Electronic Supporting Information

Catalytic enantioselective synthesis of α-nitro epoxides via aminolytic kinetic resolution

Sara Meninno, Loris Napolitano and Alessandra Lattanzi*

Dipartimento di Chimica e Biologia, Università di Salerno, Via Giovanni Paolo II, 84084, Fisciano, Italy, e-mail:lattanzi@unisa.it

Table of contents

General Methods ........................................................................................................................................................................................................S2
Experimental Procedures and Compounds Characterization Data .................................................................S3
  General procedure for the epoxidation of nitroalkenes ..................................................................................S3
  General procedure for the aminolytic kinetic resolution (AKR) of racemic α-nitro epoxides ......S3
  General procedure for the kinetic resolution of 1a-(±) with thiol 5 ......................................................S3
  General procedure for the kinetic resolution of 1a-(±) with diamine 7 ............................................S4
  General procedure for one-pot stereoselective ring-opening/reduction sequence to amino alcohol 4a ........................................................................................................................................S4
References .............................................................................................................................................................S15
NMR Spectra ..........................................................................................................................................................S16
HPLC Chromatograms ..............................................................................................................................................S58
General Methods

All reactions requiring dry or inert conditions were conducted in flame dried glassware under a positive pressure of nitrogen. THF and DCM were freshly distilled prior to use respectively over LiAlH₄ and calcium hydride and stored under nitrogen, all other solvents were dried over molecular sieves. Molecular sieves (Aldrich Molecular Sieves, 3 Å, 1.6 mm pellets) were activated under vacuum at 200°C overnight. Reactions were monitored by thin layer chromatography (TLC) on Merck silica gel plates (0.25 mm) and visualised by UV light or by phosphomolybdic acid/ethanol spray test. Flash chromatography was performed on Merck silica gel (60, particle size: 0.040–0.063 mm). ¹H NMR and ¹³C NMR spectra were recorded on Bruker Avance-400 spectrometer, Bruker Avance-300 spectrometer and Bruker Avance-250 spectrometer at room temperature in CDCl₃ as solvent. Chemical shifts for protons are reported using residual CHCl₃ as internal reference (δ = 7.26 ppm). Carbon spectra were referenced to the shift of the ¹³C signal of CDCl₃ (δ = 77.0 ppm). Optical rotation of compounds was performed on a Jasco Dip-1000 digital polarimeter using the Na lamp (582 nm). FTIR spectra were recorded as thin films on KBr plates using Bruker Tensor 27 spectrometer and absorption maxima are reported in wavenumber (cm⁻¹). ESI-MS was performed using a Bio-Q triple quadrupole mass spectrometer (Micromass, Manchester, UK) equipped with an electrospray ion source. Elemental analyses were carried out by using Flash EA 1112 (Thermo Electron Corporation) analyzer. Melting points were measured with a Stuart Model SMP 30 melting point apparatus. Petrol ether (PE) refers to light petroleum ether (boiling point 40-60°C). Anhydrous toluene, dry methanol and all starting materials (unless otherwise noted) were purchased from Aldrich and used as received. Catalysts I, III were purchased from Aldrich and compound IV from Strem Chemicals and used as received. Catalysts II,¹ V,² VI,² VII² and VIII³ were prepared according to the literature. Enantiomeric excesses of α-nitroepoxides 1a, 1e-m and compound 4a were determined by HPLC (Waters-Breeze 2487, UV dual λ absorbance detector and 1525 Binary HPLC Pump) using Daicel chiral columns.
Experimental Procedures and Compounds Characterization Data

General procedure for the epoxidation of nitroalkenes
The (E)-α,β-disubstituted nitroalkenes were synthesized according to the literature.α-Nitroepoxides were prepared according to published procedures.β To a stirred ice-bath cold suspension of (E)-α,β-disubstituted nitroalkene (6 mmol) in methanol (12 mL) and hydrogen peroxide 50% aqueous solution (450 μL, 7.8 mmol), aqueous NaOH 2M (1.5 mL, 3 mmol) was added rapidly (ca. 5 minutes) with stirring. The reaction was stirred at 0°C for 1 h (5 h for compound 1h). Then, water was added (30 mL), extracted with diethyl ether (3 x 30 mL) and the combined ethereal extracts were washed with brine (40 mL), dried with Na₂SO₄ and concentrated under vacuum. The residue was purified by flash chromatography (PE/ diethyl ether 100:5) to give compounds 1a, 1e-m (13-72% yields).

General procedure for the aminolytic kinetic resolution (AKR) of racemic α-nitro epoxides
A sample vial was charged with nitroepoxide 1 (0.20 mmol) and catalyst VI (22.5 mg, 0.04 mmol) in anhydrous toluene (2 mL). Aniline (55 μL, 0.60 mmol) was added and the reaction stirred at room temperature for 84-115 h, monitored by TLC (eluent PE/ diethyl ether 95:5 or 90:10 and PE/ethyl acetate 90:10 only for compounds 1,3g and 1,3k). The enantioenriched α-nitroepoxides 1a, 1e-m and products 3a-3e-m were isolated by flash chromatography (eluting from PE/ diethyl ether 100:2 to 100:5 and to 80:20 only for compound 3m. In particular, aniline and α-amino ketone 3m have the same polarity. To remove aniline from the mixture of the two products, recovered after silica gel chromatography, the mixture was diluted with Et₂O and washed with water. As a general note, α-amino ketone 3 showed to be relatively unstable compounds and they have to be stored under nitrogen at low temperature.

