Palladium-Catalyzed Reaction of Vinyl Triflates and Vinyl/Aryl Halides with 4-Alkynoic Acids: Regio- and Stereoselective Synthesis of (*E*)-δ-Vinyl/aryl-γ-methylene-γ-butyrolactones

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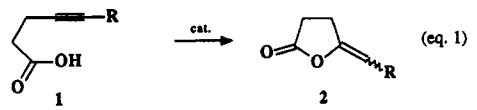
The palladium-catalyzed reaction of vinyl triflates and vinyl/aryl halides with 4-pentynoic acid, 2,2-disubstituted 4-pentynoic acids, and 5-substituted 4-pentynoic acids produced regio- and stereoselectively the corresponding (*E*)-δ-vinyl/aryl-γ-methylene-γ-butyrolactones in good to high yield. Reactions were carried out in the presence of catalytic amounts of $Pd(OAc)_2(PPh_3)_2$ or $Pd(PPh_3)_4$, Et_3N, and *n*-Bu_4NCl. The presence of chloride anions was found to be necessary to obtain the best results. The proposed mechanism involves an intramolecular nucleophilic attack of the carboxylate anion on the palladium-coordinated carbon-carbon triple bond and subsequent reductive elimination of Pd(0) species from the resulting σ-vinylpalladium complex which regenerates the catalyst and releases the exocyclic enol lactone.

In recent years, several synthetic approaches to exocyclic enol lactones **2** based on transition metal-catalyzed cyclization of 4-alkynoic acids **1** have been reported (eq 1).[1-6]



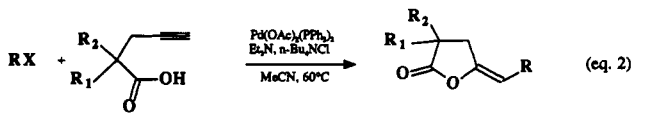
(eq. 1)

1 **2**

Interest in these compounds arises from the biological activities[7] that a number of natural products containing this moiety show and from their utility as synthetic intermediates.[5b]

Best results in terms of reaction conditions and regio- and stereoselectivity have been obtained by using palladium[5] and rhodium[6] catalysts. Anti oxymetalation of the coordinated carbon–carbon triple bond producing five-membered rings was always found to be the preferred reaction pathway.

As part of our ongoing interest in developing methods for the preparation of five-membered oxygen heterocycles,[8] and based on the results obtained in the palladium-catalyzed reactions of organic triflates with 1-alkynes,[9] we decided to explore the use of 4-pentynoic acid and vinyl triflates as building blocks for the preparation of functionalized δ-vinyl-γ-methylene-γ-butyrolactones. Since vinyl triflates can be easily prepared from a wide variety of ketones,[10] this process may be expected to broaden the scope of the transition metal-catalyzed approach to this class of compounds. This transformation has now been actually achieved, and a variety of vinyl triflates (and aryl/vinyl halides) **3** were found to react with 4-pentynoic acid **4** in the presence of Et_3N, *n*-Bu_4NCl, and catalytic amounts of $Pd(OAc)_2(PPh_3)_2$ to give regio- and stereoselectively (*E*)-δ-vinyl/aryl-γ-methylene-γ-butyrolactones **6** (eq 2).



(eq. 2)

3 **4**: $R_1 = R_2 = H$; **5**: $R_1 = COOMe$; R_2 = alkyl — **6**: $R_1 = R_2 = H$; **7**: $R_1 = COOMe$; R_2 = alkyl

R = vinyl, aryl; X = OTf, I, Br

Reaction of 4-Pentynoic Acid (4) with Vinyl Triflates and Aryl Halides (3). A variety of *exo*-enol lactones **6** were prepared by reacting vinyl triflates in MeCN with 1.5 equiv of 4-pentynoic acid, 1.5 equiv of *n*-Bu_4NCl, and 0.05 equiv of $Pd(OAc)_2(PPh_3)_2$ in the presence of Et_3N at 60 °C. $Pd(OAc)_2/2PPh_3$ can also be used as a catalyst. Reactions were usually fast (10–100 min). Reaction conditions were by no means optimized; however, we observed that the presence of *n*-Bu_4NCl strongly affects the reaction course. For example, reacting **3f** under usual conditions produced the corresponding enol lactone **6f** in 74% yield (Table I, entry 6) while in the absence of the ammonium salt the enol lactone **6f** was isolated in 20% yield (45 min).

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(1) For the use of silver nitrate see: (a) Castaner, J.; Pascual, J. *J. Chem. Soc.* **1958**, 3962. (b) Willioard, P. G.; Jong, T. T.; Porwoll, J. P. *J. Org. Chem.* **1984**, *49*, 736.

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(5) For the use of palladium catalysts see: (a) Lambert, C.; Utimoto, K.; Nozaki, H. *Tetrahedron Lett.* **1984**, *25*, 5323. (b) Yanagihara, N.; Lambert, C.; Iritani, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 2753. (c) Tsuda, T.; Ohashi, Y.; Nagahama, N.; Sumiya, R.; Saegusa, T. *J. Org. Chem.* **1988**, *53*, 2650.

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(7) See for example: (a) Kupchan, S. M.; Britto, R. W.; Ziegler, M. P.; Gilmore, C. J.; Restivo, R. G.; Bryan, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 1335. (b) Niwa, M.; Iguchi, M.; Yamamura, S. *Tetrahedron Lett.* **1975**, 4395. (c) Amos, R. A.; Katzenellenbogen, J. A. *J. Org. Chem.* **1978**, *43*, 560. (d) Yamamoto, M. *J. Chem. Soc., Perkin Trans. 1* **1982**, 582. (e) Mason, C. P.; Edwards, K. R.; Carlson, R. E.; Pignatello, J.; Gleason, F. K.; Wood, J. M. *Science (Washington, D.C.)* **1982**, *215*, 400.

(8) (a) Arcadi, A.; Cacchi, S.; Marinelli, F. *Synthesis* **1986**, 749. (b) Arcadi, A.; Bernocchi, E.; Burini, A.; Cacchi, S.; Marinelli, F.; Pietroni, B. *Tetrahedron* **1988**, *44*, 481. (c) Arcadi, A.; Burini, A.; Cacchi, S.; Delmastro, M.; Marinelli, F.; Pietroni, B. *Synlett.* **1990**, 47. (d) Arcadi, A.; Bernocchi, E.; Cacchi, S.; Marinelli, F. *Synlett.* **1991**, 27. (e) Arcadi, A.; Bernocchi, E.; Cacchi, S.; Marinelli, F. *Tetrahedron* **1991**, *47*, 1525.

(9) (a) Cacchi, S.; Morera, E.; Ortar, G. *Synthesis* **1986**, 319. (b) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1989**, *30*, 2581.

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The starting triflate was recovered in 20% yield and only traces, if any, of 5-(4-phenylcyclohex-1-en-1-yl)-4-pentynoic acid were detected. Vinyl triflates were indeed reported to react with 1-alkynes in the presence of catalytic amounts of palladium to give conjugated enynes[9a] and these compounds could be reasonably expected as possible products or by-products of the reaction.

Essentially the same result was obtained changing the solvent from MeCN to DMSO (in the absence of *n*-Bu_4NCl, **6f** was isolated in 25% yield). Even the amount of *n*-Bu_4NCl appears to be critical. Compound **6f** was isolated in only 59% yield in the presence of 1.0 equiv of *n*-Bu_4NCl. The starting material was recovered in 12% yield. The results obtained with vinyl triflates are summarized in Table I (entries 1–6).

