Versatile Carbon−Carbon Bond-Forming Polycondensation between Terpene Derivatives and Malonic Esters via Palladium-Catalyzed Allylic Substitution Reaction

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The palladium-catalyzed allylic substitution reaction between allylic esters and malonic esters is a versatile carbon−carbon bond-forming reaction, which is well-known as the Tsuji−Trost reaction[1] (Scheme 1). Although there are some already known polymerizations including the partial process of this reaction,[2−4] the polymerization reaction via the typical Tsuji−Trost reaction has not been reported in polymer synthesis until recently[5] (eq 1). We believed that great diversity of the Tsuji−Trost reaction should be a potential methodology for designing functional polymers aimed at novel environmentally benign materials. Specifically, some of the ubiquitous natural terpene alcohols (Chart 1) could be utilized after simple derivatization. Only two polymers with relatively lower molecular weights ($M_n \leq 7600$), which were consisted of carbon−carbon bonds in the main chains, were reported,[5a] and hence establishment of the efficient polycondensation system between terpene derivatives and malonic esters has been highly desired. In this report, we optimized the polymerization conditions and succeeded in the general synthesis of some terpene-derived polymers with higher molecular weights. We also examined the functional group tolerance in the system, and the present polymerization conditions appeared compatible with various functional groups such as ether, amine, and even ester groups in the polymer main chains.

We first synthesized the bifunctional monomer **1** derived from geraniol (Table 1). An AB-type monomer such as **1** is suitable to elucidate the optimized conditions, for an accidental material imbalance in the two-component polycondensation determines the degree of polymerization without reflection of the polymerization conditions. The main chain of the polymer consisted of only C−C and C═C bonds, and cleavage of the main chain was not considered possible during the polymerization.[6] The polymerization reactions were catalyzed by 1 mol % $Pd_2(dba)_3$−2 mol % dppb in CH_2Cl_2 at 40 °C in the presence of *N*,*O*-bis(trimethylsilyl)acetamide (BSA) as a base. It was reported that the polymerization reaction of the acetate ester of the terpene alcohol derivative is sluggish under these conditions, while the carbonate **1a** was polymerized under the same conditions and the desired polymer was obtained in good yield[5a] (entry 1). The benzoate ester **1b** was superior to **1a** for the synthesis of the higher molecular weight polymer (entry 2). The *E*-stereochemistry of the monomer was retained in each case (^1H and ^{13}C NMR). To synthesize the polymer with a higher M_n, we screened some polar cosolvents to enhance the nucleophilicity of the malonate anion, and 1,3-dimethyl-2-imidazolidinone (DMI) appeared the most effective[7] (entry 3). The narrow polydispersity indices (PDIs) throughout the polymerization in entries 1−3 indicated that allylation under these conditions was not reversible and that C−C bond cleavage of the main chain did not occur. Monomer **2**, which is an allylic regioisomer of **1b**, gave the polymer with the same structure pattern as that from **1b** (entry 4). The higher M_n was obtained from the terminal olefinic substrate **2**, while stereoselectivity of the olefin was moderate ($E/Z = 8/1$). Under these optimal conditions, the scope of this polymerization was examined using various combinations of monomers. Monomer **3**, which was synthesized from citronellol, gave the desired polymer. The higher flexibility of **3**, compared with that of **2**, might have produced the higher M_n because it is well-known that the π-allylpalladium complexes are extremely sensitive to steric effects of both the nucleophilic and allylic moieties.[1] The two-component polycondensation between **4** and diethyl malonate (**5**) afforded the corresponding polyether **6** in high yield. The tetramethylene-linked dual malonate **7** was also a good nucleophile (entry 7). On the contrary, the rigid nucleophile **8** revealed the steric sensitivity of this catalysis, and only oligomerization occurred (entry 8). It is consistent with the results of entries 4 and 5. The ethereal monomer **9** derived from the hemiterpene prenyl alcohol showed an interesting reactivity (entries 9−11). The M_n's of the obtained polymers from **9** were higher than those from **4**, which indicated that the degrees of polymerization using **9** were apparently higher, especially when the nucleophile **8** was used (entry 11). Coordination of the oxygen atom in the appropriate position of **9** to the palladium center was likely to accelerate the coupling process. The tosylamide monomer **10** was also polymerized without any difficulty (entry 12). We then prepared the monomer **11** to synthesize the corresponding polyester. Since ester functional groups are easily cleaved under both acidic and basic conditions, it is a challenging topic to introduce ester functions into the polymer main chains via carbon−carbon bond formation.[3c] To our delight, the polymerization of **11** afforded the corresponding polyester **12** in the same procedure. On the basis of the

Scheme 1. Palladium-Catalyzed Allylic Substitution Reaction (Tsuji−Trost Reaction)

