New Luminescent Materials Based on a Steroid Molecule

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An efficient way to synthesize new steroid derivatives substituted in the A ring is described; based on a new route to stable diazo steroid 3-diazoandrosta-1,4-dien-17-one (**4**). Using the Barton–Kellogg olefination, it is possible to combine the steroid molecule with a heterocyclic substructure: the oxazoline ring system. Unlike the starting material, the resulting oxazinylidene products **2** are luminescence dyes with high quantum yields, and possess Stokes shifts of about 100 nm. The described synthetic method opens the way for the development of new diagnostic and pharmaceutical materials containing a steroidal substructure.

Introduction

Luminescence dyes play an important role in the field of biochemistry and modern diagnostic approaches.[1] Some of these dyes, such as fluoresceine or rhodamine, are widely used and easily available.[2] However, there are often problems concerning their purity as well as their rapid decomposition during irradiation with ultraviolet light. In addition, it is difficult to add linker groups to the dye molecule. It is thus obvious that there exists a need for new dyes with made-to-measure properties. In addition, intracellular diagnostics, as a new field in diagnostics, need completely new types of dyes. They must be able to permeate through membranes, should be stable against enzymatic attack and should produce special interactions with different parts of the cell. From our point of view, the steroid molecule represents the ideal basis for the construction of such new dyes. We therefore focused upon synthetic modification of steroids, and developed a new synthetic method to modify the A ring of steroids.

Results and Discussion

Using the Barton−Kellogg olefination, which constitutes an elegant pathway to overcrowded olefins, 3-thioxoandrosta-1,4-dien-17-one **1**[3] was treated with a diazoalkane. Even at room temperature, the 1,3,4-thiadiazoline, preformed by 1,3-dipolar cycloaddition, eliminates nitrogen and sulfur, thus leading directly to the cross-conjugated olefin **2**.[4] This olefination reaction is very easy to carry out. Small amounts of the solid thioxo steroid were added in the manner of a titration to a solution of the diazoalkane in ether. The intense colour of the starting materials immediately faded, nitrogen gas was evolved and sulfur precipitated. The resulting olefins could be isolated from the solutions by chromatography in yields of up to 70% (Figure 1, path 1). It was of especial interest to us to be able to introduce an oxazoline substructure because of their well-known fluorescence properties. Unfortunately, all attempts to prepare the corresponding diazo compounds starting from the heterocycle were unsuccessful. Here an inverse synthesis was the method of choice. Accordingly, the steroid hydrazone **3** was synthesized first,[5] oxidized to the diazo steroid **4** and then treated with the heterocyclic thio ketones **6a−g** (Figure 1, path 2). The steroid-substituted oxazolinylidenes **2a−g** were formed as mixtures of diastereomers in a 1:1 ratio. Diazo steroid **4**, obtained by careful oxidation of the appropriate hydrazone in ether by manganese oxide at room temperature, is to the best of our knowledge the first pure diazo steroid. Other diazo steroids are either diazocarbonyl compounds in which the diazo group is stabilized by a neighboring carbonyl group,[6] or are only postulated as reactive intermediates.[7] Under the conditions used, **4** forms a slightly blue solution that is stable for several hours. In its ^{13}C NMR spectrum at room temperature, the signal of the diazocarbonyl carbon atom is not apparent. However, it could be detected at −20 °C as a broad singlet at δ = 61.1. Furthermore, the presence of the diazo group

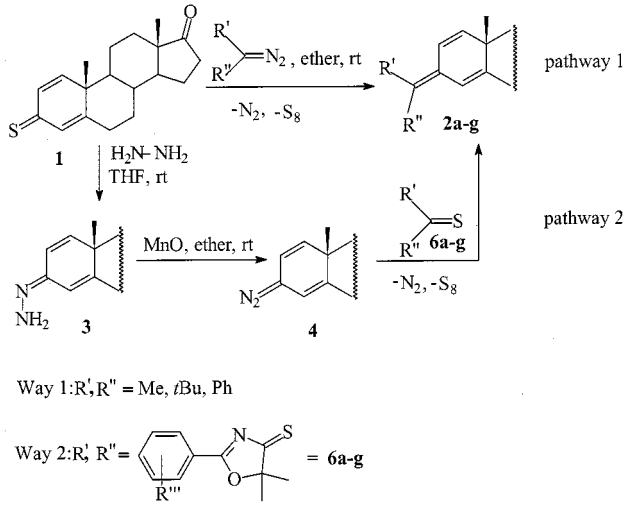

Figure 1. Synthesis of steroid olefins

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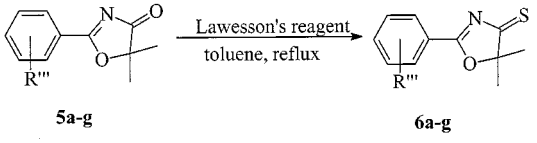
could also be detected by its typical IR absorption at 2042 cm^{-1}.

The thio ketones **6a−g** were isolated in high yields from the corresponding carbonyl compounds **5a−g** using Lawesson's reagent (Figure 2). These new thioxo derivatives are orange or red substances with an H_2S-like odor.



R''' = F, Cl, OCH_3, NO_2, $N(CH_3)_2$

Figure 2. Synthesis of thiocarbonyl compounds

The oxazolinones **5a−g** were prepared as described in the literature.[8] These substances show no or only weak luminescence in solution. In contrast to this, the oxazolinylidenes **2a−g** are excellent luminescence dyes. The wavelength of luminescence depends on the nature of the aromatic substituent R′′′, and ranges from 489 nm up to 629 nm. In all luminescence spectra, a large Stokes shift of about 100 nm was observed (Table 1).