As an example of vinyl halides, we reacted a commercially available *E*/*Z* mixture of β-bromostyrene. As found in other palladium-catalyzed reactions,[11] only the product containing the *E*-styryl moiety was isolated in good yield (Table I, entry 7). In this case best results were obtained in the presence of 3 equiv of pentynoic acid. Under usual conditions compound **6g** was isolated in 49% yield.

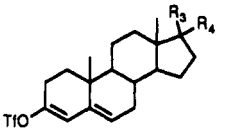
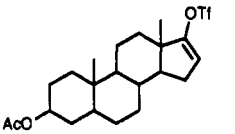
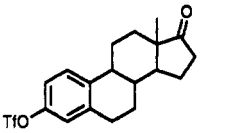
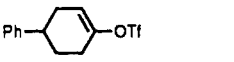
Attempts were made to extend the reaction to aryl triflates. However, at least with our model system, unsatisfactory results were obtained. Indeed, under usual conditions, compound **3e** was converted into the corresponding lactone **6e** in 20% yield (1.25 h). The starting triflate was recovered in 65% yield. Similar results were obtained using diphenylphosphinoferrocene (dppf) as the ligand (**6e**: 17% yield; recovered **3e**; 69% yield) or DMSO as the solvent (**6e**: 23% yield; recovered **3e**: 62% yield). A moderate increase of the yield was observed when the reaction was carried out in DMF at 80 °C (1.25 h) and the lactone **6e** was isolated in 39% yield (the starting triflate was recovered in 42% yield). Aryl halides afforded better results (Table I, entries 8–12).

Reaction of Vinyl Triflates with 2,2-Disubstituted 4-Pentynoic Acids (5). The efficiency of this new route to exocyclic enol lactones was also tested by using a variety of substituted 4-pentynoic acids, i.e., 2,2-disubstituted 4-pentynoic acids **5** and 5-substituted 4-pentynoic acids **8**. Compounds **5** were easily prepared in good to high yield from Meldrum's acid[12] and their cyclization was carried out as usual. The results are summarized in Table II. High reaction rates were usually observed (5–40 min). Compounds **7** were isolated as mixtures of diastereoisomers, and no attempts were made to separate them. For example, **7b** was isolated as an about 70/30 diastereoisomeric mixture (based on ^1H NMR analysis (300 MHz) of the methylene protons of the butyrolactone ring).

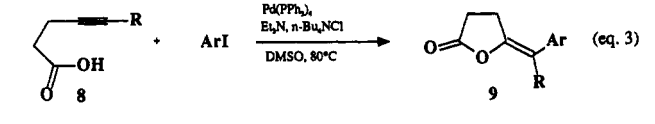
As found with 4-pentynoic acid, treatment of model aryl triflate **3e** under usual conditions with 2-methyl-2-carbomethoxy-4-pentynoic acid produced the corresponding exocyclic enol lactone in low yield (24%; 1.5 h). The starting triflate was recovered in 66% yield.

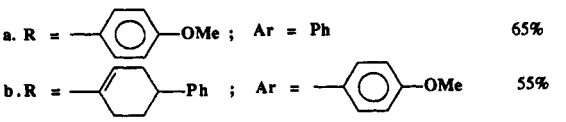
Reaction of Aryl Iodides with 5-Substituted 4-Pentynoic Acids (8). Compounds **8**[13] were reacted with aryl iodides in the presence of $Pd(PPh_3)_4$ at 80 °C. The corresponding enol lactones **9** were isolated in good yield (eq 3). The presence of a substituent on the C-5 of 4-pentynoic acid, at least with the examples we tested, does not change the regiochemical trend of the reaction.

Table I. Palladium-Catalyzed Reaction of Vinyl/Aryl Triflates and Halides with 4-Pentynoic Acid 4 (eq 2; R_1 = R_2 = H)[a]

entry	compd 3	reaction time (min)	yield (%) of 6[b]
1	 **3a**, R_3 = R_4 = O	20	**6a**, 63
2	**3b**, R_3 = β-OAc, R_4 = H	20	**6b**, 74
3	**3c**, R_3 = β-Ac, R_4 = H	20	**6c**, 73
4	 **3d**	100	**6d**, 60
5	 **3e**	85	**6e**, 39[c]
6	 **3f**	45	**6f**, 74
7	 **3g**	55	**6g**, 74[d,e]
8	4-$MeOC_6H_4I$ (**3h**)	30	**6h**, 70
9	4-$MeCOC_6H_4Br$ (**3i**)	20	**6i**, 60
10	4-$MeOCOC_6H_4I$ (**3j**)	20	**6j**, 60
11	4-$MeCONHC_6H_4I$ (**3k**)	15	**6k**, 74
12	PhI (**3l**)	10	**6l**, 82

[a] Unless otherwise stated, reactions were carried out at 60 °C in MeCN in the presence of Et_3N under an argon atmosphere using the following molar ratios: 3:4:*n*-Bu_4NCl:$Pd(OAc)_2(PPh_3)_2$ = 1:1.5:1.5:0.05. [b] Yields refer to single runs, are given for pure isolated products, and are calculated on **3**. [c] The reaction was carried out in DMF at 80 °C. The starting triflate was recovered in 42% yield. Under usual conditions, compound **6e** was isolated in 20% yield and the starting triflate was recovered in 65% yield. [d] 3:4 = 1:3. [e] The reaction was carried out with a commercially available *E*/*Z* mixture of β-bromostyrene. Only the product containing the (*E*)-styryl moiety was isolated.





Discussion

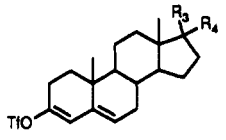
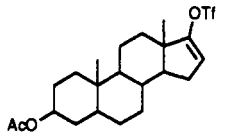
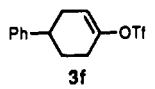
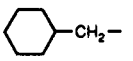
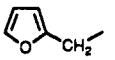
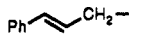
Presumably, the reaction proceeds according to the Scheme I depicted for 4-pentynoic acid and vinyl triflates.

(11) (a) Andreini, B. P.; Carpita, A.; Rossi, R. *Tettrahedron Lett.* **1986**, *27*, 5533. (b) Arcadi, A.; Bernocchi, E.; Burini, A.; Cacchi, S.; Marinelli, F.; Pietroni, B. *Ibid.* **1989**, *30*, 3465. (c) Arcadi, A.; Bernocchi, E.; Cacchi, S.; Marinelli, F.; Ortar, G. *J. Organomet. Chem.* **1989**, *368*, 249.

(12) Arcadi, A., Cacchi, S., Delmastro, M., Marinelli, F. *Synlett.* **1991**, 407.

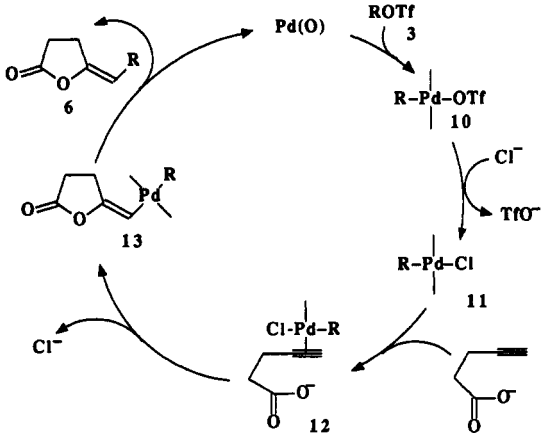
(13) Arcadi, A., Cacchi, S., Delmastro, M., Marinelli F. *Synlett.* **1991**, 409.