General procedure for the kinetic resolution of 1a-(±) with thiol 5
A sample vial was charged with nitroepoxide 1a-(±) (17.9 mg, 0.10 mmol), K₂CO₃ (2.8 mg, 0.02 mmol) and catalyst VI (8.5 mg, 0.015 mmol) in anhydrous toluene (1 mL). Then, 2-naphthalenethiol (19.2 mg, 0.12 mmol) was added and the reaction stirred at room temperature for 70 h, monitored by TLC (eluent PE/ diethyl ether 95:5). The enantioenriched α-nitroepoxide 1a (4.5 mg, 25% yield) and product 6 (21.3 mg, 73% yield) were isolated by flash chromatography (eluting from PE/ diethyl ether 100:1 to 80:20).
General procedure for the kinetic resolution of 1a-(±) with diamine 7
A sample vial was charged with nitroepoxide 1a-(±) (26.9 mg, 0.15 mmol) and catalyst VI (12.7 mg, 0.022 mmol) in anhydrous toluene (1.5 mL). Then o-phenylenediamine (19.5 mg, 0.18 mmol) was added and the reaction was stirred at room temperature for 47 h, monitored by TLC (eluent PE/diethyl ether 95:5). The enantioenriched α-nitroepoxide 1a (8.6 mg, 32% yield) and product 8 (18.5 mg, 56% yield) were isolated by flash chromatography (eluting from PE/diethyl ether 100:2 to 90:10).

General procedure for one-pot stereoselective ring-opening/reduction sequence to amino alcohol 4a
To a solution of nitroepoxide 1a-(±) (22.6 mg, 0.126 mmol) in dry CHCl₃ (315 μL), pyrrolidine (21 μL, 0.252 mmol) was added at 0°C. The resulting mixture was stirred for 6 hours at 0 °C (TLC eluent PE/diethyl ether 95:5). After completion, dry MeOH (105 μL) was added at 0 °C, followed by dry CeCl₃ (31.1 mg, 0.126 mmol, finely ground CeCl₃•7H₂O dried at 100°C under vacuum overnight). The reaction mixture was stirred for 10 min at the same temperature and then NaBH₄ (4.8 mg, 0.126 mmol) was added. After stirring at 0 °C for 2.5 h, a second portion of NaBH₄ (4.8 mg, 0.126 mmol) and CeCl₃ (31.1 mg, 0.126 mmol) was added, and stirring continued for additional 3 h. After complete conversion of the ketone to the alcohol (TLC eluent ethyl acetate/MeOH 10 mL : 1 mL with 6 drops of NH₄OH, stained with permanganate) the reaction was quenched by diluting with brine (20 mL) and extracting with ethyl acetate (3x20 mL). The combined organic layers were washed with brine, dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. Purification by flash chromatography eluting with CH₂Cl₂ and then with diethyl ether afforded anti-1,2-amino alcohol 4a in 78% yield (20.2 mg). Absolute configuration of (1R,2S)-1-phenyl-1-(pyrrolidin-1-yl)propan-2-ol 4a was determined by comparison of optical rotation with the literature. The absolute configuration of α-nitroepoxide 1a was assigned to be (2R,3S) and the absolute configuration of α-nitroepoxides 1 was assigned to be (2R,3S) by analogy.
(2R, 3S)-2-Methyl-2-nitro-3-phenyloxirane (1a)

Data for this compound were consistent with those reported in the literature.\textsuperscript{5c}

Yellow oil, 10 mg, 28 % yield. $[\alpha]_D^{17} = -36.7$ (c 0.48, CHCl$_3$), $ee$ 72%. \textbf{FTIR} $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3066, 3035, 2947, 1558, 1451, 1357, 1159, 1107, 770, 754, 703, 602. \textbf{1H NMR} (CDCl$_3$, 400 MHz): $\delta$ 7.46-7.40 (m, 3H), 7.32-7.29 (m, 2H), 4.54 (s, 1H), 1.80 (s, 3H). \textbf{13C NMR} (CDCl$_3$, 100 MHz): $\delta$ 130.9, 129.4, 128.7, 126.4, 88.9, 62.6, 12.4. \textbf{HPLC} analysis with Chiralpak AS-H column, 95:5 n-hexane:2-propanol, 1 mL/min, 254 nm; minor enantiomer $t_R = 6.1$ min, major enantiomer $t_R = 6.8$ min.

(2R, 3S)-2-Methyl-2-nitro-3-p-tolyloxirane (1e)

Data for this compound were consistent with those reported in the literature.\textsuperscript{5c}

Yellow oil, 6.6 mg, 17% yield. $[\alpha]_D^{24} = -33.5$ (c 0.50, CHCl$_3$), $ee$ 84%. \textbf{FTIR} $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3028, 2925, 1559, 1452, 1346, 1159, 1106, 903, 848, 817, 772. \textbf{1H NMR} (CDCl$_3$, 300 MHz): $\delta$ 7.25-7.16 (m, 2H), 4.50 (s, 1H), 2.38 (s, 3H), 1.80 (d, 3H, $J = 1.3$ Hz). \textbf{13C NMR} (CDCl$_3$, 100 MHz): $\delta$ 139.5, 129.4, 127.9, 126.3, 89.0, 62.8, 21.3, 12.4. \textbf{MS} (ESI m/z) 216.5 [MNa$^+$, 12%]. \textbf{HPLC} analysis with Chiralpak IE-3 column, 98:2 n-hexane:2-propanol, 0.7 mL/min, 220 nm; minor enantiomer $t_R = 16.2$ min, major enantiomer $t_R = 14.2$ min.

