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# The Conversion of Vinyl Triflates into γ'-Hydroxy-α,β-enones

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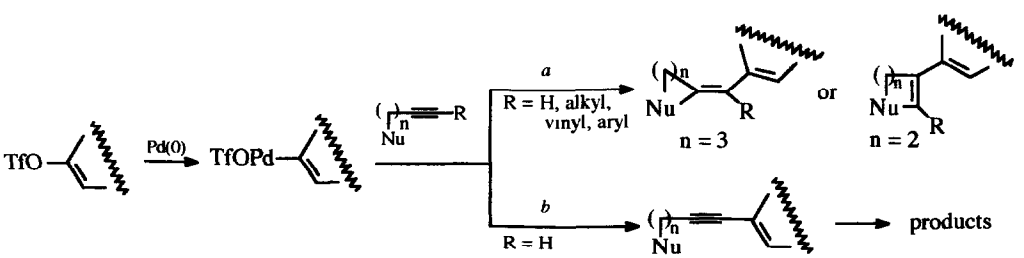
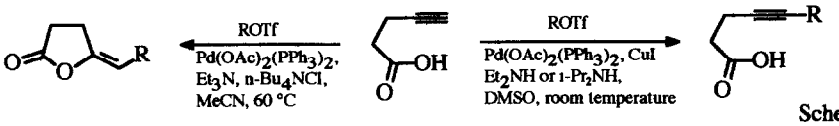
***Abstract:*** *Vinyl triflates have been converted into γ'-hydroxy-α,β-enones through their palladium-catalysed coupling with 1-butyn-4-ols followed by the reaction of the obtained 1-hydroxy-3-yn-5-enes in an acidic $CH_2Cl_2$/3 N HCl two-phase system in the presence of the n-$BuN_4Cl$/$PdCl_2$ combination. Both the coupling step and the conversion of the carbon-carbon triple bond into the ketonic group have been performed at room temperature. The conversion of vinyl triflates into γ'-hydroxy-α,β-enones can be carried out through a one-flask process, without the isolation of 1-hydroxy-3-yn-5-enes.*

We have previously reported that 1-alkynes react with vinyl triflates in the presence of catalytic amounts of a palladium catalyst to produce conjugate enynes.[1] The reaction occurs with a wide variety of alkyl- and aryl acetylenes, can tolerate numerous functionalities both on the vinyl triflate and the alkyne moiety, and appears to be a useful tool in organic synthesis. For example, it has been applied to the preparation of dienynes related to vitamin D[2] and of dienediynes related to neocarzinostatin[3], a potent antitumor agent. Its scope is considerably widened by the observation that nucleophiles near the carbon-carbon triple bond can participate in the palladium-catalysed reaction with vinyl triflates through intramolecular attack on the multiple bond activated by the coordination to the in situ generated σ-vinylpalladium complex. Cyclic compounds are obtained thus providing an interesting route for conversion of vinyl triflates into derivatives not easily available by known procedures (Scheme 1a).[4] Alternatively, vinyl triflates and 1-alkynes may produce functionalized enynes that can be subsequently reacted to give the desired products (Scheme 1b).[5]



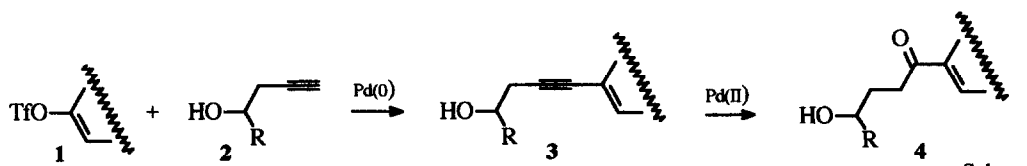

Scheme 1

In some cases, products derived from both pathway *a* and pathway *b* can be easily prepared by introducing apparently minor changes in the reaction mixture composition. The palladium-catalysed reaction of 4-pentynoic acid with vinyl triflates represents an impressive example of this. (*E*)-δ-Vinyl-γ-methylene-γ-butyrolactones are obtained when the reaction is carried out in the presence of $Et_3N$ and *n*-$Bu_4NCl$[4a] while 5-vinyl-4-pentynoic acids are the main products when the reaction is carried in the presence of $Et_2NH$ or *i*-$Pr_2NH$ and CuI[5a] (Scheme 2).




Scheme 2

Since we are currently investigating new strategies for the preparation of heterocyclic derivatives[6] and part of this program is devoted to the development of methodologies based on the reaction of vinyl triflates with functionalized alkynes,[4,5] we decided to examine the feasibility of the sequence sketched in the Scheme 3. 1-Hydroxy-4-ketones **4** are useful intermediates for the preparation of five-membered hetero-[7] and carbo-cycles[8] via their oxidation to 1,4-dicarbonyl compounds and the whole process represents a convenient approach to the conversion of ketones into cyclic derivatives.




