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Alkynylation of steroids *via* Pd-free Sonogashira coupling

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Cu-catalyzed Pd-free Sonogashira coupling has been proposed as a straightforward and convenient route to valuable steroidal enynes. A biligand catalyst system based on Ph_3P and TMEDA has been designed. The protocol was utilized for the efficient coupling of iodosteroids with diverse terminal alkynes and 1-trimethylsilylalkynes. A possible role of auxiliary ligand as a phase-transfer catalyst for sparingly soluble inorganic base (K_2CO_3) was revealed.

Introduction

The Sonogashira reaction is one of the most efficient and convenient ways for C(sp^2)–C(sp) bond formation by cross-coupling of aryl or vinyl halides with terminal acetylenes.[1] An important trend in modern development of synthetic methods is the search for cheaper starting materials, ligands, and catalysts. Thus, *e.g.* copper derivatives are replacing very expensive palladium in the cross-coupling and related processes.[2]

The Pd-free Cu-catalyzed Sonogashira coupling has been attracting a significant interest for two last decades since its discovery.[3] A large number of new catalytic systems based on copper complexes have been proposed. These catalysts involve not only phosphines,[4] but also N- and O-donating ligands,[5] some of which are quite simple and readily available. Following principles of green chemistry, "ligand-free",[6] aqueous,[7] and solvent-free[8] systems were reported. Efficient and recyclable heterogeneous catalysts were designed utilizing metallic copper, copper oxides,[9] and immobilized copper complexes.[10] Apart from the synthesis of enynes and arylacetylenes, Pd-free Sonogashira coupling was applied as a key step of new cascade processes leading to various heterocycles such as indoles, benzofurans, isocoumarins, and other fused systems.[11] However, the synthetic potential of this method toward the preparation of rather complex molecules, in particular, for the derivatization of polyfunctional natural products, remains largely unexplored.

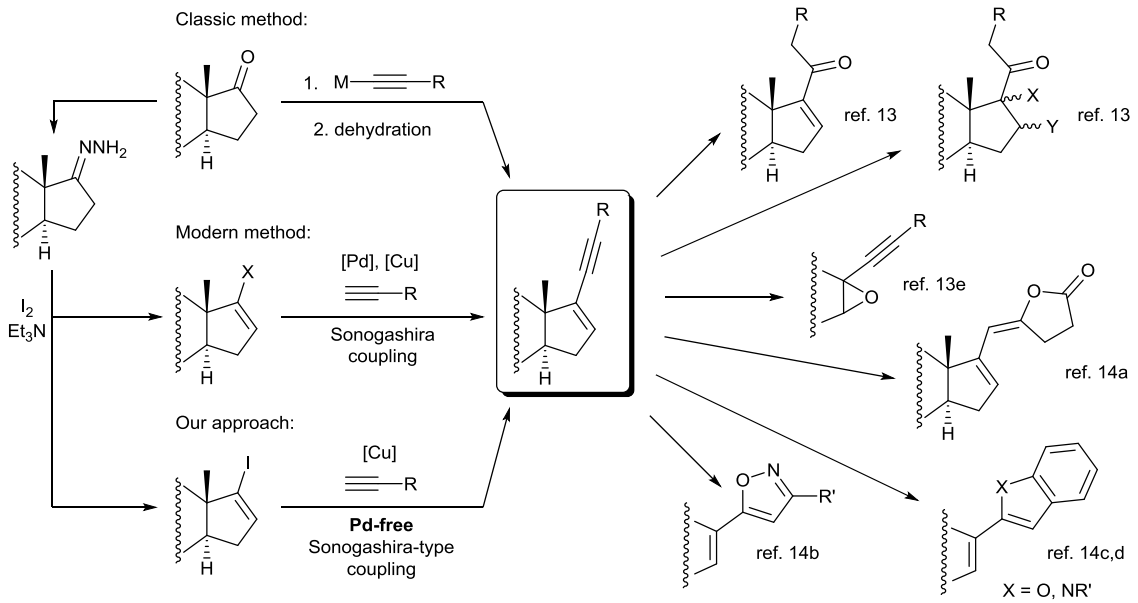
The steroids represent an important class of widespread multirole signalling molecules regulating diverse processes in living organisms, such as salt and water balance, metabolism, immune response, reproductive cycle, *etc*. Modification of steroidal drugs provides a well-established and efficient route for fine-tuning their biological activity.[12] Sonogashira coupling is a convenient approach to steroidal enynes, which are valuable synthetic intermediates to be easily transformed to pharmacologically significant 20-ketosteroids[13] as well as a large number of diverse heterocycles[14] (Scheme 1).

The conventional Pd-catalyzed Sonogashira coupling of steroids was successfully applied for the synthesis of new biologically active compounds exhibiting anticancer[15] and antiviral[16] effects, supramolecular structures (such as dendrimers,[17] macrocycles,[18] and molecular machines[19]), bioconjugates with porphyrins,[20] nucleosides,[21] and oligosaccharides.[22] The same approach became popular for introduction of various radioactive,[23] electrochemical,[24] and luminescent labels[25] into steroid molecules.

So far, all of the catalyst systems proposed for the synthesis of alkynylsteroids *via* Sonogashira reaction were based on palladium complexes. Moreover, in some cases the cross-coupling could be performed in high yield only with tandem catalytic effect of palladium and silver.[26] Herein, we report a new protocol for the synthesis of steroidal enynes *via* Pd-free Sonogashira coupling.

Results and discussion

Preparation of steroidal enynes was performed by Cu-catalyzed cross-coupling of steroidal vinyl iodides with terminal acetylenes. The starting iodosteroids were prepared according to the previously reported procedures[27] from readily available ketosteroids by Barton's method, which is the cleavage of hydrazones by iodine in the presence of base (Scheme 1).



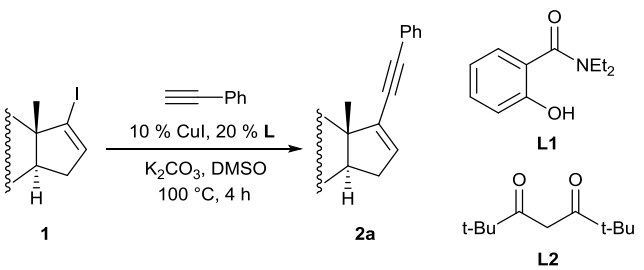
Scheme 1 Synthetic routes to steroidal enynes and their post-transformation.

Conditions for the reaction between steroidal vinyl iodides and terminal acetylenes were optimized by using **1** as a model substrate (Scheme 2, Table 3). Iodosteroid **1** is known to be challenging compound for cross-couplings and generally demonstrates poor reactivity due to a steric hindrance. Only moderate or low yields of the respective coupling products are often accessible under either Cu-[27] or even Pd-catalysis.[28] It is worth mentioning that a strong negative effect of steric bulk for Ullmann-type chemistry is a well-known feature substantially limiting the scope of the methods.[29]

Taking into consideration a large number of ligands proposed for the Cu-catalyzed Sonogashira coupling,[3-5] it was interesting to compare the performance of different catalytic systems (Table 1). Although the alkynylation of **1** with phenylacetylene proceeds in the presence of CuI even under "ligand-free" conditions (entry 1), an addition of some N- and O-donating ligands increases the yield significantly (entries 3–5). Nevertheless, the best ligand was found to be Ph_3P (entry 6), in the presence of which the conversion of **1** within 4 h at 100 °C in DMSO with K_2CO_3 as a base was nearly quantitative. In contrast to Ph_3P bidentate phosphines demonstrated an extremely low activity (entries 7–10), and in the case of BINAP and dppe the reaction didn't take place at all. Apparently, the chelating diphosphines form with copper(I) ions too stable and inert complexes blocking all coordination sites and thus quenching the reaction.

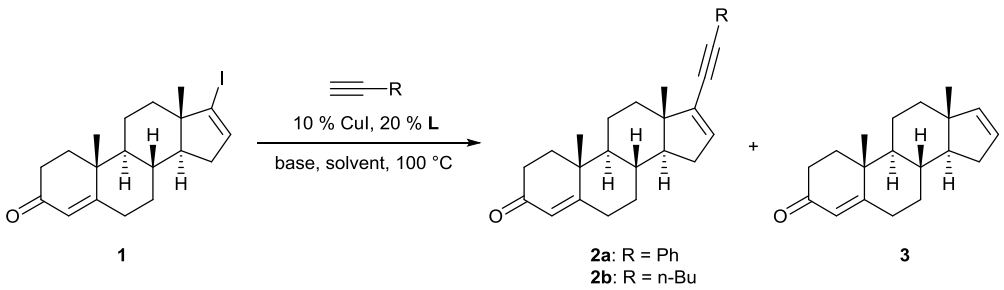
Interestingly, phosphines are rarely used in other Cu-catalyzed reactions, and always never outperform N- or O-chelators. Therefore, we suspected that the results could be accounted for not by Cu-catalysis, but rather by trace impurities of Pd.[30] However, carrying out the cross-coupling of **1** with 1-hexyne in the presence of 100 ppb $Pd(Ph_3P)_2Cl_2$ (10^{-5} mol%) revealed no effect of palladium. Therefore, we didn't take into account any significant contribution of Pd to catalysis of the reaction under investigation.

Table 1 Ligand effect on the Cu-catalyzed coupling of **1** with phenylacetylene



Entry	Ligand	Yield **2a**[a] (%)	Entry	Ligand	Yield **2a**[a] (%)
1	–	39	6	20 % Ph_3P	100
2	20 % DMEDA	36	7	10 % BINAP	0
3	20 % L-Pro	52	8	10 % dppe	0
4	20 % **L1**	63	9	10 % dppp	15
5	20 % **L2**	84	10	10 % dppf	21

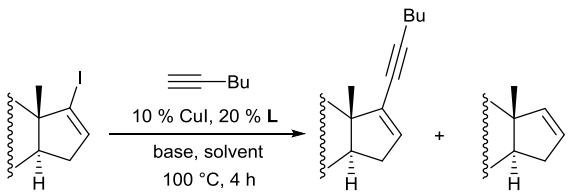
[a] By ^1H NMR.



Scheme 2 Cu-catalyzed alkynylation of iodosteroid **1**.

Aliphatic 1-alkynes are known to be less reactive than arylacetylenes requiring a more careful tuning of the catalytic system. As expected, 1-hexyne reacted with **1** much more slowly than phenylacetylene (Table 2). Moreover, the formation of the target coupling product **2b** was accomplished by an undesirable reductive dehalogenation giving product **3**. The decrease in the coupling rate led to a higher yield of **3**, as the dehalogenation rate is believed not to depend on the acetylene used. Changing solvent from DMSO to DMF doesn't affect the yield of the products (*cf.* entries 1 and 2). The use of K_3PO_4 instead of K_2CO_3 affords practically the same result, while the use of KOH increases the amount of reduction product **3**, and in the case of Cs_2CO_3 and pyridine no reaction was observed (entries 3–6). Changing Ph_3P to phosphines bearing donating alkyl substituents leads to a negative effect (entries 7 and 8). Thus, the initial variation of conditions didn't allow us to improve the rate and selectivity in the reaction of **1** with 1-hexyne.

