Palladium-Catalyzed Regioselective [3 + 2] Cycloaddition of Vinylic Oxiranes with Activated Olefins. A Facile Synthesis of Tetrahydrofuran Derivatives

Jae-Goo Shim and Yoshinori Yamamoto*

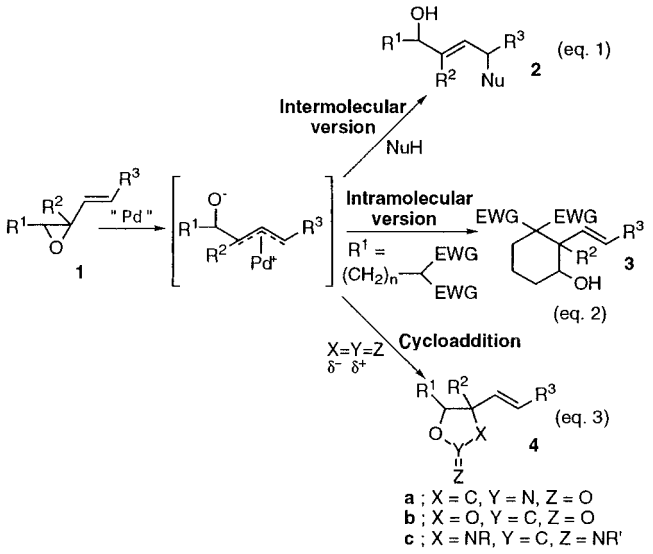
Department of Chemistry, Graduate School of Science, Tohoku University, Sendai 980-77, Japan

Received December 31, 1997

The reaction of certain activated olefins (Michael acceptors) **5** with vinylic oxiranes **1** in the presence of catalytic amounts of $Pd(PPh_3)_4$ (5 mol %) in THF at 40 °C gave the corresponding [3 + 2] cycloaddition products **6**. In all cases the reactions proceeded in regioselective manner, affording the corresponding polysubstituted tetrahydrofuran derivatives. The nature of electron-withdrawing group in activated olefins affected significantly the reactivity of substrates. Michael acceptors having sterically less bulky electron-withdrawing groups were essential for the cycloaddition reaction, and the presence of two electron-withdrawing groups at the α-position was needed. Accordingly, activated olefins having (CN, CN), (CN, CO_2Et), (CN, SO_2Ph), (Meldrum's type), and (SO_2Ph, SO_2Ph) could be used as a Michael acceptor. The present reaction provides a new method for the synthesis of tetrahydrofuran derivatives from vinylic oxiranes and Michael acceptors.

Introduction

It is well-known that palladium-catalyzed reaction of vinylic oxiranes **1** with nucleophiles (Nu^-) produces allylic alcohols **2** via a π-allylpalladium intermediate; 1,4-addition of Nu^- to vinylic oxiranes **1** takes place under neutral conditions (eq 1).[1−3] Stable carbon pronucleophiles, such as $CH_2(CO_2Et)_2$, $CH_2(CO_2Me)(COCH_3)$, $CH_2(COPh)(CO_2H)$, and $CH_2(CO_2R)(SO_2Tol)$, are used as a NuH,[4−6] giving the corresponding carbon chain elongated allylic alcohols in good yields. Organometallic compounds such as organostannanes ($PhSnR_3$) and vinylboronates ($CH_2{=}CHBR_2$) can be utilized also as a carbon nucleophile; phenyl and vinyl groups are introduced as a Nu^-, respectively.[7,8] Furthermore, heteroatom nucleophiles such as N_3^-, RO^-, ArO^-, $RCOO^-$, and R_2N^- may be introduced as a Nu^-, by using NaN_3, ROH, ArOAc, $(RCO)_2O$, and R_2NH, respectively, as a substrate.[9−11] Finally, even a hydride (H^-) introduction is possible by the use of HCO_2H.[12] A much more useful extension of this vinyl epoxide-based transformation is its intramolecular version; when a pronucleophile [−CH-$(SO_2Ph)_2$] is involved in the carbon chain R^1, the intramolecular attack of the nucleophile to the π-allylpalladium takes place, giving the corresponding carbocycles **3** (eq 2).[13]



On the other hand, the palladium-catalyzed cycloaddition of vinylic oxiranes to unsaturated compounds X=Y=Z is less common (eq 2).[14−18] Heterocumulenes such as N=C=O, O=C=O, and N=C=N have been used

(1) (a) Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons: Chichester, 1995; p 325. (b) Trost, B. M.; Molander, G. A. *J. Am. Chem. Soc.* **1981**, *103*, 5969. (c) Trost, B. M.; Luengo, J. I. *J. Am. Chem. Soc.* **1988**, *110*, 8239.

(2) Deardorff, D. R.; Shambayati, S.; Linde, R. G., II; Dunn, M. M. *J. Org. Chem.* **1988**, *53*, 189.

(3) (a) Trost, B. M.; Chen, S.-F. *J. Am. Chem. Soc.* **1986**, *108*, 6053. (b) Trost, B. M.; Scanlan, T. S. *Tetrahedron Lett.* **1986**, *27*, 4141.

(4) Tsuji, J.; Kataoka, H.; Kobayashi. Y. *Tetrahedron Lett.* **1981**, *22*, 2575.

(5) Takahashi, T.; Ootake, A.; Tsuji, J. *Tetrahedron Lett.* **1984**, *25*, 1921; *Tetrahedron* **1985**, *41*, 5747.

