Catalytic Ester-Amide Exchange Using Group (IV) Metal Alkoxide-Activator Complexes

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I. General Information: ^1H NMR spectra were recorded on a 400 MHz spectrometer at ambient temperature. ^{13}C NMR spectra were recorded on a 75.0 MHz spectrometer at ambient temperature with complete proton decoupling. Variable temperature, DQF-COSY, and T-ROESY ^1H NMR experiments were recorded on a 500 MHz spectrometer. Chemical shifts for characterized compounds are reported in parts per million relative to CDCl_3 (^1H , δ 7.27; ^{13}C , δ 77.23) unless otherwise stated. Data for ^1H NMR are reported as follows: chemical shift, integration, multiplicity (app = apparent, br = broad, ovrlp = overlapping, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet) and coupling constants. Infrared spectra were recorded on a Nicolet Nexus 670 FT-IR spectrophotometer. React-IR spectra were recorded using a METTLER TOLEDO Autochem React-IR 3.0 spectrophotometer. Enantiomeric excess values were determined by chiral HPLC analysis performed on an Agilent 1100 series HPLC (column: Chiralcel[®]OD, Chiral technologies Inc., 24 cm x 4.6 mm). High-resolution mass spectra were obtained in the Boston University Mass Spectrometry Laboratory using a Finnegan MAT-90 spectrometer. Analytical thin layer chromatography was performed on 0.25 mm silica gel 60-F plates. Flash chromatography was performed using 200~400 mesh silica gel (Scientific Absorbents Incorporated). $\text{Zr}(\text{Ot-Bu})_4$ was obtained from Strem Chemicals and 1-hydroxy-7-azabenzotriazole (HOAt) was obtained from TCI-America Chemicals. Benzene- d_6 was distilled from calcium hydride. Yields refer to chromatographically and spectroscopically pure materials unless otherwise stated. All other reagents were used as supplied by Sigma-Aldrich, Alfa-Aesar, Lancaster, Fluka, Strem, and Bachem Chemicals. All reactions were performed in oven-dried glassware under an argon atmosphere unless otherwise noted. Compounds **1b**¹, **1c**², and **1d**³ were prepared according to procedures.

II. General procedure for ester-amide exchange catalyzed by $\text{Zr}(\text{Ot-Bu})_4$ and HOAt as additive (Table 3):

To a solution of carboxylic ester (1.00 mmol) and amine (1.10 mmol) in 1 mL (1.00 M in ester substrate) of toluene was added HOAt (0.05 mmol) followed by $\text{Zr}(\text{Ot-Bu})_4$ (0.05 mmol). The reaction was stirred at the desired temperature for the indicated time and quenched by addition of MeOH (2 mL) and CH_2Cl_2 (2 mL). The reaction mixture was filtered through a silica gel pad and concentrated *in vacuo*. Conversions were determined by ^1H NMR analysis of the crude reaction mixtures. Amide products were isolated by flash column chromatography using silica gel.

(1) Shieh, W.-C.; Dell, S.; Repič, O. *J. Org. Chem.* **2002**, 67, 2188.

(2) Maguire, A. R.; Plunkett, S. J.; Papot, S.; Clynes, M.; O'Connor, R.; Touhey, S. *Bioorg. Med. Chem.* **2001**, 9, 745.

(3) Kim, H. K.; Na, H. S.; Park, M. S.; Oh, T. K.; Lee, T. S. *J. Mol. Catal. B: Enzym.* **2004**, 27, 237.

III. Metal catalyst evaluation in the presence of HOBt:

catalyst	conversion (%) ^a	catalyst	conversion (%) ^a
Zr(<i>Ot</i> -Bu) ₄ + 2HOBt	79	HfCl ₄ + 2HOBt	33
Zr(<i>Oi</i> -Pr) ₄ + 2HOBt	65	Sb(<i>Oi</i> -Pr) ₃ + 2HOBt	21
Hf(<i>Ot</i> -Bu) ₄ + 2HOBt	80	ZnEt ₂ + 2HOBt	9
Hf(<i>Oi</i> -Pr) ₄ + 2HOBt	60	Cu(OBt) ₂	26

^a Conversion based on ¹H NMR analysis of the crude reaction mixture.

IV. Compound characterization:

Compounds **2a**,⁴ **2i**,⁵ **2l**,⁶ **2m**,⁷ **2o**,⁸ and **2p**,⁹ were characterized by comparing their ¹H NMR and ¹³C NMR data with those previously reported in the literature. Compound **2q** were characterized by comparing its ¹H NMR and ¹³C NMR data with spectra obtained from a commercially available sample (Aldrich).