Scheme 3

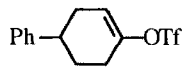
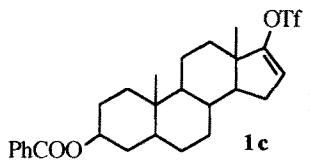
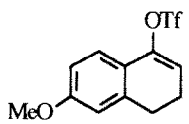
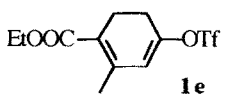
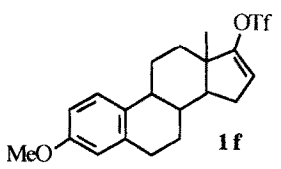
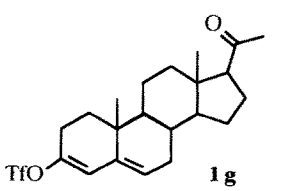
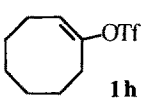
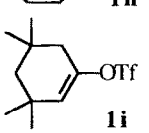
This process attracted our attention because of other specific features. It offers the possibility of evaluating potential competition between coupling and cyclization reactions in the first step and provides an approach to the preparation of α,β-enones from vinyl triflates. The conversion of vinyl triflates into α,β-enones has been realised via palladium-catalysed carbonylative cross-coupling with organostannanes[9] or via palladium-catalysed cross-coupling with 1-ethoxy-1-(trimethylstannyl)-ethylene followed by a hydrolytic step.[10] Since compounds **2** are easily available,[11] the present protocol may represent a useful, alternative route to this class of compounds. No less than four carbons containing an hydroxy substituent can be linked to the vinyl fragment. However, the simultaneous presence of a conjugated enone system and of an hydroxy group makes **4** versatile synthetic intermediates and stimulates new applications.

Now we report that the conversion of vinyl triflates **1** into γ'-hydroxy-α,β-enones **4** occurs under mild conditions and in moderate to high overall yield. It is also possible to prepare compounds **4** through a one-flask process, without the isolation of the intermediate enyne **3**.

Our results are summarised in Table 1.

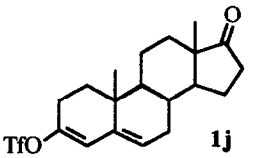
The coupling reaction was initially attempted treating the vinyl triflate **1h** with 1-butyn-3-ol in the presence of $Pd(OAc)_2(PPh_3)_2$ and $Et_3N$ in DMF at 60 °C. Under these conditions, the corresponding 4-hydroxy-3-yn-5-ene **3h** was isolated as the main product from a complex reaction mixture in only 39% yield (see Table 1, note l). In spite of the low yield, this result shows a tendency of 1-butyn-3-ol to react with σ-vinylpalladium complexes giving rise to the preferential formation of coupling products instead of cyclic derivatives.

**Table 1.** Palladium-Catalysed Synthesis of γ'-Hydroxy-α,β-enones **4** from Vinyl Triflates.

| entry | vinyl triflate **1** | 1-butyn-4-ol **2** R | reaction time (h)[a] | 1-en-3-yn-6-ol **3** (% yield)[b] | reaction time (h) | procedure[c,d] | γ'-hydroxy-α,β-enone **4** (% yield)[e] |
|---|---|---|---|---|---|---|---|
| a |  **1a** | H | 5 | **3a** 90 | 0.75 | A | **4a** 67 |
| b | | " | " | **3a** " | 2 | B | **4a** 88 |
| c | | " | " | - | " | C[f] | **4a** 85 |
| d | | Me | 7 | **3b** 83 | 3 | B | **4b** 73 |
| e |  **1c** | H | 4 | **3c** 96 | 6 | B | **4c** 62 |
| f |  **1d** | " | 4g | **3d** 86 | 10 | B[h] | **4d** 25 |
| g |  **1e** | Me | 6[i] | **3e** 89 | 6.5 | B[h] | **4e** 57 |
| h |  **1f** | H | 5 | **3f** 93 | 1 | A | **4f** 87 |
| i | | " | " | **3f** " | 5 | B | **4f** 71 |
| j | | " | " | - | 5.5 | C[f] | **4f** 82 |
| k |  **1g** | H | 3 | **3g** 85 | 3 | A | **4g** 78 |
| l | | " | " | **3g** " | 3 | B | **4g** 84 |
| m | | " | " | - | 5 | C[f] | **4g** 56 |
| n |  **1h** | " | 5 | **3h** 95 (39)[l] | 0.75 | A | **4h** 74 |
| o | | " | " | **3h** " | 1.5 | C[f] | **4h** 60 (90)[m] |
| p |  **1i** | Me | 5 | - | 6.5 | C[f] | **4i** 45 |

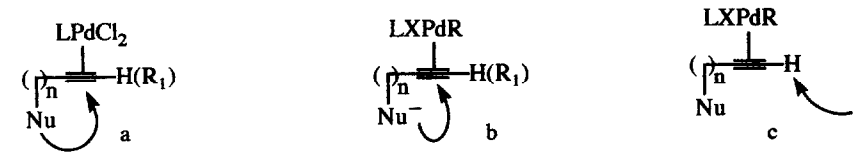
(continued)

**Table 1** - (continued)

| entry | vinyl triflate **1** | 1-butyn-4-ol **2** R | reaction time (h)[a] | 1-en-3-yn-6-ol **3** (% yield)[b] | reaction time (h) | procedure[c,d] | γ'-hydroxy-α,β-enone **4** (% yield)[e] |
|---|---|---|---|---|---|---|---|
| q |  **1j** | H | 4.5 | **3j** 93 . | 3 | B | **4j** 79 |
| r | | " | " | - | 3.5 | C[f] | **4j** 52 |

