SUPPORTING INFORMATION for the article entitled

A mild method for the efficient, [3,3]-sigmatropic rearrangement of N,O-diacyl hydroxylamines

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General Methods

Melting points were determined using a hot stage melting point apparatus. Optical Rotations were obtained using an automatic polarimeter, using 1dm cell with chloroform as the solvent, at a wavelength of 589 nm (sodium D line), and are quoted as $\alpha_D$, concentration $c$ (g/100 mL) and recorded at room temperature. Proton nuclear magnetic resonance ($^1$H NMR) spectra were recorded on a 300 MHz or 400 MHz spectrometer. The $^1$H spectra were run in deuterchloroform (CDCl$_3$) with $\delta$ 7.26 (residual CHCl$_3$) used as an internal reference. Carbon nuclear magnetic resonance ($^{13}$C NMR) spectra were recorded at 75 MHz or at 100 MHz with a 300 MHz or 400 MHz spectrometer and were run in deuterchloroform (CDCl$_3$) solutions with $\delta$ 77.16 (CDCl$_3$ solvent resonance) used as an internal reference. Accurate mass determinations were made at high resolution on an accurate mass LC-TOF system; ESI Conditions: 6L/min N$_2$, 325 °C drying gas temp., capillary voltage: 3500v, Fragmentor voltage: 150v. Infrared (IR) spectra were recorded neat on a FTIR equipped with a diamond ATR (cm$^{-1}$ scale) and MCT detector. Analytical thin layer chromatography (TLC) was performed on silica gel 60 F$_{254}$. Detection was by UV light or stained using potassium permanganate dip. Flash Chromatography was performed using silica gel 60 (230-400 mesh).

Dichloromethane was distilled over P$_2$O$_5$. Triethylamine (NEt$_3$) was distilled over sodium wire. Trimethylsilyl trifluoromethanesulfonate (TMSOTf) and other commercially available reagents were purchased and used as received. All reactions were carried out under an argon atmosphere.

$N,O$-diacyl hydroxylamine starting materials were prepared according to the literature.$^1$
General [3,3] sigmatropic rearrangement procedure using a 1:1 ratio of TMSOTf to NEt₃: Preparation of 2-(methylamino)-2-oxo-1-phenylethyl benzoate (6a)

N-(benzoyloxy)-N-methyl-2-phenylacetamide (5a) (200 mg, 0.743 mmol) was dissolved in 3 mL dry DCM and the temperature lowered to -78 °C. To this, TMSOTf (135 μL, 0.743 mmol) was added, followed 5 min later by NEt₃ (104 μL, 0.743 mmol). After stirring at this temperature for 30 min, the reaction was removed from the cooling bath, allowed to warm to room temperature, sealed and left to stir overnight. The reaction was quenched by pouring directly onto a silica gel plug and eluted with EtOAc. Solvent removal in vacuo left a white solid which upon spectroscopic analysis, proved to be pure 6a (150 mg, 75%).

In all other examples where a mixture of products 6 and 7 were present, a crude ¹H NMR after the plug was used to determine product ratios. Then further column chromatography to separate the two products was undertaken.

General [3,3] sigmatropic rearrangement procedure using a 2:2 ratio of TMSOTf to NEt₃: Preparation of 3-methyl-2,5-diphenyl-2-(trimethylsilyloxy)oxazolidin-4-one (7a)

N-(benzoyloxy)-N-methyl-2-phenylacetamide (5a) (100 mg, 0.371 mmol) was dissolved in 1.5 mL dry DCM and the temperature lowered to -78 °C. To this, TMSOTf (135 μL, 0.743 mmol) was added, followed 5 min later by NEt₃ (104 μL, 0.743 mmol). After stirring at this temperature for 30 min, the reaction was removed from the cooling bath, allowed to warm to room temperature, sealed and left to stir overnight. The reaction was quenched by pouring directly onto a silica gel plug and eluted with EtOAc. Solvent removal in vacuo left a white solid which upon spectroscopic analysis, showed a 10:1 mixture of 7a:6a in a combined 90% yield. Column chromatography (20% EtOAc/Hexane) afforded 7a as a white solid (102 mg, 80%).
2-(methylamino)-2-oxo-1-phenylethyl benzoate (6a)