(2R, 3S)-3-(4-Chlorophenyl)-2-methyl-2-nitrooxirane (1f)

White solid, 12.4 mg, 29% yield. Mp 55.9-57.9 °C. $[\alpha]_D^{22} = -53.8$ (c 0.65, CHCl$_3$), $ee$ 86%. \textbf{FTIR} $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 1561, 1495, 1436, 1352, 1159, 1091, 1015, 900, 763. \textbf{1H NMR} (CDCl$_3$, 400 MHz): $\delta$ 7.41 (d, 2H, $J = 8.2$ Hz), 7.25 (d, 2H, $J = 8.2$ Hz), 4.52 (s, 1H), 1.79 (s, 3H). \textbf{13C NMR} (CDCl$_3$, 100 MHz): $\delta$ 135.6, 129.4, 129.1, 127.8, 88.6, 62.0, 12.4. Elemental analysis calcd (%) for $C_9H_8ClNO_3$: C, 50.60; H, 3.77; N, 6.56; found C, 50.89; H, 3.97; N, 6.60. \textbf{HPLC} analysis with Chiralpak AS-H column, 90:10 n-hexane:2-propanol, 1 mL/min, 220 nm; minor enantiomer $t_R = 6.9$ min, major enantiomer $t_R = 7.5$ min.
(2R, 3S)-2-Methyl-2-nitro-3-(4-(trifluoromethyl)phenyl)oxirane (1g)

Yellow solid, 18 mg, 36% yield. **Mp** 58.2-62.6 °C. **[α]_D^{23}** = -30.9 (c 0.53, CHCl₃), ee 77%. **FTIR** νₘₐₓ (KBr)/cm⁻¹ 1561, 1325, 1167, 1127, 1067, 1019, 857, 832. **¹H NMR** (CDCl₃, 250 MHz): δ 7.69 (d, 2H, J = 8.1 Hz), 7.45 (d, 2H, J = 8.1 Hz), 4.61 (s, 1H), 1.78 (s, 3H). **¹³C NMR** (CDCl₃, 75 MHz): δ 134.9, 131.7 (q, ²J(C-C-F) = 32.8 Hz), 126.9, 125.9, 125.8, 123.6 (q, ¹J(C-F) = 271.0 Hz), 88.5, 61.8, 12.4. **MS** (ESI m/z) 285.6 [MK⁺, 20%]. Elemental analysis calcd (%) for C₁₀H₈F₃NO₃: C, 48.59; H, 3.26; N, 5.67; found C, 48.94; H, 3.48; N, 5.40. HPLC analysis with Chiralpak IE-3 column, 98:2 n-hexane:2-propanol, 0.7 mL/min, 220 nm; minor enantiomer tᵣ = 18.4 min, major enantiomer tᵣ = 13.2 min.

(2R, 3S)-2-Methyl-3-(naphthalen-2-yl)-2-nitrooxirane (1h)

Pale yellow solid, 11.9 mg, 26% yield. **Mp** 63.8-65.7 °C. **[α]_D^{20}** = -72.2 (c 0.67, CHCl₃), ee 95%. **FTIR** νₘₐₓ (KBr)/cm⁻¹ 3057, 2925, 1559, 1343, 1105, 893, 861, 821, 756. **¹H NMR** (CDCl₃, 300 MHz): δ 7.92-7.85 (m, 3H), 7.79 (s, 1H), 7.58-7.53 (m, 2H), 7.39 (dd, 1H, J₁ = 8.4 Hz, J₂ = 1.5 Hz), 4.71 (s, 1H), 1.83 (s, 3H). **¹³C NMR** (CDCl₃, 100 MHz): δ 133.6, 132.8, 128.8, 128.3, 128.0, 127.9, 126.9, 126.1, 123.2, 80.0, 62.9, 12.5. **MS** (ESI m/z) 230.0 [MH⁺, 6%], 248.6 [M+H₃O⁺, 38%]. Elemental analysis calcd (%) for C₁₃H₁₁NO₃: C, 68.11; H, 4.84; N, 6.11; found C, 68.44; H, 5.10; N, 6.24. HPLC analysis with Chiralpak IE-3 column, 98:2 n-hexane:2-propanol, 0.7 mL/min, 254 nm; minor enantiomer tᵣ = 24.7 min, major enantiomer tᵣ = 20.3 min.

(2R, 3S)-2-Ethyl-2-nitro-3-phenyloxirane (1i)

Yellow oil, 8 mg, 21% yield. **[α]_D^{22}** = -25.1 (c 0.67, CHCl₃), ee 92%. **FTIR** νₘₐₓ (KBr)/cm⁻¹ 2918, 1557, 1458, 1435, 1351, 938, 813, 768. **¹H NMR** (CDCl₃, 300 MHz): δ 7.44-7.38 (m, 3H), 7.33-7.29 (m, 2H), 4.52 (s, 1H), 2.55-2.41 (m, 1H), 1.69 (dq, 1H, J₁ = 15.1 Hz, J₂ = 7.3 Hz), 1.07 (t, 3H, J₁ = 7.4 Hz). **¹³C NMR** (CDCl₃, 100 MHz): δ 131.1, 129.4, 128.7, 126.3, 92.5, 63.2, 19.5, 7.6. **MS** (ESI m/z) 193.8 [MH⁺, 7%], 216.5 [MNa⁺, 15%]. Elemental analysis calcd (%) for C₁₀H₁₁NO₃: C, 62.17; H, 5.74; N, 7.25; found C, 62.46; H, 5.50; N, 7.48. HPLC analysis with Chiralpak IE-3
column, 98:2 n-hexane:2-propanol, 0.7 mL/min, 220 nm; minor enantiomer \( t_R = 13.7 \) min, major enantiomer \( t_R = 11.9 \) min.

\((2R, 3S)-2\text{-Ethyl-2-nitro-3-m-tolyloxirane (1j)}\)

![Structure](image)

Yellow oil, 12.8 mg, 31% yield. \([\alpha]_D^{23} = -30.6 \) (c 0.57, CHCl\(_3\)), ee 92%. FTIR \( \nu_{\text{max}} \) (KBr)/cm\(^{-1}\) 2984, 2945, 1559, 1462, 1435, 1351, 1152, 1083, 969, 815, 790. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 7.30 (t, 1H, \( J = 7.5 \) Hz), 7.23-7.18 (m, 1H), 7.12-7.07 (m, 2H), 4.47 (s, 1H), 2.48 (dq, 1H, \( J_1 = 15.1 \) Hz, \( J_2 = 7.4 \) Hz), 2.38 (s, 3H), 1.69 (dq, 1H, \( J_1 = 15.1 \) Hz, \( J_2 = 7.4 \) Hz), 1.08 (t, 3H, \( J = 7.4 \) Hz). \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \( \delta \) 138.6, 131.0, 130.1, 128.6, 126.9, 123.3, 92.6, 63.3, 21.4, 19.5, 7.6. MS (ESI \( m/z \) 207.9 [MH\(^+\)], 8%), 230.5 [MNa\(^+\), 10%]. Elemental analysis calcd (%) for C\(_{11}\)H\(_{13}\)NO\(_3\): C, 63.76; H, 6.32; N, 6.76; found C, 64.07; H, 6.53; N, 6.63. HPLC analysis with Chiralpak IE-3 column, 98:2 n-hexane:2-propanol, 0.7 mL/min, 254 nm; minor enantiomer \( t_R = 13.4 \) min, major enantiomer \( t_R = 11.6 \) min.

