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SYNTHESIS OF CYCLOALKYL/STEROIDAL HETEROARYL SULFIDES USING RHODIUM-CATALYZED HETEROARYL EXCHANGE REACTION

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Abstract – Cycloalkyl heteroaryl sulfides are efficiently synthesized by the single-bond cleavage and exchange reaction of *S*-cycloalkyl thioesters and heteroaryl ethers without using a base. The method is applicable to steroids at the A- and D-rings, and provides diverse heteroarylthiolated steroids with five- and six-membered heteroarenes.

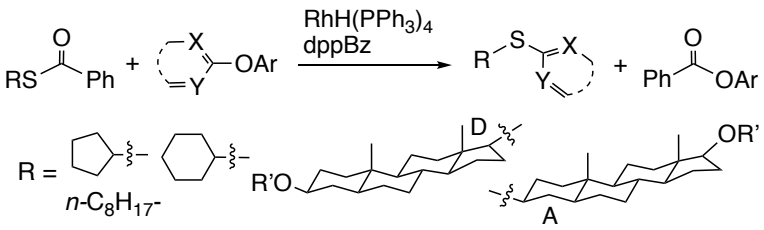
INTRODUCTION

Unsymmetrical diheteroaryl HetAr–X–HetAr' compounds, in which two different heteroarenes are linked by one heteroatom linker X, are expected to exhibit diverse biological activities.[1] These compounds possess rigid heteroarenes with various heteroatoms and flexible linker C–X bonds, which can assume various conformations. Consequently, diverse shapes can be formed from a single compound, which can flexibly fit to biomacromolecular surfaces such as proteins and nucleic acids. Synthesis of unsymmetrical HetAr–X–HetAr' compounds, however, are quite limited. We have developed an efficient method to synthesize unsymmetric HetAr–X–HetAr' compounds (X = O, S, CH_2) using transition-metal-catalyzed heteroaryl exchange reactions.[2] This method has the advantages of 1) involvement of cleavage and exchange of covalent bonds between two organoheteroaryl compounds, which are stable and readily available, 2) its employment under equilibrium condition of the exchange reactions, whose reaction rate and yield can be controlled by reaction conditions and substrate/product structures, 3) broad substrate applicabilities, because the reactivity is relatively insensitive to the structures of heteroarenes, 4) producing various new compounds, and 5) not using metal reagents and metal bases, which avoids the formation of inorganic byproducts as waste materials that are difficult to recycle. Using this method, we

previously synthesized HetAr–S–HetAr' compounds,[2a] and in this paper, we describe the extension of this method to the synthesis of cycloalkyl heteroaryl sulfides, in which one of the heteroarenes in HetAr–S–HetAr' is substituted by a cycloalkane with special emphasis on steroids. It is expected that such steroidal–S–HetAr compounds will exhibit interesting biological activities by taking advantage of the strong biological activities of steroid derivatives.

Synthesis of cycloalkyl heteroaryl sulfides by alkylation of heteroaryl thiolates has been rare,[3] which may be due to enhanced steric hindrances and competitive elimination reactions. Such compounds have been synthesized by the copper-catalyzed coupling reaction of cyclohexylthiol and 2- or 3-pyridyl halides in the presence of a base.[4] The heteroaryl substrate, however, has been limited to 2- or 3-pyridyl halides, and only two examples of the successful synthesis have been shown. Several other methods not using halides were reported. The palladium-catalyzed cross-coupling reaction of methylthioheteroarenes and cycloalkyl thiols (2 equiv.) in the presence of lithium bis(trimethylsilyl)amide (3.6 equiv.) showed a broader applicability yielding benzothiazolyl-, pyridyl-, and pyrazyl-cycloalkyl sulfides.[5] The palladium-catalyzed decarboxylative coupling of 2-pyridylcarboxylic acid and cyclohexane thiol in the presence of $CuCO_3/Cu(OH)_2$ (1.5 equiv.) and KF (3.0 equiv.) was also reported.[6] The use of a stoichiometric amount of a base, however, is essential for these methods to form reactive thiolates. An interesting radical approach to thiolation was reported; it employed excess cycloalkanes and 2-benzothiazolyl-, 2-pyridyl-, 2-thienyl-, and *N*-phenyltetrazolyl disulfides in the presence of di-*t*-butyl peroxide (DTBT).[7] However, this method is limited to the reactions of simple cycloalkane such as cyclopentane, cyclohexane, and cyclooctane.

Described here is the efficient synthesis of cycloalkyl heteroaryl sulfides by the single-bond cleavage and exchange reaction of *S*-cycloalkyl thioesters and heteroaryl ethers without using a base. It is emphasized that the method is applicable to the reaction of steroids at A- and D-rings, and provides heteroarylthiolated steroids. The introduction of a heteroarylthio group to steroid A- or D-rings has not been reported (Scheme 1).

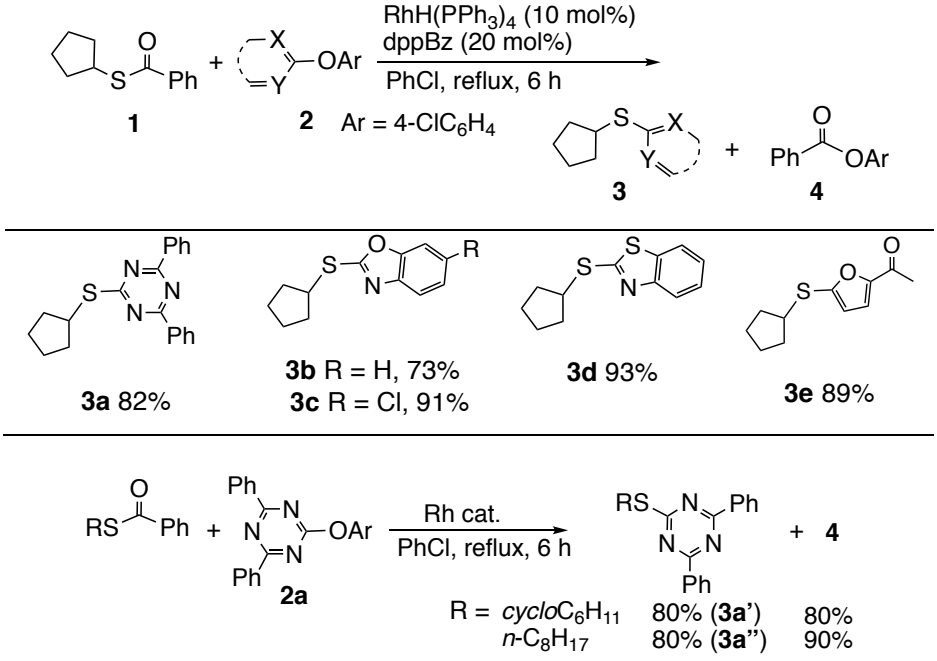


Scheme 1. Synthesis of cycloalkyl/steroidal heteroaryl sulfides

RESULTS AND DISCUSSION

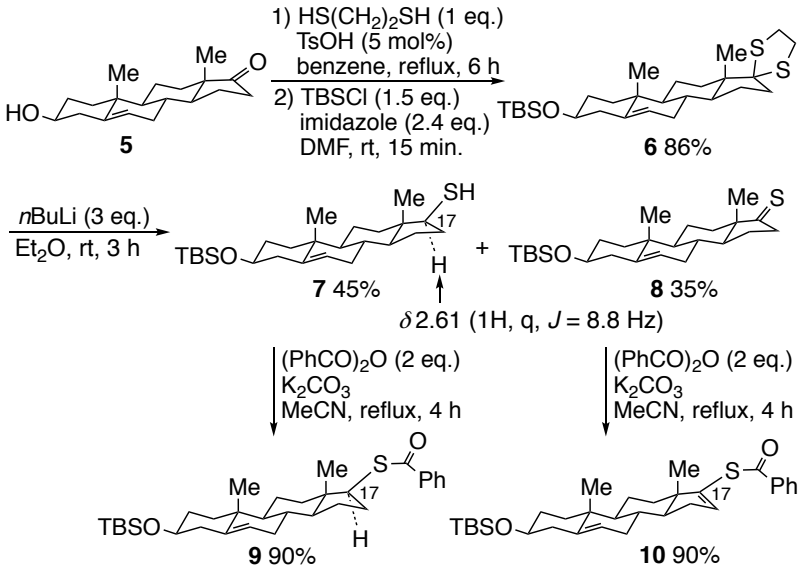
The study was initiated with the examination of rhodium-catalyzed heteroaryl exchange reactions of

