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Communications

Ortho Lithiation of Tetrahydroquinoline Derivatives and Its Use for the Facile Construction of Polymerization Catalysts

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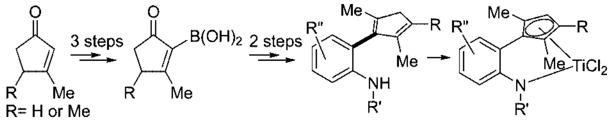
Summary: Ortho lithiation is achieved by the treatment of tBuLi to the lithium carbamate compounds derived from 2-R-1,2,3,4-tetrahydroquinolines (R = H, methyl, n-butyl, tert-butyl, and 6-tert-butoxyhexyl), which enables the facile construction of the o-phenylene-bridged (Me_4C_5, indenyl, or fluorenyl)/amido titanium complexes. The titanium complex derived from 2-methyltetrahydroquinoline exhibits higher activity, higher 1-octene incorporation, and higher molecular weight in ethylene/1-octene copolymerization than the standard CGC, $[Me_2Si(\eta^5\text{-}Me_4C_5)(N^tBu)]TiCl_2$.

Recently, we disclosed a synthetic route for *o*-phenylene-bridged (dimethyl or trimethylcyclopentadienyl)/amido titanium complexes.[1] The Suzuki coupling reaction of the boronic acids of cyclopentenones is a key step for the route (eq 1). Some of them exhibit a comparable catalytic performance in ethylene/α-olefin copolymerizations to the standard "constrained geometry catalyst" (CGC), $[Me_2Si(\eta^5\text{-}Me_4C_5)(N^tBu)]TiCl_2$.[2] However, the number of steps to reach the final titanium complexes from commercially available starting materials is too many for usage in a commercial process (eq 1). The route does not allow for more attractive tetramethylcyclopentadienyl, indenyl, or fluorenyl complexes because the corresponding boronic acids are not available.



(1)

The regioselective ortho lithiation of aryl compounds containing various functional groups such as −F, −OR, $-CH_2NR_2$, and $-C(O)NR_2$ has been widely used in organic synthesis.[3] The coordination of the lithium ion on the heteroatom brings the reactive carbanion into proximity for the directed deprotonation of the ortho proton (directed ortho lithiation). The ortho lithiation of *N*-alkylaniline derivatives may allow for a simple and efficient synthetic route for the *o*-phenylene-bridged Cp/amide ligand system. A lithiated *tert*-butyl carbamate group ($-N(Li)C(O)O^t\text{-}Bu$) acts as the directing group,[4] but the carbonyl attack of its ortho-lithiated carbanion onto the cyclopentenone is unsuccessful. This is possibly due to the side reactions caused by the strongly basic nature of the appended $-N(Li)C(=O)^tBu$ group. We envisioned that the lithium carbamate group (−N(R)COOLi)

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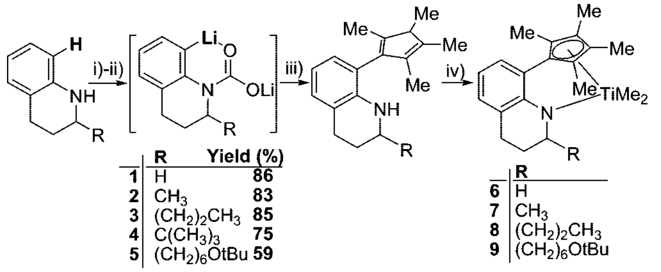
Scheme 1[a]



[a] Legend: (i) ^{n}BuLi (1.0 equiv) and then CO_2; (ii) THF (1.1 equiv) and then ^{t}BuLi (1.1 equiv); (iii) $Me_4C_5H_2(=O)$ and then aqueous HCl; (iv) MeLi (4.0 equiv) and then $TiCl_4(DME)_2$.

may act as an ortho-directing group. Not only is the $-N(R)COOLi$ group easily generated from the $-N(R)H$ group but it can also be easily brought back to the original $-N(R)H$ group after a reaction. The $-N(R)COOLi$ group might not be basic enough to cause side reactions. Almost two decades ago, Katritzky reported the lithiation reactions of the lithium carbamates of tetrahydroquinoline, tetrahydroisoquinoline, indoline, and indole, but the main reaction was α-lithiation, not ortho lithiation, through the treatment of ^{t}BuLi−KO^{t}Bu in THF at −78 to −50 °C.[5] In this paper, we report the conditions that lead to ortho lithiation and its utilization in the facile construction of various titanium complexes. Several of them exhibit excellent catalytic performance in ethylene/1-octene copolymerization.