Table II. Palladium-Catalyzed Reaction of Vinyl Triflates with 2,2-Disubstituted 4-Pentynoic Acids 5 (eq 2; R_1 = COOMe, R_2 = Alkyl)[a]

no.	vinyl triflate 3	2,2-disubstd 4-pentynoic acid 5 R_2	reactn time (min)	yield (%) of 7[b,c]
1	 3a, R_3 = R_4 = O	Me	30	**7a**, 69
2	3b, R_3 = β-OAc, R_4 = H		20	**7b**, 68
3	 3d	Me	10	**7d**, 69
4	 3f	Me	15	**7f**, 64
5		$EtCOCH_2CH_2$–	30	**7g**, 61
6			10	**7h**, 86
7			40	**7i**, 62
8			5	**7j**, 65

[a] Reactions were carried out at 60 °C in MeCN under an argon atmosphere in the presence of Et_3N using the following molar ratios: 3:5:*n*-Bu_4NCl:$Pd(OAc)_2(PPh_3)_2$ = 1:1.5:1.5:0.05. [b] Isolated and characterized as mixture of diastereoisomers. [c] Yields refer to single runs, are given for isolated products, and are calculated on the basis of 3.

Scheme I

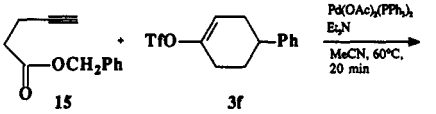


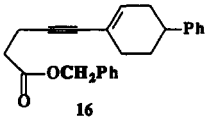
Pd(0) species, most likely derived from reductive coupling of acetylene units, react with the vinyl triflate **3** producing the σ-vinylpalladium triflate complex **10** which, through a ligand exchange mechanism, undergoes the substitution of chloride anion for the poorly coordinating triflate anion to give the σ-vinylpalladium chloride complex **11**.

The triflate–chloride exchange has been reported to affect the reactivity and/or to enhance the reaction yield in a variety of palladium-catalyzed reactions of organotriflates.[14] In the present reaction, the involvement of this mechanism along the reaction pathway is supported by the observation that in the absence of *n*-Bu_4NCl a more complex reaction mixture is usually obtained and the enol lactone is produced in low yield.

Apparently, in the absence of chloride anions, vinyl triflates and 4-alkynoic acids are unable to enter efficiently both the catalytic cycle producing enol lactones and that producing conjugated enynes.[9] The role of chloride anions is further stressed by the observation that the use of *n*-Bu_4NHSO_4 instead of *n*-Bu_4NCl in the reaction of **3d** with 4-pentynoic acid produced quite the same result obtained in the absence of the ammonium salt, while good results were obtained by using an excess of LiCl.

A reasonable working hypothesis envisions that, in the absence of chloride anions, the strongly electrophilic palladium of the σ-organopalladium triflate complex reacts with the free carboxylate to give a σ-organopalladium carboxylate complex **14**,[15] and that this complex is prone to undergo side reactions.





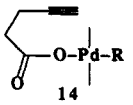
(eq. 4)

In practice, in the absence of chloride anions, the free carboxylate group, obviously necessary for the lactonization step, might be responsible for the failure in the formation

(14) (a) Scott, W. J.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 3033. (b) Echavarren, A. M.; Stille, J. K. *Ibid* **1987**, *109*, 5478. (c) Andersson, C.-M.; Hallberg, A. *J. Org. Chem.* **1988**, *53*, 2112. (d) Fiess, B.; Cazes, B.; Gore, J. *Tetrahedron Lett.* **1988**, *29*, 4089. (e) Cacchi, S.; Ciattini, P. G.; Morera, E.; Ortar, G. *Ibid.* **1988**, *29*, 3117.

(15) Ligand exchange mechanisms producing σ-vinyl/arylpalladium acetates (from triflates (a) and from halides (b)) and halides (from triflates)[14] have been invoked to account for the results of palladium-catalyzed reactions: (a) Amorese, A.; Arcadi, A.; Bernocchi, E.; Cacchi, S.; Cerrini, S.; Fedeli, W.; Ortar, G. *Tetrahedron* **1989**, *45*, 813. (b) Arcadi, A.; Cacchi, S.; Marinelli, F.; Morera, E.; Ortar, G. *Tetrahedron* **1990**, *46*, 7151.

of both enol lactones and enynes. Accordingly, when **3f** was reacted with benzyl 4-pentynoate **15**, enyne **16** was isolated in 63% yield (eq 4). Quite the same result was obtained in the presense of n-Bu_4NCl.



14

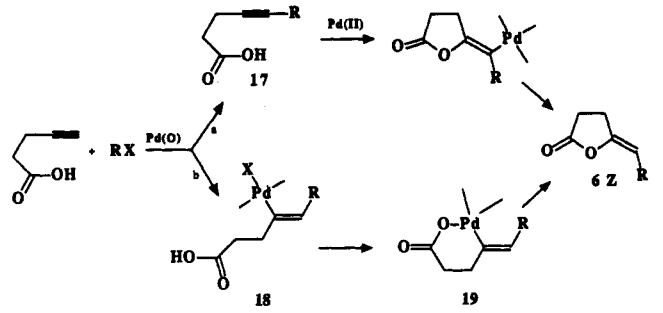
The addition of chloride anions induces the formation of σ-organopalladium chloride intermediates which preferentially undergo π-interactions with the alkyne moiety of the alkynoic acid producing the π-palladium complex **12** from which the σ-vinylpalladium intermediate **13** is generated through regioselective trans addition[5b,c] of the carboxylate anion across the carbon–carbon triple bond. Subsequent reductive elimination of Pd(0) species from **13** produces enol lactones **6**.

The results obtained with vinyl and aryl halides in the absence of n-Bu_4NCl appear to be in agreement with this hypothesis. Indeed, β-bromostyrene, 4-methoxyphenyl iodide, and 4-acetylphenyl bromide produced the corresponding enol lactones in 35, 47, and 40% yield, respectively. Yields are lower than those obtained in the presence of n-Bu_4NCl (74, 70, and 60% yield, respectively) but significantly higher than those obtained with vinyl triflates omitting the ammonium chloride salt. When vinyl and aryl bromides or iodides are used, σ-organopalladium bromides and iodides are formed through oxidative addition. of Pd(0) species and the involvement of a ligand exchange mechanism with chloride anions along the reaction coordinate is less crucial for the formation of π-palladium complexes with the alkynoic acid.

