

Ring-closing Metathesis at Room Temperature within Nanometer Micelles Using Water as the Only Solvent

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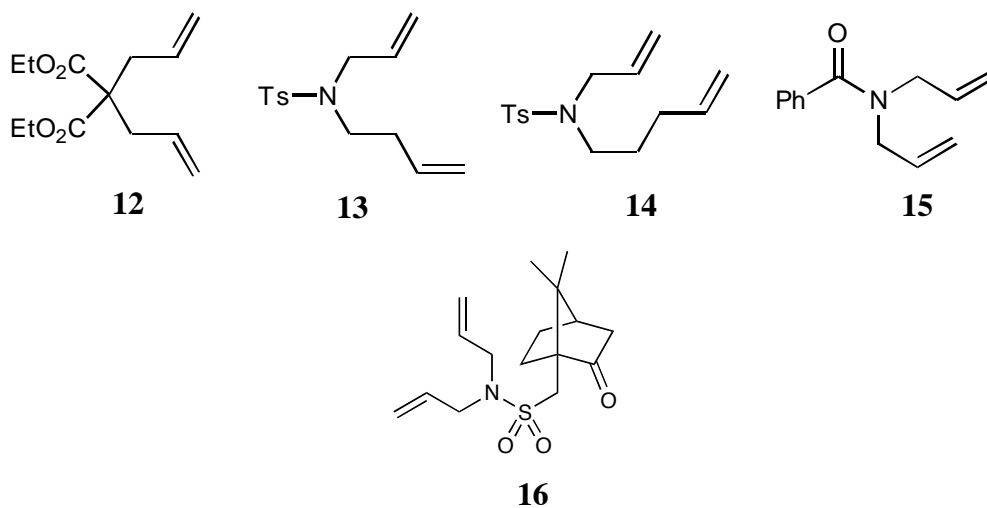
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Supporting Information

General Considerations: All reactions were performed in Biotage 2-5 mL microwave reactor vials containing a Teflon-coated stir bar. A stock solution of 2.5% (w/w) PTS in ultrapure H₂O was made and stored in a sealed serum bottle on the bench-top. Column chromatography was performed using Silicycle Silia-P 60 Å flash silica gel. Thin-Layer-Chromatography analysis was conducted using commercially available EMD silica gel 60 F₂₅₄ plates. Nuclear Magnetic Resonance spectra were obtained on a Varian Inova system, in CDCl₃, with proton and carbon resonances at 400 and 100 MHz, respectively, and are referenced to the residual solvent signal at 7.27 ppm. Infrared spectra were obtained either neat or by thin-film on NaCl plates using a JASCO FT/IR-430 series spectrometer and are reported as cm⁻¹. Mass spectral data were acquired on either a VF Autospec or an analytical VG-70-250 HF spectrometer. Grubbs and Grubbs-Hoveyda second generation catalysts were obtained from Materia, Inc. and stored in a glove box under an Ar atmosphere. Compounds **2**¹, **3**¹, **4**², **6**¹, **8**³, **10**⁴, **12**⁵, **13**¹, **14**⁶ and **15**¹ were all synthesized and characterized according to known procedures and data.

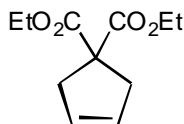


Representative Procedure for Ring-Closing Metathesis; 1-((2,5-Dihydro-1H-pyrrol-1-ylsulfonyl)methyl)-7,7-dimethylbicyclo[2.2.1]heptan-2-one (Table 1, Entry F): Sulfonamide **16** (47 mg, 0.15 mmol) and Grubbs second generation catalyst (2.6 mg, 0.003 mmol) were both added into a Teflon-coated-stir-bar-containing Biotage 2-5 mL microwave reactor vial at rt, and sealed with a septum. An aliquot of PTS/H₂O (1.5 mL; all RCM reactions were conducted at 0.1 M unless stated otherwise) was added, via syringe, and the resulting emulsion was allowed to stir at rt for 3 h. The homogeneous reaction mixture was then diluted with EtOAc (5 mL), filtered through a bed of silica gel layered over Celite, and the bed further washed (3 x 10 mL) with EtOAc to collect the cyclized material. The volatiles were removed *in vacuo* to afford the crude product which was subsequently purified by flash chromatography on silica gel (12%