(6) (a) Takahashi, T.; Kataoka, H.; Tsuji, J. *J. Am. Chem. Soc.* **1983**, *105*, 147. (b) Takahashi, T.; Miyazawa, M.; Ueno, H.; Tsuji, J. *Tetrahedron Lett.* **1986**, *27*, 3881.

(7) Echavarren, A. M.; Tueting, D. R.; Stille, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 4039; *Tetrahedron* **1989**, *45*, 979.

(8) Miyaura, N.; Tanabe, Y.; Suginome, H.; Suzuki, A. *J. Organomet. Chem.* **1982**, *233*, C13.

(9) Tenaglia, A.; Waegell, B. *Tetrahedron Lett.* **1988**, *29*, 4851.

(10) (a) Trost. B. M.; Kuo, G. H.; Benneche, T. *J. Am. Chem. Soc.* **1988**, *110*, 621. (b) Peel, M. R.; Sternbach, D. D.; Johnson, M. R. *J. Org. Chem.* **1991**, *56*, 4990.

(11) Deardorff, D. R.; Myles, D. C.; MacFerrin, K. D. *Tetrahedron Lett.* **1985**, *26*, 5615.

(12) (a) Shimizu, I.; Oshima, M.; Nisar, M.; Tsuji, J. *Chem. Lett.* **1986**, 1775. (b) Oshima, M.; Yamazaki, H.; Shimizu, I.; Tsuji, J. *J. Am. Chem. Soc.* **1989**, *111*, 6280.

(13) Trost, B. M.; Vos, B. A.; Brezezowski, C. M.; Martina, D. P. *Tetrahedron Lett.* **1992**, *33*, 717.

(14) Trost, B. M.; Angle, S. R. *J. Am. Chem. Soc.* **1985**, *107*, 6123.

(15) Trost, B. M.; Sudhakar, A. R. *J. Am. Chem. Soc.* **1987**, *109*, 3792.

(16) Suzuki. S.; Fugita, Y.; Kobayashi, Y.; Sato, F. *Tetrahedron Lett.* **1986**, *27*, 69.

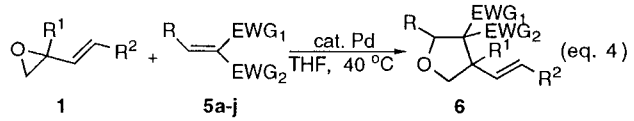
(17) Fujinami, T.; Suzuki, T.; Kamiya, M.; Fukuzawa, S.-I.; Sakai, S. *Chem. Lett.* **1985**, 199.

(18) Larksarp, C.; Alper, H. *J. Am. Chem. Soc.* **1997**, *119*, 3709.

S0022-3263(97)02317-7 CCC: $15.00
Published on Web 04/17/1998

as $X^{\delta-}=Y^{\delta+}=Z$. Isocyanates (RNC=O) gave oxazolidinones **4a**, carbon dioxide (O=C=O) afforded cyclic carbonates **4b**, and carbodiimide (RN=C=NR′) produced oxazolidinone derivatives **4c**. Accordingly, before we started the research in this area, only heterocumulenes and aldehydes had been used as a partner of the cycloaddition of vinyl oxiranes. It occurred to us that if a carbon−carbon double bond is utilized as the partner, five-membered cyclic ethers can be obtained from vinyl epoxides and that this type of cyclization would be more synthetically useful than the previously known heterocumulene addition (eq 3) since the tetrahydrofuran skeleton is frequently found in important natural products such as altholactone,[19] monensin,[20] and nonactin.[21] This simple extension has not been studied. It was rather curious to us that there were no prior reports of this transformation, unless previous trials were not successful. Actually, when we used simple Michael acceptors, such as $RCH=CHCO_2Et$ and $RCH=C(CO_2Et)_2$, or simple olefins and dienes, no cyclization products were obtained. Therefore, the desired tetrahydrofuran derivatives are not available by the use of ordinary nonpolar and/or polarized carbon−carbon double bonds. After a number of trials, we discovered that the use of more activated Michael acceptors having *sterically less bulky electron-withdrawing groups* is essential for the cyclization to occur.

Herein we wish to report that the palladium-catalyzed reaction of vinylic oxiranes **1** with certain Michael acceptors **5**, possessing sterically less demanding electron-withdrawing groups, gives the products of [3 + 2] cycloaddition, tetrahydrofuran derivatives **6**, in good to excellent yields (eq 4).[22]



