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Ni(0)-Catalyzed Formation of Azaaluminacyclopentenes via Azanickelacyclopentenes: A Unique Nickel/Aluminum Double Transmetalation Reaction

Masato Ohashi, Osamu Kishizaki, Haruo Ikeda, and Sensuke Ogoshi*

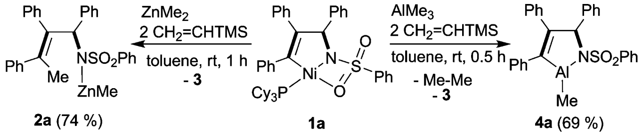
Department of Applied Chemistry, Graduate School of Engineering, Osaka University, Suita, Osaka 565-0871, Japan

Received April 21, 2009; E-mail: ogoshi@chem.eng.osaka-u.ac.jp

Oxidative cyclization of two π components with low-valent transition metals has been the focus of a great deal of attention because of its promise as a method for constructing C−C bonds between a variety of functional groups.[1] Among these methods, the formation of heteronickelacycles is assumed to be a key step in multicomponent nickel-catalyzed coupling reactions.[2−6] We recently developed the nickel-catalyzed [2 + 2 + 2] cycloaddition reaction of two alkynes and an imine to afford 1,2-dihydropyridines, in which the oxidative cyclization of an alkyne and an imine was proposed as a key step.[6e] The formation of a key intermediate (**1a**) by oxidative cyclization of diphenylacetylene and *N*-benzylidene benzenesulfonamide (*N*-BBSA) with Ni(0) was observed.[6e] Azanickelacycles were also assumed to be an important intermediate in the three-component reaction of an alkyne, an imine, and an alkylmetal reagent,[4] and therefore, investigation of the reactivity of **1a** toward alkylmetal reagents was warranted. Herein, we report the stoichiometric reactions of **1a** with ZnMe$_2$ and AlMe$_3$. Treatment with ZnMe$_2$ gave a three-component coupling product, while the reaction with AlMe$_3$ resulted in the unexpected formation of an azaaluminacyclopentene by nickel/aluminum double transmetalation. We also achieved the construction of a novel nickel-catalyzed three-component cyclocondensation of an alkyne, an imine, and AlMe$_3$.

The reaction of **1a** with ZnMe$_2$ in toluene at room temperature in the presence of 2 equiv of TMSCH═CH$_2$ afforded the expected methylzincamido product **2a** in 74% isolated yield together with the formation of (PCy$_3$)Ni(CH$_2$═CHTMS)$_2$ (**3**) (Scheme 1).[7] In addition, the three-component coupling reaction of diphenylacetylene, *N*-BBSA, and ZnMe$_2$, which afforded **2a**, also proceeded in the presence of Ni(cod)$_2$ and PCy$_3$ (10 and 20 mol %, respectively). Although **1a** was analogous to the reaction intermediate proposed in Jamison's work,[4] **1a** did not react with BEt$_3$ even when heated at 60 °C for 2 h. This is consistent with the fact that *N*-tosyl imines do not react in the Ni-catalyzed three-component coupling of alkyne, imine, and triethylborane.[4]

Scheme 1. Reaction of **1a** with Alkylmetal Reagents



In contrast, treatment of **1a** with an equimolar amount of AlMe$_3$ under identical reaction conditions unpredictably gave the five-membered azaaluminacycle **4a** in 69% isolated yield (Scheme 1). Monitoring of the reaction by means of ^{1}H NMR spectroscopy indicated a concomitant generation of ethane (δ_H 0.80 in C$_6$D$_6$) and **3**. X-ray crystallography of **4a** showed that the aluminum atom was covalently bonded to both the carbon and nitrogen atoms to form a five-membered ring and that one methyl group also was bound to the aluminum center (Figure 1).

