N-Heterocyclic Carbene Catalyzed Amidation of Unactivated Esters with Amino Alcohols.

Mohammad Movassaghi* and Michael A. Schmidt

Massachusetts Institute of Technology, Department of Chemistry, Massachusetts 02139

Supporting Information

General Procedures. All reactions were performed in oven-dried or flame-dried round bottomed flasks, modified Schlenk (Kjeldahl shape) flasks, or where indicated in modified Schlenk vessels designed for the probe of the React-IR¹ instrument. The flasks were fitted with rubber septa and reactions were conducted under a positive pressure of argon. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Flash column chromatography was performed as described by Still et al. using silica gel (60-Å pore size, 32–63 μm , standard grade, Sorbent Technologies).² Analytical thin-layer chromatography was performed using glass plates pre-coated with 0.25 mm 230–400 mesh silica gel impregnated with a fluorescent indicator (254 nm). Thin layer chromatography plates were visualized by exposure to ultraviolet light and/or by exposure to an ethanolic phosphomolybdic acid (PMA), an acidic solution of *p*-anisaldehyde (Anis), an aqueous solution of ceric ammonium molybdate (CAM), an aqueous solution of potassium permanganate (KMnO_4) or an ethanolic solution of ninhydrin followed by heating (<1 min) on a hot plate (~250 °C). Organic solutions were concentrated on Büchi R-200 rotary evaporators at ~20 Torr (house vacuum) at 25–35 °C.

Materials. Commercial reagents and solvents were used as received with the following exceptions: Dichloromethane, diethyl ether, tetrahydrofuran, acetonitrile, and toluene were purchased from J.T. Baker (CycletainerTM) and were purified by the method of Grubbs et al. under positive argon pressure,³ Triethylamine was distilled from calcium hydride at 760 Torr under a nitrogen atmosphere. Methanol was distilled from magnesium methoxide at 760 Torr under a nitrogen atmosphere. Acetic acid was distilled from 5% v/v acetic anhydride and 2% wt/v CrO_3 . Perdeuterobenzene was distilled from CaH_2 and stored over 5 Å MS pellets. All reagents for NMR experiments were degassed via an argon purge for at least 10 min. *i*-Propyl acetate, *t*-butyl acetate, methyl benzoate, L-leucinol, L-prolinol, methyl 2-furate and benzyl alcohol were distilled from K_2CO_3 . Ethanolamine and methylphenyl acetate were distilled from KOH. Methyl 4-methoxybenzoate was purified by bulb-to-bulb distillation. Phthalide (**11**) was recrystallized from toluene. LiCl was dried at 200 °C under vacuum (~1 Torr) for 24 h then flame dried and stored in a glove box.

Instrumentation. Proton nuclear magnetic resonance (¹H NMR) spectra were recorded with Varian inverse probe 500 INOVA and Varian 500 INOVA spectrometers and are recorded in parts per million from internal tetramethylsilane on the δ scale and are referenced from the residual protium in the NMR solvent (CHCl_3 : δ 7.27, C_6D_6 : δ 7.16, $\text{DMSO}-d_6$: δ 2.50, $\text{THF}-d_8$: δ 1.73, δ 3.58). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, q

¹ www.asirxn.com

² Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

³ Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.

= quartet, m = multiplet), coupling constant(s) in Hertz, integration, assignment]. Carbon-13 nuclear magnetic resonance spectra were recorded with a Varian 500 INOVA spectrometer and are recorded in parts per million from internal tetramethylsilane on the δ scale and are referenced from the carbon resonances of the solvent (CDCl_3 : δ 77.23, $\text{DMSO}-d_6$: δ 39.51, C_6D_6 : δ 128.39, $\text{THF}-d_8$: δ 67.57, δ 25.37). Data is reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, q = quartet, m = multiplet), coupling constant(s) in Hertz, assignment]. Infrared data were obtained with a Perkin-Elmer 2000 FTIR and are reported as follows: [frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad), assignment]. React-IR experiments were performed on an ASI ReactIR 1000 fitted with a silicon probe. Infrared (IR) spectra were obtained using a Perkin Elmer System 2000 FT-IR spectrophotometer referenced to a polystyrene standard. Data are represented as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak) and assignment where appropriate. Melting points were determined on an Electrothermal Mel-Temp melting point apparatus. Gas chromatography was performed on an Agilent Technologies 6890N Network GC System with a HP-5 5% Phenyl Methyl Siloxane column. We are grateful to Dr. Li Li for obtaining the mass spectroscopic data at the Department of Chemistry's Instrumentation Facility, Massachusetts Institute of Technology. The structure of *N,N*-bismesitylimidazolylidene-methanol complex **8b** was obtained with the assistance of Dr. Peter Mueller at the X-ray crystallography laboratory of the Department of Chemistry, Massachusetts Institute of Technology.

Procedure A

Use of Recrystallized IMes as Catalyst:

N-(2-Hydroxyethyl)-2-phenyl acetamide (4aa, Table 1, entry 1):

To a solution of IMes (**3**, 30 mg, 98 μ mol, 0.05 equiv.) in THF (1.95 mL) was added ester **1a** (285 μ L, 1.97 mmol, 1 equiv) and ethanolamine **2a** (120 μ L, 1.97 mmol, 1.00 equiv) sequentially via a gas-tight syringe. Monitoring the reaction mixture by TLC and GC analysis indicated complete conversion after 8 h. The volatiles were removed under reduced pressure on a rotary evaporator, and the resulting residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4aa** as a white powder (355 mg, 100%). For characterization data, please see below.

Procedure B

In Situ Generation of IMes as Catalyst:

N-(2-Hydroxyethyl)-2-phenyl acetamide (4aa):

A flame-dried flask was charged with IMes·HCl (44 mg, 128 μ mol, 0.065 equiv) and *tert*-BuOK (11 mg, 98 μ mol, 0.050 equiv) and sealed under an argon atmosphere. THF (1.95 mL) was added via a gas-tight syringe and the resulting suspension was vigorously stirred for 30 min. Ester **1a** (285 μ L, 1.97 mmol, 1 equiv) and ethanolamine **2a** (120 μ L, 1.97 mmol, 1.00 equiv) were sequentially added via a gas-tight syringe. After 2 h, the yellow homogenous mixture was concentrated under reduced pressure on a rotary-evaporator. The resulting residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4aa** as a white solid (340 mg, 96%).

Use of 1,3-dimethylimidazolium iodide (IMe·HI) and 1,3-dicyclohexyl-imidazolium chloride (ICHx·HCl) in place of IMes·HCl provided the desired product in 95 and 88% yield, respectively.

^1H NMR (500 MHz, CDCl_3 , 20 °C):

δ 7.35–7.38 (m, 2H, PhH_m), 7.26–7.32 (m, 3H, $\text{PhH}_{o,p}$), 5.97 (br-s, 1H, NH), 3.66 (app-q, J = 5.0 Hz, 2H, CH_2OH), 3.59 (s, 2H, PhCH_2), 3.37 (app-q, J = 5.0 Hz, 2H, NCH_2), 2.87 (br-s, 1H, OH).

^{13}C NMR (125.8 MHz, CDCl_3 , 20 $^\circ\text{C}$):	δ 172.7 (C_{amide}), 134.8 (PhC_{ipso}), 129.7 ($\text{PhC}_{\text{ortho}}$), 129.3 (PhC_{meta}), 127.7 (PhC_{para}), 62.7 (CH_2OH), 43.9 (PhCH_2), 42.9 (NCH_2).
FTIR (thin film) cm^{-1} :	3293 (s, O-H), 3087 (w), 2925 (m), 1645 (s, C=O), 1550 (m).
HRMS (ESI):	Calc for $\text{C}_{10}\text{H}_{13}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 180.1019 Found: 180.1018
m.p.:	65–66 $^\circ\text{C}$
TLC (5% MeOH in CH_2Cl_2):	Prod. 4aa : 0.40 (UV, KMnO_4).

Control Experiments:

All experiments were conducted under standard conditions used above for direct comparison. In the absence of IMes (**3**), incubation of equimolar amounts of esters **1a** and **1b** with **2a** at 23 $^\circ\text{C}$ for 12 h provides less than 2 and 1%, respectively, of the corresponding amides **4aa** and **4ba**. The use of sodium methoxide and potassium *t*-butoxide in place of IMes (**3**) in the coupling of **1a** and **2a** resulted in complete consumption of **1a** within 5 h and gave 60% and 74% isolated yield of **4aa**, respectively. Use of 1,3-bis(2,4,6-trimethylphenyl)imidazolin-2-ylidene (SIMes), prepared by in situ deprotonation (SIMes $\cdot\text{HCl}$ 6.5 mol% and potassium *t*-butoxide 5 mol%) did not provide a detectable amount of product (<2%) in 5 h and returned the starting ester **1a**.

Competition Experiment (Equation 2):

N-(2-Hydroxyethyl)-2-phenyl acetamide (**4aa**):

To a solution of IMes (30 mg, 98 μmol , 0.05 equiv) in THF (1.95 mL) was added the ester **1a** (255 μL , 1.97 mmol, 1 equiv), ethanolamine (**2a**, 120 μL , 1.97 mmol, 1.00 equiv), and benzylamine (**6**, 215 μL , 1.97 mmol, 1.00 equiv) sequentially via a gas-tight syringe under an argon atmosphere. After 4 h, TLC analysis indicated complete conversion of ester **1a** to the desired amide **4aa**. The volatiles were removed under reduced pressure on a rotary-evaporator. ^1H NMR analysis of the residue indicated an equal mixture of amide **4aa** and benzylamine (**6**). To facilitate chromatographic separation, acetic acid (100 μL , 1.75 mmol, 0.89 equiv) was added and the residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4aa** as a white solid (350 mg, 98.5%). For characterization data, please see above.