1 **5a-j** **6**

a = $R^1 = R^2 = H$
b = $R^1 = CH_3$, $R^2 = H$
c = $R^1 = H$, $R^2 = Ph$

Results and Discussion

The reaction of benzylidene malononitrile (**5a**, 0.5 mmol) with 1,3-butadiene monoxide (**1a**, 1.2 equiv) in THF in the presence of $Pd(PPh_3)_4$ (5 mol %) at 40 °C was monitored by analytical TLC, and the starting material **5a** was consumed completely after 1 h. GLPC analysis of the reaction mixture revealed that 2-phenyl-3,3-dicyano-4-vinyltetrahydrofuran (**6a**) was produced in essentially quantitative yield. Purification with silica gel column chromatography using *n*-hexanes−ethyl acetate (15:1) as eluant gave **6a** in 90% yield (eq 4). The effect of solvents and catalysts upon the chemical yield was investigated (Table 1). The use of DMF, CH_3CN, and 1,4-dioxane gave **6a** in 86−88% yields (entries 2−4), while the use of *n*-hexane afforded **6a** in only 10% yield (entry 5). The use of $Pd(dba)_2$ as a catalyst, instead of $Pd(PPh_3)_4$, in THF gave a poor result (entry 6). Other catalyst systems, such as $Pd(dba)_2$−2DPPE and $Pd(dba)_2$−$4PPh_3$, were also tested (entries 7−8), but $Pd(PPh_3)_4$ was the best among the catalysts examined. Other catalysts, such as $Pd(OAc)_2$, $PdCl_2(PPh_3)_2$, $RhCl(PPh_3)_3$, and $RuCl_2(PPh_3)_3$, were totally ineffective. The [3 + 2] cycloaddition did not take place without Pd catalyst even after heating both substrates at 40 °C for a prolonged period of time. As we mentioned above, the use of benzylidene methylmalonate and benzylidene ethylmalonate instead of benzylidene malononitrile did not give the desired [3 + 2] cycloadducts at all under a variety of reaction conditions.

Table 1. Pd-Catalyzed [3 + 2] Cycloaddition of Benzylidene Malononitrile 5a with 1,3-Butadiene Monoxide 1a[a]

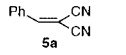
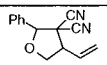
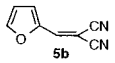
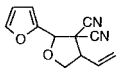
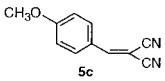
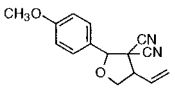
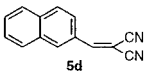
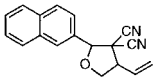
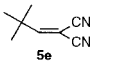
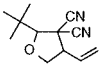
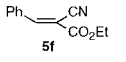
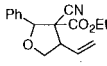
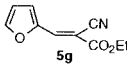
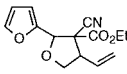
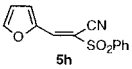
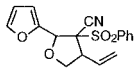
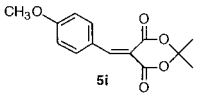
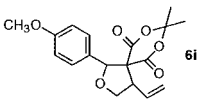
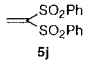
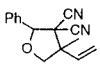
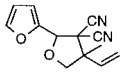
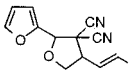
entry	catalyst	solvent	product	yield,[b] %
1	$Pd(PPh_3)_4$	THF	**6a**	>99 (90)[c]
2	$Pd(PPh_3)_4$	DMF	**6a**	87
3	$Pd(PPh_3)_4$	CH_3CN	**6a**	88
4	$Pd(PPh_3)_4$	1,4-dioxane	**6a**	86
5	$Pd(PPh_3)_4$	*n*-hexane	**6a**	10
6	$Pd(dba)_2$	THF	**6a**	17
7	$Pd(dba)_2$−2DPPE	THF	**6a**	84
8	$Pd(dba)_2$−$4PPh_3$	THF	**6a**	86

[a] All reactions were conducted at 40 °C for 1 h in the presence of 5 mol % of catalyst. [b] ^1H NMR yield. *p*-Xylene was used for an internal standard. [c] Isolated yield based on **5a**.

We next examined the effect of substituents at the β-position of activated olefins **5** on reactivity (Table 2). The activated olefins **5a**−**d** containing aryl and furyl substituents reacted effectively with vinyl oxirane **1a** to afford the five-membered O-heterocycles **6a**−**d**, respectively, in good to excellent yields (entries 1−4). Even activated olefin **5e** having a sterically bulky alkyl substituent afforded **6e** in good yield (entry 5). The effect of the electron-withdrawing groups of activated olefins was investigated. Under the same reaction conditions, activated olefins **5f**−**h** containing CN and CO_2Et or CN and SO_2Ph in place of two CN groups were converted smoothly to the corresponding five-membered O-heterocycles **6f**−**h**, respectively, in high yields (entries 6−8). In these cases, interestingly, only two stereoisomers were obtained, although there was a possibility that four diastereoisomers would be produced. Accordingly, one CN group among two electron-withdrawing groups is required to accomplish the cycloaddition reaction. One CN group was not sufficient to activate the double bond since β-cyanostyrene did not react with **1a** under the same reaction conditions as above. The reaction using Meldrum's acid derivative **5i** also proceeded well to give **6i** in moderate yield (entry 9). It should be noted that the corresponding diethylmalonate derivative did not give the desired tetrahydrofuran derivative at all, indicating that the steric bulkiness of electron-withdrawing groups is a key for the cycloaddition. In this regard, the substituent effects in the dienophile on the rate of cyclization of substrates via the intramolecular Diels−Alder reaction should be mentioned.[23] The reactivity of the dienophiles (C=CXY) was dependent upon the substituents (X, Y) and the order as follows: (CN, CN) > (CN, CO_2CH_3) ≫ (CO_2CH_3, CO_2CH_3). This order is very similar to the order of the present [3 + 2] cycloaddition.

