Highly Efficient and Selective Procedures for the Synthesis of γ-Alkylidenebutenolides via Palladium-Catalyzed Ene-Yne Coupling and Palladium- or Silver-Catalyzed Lactonization of (*Z*)-2-En-4-ynoic Acids. Synthesis of Rubrolides A, C, D, and E

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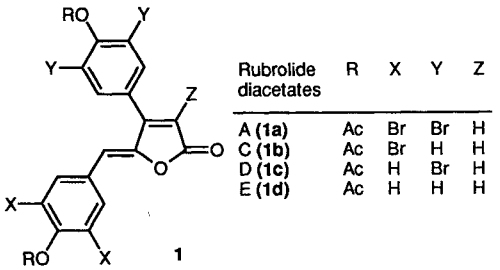
Received 5 July 1996; revised 9 August 1996

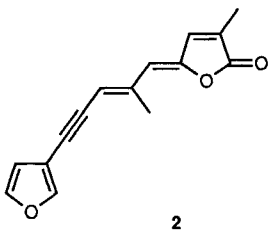
The diacetates of rubrolides A, C, D, and E **(1a–d)** were prepared in modest yields by the Pd-catalyzed cross coupling-lactonization tandem reaction of **5a** or **5b** with **6a** or **6b** using $Cl_2Pd(PPh_3)_2$ and CuI as catalysts. The feasibility of converting the diacetates into rubrolides was demonstrated by the synthesis of rubrolide C by treatment of **1b** with methanolic K_2CO_3 in THF. A detailed investigation of various parameters and conditions has indicated that formation of the corresponding six-membered lactones **7** and/or the cross coupling-lactonization-Heck substitution products **11** can be serious side reactions under non-optimized conditions and that the use of $Pd(PPh_3)_4$ rather than phosphine-free complexes, e.g., $Cl_2Pd(PhCN)_2$, or complexes of low phosphine content, e.g., $Cl_2Pd(PPh_3)_2$, along with CuI and NEt_3 in MeCN provides satisfactory conditions for the cross coupling-lactonization tandem reaction. Thus, the diacetate of rubrolide A **(1a)** was prepared in 70% isolated yield. The optimized conditions reported herein appear to be generally applicable to the stereoselective and regioselective synthesis of γ-alkylidenebutenolides in a highly efficient manner.

(*Z*)-γ-Alkylidenebutenolides represent a wide variety of natural products, such as rubrolides (**1**, R = H)[1] and freelingyne (**2**).[2] Rubrolides are marine tunicate metabolites exhibiting potent in vitro antibiotic activities and moderate but selective inhibition of protein phosphatases 1 and 2A.



Rubrolide diacetates	R	X	Y	Z
A (1a)	Ac	Br	Br	H
C (1b)	Ac	Br	H	H
D (1c)	Ac	H	Br	H
E (1d)	Ac	H	H	H

1



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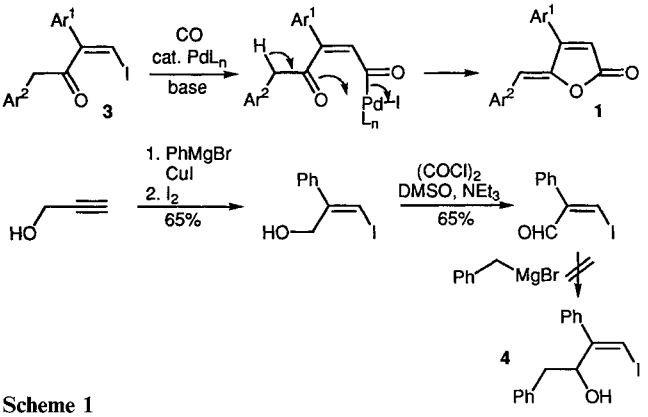
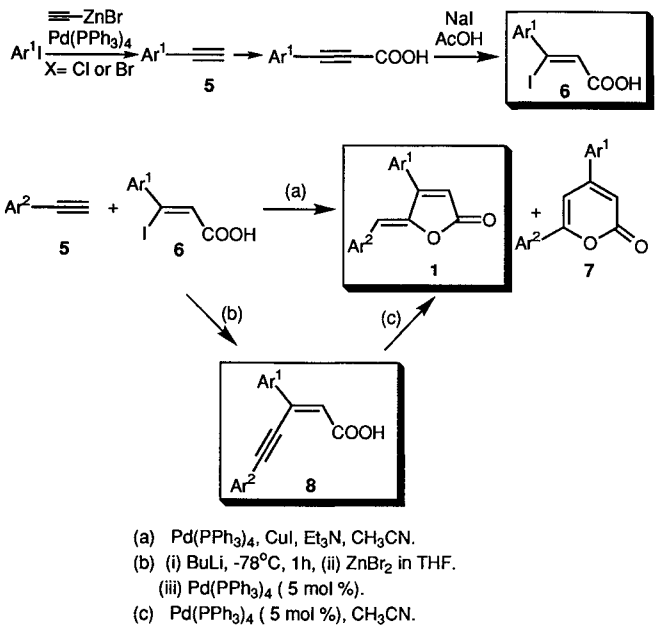
We first envisioned the synthesis of **1** through the use of a Pd-catalyzed intramolecular trapping of acylpalladium derivatives by enolates[3] (Scheme 1). However, the preparation of the requisite precursors **3** for the synthesis of rubrolides **1** proved to be quite challenging and problematical. Specifically, conversion of propargyl alcohol into (*Z*)-3-iodo-2-phenylprop-2-enol using PhMgBr and cat. CuI[4] followed by iodinolysis proceeded in 65% yield. Swern oxidation[5] of the iodo alcohol to give the corresponding aldehydes also proceeded as desired. However, its conversion to **4** by its treatment with benzylmagnesium bromide led to an intractable mixture which did not contain **4** in a useful yield.