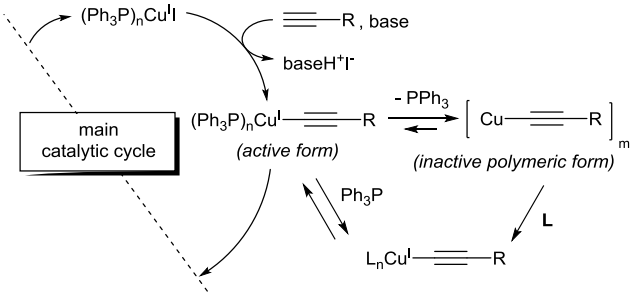
Table 2 The effect of reaction conditions on the Cu-catalyzed coupling of **1** with 1-hexyne



Entry	Ligand	Base	Solvent	Yield **2b**/**3**[a] (%)
1	Ph_3P	K_2CO_3	DMSO	40/<5
2	Ph_3P	K_2CO_3	DMF	40/<5
3	Ph_3P	K_3PO_4	DMSO	37/4
4	Ph_3P	KOH	DMF	22/13
5	Ph_3P	Cs_2CO_3	DMSO	0/8
6	Ph_3P	pyridine	DMSO	0/0
7	Cy_3P	K_2CO_3	DMSO	6/<5
8	$(t\text{-Bu})_3P{\cdot}HBF_4$	K_2CO_3	DMSO	30/0

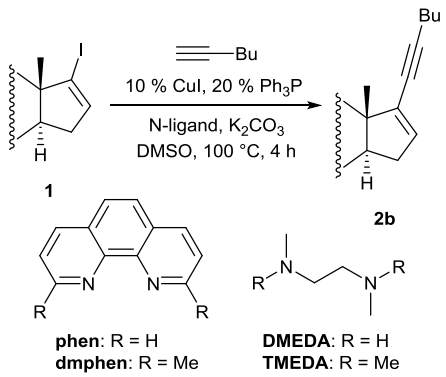
[a] By ^{1}H NMR.

Since copper acetylides tend to form oligomeric or polymeric associates, which are often sparingly soluble, we supposed that an introduction of additional N-donating ligands **L** (Scheme 3) could increase the amount of soluble copper acetylide complexes. The subsequent ligand exchange with Ph_3P should afford catalytically active monomeric copper(I) complex.



Scheme 3 Possible equilibrium of copper acetylides.

Table 3 The effect of additional ligand on the Cu-catalyzed coupling of **1** with 1-hexyne



Entry	Ligand	Additive	Yield **2b**[a] (%)
1	Ph_3P	–	40
2	Ph_3P	100 % pyridine	41
3	Ph_3P	100 % Et_3N	23
4	Ph_3P	10 % DMEDA	48
5	Ph_3P	10 % dmphen	50
6	Ph_3P	10 % EDTA	54
7	Ph_3P	10 % phen	61
8	Ph_3P	10 % TMEDA	89
9	–	10 % TMEDA	7

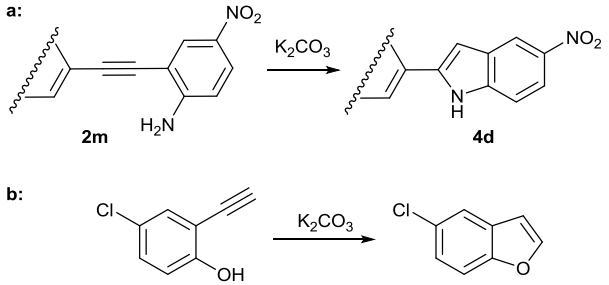
[a] By ^{1}H NMR.

Thus, we applied a biligand catalyst system comprising Ph_3P and an additional N-donating ligand (Table 3). The use of pyridine didn't allow us to improve the result (entry 2), although it is a common solvent for the coupling of copper(I) acetylides in non-catalytic Castro-Stephens variant.[31] In the case of Et_3N the conversion was even lower (entry 3), thus confirming an inhibitory effect of amines on the reaction.[3b]

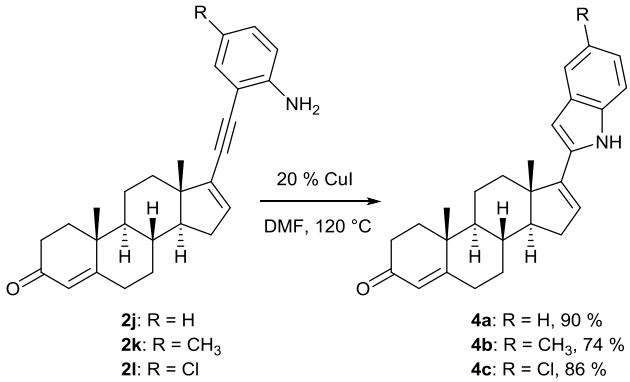
However, the application of N,N-donating chelating ligands led to a significant improvement (entries 4–8). Thus, the addition of TMEDA not only results in increase of the yield of enyne **2b** from 40 to 89 % (*cf.* entries 1 and 8), but also suppresses the formation of undesired product **3** almost completely. It is noteworthy that the use of TMEDA without Ph_3P leads to unsatisfactory result (entry 9).

The potential of the developed biligand catalytic system (CuI : Ph_3P : TMEDA = 10:20:10 mol%) was revealed in the reaction of iodosteroid **1** with various terminal alkynes (Table 4). Good to excellent yields of steroidal enynes **2** were obtained in a majority of cases despite the above mentioned inertness of **1** in Cu(I)-catalyzed reactions due to steric hindrance. The reaction proceeds smoothly with arylacetylenes containing electron-donating (**2c**) or weak electron-withdrawing (**2d**) groups. Substantially lower reactivity of C-Br bond compared to C-I allow to preserve aryl bromide fragment during the coupling providing **2d** with almost quantitative yield. The obtained aryl bromide moiety is a convenient precursor for further modifications of the steroid side chain *via* well-established palladium-catalyzed chemistry. However, strong electron-acceptors in arylacetylene lead either to significantly diminished yields or to the complete suppression of the coupling (Table 4, entries 5 and 6). This is probably caused by the high propensity of these alkynes to undergo Michael addition in basic media leading to the complex mixture of products. However, such a strongly electron-deficient substrate as 2-ethynylpyridine afforded a very good yield of the enyne **2g**. Almost the same yields were achieved with other electron-deficient and electron-donating heteroaryl alkynes (**2h**, **2i**). Good yields were also achieved with less reactive aliphatic terminal alkynes including 1-hexyne (**2b**, 86 %) and 3-diethylaminopropyne (**2o**, 68 %). However, propargyl alcohol which is known to be inert in Cu-catalyzed Sonogashira coupling gave no product **2r** under these conditions.

Various *o*-alkynylanilines were competent substrates in the coupling, affording *o*-aminoenynes **2j-m** in excellent yields. Both donor methyl and electron-withdrawing chlorine substituents were tolerated. The coupling of 4-nitro-2-ethynylaniline was also very efficient but the product **2m** was isolated as an equimolar mixture with the corresponding indole **4d** (Scheme 4a). The observed 5-*endo-dig* cyclization of **2m** to **4d** is probably facilitated by increased NH-acidity of 4-nitroaniline core. In the case of much more acidic *o*-ethynylphenol, no coupling product **2n** was detected in the reaction mixture due to fast intramolecular cyclization of the terminal alkyne to 5-chlorobenzo[*b*]furan (Scheme 4b). The other aminoenynes **2j-l** are less acidic than **2m**, so the cyclization to indole requires the assistance of Lewis acid capable of effective coordination with triple bond. Since Ph_3P lowers the Lewis acidity of Cu(I), no cyclization is observed for **2j-l** in the reaction media. However, good yields of indoles were obtained by heating these aminoenynes under "ligand-free" conditions (CuI, DMF, 120 °C, Scheme 5). Various Cu(I) and Cu(II) complexes ($[Cu(MeCN)_4]BF_4$, $(CuOTf)_2{\cdot}C_6H_6$, $Cu(OTf)_2$) were all equally useful in this transformation. It is worth noting that **2m**, containing electron-withdrawing nitro-group, did not afford **4d** on heating with Cu salts, probably due to a lower nucleophilicity of amino-group.



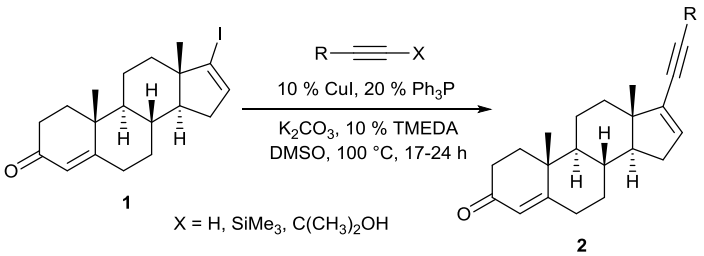
Scheme 4 Base-promoted cyclizations of aminoenyne **2m** (*a*) and *o*-ethynylphenol (*b*).

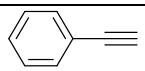
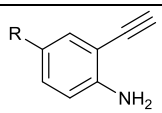
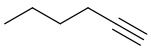
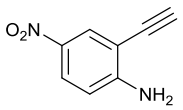
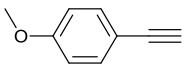
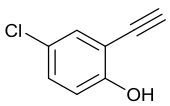
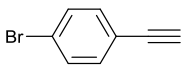
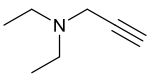
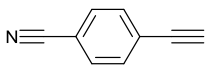
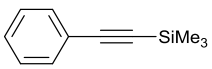
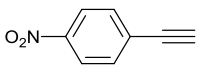
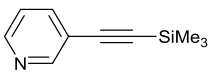
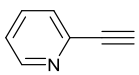
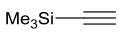
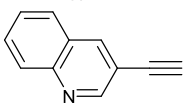
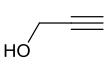
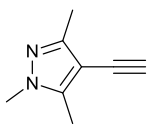
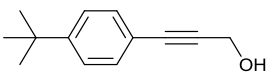
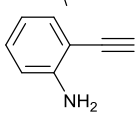
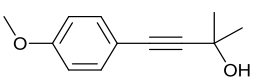


Scheme 5 Cu-catalyzed transformation of *o*-aminoenynes to indoles **4a-c**.

