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A Simple and Practical Phase-Separation Approach to the Recycling of a Homogeneous Metathesis Catalyst

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Contents

1. General

Unless otherwise noted, all reactions were carried out under Ar in the "Radleys Heated Carousel Reaction Station" parallel reactor (www.radleys.com). The solvents were dried by distillation over the following drying agents and were transferred under argon: THF (K/benzophenone), toluene (Na), *n*-pentane, *n*-hexane, CH_2Cl_2 (CaH_2), Et_2O ($LiAlH_4$), MeOH (Mg). Flash column chromatography: Merck silica gel 60 (230–400 mesh). NMR: Spectra were recorded on Bruker AVANCE 500, Varian Gemini 200 and 400 spectrometers in $CDCl_3$; chemical shifts (δ) are given in ppm relative to TMS, coupling constants (J) in Hz. IR: Perkin-Elmer Spectrum 2000 FT-IR, wavenumbers in cm^{-1}. MS (EI, LSIMS): AMD 604 Intectra GmbH. MS (ESI): Mariner Perseptive Biosystems, Inc. GC: HP 6890 with HP 5 column. GC/MS: HP 5890 with HP 5 column. Micro-analyses were provided by Institute of Organic Chemistry, PAS, Warsaw.

2. Preparation of catalysts 16

Carbene complex **1b** (102 mg, 0.12 mmol), CuCl (13 mg, 0.132 mmol) and CH_2Cl_2 (8 mL) were placed in a Schlenk flask equipped with a condenser. A solution of (*Z*)-asarone, (28 mg, 0.12 mmol, Fluka) in CH_2Cl_2 (4 mL) was then added and the resulted solution was stirred under argon at 40 °C for 1 h. From this point forth, all manipulations were carried out in air with reagent-grade solvents. The reaction mixture was concentrated in vacuo and the resulted material was purified by column chromatography on silica. Elution with CH_2Cl_2:EtOAc (5:1) removes **16** as a khaki band. Removal of solvent, washing with a minimal amount of cold *n*-pentane and drying under vacuum afforded **16** (77 mg, 93%) as a olive-green microcrystalline solid (79 mg, 96% of yield).[i] $R_f = 0.00$ (CH_2Cl_2), ^{1}H NMR (500 MHz, $CDCl_3$) δ_H/ppm: 2,41 (s, 6H), 2,46 (s, 12H), 3,78 (s, 3H), 3,79 (s, 3H), 3,84 (s, 3H), 4,15 (s, 4H), 6,36 (s, 1H), 6,43 (s, 1H), 7,08 (s, 4H), 7,37 (s, 1H), 16,03 (br. s, 1H), ^{13}C NMR (125 MHz, $CDCl_3$) δ_C/ppm: 19,2, 21,1, 51,6, 56,2, 56,3, 58,9, 96,9, 105,4, 128,3, 129,7, 137,7, 138,6, 138,8, 144,6, 149,3, 150,7, 211,9, 294,7, MS (ESI) 623 $[M-Cl]^+$; Elemental analysis calculated (%) for $C_{31}H_{38}Cl_2N_2O_3Ru$ (658,64): C 56,53, H 5,82, N 4,25; found: C 56,41; H 6,01, N 4,18.

3. General procedures for metathesis and catalyst recovery

3.1. Ring-closing metathesis

A reaction flask equipped with a magnetic stirring bar was charged under argon with CH_2Cl_2 (30 mL), catalyst **16** (20.2 mg, 0.031 mmol) and diene (0.61 mmol). The reaction mixture was stirred at 24–45 °C. After complete conversion (TLC), the reaction mixture was passed through a cartridge containing silica gel (1.2–1.8 g). The cartridge was washed with an additional portion of CH_2Cl_2 (10 mL) and then with EtOAc (20 mL). The CH_2Cl_2 fraction was concentrated under reduced pressure to yield crude product **19–25**. After evaporation of the EtOAc fraction catalyst **16** was obtained as a olive green microcrystalline solid.

[i] Grela, K.; Kim, M. *Eur. J. Org. Chem.* **2003**, 963

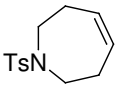
3.2. Cross- and homo-metathesis

A reaction flask equipped with a magnetic stirring bar was charged under argon with CH_2Cl_2 (30 mL), catalyst **16** (20.2 mg, 0.031 mmol) and alkene (0.61 mmol). In the case of products **26**, **28**, **29**, the appropriate cross-metathesis partner: 2-methyl-2-butene (6.1 mmol, 10 equiv), methyl acrylate (1.22 mmol, 2 equiv) or (Z)-4-(acetyloxy)-2-butenyl acetate (1.22 mmol, 2 equiv) was added. The reaction mixture was stirred at 24–45 °C. After complete conversion (TLC), the reaction mixture was passed through a cartridge containing silica gel (1.2–1.8 g). The cartridge was washed with an additional portion of CH_2Cl_2 (10 mL) and then with EtOAc (20 mL). The CH_2Cl_2 fraction was concentrated under reduced pressure and dried under high vacuum to yield crude products **26–29**. After evaporation of the EtOAc fraction catalyst **16** was obtained as a olive green microcrystalline solid.