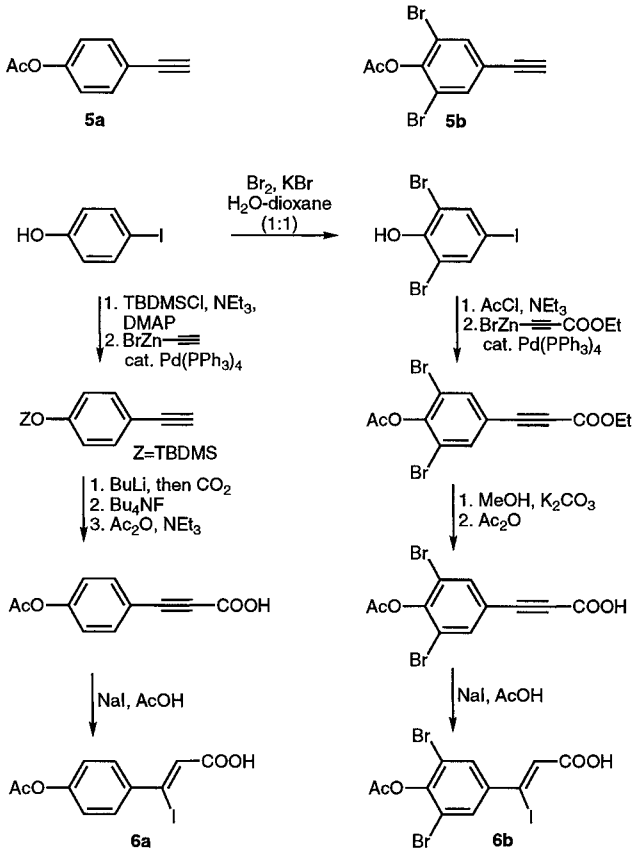


Scheme 1

In view of the difficulty mentioned above, we turned our attention to the application of the catalytic oxypalladation reaction of alkynoic acids[6,7] (Scheme 2). In particular, a recent tandem cross coupling-oxypalladation reaction of Lu[8] which was run essentially under the conditions of the Sonogashira coupling[9] appeared directly applicable to the synthesis of **1**. We therefore prepared **5a** and **5b** in 73 and 72% isolated yields, respectively, by direct ethynylation of the corresponding aryl iodides using ethynylzinc bromide and a catalytic amount of $Pd(PPh_3)_4$.[10] Although **6** may be preparable from **5**, the following indirect routes were employed to avoid any potential chemoselectivity problems (Scheme 3). Selective dibromination of 4-iodophenol required careful control of the reaction conditions to avoid displacement of iodine with bromine. After several attempts, the desired 2,6-dibromo-4-iodophenol (73% isolated yield) and 2,4,6-tribromophenol were obtained in a 6:1 ratio in 1:1 mixture of water and dioxane using Br_2 and KBr as brominating agents. The acetyl protective group was chosen in part because it proved to be compatible with hydroiodination and the Pd-catalyzed cross coupling-lactonization reaction and in part because of the ease of its removal. In contrast, the use of TBDMS in place of Ac in the cross coupling-lactonization reaction led to complex product mixtures. The preparation of **6a** and **6b** via hydroiodination was carried out with NaI in HOAc by applying a reported procedure for hydroiodination of alkynoic esters[11] to that of free alkynoic acids.



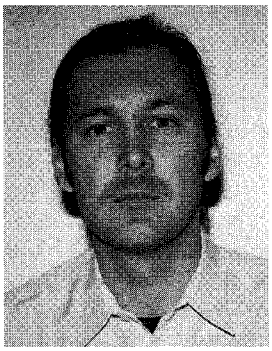
Scheme 2



Scheme 3

The cross coupling-lactonization reaction of **5** with **6** was initially carried out under essentially the same conditions as reported by Lu[8] in a 1.5/1 molar ratio in MeCN at 25 °C using NEt_3 as a base in the presence of 5 mol% each of $Cl_2Pd(PPh_3)_2$ and CuI. The two terminal alkynes,

Biographical Sketches



Ei-ichi Negishi received the bachelor's degree from the University of Tokyo in 1958. While he was a research chemist at Teijin, Ltd., Japan, he came to the University of Pennsylvania as a Fulbright Scholar in 1960 and received his Ph.D. degree in 1963. He joined Professor H.C. Brown's research group at Purdue University as a postdoctoral associate in 1966 and became his assistant in 1968. In 1972 he moved to Syracuse University as Assistant Professor and was promoted to Associate Professor in 1976. He returned to Purdue University as Professor in 1979. He is the author of about 250 scientific publications. His recent work has centered on the use of transition-metal complexes as catalytic reagents in organic synthesis. Some transition metal-catalyzed reactions developed by him and his students include Pd- or Ni-catalyzed cross-coupling, Pd-catalyzed cyclic carbopalladation reactions, and Zr- or Ti-catalyzed carbometallation reactions.

Martin Kotora received his first degree from Charles University (Prague, Czech Republic) in 1986. He then moved to Institute of Chemical Process Fundamentals as a graduate student, and received a Ph.D. degree in 1991. After working in the same institute he joined Professor Takahashi's group at Institute for Molecular Science (Japan) as a JSPS Fellow in 1993. Two years later he joined Professor Negishi's group at Purdue University. His research interest lies in the development of new synthetic methodologies with emphasis on organometallic chemistry of both main group and transition metals and their application in organic synthesis.

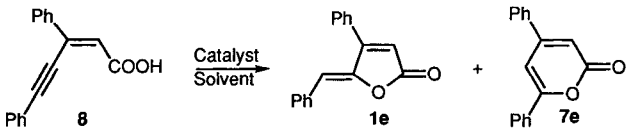
i.e., **5a** and **5b**, and the two (*Z*)-β-iodocinnamic acids, i.e., **6a** and **6b**, prepared as above provide four different combinations of **5** and **6**, and their reactions under the above-mentioned conditions indeed produced the corresponding diacetates of rubrolides A (**1a** from **5b** and **6b**, 38% isolated and 50% NMR yields), C (**1b** from **5b** and **6a**, 54% isolated and 63% NMR yields), D (**1c** from **5a** and **6b**, 54% isolated and 56% NMR yields) and E (**1d** from **5a** and **6a**, 50% isolated and 69% NMR yields) in the yields indicated in parentheses. In each case, the *Z*/*E* ratio was ≥ 50/1. Inspection of the concentrated reaction mixtures indicated that the amounts of **7a–d** were ≤ 2–3%. However, the presence of significant amounts of other unidentified byproducts was evident. The feasibility of converting the diacetates into rubrolides was demonstrated by the synthesis of rubrolide C in 78% isolated yield by treatment of its diacetate **1b** with methanolic K_2CO_3 in 1:1 MeOH/THF.

In the cross coupling-lactonization tandem process,[8] two critical bond formation reactions take place under one set of reaction conditions. Consequently, it is not clear which of the two processes is primarily responsible for the observed modest yields. In order to accurately diagnose possible difficulties in each process, in particular the lactonization step, and optimize the reaction conditions, we prepared (*Z*)-3,5-diphenylpent-2-en-4-ynoic acid (**8**) from phenylethynylzinc bromide and (*Z*)-3-iodocinnamic acid (**6e**) via Pd-catalyzed cross coupling.[10] Under these conditions, no lactonization took place. Lactonization of ≥ 99% pure **8** was then carried out using Pd-, Ag-, and Hg-containing catalysts. The results summarized in Table 1 reveal the following useful and intriguing features. Firstly, the use of $Cl_2Pd(PhCN)_2$, a phosphine-free complex employed by Utimoto et al.,[6] or various reagent combinations in which the ratio of PPh_3 to Pd was 2/1, i.e., $Cl_2Pd(PPh_3)_2$ employed by Lu et al.[8] as well as $Pd(dba)_2$ and $Pd(OAc)_2$ used in conjunction with 2 equivalents of PPh_3 led only to poor-to-modest yields of **1e**. Unexpectedly, the use of $Pd(PPh_3)_4$ led to significantly higher yields of **1e**. As such, this represents a rare example of those Pd-catalyzed reactions in which the 4/1 ratio of PPh_3 to Pd leads to more favorable results than the 2/1 ratio. Secondly, the yield of **1e** also depends on solvents, and MeCN appears to be superior to THF and DMF. Thirdly, the formation of **7e** (Ar = Ph) is a significant side reaction in this lactonization reaction. However, it can be suppressed to a level of 6% under the optimal conditions using $Pd(PPh_3)_4$ and MeCN. Fourthly, the use of $AgNO_3$[12,13] in MeOH as a catalyst can lead to up to a 95% yield of **1e** along with a only a minor amount (< 5%) of **7e** under very dilute conditions (0.01 M). However, the ratio of **1e** to **7e** is very much concentration dependent. Fifthly, $Hg(OCOCF_3)_2$[14] was totally ineffective under the conditions used.

