 mL/mL) mixture, in the presence of PdI_2 (3.3 mol %) and KI (KI/PdI_2 molar ratio = 10), under 32 bar (at 25 °C) of a 3:1 mixture of CO and air. [b] Based on starting **6**, by GLC. [c] GLC yield (isolated yield) based on **6**. [d] The reaction also led to the formation of 3-ethyl-2-methyl-5-oxocyclopent-1-ene-1,3-dicarboxylic acid dimethyl ester **8b** (32% GLC yield, 21% isolated). [e] The ratio of the mixture MeCN/MeOH was 4.5/1.0 mL/mL.

SCHEME 3



(eq 3 and Table 1). In some cases, only the most abundant diastereoisomer **7** was isolated, and its stereochemistry was determined by 2D NOESY NMR experiments. It is interesting to note that, in contrast to the reaction of 2-alkynylbenzaldehydes or 2-alkynylphenyl ketones **3** carried out under analogous conditions,[6] 4-ynones **6** underwent 5-*exo-dig* cyclization exclusively (Scheme 3)

Diastereoselectivity toward **7** was moderate when R^2 = H (entries 1 and 2) or when R^1 = Ph (entries 9 and 10), whereas it was higher when both R^1 and R^2 were alkyl groups (entries 3−7). For example, carbonylation of 2-acetyl-2-ethylpent-4-ynoic acid methyl ester **6b**, carried out at 65 °C for 36 h, led to a 65% GLC yield of **7b** and only 3% of **7′b** at 72% substrate conversion (entry 3). Interestingly, when the same reaction was carried out at 100 °C, its conversion reached 89% after 24 h, but the diastereoselectivity was lower; moreover, in this case, a

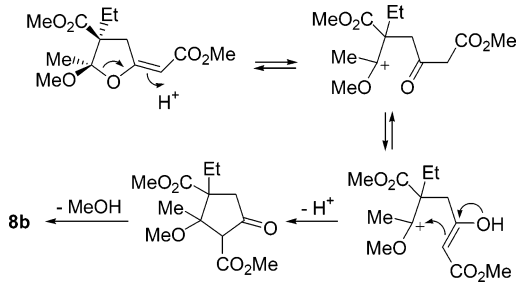


8b

rearrangement product, 3-ethyl-2-methyl-5-oxocyclopent-1-ene-1,3-dicarboxylic acid dimethyl ester **8b**, was also formed as coproduct (entry 4).

As already reported in the literature,[7] product **8b** was also obtained by acid treatment of **7b**. A plausible mechanism for its formation is shown in Scheme 4.

SCHEME 4



The diastereoselectivity of the cyclization products is controlled by the presence of neighboring groups in the α position to the ketonic CO. On the other hand their presence is not necessary for the cyclization to occur, as shown by the formation of compound **7f** (yield 77%, entry 8).

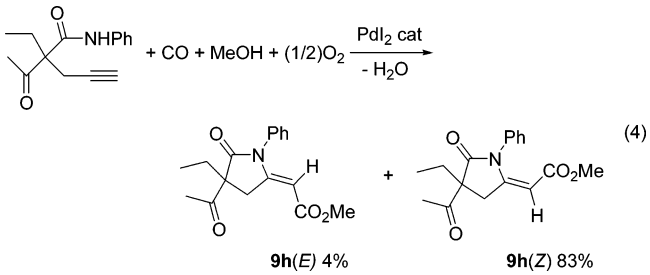
Some differences should now be pointed out between the behavior of our catalytic system (PdI_2/KI) and the one previously used,[7] $(MeCN)_2PdCl_2$, in the oxidative carbonylation of **6**. The latter catalyst allowed the reaction to be carried out under milder conditions (0 °C and atmospheric pressure of CO) but required a stoichiometric amount of an organic reoxidant (1,4-benzoquinone) because, contrary to the PdI_2/KI system, air was not active for Pd(0) reoxidation. On the other hand no significant difference in diastereoselectivity was observed for the carbonylation reaction of the common substrates **6a**, **6b**, and **6e** using the two catalytic systems, under appropriate reaction conditions. Other substrates **6**, used in this work, however, showed a good stereoselectivity toward isomers **7**.

As regards the mechanism, Kato et al.[7] suggested that a cyclic oxonium intermediate plays a key role in controlling the diastereoselectivity of the reaction and enabling the formation of a not negligible amount of acyclic methoxyacrylate derivative in addition to the desired cyclic ketal. In our case, the intermediacy of the cyclic oxonium ion in the reaction mechanism cannot be excluded even if the formation of an acyclic methoxyacrylate derivative did not occur. This different behavior could tentatively be attributed to the presence, in our catalytic system, of I^- ions, which may cause a greater steric hindrance than the Cl^- ones, thus preventing the attack of MeOH to the olefinic carbon of vinyl palladium intermediate (Scheme 3a). An alternative to the formation of a cyclic oxonium ion could be MeOH addition to the keto group in a concerted fashion with carbonyl oxygen attack on the PdI_2-activated alkyne to give the ketal intermediate directly as shown in Scheme 3b.

Oxidative Carbonylation of 4-Ynones Bearing an α-Amido Group. In sharp contrast with 4-yn-1-ones bearing an ester group at the α position (Table 1, entries

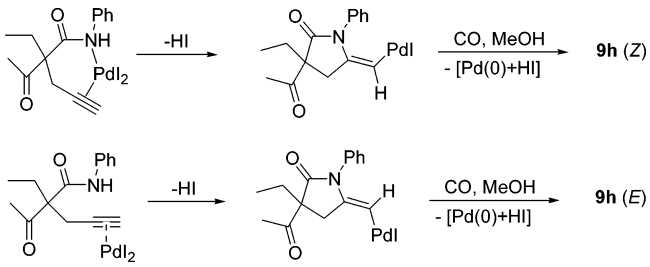
(7) Kato, K.; Yamamoto, Y.; Akita, H. *Tetrahedron Lett.* **2002**, *43*, 4915−4917.

1−7 and 9 and 10), the oxidative carbonylation of 4-yn-1-ones bearing an α-amido group selectively afforded a γ-lactam derivative resulting from nucleophilic attack of amide nitrogen on the activated triple bond. For example, the reaction of 2-acetyl-2-ethyl-pent-4-ynoic acid phenylamide **6h**, carried out under the same conditions reported in Table 1, afforded the two geometric isomers (*E*:*Z* = 1:20) of (4-acetyl-4-ethyl-5-oxo-1-phenyl-pyrrolidin-2-ylidene) acetic acid methyl ester **9h** (total yield 87%) (eq 4, Scheme 5). Acid treatment with HCl (0.22 M



(4)

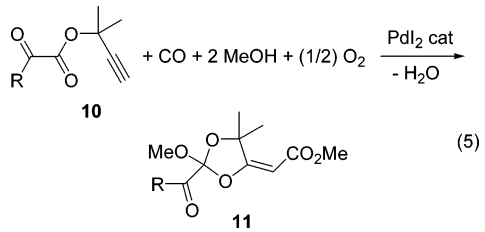
SCHEME 5



in dioxane/water = 4/1 v/v) at room temperature for 15−20 min caused the practically complete isomerization of **9h**(*Z*) into **9h**(*E*).

Oxidative Carbonylation of Prop-2-ynyl α-Ketoesters and α-Ketoamides. The observation (Scheme 4) that a C−O to C−C rearrangement could take place under the carbonylation conditions prompted us to study the behavior of acetylenic substrates containing an α-dicarbonyl functionality, which could lead in one step to highly functionalized five- or six-membered rings. We thus applied our methodology to prop-2-ynyl α-ketoesters **10** and α-ketoamides **12**.

