

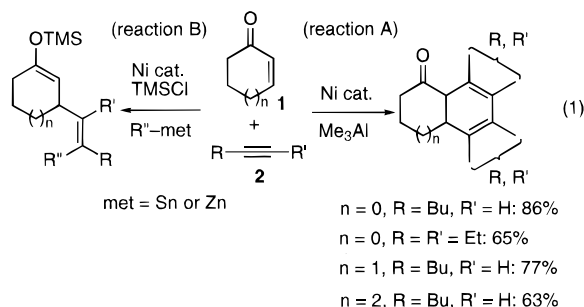
## Regioselective Cyclic Cotrimerization of $\alpha,\beta$ -Enones and Alkynes by a Nickel–Aluminum Catalyst System

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We report here a new example of cyclic cotrimerization. The reaction of  $\alpha,\beta$ -enones **1** (1 equiv) and alkynes **2** (2 equiv) proceeded smoothly in the presence of a nickel–organoaluminum catalyst system to give the corresponding cyclic adducts (reaction A in eq 1). Moreover, regioselective cotrimerization was observed in the reaction with 1-alkyne.



We recently reported the nickel-catalyzed tandem reaction of **1**, **2**, chlorotrimethylsilane (TMSCl), and organotin or organozinc to provide the corresponding coupling products (reaction B in eq 1).<sup>1</sup> During this research, we found that the reaction of trimethylaluminum (Me<sub>3</sub>Al) with 2-cyclopenten-1-one (**1a**), 1-hexyne (**2a**), and TMSCl in the presence of a nickel–triphenylphosphine (PPh<sub>3</sub>) catalyst in THF at room temperature gave an unexpected cyclic cotrimerization adduct (n = 0, R = Bu, R' = H; isomer mixture) derived from one molecule of **1a** and two molecules of **2a** in a total yield of 48% (reaction A). To the best of our knowledge, there is no example of the cotrimerization of enone **1** with alkyne **2**.<sup>2</sup> Therefore, we started to investigate the nickel-catalyzed (5 mol %) reaction of **1a** with a stoichiometric amount of **2a** (i.e., 2 equiv vs **1a**) in the presence of Me<sub>3</sub>Al to determine the optimum conditions for obtaining the adducts in high yield. A palladium complex such as Pd(acac)<sub>2</sub> did not catalyze the reaction. TMSCl was not required for cotrimerization. The amount of Me<sub>3</sub>Al could be reduced to 40 mol %. When phenol (ca. 3 equiv vs Me<sub>3</sub>Al) was added to the reaction system, the yield of the adduct increased to 86%.<sup>3</sup> Other enones and alkynes could also be applied to this cotrimerization.<sup>4</sup>

(1) (a) Ikeda, S.; Sato, Y. *J. Am. Chem. Soc.* **1994**, *116*, 5975. (b) Ikeda, S.; Yamamoto, H.; Kondo, K.; Sato, Y. *Organometallics* **1995**, *14*, 5015. (c) Ikeda, S.; Kondo, K.; Sato, Y. *J. Org. Chem.* **1996**, *61*, 8248. Also see: Montgomery, J.; Savchenko, A. V. *J. Am. Chem. Soc.* **1996**, *118*, 2099. Montgomery, J.; Seo, J.; Chui, H. M. P. *Tetrahedron Lett.* **1996**, *37*, 6839.

(2) For the cyclic cotrimerization of alkenes and alkynes, see: Kein, W.; Behr, A.; Röper, M. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon Press: Oxford, 1982; Vol. 8, Chapter 52. Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 4, Chapter 9.4. Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Hegedus, L. S., Ed.; Pergamon Press: Oxford, 1995; Vol. 12, Chapter 7.4.

(3) Maruoka, K.; Yamamoto, H. *J. Synth. Org. Chem. Jpn.* **1993**, *51*, 1074 and references cited therein. When the nickel–aluminum-catalyzed reaction of **1a** with **2a** proceeded in the absence of PPh<sub>3</sub>, the corresponding adduct was produced in 49% yield.

(4) While the reaction of methyl vinyl ketone with **2b** also gave the desired product, methyl acrylate did not react in the catalytic system.

