A green catalyst for green chemistry: Synthesis and application of an olefin metathesis catalyst bearing a quaternary ammonium group

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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$_2$Cl$_2$ (CaH$_2$), Et$_2$O (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. 4-(Diethylamino)-2-hydroxybenzaldehyde (9), methyl iodide, 2-propyl iodide, CuCl and carbene $\text{1b}$ were purchased from Aldrich.

2. Preparation of catalysts 8

2.1. N,N-diethyl-N-3-isopropoxy-4-[(E,Z)-1-propenyl]-phenylamine (10)

K$_2$CO$_3$ (1.24 g, 9.0 mmol) and Cs$_2$CO$_3$ (410 mg, 1.26 mmol) were placed in a round bottom flask. A solution of 4-(diethylamino)-2-hydroxybenzaldehyde (1.16 g, 6.0 mmol) in dry DMF (15 mL) was added. After stirring for 10 minutes at room temperature 2-iodopropane (0.9 mL, 9.0 mmol) was added. The reaction was carried out for the next 24 hours at room temperature. After pouring onto a saturated aqueous solution of K$_2$CO$_3$ the reaction mixture was extracted with MTBE. The combined organic layers were washed with 1M solution of NaOH and then with brine, dried (MgSO$_4$) and the solvent was removed under reduced pressure. Crude 4-(diethylamino)-2-isopropoxybenzaldehyde (10) was obtained as a dark red oil (1.28 g, 5.4 mmol; 91%). IR (film) $\nu$/cm$^{-1}$: 2976, 2930, 2867, 2836, 2758, 1658, 1587, 1547, 1521, 1471, 1406, 1391, 1356, 1299, 1238, 1210, 1106, 1076, 1015, 979, 930.; $^1$H NMR (200 MHz, C$_6$D$_6$) $\delta$/ppm: 10.72 (s, 1H), 8.10 (d, $J = 9.2$ Hz, 1H), 6.03 (dd, $J = 9.2$, 2.1 Hz, 1H), 5.93 (d, $J = 2.1$ Hz, 1H), 4.30 (septet, $J = 6.0$ Hz, 1H), 2.87 (q, $J = 7.1$ Hz, 4H), 1.09 (d, $J = 6.0$ Hz, 6H), 0.82 (t, $J = 7.1$ Hz, 6H); $^{13}$C NMR (50 MHz, C$_6$D$_6$) $\delta$/ppm: 186.4, 163.0, 153.6, 130.5, 116.6, 105.1, 95.7, 70.7, 44.6, 22.0, 12.6; MS (EI) m/z 235 (32) [M$^+$], 220 (31), 192 (7), 178 (100), 162 (9), 150 (14), 148 (8), 136 (2), 122 (4), 106 (2), 94 (4), 77 (5), 65 (9), 41 (9), HRMS (EI) calcd. for C$_{14}$H$_{21}$O$_2$N: 235.1572 [M$^+$]; found: 235.1580.

To a solution of dry THF (450 mL) and ethyltriphenylphosphonium bromide (22.08 g, 59.46 mmol) under argon at $-78^\circ$C was added dropwise n-BuLi (2.5 M in hexane 25.6 ml, 63.7 mmol). After 15 minutes at $-78^\circ$C the solution was heated at 30°C for three hours. After this period the solution was cooled again to $-78^\circ$C and 4-(diethylamino)-2-isoproxybenzaldehyde (10 g, 42.26 mmol) was added. After 30 minutes the reaction mixture was warmed to room temperature and was stirred overnight at this temperature. After pouring onto a saturated aqueous solution of NaHCO$_3$ the reaction mixture was extracted with MTBE. The combined organic layers were dried (MgSO$_4$) and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (5% ethyl acetate in hexane with 1.5% triethyl amine) to afford 10 as a yellow oil (10.3 g, 41.6 mmol, 98%; (E)/(Z) = 2:1).
2.2. Diethyl(methyl)[3-izopropoxy-4-[(E/Z)-prop-1-en-1-yl]phenyl]ammonium iodide (11)

Amine 10 (0.074 g, 0.3 mmol) and neat MeI (0.23 mL, 3.6 mmol) were placed in a round bottom flask and stirred at room temperature for 2 days. Excess of MeI was evaporated to dryness to give 11 (0.116 g, 0.3 mmol, 100 %) as a colourless solid ((E):(Z) = 4:1).
2.3. Quaternary salt 8

