Supplementary Material

Highly efficient, solvent-free esterification of testosterone promoted by a recyclable polymer-supported tosyllic acid catalyst under microwave irradiation

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Table S1. Analytical HPLC conditions of different testosterone esters by Chiralcel OD-H (Daicel) column

| Compound | Ratio of n-hexane to 2-propanol<sup>b</sup> | Retention time [min] |
|----------|--------------------------------------------|----------------------|
|          | 85:15                                      | 12.482               |
|          | 90:10                                      | 18.810               |
|          | 95:5                                       | 40.468               |
|          | 85:15                                      | 12.792               |
|          | 90:10                                      | 16.736               |
|          | 95:5                                       | 26.785               |
|          | 85:15                                      | 11.618               |
|          | 85:15                                      | 10.752               |
|          | 85:15                                      | 8.715                |
|          | 85:15                                      | 8.372                |

<sup>a</sup> The samples were carried out at 254 nm and 30 °C. The elution velocity was set at 0.8 mL/min.
Testosterone (1):

$^1$H NMR spectrum of 1 (500 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of 1 (126 MHz, CDCl$_3$)
HRMS spectrum of 1 (ESI-TOF)

IR spectrum of 1 (Mineral oil, Nujol)
HPLC chromatogram of 1

HPLC conditions: \( n\)-hexane-2-ProH (85:15, \( v/v \)); \( f=0.8\) mL/min; \( \lambda=254\) nm; \( p=3.3\) MPa

| Peak# | Ret. Time (min) | Area (a.u.) | Height (a.u.) | Area % | Height % |
|-------|----------------|-------------|---------------|--------|---------|
| 1     | 12.482         | 21085669    | 838158        | 100.000 | 100.000 |
| Total |                | 21085669    | 838158        | 100.000 | 100.000 |

HPLC conditions: \( n\)-hexane-2-ProH (90:10, \( v/v \)); \( f=0.8\) mL/min; \( \lambda=254\) nm; \( p=3.2\) MPa

| Peak# | Ret. Time (min) | Area (a.u.) | Height (a.u.) | Area % | Height % |
|-------|----------------|-------------|---------------|--------|---------|
| 1     | 18.810         | 24678063    | 528516        | 100.000 | 100.000 |
| Total |                | 24678063    | 528516        | 100.000 | 100.000 |
HPLC conditions: \( n\)-hexane-2-ProH (95:5, v/v); \( f=0.8 \text{ mL/min} \); \( \lambda=254 \text{ nm} \); \( p=3.0 \text{ MPa} \)

| Peak# | Ret. Time | Area  | Height | Area %  | Height % |
|-------|-----------|-------|--------|---------|----------|
| 1     | 40.468    | 18423378 | 182495 | 100.000 | 100.000  |
| Total |           | 18423378 | 182495 | 100.000 | 100.000  |
Testosterone acetate (2a):

$^1$H NMR spectrum of 2a (500 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of 2a (126 MHz, CDCl$_3$)
HRMS spectrum of 2a (ESI-TOF)

IR spectrum of 2a (Mineral oil, Nujol)
UV/VIS spectrum of 2a (EtOH)

| Wavelength (nm) | Abs   |
|-----------------|-------|
| 245.00          | 4.807 |
| 242.00          | 4.928 |
| 240.00          | 4.850 |
| 237.00          | 4.781 |
| 235.00          | 4.776 |
HPLC chromatograms of 2a

2a (93% purity) obtained after DMAP-catalyzed reaction (Method A).

Acetyl chloride (1.5 equiv), Et₃N (1.5 equiv), DMAP (cat.).

dry CH₂Cl₂, 24 h at 25 °C (magnetic stirring)

METHOD A

| Peak | Ret. Time | Abs. | Height | Area % | Height % |
|------|-----------|------|--------|--------|----------|
| 1    | 13.72     | 29039718 | 1224494 | 92.847 | 94.317   |
| 1    | 15.54     | 3000766  | 17147   | 7.153  | 5.683    |
| Total| 294.6853  | 1195488  | 801.980 | 100.00 | 100.00   |
2a (97% purity) obtained after TsOH-catalyzed reaction (normal mode) (Method B).

Acetyl chloride (1.1 equiv), imm. p-TsOH (0.04 equiv).

CH₂Cl₂, 24 h at 25 °C (magnetic stirring) (METHOD B)
2a (91% purity) obtained after TsOH-catalyzed reaction (5 min MW mode) (Method C).

2a (94% purity) obtained after TsOH-catalyzed reaction (2.5 min MW mode) (Method C).
Testosterone propionate (2b):

$^1$H NMR spectrum of 2b (500 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of 2b (126 MHz, CDCl$_3$)
HRMS spectrum of 2b (ESI-TOF)

IR spectrum of 2b (Mineral oil, Nujol)
UV/VIS spectrum of 2b (EtOH)

| Wavelength (nm) | Abs  |
|-----------------|------|
| 251.00          | 4.840|
| 249.00          | 5.128|
| 247.00          | 5.145|
| 244.00          | 5.288|
| 239.00          | 5.238|
| 237.00          | 5.088|
| 235.00          | 4.961|
| 230.00          | 5.007|
| 227.00          | 4.960|
| 225.00          | 4.886|
HPLC chromatograms of 2b

2b (>99% purity) obtained after DMAP-catalyzed reaction (Method A).

[Diagram showing reaction and chromatogram]

2b (90% purity) obtained after TsOH-catalyzed reaction (normal mode) (Method B).

