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An Efficient Protocol of Iridium-Catalyzed Allylic Substitution Reaction and Its Application to Polymer Synthesis: Complementary Regio- and Stereoselective Allylation Polycondensation via Ir and Pd Catalyses

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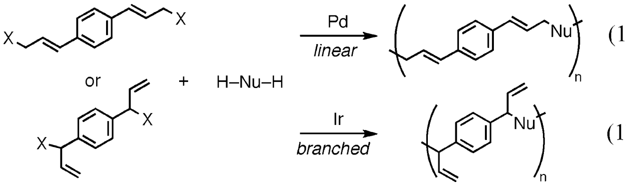
The development of regio- and stereoselective polymerizations continues to be an important topic[1] because these selectivities are fundamental elements that determine the properties of a polymeric material. For the synthesis of polymers whose main chains consist of only C−C bonds, vinyl polymerizations have arguably dominated[2] the polymeric materials in our daily life. However, there are crucial drawbacks in the vinyl polymerizations, for example, a limitation of only two carbons as the repeating unit in the main chain and loss of the double bond in every monomer. Under such circumstances, a regioselective C−C bond-forming allylation polycondensation via the Tsuji−Trost reaction[3] (TTR) was developed[4,5] (eq 1a), and a Pd-catalyzed polycondensation that proceeds without strict stoichiometric balance was realized in certain cases.[6] A characteristic of this polycondensation is that a new C−C bond is formed between the sp^3-hybridized carbons (Csp^3's) of the monomers without losing the double bond of the allylic monomer. Although transition metal-catalyzed allylation reactions[7,8] whose major products are not easily accessible via the TTR have been reported,[9−12] they have not been applied in polymer synthesis. This is due to the severe limitations of the polycondensation reaction.[13] We now report an efficient protocol of the Ir-catalyzed allylic substitution reaction, which we may call the "Takeuchi reaction",[12] and its applications in polymer synthesis[14] (eq 1b). This Ir-catalyzed regio- and stereoselective polycondensation can fill in some of the methodological gaps of the polymerization via the TTR.

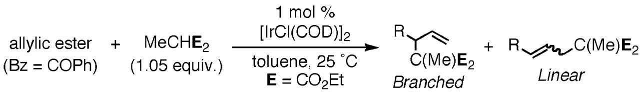


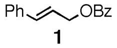
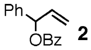
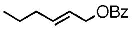
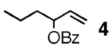
(1a)

(1b)

In spite of extensive studies of the Ir-catalyzed allylic substitution reaction,[12] the quantitative formation of quaternary (4°-) carbon centers with a branched selectivity by the Ir catalysis has been hardly studied.[15] *N*,*O*-Bis(trimethylsilyl)acetamide[16] (BSA) has rarely been utilized in the Ir-catalyzed C−C bond-forming allylic substitution reaction,[17,18] although it is an excellent reagent in the TTR[3] and the polycondensation via the TTR.[4] No reaction occurred between cinnamyl acetate and commercially available diethyl methylmalonate ($MeCH\mathbf{E}_2$, $\mathbf{E} = CO_2Et$) in CH_2Cl_2 similar to the conditions of the Pd system.[5a] By examination of the reaction conditions, non-halogenated solvents such as toluene and THF were suitable, and a catalytic amount of $n\text{Bu}_4\text{NF}$ (TBAF) (10 mol %) smoothly promoted the reaction. The scope is presented in Table 1. Nearly 1 equiv of $MeCH\mathbf{E}_2$ (1.05 equiv) was sufficient to complete the reaction in a short time, and the products with a 4°-carbon were obtained in excellent yields. Cinnamyl benzoate **1** was superior to the corresponding acetate ester (99% yield, $B/L = 86/14$) regarding the regioselectivity (entry 1). The addition of $P(OPh)_3$ improved the branched regioselectivity as expected[12a,c,e] (entry 2). To our surprise, PPh_3 was superior to $P(OPh)_3$ based on the regioselectivity (entry 3). As far as we know, this is the first Ir-catalyzed allylic substitution reaction system where PPh_3 showed a higher branched regioselectivity than $P(OPh)_3$. Branched substrate **2** also selectively afforded the branched product (entries 4 and 5). On the other hand, linear alkyl-substituted **3** selectively gave a linear product (entry 6). In contrast, branched **4**, which was an allylic isomer of **3**, selectively afforded the branched product (entries 7 and 8). For this electrophile, PPh_3 slightly decreased the regioselectivity.