[a] Unless otherwise stated reactions were carried out at room temperature in DMF (0.5- 1 mL) and $Et_2NH$ (2-5 mL) under a nitrogen atmosphere using the following molar ratios. **1**. **2**: $Pd(PPh_3)_4$: CuI = 1: 1.1. 0.01· 0.02. 0 015 equiv of $Pd(PPh_3)_4$ and 0 03 equiv of CuI were used when reactions were carried out starting from less than 1 mmol of **1**. [b] Yields refer to single run, are given on pure isolated products, and are calculated on **1** [c] Reactions were carried out on a mmol scale. d Procedure A: [MeCN (9-15 mL), $H_2O$ (1 mL), reflux] **3**:$PdCl_2$ = 1: 0.05. Procedure B· [$CH_2Cl_2$ (5 mL), 3 N HCl (5 mL), room temperature] **1** $PdCl_2$· *n*-$Bu_4NCl$ = 1: 0 05: 0 10 Procedure C: $CH_2Cl_2$, 3 N HCl, $PdCl_2$, and *n*-$Bu_4NCl$ are added to the reaction mixture derived from the coupling step after evaporation of the solvent. [e] Unless otherwise stated, yields refer to single run, are given on pure isolated products, and are calculated on **3** [f] Yields are calculated on **1**. [g] **1**: **2** $Pd(PPh_3)_4$: CuI = 1 1 5: 0.01: 0.02. [h] **1**· $PdCl_2$· *n*-$Bu_4NCl$ = 1: 0.1 0.2. [i] **1**: **2**: $Pd(PPh_3)_4$ CuI = 1: 1.2: 0.01: 0.02. [l] The reaction was carried out in DMF at 60 °C (4.5 h) under an argon atmosphere using the following molar ratios: **1h**: 1-butyn-3-ol ·$Pd(OAc)_2(PPh_3)_2$: $Et_3N$: = 1· 1 1: 0.05: 20. [m] HPLC yield

Some general conclusions on the reactivity of alkynes containing nucleophiles near the alkyne moiety in palladium-catalysed reactions can be drawn. Their behaviour is clearly dependent on an intriguing combination of electronic, coordinating, and medium factors. Among them, the nature of palladium species interacting with the carbon-carbon triple bond, the strength of the nucleophile, and the strength of the added base appear to play dominant roles. Thus, while the reaction of palladium dichloride with functionalized alkynes generates π-palladium complexes able to react with nucleophiles such as the hydroxy,[12] the amino,[5b,12d,13] and the amido groups[13c,14] (Fig. 1a), π-allyl-[15] and σ-vinyl(aryl)palladium intermediates[16] react with functionalized alkynes affording π-palladium complexes that apparently need anionic nucleophiles to allow the intramolecular nucleophilic attack (Fig. 1b). For example, in our palladium-catalysed synthesis of 2,3-disubstituted indoles,[4b] no indole derivatives were formed by reacting vinyl triflates and aryl halides with *o*-alkynylanilines or *o*-alkynylacetanilides and using $K_2CO_3$ as the base. Good results were instead obtained with *o*-alkynyltrifluoroacetanilides, which are more prone to generate anionic nucleophiles. The formation of π-palladium complexes from 1-alkynes and organopalladium intermediates might even affect the tendency of the $C_{sp}$-H bond to dissociate. Consequently, depending on the relative strength of the nucleophile and of the added base, base attack on the terminal hydrogen (Fig. 1c) could prevail over the intramolecular nucleophilic attack on the carbon-carbon triple bond, favouring the formation of the carbon-palladium bond between the incipient acetylide anion and the coordinated palladium. The resultant σ-alkynyl,σ-vinyl(aryl)palladium complex[17] affords coupling products through reductive elimination of a Pd(0) species. This mechanism could be involved in the formation of the coupling product **3h** in the above reaction of **1h** with 1-butyn-3-ol in the presence of $Et_3N$ (Table 1, note l).

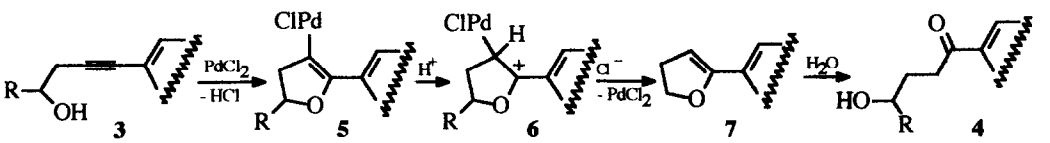



Nu = OH, $NH_2$, NHCOMe  Nu = O, NTs, $NCOCF_3$, $C(COOEt)_2$  Nu = OH, $NH_2$, NHCOMe

Fig. 1

Best results in the coupling step were obtained by reacting vinyl triflates with 1-butyn-4-ols **2** in the presence of $Pd(PPh_3)_4$, $Et_2NH$, and CuI as co-catalyst at *room temperature*.[1] Under these conditions compounds **3** were isolated in high to excellent yield.