(19) Gesson, J.-P.; Jacquesy, J.-C. *Tetrahedron Lett.* **1987**, *28*, 69.
(20) Collum, D. B.; McDonald, J. H.; Still, C. W., III *J. Am. Chem. Soc.* **1980**, *102*, 2117, 2118, 2120.
(21) Bartlett, P. A.; Meadows, J. D.; Ottow, E. *J. Am. Chem. Soc.* **1984**, *106*, 5304.
(22) Free radical mediated [3 + 2] addition of vinyl oxiranes with certain activated olefins was reported. Feldman, K. S.; Fisher, T. E. *Tetrahedron* **1989**, *45*, 2969.
(23) Boeckman, R. K., Jr.; Ko, S. S. *J. Am. Chem. Soc.* **1982**, *104*, 1033.

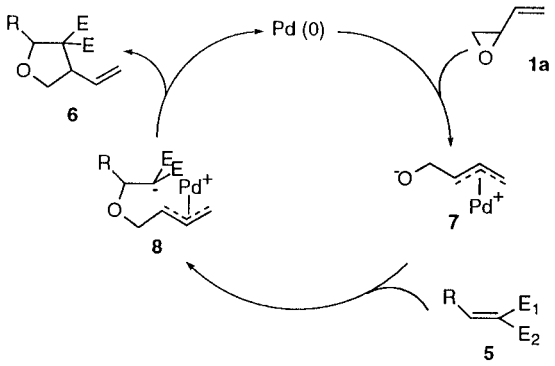
Table 2. Pd-Catalyzed [3 + 2] Cycloaddition of 5 with 1[a]

Entry	Michael acceptor 5	Vinylic oxirane 1	Product 6	Yield(%)[b]
1	 5a	1a	 6a	90 (56:44)[c]
2	 5b	1a	 6b	94 (55:45)[c]
3	 5c	1a	 6c	77 (61:39)[c]
4	 5d	1a	 6d	71 (51:49)[c]
5	 5e	1a	 6e	74 (54:46)[c]
6	 5f	1a	 6f	81 (64:36)[c]
7	 5g	1a	 6g	89 (66:34)[c]
8	 5h	1a	 6h	88 (72:28)[c]
9	 5i	1a	 6i	61 (55:45)[c]
10[d]	 5j	1a	 6j	47
11[e]	5a	1b	 6k	68 (55:45)[c]
12[f]	5a	1c	 6l	58 (52:48)[c]
13[g]	5b	1b	 6m	66 (68:32)[c]
14[h]	5b	1c	 6n	66 (55:45)[c]

[a] All reactions were conducted in THF at 40 °C for 1 h, except where otherwise indicated. [b] Isolated yields were based on **5**. [c] Diastereomeric ratios were indicated in parentheses. The stereochemistries of diastereoisomers were not determined since the selectivities were low. [d] The reaction was carried out in THF at 40 °C for 18 h. [e] 10 mol % of catalyst was used. The reaction was carried out for 30 h. [f] The reaction was carried out for 4 h. [g] The reaction was carried out for 1.5 days. [h] The reaction was carried out for 3 h.

Boeckman and Ko interpreted the effects on the rate of cyclization upon substitution of a cyano group by the concept of steric inhibition of resonance;[23] complete coplanarity of two esters is difficult due to the steric interactions, but cyano produces much less disruption of the ester overlap. The present observation can be explained by the same concept: the coplanarity can be maintained in the case of Meldrum's acid derivative (entry 9). The reaction of 1,1-bis(phenylsulfonyl)ethylene **5j** afforded **6j**, a tetrahydrofuran derivative unsubstituted at the position α to the oxygen atom, in moderate yield (entry 10). In all cases, seven-membered O-heterocycles were not obtained.

Scheme 1



Meanwhile, to understand the effect of substituents of vinylic oxiranes, we examined the reaction of substituted vinylic oxiranes **1b** and **1c**. Although the reaction of **1b** or **1c** was sluggish in comparison with that of **1a** (entries 11−14), presumably due to the steric congestion of a π-allylpalladium intermediate **7** (vide infra), the [3 + 2] cycloaddition products **6k**−**n** were obtained in acceptable to good yields.

The following mechanistic rationale may account for the present Pd-catalyzed regioselective [3 + 2] cycloaddition (Scheme 1). Initially, Pd(0) catalyst would add oxidatively to vinyl oxirane **1a** to give π-allylpalladium intermediate **7**. The Michael addition of the oxygen nucleophile of **7** to activated olefins **5** would produce **8**. Then the resulting intermediate **8** would undergo intramolecular nucleophilic attack on the inner π-allylic carbon atom to give cyclized products **6** and the Pd(0) species would be regenerated. A key point of the present [3 + 2] cycloaddition is the Michael addition of **7** to activated olefins. If an ordinary Michael acceptor such as β-cyanostyrene (substituted with a mono-electron-withdrawing group) was used, no cycloaddition took place; the use of the double substituted olefins **5** is essential.

Conclusions

In summary, we have developed a palladium-catalyzed regioselective [3 + 2] cycloaddition of certain activated olefins **5** with vinylic oxiranes **1**. The reaction proceeds under neutral conditions at 40 °C, the starting substrates are easily available, and therefore the present finding may provide a new and convenient procedure for the preparation of five-membered O-heterocycles.