Table 1. Ir-Catalyzed Regioselective Allylic Substitution Reaction[a]



entry	allylic ester	additive[b]	time, h	yield,[c] %	*B*/*L* ratio[d] (*E*/*Z*)[d]
1	 **1**	–	4	98	90/10 (10/0)
2		$P(OPh)_3$	4	95	92/ 8 (8/0)
3		PPh_3	4	99	95/ 5 (5/0)
4	 **2**	–	6[e]	97	95/ 5 (4/1)
5		PPh_3	6	97	92/ 8 (4/4)
6	 **3**	–	2	98	10/90 (–)[f]
7	 **4**	–	4	95	79/21 (–)[f]
8		PPh_3	6	98	69/31 (–)[f]

[a] Reaction conditions: allylic ester, 0.50 mmol; $MeCH(CO_2Et)_2$, 90 μL (0.52 mmol), $[IrCl(COD)]_2$, 3.3 mg (4.9 μmol); 1 M $n\text{Bu}_4\text{NF}$ in THF, 0.050 mL (0.050 mmol); BSA, 0.37 mL (1.5 mmol); toluene, 1.0 mL. [b] 2 mol %. [c] Isolated yield after column chromatography. [d] The branched/linear (*B*/*L*) ratio of the products and the *E*/*Z* ratio (%) of the linear product were determined by GC. [e] Allylic substrate **2** remained after 4 h (7% by ^{1}H NMR). [f] The *Z*-isomer was not detectable/separable by GC.

This efficient protocol synthesizing the branched products was applicable to the regio- and stereoselective Csp^3-Csp^3 bond-forming polycondensation. Table 2 illustrates the complementary regio- and stereoselective polycondensations catalyzed by Ir and Pd. In the absence of ligands, precipitation due to metal aggregation was observed when the reaction time increased, so that PPh_3 as a ligand was added to the Ir-catalyzed allylation polycondensation reaction to keep the reaction homogeneous. Electrophile **5** and nucleophile **6** afforded branched and linear polymers when using the Ir and Pd catalysts, respectively (entry 1). Electrophile **7** produced results consistent with those of its allylic isomer **5** (entry 2). The branched electrophile **8**, in which two branched allylic moieties were connected to a trimethylene group, also gave the expected branched and linear polymers using each catalyst (entry 3). The regioselectivity of the Ir catalyst

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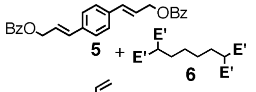
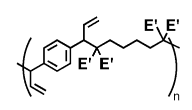
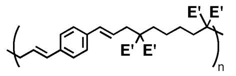
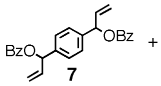
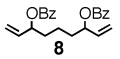
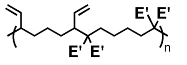
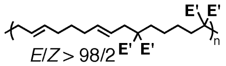
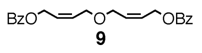
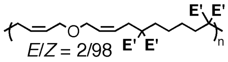
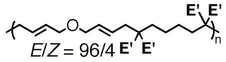
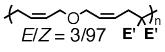
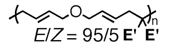
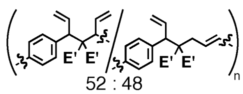
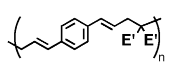
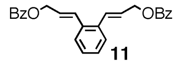
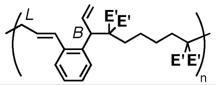
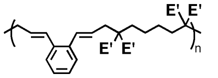
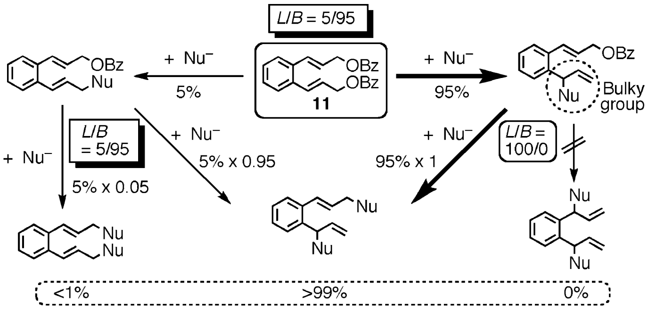
Table 2. Complementary Regio- and Stereoselective Ir- and Pd-Catalyzed Allylation Polycondensation[a]