\((2R, 3S)-3-(4-Bromophenyl)-2\text{-ethyl-2-nitrooxirane (1k)}\)

White solid, 18.2 mg, 33% yield. \( \text{Mp} 59.6-60.3 \) °C. \([\alpha]_D^{21} = -29.0 \) (c 0.53, CHCl\(_3\)), ee 90%. FTIR \( \nu_{\text{max}} \) (KBr)/cm\(^{-1}\) 2984, 1557, 1489, 1463, 1434, 1346, 1071, 1011, 936, 808. \(^1\)H NMR (CDCl\(_3\), 300 MHz): \( \delta \) 7.56 (d, 2H, \( J = 8.4 \) Hz), 7.19 (d, 2H, \( J = 8.4 \) Hz), 4.48 (s, 1H), 2.46 (dq, 1H, \( J_1 = 15.1 \) Hz, \( J_2 = 7.4 \) Hz), 1.66 (dq, 1H, \( J_1 = 15.1 \) Hz, \( J_2 = 7.4 \) Hz), 1.07 (t, 3H, \( J = 7.4 \) Hz). \(^{13}\)C NMR (CDCl\(_3\), 100 MHz): \( \delta \) 132.0, 130.1, 127.9, 123.7, 92.2, 62.6, 19.5, 7.6. MS (ESI \( m/z \) 225.8 [M-H\(^+\)-NO\(_2\)], 5%), 261.7 [M-H\(^+\)-NO\(_2\)+2H\(_2\)O, 20%]. Elemental analysis calcd (%) for C\(_{10}\)H\(_{10}\)BrNO\(_3\): C, 44.14; H, 3.70; N, 5.15; found C, 43.87; H, 3.88; N, 5.37. HPLC analysis with Chiralpak IE-3 column, 98:2 n-hexane:2-propanol, 0.7 mL/min, 220 nm; minor enantiomer \( t_R = 17.4 \) min, major enantiomer \( t_R = 14.6 \) min.

\((2R, 3S)-3-(3,4-Dichlorophenyl)-2\text{-ethyl-2-nitrooxirane (1l)}\)

Yellow oil, 18.1 mg, 35% yield. \([\alpha]_D^{25} = -18.3 \) (c 0.76, CHCl\(_3\)), ee 61%. FTIR \( \nu_{\text{max}} \) (KBr)/cm\(^{-1}\) 2984, 2944, 1561, 1474, 1435, 1350, 1133, 1033, 944, 811. \(^1\)H NMR (CDCl\(_3\), 400 MHz): \( \delta \) 7.51 (d, 1H, \( J = 8.3 \) Hz), 7.40 (d, 1H, \( J = 1.9 \) Hz), 7.16 (dd, 1H, \( J_1 = 8.3 \) Hz, \( J_2 = 1.9 \) Hz), 4.48 (s, 1H), 2.46
(dq, 1H, $J_1 = 15.1$ Hz, $J_2 = 7.4$ Hz), 1.65 (dq, 1H, $J_1 = 15.1$ Hz, $J_2 = 7.4$ Hz), 1.09 (t, 3H, $J = 7.4$ Hz).

$^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ 133.8, 133.3, 131.3, 130.9, 128.2, 125.6, 92.0, 61.8, 19.5, 7.6. MS (ESI m/z) 251.6 [M$^+$-NO$_2$+2H$^+$, 100%]. Elemental analysis calcd (%) for C$_{10}$H$_9$Cl$_2$NO$_3$: C, 45.83; H, 3.46; N, 5.34; found C, 46.16; H, 3.24; N, 5.55. HPLC analysis with Chiralpak IE-3 column, 98:2 $n$-hexane:2-propanol, 0.7 mL/min, 254 nm; minor enantiomer $t_R = 17.3$ min, major enantiomer $t_R = 13.5$ min.

2-Methyl-2-nitro-3-phenethyloxirane (1m)

Yellow oil, 14.5 mg, 35% yield. $[\alpha]_D^{25} = -4.6$ (c 0.88, CHCl$_3$), ee 16%.

FTIR $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3027, 2924, 1557, 1496, 1455, 1388, 1357, 1112, 1083, 751, 699.

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.35-7.24 (m, 3H), 7.21-7.16 (m, 2H), 3.48 (t, 1H, $J = 6.3$ Hz), 2.95-2.87 (m, 1H), 2.83-2.74 (m, 1H), 2.06-1.95 (m, 1H), 1.93-1.83 (m, 1H), 1.74 (s, 3H).

$^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 139.6, 128.8, 128.3, 126.7, 62.4, 31.9, 29.8, 13.5. Elemental analysis calcd (%) for C$_{11}$H$_{13}$NO$_3$: C, 63.76; H, 6.32; N, 6.76; found C, 64.11; H, 6.58; N, 6.65. HPLC analysis with Chiralpak AS-H column, 99:1 $n$-hexane:2-propanol, 0.8 mL/min, 220 nm; minor enantiomer $t_R = 12.7$ min, major enantiomer $t_R = 11.5$ min.

1-Phenyl-1-(phenylamino)propan-2-one (3a)

Data for this compound were consistent with those reported in the literature.$^7$

Wax, 29.3 mg, 65% yield. $[\alpha]_D^{27} = +27.9$ (c 0.50, CHCl$_3$), ee 16%.

