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Alkylzirconation of Alkynes Catalyzed by Triphenylcarbenium Tetrakis(pentafluorophenyl)borate

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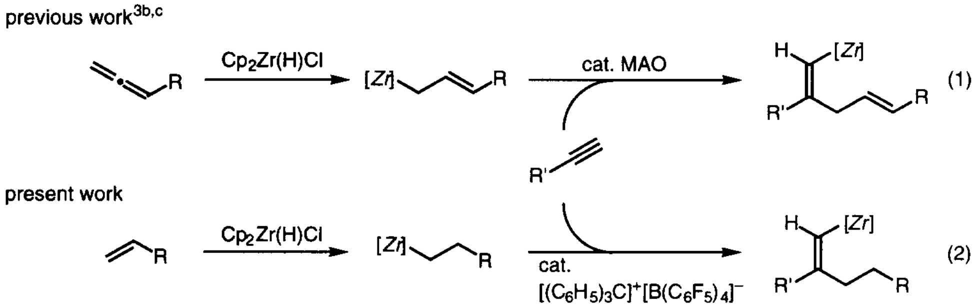
Abstract: $[(C_6H_5)_3C]^+[B(C_6F_5)_4]^-$ effectively catalyzes the alkylmetallation of alkynes by using the alkylzirconium species, which is generated by the hydrozirconation of alkenes.

Carbometallation of alkenes/alkynes is attracting considerable interest as a potential new method for C–C bond formation.[1] Among the precedents, the Negishi reaction is a pioneering example that has found wide synthetic applications,[2] which, however, is virtually limited to the transfer of a methyl group, and the corresponding reaction for higher alkyls ($R \neq CH_3$) is hampered by the limited availability of R_3Al as well as the poorer regioselectivity.[2a]

We recently reported the allylzirconation of 1-alkynes by using the allylzirconium species generated by the hydrozirconation of allenes (eq. 1), in which methylaluminoxane (MAO) effectively worked for generating the key cationic zirconocene species.[3,4] In order to extend the scope of the reaction, we examined the feasibility of the corresponding *alkyl*zirconation by using the alkylzirconium generated by the hydrozirconation of 1-alkene (eq. 2).[5] It turned out, however, that the reaction proceeded only slowly, requiring a stoichiometric amount of MAO (vide infra).



After considerable experimentation to find out the alternative catalyst(s), triphenylcarbenium tetrakis(pentafluorophenyl)borate, $[(C_6H_5)_3C]^+[B(C_6F_5)_4]^-$, was found as the reagent of choice.[4] In this communication, we wish to feature the trityl salt-catalyzed alkylmetallation of alkynes.

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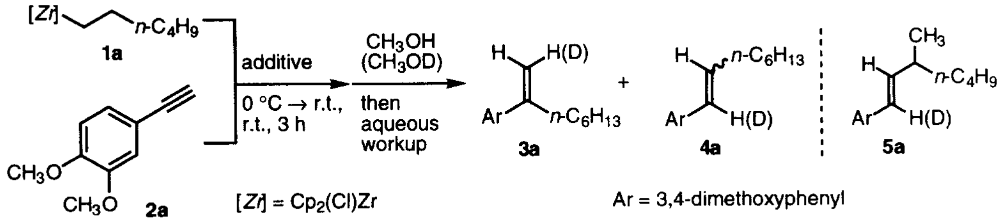
Table 1



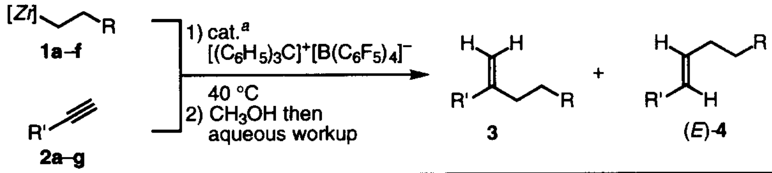
run	additive (equiv.)	total yield/%[a]	3a : 4a[b] : 5a
1	MAO (0.6)	59	–[c]
2	MAO (1.1)	82	–[c]
3	MAO (1.5)	90	89 : 9 : 2
4	$\{(i\text{-}C_4H_9)_2Al\}_2O$ (0.75)	3	–[c]
5	$\{(C_2H_5)Al(Cl)\}_2O$ (1.5)	17	–[c]
6	$[C_6H_5N(CH_3)_2H]^+[B(C_6F_5)_4]^-$ (0.2)	72	78 : 22 : 0
7	$[(C_6H_5)_3C]^+[B(C_6F_5)_4]^-$ (0.05)	93	91 : 8 : 1
8	$[(C_6H_5)_3C]^+[B(C_6F_5)_4]^-$ (0.05)	95	91 : 9 : 0[d]