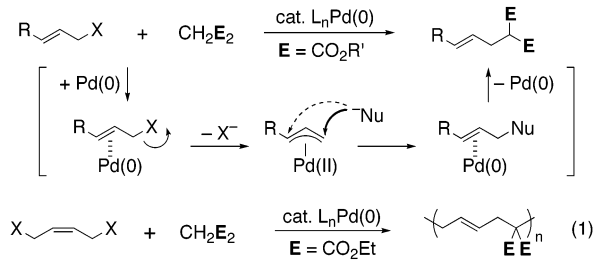

Chart 1. Some Ubiquitous Terpenes

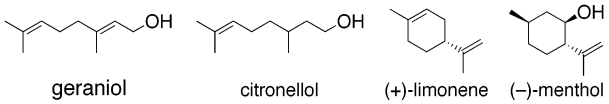

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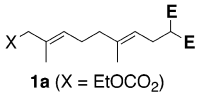
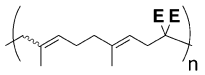
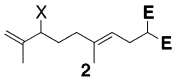
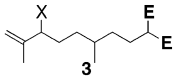
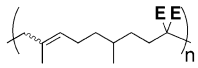
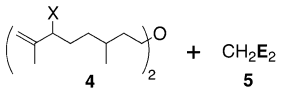
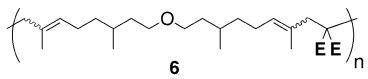
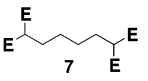
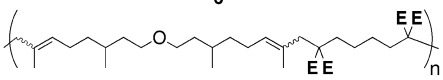
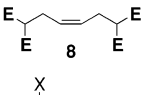
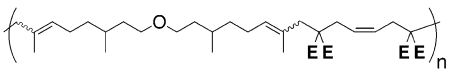
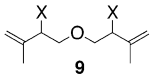
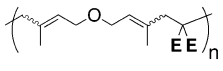
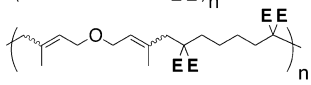
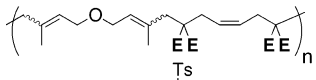
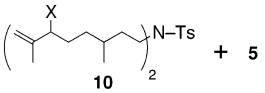
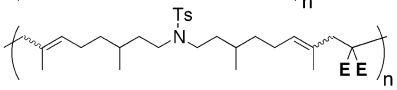
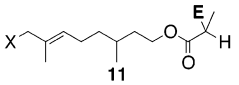
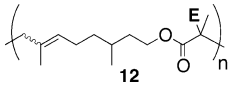
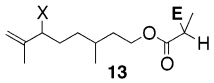
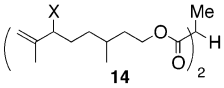
Table 1. Pd-Catalyzed Allylation Polycondensation between Terpene Derivatives and Malonic Esters[a] (E = CO_2Et)

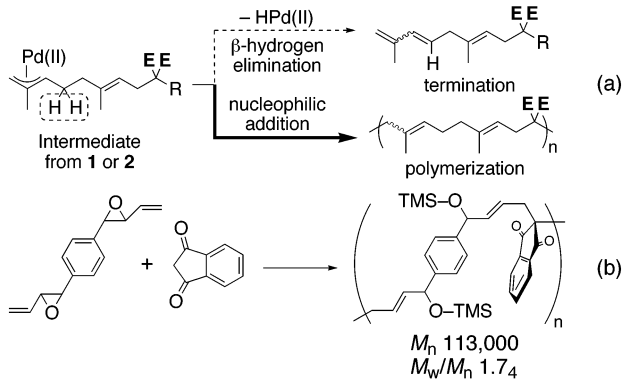
entry	monomer(s)	polymer	yield, %[b]	*E*/*Z*[c]	M_n x 10^{-3}	PDI[d]
1[e,f]	 **1a** (X = $EtOCO_2$)		98	≥20/1	7.6	1.4_6
2[e]	**1b** (X = $PhCO_2$)		95	≥20/1	11	1.6_1
3	**1b**		92	≥20/1	23	1.6_8
4	 **2**		86	8/1	34	1.5_9
5	 **3**		87	7/1	44	1.6_7
6	 **4** + CH_2E_2 **5**	 **6**	98	4/1	14	1.6_5
7	**4** +  **7**		93	10/1	25	1.5_6
8	**4** +  **8**		92	≥20/1	3.5	1.4_9
9	 **9** + **5**		98	5/1	27	1.6_1
10	**9** + **7**		98	8/1	30	1.5_8
11	**9** + **8**		91	10/1	15	1.7_3
12	 **10** + **5**		91	4/1	14	1.4_4
13	 **11**	 **12**	92	≥20/1	29	1.5_8
14	 **13**	**12**	94	4/1	36	1.6_6
15	 **14**	hyperbranched polyester	92	—[g]	14	1.7_4