FTIR $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3393, 2863, 1714, 1600, 1505, 1312, 1230, 1165, 745, 692.

$^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.55-7.32 (m, 5H), 7.13-7.06 (m, 2H), 6.73-6.66 (m, 1H), 6.63-6.57 (m, 2H), 5.01 (brd, 1H), 2.14 (s, 3H).

$^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ 203.8, 145.4, 137.6, 129.7, 129.2, 129.1, 128.8, 127.8, 118.0, 113.7, 68.4, 26.7. MS (ESI m/z) 248.5 [MNa$^+$, 10%]. HPLC analysis with Chiralpak IE-3 column, 95:5 $n$-hexane:2-propanol, 0.7 mL/min, 254 nm; minor enantiomer $t_R = 18.8$ min, major enantiomer $t_R = 15.6$ min.
1-(naphthalen-1-ylamino)-1-phenylpropan-2-one (3b)

Red solid, 12.4 mg, 30% yield. Mp 81 °C (Decomp.). FTIR νmax (KBr)/cm⁻¹ 3415, 3064, 1715, 1625, 1582, 1526, 1476, 1365, 769, 701. ¹H NMR (CDCl₃, 400 MHz): δ 8.09 (d, 1H, J = 8.2 Hz), 7.76 (d, 1H, J = 8.0 Hz), 7.58-7.44 (m, 3H), 7.41-7.29 (m, 3H), 7.20-7.13 (m, 2H), 6.36-6.30 (m, 2H), 5.15 (d, 1H, J = 2.7 Hz), 2.20 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ 204.0, 140.9, 137.8, 134.3, 129.3, 128.6, 128.5, 127.8, 126.3, 125.8, 124.9, 123.4, 120.2, 117.6, 105.3, 68.2, 26.6. MS (ESI m/z) 276.7 [MH⁺, 28%], 298.6 [MNa⁺, 100%]. Elemental analysis calcd (%) for C₁₉H₁₇NO: C, 82.88; H, 6.22; N, 5.09; found C, 83.25; H, 6.47; N, 4.94.

1-(naphthalen-2-ylamino)-1-phenylpropan-2-one (3c)

Red solid, 12.8 mg, 31% yield. Mp 83 °C (Decomp.). FTIR νmax (KBr)/cm⁻¹ 3398, 3057, 1714, 1629, 1519, 1482, 1358, 1190, 827, 748, 701. ¹H NMR (CDCl₃, 400 MHz): δ 7.64-7.58 (m, 2H), 7.54-7.45 (m, 3H), 7.42-7.37 (m, 2H), 7.34-7.28 (m, 1H), 7.18-7.13 (m, 1H), 6.96 (dd, 1H, J₁ = 8.8 Hz, J₂ = 2.5 Hz), 6.63-6.60 (m, 2H), 5.61 (brs, 1H), 5.13 (d, 1H, J = 4.3 Hz), 2.18 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ 203.9, 143.5, 137.8, 134.8, 129.3, 129.0, 128.5, 127.8, 126.3, 125.9, 122.1, 118.1, 105.4, 68.1, 26.7. MS (ESI m/z) 276.7 [MH⁺, 26%], 298.6 [MNa⁺, 100%]. Elemental analysis calcd (%) for C₁₉H₁₇NO: C, 82.88; H, 6.22; N, 5.09; found C, 83.22; H, 6.50; N, 4.84.

1-(4-methoxyphenylamino)-1-phenylpropan-2-one (3d)

Ochre wax, 14.6 mg, 38% yield. FTIR νmax (KBr)/cm⁻¹ 3404, 1719, 1654, 1513, 1239, 1178, 1035, 820, 762, 701. ¹H NMR (CDCl₃, 300 MHz): δ 7.48-7.30 (m, 5H), 6.69 (d, 2H, J = 8.8 Hz), 6.50 (d, 2H, J = 8.8 Hz), 5.15 (brs, 1H), 4.93 (s, 1H), 3.68 (s, 3H), 2.12 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ 204.4, 152.1, 140.3, 138.3, 129.2, 128.3, 127.8, 114.8, 114.5, 69.1, 55.7, 26.7. MS (ESI m/z) 276.7 [MH⁺, 28%], 298.6 [MNa⁺, 100%]. Elemental analysis calcd (%) for C₁₉H₁₇NO: C, 82.88; H, 6.22; N, 5.09; found C, 83.22; H, 6.50; N, 4.84.
m/z) 255.7 [MH⁺, 13%], 278.0 [MNa⁺, 16%]. Elemental analysis calcd (%) for C₁₆H₁₇NO₂: C, 75.27; H, 6.71; N, 5.49; found C, 75.58; H, 7.00; N, 5.72.

1-(phenylamino)-1-p-tolylpropan-2-one (3e)

Red wax, 37.8 mg, 79% yield. FTIR νₘₚₓ(KBr)/cm⁻¹ 3422, 2921, 1707, 1668, 1496, 1444, 1314, 1159, 1113, 1030, 901, 823, 744. ¹H NMR (CDCl₃, 400 MHz): δ 7.32 (d, 2H, J = 7.7 Hz), 7.17 (d, 2H, J = 7.7 Hz), 7.13-7.06 (m, 2H), 6.72-6.66 (m, 1H), 6.64-6.58 (m, 2H), 4.99 (brs, 1H), 2.33 (s, 3H), 2.13 (s, 3H). ¹³C NMR (CDCl₃, 75 MHz): δ 204.2, 145.8, 138.2, 134.8, 130.4, 129.9, 129.5, 129.1, 127.6, 117.6, 113.3, 67.8, 26.6, 21.1. MS (ESI m/z) 240.8 [MH⁺, 10%], 262.8 [MNa⁺, 14%]. Elemental analysis calcd (%) for C₁₆H₁₇NO: C, 80.30; H, 7.16; N, 5.85; found C, 79.98; H, 7.41; N, 6.06.