The preference of π-palladium complexes of 4-alkynoic acids to produce five- vs six-membered rings has been already reported.[5] In addition, IR spectral bands for compounds **6**, **7**, and **9** range from 1786 to 1803 cm^{-1} in agreement with reported frequencies for five-membered exocyclic enol lactone carbonyls.[2a,3a,5a,c,16,17]

The stereochemistry of the reaction is in agreement with the sequence illustrated in the Scheme I since only E isomers were isolated. The E stereochemistry of enol lactones **6** and **7** was assigned on the basis of ^1H NMR chemical shifts of C-5 olefinic protons. These values range from δ 5.69 to 6.03 for enol lactones derived from vinyl triflates or halides and from δ 6.17 to 6.38 for enol lactones derived from aryl halides and are compatible with the calculated shifts.[18] In addition, we independently prepared some Z isomers of enol lactones through Pd(II)-catalyzed cyclization of 5-substituted 4-pentynoic acids.[5a,13] According to the values reported for similar compounds,[2a,5a,c,6b,17,19] E isomers show the C-5 vinyl proton signals at lower fields than Z isomers due to the deshielding by the lactone oxygen. For example, Z isomers of **6d**, **6c** (vinyl derivatives), and **6l** (aryl derivative) show C-5 vinyl proton signals at δ 5.00, 5.18, and 5.51 while the corresponding E isomers show C-5 proton signals at δ 5.69, 5.90, and 6.31, respectively. The assignments were confirmed by the proton NOE measurements: when the allylic protons of the lactone ring were irradiated, the Z isomers showed a strong enhancement of the olefinic proton signal, whereas the E isomers gave no such enhancement. The

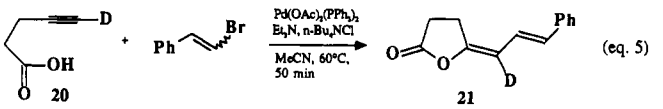
Scheme II



stereochemistry of compounds **9**, expected to be that depicted in the eq 3 on the basis of a likely uniformity of the cyclization mechanism, was unambiguously assigned on the basis of X-ray analysis.[20]

The stereochemical outcome of the reaction rules out the possible formation of enol lactones through an alternative pathway involving Pd(II)-catalyzed cyclization of the initially formed enyne **17**. This mechanism is known to produce the Z isomer of the product **6** (Scheme IIa).[5a]

Furthermore, when the reaction was carried out with 5-deuterio-4-pentynoic acid **20**, only the corresponding deuterio enol lactone **21** was obtained, thus showing that breaking of the C_{sp}–H bond is not involved in the reaction (eq 5).



(eq. 5)

In addition, on the grounds of the stereochemical outcome of the reaction, it is also possible to rule out the formation of enol lactones via the Pd(0) reductive elimination from the postulated intermediate **19**, in turn derived from the syn addition intermediate **18** (Scheme IIb). This mechanism would produce Z isomers as well.

The mechanism proposed here, based on the activation of the carbon–carbon triple bond toward the intramolecular nucleophilic attack of the carboxylate anion by a σ-vinyl(aryl)palladium complex, is closely related to the proposed one for the palladium-catalyzed heterocyclization/allylation of lithium salts and allyl esters of 4-pentynoic acids.[5c] π-Allylpalladium cation complexes in that case were supposed to activate the acetylenic system. While this work was in progress, the activation of the carbon–carbon triple bond toward carbon nucleophiles by σ-vinyl(aryl)palladium complexes in related palladium-catalyzed carbocyclization reaction has been reported.[21]

In conclusion, the regio- and stereoselective heterocyclization described above provides easy access to functionalized (E)-δ-vinyl/aryl-γ-methylene-γ-butyrolactones and holds promise as a useful and versatile tool for the preparation of this class of compounds. The utility of the present reaction may be apparent from the ready availability of the starting alkynoic acids and the general applicability to 4-pentynoic acids containing a variety of substituents. Work along this line is in progress.

Experimental Section

Melting points are uncorrected. All the starting materials such as catalysts, amines, salts, aryl halides (**3h**, **3i**, **3l**), and solvents are commercially available and were used without further purification. 17-Oxoandrosta-3,5-dien-3-yl triflate, 17β-acetoxy-

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androsta-3,5-dien-3-yl triflate,[22] 17β-acetylandrosta-3,5-dien-3-yl triflate, 3β-acetoxy-5β-androst-16-en-17-yl triflate,[23] and 4-phenylcyclohex-1-en-1-yl triflate were prepared according to ref 10. 17-Oxoestra-1,3,5(10)-trien-3-yl triflate was prepared according to ref 24. Compounds **5**,[12] **8**,[13] and 4-iodoacetanilide[25] were prepared according to literature methods. Methyl 4-iodobenzoate[26] was prepared according to the procedure given in ref 27 for the synthesis of methyl 2-iodobenzoate and purified by chromatography on silica gel eluting with *n*-hexane/ethyl acetate (90/10 v/v). Compound **15** was prepared according to the procedure reported in ref 28. Reactions were carried out on a 0.3–0.8 mmol scale. Reaction products were purified by preparative HPLC (Chromatospac Prep 10 from Jobin Yvon, equipped with a PrepLC 500/A solvent delivery system and a refractive index detector, from Waters Ass.) on axially compressed columns packed with SiO_2, 20–45 μm (Amicon), eluting with *n*-hexane/ethyl acetate mixtures.

^1H NMR spectra ($CDCl_3$, unless otherwise stated, TMS internal standard) were recorded at 90 or 300 MHz. ^{13}C NMR spectra were recorded at 75 MHz. IR spectra were recorded in KBr dispersions unless otherwise indicated.

General Procedure for the Preparation of Vinyl Triflates (3a,c,f). 4-Phenylcyclohex-1-en-1-yl Triflate (3f). To a solution of 2,6-di-*tert*-butyl-4-methylpyridine (1.77 g, 8.61 mmol) and trifluoromethanesulfonic anhydride (2.10 g, 7.46 mmol) in dry dichloromethane (15 mL) was slowly added 4-phenylcyclohexanone (1.00 g, 5.74 mmol) in CH_2Cl_2 (10 mL). The resulting solution was stirred for 2.5 h at rt. The solvent was removed in vacuo and the residue combined with ether. The ethereal solution was washed with 2 N HCl, water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel eluting with *n*-hexane to afford 1.20 g (68%) of **3f**: mp oil; IR 1417, 1212, 1138 cm^{-1}; ^1H NMR δ 1.87–2.20 (m, 2 H), 2.23–2.63 (m, 4 H), 2.67–3.07 (m, 1 H), 5.87 (m, 1 H), 7.13–7.53 (m, aromatic, 5 H). Anal. Calcd for $C_{13}H_{13}F_3O_3S$: C, 50.98; H, 4.28. Found: C, 52.00; H, 4.35. The following vinyl triflates were prepared and isolated according to this procedure.

17-Oxoandrosta-3,5-dien-3-yl triflate (3a, 83%): mp 121–123 °C; IR 1737, 1417, 1204, 1138 cm^{-1}; ^1H NMR δ 0.90 (s, 3 H), 0.99 (s, 3 H), 5.63 (m, 1 H), 6.04 (m, 1 H). Anal. Calcd for $C_{20}H_{25}F_3O_4S$: C, 57.40; H, 6.02. Found: C, 57.57; H, 5.87.

17β-Acetylandrosta-3,5-dien-3-yl triflate (3c, 55%): mp 98–100 °C; IR 1712, 1417, 1212, 1130 cm^{-1}; ^1H NMR δ 0.67 (s, 3 H), 0.97 (s, 3 H), 2.13 (s, 3 H), 5.63 (m, 1 H), 6.04 (m, 1 H). Anal. Calcd for $C_{22}H_{29}F_3O_4S$: C, 59.18; H, 6.55. Found: C, 59.14; H, 6.48.