Compounds **3** were then reacted in the presence of palladium dichloride in refluxing aqueous acetonitrile (procedure A) according to Utimoto conditions[12] and the title derivatives were selectively obtained (see Table 1, entries a,h,k,n). However, we envisioned that the use of an acidic medium might favour the protic cleavage of the carbon-palladium bond[18] in the presumed σ-vinylpalladium complex **5** and quite probably the hydrolysis of the dihydrofuran intermediate **7** (Scheme 4).




Scheme 4

Therefore, using **3a** as the model system, we examined its conversion into **4a** under an acidic $CH_2Cl_2$/3 N HCl two-phase system in the presence of the *n*-$BuN_4Cl/PdCl_2$ combination (procedure B). These conditions were found to promote our palladium-catalysed conjugate addition-type reaction of arylmercury and aryl tin compounds to α,β-enones.[19] We were pleased to find that **3a** reacted smoothly at *room temperature* to give **4a** in 88% isolated yield. The acid concentration was found to affect greatly the reaction outcome (see Table 2). The role of palladium catalysis in the conversion of enynols **3** into γ'-hydroxy-α,β-enones **4**, even under acidic conditions, is stressed by the observation that omitting palladium dichloride led to the recovery of **3a** in 96% yield (2 h). A variety of enynols **3** were reacted under two-phase conditions to produce γ'-hydroxy-α,β-enones **4** in good to high yield (see Table 1, entries b,d,e,f,g,i,l,q).

Two-phase conditions proved to be particularly convenient when the preparation of **4** was attempted through a one-flask process, without the isolation of **3** (procedure C; see Table 1, entries c,j,m,o,p,q). For example, **1a** produced the corresponding γ'-hydroxy-α,β-enone in only 10% overall yield when the crude mixture obtained from the palladium-catalysed coupling with 1-butyn-4-ol was reacted, after evaporation under vacuum at the rotary evaporator, with $PdCl_2$ in aqueous acetonitrile (reflux, 2 h). The starting triflate was recovered in 10% yield and the intermediate enynol **3a** was isolated in 72% yield. Treating the reaction mixture derived from the coupling step with $CH_2Cl_2$, 3 N HCl, *n*-$BuN_4Cl$, and $PdCl_2$ at room temperature for 2 h allowed the isolation of **4a** in 85% overall yield. The same trend was observed with **1h**. Homogeneous conditions afforded the target compound in 20% yield (the intermediate enynol was isolated in 50% yield) while two-phase conditions gave **4h** in 60% overall yield.

**Table 2.** Acid Concentration and Synthesis of **4a** from **3a** under a $CH_2Cl_2$/HCl two-phase system in the presence of *n*-$BuN_4Cl$/$PdCl_2$.[a]

| acid concentration | recovered **3a** yield %[b] | **4a** yield %[b] |
|---|---|---|
| 0.1 | 89 | 3 |
| 0.5 | 83 | 13 |
| 1.0 | 29 | 62 |
| 2.0 | - | 85 |
| 3.0 | - | 88 |

[a] Reactions were carried out at room temperature (2 h), under a nitrogen atmosphere, using the following molar ratios: **3a** $PdCl_2$: *n*-$BuN_4Cl$ = 1: 0.05- 0.10. [b] Yields refer to single run and are given on pure isolated products

## Experimental Section

Melting points were determined with a Büchi apparatus and are uncorrected. All the starting materials such as catalysts, amines, salts, and solvents are commercially available and were used without further purification. Vinyl triflates **1a**,[4a] **1c-e**, **1f**,[20] **1g**,[4a] **1h-i**, and **1j**[4a] were prepared according to reference 21 and purified by flash chromatography on silica gel eluting with *n*-hexane/EtOAc mixtures. Coupling reactions were carried out on a 0.6 - 2.5 mmol scale. Palladium-catalysed conversion of **3** into **4** were carried out on a 0.2 - 2.0 mmol scale. One-pot conversion of vinyl triflates into γ'-hydroxy-α,β-enones were carried out on a 0.5 - 1.5 mmol scale. The products were purified by flash chromatography on silica gel eluting with *n*-hexane/EtOAc mixtures. $^1H$ NMR and $^{13}C$ NMR spectra ($CDCl_3$; TMS as internal standard) were recorded with a Bruker AC 200 E spectrometer. IR spectra (KBr, unless otherwise indicated) were recorded with a Perkin-Elmer 683 spectrometer.