Since the basic media will favor the cleavage of alkynylsilanes we investigated tandem desilylation-Sonogashira-type coupling with readily available trimethylsilylalkynes. Indeed both aryl- (**2a**, Table 4, entry 15) and hetarylenynes (**2p**, entry 16) were prepared under the optimized conditions in excellent yields. Accordingly, no coupling product was observed neither with trimethylsilylacetylene nor with bis(trimethylsilyl)acetylene, since formation of volatile acetylene should proceed much faster than the coupling. The other internal alkynes capable to give terminal alkynes *in situ* were also considered. Propargyl alcohols are known to be versatile sources of terminal alkynes *via* base-catalyzed retro-Favorsky reaction. While no reaction was observed with 3-arylpropargyl alcohol (Table 4, entry 19), a significant amount of coupling product **2c** was observed for 3-aryl-1,1-dimethylpropargyl alcohol (entry 20). The process has a well-known counterpart in Pd-catalyzed Sonogashira coupling,[32] though it is not quite efficient to be preparatively useful.

Table 4 Yields of alkynylation products in the Cu-catalyzed coupling of **1** with acetylenes

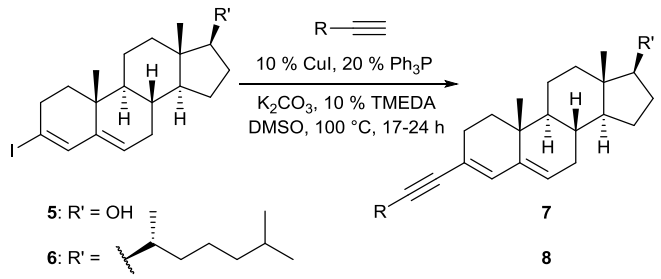


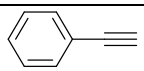
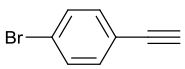
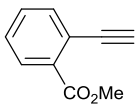
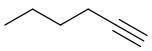
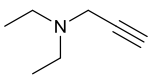
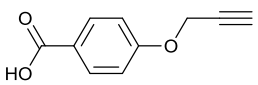
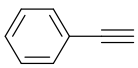
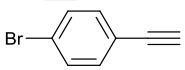
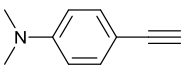
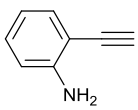
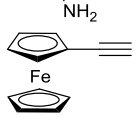
Entry	Alkyne	Product	Isolated yield (%)	Entry	Alkyne	Product	Isolated yield (%)
1		**2a**	100[a]	11		**2k**, R = CH_3 **2l**, R = Cl	85 90
2		**2b**	86	12		**2m** + **4d** (44:56)	96[c]
3		**2c**	75	13		**2n**	0[d]
4		**2d**	99	14		**2o**	68[e]
5		**2e**	(34)[b]	15		**2a**	100
6		**2f**	0	16		**2p**	92
7		**2g**	85	17		**2q**	0
8		**2h**	87	18		**2r**	0
9		**2i**	86	19		**2s**	0
10		**2j**	94	20		**2c**	(59)[b]

[a] Reaction for 4 h. [b] ^{1}H NMR yield in parentheses. [c] Yield for mixture of **2m** and **4d**. [d] Cyclization of starting acetylene to 5-chlorobenzo[*b*]furan was observed. [e] Reaction for 48 h.

The scope of protocol was expanded to testosterone and cholestenone-derived steroidal iododienes **5** and **6** (Table 5). Since these dienes are much less sterically encumbered than **1**, the Cu-catalyzed coupling with these substrates was much smoother. In fact, we have never detected any traces of protodeiodinated by-products in these reactions. Arylacetylenes with both electron-donating (**8c**-**e**), weak (**7b**, **8b**) and even moderate (**7c**) electron-withdrawing groups were tolerated. The coupling with *o*-ethynylaniline afforded uncyclized *o*-aminophenylenyne **8d** in a good isolated yield. The developed method was used to prepare ferrocene-cholesterol conjugate **8e** in 84 % yield. It is noteworthy that this route to steroids containing electrochemical probe gives almost the same yield as palladium-catalyzed reaction of ethynylferrocene with the corresponding vinyl triflate.[24a] High yields were also achieved for aliphatic alkynes including 3-diethylaminopropyne (**7e**), which was expected to poison catalyst due to known detrimental effect of trialkylamines on Cu-catalyzed Sonogashira reaction.[3b] However, the presence of free carboxy group led to slowdown of the coupling, though the product **7f** was isolated in 79 % yield after heating the reaction mixture for 66 h.

Table 5 Yields of alkynylation products in the Cu-catalyzed coupling of **5** and **6** with acetylenes



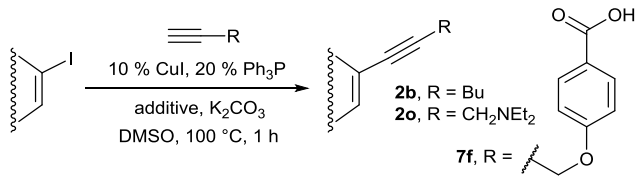
Entry	Substrate	Alkyne	Product	Isolated yield (%)
1	**5**		**7a**	100
2	**5**		**7b**	98
3	**5**		**7c**	83
4	**5**		**7d**	95
5	**5**		**7e**	97
6	**5**		**7f**	79[a]
7	**6**		**8a**	90
8	**6**		**8b**	87
9	**6**		**8c**	87
10	**6**		**8d**	80
11	**6**		**8e**	84

[a] Reaction for 66 h.

It is known that diamines in Cu-catalyzed amination can act not only as ligands for copper but as mass-transfer agents for sparingly soluble inorganic base.[33] To clarify the effect of TMEDA addition on the reaction rate we carried out the coupling of 1-hexyne with iodosteroid **1** in the presence of various phase-transfer catalysts (Table 6). The acceleration of the coupling was observed for all additives except Bu_4NI (entry 11), which completely inhibited the reaction. The most prominent acceleration was observed with Bu_4NBr and aliquat-336 (entries 5 and 7), which were even more efficient than TMEDA (entry 2). However, the increase of the reaction rate proved to be very dependent on the nature of the substrate. For instance, Bu_4NBr and TMEDA led to the same yield in the reaction of **1** with 3-diethylaminopropyne (entries 12 and 13). The rather slow coupling of **5** with 4-(propargyloxy)benzoic acid is much less efficient when Bu_4NBr (entry 15) or aliquat-336 (entry 16) are used instead of TMEDA (entry 14).

Surprisingly, the increase of additive amount led to deceleration of the reaction rate (*cf.* entries 3 *vs.* 4 and 5 *vs.* 6). Since Bu_4NI inhibits the coupling (entry 11), the observed effect is probably caused by the formation of tetraalkylammonium iodide due to anion exchange with iodide anion, which is formed in the course of the coupling.

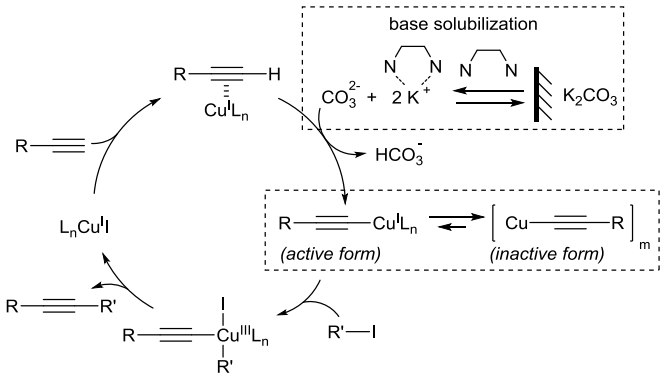
Table 6 Effect of phase transfer agents



Entry	Additive	Product	Yield[a] (%)
1	–	**2b**	4
2	10 % TMEDA	**2b**	89[b]
3	10 % TEBAC	**2b**	29
4	20 % TEBAC	**2b**	19
5	10 % $(n\text{-}Bu)_4NBr$	**2b**	97
6	20 % $(n\text{-}Bu)_4NBr$	**2b**	41[b]
7	10 % aliquat-336[c]	**2b**	79
8	10 % $(n\text{-}Bu)_4NHSO_4$	**2b**	9
9	10 % 18-crown-6	**2b**	23
10	100 % PEG-1500	**2b**	23
11	10 % $(n\text{-}Bu)_4NI$	**2b**	0
12	10 % TMEDA	**2o**	66[d]
13	10 % $(n\text{-}Bu)_4NBr$	**2o**	66[d]
14	10 % TMEDA	**7f**	53[d]
15	10 % $(n\text{-}Bu)_4NBr$	**7f**	33[d]
16	10 % aliquat-336[c]	**7f**	17[d]

[a] By ^1H NMR. [b] Reaction for 4 h. [c] $Me(Oct)_3NCl$. [d] Reaction for 17 h.

A notable acceleration of the coupling was also observed in the presence of 18-crown-6 (*cf.* entries 1 and 9 in Table 6), which is an excellent ligand for potassium cation. Improving the solubility of K_2CO_3, thus increasing an amount of carbonate anion in a solution should accelerate the formation of copper acetylide. It prompted us to suppose that the formation of copper acetylides might be the rate-limiting stage for Cu-catalyzed Sonogashira coupling. Indeed, an addition of Ph_3P to stoichiometric reaction of CuI with terminal alkyne (2-(4-nitrophenyloxy)prop-1-yne) in the presence of K_2CO_3 led to catastrophic slowdown of Cu acetylide formation with incomplete conversion of starting alkyne even after 5 h (HPLC monitoring), whereas in the absence of Ph_3P a full conversion was observed within a few minutes. The addition of TMEDA (1 equiv.) led to partial improvement of alkyne conversion, while no effect of TMEDA was observed in the reaction of preformed copper acetylide with iodosteroid **1**. Therefore, we believe that the addition of co-ligands in Cu-catalyzed Sonogashira coupling improves the solubility of inorganic base leading to the increased amount of catalytically active acetylide copper complexes (Scheme 6).



Scheme 6 Plausible mechanism of the Cu-catalyzed Sonogashira coupling.

Conclusions

We developed a new synthetic approach to important steroidal enynes based on Pd-free Sonogashira reaction. The introduction of additives, acting as phase-transfer agents for sparingly soluble inorganic base, was found to considerably improve catalytic performance of CuI/Ph_3P system. Though Cu-catalyzed protocols in Sonogashira reaction are generally less effective and versatile than the classical Pd-catalyzed methods, a wide range of aryl- and hetarylacetylenes as well as aliphatic 1-alkynes can be efficiently coupled with steroidal vinyl iodides affording the corresponding enynes in up to quantitative yields. Trimethylsilylalkynes can also be viable substitutes for terminal alkynes in this protocol due to the *in situ* desilylation. The limitations of the procedure are mainly imposed by relatively basic media which induces side reactions with strongly electron-deficient acetylenes, propargyl alcohols, and some base-sensitive *o*-ethynylanilines and phenols. Notwithstanding, the protocol appeared highly efficient in coupling of *o*-ethynylanilines, which can be easily transformed to steroid-anchored indoles.