Typical Procedure for the Synthesis of Exocyclic Enol Lactones 6 and 7. 5(*E*)-[(4-Phenylcyclohex-1-en-1-yl)-methylidene]tetrahydrofuran-2-one (6f) (Table I, entry 6). To a solution of triflate **3f** (0.15 g, 0.49 mmol), 4-pentynoic acid (0.072 g, 0.74 mmol), tetrabutylammonium chloride (0.217 g, 0.74 mmol), and triethylamine (1.09 g, 10.78 mmol) in acetonitrile (1.5 mL) was added bis(triphenylphosphine)palladium diacetate (0.018 g, 0.024 mmol) under Ar. The mixture was warmed at 60 °C and stirred for 45 min. Then, the reaction mixture was cooled, acidified with 2 N HCl, and extracted with ethyl acetate. The organic layer was separated and washed with water, dried over Na_2SO_4, and evaporated under vacuum. The residue was chromatographed on silica gel eluting with *n*-hexane/ethyl acetate (85/15 v/v) to afford 0.094 g (75%) of **6f**: mp 129.5–131 °C (CH_2Cl_2/*n*-hexane); IR 1786, 1672, 1122, 761, 704 cm^{-1}; ^1H NMR δ 1.70–2.10 (m, 2 H), 2.15–2.60 (m, 4 H), 2.60–2.90 (m, 3 H), 3.00–3.20 (m, 2 H), 5.72 (m, 1 H), 5.84 (bs, 1 H), 7.34–7.15 (m, aromatic, 5 H); ^{13}C NMR δ 146.5, 148.8, 174.5; MS *m/e* (relative intensity) 254 (M^+, 47), 150 (73), 122 (100), 91 (28). Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.20; H, 7.09. The following enol lactones were prepared and isolated in a similar manner.

5(*E*)-[(17-Oxoandrosta-3,5-dien-3-yl)methylidene]tetrahydrofuran-2-one (6a): mp 139–141 °C; IR 1803, 1729, 1655 cm^{-1}; ^1H NMR δ 0.90 (s, 3 H), 0.97 (s, 3 H), 3.03–3.33 (m, 2 H), 5.50 (m, 1 H), 5.90 (bs, 2 H); ^{13}C NMR δ 109.9, 123.4, 129.1, 129.4, 141.9, 149.4, 174.1, 220.3; MS *m/e* (relative intensity) 366 (M^+, 100). Anal. Calcd for $C_{24}H_{30}O_3$: C, 78.65; H, 8.25. Found: C, 78.55; H, 8.19.

5(*E*)-[(17β-Acetoxyandrosta-3,5-dien-3-yl)methylidene]-tetrahydrofuran-2-one (6b): mp 173–175 °C; IR 1786, 1721, 1663 cm^{-1}; ^1H NMR δ 0.87 (s, 3 H), 0.97 (s, 3 H), 2.07 (s, 3 H), 2.57–2.87 (m, 2 H), 3.03–3.33 (m, 2 H), 4.68 (m, 1 H), 5.49 (m, 1 H), 5.90 (bs, 2 H); ^{13}C NMR δ 109.9, 123.9, 129.2, 141.8, 149.3, 171.2, 174.4; MS *m/e* (relative intensity) 410 (M^+, 100). Anal. Calcd for $C_{26}H_{34}O_4$: C, 76.06; H, 8.35. Found: C, 75.97; H, 8.30.

5(*E*)-[(17β-Acetylandrosta-3,5-dien-3-yl)methylidene]-tetrahydrofuran-2-one (6c): mp 156–157 °C; IR 1803, 1696, 1655 cm^{-1}; ^1H NMR δ 0.67 (s, 3 H), 0.97 (s, 3 H), 2.13 (s, 3 H), 3.03–3.33 (m, 2 H), 5.49 (m, 1 H), 5.90 (bs, 2 H); ^{13}C NMR δ 109.9, 124.1, 129.1, 141.7, 149.3, 174.4, 209.6; MS *m/e* (relative intensity) 394 (M^+, 100). Anal. Calcd for $C_{26}H_{34}O_3$: C, 79.15; H, 8.69. Found: C, 79.27; H, 8.65.

5(*E*)-[(3β-Acetoxy-5β-androst-16-en-17-yl)methylidene]-tetrahydrofuran-2-one (6d): mp 159–160 °C; IR 1803, 1729, 1663 cm^{-1}; ^1H NMR δ 0.82 (s, 3 H), 0.90 (s, 3 H), 2.03 (s, 3 H), 4.75 (m, 1 H), 5.50 (m, 1 H), 5.69 (m, 1 H); ^{13}C NMR δ 99.2, 124.7, 148.3, 151.7, 170.7, 174.3; MS *m/e* (relative intensity) 412 (M^+, 57). Anal. Calcd for $C_{26}H_{36}O_4$: C, 75.69; H, 8.80. Found: C, 75.35; H, 8.71.

5(*E*)-[(17-Oxoestra-1,3,5(10)-trien-3-yl)methylidene]-tetrahydrofuran-2-one (6e): mp 197–199 °C; IR 1803, 1745, 1672 cm^{-1}; ^1H NMR δ 0.73 (s, 3 H), 6.30 (m, 1 H), 6.93–7.41 (m, aromatic, 3 H); ^{13}C NMR δ 106.7, 125.0, 125.7, 128.5, 131.9, 136.8, 138.4, 150.7, 174.2, 220.7; MS *m/e* (relative intensity) 350 (M^+, 100). Anal. Calcd for $C_{23}H_{26}O_3$: C, 78.83; H, 7.48. Found: C, 79.05; H, 7.44.

5(*E*)-(3-Phenylprop-2-enylidene)tetrahydrofuran-2-one (6g): mp 125–126.5 °C; IR 1803, 1663, 753, 695 cm^{-1}; ^1H NMR δ 2.67–2.73 (m, 2 H), 2.99–3.06 (m, 2 H), 6.05 (dt, J = 11, 2 Hz, 1H), 6.48 (d, J = 15.3 Hz, 1 H), 6.62 (dd, J = 15.3, 11 Hz, 1 H), 7.21–7.39 (m, aromatic, 5 H); ^{13}C NMR δ 151.8, 174.4; MS *m/e* (relative intensity) 200 (M^+, 83), 115 (100). Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 77.84; H, 6.00.

5(*E*)-[(4-Methoxyphenyl)methylidene]tetrahydrofuran-2-one (6h): mp 110–110.5 °C; IR 1803, 1672, 1606, 818 cm^{-1}; ^1H NMR δ 2.57–2.87 (m, 2 H), 3.0–3.30 (m, 2 H), 3.82 (s, 3 H), 6.29 (m, 1 H), 6.95 (d, J = 7.5 Hz, aromatic, 2 H), 7.22 (d, J = 7.5 Hz, aromatic, 2 H); ^{13}C NMR δ 149.7, 158.3, 174.3; MS *m/e* (relative intensity) 204 (M^+, 100). Anal. Calcd for $C_{12}H_{12}O_3$: C, 70.58; H, 5.92. Found: C, 70.78; H, 5.88.