S-cyclopentyl benzenethiocarboxylate and heteroaryl aryl ethers (Scheme 2). When **1** was reacted with 4,6-diphenyl-2-(4-chlorophenoxy)triazine **2a** in the presence of $RhH(PPh_3)_4$ (10 mol%) and dppBz [20 mol%, dppBz = 1,2-bis(diphenylphosphino)benzene] in refluxing chlorobenzene for 6 h, 2-cyclopentylthio-4,6-diphenyltriazine **3a** and 4-chlorophenyl benzoate **4** were obtained in 82% and 99% yields, respectively. The heteroaryl 4-chlorophenyl ethers containing 6-chloro-2-benzoxazolyl, 2-benzoxazolyl, 2-benzothiazolyl, and 5-acetyl-2-furyl groups were reacted with **1**, and the corresponding cyclopentyl heteroaryl sulfides **3b**–**3e** were obtained in high yields. The reaction of *S*-cyclohexyl and *S*-octyl benzenethiocarboxylates with **2a** also gave the corresponding sulfides **3a'** and **3a''**. The rhodium-catalyzed heteroarylthiolation of *S*–cycloalkyl/*S*–alkylbenzenethiocarboxylates proceeds effectively without the reactivity being significantly affected by the structure of the heteroarenes. Note that no base is employed here.



Scheme 2. Rhodium-catalyzed heteroarylthiolation of *S*–cycloalkyl/*S*–alkylbenzenethiocarboxylates

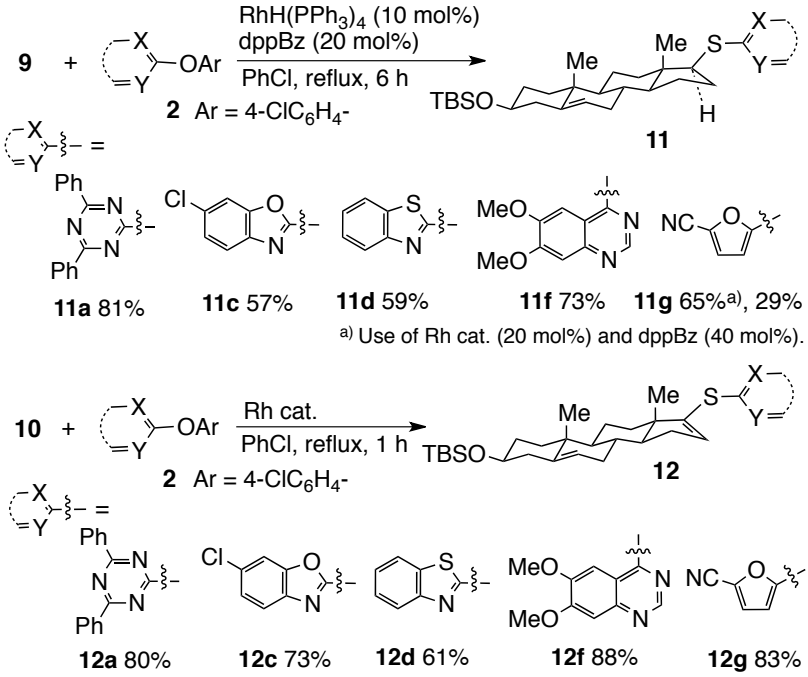
The heteroarylthiolation of steroids was examined in the presence of the rhodium catalyst, employing benzoylthiolated steroids as the substrate. Benzoylthiolated 17β-steroids **9** and **10** were synthesized in accordance with the method of Wilson (Scheme 3).[8] Thioketal **6** derived from dehydroepiandrosterone was reduced using butyllithium to give thiol **7** and thione **8** in 45% and 35% yields, respectively. The use of butyllithium (4 equiv.) increased the yield of **7** to 80%, which was accompanied by **8** (10%). ^{1}H-NMR analysis of **7** showed the proton peak at C17 at δ 2.61 (1H, q, J = 8.8 Hz), which indicated the 17α-H configuration according to the literature.[9] Thioester **9** was obtained by benzoylation of **7**, and unsaturated thioester **10** was obtained from **8**.



Scheme 3. Synthesis of benzoylthiolated 17β-steroids **9** and **10**

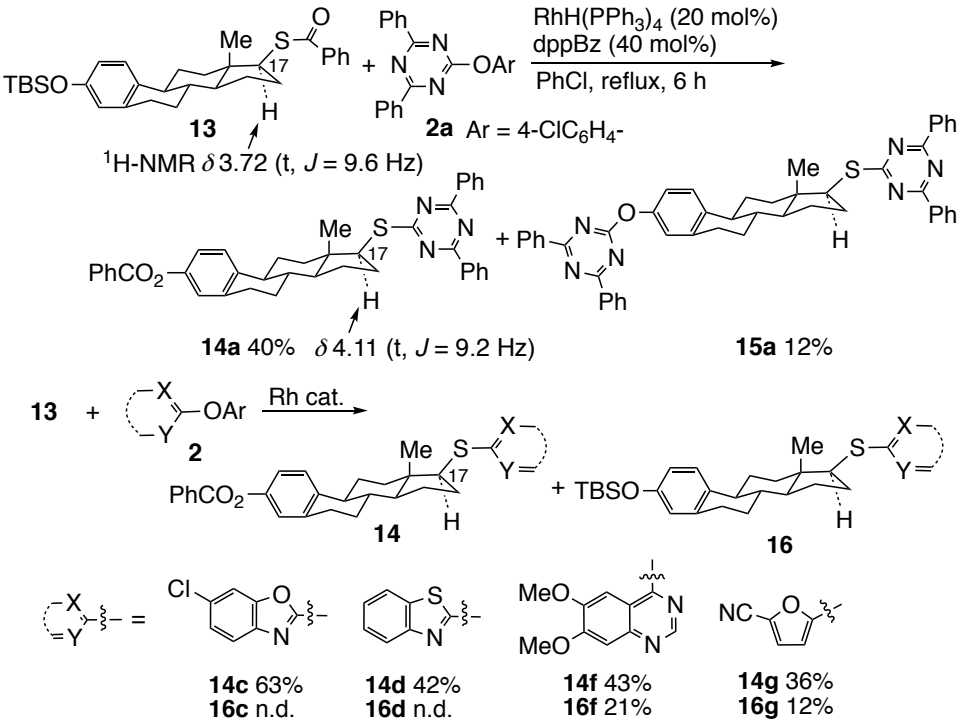
When **9** was reacted with **2a** (1 equiv.) in the presence of $RhH(PPh_3)_4$ (10 mol%) and dppBz (20 mol%) in refluxing chlorobenzene for 6 h, the 17β-(4,6-diphenyl-2-triazyl)-thiolated product **11a** was obtained in 81% yield (Scheme 4). Steroid **9** was also reacted with five- and six-membered heteroaryl ethers such as 6,7-dimethoxy-2-qinazolyl, 6-chloro-2-benzoxazolyl, 2-benzothiazolyl, and 5-cyano-2-furyl ethers to form the corresponding sulfides **11b**, **11d**, **11f**, and **11g**, respectively.

Using the same rhodium-catalyzed method, heteroarylthiolation of enol thioester **10** gave heteroaryl sulfides **12a**, **12c**, **12d**, **12f**, and **12g**. It was noted that **10** reacted faster than **9**, with the reaction of **10** completed within 1 h.