React-IR Monitoring of the Amidation Reaction

4-Hydroxy-N-(2-hydroxyethyl)-butyramide (**4ma**, Table 1, entry 15):

An oven-dried React-IR flask was charged with IMes (30 mg, 98 μ mol, 0.05 equiv) under a nitrogen atmosphere and the reaction vessel was sealed, moved out of the glove-box, and fitted to the React-IR probe under a stream of Argon. Anhydrous and deoxygenated THF (1.95 mL) was added to dissolve the IMes. A background spectrum was collected, ester **1m** (150 μ L, 1.97 mmol, 1 equiv) followed by ethanolamine (**2a**, 120 μ L, 1.97 mmol, 1.00 equiv) were added sequentially via a gas-tight syringe, and the reaction progress was monitored. After 6 h, the reaction was complete, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4ma** as a solid (261 mg, 88%).

^1H NMR (500 MHz, $\text{DMSO}-d_6$, 20 °C): δ 7.78 (br-t, J = 5.0 Hz, 1H, CONH), 4.61 (t, J = 5.5 Hz, 1H, OH), 4.45 (t, J = 5.5 Hz, 1H, OH), 3.34–3.38 (m, 4H, $\text{NCH}_2\text{CH}_2\text{OH}$, $\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$), 3.08 (q, J = 6.0 Hz, 2H, NCH_2), 2.09 (t, J = 7.5 Hz, 2H, CH_2CONH), 1.61 (app-quintet, J = 7.3 Hz, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2$).

^{13}C NMR (125.8 MHz, $\text{DMSO}-d_6$, 20 °C): δ 172.3 (C_{amide}), 60.4 (CH_2OH), 60.0 (CH_2OH), 41.5 (NCH_2), 32.1 (CH_2CONH), 28.7 ($\text{CH}_2\text{CH}_2\text{CH}_2$).

FTIR (CHCl_3) cm^{-1} : 3447 (m, O-H), 3006 (w), 2946 (w), 1654 (s, C=O), 1525 (m).

HRMS (ESI): Calc for $\text{C}_6\text{H}_{13}\text{NO}_3$ $[\text{M}+\text{Na}]^+$: 170.0788
Found: 170.0786

m.p.: 55.5–56.5 °C

TLC (5% MeOH in CH_2Cl_2): Prod. **4ma**: 0.18 (UV, KMnO_4)

React-IR Monitoring of IMesNHC-catalyzed amidation of γ -lactone **1m** to amide **4ma**.

The intermediate ester **12ma** was observed within 2 min. Although ester **12ma** proved to be exceedingly difficult to isolate for direct verification of the absorbance at 1736 cm^{-1} , a similar ester ($\text{Ph}(\text{CH}_2)_{14}\text{CO}_2\text{CH}_2\text{CH}_2\text{N}(\text{CH}_3)_2$) has been reported to have an absorbance at 1730 cm^{-1} (T. Siatra-Prpastaikoudi, A. Papadaki-Valiraki, A. Tsantili-Kakoulidou, L. Tzouvelekis, A. Mentis, *Chem. Pharm. Bull.* **1994**, 42, 392–394). Additionally, we have prepared samples of *O*-benzoyl ethanolamine (see below) and *O*-4-hydroxybutanoyl-*N,N*-dimethylethanolamine and detected their carbonyl absorbances at 1721 cm^{-1} and 1741 cm^{-1} , respectively.

¹H NMR Monitoring of the Amidation Reaction

N-(2-Hydroxyethyl)-benzamide (4ba):

An NMR tube was charged with IMes (**3**, 11 mg, 35 μmol , 0.05 equiv) and THF- d_8 (700 μL) and sealed under a nitrogen atmosphere in a glove-box. Methyl benzoate **1b** (87 μL , 0.71 mmol, 1 equiv) and ethanolamine (**2a**, 43 μL , 0.71 mmol, 1.0 equiv) were added sequentially via a gas-tight syringe and the reaction progress was monitored by ¹H NMR spectroscopy over 24 h. The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting yellow residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4ba**⁴ as a white solid (101 mg, 85%).

¹H NMR (500 MHz, CDCl_3 , 20 °C):

δ 7.78–7.79 (m, 2H, PhH_o), 7.49–7.53 (m, 1H, PhH_p), 7.27–7.45 (m, 1H, PhH_m), 6.74 (br-s, 1H, NH), 3.83 (app-q, $J = 6.0\text{ Hz}$, 2H, CH_2OH), 3.64 (app-q, $J = 5.5\text{ Hz}$, 2H, NCH_2), 2.89 (br-s, 1H, OH).

⁴ For a previous synthesis of amide **4ba** using benzoyl chloride, see: Morcuende, A.; Ors, M.; Valverde, S.; Herrandón, B. *J. Org. Chem.* **1996**, 61, 5264–5270.

^{13}C NMR (125.8 MHz, CDCl_3 , 20 $^\circ\text{C}$):	δ 168.8 (C_{amide}), 134.3 (PhC_{ipso}), 131.9 (PhC_p), 128.8 (PhC_m), 127.2 (PhC_o), 62.7 (CH_2OH), 43.1 (NCH_2).
FTIR (thin film) cm^{-1} :	3326 (s, O–H), 2936 (w), 2879 (w), 1636 (s, C=O), 1542 (s).
HRMS (ESI):	Calc for $\text{C}_9\text{H}_{11}\text{NO}_2$ $[\text{M}+\text{Na}]^+$: 188.0682 Found: 188.0678
m.p.:	54–55 $^\circ\text{C}$
TLC (5% MeOH in CH_2Cl_2):	Prod. 4ba : 0.43 (UV, KMnO_4)

React-IR Monitoring of the Amidation Reaction

N-(2-Hydroxyethyl)-benzamide (**4ba**):

A flame dried React-IR cell was charged with IMes (**3**, 60.0 mg, 197 μmol , 0.100 equiv) and anhydrous LiCl (8 mg, 0.2 mmol, 0.1 equiv), and was sealed under a nitrogen atmosphere in a glove-box. The reaction vessel was placed onto the probe under a stream of Argon and THF (1.95 mL) was added via a gas-tight syringe to give a clear colorless solution. Methyl benzoate **1b** (246 μL , 1.97 mmol, 1 equiv) and ethanolamine (**2a**, 120 μL , 1.97 mmol, 1.00 equiv) were added sequentially via a gas-tight syringe. The reaction progress was monitored for 2 h (41% conversion). A solution of the sensitive ester **12ba** (0.12 equiv, the sample was a 43:57 ratio of **12ba**:**4ba**, see below for preparation; 27% expected increase in final product) in THF (535 μL) was added to the reaction in progress. Monitoring of the reaction mixture (IR and TLC) was continued for an additional 8 h. The conversion to amide **4ba** proceeded as expected after an initial burst upon addition of ester **12ba**. The ester **12ba** was rapidly consumed and within 20 min the ester was no longer detectable by TLC (the carbonyl frequencies of esters **12ba** and **1b** were not sufficiently resolved for clear monitoring by IR). The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting crude orange residue was purified by flash column chromatography on silica gel (100% THF) to afford the amide **4ba** as a white solid (370 mg, 90%). For characterization data, please see above.

Preparation of the ester **12ba:** A suspension of *O*-benzoyl-*N*-Cbz-ethanolamine (197 mg, 657 μmol , 1.00 equiv) and palladium on carbon (5% wt/wt, 197 mg, 92.6 μmol , 0.14 equiv) in THF (650 μL) was vigorously stirred under a hydrogen atmosphere. Monitoring the reaction

mixture by TLC indicated complete removal of the nitrogen protective group and formation of ester **12ba** in 2 h. To avoid IMes deactivation in the amidation reaction, the ester **12ba** was purified under a nitrogen-atmosphere (glove-box) by flash column chromatography (0.5 × 2.5 cm, 100% THF) on dry silica gel (dehydrated by heating 200 °C for 48 h) to give a sample of the sensitive ester **12ba** along with the corresponding amide **4ba** as a clear oil (88.5 mg, 82%, 536 μmol, 43:57 ratio of **12ba**:**4ba**) which was diluted with THF (535 μL) and used above.

¹H NMR (500 MHz, CDCl₃, 20 °C, 43:57 mixture of **12ba**:**4ba**, ester **12ba** noted by *): δ 8.06–8.08 (m, 2H, PhH_o*), 7.78–7.80 (m, 2H, PhH_o), 7.58 (tt, *J* = 7.5 Hz, 1.5 Hz, 1H, PhH_p*), 7.53 (tt, *J* = 7.0 Hz, 1.5 Hz, 1H, PhH_p), 7.44–7.48 (m, 4H, PhH_m, PhH_m*), 6.61 (br s, 1H, NH) 4.37 (app-t, *J* = 5.5 Hz, 2H, OCH₂*), 3.86 (app-t, *J* = 5.0 Hz, 2H, CH₂OH), 3.66 (app-q, *J* = 5.2 Hz, 2H, NCH₂), 3.10 (app-t, *J* = 5.5 Hz, 2H, NCH₂*), 1.72 (br-s, 3H, NH₂*, OH).

Experimental Procedures for Remainder of Compounds in Table 1

N-(2-Hydroxyethyl)-benzamide (**4ba**, Table 1, entry 2):

To a solution of IMes (**3**, 30 mg, 66 μmol, 0.05 equiv) and anhydrous lithium chloride (3 mg, 7 μmol, 0.05 equiv) in THF (1.30 mL) was added methyl benzoate **1b** (190 μL, 1.31 mmol, 1 equiv) and ethanolamine (**2a**, 80 μL, 1.9 mmol, 1.0 equiv) sequentially via a gas-tight syringes at 23 °C under an Argon atmosphere. After 9.5 h, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting orange residue was purified by flash column chromatography on silica gel (100 % THF) to afford the amide **4ba** as a white solid (205 mg, 94%). For characterization data, please see above.

4-Acetyl-N-(2-hydroxyethyl)-benzamide (4ca, Table 1, entry 3):

A solution of IMes (**3**, 30 mg, 98 μmol , 0.05 equiv) in THF (1.95 mL) followed by ethanolamine (**2a**, 120 μL , 1.97 mmol, 1.00 equiv) was added sequentially via a gas-tight syringe to a flame-dried round bottom flask containing the ester **1c** (351 mg, 1.97 mmol, 1 equiv) under an argon atmosphere. Amide **4ca** began to precipitate after 40 min. After 24 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting red residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4ca** as a white powder (354 mg, 87%).