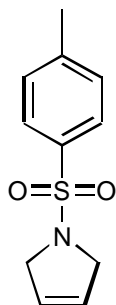
EtOAc/hexanes) to yield the product as a colorless solid (41 mg, 96%); mp = 86-88 °C; IR (thin-film): 2971, 2912, 2876, 1744, 1483, 1470, 1415, 1403, 1379, 1331, 1217, 1146, 1111, 1051, 982, 966, 945 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 5.78 (t, *J* = 4.0 Hz, 2H), 4.26-4.17 (m, 4H), 3.38 (d, *J* = 14.8 Hz, 1H), 2.81 (d, *J* = 14.8 Hz, 1H), 2.52 (ddd, *J* = 14.4, 11.5, 4.0 Hz, 1H), 2.37 (dt, *J* = 18.4, 4.0 Hz, 1H), 2.09 (t, *J* = 4.8 Hz, 1H), 2.07-1.99 (m, 1H), 1.92 (d, *J* = 18.4 Hz, 1H), 1.64 (ddd, *J* = 14.4, 9.6, 4.8 Hz, 1H), 1.41 (ddd, *J* = 12.4, 9.2, 4.0 Hz, 1H), 1.12 (s, 3H), 0.88 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 215.8, 125.8, 58.4, 55.0, 48.1, 44.7, 42.92, 42.76, 27.1, 25.3, 20.1, 19.9; MS (CI) *m/z* (%): 284 (M + H, 21), 215 (18), 151 (11), 123 (12), 109 (20), 68 (100); HRMS (CI) calcd for C₁₄H₂₂NO₃S [M + H]⁺ = 284.1320, found 284.1322.

Notes:

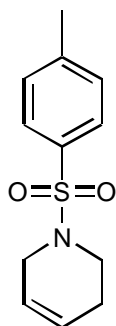
- Reaction mixtures can be analyzed via TLC directly from the reaction solution with no “mini work-up” needed.
- Thorough stirring of the reaction mixture is needed for the success of the reported reactions, especially when using solid substrates.
- Washing the silica gel bed with EtOAc is ideal because the PTS can be easily separated from the reaction mixture with no problem.
- Reactions can be preformed either under an blanket of Ar, in an open system (i.e., a vent needle is placed through the septum), or in a closed system. All conditions yield similar results at the reaction scale mentioned.



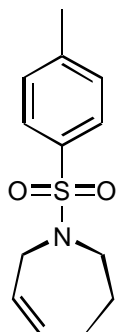
Diethyl cyclopent-3-ene-1,1-dicarboxylate (Table 1, Entry A): The representative procedure was followed using **12** (50 mg, 0.208 mmol) and Grubbs second-generation catalyst (3.54 mg, 0.004 mmol). Column chromatography on silica gel (eluting with 16% EtOAc/hexanes) afforded the product as a colorless oil (41 mg, 92%). The spectroscopic data obtained for the product was in accord with that previously reported for this compound.⁷



***N*-Tosyl-2,5-dihydro-1*H*-pyrrole (Table 1, Entry B):** The representative procedure was followed using **2** (50 mg, 0.20 mmol) and Grubbs second-generation catalyst (3.4 mg, 0.004 mmol). Column chromatography on silica gel (eluting with 5% EtOAc/hexanes) afforded the product as a colorless solid (44 mg, 99%). The spectroscopic data obtained for the product was in accord with that previously reported for this compound.⁷

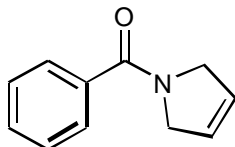


***N*-Tosyl-1,2,3,6-tetrahydropyridine (Table 1, Entry C):** The representative procedure was followed using **13** (55 mg, 0.207 mmol) and Grubbs second-generation catalyst (3.52 mg, 0.004 mmol). Column chromatography on silica gel (eluting with 4% EtOAc/hexanes) afforded the product as a colorless solid (49 mg, 99%). The spectroscopic data obtained for the product was in accord with that previously reported for this compound.⁷

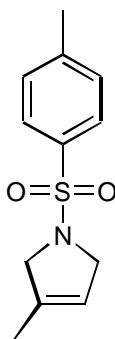


***(Z)*-N-Tosyl-2,3,4,7-tetrahydro-1*H*-azepine (Table 1, Entry D):** The representative procedure was followed using **14** (58 mg, 0.208 mmol) and Grubbs second-generation catalyst (3.54 mg, 0.004 mmol). Column chromatography on silica gel (eluting with 4% EtOAc/hexanes) afforded

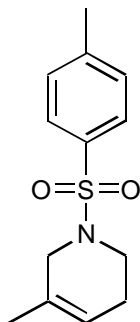
the product as a colorless oil (45 mg, 85%). The spectroscopic data obtained for the product was in accord with that previously reported for this compound.⁶



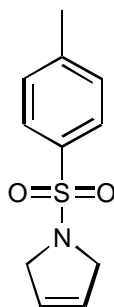
N-Benzoyl-3-pyrroline (Table 1, Entry E): The representative procedure was followed using **15** (58 mg, 0.288 mmol) and Grubbs second-generation catalyst (5.23 mg, 0.006 mmol). Column chromatography on silica gel (eluting with 15% EtOAc/hexanes) afforded the product as a colorless oil (48 mg, 96%). The spectroscopic data obtained for the product was in accord with that previously reported for this compound.⁸



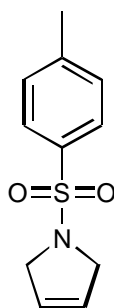
3-Methyl-N-tosyl-2,5-dihydro-1H-pyrrole (7): The representative procedure was followed using **6** (55 mg, 0.207 mmol) and Grubbs second-generation catalyst (3.52 mg, 0.004 mmol). Column chromatography on silica gel (eluting with 5% EtOAc/hexanes) afforded the product as a colorless solid (48 mg, 97%). The spectroscopic data obtained for the product was in accord with that previously reported for this compound.⁹