Under conditions similar to those previously used for 4-yn-1-ones **6**, but in MeOH as the only solvent, prop-2-ynyl α-ketoesters **10** selectively afforded 2-methoxy-5-(alkoxycarbonyl)methylene-[1,3]dioxolane derivatives **11**, resulting from MeOH attack on the ester carbonyl group followed by 5-*exo-dig* cyclization and methoxycarbonylation, in good yields (eq 5 and Table 2). The addition of



(5)

MeCN to MeOH depressed the yield of the reaction. Neither products deriving from 6-*exo-dig* cyclization (ensuing from MeOH attack on the ketonic carbonyl

TABLE 2. Synthesis of 2-Methoxy-5-[(methoxycarbonyl)methylene]dioxolanes 11 by Oxidative Carbonylation of Prop-2-ynyl-α-ketoesters 10 (2.0 mmol)[a]

entry	10	R	*T* (°C)	*t* (h)	conv **10** (%)[b]	yield **11** (%)[c]
12	**10a**	Me	65	30	99	75 (61)
13	**10b**	Ph	65	24	99	70 (58)

[a] In MeOH (5.6 mL), in the presence of PdI_2 (3.3 mol %) and KI (KI/PdI_2 molar ratio = 10), under 32 bar (at 25 °C) of a 3:1 mixture of CO and air. [b] Based on starting **10**, by GLC. [c] GLC yield (isolated yield) based on **10**.

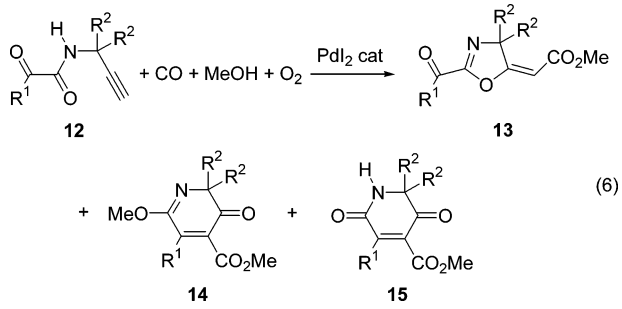
TABLE 3. Cyclization−Alkoxycarbonylation Reactions of Prop-2-ynyl-α-ketoamides 12 (2.0 mmol)[a]

entry	12	R^1	R^2	*T* (°C)	*t* (h)	conv **12** (%)[b]	yield **13** (%)[c]	yield **14** (%)[c]	yield **15** (%)[b]c
14	**12a**	Me	Me	75	16	100	85 (74)	8 (5)	
15	**12a**	Me	Me	75	40	100	52 (43)	39 (30)	6 (3)
16	**12b**	Ph	Me	75	16	98	81 (70)	14 (8)	
17	**12b**	Ph	Me	75	40	100	67 (59)	30 (23)	

[a] In MeCN/MeOH (5.0/0.5 mL/mL) mixture, in the presence of PdI_2 (3.33 mol %) and KI (KI/PdI_2 molar ratio = 10), under 32 bar (at 25 °C) of a 3:1 mixture of CO and air. [b] Based on starting **12**, by GLC. [c] GLC yield (isolated yield) based on **12**.

group) nor products deriving from a subsequent rearrangement of **11** were observed under these conditions. In particular acid treatment of **11** (10% HCl in dry MeOH or 0.22 M HCl in dioxane/water = 4/1 v/v) at room temperature, led to its complete decomposition without formation of new products.

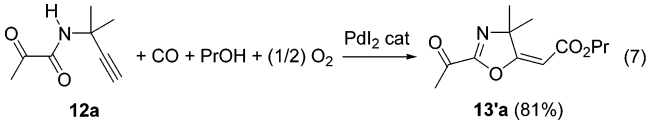
In contrast to **10**, the PdI_2/KI-catalyzed oxidative carbonylation of prop-2-ynyl-α-ketoamides **12** with MeOH as the nucleophile led to a mixture of different cyclization products **13**, **14**, and **15** (eq 6 and Table 3). The structures



(6)

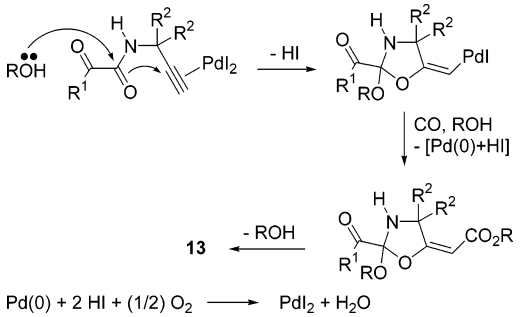
of products **14b** and **15a** were confirmed by X-ray diffraction analysis (see Supporting Information).

Interestingly, no six-membered products were formed using propan-1-ol in place of MeOH as the nucleophile under similar conditions; for example, the reaction of *N*-(1,1-dimethylprop-2-ynyl)-2-oxopropionamide **12a**, carried out under the same conditions reported in entry 15 but at 70 °C and with 1.0 mL of PrOH, afforded oxazoline **13′a** as the sole product in 92% GLC yield (81% isolated) at total substrate conversion (eq 7).



(7)

SCHEME 6



Formation of oxazolines **13a,b** and **13′a** corresponded to the usual alkoxylation-5-*exo-dig* cyclization−alkoxycarbonylation sequence, followed in this case by a final ROH elimination from the 2-alkoxyoxazolidine intermediate, with formation of a C=N double bond (Scheme 6).

On the other hand, six-membered compounds **14a,b** and **15a** derived from subsequent transformations of **13a,b**, as shown by experiments carried out at different reaction times (compare entries 14 and 16 with entries 15 and 17, respectively). These unusual rearrangements also occurred under acidic conditions. For example, when pure oxazolines **13a,b** (1.0 mmol) were treated with a 10% solution of HCl in anhydrous MeOH (10 mL) at room temperature, a fast conversion (15−20 min) of **13a,b** into 6-methoxy-3-oxo-2,3-dihydropyridines **14a,b** was observed in almost quantitative yield (eq 8).

$$\mathbf{13a,b} \xrightarrow[\text{rt}]{\text{10\% HCl/MeOH}} \mathbf{14a,b}\ (96-92\%) \qquad (8)$$

On the other hand, the reaction of pure **13a,b** and **13′a** (1.0 mmol) with HCl (0.22 M in dioxane/water 4/1 v/v, 10 mL) at room temperature for 15−20 min led to the formation of 3,6-dioxo-1,2,3,6-tetrahydro-pyridines **15a,b** and **15′a** in 92−96% yields (eq 9). Products **14a,b** could also be converted into **15a,b** under analogous conditions (eq 10).