Experimental Section

General Information. All solvents were purified and dried before use according to the standard procedure. Reactions were conducted under an argon atmosphere in oven-dried glassware. 1,3-Butadiene monoxide (**1a**) and 2-methyl-2-vinyloxirane (**1b**) were purchased from Aldrich Chemical Co. β-Styryloxirane (**1c**) was prepared according to the method described in the published paper.[24] The starting activated olefins (**5**) were prepared by the Knoevenagel condensation of the corresponding aldehydes with acidic methylenes. $Pd(PPh_3)_4$ was prepared according to the method described in the literature.[25] ^1H and ^{13}C NMR spectra were recorded on a JEOL LA-300 spectrometer. All chemical shifts (δ) were measured relative to tetramethylenesilane (TMS). Melting points were determined with a Yamato MP-21 and were

(24) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353.
(25) Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121.

uncorrected. High-resolution mass spectra (HRMS) were obtained on a JEOL HX-110 instrument.

General Procedure (2-Phenyl-3,3-dicyano-4-vinyltetrahydrofuran, 6a). To a solution of $Pd(PPh_3)_4$ (0.029 g, 5 mol %) and **5a** (0.077 g, 0.5 mmol) in THF (5.0 mL) was added vinyl oxirane **1a** (0.046 mL, 1.2 equiv) under an Ar atmosphere. The reaction mixture was stirred at 40 °C, and the reaction progress was monitored by TLC. When the starting substrate **5a** was consumed completely, the reaction mixture was filtered through a Celite short column using diethyl ether as eluent. After the usual workup, analytically pure product **6a** was isolated in 90% yield (0.101 g) by column chromatography on silica gel using *n*-hexanes−ethyl acetate (15:1) as eluant.

2-Phenyl-3,3-dicyano-4-vinyltetrahydrofuran (6a): HRMS calcd for $C_{14}H_{12}N_2O$ 224.0948, found 224.0942. Anal. Calcd: C, 74.981; H, 5.393; N, 12.491. Found: C, 74.735; H, 5.475; N, 12.142.

Major diastereoisomer: white solid: mp 56 °C; ^{1}H NMR ($CDCl_3$) δ 7.47 (m, 5H), 6.01−5.89 (m, 1H), 5.50 (m, 2H), 5.25 (s, 1H), 4.56 (dd, 1H, J = 9.5, 7.1 Hz), 3.96 (dd, 1H, J = 9.5, 7.1 Hz), 3.60 (q, 1H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$) δ 133.612, 130.100, 130.034, 128.907, 126.144, 123.199, 113.033, 112.589, 87.100, 71.917, 53.658, 47.366.

Minor diastereoisomer: colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.54 (m, 2H), 7.46 (m, 3H), 5.94 (m, 1H), 5.54 (m, 2H), 5.26 (s, 1H), 4.41 (t, 1H, J = 9.0 Hz), 4.15 (t, 1H, J = 9.2 Hz), 3.70 (q, 1H, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$) δ 132.872, 130.092, 129.368, 128.866, 126.144, 123.561, 113.017, 110.483, 86.993, 70.585, 54.653, 48.394.

2-(2-Furyl)-3,3-dicyano-4-vinyltetrahydrofuran (6b): HRMS calcd for $C_{12}H_{10}N_2O_2$ 214.0741, found 214.0744. Anal. Calcd: C, 67.281; H, 4.705; N, 13.077. Found: C, 66.977; H, 4.809; N,12.814.

Major diastereoisomer: colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.51 (m, 1H), 6.57 (d, 1H, J = 3.5 Hz), 6.44 (m, 1H), 5.91 (m, 1H), 5.54 (m, 2H), 5.48 (s, 1H), 4.48 (t, 1H, J = 8.2 Hz), 3.96 (t, 1H, J = 9.2 Hz), 3.78 (q, 1H, J = 8.3 Hz); ^{13}C NMR ($CDCl_3$) δ 147.528, 144.321, 128.726, 123.882, 112.441, 112.013, 111.183, 110.771, 81.063, 71.391, 52.819, 45.441.

Minor diastereoisomer: colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.52 (m, 1H), 6.67 (d, 1H, J = 3.5 Hz), 6.46 (dd, 1H, J = 3.3., 1.8 Hz), 5.92 (m, 1H), 5.53 (m, 2H), 5.30 (s, 1H), 4.34 (dd, 1H, J = 9.2, 8.4 Hz), 4.10 (t, 1H, J = 9.2 Hz), 3.64 (dd, 1H, J = 17.6, 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ 146.188, 144.164, 128.915, 123.808, 112.630, 110.829, 110.508, 81.548, 70.568, 54.439, 46.173.

2-(4-Methoxyphenyl)-3,3-dicyano-4-vinyltetrahydrofuran (6c): HRMS calcd for $C_{15}H_{14}N_2O_2$ 254.1054, found 254.1054. Anal. Calcd: C, 70.850; H, 5.549; N, 11.016. Found: C, 70.979; H, 5.625; N, 11.387.

Major diastereoisomer: colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.41 (d, 1H, J = 8.6 Hz), 6.97 (d, 1H, J = 8.6 Hz), 5.94 (m, 1H), 5.50 (m, 2H), 5.21 (s, 1H), 4.54 (m, 1H), 3.91 (m, 1H), 3.83 (s, 3H), 3.59 (dd, 1H, J = 15.7, 7.7 Hz); ^{13}C NMR ($CDCl_3$) δ 160.853, 130.240, 127.608, 125.477, 123.084, 114.300, 113.231, 112.680, 87.149, 71.853, 55.319, 53.633, 47.522.