Carbene complex 1b (0.081 g, 0.10 mmol), CuCl (0.014 g, 0.14 mmol) and CH₂Cl₂ (3 mL) were placed in a Schlenk flask equipped with a condenser. A solution of 11 (0.045 g, 0.11 mmol) in CH₂Cl₂ (3 mL) was then added and the resulted solution was stirred under argon at 40 °C for 15 min. From this point forth, all manipulations were carried out in air with reagent-grade solvents. The reaction mixture was concentrated in vacuo and to the residue EtOAc (10 mL) was added. The solution was filtered off and the residue was washed on a Buchner funnel with MeOH (20 mL) and dried under vacuum to give complex 8 as green microcrystalline solid (0.051 g, 63 %).

IR (KBr) \( \nu/\text{cm}^{-1} \): 3431, 2928, 2852, 1629, 1592, 1484, 1448, 1398, 1384, 1295, 1262, 1214, 1168, 1141, 1098, 1030, 980, 898, 852, 821. \(^1\)H NMR (500 MHz, CDCl₃) \( \delta/\text{ppm} \): 1.05 (br.s, 6H), 1.34–1.55 (m, 6H), 2.40 (s, 6H), 2.46 (s, 12H), 3.60 (s, 3H), 4.18 (s, 4H), 4.20–4.65 (m, 4H), 5.25–5.45 (m, 1H), 6.90–7.15 (m, 6H), 7.60 (s, 1H), 16.59 (s, 1H). \(^{13}\)C NMR (125 MHz, CDCl₃) \( \delta/\text{ppm} \): 8.9, 19.4, 21.1, 22.0, 35.1, 51.5, 64.6, 78.3, 108.0, 115.7, 122.0, 126.8, 128.7, 129.4, 139.1, 139.5, 145.4, 153.5, 208.3, 290.1. HRMS (ESI (+)): calcd for \([M-126]^+\) \(\text{C}_{36}\text{H}_{50}\text{N}_3\text{O}^3\text{Cl}_2\text{Ru}\): 712.23744. found 712.2379. \(^a\)


3. General procedures for metathesis

3.1. Representative procedure of metathesis in CH₂Cl₂

A reaction tube equipped with a magnetic stirring bar was charged with CH₂Cl₂ (10 mL), catalyst 8 (1–5 mol %) and substrate 12 (0.2 mmol). The reaction mixture was stirred at 25 °C. After complete conversion (TLC), the reaction mixture was passed through a cartridge containing silica gel (1–2 g). The cartridge was washed with an additional portion of CH₂Cl₂ (10–20 mL). The CH₂Cl₂ fraction was concentrated under reduced pressure to yield crude product 13.

3.2. Representative procedure of metathesis in EtOH–H₂O and MeOH–H₂O

A reaction tube equipped with a magnetic stirring bar was charged with catalyst 8 (6 mg, 0.007 mmol, 5 mol %) and non-degassed water (2 mL). To the resulting suspension a solution of substrate 12 (0.14 mmol) in MeOH or EtOH (5 mL) was added. The reaction mixture was stirred at 25 °C. After complete conversion (TLC), the reaction mixture was evaporated to dryness, dissolved in CH₂Cl₂ (5 mL) and passed through a cartridge containing silica gel (1–2 g). The cartridge was washed with an additional portion of CH₂Cl₂ (15–25 mL). The CH₂Cl₂ fraction was concentrated under reduced pressure to yield crude product 13.
4. General procedure for residual ruthenium analyses

Samples of the crude metathesis product were digested with subboiled HNO₃ (4 mL) and H₂O₂ (1 mL, p.a.; Merck), and diluted with dist. water (to 250 mL). The Ru determination was carried out with an inductively coupled plasma mass spectrometer (ICP-MS) Thermo X7 ICP-MS (Thermo Electron GmbH, Dreieich, Germany, www.thermo.com). This quadrupole instrument had a power of 1200W throughout the measurement. The gas flow rates were 1.0 ml/min (Nebuliser), 1.2 mL/min (Auxiliary) and 13 mL/min (Cool) argon 4.8, respectively. Quantification was performed with liquid Ru standards from 0.01–50 µg/L. For drift corrections during the measurements a standard of 1 µg/L Ru was interspaced after every second sample measurement.