[a] X = OCOPh unless otherwise noted. The polymerization conditions: each monomer, 0.50 mmol; CH_2Cl_2, 0.90 mL; DMI, 0.10 mL; $Pd_2(dba)_3$, 5.0 μmol (1.0 mol %); 1,4-bis(diphenylphosphino)butane (dppb), 10 μmol (2.0 mol %); BSA, 1.5 mmol (entries 1−5 and 13−15) or 3.0 mmol (entries 6−12); temperature, 40 °C. [b] Isolated yield. [c] By ^1H NMR. [d] Polydispersity index (M_w/M_n) by SEC. [e] Only CH_2Cl_2 (1.0 mL) was used as the solvent, and DMI was not added. [f] Reference 5a. [g] Not determined.

obtained M_n with the relatively small PDI in a high yield, no or scarce cleavage of the acyl−oxygen bonds in the main chains occurred during the polymerization and the workup procedure. Since few methodologies for functional polyesters have been reported in the literature,[8] this process is attractive for this purpose. Monomer **13**, which is the allylic regioisomer of **11**, led to the higher M_n, while the stereoselectivity was moderate as expected. Monomer **14**, which has two electrophilic sites and one nucleophilic site, was polymerized under the same conditions. The ^1H NMR spectrum indicated a relatively similar structure to that of **12**, while the ^{13}C NMR spectra suggested the hyperbranched structure based on the multiple peaks.

The π-allylpalladium intermediates in all entries of Table 1 have β-hydrogens, which easily cause the β-H−Pd(II) elimination[2,4] (Scheme 2a). In our system, however, such a side reaction was diminished to the undetectable level by ^1H and ^{13}C NMR analyses, and the polymerization reaction effectively proceeded as illustrated in Table 1. As a matter of fact, the present system is also applicable to the polyaddition reported

Scheme 2. β-H−Pd Elimination vs Nucleophilic Addition



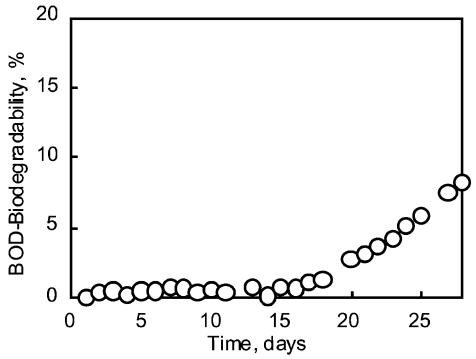


Figure 1. BOD measurements of polyether **6**.

by Koizumi and Endo, which suffered from β-H−Pd elimination.[4] Although incident β-H−Pd elimination terminated the polymerization in their conditions ($M_n \leq 9200$, PDI = 1.9_6), we obtained the desired polymer with a higher molecular weight as TMS ether under our optimal conditions[9] (Scheme 2b). Treatment of TMS ether with 1 N HCl(aq) in THF for desilylation afforded an insoluble material in common organic solvents because of higher molecular weight. The PDIs of the obtained polymers in Table 1 were relatively small considering the conventional polycondensations as well as the palladium-catalyzed polymerization via π-allylpalladium intermediates.[10]

All of the polymers obtained in Table 1 were amorphous.[11] This might be reasonable when thinking of natural rubber that consists of isoprene units. Because the polymers contain the terpene derivatives, we expected some of these polymers to be biodegradable. Biochemical oxygen demand (BOD) measurements on polyether **6** and polyester **12** were carried out in an activated sludge.[12] Polyether **6** showed a slow but apparent biodegradability that reached 8% after 28 days (Figure 1). To our surprise, polyester **12**, which we had expected to be readily biodegradable, was not degraded at all (0% after 28 days). The quaternary bulky α-carbons of the ester functional groups might have interfered with degradation.

We have reported the versatile carbon−carbon bond-forming polycondensation between terpene derivatives and malonic esters via the Tsuji−Trost reaction. The highly incident β-H−Pd elimination was diminished, and the relatively higher polymers were synthesized using various types of the monomers with some functional groups in the polymer main chains. The studies of biodegradation of the synthesized polymers and also asymmetric polymerization are now under investigation.

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Supporting Information Available: Experimental procedures, preparation of monomers, and spectroscopic data (^{1}H and ^{13}C NMR) of polymers in Table 1. This material is available free of charge via the Internet at http://pub.acs.org.