With the findings gained in the above-described study in mind, we then investigated the Pd-catalyzed cross coupling-lactonization tandem reaction between phenylethyne and (*Z*)-β-halocinnamic acid containing I (**6e**) and Br (**6f**). Specifically, the reaction of phenylethyne with **6e** or **6f** was carried out using 5 mol% of a Pd–PPh_3 complex, CuI (5%), and NEt_3 (4 equiv.) in MeCN at 25 °C, and the results are summarized in Table 2. The following findings are noteworthy. Firstly, $Pd(PPh_3)_4$ is uniformly superior to $Cl_2Pd(PPh_3)_2$ even in this tandem reaction. That it has primarily to do with the PPh_3 to Pd ratio is indicated by the observation that the mere addition of 2 equivalents of PPh_3 to $Cl_2Pd(PPh_3)_2$ substantially increases the yield of **1e**. Secondly, the *Z*/*E* ratio is at least 50/1. Thirdly, both **6e** and **6f** are effective in this particular case. Using 5 mol% of $Pd(PPh_3)_4$ in place of $Cl_2Pd(PPh_3)_2$ along with CuI (5%) and NEt_3 (4 equiv.) in MeCN at 25 °C the diacetate of rubrolide A (**1a**) was obtained in 70% isolated yield (78% by NMR) from **5b** and **6b**. This corresponds to an improvement of yield by 32%. It is noteworthy that the use of the bromo analogue of **6b** under the same reaction conditions was much more sluggish, producing **1a** in only 20% yield even after 36 h at 25 °C. The rest of the bromide was recovered unreacted. It thus appears that the relative merits of iodides and bromides are strongly dependent on other substituents in the substrates.

To probe the generality of the optimized Pd-catalyzed tandem cross coupling-lactonization procedure, the reac-

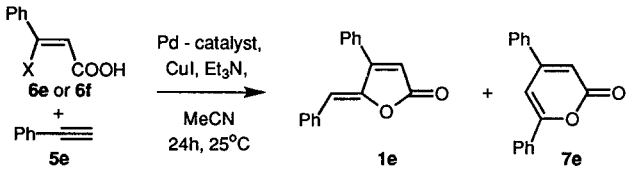
Table 1. Lactonization of (Z)-2,5-Diphenyl-2-penten-4-ynoic Acid **8** Catalyzed by Metal Complexes Containing Pd, Ag, and Hg



Catalyst	Solvent	Time[a] (h)	Product yield[b] (%) 1e	7e
$PdCl_2(PhCN)_2$	THF	3[c]	49	36
$PdCl_2(PhCN)_2$	THF	24	53	31
$PdCl_2(PhCN)_2$	CH_3CN	24	50	44
$PdCl_2(PPh_3)_2$	CH_3CN	24	27	10
$Pd(dba)_2 + 2PPh_3$	CH_3CN	24	27	6
$Pd(OAc)_2 + 2PPh_3$	CH_3CN	24	17	27
$Pd(PPh_3)_4$	CH_3CN	24	83	6
$Pd(PPh_3)_4$	DMF	24	64	17
$Pd(PPh_3)_4$	THF	24	20	22
$AgNO_3$[d]	CH_3OH	1	95	5
$Hg(OCOCF_3)_2$	CH_2Cl_2	192	<2	36

[a] Unless otherwise mentioned, the reaction was run at 25°C.
[b] ^1H NMR yield.
[c] Under reflux.
[d] The **1e**/**7e** ratio of 95/5 was observed at ≤ 0.01M in **8**. At its concentration of 0.1M, the ratio was 74/26.

Table 2. Cross Coupling-Lactonization of **6e** or **6f** with **5e** Catalyzed by Pd Complexes



6e (X=I), 6f (X=Br)

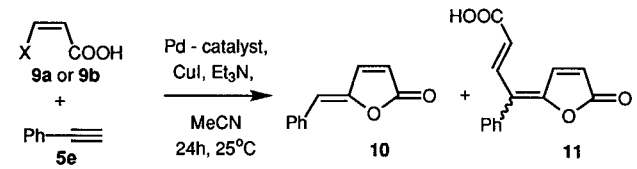
Catalyst	X	Product yield[a] (%) 1e[b]	7e
$PdCl_2(PPh_3)_2$	I	52	<2
$PdCl_2(PPh_3)_2$	Br	55	4
$Pd(PPh_3)_4$	I	80	<2
$Pd(PPh_3)_4$	Br	95	4
$PdCl_2(PPh_3)_2$ + $2PPh_3$	I	78	4
$Pd(dba)_2$ + $4PPh_3$	I	80	3

[a] ^1H NMR yield.
[b] Z/E ratio ≥ 50/1.

tion of phenylethyne **(5e)** with (*Z*)-β-haloacrylic acids **9a** (X = I) and **9b** (X = Br) was examined using $Pd(PPh_3)_4$ and $Cl_2Pd(PPh_3)_2$. One of the objectives is to see if the effect of the amount of PPh_3 observed above is general. Another is to see if the high *Z*/*E* ratio observed with **6** would be maintained even with **9** containing a β-H atom rather than a bulky aryl group. This is a potentially important issue in the synthesis of various γ-alkylidenebutenolides containing a β-H atom, such as freelingyne **(2)**. The results summarized in Table 3 indicate the following. Firstly, $Pd(PPh_3)_4$ is, once again, uniformly superior to $Cl_2Pd(PPh_3)_2$. Secondly, (*Z*)-β-bromoacrylic acid **(9b)** is superior to its iodo analogue **9a** in this case. Thirdly, one side reaction, which can be serious, is the formation of **11** which must arise via the Heck reaction[15] of **9** with **10**. When only 1.5 equivalents of phenylethyne were used, the formation of **11** was indeed a serious side reaction in cases where $Cl_2Pd(PPh_3)_2$ and/or (*Z*)-β-iodoacrylic acid **(9a)** were employed. This appears to provide an explanation for the first and second generalizations mentioned above. Fourthly, the *Z*/*E* ratio is at least 30/1. It thus appears that the *Z*/*E* ratio is mechanistically and kinetically controlled and that it most likely is essentially independent of the steric requirement of the β-substituent in γ-alkylidenebutenolides. If this should indeed be the case, the reaction would distinguish itself from most of the previously developed syntheses of γ-alkylidenebutenolides, such as carbonyl-olefination[2] and trapping of acylpalladiums by *O*-enolates.[3]

Despite a number of related previous studies,[6-8] the rubrolide synthesis herein reported appears to represent the first set of results demonstrating the practical applicability of the Pd-catalyzed alkynoic acid lactonization methodology to highly efficient and selective syntheses of natural products.