Minor diastereoisomer: white solid; mp 82 °C; ^{1}H NMR ($CDCl_3$) δ 7.47 (m, 1H), 6.97 (m, 1H), 5.94 (m, 1H), 5.52 (m, 2H), 5.21 (s, 1H), 4.39 (t, 1H, J = 9.0 Hz), 4.13 (t, 1H, J = 9.2 Hz), 3.84 (s, 3H), 3.68 (dd, 1H, J = 17.6, 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ 160.943, 129.532, 127.616, 124.680, 123.405, 114.259, 113.107, 110.681, 87.034, 70.453, 55.319, 54.530, 48.542.

2-(2-Naphthyl)-3,3-dicyano-4-vinyltetrahydrofuran (6d): HRMS calcd for $C_{18}H_{14}N_2O$ 274.1105, found 274.1103. Anal. Calcd: C, 78.813; H, 5.144; N, 10.212. Found: C, 78.727; H, 5.298; N, 10.301.

Major diastereoisomer: colorless oil; ^{1}H NMR ($CDCl_3$) δ 8.03−7.86 (m, 4H), 7.64−7.50 (m, 3H), 6.02−5.90 (m, 1H), 5.53 (m, 2H), 5.42 (s, 1H), 4.45 (t, 1H, J = 9.1 Hz), 4.21 (t, 1H, J = 9.1 Hz), 3.75 (q, 1H, J = 8.8 Hz); ^{13}C NMR ($CDCl_3$) δ 134.081, 132.946, 130.314, 129.327, 128.858, 128.414, 127.838, 126.966, 126.678, 126.028, 123.602, 123.002, 113.115, 110.525, 87.158, 70.683, 54.743, 48.394.

Minor diastereoisomer: white solid; ^{1}H NMR ($CDCl_3$) δ 7.97−7.85 (m, 4H), 7.54 (m, 3H), 6.02−5.91 (m, 1H), 5.51 (m, 2H), 5.42 (s, 1H), 4.61 (dd, 1H, J = 9.5, 7.1 Hz), 4.00 (dd, 1H, J = 9.5, 7.7 Hz), 3.63 (dd, 1H, J = 15.8, 7.7 Hz); ^{13}C NMR ($CDCl_3$) δ 133.974, 132.913, 131.037, 130.026, 128.907, 128.356, 127.863, 126.983, 126.719, 125.963, 123.240, 123.043, 113.050, 112.671, 87.256, 71.975, 53.748, 47.325.

2-*tert*-Butyl-3,3-dicyano-4-vinyltetrahydrofuran (6e): HRMS calcd for $C_{12}H_{16}N_2O$ 204.1262, found 204.1263. Anal. Calcd: C, 70.559; H, 7.895; N, 13.714. Found: C, 70.460; H, 7.871; N, 13.363.

Major diastereoisomer: colorless oil; ^{1}H NMR ($CDCl_3$) δ 5.96−5.84 (m, 1H), 5.50 (m, 2H), 4.19 (m, 1H), 3.92 (m, 1H), 3.87 (s, 1H), 3.49 (m, 1H), 1.19 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 129.154, 123.577, 114.242, 112.063, 92.932, 69.869, 55.739, 41.419, 34.683, 26.376.

Minor diastereoisomer: colorless oil; ^{1}H NMR ($CDCl_3$) δ 5.93−5.81 (m, 1H), 5.47 (m, 2H), 4.29 (dd, 1H, J = 9.3, 6.9 Hz), 3.81 (s, 1H), 3.64 (t, 1H, J = 9.1 Hz), 3.38 (dd, 1H, J = 15.8, 8.8 Hz), 1.20 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 129.869, 123.125, 115.106, 113.699, 94.437, 71.062, 56.249, 40.950, 34.453, 25.965.

2-Phenyl-3-ethoxycarbonyl-3-cyano-4-vinyltetrahydrofuran (6f): inseparable mixture; colorless oil; HRMS calcd for $C_{16}H_{17}NO_3$ 271.1207, found 271.1200. Anal. Calcd: C, 70.831; H, 6.316; N, 5.163. Found: C, 70.300; H, 6.284; N, 5.169.

Major diastereoisomer: ^{1}H NMR ($CDCl_3$) δ 7.45−7.36 (m, 5H), 5.83−5.71 (m, 1H), 5.48 (s, 1H), 5.35−5.29 (m, 2H), 4.48 (m, 1H), 4.35−4.17 (m, 2H), 3.91 (m, 1H), 3.61 (m, 1H), 1.31−1.22 (m, 3H).

Minor diastereoisomer: ^{1}H NMR ($CDCl_3$) δ 7.45−7.36 (m, 5H), 6.00−5.88 (m, 1H), 5.35−5.29 (m, 2H), 5.25 (s, 1H), 4.36 (m, 1H), 4.35−4.17 (m, 2H), 4.11 (m, 1H), 3.77 (m, 1H), 1.31−1.22 (m, 3H).

2-(2-Furyl)-3-ethoxycarbonyl-3-cyano-4-vinyltetrahydrofuran (6g): HRMS calcd for $C_{14}H_{15}NO_4$ 261.1001, found 261.1006. Anal. Calcd: C, 64.358; H, 5.786; N, 5.361. Found: C, 63.899; H, 5.722; N, 5.343.