**General Procedure for the Preparation of Vinyl Triflates. 3β-Benzoyloxy-androst-16-en-17-yl Triflate (1c).** To a solution of 2,6-di-*tert*-butyl-4-methylpyridine (1.21 g, 5.89 mmol) in dry dichloromethane (30 mL) trifluoromethansulfonic anhydride (0.82 mL, 4.91 mmol) was added rapidly from a syringe and 3β-benzoyloxy-androstan-17-one (1.55 g, 3.93 mmol) in dry dichloromethane (20 mL) was added, dropwise and with stirring, during 15-20 min. The mixture was stirred at room temperature for 7 h and poured into a separatory funnel containing saturated aqueous $Na_2CO_3$. The organic layer was separated, dried ($Na_2SO_4$), and evaporated under vacuum. The residue was chromatographed on silica gel eluting with *n*-hexane to recover 2,6-di-*tert*-butyl-4-methylpyridine and then with a 90/10 *n*-hexane/EtOAc mixture to afford 1.45 g (70% yield) of **1c**: mp 141-3 °C; IR 1720, 1630, 1410, 1190 $cm^{-1}$; $^1H$ NMR δ 8.07-8.01 (m, 2 H), 7.59-7.17 (m, 3, H), 5.56 (dd, J = 1.5 Hz, J = 1.7 Hz, 1 H), 5.03-4.87 (m, 1 H), 0.97 (s, 3 H), 0.90 (s, 3 H); $^{13}C$ NMR δ 166.1, 159.3, 132.7, 130.7, 129.5, 128.3, 118.6 (q, $J_{CF}$ = 320 Hz), 114.5, 74.1. Anal. Calcd for $C_{27}H_{33}F_3O_5S$: C, 61.58; H, 6.32. Found: C, 61.44; H, 6.21.

**6-Methoxy-3,4-dihydro-1-naphthyl Triflate (1d, 62%):** oil; IR (neat) 1640, 1400, 1190 $cm^{-1}$; $^1H$ NMR δ 7.29-7.23 (m, 1 H), 6.78-6.71 (m, 2 H), 5.85 (t, J = 4.8 Hz, 1 H), 3.79 (s, 3 H), 2.82 (t, J = 8.0 Hz, 2 H), 2.51-2.40 (m, 2 H); $^{13}C$ NMR δ 160.3, 146.4, 138.4, 122.7, 121.7, 118.8 (q, $J_{CF}$ = 320), 114.9, 114.3, 111.3. Anal. Calcd for $C_{12}H_{11}F_3O_4S$: C, 46.76; H, 3.6. Found: C, 46.31; H, 3.42.

**4-Carbethoxy-3-methyl-cyclohexa-1,3-dien-1-yl Triflate (1e, 74%):** oil; IR (neat) 1690, 1410, 1190 $cm^{-1}$; $^1H$ NMR δ 5.94 (t, J = 1.4 Hz, 1H), 4.22 (q, J + 7.1 Hz, 2 H), 2.75-2.69 (m, 2 H), 2.59-2.53 (m, 2 H), 2.19 (t, J = 1.8 Hz, 3 H), 1.31 (t, J = 7.1 Hz, 1 H); $^{13}C$ NMR ($Me_2CO$-$d_6$) δ 167.3, 153.1, 140.5, 122.9, 121.4, 119.4 (q, $J_{CF}$ = 320). Anal. Calcd for $C_{11}H_{13}F_3O_5S$: C, 42.04; H, 4.17. Found: C, 41.62; H, 4.02.

**Cycloott-1-en-1-yl Triflate (1h, 66%):** oil; IR (neat) 1670, 1400, 1190 $cm^{-1}$; $^1H$ NMR δ 5.69 (t, J = 8.7 Hz, 1 H), 2.50-2.44 (m, 2 H), 2.22-2.12 (m, 2 H), 1.50-1.80 (m, 8 H); $^{13}C$ NMR δ 151.0, 120.7, 118.6 (q, $J_{CF}$ = 320). Anal. Calcd for $C_9H_{13}F_3O_3S$: C, 41.86; H, 5.07. Found: C, 41.53; H, 4.86.

**3,3,5,5-Tetrametyl-cyclohex-1-en-1-yl Triflate (1i, 74%):** oil; IR (neat) 1670, 1400, 1190 $cm^{-1}$; $^1H$ NMR δ 5.52 (t, J = 1.4 Hz, 1H), 2.09 (d, J = 1.4 Hz, 2 H), 1.36 (s, 2 H), 1.10 (s, 6 H), 1.05 (s, 6 H); $^{13}C$ NMR 147.1, 126.7, 118.7 (q, $J_{CF}$ = 320). Anal. Calcd for $C_{11}H_{17}F_3O_3S$: C, 46.15; H, 5.98. Found: C, 45.66; H, 5.81.

**General Procedure for the Preparation of 1-Hydroxy-3-yn-5-enes (3). 4-Hydroxy-1-(17-Oxo-androsta-3,5-dien-3-yl)-1-butyne (3j).** To a stirred solution of 17-oxo-androsta-3,5-dien-3-yl triflate (0.290 g, 0.69 mmol) in DMF (0.5 mL) and $Et_2NH$ (3 mL) were added 1-butyn-4-ol (0.057 mL, 0.76 mmol), $Pd(PPh_3)_4$ (0.012 g, 0.01 mmol), and CuI (0.004 g, 0.02 mmol) under nitrogen. The mixture was stirred for 4.5 h at room temperature. Then, the reaction mixture was acidified with 0.1 N HCl and extracted with diethyl ether. The organic layer was separated, washed with water, dried over $Na_2SO_4$, and evaporated under vacuum. The residue was chromatographed on silica gel eluting with *n*-hexane/EtOAc (70/30 v/v) to afford 0.220 g (93% yield) of **3j**: mp 146-7 °C; IR 3400, 1710 $cm^{-1}$; $^1H$ NMR δ 6.24 (bs, 1 H), 5.50 (bs, 1 H), 3.74 (t, J = 6.3 Hz, 2 H), 2.62 (t, J = 6.3 Hz, 2 H), 0.96 (s, 3 H), 0.92 (s, 3 H); $^{13}C$ NMR δ 221.2, 141.3, 134.6, 124.7, 117.5, 86.1, 84.3, 61.2. Anal. Calcd for $C_{23}H_{30}O_2$: C, 81.61; H, 8.93. Found: C, 81.86; H, 8.81.