Scheme 4. Rhodium-catalyzed heteroarylthiolation of benzoylthiolated 17β-steroids **9** and **10**

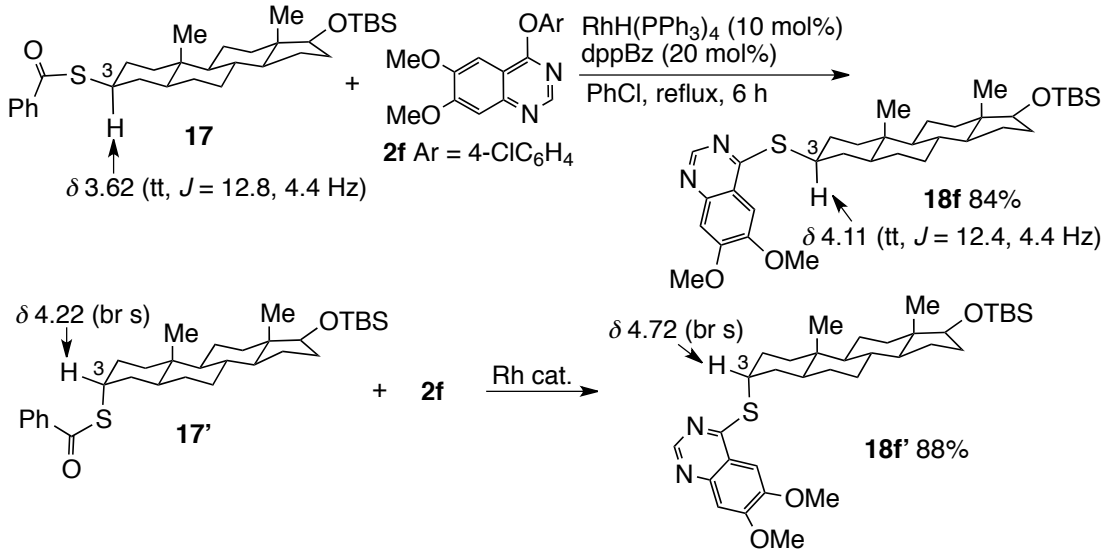
17β-(Benzoylthio)-3-(*tert*-butyldimethylsilyloxy)estra-1,3,5(10)-triene **13** containing an aromatic A-ring was heteroarylthiolated by the rhodium-catalyzed heteroaryl exchange reaction at the 17-position (Scheme 5). When **13** was reacted with **2a** (1 equiv.) in the presence of $RhH(PPh_3)_4$ (20 mol%) and dppBz (40 mol%) in refluxing chlorobenzene for 6 h, 17β-(4,6-diphenyl-2-triazylthio)estra-1,3,5(10)-trien-3-ol benzoate **14a** (40%) was obtained. Notably, no heteroarylated TBS ether was detected, and the TBS group was replaced by benzoyl group, which was derived from **13**, along with the formation of 1-*tert*-butyldimethylsilyloxy-4-chlorobenzene (80%). The 17β-stereochemistry of **14a** was determined by the coupling constant J = 9.2 Hz of the proton at C17. The coupling constant of 17α-H of the estrone derivatives is generally about 9 Hz.[10] In addition to **14a**, compound **15a** with a 4,6-diphenyl-2-triazylthio group at both the D-ring and the A-ring was obtained in 12% yield. The reactions of 4-(4-chlorophenoxy)-6,7-dimethoxyquinazoline **2f** and 5-(4-chlorophenoxy)-2-furancarbonitrile **2g** with **13** gave heteroarylthiolated **14f** (43%) and **14g** (36%), respectively. In these cases, the products **16f** (21%) and **16g** (12%) which retained the TBSO group were formed in small amounts. The steroidal heteroaryl sulfides with five-/six-membered heteroaryl group were successfully.



Scheme 5. Rhodium-catalyzed synthesis of steroidal heteroaryl sulfides

The heteroarylthiolation of the A-ring at the 3-position in andorostane derivatives was examined (Scheme 6). The reaction of 3β-benzoylthio-17β-silyloxy-5α-androstane **17** with **2f** provided **18f**, which contains the 3β-[2-(6,7-dimethoxyquinazolyl)thio] group at the equatorial position, in 80% yield. The 3β-configuration of **18f** was determined by the ^{1}H-NMR coupling constant of the proton at C3-position (δ

4.11, tt, J = 12.4, 4.4 Hz). The reaction of the 3α-thioester derivative **17'** with **2f** gave the 3α-[2-(6,7-dimethoxyquinazolyl)thio] product **18f'** with the axial configuration. The 3α-configuration of **18f'** was determined from the ^{1}H-NMR of the proton at C-3 at δ 4.72, appearing as a broad singlet. The stereochemistry of steroid 3-thioester was retained during rhodium-catalyzed heteroarylthiolation.



Scheme 6. Rhodium-ctalyzed heteroarylthiolation of the A-ring in andorostane derivatives

In summary, cycloalkyl heteroaryl sulfides were synthesized by a rhodium-catalyzed heteroaryl exchange reaction of *S*-cycloalkyl thioesters and heteroaryl ethers. This method can introduce various five-/six-membered heteroarenes into cycloalkanes and also into the A- and D-rings of steroids. Studies of the biological activity of heteroarylthiolated steroids are underway.

EXPERIMENTAL

^{1}H- and ^{13}C-NMR spectra were recorded on a Varian Mercury (400 MHz) and tetramethylsilane were used as standard. IR spectra were measured on a JASCO FT/IR-410 spectrophotomer. Melting points were determined with a Yanagimoto micro melting point apparatus without correction. High- and low-resolution mass spectra were measured on a JEOL JMS-DX-303, a JEOL JMS-700, or a JMS-T100GC spectrometer. Kanto Chemical. Co. Inc. silica gel 60 (63-210 μm) was employed for flash column chromatography.

Typical procedures for synthesis of the 2-(6-chlorobenzoxazolyl) cyclopentyl sulfide (3c)

In a two-necked flask were placed $RhH(PPh_3)_4$ (28.8 mg, 10 mol%), 1,2-bis(diphenylphosphino)benzene (dppBz, 22.3 mg, 20 mol%), benzenecarbothioic acid *S*-cyclopentyl ester (0.25 mmol, 51.5 mg), and 6-chloro-2-(4-chlorophenoxy)benzoxazole **2c** (0.25 mmol, 69.8 mg) in chlorobenzene (1 mL) under an argon atomosphere, and the mixture was heated at reflux for 6 h. The solvent was removed under reduced

pressure, and the residue was purified by flash column chromatography on silica gel giving 2-(6-chlorobenzoxazolyl) cyclopentyl sulfide **3c** (57.7 mg, 91%). **3c**: Colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.68-1.83 (6H, m), 2.27-2.33 (2H, m), 4.10 (1H, quintet, J = 6.4 Hz), 7.25 (1H, dd, J = 8.4, 1.6 Hz), 7.44 (1H, d, J = 1.6 Hz), 7.49 (1H, d, J = 8.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 24.7, 33.7, 45.4, 110.5, 118.7, 124.7, 129.3, 140.9, 151.7, 166.1. IR (neat) 2961, 2869, 1498, 1461, 1257, 1214, 1134, 915 cm^{-1}. MS (EI) *m/z* 253 (M^+, 16%), 185 (M^+-68, 100%). HRMS Calcd for $C_{12}H_{12}ClNOS$: 253.0318. Found: 253.0354.

2-(4,6-Diphenyl-1,3,5-triazyl) cyclopentyl sulfide (3a)

Colorless solid. Mp 98.0-99.0 °C (Hexane:EtOAc = 4:1). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.72-1.86 (6H, m), 2.32-2.39 (2H, m), 4.26 (1H, quintet, J = 6.0 Hz), 7.53 (1H, td, J = 8.8, 1.6 Hz), 7.58 (2H, t, J = 7.2 Hz), 8.61 (4H, dd, J = 7.2, 1.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.0, 33.2, 43.5, 128.6, 128.9, 132.5, 135.7, 169.9, 183.4. IR (KBr) 2961, 2869, 1498, 1461, 1257, 1214, 1134, 915 cm^{-1}. MS (EI) *m/z* 333 (M^+, 34%), 300 (M^+-33, 100%). HRMS Calcd for $C_{20}H_{19}N_3S$: 333.1300. Found: 333.1302.

2-Benzoxazolyl cyclopentyl sulfide (3b)

Colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.67-1.82 (6H, m), 2.23-2.31 (2H, m), 4.11 (1H, quintet, J = 7.6 Hz), 7.21 (1H, td, J = 7.6, 1.6 Hz), 7.26 (1H, td, J = 7.6, 1.6 Hz), 7.41 (1H, dd, J = 7.6, 0.8 Hz), 7.59 (1H, dd, J = 7.2, 1.2 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 24.7, 33.7, 45.3, 109.8, 118.4, 123.7, 124.2, 142.0, 151.6, 165.3. IR (neat) 2960, 2870, 1498, 1454, 1128, 1095, 742 cm^{-1}. MS (EI) *m/z* 219 (M^+, 16%), 151 (M^+-68, 100%). HRMS Calcd for $C_{12}H_{13}NOS$: 219.0717. Found: 219.0719.