^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 8.02 (dt, J = 8.0 Hz, 1.5 Hz, 2H, C_4H), 7.88 (dt, J = 8.0 Hz, 1.5 Hz, 2H, C_3H), 6.71 (br-s, 1H, NH), 3.88 (app-q, J = 5.0 Hz, 2H, CH_2OH), 3.67 (app-q, J = 5.2 Hz, 2H, NCH_2), 2.64 (s, 3H, CH_3), 2.43 (t, J = 4.8 Hz, 1H, OH).

^{13}C NMR (125.8 MHz, CD_3OD , 20 $^\circ\text{C}$): δ 199.8 (C_{ketone}), 169.6 (C_{amide}), 140.6 (C_5), 139.9 (C_2), 129.7 (C_4), 128.8 (C_3), 61.6 (CH_2OH), 43.8 (NCH_2), 27.0 (COCH_3).

FTIR (CHCl_3) cm^{-1} : 3452 (m, O–H), 3020 (w), 2995 (w), 1687 (s, C=O), 1660 (s, C=O).

HRMS (ESI): Calc for $\text{C}_{11}\text{H}_{13}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 208.0968
Found: 208.0968

m.p.: 136–137 $^\circ\text{C}$

TLC (10% MeOH / CH_2Cl_2): Prod. **4ca**: 0.44 (UV, KMnO_4)

4-Cyano-N-(2-hydroxyethyl)-benzamide (4da, Table 1, entry 4):

A solution of IMes (**3**, 30 mg, 98 μmol , 0.05 equiv) in THF (1.95 mL) followed by ethanolamine (**2a**, 120 μL , 1.97 mmol, 1.00 equiv) was added sequentially via a gas-tight syringe to a flame-dried round bottom flask containing the ester **1d** (317 mg, 1.97 mmol, 1 equiv) under an argon atmosphere to give a maroon mixture. After 24 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4da** as a white powder (361 mg, 96%).

^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 7.90 (d, J = 7.5 Hz, 2H, C_4H), 7.75 (d, J = 8.0 Hz, 2H, C_3H), 6.69 (br-s, 1H, NH), 3.87 (app-q, J = 4.8 Hz, 2H, CH_2OH), 3.66 (app-q, J = 5.2 Hz, 2H, NCH_2), 2.26 (br-t, J = 4.3 Hz, 1H, OH).

^{13}C NMR (125.8 MHz, $\text{DMSO}-d_6$, 20 $^\circ\text{C}$): δ 165.0 (C_{amide}), 138.6 (C_2), 132.4 (C_4), 128.1 (C_3), 118.4 (CN), 113.5 (C_5), 59.6 (CH_2OH), 42.4 (NCH_2).

FTIR (CHCl_3) cm^{-1} : 3451 (m, O–H), 2995 (w), 2940 (w), 2234 (m, nitrile), 1664 (s, C=O).

HRMS (ESI): Calc for $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 191.0815
Found: 191.0816

m.p.: 108–109 $^\circ\text{C}$

TLC (10% MeOH in CH_2Cl_2): Prod. **4da**: 0.58 (UV, KMnO_4)

N-(2-Hydroxyethyl)-4-trifluoromethyl benzamide (4ea, Table 1, entry 5):

A flame dried React-IR cell was charged with IMes (**3**, 30 mg, 98 μmol , 0.05 equiv) and sealed under a nitrogen atmosphere in a glove-box. The reaction vessel was placed onto the probe under a stream of Argon and THF (1.95 mL) was added via a gas-tight syringe to give a clear colorless solution. Ester **1e** (317 μL , 1.97 mmol, 1 equiv) and ethanolamine (**2a**, 120 μL , 1.97 mmol, 1.00 equiv) were added sequentially via a gas-tight syringe. The reaction progress was monitored for 24 h. The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting orange residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4ea** as a white powder (436 mg, 95%).

^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 7.89 (dd, J = 8.5 Hz, 1.0 Hz, 2H, C_4H), 7.70 (dd, J = 8.3 Hz, 1.0 Hz, C_3H), 6.76 (br-s, 1H, NH), 3.86 (app q, J = 5.0 Hz, 2H, CH_2OH), 3.66 (app-q, J = 5.3 Hz, 2H, NCH_2), 2.56 (t, J = 5.0 Hz, 1H, OH).

^{13}C NMR (125.8 MHz, $\text{DMSO}-d_6$, 20 $^\circ\text{C}$): δ 165.2 (C_{amide}), 138.3 (C_2), 131.0 (q, J_{CF}^2 = 31.9 Hz, C_5), 128.1 (C_3), 125.3 (app-t, J_{CF}^3 = 3.8 Hz, C_4), 124.0 (q, J_{CF} = 272.6 Hz, CF_3), 59.6 (CH_2OH), 42.3 (NCH_2).

FTIR (CHCl_3) cm^{-1} : 3452 (m O–H), 2997 (w), 2943 (w), 1662 (s, C=O), 1327 (s, C–F).

HRMS (ESI): Calc for $\text{C}_{10}\text{H}_{10}\text{F}_3\text{NO}_2$ $[\text{M}+\text{H}]^+$: 234.0736
Found: 234.0735

m.p.: 118–119.5 $^\circ\text{C}$

TLC (10% MeOH in CH_2Cl_2): Prod. **4ea**: 0.42 (UV, KMnO_4)

4-Fluoro-N-(2-hydroxyethyl)-benzamide (4fa, Table 1, entry 6):

To a solution of IMes (**3**, 30 mg, 98 μmol , 0.05 equiv) in THF (1.95 mL) at 23 $^\circ\text{C}$, was added ester **1f** (255 μL , 1.97 mmol, 1.00 equiv) followed by ethanolamine (**2a**, 120 μL , 1.97 mmol, 1 equiv) sequentially via a gas-tight syringe. After 18.5 h, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4fa**⁵ as a white solid (318 mg, 88%).

^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 7.80 (m, 2H, C_4H), 7.10 (m, 2H, C_3H), 6.70 (br-s, 1H, NH), 3.83 (app-t, $J = 5.0$ Hz, 2H, CH_2OH), 3.62 (app-q, $J = 5.2$ Hz, 2H, NCH_2), 2.82 (br-s, 1H, OH).

^{13}C NMR (125.8 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 167.7 (C_{amide}), 165.0 (d, $J_{\text{CF}} = 252.2$ Hz, C_5), 130.5 (d, $J_{\text{CF}}^4 = 3.5$ Hz, C_2), 129.5 (d, $J_{\text{CF}}^3 = 8.6$ Hz, C_3), 115.8 (d, $J_{\text{CF}}^2 = 21.9$ Hz, C_4), 62.4 (CH_2OH), 43.0 (NCH_2).

FTIR (thin film) cm^{-1} : 3292 (s, O–H), 2980 (w), 1636 (s, C=O), 1560 (m), 854 (m).

HRMS (ESI): Calc for $\text{C}_9\text{H}_{10}\text{FNO}_2$ $[\text{M}+\text{H}]^+$: 184.0768
Found: 184.0769

m.p.: 91.5–92.5 $^\circ\text{C}$

TLC (10% MeOH in CH_2Cl_2): Prod. **4fa**: 0.56 (UV, KMnO_4)

⁵ For an alternative synthesis of amide **4fa** using an electrochemical method starting with ester **1f**, see: Arai, K.; Tamura, S.; Masumizu, T.; Kawai, K.-i.; Nakajima, S.; Ueda, A. *Can. J. Chem.* **1990**, 68, 903–907.

N-(2-Hydroxyethyl)-4-methoxy benzamide (4ga, Table 1, entry 7):

A solution of IMes (**3**, 30 mg, 98 μ mol, 0.05 equiv) and anhydrous lithium chloride (4 mg, 0.1 mmol, 0.05 equiv) in THF (1.95 mL) followed by ethanolamine (**2a**, 120 μ L, 1.97 mmol, 1.00 equiv) was added sequentially via a gas-tight syringe to a flame-dried round bottom flask containing the ester **1g** (327 mg, 1.97 mmol, 1 equiv) under an argon atmosphere to give a maroon mixture. After 24 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting residue was purified by flash column chromatography on silica gel (5% MeOH in CH₂Cl₂) to afford the amide **4ga** as a white powder (264 mg, 69%).

¹H NMR (500 MHz, CDCl₃, 20 °C): δ 7.76 (d, J = 8.5 Hz, 2H, C₃H), 6.93 (d, J = 8.5 Hz, 2H, C₄H), 6.57 (br-s, 1H, NH), 3.86 (s, 3H, OCH₃), 3.84 (m, 2H, CH₂OH), 3.63 (app-q, J = 5.2 Hz, 2H, NCH₂), 2.79 (br-s, 1H, OH).

¹³C NMR (125.8 MHz, CDCl₃, 20 °C): δ 168.5 (C_{amide}), 162.5 (C₅), 129.0 (C₃), 126.5 (C₂), 113.9 (C₄), 62.6 (CH₂OH), 55.6 (OCH₃), 43.1 (NCH₂).

FTIR (thin film) cm⁻¹: 3332 (s, O–H), 2940 (w), 1633 (s, C=O), 1559 (m), 1252 (m).

HRMS (ESI): Calc for C₁₀H₁₃NO₃ [M+H]⁺: 196.0968
Found: 196.0964

m.p.: 97–98 °C

TLC (5% MeOH in CH₂Cl₂): Prod. **4ga**: 0.38 (UV, KMnO₄)

N-(2-Hydroxyethyl)-acetamide (4ha, Table 1, entry 8):

A flame dried React-IR cell was charged with IMes (**3**, 30 mg, 98 μmol , 0.05 equiv) and sealed under a nitrogen atmosphere in a glove-box. The reaction vessel was placed onto the probe under a stream of Argon and THF (1.95 mL) was added via a gas-tight syringe to give a clear colorless solution. Ester **1h** (265 μL , 1.97 mmol, 1 equiv) and ethanolamine (**2a**, 120 μL , 1.97 mmol, 1.00 equiv) were added sequentially via a gas-tight syringe. The reaction progress was monitored for 24 h. The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting orange residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4ha**⁶ (200 mg, 99%).