4. Analytical data of isolated products

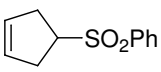
2,5-Dihydro-1-tosyl-1*H*-pyrrole (19)
Colourless crystals,[a] IR (film) ν/cm^{-1} 3048, 2910, 2854, 1928, 1595, 1492, 1476, 1450, 1336, 1305, 1288, 1161, 1103, 1070, 1017, 1001, 947, 819, ^{1}H NMR (200 MHz, $CDCl_3$) δ_H/ppm: 2,42 (s, 3H), 4,12 (d, J= 4,5 Hz, 4H), 5,65 (d, J= 4,5 Hz, 2H), 7,32 (d, J= 8,3 Hz, 2H), 7,72 (d, J= 8,3 Hz, 2H), ^{13}C NMR (50 MHz, $CDCl_3$) δ_C/ppm: 21,8, 55,1, 125,7, 127,7, 130,0, 134,6, 143,7, MS (EI) *m/z* 223 (20, $[M]^{+\cdot}$), 155 (25), 91 (100), 68 (80), 65 (52), 51 (12), 41 (44), 39 (52),

[a] Fürstner, A.; Liebl, M.; Lehmann, C.; Piquet, M.; Kunz, R.; Bruneau, C.; Touchard, D.; Dixneuf, P. H. *Chem. Eur. J.* **2000**, *6*, 1847.



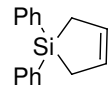
1-[(4-Methylphenyl)sulfonyl]-2,3,6,7-tetrahydro-1*H*-azepine (20)
Colourless crystalline solid,[a] IR (KBr) ν/cm^{-1} 3030, 2942, 2899, 2855, 1657, 1596, 1450, 1332, 1286, 1162, 910, 816, 712, ^{1}H NMR (200 MHz, $CDCl_3$) δ_H/ppm: 2,28 (m, 4H), 2,39 (s, 3H), 3,25 (m, 4H), 5,72 (m, 2H), 7,25 (d, J= 8,2 Hz, 2H), 7,64 (d, J= 8,2 Hz, 2H), ^{13}C NMR (50 MHz, $CDCl_3$) δ_C/ppm: 21,5, 29,9, 48,2, 126,9, 129,5, 130,1, 136,2, 142,9, MS (EI) *m/z* 251 (5, $[M]^{+\cdot}$), 223 (2), 184 (6), 155 (4), 105 (2), 91 (19), 96 (16), 77 (1), 65 (13), 42 (100), HRMS (EI): calculated for $[M]^{+\cdot}$ ($C_{13}H_{17}NO_2S$): 251,0980. Found 251,0979.

[a] Grela, K.; Kim, M. *Eur. J. Org. Chem.* **2003**, 963.



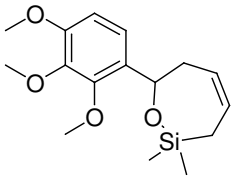
3-Cyclopentenyl phenyl sulfone (21)
Colourless oil,[a] ^{1}H NMR (200 MHz, $CDCl_3$) δ_H/ppm: 2,60–2,64 and 2,88–2,94 (m, 4H), 3,83–3,88 (m, 1H), 5,60 (s, 2H), 7,57–7,62 (m, 3H), 7,89–7,93 (m, 2H), ^{13}C NMR (50 MHz, $CDCl_3$) δ_C/ppm: 32,7, 60,5, 127,2, 127,4, 128,1, 132,5, 137,4, MS (EI) *m/z* 209 (1), 143 (100), 125 (17), 77 (22), 66 (95).

[a] Mioskowski, C. *Tetrahedron Lett.* **1994**, *35* , 5437.

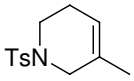


1,1-Diphenyl-1-sila-3-cyclopentene (22)
Colourless oil,[a] IR (film) ν/cm^{-1} 3068, 3047, 3005, 2931, 2870, 1641, 1621, 1427, 1402, 1150, 1114, 1055, 1029, 998, 816, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H/ppm: 1,91 (d, J = 1,0 Hz, 4H), 6,09 (s, 2H), 7,41–7,46 (m, 6H), 7,60–7,65 (m, 4H), ^{13}C NMR (125 MHz, $CDCl_3$) δ_C/ppm: 16,8, 127,9, 129,4, 131,0, 134,7, 135,8, MS (EI) *m/z* 236 (65, $[M]^{+\cdot}$), 221 (3), 208 (15), 182 (43), 181 (69), 180 (15), 173 (31), 159 (13), 158 (53), 155 (6), 145 (4), 131 (5), 130 (7), 106 (10), 105 (100), 82 (3), 79 (8), 77 (31), 68 (4), 53 (11), 51 (12), 41 (4), 39 (6), HRMS (EI): calculated for $[M]^{+\cdot}$ ($C_{16}H_{16}Si$): 236,1021. Found 236,1014.

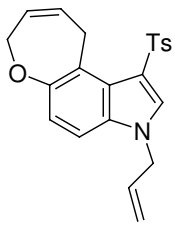
[a] Miguani, S.; Damour, D.; Bastart, J. P.; Manuel, G. *Synth. Commun.* **1995**, *25* , 3855.



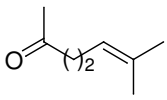
(4*Z*)-8,9,10-Trimethoxy-2,2-dimethyl-3,6-dihydro-2*H*-1,2-benzoxasilocine (23)
Colourless oil, IR (film) ν/cm^{-1} 3397, 2957, 2937, 1602, 1494, 1464, 1416, 1304, 1277, 1253, 1198, 1161, 1096, 1045, 1022, 938, 907, 839, 798, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H/ppm: 0,20 (d, J= 3,1 Hz, 6H), 1,43–1,57 (m, 1H), 1,81–1,94 (m, 1H), 2,25–2,35 (m, 1H), 2,54–2,66 (m, 1H), 3,83 (s, 3H), 3,84 (s, 3H), 3,90 (s, 3H), 5,20 (dd, J= 9,3, 1,4 Hz, 1H), 5,62–5,73 (m, 1H), 5,85–5,96 (m, 1H), 6,61–6,72 (m, 1H), 7,20 (dd, J= 8,6, 0,5 Hz, 1H),^{13}C NMR (100 MHz, $CDCl_3$) δ_C/ppm: −2,2, 18,5, 39,0, 56,0, 60,7, 60,9, 69,5, 107,2, 120,5, 126,9, 128,6, 131,6, 141,7, 149,9, 152,6, MS (EI) *m/z* 308 (19, $[M]^{+\cdot}$), 295 (7), 253 (5), 240 (17), 239 (100), 223 (26), 221 (6), 195 (7), 181 (5), 164 (6), 149 (5), 89 (13), 77 (4), 75 (7), 59 (7), 43 (2), 39 (2), HRMS (EI): calculated for $[M]^{+\cdot}$ ($C_{16}H_{24}O_4Si$): 308,1444. Found 308,1457.



