

Highly efficient binding of trivalent f-elements with a C_3 -symmetric tripodal ligand containing diglycolamide arms

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General Consideration

Elemental analyses were performed at the in-house facility of Department of Chemistry at University of Florida. The ^1H , ^{13}C , and spectra were recorded on a Varian VXR-300 or Mercury-300 spectrometer at 299.95 and 75.4 MHz for the proton and carbon channels respectively. Mass spectrometry samples were analyzed on a Bruker Apex II 4.7T Fourier transform ion cyclotron resonance mass spectrometer.

The synthetic pathways for preparation of compounds **1**, **2** and **4** have been adapted from general procedures for variety of diamides.^{1, 2} Amine **3** was synthesized according to previously developed procedure.³

Experimental Procedures

[(Diisopropylcarbamoyl)-methoxy]-acetic acid 1. A mixture of 6.09 ml (0.043 mol) of diisopropyl amine and 3.50 ml (0.043) of pyridine was slowly added to a solution of 5.15 g (0.043 mol) of diglycolic anhydride in 40 ml of 1, 4-dioxane, under an ice bath condition. After stirring the reaction mixture for approximately 20 h at room temperature, solvent was evaporated under reduced pressure, and 6 M hydrochloric acid was added. The organic phase was further extracted with dichloromethane, dried over magnesium sulfate, and partially evaporated. Clean product crystallized upon slow solvent evaporation. Yield: 4.5g (48 %).

^1H NMR (CDCl_3): δ = 1.26 (d, J = 6.7 Hz, 6H; NCHCH_3), 1.38 (d, J = 6.9 Hz, 6H; NCHCH_3), 3.40 – 3.63 (two multiplets, 2H; NCHCH_3), 4.10 (s, 2H; CH_2CON), 4.30 (s, 2H; CH_2COOH). ^{13}C NMR (CDCl_3): δ = 20.1, 20.3 (aliphatic); 46.7, 47.8 (CH-N); 72.0, 72.4 (O- CH_2); 169.9, 172.3 (C=O). HR LSIMS $[\text{M}+\text{H}]^+ = 218.1392$, (Theoretical $[\text{M}+\text{H}]^+ = 218.1392$).

2-[(Diisopropylcarbamoil)-methoxy]-N,N-diisopropyl-acetamiden 2. A cold solution of mono-substituted amide **1** (2.0 g, 9.20 mmol) in 40 ml of dry dichloromethane was gradually treated with oxalyl chloride (1.46 ml, 18.40 mmol). After 4 h solvent was evaporated and the orange sticky residue was dissolved in 20 ml of dioxane. Subsequently, 6.45 ml (0.046 mol) of diisopropyl amine was slowly added to the solution, and stirred overnight at room temperature. The solvent was evaporated, and the residue was dissolved in a mixture of diethyl ether and pentane, extracted with 1 M hydrochloric acid followed by the extraction with 1 M sodium hydroxide, and dried over magnesium sulfide. Pure product crystallized upon slow evaporation of solvent with 43 % yield (1.10g).

^1H NMR (CDCl_3): δ = 1.18 (d, J = 6.4 Hz, 12H; NCHCH_3), 1.40 (d, J = 5.4 Hz, 12H; NCHCH_3), 3.44 (m, 2H; NCHCH_3), 3.90 (m, 2H; NCHCH_3), 4.22 (s, 4H; OCH_2). ^{13}C NMR (CDCl_3): δ = 20.2, 20.5 (CH_3); 46.0, 48.0 (CH-NH); 70.4 (O-CH_2); 168.1 (C=O). HR LSIMS m/z $[\text{M}+\text{H}]^+ = 301.2487$, (Theoretical m/z $[\text{M}+\text{H}]^+ = 301.2491$).

Compound 4. Method I. To a mixture of 0.85 g (7.12 mmol) of 2-mercaptothiazoline, DCC (1.47g, 7.12 mmol) and DMAP (0.11, 0.89 mmol) in 60 ml of dichloromethane (DCM), 1.55g (7.12 mmol) of mono-substituted oxa-pentaneamide **1** was added and stirred for 5 h. Subsequently, 1.50 g (1.78 mmol) of amine **3** dissolved in 10 ml of DCM was added dropwise, and the solution was stirred for 48 h. White precipitate was filtered away, and solvent was evaporated in vacuo. The residue was treated with diethyl ether followed by addition of pentane. The crashed out solid was filtered away and remaining solution of product was evaporated. The crude material was dissolved in mixture of DCM and hexamethyldisiloxane and left for crystallization. Yield: 1.50 g (59 %).