**4-Hydroxy-1-(4-phenylcyclohex-1-en-1-yl)-1-butyne (3a)**: mp 90-1 °C; IR 3300, $cm^{-1}$; $^1H$ NMR δ 7.35- 7.16 (m, 5 H), 6.14 (bs, 1 H), 3.74 (t, J = 6.2 Hz, 2 H), 2.60 (t, J = 6.2 Hz, 2 H); $^{13}C$ NMR δ 146.4, 133.6, 128.4, 126.8, 126.2, 120.5, 84.0, 83.9, 61.2. Anal. Calcd for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 84.8; H, 8.19.

**4-Hydroxy-1-(4-phenylcyclohex-1-en-1-yl)-1-pentyne (3b)**; mp 60-2 °C; IR 3300, $cm^{-1}$; $^1H$ NMR δ 7.34-7.16 (m, 5 H), 6.13 (m, 1 H), 4.08-3.88 (m, 1H), 2.52-2.46 (m, 2 H), 1.27 (d, J = 6.2 Hz, 3 H); $^{13}C$ NMR δ 146.4, 133.5, 128.4, 126.8, 126.2, 120.5, 84.4, 83.8, 66.5. Anal. Calcd for $C_{17}H_{20}O$: C, 84.96; H, 8.39. Found: C, 84.79; H, 8.34.

**4-Hydroxy-1-(3β-benzoyloxy-androst-16-en-17-yl)-1-butyne (3c)**: mp 159-161 °C; IR 3380, 1710 $cm^{-1}$; $^1H$ NMR δ 8.06-8.01 (m, 2 H), 7.58-7.38 (m, 3 H), 5.95 (t, J = 2.0 Hz, 1 H), 5.03-4.87 (m, 1 H), 3.74 (t, J = 6.2 Hz, 2 H), 2.64 (t, J = 6.2 Hz, 2 H), 0.91 (s, 3 H), 0.83 (s, 3 H); $^{13}C$ NMR δ 166.1, 137.2, 135.1, 132.7, 130.9, 129.5, 128.2, 89.3, 78.1, 74.2, 61.2. Anal. Calcd for $C_{30}H_{38}O_3$: C, 80.68; H, 8.58. Found: C, 80.58; H, 8.72.

**4-Hydroxy-1-(6-methoxy-3,4-dihydro-1-naphthyl)-1-butyne (3d)**: oil; IR (neat) 3340 $cm^{-1}$; $^1H$ NMR δ 7.46 (d, J = 8.4 Hz, 1 H), 6.77-6.66 (m, 2 H), 6.28 (t, J = 4.7 Hz, 1 H), 3.81 (t, J = 6.3 Hz, 2 H), 3.80 (s, 3 H), 2.79-2.66 (m, 4 H); $^{13}C$ NMR δ 159.1, 136.9, 132.4, 126.2, 126.0, 121.1, 113.5, 111.1, 86.8, 80.5, 61.3. Anal. Calcd for $C_{15}H_{16}O_2$: C, 78.92; H, 7.06. Found: C, 78.47; H, 6.91.

**4-Hydroxy-1-(4-carbethoxy-3-methyl-cyclohexa-1,3-dien-1-yl)-1-pentyne (3e)**: oil; IR (neat) 3380, 1680 $cm^{-1}$; $^1H$ NMR δ 6.17 (bs, 1 H), 4.20 (q, J = 7.1 Hz, 2 H), 4.08-3.92 (m, 1 H), 2.58-2.43 (m, 4

H), 2.14 (t, J = 1.7 Hz, 2 H), 1.39-1.26 (m, 6 H); $^{13}$C NMR δ 168.2, 142.4, 135.5, 125.2, 121.8, 91.6, 83.6, 66.5. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.06; H, 7.98.

**4-Hydroxy-1-(3-methoxy-estra-1,3,5(10),16-tetraen-17-yl)-1-butyne (3f)**: mp 50-2 °C; IR 3350, cm$^{-1}$; $^1$H NMR δ 7.20 (d, J = 8.5 Hz, 1 H), 6.74-6.63 (m, 2 H), 5.99 (bs, 1 H), 3.78 (s, 3 H), 3.76 (t, J = 6.2 Hz, 2 H), 2.66 (t, J = 6.2 Hz, 2 H), 0.86 (s, 3 H); $^{13}$C NMR δ 157.4, 137.8, 137.4, 134.8, 132.7, 126.0, 113.8, 111.4, 89.6, 77.8, 61.2. Anal. Calcd for $C_{23}H_{28}O_2$: C, 82.1; H, 8.39. Found: C, 82.21; H, 8.26.

