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Iridium complex-catalyzed [2+2+2] cycloaddition of α,ω-diynes with monoalkynes: a new and efficient catalyst for cyclotrimerization of alkynes

Ryo Takeuchi,* Shigeru Tanaka and Yoshihiko Nakaya

Department of Environmental Science, Faculty of Science and Graduate School of Integrated Science, Yokohama City University, 22-2 Seto, Kanazawa-ku, Yokohama 236-0027, Japan

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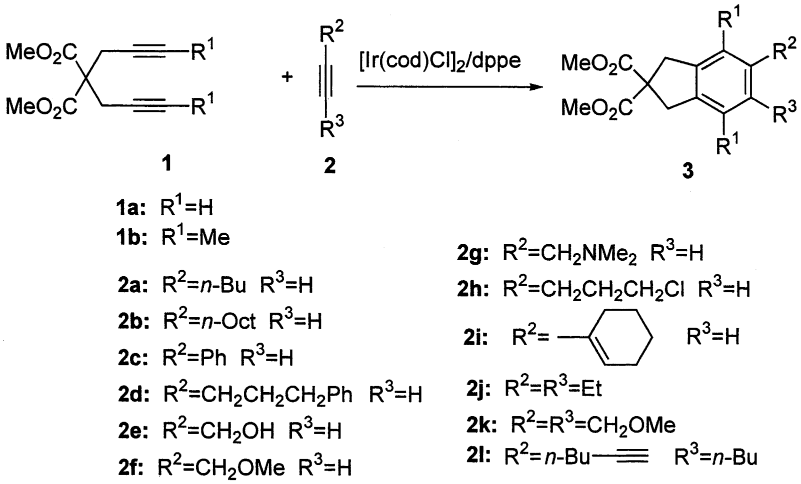
Abstract—[Ir(cod)Cl]$_2$ combined with dppe was found to be a new and efficient catalyst for [2+2+2] cycloaddition. Dimethyl dipropargylmalonate reacted with 1-hexyne in the presence of a catalytic amount of [Ir(cod)Cl]$_2$ combined with dppe at room temperature in 20 min to give an indane derivative in 84% yield. Various functionalized monoalkynes can be used for this [2+2+2] cycloaddition. © 2001 Elsevier Science Ltd. All rights reserved.

The transition metal complex-catalyzed synthetic transformation of alkynes has been studied extensively. From the standpoint of atom economy, dimerization and cyclotrimerization are particularly important.[1] The synthetic application of the cyclotrimerization of alkynes to give substituted benzene derivatives has not been developed due to the low regioselectivity. Vollhardt enhanced the synthetic value of the cyclotrimerization of alkynes by using α,ω-diyne as one component and a monoalkyne as the other component.[2] Several transition metal complexes, such as those of Co,[2] Ni,[3] Rh,[4] Pd,[5] and Ru,[6] have been reported to be catalysts for this reaction. However, new catalysts are still valuable to expand the reaction scope and selectivity.

Less attention has been paid to iridium complexes as catalysts for organic synthesis compared to palladium and rhodium complexes. Recently, synthetically useful reactions catalyzed by an iridium complex have been reported.[7] Collman et al. first prepared an iridiacy-



1a: R^1=H
1b: R^1=Me

2a: R^2=*n*-Bu R^3=H
2b: R^2=*n*-Oct R^3=H
2c: R^2=Ph R^3=H
2d: R^2=$CH_2CH_2CH_2Ph$ R^3=H
2e: R^2=CH_2OH R^3=H
2f: R^2=CH_2OMe R^3=H
2g: R^2=CH_2NMe_2 R^3=H
2h: R^2=$CH_2CH_2CH_2Cl$ R^3=H
2i: R^2= R^3=H
2j: R^2=R^3=Et
2k: R^2=R^3=CH_2OMe
2l: R^2=*n*-Bu—≡ R^3=*n*-Bu

Scheme 1.

Keywords: iridium and compounds; diynes; cycloadditions; metallacycles; alkynes.

* Corresponding author.