Experimental

General information

NMR spectra were recorded with a Bruker Avance 400 and an Agilent 400MR spectrometers (^{1}H 400 MHz, ^{13}C 100.6 MHz) at ambient temperature in $CDCl_3$ or in $CDCl_3$–DMSO-d^6 and $CDCl_3$–CD_3OD mixtures for compounds with low solubility in $CDCl_3$. Chemical shifts are presented in ppm (δ scale) and referenced to hexamethyldisiloxane (δ = 0.05 ppm) in the ^{1}H NMR spectra and to the solvent signal in the ^{13}C NMR spectra. IR spectra were recorded with a Thermo Nicolet 200 FT-IR instrument in KBr pellets. MALDI-TOF spectra were recorded with a Bruker Daltonics UltraFlex instrument in a dithranol matrix using PEG 400 or PEG 600 as the internal standard. Elemental analyses were performed with an Elementar Vario MICRO cube apparatus. Column chromatography was carried out on Macherey–Nagel silica gel 60 (0.040–0.063 mm). Steroidal vinyl iodides **1**, **5** and **6** were prepared from the corresponding ketones according to previously reported procedures.[27]

Copper-catalyzed Sonogashira coupling of iodosteroids and terminal acetylenes

General Procedure

In a vial with a screw cap, iodosteroid **1**, **5** or **6** (0.150 mmol), terminal acetylene (0.180 mmol), anhydrous K_2CO_3 (41.5 mg, 0.300 mmol), CuI (2.9 mg, 15 μmol, 10 mol%), triphenylphosphine (7.9 mg, 30 μmol, 20 mol%), and N,N,N',N'-tetramethylethylenediamine (TMEDA) (2.2 μL, 15 μmol, 10 mol%) were mixed under an Ar atmosphere in DMSO (0.5 mL). The reaction mixture was stirred at 100 °C for 4–66 h, then diluted with CH_2Cl_2 (25 mL) and washed with water (4 × 25 mL). The organic layer was dried with anhydrous Na_2SO_4, and the solvents were evaporated *in vacuo*. The residue was purified by column chromatography.

Copper-catalyzed synthesis of indoles from *o*-ethynylanilines

General Procedure

In a vial with a screw cap, steroidal aniline **2j-l** (0.150 mmol) and CuI (5.7 mg, 30 μmol, 20 mol%) were mixed under an Ar atmosphere in DMF (0.5 mL). The reaction mixture was stirred at 100 °C for 24 h, then diluted with CH_2Cl_2 (25 mL) and washed with water (4 × 25 mL). The organic layer was dried with anhydrous Na_2SO_4, and the solvents were evaporated *in vacuo*. The residue was purified by column chromatography.

17-(phenylethynyl)androsta-4,16-dien-3-one (2a). Prepared from **1** (59.4 mg, 0.15 mmol) and phenylacetylene (19.8 μL, 0.18 mmol) without addition of TMEDA; heating 4 h. Yield 55.8 mg (100 %). Prepared from **1** (59.4 mg, 0.15 mmol) and (trimethylsilyl)phenylacetylene (0.18 mmol, 35.4 μL); heating 24 h; eluent: CH_2Cl_2–MeOH = 100 : 1. Yield 55.8 mg (100 %). Light-brown solid; mp 209–210 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.39 [m, 2H, 2,6-CH(Ph)], 7.32–7.23 [m, 3H, 3,4,5-CH(Ph)], 6.07 (m, 1H, 16-CH), 5.72 (s, 1H, 4-CH), 2.48–2.20 (m, 5H), 2.11–1.36 (m, 10H), 1.20 (s, 3H, 19-CH_3), 1.18–0.97 (m, 2H), 0.94 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.3 [C(3)=O], 170.8 (5-C), 137.0 (17-C), 135.5 (16-CH), 131.5 [2C, 2,6-CH(Ph)], 128.2 [2C, 3,5-CH(Ph)], 127.9 [4-CH(Ph)], 123.9 (4-CH), 123.5 [1-C(Ph)], 92.9 (C≡C), 84.8 (C≡C), 55.4, 54.1, 47.9 (quat.), 38.7 (quat.), 35.5, 34.33, 34.30, 33.9, 32.7, 32.0, 31.7, 20.8, 17.2, 16.2; IR (KBr) ν = 2195 (C≡C), 1668 (C=O), 760 (Ph) cm^{-1}; HRMS (MALDI-TOF) calcd for $C_{27}H_{31}O$ $[M+H]^+$ 371.2375; found 371.2373; Anal. calcd for $C_{27}H_{30}O$: C, 87.52; H, 8.16; found C, 87.12; H, 8.07.

17-(hex-1-yn-1-yl)androsta-4,16-dien-3-one (2b). Prepared from **1** (59.4 mg, 0.15 mmol) and hex-1-yne (0.18 mmol, 20.7 μL); heating 17 h; eluent: CH_2Cl_2–MeOH = 100 : 1. Yield 45.1 mg (86 %). Light-yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (m, 1H, 16-CH), 5.72 (s, 1H, 4-CH), 2.47–2.24 (m, 6H), 2.17 (ddd, J = 15.9, 6.6, 3.5 Hz, 1H), 2.04–1.93 (m, 2H), 1.89–

1.80 (m, 2H), 1.78–1.22 (m, 10H), 1.20 (s, 3H, 19-CH_3), 1.16–0.95 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H, CH_2CH_3), 0.86 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.4 [C(3)=O], 171.1 (5-C), 137.6 (17-C), 133.3 (16-CH), 123.9 (4-CH), 93.9 (C≡C), 75.6 (C≡C), 55.3, 54.1, 47.6 (quat.), 38.7 (quat.), 35.5, 34.33, 34.26, 33.9, 32.7, 31.74, 31.68, 30.9, 21.8, 20.8, 19.2, 17.2, 16.0, 13.6 (CH_2CH_3); HRMS (MALDI-TOF) calcd for $C_{25}H_{35}O$ $[M+H]^+$ 351.2688; found 351.2697.

17-[(4-methoxyphenyl)ethynyl]androsta-4,16-dien-3-one (2c). Prepared from **1** (59.4 mg, 0.15 mmol) and (4-methoxyphenyl)acetylene (23.3 μL, 0.18 mmol); heating 24 h; eluent: CH_2Cl_2–MeOH = 100 : 1. Yield 44.8 mg (75 %). White solid; mp 221–223 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 [d, J = 8.6 Hz, 2H, 2,6-CH(Ar)], 6.82 [d, J = 8.6 Hz, 2H, 3,5-CH(Ar)], 6.03 (m, 1H, 16-CH), 5.73 (s, 1H, 4-CH), 3.79 (s, 3H, CH_3O), 2.48–2.20 (m, 5H), 2.11–1.35 (m, 10H), 1.21 (s, 3H, 19-CH_3), 1.18–0.98 (m, 2H), 0.93 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.4 [C(3)=O], 171.0 (5-C), 159.4 [4-C(Ar)], 137.2 (17-C), 134.7 (16-CH), 132.9 [2C, 2,6-CH(Ar)], 123.9 (4-CH), 115.6 [1-C(Ar)], 113.8 [2C, 3,5-CH(Ar)], 92.9 (C≡C), 83.4 (C≡C), 55.4, 55.2 (CH_3O), 54.1, 47.9 (quat.), 38.7 (quat.), 35.5, 34.3 (2C), 33.9, 32.7, 32.0, 31.7, 20.8, 17.2, 16.2; HRMS (MALDI-TOF) calcd for $C_{28}H_{33}O_2$ $[M+H]^+$ 401.2481; found 401.2482.

17-[(4-bromophenyl)ethynyl]androsta-4,16-dien-3-one (2d). Prepared from **1** (59.4 mg, 0.15 mmol) and (4-bromophenyl)acetylene (32.6 mg, 0.18 mmol); heating 17 h; eluent: CH_2Cl_2–MeOH = 100 : 1. Yield 67.0 mg (99 %). White solid; mp 219–222 °C (dec.); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.40 [m, 2H, CH(Ar)], 7.30–7.26 [m, 2H, CH(Ar)], 6.10 (dd, J = 3.0, 2.0 Hz, 1H, 16-CH), 5.73 (s, 1H, 4-CH), 2.48–2.21 (m, 5H), 2.11–1.37 (m, 10H), 1.21 (s, 3H, 19-CH_3), 1.19–0.97 (m, 2H), 0.93 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.4 [C(3)=O], 170.8 (5-C), 136.8 (17-C), 136.3 (16-CH), 132.9 [2C, CH(Ar)], 131.5 [2C, CH(Ar)], 124.0 (4-CH), 122.5 [1- or 4-C(Ar)], 122.1 [1- or 4-C(Ar)], 91.9 (C≡C), 86.0 (C≡C), 55.5, 54.1, 48.0 (quat.), 38.7 (quat.), 35.5, 34.3 (2C), 33.9, 32.7, 32.1, 31.7, 20.8, 17.2, 16.3; HRMS (MALDI-TOF) calcd for $C_{27}H_{30}BrO$ $[M+H]^+$ 449.1480; found 449.1494.

17-[(pyridin-2-yl)ethynyl]androsta-4,16-dien-3-one (2g). Prepared from **1** (59.4 mg, 0.15 mmol) and 2-ethynylpyridine (18.6 mg, 0.18 mmol); heating 20 h; eluent: hexanes–EtOAc = 2 : 1. Yield 47.2 mg (85 %). White solid; mp 204–205 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.57 [d, J = 4.6 Hz, 1H, 6-CH(pyridine)], 7.62 [td, J = 7.7, 1.8 Hz, 1H, 4-CH(pyridine)], 7.41 [d, J = 7.7 Hz, 1H, 3-CH(pyridine)], 7.18 [dd, J = 7.7, 4.6 Hz, 1H, 5-CH(pyridine)], 6.22 (m, 1H, 16-CH), 5.73 (s, 1H, 4-CH), 2.49–2.23 (m, 5H), 2.14–1.39 (m, 10H), 1.21 (s, 3H, 19-CH_3), 1.19–0.98 (m, 2H), 0.96 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.3 [C(3)=O], 170.8 (5-C), 150.0 [6-CH(pyridine)], 143.7 [2-C(pyridine)], 138.1 [16-CH or 4-CH(pyridine)], 136.3 (17-C), 135.9 [16-CH or 4-CH(pyridine)], 127.1 [3-CH(pyridine)], 124.0 (4-CH), 122.4 [5-CH(pyridine)], 92.2 (C≡C), 84.9 (C≡C), 55.5, 54.1, 48.1 (quat.), 38.7 (quat.), 35.5, 34.33, 34.27, 33.9, 32.7, 32.2, 31.7, 20.7, 17.2, 16.2; HRMS (MALDI-TOF) calcd for $C_{26}H_{30}NO$ $[M+H]^+$ 372.2327; found 372.2318.