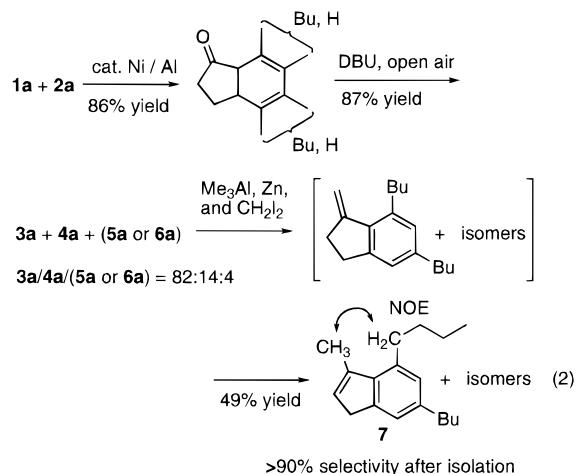
Table 1. Nickel–Aluminum-Catalyzed Cotrimerization of **1** and **2a**

entry	<b>1</b>	<b>2</b>	total yield of <b>3–6</b> , <sup>b</sup> %	ratio, <sup>c</sup> <b>3:4</b> :( <b>5</b> or <b>6</b> )
1	<b>1a</b>	<b>2a</b>	<b>a</b> , 71	82:14:4
2	<b>1a</b>	<b>2b</b>	<b>b</b> , 62	
3 <sup>d</sup>	<b>1a</b>	<b>2c</b>	<b>c</b> , 42	<b>3c</b> , >98%
4 <sup>d</sup>	<b>1a</b>	<b>2d</b>	<b>d</b> , 81	92:<2:6
5 <sup>d</sup>	<b>1a</b>	<b>2e</b>	<b>e</b> , 45 <sup>e</sup>	<b>4e</b> , 89%
6 <sup>d</sup>	<b>1a</b>	<b>2f</b>	<b>f</b> , 33	<b>4f</b> , >98%
7	<b>1b</b>	<b>2a</b>	<b>g</b> , 83	91:7:<2
8 <sup>f</sup>	<b>1b</b>	<b>2g</b>	<b>h</b> , 50	89:9:<2
9	<b>1c</b>	<b>2a</b>	<b>i</b> , 70	85:0:15

<sup>a</sup> Unless stated otherwise, all reactions were carried out with Ni(acac)<sub>2</sub> (0.05 mmol), PPh<sub>3</sub> (0.1 mmol), Me<sub>3</sub>Al (1.0 M in hexane, 0.4 mL), phenol (1.1 mmol), enone (1 mmol), alkyne (2.05 mmol), and THF (5 mL) at room temperature for 2 h under N<sub>2</sub> and followed by treatment with DBU (2 mmol) overnight under open air. <sup>b</sup> Isolated yield. <sup>c</sup> Ratio based on <sup>1</sup>H NMR. <sup>d</sup> The reaction was carried out with Ni(acac)<sub>2</sub> (0.1 mmol), PPh<sub>3</sub> (0.2 mmol), Me<sub>3</sub>Al (0.8 mmol), and phenol (2.0 mmol). <sup>e</sup> Aromatization was performed with 0.2 M NaOH in methanol instead of DBU. <sup>f</sup> Gaseous **2g** (ca. 25 mmol) was used.

<sup>a</sup> Unless stated otherwise, all reactions were carried out with Ni(acac)<sub>2</sub> (0.05 mmol), PPh<sub>3</sub> (0.1 mmol), Me<sub>3</sub>Al (1.0 M in hexane, 0.4 mL), phenol (1.1 mmol), enone (1 mmol), alkyne (2.05 mmol), and THF (5 mL) at room temperature for 2 h under N<sub>2</sub> and followed by treatment with DBU (2 mmol) overnight under open air. <sup>b</sup> Isolated yield. <sup>c</sup> Ratio based on <sup>1</sup>H NMR. <sup>d</sup> The reaction was carried out with Ni(acac)<sub>2</sub> (0.1 mmol), PPh<sub>3</sub> (0.2 mmol), Me<sub>3</sub>Al (0.8 mmol), and phenol (2.0 mmol). <sup>e</sup> Aromatization was performed with 0.2 M NaOH in methanol instead of DBU. <sup>f</sup> Gaseous **2g** (ca. 25 mmol) was used.

The most notable feature is that the regioselective cotrimerization occurred in the reaction with 1-alkynes. Since the regiochemistry of the adducts was equivocal by spectroscopic analyses, it was determined after aromatization. When the adducts derived from the reaction of **1a** with **2a** were treated with DBU under open air, three kinds of regioisomers (i.e., **3a**, **4a**, and **5a** or **6a**) were produced on the basis of <sup>1</sup>H NMR spectral data (total yield 87%) (eq 2). One of the minor products



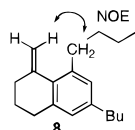
(14% selectivity) was considered to be 4,7-dibutyl-1-indanone (**4a**) on the basis of the coupling constant ( $J = 8.1$  Hz) between two aromatic protons. The major isomer (82% selectivity) was determined to be 5,7-dibutyl-1-indanone (**3a**) on the basis of spectral analyses of product **7** derived from further chemical transformation of the aromatic compound mixture.<sup>5</sup>