5(*E*)-[(4-Acetylphenyl)methylidene]tetrahydrofuran-2-one (6i): mp 120–122 °C; IR 1795, 1672, 1598, 810 cm^{-1}; ^1H NMR δ 2.58 (s, 3 H), 2.67–2.93 (m, 2 H), 3.07–3.40 (m, 2 H), 6.37 (m, 1 H), 7.37 (d, J = 9 Hz, aromatic, 2 H), 8.00 (d, J = 9 Hz, aromatic, 2 H); ^{13}C NMR δ 153.3, 173.8, 197.4; MS *m/e* (relative intensity) 216 (M^+, 39), 201 (100). Anal. Calcd for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 72.02; H, 5.57.

5(*E*)-[(4-Carbomethoxyphenyl)methylidene]tetrahydrofuran-2-one (6j): mp 160–160.5 °C; IR 1803, 1704, 1671, 1606, 843 cm^{-1}; ^1H NMR δ 2.65–2.93 (m, 2 H), 3.02–3.33 (m, 2 H), 3.92 (s, 3 H), 6.38 (m, 1 H), 7.33 (d, J = 7.5 Hz, aromatic, 2 H), 8.10 (d, J = 7.5 Hz, aromatic, 2 H); ^{13}C NMR δ 153.1, 166.1, 173.8; MS *m/e* (relative intensity) 232 (M^+, 78), 145 (100). Anal. Calcd for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 67.30; H, 5.24.

5(*E*)-[(4-Acetamidophenyl)methylidene]tetrahydrofuran-2-one (6k): mp 200–202 °C; IR 1803, 1671, 1598, 1532, 867 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.03 (s, 3 H), 2.63–2.93 (m, 2 H), 3.00–3.30 (m, 2 H), 6.23 (m, 1 H), 7.28 (d, J = 9 Hz, aromatic, 2 H), 7.67 (d, J = 9 Hz, aromatic, 2 H), 10.05 (bs, 1 H); ^{13}C NMR δ 151.6, 168.1, 174.7; MS *m/e* (relative intensity) 231 (M^+, 100), 189 (84), 133 (93). Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.67; N, 6.06. Found: C, 67.23; H, 5.62; N, 5.94.

5(*E*)-Benzylidenetetrahydrofuran-2-one (6l): mp 96–97 °C; IR 1794, 1679, 753, 695 cm^{-1}; ^1H NMR δ 2.55–2.88 (m, 2 H), 2.97–3.30 (m, 2 H), 6.33 (m, 1 H), 7.17–7.57 (m, aromatic, 5 H);

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^{13}C NMR δ 151.2, 173.8; MS m/e (relative intensity) 174 (M^+, 100), 90 (89). Anal. Calcd for $C_{11}H_{10}O_2$: C, 75.84; H, 5.79. Found: C, 75.74; H, 5.74.

3-Methyl-3-carbomethoxy-5(*E*)-[(17-oxoandrosta-3,5-dien-3-yl)methylidene]tetrahydrofuran-2-one (7a): IR 1795, 1754, 1728, 1663, cm^{-1}; ^1H NMR δ 0.91 (s, 3 H), 0.97 (s, 3 H), 1.60 (s, 3 H), 2.97–3.07 (m, 1 H), 3.60–3.71 (m, 1 H), 3.82 (s, 3 H), 5.50 (m, 1 H), 5.92 (m, 2 H); ^{13}C NMR δ 141.8, 145.7, 169.8, 172.3, 221.1; MS m/e (relative intensity) 438 (M^+, 100). Anal. Calcd for $C_{27}H_{34}O_5$: C, 73.95; H, 7.81. Found: C, 73.86; H, 7.73.

3-Methyl-3-carbomethoxy-5(*E*)-[(17β-acetoxyandrosta-3,5-dien-3-yl)methylidene]tetrahydrofuran-2-one (7b): IR 1795, 1729, 1663, cm^{-1}; ^1H NMR δ 0.82 (s, 3 H), 0.94 (s, 3 H), 1.58 (s, 3 H), 2.03 (s, 3 H), 2.90–3.03 (m, 1 H), 3.52–3.64 (m, 1 H), 3.82 (s, 3 H), 4.63 (m, 1 H), 5.48 (m, 1 H), 5.92 (bs, 2 H); ^1H NMR (300 MHz) of methylene protons: δ 2.95 (dd, J = 17.0, 2.3 Hz, 0.3 H), 2.97 (dd, J = 17.0, 2.3 Hz, 0.7 H), 3.57 (dd, J = 17.0, 1.9 Hz, 0.7 H), 3.60 (dd, J = 17.0, 1.9 Hz, 0.3 H); ^{13}C NMR δ 141.7, 145.6, 170.4 171.2, 172.9; MS m/e (relative intensity) 482 (M^+, 100). Anal. Calcd for $C_{29}H_{38}O_6$: C, 72.17; H, 7.94. Found: C, 72.41; H, 7.89.

3-Methyl-3-carbomethoxy-5(*E*)-[(3β-acetoxy-5β-androst-16-en-17-yl)methylidene]tetrahydrofuran-2-one (7d): IR 1803, 1729, cm^{-1}; ^1H NMR δ 0.77 (s, 3 H), 0.86 (s, 3 H), 1.60 (s, 3 H), 2.01 (s, 3 H), 2.76–2.87 (m, 1 H), 3.36–3.47 (m, 1 H), 3.79 (s, 3 H), 4.73 (m, 1 H), 5.47 (m, 1 H), 5.72 (m, 1 H); ^{13}C NMR δ 148.0, 148.4, 170.0, 170.7, 173.1; MS m/e (relative intensity) 484 (M^+, 19). Anal. Calcd for $C_{29}H_{40}O_6$: C, 71.87; H, 8.32. Found: C, 72.11; H, 8.28.

3-Methyl-3-carbomethoxy-5(*E*)-[(4-phenylcyclohex-1-en-1-yl)methylidene]tetrahydrofuran-2-one (7f): IR 1803, 1745, 1671, 761, 704 cm^{-1}; ^1H NMR δ 1.58 (s, 3 H), 2.84–3.10 (m, 1 H), 3.52–3.77 (m, 1 H), 3.82 (s, 3 H), 5.78 (m, 1 H), 5.92 (bs, 1 H), 7.29 (m, aromatic, 5 H); ^{13}C NMR δ 145.2, 146.4, 170.3, 173.1; MS m/e (relative intensity) 326 (M^+, 53), 222 (100). Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.6; H, 6.79. Found: C, 73.85; H, 6.75.

3-(3-Oxopent-1-yl)-3-carbomethoxy-5(*E*)-[(4-phenylcyclohex-1-en-1-yl)methylidene]tetrahydrofuran-2-one (7g): IR 1795, 1737, 1713, 1680, 769, 704 cm^{-1}; ^1H NMR δ 2.97–3.07 (m, 1 H), 3.51–3.61 (m, 1 H), 3.79 (s, 3 H), 5.77 (m, 1 H), 5.93 (bs, 1 H), 7.30 (m, aromatic, 5 H); ^{13}C NMR δ 145.0, 146.4, 169.6, 171.8, 209.3; MS m/e (relative intensity) 396 (M^+, 24), 91 (100). Anal. Calcd for $C_{24}H_{28}O_5$: C, 72.71; H, 7.12. Found: C, 72.83; H, 7.08.