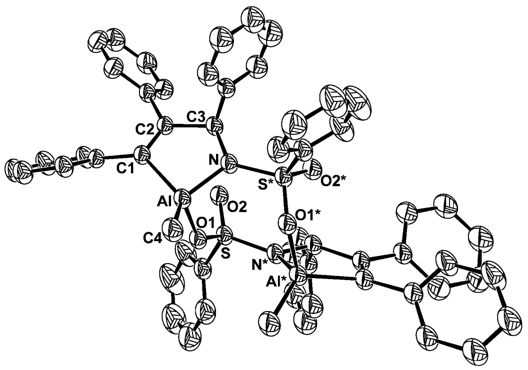
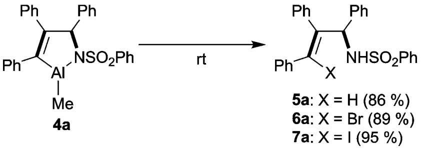


Figure 1. Molecular structure of **4a**, with thermal ellipsoids at the 30% probability level. H atoms and the solvated molecule (toluene) have been omitted for clarity. Symmetry transformation used to generate equivalent atoms S*: 2 − *X*, *Y*, 0.5 − *Z*.

In the crystal lattice, the five-membered azaaluminacycle unit formed a dimer in which one of the oxygen atoms in the benzenesulfonyl group of **4a** is coordinated to the other aluminum atom. Unlike the three-component coupling product **2a**, azaaluminacycle **4a** is an organometallic reagent in which the Al−C bond can react with electrophiles. Indeed, **4a** can be treated with electrophiles such as proton and halogenonium to afford allylamine derivatives **5a**−**7a** (Scheme 2). To the best of our knowledge, this is the first example of the catalytic formation of azaaluminacyclopentenes, although cycloalumination of either olefins or acetylenes mediated by Cp$_2$Zr derivatives has been used in the preparation of organoaluminum compounds.[8,9]

Scheme 2. Transformation of **4a** into Allylamine Derivatives[a]



[a] Reaction conditions: for **5a**, MeOH/toluene; for **6a**, NBS (2 equiv) in MeCN, 0.5 h, then MeOH; for **7a**, I$_2$ (excess) in CH$_3$CN, 2 h, then HCl.

As anticipated from the regeneration of the Ni(0) complex **3**, the transformation of diphenylacetylene, *N*-BBSA, and AlMe$_3$ into **4a**, in which the oxidative cyclization of diphenylacetylene and *N*-BBSA is a key step, proceeded catalytically. However, as shown by the equation in Table 1, the addition reaction of AlMe$_3$ and *N*-BBSA, which gave the corresponding amide **8**, also took place

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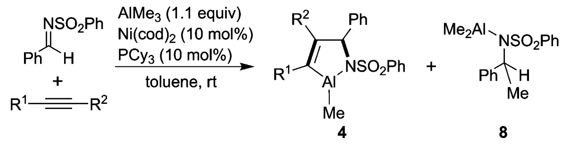
Table 1. Nickel-Mediated Cyclocondensation of Alkynes, *N*-BBSA, and AlMe$_3$[a]



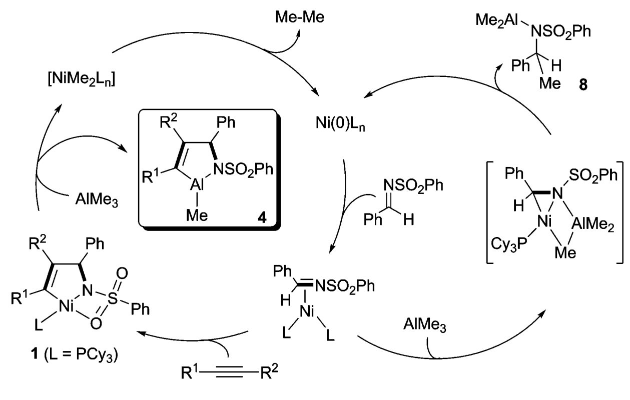
run	alkyne		product	yield (%)[b]	yield of **8** (%)[c]
	R^1	R^2			
1	Ph	Ph	**4a**	86 (71)	–
2	*p*-MeC$_6$H$_4$	*p*-MeC$_6$H$_4$	**4b**	85 (82)	–
3	*p*-CF$_3$C$_6$H$_4$	*p*-CF$_3$C$_6$H$_4$	**4c**	90 (99)	–
4[d]	Ph	TMS	**4d**	85 (73)	7
5[e]	Ph	Me	**4e**[f]	65 (44)	13
6	Et	Et	**4f**[g]	27	59

