Supporting Information for

Simple and convenient access to $\alpha,\alpha,\alpha$-trisubstituted amides by double addition of Grignard reagents to acyl cyanohydrins

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I. General information

All experiments were carried out under N₂ atmosphere. THF and CH₂Cl₂ were purified by passing through neutral alumina columns under nitrogen. The Grignard reagents for the synthesis of amides 5a-r were prepared in anhydrous THF using the conventional method from the appropriate bromide precursors and Mg turnings.

Analytical TLC were performed on Alugram SIL G/UV254 silica gel sheets (Macherey-Nagel) with detection by 5% ethanolic potassium permanganate solution. Column chromatography was carried out using silica gel 60 (0.040-0.063 mm) from Merck. Melting points were determined with a Büchi B-540 melting point apparatus and are uncorrected. ¹H and ¹³C NMR spectra were recorded on a Bruker DPX-200 or Bruker AC-400 spectrometer. Chemical shifts (δ) are expressed in ppm units, relative to the residual solvent peak. Coupling constants are given in Hz. The multiplicities are reported as follows: singlet (s), doublet (d), triplet (t), quadruplet (q), sextuplet (sext), multiplet (m), and broad signal (bs). IR spectra were obtained on a Perkin Elmer Spectrum One spectrometer on a single-reflection diamond ATR unit. High resolution mass spectra were recorded on a Waters Micromass GCT Premier spectrometer.

II. Synthesis and analytical data of amides 5a-r

General procedure for the synthesis of amides 5a-r

To a solution of cyanoester 2a-j (1 mmol, unless otherwise mentioned) in THF (5 mL) cooled to 0 °C was added dropwise a solution of the appropriate Grignard reagent in THF (2.2 mmol). The mixture was allowed to warm up to room temperature and stirred at this temperature for 1 h. After addition of water (5 mL) and 1M aqueous HCl solution (1 mL), the aqueous phase was extracted with EtOAc (3 × 10 mL) and the combined organic layers were washed with brine. After drying over MgSO₄, the organic fraction was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel or recrystallization to afford the pure amides 5a-r.
**N-(3-(Hydroxymethyl)pentan-3-yl)benzamide (5a)**

![Chemical structure](image)

General procedure applied on 3 mmol of cyanoester 2a. Purification by flash chromatography (cyclohexane–EtOAc, 5:5) afforded amide 5a as a yellow oil (432 mg, 65%).

\[ R_f = 0.30 \text{ (cyclohexane–EtOAc, 5:5).} \]

\[ \text{^1H NMR (400 MHz, CDCl}_3\text{): } \delta 7.73 - 7.69 \text{ (m, 2H, Harom), 7.52 - 7.46 \text{ (m, 1H, Harom), 7.44 - 7.38 \text{ (m, 2H, Harom), 6.12 (bs, 1H, NH), 5.03 (bs, 1H, OH), 3.74 (s, 2H, CH}_2\text{), 1.84 - 1.68 \text{ (m, 4H, CH}_2\text{), 0.92 (t, } J = 7.5 \text{ Hz, 6H, CH}_3\text{).} \]

\[ \text{^13C NMR (100 MHz, CDCl}_3\text{): } \delta 168.7 \text{ (C}=O)\text{), 135.1 (1 Carom), 131.7 (1 Carom), 128.8 (2 Carom), 127.0 (2 Carom), 67.1 (CH}_2\text{OH), 62.0 (C), 26.5 (2 CH}_2\text{), 7.7 (2 CH}_3\text{).} \]

\[ \text{IR (neat): } 3174, 3067, 2972, 2947, 2865, 1727, 1635, 1489, 1454, 1319, 1252, 1054 \text{ cm}^{-1}. \]

\[ \text{HRMS (CI-NH}_3/\text{CH}_4\text{): m/z } [\text{M + H}]^+ \text{ calcld for C}_{13}\text{H}_{20}\text{NO}_2: 222.1494; \text{ found: 222.1489.} \]

**N-(1-Hydroxy-2-methylpropan-2-yl)benzamide (5b)**

![Chemical structure](image)

Purification by flash chromatography (cyclohexane–EtOAc, 5:5) afforded amide 5b as a white solid (112 mg, 58%).