The results of regioselective cotrimerization of a variety of combinations of **1a–c** and **2a–g** are summarized in Table 1.<sup>6</sup> The reaction of **1a** with propargyl silyl ether **2c** gave **3c** as a sole product (entry 3). When silyl ether **2d** was treated instead of **2c**, the regioselectivity of **3d** decreased to 92% (entry 4). The six- and seven-membered enones **1b** and **1c** also reacted to provide **3g** (from the reaction with **2a**, 91% selectivity), **3h** (from the reaction with **2g**, 89% selectivity), and **3i** (from the reaction with **2a**, 85% selectivity) as the major products (entries 7–9). The products **4e** (89% selectivity) and **4f** (>98% selectivity) were synthesized from the reaction of **1a** with *tert*-butylacetylene (**2e**) and (trimethylsilyl)acetylene (**2f**), respectively (entries 5 and 6).

Plausible mechanisms are shown in Scheme 1. The aluminum catalyst functions as a Lewis acid and activates enone **1**.<sup>7</sup> The reaction of nickelacyclopentene **9**,<sup>1c,8</sup> which was generated from a Ni(0) species, one molecule of alkyne **2**, and a 1–aluminum complex, with another molecule of **2** may produce intermediate **10** followed by reductive elimination. Alternatively, a pathway which involves the generation of nickelacyclopentadiene **11** has also been suggested.<sup>9,10</sup> Regioselectivity is due

(5) Takai, K.; Hotta, Y.; Oshima, K.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1698.

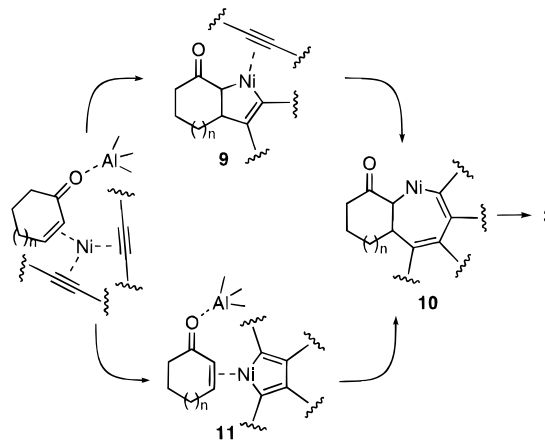
(6) All new compounds were characterized by NMR, IR, and mass spectral data and by elemental analyses or high-resolution mass spectra. The structures of major products were determined as follows: **3g**, the transformation to **8**;<sup>5</sup> **3c**, the NOE experiment; **3h**, the comparison with <sup>1</sup>H NMR spectral data of commercially available **5h**; **3d** and **3i**, the comparison with <sup>1</sup>H and <sup>13</sup>C NMR spectral data of **3a**, **3g**, and **3h**; **4e** and **4f**, the coupling constant between two aromatic protons. See the Supporting Information.



total 39% yield from **3e–6e** mixture;  
**8**: >95% selectivity after isolation

(7) In the first step, an aluminum–nickel complex based on Lewis acid–Lewis base interaction may be prepared; see: Fischer, K.; Jonas, K.; Misbach P.; Stabba, R.; Wilke, G. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 943.

### Scheme 1



to steric and/or electronic characteristics of **1** and **2** in the production of intermediate **9** or **11**.<sup>9c,11</sup>

In summary, we have described the novel regioselective cyclic cotrimerization of enones **1** and 1-alkynes **2** by a nickel–aluminum catalyst system. More detailed studies on the scope of this reaction are in progress.

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**Supporting Information Available:** Experimental procedure and spectrographic data for all new compounds (7 pages). See any current masthead page for ordering and Internet access instructions.

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(8) For production of a cobaltacyclopentene complex, see: Wakatsuki, Y.; Aoki, K.; Yamazaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 5284. Wakatsuki, Y.; Aoki, K.; Yamazaki, H. *J. Am. Chem. Soc.* **1979**, *101*, 1123.

(9) (a) Eisch, J. J.; Galle, J. E. *J. Organomet. Chem.* **1975**, *96*, C23. (b) Eisch, J. J.; Piotrowski, A. M.; Han, K. I.; Krüger, C.; Tsay, Y. H. *Organometallics* **1985**, *4*, 224. For production of a cobaltacyclopentadiene complex, see: (c) Wakatsuki, Y.; Nomura, O.; Kitaura, K.; Morokuma, K.; Yamazaki, H. *J. Am. Chem. Soc.* **1983**, *105*, 1907.

(10) The possibility of a Diels–Alder process cannot be ruled out in the reaction; see: McAlister, D. R.; Bercaw, J. E.; Bergman, R. G. *J. Am. Chem. Soc.* **1977**, *99*, 1666.

(11) Stockis, A.; Hoffmann, R. *J. Am. Chem. Soc.* **1980**, *102*, 2952.