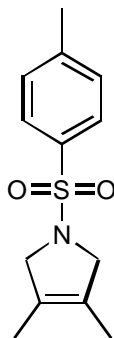
5-Methyl-N-tosyl-1,2,3,6-tetrahydropyridine (9): The representative procedure was followed using **8** (140 mg, 0.501 mmol) and Grubbs second-generation catalyst (8.52 mg, 0.01 mmol). Column chromatography on silica gel (eluting with 6% EtOAc/hexanes) afforded the product as a tan solid (125 mg, 99%). The spectroscopic data obtained for the product was in accord with that previously reported for this compound.¹⁰



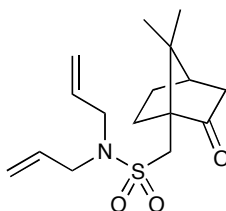
N-Tosyl-2,5-dihydro-1H-pyrrole (5): The representative procedure was followed using **3** (53 mg, 0.20 mmol) and Grubbs second-generation catalyst (3.52 mg, 0.004 mmol). Column chromatography on silica gel (eluting with 5% EtOAc/hexanes) afforded the product as a colorless solid (44 mg, 99%). The spectroscopic data obtained for the product was in accord with that previously reported for this compound.⁷



N-Tosyl-2,5-dihydro-1H-pyrrole (5): The representative procedure was followed using **4** (56 mg, 0.20 mmol) and Grubbs second-generation catalyst (3.52 mg, 0.004 mmol). Column chromatography on silica gel (eluting with 5% EtOAc/hexanes) afforded the product as a colorless solid (44 mg, 99%). The spectroscopic data obtained for the product was in accord with that previously reported for this compound.⁷



***N*-Tosyl-3,4-dimethyl-2,5-dihydro-1*H*-pyrrole (11):** The representative procedure was followed using **10** (56 mg, 0.20 mmol) and Grubbs second-generation catalyst (8.5 mg, 0.01 mmol). Resulting solution was allowed to stir at 60 °C for 24 h. Column chromatography on silica gel (eluting with 5% EtOAc/hexanes) afforded the product as a white solid (33 mg, 66%). The spectroscopic data obtained for the product was in accord with that previously reported for this compound.¹¹



***N,N*-Diallyl-1-(7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)methanesulfonamide (16):** To a 50 mL round-bottomed-flask 10-camphorsulfonyl chloride (1.0 g, 4.0 mmol) in CH₂Cl₂ (5 mL) was added dropwise to a mixture of diallylamine (1.0 mL, 8.0 mmol), and 4-dimethylamino-pyridine (24 mg, 0.20 mmol) in CH₂Cl₂ (10 mL) at 0 °C, and the resulting mixture was allowed to stir for 2 h at this temperature. The reaction mixture was quenched with 10% aqueous citric acid, extracted with CH₂Cl₂, and dried using anhydrous Na₂SO₄. Removal of the volatiles *in vacuo* afforded the crude residue, which was purified by column chromatography on silica gel (eluting with 8% EtOAc/hexanes) to yield the product as a colorless oil (1.03 g, 88%). IR (neat) 3082, 2960, 1746, 1643, 1471, 1442, 1418, 1393, 1374, 1344, 1267, 1217, 1200, 1146, 1106, 1051, 994, 931, 907 cm⁻¹; ¹H NMR (400 MHz, CDCl₃): δ 5.82 (ddt, *J* = 16.4, 10.0, 6.4 Hz, 2H), 5.28-5.23 (m, 4H), 3.91 (dd, *J* = 15.6, 6.4 Hz, 2H), 3.81 (dd, *J* = 15.6, 6.4 Hz, 2H), 3.38 (d, *J* = 14.8 Hz, 1H), 2.82 (d, *J* = 14.8 Hz, 1H), 2.53 (ddd, *J* = 14.4, 11.2, 4.0 Hz, 1H), 2.37 (dt, *J* = 18.4, 4.0 Hz, 1H), 2.09 (t, *J* = 4.4 Hz, 1H), 2.06-1.99 (m, 1H), 1.92 (d, *J* = 18.4 Hz, 1H), 1.63 (ddd, *J* = 14.4, 9.6, 4.4 Hz, 1H), 1.41 (ddd, *J* = 12.4, 9.2, 4.0 Hz, 1H), 1.13 (s, 3H), 0.86 (s, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 215.5, 133.1, 119.4, 58.7, 49.34, 49.30, 48.0, 43.0, 42.7, 27.1, 25.3, 20.2, 19.9;

MS (CI) m/z (%): 312 (M + H, 13), 215 (10), 151 (7), 123 (14), 109 (20), 96 (100), 81 (19); HRMS (CI) calcd for $C_{16}H_{26}NO_3S$ $[M + H]^+ = 312.1633$, found 312.1638.

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