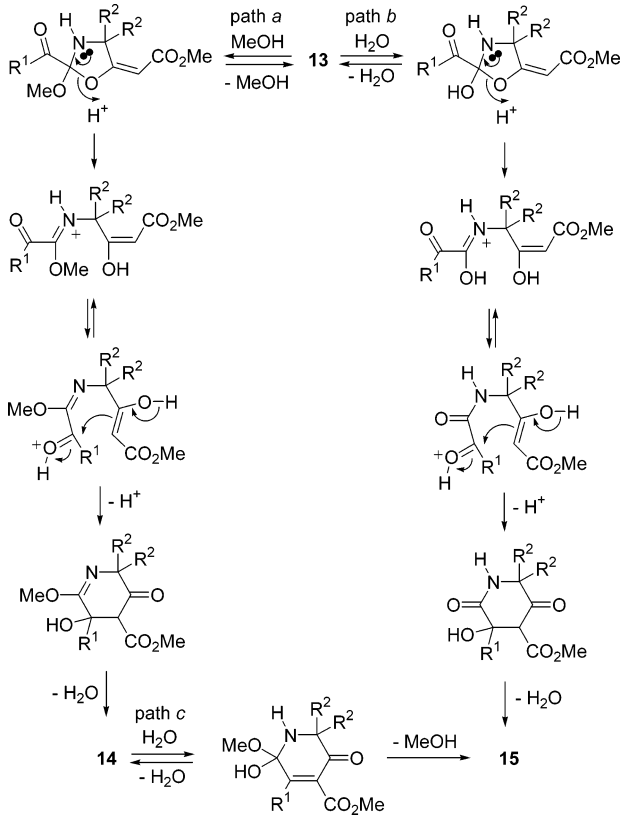
$$\mathbf{13a,a',b} \xrightarrow[\text{dioxane/H}_2\text{O, rt}]{\text{10 \% HCl}} \mathbf{15a,a',b}\ (92-96\%) \qquad (9)$$

$$\mathbf{14a,b} \xrightarrow[\text{dioxane/H}_2\text{O, rt}]{\text{10 \% HCl}} \mathbf{15a,b}\ (92-95\%) \qquad (10)$$

A likely mechanism for these transformations is shown in Scheme 7. In anhydrous MeOH, a reversible MeOH addition to the C=N double bond of **13** with formation of a 2-alkoxyoxazolidine intermediate takes place (path *a*), followed by cleavage of the endocyclic C−O bond and C−C bond formation through nucleophilic attack of the enolic *β*-carbon to the carbonyl group; elimination of water then gives **14**. A similar sequence of steps, with H_2O instead of MeOH as the initial nucleophile, accounts for the formation of **15** from **13** in aqueous dioxane (path *b*). In the latter medium, conversion of **14** into **15** is easily explained by addition of H_2O to the C=N double bond followed by MeOH elimination (path *c*).

We have ascertained that is also possible to directly convert products **13a,b** into 3,6-dioxo-1,2,3,6-tetrahydropyridines **15a,b** by Pd-catalyzed carbonylation followed by one-pot acid-catalyzed ring enlargement. Thus, the carbonylation mixture deriving from **12a** or **12b** was

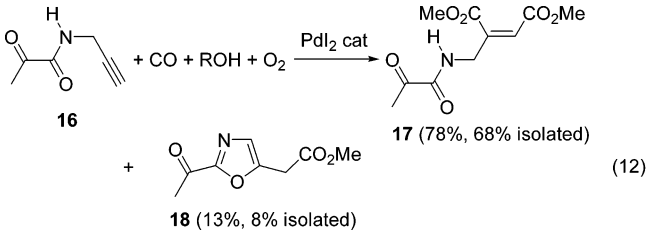
SCHEME 7



added with a solution of HCl (0.22 M in dioxane/water 4/1 v/v, 15 mL) and the resulting mixture was let to react at room temperature. After 0.5 h, **15a** or **15b** was formed as the sole product in 71% and 69% yield, respectively (eq 11) of isolated product. Thus, this procedure offers a convenient method for the one-pot synthesis of new 3,6-dioxo-pyridine derivatives starting from very simple and readily available substrates.

$$\mathbf{12a,b} \xrightarrow[\text{2) H}^+]{\text{1) CO, O}_2\text{, MeOH; PdI}_2\text{/KI}} \mathbf{15a,b}\ (71\%, 69\%) \qquad (11)$$

That geminal groups α to the triple bond direct the process toward cyclization[8] was clearly shown using 2-oxo-*N*-prop-2-ynylpropionamide **16** bearing an α-unsubstituted triple bond. The oxidative carbonylation of this substrate, carried out under the usual conditions at 70 °C for 40 h, afforded maleic diester **17** as the main product (78% yield, 68% isolated, deriving from triple bond dicarbonylation)[4] together with small amounts (13%, 8% isolated yield) of (2-acetyloxazol-5-yl)acetic acid methyl ester **18**, clearly resulting from aromatization of the initially formed oxazoline derivative (eq 12).



(12)

Conclusions

In summary, we have found a simple and efficient route for the synthesis of new heterocyclic compounds starting from readily available acetylenic derivatives.

The catalytic system, based on PdI_2 with an excess of KI in the presence of oxygen as oxidant, has proven to be particularly effective in promoting the oxidative cyclization−alkoxycarbonylation of 4-yn-1-ones, prop-2-ynyl α-ketoesters, and α-ketoamides to give different heterocyclic carbonyl compounds under mild conditions. Interestingly, in the case of prop-2-ynyl α-ketoamides, the oxidative carbonylation gave a mixture of five-membered and six-membered heterocycles, the latter deriving from an unusual rearrangement of the initially formed five-membered compounds. This rearrangement was acid-catalyzed, so the substrates could be conveniently converted in high yields into new 3,6-dioxo-1,2,3,6-tetrahydro-pyridine derivatives through a two-step, one-pot procedure corresponding to carbonylation followed by acid-catalyzed rearrangement.

Experimental Section

Preparation of Substrates. Methyl acetoacetate, methyl 2-ethylacetoacetate, 3-ethyl-2,4-pentanedione, ethyl 2-benzyl-acetoacetate, methyl cyclohexanone-2-carboxylate, ethyl benzoyl acetate, acetoacetanilide, oxalyl chloride, methyl sulfoxide, 4-pentyn-1-ol, α,α-dichloromethyl methyl ether, pyruvic acid, benzoylformic acid, prop-2-ynylamine, *N*-methylprop-2-ynylamine, 2-methyl-3-butyn-2-ol, bromoethane, and iodomethane were commercially available and were used without further purification. 1,1-Dimethylprop-2-ynylamine,[9] substrates **6a**,[10] **6b**,[11] **6c**,[11] **6d**,[11] **6e**,[11] **6f**,[12] **6g**,[11] and **6h**[11] were prepared according to the procedures reported in the literature. Alkylations of ethyl benzoyl acetate and acetoacetanilide were carried out according to a reported procedure[13] using EtBr or MeI as alkylating agents of the respective sodium enolates. Propynyl esters, secondary propynylamides of pyruvic or benzoylformic acids were prepared through standard procedures[14] starting from the respective acid chlorides obtained according a preparation reported in the literature.[15] The substrates were purified by column chromatography using suitable eluents. ^1H, ^{13}C NMR, IR, mass spectra, and elemental analyses confirmed the assigned structures (see Supporting Information).