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Table 1. Effect of ligands on the reaction of **1a** with **2a**[a]

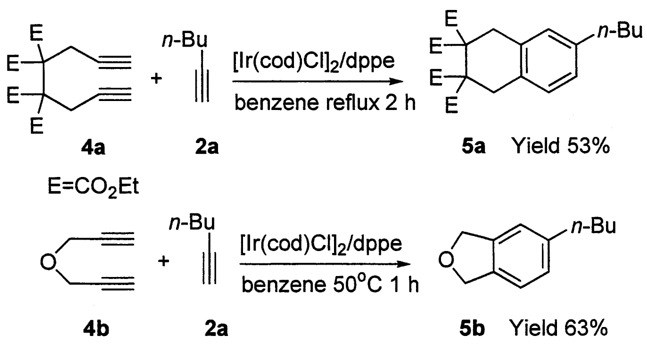
Entry	Ligand	Conditions	Yield of **3aa** (%)[b]
1	PPh_3	50°C 24 h	45
2	dppm	50°C 24 h	45
3	dppe	rt 20 min	84
4	dppp	50°C 24 h	68
5	None	50°C 24 h	35
6	$P(OPh)_3$	Reflux 24 h	12

[a] A mixture of **1** (1 mmol), **2a** (3 mmol), $[Ir(cod)Cl]_2$ (0.02 mmol), ligand (P/Ir = 2) and benzene (5 ml) was stirred under Ar.

[b] Isolated yield based on **1**.

clopentadiene complex by the reaction of $IrCl(N_2)(PPh_3)_2$ with dimethyl acetylenecarboxylate and found that an iridiacyclopentadiene complex was a potential catalyst for the cyclotrimerization of alkynes.[8] However, this chemistry has not yet been developed. In the course of our study on iridium complex-catalyzed carbon–carbon bond forming reactions,[9] we first found that $[Ir(cod)Cl]_2$ combined with dppe was an efficient catalyst for the [2+2+2] cycloaddition of α,ω-diynes with monoalkynes to give polysubstituted benzene derivatives (Scheme 1).

Diyne **1a** reacted with 3 equiv. of 1-hexyne (**2a**) to give an indane derivative **3aa** in the presence of a catalytic amount of $[Ir(cod)Cl]_2$ (Ir atom 4 mol%; cod = 1,5-cyclooctadiene). The catalytic activity depended on the ligand used. The results are summarized in Table 1. Dppe was found to be the most efficient ligand (entry 3). The reaction was completed in 20 min at room temperature to give **3aa** in 84% yield. Dppp, dppm and PPh_3 were all inferior to dppe. Reactions using dppp, dppm or PPh_3 as a ligand required heating to give **3aa**, and the yield of **3aa** decreased (entries 1, 2 and 4). $[Ir(cod)Cl]_2$ without any ligand gave **3aa** in 35% yield (entry 5). We previously reported that $P(OPh)_3$ was an efficient ligand for $[Ir(cod)Cl]_2$-catalyzed allylic substitution.[9] However, $P(OPh)_3$ was a less efficient ligand



Scheme 2.

than dppe for [2+2+2] cycloaddition (entry 6). Iridium complexes such as $[Ir(cod)OMe]_2$ and $[Ir(cod)_2]BF_4$ combined with dppe were less efficient than $[Ir(cod)Cl]_2$ combined with dppe.

Diyne **1a** reacted with 3 equiv. of monoalkynes **2** to give indane derivatives **3** in good to excellent yields (Scheme 1). Various functionalized monoalkynes could be used. The results were summarized in Table 2. The optimal reaction conditions depended on the monoalkyne component used. Diyne **1a** reacted with 1-hexyne (**2a**), 1-decyne (**2b**), 5-phenyl-1-pentyne (**2d**) and 5-chloro-1-pentyne (**2h**) at room temperature to give **3aa**, **3ab**, **3ad** and **3ah** in excellent yields (entries 1, 2, 4 and 8). The reaction with phenylacetylene (**2c**) required more demanding conditions. The reaction with **2c** under refluxing dioxane for 2 h gave **3ac** in 83% yield (entry 3). Propargylic alcohol (**2e**), propargylic ether (**2f**) and conjugated enyne (**2i**) could each be used as a monoalkyne component. The reaction with **2e** under refluxing in dioxane for 8 h gave **3ae** in 85% yield (entry 5). Reactions with **2f** and **2i** gave the corresponding products in decreased yields compared to **3aa**–**ae** (entries 6 and 9). Interestingly, the reaction with *N*,*N*-dimethylpropargylic amine (**2g**) gave **3ag** in 65% yield (entry 7). The reaction of α,ω-diyne with **2g** has been