Compound 4. Method II. A mixture of 1.0 equivalence of mono-substituted amide (**1**), 2.0 eq. of ethyl-diisopropyl-amine, and 1.1 eq. PyBOP (Benzotriazole-1-yl-oxy-trispyrrolidinophosphonium hexafluorophosphate) was stirred in DMF for approximately 30 min. Subsequently, 0.3 eq. of amine (**3**) was added and stirred for 48h. Upon following treatment with 10% hydrochloric acid, white solid crashed out of solution. A precipitate was extracted with diethyl ether, and the organic solution was further washed with 0.5 M sodium hydroxide, and dried over magnesium sulfide. A solvent was evaporated under reduced pressure leaving clean light yellowish product in 73% yield.

^1H NMR (CDCl_3): δ = 0.52 (m, 18H; CH_2CH_3), 1.13 (s, 18H; CCH_3), 1.20 (d, J = 5.9 Hz, 18H; NCHCH_3), 1.31 (s, 18H; CCH_3), 1.39 (d, J = 6.1 Hz, 18H; NCHCH_3), 1.20 – 1.70 (two broad multiplets,

6H + 6H; CH_2CH_3), 3.20 – 3.90 (broad multiplets: 6H, $\text{CH}_2\text{CH}_2\text{-NH}_2$; 6H, NCHCH_3 ; 6H, $\text{O-CH}_2\text{CH}_2$), 4.10 (s, 6H; OCH_2), 4.22 (s, 6H; OCH_2), 6.43 (s, 1H; CH), 7.02 (s, 3 H; Ar-H), 7.11 (s, 3 H; Ar-H), 7.89 (bt, 3 H; N-H). ^{13}C NMR (CDCl_3): $\delta = 9.2, 9.7, 20.6, 21.0, 28.9, 29.7, 35.4, 37.0, 37.7, 38.6, 39.3, 39.5, 46.2, 47.8$ (aliphatic); 70.2, 71.1 (O-CH_2); 125.0, 127.9, 137.8, 139.9, 142.9, 153.0 (aromatic); 167.6, 170.2 (C=O). HR ESI-ICR MS $[\text{M}+\text{K}+\text{H}]^{2+} = 739.5151$, (Theoretical $\text{m/z} [\text{M}+\text{K}+\text{H}]^{2+} = 739.5200$). Anal. Found: C, 71.3; H, 10.2; N, 5.7. Calc. for $\text{C}_{85}\text{H}_{142}\text{N}_6\text{O}_{12}$: C, 70.9; H, 9.9; N, 5.8 %.

General procedure for preparation of **5** and **6**.

A solution of 0.7 equivalent of $\text{Ln}(\text{NO}_3)_3 \cdot x\text{H}_2\text{O}$ in methanol was added to a solution of 1 equivalent of **4** in methanol, and mixture was stirred at room temperature for approximately 4 h. The Ce complex, was formed in reaction of $(\text{NH}_4)_2\text{Ce}(\text{NO}_3)_6$ and ligand **4**. However, due to instability of Ce(IV) in the organic solvents, the crystalline material collected after diffusion of ether into the reaction mixture in methanol contained complex of Ce(III) exclusively. Upon slow diffusion of ether to a methanol solution of Yb complex, clear crystals were formed in 50 – 60% yields.

Compound **5**, $[\text{4 Ce}](\text{NO}_3)_3$ HR ESI-ICR MS $\text{m/z} [\text{M}+\text{Ce}(\text{NO}_3)_2]^+ = 1702.9413$, (Theoretical $\text{m/z} [\text{M}+\text{Ce}(\text{NO}_3)_2]^+ = 1702.9491$).

Compound **6**, $[\text{4 Yb}](\text{NO}_3)_3$ HR ESI-ICR MS $\text{m/z} [\text{M}+\text{Yb}(\text{NO}_3)_2]^+ = 1736.9813$, (Theoretical $\text{m/z} [\text{M}+\text{Yb}(\text{NO}_3)_2]^+ = 1736.9842$).

References:

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