Typical Procedure for the Oxidative Cyclization−Alkoxycarbonylation of 4-Yn-1-ones 6a−g, 2-Acetyl-2-ethylpent-4-ynoic Acid Phenylamide 6h, Prop-2-ynyl α-Ketoesters 10a,b, Prop-2-ynyl α-Ketoamides 12a,b, and 2-Oxo-*N*-prop-2-ynylpropionamide 16, and Separation of Products. All carbonylations were carried out in a 45 mL stainless steel autoclave. In a typical experiment, the autoclave was charged in the presence of air with PdI_2 (24.0 mg, 6.7×10^{-2} mmol), KI (111.0 mg, 0.7 mmol), and a solution of **6** (2.0 mmol) in MeCN/MeOH or pure MeOH as the solvent. The autoclave was pressurized at room temperature with CO (24 bar) and air (up to 32 bar) and stirred at the required temperature for the required time (see Tables 1−3 for the solvent, temperature, reaction time, and product yield for each substrate). After cooling, the autoclave was degassed and opened. The crude reaction mixture was filtered, the solvent was evaporated under vacuum and products were isolated by column chromatography (SiO_2): **7a** (4:1 hexane/AcOEt, 191 mg, 39%); **7′a** (4:1 hexane/AcOEt, 63 mg, 13%); **7b** (4:1 hexane/AcOEt, 249 mg, 65%); **7c** (3:2 hexane/AcOEt, 432 mg, 62%); **7d** (4:1 hexane/AcOEt, 347 mg, 73%); **7e** (4:1 hexane/AcOEt, 443 mg, 78%);**7f** (10:1 hexane/AcOEt, 322 mg, 65%); **7g** (10:1 hexane/AcOEt, 307 mg, 46%); **7′g** (10:1 hexane/AcOEt, 94 mg, 14%); **8b** (10:1 hexane/AcOEt, 101 mg, 21%); **9h**(*Z*) (6:1 hexane/AcOEt, 427 mg, 71%); **11a** (10:1 hexane/AcOEt, 298 mg, 61%); **11b** (10:1 hexane/AcOEt, 355 mg, 58%); **11b** (10:1 hexane/AcOEt, 312 mg, 74%); **13′a** (10:1 hexane/AcOEt, 387 mg, 81%); **13b** (10:1 hexane/AcOEt, 382 mg, 70%); **14a** (10:1 hexane/AcOEt, 23 mg, 5%); **14b** (10:1 hexane/AcOEt, 46 mg, 8%); **17** (1:1 hexane/AcOEt, 330 mg, 68%); **18** (4:1 CH_2Cl_2/AcOEt, 30 mg, 8%).

Acid-Promoted Isomerization of 9h(Z) into 9h(E). Treatment with HCl in Anhydrous Methanol. A mixture of pure (*Z*)-(4-Acetyl-4-ethyl-5-oxo-1-phenyl-pyrrolidin-2-ylidene)-acetic acid methyl ester **9h*(Z)*.** Next, (1.0 mmol) in HCl (10% weight in dry methanol, 10 mL) was stirred at room temperature for 20 min. The solution was neutralized with Na_2CO_3 and then filtered. The solvent was eliminated under reduced pressure and (*E*)-(4-acetyl-4-ethyl-5-oxo-1-phenyl-pyrrolidin-2-ylidene)-acetic acid methyl ester **9h*(E)*** (287 mg, 95%) was recovered as pure product.

Typical Procedure for the Acid-Catalyzed Rearrangement of Oxazolines 13a, 13b, 13′a, and 6-Methoxy-3-oxo-2,3-dihydropyridines 14a, 14b. Treatment with HCl in Anhydrous Methanol. A mixture of pure oxazoline **13a** or **13b** (1.0 mmol) in HCl (10% weight in dry methanol, 10 mL) was stirred at room temperature for 20 min. The solution was neutralized with Na_2CO_3 and then filtered. The solvent was eliminated under reduced pressure and 6-methoxy-3-oxo-2,3-dihydropyridines **14a** or **14b** were recovered as pure products in 96% or 92% yield, respectively.

Treatment with HCl in Dioxane/Water. A mixture of pure oxazolines **13a**, **13′a**, **13b**, or 6-methoxy-3-oxo-2,3-dihydropyridines **14a** and **14b** (1.0 mmol) respectively in HCl (0.22 M in dioxane/water 4/1 v/v, 10 mL) was stirred at room temperature for 15−20 min. The solution was neutralized with Na_2CO_3 and then extracted several times with Et_2O. The collected organic layers were dried over Na_2SO_4 and filtered, and the solvent was eliminated by rotatory evaporation. The 3,6-dioxo-1,2,3,6-tetrahydro-pyridines **15a**, **15′a**, and **15b**, respectively**,** were recovered as pure products in yields ranging from 92% to 96%: **15a** (203 mg, 96%); **15′a** (222 mg, 93%); **15b** (251 mg, 92%).

Typical Procedure for the Acid-Catalyzed Rearrangement of Crude Carbonylation Mixture of 12a or 12b. A solution of HCl (0.22 M in dioxane/water 4/1 v/v, 15 mL) was slowly added to the crude reaction mixture deriving from carbonylation of **12a,b**, and the resulting mixture was stirred at room temperature for 0.5 h. The mixture was extracted several times with Et_2O and the collected organic layers were dried over Na_2SO_4. After filtration and elimination of the solvent by rotatory evaporation, 3,6-dioxo-1,2,3,6-tetrahydro-pyridine **15a** was purified by column chromatography (SiO_2) using hexane/AcOEt 10/1 as eluent (300 mg, 71% yield based on **12a**). An analogous procedure was used for the crude mixture of the oxidative carbonylation of **12b**, to obtain pure **15b** by column chromatography (SiO_2) using hexane/AcOEt 10/1 as eluent (370 mg, 68% yield).

(8) For a review on the *gem*-dialkyl effect on cyclizations, see: Sammes, P. G.; Weller, D. J. *Synthesis* **1995**, 1205−1222.

(9) (a) Straziota, M. Ger. Offen Appl. DE 2530003, 1976; *Chem. Abstr.* **1976**, *84*, 135100n. (b) Foschi, C.; Carrillo, G.; Colombo, M. Ger. Offen Appl. DE 2600706, 1976; *Chem. Abstr.* **1976**, *85*, 142612e.

(10) Cruciani, P.; Stammler, R.; Aubert, C.; Malacria, M. *J. Org. Chem.* **1996**, *61*, 2699−2708.

(11) Polo, E.; Bellabarba, R. M.; Prini, G.; Traverso, O.; Green, M. L. H. *J. Organomet. Chem.* **1999**, *577*, 211−218.

(12) Adams, T. C.; Dupont, A. C.; Carter, J. P.; Kachur, J. F.; Guzewska, M. E.; Rzeszotarski, W. J.; Farmer, S. G.; Noronha-Blob, L.; Kaiser, C. *J. Med. Chem.* **1991**, *34*, 1585−1593.

(13) Searles, A. L.; Lindwall, H. G. *J. Am. Chem. Soc.* **1946**, *68*, 988−990.

(14) Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R. *Vogel's Textbook of Practical Organic Chemistry*, 5th ed.; Longmann Scientific & Techical; Essex, U.K., 1991; pp 698, 708.

(15) Ottenheijm, H. C. J.; de Man, J. H. M. *Synthesis* **1975**, 163−164.

Characterization of Products. All products were fully characterized by IR, ^{1}H NMR and ^{13}C spectroscopies, MS spectrometry, elemental analysis, and in the case of **14b** and **15a**, also by X-ray diffraction analysis (see Supporting Information). Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solutions at 300 and 75 MHz, respectively, with Me_4Si as internal standard. Chemical shifts and coupling constants (J) are given in ppm (δ) and in Hz, respectively. IR spectra were taken on a FT-IR spectrometer. Mass spectra were obtained at 70 eV on a GC−MS apparatus. Microanalyses were performed at our analytical laboratory.