Purified by flash chromatography on silica gel (hexane: EtOAc= 3:1). mp. 38-39 °C; IR (neat): 3279, 3082, 2929, 2858, 1656, 1619, 1557, 1451, 1341, 1224, 979, 865, 762, 682 cm⁻¹; ¹H NMR: δ 7.61 (1H, d, *J* = 15.2 Hz), 7.47-7.45 (2H, m), 7.35-7.30 (3H, m), 6.38 (1H, d, *J* = 15.2 Hz), 5.69 (1H, br), 3.37 (2H, dt, *J* = 7.2, 6.0 Hz), 1.57 (2H, tt, *J* = 7.2, 7.2 Hz), 1.36-1.25 (6H, m), 0.87 (3H, t, *J* = 6.8 Hz) ppm; ¹³C NMR: δ 166.2, 140.4, 134.9, 129.5, 128.7 (2C), 127.7 (2C), 121.2, 39.9, 31.6, 29.7,

(4) Matsuura, I.; Ueda, T.; Murakami, N.; Nagai, S.; Sakakibara, J. *J. Chem. Soc. Perkin Trans. 1* **1991**, 2821.

(5) Prashad, M.; Hu, B.; Har, D.; Repič, O.; Blacklock, T. J. *Tetrahedron Lett.* **2000**, 41, 9957.

(6) Ishihara, K.; Ohara, S.; Yamamoto, H. *J. Org. Chem.* **1996**, 61, 4196.

(7) Kim, J. M.; Wilson, T. E.; Norman, T. C.; Schultz, P. G. *Tetrahedron Lett.* **1996**, 37, 5309.

(8) Sanchez, R.; Vest, G.; Despres, L. *Synth. Commun.* **1989**, 19, 2909.

(9) Kunishima, M.; Kawachi, C.; Hioki, K.; Terao, K.; Tani, S. *Tetrahedron* **2001**, 57, 1551.

26.8, 22.6, 14.0 ppm; CI-HRMS calcd. for C₁₅H₂₂NO [M+H]⁺: 232.1701, found 232.1707.

Purified by flash chromatography on silica gel (hexane: EtOAc= 1:2). mp. 66-68 °C; IR (neat): 3285, 2986, 2961, 2937, 1636, 1539, 1380, 1372, 1252, 1217, 1158, 1074, 847, 762 cm⁻¹; ¹H NMR: δ 6.14 (1H, bs), 4.20 (1H, tt, *J* = 7.2, 6.8 Hz), 4.01 (1H, dd, *J* = 7.6, 7.2 Hz), 3.60 (1H, dd, *J* = 7.6, 7.2 Hz), 3.60 (1H, dd, ovrlp, *J* = 14.0, 6.8 Hz), 3.22 (1H, dd, *J* = 14.0, 6.8 Hz), 1.41 (3H, s), 1.31 (3H, s), 0.18 (9H, s) ppm; ¹³C NMR: δ 153.2, 109.8, 97.5, 92.2, 66.9, 42.3, 27.0, 25.4, -0.52 ppm; CI-HRMS calcd. for C₁₂H₂₂NO₃Si [M+H]⁺: 256.1369, found 256.1369.

Purified by flash chromatography on silica gel (hexane: EtOAc= 3:2). IR (neat): 3413, 2992, 2938, 1692, 1516, 1454, 1375, 1260, 1237, 1185, 1145, 1121, 1094, 1029, 915, 868, 831, 763 cm⁻¹; ¹H NMR: δ 7.20 (1H, bs), 6.75-6.71 (3H, m), 4.55 (1H, s), 4.27 (1H, d, *J* = 1.6 Hz), 4.13 (1H, d, *J* = 1.6 Hz), 4.06 (1H, dd, *J* = 14.0, 1.6 Hz), 4.00 (1H, d, *J* = 14.0 Hz), 3.83 (3H, s), 3.81 (3H, s), 3.57 (1H, ddt, *J* = 13.2, 7.6, 6.0 Hz), 3.37 (1H, ddt, *J* = 13.2, 7.6, 6.0 Hz), 2.74 (2H, dd, *J* = 7.6, 7.6 Hz), 1.52 (3H, s), 1.50 (3H, s), 1.38 (3H, s), 1.21 (3H, s) ppm; ¹³C NMR: δ 167.5, 149.2, 147.8, 131.4, 120.9, 114.7, 112.1, 111.6, 110.8, 97.7, 88.1, 73.7, 72.6, 60.3, 56.1, 56.0, 44.5, 35.5, 29.3, 27.3, 25.9, 18.7 ppm; CI-HRMS calcd. for C₂₂H₃₁NO₈ [M+H]⁺: 438.2128, found 438.2145. [α]_D²⁵ = - 12.8 (*c* = 1.88, CHCl₃)