Major diastereoisomer: colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.47 (m, 1H), 6.51 (m, 1H), 6.40 (m, 1H), 5.71 (m, 1H), 5.50 (s, 1H), 5.34 (m, 2H), 4.42−4.22 (m, 3H), 3.94 (t, 1H, J = 8.7 Hz), 3.69 (q, 1H, J = 8.0 Hz), 1.33 (t, 3H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 165.401, 149.379, 143.473, 130.166, 121.661, 116.446, 110.500, 109.455, 79.936, 71.654, 63.281, 57.334, 54.513, 14.063.

Minor diastereoisomer: colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.35 (m, 1H), 6.52 (m, 1H), 6.34 (m, 1H), 5.86 (m, 1H), 5.28 (s, 1H), 5.25 (m, 2H), 4.30−4.19 (m, 3H), 4.00 (t, 1H, J = 9.3 Hz), 3.65 (q, 1H, J = 9.0 Hz), 1.22 (t, 3H, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 165.393, 148.433, 143.153, 130.873, 121.579, 114.185, 110.615, 109.110, 81.450, 70.988, 63.462, 59.432, 53.493, 14.006.

2-(2-Furyl)-3-cyano-3-phenylsulfonyl-4-vinyltetrahydrofuran (6h): inseparable mixture; white solid; HRMS calcd for $C_{17}H_{15}NO_4S$ 329.0720, found 329.0720. Anal. Calcd: C, 61.803; H, 4.881; N, 4.239; S, 9.706. Found: C, 61.779; H, 4.589; N, 4.183; S, 9.430.

2-(4-Methoxyphenyl)-4-vinyltetrahydrofuran-3-spiro-4,4-dimethyl-3,5-dioxane-2,6-dione (6i): HRMS calcd for $C_{18}H_{20}O_6$ 332.1259, found 332.1261. Anal. Calcd: C, 65.050; H, 6.065. Found: C, 65.320; H, 6.178.

Major diastereoisomer: white solid; mp 84 °C; ^{1}H NMR ($CDCl_3$) δ 7.24 (m, 2H), 6.84 (m, 2H), 5.96 (m, 1H), 5.51 (s, 1H), 5.25 (m, 2H), 4.47 (m, 1H), 4.00 (m, 1H), 3.79 (s, 3H), 3.74 (m, 1H), 1.58 (s, 3H), 1.51 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 167.704, 159.931, 132.650, 127.756, 126.851, 120.995, 113.601, 105.220, 92.932, 73.603, 64.885, 55.451, 55.130, 30.595, 27.955.

Minor diastereoisomer: white solid; mp 69 °C; ^{1}H NMR ($CDCl_3$) δ 7.26 (m, 2H), 6.85 (m, 2H), 5.79 (m, 1H), 5.50 (s, 1H), 5.28 (m, 2H), 4.43 (dd, 1H, J = 9.3, 8.1 Hz), 4.34 (dd, 1H, J = 9.3, 8.1 Hz), 4.10 (q, 1H, J = 9.3 Hz), 3.78 (s, 3H), 1.55 (s, 3H), 1.12(s, 3H); ^{13}C NMR ($CDCl_3$) δ 167.630, 160.260, 132.041, 127.797, 126.497, 121.521, 113.823, 105.614, 90.727, 72.262, 65.773, 55.196, 54.974, 30.472, 28.070.

3,3-Diphenylsulfonyl-4-vinyltetrahydrofuran (6j): white solid; mp 87−88 °C; HRMS calcd for $C_{18}H_{18}S_2O_5$ 378.0594, found 378.0580; ^{1}H NMR ($CDCl_3$) δ 8.14 (m, 4H), 7.72 (m, 2H),

7.60 (m, 4H), 6.08 (m, 1H), 5.00 (d, 1H, J = 10.2 Hz), 4.70 (m, 2H), 4.52 (d, 1H, J = 11.6 Hz), 4.13 (t, 1H, J = 7.9 Hz), 3.93 (dd, 1H, J = 10.2, 8.3 Hz), 3.65 (dd, 1H, J = 18.0, 7.7 Hz); ^{13}C NMR ($CDCl_3$) δ 137.872, 135.923, 134.895, 134.829, 131.646, 131.613, 129.179, 128.751, 128.512, 120.608, 93.137, 73.389, 71.958, 52.950. Anal. Calcd: C, 57.124; H, 4.794. Found: C, 57.030; H, 4.834.

2-Phenyl-3,3-dicyano-4-methyl-4-vinyltetrahydrofuran (6k): HRMS calcd for $C_{15}H_{14}N_2O$ 238.1105, found 238.1106. Anal. Calcd: C, 75.608; H, 5.922; N, 11.756. Found: C, 75.642; H, 5.928; N, 11.618.

Major diastereoisomer: white solid; mp 64 °C; ^{1}H NMR ($CDCl_3$) δ 7.53−7.43 (m, 5H), 6.13 (dd, 1H, J = 17.2, 10.8 Hz), 5.56 (m, 2H), 5.32 (s, 1H), 4.33 (d, 1H, J = 9.5 Hz), 4.15 (d, 1H, J = 9.5 Hz), 1.56 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 136.581, 133.965, 129.861, 128.817, 126.061, 119.399, 111.989, 111.520, 85.751, 75.824, 53.666, 52.663, 20.405.