The stereochemistry of **7g** and **7′g** was attributed on the basis of ^{1}H NMR chemical shifts of the protons of geminal CH_3 (R^2) and $CO_2CH_2CH_3$ (R^3) groups, respectively. The CH_3 protons or alternatively the $CO_2CH_2CH_3$ group ones suffer from the induced field generated by the ring current when the B_0 field is perpendicular to the plane of the vicinal phenyl ring (R^1). The geometry of the system is such that the protons in question are situated "inside" the diamagnetic circulation of electrons, undergoing an average higher-field shift. Thus it is possible to distinguish the two configurations when the phenyl and the vicinal CH_3 groups are on the same side [δ 0.86 (s) CH_3, 1.27 (t) OCH_2CH_3, 3.10 (s) OCH_3, 4.15−4.26 (m) OCH_2-CH_3] or when they are on the opposite side [δ 0.77 (t) OCH_2CH_3, 1.47 (s) CH_3, 3.09 (s) OCH_3, 3.44−3.70 (m) OCH_2-CH_3], the absorption of the OCH_3 protons being shifted at higher field of about the same value for both diastereoisomers.

2-Methoxy-5-methoxycarbonylmethylene-2-methyltetrahydrofuran-3-carboxylic Acid Methyl Ester 7a. Pale yellow oil. IR (film) ν_{max} cm^{-1} 3015 (w), 2956 (m), 1740 (s), 1719 (s), 1438 (m), 1360 (m), 1326 (m), 1265 (m), 1154 (m); ^{1}H NMR δ_H 5.33 (t, 1 H, J = 1.9), 3.74 (s, 3 H), 3.67 (s, 3 H), 3.50−3.47 (m, 1 H), 3.27 (s, 3 H), 3.37−3.23 (m, 2 H), 1.71 (s, 3 H); MS *m/z* 244 (M$^+$, 3), 212 (60), 181 (100), 153 (55), 111 (33), 69 (25), 59 (21). Anal. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found C, 53.96; H, 6.56.

2-Methoxy-5-methoxycarbonylmethylene-2-methyltetrahydrofuran-3-carboxylic Acid Methyl Ester 7′a. Pale yellow oil, impure of **7a**. IR (film) ν_{max} cm^{-1} 3015 (w), 2956 (m), 1740 (s), 1719 (s), 1438 (m), 1360 (m), 1326 (m), 1265 (m), 1154 (m); ^{1}H NMR δ_H 5.36 (t, 1 H, J = 1.8), 3.72 (s, 3 H), 3.66 (s, 3 H), 3.36−3.33 (m, 1 H), 3.31 (s, 3 H), 3.34−3.20 (m, 2 H), 1.49 (s, 3 H); MS *m/z* 244 (M$^+$, 4), 213 (80), 181 (100), 171 (38), 153 (78), 111 (70), 85 (37), 59 (30). Anal. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found C, 53.93; H, 6.54.

3-Ethyl-2-methoxy-5-methoxycarbonylmethylene-2-methyltetrahydrofuran-3-carboxylic Acid Methyl Ester 7b. Pale yellow oil. IR (film) ν_{max} cm^{-1} 2953 (s), 2884 (m), 2841 (m), 1750 (s), 1710 (s), 1646 (s), 1436 (s), 1360 (s), 1244 (s); ^{1}H NMR δ_H 5.28 (dd, 1 H, J = 2.3, 1.3), 3.67 (s, 3 H), 3.64 (s, 3 H), 3.52 (ddd, 1 H, J = 18.6, 2.3, 1.4), 3.36 (dd, 1 H, J = 18.6, 1.3), 3.20 (s, 3 H), 1.91 (qdd, 1 H, J = 13.3, 7.3, 1.4), 1.53 (s, 3 H), 1.24 (qd, 1 H, J = 13.3, 7.3), 0.79 (t, 3 H, J 7.3) (the stereochemistry of the substituents of the ring was confirmed by a 2D NOESY experiment); ^{13}C NMR δ_C 172.9, 171.4, 168.2, 111.8, 92.2, 59.8, 51.9, 50.6, 49.6, 35.2, 25.9, 14.9, 8.8; MS *m/z* 272 (M$^+$, 1), 257 (1), 225 (1), 208 (50), 180 (90), 154 (5), 149 (100), 135 (20), 121 (30), 93 (35), 77 (30), 59 (30), 53 (20). Anal. Calcd for $C_{13}H_{20}O_6$: C, 57.34; H, 7.40. Found: C, 57.26; H, 7.43.

3-Benzyl-2-methoxy-5-methoxycarbonylmethylene-2-methyltetrahydrofuran-3-carboxylic Acid Ethyl Ester 7c. Pale yellow oil. IR (film) ν_{max} cm^{-1} 2981 (s), 2945 (s), 2832 (m), 1744 (s), 1713 (s), 1654 (s), 1598 (m), 1437 (s); ^{1}H NMR δ_H 7.26−7.23 (m, 3 H), 7.02−6.98 (m, 2 H), 5.40 (dd, 1 H, J = 2.3, 1.3), 4.21−4.09 (m, 2 H) 3.68 (s, 3 H), 3.41 (d, 1 H, J = 18.0, 1.3), 3.38 (d, 1 H, J = 12.9), 3.36 (dd, 1 H, J = 18.0, 2.3), 3.27 (s, 3 H), 2.38 (d, 1 H, J = 12.9), 1.70 (s, 3 H), 1.20 (t, 3 H, J = 7.2) (the stereochemistry of the substituents of the ring was confirmed by a 2D NOESY experiment); ^{13}C NMR δ_C 172.4, 170.5, 168.0, 135.6, 129.8, 128.4, 127.0, 111.7, 92.6, 60.9, 60.2, 50.6, 49.8, 38.7, 34.8, 15.0, 13.9; MS *m/z* 348 (M$^+$, 1), 317 (5), 316 (10), 285 (5), 257 (10), 243 (10), 225 (90), 197 (5), 179 (5), 165 (5), 141 (5), 115 (5), 91 (100), 69 (5), 59 (5). Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.42; H, 7.00.

(4-Acetyl-4-ethyl-5-methoxy-5-methyldihydrofuran-2-ylidene)acetic Acid Methyl Ester 7d. Pale yellow oil. IR (film) ν_{max} cm^{-1} 2972 (m), 1711 (s), 1654 (s), 1462 (m), 1437 (s), 1360 (s), 1284 (m), 1138 (s); ^{1}H NMR δ_H 5.34 (dd, 1 H, J = 2.4, 1.3), 3.69 (s, 3 H), 3.52 (ddd, 1 H, J = 18.3, 2.3, 1.6), 3.44 (dd, 1 H, J = 18.3, 1.3), 3.25 (s, 3 H), 2.19 (s, 3 H), 1.94 (qdd, 1 H, J = 13.5, 7.4, 1.6), 1.59 (s, 3 H), 1.30 (qd, 1 H, J = 13.5, 7.4), 0.81 (t, 3 H, J = 7.4) (the stereochemistry of the substituents of the ring was confirmed by a 2D NOESY experiment); ^{13}C NMR δ_C 206.2, 172.9, 168.4, 112.17, 92.0, 63.9, 50.7, 49.5, 35.3, 28.8, 25.8, 15.5, 8.6; MS *m/z* 256 (M$^+$, 1), 241 (1), 225 (10), 195 (5), 182 (100), 167 (30), 151 (20), 139 (10), 123 (20), 113 (50), 101 (40), 79 (10), 69 (15), 55 (15). Anal. Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 60.84; H, 7.92.