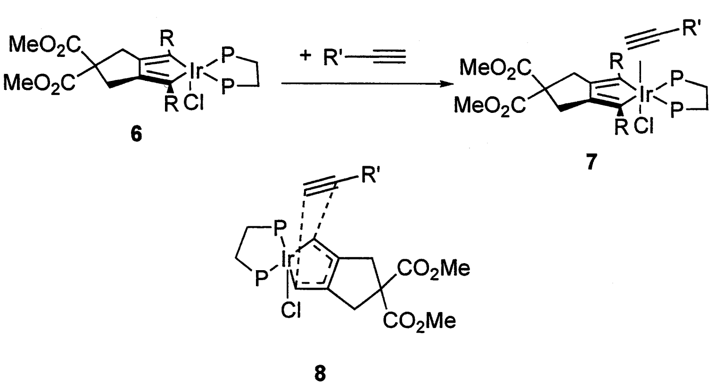
Table 2. [2+2+2] Cycloaddition of **1** with **2**[a]

Entry	Substrate	Alkyne	Conditions	Product	Yield (%)[b]
1	**1a**	**2a**	Benzene, rt 20 min	**3aa**	84
2	**1a**	**2b**	Benzene, rt 20 min	**3ab**	82
3	**1a**	**2c**	Dioxane, reflux 2 h	**3ac**	83
4	**1a**	**2d**	Benzene, rt 1 h	**3ad**	81
5	**1a**	**2e**	Dioxane, reflux 8 h	**3ae**	85
6	**1a**	**2f**	Benzene, reflux 10 h	**3af**	66
7[c]	**1a**	**2g**	Dioxane, reflux 2 h	**3ag**	65
8	**1a**	**2h**	Benzene, rt 30 min	**3ah**	86
9	**1a**	**2i**	Benzene, reflux 6 h	**3ai**	65
10	**1b**	**2a**	Toluene, reflux 7 h	**3ba**	87
11	**1b**	**2c**	Toluene, reflux 4 h	**3bc**	77
12	**1b**	**2f**	Toluene, reflux 5 h	**3bf**	79
13	**1b**	**2j**	Benzene, rt 2 h	**3bj**	87
14	**1b**	**2k**	Benzene, rt 30 min	**3bk**	94
15	**1b**	**2l**	Benzene, rt 15 min	**3bl**	86

[a] A mixture of **1** (1 mmol), **2** (3 mmol), $[Ir(cod)Cl]_2$ (0.02 mmol), dppe (0.04 mmol) and solvent (5 ml) was stirred under Ar.

[b] Isolated yield based on **1**.

[c] $[Ir(cod)Cl]_2$ (0.03 mmol), dppe (0.06 mmol).



Scheme 3.

reported to require a stoichiometric amount of a Ni(0) complex.[10] Diyne **1b** also reacted smoothly with **2**. Reactions with 1-hexyne (**2a**) and phenylacetylene (**2c**) gave **3ba** and **3bc** in respective yields of 87 and 77% (entries 10 and 11). The reaction with propargylic ether (**2f**) gave **3bf** in 79% yield (entry 12). Diyne **1b** reacted with internal alkynes **2j** and **2k** at room temperature to give **3bj** and **3bk** in respective yields of 87 and 94% (entries 13 and 14). Conjugated diyne could also be used for this reaction. The reaction with 5,7-dodecadiyne (**2l**) gave **3bl** in 86% yield (entry 15).

Other diynes could be used for this [2+2+2] cycloaddition (Scheme 2). 1,7-Diyne (**4a**) reacted with 1-hexyne (**2a**) to give **5a** in 53% yield. Dipropargyl ether (**4b**) also reacted with 1-hexyne (**2a**) to give **5b** in 63% yield.

The reaction mechanism may involve the formation of an iridiacyclopentadiene complex as an intermediate (Scheme 3).[8,11] The reaction of $[Ir(cod)Cl]_2$ with dppe gives a mononuclear species Ir(cod)Cl(dppe). Oxidative cyclization of diynes with Ir(cod)Cl(dppe) would give an iridiacyclopentadiene **6**. The reaction of **6** with an monoalkyne by insertion or a Diels–Alder type process[12] followed by reductive elimination gives a final product. Bidentate coordination of dppe produces a vacant coordination site above the plane of an iridiacyclopentadiene **6**.[13] Coordination of a monoalkyne to this position[14] would facilitate a Diels–Alder type process via transition state **8**. Among bidentate ligands, dppe might give the most stable chelation. This may explain the efficiency of dppe.

$[Ir(cod)Cl]_2$ and dppe are commercially available, air-stable solids. Our simple procedure is useful for the selective synthesis of polysubstituted benzene derivatives. Further mechanistic study and the synthetic application of this [2+2+2] addition are underway.