1-(4-chlorophenyl)-1-(phenylamino)propan-2-one (3f)

Red wax, 34.9 mg, 67% yield. FTIR νₘₚₓ(KBr)/cm⁻¹ 3449, 1715, 1670, 1601, 1542, 1500, 1489, 1441, 1315, 1162, 1091, 836, 752, 693. ¹H NMR (CDCl₃, 400 MHz): δ 7.46-7.33 (m, 4H), 7.14-7.07 (m, 2H), 6.70-6.66 (m, 1H), 6.55-6.50 (m, 2H), 4.98 (brs, 1H), 2.14 (s, 3H). ¹³C NMR (CDCl₃, 100 MHz): δ 203.2, 145.5, 136.6, 131.7, 129.4, 129.2, 129.1, 117.9, 113.3, 67.4, 26.6. MS (ESI m/z) 260.5 [MH⁺, 37%], 282.5 [MNa⁺, 10%]. Elemental analysis calcd (%) for C₁₅H₁₄ClNO: C, 69.36; H, 5.43; N, 5.39; found C, 69.70; H, 5.60; N, 5.21.

1-(phenylamino)-1-(4-(trifluoromethyl)phenyl)propan-2-one (3g)
Yellow wax, 28.1 mg, 48% yield. FTIR $\nu_{\text{max}}$(KBr)/cm$^{-1}$ 3392, 3052, 2926, 1721, 1603, 1505, 1417, 1325, 1279, 1166, 1125, 1066, 1017, 845, 751, 692. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.67-7.58 (m, 4H), 7.12-7.07 (m, 2H), 6.70-6.66 (m, 1H), 6.53-6.48 (m, 2H), 5.47 (brs, 1H), 5.06 (brs, 1H), 2.16 (s, 3H). $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 202.7, 145.5, 142.3, 130.7 (q, $^2J_{(C-C-F)}$ = 32.3 Hz), 129.3, 128.2, 126.2 (q, $^3J_{(C-C-C-F)}$ = 3.6 Hz), 123.9 (q, $^1J_{(C-F)}$ = 270.5 Hz), 118.1, 113.3., 67.8, 26.8. MS (ESI $m/z$) 293.6 [MH$^+$, 17%), 316.7 [MNa$^+$, 21%]. Elemental analysis calcd (%) for C$_{16}$H$_{14}$F$_3$NO: C, 65.52; H, 4.81; N, 4.78; found C,65.79; H, 4.97; N, 4.63.

1-(naphthalen-2-yl)-1-(phenylamino)propan-2-one (3h)

Red wax, 39.6 mg, 72% yield. FTIR $\nu_{\text{max}}$(KBr)/cm$^{-1}$ 3056, 1711, 1667, 1598, 1544, 1496, 1444, 1313, 1232, 1155, 1028, 821, 753, 693. $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ 7.99 (s, 1H), 7.93-7.80 (m, 2H), 7.58-7.35 (m, 5H), 7.17-7.05 (m, 2H), 6.70-6.58 (m, 2H), 5.17 (s, 1H), 2.16 (s, 3H). $^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ 203.9, 145.9, 135.5, 133.4, 133.2, 129.2, 129.1, 128.3, 127.8, 127.7, 127.3, 126.5, 126.3, 124.9, 117.7, 113.3, 68.3, 26.8. MS (ESI $m/z$) 276.6 [MH$^+$, 39%], 298.6 [MNa$^+$, 77%]. Elemental analysis calcd (%) for C$_{19}$H$_{17}$NO: C, 82.88; H, 6.22; N, 5.09; found C, 82.58; H, 6.38; N, 5.37.

1-phenyl-1-(phenylamino)butan-2-one (3i)

Ochre solid, 28.2 mg, 59% yield. Mp 84.2-86.7 °C. FTIR $\nu_{\text{max}}$(KBr)/cm$^{-1}$ 3395, 2923, 1716, 1603, 1504, 1454, 1428, 1317, 1260, 1111, 1034, 749. $^1$H NMR (CDCl$_3$, 400 MHz): $\delta$ 7.47-7.42 (m, 2H), 7.39-7.34 (m, 3H), 7.30 (d, 1H, J= 7.2 Hz), 7.12-7.05 (m, 2H), 6.65 (t, 1H, J= 7.3 Hz), 6.57-6.53 (m, 2H), 5.50 (brs, 1H), 5.00 (s, 1H), 2.53-2.40 (m, 2H), 0.99 (t, 3H, J= 7.3 Hz). $^{13}$C NMR (CDCl$_3$, 100 MHz): $\delta$ 206.9, 146.0, 138.3, 129.14, 129.12, 128.3, 127.8, 117.6, 113.3., 76.4, 32.5, 7.86. MS (ESI $m/z$) 240.7 [MH$^+$, 18%], 262.6 [MNa$^+$, 43%]. Elemental analysis calcd (%) for C$_{16}$H$_{17}$NO: C, 80.30; H, 7.16; N, 5.85; found C, 80.57; H, 7.41; N, 6.12.
1-(phenylamino)-1-m-tolylbutan-2-one (3j)

Orange wax, 33.4 mg, 66% yield.  
**FTIR** $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3386, 1716, 1603, 1505, 1428, 1321, 1111, 1035, 749, 692.  
**$^1$H NMR** (CDCl$_3$, 300 MHz): $\delta$ 7.31-7.23 (m, 3H), 7.16-7.08 (m, 3H), 6.68 (t, 1H, $J$= 7.3 Hz), 6.61-6.56 (m, 2H), 5.48 (brs, 1H), 4.98 (s, 1H), 2.48 (q, 2H, $J$= 7.3 Hz), 2.36 (s, 3H), 1.01 (t, 3H, $J$= 7.3 Hz).  
**$^{13}$C NMR** (CDCl$_3$, 75 MHz): $\delta$ 207.1, 146.2, 138.9, 138.3, 129.13, 129.09, 128.95, 128.21, 125.0, 117.5, 113.3, 67.4, 32.4, 21.4, 7.9.  
**MS** (ESI m/z) 276.5 [MNa$^+$, 100%].  
Elemental analysis calcd (%) for C$_{17}$H$_{19}$NO: C, 80.60; H, 7.56; N, 5.53; found C, 80.28; H, 7.81; N, 5.80.