**4-Hydroxy-1-(17β-acetyl-androsta-3,5-dien-3-yl)-1-butyne (3g)**: mp 119-122 °C; IR 3420, 1710 cm$^{-1}$; $^1$H NMR δ 6.23 (s, 1 H), 5.48 (bs, 1 H), 3.74 (t, J = 6.2 Hz, 2 H), 2.62 (t, J = 6.2 Hz, 2 H), 2.13 (s, 3 H), 0.93 (s, 3 H), 0.65 (s, 3H); $^{13}$C NMR δ 209.6, 141.2, 134.9, 125.4, 117.3,86.0, 84.5, 61.3. Anal. Calcd for $C_{25}H_{34}O_2$: C, 81.92; H, 9.35. Found: C, 82.03; H, 9.43.

**4-Hydroxy-1-(cycloott-1-en-1-yl)-1-butyne (3h)**: oil; IR (neat) 3450, cm$^{-1}$; $^1$H NMR δ 6.03 (t, J = 8.3 Hz, 1 H), 3.72 (t, J = 6.2 Hz, 2 H), 2.58 (t, J = 6.2 Hz, 2H); $^{13}$C NMR δ 137.1, 123.6, 85.1, 82.6, 61.3. Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.39; H, 10.02.

**General Procedure for the Preparation of γ'-Hydroxy-α,β-unsaturated ketones (4) from 1-Hydroxy-3-yn-5-enes (3). 4-Hydroxy-butan-1-(17-Oxo-androsta-3,5-dien-3-yl)-1-one (4j).** To a solution of 4-hydroxy-1-(17-Oxo-androsta-3,5-dien-3-yl)-1-butyne **3j** (0.191 g, 0.56 mmol) in dichloromethane (5 mL) were added 3 N HCl (5 mL), $PdCl_2$ (0.005 g, 0.028 mmol), and *n*-$Bu_4NCl$ monohydrate (0.017 g, 0.056 mmol). The reaction mixture was stirred for 3 h at room temperature under nitrogen and poured into a separatory funnel containing diethyl ether and saturated aqueous $NaHCO_3$.The organic layer was separated, dried over $Na_2SO_4$ and evaporated under vacuum. The residue was chromatographed on silica gel eluting with a 50/50 *n*-hexane/EtOAc mixture to afford 0.160 g (79% yield) of **4j**: mp 141-2 °C; IR 3500, 1710, 1650 cm$^{-1}$; $^1$H NMR δ 6.99 (bs, 1 H), 5.91 (bs, 1 H), 3.68 (t, J = 6.1 Hz, 2 H), 2.85 (t, J = 7.1Hz, 2 H), 0.93 (bs, 6 H); $^{13}$C NMR δ 220.7, 201.4, 141.7, 138.4, 134.1, 131.8, 62.0. Anal. Calcd for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.37; H, 9.11.

**4-Hydroxy-pentan-1-(4-phenylcyclohex-1-en-1-yl)-1-one (4b)**: oil; IR (neat) 3400,1650 cm$^{-1}$; $^1$H NMR δ 7.24-7.06 (m, 5 H), 6.94 (bs, 1 H), 3.76-3.67 (m, 1 H), 2.74 (t, J = 7.4 Hz, 2 H), 1.12 (d, J = 6.2 Hz, 3 H); $^{13}$C NMR δ 201.5, 145.7, 139.4, 138.6, 128.3, 126.6, 126.1, 67.1. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.54; H, 8.42.

**4-Hydroxy-butan-1-(3β-benzoyloxy-androst-16-en-17-yl)-1-one (4c)**: mp 134-6 °C; IR 3400, 1700, 1650 cm$^{-1}$; $^1$H NMR δ 8.06-8.01 (m, 2 H), 7.58-7.38 (m, 3 H), 6.74 (bs, 1 H), 5.03-4.87 (m, 1 H), 3.67 (t, J = 5.8 Hz, 2 H), 2.76 (dt, J = 6.7 Hz, J = 3.2 Hz, 2 H), 0.91 (s, 3 H), 0.90 (s, 3 H); $^{13}$C NMR δ 199.6, 166.2, 155.0, 144.0, 132.7, 130.9, 129.5, 128.3, 74.3, 62.5. Anal. Calcd for $C_{30}H_{40}O_4$: C, 77.55; H, 8.68. Found: C, 77.44; H, 8.59.

**4-Hydroxy-butan-1-(6-methoxy-3,4-dihydro-1-naphthyl)-1-one (4d)**: oil; IR (neat) 3340,1680 cm$^{-1}$; $^1$H NMR δ 7.57 (d, J = 7.4 Hz, 1 H), 6.87 (t, J = 4.9 Hz, 1 H), 6.76-6.69 (m, 2 H), 3.78 (s, 3H), 3.70 (t, J = 6.1 Hz, 2 H), 2.92 (t, J = 7.0 Hz, 2 H), 2.01-192 (m, 2 H); $^{13}$C NMR δ 202.6, 62.0. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.47; H, 7.24.