5-methyl-1-[(4-methylphenyl)sulfonyl]-1,2,3,6-tetrahydropyridine (24)
Colourless crystalline solid, MS (EI) *m/z* 251 (70, $[M]^{+\cdot}$), 236 (21), 155 (20), 96 (55), 91 (100), 65 (60), 80 (16), 65 (60), 53 (19), 41 (68),



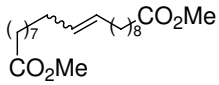
3-Allyl-1-[(4-methylphenyl)sulfonyl]-7,10-dihydro-3*H*-oxepino[3,2-e]indole (25)
Colourless oil, IR (KBr) ν/cm^{-1} 3143, 2924, 2854, 1640, 1595, 1578, 1509, 1479, 1444, 1417, 1394, 1353, 1340, 1288, 1262, 1228, 1204, 1172, 1138, 1091, 1065, 1051, 1019, 999, 976, 954, 947, 910, 876, 815, 767, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H/ppm: 2,39 (s, 3H), 3,82–3,89 (m, 2H), 4,51–4,55 (m, 2H), 4,72–4,78 (m, 2H),5,14–5,24 (m, 1H), 5,24–5,30 (m, 1H), 5,30–5,37 (m, 1H), 5,45–5,59 (m, 1H), 5,90–6,09 (m, 1H), 7,05–7,11 (m, 1H), 7,13–7,19 (m, 1H), 7,24–7,30 (m, 2H), 7,72–7,79 (m, 2H), 8,00 (s, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ_C/ppm: 21,5, 26,6, 49,7, 71,4, 109,2, 114,7, 118,6, 119,2, 122,4, 125,8, 126,7, 127,2, 129,6, 129,7, 131,5, 134,9, 136,8, 137,2, 140,6, 143,1, 154,4, MS (EI) *m/z* 379 (77, $[M]^{+\cdot}$), 364 (28), 258 (2), 252 (4), 225 (17), 224 (100), 223 (14), 211 (14), 208 (10), 207 (20), 196 (6), 183 (47), 182 (25), 170 (4), 167 (5), 154 (14), 139 (5), 127 (9), 115 (7), 91 (11), 65 (9), 41 (40), 39 (9), HRMS (EI): calculated for $[M]^{+\cdot}$ ($C_{22}H_{21}NO_3S$): 379,1242. Found 379,1252.



6-Methylhept-5-en-2-one (26)

Colourless liquid,[a] IR (film from DCM) ν/cm^{-1} 2954, 2926, 2855, 1744, 1690, 1610, 1590, 1521, 1478, 1449, 1430, 1381, 1342, 1270, 1213, 1145, 1125, 1094, 1075, 1046, 974, 944, 819, ^{1}H NMR (400 MHz, $CDCl_3$) δ_H/ppm: 1,61 (s, 3H), 1,68 (s, 3H), 2,14 (s, 3H), 2,20–2,31 (m, 2H), 2,41–2,50 (m, 2H), 5,02–5,10 (m, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ_C/ppm: 17,6, 22,5, 25,6, 29,9, 43,7, 122,6, 132,7, 208,8, MS (EI) *m/z* 126 (8, $[M]^{+\cdot}$), 111 (16), 108 (42), 93 (14), 83 (7), 71 (12), 69 (27), 68 (11), 67 (12), 58 (14), 55 (28), 53 (6), 43 (100), 41 (59), 39 (18), HRMS (EI): calculated for $[M]^{+\cdot}$ ($C_8H_{14}O$): 126,1045. Found 126,1049.

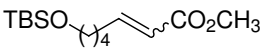
[a] Jansen, F. J.; Lugtenburg, *J. Eur. J. Org. Chem.* **2000**, *5*, 829.



Dimethyl icos-10-endioate (27)

Pale yelow solid,[a] (*E*):(*Z*) = 1,2:1, IR (film) ν/cm^{-1} 2926, 2854, 1741, 1436, 1362, 1260, 1196, 1171, 1094, 1018, 964, 865, 799, ^{1}H NMR (500 MHz, $CDCl_3$) δ_H/ppm: 5,11 (m, 1H), 3,66 (s, 6H), 2,29 (t, J = 6,8 Hz, 4H), 1,92–1,98 (m, 4H), 1,80–1,10 (m, 24H). Isomer (*E*). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C/ppm: 25,7, 29,1, 29,3, 29,5, 29,8, 29,9, 32,6, 34,1, 51,4, 131,1, 174,3 . Isomer (*E*). MS (EI) *m/z* 368 (10, $[M]^{+\cdot}$), 354 (8), 336 (27), 322 (22), 308 (15), 304 (34), 294 (9), 291 (10), 290 (27), 276 (19), 262 (12), 248 (8), 234 (4), 220 (4), 207 (4), 194 (6), 179 (8), 165 (12), 151 (17), 137 (18), 123 (19), 112 (23), 109 (27), 98 (49), 95 (55), 87 (29), 83 (36), 81 (70), 74 (48), 69 (60), 67 (62), 59 (28), 55 (100), HRMS (EI): calculated for $[M]^{+\cdot}$ ($C_{22}H_{40}O_4$): 368,2926. Found 368,2935.