1-(4-Bromophenyl)-1-(phenylamino)butan-2-one (3k)

Red wax, 40.7 mg, 64% yield.  
**FTIR** $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3066, 1719, 1602, 1505, 1428, 1404, 1316, 1140, 1111, 1071, 1010, 833, 750, 692.  
**$^1$H NMR** (CDCl$_3$, 300 MHz): $\delta$ 7.50 (d, 2H, $J$= 8.3 Hz), 7.34 (d, 2H, $J$= 8.3 Hz), 7.13-7.05 (m, 2H), 6.67 (t, 1H, $J$= 7.2 Hz), 6.54-6.49 (m, 2H), 4.96 (s, 1H), 2.50-2.40 (m, 2H), 1.00 (t, 3H, $J$= 7.3 Hz).  
**$^{13}$C NMR** (CDCl$_3$, 100 MHz): $\delta$ 206.1, 145.6, 137.4, 132.3, 129.3, 129.1, 122.2, 117.8, 113.8, 66.7, 32.4, 7.8.  
**MS** (ESI m/z) 318.5 [MH$^+$, 45%].  
Elemental analysis calcd (%) for C$_{16}$H$_{16}$BrNO: C, 60.39; H, 5.07; N, 4.40; found C, 60.13; H, 5.28; N, 4.63.

1-(3,4-Dichlorophenyl)-1-(phenylamino)butan-2-one (3l)

Red wax, 29 mg, 47% yield.  
**FTIR** $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3390, 1720, 1604, 1505, 1467, 1429, 1394, 1318, 1135, 1031, 752, 740, 692.  
**$^1$H NMR** (CDCl$_3$, 300 MHz): $\delta$ 7.56 (s, 1H), 7.48-7.42 (m, 1H), 7.35-7.28 (m, 1H), 7.16-7.07 (m, 2H), 6.70 (t, 1H, $J$= 7.3 Hz), 6.55-6.48 (m, 2H), 5.55 (brs, 1H),
4.95 (s, 1H), 2.53-2.41 (m, 2H), 1.02 (t, 3H, J= 7.3 Hz). $^{13}$C NMR (CDCl$_3$, 75 MHz): δ 205.5, 145.4, 138.9, 133.4, 132.5, 131.1, 129.5, 129.2, 127.0, 118.1, 113.3, 66.4, 32.6, 7.7. MS (ESI m/z) 307.7 [M+H$^+$, 19%], 331.4 [M+Na$^+$, 12%]. Elemental analysis calcd (%) for C$_{16}$H$_{15}$Cl$_2$NO: C, 62.35; H, 4.91; N, 4.54; found C, 62.57; H, 5.07; N, 4.37.

5-Phenyl-3-(phenylamino)pentan-2-one (3m)

![Structure of 5-Phenyl-3-(phenylamino)pentan-2-one (3m)]

Yellow oil, 14.2 mg, 28% yield. Aniline and $\alpha$-amino ketone 3m have the same polarity. To remove aniline from the mixture of the two products, recovered after silica gel chromatography, the mixture was diluted with Et$_2$O and washed with water. FTIR $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3441, 2918, 2850, 1705, 1635, 1602, 1506, 1454, 1260, 1093, 799, 748, 693. $^1$H NMR (CDCl$_3$, 400 MHz): δ 7.33-7.15 (m, 7H), 6.77-6.72 (m, 1H), 6.59-6.52 (m, 2H), 4.32 (brs, 1H), 4.07-4.02 (m, 1H), 2.94-2.84 (m, 1H), 2.80-2.65 (m, 2H), 2.19 (s, 3H), 2.03-1.93 (m, 1H). $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 210.0, 146.8, 140.8, 129.4, 128.5, 128.4, 126.2, 118.1, 113.2, 62.8, 33.4, 31.5, 26.4. Elemental analysis calcd (%) for C$_{17}$H$_{19}$NO: C, 80.60; H, 7.56; N, 5.53; found C, 82.32; H, 7.72; N, 5.70.

(1R,2S)-1-phenyl-1-(pyrrolidin-1-yl)propan-2-ol (4a)

![Structure of (1R,2S)-1-phenyl-1-(pyrrolidin-1-yl)propan-2-ol (4a)]

Data for this compound were consistent with those reported in the literature.$^6$

White solid, 20.2 mg, 78% yield. $[\alpha]_D^{24} = -53.0$ (c 0.82, CH$_2$Cl$_2$), ee 67%. $^1$H NMR (CDCl$_3$, 400 MHz): δ 7.32-7.27 (m, 5H), 4.27-4.21 (m, 1H), 2.99 (d, 1H, J= 3.3 Hz), 2.69-2.60 (m, 2H), 2.47-2.40 (m, 2H), 1.79-1.74 (m, 4H), 0.83 (d, 3H, J= 6.4 Hz). $^{13}$C NMR (CDCl$_3$, 100 MHz): δ 138.4, 129.4, 127.8, 127.4, 75.7, 66.9, 52.8, 23.3, 19.1. HPLC analysis with Chiralcel OD-H column, 99:1 n-hexane: ethanol, 1 mL/min, 220 nm; minor enantiomer $t_R = 7.5$ min, major enantiomer $t_R = 8.4$ min, ee 67 %.
1-(Naphthalen-2-ylthio)-1-phenylpropan-2-one (6)

![Chemical structure](image)

Pink solid, 21.3 mg, 73% yield. **Mp 70.8-74.3 °C.** **FTIR** $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 2923, 1712, 1585, 1493, 1454, 1355, 1067, 815, 744, 699, 569. **$^1$H NMR** (CDCl$_3$, 300 MHz): $\delta$ 7.81-7.68 (m, 4H), 7.48-7.44 (m, 2H), 7.41-7.31 (m, 6H), 5.10 (s, 1H), 2.21 (s, 3H). **$^{13}$C NMR** (CDCl$_3$, 100 MHz): $\delta$ 203.1, 135.4, 133.5, 132.5, 131.3, 131.0, 129.3, 128.9, 128.6, 128.5, 127.6, 127.5, 126.5, 126.4, 64.4, 27.3. **MS** (ESI $m/z$) 293.4 [MH$^+$, 14%]. Elemental analysis calcd (%) for C$_{19}$H$_{16}$OS: C, 78.05; H, 5.52; S, 10.97; found C, 78.27; H, 5.34; S, 11.12.