¹H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 6.29 (br-s, 1H, NH), 3.72 (t, J = 4.5 Hz, 2H, CH_2OH), 3.41 (app-q, J = 5.2 Hz, 2H, NCH_2), 3.25 (br-s, 1H, OH), 2.02 (s, 3H, CH_3).

¹³C NMR (125.8 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 171.7 (C_{amide}), 62.3 (CH_2OH), 42.7 (NCH_2), 23.4 (CH_3).

FTIR (thin film) cm^{-1} : 3298 (s, O–H), 2963 (m), 1652 (s, C=O), 1559 (m), 1261 (s).

HRMS (ESI): Calc for $\text{C}_4\text{H}_9\text{NO}_2$ $[\text{M}+\text{Na}]^+$: 126.0525
Found: 126.0531

TLC (10% MeOH in CH_2Cl_2): Prod. **4ha**: 0.29 (KMnO_4)

N-(2-Hydroxyethyl)-acetamide (4ha, Table 1, entries 9-11):

The same procedure as above was used for entries 9–11 (Table 1). For consistency all experiments were allowed to proceed only for 24 h prior to isolation of the product. The experiments with benzyl acetate, *i*-propyl acetate, and *t*-butyl acetate gave 95, 34, and 0% yield of the desired amide **4ha**. For characterization data, please see above.

⁶ For a previous synthesis of amide **4ha** using acetic acid, Ph_3SbO , and P_4S_{10} at 50 $^\circ\text{C}$, see: Nomura, R.; Nakano, T.; Yamada, Y.; Matsuda, H. *J. Org. Chem.* **1991**, 56, 4076–4078.

N-(3-Hydroxypropyl)-2-phenyl acetamide (4ab, Table 1, entry 12):

To a solution of IMes (**3**, 30 mg, 98 μmol , 0.05 equiv) in THF (1.95 mL) at 23 $^\circ\text{C}$, was added ester **1a** (285 μL , 1.97 mmol, 1 equiv) and 1-amino-3-propanol **2b** (151 μL , 1.97 mmol, 1.00 equiv) sequentially via a gas-tight syringes. After 4.5 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4ab**⁷ as a white solid (379 mg, 99%).

¹ H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$):	δ 7.36–7.39 (m, 2H, PhH _m), 7.30–7.33 (m, 2H, PhH _o), 7.27–7.27 (m, 1H, PhH _p), 5.76 (br-s, 1H, NH), 3.61 (s, 2H, PhCH ₂), 3.58 (app-q, J = 5.5 Hz, 2H, CH ₂ OH), 3.38 (app-q, J = 6.5 Hz, 2H, NCH ₂), 3.09 (br-s, 1H, OH), 1.61 (app-pentet, J = 6.0 Hz, 2H, CH ₂ CH ₂ CH ₂).
¹³ C NMR (125.8 MHz, CDCl_3 , 20 $^\circ\text{C}$):	δ 172.6 (C _{amide}), 134.9 (PhC _{ipso}), 129.6 (PhC _o), 129.2 (PhC _m), 127.6 (PhC _p), 59.3 (CH ₂ OH), 43.8 (PhCH ₂), 36.6 (NCH ₂), 32.3 (CH ₂ CH ₂ CH ₂).
FTIR (thin film) cm^{-1} :	3247 (s, O–H), 3084 (m), 2946 (m), 1630 (s, C=O), 1567 (s).
HRMS (ESI):	Calc for C ₁₁ H ₁₅ NO ₂ [M+Na] ⁺ : 216.0995 Found: 216.0994
m.p.:	62.5–63.5 $^\circ\text{C}$
TLC (5% MeOH in CH_2Cl_2):	Prod. 4ab : 0.31 (UV, KMnO_4)

⁷ For an alternative synthesis of amide **4ab** at 150 $^\circ\text{C}$ using phenylacetic acid, see: Cossy, J.; Pale–Grosdemange, C. *Tetrahedron Lett.* **1989**, 30, 2771–2774.

N-(3-Hydroxypropyl)-benzamide (4bb, Table 1, entry 13):

To a solution of IMes (**3**, 20 mg, 66 μmol , 0.05 equiv) and anhydrous LiCl (3 mg, 0.07 mmol, 0.05 equiv) in THF (1.30 mL) was added ester **1b** (164 μL , 1.31 mmol, 1 equiv) and 1-amino-3-propanol **2b** (100 μL , 1.31 mmol, 1.00 equiv) sequentially via a gas-tight syringe. After 9 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4bb**⁸ as a clear oil (229 mg, 97%).

¹H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 7.78–7.79 (m, 2H, PhH_o), 7.52 (tt, $J = 7.0, 1.5$ Hz, 1H, PhH_p), 7.44–7.47 (m, 2H, PhH_m), 6.64 (br-s, 1H, NH), 3.73 (app-q, $J = 6.0$ Hz, 2H, CH_2OH), 3.66 (app-q, $J = 6.0$ Hz, 2H, NCH_2), 3.15 (br-t, $J = 6.0$ Hz, 1H, OH), 1.81 (app-quintet, $J = 6.0$ Hz, 2H, $\text{CH}_2\text{CH}_2\text{CH}_2$).

¹³C NMR (125.8 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 168.8 (C_{amide}), 134.2 (PhC_{ipso}), 131.6 (PhC_p), 128.5 (PhC_m), 127.0 (PhC_o), 59.9 (CH_2OH), 37.4 (NCH_2), 31.8 ($\text{CH}_2\text{CH}_2\text{CH}_2$).

FTIR (thin film) cm^{-1} : 3323 (s, O–H), 3066 (m), 2944 (s), 1639 (s, C=O), 1545 (s).

HRMS (ESI): Calc for $\text{C}_{10}\text{H}_{13}\text{NO}_2$ $[\text{M}+\text{Na}]^+$: 202.0838
Found: 202.0837

TLC (5% MeOH in CH_2Cl_2): Prod. **4bb**: 0.22 (UV, KMnO_4)

⁸ For a previous synthesis of amide **4bb** using benzoyl chloride, see: Morcuende, A.; Ors, M.; Valverde, S.; Herrandón, B. *J. Org. Chem.* **1996**, *61*, 5264–5270.

N-(2-Hydroxyethyl)-2-hydroxymethyl benzamide (4la, Table 1, entry 14):

A flame dried React-IR cell was charged with IMes (**3**, 30 mg, 98 μ mol, 0.05 equiv) and sealed under a nitrogen atmosphere in a glove-box. The reaction vessel was placed onto the probe under a stream of Argon and THF (1.00 mL) was added via a gas-tight syringe to give a clear colorless solution. A solution of ester **1l** (264 mg, 1.97 mmol, 1 equiv) in THF (0.95 mL) was added to the cell followed by ethanolamine (**2a**, 120 μ L, 1.97 mmol, 1.00 equiv) via a gas-tight syringe. The reaction progress was monitored for 24 h. The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting yellow residue was purified by flash column chromatography on silica gel (10% MeOH in CH_2Cl_2) to afford the amide **4la** as a solid (105 mg, 66%).

^1H NMR (500 MHz, $\text{DMSO}-d_6$, 20 $^\circ\text{C}$): δ 8.34 (br-t, $J = 5.3$ Hz, 1H, NH), 7.52 (d, $J = 7.5$ Hz, 1H, C_3H), 7.42–7.44 (m, 2H, C_5H and C_6H), 7.29 (t, $J = 7.5$ Hz, 1H, C_4H), 5.28 (t, $J = 6.5$ Hz, 1H, ArCH_2OH), 4.73 (t, $J = 6.5$ Hz, 1H, CH_2OH), 4.58 (d, $J = 6.0$ Hz, 2H, ArCH_2OH), 3.49 (app-q, $J = 6.5$ Hz, 2H, CH_2OH), 3.29 (app-q, $J = 6.0$ Hz, 2H, NCH_2).

^{13}C NMR (125.8 MHz, $\text{DMSO}-d_6$, 20 $^\circ\text{C}$): δ 168.8 (C_{amide}), 140.2 (C_7), 135.2 (C_2), 129.7 (C_5), 127.6 (C_3), 127.4 (C_4), 126.6 (C_6), 61.1 (CH_2OH), 59.8 (ArCH_2OH), 42.0 (NCH_2).

FTIR (CHCl_3) cm^{-1} : 3442 (m, O–H), 3003 (w), 2940 (w), 1644 (s, C=O), 1526 (w).

HRMS (ESI): Calc for $\text{C}_{10}\text{H}_{13}\text{NO}_3$ $[\text{M}+\text{Na}]^+$: 218.0788
Found: 218.0783

m.p.: 63–64 $^\circ\text{C}$

TLC (10% MeOH in CH_2Cl_2): Prod. **4la**: 0.40 (UV, KMnO_4)

N-(1-(S)-Benzyl-2-hydroxyethyl)-pyridin-4-yl acetamide (4nc, Table 1, entry 16):

Ester **1n** (265 μL , 1.97 mmol, 1.00 equiv) was added via a gas-tight syringe to a solution of IMes (**3**, 30 mg, 98 μmol , 0.05 equiv.) in THF (1.95 mL) at 23 $^\circ\text{C}$ under an argon atmosphere. The resulting bright-yellow solution was transferred via cannula to a flask containing solid L-phenylalaninol (**2c**, 298 mg, 1.97 mmol, 1 equiv) under an argon atmosphere and the resulting mixture was set to stir vigorously. After 15 min, a yellow-homogenous solution resulted and after an additional 30 min, the amide product **4nc** began to precipitate. After 4 h, monitoring of the reaction mixture by TLC indicated complete conversion to the desired amide **4nc**. The volatiles were removed under reduced pressure on a rotary-evaporator and the resulting beige-residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4nc** as an off-white solid (461 mg, 86%).