\[ \text{Mp 87 - 89 °C; } R_f = 0.35 \text{ (cyclohexane–EtOAc, 5:5).} \]

\[ \text{^1H NMR (200 MHz, CDCl}_3\text{): } \delta 7.74 - 7.67 \text{ (m, 2H, Harom), 7.53 - 7.33 \text{ (m, 3H, Harom), 6.38 (bs, 1H, NH), 5.02 (bs, 1H, OH), 3.64 (s, 2H, CH}_2\text{), 1.39 (s, 6 H, CH}_3\text{).} \]

\[ \text{^13C NMR (50 MHz, CDCl}_3\text{): } \delta 168.6 \text{ (C}=O)\text{), 134.9 (1 Carom), 131.7 (1 Carom), 128.7 (2 Carom), 127.0 (2 Carom), 70.7 (CH}_2\text{OH), 56.4 (C), 24.6 (2 CH}_3\text{).} \]

\[ \text{IR (neat): } 3174, 3067, 2972, 2947, 2865, 1727, 1635, 1549, 1489, 1454, 1319, 1252, 1054 \text{ cm}^{-1}. \]

\[ \text{HRMS (CI-NH}_3/\text{CH}_4\text{): m/z } [\text{M + H}]^+ \text{ calcld for C}_{11}\text{H}_{16}\text{NO}_2: 194.1181; \text{ found: 194.1181.} \]
**N-(5-(Hydroxymethyl)nonan-5-yl)benzamide (5c)**

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide 5c as a pale yellow oil (135 mg, 49%).

$R_f = 0.40$ (cyclohexane–EtOAc, 7:3).

$^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 7.74 – 7.66 (m, 2H, Harom), 7.53 – 7.33 (m, 3H, Harom), 6.19 (bs, 1H, NH), 5.18 (bs, 1H, OH), 3.72 (m, 2H, CH$_2$), 1.79 – 1.61 (m, 4H, CH$_2$), 1.41 – 1.19 (m, 8H, CH$_2$), 0.90 (t, $J$ = 6.6 Hz, 6H, CH$_3$).

$^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ 168.6 (C=O), 135.2 (1 Carom), 131.8 (1 Carom), 128.8 (2 Carom), 127.0 (2 Carom), 68.0 (CH$_2$OH), 61.9 (C), 34.4 (2 CH$_2$), 25.6 (2 CH$_2$), 23.3 (2 CH$_2$), 14.2 (2 CH$_3$).

IR (neat): 3309, 2955, 2930, 2862, 1739, 1638, 1525, 1488, 1466, 1365, 1217, 1054 cm$^{-1}$.

HRMS (CI-NH$_3$/CH$_4$): m/z [M + H]$^+$ calcld for C$_{17}$H$_{28}$NO$_2$: 277.2120; found: 277.2121.

**N-(2-Hydroxy-1,1-diphenylethyl)benzamide (5d)**

General procedure applied on 12 mmol of cyanoester 2a. Purification by recrystallization from toluene afforded amide 5d as white crystals (3.05 g, 80%).

Mp 185–187 °C.

$^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 7.86 – 7.80 (m, 2H, Harom), 7.61 – 7.29 (m, 13H, Harom), 6.99 (bs, 1H, NH), 5.31 (t, $J$ = 6.4 Hz, 1H, OH), 4.50 (d, $J$ = 6.4 Hz, 2H, CH$_2$).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 168.5 (C=O), 142.0 (2 Carom), 134.3 (1 Carom), 132.2 (1 Carom), 128.9 (2 Carom), 128.8 (4 Carom), 128.0 (2 Carom), 127.4 (4 Carom), 127.2 (2 Carom), 70.1 (CH$_2$OH), 69.4 (C).

IR (neat): 3271, 3059, 3027, 2920, 2867, 1726, 1638, 1600, 1578, 1525, 1485, 1444, 1312, 1283, 1075 cm$^{-1}$.

HRMS (CI-NH$_3$/CH$_4$): m/z [M + H]$^+$ calcld for C$_{21}$H$_{20}$NO$_2$: 318.1494; found: 318.1495.
N-(2-Hydroxy-1,1-di(thiophen-2-yl)ethyl)benzamide (5e)

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide 5e as a dark red solid (197 mg, 60%).

Mp 156.5–158.5 °C; \( R_f = 0.31 \) (cyclohexane–EtOAc, 7:3).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta 7.83 \) (d, \( J = 7.3 \) Hz, 2H, Harom), 7.56 (t, \( J = 7.4 \) Hz, 1H, Harom), 7.47 (t, \( J = 7.6 \) Hz, 2H, Harom), 7.31 (dd, \( J = 5.1 \) Hz, \( J = 1.0 \) Hz, 2H, Harom), 7.21 (bs, 1H, NH), 7.09 (dd, \( J = 3.6 \) Hz, \( J = 1.0 \) Hz, 2H, Harom), 7.02 (dd, \( J = 5.1 \) Hz, \( J = 3.6 \) Hz, 2H, Harom), 4.96 (bs, 1H, OH), 4.45 (s, 2H, \( CH_2 \)).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 167.9 \) (C=O), 146.3 (2 Carom), 134.2 (1 Carom), 132.2 (1 Carom), 128.9 (2 Carom), 127.3 (2 Carom), 127.0 (2 Carom), 126.1 (2 Carom), 125.5 (2 Carom), 71.1 (CH\(_2\)OH), 64.9 (C).