Purified by flash chromatography on silica gel (hexane: EtOAc= 5:1). mp. 132-134 °C; IR (neat): 3324, 2949, 1733, 1644, 1595, 1539, 1502, 1487, 1443, 1306, 1251, 1217, 1170, 1095, 1037, 1015, 926, 847 cm⁻¹; ¹H NMR: δ 8.03 (1H, bs), 7.66 (2H, d, *J* = 8.4 Hz), 7.31 (2H, d, *J* = 8.4 Hz), 7.06 (1H, d, *J* = 8.8 Hz), 6.94 (1H, d, *J* = 2.0 Hz), 6.76 (1H, s), 6.73-6.70 (3H, m), 5.89 (2H, s), 4.44 (2H, d, *J* = 6.0 Hz), 3.81 (3H, s), 3.62 (2H, s), 2.31 (3H, s) ppm; ¹³C NMR: δ 172.9, 166.6, 154.3, 148.2, 147.3, 138.0, 133.9, 132.9, 132.1, 130.4, 129.0 (2C), 128.7 (2C), 121.4, 111.3, 111.0, 108.7, 108.6, 104.4, 101.3, 100.6, 56.1, 52.1, 44.2, 30.5, 12.0 ppm; CI-HRMS calcd. for C₂₇H₂₄ClN₂O₂ [M+H]⁺: 491.1373, found 491.1326.

Purified by flash chromatography on silica gel (CH₂Cl₂: acetone= 6:1, 1% Et₃N). mp. 88-90 °C; IR (neat): 3339, 2962, 2932, 2884, 1642, 1579, 1540, 1475, 1443, 1362, 1339, 1309, 1268, 1230, 1146, 1105, 1033, 945, 754, 713 cm⁻¹; ¹H NMR: δ 7.76 (2H, d, *J* = 7.2 Hz), 7.41 (1H, dd, *J* = 7.2, 7.2 Hz), 7.34

(2H, dd, $J = 7.2$, 7.2 Hz), 7.34 (1H, bs, ovrlp), 4.17 (2H, d, $J = 4.0$ Hz), 3.89 (4H, s), 3.65 (2H, t, $J = 6.0$ Hz), 3.43 (2H, t, $J = 6.0$ Hz), 1.63 (4H, t, $J = 6.0$ Hz) ppm; ^{13}C NMR: δ 167.4, 166.5, 134.1, 131.8, 128.7 (2C), 127.3 (2C), 106.8, 64.7 (2C), 42.6, 41.9, 40.5, 35.4, 34.9 ppm; CI-HRMS calcd. for $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$: 305.1501, found 305.1504.

Purified by flash chromatography on silica gel (CH_2Cl_2 : MeOH = 20:1). mp. 147-148 °C; IR (neat): 3251, 3074, 2931, 2882, 1636, 1559, 1457, 1297, 1199, 1127, 1987, 1022, 922, 718, 683 cm^{-1} ; ^1H NMR: δ 8.02 (3H, s), 7.57 (3H, bs), 3.59 (6H, t, $J = 4.4$ Hz), 3.52 (6H, t, $J = 4.4$ Hz), 3.36 (9H, s) ppm; ^{13}C NMR: δ 165.7 (3C), 134.9 (3C), 127.9 (3C), 71.2 (3C), 58.7 (3C), 40.2 (3C) ppm; CI-HRMS calcd. for $\text{C}_{18}\text{H}_{28}\text{N}_3\text{O}_6$ $[\text{M}+\text{H}]^+$: 382.1978, found 382.1999.