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(1) Reviews: (a) Tsuji, J. In *Palladium Reagents and Catalysts, Innovations in Organic Synthesis*; John Wiley: New York, 1995; p 290. (b) Godleski, S. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Semmelhack, M. F., Eds.; Pergamon Press: Oxford, 1991; Vol. 4, p 585. (c) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395. (d) Frost, C. G.; Howarth, J.; Williams, J. M. J. *Tetrahedron: Asymmetry* **1992**, *3*, 1089.

(2) (a) Suzuki, M.; Sawada, S.; Saegusa, T. *Macromolecules* **1989**, *22*, 1505. (b) Suzuki, M.; Sawada, S.; Yoshida, S.; Eberhardt, A.; Saegusa, T. *Macromolecules* **1993**, *26*, 4748.

(3) (a) Miyaki, N.; Tomita, I.; Endo, T. *Macromolecules* **1996**, *29*, 6685. (b) Miyaki, N.; Tomita, I.; Endo, T. *J. Polym. Sci., Part A: Polym. Chem.* **1997**, *35*, 1211. (c) Miyaki, N.; Tomita, I.; Endo, T. *J. Polym. Sci., Part A: Polym. Chem.* **1997**, *35*, 2097. (d) Miyaki, N.; Tomita, I.; Endo, T. *Chem. Lett.* **1997**, 685. (e) Miyaki, N.; Tomita, I.; Kido, J.; Endo, T. *Macromolecules* **1997**, *30*, 4504.

(4) After our preliminary report,[5a] another type of palladium-catalyzed polymerization via π-allylpalladium intermediates was reported: (a) Koizumi, T.; Sakamoto, J.; Gondo, Y.; Endo, T. *Macromolecules* **2000**, *33*, 7235. (b) Koizumi, T.; Sakamoto, J.; Gondo, Y.; Endo, T. *Macromolecules* **2002**, *35*, 2898. (c) Koizumi, T.; Sakamoto, J.; Gondo, Y.; Endo, T. *J. Polym. Sci., Part A: Polym. Chem.* **2002**, *40*, 2487.

(5) (a) Nomura, N.; Tsurugi, K.; Okada, M. *J. Am. Chem. Soc.* **1999**, *121*, 7268. (b) Nomura, N.; Tsurugi, K.; Okada, M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1932. (c) Tsurugi, K.; Nomura, N.; Aoi, K. *Tetrahedron Lett.* **2002**, *43*, 469.

(6) Since reversible ionization of the Tsuji−Trost reaction has been reported, the cleavage of C−C bonds during polymerization could not be ruled out at this stage: Amatore, C.; Gamez, S.; Jutand, A.; Meyer, G.; Moreno-Mañas, M.; Morral, L.; Pleixats, R. *Chem.—Eur. J.* **2000**, *6*, 3372.

(7) Ten percent of the other following cosolvents were examined: THF, DMF, DMSO, and HMPA. These cosolvents might have participated in the catalysis somehow, not only as a polar cosolvent.

(8) A review: Stridsberg, K. M.; Ryner, M.; Albertsson, A.-C. *Adv. Polym. Sci.* **2002**, *157*, 41.

(9) We believe that BSA as a weak and soft base must play an important role in diminished β-H−Pd elimination. The β-H-Pd elimination promoted by the strong base such as DBU and ^{i}Bu$_3$N has been reported: (a) Andersson, P. G.; Schab, S. *Organometallics* **1995**, *14*, 1. See also: (b) Takacs, J. M.; Lawson, E. C.; Clement, F. *J. Am. Chem. Soc.* **1997**, *119*, 5956. The further mechanistic discussions about BSA and β-H−Pd elimination will be made with additional experiments in a future article.

(10) The palladium-catalyzed polyaddition via π-allylpalladium intermediates using bifunctional vinyloxiranes was reported, where the PDIs were quite large (2.5_7−5.3_8) once the M_n's got over 10 000; see ref 4c.

(11) Some T_g's: poly[(1*E*,5*E*)-8,8-bis(ethoxycarbonyl)-1,5-dimethylnona-1,5-dienylene] (entry 3), −16.5 °C; poly{oxy-[(2*E*,7*E*)-5,5-bis(ethoxycarbonyl)-3,7-dimethylnona-2,7-dienylene]} (entry 9), −3.2 °C; poly{(*p*-toluenesulfonylimino-[(6*E*,11*E*)-9,9-bis(ethoxycarbonyl)-3,7,11,15-tetramethylheptadeca-6,11-dienylene]) (entry 12), −23.0 °C; poly{oxy[(*E*)-2-ethoxycarbonyl-2,4,8-trimethyl-1-oxodec-4-enylene]} (**12**, entry 14), not detected.

(12) An activated sludge was prepared so that the suspension concentration was 30 mg/L according to the Japan Industrial Standard JIS K 6950. The data were obtained by the average of three samples.

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