3-(Cyclohexylmethyl)-3-carbomethoxy-5(*E*)-[(4-phenylcyclohex-1-en-1-yl)methylidene]tetrahydrofuran-2-one (7h): IR 1795, 1737, 1680, 761, 704 cm^{-1}; ^1H NMR δ 2.93–3.20 (m, 1 H), 3.60–3.84 (m, 1 H), 3.81 (s, 3 H), 5.80 (m, 1 H), 5.90 (bs, 1 H), 7.28 (m, aromatic, 5 H); ^{13}C-NMR δ 145.6, 146.5, 169.9, 172.4; MS m/e (relative intensity) 408 (M^+, 43). Anal. Calcd for $C_{26}H_{32}O_4$: C, 76.44; H, 7.90. Found: C, 76.24; H, 7.96.

3-(2-Furylmethyl)-3-carbomethoxy-5(*E*)-[(4-phenylcyclohex-1-en-1-yl)methylidene]tetrahydrofuran-2-one (7i): mp oil; IR (liquid film) 1795, 1745, 1677, 1196, 767, 704 cm^{-1}; ^1H NMR δ 3.03–3.30 (m, 1 H), 3.47–3.73 (m, 1 H), 3.82 (s, 3 H), 5.73 (m, 1 H), 5.83 (bs, 1 H), 6.00–6.40 (m, 2 H), 7.22–7.43 (m, aromatic, 6 H); ^{13}C NMR δ 141.7, 142.6, 145.3, 146.5, 149.3, 169.1, 171.7; MS m/e (relative intensity) 392 (M^+, 67), 81 (100). Anal. Calcd for $C_{24}H_{24}O_5$: C, 73.45; H, 6.16. Found: C, 73.67; H, 6.13.

3-(3-Phenylprop-2-en-1-yl)-3-carbomethoxy-5(*E*)-[(4-phenylcyclohex-1-en-1-yl)methylidene]tetrahydrofuran-2-one (7j): IR 1786, 1737, 1672, 745, 695 cm^{-1}; ^1H NMR δ 2.92 (d, J = 7.5 Hz, 2 H), 3.03–3.33 (m, 1 H), 3.51–3.78 (m, 1 H), 3.82 (s, 3 H), 5.76 (m, 1 H), 5.92 (m, 1 H), 6.12 (dt, J = 15.7, 7.5 Hz, 1 H), 6.62 (d, J = 15.7 Hz, 1 H), 7.13–7.67 (m, aromatic, 10 H); ^{13}C NMR δ 145.4, 146.5, 169.4, 171.8; MS m/e (relative intensity) 384 (40), 325 (100). Anal. Calcd for $C_{28}H_{28}O_4$: C, 78.48; H, 6.59. Found: C, 78.87; H, 6.55.

5-Deuterio-4-pentynoic Acid (20). Compound **20** was obtained by treating 4-pentynoic acid (5.1 mmol) with a pentane solution of *tert*-butyl lithium (11.22 mmol) at −78 °C in anhydrous THF (7 mL) under Ar. After 15 min the reaction mixture was allowed to reach rt and maintained at that temperature for 15 min. Then the mixture was recooled at −78 °C and D_2O was added. The refrigerating bath was removed, and the mixture was stirred at rt for 15 min. Then 2 N HCl was added, and the deuteriated product was extracted with ether in almost quantitative yield.

The 4-pentynoic acid % D was determined by ^1H NMR. From this analysis an abundance of D greater than 95% was calculated.

Palladium-Catalyzed Reaction of 5-Deuterio-4-pentynoic Acid (20) with β-Bromostyrene. To a solution of β-bromostyrene **3g** (0.150 g, 0.82 mmol), **20** (0.243 g, 2.46 mmol), tetrabutylammonium chloride (0.364 g, 1.23 mmol), and triethylamine (1.82 g, 18.02 mmol) in MeCN (1.5 mL) was added bis(triphenylphosphine)palladium diacetate (0.031 g, 0.041 mmol) under Ar. The reaction mixture was warmed at 60 °C and stirred for 50 min. It was then worked up as usual. After chromatography on silica gel, using *n*-hexane/ethyl acetate (80/20 v/v) as the eluant, a white solid was obtained in 50% yield (0.082 g): mp 120–122 °C. The ^1H NMR spectrum of (*E*)-enol lactone **21** showed a vinyl proton integration lower then 0.05 H: ^1H NMR δ 2.66–2.77 (m, 2 H), 3.04–3.09 (m, 2 H), 6.57 (q, J = 15.6 Hz, 2 H), 7.29–7.39 (m, aromatic, 5 H).

Typical Procedure for the Synthesis of Exocyclic Enol Lactones 9. 5(*E*)-[1-(4-Phenylcyclohex-1-en-1-yl)-1-(4-methoxyphenyl)methylidene]tetrahydrofuran-2-one (9b). To a solution of 5-(4-phenylcyclohex-1-en-1-yl)-4-pentynoic acid **8b** (0.2 g, 0.79 mmol), 4-methoxyphenyl iodide (0.37 g, 1.57 mmol), tetrabutylammonium chloride (0.23 g, 0.79 mmol), and triethylamine (1.75 g, 17.32 mmol) in DMSO (4 mL) was added tetrakis(triphenylphosphine)palladium(0) (0.044 g, 0.38 mmol) under Ar. The reaction mixture was warmed at 80 °C and stirred for 4.5 h. It was then cooled, acidified with 2 N HCl, and extracted with ethyl acetate. The organic layer was separated and washed with water, dried over Na_2SO_4 and evaporated under reduced pressure. The residue was chromatographed on silica gel eluting with *n*-hexane/ethyl acetate (85/15 v/v) to afford 0.077 g (55%) of **9b** as a pale yellow oil: IR (liquid film) 1803, 826, 761, 704 cm^{-1}; ^1H NMR δ 1.73–3.00 (m, 11 H), 3.83 (s, 3 H), 5.65 (m, 1 H), 6.95 (d, J = 7.5 Hz, aromatic, 2 H), 7.13–7.47 (m, aromatic, 7 H); ^{13}C NMR δ 144.4, 147.1, 158.6, 175.2; MS m/e (relative intensity) 360 (M^+, 100), 256 (37). Anal. Calcd for $C_{24}H_{24}O_3$: C, 79.97; H, 6.71. Found: C, 80.32; H, 6.57.

5(*E*)-[1-Phenyl-1-(4-methoxyphenyl)methylidene]tetrahydrofuran-2-one (9a): mp 118 °C dec; IR 1795, 1655, 835, 777, 703 cm^{-1}; ^1H NMR δ 2.50–3.03 (m, 4 H), 3.78 (s, 3 H), 6.87 (d, J = 7.5 Hz, aromatic, 2 H), 7.17–7.50 (m, aromatic, 7 H); ^{13}C NMR δ 139.0, 145.3, 158.4, 174.9; MS m/e (relative intensity) 280 (M^+, 100), 196 (93), 152 (84). Anal. Calcd for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 76.95; H, 5.83.

Benzyl 4-Pentynoate (15). To a solution of 4-pentynoic acid (0.39 g, 4.02 mmol) and n-Bu_4NCl (1.12 g, 4.02 mmol) in 2 N NaOH (5 mL) was added benzyl bromide (0.72 mL, 6.05 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred at 40 °C for 6 h. Then, ether and water were added. The organic layer was separated, washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel, eluting with *n*-hexane/EtOAc (97.3 v/v) to afford 0.26 g (34%) of **15**: mp oil; IR (film) 3260, 2080, 1720, 1150, 730, 680 cm^{-1}; ^1H NMR δ 1.97 (t, J = 2.5 Hz, 1 H), 2.53 (m, 4 H), 5.14 (s, 2 H), 7.35 (m, aromatic, 5 H); ^{13}C NMR δ 14.4, 33.31, 66.5, 69.1, 82.4, 128.2, 128.3, 128.5, 135.7, 171.6. Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43. Found: C, 76.71; H, 6.50.