2-Benzothiazolyl cyclopentyl sulfide (3d)

Colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.67-1.82 (6H, m), 2.26-2.30 (2H, m), 4.12 (1H, quintet, J = 7.6 Hz), 7.28 (1H, td, J = 8.0, 1.2 Hz), 7.41 (1H, td, J = 8.0, 1.2 Hz), 7.75 (1H, dd, J = 8.0, 0.8 Hz), 7.87 (1H, d, J = 8.0 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 24.8, 33.7, 46.6, 120.8, 121.5, 124.1, 125.9, 135.2, 153.4, 167.5. IR (neat) 3060, 2958, 2867, 1456, 992 cm^{-1}. MS (EI) *m/z* 235 (M^+, 21%), 180 (M^+-68, 100%). HRMS Calcd for $C_{12}H_{13}NS_2$: 235.0489. Found: 235.0506.

2-(5-Acetylthienyl) cyclopentyl sulfide (3e)

Yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.61-1.68 (4H, m), 1.75-1.79 (2H, m), 2.02-2.06 (2H, m), 2.46 (3H, s), 3.64 (1H, quintet, J = 6.4 Hz), 6.49 (1H, d, J = 3.6 Hz), 7.15 (1H, d, J = 3.2 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 24.6, 25.8, 33.6, 47.3, 116.1, 118.5, 153.4, 154.2, 185.9. IR (neat) 2959, 2868, 1681, 1565, 1454, 1291, 1025 cm^{-1}. MS (EI) *m/z* 210 (M^+, 22%), 142 (M^+-68, 100%). HRMS Calcd for $C_{11}H_{14}O_2S$: 210.0714. Found: 210.0740.

2-(4,6-Diphenyl-1,3,5-triazyl) cyclohexyl sulfide (3a')

Colorless solid. Mp 119.0-120.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.38-1.44 (1H, m), 1.52-1.72 (5H, m), 1.84-1.88 (2H, m), 2.21-2.26 (2H, m), 4.06 (1H, quintet, J = 6.8 Hz), 7.53 (4H, td, J =

7.2, 1.6 Hz), 7.59 (2H, t, J = 6.8 Hz), 8.61 (4H, dd, J = 6.8, 1.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 25.7, 26.0, 32.7, 43.6, 128.6, 128.9, 132.5, 135.7, 170.0, 182.8. IR (KBr) 2928, 2852, 1507, 1362, 1250 cm^{-1}. MS (EI) *m/z* 347 (M^+, 73%), 104 (M^+-243, 100%). HRMS Calcd for $C_{21}H_{21}N_3S$: 347.1456. Found: 347.1432.

2-(4,6-Diphenyl-1,3,5-triazyl) octyl sulfide (3a")

Colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.88 (3H, t, J = 6.4 Hz), 1.30-1.40 (8H, m), 1.53 (2H, quintet, J = 7.2 Hz), 1.86 (2H, quintet, J = 7.2 Hz), 3.32 (2H, t, J = 7.2 Hz), 7.53 (4H, td, J = 7.6, 1.6 Hz), 7.61 (2H, td, J = 7.2, 1.6 Hz), 8.62 (4H, dd, J = 7.2, 1.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.1, 22.6, 29.0, 29.21, 29.22, 30.5, 31.8, 128.5, 128.9, 132.6, 135.6, 170.0, 182.9. IR (KBr) 3064, 2925, 1508, 1362, 1252 cm^{-1}. MS (EI) *m/z* 377 (M^+, 21%), 265 (M^+-112, 100%). HRMS Calcd for $C_{23}H_{27}N_3S$: 377.1926. Found: 377.1920. One carbon peak of aliphatic region was piled up in ^{13}C-NMR.

Typical procedures for synthesis of the (3ß,17ß)-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-17-[2-(4,6-diphenyl-1,3,5-triazyl)thio]androst-5-ene (11a)

In a two-necked flask were placed $RhH(PPh_3)_4$ (14.4 mg, 10 mol%), 1,2-bis(diphenylphosphino)benzene (dppBz, 11.1 mg, 20 mol%), (3ß,17ß)-17-(benzoylthio)-3-[[(1,1-dimethyl)dimethylsilyl]oxy]androst-5-ene **9** (0.125 mmol, 65.5 mg) and 4,6-diphenyl-2-(4-chlorophenoxy)triazine **2a** (0.125 mmol, 44.9 mg) in chlorobenzene (0.5 mL) under an argon atomosphere, and the mixture was heated at reflux for 6 h. The solvent was removed under reduced pressure, and the residue was purified by flash column chromatography on silica gel giving (3ß,17ß)-3-[[(1,1-dimethyl)dimethylsilyl]oxy]-17-[2-(4,6-diphenyltriazyl)thio]androst-5-ene **11a** (66.1 mg, 81%) and **4** (23.2 mg, 80%). **11a**: Colorless solid. Mp 196.0-196.5 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.07 (6H, s), 0.90 (12H, s), 1.03 (3H, s), 1.06-1.11 (1H, m), 1.25-1.43 (4H, m), 1.48-1.66 (4H, m), 1.71 (2H, t, J = 13.2 Hz), 1.78-1.96 (4H, m), 2.07 (1H, dd, J = 17.2, 2.0 Hz), 2.20 (1H, dd, J = 13.2, 3.2 Hz), 2.29 (1H, t, J = 11.2 Hz), 2.54-2.64 (1H, m), 3.50 (1H, septet, J = 4.8 Hz), 4.00 (1H, t, J = 9.2 Hz), 5.36 (1H, d, J = 4.8 Hz), 7.53 (4H, t, J = 7.2 Hz), 7.58 (2H, d, J = 7.2 Hz), 8.61 (4H, d, J = 7.2 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.6, 13.9, 18.3, 19.4, 20.7, 24.8, 25.9, 30.1, 31.8, 32.0, 32.4, 36.7, 36.9, 37.4, 42.8, 43.7, 50.2, 53.6, 54.6, 72.5, 120.8, 128.6, 128.9, 132.5, 135.7, 141.7, 169.9, 183.5. IR (KBr) 2928, 2854, 1504, 1362, 1253, 1083 cm^{-1}. MS (EI) *m/z* 651 (M^+, 26%), 594 (M^+-57, 100%). HRMS Calcd. for $C_{40}H_{53}N_3OSSi$: 651.3679. Found: 651.3668.

(3ß,17ß)-17-[2-(6-Chlorobenzoxazolyl)thio]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]androst-5-ene (11c)

Colorless solid. Mp 142.5-143.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.84 (3H, s), 0.89 (9H, s), 0.98-1.01 (1H, m), 1.01 (3H, s), 1.01-1.10 (1H, m), 1.17-1.40 (3H, m), 1.45-1.62 (5H, m), 1.73 (1H, bd, J = 12.8 Hz), 1.76-1.86 (4H, m), 2.01-2.06 (1H, m), 2.18 (1H, bddd, J = 13.2, 4.8, 2.0 Hz), 2.28 (1H, td, J = 11.2, 2.0 Hz), 2.50-2.59 (1H, m), 3.49 (1H, septet, J = 4.8 Hz), 3.74 (1H, t, J = 9.2 Hz),

5.33 (1H, d, J = 4.8 Hz), 7.24 (1H, dd, J = 8.4, 1.6 Hz), 7.43 (1H, d, J = 1.6 Hz), 7.74 (1H, d, J = 7.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.6, 13.5, 18.3, 19.4, 20.7, 24.6, 25.9, 30.5, 31.7, 32.0, 32.4, 36.6, 37.3, 42.7, 43.8, 50.1, 54.1, 56.3, 72.5, 110.4, 118.6, 120.7, 124.7, 129.3, 140.8, 141.7, 151.8, 166.5. IR (KBr) 2930, 2854, 1498, 1461, 1256, 1094, 836 cm^{-1}. MS (EI) *m/z* 571 (M^+, 10%), 514 (M^+-57, 100%). HRMS Calcd. for $C_{32}H_{47}NOS_2Si$: 571.2707. Found: 571.2708. One carbon peak of aliphatic region was piled up in ^{13}C-NMR.