[a] (a) Ruzicka, L.; Platter, P. A.; Widmer, W. *Helv. Chim. Acta* **1942**, *25*, 604; (b) Baker, R.; Crimnin, M. J. *Tetrahedron Lett.* **1977**, 441.



Methyl-7-[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy-2-heptenoate (28)

Colourless oil,[a] (*E*):(*Z*) = 95:5 IR (film) ν/cm^{-1} 2952, 2933, 2859, 1729, 1659, 1472, 1437, 1389, 1317, 1258, 1201, 1165, 1102, 1040, 983, 838, 777, ^{1}H NMR (500 MHz, $CDCl_3$) δ_H/ppm: 0,03 (s, 6H), 0,88 (s, 9H), 1,46–1,57 (m, 4H), 2,17–2,25 (m, 2H), 3,61 (t, J= 5,9 Hz, 2H), 3,71 (s, 3H), 5,81 (dt, J= 15,7, 1,6 Hz, 1H), 6,96 (dt, J= 15,7, 7,0 Hz, 1H), Isomer (*E*). ^{13}C NMR (125 MHz, $CDCl_3$) δ_C/ppm: −5,3, 18,3, 24,4, 25,9, 31,9, 32,2, 51,3, 62,7, 121,0, 149,4, 167,1, Isomer (*E*). MS (EI) *m/z* 257 (1, $[M-15]^+$), 241 (3), 217 (4), 215 (23), 183 (15), 171 (0,5), 155 (1), 139 (3), 119 (3), 101 (3), 89 (100), 81 (53), 79 (13), 75 (32), 73 (25), 59 (24), 47 (11), 41 (21), 39 (10), HRMS (ESI): calculated for $[M+Na]^+$($C_{14}H_{28}O_3SiNa$): 295,1700. Found 295,1691.

[a] Nicolaou, K. C.; Hwang, C.-K.; Marron, B. E.; DeFrees, S. A.; Couladouros, E. A. *J. Am. Chem. Soc.* **1990**, *112*, 3040.

***(2E)*-Octadec-2-en-1-yl acetate (29)**

Colourless oil,[a] (*E*):(*Z*) = 9:1, IR (film from DCM) ν/cm^{-1} 2924, 2854, 1744, 1464, 1378, 1363, 1229, 1024, 967, izomer (*E*): ^{1}H NMR (400 MHz, $CDCl_3$) δ_H/ppm: 0,88 (t, *J*= 6,7 Hz, 3H), 1,19–1,33 (m, 26H), 2,00–2,13 (m, 5H), 4,51 (dd, *J*= 6,6, 1,1 Hz, 2H), 5,48–5,60 (m, 1H), 5,72–5,82 (m, 1H), izomer (*Z*): ^{1}H NMR (400 MHz, $CDCl_3$) δ_H/ppm: 0,88 (t, *J*= 6,7 Hz, 3H), 1,33–1,44 (m, 26H), 2,00–2,13 (m, 5H), 4,62 (dd, *J*= 6,8, 1,1 Hz, 2H), 5,48–5,60 (m, 1H), 5,72–5,82 (m, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) δ_C/ppm: 14,1, 21,0, 22,7, 26,9, 28,9, 29,2, 29,3, 29,4, 29,5, 29,6, 29,7, 30,1, 32,0, 32,2, 65,3, 135,5, 136,8, 170,9, Isomer (*E*). MS (EI) *m/z* 310 (1, $[M]^{+\cdot}$), 268 (9), 250 (10), 239 (5), 222 (11), 208 (4), 152 (3), 138 (4), 137 (4), 124 (7), 123 (8), 114 (10), 113 (5), 110 (14), 109 (13), 100 (8), 97 (20), 96 (49), 95 (25), 85 (5), 83 (24), 82 (48), 81 (31), 71 (10), 69 (24), 68 (35), 67 (29), 57 (25), 55 (42), 54 (28), 43 (100), 41 (40), 39 (6), Elemental analysis calculated (%) for $C_{20}H_{38}O_2$ (310,54): C 77,36, H 12,33; found: C 77,49, H 12,36.

[a] Attygalle, A. B.; Svatos, A,; Wilcox, Ch.; Voerman, S. *Anal. Chem.* **1995**, *67*, 1558.

5. Purification of RCM product 19

a.  b.  c. 

*(a–c) Loading cartridges. Left: Hoveyda-Grubbs (**2b**), right: Asarone catalyst (**16**).*[ii]

[ii] We thank Ms. Zuzanna Kaczmarska for the photographic documentation of this experiment. ImageMagick 6.2.2 and GIMP 2.2.8 were used for image conversions

d.  e.  f. 

g.  h.  i. 

*(d–i) Eluting cartridges with CH_2Cl_2. Left: Hoveyda-Grubbs (**2b**), right: Asarone catalyst (**16**).*

j.  k.  l. 