Table 1. Absorption maximum, emission maximum and quantum yield of the steroid olefins **2a−g**

	R′′′	$[\lambda]_{max,abs}$ [nm][a]	$[\lambda]_{max,em}$ [nm][a]	[Φ]
2a	4-OMe	385	489	0.26
2b	3-OMe	386	494	0.67
2c	2-OMe	354	514	0.24
2d	4-Cl	393	502	0.76
2e	4-F	383	488	0.59
2f	4-NMe_2	395	502	0.10
2g	4-NO_2	447	629	0.05

[a] Solvent: dioxane.

Experimental Section

General Remarks: Melting points (uncorrected): Galen TM3. − ^1H and ^{13}C NMR: Bruker AC 250 or DRX 400, TMS as internal standard, diastereomeric pair *E*/*Z* ratio determined by ^1H NMR. − IR: Nicolet. − UV/Vis: Perkin−Elmer UV/Vis/NIR spectrophotometer, dioxan as solvent. − Fluorescence spectra: Perkin−Elmer luminescence spectrophotometer LS 50, dioxan as solvent, quinine sulfate as standard. − MS: Finnigan MAT SSQ 710. − HRMS: Intectra AMD 402. − Elemental analyses: Leco CHNS-932. − Thin-layer chromatography (TLC): 0.25 mm Merck silica gel plates (60 F_{254}), detection by UV light or vanillin/H_2SO_4 and heating. − Column chromatography: 0.040−0.063 mm Merck silica gel. − Solvents were used as commercial grade without further purification. THF was distilled from Na/benzophenone. The yields of the isolated products **2a−g** are based on **6a−g**.

3-Diazoandrosta-1,4-dien-17-one (4): A manganese(IV) oxide/charcoal powder[9] (3 g) was suspended in ether (20 mL) and subjected to ultrasound for about 5 min. To this suspension the freshly prepared steroid hydrazone (0.3 g, 1.0 mmol) was added. This mixture was stirred vigorously for about 1 h, after this time the reaction was complete. The pale violet ethereal solution was decanted from the charcoal and used without further purification. To obtain the NMR spectrum, the reaction was also carried out in $[D_{10}]$diethyl ether. − IR (Et_2O): ν = 3029, 2042 (C=N=N), 1745 (C=O) cm^{-1}. − UV/Vis (Et_2O): λ_{max} = 577 nm. − ^1H NMR ($[D_{10}]Et_2O$): δ = 0.86 (s, 3 H, 18-CH_3), 1.20 (s, 3 H, 19-CH_3), 5.27 (d, *J* = 10.0 Hz, 1 H, 1-H), 5.65 (s, 1 H, 4-H), 5.96 (dd, *J* = 10.0 Hz, 1 H, 2-H). − ^{13}C NMR (0 °C, $[D_{10}]Et_2O$): δ = 13.9 (C-18), 20.7 (CH_2), 22.1 (C-19), 22.2, 32.3, 32.9, 33.0, 35.6 (5 CH_2), 36.6 (CH), 42.0 (C-10), 47.8 (C-13), 51.9, 54.7 (2 HCH), 61.1 (C-3), 106.6 (C-4), 113.27 (C-2), 128.24 (C-1), 140.4 (C-5), 217.3 (C-17). − MS (70 eV): *m*/*z* = 296 [M^+], 279, 167, 149, 108.

General Procedure for the Synthesis of the Thiocarbonyl Compounds 6a−g: Lawesson's reagent (1.5 mmol) was added to a solution of the oxazolinones **5a−g** (2.3 mmol) in dry toluene (50 mL). The mixture was stirred and refluxed for about 3 h. After this time, the starting material had been complete consumed (TLC monitoring). The solvent was removed under vacuum and the orange or red residue chromatographed on silica gel.

2-(4-Methoxyphenyl)-5,5-dimethyloxazole-4-thione (6a): Reaction time 4 h, yield 0.48 g (2.04 mmol, 89%) orange crystals, m.p. 127−129 °C (petroleum ether). − IR (KBr): ν = 2985, 2934, 2838, 1610, 1541, 1491, 1431, 1365, 1258 (C=S), 1175, 1133, 1059, 1013, 850, 761 cm^{-1}. − UV/Vis (dioxane): λ_{max} (lgε) = 237 (3.89), 293 (3.97), 349 (4.54), 494 (2.80) nm. − ^1H NMR ($CDCl_3$, AC-250): δ = 1.65 (s, 6 H, CH_3), 3.88 (s, 3 H, OCH_3), 6.98 (d, ^3J = 8.7 Hz, 2 H, 3-H), 8.23 (d, ^3J = 8.7 Hz, 2 H, 2-H). − ^{13}C NMR ($CDCl_3$, AC-250): δ = 27.1 (CH_3), 55.6 (OCH_3), 100.6 (C-5), 114.5 (C-3), 117.3 (C-1), 133.1 (C-2), 165.6 (C-4), 182.3 (C-2), 233.4 (C-4). − MS (70 eV): *m*/*z* (%) = 235 (78) [M^+], 177 (81) [$C_9H_7NOS^+$], 133 (100) [$C_8H_7NO^+$], 103 (16), 92 (21), 77 (23). − $C_{12}H_{13}NO_2S$ (235.3): calcd. C 61.25, H 5.57, N 5.95, S 13.63; found C 61.19, H 5.56, N 5.91, S 13.48.