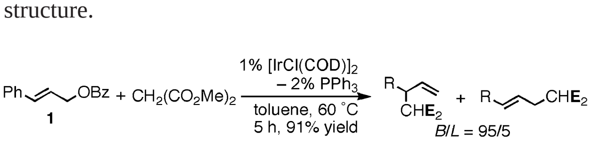
entry	monomers (**E'** = CO_2Me)	major structure(s) by Ir	time, h	B/L^b	M_n^c $(M_w/M_n)^c$ yield,[d] %	major structure by Pd	time, h	B/L^b	M_n^c $(M_w/M_n)^c$ yield,[d] %
1			6	95/ 5	43,000 (1.5_7) 90		72	6/94	29,600 (1.6_0) 92
2	 + **6**		8	94/ 6	15,000 (1.5_0) 89		11[e]	8/92	10,300 (1.4_2) 93
3	 + **6**		72	91/ 9	14,600 (1.5_6) 93		72	<1/99	11,200 (1.4_2) 84
4	 + **6**		6	6/94	23,500 (1.5_0) 90		24	2/98	17,400 (1.5_0) 91
5	**9** + $CH_2E'_2$ **10**		48[f]	4/96	10,600 (1.4_6) 94		24	2/98	16,000 (1.5_3) 96
6	**5** + **10**		6[f]	76/24	28,400 (1.5_0) 88		6	4/96	43,100 (1.7_0) 99
7	 + **6**		10 days[g]	49/51	20,300 (1.6_9) 92		6	<1/99	24,200 (1.5_6) 99

[a] Polymerization conditions unless otherwise noted: allylic substrate, 0.50 mmol; nucleophile, 0.50 mmol; catalyst 5 μmol; PPh_3 for Ir catalyst or bis(diphenylphosphino)butane for Pd catalyst, 10 μmol); BSA, 3.0 mmol; toluene (Ir) or CH_2Cl_2 (Pd), 1.0 mL; 25 °C for Ir catalyst or 40 °C for Pd catalyst. nBu$_4$NF (1 M in THF, 50 μL, 50 μmol) was added to the Ir system. The polymerization was traced by SEC analysis of the crude reaction mixture. [b] The branched/linear ratio by ^{1}H NMR. [c] M_n, number-average molecular weight of the crude product by size-exclusion chromatography (SEC, polystyrene standards, $CHCl_3$, 40 °C); M_w/M_n, polydispersity index of the crude product by SEC. All of the values of M_n and M_w/M_n were consistent after purification. [d] Purified by gel filtration (Sephadex LH-60, MeOH/$CHCl_3$ = 2/1). [e] Data using a corresponding acetate as an electrophile (**E'** = CO_2Et); see ref 5a. [f] Reaction temp, 60 °C. [g] The polymerization time was not optimized.