[a] General conditions: alkyne and *N*-BBSA (0.3 mmol each), solvent (10 mL). After dropwise addition of AlMe$_3$, the reaction mixture was stirred until the color derived from **1** (typically purple) disappeared (1.0−6.0 h). [b] Isolated yields as allylamines **5** after protolysis. Cited yields in parentheses are of isolated **4**. [c] The cited yields, determined by ^{1}H NMR, were of the corresponding protonated products. [d] The reaction was carried out using 1.5 mmol of $TMSC{\equiv}CPh$. [e] The reactions were carried out with concomitant addition of AlMe$_3$ and the alkyne. [f] The minor regioisomer (11%) was also obtained. [g] Formation of a 1,2-dihydropyridine derivative was also observed (also see ref 6e).

and was found to accelerate with the addition of 10 mol % Ni(cod)$_2$ and PCy$_3$ (Scheme 3, right circle).[10] Therefore, the slow addition of AlMe$_3$ improved the yield of **4a** as a result of suppression of the competitive reaction. Finally, the three-component cyclocondensation of *N*-BBSA, diphenylacetylene, and AlMe$_3$ (via slow addition over 30 min) in the presence of 10 mol % Ni(cod)$_2$ and PCy$_3$ afforded **4a** in 71% isolated yield (Table 1, run 1).[11] While the isolated yield of **4a** was somewhat decreased because of losses during the purification process, NMR analysis indicated that this catalytic reaction proceeded quantitatively. In fact, protolysis of the crude product gave the corresponding allylamine **5a** in 86% isolated yield (run 1). The same reaction conditions were applied successfully to diphenylacetylene derivatives, which led to clean formation of **4b** and **4c** (runs 2 and 3, respectively).

Nonsymmetric alkynes were used as coupling components in the cyclocondensation with *N*-BBSA and AlMe$_3$; **4d** was formed in 85% yield as a single regioisomer, but use of 5 equiv of 1-phenyl-2-trimethylsilylacetylene was essential for the promotion of a smooth reaction, probably as a result of its diminished ability to coordinate to Ni(0) (run 4). In contrast, the reaction with 1-phenyl-1-propyne gave **4e** with 86:14 regioselectivity only when slow addition of both AlMe$_3$ and the alkyne was conducted in order to circumvent the insertion of the second alkyne into a five-membered azanickelacycle (run 5).[6e] 1,2-Dialkyl-substituted alkynes such as 3-hexyne did not react efficiently because of the rapid formation of the undesired seven-membered azanickelacycle even with slow addition of a mixture of the alkyne and AlMe$_3$ (run 6).[6e] For several cases cited in runs 4, 5, and 6, formation of **8** was observed in the ^{1}H NMR spectra of the crude products. These results are consistent with the mechanism proposed in Scheme 3.

Scheme 3. Plausible Mechanism for Catalytic Formation of **4**



In summary, we have demonstrated the nickel-catalyzed three-component cyclocondensation of imines, alkynes, and AlMe$_3$ to yield unique azaaluminacyclopentenes. Nickelacycle **1**, generated by the oxidative cyclization of an alkyne and an imine, is a key intermediate in the cyclocondensation reaction as well as in the three-component coupling reaction with ZnMe$_2$. Further study will focus on the related formation of oxaaluminacyclopentenes.

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Supporting Information Available: Detailed experimental procedures, analytical and spectral data for all new compounds, and crystallographic data (CIF) for **2a** and **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(11) In contrast, slow addition of ZnMe$_2$ was unnecessary because the corresponding direct addition in the Ni-catalyzed three-component coupling reaction did not occur.

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