^1H NMR (500 MHz, $\text{DMSO}-d_6$, 20 $^\circ\text{C}$): δ 8.40 (d, J = 5.8 Hz, 2H, $\text{CH}_{2,6\text{-pyr}}$), 8.07 (d, J = 8.5 Hz, 1H, NH), 7.21–7.24 (m, 2H, PhCH_m), 7.16–7.19 (m, 3H, $\text{PhCH}_{o,p}$), 7.08 (d, J = 6.1 Hz, 2H, $\text{CH}_{3,5\text{-pyr}}$), 4.86 (t, J = 5.5 Hz, 1H, OH), 3.91 (m, 1H, NCH), 3.30–3.43 (m, 4H, CH_2CONH , CH_2OH), 2.85 (dd, J = 13.7, 5.2 Hz, 1H, PhCH_2), 2.60 (dd, J = 13.6, 9.1 Hz, 1H, PhCH_2).

^{13}C NMR (125.8 MHz, $\text{DMSO}-d_6$, 20 $^\circ\text{C}$): δ 168.4 (C_{amide}), 149.2 ($\text{C}_{2,6\text{-pyr}}$), 145.3 ($\text{C}_{4\text{-pyr}}$), 139.1 (PhC_{ipso}), 129.1 (PhC_o), 128.1 (PhC_m), 125.9 (PhC_p), 124.3 ($\text{C}_{3,5\text{-pyr}}$), 62.7 (CH_2OH), 52.5 (NCH), 41.6 (CH_2CONH), 36.6 (CH_2Ph).

FTIR (thin film), cm^{-1} : 3316 (s, O–H), 3059 (w), 2919 (w), 1637 (s, C=O), 1538 (m).

HRMS (ESI): Calc for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 271.1441
Found: 271.1433

m.p.: 144.5–145 $^\circ\text{C}$

TLC (10% MeOH in CH_2Cl_2): S.M. **1n**: 0.74 (UV, KMnO_4)
Prod. **4nc**: 0.30 (UV, KMnO_4)

N-(2-Furoyl) L-Phenylalaninol (4oc, Table 1, entry 17):

Ester **1o** (211 μ L, 1.97 mmol, 1 equiv) was added via a gas-tight syringe to a solution of IMes (**3**, 30 mg, 98 μ mol, 0.05 equiv.) in THF (1.95 mL) at 23 °C under an argon atmosphere. The resulting bright-yellow solution was transferred via cannula to a flask containing solid L-phenylalaninol (**2c**, 298 mg, 1.97 mmol, 1.00 equiv) under an argon atmosphere. After 24 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting beige-residue was purified by flash column chromatography on silica gel (2% MeOH in CH₂Cl₂) to afford the amide **4oc** as an off-white solid (428 mg, 89%).

¹H NMR (500 MHz, CDCl₃, 20°C): δ 7.42 (m, 1H, C₃H), 7.31–7.34 (m, 2H, PhH_m), 7.23–7.28 (m, 3H, PhH_{o,p}), 7.10 (m, 1H, C₅H), 6.65 (br-d, J = 6.0 Hz, 1H, NH), 6.49 (dd, J = 3.2, 2.5 Hz, 1H, C₄H), 4.35 (m, 1H, NCH), 3.77 (m, 1H, CH₂OH), 3.67 (m, 1H, CH₂OH), 2.99 (d, J = 7.5 Hz, 2H, PhCH₂), 2.74–2.77 (br-d, 1H, OH).

¹³C NMR (125.8 MHz, CDCl₃, 20 °C): δ 158.8 (C_{amide}), 147.7 (C₂), 144.2 (C₅), 137.7 (PhC_{ipso}), 129.4 (PhC_o), 128.7 (PhC_m), 126.8 (PhC_p), 114.6 (C₃), 112.3 (C₄), 63.5 (CH₂OH), 52.6 (NCH₂), 37.2 (CH₂Ph).

FTIR (CHCl₃) cm⁻¹: 3425 (m, O–H), 3000 (w), 2948 (w), 1653 (s (C=O), 1595 (s).

HRMS (ESI): Calc for C₁₄H₁₅NO₃ [M+H]⁺: 246.1125
Found: 246.1126

m.p.: 94.5–95.5 °C

TLC (5% MeOH in CH₂Cl₂): Prod. **4oc**: 0.34 (UV, KMnO₄)

N-(1-(S)-Hydroxymethyl-3-methylbutyl)-2-pyridin-4-yl acetamide (4nd):

Ester **1n** (265 μL , 1.97 mmol, 1.00 equiv) was added via a gas-tight syringe to a solution of IMes (**3**, 30 mg, 98 μmol , 0.05 equiv.) in THF (1.95 mL) at 23 $^\circ\text{C}$ under an argon atmosphere. To the resulting bright-yellow solution was added L-leucinol (**2d**, 255 μL , 1.97 mmol, 1 equiv) under an argon atmosphere and the resulting mixture was set to stir vigorously. After 1.5 h, the amide product **4nd** began to precipitate. After 15 h, monitoring of the reaction mixture by TLC indicated complete conversion to the desired amide **4nd**. The volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting beige residue was purified by flash column chromatography on silica gel (5 $\rightarrow$ 10% MeOH in CH_2Cl_2) to afford the amide **4nd** as an off-white solid (391 mg, 84%).

^1H NMR (500 MHz, $\text{DMSO}-d_6$, 20 $^\circ\text{C}$) δ 8.46 (d, J = 5.0 Hz, 2H, $\text{CH}_{2,6\text{-pyr}}$), 7.90 (d, J = 8.5 Hz, 1H, NH), 7.26 (d, J = 5.5 Hz, 2H, $\text{CH}_{3,5\text{-pyr}}$), 4.70 (t, J = 5.3 Hz, 1H, OH), 3.77 (m, 1H, NCH), 3.47 (d, J = 14.5 Hz, 1H, CH_2CONH), 3.43 (d, J = 14.0 Hz, 1H, CH_2CONH), 3.32 (m, 1H, CH_2OH), 3.24 (m, 1H, CH_2OH), 1.55 (septet, J = 6.5 Hz, 1H, CH_3CHCH_3), 1.29 (m, 2H, $\text{CH}_2i\text{-Pr}$), 0.84 (d, J = 6.5 Hz, 3H, CH_3), 0.79 (d, J = 6.5 Hz, 3H, CH_3).

^{13}C NMR (125.8 MHz, $\text{DMSO}-d_6$, 20 $^\circ\text{C}$) δ 168.5 (C_{amide}), 149.4 ($\text{C}_{2,6\text{-pyr}}$), 145.6 ($\text{C}_{4\text{-pyr}}$), 124.4 ($\text{C}_{3,5\text{-pyr}}$), 63.8 (CH_2OH), 48.8 (CH_2CONH), 41.7 (NCH), 24.3 ($\text{CH}(\text{CH}_3)_2$), 23.3 ($\text{CH}_2i\text{-Pr}$), 21.8 (CH_3).

FTIR (CHCl_3) cm^{-1} : 3430 (m, O–H), 2993 (m), 2959 (m), 1666 (s, C=O), 1603 (m).

HRMS (ESI): Calc for $\text{C}_{13}\text{H}_{20}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 237.1598
Found: 237.1608

m.p. 106.5–107.5 $^\circ\text{C}$

TLC (10% MeOH in CH_2Cl_2): S.M. **1n**: 0.74 (UV, KMnO_4)
Prod. **4nd**: 0.22 (UV, KMnO_4)

N-(2-thiophenecarbonyl) L-Leucinol (4pd, Table 1, entry 19):

Ester **1p** (228 μ L, 1.97 mmol, 1.00 equiv) was added via a gas-tight syringe to a solution of IMes (**3**, 30 mg, 98 μ mol, 0.05 equiv) in THF (1.95 mL) at 23 °C under an argon atmosphere. To the resulting bright-yellow solution was added L-leucinol (**2d**, 255 μ L, 1.97 mmol, 1 equiv) under an argon atmosphere. After 24 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting yellow-residue was purified by flash column chromatography on silica gel (5% MeOH in CH₂Cl₂) to afford the amide **4pd** as a white solid (343 mg, 77%).

¹ H NMR (500 MHz, CDCl ₃ , 20°C):	δ 7.51 (m, 1H, C ₃ H), 7.48 (dd, J = 5.0, 1.0 Hz, 1H, C ₅ H), 7.07, (m, 1H, C ₄ H), 6.19 (br-s, 1H, NH), 4.32 (m, 1H, NCH), 3.78 (d, J = 11.0 Hz, 1H, CH ₂ OH), 3.65 (dd, J = 10.5, 5.0 Hz, 1H, CH ₂ OH), 2.82, (br-s, 1H, OH), 1.70 (m, 1H, CH ₃ CHCH ₃), 1.54 (ddd, J = 9.5, 6.0, 5.5 Hz, 1H, CH ₂ <i>i</i> -Pr), 1.44 (ddd, J = 5.5, 5.5, 8.5 Hz, CH ₂ <i>i</i> -Pr), 0.97 (d, J = 1.5 Hz, 3H, CH ₃), 0.96 (d, J = 1.5 Hz, 3H, CH ₃).
¹³ C NMR (125.8 MHz, CDCl ₃ , 20 °C):	δ 162.8 (C _{amide}), 139.1 (C ₂), 130.4 (C ₅), 128.4 (C ₃), 127.8 (C ₄), 65.8 (CH ₂ OH), 50.5 (NCH), 40.4 (CH ₃ CHCH ₃), 25.2 (C <i>i</i> -Pr), 23.2 (CH ₃), 22.5 (CH ₃).
FTIR (CHCl ₃) cm ⁻¹ :	3438 (m, O–H), 3003 (w), 2959 (w), 1641 (s, C=O), 1537 (m).
HRMS (ESI):	Calc for C ₁₁ H ₁₇ NO ₂ S [M+H] ⁺ : 228.1053 Found: 228.1045
m.p.:	67-70 °C
TLC (10% MeOH in CH ₂ Cl ₂):	Prod. 4pd : 0.53 (UV, KMnO ₄)

N-Phenylacetyl-L-Prolinol (4ae, Table 1, entry 20):

Ester **1a** (283 μL , 1.97 mmol, 1.00 equiv) and L-prolinol (**2e**, 192 μL , 1.97 mmol, 1 equiv) were added sequentially via a gas-tight syringe to a solution of IMes (**3**, 30 mg, 98 μmol , 0.05 equiv) in THF (1.95 mL) at 23 $^\circ\text{C}$ under an argon atmosphere. After 4 h, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting yellow-residue was purified by flash column chromatography on silica gel (5% MeOH in CH_2Cl_2) to afford the amide **4ae**⁹ as a pale yellow oil (428 mg, 99%).