17-[(quinolin-3-yl)ethynyl]androsta-4,16-dien-3-one (2h). Prepared from **1** (59.4 mg, 0.15 mmol) and 3-ethynylquinoline (27.6 mg, 0.18 mmol); heating 24 h; eluent: hexanes–EtOAc = 2 : 1. Yield 55.1 mg (87 %). Off-white solid; mp 170–173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 [br. s, 1H, 2-CH(quinoline)], 8.20 [s, 1H, 4-CH(quinoline)], 8.07 [d, J = 7.8 Hz, 1H, 5- or 8-CH(quinoline)], 7.76 [d, J = 7.8 Hz, 1H, 5- or 8-CH(quinoline)], 7.70 [t, J = 7.8 Hz, 1H, 6- or 7-CH(quinoline)], 7.54 [t, J = 7.8 Hz, 1H, 6- or 7-CH(quinoline)], 6.19 (m, 1H, 16-CH), 5.74 (s, 1H, 4-CH), 2.49–2.25 (m, 5H), 2.16–1.40 (m, 10H), 1.22 (s, 3H, 19-CH_3), 1.20–1.00 (m, 2H), 0.98 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.3 [C(3)=O], 170.7 (5-C), 152.2 [2-CH(quinoline)], 146.7 [8a-C(quinoline)], 137.9 [16-CH or 4-CH(quinoline)], 137.2 [16-CH or 4-CH(quinoline)], 136.6 (17-C), 129.9, 129.4, 127.5, 127.2 [2C, CH(quinoline) + 4a-C(quinoline)], 124.0 (4-CH), 117.7 [3-C(quinoline)], 90.2 (C≡C), 88.2 (C≡C), 55.5, 54.1, 48.1 (quat.), 38.7 (quat.), 35.6, 34.4 (2C), 33.9, 32.7, 32.2, 31.8, 20.8, 17.2, 16.3; HRMS (MALDI-TOF) calcd for $C_{30}H_{32}NO$ $[M+H]^+$ 422.2484; found 422.2486.

17-[(1,3,5-trimethyl-1H-pyrazol-4-yl)ethynyl]androsta-4,16-dien-3-one (2i). Prepared from **1** (59.4 mg, 0.15 mmol) and 4-ethynyl-1,3,5-trimethyl-1H-pyrazole (24.2 mg, 0.18 mmol); heating 24 h; eluent: hexanes–EtOAc = 1 : 1. Yield 51.7 mg (86 %). White solid; mp 190–193 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (m, 1H, 16-CH), 5.72 (s, 1H, 4-CH), 3.68 (s, 3H, CH_3N), 2.48–2.18 (m, 5H), 2.26 [s, 3H, CH_3C(pyrazole)], 2.23 [s, 3H, CH_3C(pyrazole)], 2.09–1.35 (m, 10H), 1.21 (s, 3H, 19-CH_3), 1.18–0.96 (m, 2H), 0.93 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.3 [C(3)=O], 170.9 (5-C), 149.2 [3-C(pyrazole)], 141.4 [5-C(pyrazole)], 137.4 (17-C), 133.1 (16-CH), 123.9 (4-CH), 102.0 [4-C(pyrazole)], 87.9 (C≡C), 84.9 (C≡C), 55.4, 54.1, 47.8 (quat.), 38.7 (quat.), 36.0 (CH_3N), 35.5, 34.3 (2C), 33.9, 32.7, 31.9, 31.7, 20.8, 17.1, 16.2, 12.3 [CH$_3$C(pyrazole)], 10.4 [CH$_3$C(pyrazole)]; HRMS (MALDI-TOF) calcd for $C_{27}H_{35}N_2O$ $[M+H]^+$ 403.2749; found 403.2757; Anal. calcd for $C_{27}H_{34}N_2O$: C, 80.55; H, 8.51; N, 6.96; found C, 80.26; H, 8.65; N, 6.71.

17-[(2-aminophenyl)ethynyl]androsta-4,16-dien-3-one (2j). Prepared from **1** (118.8 mg, 0.30 mmol) and 2-ethynylaniline (41.0 μL, 0.36 mmol); heating 24 h; eluent: CH_2Cl_2–MeOH = 200 : 1. Yield 108.3 mg (94 %). Off-white solid; mp 217–219 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 [dd, J = 7.6, 1.1 Hz, 1H, 6-CH(Ar)], 7.13–7.06 [m, 1H, 4-CH(Ar)], 6.74–6.65 [m, 2H, 3- and 5-CH(Ar)], 6.07 (dd, J = 2.8, 2.0 Hz, 1H, 16-CH), 5.73 (s, 1H, 4-CH), 4.36 (br. s, 2H, NH_2), 2.49–2.21 (m, 5H), 2.13–1.38 (m, 10H), 1.21 (s, 3H, 19-CH_3), 1.19–0.97 (m, 2H), 0.95 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.5 [C(3)=O], 171.0 (5-C), 147.4 [2-C(Ar)], 136.9 (17-C), 135.1 (16-CH), 132.0 [4- or 6-CH(Ar)], 129.4 [4- or 6-CH(Ar)], 124.0 (4-CH), 117.9 [3- or 5-CH(Ar)], 114.2 [3- or 5-CH(Ar)], 108.3 [1-C(Ar)], 90.1 (C≡C), 89.3 (C≡C), 55.4, 54.1, 47.9 (quat.), 38.7 (quat.), 35.5, 34.4, 34.3, 33.9, 32.7, 32.1, 31.7,

20.8, 17.2, 16.3; HRMS (MALDI-TOF) calcd for $C_{27}H_{32}NO$ $[M+H]^+$ 386.2484; found 386.2479.

17-[(2-amino-5-methylphenyl)ethynyl]androsta-4,16-dien-3-one (2k). Prepared from **1** (118.8 mg, 0.30 mmol) and 2-ethynyl-4-methylaniline (47.2 mg, 0.36 mmol); heating 24 h; eluent: CH_2Cl_2–MeOH = 200 : 1. Yield 101.6 mg (85 %). Off-white solid; mp 160–163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 [d, J = 2.4 Hz, 1H, 6-CH(Ar)], 6.89 [dd, J = 8.2, 2.4 Hz, 1H, 4-CH(Ar)], 6.59 [d, J = 8.2 Hz, 1H, 3-CH(Ar)], 6.03 (dd, J = 3.1, 2.0 Hz, 1H, 16-CH), 5.72 (s, 1H, 4-CH), 4.08 (br. s, 2H, NH_2), 2.47–2.19 (m, 5H), 2.18 [s, 3H, CH_3C(Ar)], 2.10–1.36 (m, 10H), 1.19 (s, 3H, 19-CH_3), 1.16–0.96 (m, 2H), 0.93 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.3 [C(3)=O], 170.9 (5-C), 145.1 [2-C(Ar)], 136.9 (17-C), 134.8 (16-CH), 132.0 [4- or 6-CH(Ar)], 130.2 [4- or 6-CH(Ar)], 127.0 [5-C(Ar)], 123.9 (4-CH), 114.3 [3-CH(Ar)], 108.2 [1-C(Ar)], 89.8 (C≡C), 89.5 (C≡C), 55.3, 54.0, 47.8 (quat.), 38.6 (quat.), 35.4, 34.4, 34.3, 33.9, 32.7, 32.0, 31.7, 20.8, 20.2 [CH_3C(Ar)], 17.1, 16.2; HRMS (MALDI-TOF) calcd for $C_{28}H_{34}NO$ $[M+H]^+$ 400.2640; found 400.2632.

17-[(2-amino-5-chlorophenyl)ethynyl]androsta-4,16-dien-3-one (2l). Prepared from **1** (118.8 mg, 0.30 mmol) and 2-ethynyl-4-chloroaniline (54.6 mg, 0.36 mmol); heating 24 h; eluent: CH_2Cl_2–MeOH = 200 : 1. Yield 113.0 mg (90 %). Off-white solid; mp 148–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 [d, J = 2.5 Hz, 1H, 6-CH(Ar)], 7.02 [dd, J = 8.6, 2.5 Hz, 1H, 4-CH(Ar)], 6.60 [d, J = 8.6 Hz, 1H, 3-CH(Ar)], 6.08 (dd, J = 3.1, 2.0 Hz, 1H, 16-CH), 5.72 (s, 1H, 4-CH), 4.23 (br. s, 2H, NH_2), 2.47–2.21 (m, 5H), 2.12–1.36 (m, 10H), 1.20 (s, 3H, 19-CH_3), 1.17–0.96 (m, 2H), 0.93 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.4 [C(3)=O], 170.8 (5-C), 146.0 [2-C(Ar)], 136.5 (17-C), 136.0 (16-CH), 131.1 [4- or 6-CH(Ar)], 129.3 [4- or 6-CH(Ar)], 123.9 (4-CH), 122.0 [5-CCl(Ar)], 115.2 [3-CH(Ar)], 109.5 [1-C(Ar)], 91.1 (C≡C), 88.0 (C≡C), 55.4, 54.0, 47.9 (quat.), 38.6 (quat.), 35.4, 34.3, 34.2, 33.9, 32.6, 32.1, 31.6, 20.7, 17.1, 16.2; HRMS (MALDI-TOF) calcd for $C_{27}H_{31}ClNO$ $[M+H]^+$ 420.2094; found 420.2102.

17-[(2-amino-5-nitrophenyl)ethynyl]androsta-4,16-dien-3-one (2m) and 17-(5-nitro-1H-indol-2-yl)androsta-4,16-dien-3-one (4d). Prepared from **1** (118.8 mg, 0.30 mmol) and 2-ethynyl-4-nitroaniline (58.4 mg, 0.36 mmol); heating 24 h; eluent: CH_2Cl_2–MeOH = 50 : 1. A 46 : 54 inseparable mixture of **2m** and **4d** was obtained. Yield 124.5 mg (96 %). Yellow oil. HRMS (MALDI-TOF) calcd for $C_{27}H_{31}N_2O_3$ $[M+H]^+$ 431.2335; found 431.2342.