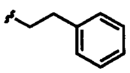
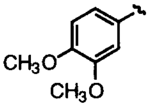
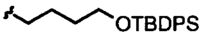
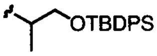
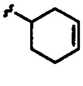
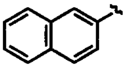
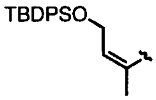
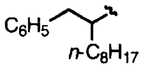
[a] Combined yields of **3a**, **4a** and **5a**. The ratios were assessed by capillary GC. See also ref. 6 [b] *E/Z*: 3.5/1 for run 3; 1/3.4 for run 6; 3/1 for run 7; 8/1 for run 8. [c] Not determined. [d] At 40 °C (30 min), see text.

As a model reaction, the *n*-hexylzirconium species **1a** was generated from 1-hexene and $Cp_2Zr(H)Cl$ (CH_2Cl_2, 25 °C, 20 min) and treated with the alkyne **2a** at 0 °C. No reaction was observed at this stage (TLC assay). However, the carbometallation was induced with varying efficiency upon addition of the reagents that would potentially generate a cationic zirconocene species (Table 1).[4,6] MAO, which was used for the *allyl*zirconation,[3b,c] turned out to be less effective; an excess amount was required for completing the reaction (runs 1–3). Dialuminoxanes were not effective (runs 4, 5).[7] On the other hand, $[C_6H_5N(CH_3)_2H]^+[B(C_6F_5)_4]^-$ showed a good catalytic activity. However, a considerable amount of **4a** was produced. Eventually, the best result was obtained with $[(C_6H_5)_3C]^+[B(C_6F_5)_4]^-$ (runs 7, 8):[8] Only 5 mol% was enough for the complete consumption of **2a**, and the regioselectivity was better than the case of MAO, albeit slightly. Furthermore, the formation of **5a** was completely suppressed by performing both the hydrozirconation and the carbometallation at 40 °C, and the reaction was completed more quickly (30 min) to give 95% yield of the products (run 8). When the reaction was quenched with methanol-d_1, a deuterium was incorporated as shown in the equation in Table 1 (76% incorporation for **3a**).

This optimal procedure was applied to various alkylzirconiums and alkynes (Table 2). As runs 1–5 show, various ***higher alkyl groups*** are combined with the alkyne **2a** in high yields. Interestingly, the alkylzirconium possessing an internal C=C bond (**1e**) or a bromine (**1f**) smoothly took part in the reaction (runs 4, 5).[9] Runs 6–9 illustrate the variation of alkynes. The regioselectivities for the alkynes with a bulky substituent (**2b–d**) were high, whereas low for the alkyne **2g** with a *prim*-alkyl substituent. This is the trend already seen for the case of the allylzirconation,[3b,c] where the critical factor was the steric demand of the alkyne substituent R'. Conjugated enyne **2c** reacted selectively at its C≡C bond, while the C=C bond remained intact.

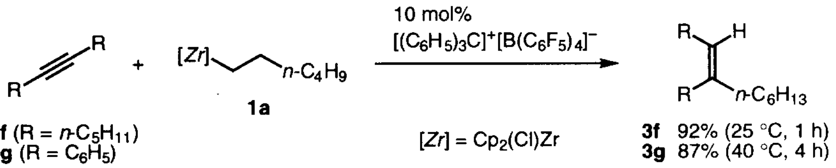
Table 2



run	R		R'		period/h	Yield/%[b]	3 : (E)-4[c]
1		(1b)		(2a)	1	91	92 : 8[f]
2		(1c)	2a		1.4	88	94 : 6
3		(1d)	2a		1	84[d]	92 : 8
4		(1e)	2a		0.5	86	93 : 7
5		(1f)	2a		0.3	80[d,e]	93 : 7
6	n-C_4H_9	(1a)		(2b)	0.5	93	89 : 11
7	1a			(2c)	1	73	>98 : <2
8	1a			(2d)	1	89[d]	96 : 4
9	1a		n-$C_{10}H_{21}$	(2e)	0.5	91	75 : 25

[a] 0.05 equiv. [b] Combined yields of **3** and **4**. [c] Any (*Z*)-**4** or **5** (for their structures, see the equation in Table 1) was not observed (GC), otherwise noted. [d] 0.1 equiv. of the catalyst was used. [e] The reaction was carried out at 0 °C. [f] Small amount of **5** (2%) was included.