¹ H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$):	δ 7.33–7.36 (m, 2H, PhH_m), 7.26–7.29 (m, 3H, $\text{PhH}_{o,p}$), 5.08 (dd, $J = 8.0, 2.5$ Hz, 1H, OH), 4.25 (ddd, $J = 14.1, 8.5, 2.5$ Hz, 1H, NCHCH_2OH), 3.66–3.71 (m, 3H, PhCH_2 , CH_2OH), 3.56–3.62 (m, 2H, CH_2OH , NCH_2), 3.45 (dt, $J = 10.5, 7.0$ Hz, 1H, NCH_2), 2.05 (dt, $J = 19.9, 7.5$ Hz, 1H, $\text{NCHCH}_2\text{CH}_2$), 1.91 (app-septet, $J = 7.0$ Hz, 1H, $\text{NCHCH}_2\text{CH}_2$), 1.85 (m, 1H, $\text{NCHCH}_2\text{CH}_2$), 1.57 (sextet, $J = 7.0$ Hz, 1H, $\text{NCHCH}_2\text{CH}_2$).
¹³ C NMR (125.8 MHz, CDCl_3 , 20 $^\circ\text{C}$):	δ 172.7 (C_{amide}), 134.5 (PhC_{ipso}), 129.1 (PhC_o), 129.0 (PhC_m), 127.2 (PhC_p), 67.8 (NCHCH_2OH), 61.8 (NCHCH_2OH), 48.2 (NCH_2), 42.7 (PhCH_2), 28.6 ($\text{NCHCH}_2\text{CH}_2$), 24.7 ($\text{NCHCH}_2\text{CH}_2$).
FTIR (thin film) cm^{-1} :	3383 (s, O–H), 3062 (w), 2954 (m), 1620 (s, C=O), 1430 (m).
HRMS (ESI):	Calc for $\text{C}_{13}\text{H}_{17}\text{NO}_2$ $[\text{M}+\text{Na}]^+$: 242.1151 Found: 242.1148
TLC (5% MeOH in CH_2Cl_2):	Prod. 4ae : 0.33 (UV, KMnO_4)

⁹ For a previous synthesis of amide **4ae** by acylation of the phenylacetyl chloride, see: Davis, F. A.; Vishwakarma, L. C. *Tetrahedron Lett.* **1985**, 26, 3539–3542.

N-(N-Boc-Glycyl)-L-Phenylalaninol (4qc, Table 1, entry 21):

A solution of IMes (**3**, 30 mg, 98 μmol , 0.05 equiv) in THF (1.95 mL) was added to a suspension of *N*-Boc-glycine methyl ester (**1q**, 373 mg, 1.97 mmol, 1.00 equiv) and L-phenylalaninol (**2c**, 298 mg, 1.97 mmol, 1 equiv) via a gas-tight syringe under an argon atmosphere. Within 5 min, amide **4qc** began to precipitate. After 17 h, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting yellow-residue was purified by flash column chromatography on silica gel (5 $\rightarrow$ 10% MeOH in CH_2Cl_2) to afford the amide **4qc** as a white crystalline solid (506 mg, 83%).

^1H NMR (500 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 7.30–7.33 (m, 2H, PhH_m), 7.21–7.26 (m, 3H, $\text{PhH}_{p,o}$), 6.34 (br-d, 1H, $\text{N}_{\text{amide}}\text{H}$), 5.10 (br-s, 1H, $\text{N}_{\text{carbamate}}\text{H}$), 4.19 (m, 1H, NCH), 3.75 (d, $J = 5.5$ Hz, 2H, CH_2CONH), 3.70 (m, 1H, CH_2OH), 3.59 (m, 1H, CH_2OH), 2.92 (d, $J = 7.5$ Hz, 1H, CH_2Ph), 2.89 (dd, $J = 7.5, 4.5$ Hz, 2H, CH_2Ph), 2.58–2.75 (br-d, 1H, OH), 1.46 (s, 9H, $(\text{CH}_3)_3$).

^{13}C NMR (125.8 MHz, CDCl_3 , 20 $^\circ\text{C}$): δ 170.1 (C_{amide}), 156.5 ($\text{C}_{\text{carbamate}}$), 137.7 (PhC_{ipso}), 129.4 (PhC_o), 128.8 (PhC_m), 126.9 (PhC_p), 80.6 ($\text{C}(\text{CH}_3)_3$), 63.7 (CH_2OH), 53.0 (NCH), 44.6 (BocNHCH_2), 37.2 (PhCH_2), 28.5 ($(\text{CH}_3)_3$).

FTIR (CHCl_3) cm^{-1} : 3424 (m, O–H), 2984 (m), 2935 (m), 1699 (s, C=O), 1674 (s, C=O).

HRMS (ESI): Calc for $\text{C}_{16}\text{H}_{24}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$: 309.1809
Found: 309.1811

m.p.: 134–135 $^\circ\text{C}$

TLC (10% MeOH in CH_2Cl_2): S.M. **1q**: 0.67 (ninhydrin)
Prod. **4qc**: 0.49 (UV, ninhydrin)

N-(N-Boc-Glycyl)-L-1-Methyl-Tryptophanol (4qf, Table 1, entry 22):

A solution of IMes (**3**, 30 mg, 98 μ mol, 0.05 equiv) in THF (1.95 mL) was added via a gas-tight syringe to a suspension of *N*-Boc-glycine methyl ester (**1q**, 373 mg, 1.97 mmol, 1.00 equiv) and L-1-methyl-tryptophanol (**2f**, 402 mg, 1.97 mmol, 1 equiv) under an argon atmosphere at 23 °C. After 1.5 h, the volatiles were removed under reduced pressure on a rotary-evaporator and the resulting yellow residue was purified by flash column chromatography on silica gel (5% MeOH in CH₂Cl₂) to afford the amide **4qf** as a white foam (628 mg, 88%).

¹H NMR (500 MHz, DMSO-*d*₆, 20 °C)

δ 7.61 (m, 2H, C₄H, N_{amide}H), 7.36 (d, *J* = 8.0 Hz, 1H, C₇H), 7.12 (t, *J* = 7.8 Hz, 1H, C₆H), 7.08 (s, 1H, C₁H), 7.01 (t, 1H, C₅H), 6.91 (br-t, *J* = 5.8 Hz, 1H, N_{carbamate}H), 4.76 (br-t, *J* = 5.0 Hz, 1H, OH), 3.94 (m, 1H, NCH), 3.72 (s, 3H, NCH₃), 3.54 (dd, *J* = 16.5, 6.5 Hz, 1H, BocNHCH₂), 3.49 (dd, *J* = 16.5, 6.0 Hz, 1H, BocNHCH₂), 3.30–3.40 (m, 2H, CH₂OH), 2.29 (dd, *J* = 14.5, 6.5 Hz, 1H, CH₂Ar), 2.74 (dd, *J* = 14.0, 6.3 Hz, 1H, CH₂Ar), 1.38 (s, 9H, (CH₃)₃).

¹³C NMR (125.8 MHz, CDCl₃, 20 °C):

δ 170.2 (C_{amide}), 156.4 (C_{carbamate}), 137.1 (C₈), 128.2 (C₃), 127.7 (C₁), 121.9 (C₄), 119.3 (C₅), 119.0 (C₆), 110.1 (C₇), 109.5 (C₂), 80.5 (C(CH₃)₃), 64.0 (CH₂-OH), 52.5 (NHCH), 44.6 (BocNHCH₂), 32.9 (NCH₃), 28.5 (C(CH₃)₃), 26.6 (CH₂Ar).

FTIR (CHCl₃) cm⁻¹:

3424 (m, O–H), 3004 (m), 2935 (m), 1706 (s, C=O), 1673 (s, C=O).

HRMS (ESI):

Calc for C₁₉H₂₇N₃O₄ [M+H]⁺: 362.2074
Found: 362.2077

m.p.:

64–66 °C

TLC (10% MeOH in CH₂Cl₂):

S.M. **1q**: 0.67 (ninhydrin)
Prod. **4qf**: 0.42 (UV, ninhydrin).

N-(N-Boc-1-Methyl-L-Tryptophanoyl)-L-Phenylalaninol (4rc-(S,S), Table 1, entry):

A solution of IMes (**3**, 30 mg, 98 μ mol, 0.05 equiv) in THF (1.95 mL) was added via a cannula to a suspension of *N*-Boc-1-methyl-tryptophan methyl ester (**1r**, 655 mg, 1.97 mmol, 1.00 equiv) and L-phenylalaninol (**2c**, 298 mg, 1.97 mmol, 1 equiv) under an argon atmosphere. After 18.5 h, the volatiles were removed under reduced pressure on a rotary-evaporator, and the resulting yellow-residue was purified by flash column chromatography on silica gel (2% MeOH in CH₂Cl₂) to afford the amide **4rc** as a white crystalline solid (781 mg, 88%). Chromatographic enrichment of amide **4rc** was not attempted (crude product, >94%*de*). The product was found to be >94%*de* and >98%*ee* by chiral HPLC analysis [Chirapak AD-H; 3.0 mL/min; 10% *i*-PrOH in hexanes; *t*_R(major-**4rc-S,S**) = 8.12 min, *t*_R(minor-**4rc-R,S**) = 11.8 min, *t*_R(not present-**4rc-S,R**) = 9.9 min, *t*_R(not present-**4rc-R,R**) = 14.8 min]. The L-phenylalaninol (**2c**) and the precursor to ester **1r**, 1-methyl L-tryptophan, were used as received from Aldrich (>98%*ee*).