7a-Methoxy-2-methoxycarbonylmethylenehexahydrobenzofuran-3a-carboxylic Acid Methyl Ester 7e. Colorless oil. IR (film) ν_{max} cm^{-1} 2948 (s), 1759 (s), 1652 (s), 1462 (m), 1435 (s), 1368 (s), 1360 (s), 1330 (m), 1292 (m), 1277 (s), 1237 (s), 1188 (m), 1156 (m), 1124 (s), 1105 (s), 1079 (m), 1040 (s), 994 (s); ^{1}H NMR δ_H 5.34 (dd, 1 H, J = 2.3, 1.0), 3.65 (s, 3 H), 3.61 (s, 3 H), 3.46 (dd, 1 H, J = 18.0, 2.3), 3.18 (s, 3 H), 3.17 (d, broad, 1 H, J = 18.0), 2.26 (d, broad, 1 H, J = 13.3), 1.87−1.58 (m, 4 H), 1.44 (d, broad, 1 H, J = 13.3), 1.33−1.15 (m, 2 H); ^{13}C NMR δ_C 172.7, 171.6, 168.1, 109.1, 93.1, 53.1, 51.7, 50.6, 48.9, 40.3, 33.7, 26.8, 21.4, 20.6; MS *m/z* 284 (M$^+$, 2), 252 (23), 237 (2), 221 (30), 194 (13), 193 (100), 168 (63), 153 (19), 137 (45), 109 (24), 101 (11), 91 (15), 69 (15), 55 (10). Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.14; H, 7.09. Found: C, 59.05; H, 7.16.

(5-Methoxy-5-phenyl-dihydrofuran-2-ylidene)acetic Acid Methyl Ester 7f. Pale yellow oil. IR (film) ν_{max} cm^{-1} 2993 (w), 2945 (m), 2834 (w), 1745 (w), 1708 (s), 1650 (s), 1434 (s), 1359 (s), 1324 (m), 1269 (m), 1245 (m), 1189 (m), 1115 (s), 1041 (s), 972 (s), 700 (s); ^{1}H NMR δ_H 7.46−7.31 (m, 5 H), 5.54 (dd, 1 H, J = 1.8, 1.5), 3.69 (s, 3 H), 3.40−3.29 (m, 1 H), 3.26−3.13 (m, 1 H), 3.11 (s, 3 H), 2.53−2.45 (m, 1 H), 2.08−1.97 (m, 1 H); ^{13}C NMR δ_C 175.4, 168.5, 138.5, 128.5, 128.4, 125.7, 112.6, 91.4, 50.9, 50.6, 38.1, 29.8; MS *m/z* 248 (M$^+$, 19), 230 (3), 216 (47), 201 (23), 187 (4), 185 (10), 159 (40), 147 (100), 129 (17), 115 (33), 101 (54), 91 (10), 77 (56), 69 (25). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.65; H, 6.55.

2-Methoxy-5-methoxycarbonylmethylene-3-methyl-2-phenyltetrahydrofuran-3-carboxylic Acid Ethyl Ester 7g. Colorless oil; IR (film) ν_{max} cm^{-1} 2981 (m), 2946 (m), 1736 (s), 1732 (s), 1712 (s), 1450 (m), 1436 (m), 1360 (s), 1301 (m), 1273 (m), 1125 (s), 1039 (s), 983 (s); ^{1}H NMR δ_H 7.50−7.47 (m, 2 H), 7.39−7.36 (m, 3 H), 5.54 (dd, 1 H, J = 2.4, 1.3), 4.26−4.15 (m, 2 H) 3.94 (dd, 1 H, J = 18.3, 2.4), 3.70 (s, 3 H), 3.34 (dd, 1 H, J = 18.3, 1.3), 3.10 (s, 3 H), 1.27 (t, 3 H, J = 7.1), 0.86 (s, 3 H); ^{13}C NMR δ_C 172.6, 171.2, 168.3, 133.5, 129.0, 128.2, 127.7, 113.3, 92.8, 61.1, 55.6, 51.3, 50.9, 40.3, 22.0, 14.0; MS *m/z* 334 (M$^+$, 1), 319 (2), 302 (45), 289 (15), 271 (8), 229 (100), 137 (15), 105 (15), 77 (9). Anal. Calcd for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63. Found: C, 64.59; H, 6.67.

2-Methoxy-5-methoxycarbonylmethylene-3-methyl-2-phenyltetrahydrofuran-3-carboxylic Acid Ethyl Ester 7′g. Colorless oil. IR (film) ν_{max} cm^{-1} 2982 (m), 2946 (m), 1737 (s), 1732 (s), 1712 (s), 1450 (m), 1436 (m), 1360 (s), 1299 (m), 1211 (m), 1125 (s), 1039 (s), 983 (s); ^{1}H NMR δ_H 7.50−7.46 (m, 2 H), 7.37−7.31 (m, 3 H), 5.52 (dd, 1 H, J = 2.3, 1.3), 3.81 (dd, 1 H, J = 17.8, 1.3), 3.68 (s, 3 H), 3.70−3.44 (m, 2 H) 3.09 (s, 3 H), 2.59 (dd, 1 H, J = 17.8, 2.3), 1.47 (s, 3 H) 0.77 (t, 3 H, J = 7.1); ^{13}C NMR δ_C 173.7, 172.3, 168.5, 134.4, 129.0, 128.1, 126.7, 111.8, 91.5, 60.9, 57.4, 50.8, 50.7, 41.4, 16.3, 13.3; MS *m/z* 334 (M$^+$, 1), 319 (2), 302 (45), 289 (15), 271 (8), 229 (100),

137 (15), 105 (15), 77 (9). Anal. Calcd for $C_{18}H_{22}O_6$: C, 64.66; H, 6.63. Found: C, 64.60; H, 6.68.

3-Ethyl-2-methyl-5-oxocyclopent-1-ene-1,3-dicarboxylic Acid Dimethyl Ester 8b. Colorless oil. IR (film) ν_{max} cm^{-1} 2955 (m), 1713 (s), 1632 (s), 1435 (m), 1328 (m), 1233 (s), 1018 (m); ^{1}H NMR δ_H 3.80 (s, 3 H), 3.67 (s, 3 H), 2.90 (d, 1 H, J = 18.6), 2.36 (d, 1 H, J = 18.6), 2.24 (s, 3 H), 2.14−2.04 (m, 1 H), 1.81−1.70 (m, 1 H), 0.77 (t, 3 H, J = 7.4); ^{13}C NMR δ_C 200.4, 182.6, 172.4, 163.1, 133.2, 56.9, 52.8, 52.0, 43.6, 27.1, 15.2, 8.4; MS *m/z* 240 (M$^+$, 10), 225 (1), 212 (35), 208 (50), 181 (55), 180 (92), 154 (5), 149 (100), 135 (15), 121 (27), 107 (5), 93 (32), 77 (20), 59 (28). Anal. Calcd for $C_{12}H_{16}O_5$: C, 59.99; H, 6.71. Found: C, 59.90; H, 6.75.

(*Z*)-(4-Acetyl-4-ethyl-5-oxo-1-phenylpyrrolidin-2-ylidene)acetic Acid Methyl Ester 9h (*Z*). Pale yellow oil. IR (film) ν_{max} cm^{-1} 2971 (m), 1714 (s), 1650 (s), 1594 (m), 1434 (m), 1360 (m), 1124 (s), 1071 (s); ^{1}H NMR δ_H 7.31 (t, 2 H, J = 7.8), 7.14−7.06 (m, 3 H), 5.55 (t, 1 H, J = 2.0), 4.00 (dd, 1H, J = 19.3, 2.0), 3.68 (s, 3 H), 3.04 (dd, 1H, J = 19.3, 2.0), 2.42 (s, 3 H), 2.21−2.01 (m, 2 H), 0.96 (t, 3 H, J = 7.4); ^{13}C NMR δ_C 203.0, 168.0, 167.1, 156.5, 144.6, 128.7, 125.0, 122.5, 95.4, 60.5, 51.2, 33.4, 29.3, 25.1, 8.8; MS *m/z* 301 (M$^+$, 38), 273 (100), 259 (66), 241 (49), 226 (50), 212 (34), 198 (65), 158 (88), 144 (49), 104 (48), 77 (89), 59 (5). Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.66; H, 6.40; N, 4.60.