The successive addition of ^{n}BuLi and CO_2 gas to tetrahydroquinoline at −78 °C in diethyl ether afforded a slurry of the corresponding lithium carbamate compound. The treatment of ^{t}BuLi (1.1 equiv) to the slurry at −20 °C after the addition of THF (1.1 equiv) provided the ortho-lithiated compound (Scheme 1). In the ^1H NMR spectrum of the D_2O-quenched product, the intensity of the ortho proton was reduced from 1.0 to 0.14, indicating the ortho lithiation in 86% yield. The addition of 1 equiv of THF in diethyl ether solvent is crucial to attain the high yield. When 1 equiv of ^{t}BuLi was added to the slurry in diethyl ether in the absence of THF or to just the THF solution, the ortho-lithiation yields were lowered to 50 and 60%, respectively. Similar sensitivity on the yield or on the regioselectivity of the lithiation through solvent or additive variation has been reported in other cases as well.[6] Using the same treatment, various tetrahydroquinoline derivatives were ortho-lithiated in high yields (Scheme 1). The *tert*-butoxy group decreased the yield, and the *tert*-butoxyhexyl-substituted tetrahydroquinoline was lithiated in only 59% yield.

The desired *o*-phenylene-bridged Me_4C_5/amide ligands were obtained through the addition of tetramethylcyclopentenone in the presence of $CeCl_3-LiCl$[7] to in situ generated ortho-lithiated compounds. During the aqueous HCl workup, the elimination reaction of the resulting tertiary alcohol occurred, and the lithium carbamate group was converted to the original amino group. The operation can be carried out in one pot and, in some cases, on a large scale (15 g scale with 1 L apparatus) without column chromatography. The metalation was also carried out efficiently in one step and resulted in good yields (53–82%) using the method introduced by Resconi.[8] A complex containing the *tert*-butoxy group at a sidearm (**9**) can be used to immobilize the complex on a silica surface.[9]

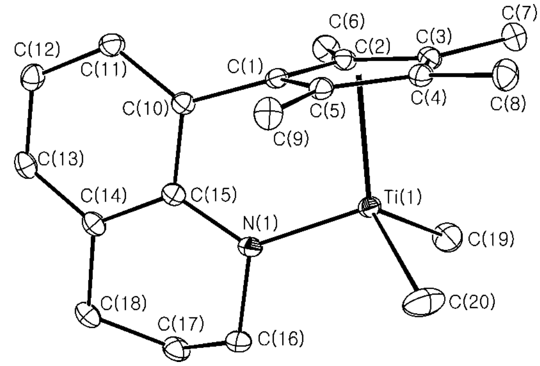
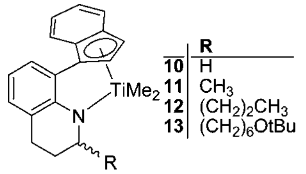
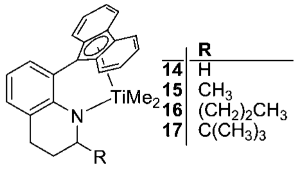


Figure 1. Thermal ellipsoid plot (30% probability level) of **6**. Selected bond distances (Å) and angles (deg): Ti−Cp(centroid), 2.020; Ti(1)−N(1), 1.9288(16); Ti(1)−C(19), 2.104(3); Ti(1)−C(20), 2.102(2); Cp(centroid)−Ti(1)−N(1), 106.10; C(10)−C(1)−Cp(centroid), 169.68; C(1)−Cp(centroid)−Ti(1), 88.84; C(19)−Ti(1)−C(20), 101.38(13); C(15)−N(1)−Ti(1), 126.19(12); C(15)−N(1)−C(16), 115.85(16); C(16)−N(1)−Ti(1), 117.93(13).