Table 3. Cross Coupling-Lactonization of **9a** or **9b** with **5e** Catalyzed by Pd Complexes



9a (X=I), 9b (X=Br)

Catalyst	Alkyne(eq.)	X	Product yield[a] (%) 10[b]	11
$PdCl_2(PPh_3)_2$	1.5	I	24	38
$PdCl_2(PPh_3)_2$	4	I	37	19
$Pd(PPh_3)_4$	1.5	I	46	23
$Pd(PPh_3)_4$	10	I	60	3
$PdCl_2(PPh_3)_2$	1.5	Br	42	27
$Pd(PPh_3)_4$	1.5	Br	74	11
$Pd(PPh_3)_4$	4	Br	78	<2
$Pd(PPh_3)_4$	10	Br	80	<2
$PdCl_2(PPh_3)_2$ + $2PPh_3$	1.5	Br	86	5

[a] ^1H NMR yields.
[b] Z/E ratio ≥ 30/1.

All reactions involving organometallic reagents were conducted under dry Ar atmosphere. ^1H and ^{13}C NMR spectra were recorded in $CDCl_3$, unless otherwise noted, on a Varian Gemini 200 spectrometer (200 MHz for ^1H and 50.3 MHz for ^{13}C, respectively). IR spectra were recorded on Perkin–Elmer 1800 FTIR. HRMS data were recorded on a Kratos MS-50 mass spectrometer. Solvents were purified and dried according to standard procedures. Reagents were purchased from commercial sources, and used as obtained, unless otherwise stated. $PdCl_2$ was received from Johnson Matthey. $Pd(PPh_3)_4$ and $PdCl_2(PPh_3)_2$ were prepared as reported.[16]

2,6-Dibromo-4-iodophenol:
To a solution of 4-iodophenol (4.40 g, 20 mmol) in dioxane-H_2O (100 mL, 1:1) was added dropwise a brominating agent (70 mL) prepared from Br_2 (32 mL) and KBr (150 g) in H_2O (1 L). The mixture was stirred for additional 30 min, treated with brine (100 mL), and extracted with Et_2O (4 × 25 mL). The organic layer was washed with brine (25 mL) and $Na_2S_2O_3$ (25 mL), dried (Na_2SO_4), and concentrated in vacuo. Column chromatography on silica gel (4/1 hexane/Et_2O) afforded 6.21 g of an inseparable mixture of the title compound (5.41 g, 71 %) and 2,4,6-tribromophenol (0.80 g, 12 %) as a white solid, mp 99–103 °C.

^1H NMR ($CDCl_3$): δ = 5.89 (br s, 1 H), 7.73 (s, 2 H).

^{13}C NMR ($CDCl_3$): δ = 81.69, 110.71 (2C), 139.63 (2C), 149.45.

4-Acetoxyphenylethyne (5a):
Acetylation of 4-iodophenol (2.20 g, 10 mmol) was carried out in CH_2Cl_2 (50 mL) with AcCl (0.86 g, 11 mmol) and Et_3N (1.20 g,

12 mmol). The product was treated with ethynylzinc bromide (15 mmol) in the presence of $Pd(PPh_3)_4$ (0.42 g, 0.36 mmol) according to a previously reported procedure.[10] The crude product was purified by column chromatography on silica gel (4/1 hexane/Et_2O) to afford the title compound (1.17 g, 73%) as a white solid, mp 63 °C.

^1H NMR ($CDCl_3$): $\delta = 2.29$ (s, 3H), 3.07 (s, 1H), 7.06 (d, $J = 8.7$ Hz, 2H), 7.51 (d, $J = 8.7$ Hz, 2H).

^{13}C NMR ($CDCl_3$): $\delta = 21.04$, 77.29, 82.74, 119.69, 121.64 (2C), 133.26 (2C), 150.77, 169.00.

IR ($CDCl_3$): $\nu = 3308$, 1759, 1602, 1502, 1207, 1016 cm^{-1}.

HRMS for $C_{10}H_8O_2$ calc. 160.0524, found 160.0521.

4-(*tert*-Butyldimethylsilyloxy)phenylethyne:
Silylation of 4-iodophenol (4.40 g, 20 mmol) was carried out in CH_2Cl_2 (50 mL) with *tert*-butyldimethylchlorosilane (3.32 g, 22 mmol), Et_3N (2.42 g, 24 mmol), and DMAP (0.12 g, 1 mmol). Its ethynylation as above followed by distillation afforded the title compound (2.84 g, 75%) as a colorless oil (84–86 °C/0.25 mmHg).

^1H NMR ($CDCl_3$): $\delta = 0.20$ (s, 6H), 0.98 (s, 9H), 3.00 (s, 1H), 6.78 (d, $J = 8.7$ Hz, 2H), 7.37 (d, $J = 8.7$ Hz, 2H).

^{13}C NMR ($CDCl_3$): $\delta = -4.42$ (2C), 18.21, 25.61 (3C), 75.89, 83.69, 114.77, 120.15 (2C), 133.57 (2C), 156.32.

IR (neat): $\nu = 3318$, 3296, 2958, 2932, 2860, 1602, 1504, 1472, 1266, 1166, 911 cm^{-1}.

HRMS for $C_{14}H_{20}OSi$ calc. 160.0524, found 160.0521.

4-Acetoxy-2,6-dibromophenylethyne:
Acetylation of a mixture of 2,6-dibromo-4-iodophenol (0.76 g, 2 mmol) and 2,4,6-tribromophenol (88 mg, 0.27 mmol) in CH_2Cl_2 (20 mL) was carried out with AcCl (0.24 g, 3 mmol) and Et_3N (0.30 g, 3 mmol). Ethynylation as above followed by column chromatography on silica gel (9/1 hexane/Et_2O) afforded 4-acetoxy-2,6-dibromophenylethyne (0.46 g, 72%) as a white solid, mp 93–94 °C.

^1H NMR ($CDCl_3$): $\delta = 2.40$ (s, 3H), 3.14 (s, 1H), 7.67 (s, 2H).

^{13}C NMR ($CDCl_3$): $\delta = 20.44$, 79.75, 79.97, 117.52 (2C), 122.66, 135.61 (2C), 146.76, 166.91.

IR ($CDCl_3$): $\nu = 3304$, 1774, 1558, 1468, 1204, 1182, 1010 cm^{-1}.

HRMS for $C_{10}H_6Br_2O_2$ calc. 315.8734, found 315.8730.

3-(4-Hydroxyphenyl)prop-2-ynoic Acid:
To a solution of 4-(*tert*-butyldimethylsilyloxy)phenylethyne (2.10 g, 9.1 mmol) in THF (50 mL) was added dropwise BuLi (3.5 mL of 2.6 M in hexanes, 9.1 mmol) at −78 °C. The mixture was stirred at −78 °C for 1 h, treated with an excess of finely powdered dry ice, warmed to 25 °C, quenched with 3M HCl, extracted with Et_2O (4 × 25 mL), dried (Na_2SO_4), and concentrated in vacuo to afford crude 3-(4-(*tert*-butyldimethylsilyloxy)phenyl)prop-2-ynoic acid (2.18 g, 87%) as a white solid. To a solution of 3-(4-(*tert*-butyldimethylsilyloxyphenyl)prop-2-ynoic acid (1.38 g, 5 mmol) in THF (10 mL) was added Bu_4NF (10 mL of 1.0 M solution, 10 mmol). The mixture was stirred for 1 h at 25 °C, diluted with 3M HCl (10 mL), extracted with Et_2O (4 × 10 mL), and dried (Na_2SO_4). Concentration and complete removal of solvents in vacuo afforded the title compound[17] (0.81 g, 94%) as a white solid, mp > 120 °C (dec.).

