

The Catalytic Synthesis of Amines and N-Containing Heterocycles. Amidate Complexes for Selective C–N and C–C Bond Forming Reactions.

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Supplementary Information

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General remarks

Synthesis and techniques

All preparative scale reactions were conducted in oven dried (160 °C) glass ware with magnetic stirring using Schlenk-line techniques or a glove box under an atmosphere of dry dinitrogen. Experiments on NMR tube scale were carried out in Teflon cap sealed NMR tubes (5 mm). Toluene, benzene, hexanes and pentanes were purified by passage over an activated aluminum oxide column and degassed prior to use. [D₆]-Benzene and [D₈]-toluene were dried over 4 Å molecular sieves and degassed by 3 freeze-pump-thaw cycles. Solvents for chromatography were used as received from commercial sources and were at least of ACS reagent grade. Silica gel G60 (70 – 230 mesh) and F60 (230 – 400 mesh) was purchased from Silicycle. TLC were run on silica gel coated glass plates with UV indicator obtained by Merck and analyzed by UV/VIS and stained using a cerium ammonium molybdate solution.

Reagents and materials

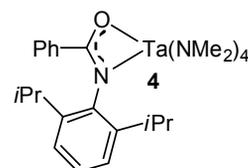
Reagents for amide synthesis were used as received from Aldrich without further purification. The amides were synthesized from the corresponding commercial acid chlorides and amines and rigorously dried by heating to 80 °C under vacuum or by sublimation. The known group 4 complexes **1** and **2**^[1] and the Ta(V) complexes **3**, **6** and **7** were synthesized as reported in the literature.^[2] All commercial amines and olefins for catalytic reactions were distilled under reduced pressure from CaH₂ and degassed by 3 freeze-pump-thaw cycles or sublimed in the case of solids. [Ta(NMe₂)₅] was purchased from Strem and used as received. Known catalysis products matched the published data.^[1,2,3]

Characterization

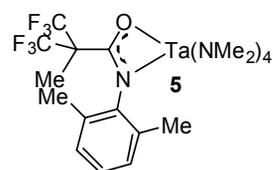
NMR spectra were recorded on Bruker Avance 300 (¹H: 300.13 ¹³C: 75.47) or Bruker Avance 400 (¹H: 400.19, ¹³C: 100.63) instruments operating at the denoted spectrometer frequency given in mega Hertz (MHz) for the specified nucleus. The samples were measured as solutions in the stated solvent at ambient temperature in non-spinning mode if not mentioned otherwise. To specify the signal multiplicity, the following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, qu = quintet, sept = septet, oct = octet, and m = multiplet; br. indicates a broad resonance. Shifts δ are reported in parts per million (ppm) relative to tetramethylsilane (TMS) as an external standard for ¹H- and ¹³C NMR spectra and calibrated against the solvent residual peak.^[4] Coupling constants *J* are given in Hertz (Hz). **HPLC** analyses were run on an Agilent Series 1100 (detector: UV/VIS, operating at the state wave length given in nm) using the specified column (AS-H, length: 25 cm, inner diameter: 4.6 mm, particle size: 5 μ m), flow rate of the solvent (mL/min), ratio of hexanes/*i*-PrOH, and sample injection volume (μ L; sample concentration approximately 1 mg/mL). Retention times *t_R* are stated in minutes (min). **GC-MS** measurements were performed on an Agilent Technologies GC 6890N/ MS 5973N equipped with an Agilent Technologies HP-5HS column (length: 30 m, 0.25 mm inner diameter, 0.25 μ m coating thickness) coupled to a quadrupole mass filter. Helium was used as the carrier gas with a constant flow of 1.2 mL/min. Separation of the injected species was achieved using the denoted temperature program and retention times *t_R* are given in minutes (min). High resolution mass-spectra (**HRMS**) and elemental analyses (**EA**) were measured by the mass spectrometry and microanalysis service at University of British Columbia, UBC Vancouver. Mass spectra were measured on a Kratos MS-50. Fragment signals are given in mass per charge number (*m/z*). Elemental analysis were performed on a Carlo Erba Elemental Analyzer EA 1108. The content of the specified element is expressed in percent (%).