Indenyl and fluorenyl analogues were also efficiently prepared using **1**–**3** and **5**. The ligands for the indenyl complexes **10**–**13** were obtained by the same procedure and conditions using 1-indanone instead of tetramethylcyclopentenone. The lithiated compounds **1**–**4** can attack the carbonyl on 9-fluorenone in the absence of $CeCl_3-LiCl$ to yield tertiary alcohols, which were reduced to the desired fluorenyl ligands by treatment with HI in acetic acid.[10] Reactions between the *tert*-butyl-substituted ortho-lithiated compound **4** and 2,3,4,5-tetramethyl-2-cyclopentenone and 1-indanone were unsuccessful. The reaction between the *tert*-butoxyhexyl-substituted ortho-lithiated compound **5** and 9-fluorenone was successful, but the next reduction reaction was problematic. The *tert*-butyl ether group is not compatible with the generated I_2 in the reaction medium. Metalations were also conducted using the same method applied for the tetramethylcyclopentadienyl complexes. The indenyl titanium complexes were obtained as a mixture of two diastereomers when the racemic chiral tetrahydroquinolines were employed as starting materials.





The molecular structures of **6**, **11**, and **14** were determined by X-ray crystallography (Figures 1−3). The Cp(centroid)−Ti−N angles, which have been used as a qualitative measure for the "constrained geometry", are 106.10, 106.12, and 106.88° for **6**, **11**, and **14**, respectively. The angles are smaller than those observed for the corresponding Me_2Si-bridged CGC complexes

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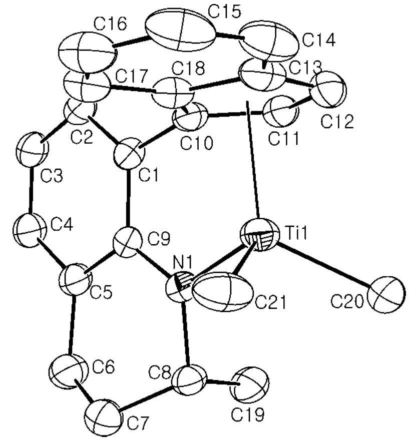

Figure 2. Thermal ellipsoid plot (30% probability level) of **11**. Selected bond distances (Å) and angles (deg): Ti−Ind(centroid), 2.061; Ti(1)−N(1), 1.927(3); Ti(1)−C(20), 2.082(6); Ti(1)−C(21), 2.103(5); Ind(centroid)−Ti(1)−N(1), 106.12; C(1)−C(10)−Ind(centroid), 170.04; C(10)−Ind(centroid)−Ti(1), 87.88; C(20)−Ti(1)−C(21), 100.4(3); C(9)−N(1)−Ti(1), 125.8(2); C(8)−N(1)−Ti(1), 118.6(2); C(9)−N(1)−C(8), 115.4(3).

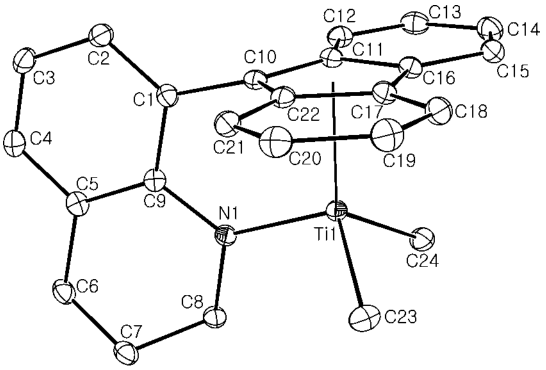

Figure 3. Thermal ellipsoid plot (30% probability level) of **14**. Selected bond distances (Å) and angles (deg): Ti−Flu(centroid), 2.072; Ti(1)−N(1), 1.9212(16); Ti(1)−C(23), 2.103(2); Ti(1)−C(24), 2.104(2); Flu(centroid)−Ti(1)−N(1), 106.88; C(1)−C(10)−Flu(centroid), 171.14; C(10)−Flu(centroid)−Ti(1), 86.29; C(23)−Ti(1)−C(24), 101.27(9); C(9)−N(1)−Ti(1), 125.97(12); C(8)−N(1)−Ti(1), 118.26(12); C(9)−N(1)−C(8), 115.77(15).