^1H NMR (acetone-d_6): $\delta = 6.91$ (d, $J = 8.7$ Hz, 2H), 7.49 (d, $J = 8.7$ Hz, 2H), 9.20 (br s, 2H).

^{13}C NMR (acetone-d_6): $\delta = 80.78$, 87.20, 110.84, 116.82 (2C), 135.76 (2C), 154.84, 160.75.

HRMS for $C_9H_6O_3$ calc. 162.0317, found 162.0315.

3-(4-Acetoxyphenyl)prop-2-ynoic Acid:
Acetylation of 3-(4-hydroxyphenyl)prop-2-ynoic acid (0.74 g, 4.6 mmol) was carried out in CH_2Cl_2 (20 mL) with Ac_2O (1.12 g, 11 mmol) and Et_3N (1.40 g, 14 mmol) at 25 °C for 3 h, followed by dilution with 3 M HCl (10 mL), extraction with Et_2O (3 × 20 mL), drying (Na_2SO_4), and concentration in vacuo to afford the title compound (0.89 g, 95%) as a white solid, mp 141–143 °C.

^1H NMR ($CDCl_3$): $\delta = 2.32$ (s, 3H), 7.14 (d, $J = 8.9$ Hz, 2H), 7.63 (d, $J = 8.9$ Hz, 2H), 11.26 (br s, 1H).

^{13}C NMR ($CDCl_3$): $\delta = 21.11$, 80.14, 88.12, 116.59, 122.17 (2C), 134.69 (2C), 152.64, 158.29, 169.00.

IR ($CDCl_3$): $\nu = 2232$, 1772, 1683, 1600, 1506, 1412, 1202, 1142, 1016 cm^{-1}.

HRMS for $C_{11}H_8O_4$ calc. 204.0423, found 204.0421.

Ethyl 3-(4-Acetoxy-3,5-dibromophenyl)prop-2-ynoate:
To a solution of ethyl propynoate (0.59 g, 6 mmol) in THF (15 mL) cooled to −78 °C was added dropwise BuLi (2.3 mL of 2.6 M in hexanes, 6 mmol) over 10 min. The mixture was stirred at −78 °C for 1 h, treated with a solution of $ZnBr_2$ (1.35 g, 6 mmol) in THF (20 mL) chilled with dry ice, warmed to 0 °C, and stirred for 1 h. To this solution were added a 6:1 mixture of acylated 2,6-dibromo-4-iodophenol (2.60 g, 6.2 mmol) and acylated 2,4,6-tribromophenol (0.87 g, 2.3 mmol), and $Pd(PPh_3)_4$ (0.34 g, 0.3 mmol). After stirring for 6 h at 25 °C the mixture was quenched with 3M HCl (10 mL), extracted with pentane (4 × 10 mL), dried (Na_2SO_4), and concentrated in vacuo. Column chromatography on silica gel (70/15/15 hexane/Et_2O/CH_2Cl_2) afforded the title compound (1.24 g, 55%) as light yellow solid, mp 96–97 °C.

^1H NMR ($CDCl_3$): $\delta = 1.33$ (t, $J = 7.2$ Hz, 3H), 2.39 (s, 3H), 4.28 (q, $J = 7.2$ Hz, 2H), 7.76 (s, 2H).

^{13}C NMR ($CDCl_3$): $\delta = 13.96$, 20.39, 62.39, 81.48, 82.22, 117.96 (2C), 120.16, 136.26 (2C), 148.24, 153.20, 166.62.

IR ($CDCl_3$): $\nu = 3078$, 2986, 2224, 1778, 1706, 1542, 1452, 1370, 1300, 1235, 1187, 1010 cm^{-1}.

HRMS for $C_{13}H_{10}Br_2O_4$ calc. 387.8946, found 387.8950.

3-(4-Acetoxy-3,5-dibromophenyl)prop-2-ynoic Acid:
To a solution of ethyl 3-(4-acetoxy-3,5-dibromophenyl)prop-2-ynoate (0.94 g, 2.4 mmol) in MeOH (10 mL) was added 1 M solution of K_2CO_3 in H_2O (3 mL, 3 mmol). The mixture was stirred at 50 °C for 12 h, quenched with 3M HCl (10 mL), extracted with Et_2O (5 × 10 mL), dried (Na_2SO_4), and concentrated in vacuo to afford 3-(3,5-dibromo-4-hydroxyphenyl)prop-2-ynoic acid as a white powder, which was used immediately in the next step.

Acetylation of 3-(3,5-dibromo-4-hydroxyphenyl)prop-2-ynoic acid (0.76 g, 2.4 mmol) was carried out in a mixture of CH_2Cl_2 (14 mL) and Et_2O (7 mL) with Ac_2O (0.82 g, 7.5 mmol) and Et_3N (1.01 g, 10 mmol) at 25 °C for 3 h. The mixture was diluted with 3M HCl (10 mL), extracted with Et_2O (5 × 10 mL), and dried (Na_2SO_4). Concentration and complete removal of solvents in vacuo afforded the title compound (0.80 g, 93%) as a white solid, mp 131–132 °C.

^1H NMR ($CDCl_3$): $\delta = 2.42$ (s, 3H), 7.80 (s, 2H), 11.50 (br s, 1H).

^{13}C NMR ($CDCl_3$): $\delta = 20.45$, 81.44, 84.34, 118.14 (2C), 119.62, 136.58 (2C), 148.70, 157.43, 166.86.

IR ($CDCl_3$): $\nu = 2224$, 1774, 1690, 1588, 1542, 1454, 1410, 1372, 1296, 1242, 1178, 1008 cm^{-1}.

HRMS for $C_{11}H_6Br_2O_4$ calc. 359.8633, found 359.8629.

(Z)-3-(4-Acetoxyphenyl)-3-iodoprop-2-enoic Acid **(6a):**
Hydroiodination of 3-(4-acetoxyphenyl)prop-2-ynoic acid (0.41 g, 2 mmol) with NaI (1.28 g, 8 mmol) in HOAc (5 mL) at 115 °C for 1 h according to a previously reported procedure[11] followed by column chromatography on silica gel (1/1 hexane/Et_2O) afforded the title compound (0.51 g, 77%) as a light yellow solid, mp 150–152 °C.

^1H NMR ($CDCl_3$): $\delta = 2.33$ (s, 3H), 6.70 (s, 1H), 7.11 (d, $J = 8.5$ Hz, 2H), 7.68 (d, $J = 8.5$ Hz, 2H), 10.50 (br s, 1H).

^{13}C NMR ($CDCl_3$): $\delta = 21.11$, 118.09, 121.56 (2C), 126.24, 130.01 (2C), 140.73, 152.04, 169.22 (2C).

IR ($CDCl_3$): $\nu = 3588$, 1767, 1744, 1697, 1598, 1502, 1276, 1210, 1168, 1016, 842 cm^{-1}.

HRMS for $C_{11}H_9IO_4$ calc. 331.9546, found 331.9548.