[Diagram showing reaction and chromatogram]
2b (97% purity) obtained after TsOH-catalyzed reaction (5 min MW mode) (Method C).

2b (98% purity) obtained after TsOH-catalyzed reaction (2.5 min MW mode) (Method C).
Testosterone butanoate (2c):

$^1$H NMR Spectrum of 2c (500 MHz, CDCl$_3$)

$^{13}$C NMR Spectrum of 2c (126 MHz, CDCl$_3$)
HRMS spectrum of 2c (ESI-TOF)

IR spectrum of 2c (Mineral oil, Nujol)
UV/VIS spectrum of 2c (EtOH)

| Wavelength (nm) | Abs  |
|----------------|------|
| 246.00         | 10.000 |
| 244.00         | 6.084  |
| 238.00         | 5.754  |
| 236.00         | 5.259  |
| 233.00         | 5.509  |
| 231.00         | 5.227  |
| 228.00         | 5.068  |
HPLC chromatograms of 2c

2c (97% purity) obtained after DMAP-catalyzed reaction (Method A).

2c (98% purity) obtained after TsOH-catalyzed reaction (normal mode) (Method B).
2c (98% purity) obtained after TsOH-catalyzed reaction (5 min MW mode) (Method C).

\[
\text{Butanoyl chloride (3.0 equiv), imm. p-TsOH (0.025 equiv).} \\
\text{5 min at 100 } ^\circ \text{C} \\
\text{(MW irradiation, 200 W) (METHOD C)}
\]

**Table**

| Peak | Ret. Time | Area | Height | Area % | Height % |
|------|-----------|------|--------|--------|----------|
| 1    | 0.740     | 18451| 32117  | 1.289  | 2.096    |
| 2    | 1.013     | 29650| 8862   | 3.345  | 0.851    |
| 3    | 1.000     | 10307| 3222   | 1.201  | 0.405    |
| 4    | 1.290     | 5068  | 3284   | 1.289  | 0.185    |
| 5    | 1.071     | 507080| 231264| 10.353 | 5.402    |
| Total| 2900461   | 227221| 111.093| 53.600 |

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2c (98% purity) obtained after TsOH-catalyzed reac. (2.5 min MW mode) (Method C).

\[
\text{Butanoyl chloride (3.0 equiv), imm. p-TsOH (0.025 equiv).} \\
\text{5 min at 100 } ^\circ \text{C} \\
\text{(MW irradiation, 200 W) (METHOD C)}
\]

**Table**

| Peak | Ret. Time | Area | Height | Area % | Height % |
|------|-----------|------|--------|--------|----------|
| 1    | 1.046     | 6137 | 4246   | 1.272  | 0.206    |
| 2    | 1.087     | 245632| 193754 | 10.365 | 90.674   |
| 3    | 1.371     | 122021| 4912   | 0.493  | 0.452    |
| 4    | 1.358     | 20941 | 1078   | 1.092  | 0.513    |
| Total| 2184414   | 1302306| 100.183| 100.000|
Testosterone decanoate (2d):

$^1$H NMR spectrum of 2d (500 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of 2d (126 MHz, CDCl$_3$)
HRMS spectrum of 2d (ESI-TOF)

IR spectrum of 2d (Mineral oil, Nujol)
UV/VIS spectrum of 2d (EtOH)

| Wavelength (nm) | Abs  |
|-----------------|------|
| 241.00          | 4.401|
| 239.00          | 4.407|
HPLC chromatograms of 2d

**2d (99% purity) obtained after DMAP-catalyzed reaction (Method A).**

Decanoyl chloride (1.5 equiv), Et₃N (1.5 equiv), DMAP (cat.), dry CH₂Cl₂, 24 h at 25 °C (magnetic stirring) (METHOD A)

**2d (95% purity) obtained after TsOH-catalyzed reaction (normal mode) (Method B).**

Decanoyl chloride (1.1 equiv), imm. p-TsOH (0.04 equiv), CH₂Cl₂, 24 h at 25 °C (magnetic stirring) (METHOD B)
2d (95% purity) obtained after TsOH-catalyzed reaction (5 min MW mode) (Method C).

Decanoyl chloride (3.0 equiv), Imm. p-TsOH (0.025 equiv).

5 min at 100 °C
(MW irradiation, 200 W) (METHOD C)

Decanoyl chloride (3.0 equiv), Imm. p-TsOH (0.025 equiv).

2.5 min at 100 °C
(MW irradiation, 200 W) (METHOD C)

2d (98% purity) obtained after TsOH-catalyzed reaction. (2.5 min MW mode) (Method C).
**Testosterone laurate (2e):**

$^1$H NMR Spectrum of 2e (500 MHz, CDCl$_3$)

$^{13}$C NMR Spectrum of 2e (126 MHz, CDCl$_3$)
HRMS spectrum of 2e (ESI-TOF)

IR spectrum of 2e (Mineral oil, Nujol)
UV/VIS spectrum of 2e (EtOH)

| Wavelength (nm) | Abs  |
|-----------------|------|
| 240.00          | 4.193|
HPLC chromatograms of 2e

2e (>99% purity) obtained after DMAP-catalyzed reaction (Method A).

2e (91% purity) obtained after TsOH-catalyzed reaction (normal mode) (Method B).
2e (97% purity) obtained after TsOH-catalyzed reaction (5 min MW mode) (Method C).

2e (97% purity) obtained after TsOH-catalyzed reac. (2.5 min MW mode) (Method C).