IR (neat): 3283, 1739, 1650, 1578, 1515, 1483, 1290, 1060 cm\(^{-1}\).

HRMS (CI-NH\(_3\)): m/z [M + H]\(^+\) calcd for C\(_{17}\)H\(_{16}\)NO\(_2\)S\(_2\): 330.0622; found: 330.0616.

N-(3-(Hydroxymethyl)penta-1,4-dien-3-yl)benzamide (5f)

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide 5f as a pale yellow solid (155 mg, 71%).

Mp 82–84 °C; \( R_f = 0.17 \) (cyclohexane–EtOAc, 7:3).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta 7.81 – 7.76 \) (m, 2H, Harom), 7.49 (m, 1H, Harom), 7.45 – 7.40 (m, 2H, Harom), 6.59 (bs, 1H, NH), 6.02 (dd, \( J = 17.4 \) Hz, \( J = 10.7 \) Hz, 2H, CH\(_2\)), 5.33 (d, \( J = 10.7 \) Hz, 2H, CH\(_2\)), 5.26 (d, \( J = 17.4 \) Hz, 2H, CH\(_2\)), 4.47 (bs, 1H, OH), 3.77 (s, 2H, CH\(_2\)).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 167.9 \) (C=O), 137.7 (2 CH), 134.6 (1 Carom), 131.9 (1 Carom), 128.8 (2 Carom), 127.1 (2 Carom), 115.9 (2 CH\(_2\)), 67.9 (CH\(_2\)), 64.9 (C).

IR (neat): 3292, 3151, 3065, 2917, 2857, 1727, 1632, 1601, 1579, 1548, 1489, 1409, 1347, 1315, 1260, 1163, 1091 cm\(^{-1}\).

HRMS (CI-NH\(_3\)): m/z [M + H]\(^+\) calcd for C\(_{17}\)H\(_{16}\)NO\(_2\): 218.1181; found: 218.1181.
**N-(4-(Hydroxymethyl)hepta-1,6-dien-4-yl)benzamide (5g)**

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide 5g as a colorless oil (157 mg, 64%).

$R_f = 0.20$ (cyclohexane–EtOAc, 7:3).

$^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 7.75 – 7.67 (m, 2H, Harom), 7.57 – 7.39 (m, 3H, Harom), 6.39 (bs, 1H, NH), 5.92 (dddd, $J = 18.9$ Hz, $J = 9.3$ Hz, $J = 8.5$ Hz, 2H, CH), 5.28 – 5.17 (m, 4H, CH$_2$), 5.08 (t, $J = 5.6$ Hz, 1H, OH), 3.78 (d, $J = 5.6$ Hz, 2H, CH$_2$), 2.66 (dd, $J = 13.9$ Hz, $J = 6.6$ Hz, 2H, CH$_2$), 2.38 (dd, $J = 13.9$ Hz, $J = 8.5$ Hz, 2H, CH$_2$).

$^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ 168.4 (C=O), 134.8 (1 Carom), 133.1 (2 CH), 131.9 (1 Carom), 128.9 (2 Carom), 127.0 (2 Carom), 120.1 (2 CH$_2$), 68.3 (CH$_2$), 60.4 (C), 39.1 (2 CH$_2$).

IR (neat): 3343, 3075, 2978, 2922, 1735, 1638, 1602, 1579, 1520, 1487, 1439, 1326, 1308, 1058 cm$^{-1}$.

HRMS (CI-NH$_3$): m/z [M + H]$^+$ calcd for C$_{15}$H$_{20}$NO$_2$: 246.1494; found: 246.1499.

**N-(5-(Hydroxymethyl)nona-1,8-dien-5-yl)benzamide (5h)**

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide 5h as a yellow oil (145 mg, 53%).

$R_f = 0.30$ (cyclohexane–EtOAc, 7:3).

$^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 7.75 – 7.67 (m, 2H, Harom), 7.54 – 7.36 (m, 3H, Harom), 6.23 (bs, 1H, NH), 5.83 (ddt, $J = 16.7$ Hz, $J = 10.0$ Hz, $J = 6.4$ Hz, 2H, CH), 5.16 – 4.92 (m, 4H, CH$_2$), 3.78 (s, 2H, CH$_2$), 2.25 – 1.99 (m, 4H, CH$_2$), 1.85 (t, $J = 7.9$ Hz, 4H, CH$_2$).