(Z)-3-(4-Acetoxy-3,5-dibromophenyl)-3-iodoprop-2-enoic Acid **(6b):**
Hydroiodination of 3-(4-acetoxy-3,5-dibromophenyl)prop-2-ynoic acid (0.68 g, 1.9 mmol) with NaI (1.11 g, 7.5 mmol) in HOAc (5 mL) as above, followed by column chromatography on silica gel (1/1

hexane/Et_2O) afforded the title compound (0.66 g, 72%) as a light yellow solid, mp 171–172°C.

^1H NMR ($CDCl_3$): δ = 2.42 (s, 3H), 6.72 (s, 1H), 7.73 (s, 2H), 10.3 (br s, 1H).

^{13}C NMR ($CDCl_3$): δ = 20.51, 113.81, 117.62 (2C), 127.98, 132.38 (2C), 143.34, 147.57, 167.03, 168.52.

IR ($CDCl_3$): ν = 3512, 1792, 1738, 1702, 1602, 1546, 1452, 1298, 1248 cm^{-1}.

HRMS for $C_{11}H_7Br_2IO_4$ calc. 487.7756, found 487.7751.

(Z)-3-(4-Acetoxy-3,5-dibromophenyl)-3-bromoprop-2-enoic Acid **(6c):**

Hydrobromination of 3-(4-acetoxy-3,5-dibromophenyl)prop-2-ynoic acid (0.30 g, 0.83 mmol) with LiBr (0.92 g, 3.3 mmol) in HOAc (2 mL) as above, followed by column chromatography on silica gel (1/1 hexane/Et_2O) afforded the title compound (0.27 g, 59%) as a light yellow solid, mp 185–186°C.

^1H NMR ($CDCl_3$): δ = 2.42 (s, 3H), 6.77 (s, 1H), 7.84 (s, 2H), 9.4 (br s, 1H).

^{13}C NMR ($CDCl_3$): δ = 20.47, 117.98 (2C), 121.35, 131.91 (2C), 135.95, 139.22, 148.04, 166.90, 168.41.

IR ($CDCl_3$): ν = 3500, 1702, 1612, 1460, 1184 cm^{-1}.

HRMS for $C_{11}H_7Br_3O_4$ calc. 440.7973, found 440.7977.

(Z)-3-Iodo-3-phenylpropenoic acid **(6e):**

Hydroiodination of 3-phenylprop-2-ynoic acid (1.46 g, 10 mmol) with NaI (6.00 g, 40 mmol) in HOAc (7 mL) as above, followed by column chromatography on silica gel (1/1 hexane/Et_2O) afforded the title compound (2.35 g, 86%) as a light yellow solid, mp 139–140°C (lit.[18] mp 127–128°C).

^1H NMR ($CDCl_3$): δ = 6.73 (s, 1H), 7.70–7.90 (m, 3H), 8.00–8.20 (m, 2H), 11.70 (br s, 1H).

^{13}C NMR ($CDCl_3$): δ = 119.71, 126.11, 128.44 (2C), 128.79 (2C), 130.32, 143.22, 169.70.

IR ($CDCl_3$): ν = 3512, 1695, 1599, 1576, 1444, 1297, 1213, 1124 cm^{-1}.

HRMS for $C_9H_7IO_2$ calc. 273.9491, found 273.9491.

(Z)-3-Bromo-3-phenylpropenoic Acid **(6f):**

Hydrobromination of 3-phenylprop-2-ynoic acid (1.46 g, 10 mmol) with LiBr (2.6 g, 30 mmol) in HOAc (5 mL) as above, followed by recrystallization from hexane/Et_2O afforded the title compound (1.00 g, 44%) as colorless crystals, mp 135°C (lit.[19] mp 135°C).

^1H NMR ($CDCl_3$): δ = 6.80 (s, 1H), 7.40–7.50 (m, 3H), 7.60–7.70 (m, 2H), 11.90 (br s, 1H).

^{13}C NMR ($CDCl_3$): δ = 119.47, 128.11 (2C), 128.56 (2C), 130.83, 139.13, 140.82, 169.79.

IR ($CDCl_3$): ν = 3500, 1703, 1612, 1410, 1324, 1284, 1238, 1187 cm^{-1}.

(Z)-3-Iodoprop-2-enoic Acid **(9a):**

Hydroiodination of propynoic acid (1.4 g, 20 mmol) with NaI (4.8 g, 32 mmol) in HOAc (7 mL) as above, followed by filtration over a short column of silica gel and concentration in vacuo afforded the title compound[20] (2.0 g, 51%) as a white solid, mp 66–67°C (lit.[21] mp 63–65°C).

^1H NMR ($CDCl_3$): δ = 6.98 (d, J = 9.0 Hz, 1H), 7.70 (d, J = 9.0 Hz, 1H), 12.30 (br s).

^{13}C NMR ($CDCl_3$): δ = 98.34, 129.39, 170.04.

IR ($CDCl_3$): ν = 3500, 1701, 1598, 1404, 1312, 1282, 1228 cm^{-1}.

(Z)-3-Bromoprop-2-enoic Acid **(9b):**

Hydrobromination of propynoic acid (0.70 g, 10 mmol) with LiBr (1.74 g, 20 mmol) in HOAc (2 mL) as above, followed by filtration over a short column of silica gel and concentration in vacuo afforded the title compound (1.40 g, 93%) as a white solid, mp 60°C (lit.[22] mp 55°C).

^1H NMR ($CDCl_3$): δ = 6.69 (d, J = 8.5 Hz, 1H), 7.18 (d, J = 8.5 Hz, 1H), 12.20 (br s, 1H).

^{13}C NMR ($CDCl_3$): δ = 123.86, 124.47, 169.56.

IR ($CDCl_3$): ν = 3500, 1699, 1612, 1578, 1490, 1446, 1398, 1296, 1232, 1204 cm^{-1}.

Synthesis of Rubrolide Diacetates (1a–d);[8] General Procedure:

To a solution of (*Z*)-3-iodocinnamic acid (0.25 mmol) in MeCN (5 mL) was added an alkyne (0.38 mmol), $PdCl_2(PPh_3)_2$ (8.8 mg, 12.5 μmol), CuI (2.4 mg, 12.5 μmol), and Et_3N (101 mg, 1 mmol). The mixture was stirred at 25°C for 36 h, concentrated in vacuo, dissolved in $CDCl_3$, and analyzed by ^1H NMR spectroscopy. This solution was diluted with 3M HCl, extracted with Et_2O or CH_2Cl_2, dried (Na_2SO_4), and concentrated in vacuo.

Rubrolide A Diacetate **(1a)**:

This compound was prepared as above from **6b** (122 mg, 0.25 mmol) and **5b** (115 mg, 0.38 mmol). Column chromatography on silica gel (5/4/1 hexane/$CHCl_3$/EtOAc) afforded the title compound[1] (65 mg, 38%) as a light yellow solid.

^1H NMR ($CDCl_3$): δ = 2.41 (s, 3H), 2.46 (s, 3H), 5.97 (s, 1H), 6.31 (s, 1H), 7.66 (s, 2H), 8.00 (s, 2H).

^{13}C NMR ($CDCl_3$): δ = 20.52 (2C), 110.01, 117.05, 118.19 (2C), 118.86 (2C), 130.05, 132.02 (2C), 132.94, 134.02 (2C), 146.70, 148.15, 148.47, 154.70, 166.96, 167.01, 167.06.