References

1. (a) Saito, S.; Yamomoto, Y. *Chem. Rev.* **2000**, *100*, 2901–2915; (b) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49–92; (c) Grotjahn, D. B. In *Comprehensive Organometallic Chemistry II*; Abel, E. W.; Stone, F. G. A.; Wilkinson, W., Eds.; Pergamon: Oxford, 1995; Vol. 12, pp. 741–770; (d) Schore, N. E. In *Comprehensive Organic Synthesis*; Trost, B. M.; Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp. 1129–1162.
2. Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539–644.
3. (a) Sato, Y.; Nishimata, T.; Mori, M. *J. Org. Chem.* **1994**, *59*, 6133–6155; (b) Sato, Y.; Ohashi, K.; Mori, M. *Tetrahedron Lett.* **1999**, *40*, 5231–5234.
4. (a) Grigg, R.; Scott, R.; Stevenson, P. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1357–1364; (b) McDonald, F. E.; Zhu, H. Y. H.; Holmquist, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 6605–6606; (c) Witulski, R.; Stengel, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 2426–2430.
5. (a) Yamamoto, Y.; Nagata, A.; Itoh, K. *Tetrahedron Lett.* **1999**, *40*, 5035–5038; (b) Yamamoto, Y.; Nagata, A.; Arikawa, Y.; Tatsumi, K.; Itoh, K. *Organometallics* **2000**, *19*, 2403–2405.
6. (a) Yamamoto, Y.; Ogawa, R.; Itoh, K. *J. Chem. Soc., Chem. Commun.* **2000**, 549–550; (b) Witulski, B.; Stengel, T.; Fernández-Hernández, J. M. *J. Chem. Soc., Chem. Commun.* **2000**, 1965–1966; (c) Peters, J.-U.; Blechert, S. *J. Chem. Soc., Chem. Commun.* **1997**, 1983–1984.
7. (a) Matsumoto, T.; Taube, D. J.; Periana, R. A.; Taube, H.; Yoshida, H. *J. Am. Chem. Soc.* **2000**, *122*, 7414–7415; (b) Murahashi, S.; Takaya, H. *Acc. Chem. Res.* **2000**, *33*, 225–233; (c) Ohmura, T.; Yorozuya, S.; Yamamoto, Y.; Miyaura, N. *Organometallics* **2000**, *19*, 365–367; (d) Jun, C.-H.; Lu, Z.; Crabtree, R. H. *Tetrahedron Lett.* **1992**, *33*, 7119–7120.
8. Collman, J. P.; Kang, J. W.; Little, W. F.; Sullivan, M. F. *Inorg. Chem.* **1968**, *7*, 1298–1303.
9. (a) Takeuchi, R.; Kashio, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 263–265; (b) Takeuchi, R.; Kashio, M. *J. Am. Chem. Soc.* **1998**, *120*, 8647–8655; (c) Takeuchi, R. *Polyhedron* **2000**, *19*, 557–561; (d) Takeuchi, R.; Tanabe, K. *Angew. Chem., Int. Ed.* **2000**, *39*, 1975–1978; (e) Allylic amination, see: Takeuchi, R.; Shiga, N. *Org. Lett.* **1999**, *1*, 265–267.
10. Duckworth, D. M.; Wang, S.-L.; Slawin, A. M. Z.; Smith, E. H.; Williams, D. J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 815–821.
11. (a) O'Connor, J. M.; Hiibner, K.; Merwin, R.; Gantzel, P. K.; Fong, B. S.; Adams, M.; Rheingold, A. L. *J. Am. Chem. Soc.* **1997**, *119*, 3631–3632; (b) O'Connor, J. M.; Pu, L.; Rheingold, A. L. *J. Am. Chem. Soc.* **1990**, *112*, 6232–6247; (c) Rappoli, B. J.; Churchhill, M. R.; Janik, T. S.; Rees, W. M.; Atwood, J. D. *J. Am. Chem. Soc.* **1987**, *109*, 5145–5149.

12. Reaction of a metallacyclopentadiene with a monoalkyne via Diels–Alder type process, see: McAlister, D. R.; Bercaw, J. E.; Bergman, R. G. *J. Am. Chem. Soc.* **1977**, *99*, 1666–1668.
13. A vacant coordination site on an iridiacyclopentadiene is necessary for the incoming monoalkyne. Blocking a vacant coordination site by carbon monoxide inhibits [2+2+2] cycloaddition, see Ref. 8.
14. A metallacyclopentadiene bearing an alkyne ligand, see: Diercks, R.; Eaton, B. E.; Gurtzgen, S.; Jalisatgi, S.; Matzger, A. J.; Radde, R. H.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1998**, *120*, 8247–8248.