(3ß,17ß)-17-(2-Benzothiazolylthio)-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]androst-5-ene (11d)

Colorless solid. Mp 112.5-113.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.85 (3H, s), 0.89 (9H, s), 1.01 (3H, s), 0.95-1.09 (1H, m), 1.20-1.38 (4H, m), 1.45-1.61 (6H, m), 2.02-2.05 (1H, m), 2.16-2.21 (1H, m), 2.25 (1H, t, J = 11.2 Hz), 2.50-2.60 (1H, m), 3.49 (1H, septet, J = 6.4 Hz), 3.80 (1H, t, J = 9.2 Hz), 5.33 (1H, bd, J = 5.2 Hz), 7.28 (1H, td, J = 7.2, 0.8 Hz), 7.40 (1H, td, J = 8.0, 0.8 Hz), 7.74 (1H, d, J = 8.4 Hz), 7.40 (1H, td, J = 8.0, 0.8 Hz), 7.74 (1H, d, J = 8.4 Hz), 7.84 (1H, d, J = 8.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.6, 13.5, 18.3, 19.4, 20.7, 24.7, 25.9, 30.5, 31.7, 32.0, 32.4, 36.7, 36.9, 37.4, 42.7, 44.1, 50.1, 54.2, 57.5, 72.5, 120.7, 120.8, 121.4, 124.1, 125.9, 135.3, 141.7, 153.3, 167.7. IR (KBr) 2940, 2854, 1459, 1428, 1255, 1086 cm^{-1}. MS (EI) *m/z* 553 (M^+, 20%), 496 (M^+-57, 100%). HRMS Calcd. for $C_{32}H_{47}NOS_2Si$: 553.2868. Found: 553.2860.

(3ß,17ß)-17-[4-(6,7-Dimethoxyquinazolyl)thio]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]androst-5-ene (11f)

Colorless solid. Mp 183.0-184.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.07 (6H, s), 0.90 (9H, s), 0.92 (3H, s), 1.03 (3H, s), 0.99-1.11 (1H, m), 1.25-1.38 (3H, m), 1.41-1.66 (6H, m), 1.72-1.77 (1H, m), 1.80-1.84 (2H, m), 2.03-2.09 (1H, m), 2.19 (1H, ddd, J = 12.4, 5.2, 2.0 Hz), 2.26 (1H, td, J = 11.2, 2.0 Hz), 2.50-2.56 (1H, m), 3.50 (1H, septet, J = 5.2 Hz), 4.04 (3H, s), 4.05 (3H, s), 4.16 (1H, t, J = 9.6 Hz), 5.34-5.36 (1H, m), 7.26 (1H, s), 7.27 (1H, s), 8.81 (1H, s). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.6, 14.2, 18.2, 19.5, 20.7, 24.7, 25.9, 30.2, 31.7, 32.0, 32.4, 36.66, 36.69, 37.4, 42.8, 43.5, 50.2, 52.8, 54.3, 56.27, 56.33, 72.5, 101.8, 106.9, 119.3, 120.8, 141.6, 145.3, 149.8, 152.3, 155.3, 168.5. IR (KBr) 2930, 2853, 1506, 1344, 1252, 1100, 835 cm^{-1}. MS (EI) *m/z* 608 (M^+, 100%), 222 (M^+-386, 90%). HRMS Calcd. for $C_{35}H_{52}N_2O_3SSi$: 608.3468. Found: 608.3470.

(3ß,17ß)-17-[5-(2-Cyanofuranyl)thio]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]androst-5-ene (11g)

Colorless solid. Mp 96.0-97.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.07 (6H, s), 0.80 (3H, s), 0.88 (9H, s), 1.00 (3H, s), 1.00-1.18 (2H, m), 1.23-1.30 (2H, m), 1.41 (1H, dd, J = 13.2, 4.0 Hz), 1.49-1.62 (5H, m), 1.64-1.74 (4H, m), 1.80 (1H, dd, J = 13.2, 3.2 Hz), 1.96-2.03 (1H, m), 2.16 (2H, dd, J = 14.8, 4.8 Hz), 2.26 (1H, bt, J = 13.2 Hz), 3.14 (1H, t, J = 9.2 Hz), 3.47 (1H, septet, J = 4.8 Hz), 5.31 (1H, dd, J = 5.2, 2.0 Hz), 6.44 (1H, d, J = 3.6 Hz), 7.03 (1H, d, J = 3.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.6, 13.0, 18.3, 19.4, 20.7, 24.4, 25.9, 30.0, 31.7, 32.0, 32.4, 36.6, 36.8, 37.3, 42.7, 44.0, 50.0, 54.3,

58.5, 72.5, 111.4, 114.6, 120.7, 123.5, 127.0, 141.6, 154.4. IR (KBr) 2959, 2941, 2856, 2228, 1463, 1259, 1085 cm^{-1}. MS (EI) *m/z* 511 (M^+, 2%), 454 (M^+-57, 100%). HRMS Calcd. for $C_{30}H_{45}NO_2SSi$: 511.2940. Found: 511.2917.

(3ß)-3-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-17-[2-(4,6-diphenyl-1,3,5-triazyl)thio]androsta-5,16-diene (12a)

Colorless solid. Mp 158.5-159.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.89 (9H, s), 0.95 (3H, s), 1.04 (3H, s), 1.46-1.62 (6H, m), 1.65-1.82 (6H, m), 2.11-2.21 (3H, m), 2.29 (1H, bt, *J* = 11.2 Hz), 2.48 (1H, ddd, *J* = 15.6, 5.6, 3.2 Hz), 3.50 (1H, septet, *J* = 6.0 Hz), 5.38 (1H, d, *J* = 4.8 Hz), 6.49 (1H, dd, *J* = 3.2, 1.6 Hz), 7.53 (4H, td, *J* = 7.6, 1.2 Hz), 7.59 (2H, tt, *J* = 7.2, 1.6 Hz), 8.61 (4H, d, *J* = 7.2, 1.2 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.6, 16.1, 18.3, 19.4, 20.7, 25.9, 30.9, 31.6, 32.0, 32.7, 33.8, 36.8, 37.2, 42.8, 49.7, 50.7, 56.2, 72.5, 120.6, 128.6, 129.0, 132.6, 135.5, 141.0, 141.4, 142.1, 170.1, 183.4. IR (KBr) 2933, 2845, 1507, 1361, 1247 cm^{-1}. MS (EI) *m/z* 649 (M^+, 100%), 592 (M^+-57, 77%). HRMS Calcd. for $C_{40}H_{51}N_3OSSi$: 649.3522. Found: 649.3524.

(3ß)-17-[2-(6-Chlorobenzoxazolyl)thio]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]androsta-5,16-diene (12c)

Colorless solid. Mp 103.0-104.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.89 (9H, s), 0.93 (3H, s), 1.02 (3H, s), 1.00-1.07 (1H, m), 1.40 (1H, ddd, *J* = 21.6, 12.0, 4.8 Hz), 1.47-1.78 (8H, m), 2.02-2.11 (2H, m), 2.18 (1H, ddd, *J* = 13.6, 5.2, 2.0 Hz), 2.27 (1H, td, *J* = 13.2, 2.0 Hz), 2.39 (1H, ddd, *J* = 15.6, 6.0, 3.2 Hz), 3.48 (1H, septet, *J* = 6.0 Hz), 5.34 (1H, d, *J* = 5.2 Hz), 6.43 (1H, dd, *J* = 2.8, 1.6 Hz), 7.28 (1H, dd, *J* = 8.8, 2.0 Hz), 7.48 (1H, d, *J* = 1.6 Hz), 7.53 (1H, d, *J* = 8.8 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.6, 15.9, 18.3, 19.3, 20.6, 25.9, 30.8, 31.3, 32.0, 32.5, 33.7, 36.8, 37.2, 42.8, 49.5, 50.3, 55.8, 72.5, 110.7, 119.4, 120.5, 125.0, 130.0, 139.6, 139.8, 140.8, 141.9, 151.7, 163.7. IR (KBr) 2926, 2901, 2855, 1503, 1462, 1258, 1084, 839 cm^{-1}. MS (EI) *m/z* 569 (M^+, 9%), 512 (M^+-57, 100%). HRMS Calcd. for $C_{32}H_{44}ClNO_2SSi$: 569.2551. Found: 569.2557.