IR (CH_2Cl_2): ν = 1772, 1546, 1372, 1182, 1010, 850 cm^{-1}.

Rubrolide C Diacetate **(1b)**:

This compound was prepared as above from **6a** (83 mg, 0.25 mmol) and **5b** (115 mg, 0.38 mmol). Column chromatography on silica gel with (3/1/1 hexane/CH_2Cl_2/EtOAc) afforded the title compound[1] (70 mg, 54%) as a light yellow solid.

^1H NMR ($CDCl_3$): δ = 2.36 (s, 3H), 2.40 (s, 3H), 6.00 (s, 1H), 6.26 (s, 1H), 7.26 (d, J = 8.7 Hz, 2H), 7.50 (d, J = 8.7 Hz, 2H), 7.98 (s, 2H).

^{13}C NMR ($CDCl_3$): δ = 20.51, 21.15, 109.70, 115.69, 118.08 (2C), 122.63 (2C), 127.35, 129.69 (2C), 133.35, 133.89 (2C), 146.40, 149.19, 152.50, 157.52, 167.08, 167.77, 169.10.

IR (CH_2Cl_2): ν = 1776, 1504, 1458, 1371, 1213, 1200, 1180, 1168, 1065 cm^{-1}.

Rubrolide D Diacetate **(1c)**:

This compound was prepared as above from **6b** (122 mg, 0.25 mmol) and **5a** (61 mg, 0.38 mmol). Column chromatography on silica gel (7/3 hexane/EtOAc) afforded the title compound[1] (70 mg, 54%) as a light yellow solid.

^1H NMR ($CDCl_3$): δ = 2.32 (s, 3H), 2.45 (s, 3H), 6.12 (s, 1H), 6.25 (s, 1H), 7.15 (d, J = 8.8 Hz, 2H), 7.69 (s, 2H), 7.85 (d, J = 8.8 Hz, 2H).

^{13}C NMR ($CDCl_3$): δ = 20.52, 21.16, 113.17, 115.97, 118.70 (2C), 122.16 (2C), 130.22, 130.58, 132.10 (2C), 132.17 (2C), 147.07, 147.92, 151.51, 154.88, 167.02, 167.76, 169.07.

IR (CH_2Cl_2): ν = 1765, 1506, 1454, 1370, 1217, 1198, 1169, 947 cm^{-1}.

Rubrolide E Diacetate **(1d)**:

This compound was prepared as above from **6a** (83 mg, 0.25 mmol) and **5b** (61 mg, 0.38 mmol). Column chromatography on silica gel with (5/2.5/2.5 hexane/CH_2Cl_2/EtOAc) afforded the title compound[1] (46 mg, 50%) as a white solid.

^1H NMR ($CDCl_3$): δ = 2.31 (s, 3H), 2.36 (s, 3H), 6.16 (s, 1H), 6.21 (s, 1H), 7.14 (d, J = 8.8 Hz, 2H), 7.26 (d, J = 8.7 Hz, 2H), 7.52 (d, J = 8.7 Hz, 2H), 7.83 (d, J = 8.8 Hz, 2H).

^{13}C NMR ($CDCl_3$): δ = 21.12 (2C), 112.82, 114.66, 122.03 (2C), 122.46 (2C), 123.71 (2C), 127.83, 130.56, 131.96 (2C), 147.72, 151.21, 152.30, 157.70, 168.48, 169.08, 169.14.

IR (CH_2Cl_2): ν = 1763, 1610, 1502, 1372, 1201, 1168, 1086, 1018, 960 cm^{-1}.

Improved Procedure for the Preparation of Diacetate of Rubrolide A:

The reaction was carried out on a 0.25 mmol scale under the same conditions as above, except that $Pd(PPh_3)_4$ (14.5 mg, 12.5 μmol) was used as a catalyst. Column chromatography on silica gel (5/4/1 hexane/$CHCl_3$/EtOAc) afforded the title compound (100 mg, 70%) as a light yellow solid.

Diacetate of Rubrolide A from (*Z*)-Bromocinnamic Acid (6c):
The reaction was carried out on a 0.25 mmol scale under the same conditions as above, except that (*Z*)-bromocinnamic acid (111 mg, 0.25 mmol) and $Pd(PPh_3)_4$ (14.5 mg, 12.5 μmol) were used. However, ^1H NMR ($CDCl_3$) analysis of a mixture showed that rubrolide A diacetate was formed in 20% yield under these conditions.

Rubrolide C:
To a solution of rubrolide C diacetate (18 mg, 35 μmol) in a mixture of CH_3OH-THF (1/1, 2 mL) was added 1 M K_2CO_3 (0.2 mL, 0.2 mmol). The mixture was stirred at 25°C for 1 h, quenched with 3M HCl (2 mL), extracted with Et_2O (5 × 2 mL), dried (Na_2SO_4), and concentrated in vacuo. Column chromatography on silica gel (1/1 hexane/EtOAc) afforded the title compound[1] (12 mg, 78%) as a yellow solid.

^1H NMR ($CDCl_3$): $\delta = 6.43$ (s, 1H), 6.52 (s, 1H), 6.95 (d, $J = 8.6$ Hz, 2H), 7.54 (d, $J = 8.6$ Hz, 2H), 8.10 (s, 2H), 10.20 (br s, 1H), 10.50 (br s, 1H).

(*Z*)-3,5-Diphenylpent-2-en-4-ynoic Acid (8):
To a solution of phenylethynylzinc bromide, prepared from phenylacetylene (3.10 g, 30 mmol), BuLi (12 mL of 2.6 M in hexanes, 30 mmol), and $ZnBr_2$ (6.80 g, 30 mmol) in THF (100 mL), were added (*Z*)-3-iodo-3-phenylpropenoic acid **6e** (2.74 g, 10 mmol) and $Pd(PPh_3)_4$ (0.23 g, 0.2 mmol) at 0°C. The mixture was stirred at 0°C for 1 h and at 25°C for 3 h, quenched with 3M HCl (20 mL), extracted with Et_2O (4 × 25 mL), dried (Na_2SO_4), and concentrated in vacuo. Recrystallization from hexane-Et_2O afforded the title compound (1.50 g, 52%) as colorless crystals, mp 122–123°C.

^1H NMR ($CDCl_3$): $\delta = 6.68$ (s, 1H), 7.30–7.50 (m, 6H), 7.60–7.70 (m, 2H), 7.80–7.90 (m, 2H), 12.65 (br s, 1H).

^{13}C NMR ($CDCl_3$): $\delta = 86.77$, 103.82, 121.60, 122.46, 127.31 (2C), 128.45 (2C), 128.70 (2C), 128.43, 130.28, 132.14 (2C), 136.71, 138.65, 171.10

IR ($CDCl_3$): $\nu = 2198$, 1685, 1600, 1590, 1574, 1490, 1450, 1284 cm^{-1}.

HRMS for $C_{17}H_{12}O_2$ calc. 248.0837, found 240.0831.