2-(3-Methoxyphenyl)-5,5-dimethyloxazole-4-thione (6b): Reaction time 10 h, yield 0.40 g (1.7 mmol, 74%) orange mass, m.p. glasslike (decomp). − IR (KBr): ν = 2957, 2932, 1633, 1601, 1586, 1532, 1489, 1461, 1364, 1280 (C=S), 1231 (C=S), 1172, 1104, 1051, 942, 900, 847, 817, 752, 685 cm^{-1}. − UV/Vis (dioxane): λ_{max} (lgε) = 235 (3.93), 270 (3.76), 337 (4.09), 491 (1.95) nm. − ^1H NMR ($CDCl_3$, AC-250): δ = 1.68 (s, 6 H, CH_3), 3.86 (s, 3 H, OCH_3), 7.23 (d, ^3J = 8.3 Hz, 1 H, 4-H), 7.42 (t, $^3J_1$ = 7.9 Hz, $^3J_2$ = 8.0 Hz, 1 H, 5-H), 7.80 (s, 1 H, 2-H), 7.86 (d, ^3J = 7.6, 1 H, 6-H). − ^{13}C NMR ($CDCl_3$, AC-250): δ = 27.3 (CH_3), 55.60 (OCH_3), 100.9 (C-5), 114.25 (C-2′), 122.5 (C-4′), 123.0 (C-6′), 126.6 (C-1′), 130.0 (C-5′), 159.89 (C-3′), 182.79 (C-2), 233.99 (C-4). − MS (70 eV): *m*/*z* (%) = 235 (54) [M^+], 177 (80) [$C_9H_7NOS^+$], 133 (100) [$C_8H_7NO^+$], 103 (13), 92 (13), 77 (14). − $C_{12}H_{13}NO_2S$ (235.3): calcd. C 61.25, H 5.57, N 5.95, S 13.63; found C 61.13, H 5.88, N 5.89, S 13.80

2-(2-Methoxyphenyl)-5,5-dimethyloxazole-4-thione (6c): Reaction time 12 h, yield 0.18 g (0.75 mmol, 33%) orange oil. − IR (KBr): ν = 2979, 2930, 2857, 1603, 1581, 1515, 1473, 1362, 1279 (C=S), 1243 (C=S), 1163, 1105, 1017, 959, 918, 842, 756 cm^{-1}. − UV/Vis (dioxane): λ_{max} (lgε) = 232 (3.92), 267 (3.86), 353 (4.26), 497 (2.04) nm. − ^1H NMR ($CDCl_3$, AC-250): δ = 1.65 (s, 6 H, CH_3), 3.93 (s, 3 H, OCH_3), 7.00−7.07 (m, 2 H, 3-H, 5-H), 7.57−7.64 (m, 1 H, 4-H), 8.25−8.29 (m, 1 H, 6-H). − ^{13}C NMR ($CDCl_3$, AC-250): δ = 27.2 (CH_3), 56.0 (OCH_3), 100.1 (C-5), 112.3 (C-3′), 114.12 (C-1′), 120.5 (C-5′), 134.0 (C-6′), 136.7 (C-4′), 161.1 (C-2′), 183.2 (C-2), 233.9 (C-4). − MS (DCI with H_2O): *m*/*z* (%) = 236 (100) [M^+ + H], 154 (12), 119 (14), 93 (25). − $C_{12}H_{13}NO_2S$ (235.3): calcd. C 61.25, H 5.57, N 5.95, S 13.63; found C 61.23, H 5.76, N 5.93, S 13.74.

2-(4-Chlorophenyl)-5,5-dimethyloxazole-4-thione (6d): Reaction time 6 h, yield 0.33 g (1.4 mmol, 60%) orange crystals, m.p. 66−68 °C (petroleum ether). − IR (KBr): ν = 2982, 2932, 1596, 1578, 1530, 1478, 1457, 1410, 1362, 1267 (C=S), 1250 (C=S), 1162, 1132, 1089, 1043, 1013, 957, 917, 844, 755, 676, 660, 483 cm^{-1}. − UV/Vis (dioxane): λ_{max} (lgε) = 269 (4.07), 337 (4.32), 498 nm (2.04). − ^1H NMR ($CDCl_3$, AC-250): δ = 1.67 (s, 6 H, CH_3), 7.50 (d, ^3J = 8.7 Hz, 2 H, 3-H), 8.21 (d, ^3J = 8.7 Hz, 2 H, 2-H). − ^{13}C NMR ($CDCl_3$, AC-250): δ = 27.4 (CH_3), 101.2 (C-5), 124.0 (C-1′), 129.5 (C-3′), 131.8 (C-2′), 142.0 (C-4′), 181.8 (C-2), 233.6 (C-4). − MS (70 eV): *m/z* (%) = 241 (16) [M^+ + 2], 239 (43) [M^+], 183 (28), 181 (81) [$C_8H_4ClNS^+$], 139 (45), 137 (100) [$C_7H_4ClN^+$], 111 (21), 102 (13), 75 (18). − HRMS (70 eV): $C_{11}H_{10}ClNOS$ calcd. 239.0172; found 239.0184. − $C_{11}H_{10}ClNOS$ (239.7): calcd. C 55.11, H 4.20, N 5.84, S 13.38; found C 54.66, H 4.31, N 5.70, S 13.80.