$^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ 168.5 (C=O), 138.1 (2 CH), 134.9 (1 Carom), 131.9 (1 Carom), 128.8 (2 Carom), 127.0 (2 Carom), 115.4 (2 CH$_2$), 67.7 (CH$_2$), 61.6 (C), 33.9 (2 CH$_2$), 27.8 (2 CH$_2$).

IR (neat): 3315, 3074, 2931, 1727, 1639, 1603, 1578, 1520, 1488, 1450, 1289, 1068 cm$^{-1}$.

HRMS (CI-NH$_3$/CH$_4$): m/z [M + H]$^+$ calcd for C$_{17}$H$_{24}$NO$_2$: 274.1807; found: 274.1807.
**N-(6-(Hydroxymethyl)undeca-1,10-dien-6-yl)benzamide (5i)**

![Chemical Structure](image)

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide 5i as a pale yellow oil (172 mg, 57%).

\[ R_f = 0.50 \text{ (cyclohexane–EtOAc, 7:3).} \]

\[ \text{^1H NMR (200 MHz, CDCl}_3): \delta 7.76 - 7.67 \text{ (m, 2H, Harom), 7.56 - 7.39 (m, 3H, Harom),} \]

\[ \text{6.06 (bs, 1H, NH), 5.80 (ddt, J = 16.8 Hz, J = 10.0 Hz, J = 6.6 Hz, 2H, CH), 5.08 - 4.95 (m, 5H, CH}_2, \text{ OH), 3.77 (s, 2H, CH}_2), 2.09 (q, J = 7.1 Hz, 4H, CH}_2), 1.81 - 1.68 (m, 4H, CH}_2), 1.49 - 1.36 (m, 4H, CH}_2).} \]

\[ \text{\^13C NMR (50 MHz, CDCl}_3): \delta 168.6 (C=O), 138.3 (2 CH), 135.0 (1 Carom), 131.9 (1 Carom), 128.9 (2 Carom), 127.0 (2 Carom), 115.4 (2 CH}_2), 67.9 (CH}_2), 61.8 (C), 34.2 (2 CH}_2), 34.1 (2 CH}_2), 22.8 (2 CH}_2).} \]

\[ \text{IR (neat): 3317, 3281, 3004, 2971, 2934, 2878, 1726, 1627, 1548, 1461, 1254, 1174, 1035 cm}^{-1}. \]

\[ \text{HRMS (CI-NH}_3/CH}_4: m/z [M + H]^+ \text{ calc for C}_{19}H_{28}NO}_2: 302.2120; \text{ found: 302.2110.} \]

**N-(3-(Hydroxymethyl)pentan-3-yl)-4-methoxybenzamide (5j)**

General procedure applied on 2 mmol of cyanoester 2b. Purification by flash chromatography (cyclohexane–EtOAc, 5:5) afforded amide 5j as a white solid (367 mg, 73%).

\[ \text{Mp 70.5–72.5 °C; } R_f = 0.41 \text{ (cyclohexane–EtOAc, 5:5).} \]

\[ \text{\^1H NMR (400 MHz, CDCl}_3): \delta 7.69 (d, J = 8.8 Hz, 2H, Harom), 6.92 (d, J = 8.8 Hz, 2H, Harom), 5.97 (bs, 1H, NH), 5.26 (bs, 1H, OH), 3.84 (s, 3H, CH}_3)O), 3.75 (s, 2H, CH}_2), 1.83 - 1.67 (m, 4H, CH}_2), 0.93 (t, J = 7.5 Hz, 6H, CH}_3).} \]

\[ \text{\^13C NMR (100 MHz, CDCl}_3): \delta 168.3 (C=O), 162.4 (1 Carom), 128.8 (2 Carom), 127.2 (1 Carom), 114.0 (2 Carom), 67.6 (CH}_2)OH), 61.9 (C), 55.6 (CH}_3)O), 26.6 (2 CH}_2), 7.8 (2 CH}_3).} \]

\[ \text{IR (neat): 3318, 3281, 3004, 2965, 2934, 2878, 1726, 1627, 1548, 1461, 1254, 1174, 1035 cm}^{-1}. \]

\[ \text{HRMS (CI-NH}_3/CH}_4: m/z [M + H]^+ \text{ calc for C}_{16}H}_{22}NO}_3: 252.1600; \text{ found: 252.1604.} \]
4-Bromo-N-(3-(hydroxymethyl)pentan-3-yl)benzamide (5k)

Purification by flash chromatography (cyclohexane–EtOAc, 5:5) afforded amide 5k as a white solid (174 mg, 58%).