mp 142-143 ºC; \( ^1H \) NMR (300 MHz, CDCl\(_3\)) \( \delta \) 8.10-8.14 (2H, m), 7.28-7.65 (8H, m), 6.37 (1H, s), 6.20 (1H, brs), 2.90 (3H, d, \( J=4.8 \)); \( ^{13}C \) NMR (75 MHz, CDCl\(_3\)) 169.1, 165.1, 135.8, 133.8, 130.0, 129.5, 128.9, 128.8, 127.5, 76.1, 26.4; FT-IR \( \nu_{\max}/cm^{-1} \) 3311s, 3092w, 3065w, 3036w, 2949w, 1725vs, 1661vs, 1561s, 1496m, 1449m, 1315s, 1245vs, 1113s, 1025m, 985m, 708m, 683m; ESI-HRMS \( m/z \) 270.1124, 292.0947 (C\(_{16}\)H\(_{15}\)NO\(_3\) + H\(^+\) requires 270.1130, C\(_{16}\)H\(_{15}\)NO\(_3\) + Na\(^+\) requires 292.0950).

3-methyl-2,5-diphenyl-2-(trimethylsilyloxy)oxazolidin-4-one (7a)

mp 62-63 ºC; \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.20-7.62 (10H, m), 5.52 (1H, s), 2.70 (3H, s), 0.22 (9H, s); \( ^{13}C \) NMR (100 MHz, CDCl\(_3\)) 169.5, 139.5, 135.5, 129.5, 128.9, 128.7, 128.4, 127.0, 126.9, 126.8, 110.7, 78.6, 25.7, 1.2; FT-IR \( \nu_{\max}/cm^{-1} \) 3035w, 2957w, 1716s, 1424m, 1231m, 1090m, 1062m, 1035m, 869m, 839m, 760m, 698m; ESI-HRMS \( m/z \) 342.1519 (C\(_{19}\)H\(_{23}\)NO\(_3\)Si + H\(^+\) requires 342.1525).
2-(methylamino)-2-oxo-1-phenylethyl 2-phenylacetate (6b)

mp 91-93 ºC; \( ^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.26-7.40 (10H, m), 6.10 (1H, s), 5.73 (1H, brs), 3.76 (2H, s), 2.7 (3H, d, \( J=4.8 \)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) 169.5, 168.9, 135.5, 133.6, 129.4, 129.0, 129.0, 128.8, 127.6, 127.4, 75.7, 41.6, 26.1; FT-IR \( \nu_{\text{max}}/\text{cm}^{-1} \) 3302s, 3092w, 3064w, 3032w, 2947w, 2917w, 1732s, 1663vs, 1566m, 1498m, 1453m, 1410m, 1355m, 1191m, 1155s, 866m; ESI-HRMS \( m/z \) 284.1281 (C\(_{17}\)H\(_{17}\)NO\(_3\) + H\(^{+}\) requires 284.1287).

\[ \text{N} \]
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2-benzyl-3-methyl-5-phenyl-2-(trimethylsilyloxy)oxazolidin-4-one (7b)

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.16-7.26 (8H, m), 6.98-7.00 (2H, m), 5.25 (1H, s), 3.21 (2H, s), 2.97 (3H, s), 0.15 (9H, s); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) 170.3, 135.4, 134.6, 131.0, 130.5, 128.7, 128.6, 128.5, 128.4, 127.5, 127.2, 127.1, 111.6, 79.2, 45.7, 26.2, 1.1; FT-IR \( \nu_{\text{max}}/\text{cm}^{-1} \) 3089w, 3064m, 3032m, 2957m, 2930m, 2899m, 1719vs, 1453m, 1432s, 1395s, 1252s, 1162m, 1087s, 1070s, 1017m, 840s, 697m, 638m; ESI-HRMS \( m/z \) 356.1674 (C\(_{20}\)H\(_{25}\)NO\(_3\)Si + H\(^{+}\) requires 356.1682).
1-(methylamino)-1-oxopent-4-en-2-yl hex-5-enoate (6c)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.08 (1H, br), 5.84 (1H, dddd, $J_{1}=6.4$, $J_{2}=10.2$, $J_{3}=12.5$, $J_{4}=16.7$), 5.71 (1H, dddd, $J_{1}=7.1$, $J_{2}=10.2$, $J_{3}=14.2$, $J_{4}=17.1$), 5.27 (1H, dd, $J_{1}=4.7$, $J_{2}=7$), 5.06-5.13 (4H, m), 2.82 (3H, d, $J_{1}=3.8$), 2.65-2.71 (1H, m), 2.53-2.60 (1H, m), 2.48-2.52 (2H, m), 2.40-2.44 (2H, m); $^{13}$C NMR (100 MHz, CDCl$_3$) 171.6, 169.8, 136.7, 132.4, 118.9, 116.0, 73.2, 36.4, 33.6, 28.9, 26.0; FT-IR $\nu_{\text{max}}$/cm$^{-1}$ 3306br, 3080m, 2980m, 2942m, 1742vs, 1660vs, 1543s, 1370m, 1243m, 1160m, 918m, 843m; ESI-HRMS $m/z$ 212.1282 (C$_{11}$H$_{17}$NO$_3$ + H$^+$ requires 212.1287).