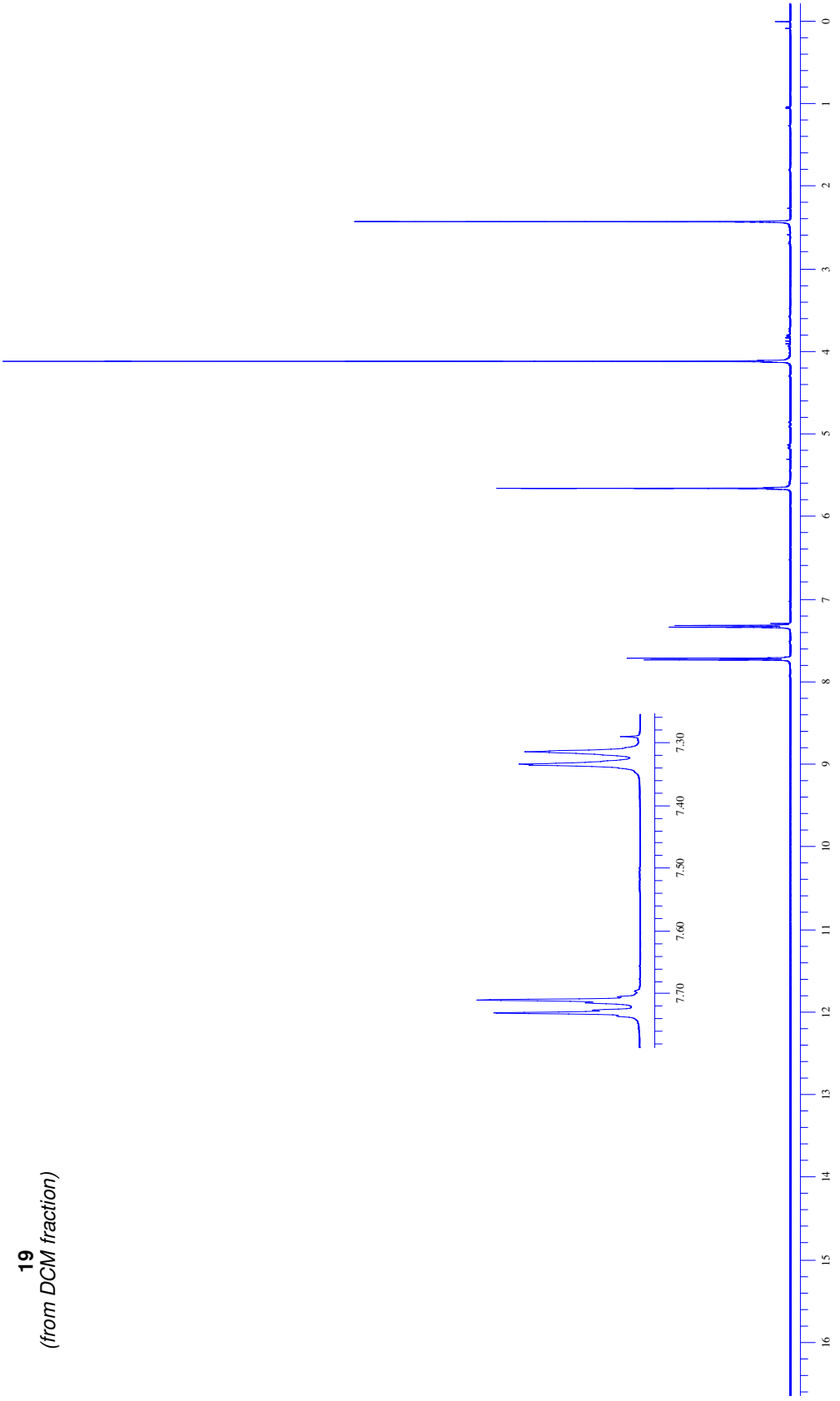
m.  n.  o. 

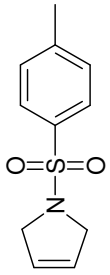
p.  q.  r. 

*(j–r) Eluting cartridges with EtOAc. Left: Hoveyda-Grubbs (**2b**), right: Asarone catalyst (**16**).*

6. Sample NMR spectra

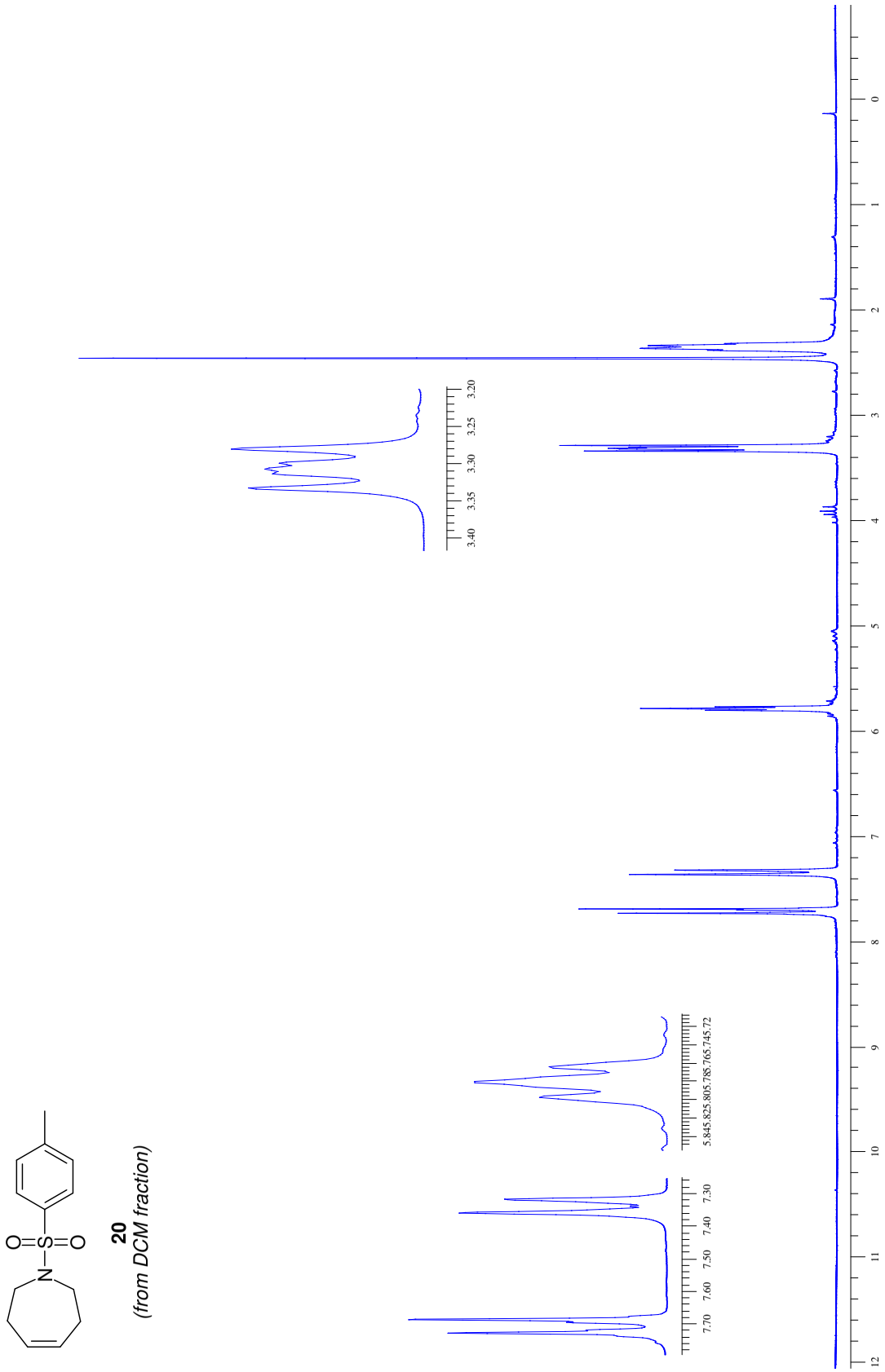
6.1. Representative NMR spectra of products obtained from DCM filtrates