Palladium-Catalyzed Reaction of Benzyl 4-Pentynoate (15) with 3f. Benzyl 5-(4-Phenylcyclohex-1-en-1-yl)-4-pentynoate (16). To a solution of **3f** (0.30 g, 0.98 mmol), benzyl ester **15** (0.28 g, 1.47 mmol), and triethylamine (2.18 g, 21.6 mmol) in acetonitrile (3.0 mL) was added bis(triphenylphosphine)palladium diacetate (0.036 g, 0.049 mmol) was added under Ar. The mixture was warmed at 60 °C and stirred for 20 min. After cooling, the reaction mixture was acidified with 2 N HCl and extracted with ethyl acetate. The organic layer was separated and washed with water, dried over Na_2SO_4, and evaporated under vacuum. The residue was chromatographed on silica gel, eluting with *n*-hexane/ethyl acetate (90/10 v/v) to afford 0.212 g (63%) of **16** as colorless oil: IR (film) 1728, 1606 cm^{-1}; ^1H NMR δ 2.62 (s, 4 H), 5.17 (s, 2 H), 6.10 (m, 1 H), 7.28 (m, aromatic, 5 H), 7.38 (m, aromatic, 5 H); ^{13}C NMR δ 146.4, 171.8. Anal. Calcd for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02. Found: C, 83.80; H, 6.08.

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Registry No. **3a**, 95667-41-7; **3b**, 81827-59-0; **3c**, 95667-43-9; **3d**, 96150-02-6; **3e**, 92817-04-4; **3f**, 122948-47-4; **3h**, 696-62-8; **3i**, 99-90-1; **3j**, 619-44-3; **3k**, 622-50-4; **3l**, 591-50-4; **4**, 6089-09-4; **5** (R_2 = Me), 136041-11-7; **5** (R_2 = $(CH_2)_2COEt$), 136041-10-6; **5** (R_2 = CH_2cyclohexane), 136041-09-3; **5** (R_2 = $CH_2C_4H_3O$), 136041-07-1; **5** (R_2 = CH_2CH:CHPh), 137742-20-2; **6a**, 137742-21-3; **6b**, 137742-22-4; **6c**, 137768-00-4; **6d**, 137742-23-5; **6e**, 137742-24-6; **6f**, 137742-25-7; **6g**, 137742-26-8; **6h**, 137742-27-9; **6i**, 137742-28-0; **6j**, 137742-29-1; **6k**, 137742-30-4; **6l**, 69063-22-5; **7a** (isomer 1), 137742-31-5; **7a** (isomer 2), 137820-53-2; **7b** (isomer 1), 137742-32-6; **7b** (isomer 2), 137820-54-3; **7d** (isomer 1), 137742-33-7; **7d** (isomer 2), 137820-55-4; **7f** (isomer 1), 137742-34-8; **7f** (isomer 2), 137742-35-9; **7g** (isomer 1), 137742-36-0; **7g** (isomer 2), 137742-37-1; **7h** (isomer 1), 137742-38-2; **7h** (isomer 2), 137742-39-3; **7i** (isomer 1), 137742-40-6; **7i** (isomer 2), 137742-41-7; **7j** (isomer 1), 137742-42-8; **7j** (isomer 2), 137742-43-9; **8a**, 137742-44-0; **8b**, 135129-15-6; **9a**, 137742-45-1; **9b**, 137742-46-2; **15**, 126378-11-8; **16**, 137742-47-3; **20**, 137742-48-4; **21**, 137742-49-5; $Pd(OAc)_2(PPh_3)_2$, 14588-08-0; $Pd(PPh_3)_4$, 14221-01-3; n-Bu_4NCl, 1112-67-0; PhI, 591-50-4; p-$MeOC_6H_4I$, 696-62-8; 4-phenylcyclohexanone, 4894-75-1; trifluoromethanesulfonic anhydride, 358-23-6.

Supplementary Material Available: ^1H and ^{13}C NMR spectra of compounds **6d**, **9a**, and **16** (6 pages). Ordering information is given on any current masthead page.

Trapping of Cyclopentanediyl and Trimethylenemethane Triplet Diradicals with the Nitroxide 1,1,3,3-Tetramethyl-1,3-dihydroisoindolin-2-yloxyl

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Nitroxide trapping constitutes a convenient and effective alternative to dioxygen for the detection of triplet diradical intermediates. Thus, photolysis of the azoalkanes **1a–c** in the presence of the nitroxide 1,1,3,3-tetramethyl-1,3-dihydroisoindolin-2-yloxyl produced the bisalkoxyamines **3a–c** by trapping of the transient triplet diradicals **5a–c**. The resulting bis-adducts **3a–c** were fully characterized, and their regio- and stereochemistry were established on the basis of spectral and X-ray data for *trans*-**3a** and *trans*-**3b**. The novel bis-azoalkane **1d** was prepared and its photochemical loss of nitrogen studied in the presence of the above nitroxide or dioxygen as scavengers. In the case of the nitroxide, the tetrakis-adduct **3d** was obtained, tentatively assigned in view of its thermal instability, while with dioxygen the stable bis-peroxide **4d** was isolated and rigorously characterized. Instead of concurrent double denitrogenation to afford the high-spin non-Kekule species **5d** or its low-spin quinoid diradical **5d′**, stepwise loss of dinitrogen and trapping is proposed to be the pathway to these products.

The importance of diradicals in chemical reactions is reflected in the large number of recent studies on these short-lived intermediates, especially in photochemical transformations.[1] While most investigations of reactive diyl intermediates have utilized time-resolved laser flash techniques[2] and oxygen trapping, the latter technique has proven particularly useful both for lifetime determinations[3] and even for some synthetic purpose.[4] Oxygen trapping of diradicals has the advantage that no chromophores are needed and also that subtle features such as conformational effects on the ISC process[5] may be investigated. However, there exist some limitations with this trapping method in that the paramagnetic dioxygen molecule may enhance triplet to singlet ISC and that the peroxide trapping products are often unstable. Nonetheless, to date the use of other intermolecular trapping agents is quite limited, e.g. SO_2[6] and alkenes[7] have been employed to scavenge transient diradical species, which have been generated by laser flash photolysis (LFP).

Besides the well-established trapping by dioxygen, nitroxide radicals represent potentially useful scavenging agents for detecting diradicals. It is known that nitroxides bind to carbon-centered radicals at close to diffusion-controlled rates[8] and that the resultant alkoxyamine adducts can be readily isolated and characterized.[9] The nitroxide 1,1,3,3-tetramethyl-1,3-dihydroisoindolin-2-yloxyl appears to be ideal for this purpose as it contains a UV chromophore, which facilitates detection and structural elucidation of the resulting alkoxyamines. Despite these apparent advantages, the use of nitroxides has received much less attention in the detection of triplet diradicals, presumably due to enhanced ISC,[10] which has been claimed responsible for the lack of incorporation of nitroxides in the final diradical product. For photomechanistic purposes, nitroxides have been employed in LFP quenching studies of triplet diradicals.[10,11]

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