Purified by flash chromatography on silica gel (CH_2Cl_2 : acetone = 8:1). mp. 135-136 °C; IR (neat): 3291, 3078, 2927, 1642, 1551, 1444, 1223, 1151, 1015, 924, 731, 701 cm^{-1} ; ^1H NMR: δ 7.21 (2H, d, $J = 2.4$ Hz), 7.16 (1H, dd, $J = 7.6$, 7.6 Hz), 7.00 (2H, d, $J = 7.6$ Hz), 6.92 (1H, s), 6.34 (2H, bs), 6.21 (2H, dd, $J = 2.4$ Hz), 5.95 (2H, d, $J = 2.4$ Hz), 4.21 (4H, d, $J = 5.6$ Hz), 2.91 (4H, t, $J = 3.6$ Hz), 2.47 (4H, t, $J = 3.6$ Hz) ppm; ^{13}C NMR: δ 172.1 (2C), 154.6 (2C), 141.4 (2C), 138.9 (2C), 129.2, 127.1, 126.9 (2C), 110.5 (2C), 105.7 (2C), 43.5 (2C), 35.0 (2C), 24.2 (2C) ppm; CI-HRMS calcd. for $\text{C}_{22}\text{H}_{25}\text{N}_2\text{O}_4$ $[\text{M}+\text{H}]^+$: 381.1814, found 381.1812.

Purified by flash chromatography on silica gel (EtOAc: CH_2Cl_2 : MeOH: Et_3N = 5:2:2:1). mp. 155-157 °C; IR (neat): 3229, 2935, 2843, 2795, 1655, 1618, 1604, 1541, 1474, 1449, 1373, 1348, 1294, 1238, 1149, 1048, 1007 cm^{-1} ; ^1H NMR: δ 10.29 (1H, t, $J = 6.0$ Hz), 8.61 (1H, s), 7.67 (1H, d, $J = 12.4$ Hz), 7.33 (1H, d, $J = 2.0$ Hz), 6.27 (1H, d, $J = 2.0$ Hz), 6.24 (1H, d, $J = 2.0$ Hz), 4.64 (1H, dd, $J = 6.0$, 16.0 Hz), 4.59 (1H, dd, $J = 6.0$, 16.0 Hz), 4.39-4.26 (3H, m), 3.39 (4H, bs), 2.62 (4H, bs), 2.40 (3H, s), 1.55 (3H, d, $J = 6.8$ Hz) ppm; ^{13}C NMR: δ 175.3, 165.1, 157.6, 154.3, 152.2, 144.3, 142.1, 139.7, 132.2, 68.3, 55.9 (2C), 55.0, 50.8 (2C), 46.6, 36.4, 18.5 ppm; CI-HRMS calcd. for $\text{C}_{23}\text{H}_{26}\text{FN}_4\text{O}_4$: 440.1860, found 440.1885. $[\alpha]_{\text{D}}^{25} = -64.7$ ($c = 0.53$, CHCl_3)

Purified by flash chromatography on silica gel (CH_2Cl_2 : acetone = 6:1). mp. 178-179 °C; IR (neat): 3335, 2955, 2870, 1660, 1621, 1540, 1457, 1373, 1306, 1165, 1136, 834 cm^{-1} ; ^1H NMR: δ 6.62 (1H, d, $J = 9.6$ Hz), 6.17 (1H, d, $J = 9.6$ Hz), 5.77 (1H, bs), 4.48 (1H, d, $J = 9.6$ Hz), 3.64

(1H, bs), 3.27 (1H, ddt, $J = 13.2, 7.2, 5.6$ Hz), 3.24 (1H, ddt, $J = 13.2, 7.2, 5.6$ Hz), 2.57 (1H, dq, $J = 7.2, 4.0$ Hz), 1.94-1.86 (1H, m), 1.74-1.53 (5H, m), 1.36 (2H, dt, $J = 7.2, 7.2$ Hz), 1.22 (3H, d, $J = 7.2$ Hz), 1.18 (3H, s), 0.87 (6H, d, $J = 6.8$ Hz) ppm; ^{13}C NMR: δ 188.0, 176.4, 159.5, 156.7, 129.8, 125.8, 74.5, 50.2, 42.8, 42.2, 38.7, 38.3, 38.2, 26.1, 23.7, 23.5, 22.7, 22.6, 14.4, 11.6 ppm; CI-HRMS calcd. for $\text{C}_{20}\text{H}_{32}\text{NO}_3$ $[\text{M}+\text{H}]^+$: 334.2382, found 334.2359. $[\alpha]_{\text{D}}^{25} = -48.3$ ($c = 1.12$, CHCl_3)