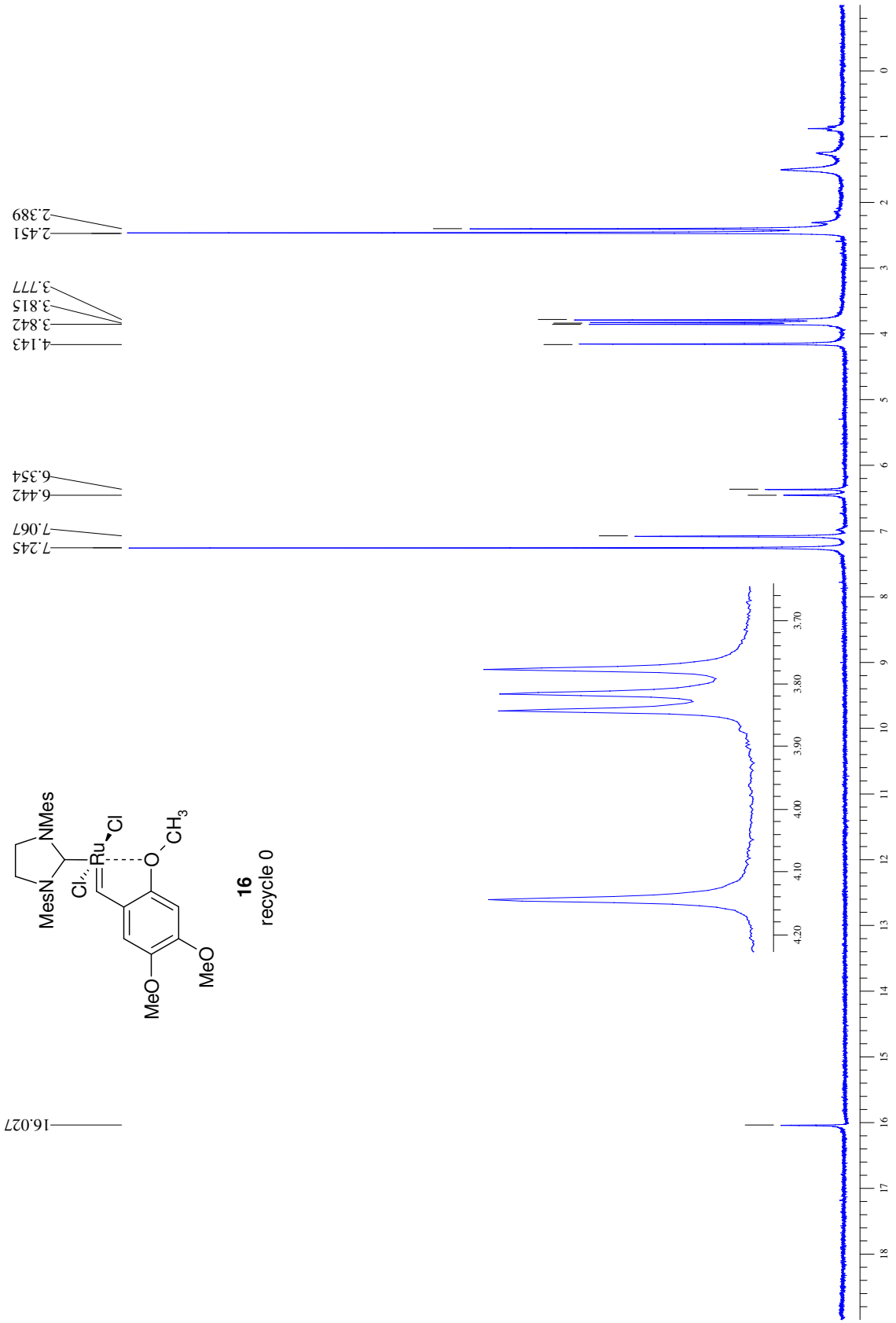
19
(from DCM fraction)