(3ß)-17-(2-Benzothiazolylthio)-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]androsta-5,16-diene (12d)

Colorless solid. Mp 170.0-170.5 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.05 (6H, s), 0.88 (9H, s), 0.93 (3H, s), 1.02 (3H, s), 0.98-1.09 (1H, m), 1.38-1.57 (4H, m), 1.60-1.77 (7H, m), 2.04-2.11 (2H, m), 2.19 (1H, ddd, *J* = 13.6, 4.8, 2.0 Hz), 2.27 (1H, td, *J* = 11.6, 1.2 Hz), 2.39 (1H, ddd, *J* = 15.6, 6.0, 2.8 Hz), 3.47 (1H, septet, *J* = 5.2 Hz), 5.34 (1H, d, *J* = 5.2 Hz), 6.45 (1H, d, *J* = 1.2 Hz), 7.30 (1H, td, *J* = 7.2, 0.8 Hz), 7.41 (1H, td, *J* = 7.6, 0.2 Hz), 7.74 (1H, d, *J* = 7.6 Hz), 7.88 (1H, d, *J* = 8.0 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.6, 16.0, 18.2, 19.3, 20.6, 25.9, 30.9, 31.3, 32.0, 32.5, 33.9, 36.8, 37.2, 42.8, 49.6, 50.4, 56.3, 72.5, 120.5, 120.8, 122.0, 124.4, 126.1, 135.7, 141.6, 142.0, 143.8, 154.0, 168.4. IR (KBr) 2926, 1424, 1253, 1084, 1004 cm^{-1}. MS (EI) *m/z* 551 (M^+, 100%), 494 (M^+-57, 90%). HRMS Calcd. for $C_{32}H_{45}NOS_2Si$: 551.2712. Found: 551.2698.

(3ß)-17-[4-(6,7-Dimethoxyquinazolyl)thio]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]androsta-5,16-diene (12f)

Pale yellow solid. Mp 202.0- 203.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.89 (9H, s), 0.93 (3H, s), 1.02 (3H, s), 1.05-1.09 (2H, m), 1.19-1.23 (1H, m), 1.47-1.57 (5H, m), 1.66-1.79 (4H, m), 2.07-2.13 (2H, m), 2.19 (1H, dd, *J* = 13.2, 3.2 Hz), 2.28 (1H, t, *J* = 11.2 Hz), 2.45 (1H, ddd, *J* = 16.0, 6.0, 3.2 Hz), 3.49 (1H, septet, *J* = 6.0 Hz), 4.04 (3H, s), 4.06 (3H, s), 5.35 (1H, t, *J* = 5.2 Hz), 6.42 (1H, dd, *J* = 3.2, 2.0 Hz), 7.27 (1H, s), 7.36 (1H, s), 8.85 (1H, s). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.6, 16.2, 18.3, 19.3, 20.7, 25.9, 31.0, 31.4, 31.9, 32.8, 34.1, 36.8, 37.2, 42.8, 50.0, 50.4, 55.5, 56.3, 56.4, 72.5, 101.9, 107.1, 119.3, 120.7, 141.3, 141.4, 141.9, 146.2, 150.1, 152.7, 155.6, 167.7. IR (KBr) 2928, 2857, 1505, 1342, 1231, 1157, 1094 cm^{-1}. MS (EI) *m/z* 606 (M^+, 97%), 260 (M^+-346, 100%). HRMS Calcd. for $C_{35}H_{50}N_2O_3SSi$: 606.3311. Found: 606.3328.

(3ß,17ß)-17-[5-(2-Cyanofuranyl)thio]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]androsta-5,16-diene (12g)

Colorless solid. Mp 144.0-145.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.06 (6H, s), 0.88 (9H, s), 0.89 (3H, s), 1.02 (3H, s), 0.96-1.08 (1H, m), 1.19-1.31 (3H, m), 1.42-1.55 (3H, m), 1.59-1.70 (4H, m), 1.77 (1H, dt, *J* = 12.8, 3.6 Hz), 1.93 (1H, ddd, *J* = 15.2, 11.6, 2.0 Hz), 1.98-2.03 (1H, m), 2.15-2.22 (2H, m), 2.26-2.30 (1H, m), 3.47 (1H, septet, *J* = 4.8 Hz), 5.32 (1H, d, *J* = 5.2 Hz), 5.67 (1H, dd, *J* = 2.8, 1.6 Hz), 6.59 (1H, d, *J* = 3.6 Hz), 7.07 (1H, d, *J* = 3.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.6, 15.8, 18.2, 19.3, 20.6, 25.9, 30.6, 31.3, 31.8, 32.0, 33.9, 36.7, 37.2, 42.8, 48.9, 50.3, 56.4, 72.5, 111.1, 116.8, 120.6, 123.5, 128.6, 131.5, 141.9, 144.5, 151.2. IR (neat) 2928, 2856, 2238, 1465, 1256, 1098 cm^{-1}. MS (EI) *m/z* 509 (M^+, 2%), 452 (M^+-57, 100%). HRMS Calcd. for $C_{30}H_{43}NO_2SSi$: 509.2784. Found: 509.2783.

(17ß)-17-(Benzoylthio)-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]estra-1,3,5(10)-triene (13)

Colorless solid. Mp 142.5-143.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.19 (6H, s), 0.83 (3H, s), 0.98 (9H, s), 1.34-1.46 (6H, m), 1.59-1.79 (1H, m), 1.85-1.91 (3H, m), 2.25-2.38 (3H, m), 2.80-2.85 (2H, m), 3.72 (1H, t, *J* = 9.6 Hz), 6.56 (1H, d, *J* = 2.4 Hz), 6.61 (1H, dd, *J* = 8.4, 2.8 Hz), 7.12 (1H, d, *J* = 8.4 Hz), 7.44 (2H, td, *J* = 8.0, 1.6 Hz), 7.55 (1H, t, *J* = 7.6 Hz), 7.99 (2H, d, *J* = 7.2 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.4, 14.3, 18.2, 24.3, 25.7, 26.2, 27.6, 29.5, 29.6, 36.7, 39.2, 43.8, 44.1, 52.7, 53.1, 117.1, 119.9, 126.1, 127.2, 128.5, 132.9, 133.1, 137.4, 137.7, 153.3, 192.2. IR (KBr) 2933, 2857, 1658, 1496, 1255, 907, 842 cm^{-1}. MS (EI) *m/z* 506 (M^+, 59%), 449 (M^+-57, 67%), 105 (M^+-401, 100%). HRMS Calcd. for $C_{31}H_{42}O_2SSi$: 506.2675. Found: 506.2652.

(17ß)-[2-(4,6-Diphenyl-1,3,5-triaziyl)thio]estra-1,3,5(10)-trien-3-ol benzoate (14a)

Colorless solid. Mp 236.0-238.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.94 (3H, s), 1.46-1.59 (6H, m), 1.85-1.93 (1H, m), 1.95-2.01 (2H, m), 2.06 (1H, bd, *J* = 9.2 Hz), 2.36 (2H, bd, *J* = 6.0 Hz), 2.52-2.68 (1H, m), 2.94 (2H, br s), 4.11 (1H, t, *J* = 9.2 Hz), 6.95 (1H, s), 6.97 (1H, dd, *J* = 8.4, 3.6 Hz), 7.34 (1H, d,

J = 8.8 Hz), 7.49-7.65 (9H, m), 8.20 (2H, dd, *J* = 7.2, 0.9 Hz), 8.63 (4H, dd, *J* = 6.8, 1.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.0, 24.4, 26.1, 27.5, 29.6, 30.2, 37.0, 38.8, 44.06, 44.14, 53.4, 53.7, 118.7, 121.6, 126.5, 128.5, 128.6, 128.9, 129.6, 130.1, 132.5, 133.5, 135.7, 137.8, 138.2, 148.7, 165.5, 169.9, 183.4. IR (KBr) 3061, 2925, 1738, 1506, 1249, 755 cm^{-1}. MS (EI) *m/z* 623 (M^+, 32%), 105 (M^+-518, 100%). HRMS Calcd. for $C_{40}H_{37}N_3O_2S$: 623.2606. Found: 623.2608.

(17ß)-[2-(4,6-Diphenyl-1,3,5-triazyl)thio]-3-[2-(4,6-diphenyl-1,3,5-triazyl)oxy]estra-1,3,5(10)-triene (15a)

Colorless solid. Mp 145.0-146.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.99 (3H, s), 1.49-1.68 (6H, m), 1.91 (1H, bq, *J* = 14.0 Hz), 2.01-2.10 (3H, m), 2.40-2.44 (2H, m), 2.61-2.71 (1H, m), 2.95-3.00 (2H, m), 4.14 (1H, t, *J* = 9.6 Hz), 7.07 (1H, d, *J* = 2.8 Hz), 7.12 (1H, dd, *J* = 8.4, 2.8 Hz), 7.39 (1H, d, *J* = 8.4 Hz), 7.40-7.62 (12H, m), 8.57 (4H, d, *J* = 6.8 Hz), 8.63 (4H, d, *J* = 6.8 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.1, 24.5, 26.2, 27.6, 29.7, 30.2, 37.1, 38.9, 44.1, 44.2, 53.5, 53.7, 118.8, 121.3, 126.2, 128.58, 128.60, 129.0, 129.1, 132.6, 132.8, 135.4, 135.7, 137.5, 138.1, 149.9, 169.9, 171.7, 174.0, 183.5. IR (KBr) 2933, 2878, 1542, 1507, 1361 cm^{-1}. MS (EI) *m/z* 750 (M^+, 13%), 44 (M^+-706, 100%). HRMS Calcd. for $C_{48}H_{42}N_6OS$: 750.3141. Found: 750.3123.