Mp 95–97 °C; \( R_f = 0.40 \) (cyclohexane–EtOAc, 5:5).

\(^1\)H NMR (200 MHz, CDCl\(_3\)): \( \delta 7.61 – 7.49 \) (m, 4H, Harom), 6.10 (bs, 1H, NH), 4.83 (bs, 1H, OH), 3.73 (bs, 2H, CH\(_2\)), 1.75 (q, \( J = 7.5 \) Hz, 4H, CH\(_2\)), 0.90 (t, \( J = 7.5 \) Hz, 6H, CH\(_3\)).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 167.7 \) (C=O), 134.0 (1 Carom), 132.0 (2 Carom), 128.6 (2 Carom), 126.4 (1 Carom), 66.9 (CH\(_2\)OH), 62.1 (C), 26.5 (2 CH\(_2\)), 7.8 (2 CH\(_3\)).

IR (neat): 3196, 3071, 2938, 2877, 1737, 1634, 1591, 1548, 1481, 1455, 1443, 1343, 1250, 1053 cm\(^{-1}\).

HRMS (Cl-NH\(_3\)): m/z [M + H]\(^+\) calcd for C\(_{13}\)H\(_{19}\)NO\(_2\)Br: 300.0599; found: 300.0602.

\( N\)-(3-(Hydroxymethyl)pentan-3-yl)butyramide (5l)

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide 5l as a pale yellow oil (97 mg, 52%).

\( R_f = 0.33 \) (cyclohexane–EtOAc, 7:3).

\(^1\)H NMR (200 MHz, CDCl\(_3\)): \( \delta 5.38 \) (bs, 1H, NH), 5.16 (bs, 1H, OH), 3.65 (s, 2H, CH\(_2\)), 2.18 (t, \( J = 7.4 \) Hz, 2H, CH\(_2\)), 1.76 – 1.54 (m, 6H, CH\(_2\)), 0.95 (t, \( J = 7.4 \) Hz, 3H, CH\(_3\)), 0.86 (t, \( J = 7.5 \) Hz, 6H, CH\(_3\)).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta 174.5 \) (C=O), 67.5 (CH\(_2\)OH), 61.6 (C), 39.3 (CH\(_2\)C=O), 26.6 (2 CH\(_2\)), 19.5 (CH\(_2\)), 13.7 (CH\(_3\)), 7.6 (2 CH\(_3\)).

IR (neat): 3300, 3083, 2966, 2936, 2877, 1740, 1645, 1547, 1459, 1376, 1217, 1062 cm\(^{-1}\).

HRMS (Cl-NH\(_3\)/CH\(_4\)): m/z [M + H]\(^+\) calcd for C\(_{10}\)H\(_{22}\)NO\(_2\): 188.1651; found: 188.1647.
**N-(3-(Hydroxymethyl)pentan-3-yl)-3-methylbutanamide (5m)**

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide **5m** as a colorless oil (124 mg, 62%).

\( R_f = 0.35 \) (cyclohexane–EtOAc, 7:3).

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \) 5.53 (bs, 1H, NH), 5.27 (bs, 1H, OH), 3.62 (s, 2H, CH\(_2\)), 2.07 – 2.01 (m, 3H, CH\(_2\) CH), 1.69 – 1.54 (m, 4H, CH\(_2\)), 0.93 (d, \( J = 5.9 \) Hz, 6H, CH\(_3\)), 0.84 (t, \( J = 7.4 \) Hz, 6H, CH\(_3\)).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 174.0 (C=O), 67.5 (CH\(_2\)OH), 61.7 (C), 46.8 (CH\(_2\)=O), 26.7 (2 CH\(_2\)), 26.5 (CH), 22.4 (2 CH\(_3\)), 7.6 (2 CH\(_3\)).

IR (neat): 3267, 3183, 3086, 2963, 2933, 2870, 1631, 1558, 1457, 1263, 1051 cm\(^{-1}\).

HRMS (CI-NH\(_3\)/CH\(_3\)): m/z [M + H]\(^+\) calcld for C\(_{11}\)H\(_{24}\)NO\(_2\): 202.1807; found: 202.1809.

**N-(3-(Hydroxymethyl)pentan-3-yl)pivalamide (5n)**

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide **5n** as a colorless oil (110 mg, 55%).

\( R_f = 0.34 \) (cyclohexane–EtOAc, 7:3).