2-(4-Fluorophenyl)-5,5-dimethyloxazole-4-thione (6e): Reaction time 10 h, yield 0.31 g (1.42 mmol, 62%) yellow-orange crystals, m.p. 79−81 °C (petroleum ether). − IR (KBr): ν = 2985, 2865, 1600, 1541, 1490, 1463, 1421, 1375, 1361, 1285 (C=S), 1228, 1173, 1154, 1132, 1099, 1052, 1010, 969, 923, 852, 810, 758, 694, 660, 521 cm^{-1}. − UV/Vis (dioxane): λ_{max} (lgε) = 261 (4.00), 334 (4.33), 496 nm (2.46). − ^1H NMR ($CDCl_3$, AC-250): δ = 1.68 (s, 6 H, CH_3), 7.15−7.25 (m, 2 H, 3-H), 8.25−8.35 (m, 2 H, 2-H). − ^{13}C NMR ($CDCl_3$, AC-250): δ = 27.2 (CH_3), 101.2 (C-5), 116.5 (C-3, $^2J_{C,F}$ = 22.3), 121.6 (C-1′, $^4J_{C,F}$ = 2.8), 133.4 (C-2′, $^3J_{C,F}$ = 9.9), 167.2 (C-4′, $^1J_{C,F}$ = 259.0), 181.69 (C-2), 233.25 (C-4). − MS (70 eV): *m/z* (%) = 223 (51) [M^+], 165 (85) [$C_8H_4FNS^+$], 121 (100) [$C_7H_4FN^+$], 95 (39), 75 (19). − $C_{11}H_{10}FNOS$ (223.3) calcd. C 59.18, H 4.51, N 6.27, S 14.36; found C 59.17, H 4.35, N 6.26, S 14.74.

2-(4-Dimethylaminophenyl)-5,5-dimethyloxazole-4-thione (6f): Reaction time 40 min, yield 0.41 g (1.68 mmol, 73%) yellow crystals, m.p. 145−147 °C (toluene). − IR (KBr): ν = 2982, 2928, 1621, 1561, 1505, 1442, 1370, 1335, 1281 (C=S), 1231, 1199, 1166, 1126, 1046, 957, 824, 764, 665, 521 cm^{-1}. − UV/Vis (dioxane): λ_{max} (lgε) = 255 (3.72), 305 (3.62), 406 (4.79) nm. − ^1H NMR ($CDCl_3$, AC-250): δ = 1.65 (s, 6 H, CH_3), 3.11 (s, 6 H, $N(CH_3)_2$), 6.69 (d, ^3J = 9.3 Hz, 2 H, 3-H), 8.13 (d, ^3J = 9.2 Hz, 2 H, 2-H). − ^{13}C NMR ($CDCl_3$, AC-250): δ = 27.1 (CH_3), 40.1 ($N(CH_3)_2$), 99.9 (C-5), 110.8 (C-1′), 111.3 (C-3′), 133.2 (C-2′), 155.1 (C-4′), 182.37 (C-2), 232.2 (C-4). − MS (DCI with H_2O): *m/z* (%) = 249 (100) [M^+ + H], 233 (4), 148 (6). − $C_{13}H_{16}N_2OS$ (248.3): calcd. C 62.87, H 6.49, N 11.28, S 12.91; found C 62.57, H 6.52, N 11.00, S 12.71.

5,5-Dimethyl-2-(4-nitrophenyl)oxazole-4-thione (6g): Reaction time 12 h, yield: 0.35 g (1.40 mmol, 61%) orange-red crystals, m.p. 184−187 °C (Et_2O). − IR (KBr): ν = 3068, 3040, 2993, 2936, 1609, 1534, 1485, 1454, 1414, 1348, 1322, 1270 (C=S), 1241 (C=S), 1160, 1133, 1038, 1010, 959, 920, 875, 854, 723, 687 cm^{-1}. − UV/Vis (dioxane): λ_{max} (lgε) = 263 (4.22), 346m (4.24), 499 nm (2.41). − ^1H NMR ($CDCl_3$, AC-250): δ = 1.76 (s, 6 H, CH_3), 8.40 (d, ^3J = 8.9 Hz, 2 H, 2-H), 8.51 (d, ^3J = 8.9 Hz, 2 H, 3-H). − ^{13}C NMR ($CDCl_3$, AC-250): δ = 27.4 (CH_3), 102.0 (C-5), 124.0 (C-3′), 131.3 (C-1′), 131.4 (C-2′), 151.5 (C-4′), 180.6 (C-2), 233.4 (C-4). − MS (70 eV): *m/z* (%) = 250 (50) [M^+], 192 (100) [$C_8H_4N_2O_2S^+$], 150 (26), 102 (49), 76 (18). − HRMS (70 eV): $C_{11}H_{10}N_2O_3S$: calcd. 250.0412, found 250.0429. − $C_{11}H_{10}N_2O_3S$ (250.3): calcd. C 52.78, H 4.03, N 11.19, S 12.81; found C 51.45, H 4.06, N 10.66, S 12.31.

General Procedure for the Synthesis of the Steroid Olefins 2a−g: The solid thiocarbonyl compound (0.2 g, 0.85 mmol) was added to a freshly prepared solution of **4** (starting from 0.3 g hydrazone) in ether. The start of the reaction was indicated by evolution of nitrogen and, after a few minutes, the solution became cloudy as sulfur precipitated. The reaction was complete after 2 or 3 h, after which the solvent was removed in vacuum. Toluene was added to the raw material, which containes sulfur, to form a slurry and purification was performed by column chromatography on silica gel.