Varian 200 MHz, $CDCl_3$

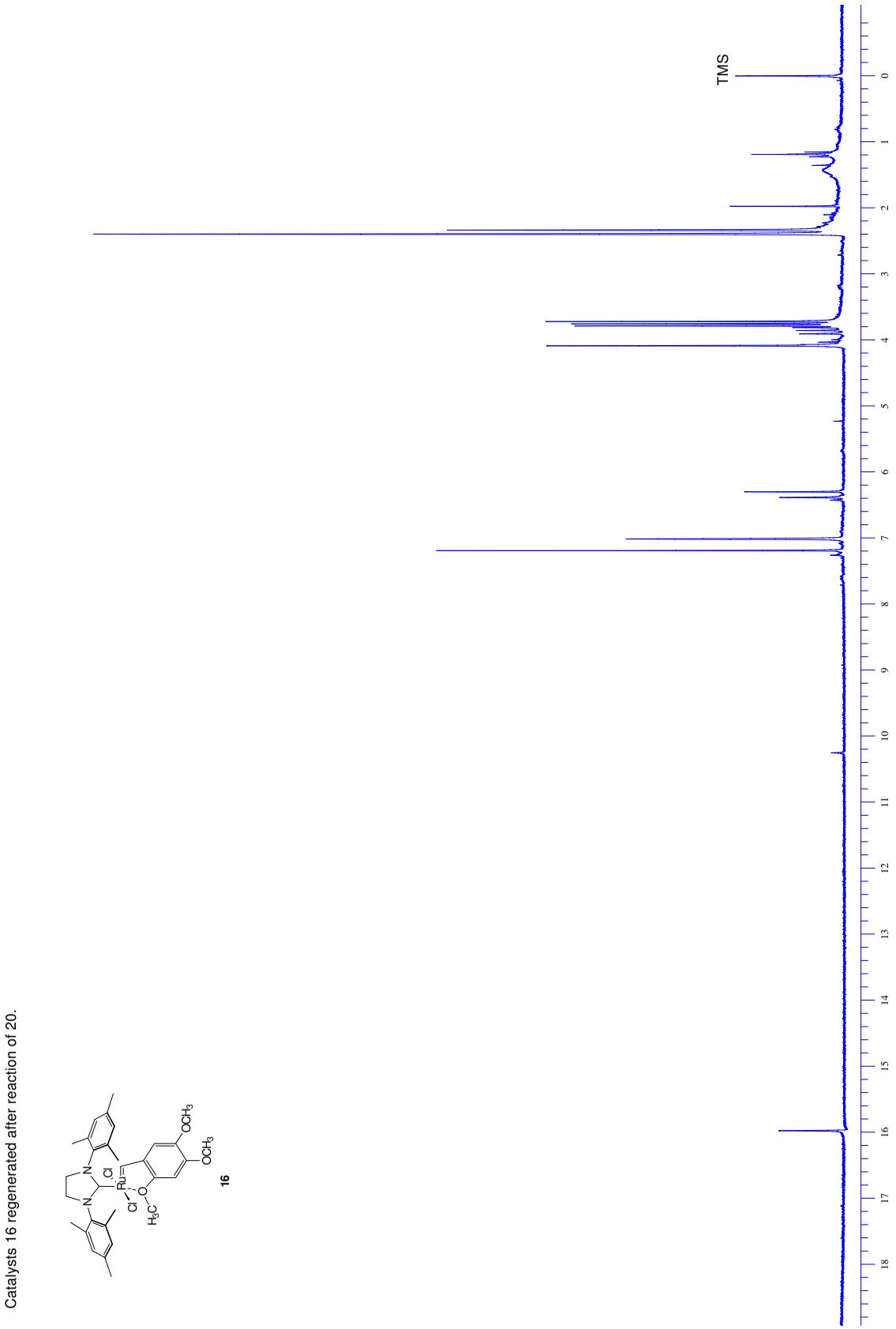


Varian 200 MHz, $CDCl_3$

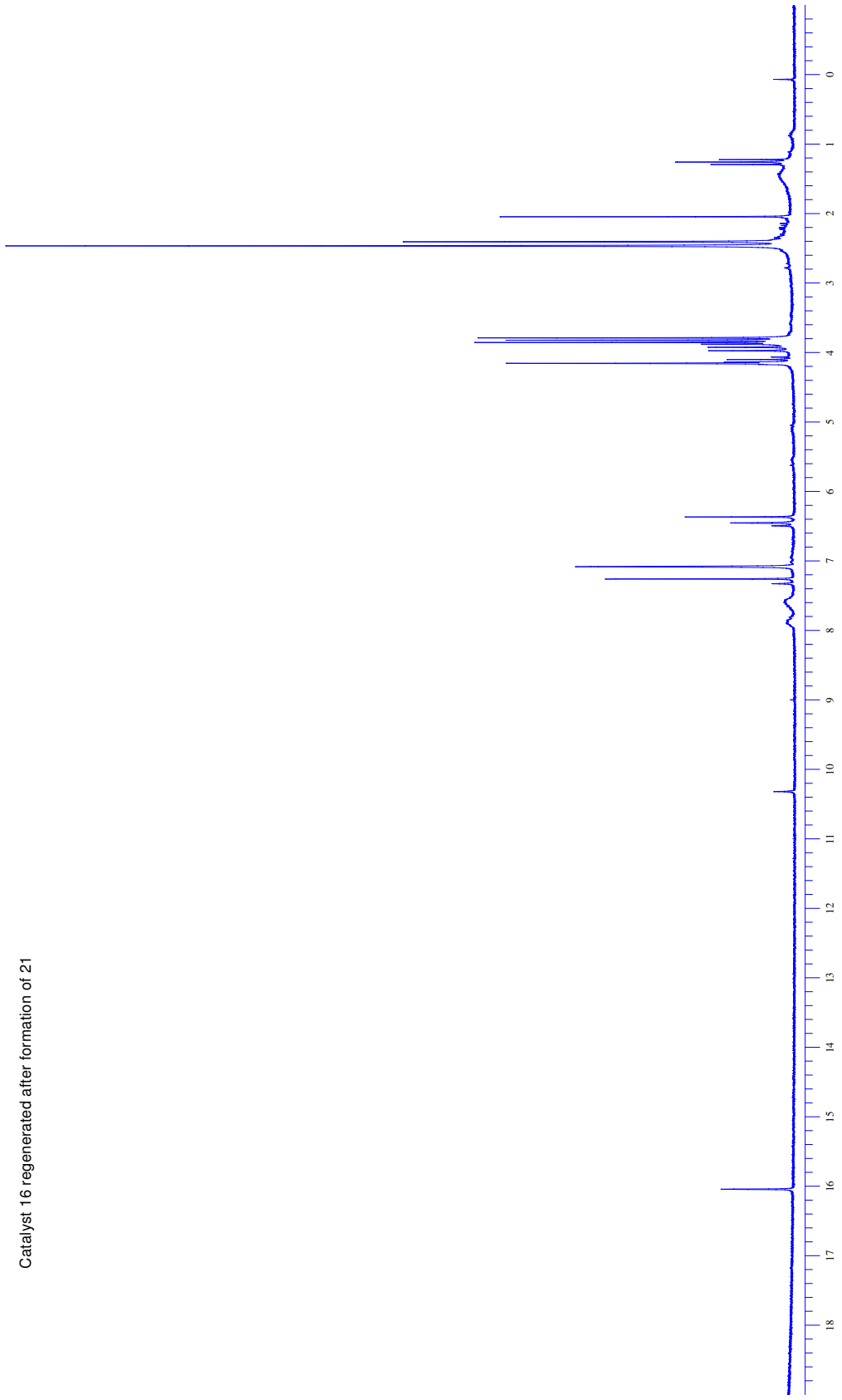
6.2. Representative NMR spectra of catalysts 16 obtained from EtOAc filtrates