Synthesis and characterization of Ta(amidate)(amido) complexes

(*N*-(2,6-Diisopropylphenyl)benzamido)tetrakis(dimethylamino)tantalum, **4**. *N*-(2,6-Diisopropylphenyl)benzamide (0.281 g, 1.0 mmol) and [Ta(NMe₂)₅] (0.402 g, 1.0 mmol) was suspended in hexanes (2 mL) and the mixture was allowed to stir over night (15 h) at ambient temperature. All volatiles were removed in vacuo after brief heating to reflux (5 min) and the remaining solid was recrystallized from hot hexanes at –30 °C. The crystals which were collected and identified as the title compound. Yield: 0.321 g (0.50 mmol, 50%). ¹H NMR ([D₆]-Benzene, 400 MHz) δ 1.06 (d, ³*J*_{H,H} = 6.8 Hz, 6H, CH(CH₃)₂), 1.40 (d, ³*J*_{H,H} = 6.8 Hz, 6H, CH(CH₃)₂), 3.48 (br. s, 24H, N(CH₃)₂), 3.65 (sept., ³*J*_{H,H} = 6.8 Hz, 2H, CH(CH₃)₂), 6.94 – 7.00 (m, 3H, CH_{arom.}), 7.26 (s, 3H, CH_{arom.}), 7.68 (d, ³*J*_{H,H} = 7.6 Hz, 2H, CH_{arom.}); ¹³C {¹H} NMR ([D₆]-Benzene, 100 MHz) δ 24.7, 24.8 (CH(CH₃)₂), 27.3 (CH(CH₃)₂), 47.0 (br. s, N(CH₃)₂), 124.2, 125.8, 127.9, 130.2, 130.7 (CH_{arom.}), 133.9, 141.4, 142.4 (C_{arom.}), 167.3 (C=O). Single crystal X-ray quality samples were obtained by recrystallization from hot hexanes at –30 °C.



***N*-(2,6-dimethylphenyl)-3,3,3-trifluoro-2-methyl-2-(trifluoromethyl)propan-amido)tetrakis(dimethylamino)tantalum, 5.** *N*-(2,6-Dimethylphenyl)-3,3,3-trifluoro-2-methyl-2-(trifluoromethyl)propanamide (0.248 g, 0.79 mmol) and [Ta(NMe₂)₅] (0.320 g, 0.80 mmol) was suspended in hexanes (3 mL) and the mixture was allowed to stir over night (19 h) at ambient temperature. The solvent was removed in vacuo after heating to reflux for 5 min and the remaining material was recrystallized from hot hexanes at -30 °C to deposit crystals which were collected and identified as the title compound. Yield: 0.329 g (0.49 mmol, 62%). ¹H NMR ([D₆]-Benzene, 400 MHz) δ 1.07 (br. s, 3H, C(CH₃)(CF₃)₂), 2.23 (s, 6H, CCH₃), 3.20 (br. s, 24H, N(CH₃)₂), 6.83 – 6.90 (m, 3H, CH_{arom}); ¹³C{¹H} NMR ([D₆]-Benzene, 100 MHz) δ: ¹⁹F NMR ([D₆]-Benzene, 282 MHz) δ -67.5 (br. s, CF₃). Single crystal X-ray quality samples were obtained by recrystallization from hot hexanes at -30 °C.

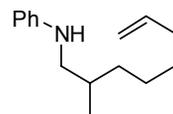


Experimental details for catalytic reactions and characterization of the corresponding products

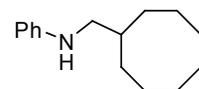
Caution: Heating reaction mixtures constituting of very volatile components beyond their boiling points in sealed glass containers is potentially dangerous, and may result in explosions. Be advised to carry out these experiments on the appropriate scale behind a blast shield!

General procedure 1 (GPI) for Ta(amidate) catalyzed α -alkylation of amines: In a nitrogen filled glove box the tantalum complex was placed in a small vial and the specified amount of (deuterated) solvent was added. The solution was transferred to a NMR tube equipped a Teflon cap and olefin followed by amine were added sequentially by means of a μ L-pipette. The NMR tube was closed, shaken and ¹H NMR spectrum was recorded. The NMR tube was placed in a preheated oil bath at the indicated temperature for the given time. After confirmation of conversion by means of ¹H NMR spectroscopy the crude reaction mixture was directly loaded onto a silica gel column and eluted using a mixture of hexanes/EtOAc/NEt₃.