¹H NMR (500 MHz, CDCl₃, 20°C)

δ 7.66 (d, *J* = 8.0 Hz, 1H, C₄H), 7.14–7.33 (m, 6H, ArH), 7.01 (m, 2H, ArH), 6.90 (s, 1H, C₁H), 5.78 (br-s, 1H, N_{amide}H), 5.16 (br-s, 1H, N_{carbamate}H), 4.36 (br-s, 1H, BocNHCH), 4.01 (br-s, 1H, NCH), 3.74 (s, 3H, NCH₃), 3.32 (m, 3H, CH₂Ar and CH₂OH), 3.10 (dd, *J* = 14.0, 7.5 Hz, 1H, CH₂OH), 2.67 (dd, *J* = 14.0, 8.0 Hz, 1H, CH₂Ph), 2.60 (m, 1H, CH₂Ph), 2.08 (br-s, 1H, OH), 1.44 (s, 9H, (CH₃)₃).

¹³C NMR (125.8 MHz, CDCl₃, 20 °C):

δ 172.0 (C_{amide}), 155.7 (C_{carbamate}), 137.6 (C₈), 137.1 (PhC_{ipso}), 129.3 (C₃), 128.6 (PhC_m), 128.0 (C₁, PhC_o), 126.7 (PhC_p), 122.1 (C₄), 119.5 (C₅), 119.1 (C₆), 109.5 (C₇), 109.2 (C₂), 80.3 (C(CH₃)₃), 63.3 (CH₂OH), 55.8 (BocNHCH), 52.9 (NHCH), 36.8 (CH₂Ph), 32.8 (NCH₃), 28.6 (CH₂Ar), 28.4 (C(CH₃)₃).

FTIR (CHCl₃) cm⁻¹:

3422 (m, O–H), 3005 (m), 2935 (m), 1705 (s, C=O), 1669 (s, C=O).

HRMS (ESI):

Calc for C₂₆H₃₃N₃O₄ [M+H]⁺: 452.2544
Found: 452.2541

m.p.:

149–150 °C

TLC (10% MeOH in CH₂Cl₂):

S.M. **1r**: 0.84 (UV, KMnO₄)
Prod. **4rc**: 0.50 (UV, KMnO₄)

IMes–Alcohol Complexes (Table 2)

Representative Experimental Procedure for Complex 8b (Table 2, entry 2):

Anhydrous methanol (14.0 μL , 32 μmol , 1.0 equiv) was added to a solution of IMes (**3**, 100 mg, 32.0 μmol , 1 equiv) and C_6D_6 (700 μL) in an NMR-tube under a nitrogen atmosphere in a glove-box. Alternatively, this complex is quantitatively formed upon removal of excess methanol from a solution of IMes in methanol under reduced pressure. Slow crystallization of complex **8b** from toluene affords high quality crystals that have the same ^1H NMR (C_6D_6) spectrum as complexes formed in solution.

IMes– HOCH_3 (**8b**):

^1H NMR (500 MHz, C_6D_6 , 20 $^\circ\text{C}$, 0.05M): δ 6.78 (s, 4H, ArH), 6.38 (s, 2H, C_4H), 4.37 (s, 1H, OH), 3.10 (s, 3H, CH_3OH), 2.13 (s, 18H, Ar CH_3).

^{13}C NMR (125.8 MHz, C_6D_6 , 20 $^\circ\text{C}$, 0.5M): δ 209.7 (C_2), 138.5 (Ar C_{ipso}), 138.1 (Ar C_o), 135.6 (Ar C_p), 129.5 (Ar C_m), 121.2 (C_4), 48.1 (CH_3OH), 21.4 ($p\text{-CH}_3$), 18.2 ($o\text{-CH}_3$).

The IMes–*tert*-butanol, –ethanolamine and –benzyl alcohol complexes (Table 2, entries 1 and 3–4) were prepared as described above and the data is shown below. For completeness and direct comparison, the relevant ^1H and ^{13}C NMR data for IMes (**3**) is listed below:

IMes– $\text{HO}t\text{Bu}$ (**8a**):

^1H NMR (500 MHz, C_6D_6 , 20 $^\circ\text{C}$, 0.05M): δ 6.80 (s, 4H, ArH), 6.43 (s, 2H, C_4H), 2.81 (s, 1H, OH), 2.16 (s, 12H, CH_3), 2.15 (s, 6H, CH_3), 1.07 (s, 3H, $\text{C}(\text{CH}_3)_3$).

IMes– $\text{HOCH}_2\text{CH}_2\text{NH}_2$ (**8c**):

^1H NMR (500 MHz, C_6D_6 , 20 $^\circ\text{C}$, 0.05M): δ 6.78 (s, 4H, ArH), 6.37 (s, 2H, C_4H), 5.24 (s, 1H, OH), 3.27 (t, $J = 5.3$ Hz, CH_2OH), 2.45 (t, $J = 5.0$ Hz, CH_2NH_2), 2.14 (s, 6H, Ar(CH_3) $_p$), 2.12 (s, 12H, Ar(CH_3) $_o$).

IMes– HOCH_2Ph (**8d**):

^1H NMR (500 MHz, C_6D_6 , 20 $^\circ\text{C}$, 0.05M): δ 7.05–7.21 (m, 5H, C_6H_5), 6.76 (s, 4H, ArH), 6.33 (s, 2H, C_4H), 5.8–6.2 (br-s, 1H, OH), 4.38 (s, 2H, CH_2), 2.14 (s, 6H, Ar(CH_3) $_p$), 2.08 (s, 12H, Ar(CH_3) $_o$).

IMes (3):

^1H NMR (500 MHz, C_6D_6 , 20 °C, 0.5 M): δ 6.81 (s, 4H, ArH), 6.50, (s, 2H, CH_4), 2.15 (s, 6H, Ar(CH_3)_p), 2.07 (s, 12H, Ar(CH_3)_o).

^{13}C NMR (125.8 MHz, C_6D_6 , 20 °C, 0.5 M): δ 219.4 (C_2), 139.6 (ArC_{ipso}), 137.6 (ArC_o), 135.7 (ArC_p), 129.5 (ArC_m), 120.9 (C_4), 21.4 ($p\text{-CH}_3$), 18.4 ($o\text{-CH}_3$).

IMes (**3**, 100 mg, 32.0 μmol , 1.0 equiv) was dissolved in methanol- d_4 (700 μL) and kept under argon atmosphere for 24 h. Removal of the methanol- d_4 under reduced pressure quantitatively afforded the hexadeuterated complex **8b-d₆**.¹⁰ Dissolution of the residue in C_6D_6 (700 μL) followed by NMR analysis indicated that the complex was >95% deuterated at the $\text{C}_{4,5}$.

IMes- d_2 -DOCD₃ (8b- d_6):

^1H NMR (500 MHz, C_6D_6 , 20 °C, 0.5M): δ 6.77 (s, 4H, ArH), 6.39, (s, <0.1H, $\text{C}_{4,5}\text{H}$ -residual), 5.88 (br-s, OH-residual), 3.11 (pentet, J = 1.5 Hz, CD_2HOD -residual), 2.11 (s, 6H, $p\text{-CH}_3$), 2.06 (s, 12H, $o\text{-CH}_3$).

^{13}C NMR (125.8 MHz, C_6D_6 , 20 °C, 0.5M): δ 203.9 (C_2), 138.4 (ArC_o), 137.9 (ArC_{ipso}), 135.5 (ArC_p), 129.5 (ArC_m), 121.1 (t, J_{CD} = 27.0 Hz, C_4), 48.0 (heptet, J_{CD} = 20.9 Hz, CD_3OD), 21.3 ($p\text{-CH}_3$), 18.2 ($o\text{-CH}_3$).

IMes- d_2 -DOCD₃ (8b- d_6):

^1H NMR (500 MHz, THF- d_8 , 20 °C, 0.5 M): δ 6.96 (s, 4H, ArH), 7.11, (s, <0.15H, $\text{C}_{4,5}\text{H}$ -residual), 5.33 (br-s, OH-residual), 2.31 (s, 6H, $p\text{-CH}_3$), 2.09 (s, 12H, $o\text{-CH}_3$).

^{13}C NMR (125.8 MHz, THF- d_8 , 20 °C, 0.5 M): δ 212.4 (C_2), 139.3 (ArC_{ipso}), 138.2 (ArC_p), 136.0 (ArC_o), 129.6 (ArC_m), 121.6 (t, J_{CD} = 29.4 Hz, C_4), 47.3 (heptet, J_{CD} = 20.8 Hz, CD_3OD), 21.3 ($p\text{-CH}_3$), 18.2 ($o\text{-CH}_3$).

¹⁰ For prior reports regarding preparation of doubly deuterated NHCs, see: Denk, M. K.; Rodezno, J. M. *J. Organometal. Chem.* **2000**, 608, 122-125 and Cole, M. L.; Jones, C.; Junk, P. C. *New J. Chem.* **2002**, 262, 1296–1303.

X-ray crystal structure of *N,N*-bismesitylimidazolylidene-methanol complex 8b:

Table 1. Crystal data and structure refinement for 04152final.