3-[2-(4-Methoxyphenyl)-5,5-dimethyloxazol-4-ylidene]androsta-1,4-dien-17-one (2a): Yield 0.17 g (0.36 mmol, 42%) of a yellow, glass-like solid, mixture of diastereomers (*E/Z* = 0.6:1). − IR (KBr): ν = 2932, 1736 (C=O), 1664 (C=N), 1607, 1581, 1553, 1504, 1468, 1422, 1343, 1305, 1255, 1176, 1137, 1107, 1068, 1027, 943, 842, 744 cm^{-1}. − UV/Vis (dioxane): λ_{max} (lgε) = 263 (4.20), 289 (4.20), 367 (4.42), 385 (4.41), 406 (4.23) sh, 434 nm (3.77) sh. − ^1H NMR ($CDCl_3$, DRX-400): δ = 0.89 (s, 3 H, 18-CH_3), 1.20 (s, 3 H, 19-CH_3), 1.64 (s, 6 H, CH_3), 3.84 (s, 3 H, OCH_3), 5.78 [d, ^3J = 10.1 Hz, 1 H, 1-H (*E*)], 5.79 [d, ^3J = 10.1 Hz,1 H, 1-H (*Z*)], 6.06 [s, 1 H, 4-H (*E*)], 6.30 [dd, ^3J = 10.1 Hz, ^4J = 1.8 Hz, 1 H, 2-H (*Z*)], 6.78 [s, 1 H, 4-H (*Z*)], 6.88−6.91 (m, 2 H, aromat), 6.98 [dd, 1 H, ^3J = 10.1, ^4J = 1.8, 2-H (*E*)], 7.92−7.97 (m, 2 H, aromat). − ^{13}C NMR ($CDCl_3$, DRX-400): δ = 13.84 (C-18), 20.64 (C-19), 20.71, 21.78 (2 × CH_2), 26.96 (CH_3), 31.40, 32.25, 32.55 (3 × CH_2), 35.61 (C-8), 35.75 (CH_2), 41.33 (C-10), 47.80 (C-13), 50.95 (C-14), 52.99 (C-9), 55.38 (OCH_3), 86.92 (C-5′), 113.73 (C-3′′), 115.38 [C-4(*E*)], 115.79 (C-3), 117.39 [C-4 (*Z*)], 120.00 [C-2 (*Z*)], 120.48 (C-1′′), 122.13 [C-2 (*E*)], 129.96 (C-2′′), 133.50 [C-1 (*E*)], 135.29 [C-1 (*Z*)], 144.75 [C-5 (*Z*)], 146.20 [C-5 (*E*)], 150.25 (C-4′), 162.22 (C-4′′), 164.24 (C-2′), 221.01 (C-17). − MS (DCI with H_2O): *m/z* (%) = 472 (86) [M^+ + H], 456 (24) [M^+ − CH_3], 307 (12), 220 (42), 177 (28), 153 (16), 135 (58), 93 (76). − HRMS (70 eV): $C_{31}H_{37}NO_3$: calcd. 471.2773; found 471.2761. − $C_{31}H_{37}NO_3$ (471.3): calcd. C 78.95, H 7.91, N 2.97; found C 77.81, H 7.96, N 2.82.

3-[2-(3-Methoxyphenyl)-5,5-dimethyloxazol-4-ylidene]androsta-1,4-dien-17-one (2b): Yield 0.12 g (0.25 mmol, 30%) yellow mass, glass-like, T_g = 49 °C, mixture of diastereomers (*E/Z* = 1:0.9). − IR (KBr): ν = 2933, 1740 (C=O), 1664 (C=N), 1599, 1553, 1491, 1461, 1373, 1333, 1306, 1238, 1225, 1136, 1045, 942, 867, 794, 731, 683 cm^{-1}. − UV/Vis (dioxane): λ_{max} (lgε) = 279 (4.06), 368 (4.14), 386 (4.16), 408 (4.02) sh, 434 nm (3.64) sh. − ^1H NMR ($CDCl_3$, DRX-400): δ = 0.89 (s, 3 H, 18-CH_3), 1.16 (s, 3 H, 19-CH_3), 1.66 (s, 6 H, CH_3), 3.84 (s, 3 H, OCH_3), 5.81 [d, ^3J = 10.1 Hz, 1 H, 1-H (*E*)], 5.83 [d, ^3J = 10.1 Hz, 1 H, 1-H (*Z*)], 6.07 [s, 1 H, 4-H (*E*)], 6.31 [dd, ^3J = 10.1, ^4J = 1.7 Hz, 1 H, 2-H (*Z*)], 6.81 [s, 1 H, 4-H (*Z*)], 6.96−6.98 (m, 1 H, aromat), 7.04 [dd, 1 H, ^3J = 10.1, ^4J = 1.4, 2-H (*E*)], 7.26−7.33 (m, 1 H, aromat), 7.51−7.54 (m, 1 H, aromat), 7.57−7.62 (m, 1 H, aromat). − ^{13}C NMR ($CDCl_3$, DRX-400): δ = 13.83 (C-18), 20.64 (C-19), 20.74, 21.79 (2 × CH_2), 27.00 (CH_3), 31.77, 32.26, 32.94 (3 × CH_2), 35.59 (C-8), 35.74 (CH_2), 41.41 (C-10), 47.80 (C-13), 50.92 (C-14), 52.97 (C-9), 55.41 (OCH_3), 87.13 (C-5′), 112.44 (C-2′′), 115.30 [C-4 (*E*)], 116.78 (C-3), 117.35 [C-4 (*Z*)], 118.04 (C-4′′), 119.91 [C-2 (*Z*)], 120.69 (C-6′′), 122.09 [C-2 (*E*)], 129.20 (C-1′′), 129.37 (C-5′′), 133.97 [C-1 (*E*)], 135.97 [C-1 (*Z*)], 145.29 [C-5 (*Z*)], 146.93 [C-5 (*E*)], 149.87 (C-4′), 159.44 (C-3′′), 164.13 (C-2′), 220.95 (C-17). − MS (DCI with H_2O): *m/z* (%) = 472 (100) [M^+ + H], 456 (19) [M^+ − CH_3], 269 (56), 251 (17), 220 (38), 205 (29), 183 (38), 153 (27), 134 (58), 113 (44), 99 (56). − HRMS (70 eV): $C_{31}H_{37}NO_3$: calcd. 471.2773; found 471.2802. − $C_{31}H_{37}NO_3$ (471.3): calcd. C 78.95, H 7.91, N 2.97; found C 77.91, H 7.97, N 2.85.