Palladium-Catalyzed Cyclization; General Procedure:
To a solution of (*Z*)-3,5-diphenylpent-2-en-4-ynoic acid (12.4 mg, 50 μmol) in a solvent (5 mL) was added a palladium catalyst [$PdCl_2(PhCN)_2$, $PdCl_2(PPh_3)_2$, $Pd(PPh_3)_4$, $Pd(dba)_2 + 2PPh_3$, or $PdCl_2(OAc)_2 + 2PPh_3$, 2.5 μmol]. The mixture was stirred at 25°C for 24 h, concentrated in vacuo, dissolved in $CDCl_3$, and analyzed by ^1H NMR spectroscopy. The results are summarized in Table 1.

Silver Nitrite Catalyzed Cyclization of (*Z*)-3,5-Diphenylpent-2-en-4-ynoic Acid (8):[12]
To a solution of (*Z*)-3,5-diphenylpent-2-en-4-ynoic acid (12.4 mg, 50 μmol) in MeOH (5 mL) was added $AgNO_3$ (5 μL of 0.1 M in H_2O, 0.5 mol). The mixture was stirred at 25°C for 1 h, concentrated in vacuo, dissolved in $CDCl_3$, and analyzed by ^1H NMR spectroscopy. The results are summarized in Table 1.

For preparative purpose, cyclization was carried out under the same conditions as above with 3,5-diphenylpent-2-en-4-ynoic acid (0.124 g, 0.5 mmol) and $AgNO_3$ (4 mg, 25 μmol) in MeOH (5 mL). Column chromatography (7/3 hexane/Et_2O) afforded (*Z*)-5-benzylidene-4-phenyl-5*H*-furan-2-one[23] (79 mg, 64%) and 4,6-diphenylpyran-2-one[24] (35 mg, 28%).

(Z)-5-Benzylidene-4-phenyl-5H-furan-2-one **(1e)**:

Mp 122–123°C (lit.[23] mp 114°C).

^1H NMR ($CDCl_3$): $\delta = 6.19$ (s, 1H), 6.20 (s, 1H), 7.30–7.45 (m, 4H), 7.45–7.60 (m, 4H), 7.75–7.85 (m, 2H).

^{13}C NMR ($CDCl_3$): $\delta = 113.83$, 114.40, 128.43 (2C), 128.72 (2C), 129.01 (2C), 129.23, 130.28, 130.39, 130.72 (2C), 132.85, 147.84, 158.69, 168.75.

IR ($CDCl_3$): $\nu = 1758$, 1648, 1492, 1450, 1350, 1220, 1186, 1030 cm^{-1}.

4,6-Diphenylpyran-2-one **(7e)**:

Mp 138–139°C (lit.[24] mp 140°C).

^1H NMR ($CDCl_3$): $\delta = 6.47$ (d, $J = 1.4$ Hz, 1H), 6.97 (d, $J = 1.4$ Hz, 1H), 7.40–7.50 (m, 6H), 7.60–7.70 (m, 2H), 7.85–7.95 (m, 2H).

^{13}C NMR ($CDCl_3$): $\delta = 101.36$, 109.26, 125.73 (2C), 126.71 (2C), 128.95 (2C), 129.23 (2C), 130.67, 130.91, 131.50, 136.03, 155.59, 160.36, 162.67.

IR ($CDCl_3$): $\nu = 1714$, 1630, 1578, 1538, 1496, 1454, 1016 cm^{-1}.

Palladium-Catalyzed Cross Coupling-Lactonization of 6e and 6f with 5e; General Procedure:
To a solution of (*Z*)-3-halocinnamic acid **6e** (X=I 69 mg, 0.25 mmol) or **6f** (X=Br 57 mg, 0.25 mmol) in MeCN (5 mL) were added phenylacetylene **5e** (39 mg, 0.38 mmol), a palladium catalyst [$PdCl_2(PPh_3)_2$, $Pd(PPh_3)_4$, $Pd(dba)_2 + 4PPh_3$, or $PdCl_2(PPh_3)_2 + 2PPh_3$, 12.5 μmol], CuI (2.4 mg, 12.5 μmol), and Et_3N (101 mg, 1.0 mmol). The mixture was stirred at 25°C for 24 h, concentrated in vacuo, dissolved in $CDCl_3$, and analyzed by ^1H NMR spectroscopy. The results are summarized in Table 2.

Palladium-Catalyzed Cross Coupling-Lactonization of 9a and 9b with 5e; General Procedure:
To a solution of (*Z*)-3-halopropenoic acid **9a** (X=I 50 mg, 0.25 mmol) or **9b** (X=Br 38 mg, 0.25 mmol) in MeCN (5 mL) were added phenylethyne **5e** (39 mg, 0.38 mmol), a palladium catalyst [$PdCl_2(PPh_3)_2$, $Pd(PPh_3)_4$, or $PdCl_2(PPh_3)_2 + 2PPh_3$, 12.5 μmol], CuI (2.4 mg, 12.5 μmol), and Et_3N (101 mg, 1 mmol). The mixture was stirred at 25°C for 24 h, concentrated in vacuo, dissolved in $CDCl_3$, and analyzed by ^1H NMR spectroscopy. The results are summarized in Table 3. Isolation and identification of **10** and **11** was performed as follows.

The reaction of (*Z*)-3-bromopropenoic acid (172 mg, 1 mmol) with phenylethyne (152 mg, 1.5 mmol) in MeCN (10 mL) in the presence of $PdCl_2(PPh_3)_2$ (35 mg, 0.05 mmol), CuI (9.5 mg, 0.05 mmol), and Et_3N (202 mg, 2 mmol) at 25°C for 24 h followed by standard workup and column chromatography (7/3 hexane/Et_2O) afforded (*Z*)-5-benzylidene-5*H*-furan-2-one[25] **10** (58 mg, 34%) and **11** (55 mg, 24%) as white solids.

(Z)-5-benzylidene-5H-furan-2-one **(10):**

Mp 86°C (lit.[14] mp 86–87°C).

^1H NMR ($CDCl_3$): $\delta = 6.03$ (s, 1H), 6.21 (d, $J = 5.5$ Hz, 1H), 7.59 (d, $J = 5.5$ Hz, 1H), 7.35–7.45 (m, 3H), 7.75–7.85 (m, 2H).

^{13}C NMR ($CDCl_3$): $\delta = 114.25$, 118.06, 128.80 (2C), 129.28, 130.70 (2C), 132.76, 145.28, 148.36, 170.20.

(5E, 1'E)-5-[(2-carboxyethen-1-yl)phenylmethylene]-5H-furan-2-one **(11):**

Mp > 160°C (dec.)

^1H NMR ($CDCl_3$): $\delta = 5.81$ (d, $J = 15.8$ Hz, 1H), 6.32 (d, $J = 5.5$ Hz, 1H), 7.20–7.35 (m, 3H), 7.40–7.55 (m, 3H), 8.23 (d, $J = 15.8$ Hz, 1H), 11.30 (br s, 1H).

^{13}C NMR ($CDCl_3$): $\delta = 121.99$, 123.91, 124.57, 128.81 (2C), 129.24, 130.46 (2C), 132.14, 140.38, 141.94, 151.50, 168.31, 171.62.

IR ($CDCl_3$): $\nu = 1714$, 1630, 1578, 1538, 1496, 1454, 1016 cm^{-1}.

We thank the National Institutes of Health (GM 36792) for support of this research.

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