Minor diastereoisomer: white solid; mp 58 °C; ^{1}H NMR ($CDCl_3$) δ 7.54−7.43 (m, 5H), 6.12 (dd, 1H, J = 17.2, 10.8 Hz), 5.47 (m, 2H), 5.42 (s, 1H), 4.36 (d, 1H, J = 9.2 Hz), 4.02 (d, 1H, J = 9.2 Hz), 1.66 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 135.907, 133.957, 129.902, 128.858, 126.045, 119.366, 112.244, 111.421, 85.875, 77.707, 53.370, 53.288, 21.359.

2-Phenyl-3,3-dicyano-4-benzylidenetetrahydrofuran (6l): HRMS calcd for $C_{20}H_{16}N_2O$.300.1261, found 300.1266.

Major diastereoisomer: white solid; ^{1}H NMR ($CDCl_3$) δ 7.58−7.28 (m, 10H), 6.82 (d, 1H, J = 15.6 Hz), 6.22 (ddd, 1H, J = 15.6, 9.0, 1.6 Hz), 5.30 (s, 1H), 4.45 (m, 1H), 4.21 (td, 1H, J = 9.2, 1.1 Hz), 3.87 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 138.053, 135.092, 132.872, 130.075, 128.891, 128.866, 128.751, 126.876, 126.135, 119.564, 113.074, 110.615, 86.969, 70.938, 54.530, 48.764.

Minor diastereoisomer: white solid; ^{1}H NMR ($CDCl_3$) δ 7.54−7.33 (m, 10H), 6.79 (d, 1H, J = 15.8 Hz), 6.24 (dd, 1H, J = 15.8, 9.1 Hz), 5.35 (s, 1H), 4.63 (dd, 1H, J = 9.5, 7.2 Hz), 4.04 (dd, 1H, J = 9.5, 8.1 Hz), 3.79 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 137.856, 135.191, 133.752, 130.026, 128.924, 128.792, 126.876, 126.152, 120.288, 113.107, 112.721, 87.322, 72.369, 53.625, 47.761.

2-(2-Furyl)-3,3-dicyano-4-methyl-4-vinyltetrahydrofuran (6m): HRMS calcd for $C_{13}H_{12}N_2O_2$ 228.0898, found 228.0900. Anal. Calcd: C, 68.409; H, 5.299; N, 12.273. Found: C, 68.310; H, 5.319; N, 12.209.

Major diastereoisomer: white solid; mp 61 °C; ^{1}H NMR ($CDCl_3$) δ 7.52 (m, 1H), 6.63 (d, 1H, J = 3.5 Hz), 6.45 (dd, 1H, J = 3.3, 1.8 Hz), 6.08 (dd, 1H, J = 17.3, 10.7 Hz), 5.53 (m, 2H), 5.36 (s, 1H), 4.23 (d, 1H, J = 9.5 Hz), 4.08 (dd, 1H, J = 9.5, 1.5 Hz), 1.58(s, 3H); ^{13}C NMR ($CDCl_3$) δ 146.928, 144.181, 135.890, 119.638, 111.857, 111.413, 110.771, 110.516, 80.808, 75.585, 53.633, 50.376, 20.117.

Minor diastereoisomer: white solid; mp 50−51 °C; ^{1}H NMR ($CDCl_3$) δ 7.53 (m, 1H), 6.65 (m, 1H), 6.46 (m, 1H), 6.13 (dd, 1H, J = 17.2, 10.8 Hz), 5.49 (m, 2H), 5.41 (s, 1H), 4.31 (d, 1H, J = 9.2 Hz), 3.96 (d, 1H, J = 9.2 Hz), 1.62 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 146.977, 144.148, 135.347, 119.630, 111.931, 111.347, 110.821, 110.335, 80.989, 76.572, 53.485, 51.067, 20.742.

2-(2-Furyl)-3,3-dicyano-4-benzylidenetetrahydrofuran (6n): HRMS calcd for $C_{18}H_{14}N_2O_2$ 290.1054, found 290.1044.

Major diastereoisomer: light yellow solid; ^{1}H NMR ($CDCl_3$) δ 7.54−7.29 (m, 6H), 6.83 (d, 1H, J = 15.6 Hz), 6.69 (d, 1H, J = 3.3 Hz), 6.47 (dd, 1H, J = 3.3, 1.9 Hz), 6.21 (dd, 1H, J = 15.6, 9.0 Hz), 5.35 (s, 1H), 4.40 (m, 1H), 4.17 (m, 1H), 3.81 (dd, 1H, J = 17.6, 8.6 Hz); ^{13}C NMR ($CDCl_3$) δ 146.212, 144.189, 138.316, 135.084, 128.948, 128.767, 126.900, 119.078, 112.712, 110.845, 110.615, 110.525, 81.589, 70.938, 54.382, 46.568.

Minor diastereoisomer: yellow solid; ^{1}H NMR ($CDCl_3$) δ 7.53−7.25 (m, 6H), 6.84 (d, 1H, J = 15.6 Hz), 6.59 (m, 1H), 6.45 (dd, 1H, J = 3.3, 1.7 Hz), 6.19 (m, 1H), 5.54 (s, 1H), 4.53 (m, 1H), 4.07−3.92 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 147.635, 144.370, 138.481, 135.191, 128.932, 128.784, 126.876, 118.832, 112.605, 112.087, 111.257, 110.812, 81.211, 71.802, 52.827, 45.852.

Acknowledgment. J.-G.S. thanks the Ministry of Education, Science and Culture of Japan for a Monbusho Scholarship.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra for **5f**, **5h**, **5l**, and **5n** (12 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO972317W