Purified by flash chromatography on silica gel (hexane: EtOAc = 3:1). mp. 172-173 °C; IR (neat): 3341, 2903, 2848, 1632, 1531, 1495, 1451, 1412, 1283, 1238, 1104, 1002, 716, 692, 667 cm^{-1} ; ^1H NMR: δ 7.29-7.19 (5H, m), 5.99 (1H, bs), 4.38 (2H, d, $J = 4.8$ Hz), 1.99 (3H, bs), 1.84 (6H, bs), 1.67 (6H, dd, $J = 12.0, 11.2$ Hz) ppm; ^{13}C NMR: δ 178.1, 139.0, 128.9 (2C), 127.8 (2C), 127.6, 43.5, 40.9, 39.5 (3C), 36.8 (3C), 28.4 (3C) ppm; CI-HRMS calcd. for $\text{C}_{18}\text{H}_{24}\text{NO}$ $[\text{M}]^+$: 270.1780, found 270.1761.

V. ^1H NMR studies:

1. HOAt as additive.

a)

b)

c)

d)

e)

f)

g)

h)

i)

j)

k)

l)

m)

n)

o)

p)

q)

r)

s)

t)

2. HOBt or HYP as additive.

a)

b)

3. Reaction monitoring.

VI. Variable temperature and 2D ^1H NMR studies:

$\text{Zr}(\text{O}t\text{-Bu})_4$: HOAt: BnNH_2 (1:1:1) in 1 mL toluene- d_8 (0.05 M) varying from -50°C to 85°C .

zirconium complex 8

proposed conformer 9

Side view of 8

Side view of 9

Expanded region (6.2-8.5 ppm):

Expanded region (3.8-5.5 ppm):

Expanded region (0.4-1.8 ppm):

Zr(*Ot*-Bu)₄+ HOAt+ PhCD₂NH₂ (1:1:1) in toluene-*d*₈ (0.05M)

T-ROESY spectrum (4.4- 5.3 ppm) at 30°C

Zr(*Ot*-Bu)₄+ HOAt+ PhCD₂NH₂ (1:1:1) in toluene-*d*₈ (0.05M)

DQF-COSY spectrum (4.5- 5.4 ppm) at 0°C

VII. X-ray crystal structure of complex **8**:

Crystals of complex **8** suitable for X-ray diffraction analysis were obtained by slow evaporation from benzene-*d*₆. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC 267260). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Table 1. Crystal data and structure refinement for complex **8**.

Identification code	Complex 8	
Empirical formula	C ₃₀ H ₃₇ D ₈ N ₅ O ₄ Zr	
Formula weight	638.98	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 12.3129(3) Å	$\alpha = 90^\circ$.
	b = 12.9150(3) Å	$\beta = 100.849(1)^\circ$.
	c = 21.3187(5) Å	$\gamma = 90^\circ$.
Volume	3329.53(14) Å ³	
Z	4	
Density (calculated)	1.275 Mg/m ³	
Absorption coefficient	0.369 mm ⁻¹	
F(000)	1328	
Crystal size	0.30 x 0.15 x 0.02 mm ³	
Theta range for data collection	1.68 to 25.23°.	
Index ranges	-13 ≤ h ≤ 14, -15 ≤ k ≤ 14, -25 ≤ l ≤ 25	
Reflections collected	25543	
Independent reflections	6021 [R(int) = 0.0426]	
Completeness to theta = 25.23°	100.0 %	
Absorption correction	Semiempirical from equivalents	
Max. and min. transmission	0.9927 and 0.8974	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	6021 / 0 / 517	
Goodness-of-fit on F ²	1.022	
Final R indices [I > 2σ(I)]	R1 = 0.0304, wR2 = 0.0684	
R indices (all data)	R1 = 0.0490, wR2 = 0.0741	
Largest diff. peak and hole	0.423 and -0.438 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for complex **8**. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	$U(\text{eq})$
Zr(1)	6400(1)	9281(1)	43(1)	21(1)
O(1)	7593(1)	9326(1)	762(1)	34(1)
O(2)	5707(1)	7972(1)	178(1)	31(1)
O(3)	7067(1)	8966(1)	-681(1)	33(1)
O(4)	4768(1)	9827(1)	-566(1)	22(1)
N(1)	4531(1)	9609(1)	-1197(1)	23(1)
N(2)	3974(2)	8749(2)	-1412(1)	33(1)
N(3)	3853(2)	8743(2)	-2042(1)	41(1)
N(4)	5333(2)	11085(2)	-1634(1)	31(1)
N(5)	6754(2)	11065(2)	-188(1)	27(1)
C(1)	8422(2)	9097(2)	1306(1)	36(1)
C(2)	9341(3)	8508(4)	1094(2)	64(1)
C(3)	7891(3)	8458(3)	1766(2)	53(1)
C(4)	8855(3)	10115(3)	1616(2)	54(1)
C(5)	5577(2)	6879(2)	202(1)	32(1)
C(6)	4718(3)	6563(2)	-372(2)	49(1)
C(7)	5200(3)	6608(2)	819(2)	44(1)
C(8)	6679(3)	6378(2)	185(2)	53(1)
C(9)	7703(2)	8618(2)	-1135(1)	35(1)
C(10)	7048(3)	7772(3)	-1529(2)	60(1)
C(11)	8791(3)	8220(3)	-766(2)	54(1)
C(12)	7888(3)	9522(3)	-1554(2)	54(1)
C(13)	4785(2)	10188(2)	-1678(1)	26(1)
C(14)	4340(2)	9623(2)	-2219(1)	35(1)
C(15)	4452(2)	10045(3)	-2811(1)	50(1)
C(16)	4985(2)	10968(3)	-2787(1)	54(1)
C(17)	5410(2)	11458(2)	-2207(1)	43(1)
C(18)	7911(2)	11420(2)	-83(2)	42(1)
D(18B)	8330(20)	10920(20)	-235(13)	57(9)
D(18A)	8220(20)	11380(20)	370(15)	73(10)
C(19)	8066(2)	12479(2)	-357(1)	31(1)
C(20)	8360(2)	13319(2)	41(2)	44(1)
C(21)	8474(3)	14288(2)	-205(2)	57(1)