17-[(2-amino-5-nitrophenyl)ethynyl]androsta-4,16-dien-3-one (2m). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 [d, J = 2.6 Hz, 1H, 6-CH(Ar)], 7.98 [dd, J = 9.0, 2.6 Hz, 1H, 4-CH(Ar)], 6.67 [d, J = 9.0 Hz, 1H, 3-CH(Ar)], 6.15 (dd, J = 3.3, 2.0 Hz, 1H, 16-CH), 5.74 (s, 1H, 4-CH), 5.04 (br. s, 2H, NH_2), 2.50–2.25 (m, 5H), 2.15–1.38 (m, 10H), 1.22 (s, 3H, 19-CH_3), 1.17–0.98 (m, 2H), 0.95 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.6 [C(3)=O], 171.1 (5-C), 152.7 [2-C(Ar)], 138.3 [17-C or 5-C(Ar)], 137.2, 136.1 [17-C or 5-C(Ar)], 128.5 [4- or 6-CH(Ar)], 125.7 [4- or 6-CH(Ar)], 123.9 (4-CH), 112.7 [3-CH(Ar)], 107.5 [1-C(Ar)], 91.8 (C≡C), 86.8 (C≡C), 55.4, 54.1, 48.0 (quat.), 38.7 (quat.), 35.5, 34.4, 34.3, 33.9, 32.7, 32.2, 31.7, 20.8, 17.2, 16.3.

17-(5-nitro-1H-indol-2-yl)androsta-4,16-dien-3-one (4d). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (br. s, 1H, NH), 8.48 [d, J = 2.2 Hz, 1H, 4-CH(indole)], 8.03 [dd, J = 8.9, 2.2 Hz, 1H, 6-CH(indole)], 7.32 [d, J = 8.9 Hz, 1H, 7-CH(indole)], 6.62 [d, J = 1.1 Hz, 1H, 3-CH(indole)], 6.13 (dd, J = 3.0, 1.8 Hz, 1H, 16-CH), 5.74 (s, 1H, 4-CH), 2.51–2.25 (m, 6H), 2.16–1.38 (m, 9H), 1.24 (s, 3H, 19-CH_3), 1.17–0.98 (m, 2H), 1.08 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.7 [C(3)=O], 171.1 (5-C), 145.4 (quat.), 141.7 (quat.), 139.3 (quat.), 137.1 (quat.), 128.3 (quat.), 127.3, 123.9 (4-CH), 117.8, 117.4, 110.2 [7-CH(indole)], 101.3 [3-CH(indole)], 56.3, 54.0, 46.9 (quat.), 38.7 (quat.), 35.5, 35.3, 33.9 (2C), 32.7, 31.7, 31.6, 20.9, 17.2, 16.6.

17-[3-(diethylamino)prop-1-yn-1-yl]androsta-4,16-dien-3-one (2o). Prepared from **1** (59.4 mg, 0.15 mmol) and diethylpropargylamine (25.0 μL, 0.18 mmol); heating 48 h; eluent: CH_2Cl_2–MeOH = 20 : 1. Yield 38.8 mg (68 %). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (m, 1H, 16-CH), 5.73 (s, 1H, 4-CH), 3.60 (s, 2H, CH_2NEt$_2$), 2.55 [q, J = 7.2 Hz, 4H, N(CH_2CH$_3$)$_2$], 2.47–2.25 (m, 4H), 2.20 (ddd, J = 16.0, 6.6, 3.4 Hz, 1H), 2.06–1.96 (m, 2H), 1.90–1.81 (m, 2H), 1.79–1.61 (m, 3H), 1.52 (qd, J = 12.8, 4.3 Hz, 1H), 1.42–1.31 (m, 2H), 1.20 (s, 3H, 19-CH_3), 1.17–0.95 (m, 2H), 1.08 [t, J = 7.2 Hz, 6H, N(CH$_2$CH_3)$_2$], 0.88 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.4 [C(3)=O], 170.9 (5-C), 136.9 (17-C), 134.5 (16-CH), 123.9 (4-CH), 87.1 (C≡C), 80.3 (C≡C), 55.3, 54.1, 47.6 (quat.), 47.2 [2C, N(CH$_2$CH$_3$)$_2$], 41.2 (CH$_2$NEt$_2$), 38.7 (quat.), 35.5, 34.3 (2C), 33.9, 32.7, 31.8, 31.7, 20.8, 17.1, 16.1, 12.6 [2C, N(CH$_2$$CH_3$)$_2$]; HRMS (MALDI-TOF) calcd for $C_{26}H_{38}NO$ $[M+H]^+$ 380.2953; found 380.2970.

17-[(pyridin-3-yl)ethynyl]androsta-4,16-dien-3-one (2p). Prepared from **1** (59.4 mg, 0.15 mmol) and 3-[(trimethylsilyl)ethynyl]pyridine (34.2 μL, 0.18 mmol); heating 24 h; eluent: hexanes–EtOAc = 2 : 1. Yield 51.1 mg (92 %). Colorless crystals; mp 214–215 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 [br. s, 1H, 2-CH(pyridine)], 8.50 [br. d, J = 5.0 Hz, 1H, 6-CH(pyridine)], 7.70 [d, J = 7.6 Hz, 1H, 4-CH(pyridine)], 7.23 [dd, J = 7.6, 5.0 Hz, 1H, 5-CH(pyridine)], 6.15 (m, 1H, 16-CH), 5.73 (s, 1H, 4-CH), 2.49–2.23 (m, 5H), 2.15–1.38 (m, 10H), 1.22 (s, 3H, 19-CH_3), 1.19–0.98 (m, 2H), 0.95 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.3 [C(3)=O], 170.7 (5-C), 152.1 [2-CH(pyridine)], 148.2 [6-CH(pyridine)], 138.3 [16-CH or 4-CH(pyridine)], 137.1 [16-CH or 4-CH(pyridine)], 136.5 (17-C), 124.0 (4-CH), 122.9 [5-CH(pyridine)], 120.7 [3-C(pyridine)], 89.4 (C≡C), 88.2 (C≡C), 55.4, 54.1, 48.0 (quat.), 38.7 (quat.), 35.5, 34.32, 34.28, 33.9, 32.7, 32.2, 31.7, 20.8, 17.2, 16.2; HRMS (MALDI-TOF) calcd for $C_{26}H_{30}NO$ $[M+H]^+$ 372.2327; found 372.2330.

17-(1H-indol-2-yl)androsta-4,16-dien-3-one (4a). Prepared from **2j** (57.8 mg, 0.15 mmol); heating 24 h; eluent: CH_2Cl_2–MeOH = 100 : 1. Yield 52.2 mg (90 %). Off-white solid; mp 195–198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (br. s, 1H, NH), 7.52 [d, J = 7.7 Hz, 1H, 4- or 7-CH(indole)], 7.31–7.27 [m, 1H, 4- or 7-CH(indole)], 7.13–7.07 [m, 1H, 5- or 6-

CH(indole)], 7.05–6.99 [m, 1H, 5- or 6-CH(indole)], 6.48 [d, J = 1.5 Hz, 1H, 3-CH(indole)], 6.01 (dd, J = 3.0, 1.9 Hz, 1H, 16-CH), 5.73 (s, 1H, 4-CH), 2.48–2.23 (m, 6H), 2.11–1.48 (m, 9H), 1.21 (s, 3H, 19-CH_3), 1.17–0.97 (m, 2H), 1.06 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.5 [C(3)=O], 171.2 (5-C), 146.1 (quat.), 136.1 (quat.), 133.8 (quat.), 128.7 [3a-C(indole)], 124.7, 123.7, 121.8, 120.1, 119.4, 110.3 [7-CH(indole)], 99.5 [3-CH(indole)], 56.1, 53.8, 46.7 (quat.), 38.5 (quat.), 35.30, 35.28, 33.8 (2C), 32.6, 31.6, 31.3, 20.8, 17.0, 16.5; HRMS (MALDI-TOF) calcd for $C_{27}H_{31}NO$ $[M]^+$ 385.2406; found 385.2397.

17-(5-methyl-1H-indol-2-yl)androsta-4,16-dien-3-one (4b). Prepared from **2k** (59.9 mg, 0.15 mmol); heating 24 h; eluent: CH_2Cl_2–MeOH = 100 : 1. Yield 44.3 mg (74 %). Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (br. s, 1H, NH), 7.31 [s, 1H, 4-CH(indole)], 7.17 [d, J = 7.9 Hz, 1H, 6- or 7-CH(indole)], 6.94 [d, J = 7.9 Hz, 1H, 6- or 7-CH(indole)], 6.41 [s, 1H, 3-CH(indole)], 5.91 (m, 1H, 16-CH), 5.73 (s, 1H, 4-CH), 2.51–2.19 (m, 6H), 2.39 [s, 3H, CH_3C(indole)], 2.11–1.46 (m, 9H), 1.21 (s, 3H, 19-CH_3), 1.17–0.96 (m, 2H), 1.05 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 199.6 [C(3)=O], 171.1 (5-C), 146.4 (quat.), 134.4 (quat.), 133.9 (quat.), 129.1 [3a- or 5-C(indole)], 128.9 [3a- or 5-C(indole)], 124.3, 123.9, 123.8, 120.0, 110.0 [7-CH(indole)], 99.6 [3-CH(indole)], 56.2, 54.0, 46.9 (quat.), 38.7 (quat.), 35.5, 35.4, 34.0, 33.9, 32.7, 31.7, 31.4, 21.4 [*C*H_3C(indole)], 21.0, 17.2, 16.6; HRMS (MALDI-TOF) calcd for $C_{28}H_{34}NO$ $[M+H]^+$ 400.2640; found 400.2651.

17-(5-chloro-1H-indol-2-yl)androsta-4,16-dien-3-one (4c). Prepared from **2l** (63.0 mg, 0.15 mmol); heating 24 h; eluent: CH_2Cl_2–MeOH = 100 : 1. Yield 54.2 mg (86 %). Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$–DMSO-d^6) δ 10.10 (br. s, 1H, NH), 7.44 [d, J = 2.0 Hz, 1H, 4-CH(indole)], 7.24 [d, J = 8.5 Hz, 1H, 7-CH(indole)], 7.01 [dd, J = 8.5, 2.0 Hz, 1H, 6-CH(indole)], 6.39 [d, J = 1.5 Hz, 1H, 3-CH(indole)], 6.16 (dd, J = 3.1, 2.0 Hz, 1H, 16-CH), 5.71 (s, 1H, 4-CH), 2.51–2.22 (m, 6H), 2.12–1.98 (m, 2H), 1.94–1.86 (m, 1H), 1.81 (qd, J = 11.1, 3.2 Hz, 1H), 1.74–1.47 (m, 5H), 1.23 (s, 3H, 19-CH_3), 1.20–0.97 (m, 2H), 1.05 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$–DMSO-d^6) δ 198.8 [C(3)=O], 170.7 (5-C), 145.5 (quat.), 135.2 (quat.), 134.5 (quat.), 129.4 [3a-C(indole)], 125.6, 124.0 [5-C(indole)], 123.3, 121.2, 118.8, 111.2 [7-CH(indole)], 98.2 [3-CH(indole)], 55.8, 53.4, 46.3 (quat.), 38.2 (quat.), 35.0, 34.9, 33.44, 33.41, 32.2, 31.2, 31.0, 20.5, 16.7, 16.1; HRMS (MALDI-TOF) calcd for $C_{27}H_{30}ClNO$ $[M]^+$ 419.2016; found 419.2028.