(17ß)-[2-(6-Chlorobenzoxazolyl)thio]estra-1,3,5(10)-trien-3-ol benzoate (14c)

Pale yellow solid. Mp 76.0 - 77.5 °C (EtOAc). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, s), 1.42-1.57 (6H, m), 1.84-1.99 (4H, m), 2.30-2.40 (2H, m), 2.55-2.65 (1H, m), 2.92 (2H, br s), 3.86 (1H, t, *J* = 9.2 Hz), 6.94 (1H, d, *J* = 2.4 Hz), 6.97 (1H, dd, *J* = 8.4, 2.4 Hz), 7.26 (1H, dd, *J* = 8.4, 2.0 Hz), 7.33 (1H, d, *J* = 8.4 Hz), 7.45 (1H, d, *J* = 2.0 Hz), 7.48-7.53 (3H, m), 7.63 (1H, t, *J* = 7.2 Hz), 8.20 (2H, dd, *J* = 7.2, 1.2 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.7, 24.2, 26.1, 27.4, 29.5, 30.5, 36.7, 38.8, 43.9, 44.3, 52.9, 56.3, 110.5, 118.6, 118.7, 121.6, 124.8, 126.5, 128.5, 129.3, 129.6, 130.1, 133.5, 137.7, 138.2, 140.8, 148.7, 151.8, 165.4, 166.3. IR (KBr) 2925, 1736, 1496, 1260, 1062, 706 cm^{-1}. MS (EI) *m/z* 543 (M^+, 8%), 105 (M^+-438, 100%). HRMS Calcd. for $C_{32}H_{30}ClNO_3$: 543.1635. Found: 543.1638.

(17ß)-[2-(Benzothiazolyl)thio]estra-1,3,5(10)-trien-3-ol benzoate (14d)

Colorless solid. Mp 166.5-168.0 °C (EtOAc). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 (3H, s), 1.42-1.56 (6H, m), 1.81-2.00 (4H, m), 2.30-2.38 (2H, m), 2.57-2.65 (1H, m), 2.91 (2H, br s), 3.94 (1H, t, *J* = 9.2 Hz), 6.94 (1H, s), 6.97 (1H, dd, *J* = 8.8, 2.0 Hz), 7.29 (1H, t, *J* = 7.6 Hz), 7.33 (1H, d, *J* = 8.4 Hz), 7.41 (1H, t, *J* = 8.0 Hz), 7.50 (2H, t, *J* = 7.6 Hz), 7.63 (1H, t, *J* = 7.6 Hz), 7.75 (1H, d, *J* = 7.6 Hz), 7.86 (1H, d, *J* = 8.0 Hz), 8.20 (2H, d, *J* = 8.0 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.7, 24.3, 26.2, 27.4, 29.5, 30.5, 37.0, 38.9, 44.0, 44.6, 53.0, 57.5, 118.7, 120.8, 121.4, 121.6, 124.1, 125.9, 126.5, 128.5, 129.7, 130.1, 133.5, 135.3, 137.8, 138.2, 148.7, 153.3, 165.4, 167.5. IR (KBr) 2923, 1734, 1426, 1263, 1064, 752, 713 cm^{-1}. MS (EI) *m/z* 525 (M^+, 24%), 105 (M^+-420, 100%). HRMS Calcd. for $C_{32}H_{31}NO_2S_2$: 525.1796. Found: 525.1782.

(17ß)-[4-(6,7-Dimethoxyquinazolyl)thio]estra-1,3,5(10)-trien-3-ol benzoate (14f)

Colorless solid. Mp 118.5-119.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.97 (3H, s), 1.44-1.61 (6H, m), 1.81 (1H, bq, J = 10.8 Hz), 1.91-2.01 (3H, m), 2.30-2.41 (2H, m), 2.54-2.64 (1H, m), 2.88-2.96 (2H, br s), 4.04 (3H, s), 4.06 (3H, s), 4.29 (1H, t, J = 9.6 Hz), 6.95 (1H, s), 6.97 (1H, d, J = 8.4 Hz), 7.25 (1H, s), 7.28 (1H, s), 7.34 (1H, d, J = 8.4 Hz), 7.50 (2H, t, J = 7.2 Hz), 7.63 (1H, t, J = 7.2 Hz), 8.20 (2H, d, J = 7.2 Hz), 8.83 (1H, s). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.3, 24.3, 26.1, 27.4, 29.6, 30.2, 36.7, 38.9, 44.0, 52.8, 53.1, 56.27, 56.32, 101.8, 107.1, 118.7, 119.3, 121.6, 126.5, 128.5, 129.6, 130.1, 133.5, 137.9, 138.2, 145.5, 148.6, 149.8, 152.4, 155.3, 165.4, 168.2. IR (KBr) 2927, 1735, 1504, 1228, 1156, 1061 cm^{-1}. MS (EI) *m/z* 580 (M^+, 35%), 105 (M^+-475, 100%). HRMS Calcd. for $C_{35}H_{36}N_2O_4S$: 580.2396. Found: 580.2396. One carbon peak of aliphatic region was piled up in ^{13}C-NMR.

(17ß)-[4-(6,7-Dimethoxyquinazolyl)thio]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]estra-1,3,5(10)-triene (16f)

Colorless solid. Mp 121.0-121.5 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.19 (6H, s), 0.95 (3H, s), 0.98 (9H, s), 1.42-1.58 (6H, m), 1.79 (1H, bq, J = 10.0 Hz), 1.88-1.96 (3H, m), 2.24-2.34 (2H, m), 2.54-2.59 (1H, m), 2.80-2.88 (2H, m), 4.04 (3H, s), 4.05 (3H, s), 4.27 (1H, t, J = 9.6 Hz), 6.57 (1H, s), 6.61 (1H, d, J = 8.4 Hz), 7.13 (1H, d, J = 8.4 Hz), 7.25 (1H, s), 7.28 (1H, s), 8.82 (1H, s). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.4, 14.4, 18.2, 24.3, 25.7, 26.2, 27.6, 29.6, 30.2, 36.8, 39.2, 43.9, 44.1, 52.9, 53.1, 56.27, 56.33, 101.8, 107.1, 117.2, 119.3, 119.9, 126.1, 132.9, 137.8, 145.5, 149.8, 152.4, 153.3, 155.3, 168.3. IR (KBr) 2927, 2856, 1504, 1251, 1231, 1157, 846 cm^{-1}. MS (EI) *m/z* 590 (M^+, 100%), 249 (M^+-341, 55%). HRMS Calcd. for $C_{34}H_{46}N_2O_3SSi$: 590.2998. Found: 590.2985.

(17ß)-[2-(5-Cyanofuranyl)thio]estra-1,3,5(10)-trien-3-ol benzoate (14g)

Colorless solid. Mp 138.0-139.5 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.85 (3H, s), 1.25-1.54 (6H, m), 1.73-1.93 (4H, m), 2.21-2.34 (3H, m), 2.89 (2H, br s), 3.24 (1H, t, J = 9.2 Hz), 6.47 (1H, t, J = 9.2 Hz), 6.93 (1H, s), 6.97 (1H, d, J = 8.4 Hz), 7.06 (1H, d, J = 3.6 Hz), 7.32 (1H, d, J = 8.4 Hz), 7.50 (2H, t, J = 8.0 Hz), 7.63 (1H, t, J = 7.6 Hz), 8.19 (2H, d, J = 7.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 13.1, 24.0, 26.1, 27.3, 29.5, 30.1, 36.8, 38.8, 43.9, 44.5, 53.1, 58.6, 111.4, 114.7, 118.7, 121.6, 123.5, 126.4, 127.0, 128.5, 129.6, 130.1, 133.5, 137.6, 138.1, 148.7, 154.3, 165.4. IR (KBr) 2926, 2225, 1734, 1457, 1263, 1063 cm^{-1}. MS (EI) *m/z* 483 (M^+, 21%), 105 (M^+-378, 100%). HRMS Calcd. for $C_{30}H_{29}NO_3S$: 483.1868. Found: 483.1880.

(17ß)-[2-(5-Cyanofuranyl)thio]-3-[[(1,1-dimethylethyl)dimethylsilyl]oxy]estra-1,3,5(10)-triene (16g)

Colorless solid. Mp 101.0-102.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.18 (6H, s), 0.84 (3H, s), 0.97 (9H, s), 1.24-1.47 (6H, m), 1.71-1.88 (4H, m), 2.20-2.29 (3H, m), 2.81 (2H, bd, J = 4.4 Hz), 3.23 (1H, t, J = 9.2 Hz), 6.46 (1H, d, J = 3.6 Hz), 6.55 (1H, d, J = 2.0 Hz), 6.61 (1H, dd, J = 8.8, 2.4 Hz), 7.05 (1H, d, J = 3.6 Hz), 7.10 (1H, d, J = 8.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.4, 13.2, 18.2, 24.0, 25.7,

26.2, 27.6, 29.5, 30.1, 36.9, 39.2, 43.7, 44.5, 53.1, 58.7, 111.4, 114.6, 117.2, 119.9, 123.5, 126.1, 127.0, 132.6, 137.7, 153.4, 154.4. IR (KBr) 2928, 2225, 1496, 1460, 1255, 842 cm^{-1}. MS (EI) *m/z* 493 (M^+, 100%), 436 (M^+-57, 82%). HRMS Calcd. for $C_{29}H_{39}NO_2SSi$: 493.2471. Found: 493.2477.

(3ß,17ß)-3-[4-(6,7-Dimethoxyquinazolyl)thio]-17-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5α-androstane (18f)

Colorless solid. Mp 216.0-217.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.003 (3H, s), 0.01 (3H, s), 0.69 (3H, s), 0.86 (3H, s), 0.88 (9H, s), 0.90-1.02 (2H, m), 1.16-1.27 (5H, m), 1.32 (2H, d, J = 13.2 Hz), 1.35-1.44 (3H, m), 1.54 (3H, t, J = 0.4 Hz), 1.65-1.76 (3H, m), 1.81-1.90 (3H, m), 2.07 (1H, d, J = 12.8 Hz), 3.54 (1H, t, J = 8.0 Hz), 4.02 (3H, s), 4.03 (3H, s), 4.11 (1H, tt, J = 12.4, 4.4 Hz), 7.19 (1H, s), 7.25 (1H, s), 8.83 (1H, s). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.8, -4.5, 11.4, 12.3, 18.1, 20.6, 23.5, 25.8, 28.5, 28.8, 30.9, 31.6, 35.4, 35.6, 35.7, 37.2, 38.9, 42.7, 43.3, 47.1, 50.6, 54.6, 56.2, 56.3, 81.8, 101.7, 107.0, 119.1, 145.5, 149.8, 152.5, 155.4, 167.9. IR (KBr) 2929, 2854, 1505, 1342, 1230, 1158, 1094 cm^{-1}. MS (EI) *m/z* 610 (M^+, 6%), 222 (M^+-388, 100%). HRMS Calcd. for $C_{35}H_{54}N_2O_3SSi$: 610.3624. Found: 610.3615.

(3α,17ß)-3-[4-(6,7-Dimethoxyquinazolyl)thio]-17-[[(1,1-dimethylethyl)dimethylsilyl]oxy]-5α-androstane (18f')

Colorless solid. Mp 104.0-105.0 °C (Hexane). ^{1}H-NMR (400 MHz, $CDCl_3$) δ -0.01 (3H, s), 0.001 (3H, s), 0.70 (3H, s), 0.87 (9H, s), 0.88 (3H, s), 0.96-0.99 (1H, m), 1.19-1.31 (6H, m), 1.38-1.46 (3H, m), 1.50-1.60 (3H, m), 1.64-1.70 (3H, m), 1.74 (2H, d, J = 12.0 Hz), 1.85-1.94 (3H, m), 2.09 (1H, dt, J = 14.0, 4.0 Hz), 3.53 (1H, t, J = 8.0 Hz), 4.03 (3H, s), 4.06 (3H, s), 4.72 (1H, br s), 7.24 (1H, s), 7.25 (1H, s), 8.83 (1H, s). ^{13}C-NMR (100 MHz, $CDCl_3$) δ -4.8, -4.5, 11.4, 11.9, 18.1, 20.4, 23.5, 25.8, 27.4, 28.4, 30.9, 31.5, 34.0, 34.6, 35.5, 36.4, 37.2, 42.3, 42.6, 43.3, 50.7, 54.5, 56.30, 56.34, 81.8, 101.7, 107.0, 119.1, 145.5, 149.8, 152.5, 155.3, 167.9. IR (KBr) 2927, 2853, 1505, 1260, 1093 cm^{-1}. MS (EI) *m/z* 610 (M^+, 12%), 222 (M^+-388, 100%). HRMS Calcd. for $C_{35}H_{54}N_2O_3SSi$: 610.3624. Found: 610.3626.

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REFERENCES AND NOTES

1. (a) M. Arisawa, S. Tanii, T. Tazawa, and M. Yamaguchi, *Heterocycles*, 2017, **94**, 2179; (b) M. Arisawa, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2019, **194**, 643.
2. (a) M. Arisawa, T. Tazawa, S. Tanii, K. Horiuchi, and M. Yamaguchi, *J. Org. Chem*., 2017, **82**, 804;

(b) S. Tanii, M. Arisawa, T. Tougo, K. Horiuchi, and M. Yamaguchi, *Synlett*, 2017, **28**, 1601; (c) G. Li, M. Arisawa, and M. Yamaguchi, *Chem. Commun*., 2014, **50**, 4328.

3. (a) M. Shimazaki, M. Hikita, T. Hosoda, and A. Ohta, *Heterocycles*, 1991, **32**, 937; (b) J. B. Baudin, G. Hareau, S. A. Julia, R. Lorne, and O. Ruel, *Bull. Soc. Chim. Fr.,* 1993, **130**, 856.
4. (a) H.-J. Xu, Y.-F. Liang, X.-F. Zhou, and Y.-S. Feng, *Org. Biomol. Chem*., 2012, **10**, 2562; (b) H.-L. Kao, C.-K. Chen, Y.-J. Wang, and C.-F. Lee, *Eur. J. Org. Chem.*, 2011, 1776; (c) M. Shahjahan Kabir, M. Lorenz, M. L. Van Linn, O. A. Namjoshi, S. Ara, and J. M. Cook, *J. Org. Chem.*, 2010, **75**, 3626.
5. Z. Lian, B. N. Bhawal, P. Yu, and B. Morandi, *Science*, 2017, **356**, 1059.
6. Z. Duan, S. Ranjit, P. Zhang, and X. Liu, *Chem. Eur. J.*, 2009, **15**, 3666.
7. (a) J. Zhao, H. Fang, J. Han, Y. Pan, and G. Li, *Adv. Synth. Catal.*, 2014, **356**, 2719; (b) B. Du, B. Jin, and P. Sun, *Org. Lett.*, 2014, **16**, 3032.
8. S. R. Wilson, G. M. Georgiadis, H. N. Khatri, and J. E. Bartmess, *J. Am. Chem. Soc.*, 1980, **102**, 3577.
9. D. A. Swann and J. H. Turnbull, *Tetrahedron*, 1968, **24**, 1441. 3β-Hydroxy-5α-androstane with the 17α and 17β-mercapto drivatives showed ^{1}H-NMR at δ 3.12 and δ 2.60, respectively.
10. The coupling constant (J = ~9 Hz) of 17α-proton of 1,3,5(10)-estratrien-3-ol derivative is larger than that of 17β-proton (J = ~6 Hz). For example, for estradiol, the coupling constant of 17α-proton is 8.8 Hz and the coupling constant of 17β-proton is 5.7 Hz. (a) Y. Liu, Y. Wang, X. Chen, Q. Wu, M. Wang, D. Zhu, and Y. Ma, *Steroids*, 2017, **118**, 17; (b) F. S. P. Cardoso, G. E. Mickle, M. A. da Silva, P. T. Baraldi, and F. B. Ferreira, *Org. Process Res. Dev.*, 2016, **20**, 306.