\(^1\)H NMR (200 MHz, CDCl\(_3\)): \( \delta \) 5.55 (bs, 1H, NH), 5.21 (bs, 1H, OH), 3.60 (s, 2H, CH\(_2\)), 1.70 – 1.54 (m, 4H, CH\(_2\)), 1.18 (s, 9H, CH\(_3\)), 0.84 (t, \( J = 7.5 \) Hz, 6H, CH\(_3\)).

\(^{13}\)C NMR (500 MHz, CDCl\(_3\)): \( \delta \) 179.8 (C=O), 67.8 (CH\(_2\)OH), 61.1 (C), 39.4 (C(CH\(_3\))\(_3\)), 27.9 (3 CH\(_3\)), 26.5 (2 CH\(_2\)), 7.7 (2 CH\(_3\)).

IR (neat): 3438, 2970, 2880, 1739, 1640, 1558, 1515, 1455, 1365, 1217 cm\(^{-1}\).

HRMS (CI-NH\(_3\)/CH\(_3\)): m/z [M + H]\(^+\) calcld for C\(_{11}\)H\(_{24}\)NO\(_2\): 202.1807; found: 202.1812.
(E)-N-(3-(Hydroxymethyl)penta-1,4-dien-3-yl)but-2-enamide (5o)

Purification by flash chromatography (cyclohexane–EtOAc, 5:5) afforded amide 5o as a yellow oil (100 mg, 55%).

$R_f = 0.20$ (cyclohexane–EtOAc, 5:5).

$^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 6.90 (dq, $J = 15.1$ Hz, $J = 6.9$ Hz, 1H, $CH$), 5.94 (dd, $J = 17.3$ Hz, $J = 10.6$ Hz, 2H, $CH$), 5.90 (dq, $J = 15.1$ Hz, $J = 1.7$ Hz, 1H, $CH$), 5.69 (bs, 1H, NH), 5.29 (dd, $J = 10.6$ Hz, $J = 0.5$ Hz, 2H, $CH_2$), 5.20 (dd, $J = 17.3$ Hz, $J = 0.5$ Hz, 2H, $CH_2$), 4.76 (t, $J = 6.7$ Hz, 1H, $OH$), 3.72 (d, $J = 6.7$ Hz, 2H, $CH_2$), 1.88 (dd, $J = 6.9$ Hz, $J = 1.7$ Hz, 3H, $CH_3$).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 166.5 ($C=O$), 141.4 ($CH$), 137.7 (2 $CH$), 124.9 ($CH$), 115.8 (2 $CH_2$), 68.0 ($CH_2$), 65.1 ($C$), 17.8 ($CH_3$).

IR (neat): 3283, 3087, 2916, 2870, 1670, 1628, 1534, 1446, 1409, 1344, 1290, 1230, 1050 cm$^{-1}$.

HRMS (CI-NH$_3$): m/z [M + H]$^+$ calcd for C$_{10}$H$_{16}$NO$_2$: 182.1181; found: 182.1183.

N-(3-(Hydroxymethyl)penta-1,4-dien-3-yl)cinnamamide (5p)

Purification by flash chromatography (cyclohexane–EtOAc, 5:5) afforded amide 5p as a yellow solid (153 mg, 63%).

Mp 79–81 °C; $R_f = 0.50$ (cyclohexane–EtOAc, 5:5).

$^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 7.67 (d, $J = 15.6$ Hz, 1H, $CH$), 7.55–7.48 (m, 2H, Harom), 7.42 – 7.35 (m, 3H, Harom), 6.50 (d, $J = 15.6$ Hz, 1H, $CH$), 5.99 (dd, $J = 17.3$ Hz, $J = 10.6$ Hz, 2H, $CH$), 5.94 (bs, 1H, NH), 5.32 (d, $J = 10.6$ Hz, 2H, $CH_2$), 5.27 (d, $J = 17.3$ Hz, 2H, $CH_2$), 4.67 (t, $J = 6.8$ Hz, 1H, $OH$), 3.77 (d, $J = 6.8$ Hz, 2H, $CH_2$).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 166.5 ($C=O$), 142.4 ($CH$), 137.6 (2 $CH$), 134.6 (1 Carom), 130.1 (1 Carom), 129.0 (2 Carom), 128.1 (2 Carom), 120.4 ($CH$), 116.0 (2 $CH_2$), 68.1 ($CH_2$), 65.4 ($C$).

IR (neat): 3260, 3060, 2920, 2855, 1718, 1654, 1615, 1578, 1549, 1498, 1448, 1416, 1348, 1228, 1057 cm$^{-1}$.