***N*-(2-Methyloct-7-enyl)aniline.** The reaction was carried out following **GPI** from 1,7-octadiene (110 μ L, 0.745 mmol, 1.5 eq.), *N*-methylaniline (54 μ L, 0.498 mmol), **3** (15.5 mg, 0.025 mmol, 5 mol%), [D₈]-toluene (0.500 g) at 130 °C for 15.5 h. FC (silica gel G60, hexanes/EtOAc/NEt₃ 100:1:1) gave the title compound as a clear, colorless oil. Yield: 0.053 g (0.244 mmol, 49%). ¹H NMR (CDCl₃, 400 MHz) δ 1.06 (d, ³J_{H,H} = 6.4 Hz, 3H, CH₃), 1.24 – 1.55 (m, 6H, CH₂), 1.82 (m, 1H, CHCH₃), 2.15 (m, 2H, CH₂CH=CH₂), 2.97 (dd, ²J_{H,H} = 12.0 Hz, ³J_{H,H} = 7.2 Hz, 1H, NCH₂), 3.13 (dd, ²J_{H,H} = 12.0 Hz, ³J_{H,H} = 5.6 Hz, 1H, NCH₂), 3.73 (br. s, 1H, NH), 5.07 (m, 2H, CH=CH₂), 5.90 (m, 1H, CH=CH₂), 6.68 (d, ³J_{H,H} = 8.4 Hz, 2H, *o*-CH_{arom}), 6.76 (t, ³J_{H,H} = 7.4 Hz, 1H, *p*-CH_{arom}), 7.25 (t, ³J_{H,H} = 7.8 Hz, 2H, *m*-CH_{arom}); ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 18.2 (CH₃), 26.6, 29.4, 33.1 (CH₂), 33.9 (CHCH₃), 34.8 (CH₂), 50.5 (NCH₂), 112.8 (*o*-CH_{arom}), 114.5 (CH=CH₂), 117.1 (*p*-CH_{arom}), 129.4 (*m*-CH_{arom}), 139.2 (CH=CH₂), 148.8 (C); HRMS(EI) Calcd. for C₁₅H₂₃N: m/z 217.18305 (M⁺); Found: m/z 217.18308 (M⁺); Anal. Calcd. for C₁₅H₂₃N: C, 82.89; H, 10.67; N, 6.44; Found: C, 83.28; H, 10.96; N, 6.46.



***N*-(Cyclooctylmethyl)aniline.** The reaction was carried out following **GPI** from cyclooctene (194 μ L, 1.49 mmol, 3.0 eq.), *N*-methylaniline (54 μ L, 0.498 mmol), **3** (30.8 mg, 0.050 mmol, 10 mol%), [D₈]-toluene (0.507 g) at 165 °C for 48 h. FC (silica gel G60, hexanes/EtOAc/NEt₃ 100:1:1) gave the title compound as a clear, colorless oil. Yield: 0.055 g (0.253 mmol, 51%). ¹H NMR (CDCl₃, 400 MHz) δ 1.18 (m, 1H, NCH₂CH), 1.35 – 1.85(m, 14H, CH₂), 2.97 (d, ³J_{H,H} = 6.8 Hz, 2H, NCH₂), 3.72 (br. s, 1H, NH), 6.63 (d, ³J_{H,H} = 8.0 Hz, 2H, *o*-CH_{arom}), 6.71 (t, ³J_{H,H} = 7.2 Hz, 1H, *p*-CH_{arom}), 7.20 (t, ³J_{H,H} = 8.8 Hz, 2H, *m*-CH_{arom}); ¹³C{¹H} NMR (CDCl₃, 100 MHz) δ 25.7 (CH₂), 26.5 (NCH₂CH), 27.3, 30.8, 37.6 (CH₂), 51.4 (NCH₂), 112.8 (*o*-CH_{arom}), 117.1 (*p*-CH_{arom}), 129.4 (*m*-CH_{arom}), 148.9 (C_{arom}N); HRMS(EI) Calcd. for C₁₅H₂₃N: m/z 217.18305 (M⁺); Found: m/z 217.18325 (M⁺); Anal. Calcd. for C₁₅H₂₃N: C, 82.89; H, 10.67; N, 6.44; Found: C, 83.26; H, 10.79; N, 6.62.



Literature

- [1] Bexrud, J. A.; Eisenberger, P.; Leitch, D. C.; Payne, P. R.; Schafer, L. L. *J. Am. Chem. Soc.* **2009**, *131*, 2116.
- [2] Eisenberger, P.; Ayinla, R. O.; Lauzon, J. M. P.; Schafer, L. L. *Angew. Chem., Int. Ed.* **2009**, *48*, 8361.
- [3] Bexrud, J. A.; Schafer, L. L. *Dalton Trans.* **2009** DOI: 10.1039/b913393c.
- [4] Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512.