2-(benzylamino)-2-oxo-1-phenylethyl benzoate (6d)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.21–8.19 (15H, m), 6.46 (1H, br), 6.39 (1H, s), 4.56 (1H, dd, $J_{1}=5.8$, $J_{2}=15.2$), 4.48 (1H, dd, $J_{1}=5.9$, $J_{2}=15.2$).

3-benzyl-2,5-diphenyl-2-(trimethylsilyloxy)oxazolidin-4-one (7d)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.00–7.61 (15H, m) 5.60 (1H, s), 4.43 (1H, d, $J_{1}=15.2$ Hz), 4.21 (1H, d, $J_{1}=15.2$ Hz), 0.88 (s, 9H).
1-(benzylamino)-1-oxopropan-2-yl benzoate (6e)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.24–8.05 (10H, m), 6.46 (1H, br), 5.54 (1H, q, $J=6.9$), 4.51 (2H, dd, $J=2.0, 5.9$), 1.65 (3H, d, $J=6.6$).

3-benzyl-5-methyl-2-phenyl-2-(trimethylsilyloxy)oxazolidin-4-one (7e)

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.99–7.48 (10H, m), 4.71 (1H, q, $J=6.7$), 4.39 (1H, d, $J=15.2$), 4.10 (1H, d, $J=15.2$), 1.63 (3H, d, $J=6.8$), 0.83 (9H, s).

1-(benzylamino)-3-methyl-1-oxobutan-2-yl benzoate (6f)

mp 112-113 ºC; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.10-8.13 (1H, m), 8.06-8.08 (2H, m), 7.58-7.63 (1H, m), 7.45-7.49 (3H, m), 7.24-7.33 (3H, m), 5.38 (1H, d, $J=4$), 4.56 (1H, dd, $J=6, 14.8$), 4.44 (1H, dd, $J=6, 14.8$), 2.49-2.53 (1H, m), 1.07 (6H, dd, $J=7.2, 10.4$); $^{13}$C NMR (100 MHz, CDCl$_3$) 169.5, 165.7, 138.0, 133.8, 130.3, 129.9, 129.5, 128.9, 128.8, 128.6, 127.7, 127.7, 78.8, 43.4, 31.0, 19.1, 17.2; FT-IR $\nu_{\max}$/cm$^{-1}$ 3257m, 3090m,
1-(benzylamino)-1-oxopent-4-en-2-yl benzoate (6g)

mp 103-104 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.12 (1H, d, J=7.12), 8.03 (1H, d, J=7.8), 7.25-7.63 (8H, m), 6.40 (1H, br), 5.83 (1H, dddd, J=7.0, 10.2, 14.2, 17.1), 5.56 (1H, dd, J=4.9, 6.8), 5.18 (1H, dm, J=17.1), 5.12 (1H, dm, J=10.2), 4.56 (1H, dd, J=6, 15), 4.46 (1H, dd, J=6, 15), 2.74-2.88 (2H, m); ¹³C NMR (100 MHz, CDCl₃) δ 169.2, 165.3, 137.8, 133.7, 132.1, 130.2, 129.8, 129.3, 128.9, 128.5, 127.6, 119.2, 73.67, 43.3, 36.4; FT-IR νmax/cm⁻¹ 3306bdm, 3066m, 3033m, 2930 m, 1722vs, 1662s, 1602w, 1539m, 1452m, 1316w, 1267s, 1176w, 1110m, 1070m, 1027w, 922w, 711m; ESI-HRMS m/z 310.1440 (C₁₉H₁₉NO₃ + H⁺ requires 310.1443).