Table 1. Ethylene/1-Octene Copolymerization Results[a]

entry	complex	time (min)	temp (°C)	yield (g)	activity[b]	[Oct][c] (mol %)	M_w ($\times 10^{-3}$)	M_w/M_n
1	**6**	2	70–80	0.57	34	22	104	2.6
2	**7**	2	70–89	1.6	96	22	64	2.3
3	**8**	2	70–87	1.4	84	19	80	2.5
4	**9**	5	70–75	0.22	5.3	16	110	2.7
5	**10**	5	70–74	0.25	6.0	20	110	2.4
6	**11**	5	70–75	0.37	8.9	21	120	2.9
7	**12**	5	70–77	0.53	13	18	170	2.8
8	**13**	5	70–72	0.12	2.9	16	25	2.0
9	**14**	5	70–73	0.20	4.8	20	120	2.3
10	**15**	5	70–81	0.81	19	18	99	2.6
11	**16**	5	70–79	0.67	16	14	120	2.5
12	**17**	5	70–72	0.15	3.6	8	240	2.7
13[d]	**7**	2	70–80	0.98	150	25	150	2.6
14[d]	**8**	2	70–79	0.72	110	21	150	2.6
15[d]	CGC[e]	2	70–72	0.073	11	19	210	3.0
16	CGC	2	70–80	0.81	49	18	120	3.4

[a] Polymerization conditions: 30 mL of a toluene solution of 1-octene (0.3 M, 1.0 g), 0.50 μmol of Ti, 2.0 μmol of $[Ph_3C][B(C_6F_5)_4]$, 0.200 mmol of $Al(iBu)_3$, 60 psig of ethylene. [b] Averaged activity in two or three runs in units of 10^6 g/((mol of Ti) h). [c] 1-Octene content in the copolymer determined by ^1H NMR. [d] Conditions: 0.20 μmol of Ti, 0.80 μmol of $[Ph_3C][B(C_6F_5)_4]$, 0.080 mmol of $Al(^iBu)_3$. [e] $[Me_2Si(\eta^5\text{-}Me_4Cp)(N^tBu)]TiCl_2$.

(107.6, 108.3, and 111.31°, respectively)[11] indicating that the *o*-phenylene-bridged complexes are more constrained than the Me_2Si-bridged analogues.

The newly prepared complexes are screened for ethylene/1-octene copolymerization after activation with $[Ph_3C]^+[B(C_6F_5)_4]^-$ (Table 1). The tetramethylcyclopentadienyl complexes (**6**–**9**) generally show better activities than the corresponding indenyl (**10**–**13**) or fluorenyl complexes (**14**–**17**). Complexes **7** and **8** exhibit the highest activity (entries 2 and 3), and the temperature increases from 70 to 89 °C by the heat of polymerization, yielding a very viscous solution in 2 min. The analysis of the ^1H NMR spectra of the obtained polymers indicates that 85 and 68% of the added 1-octene is consumed.

The catalytic performances of **7** and **8** are studied compared with the standard CGC under more carefully controlled conditions (entries 13–15). The temperature and the consumption of 1-octene are controlled not to exceed 80 °C and 50%, respectively, by reducing the catalyst amount from 0.50 to 0.20 μmol. Complexes **7** and **8** provide extremely high activities under the 0.20 μmol conditions (150×10^6 and 110×10^6 g/((mol of Ti) h), respectively). In contrast, the CGC does not provide good activity under the same conditions (~1/10 of those of **7** and **8**), even though it shows reasonably good activity under 0.50 μmol conditions (~1/3 of that of **7**). Complex **7**, which shows the highest activity, is able to incorporate more 1-octene than CGC (25 mol % versus 18 mol %). The molecular weight of the obtained polymer by **7** is also higher than that of the polymer obtained by CGC (M_w 150 000 versus 120 000).

In conclusion, the ortho lithiation of tetrahydroquinoline derivatives has been accomplished, which allows for a very efficient route for bridged (Me_4C_5, indenyl, or fluorenyl)/amido titanium complexes. Some of them exhibit higher activity, higher 1-octene incorporation, and higher molecular weight in ethylene/1-octene copolymerization than the standard CGC.

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Supporting Information Available: Text, tables, and figures giving details of the syntheses, characterization data for all new compounds, and polymerization details and CIF files giving crystal data for **6**, **11**, and **14**. This material is available free of charge via the Internet at http://pubs.acs.org.

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