5. Analytical data of isolated products

**Diethyl 3-methylcyclopent-3-ene-1,1-dicarboxylate (13a)**

Colourless oil.a IR (film) ν/cm⁻¹ 2982, 2937, 1733, 1446, 1367, 1252, 1184, 1161, 1097, 1022, 861.¹H NMR (500 MHz, CDCl₃) δH/ppm: 1.24 (t, J = 7.0 Hz, 6H), 1.70 (d, J = 1.5 Hz, 3H), 2.93 (s, 2H), 2.96 (br.s, 2H), 4.19 (q, J = 7.0 Hz, 4H), 5.18 (d, J = 1.5 Hz, 1H), ¹³C NMR (100 MHz, CDCl₃) δC/ppm: 14.0 16.0, 40.8, 44.6, 59.4, 61.4, 121.2, 137.4, 172.3, . MS (EI) m/z 226 (24, [M]+), 181 (17), 180 (15), 153 (49), 152 (100), 136 (2), 134 (3), 125 (25), 124 (25), 107 (44), 97 (8), 93 (35), 81 (25), 80 (47), 79 (64), 77 (21), 67 (9), 55 (3), 53 (7), 39 (9), HRMS (EI): calcd for [M]⁺ (C₁₂H₁₈O₄): 226.1205. found 226.1210.

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**2,5-Dihydro-1-tosyl-1H-pyrrole (13b)**

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, ¹H NMR (200 MHz, CDCl₃) δH/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), ¹³C NMR (50 MHz, CDCl₃) δC/ppm: 21.8 55.1, 125.7, 127.7, 130.0, 134.6, 143.7, MS (EI) m/z 223 (20, [M]+), 155 (25), 91 (100), 68 (80), 65 (52), 51 (12), 41 (44), 39 (52).

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Diethyl cyclopent-3-ene-1,1-dicarboxylate (13c)

Colourless oil.\textsuperscript{a} IR (film) $\nu$/cm\textsuperscript{-1} 2983, 2934, 1733, 1642, 1446, 1367, 1256, 1182, 1073, 1017, 922, $^1$H NMR (500 MHz, CDCl$_3$) $\delta$/ppm: 1.24 (t, $J$ = 7.1 Hz, 6H), 3.01 (s, 4H), 4.19 (q, $J$ = 7.1 Hz, 4H), 5.61 (s, 2H), $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$/ppm: 14.1, 36.7, 61.2, 61.5, 127.8, 172.2, MS (EI) $m$/z 212 (43, [M]$^+$), 199 (12), 195 (6), 173 (2), 167 (58), 166 (80), 153 (48), 149 (12), 139 (70), 138 (100), 127 (4), 125 (18), 111 (52), 110 (35), 94 (11), 93 (45), 83 (9), 79 (55), 67 (44), 66 (59), 65 (26), 55 (7).

\textsuperscript{a} Taber, D. F.; Frankowski, K. J. \textit{J. Org. Chem.} 2003, 68, 6047.

1-[4-Methylphenyl)sulfonyl]-2,3,6,7-tetrahydro-1H-azepine (13d)

Colourles solid.\textsuperscript{a} IR (KBr) $\nu$/cm\textsuperscript{-1} 3030, 2942, 2899, 2855, 1657, 1596, 1450, 1332, 1286, 1162, 910, 816, 712, $^1$H NMR (200 MHz, CDCl$_3$) $\delta$/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$_3$) $\delta$/ppm: 21.5, 29,948,2, 126.9, 129.5, 130.1, 136,2, 142,9, MS (EI) $m$/z 251 (5, [M]$^+$), 223 (2), 184 (6), 155 (4), 105 (2), 91 (19), 96 (16), 77 (1), 65 (13), 42 (100), HRMS (EI): calcd for [M]$^+$ (C$_{13}$H$_{17}$NO$_2$S): 251,0980. found 251,0979.