3-(phenylethynyl)androsta-3,5-dien-17β-ol (7a). Prepared from **5** (59.7 mg, 0.15 mmol) and phenylacetylene (19.8 μL, 0.18 mmol) without addition of TMEDA; heating 14 h; eluent: CH_2Cl_2–MeOH = 100 : 1. Yield 55.8 mg (100 %). White solid; mp 192–193 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.38 [m, 2H, 2,6-CH(Ph)], 7.32–7.22 [m, 3H, 3,4,5-CH(Ph)], 6.36 (s, 1H, 4-CH), 5.52 (m, 1H, 6-CH), 3.64 (t, J = 8.4 Hz, 1H, 17-CHOH), 2.45–2.16 (m, 3H), 2.06 (m, 1H), 1.89–1.79 (m, 2H), 1.75–1.55 (m, 4H), 1.50–0.92 (m, 8H), 0.97 (s, 3H, 19-CH_3), 0.77 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.4 (5-C), 135.5 (4-CH), 131.4 [2C, 2,6-CH(Ph)], 128.2 [2C, 3,5-CH(Ph)], 127.8 [4-CH(Ph)], 126.1 (6-CH), 123.7 [1-C(Ph)], 117.2 (3-C), 91.5 (C≡C), 89.3 (C≡C), 81.8 (17-CHOH), 51.4, 48.2, 42.8 (quat.), 36.5, 34.6 (quat.), 33.6, 31.8, 31.6, 30.5, 27.0, 23.3, 20.6, 19.1, 11.0; HRMS (MALDI-TOF) calcd for $C_{27}H_{32}O$ $[M]^+$ 372.2453; found 372.2446; Anal. calcd for $C_{27}H_{32}O$: C, 87.05; H, 8.66; found C, 87.27; H, 8.66.

3-[(4-bromophenyl)ethynyl]androsta-3,5-dien-17β-ol (7b). Prepared from **5** (59.7 mg, 0.15 mmol) and (4-bromophenyl)acetylene (32.6 mg, 0.18 mmol); heating 17 h; eluent: CH_2Cl_2–MeOH = 100 : 1. Yield 66.4 mg (98 %). White solid; mp 109–113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.38 [m, 2H, CH(Ar)], 7.29–7.23 [m, 2H, CH(Ar)], 6.36 (s, 1H, 4-CH), 5.53 (m, 1H, 6-CH), 3.64 (t, J = 8.5 Hz, 1H, 17-CHOH), 2.45–2.17 (m, 3H), 2.06 (m, 1H), 1.90–1.79 (m, 2H), 1.76–0.93 (m, 12H), 0.96 (s, 3H, 19-CH_3), 0.77 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.4 (5-C), 135.9 (4-CH), 132.8 [2C, CH(Ar)], 131.5 [2C, CH(Ar)], 126.5 (6-CH), 122.7 [1- or 4-C(Ar)], 121.9 [1- or 4-C(Ar)], 116.9 (3-C), 92.7 (C≡C), 88.3 (C≡C), 81.8 (17-CHOH), 51.4, 48.2, 42.9 (quat.), 36.5, 34.6 (quat.), 33.5, 31.8, 31.7, 30.5, 26.8, 23.3, 20.6, 19.1, 11.0; HRMS (MALDI-TOF) calcd for $C_{27}H_{32}BrO$ $[M+H]^+$ 451.1637; found 451.1676.

3-{[2-(methoxycarbonyl)phenyl]ethynyl}androsta-3,5-dien-17β-ol (7c). Prepared from **5** (59.7 mg, 0.15 mmol) and methyl 2-ethynylbenzoate (28.8 mg, 0.18 mmol); heating 24 h; eluent: CH_2Cl_2–MeOH = 50 : 1. Yield 53.6 mg (83 %). White solid; mp 149–151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 [d, J = 7.8 Hz, 1H, 3-CH(Ar)], 7.52 [d, J = 7.6 Hz, 1H, 6-CH(Ar)], 7.46–7.38 [m, 1H, 4- or 5-CH(Ar)], 7.34–7.28 [m, 1H, 4- or 5-CH(Ar)], 6.41 (s, 1H, 4-CH), 5.55 (m, 1H, 6-CH), 3.92 (s, 3H, CH_3O), 3.65 (t, J = 8.4 Hz, 1H, 17-CHOH), 2.49–2.17 (m, 3H), 2.06 (m, 1H), 1.90–1.81 (m, 2H), 1.76–0.95 (m, 12H), 0.98 (s, 3H, 19-CH_3), 0.77 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 166.8 (CO_2Me), 141.5 (5-C), 136.2, 133.8, 131.53, 131.46 [2-C(Ar)], 130.4, 127.3, 126.5, 124.2 [1-C(Ar)], 117.4 (3-C), 96.7 (C≡C), 88.3 (C≡C), 81.8 (17-CHOH), 52.0 (CH_3O), 51.5, 48.2, 42.9 (quat.), 36.5, 34.6 (quat.), 33.6, 31.8, 31.7, 30.5, 26.8, 23.3, 20.6, 19.1, 11.0; HRMS (MALDI-TOF) calcd for $C_{29}H_{35}O_3$ $[M+H]^+$ 431.2586; found 431.2593.

3-(hex-1-yn-1-yl)androsta-3,5-dien-17β-ol (7d). Prepared from **5** (59.7 mg, 0.15 mmol) and hex-1-yne (20.7 μL, 0.18 mmol); heating 17 h; eluent: CH_2Cl_2–MeOH = 100 : 1. Yield 50.1 mg (95 %). Light-yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.16 (c, 1H, 4-CH), 5.42 (m, 1H, 6-CH), 3.63 (t, J = 8.5 Hz, 1H, 17-CHOH), 2.31 (t, J = 6.9 Hz, 2H, CH_2Pr), 2.28–2.00 (m, 4H), 1.86–1.75 (m, 2H), 1.72–0.94 (m, 16H), 0.93 (s, 3H, 19-CH_3), 0.90 (t, J = 7.1 Hz, 3H, CH_2CH_3), 0.76 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.4 (5-C), 133.9 (4-CH), 124.6 (6-CH), 117.9 (3-C), 90.1 (C≡C), 82.4 (C≡C), 81.8 (17-CHOH), 51.5, 48.2, 42.9 (quat.), 36.5, 34.6 (quat.), 33.7, 31.8, 31.5, 31.0, 30.5, 27.4, 23.3, 21.9, 20.6, 19.2, 19.0, 13.6 (CH_2CH_3), 11.0; HRMS (MALDI-TOF) calcd for $C_{25}H_{36}O$ $[M]^+$ 352.2766; found 352.2760.

3-[3-(diethylamino)prop-1-yn-1-yl]androsta-3,5-dien-17β-ol (7e). Prepared from **5** (59.7 mg, 0.15 mmol) and

diethylpropargylamine (25.0 μL, 0.18 mmol); heating 24 h; eluent: CH_2Cl_2–MeOH = 20 : 1. Yield 55.7 mg (97 %). Light-yellow solid; mp 151–153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.21 (s, 1H, 4-CH), 5.45 (m, 1H, 6-CH), 3.63 (t, J = 8.5 Hz, 1H, 17-CHOH), 3.56 (s, 2H, CH_2NEt$_2$), 2.57 [q, J = 7.1 Hz, 4H, N(CH_2CH$_3$)$_2$], 2.35–2.12 (m, 3H), 2.05 (m, 1H), 1.87–1.76 (m, 2H), 1.73–1.54 (m, 4H), 1.50–0.91 (m, 8H), 1.08 [t, J = 7.1 Hz, 6H, N(CH$_2$CH_3)$_2$], 0.93 (s, 3H, 19-CH$_3$), 0.77 (s, 3H, 18-CH$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.3 (5-C), 134.7 (4-CH), 125.3 (6-CH), 117.2 (3-C), 87.1 (C≡C), 83.5 (C≡C), 81.7 (17-CHOH), 51.4, 48.2, 47.2 [2C, N(CH_2CH$_3$)$_2$], 42.8 (quat.), 41.4 (CH_2NEt$_2$), 36.5, 34.5 (quat.), 33.6, 31.7, 31.5, 30.5, 27.2, 23.3, 20.6, 19.0, 12.4 [2C, N(CH$_2$CH_3)$_2$], 11.0; HRMS (MALDI-TOF) calcd for $C_{26}H_{40}NO$ $[M+H]^+$ 382.3110; found 382.3104.

3-[3-(4-carboxyphenoxy)prop-1-yn-1-yl]androsta-3,5-dien-17β-ol (7f). Prepared from **5** (29.9 mg, 0.075 mmol) and 4-(prop-2-yn-1-yloxy)benzoic acid (15.9 mg, 0.090 mmol) in the presence of 3 equiv. K_2CO_3 (31.1 mg, 0.225 mmol); heating 66 h; eluent: CH_2Cl_2–MeOH = 10 : 1. Yield 26.4 mg (79 %). White solid; mp 205–208 °C; ^{1}H NMR (400 MHz, $CDCl_3$–CD_3OD) δ 8.03–7.97 [m, 2H, 3,5-CH(Ar)], 7.02–6.96 [m, 2H, 2,6-CH(Ar)], 6.26 (s, 1H, 4-CH), 5.49 (m, 1H, 6-CH), 4.87 (s, 2H, CH_2O), 3.64 (t, J = 8.6 Hz, 1H, 17-CHOH), 2.46 (br. s, 2H, OH), 2.33–1.94 (m, 4H), 1.86–1.75 (m, 2H), 1.72–0.93 (m, 11H), 0.91 (s, 3H, 19-CH$_3$), 0.75 (s, 3H, 18-CH$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$–CD_3OD) δ 168.7 (CO_2H), 161.6 [1-C(Ar)], 141.0 (5-C), 136.5 (4-CH), 131.8 [2C, 3,5-CH(Ar)], 126.7 (6-CH), 123.1 [4-C(Ar)], 116.0 (3-C), 114.5 [2C, 2,6-CH(Ar)], 89.7 (C≡C), 82.6 (C≡C), 81.5 (17-CHOH), 56.8 (CH_2O), 51.4, 48.1, 42.8 (quat.), 36.4, 34.5 (quat.), 33.4, 31.7, 31.5, 30.1, 26.6, 23.2, 20.5, 19.0, 11.0; HRMS (MALDI-TOF) calcd for $C_{29}H_{33}Na_2O_4$ $[M-H+2Na]^+$ 491.2180; found 491.2158.