(B/L = 91/9) was higher than the one in the model reaction (entry 8, Table 1), and it may be caused by intramolecular coordination of the vinyl group to the Ir catalyst.[19] The stereoselectivity of the polymer using the Pd catalyst was high, and no Z-olefin was detected by ^{1}H NMR. The polycondensation between **9** and **6** using the Ir catalyst proceeded in a regio- and stereoselective manner, and a linear Z-selective polyether was obtained without any problems in the presence of an etheral oxygen atom close to the reaction sites (entry 4, Ir). On the other hand, the polycondensation using the Pd catalyst afforded a linear E-selective polyether (entry 4, Pd). Both the Ir and Pd catalysts showed a linear regioselectivity toward the Z-electrophile, and the E/Z stereoselectivity was complementary. Simple $CH_2(CO_2Me)_2$ (**10**) also worked as a monomer, and a corresponding polyether was obtained (entry 5). The polycondensation of **5** with **10** using the Ir catalyst produced a rather lower regioselectivity (B/L = 76/24, entry 6, Ir), which was expected due to formation of the extremely congested 3°−4°−3°-carbon linkages by a doubly branched regioselectivity. On the basis of the model reactions of **1**−$CH_2(CO_2Me)_2$ (eq 2) and entry 3 in Table 1, less than 1% (5% × 0.05) of the linear−linear linkage was formed. Hence, the B/L ratio (B/L = 76/24) indicated that the ratio of $B,B/B,L$ repeating units was 52/48. Although we were surprised at the 52% formation of this congested linkage, it was also notable that nearly half of the polymer linkages (48%) were branched−linear on each nucleophile (entry 6, Ir). The Pd-catalyzed polycondensation gave the corresponding linear polymer with a high regioselectivity (entry 6, Pd). An interesting dual regioselectivity on each electrophile was achieved by the Ir catalyst (entry 7, Ir). The dramatic effects of the *ortho*-substituents were observed on electrophile **11**, and the polycondensation of **11** with **6** was slow at 25 °C. Although the obtained polymer surprisingly appeared to show no regioselectivity, the model reaction of eq 3 provided us with information about a regular repeating unit of the polymer structure.

Scheme 1. A Dual Regioselectivity on Electrophile **11**





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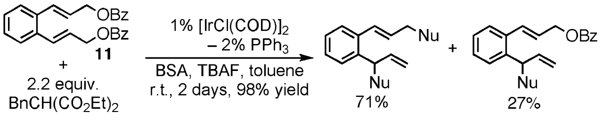
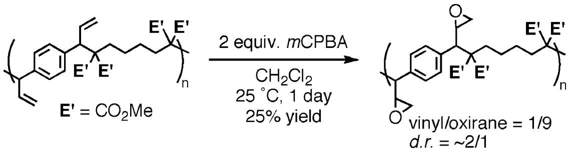


(3)

In eq 3, only a trace amount of the linear−linear product (<1%) and no branched−branched product were detected in the crude reaction mixture by ^{1}H NMR, and two products were isolated in high yields. The regioselectivity of eq 3 is explained as shown in Scheme 1. The first allylation of **11** preferentially occurred with the branched regioselectivity on the basis of entry 3 of Table 1. The second allylation then occurred with an exclusive linear selectivity because the branched−branched product was not detected in eq 3. When the linear product was afforded by the first allylation, the second reaction showed the branched regioselectivity due to the lack of the bulky malonic ester around the second reaction site. After all, branched−linear regioselectivity (>99%) was achieved on each electrophile. Therefore, we concluded that the regular polymer with a branched−linear regioselectivity on each electrophile was obtained by a single Ir catalyst. The *ortho*-substitution also brought the effects on the regioselectivity by Pd catalysis. The polymer via the TTR had a highly linear−linear structure as the repeating unit ($B/L < 1/99$, entry 7, Pd). Since the regioselectivity of the polymerization between **5** and **6** was $B/L = 6/94$ (entry 1, Pd), the exclusive regioselectivity in the polycondensation should also come from the effects of the *ortho*-substitution.

The vinyl groups[20] of the polymer can be functionalized. As an example, the polymer synthesized in entry 1 of Table 2, Ir, was reacted with *m*-chloroperbenzoic acid (*m*CPBA, 2 equiv to the olefin). Although an efficient purification method is still under investigation, the vinyl groups were converted into the oxirane groups (vinyl/oxirane = 1/9, eq 4).[21]



(4)

In conclusion, we reported the efficient protocol of the Ir-catalyzed allylic substitution reaction to form a 4°-carbon with a branched regioselectivity. The high efficiency was documented by applications to polycondensation, in which a nearly complete conversion of the functional groups under a strict stoichiometric balance is generally required. Various polymer structures from the same monomers can now be arranged using either the Ir or Pd catalyst. Further studies of other monomers and the obtained polymer properties are now in progress.

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Supporting Information Available: Experimental procedures, NMR data (^{1}H and ^{13}C) of polymers by the Ir catalyst, and functionalization of the polymer with *m*CPBA. This material is available free of charge via the Internet at http://pubs.acs.org.

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