C(22)	8281(3)	14429(2)	-854(2)	61(1)
C(23)	7994(3)	13605(3)	-1256(2)	53(1)
C(24)	7889(2)	12631(2)	-1007(1)	41(1)
C(1S)	9367(3)	4887(3)	1637(2)	73(1)
H(1S)	9794	5446	1523	88
C(2S)	8325(4)	5038(4)	1673(2)	106(2)
H(2S)	8007	5708	1602	128
C(3S)	7723(4)	4255(7)	1809(2)	135(3)
H(3S)	6966	4382	1818	162
C(4S)	8120(6)	3260(5)	1939(2)	136(3)
H(4S)	7674	2707	2040	163
C(5S)	9257(4)	3141(3)	1909(2)	86(1)
H(5S)	9607	2488	1995	104
C(6S)	9834(3)	3953(3)	1757(2)	65(1)
H(6S)	10592	3864	1735	78

VIII. Kinetic studies:

Rate order to amine concentration:

Reaction conditions: ester= 1.0 mmol; catalyst= 0.05 mmol; total volume= 1.30 mL.

amine (mol)	amine conc. (mol·L ⁻¹)	Initial rate k (mol·L ⁻¹ ·s ⁻¹)	Ln(c)	Ln(k)
0.10	0.076923	0.0000162	-2.56495	-11.0305
0.15	0.115385	0.0000229	-2.15948	-10.6844
0.20	0.153846	0.000035	-1.8718	-10.2602
0.30	0.230769	0.0000609	-1.46634	-9.70628
0.50	0.384615	0.0000823	-0.95551	-9.40514

Rate order to ester concentration:

amine= 1.0 mmol; catalyst= 0.05 mmol; total volume= 1.30 mL.

ester (mol)	ester conc. (mol·L ⁻¹)	Initial rate k (mol·L ⁻¹ ·s ⁻¹)	Ln(c)	Ln(k)
0.10	0.076923	0.0000174	-2.56495	-10.959
0.15	0.115385	0.0000222	-2.15948	-10.7154
0.20	0.153846	0.0000334	-1.8718	-10.307
0.30	0.230769	0.0000538	-1.46634	-9.83024
0.50	0.384615	0.0000792	-0.95551	-9.44353

Rate order to zirconium concentration:

ester= 1.0 mmol; amine= 1.1 mmol; total volume= 1.30 mL.

cat. (mol%)	cat. conc. (mol·L ⁻¹)	Initial rate k (mol·L ⁻¹ ·s ⁻¹)	Ln(c)	Ln(k)
2.5	0.0192308	0.0000494	-3.95124	-9.91556
5.0	0.0384615	0.0000983	-3.2581	-9.22749
7.5	0.0576923	0.0001558	-2.85263	-8.76694
10.0	0.0769231	0.0001797	-2.56495	-8.62422