3-[2-(2-Methoxyphenyl)-5,5-dimethyloxazol-4-ylidene]androsta-1,4-dien-17-one (2c): Yield 0.10 g (0.21 mmol, 25%), yellow solid, m.p. glasslike. − IR (KBr): ν = 2926, 1736 (C=O), 1661 (C=N), 1599, 1581, 1542, 1532, 1494, 1460, 1437, 1375, 1311, 1257, 1164, 1138, 1123, 1055, 1022, 945, 748 cm^{-1}. − UV/Vis (dioxane): λ_{max} (lgε) =

285 (4.06), 354 nm (4.23). – ^{1}H NMR ($CDCl_3$, DRX-400): δ = 0.88 (s, 3 H, 18-CH_3), 1.17 (s, 3 H, 19-CH_3), 1.65 (s, 6 H, CH_3), 3.90 (s, 3 H, OCH_3), 5.78 [d, 1 H, ^3J = 10.3, 1-H (*E*)], 5.81 [d, ^3J = 10.3 Hz, 1 H, 1-H (*Z*)], 6.06 [s, 1 H, 4-H (*E*)], 6.30 [dd, ^3J = 10.1, ^4J = 1.6 Hz, 1 H, 2-H (*Z*)], 6.77 [s, 1 H, 4-H (*Z*)], 6.93–6.97 (m, 2 H, aromat), 7.02 [dd, ^3J = 10.1, ^4J = 1.6 Hz, 1 H, 2-H (*E*)], 7.36–7.41 (m, 1 H, aromat), 7.82–7.86 (m, 1 H, aromat). – ^{13}C NMR ($CDCl_3$, DRX-400): δ = 13.83 (C-18), 20.60 (C-19), 20.70, 21.78 (2 × CH_2), 26.88 (CH_3), 31.39, 32.21, 32.91 (3 × CH_2), 35.58 (C-8), 35.75 (CH_2), 41.33 (C-10), 47.79 (C-13), 50.93 (C-14), 52.95 (C-9), 56.11 (OCH_3), 85.81 (C-5′), 111.94 (C-3′′), 115.39 [C-4 (*E*)], 116.72, 116.97 (C-1′′, C-3), 117.64 [C-4 (*Z*)], 120.00 [C-2 (*Z*)], 120.31 (C-5′′), 122.32 [C-2 (*E*)], 131.13 (C-6′′), 132.53 (C-4′′), 133.60 [C-1 (*E*)], 135.77 [C-1 (*Z*)], 144.77 [C-5 (*Z*)], 146.66 [C-5 (*E*)], 150.10 (C-4′), 158.91 (C-2′′), 163.28 (C-2′), 221.00 (C-17). – MS (DCI with H_2O): *m/z* (%) = 472 (66) [M^+ + H], 456 (12) [M^+ – CH_3], 254 (18), 220 (27), 153 (43), 135 (100), 102 (83), 75 (48). – HRMS (70 eV): $C_{31}H_{37}NO_3$: calcd. 471.2773; found 471.2798. – $C_{31}H_{37}NO_3$ (471.3): calcd. C 78.95, H 7.91, N 2.97; found C 77.43, H 7.80, N 2.93.

3-[2-(4-Chlorophenyl)-5,5-dimethyloxazol-4-ylidene]androsta-1,4-dien-17-one (2d): Yield 0.17 g (0.365 mmol, 43%) yellow solid, m.p. glasslike. – IR (KBr): ν = 2931, 1739 (C=O), 1664 (C=N), 1626, 1594, 1577, 1548, 1489, 1458, 1403, 1369, 1338, 1308, 1296, 1136, 1090, 1065, 1014, 943, 840, cm^{-1}. – UV/Vis (dioxane): λ_{max} (lgε) = 250 (4.15), 266 (4.16), 280 (4.16), 373 (4.22), 393 (4.24), 416 (4.12) sh, 444 nm (3.76) sh. – ^{1}H NMR ($CDCl_3$, DRX-400): δ = 0.90 (s, 3 H, 18-CH_3), 1.17 (s, 3 H, 19-CH_3), 1.76 (s, 6 H, CH_3), 5.83 [d, ^3J = 10.1 Hz, 1 H, 1-H (*E*)], 5.85 [d, ^3J = 10.1 Hz, 1 H, 1-H (*Z*)], 6.06 [s, 1 H, 4-H (*E*)], 6.30 [dd, ^3J = 10.1, ^4J = 1.7 Hz, 1 H, 2-H (*Z*)], 6.78 [s, 1 H, 4-H (*Z*)], 7.01 [dd, ^3J = 10.1, ^4J = 1.6 Hz, 1 H, 2-H (*E*)], 7.34–7.36 (m, 2 H, aromat), 7.91–7.95 (m, 2 H, aromat). – ^{13}C NMR ($CDCl_3$, DRX-400): δ = 13.83 (C-18), 20.58 (C-19), 20.70, 21.79 (2 × CH_2), 26.95 (CH_3), 31.38, 32.25, 32.57 (3 × CH_2), 35.58 (C-8), 35.74 (CH_2), 41.46 (C-10), 47.79 (C-13), 50.92 (C-14), 52.97 (C-9), 87.41 (C-5′), 115.21 [C-4 (*E*)], 117.10 (C-3), 117.24 [C-4 (*Z*)], 119.81 [C-2 (*Z*)], 121.97 [C-2 (*E*)], 126.43 (C-1′′), 128.63 (C-3′′), 129.40 (C-2′′), 134.28 [C-1 (*E*)], 136.27 [C-1 (*Z*)], 137.44 (C-4′′), 145.64 [C-5 (*Z*)], 147.28 [C-5 (*E*)], 149.53 (C-4′), 163.20 (C-2′), 220.92 (C-17). – MS (DCI with H_2O): *m/z* (%) = 476 (81) [M^+ + H], 460 (15) [M^+ – CH_3], 391 (18), 279 (19), 235 (89), 224 (70), 183 (41), 157 (22), 127 (55), 113 (84), 99 (96), 85 (100), 71 (68). – HRMS (70 eV): $C_{30}H_{34}ClNO_2$: calcd. 475.2278; found 475.2315.

3-[2-(4-Fluorophenyl)-5,5-dimethyloxazol-4-ylidene]androsta-1,4-dien-17-one (2e): Yield 0.16 g (0.33 mmol, 39%) yellow solid, m.p.: glasslike. – IR (KBr): ν = 2936, 1737 (C=O), 1665 (C=N), 1627, 1604, 1556, 1506, 1458, 1418, 1368, 1339, 1290, 1228, 1152, 1090, 1066, 943, 848, 810, 740 cm^{-1}. – UV/Vis (dioxane): λ_{max} (lgε) = 237 (4.07), 262 (4.03), 276 (4.04), 366 (4.14), 383 (4.14), 405 (4.00) sh, 434 nm (3.59) sh. – ^{1}H NMR ($CDCl_3$, DRX-400): δ = 0.90 (s, 3 H, 18-CH_3), 1.17 (s, 3 H, 19-CH_3), 1.66 (s, 6 H, CH_3), 5.82 [d, ^3J = 10.1 Hz, 1 H, 1-H (*E*)], 5.83 [d, ^3J = 10.1 Hz, 1 H, 1-H (*Z*)], 6.06 [s, 1 H, 4-H (*E*)], 6.30 [dd, ^3J = 10.1, ^4J = 1.7 Hz, 1 H, 2-H (*Z*)], 6.78 [s, 1 H, 4-H (*Z*)], 7.01 [dd, ^3J = 10.1, ^4J = 1.4 Hz, 1 H, 2-H (*E*)], 7.04–7.10 (m, 2 H, aromat), 7.97–8.03 (m, 2 H, aromat). – ^{13}C NMR ($CDCl_3$, DRX-400): δ = 13.84 (C-18), 20.63 (C-19), 20.74, 21.79 (2 × CH_2), 26.95 (CH_3), 31.39, 32.18, 32.64 (3 × CH_2), 35.59 (C-8), 35.74 (CH_2), 41.42 (C-10), 47.79 (C-13), 50.92 (C-14), 52.98 (C-9), 87.35 (C-5′), 115.22 [C-4 (*E*)], 115.54 (C-3′′, $^2J_{C-F}$ = 22.0), 116.73 (C-3), 117.26 [C-4 (*Z*)], 119.83 [C-2 (*Z*)], 121.99 [C-2 (*E*)], 125.28 (C-1′′), 130.37 (C-2′′, $^3J_{C-F}$ = 8.2), 134.07 [C-1 (*E*)], 136.01 [C-1 (*Z*)], 145.41 [C-5 (*E*)], 146.99 [C-5 (*Z*)], 149.64 (C-4′), 163.32 (C-2′), 164.70 (C-4′′, $^1J_{C-F}$ = 256.6), 220.93 (C-17). – MS (DCI with H_2O): *m/z* (%) = 460 (89) [M^+ + H], 444 (16) [M^+ – CH_3], 295 (15), 269 (43), 253 (15), 224 (60), 208 (90), 141 (43), 123 (100), 93 (41). – HRMS (70 eV): $C_{30}H_{34}FNO_2$: calcd. 459.2574; found 459.2592.

3-[2-(4-Dimethylaminophenyl)-5,5-dimethyloxazol-4-ylidene]androsta-1,4-dien-17-one (2f): Yield 0.10 g (0.22 mmol, 26%) yellow solid, m.p. glasslike. – IR (KBr): ν = 2932, 1739 (C=O), 1663 (C=N), 1609, 1567, 1518, 1446, 1365, 1300, 1192, 1137, 1068, 1005, 945, 822, 709 cm^{-1}. – UV/Vis (dioxane): λ_{max} (lgε) = 233 (4.02), 270 (4.02), 281 (4.11), 333 (4.28), 378 (4.58), 395 (4.57), 418 (4.38) sh, 446 nm (3.89) sh. – ^{1}H NMR ($CDCl_3$, DRX-400): δ = 0.89 (s, 3 H, 18-CH_3), 1.16 (s, 3 H, 19-CH_3), 1.63 (s, 6 H, CH_3), 3.01 [s, 6 H, $N(CH_3)_2$], 5.74 [d, ^3J = 10.1 Hz, 1 H, 1-H (*E*)], 5.75 [d, ^3J = 10.1 Hz, 1 H, 1-H (*Z*)], 6.05 [s, 1 H, 4-H (*E*)], 6.30 [dd, ^3J = 10.1, ^4J = 1.8 Hz, 1 H, 2-H (*Z*)], 6.63–6.66 (m. 2 H, aromat), 6.78 [s, 1 H, 4-H (*Z*)], 7.01 [dd, ^3J = 10.1, ^4J = 1.8 Hz, 1 H, 2-H (*E*)], 7.83–7.89 (m, 2 H, aromat). – ^{13}C NMR ($CDCl_3$, DRX-400): δ = 13.83 (C-18), 20.61 (CH_2), 20.76 (C-19), 21.79 (CH_2), 26.98 (CH_3), 31.41, 32.14, 32.63 (3 × CH_2), 35.64 (C-8), 35.77 (CH_2), 40.11 [$N(CH_3)_2$], 41.24 (C-10), 47.82 (C-13), 50.97 (C-14), 53.02 (C-9), 86.40 (C-5′), 111.07 (C-3′′), 114.55, 114.97 (C-1′′, C-3), 115.58 [C-4 (*E*)], 117.55 [C-4 (*Z*)], 120.22 [C-2 (*Z*)], 122.30 [C-2 (*E*)], 129.73 (C-2′′), 132.80 [C-1 (*E*)], 134.37 [C-1 (*Z*)], 143.96 [C-5 (*Z*)], 145.22 [C-5 (*E*)], 150.91 (C-4′), 152.37 (C-4′′), 165.18 (C-2′), 221.10 (C-17). – MS (DCI with H_2O): *m/z* (%) = 485 (100) [M^+ + H], 469 (10) [M^+ – CH_3], 233 (17), 220 (54), 148 (11). – HRMS (70 eV): $C_{32}H_{40}N_2O_2$ calcd.: 484.3090; found 484.3069.

3-[2-(4-Nitrophenyl)-5,5-dimethyloxazol-4-ylidene]androsta-1,4-dien-17-one (2g): Yield 0.36 g (0.74 mmol, 88%) red solid, glasslike, T_g = 180 °C. – IR (KBr): ν = 2933, 1733 (C=O), 1630 (C=N), 1593, 1543, 1522, 1455, 1344 (NO_2), 1309, 1259, 1135, 1107, 1067, 1010, 942, 859, cm^{-1}. – UV/Vis (dioxane): λ_{max} (lgε) = 298 (4.41), 447 (4.31), 466 (4.29)$_{sh}$. – ^{1}H NMR ($CDCl_3$, DRX-400): δ = 0.90 (s, 3 H, 18-CH_3), 1.18 (s, 3 H, 19-CH_3), 1.68 (s, 6 H, CH_3), 5.90 [d, ^3J = 10.2 Hz, 1 H, 1-H (*E*)], 5.92 [d, ^3J = 10.1 Hz, 1 H, 1-H (*Z*)], 6.08 [s, 1 H, 4-H (*E*)], 6.32 [dd, ^3J = 10.1, ^4J = 1.8 Hz, 1 H, 2-H (*Z*)], 6.82 [s, 1 H, 4-H (*Z*)], 7.03 [dd, ^3J = 10.2, ^4J = 1.7 Hz, 1 H, 2-H (*E*)], 8.12–8.17 (m, 2 H, aromat), 8.23–8.28 (m, 2 H, aromat). – ^{13}C NMR ($CDCl_3$, DRX-400): δ = 13.83 (C-18), 20.52 (C-19), 20.79, 21.79 (2 × CH_2), 26.98 (CH_3), 31.37, 32.28, 32.64 (3 × CH_2), 35.56 (C-8), 35.72 (CH_2), 41.70 (C-10), 47.77 (C-13), 50.89 (C-14), 52.97 (C-9), 88.08 (C-5′), 115.13 [C-4 (*E*)], 117.17 [C-4 (*Z*)], 118.95 (C-3), 119.67 [C-2 (*Z*)], 121.86 [C-2 (*E*)], 123.57 (C-3′′), 128.79 (C-2′′), 133.74 (C-1′′), 135.32 [C-1 (*E*)], 137.59 [C-1 (*Z*)], 146.85 [C-5 (*Z*)], 148.79 [C-5 (*E*)], 149.14, 149.16 (C-4′, C-4′′), 161.79 (C-2′), 220.76 (C-17). – MS (DCI with H_2O): *m/z* (%) = 487 (7) [M^+ + H], 235 (14), 93 (100). – HRMS (70 eV): $C_{30}H_{34}N_2O_4$: calcd. 486.2519; found 486.2527.

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