HRMS (CI-NH$_3$): m/z [M + H]$^+$ calcd for C$_{15}$H$_{18}$NO$_2$: 244.1338; found: 244.1341.
**N-(3-(Hydroxymethyl)penta-1,4-dien-3-yl)-3-phenylpropiolamide (5q)**

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide 5q as a yellow oil (123 mg, 51%).

\[ R_f = 0.15 \text{ (cyclohexane–EtOAc, 7:3).} \]

\(^1\)H NMR (200 MHz, CDCl\(_3\)): \( \delta \) 7.59 – 7.51 (m, 2H, Harom), 7.47 – 7.31 (m, 3H, Harom), 6.22 (bs, 1H, NH), 5.97 (dd, \( J = 17.3 \text{ Hz, } J = 10.7 \text{ Hz, } 2H, CH \)), 5.36 (d, \( J = 10.7 \text{ Hz, } 2H, CH_2 \)), 5.31 (d, \( J = 17.3 \text{ Hz, } 2H, CH_2 \)), 3.74 (d, \( J = 6.6 \text{ Hz, } 2H, CH_2 \)), 5.31 (d, \( J = 17.3 \text{ Hz, } 2H, CH_2 \)), 3.57 (t, \( J = 6.6 \text{ Hz, } 1H, OH \)).

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \) 153.5 (C=O), 136.9 (2 CH), 132.7 (2 Carom), 130.4 (1 Carom), 128.7 (2 Carom), 120.1 (1 Carom), 116.5 (2 CH\(_2\)), 85.3 (C), 83.2 (C), 67.5 (CH\(_2\)), 65.6 (C).

IR (neat): 3259, 3022, 2933, 2873, 2213, 1736, 1628, 1501, 1443, 1409, 1365, 1302, 1217, 1050 cm\(^{-1}\).

HRMS (CI-NH\(_3\)): m/z [M + H]+ calcd for C\(_{15}\)H\(_{16}\)NO\(_2\): 242.1181; found: 242.1190.

**N-(3-Ethyl-2-hydroxypentan-3-yl)benzamide (5r)**

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide 5r as a pale yellow oil (53 mg, 23%).

\[ R_f = 0.35 \text{ (cyclohexane–EtOAc, 7:3).} \]

\(^1\)H NMR (200 MHz, CDCl\(_3\)): \( \delta \) 7.77 – 7.68 (m, 2H, Harom), 7.57 – 7.37 (m, 3H, Harom), 5.93 (bs, 1H, NH), 5.74 (d, \( J = 9.5 \text{ Hz, } 1H, OH \)), 3.80 (dq, \( J = 9.5 \text{ Hz, } J = 6.4 \text{ Hz, } 1H, CH \)), 2.09 (dt, \( J = 14.6 \text{ Hz, } J = 7.4 \text{ Hz, } 1H, CH_2 \)), 1.95 (dt, \( J = 14.6 \text{ Hz, } J = 7.4 \text{ Hz, } 1H, CH_2 \)), 1.66 (m, 1H, CH\(_2\)), 1.59 (dt, \( J = 14.2 \text{ Hz, } J = 7.4 \text{ Hz, } 1H, CH_2 \)), 1.18 (d, \( J = 6.4 \text{ Hz, } 3H, CH_3 \)), 0.96 (t, \( J = 7.4 \text{ Hz, } 3H, CH_3 \)), 0.91 (t, \( J = 7.4 \text{ Hz, } 3H, CH_3 \)).

\(^{13}\)C NMR (50 MHz, CDCl\(_3\)): \( \delta \) 168.7 (C=O), 135.1 (1 Carom), 131.8 (1 Carom), 128.9 (2 Carom), 127.0 (2 Carom), 67.4 (CH), 62.1 (C), 26.7 (2 CH\(_2\)), 7.8 (3 CH\(_3\)).

IR (neat): 3308, 3210, 3061, 2975, 2931, 2882, 1729, 1630, 1600, 1577, 1539, 1489, 1451, 1334, 1315, 1274, 1107, 1028 cm\(^{-1}\).

HRMS (CI-NH\(_3\)/CH\(_4\)): m/z [M + H]+ calcd for C\(_{14}\)H\(_{22}\)NO\(_2\): 236.1651; found: 236.1652.
III. Synthesis and analytical data of amides 5s-t

**General procedure for the synthesis of amides 5s-t**

To a solution of cyanomethyl benzoate 2a (161 mg, 1 mmol) in THF (5 mL) cooled to 0 °C was added dropwise a solution of the appropriate Grignard reagent in THF (2.2 mmol) which was previously prepared from TMS-acetylene or phenylacetylene (2.2 mmol) and EtMgBr (2.2 mmol). The mixture was allowed to warm up to room temperature and stirred at 50 °C for 3 h. After addition of water (5 mL) and 1M aqueous HCl solution (1 mL), the aqueous phase was extracted with EtOAc (3 × 10 mL) and the combined organic layers were washed with brine. After drying over MgSO₄, the organic fraction was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel to afford the pure amides 5s-t.