2-methyl-3-phenylquinoxaline (8)

Data for this compound were consistent with those reported in the literature.  

White wax, 18.5 mg, 56% yield. **FTIR** $\nu_{\text{max}}$ (KBr)/cm$^{-1}$ 3060, 2924, 1562, 1483, 1445, 1396, 1374, 1343, 1191, 1132, 1006, 996, 766, 699. **$^1$H NMR** (CDCl$_3$, 400 MHz): $\delta$ 8.13-8.10 (m, 1H), 8.07-8.05 (m, 1H), 7.76-7.68 (m, 2H), 7.68-7.63 (m, 2H), 7.56-7.47 (m, 3H), 2.77 (s, 3H). **$^{13}$C NMR** (CDCl$_3$, 100 MHz): $\delta$ 154.9, 152.5, 141.1, 140.9, 138.9, 129.7, 129.21, 129.17, 129.0, 128.9, 128.5, 128.2, 24.3.
References

NMR Spectra

$^1$H NMR in CDCl$_3$ (400 MHz)

![NMR Spectrum of Compound 1f](image)
$^1$H NMR in CDCl$_3$ (250 MHz)

![NMR spectrum](image)
$^{13}$C NMR in CDCl$_3$ (75 MHz)
$^1$H NMR in CDCl$_3$ (300 MHz)
$^{13}$C NMR in CDCl$_3$ (100 MHz)
$^1$H NMR in CDCl$_3$ (300 MHz)
\[ ^{13}\text{C} \text{NMR in CDCl}_3 \text{ (100 MHz)} \]
$^1$H NMR in CDCl$_3$ (400 MHz)
$^{13}$C NMR in CDCl$_3$ (75 MHz)
$^1$H NMR in CDCl$_3$ (300 MHz)

![NMR Spectrum Image]

**Formula**

![Chemical Structure Image]
$^{13}$C NMR in CDCl$_3$ (100 MHz)

![NMR spectrum with chemical shifts]

1k
$^1$H NMR in CDCl$_3$ (400 MHz)
$^{13}$C NMR in CDCl$_3$ (75 MHz)

![Chemical Structure]

- 74.261
- 7.612
- 61.752
- 19.503
- 7.6208

![NMR Spectrum]

ppm

140 130 120 110 100 90 80 70 60 50 40 30 20 10
$^1$H NMR in CDCl$_3$ (400 MHz)
$^{13}$C NMR in CDCl$_3$ (100 MHz)
$^1$H NMR in CDCl$_3$ (400 MHz)
$^{13}$C NMR in CDCl$_3$ (100 MHz)
$^1$H NMR in CDCl$_3$ (400 MHz)
$^{13}$C NMR in CDCl$_3$ (100 MHz)

![NMR spectrum of a compound](image)

**Compound 3c**
$^1$H NMR in CDCl$_3$ (300 MHz)
$^{13}$C NMR in CDCl$_3$ (100 MHz)

![Carbon-13 NMR spectrum of molecule 3d]
$^{1}$H NMR in CDCl$_3$ (400 MHz)
$^{13}$C NMR in CDCl$_3$ (75 MHz)

![Chemical Structure](image)

**3e**
$^1$H NMR in CDCl$_3$ (400 MHz)
$^{13}$C NMR in CDCl$_3$ (100 MHz)

![Chemical Structure](image)

3f
$^1$H NMR in CDCl$_3$ (400 MHz)

![NMR Spectrum](image)

Formula: $\text{F}_3\text{C}-\text{NH}-\text{O}$

4g
$^{13}$C NMR in CDCl$_3$ (100 MHz)
$^1$H NMR in CDCl$_3$ (300 MHz)
$^{13}$C NMR in CDCl$_3$ (75 MHz)

3h
$^1$H NMR in CDCl$_3$ (400 MHz)
$^{13}$C NMR in CDCl$_3$ (100 MHz)
$\text{H NMR in CDCl}_3 (300 \text{ MHz})$
$^{13}$C NMR in CDCl$_3$ (75 MHz)
$^1$H NMR in CDCl$_3$ (300 MHz)
$^{13}$C NMR in CDCl$_3$ (100 MHz)
$^1$H NMR in CDCl$_3$ (300 MHz)
$^{13}$C NMR in CDCl$_3$ (75 MHz)
$^1$H NMR in CDCl$_3$ (400 MHz)
$^{13}$C NMR in CDCl$_3$ (100 MHz)

![Chemical Structure](image)

S55
$^1$H NMR in CDCl$_3$ (300 MHz)
$^{13}$C NMR in CDCl$_3$ (100 MHz)
### Table 1

<table>
<thead>
<tr>
<th>RT (min)</th>
<th>Area (V*sec)</th>
<th>% Area</th>
<th>Height (V)</th>
<th>% Height</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16.663</td>
<td>5136581</td>
<td>49.95</td>
<td>214265</td>
</tr>
<tr>
<td>2</td>
<td>18.689</td>
<td>5144843</td>
<td>50.05</td>
<td>124154</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>RT (min)</th>
<th>Area (V*sec)</th>
<th>% Area</th>
<th>Height (V)</th>
<th>% Height</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15.598</td>
<td>5075409</td>
<td>57.62</td>
<td>216892</td>
</tr>
<tr>
<td>2</td>
<td>18.799</td>
<td>3702638</td>
<td>42.18</td>
<td>104049</td>
</tr>
</tbody>
</table>