(*E*)-(4-Acetyl-4-ethyl-5-oxo-1-phenylpyrrolidin-2-ylidene)acetic Acid Methyl Ester 9h (*E*). Pale yellow oil. IR (film) ν_{max} cm^{-1} 2969 (m), 1736 (s), 1710 (s), 1628 (s), 1596 (w), 1496 (m), 1437 (m), 1400 (m), 1346 (m), 1167 (s), 1145 (s); ^{1}H NMR δ_H 7.53−7.41 (m, 3 H), 7.16−7.13 (m, 2 H), 5.04 (t, 1 H, J = 2.0), 4.06 (dd, 1 H, J = 19.4, 2.0), 3.67 (s, 3 H), 3.17 (dd, 1 H, J = 19.4, 2.0), 2.39 (s, 3 H), 2.17−2.08 (m, 2 H), 0.98 (t, 3 H, J = 7.5); ^{13}C NMR δ_C 203.2, 174.6, 167.4, 158.0, 133.6, 129.9, 129.3, 127.4, 93.8, 61.7, 50.9, 32.1, 28.5, 26.0, 8.7; MS *m/z* 301 (M$^+$, 6), 270 (8), 258 (100), 244 (33), 226 (47), 200 (19), 77 (18). Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.69; H, 6.38; N, 4.60.

(2-Acetyl-2-methoxy-5,5-dimethyl-[1,3]dioxolan-4-ylidene)acetic Acid Methyl Ester 11a. Colorless oil. IR (film) ν_{max} cm^{-1} 2986 (m), 1748 (s), 1719 (s), 1655 (s), 1438 (m), 1384 (s), 1359 (s), 1206 (s), 1128 (s), 1049 (s); ^{1}H NMR δ_H 5.44 (s, 1 H), 3.64 (s, 3 H), 3.37 (s, 3 H), 2.25 (s, 3 H), 1.79 (s, 3 H), 1.63 (s, 3 H); ^{13}C NMR δ_C 197.7, 172.5, 166.2, 117.1, 90.0, 86.3, 50.9, 49.2, 24.8, 24.3; MS *m/z* 244 (M$^+$, absent), 213 (3), 201 (95), 169 (16), 143 (47), 125 (60), 111 (40), 84 (25), 69 (100), 59 (32). Anal. Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 54.00; H, 6.65.

(2-Benzoyl-2-methoxy-5,5-dimethyl-[1,3]dioxolan-4-ylidene)acetic Acid Methyl Ester 11b. Colorless oil. IR (film) ν_{max} cm^{-1} 2984 (w), 2949 (w), 1713 (s), 1659 (s), 1384 (m), 1360 (m), 1133 (s); ^{1}H NMR δ_H 8.12 (dd, 2 H, J = 7.5, 1.4), 7.59 (td, 1 H, J = 7.5, 1.4), 7.46 (td, 2 H, J = 7.5, 1.4), 5.55 (s, 1 H), 3.67 (s, 3 H), 3.49 (s, 3 H), 1.88 (s, 3 H), 1.62 (s, 3 H); ^{13}C NMR δ_C 188.9, 172.3, 166.3, 133.7, 132.3, 130.5, 128.2, 90.3, 86.5, 51.0, 49.3, 24.9, 24.8; MS *m/z* 306 (M$^+$, absent), 275 (1), 247 (5), 201 (100), 169 (20), 142 (20), 125 (40), 105 (57), 77 (30), 69 (29), 59 (12). Anal. Calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.63; H, 5.95.

(2-Acetyl-4,4-dimethyl-4*H*-oxazol-5-ylidene)acetic Acid Methyl Ester 13a. Pale yellow oil. IR (film) ν_{max} cm^{-1} 2975 (w), 2942 (w), 1721 (s), 1669 (s), 1350 (m), 1166 (m), 1078 (s); ^{1}H NMR δ_H 5.78 (s, 1 H), 3.70 (s, 3 H), 2.56 (s, 3 H), 1.71 (s, 6 H); ^{13}C NMR δ_C 188.4, 176.3, 166.0, 154.3, 96.0, 73.8, 51.2, 26.7, 24.2; MS *m/z* 211 (M$^+$, 16), 180 (15), 168 (17), 141 (56), 110 (33), 84 (31), 69 (100), 59 (16). Anal. Calcd for $C_{10}H_{13}NO_4$: C, 56.86; H, 6.20; N, 6.63. Found: C, 56.80; H, 6.18; N, 6.57.

(2-Acetyl-4,4-dimethyl-4*H*-oxazol-5-ylidene)acetic Acid Propyl Ester 13′a. Pale yellow oil. IR (film) ν_{max} cm^{-1} 2975 (m), 2940 (m), 1721 (s), 1668 (s), 1461 (m), 1350 (m), 1166 (s), 1075 (s); ^{1}H NMR δ_H 5.74 (s, 1 H), 4.02 (t, 2 H, J 6.7), 2.52 (s, 3 H), 1.67 (s, 6 H) 1.67−1.59 (m, 2 H), 0.91 (t, 3 H, J 7.5); ^{13}C NMR δ_C 188.4, 176.0, 165,7, 154.3, 96.5, 73.7, 65.7, 26.7, 24.3, 21.9, 10.2; MS *m/z* 239 (M$^+$, 5), 224 (5), 198 (30), 180 (35), 154 (10), 128 (100), 111 (60), 87 (20), 83 (40), 69 (100), 59 (90). Anal. Calcd for $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; N, 5.85. Found: C, 60.16; H, 7.10; N, 5.79.

(2-Benzoyl-4,4-dimethyl-4*H*-oxazol-5-ylidene)acetic Acid Methyl Ester 13b. Pale yellow oil. IR (film) ν_{max} cm^{-1} 2974 (w), 1716 (m), 1664 (s), 1596 (m), 1578 (m), 1353 (m), 1200 (m), 1171 (m), 1101 (m); ^{1}H NMR δ_H 8.31 (dd, 2 H, J = 7.3, 1.4), 7.64 (td, 1 H, J = 7.3, 1.4), 7.49 (t, 2 H, J = 7.3), 5.84 (s, 1 H), 3.71 (s, 3 H), 1.79 (s, 6 H); ^{13}C NMR δ_C 181.1, 175.8, 166.2, 153.4, 134.7, 134.1, 130.7, 128.6, 95.8, 74.4, 51.3, 24.4; MS *m/z* 273 (M$^+$, 1), 186 (4), 142 (3), 105 (100), 77 (40), 69 (10), 59 (1), 51 (10). Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.84; H, 5.55; N, 5.08.