The reaction proved also applicable to internal alkynes **2f** and **2g**, thereby giving trisubstituted alkenes **3f** and **3g** in high yields.



In conclusion, $[(C_6H_5)_3C]^+[B(C_6F_5)_4]^-$ effectively catalyzes the addition of the alkylzirconium species to alkynes. This method has a fair generality for the introduction of an alkyl group to alkynes, and further studies to extend the scope of this reaction are in progress.

*Typical procedure is described for the reaction of 1-hexene and **2a***: To $Cp_2Zr(H)Cl$ (196 mg, 0.760 mmol)[10] at 25 °C was added 1-hexene (54.7 mg, 0.650 mmol) in CH_2Cl_2 (2.4 mL), and the mixture was stirred at 40 °C for 1 h. The resulting yellow solution was cooled to 0 °C, to which was added **2a** (61.1 mg, 0.377 mmol) in CH_2Cl_2 (2.3 mL) followed by $[(C_6H_5)_3C]^+[B(C_6F_5)_4]^-$ (17.5 mg, 19.0 μmol). After stirred for 0.5 h at 40 °C, the reaction was stopped by adding MeOH (0.5 mL) and sat. $NaHCO_3$ aq. (0.5 mL), diluted with Et_2O, and anhyd. Na_2SO_4 was added. After filtration through a SiO_2/Celite pad and evaporation, purification on preparative TLC (hexane/acetone = 4/1) gave the product (85.4 mg, 95%, **3a**:**4a** = 91:9).

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References and Notes

1. (a) Negishi, E. *Chem. Eur. J.* **1999**, *5*, 411. (b) Knochel, P. In *Comprehensive Organic Synthesis*, Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, **1991**; Vol. 4, p 865. (c) Oppolzer, W. *ibid.* Vol. 5, p 29. (d) Negishi, E.; Takahashi, T. *Synthesis* **1988**, 1. (e) Negishi, E. *Acc. Chem. Res.* **1987**, *20*, 65. (f) Zweifel, G.; Miller, J. A. *Org. React.* **1984**, *32*, 375. (g) Normant, J.-F.; Alexakis, A. *Synthesis* **1981**, 841.
2. (a) Negishi, E.; Kondakov, D. Y.; Choueiry, D.; Kasai, K.; Takahashi, T. *J. Am. Chem. Soc.* **1996**, *118*, 9577. (b) Van Horn, D. E.; Negishi, E. *ibid.* **1978**, *100*, 2252. See also Wipf, P.; Lim, S. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1068.
3. (a) Yamanoi, S.; Matsumoto, T.; Suzuki, K. *Tetrahedron Lett.* **1999**, *40*, 2793. (b) Yamanoi, S.; Matsumoto, T.; Suzuki, K. *ibid.* **1998**, *39*, 9727. (c) Yamanoi, S.; Imai, T.; Matsumoto, T.; Suzuki, K. *ibid.* **1997**, *38*, 3031. (correction) *ibid.* **1997**, *38*, 5573. See also Suzuki, K.; Imai, T.; Yamanoi, S.; Chino, M.; Matsumoto, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2469.
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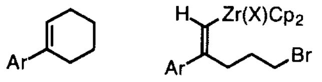
5. Schwartz, J.; Labinger, J. A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 333.
6. Identification of the minor isomers is based on the GC comparison with the authentic samples. All new compounds were fully characterized by spectroscopic means and combustion analysis/HRMS.
7. Dialuminoxanes work effectively for the *allyl*zirconation (Yamanoi, S.; Matsumoto, T.; Suzuki, K., the Annual Meeting of the Chemical Society of Japan, **1997**, 1G2 34). See also Hanawa, H.; Abe, N.; Maruoka, K. *Tetrahedron Lett.* **1999**, *40*, 5365.
8. Considering the fact that $(C_6H_5)_3CH$ was obtained after the reaction, we assume that the active catalyst is the cationic zirconocene $[Cp_2(Cl)Zr]^+[B(C_6F_5)_4]^-$, generated by the reaction of $[(C_6H_5)_3C]^+[B(C_6F_5)_4]^-$ with the alkylzirconocene or the unreacted $Cp_2Zr(H)Cl$. See ref. 4.
9. When the reaction of **1f** was carried out at 25 °C, cyclization product **6** was obtained in 44% yield, presumably by the intramolecular substitution of the intermediate **7**. A sizable amount of unidentified products were also obtained.



6 **7** Ar = 3,4-dimethoxyphenyl

10. Buchwald, S. L.; LaMaire, S. J.; Nielsen, R. B.; Watson, B. T.; King, S. M. *Org. Synth.* **1992**, *71*, 77.