**N-(3-(Hydroxymethyl)-1,5-diphenylpenta-1,4-diyn-3-yl)benzamide (5s)**

![Structure of amide 5s](image)

Purification by flash chromatography (cyclohexane–EtOAc, 7:3) afforded amide 5s as a yellow solid (234 mg, 64%).

Mp 184–186 °C; $R_f = 0.23$ (cyclohexane–EtOAc, 7:3).

$^1$H NMR (200 MHz, CDCl₃): δ 7.89 – 7.83 (m, 2H, Harom), 7.55 – 7.43 (m, 8H, Harom), 7.35 – 7.29 (m, 5H, Harom), 6.91 (bs, 1H, NH), 4.27 (s, 2H, $CH_2$), 3.76 (bs, 1H, OH).

$^{13}$C NMR (100 MHz, CDCl₃): δ 167.0 (C=O), 134.0 (1 Carom), 132.3 (4 Carom), 132.2 (1 Carom), 129.0 (2 Carom), 128.8 (2 Carom), 128.4 (4 Carom), 127.4 (2 Carom), 122.0 (2 Carom), 85.0 (2 C), 84.4 (2 C), 70.1 (CH₂OH), 51.8 (C).

IR (neat): 3438, 3327, 3059, 2962, 2932, 2231, 1727, 1629, 1601, 1577, 1532, 1489, 1451, 1402, 1370, 1312, 1260, 1069 cm⁻¹.

**N-(3-(Hydroxymethyl)-1,5-bis(trimethylsilyl)penta-1,4-diyln-3-yl)benzamide (5t)**

Purification by flash chromatography (cyclohexane–EtOAc, 8:2) afforded amide 5t as a yellow solid (198 mg, 55%).

Mp 173–175 °C; 
IR (neat): 3410, 3389, 2961, 2929, 2900, 2166, 1726, 1656, 1601, 1581, 1506, 1480, 1459, 1248, 1075 cm⁻¹.

HRMS (Cl-NH₃): m/z [M⁺] calcd for C₁₉H₂₇NO₂Si₂: 357.1580; found: 357.1593.

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V. Copies of $^1$H and $^{13}$C NMR spectra

$N$-$(3$-(Hydroxymethyl)$)pentan$-3$-yl$)benzamide (5a)
N-(1-Hydroxy-2-methylpropan-2-yl)benzamide (5b)
$N$-(5-(Hydroxymethyl)nonan-5-yl)benzamide (5c)
N-(2-Hydroxy-1,1-diphenylethyl)benzamide (5d)
N-(2-Hydroxy-1,1-di(thiophen-2-yl)ethyl)benzamide (5e)
N-(3-(Hydroxymethyl)penta-1,4-dien-3-yl)benzamide (5f)
N-(4-(Hydroxymethyl)hepta-1,6-dien-4-yl)benzamide (5g)
N-(5-(Hydroxymethyl)nona-1,8-dien-5-yl)benzamide (5h)
N-(6-(Hydroxymethyl)undeca-1,10-dien-6-yl)benzamide (5i)

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N-(3-(Hydroxymethyl)pentan-3-yl)-4-methoxybenzamide (5j)
4-Bromo-N-(3-(hydroxymethyl)pentan-3-yl)benzamide (5k)
N-(3-(Hydroxymethyl)pentan-3-yl)butyramide (5I)
N-(3-(Hydroxymethyl)pentan-3-yl)-3-methylbutanamide (5m)
N-(3-(Hydroxymethyl)pentan-3-yl)pivalamide (5n)
(E)-N-(3-(Hydroxymethyl)penta-1,4-dien-3-yl)but-2-enamide (5o)
N-(3-(Hydroxymethyl)penta-1,4-dien-3-yl)cinnamamide (5p)
N-(3-(Hydroxymethyl)penta-1,4-dien-3-yl)-3-phenylpropionamide (5q)
$N$-$(3$-Ethyl-2-hydroxypentan-3-yl)$benzamide (5r)$
$N$-(3-(Hydroxymethyl)-1,5-diphenylpenta-1,4-diyn-3-yl)benzamide (5s)
N-(3-(Hydroxymethyl)-1,5-bis(trimethylsilyl)penta-1,4-diyn-3-yl)benzamide (5t)