6-Methoxy-2,2,5-trimethyl-3-oxo-2,3-dihydropyridine-4-carboxylic Acid Methyl Ester 14a. Colorless oil. IR (film) ν_{max} cm^{-1} 2979 (m), 2951 (m), 1745 (s), 1659 (s), 1627 (s), 1439 (m), 1346 (s), 1259 (s), 1067 (s); ^{1}H NMR δ_H 3.75 (s, 3 H), 3.65 (s, 3 H), 1.96 (s, 3 H), 1.24 (s, 6 H); ^{13}C NMR δ_C 201.7, 164.9, 154.3, 140.4, 134.0, 64.6, 53.1, 52.1, 27.5, 15.2; MS *m/z* 225 (M$^+$, 6), 210 (18), 193 (100), 178 (98), 150 (46), 138 (26), 84 (30), 67 (58), 59 (8), 56 (24). Anal. Calcd for $C_{11}H_{15}NO_4$: C, 58.66; H, 6.71; N, 6.22. Found: C, 58.60; H, 6.75; N, 6.14.

6-Methoxy-2,2-dimethyl-3-oxo-5-phenyl-2,3-dihydropyridine-4-carboxylic Acid Methyl Ester 14b. Pale yellow solid, mp 94−95 °C. IR (KBr) ν_{max} cm^{-1} 2920 (w), 1738 (m), 1650 (s), 1613 (m), 1428 (w), 1292 (m), 1019 (m); ^{1}H NMR δ_H 7.34−7.41 (m, 5 H), 3.73 (s, 3 H), 3.58 (s, 3 H), 1.47 (s, 6 H); ^{13}C NMR δ_C 202.5, 164.7, 153.4, 141.1, 134.6, 132.1, 129.5, 128.5, 128.0, 65.1, 53.6, 52.3, 28.1; MS *m/z* 272 ((M-15)$^+$, 2), 255 (100), 240 (95), 212 (15), 200 (20), 156 (7), 129 (55), 115 (10), 84 (20), 75 (10), 56 (20). Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.88. Found: C, 66.79; H, 6.03; N, 4.81.

2,2,5-Trimethyl-3,6-dioxo-1,2,3,6-tetrahydropyridine-4-carboxylic Acid Methyl Ester 15a. Colorless solid, mp 121 °C; IR (KBr) ν_{max} cm^{-1} 3200 (m), 3086 (w), 1741 (s), 1685 (m), 1670 (s), 1623 (m), 1332 (s), 1208 (m); ^{1}H NMR δ_H 7.93 (s, 1 H), 3.84 (s, 3 H), 2.08 (s, 3 H), 1.43 (s, 6 H); ^{13}C NMR δ_C 193.9, 164.5, 161,7, 146.5, 135.7, 61.8, 52.6, 27.9, 15.3; MS *m/z* 211 (M$^+$, 15), 196 (4), 180 (20), 154 (75), 126 (35), 96 (70), 67 (100). Anal. Calcd for $C_{10}H_{13}NO_4$: C, 56.86; H, 6.20; N, 6.63. Found: C, 56.80; H, 6.25; N, 6.58.

2,2,5-Trimethyl-3,6-dioxo-1,2,3,6-tetrahydropyridine-4-carboxylic Acid Propyl Ester 15′a. Pale yellow oil. IR (film) ν_{max} cm^{-1} 3445 (s), 2974 (w), 2928 (w), 1733 (s), 1675 (s), 1634 (s), 1237 (m), 1210 (m); ^{1}H NMR δ_H 6.31 (s, 1 H), 4.28 (t, 2 H, J = 6.7), 2.16 (s, 3 H), 1.79−1.69 (m, 2 H), 1.49 (s, 6 H), 0.99 (t, 3 H, J = 7.5); ^{13}C NMR δ_C 193.5, 164.1, 161,3, 146.2, 136.1, 67.6, 62.0, 28.3, 21.9, 15.2, 10.2; MS *m/z* 239 (M$^+$, 12), 196 (12), 182 (18), 181 (16), 140 (10), 112 (20), 67 (19). Anal. Calcd for $C_{12}H_{17}NO_4$: C, 60.24; H, 7.16; N, 5.85. Found: C, 60.16; H, 7.18; N, 5.79.

2,2-Dimethyl-3,6-dioxo-5-phenyl-1,2,3,6-tetrahydropyridine-4-carboxylic Acid Methyl Ester 15b. Colorless oil. IR (film) ν_{max} cm^{-1} 3242 (m), 2919 (m), 1738 (s), 1732 (s), 1682 (s), 1614 (m), 1434 (m), 1171 (m), 1333 (m), 1165 (m); ^{1}H NMR δ_H 7.41−7.43 (m, 5 H), 6.32 (s, broad, 1 H), 3.64 (s, 3 H), 1.57 (s, 6 H); ^{13}C NMR δ_C 194.8, 164.3, 160.5, 146.7, 135.8, 131.7, 130.2, 129.0, 128.1, 62.3, 52.6, 28.3; MS *m/z* 273 (M$^+$, 4), 241 (5), 216 (50), 201 (10), 188 (30), 173 (4), 160 (40), 129 (100), 102 (60), 75 (20), 51 (10). Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.85; H, 5.56; N, 5.05.

2-[(2-Oxopropionylamino)methyl]but-2-enedioic Acid Dimethyl Ester 17. Colorless oil. IR (film) ν_{max} cm^{-1} 3364 (m), 3009 (w), 2957 (m), 1726 (s), 1686 (s), 1526 (m), 1438 (m), 1271 (s), 1174 (m); ^{1}H NMR δ_H 7.44 (s, 1 H), 6.00 (t, 1 H, J = 6.1), 4.10 (d, 2 H, J = 6.1), 3.74 (s, 3 H), 3.66 (s, 3 H), 2.39 (s, 3 H); ^{13}C NMR δ_C 196.2, 166.5, 165.4, 160.2, 129.8, 123.3, 52.5, 51.9, 40.9, 24.2; MS *m/z* 243 (M$^+$, 1), 212 (5), 200 (40), 172 (10), 168 (100), 142 (40), 126 (20), 98 (20), 59 (30). Anal. Calcd for $C_{10}H_{13}NO_6$: C, 49.38; H, 5.39; N, 5.76. Found: C, 49.32; H, 5.41; N, 5.70.

(2-Acetyloxazol-5-yl)acetic Acid Methyl Ester 18. Colorless oil. IR (film) ν_{max} cm^{-1} 2957 (m), 2918 (m), 2851 (m), 1740 (vs), 1704 (s), 1508 (m), 1232 (m), 1120 (m); ^1H NMR δ_H 7.21 (t, 1 H, $J = 0.7$), 3.82 (d, 2 H, $J = 0.7$), 3.75 (s, 3 H), 2.65 (s, 3 H); ^{13}C NMR δ_C 185.5, 167.8, 157.7, 148.6, 127.4, 52.6, 31.5, 26.3; MS *m/z* 183 (M^+, 100), 168 (5), 141 (15), 139 (10), 124 (60), 109 (10), 97 (10), 82 (90), 68 (15), 59 (30), 52 (5). Anal. Calcd for $C_8H_9NO_4$: C, 52.46; H, 4.95; N, 7.65. Found: C, 52.45; H, 5.01; N, 7.58.

Acknowledgment. Financial support from the Ministero dell'Università e della Ricerca Scientifica e Tecnologica is aknowledged (Progetto d'Interesse Nazionale PIN MM03027791). The facilities of Centro Interfacoltà di Misure (Università di Parma) were used for recording NMR spectra.

Supporting Information Available: Structures of **14b** and **15a** (Figures S1 and S2, respectively); X-ray structural information for **14b** and **15a** (Tables S1 and S2); spectroscopic characterization of **6b**−**h**, **10a,b**, **12a,b**, and **16** substrates; crystallographic data for **14b** and **15a** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

JO050155V