Preparation of 2-(tert-butylamino)-2-oxo-1-phenylethyl benzoate (6h):

N-(benzoyloxy)-N-tert-butyl-2-phenylacetamide (40 mg, 0.128 mmol) was dissolved in 1 mL dry DCM and the temperature lowered to -78 °C. To this, TMSOTf (47 μL, 0.257 mmol) was added, followed 5 min later by NEt₃ (36 μL, 0.257 mmol). After stirring at this temperature for 30 min, the reaction was warmed to room temperature, then heated to reflux and left overnight. The reaction was quenched by pouring directly onto a silica gel plug and eluted with EtOAc. Solvent removal in vacuo left an oil which upon spectroscopic analysis, showed approximately 25% conversion to 7h. A pure sample of 7h could not be obtained, even after extensive chromatography. Thus spectroscopic data reported here are for an impure sample with only selected resonances included (see scanned spectra for full details).
2-(tert-butylamino)-2-oxo-1-phenylethyl benzoate (6h)

$^1$H NMR (CDCl$_3$, 400 MHz) δ 7.27-8.10 (10H, m), 6.22 (1H, s), 5.97 (1H, brs), 1.37 (9H, s); $^{13}$C NMR (CDCl$_3$, 100 MHz) 167.3, 164.9, 76.1, 51.6, 28.7; ESI-HRMS $m/z$ 312.1594 (C$_{19}$H$_{22}$NO$_3$ + H$^+$ requires 312.1600).

(S)-(R)-2-(benzylamino)-2-oxo-1-phenylethyl 2-methoxy-2-phenylacetate (9)

mp 77-79 °C; [α]$_D^{25}$ = -40.0° (c 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) δ 7.26-7.32 (13H, m), 7.14-7.16 (2H, m), 6.20 (1H, br), 6.13 (1H, s), 4.89 (1H, s), 4.37 (2H, d, J=5.8), 3.40 (3H, s); $^{13}$C NMR (100 MHz, CDCl$_3$) 169.0, 168.0, 137.7, 135.7, 135.1, 129.1, 129.1, 128.9, 128.9, 128.8, 127.8, 127.2, 127.0, 82.83, 76.0, 57.8, 43.5; FT-IR $\nu_{\text{max}}$/cm$^{-1}$ 3297br, 3063m, 3031m, 2928s, 2829w, 1751v, 1661vs, 1530m, 1495m, 1453m, 1358w, 1259m, 1166s, 1103s, 1028m, 731m, 695s; ESI-HRMS $m/z$ 390.1699 (C$_{24}$H$_{23}$NO$_4$ + H$^+$ requires 390.1705).
(S)-((S)-2-(benzylamino)-2-oxo-1-phenylethyl) 2-methoxy-2-phenylacetate (10)

$\{\alpha\}_D^{25} = 58.9^\circ$ (c 1.0, CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.28-7.41 (12H, m), 7.20-7.23 (3H, m), 6.23 (1H, s), 5.80 (1H, br), 4.83 (1H, s), 4.24 (1H, dd, $J$=6, 14.8), 4.15 (1H, dd, $J$=6, 14.8), 3.38 (3H, s); $^{13}$C NMR (100 MHz, CDCl$_3$) 168.6, 168.0, 137.6, 135.9, 135.2, 129.2, 128.9, 128.8, 127.8, 127.7, 127.5, 127.2, 82.4, 75.6, 57.6, 43.3; FT-IR $\nu_{\text{max}}$/cm$^{-1}$ 3414s, 3308br, 3064m, 3032m, 2930s, 2830s, 1754vs, 1668vs, 1603s, 1527s, 1496s, 1454s, 1359s, 1243s, 1167s, 1109s, 1029w, 1002w, 734m, 697m; ESI-HRMS $m/z$ 390.1702 (C$_{24}$H$_{23}$NO$_4$ + H$^+$ requires 390.1705).

Procedure for diastereomeric product determination

$\text{N-benzyl-}$(S)-mandelamide (100 mg, 0.414 mmol), (S)-$(O$-methyl)mandelic acid (69 mg, 0.414 mmol), EDCI.HCl (240 mg, 1.243 mmol) and DMAP (152 mg, 1.243 mmol) were all combined and dissolved in 3 mL DCM. The reaction was left stirring overnight at room temperature, then quenched with water. The layers were separated, and the organics washed with 1M HCl, then brine. The solvent was removed in vacuo and the crude material was purified using column chromatography (40% EtOAc/Hexane) to give 10 in 85% yield. Spectral data was identical with that of the rearranged material.

References

$^1$H NMR (400 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)
$^1H$ NMR (400 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$) 9
$^{13}$C NMR (100 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^1$H NMR spectrum for a compound with a chemical structure diagram.