3-(phenylethynyl)cholesta-3,5-diene (8a). Prepared from **6** (74.2 mg, 0.15 mmol) and phenylacetylene (19.8 μL, 0.18 mmol) without addition of TMEDA; heating 20 h; eluent: hexanes–EtOAc = 50 : 1. Yield 63.5 mg (90 %). Light-yellow solid; mp 147–148 °C (lit.,[34] 150–152 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.37 [m, 2H, 2,6-CH(Ph)], 7.31–7.21 [m, 3H, 3,4,5-CH(Ph)], 6.36 (s, 1H, 4-CH), 5.53 (m, 1H, 6-CH), 2.45–2.15 (m, 3H), 2.01 (m, 1H), 1.89–1.77 (m, 2H), 1.76–0.79 (m, 20H), 0.95 (s, 3H, 19-CH$_3$), 0.91 (d, J = 6.4 Hz, 3H, 21-CH$_3$), 0.854 (d, J = 6.6 Hz, 3H, 26- or 27-CH$_3$), 0.851 (d, J = 6.6 Hz, 3H, 26- or 27-CH$_3$), 0.69 (s, 3H, 18-CH$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.4 (5-C), 135.6 (4-CH), 131.4 [2C, 2,6-CH(Ph)], 128.2 [2C, 3,5-CH(Ph)], 127.7 [4-CH(Ph)], 126.6 (6-CH), 123.8 [1-C(Ph)], 117.1 (3-C), 91.7 (C≡C), 89.2 (C≡C), 56.8, 56.1, 48.1, 42.5 (quat.), 39.7, 39.5, 36.2, 35.8, 34.5 (quat.), 33.6, 32.1, 31.7, 28.2, 28.0, 27.0, 24.2, 23.8, 22.8, 22.6, 21.0, 19.1, 18.7, 12.0; HRMS (MALDI-TOF) calcd for $C_{35}H_{48}$ $[M]^+$ 468.3756; found 468.3769; Anal. calcd for $C_{35}H_{48}$: C, 89.68; H, 10.32; found C, 89.78; H, 10.16.

3-[(4-bromophenyl)ethynyl)]cholesta-3,5-diene (8b). Prepared from **6** (74.2 mg, 0.15 mmol) and (4-bromophenyl)acetylene (32.6 mg, 0.18 mmol); heating 24 h; eluent: hexanes–EtOAc = 50 : 1. Yield 71.5 mg (87 %). Light-yellow solid; mp 146–148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43–7.37 [m, 2H, CH(Ar)], 7.29–7.23 [m, 2H, CH(Ar)], 6.36 (s, 1H, 4-CH), 5.54 (m, 1H, 6-CH), 2.43–2.16 (m, 3H), 2.01 (m, 1H), 1.89–1.77 (m, 2H), 1.75–0.80 (m, 20H), 0.94 (s, 3H, 19-CH$_3$), 0.91 (d, J = 6.6 Hz, 3H, 21-CH$_3$), 0.854 (d, J = 6.6 Hz, 3H, 26- or 27-CH$_3$), 0.850 (d, J = 6.6 Hz, 3H, 26- or 27-CH$_3$), 0.69 (s, 3H, 18-CH$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.3 (5-C), 136.1 (4-CH), 132.8 [2C, CH(Ar)], 131.5 [2C, CH(Ar)], 127.0 (6-CH), 122.8 [1- or 4-C(Ar)], 121.8 [1- or 4-C(Ar)], 116.8 (3-C), 92.8 (C≡C), 88.1 (C≡C), 56.8, 56.1, 48.1, 42.4 (quat.), 39.7, 39.5, 36.2, 35.8, 34.5 (quat.), 33.5, 32.1, 31.7, 28.2, 28.0, 26.9, 24.2, 23.9, 22.8, 22.6, 21.0, 19.1, 18.7, 12.0; HRMS (MALDI-TOF) calcd for $C_{35}H_{48}Br$ $[M+H]^+$ 547.2939; found 547.2944; Anal. calcd for $C_{35}H_{47}Br$: C, 76.76; H, 8.65; found C, 76.38; H, 8.52.

3-{[4-(dimethylamino)phenyl]ethynyl}cholesta-3,5-diene (8c). Prepared from **6** (74.2 mg, 0.15 mmol) and [4-(dimethylamino)phenyl]acetylene (26.1 mg, 0.18 mmol); heating 21 h; eluent: hexanes–EtOAc = 4 : 1. Yield 67.0 mg (87 %). White solid; mp 217–220 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.27 [m, 2H, 2,6-CH(Ar)], 6.65–6.58 [m, 2H, 3,5-CH(Ar)], 6.29 (s, 1H, 4-CH), 5.48 (m, 1H, 6-CH), 2.95 [c, 6H, N(CH$_3$)$_2$], 2.43–2.14 (m, 3H), 2.01 (m, 1H), 1.87–1.77 (m, 2H), 1.75–0.77 (m, 20H), 0.95 (s, 3H, 19-CH$_3$), 0.91 (d, J = 6.5 Hz, 3H, 21-CH$_3$), 0.854 (d, J = 6.6 Hz, 3H, 26- or 27-CH$_3$), 0.850 (d, J = 6.6 Hz, 3H, 26- or 27-CH$_3$), 0.69 (s, 3H, 18-CH$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 149.7 [4-C(Ar)], 141.6 (5-C), 134.1 (4-CH), 132.5 [2C, 2,6-CH(Ar)], 125.4 (6-CH), 117.8 (3-C), 111.9 [2C, 3,5-CH(Ar)], 110.7 [1-C(Ar)], 90.3 (C≡C), 89.5 (C≡C), 56.9, 56.2, 48.1, 42.5 (quat.), 40.2 [2C, N(CH$_3$)$_2$], 39.8, 39.5, 36.2, 35.8, 34.6 (quat.), 33.7, 32.1, 31.8, 28.2, 28.0, 27.2, 24.2, 23.9, 22.8, 22.6, 21.0, 19.1, 18.7, 12.0; HRMS (MALDI-TOF) calcd for $C_{37}H_{53}N$ $[M]^+$ 511.4178; found 511.4117; Anal. calcd for $C_{37}H_{53}N$: C, 86.83; H, 10.44; N, 2.74; found C, 86.47; H, 10.35; N, 2.53.

3-[(2-aminophenyl)ethynyl)]cholesta-3,5-diene (8d). Prepared from **6** (74.2 mg, 0.15 mmol) and 2-ethynylaniline (20.5 μL, 0.18 mmol); heating 24 h; eluent: hexanes–EtOAc = 15 : 1. Yield 58.3 mg (80 %). White solid; mp 203–205 °C (lit.,[35] 207–209 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 [dd, J = 7.6, 1.5 Hz, 1H, 6-CH(Ar)], 7.25 [ddd, J = 8.2, 7.4, 1.5 Hz, 1H, 4-CH(Ar)], 6.72–6.64 [m, 2H, 3- and 5-CH(Ar)], 6.35 (m, 1H, 4-CH), 5.52 (m, 1H, 6-CH), 4.30 (br. s, 2H, NH_2), 2.46–2.15 (m, 3H), 2.01 (m, 1H), 1.88–1.77 (m, 2H), 1.75–0.81 (m, 20H), 0.95 (s, 3H, 19-CH$_3$), 0.91 (d, J = 6.5 Hz, 3H, 21-CH$_3$), 0.855 (d, J = 6.7 Hz, 3H, 26- or 27-CH$_3$), 0.851 (d, J = 6.7 Hz, 3H, 26- or 27-CH$_3$), 0.69 (s, 3H, 18-CH$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 146.9 [2-C(Ar)], 141.3 (5-C), 135.1 (4-CH), 131.8 [4- or 6-CH(Ar)], 129.1 [4- or 6-CH(Ar)], 126.4 (6-CH), 118.1 [3- or 5-CH(Ar)], 117.0 (3-C), 114.3 [3- or 5-CH(Ar)], 108.8 [1-C(Ar)], 97.0 (C≡C), 85.4 (C≡C), 56.8, 56.0, 48.0, 42.4 (quat.), 39.6, 39.4, 36.1, 35.7, 34.4 (quat.), 33.5, 32.0, 31.6, 28.1, 27.9, 27.1, 24.1, 23.8, 22.7, 22.5, 20.9, 19.0, 18.6, 11.9; HRMS (MALDI-TOF) calcd for $C_{35}H_{49}N$ $[M]^+$ 483.3865; found 483.3856.

3-(ferrocenylethynyl)cholesta-3,5-diene (8e). Prepared from **6** (74.2 mg, 0.15 mmol) and ethynylferrocene (37.8 mg, 0.18

mmol); heating 24 h; eluent: hexanes–EtOAc = 50 : 1. Yield 72.5 mg (84 %). Orange solid; mp 136–138 °C (lit.,[24a] 134–136 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (s, 1H, 4-CH), 5.49 (m, 1H, 6-CH), 4.41–4.37 (m, 2H, C_5H_4), 4.22–4.14 (m, 7H, 5H C_5H_5 + 2H C_5H_4), 2.42–2.12 (m, 3H), 2.01 (m, 1H), 1.88–1.76 (m, 2H), 1.73–0.78 (m, 20H), 0.95 (s, 3H, 19-CH_3), 0.91 (d, J = 6.4 Hz, 3H, 21-CH_3), 0.854 (d, J = 6.6 Hz, 3H, 26- or 27-CH_3), 0.850 (d, J = 6.6 Hz, 3H, 26- or 27-CH_3), 0.69 (s, 3H, 18-CH_3); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 141.5 (5-C), 134.5 (4-CH), 125.7 (6-CH), 117.7 (3-C), 87.9 (C≡C), 87.7 (C≡C), 71.22 (1C, C_5H_4), 71.20 (1C, C_5H_4), 69.9 (5C, C_5H_5), 68.5 (2C, C_5H_4), 66.0 (quat., C_5H_4), 56.9, 56.2, 48.2, 42.5 (quat.), 39.8, 39.5, 36.2, 35.8, 34.5 (quat.), 33.7, 32.1, 31.8, 28.2, 28.0, 27.2, 24.2, 23.9, 22.8, 22.6, 21.0, 19.1, 18.7, 12.0; HRMS (MALDI-TOF) calcd for $C_{39}H_{52}Fe$ $[M]^+$ 576.3418; found 576.3407; Anal. calcd for $C_{39}H_{52}Fe$: C, 81.23; H, 9.09; found C, 81.58; H, 9.17.

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Notes and references

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† Electronic Supplementary Information (ESI) available: [copies of the ^{1}H and ^{13}C NMR spectra for compounds **2a-d**, **2g-m**, **2o**, **2p**, **4a-d**, **7a-f**, and **8a-e**]. See DOI: 10.1039/b000000x/

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