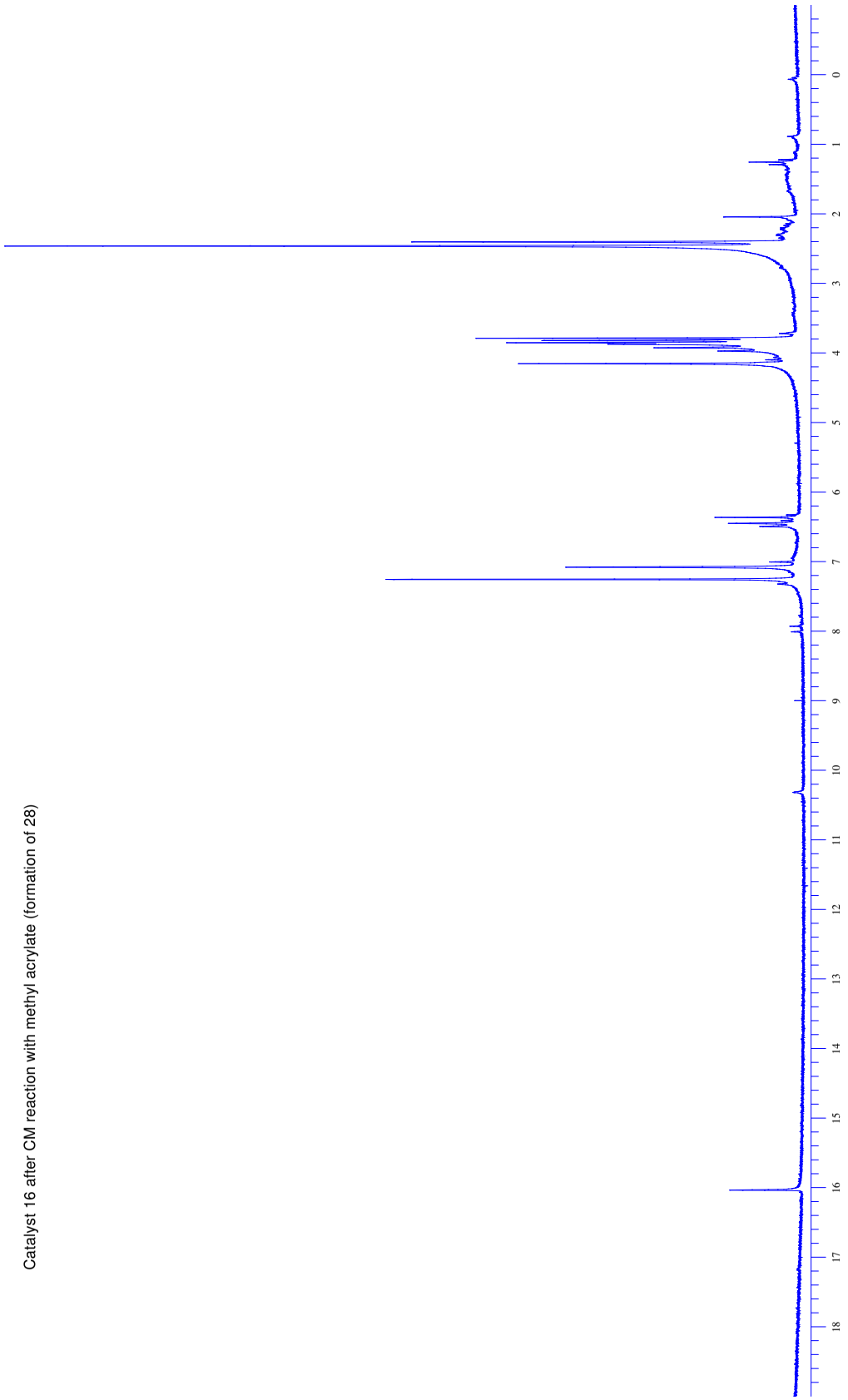
Catalyst **16** for reaction of **20**. Varian 200 MHz, $CDCl_3$



Catalyst **16** after reaction of **20**. Varian 200 MHz, $CDCl_3$



Catalyst **16** after reaction of **21**. Varian 200 MHz, $CDCl_3$



Catalyst **16** after reaction of **28**. Varian 200 MHz, $CDCl_3$