**4-Hydroxy-pentan-1-(4-carbethoxy-3-methyl-cyclohexa-1,3-dien-1-yl)-1-one (4e)**: oil; IR (neat) 3400, 1690, 1640 cm$^{-1}$; $^1$H NMR δ 6.87 (bs, 1 H), 4.24 (q, J = 7.1 Hz, 2 H), 3.85-3.81 (m, 1 H), 2.88 (dt, J = 7.1 Hz, J = 1.2 Hz, 2 H), 2.22 (t, J = 1.3 Hz, 3 H), 1.33 (t, J = 7.1 Hz, 3 H), 1.23 (d, J = 6.2 Hz, 3 H); $^{13}$C NMR δ 200.9, 167.9, 140.5, 139.3, 138.3, 128.3, 67.3. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33. Found: C, 67.87; H, 8.16.

**4-Hydroxy-butan-1-[3-methoxy-estra-1,3,5(10),16-tetraen-17-yl]-1-one (4f)**: mp 107-9 °C; IR 3530, 1660 $cm^{-1}$; $^1H$ NMR δ 7.20 (d, J = 8.5 Hz, 1 H), 6.79-6.62 (m, 3H), 3.77 (s, 3 H), 3.67 (t, J = 6.0 Hz, 2 H), 2.79 (dt, J = 6.9 Hz, J = 2.6 Hz), 0.92 (s, 3 H); $^{13}C$ NMR δ 199.6, 157.4, 155.0, 143.9, 137.7, 132.7, 126.1, 113.8, 111.4, 62.5. Anal. Calcd for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53. Found: C, 77.75; H, 8.63.
**4-Hydroxy-butan-1-(17β-acetyl-androsta-3,5-dien-3-yl)-1-one (4g)**: mp 106-8 °C; IR 3530, 1710, 1660 $cm^{-1}$; $^1H$ NMR δ 6.88 (bs, 1 H), 5.87 (bs, 1 H), 3.68 (t, J = 6.0 Hz, 2 H), 2.85 (t, J = 7.0 Hz, 2 H), 2.14 (s, 3 H), 0.90 (s, 3 H), 0.66 (s, 3 H); $^{13}C$ NMR δ 209.5, 201.6, 141.7, 138.9, 134.3, 132.8, 62.6. Anal. Calcd for $C_{25}H_{36}O_3$: C, 78.08; H, 9.44. Found: C, 77.86; H, 9.32.
**4-Hydroxy-butan-1-(cycloott-1-en-1-yl)-1-one (4h)**: oil; IR (neat) 3380, 1650 $cm^{-1}$; $^1H$ NMR δ 6.86 (t, J = 8.3 Hz, 1 H), 3.58 (t, J = 6.1 Hz, 2 H), 2.75 (t, J = 7.1 Hz, 2 H), 1.88-1.75 (m, 2 H); $^{13}C$ NMR δ 201.7, 143.1, 142.4, 62.3. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.85; H, 10.23.
**4-Hydroxy-pentan-1-(3,3,5,5-tetrametyl-cyclohex-1-en-1-yl)-1-one (4i)**: oil; IR (neat) 3400, 1650 $cm^{-1}$; $^1H$ NMR δ 6.62 (t, J = 1.5 Hz, 1 H), 3.90-3.75 (m, 1 H), 2.85 (t, J = 7.0 Hz, 2 H), 2.00 (d, J = 1.5 Hz, 2 H), 1.36 (s, 2 H), 1.22 (d, J = 6.0 Hz, 3 H), 1.10 (s, 6 H), 0.94 (s, 6 H); $^{13}C$ NMR δ 202.6, 148.1, 135.1, 67.5. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.08; H, 10.32.

**General Procedure for the Preparation of γ'-Hydroxy-α,β-unsaturated ketones (4) from Vinyl Triflates (1) and 4-Hydroxy-1-butynes (2) trough a One-Flask Process. 4-Hydroxy-butan-1-(4-phenylcyclohex-1-en-1-yl)-1-one (4a).** To a stirred solution of 4-phenylcyclohex-1-en-1-yl triflate **1a** (0.305 g, 0.99 mmol) in DMF (1 mL) and $Et_2NH$ (4 mL) were added 1-butyn-4-ol (0.083 mL, 1.09 mmol), tetrakis(triphenylphosphine)palladium (0) (0.012 g, 0.01 mmol), and CuI (0.004 g, 0.02 mmol) under nitrogen. The reaction mixture was stirred at room temperature for 5 h and then evaporated under vacuum at the rotary evaporator. The residue was dissolved in dichloromethane (5 mL) and 3 N HCl (5 mL), *n*-$Bu_4NCl$ monohydrate (0.030 g, 0.1 mmol), and $PdCl_2$ (0.009 g, 0.05 mmol) were added. The reaction mixture was stirred at room temperature for 2 h; work-up as before afforded a residue which was purified by chromatography on silica gel eluting with a 60/40 *n*-hexane/EtOAc mixture to give 0.208 g (85% yield) of **4a**: oil; IR (neat) 3380,1650 $cm^{-1}$; $^1H$ NMR δ 7.35-7.16 (m, 5 H), 7.03 (bs, 1 H), 3.68 (t, J = 6.0 Hz, 2 H), 2.83 (t, J = 6.9 Hz, 2 H), 1.97-1.87 (m, 2 H); $^{13}C$ NMR δ 201.5, 145.9, 139.6, 138.8, 128.5, 126.8, 126.4, 62.4. Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 79.07; H, 8.09.

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