2,2-Diphenyl-3-vinyl-2,5-dihydrofuran (13e)

Colourless oil.\textsuperscript{a} IR (film) $\nu$/cm\textsuperscript{-1} 3427, 3059, 3026, 2925, 1765, 1682, 1598, 1490, 1447, 1226, 1179, 1064, 758, 700, $^1$H NMR (500 MHz, CDCl$_3$) $\delta$/ppm: 4.11 (q, $J$ = 7.1 Hz, 1H), 5.10 (dd, $J$ = 11.2, 0.8 Hz, 1H), 5.31 (dd, $J$ = 17.7, 0.8 Hz, 1H), 6.16–6.18 (m, 1H), 6.20–6.27 (m, 1H), 7.10–7.40 (m, 10H), $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$/ppm: 60.3 94.5, 117.5, 124.8, 127.8, 127.9, 129.7, 143.3, 143.6, 171.1, MS (EI) $m$/z 248 (15, [M]$^+$), 229 (8), 215 (9), 205 (18), 204 (12), 203 (19), 191 (13), 189 (10), 183 (15), 182 (22), 172 (11), 171 (77), 165 (17), 157 (18), 143 (15), 141 (10), 129 (10), 128 (22), 115 (23), 105 (100), 97 (14), 95 (9), 91 (34), 83 (11), 77 (43), 71 (16), 69 (15), 57 (20), 55 (14), 51 (14), 43 (41), 41 (12), 39 (9), HRMS (EI): calcd for [M]$^+$ (C$_{18}$H$_{16}$O): 248,1201. found 248,1196.

1-Benzoyl-2,5-dihydro-1\(H\)-pyrrole (13f)

Colourless oil.\(^a\) IR (film) \(\nu/\text{cm}^{-1}\) 3480, 3061, 2862, 1638, 1616, 1575, 1447, 1418, 1355, 1198, 1000, 959, 908, 784. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta/\text{ppm}\): 4.12–4.25 (m, 2H), 4.41–4.53 (m, 2H), 5.70–5.78 (m, 1H), 5.86–5.96 (m, 1H), 7.36–7.46 (m, 3H), 7.48–7.57 (m, 2H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta/\text{ppm}\): 53.3, 55.7, 125.1, 125.9, 126.7, 128.3, 129.8, 136.8, 169.8. MS (EI) \(m/z\) 173 (55, [M]+), 106 (9), 105 (100), 78 (4), 77 (43), 68 (7), 51 (12), 41 (5), 39 (5), HRMS (EI): calcd for [M]+ (C\(_{11}\)H\(_{11}\)NO): 173.0840. found 173.0832.


(4Z)-8,9,10-trimethoxy-2,2-dimethyl-3,6-dihydro-2H-1,2-benzoxasilocine (13g)

Colourless oil.\(^a\) IR (film) \(\nu/\text{cm}^{-1}\) 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\(_3\)) \(\delta/\text{ppm}\): 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\(_3\)) \(\delta/\text{ppm}\): 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]+), 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): calcd for [M]+ (C\(_{16}\)H\(_{24}\)O\(_4\)Si): 308,1444. found 308,1457.


1-[(4-Methylphenyl)sulfonyl]-3-vinyl-2,5-dihydro-1\(H\)-pyrrole (13h)

Colourless solid.\(^a\) IR (KBr) \(\nu/\text{cm}^{-1}\) 2918, 2851, 1597, 1493, 1450, 1342, 1305, 1162, 1100, 1017, 814, 669, 588, 548. \(^1\)H NMR (200 MHz, CDCl\(_3\)) \(\delta/\text{ppm}\): 2.43 (s, 3H), 4.15–4.23 (m, 4H), 5.04 (d, J = 17.7 Hz, 1H), 5.15 (d, J = 10.2 Hz, 1H), 5.64 (br.s, 1H), 6.35 (dd, J = 17.7, 10.2 Hz, 1H), 7.32 (d, J = 8.0 Hz, 2H), 7.73 (d, J = 8.2 Hz, 2H). \(^13\)C NMR (50 MHz, CDCl\(_3\)) \(\delta/\text{ppm}\): 21.9, 53.8, 55.4, 117.1, 123.7, 127.9, 130.2, 130.3, 134.6, 137.9, 143.9. MS (EI) \(m/z\) 249 (12, [M]+), 155 (6), 139 (2), 94 (100), 91 (40), 77 (2), 67 (27), 65 (20), 51 (2).