Identification code	04152final	
Empirical formula	C ₂₂ H ₂₈ N ₂ O	
Formula weight	336.46	
Temperature	123(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 14.9026(16) Å	$\alpha = 90^\circ$.
	b = 16.6125(17) Å	$\beta = 94.235(2)^\circ$.
	c = 7.8304(8) Å	$\gamma = 90^\circ$.
Volume	1933.3(3) Å ³	
Z	4	
Density (calculated)	1.156 Mg/m ³	
Absorption coefficient	0.071 mm ⁻¹	
F(000)	728	
Crystal size	0.15 x 0.10 x 0.08 mm ³	
Theta range for data collection	1.84 to 25.00°.	
Index ranges	-17 ≤ h ≤ 17, 0 ≤ k ≤ 19, 0 ≤ l ≤ 9	
Reflections collected	25954	
Independent reflections	3411 [R(int) = 0.0501]	
Completeness to theta = 25.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9944 and 0.8925	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3411 / 1 / 234	
Goodness-of-fit on F ²	1.175	
Final R indices [I > 2sigma(I)]	R1 = 0.0509, wR2 = 0.1134	
R indices (all data)	R1 = 0.0676, wR2 = 0.1214	
Largest diff. peak and hole	0.588 and -0.167 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for 04152final. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	6662(1)	746(1)	7418(2)	22(1)
N(3)	7698(1)	67(1)	6389(2)	25(1)
C(2)	7305(1)	195(1)	7881(2)	25(1)
C(4)	7307(1)	522(1)	5047(2)	26(1)
C(5)	6654(1)	952(1)	5695(2)	25(1)
C(11)	8447(1)	-475(1)	6261(2)	25(1)
C(12)	8299(1)	-1212(1)	5450(2)	27(1)
C(13)	9030(1)	-1725(1)	5386(3)	33(1)
C(14)	9878(1)	-1525(1)	6096(3)	33(1)
C(15)	9996(1)	-783(1)	6878(3)	33(1)
C(16)	9291(1)	-243(1)	6988(2)	28(1)
C(17)	7386(1)	-1448(1)	4676(3)	37(1)
C(18)	10660(2)	-2099(2)	6002(3)	47(1)
C(19)	9440(1)	553(1)	7864(3)	40(1)
C(21)	6076(1)	1074(1)	8633(2)	22(1)
C(22)	5174(1)	852(1)	8531(2)	21(1)
C(23)	4633(1)	1157(1)	9750(2)	24(1)
C(24)	4969(1)	1669(1)	11035(2)	25(1)
C(25)	5872(1)	1874(1)	11096(2)	27(1)
C(26)	6443(1)	1585(1)	9914(2)	25(1)
C(27)	4777(1)	295(1)	7165(2)	28(1)
C(28)	4367(2)	1991(1)	12337(3)	38(1)
C(29)	7421(1)	1816(1)	10038(3)	35(1)
O(1)	7891(1)	-406(1)	11145(2)	42(1)
C(30)	8177(2)	-1189(1)	10717(3)	40(1)

Table 3. Bond lengths [Å] and angles [°] for 04152final.

N(1)-C(2)	1.355(2)
N(1)-C(5)	1.392(2)
N(1)-C(21)	1.444(2)
N(3)-C(2)	1.363(2)
N(3)-C(4)	1.388(2)
N(3)-C(11)	1.442(2)
C(4)-C(5)	1.338(3)
C(11)-C(12)	1.389(3)
C(11)-C(16)	1.396(3)
C(12)-C(13)	1.388(3)
C(12)-C(17)	1.500(3)
C(13)-C(14)	1.384(3)
C(14)-C(15)	1.381(3)
C(14)-C(18)	1.512(3)
C(15)-C(16)	1.389(3)
C(16)-C(19)	1.498(3)
C(21)-C(22)	1.390(3)
C(21)-C(26)	1.396(3)
C(22)-C(23)	1.390(3)
C(22)-C(27)	1.503(3)
C(23)-C(24)	1.382(3)
C(24)-C(25)	1.387(3)
C(24)-C(28)	1.504(3)
C(25)-C(26)	1.388(3)
C(26)-C(29)	1.503(3)
O(1)-C(30)	1.415(3)
C(2)-N(1)-C(5)	112.42(15)
C(2)-N(1)-C(21)	121.90(15)
C(5)-N(1)-C(21)	125.67(15)
C(2)-N(3)-C(4)	112.37(16)
C(2)-N(3)-C(11)	122.76(15)
C(4)-N(3)-C(11)	124.87(15)
N(1)-C(2)-N(3)	102.53(16)
C(5)-C(4)-N(3)	106.33(16)
C(4)-C(5)-N(1)	106.35(16)
C(12)-C(11)-C(16)	122.49(18)
C(12)-C(11)-N(3)	118.99(17)
C(16)-C(11)-N(3)	118.52(17)
C(13)-C(12)-C(11)	117.43(18)
C(13)-C(12)-C(17)	121.00(19)
C(11)-C(12)-C(17)	121.58(18)
C(14)-C(13)-C(12)	122.2(2)
C(15)-C(14)-C(13)	118.38(19)
C(15)-C(14)-C(18)	120.8(2)
C(13)-C(14)-C(18)	120.9(2)
C(14)-C(15)-C(16)	122.16(19)
C(15)-C(16)-C(11)	117.32(19)
C(15)-C(16)-C(19)	120.73(18)
C(11)-C(16)-C(19)	121.95(18)
C(22)-C(21)-C(26)	121.91(17)
C(22)-C(21)-N(1)	119.43(16)
C(26)-C(21)-N(1)	118.62(16)
C(23)-C(22)-C(21)	118.13(17)
C(23)-C(22)-C(27)	119.70(16)
C(21)-C(22)-C(27)	122.17(16)
C(24)-C(23)-C(22)	121.80(18)

C(23)-C(24)-C(25)	118.35(17)
C(23)-C(24)-C(28)	120.68(18)
C(25)-C(24)-C(28)	120.97(18)
C(24)-C(25)-C(26)	122.23(18)
C(25)-C(26)-C(21)	117.58(17)
C(25)-C(26)-C(29)	120.51(18)
C(21)-C(26)-C(29)	121.91(17)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for 04152final. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	22(1)	25(1)	20(1)	1(1)	1(1)	2(1)
N(3)	22(1)	30(1)	22(1)	3(1)	3(1)	3(1)
C(2)	22(1)	30(1)	24(1)	1(1)	2(1)	1(1)
C(4)	26(1)	31(1)	21(1)	3(1)	1(1)	-1(1)
C(5)	27(1)	27(1)	22(1)	4(1)	-1(1)	1(1)
C(11)	23(1)	31(1)	21(1)	5(1)	8(1)	4(1)
C(12)	27(1)	32(1)	24(1)	6(1)	6(1)	0(1)
C(13)	38(1)	31(1)	30(1)	4(1)	9(1)	6(1)
C(14)	29(1)	46(1)	24(1)	8(1)	7(1)	12(1)
C(15)	21(1)	54(1)	25(1)	5(1)	2(1)	3(1)
C(16)	25(1)	38(1)	23(1)	4(1)	4(1)	1(1)
C(17)	32(1)	38(1)	43(1)	-2(1)	3(1)	-3(1)
C(18)	42(1)	60(2)	40(1)	8(1)	5(1)	24(1)
C(19)	32(1)	48(1)	39(1)	-6(1)	0(1)	-5(1)
C(21)	24(1)	20(1)	20(1)	3(1)	2(1)	3(1)
C(22)	24(1)	19(1)	20(1)	2(1)	-2(1)	1(1)
C(23)	22(1)	25(1)	25(1)	2(1)	1(1)	2(1)
C(24)	31(1)	21(1)	22(1)	2(1)	3(1)	4(1)
C(25)	37(1)	22(1)	21(1)	-3(1)	-1(1)	-2(1)
C(26)	27(1)	22(1)	26(1)	4(1)	-1(1)	-1(1)
C(27)	26(1)	31(1)	26(1)	-5(1)	-2(1)	-1(1)
C(28)	44(1)	39(1)	34(1)	-7(1)	9(1)	3(1)
C(29)	31(1)	37(1)	37(1)	-5(1)	0(1)	-10(1)
O(1)	60(1)	37(1)	29(1)	0(1)	-2(1)	7(1)
C(30)	41(1)	43(1)	36(1)	9(1)	-1(1)	7(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for 04152_{final}.

	x	y	z	U(eq)
H(4)	7471	528	3897	31
H(5)	6262	1325	5097	30
H(13)	8945	-2233	4836	39
H(15)	10577	-638	7357	40
H(17A)	7383	-2024	4404	56
H(17B)	7245	-1138	3625	56
H(17C)	6934	-1337	5492	56
H(18A)	10453	-2591	5407	71
H(18B)	10904	-2233	7164	71
H(18C)	11130	-1844	5376	71
H(18D)	11205	-1854	6557	71
H(18E)	10754	-2212	4800	71
H(18F)	10528	-2602	6588	71
H(19A)	10085	675	7973	59
H(19B)	9212	531	9005	59
H(19C)	9121	975	7187	59
H(23)	4015	1010	9699	29
H(25)	6109	2224	11977	32
H(27A)	4631	599	6109	42
H(27B)	4227	50	7546	42
H(27C)	5212	-129	6950	42
H(28A)	4717	2341	13144	58
H(28B)	4119	1541	12962	58
H(28C)	3875	2299	11754	58
H(28D)	3757	1780	12096	58
H(28E)	4355	2580	12278	58
H(28F)	4599	1822	13485	58
H(29A)	7603	1953	8897	53
H(29B)	7783	1363	10501	53
H(29C)	7514	2282	10799	53
H(10)	7683	-195	10176	51
H(30A)	8559	-1156	9753	60
H(30B)	7650	-1524	10395	60
H(30C)	8519	-1428	11706	60

Table 6. Torsion angles [$^{\circ}$] for 04152final.

C(5)-N(1)-C(21)-C(26)	-109.9(2)
C(4)-N(3)-C(11)-C(16)	106.2(2)
C(2)-N(1)-C(5)-C(4)	0.0(2)
C(2)-N(3)-C(4)-C(5)	0.3(2)
C(2)-H(1O)-O(1)-C(30)	-25.1(12)
N(1)-C(2)-H(1O)-O(1)	175.6(10)

Symmetry transformations used to generate equivalent atoms: