Radical [3 + 2] Cycloaddition Reaction with Various Alkenes Using Iodomethylcyclopropane Derivatives as New Homoallyl Radical Precursors

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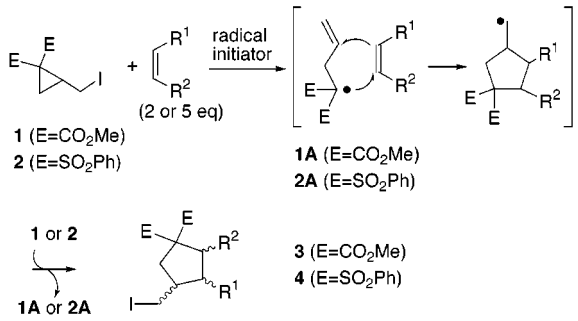
Radical iodine atom transfer [3 + 2] cycloaddition with various alkenes using dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate and 1,1-bis(phenylsulfonyl)-2-(iodomethyl)cyclopropane as new precursors of a homoallyl radical species smoothly proceeds to give functionalized cyclopentane derivatives in good yields.

Introduction

The [3 + 2] cycloaddition reaction of a homoallyl radical species with an alkene is a powerful means for one-pot transformation to a cyclopentanoide skeleton from simple substrates.[1,2] Especially, the reaction of electrophilic homoallyl radicals such as allylated active methine radicals would be synthetically very useful, because simple alkyl-substituted alkenes (without any activating groups such as electron-withdrawing groups) can be used as the partners.[2] As the precursors of such electrophilic homoallyl radical species, the use of vinylcyclopropane derivatives having an electron-withdrawing group on the ring[1e,f,2a,c] and allylated α-iodo-active methine derivatives[2b,d,e] has been reported, while there still remain several problems in these methods. For example, in Feldman and Oshima's method using vinylcyclopropane derivatives, a large excess of alkenes (15−50 equiv) is required[1e,f,2a] and there is no description concerning an application to less reactive 1,2-disubstituted alkenes.[1e,f,2a,b] On the other hand, although Curran et al. have succeeded in reactions with various 1-alkenes and 1,1- and 1,2-disubstituted alkenes by the use of allyl-α-iodomalononitrile,[2d,e] it was not applicable to the reaction with electron-rich alkenes such as enol ethers because of the nature as an electrophilic iodine source of the unstable allyl-α-iodo-active methine.[3]

We have been interested in dimethyl 2-(iodomethyl)-cyclopropane-1,1-dicarboxylate (**1**; E = CO_2Me) and 1,1-bis(phenylsulfonyl)-2-(iodomethyl)cyclopropane (**2**; E = SO_2Ph) as new homoallyl radical precursors. That is, these iodomethylcyclopropane derivatives **1** and **2** can be easily prepared through the iodocarbocyclization of allylated active methines previously found by our group[4] and may produce electrophilic homoallyl radicals **1A** and **2A** via the regioselective C(2)−C(1)E_2 bond cleavage of cyclopropylmethyl radicals formed by the reaction with a radical initiator (Scheme 1).[2a,5] Successively, the resulting **1A** and **2A** would possibly give iodoalkylated cyclopentane derivatives **3** and **4** through a radical iodine atom transfer reaction with alkenes (Scheme 1).[6] In contrast to vinylcyclopropane[2a] and allyl-α-iodo-active methine[2b,d,e] derivatives, the use of radical precursors **1** and **2**, which do not have an alkene part, may also lead to an increase in the chemical yield, because a side reaction such as the attack of the resulting homoallyl

Scheme 1



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(1) The reaction with electron-deficient alkenes: (a) Clive, D. L. J.; Angoh, *J. Chem. Soc., Chem. Commun.* **1985**, 980. (b) Cekovik, Z.; Saicic, R. *Tetrahedron Lett.* **1986**, *27*, 5893. (c) Curran, D. P.; Chen, M. *J. Am. Chem. Soc.* **1987**, *109*, 6558. (d) Barton, D. H. R.; Zard, S. Z.; da Silva, E. *J. Chem. Soc., Chem. Commun.* **1988**, 285. (e) Feldman, K. S.; Romanelli, A. L.; Ruckle, R. E., Jr.; Miller, R. F. *J. Am. Chem. Soc.* **1988**, *110*, 3300. (f) Feldman, K. S.; Ruckle, R. E., Jr.; Romanelli, A. L. *Tetrahedron Lett.* **1989**, *30*, 5845. (g) Chuang, C. P.; Ngoi, T. H. J. *J. Chin. Chem. Soc.* **1991**, *38*, 379. (h) Curran, D. P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1991; Vol. 4, p 779, and references therein.

(2) The reaction with simple alkenes: (a) Miura, K.; Fugami, K.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1988**, *29*, 5135. (b) Curran, D. P.; Chen, M.; Spletzer, E.; Seong, C. M.; Chang, C. *J. Am. Chem. Soc.* **1989**, *111*, 8872. (c) Singleton, D. A.; Church, K. M. *J. Org. Chem.* **1990**, *55*, 4780. (d) Curran, D. P.; Seong, C. M. *Tetrahedron* **1992**, *48*, 2157. (e) Curran, D. P.; Seong, C. M. *Tetrahedron* **1992**, *48*, 2175.

(3) Curran D. P.; Eichenberger, E.; Collis, M.; Roepel M. G.; Thoma, G. *J. Am. Chem. Soc.* **1994**, *116*, 4279

(4) For our review in relation to iodocarbocyclization: Kitagawa, O.; Taguchi, T. *Synlett* **1999**, 1191.

(5) For reviews in relation to the rearrangement of the cyclopropylcarbinyl radical to the homoallyl radical: (a) Motherwell, W. B.; Crich, D. *Free Radical Chain Reactions in Organic Synthesis*; Academic Press: London, 1991. (b) Nonhebel, D. C. *Chem. Soc. Rev.* **1993**, 347. (c) Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091.

(6) For reviews in relation to the reaction of carbon-centered radicals: (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon−Carbon Bonds*; Pergamon Press: New York, 1986. (b) Curran, D. P. *Synthesis* **1988**, 417. (c) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237. (d) Motherwell, W. B.; Crich, D. *Free Radical Chain Reactions in Organic Synthesis*; Academic Press: London, 1992. (e) Fossey, J.; Lefort, D.; Sorba, J. *Free Radicals in Organic Chemistry*; Wiley: New York, 1995. (f) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH: New York, 1996. For a review in relation to radical atom transfer reaction: (g) Curran, D. P. *Synthesis* **1988**, 489.

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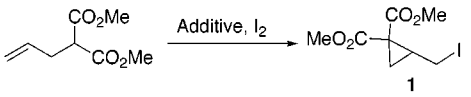
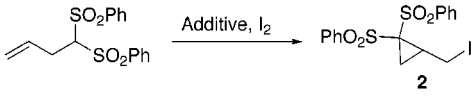
Scheme 2



	Additive	Solvent	Yield
our method	Ti(O*t*-Bu)$_4$, CuO	CH_2Cl_2	98 %
Beckwith's method	NaH	THF	81 %

Scheme 3



	Additive	Solvent	Yield
our method	$TiCl_4$, Et_3N	CH_2Cl_2	54 %
Beckwith's method	NaH	THF	49 %

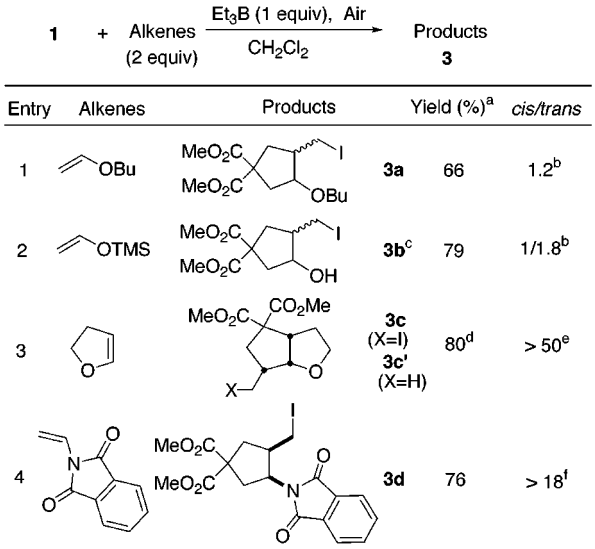
radical at the precursors can be disregarded. In addition, since the chemically stable **1** and **2**, in comparison with allyl-α-iodo-active methine derivatives, are not electrophilic iodine sources, reactions with electron-rich alkenes may be also possible. In this paper, we report radical iodine atom transfer [3 + 2] cycloaddtion with various alkenes using **1** and **2** as new homoallyl radical precursors.[7,8]

Results and Discussion

Synthesis of Iodomethylcyclopropane Derivatives (Homoallyl Radical Precursors). To avoid diastereomeric complication in the products, we chose dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate (**1**) and 1,1-bis(phenylsulfonyl)-2-(iodomethyl)cyclopropane (**2**), having the same electron-withdrawing groups at C1 as electrophilic homoallyl radical precursors. According to our previous report, **1** could be prepared in good yield through $Ti(OR)_4$-mediated iodocarbocyclization of allylmalonate (Scheme 2).[9] Beckwith's method using NaH and I_2 was also usable for the efficient preparation of **1** (Scheme 2).[10] The bis(phenylsulfonyl) cyclopropane derivative **2** could be obtained in 54% yield through the iodocarbocyclization of allylbis(phenylsulfonyl)methane using $TiCl_4-Et_3N$,[11] while $Ti(OR)_4$-mediated iodocarbocyclization did not afford **2** (Scheme 3). Although Beckwith's method[10] also gave **2** in 49% yield, in this case the formation of a side product which is difficult to separate from **2** was observed (Scheme 3).

Radical Iodine Atom Transfer [3 + 2] Cycloaddition Reaction using Dimethyl 2-(Iodomethyl)cyclopropane-1,1-dicarboxylate (1). Initially, the radical [3 + 2] cycloaddition reaction with electron-rich alkenes using dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate (**1**) as a homoallyl radical precursor was investigated. It was found that the radical iodine atom transfer

Table 1. Radical Iodine Atom Transfer [3 + 2] Cycloaddition of 1 with Various Electron-Rich Alkenes



[a] Isolated yield. [b] The ratio was determined on the basis of isolated yield. [c] The hydroxycyclopentane **3b** was obtained after desilylation by treatment with 5% HCl. [d] **3c** and **3c′** were obtained in a ratio of 3:1. [e] Other stereoisomers could not be detected by 300 MHz ^{1}H NMR and 75 MHz ^{13}C NMR. [f] The ratio was determined by ^{1}H NMR.

[3 + 2] cycloaddition reaction of **1** with various electron-rich alkenes (2 equiv) such as enol ethers and enamide smoothly proceeds in the presence of Et_3B (1 equiv)[12] in CH_2Cl_2 to give iodoalkylated cyclopentane derivatives **3** in good yields (Table 1). For example, the reaction of **1** with butyl vinyl ether and silyl enol ether gave functionalized cyclopentane derivatives **3a** and **3b** in good yields (**3a**, 66%; **3b**, 79%), respectively, while the diastereoselectivities of these reactions were low (**3a**, cis/trans = 1.2; **3b**, cis/trans = 1/1.8) (entries 1 and 2).[13]

In the reaction with 2,3-dihydrofuran, oxygen-containing bicyclic products **3c** and **3c′** were obtained with almost complete diastereoselectivity (entry 3). In this reaction, the isomer having an iodomethyl (**3c**) or a methyl (**3c′**) group of endo orientation on the bicyclo[3.3.0]octane ring was selectively formed.[13] Such preferential formation of the endo isomer, which is thermodynamically unfavorable relative to the exo isomer, has also been observed in the reaction of allylated iodomalononitrile with cyclopentene reported by Curran et al.[2e,14] Since separation of iodide **3c** and reduction product **3c′** formed in a ratio of 3/1 through this reaction was difficult, the product was isolated after complete conversion to **3c′** by subsequent treatment with $(Me_3Si)_3SiH$ and AIBN (59% overall yield).

The present reaction can be applied to not only enol ether derivatives but also an enamide derivative. In this case, aminocyclopentane derivative **3d** was obtained with high cis selectivity (cis/trans = 18) in good yield (76%) (entry 4). The higher diastereoselectivity as compared to

(7) Preliminary communication of this work: Kitagawa, O.; Fujiwara, H.; Taguchi, T. *Tetrahedron Lett.* **2001**, *42*, 2165.

(8) In relation to the present reaction of (iodomethyl)cyclopropane derivatives, we have recently succeeded in the development of radical iodine atom transfer [3 + 2] cycloaddition reactions with alkenes using *N*-tosyliodoaziridine as a new aza-homoallyl radical precursor: Kitagawa, O.; Yamada, Y.; Fujiwara, H.; Taguchi, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 3865.

(9) (a) Kitagawa, O.; Inoue, T.; Taguchi, T. *Tetrahedron Lett.* **1992**, *33*, 2167. (b) Inoue, T.; Kitagawa, O.; Ochiai, O.; Taguchi, T. *Tetrahedron: Asymmetry* **1995**, *6*, 691.

(10) Beckwith, A. L.; Zozer, M. J. *Tetrahedron Lett.* **1992**, *33*, 4975.

(11) Kitagawa, O.; Suzuki, T.; Inoue, T.; Watanabe, Y.; Taguchi, T. *J. Org. Chem.* **1998**, *63*, 9470.

(12) Oshima, K.; Uchimoto, K. *J. Synth. Org. Chem. Jpn.* **1989**, *47*, 40.

(13) The stereochemistries of the products were determined on the basis of NOESY measurement or comparison of the chemical shift of the iodomethyl group in the ^{13}C NMR. In general, the chemical shift of the iodomethyl group in cis isomers appears upfield from that of trans isomers.

(14) The model to rationalize such endo selectivity in the bicyclo[3.3.0]octane system has been reported by Curran et al.: Curran, D. P.; Rakiewicz, D. M. *Tetrahedron* **1985**, *41*, 3943.

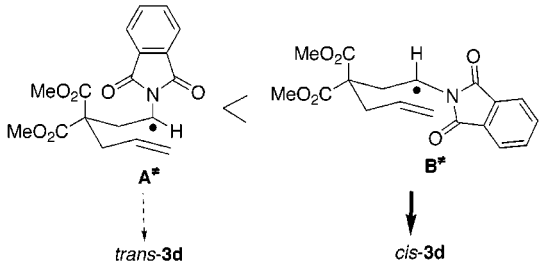
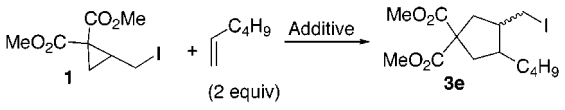


Figure 1. Stereochemical model accounting for the cis selectivity in the reaction of **1** with enamide.

Table 2. Additive Effect in Radical Iodine Atom Transfer [3 + 2] Cycloaddition of 1 with 1-Hexene



entry	additive	conditions	yield (%)[a]	cis/trans[b]
1	Et_3B (1 equiv)	CH_2Cl_2, room temp	22	8.8
2	AIBN (0.05 equiv)	C_6H_6, reflux	4	
3	$(Me_3Sn)_2$ (0.1 equiv), $h\nu$	C_6H_6	40	7.5
4[c]	Et_3B (1 equiv), $Yb(OTf)_3$ (1 equiv)	CH_2Cl_2, room temp	87	8.8
5[c]	Et_3B (1 equiv), $Yb(OTf)_3$ (1 equiv)	CH_2Cl_2, 0 °C	82	11.2

[a] Isolated yield. [b] The ratio was determined by ^{13}C NMR. [c] Air (20 mL) was introduced with a syringe.

those in the reactions with vinyl ethers may be rationalized on the basis of the cyclization model in Figure 1: that is, in the chairlike cyclization model having an equatorial olefin part, the more bulky imide group as compared to the butoxy or siloxy group should prefer equatorial orientation such as in model **B**$^{\neq}$ to avoid 1,3-diaxial repulsion. Accordingly, the cyclization reaction should preferentially proceed through model **B**$^{\neq}$ over model **A**$^{\neq}$, having an axial imide group, to give the product **3d** with high cis selectivity.

The radical [3 + 2] cycloaddition reaction with simple alkyl-substituted alkenes was further examined. In contrast to the reaction with electron-rich alkenes, reaction of **1** with 1-hexene gave the product **3e** in poor yield (22%) under the same conditions (Table 2, entry 1). No remarkable improvement was observed under other radical iodine atom transfer conditions such as AIBN and $(Me_3Sn)_2-h\nu$ (entries 2 and 3). On the other hand, the addition of $Yb(OTf)_3$ was found to lead to a remarkable increase in the chemical yield.[15,16] Thus, the reaction with 1-hexene (2 equiv) at room temperature in the presence of Et_3B (1 equiv) and $Yb(OTf)_3$ (1 equiv) gave **3e** in good yield (87%) with high diastereoselectivity (cis/trans = 8.8) (entry 4). When the same reaction was performed at 0 °C, further increase in the cis selectivity was observed (cis/trans = 11.2) (entry 5).[13] The remarkable additive effect of $Yb(OTf)_3$ may be explained as shown in Figure 2. That is, $Yb(OTf)_3$ may promote the rate of addition of the malonate radical through the formation of a more electrophilic radical on the basis of bidentate coordination with the two ester groups.[16b,c] In addition, the formation of a chelate complex with the precursor **1** may also lead to an increase in the rate of the iodine abstraction.[15h,16b]

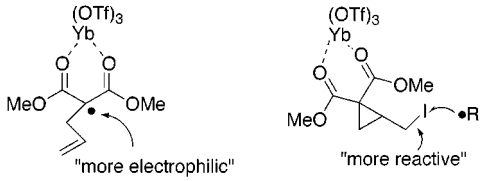
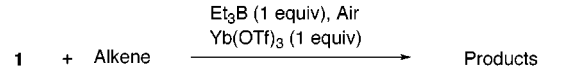
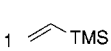
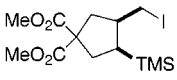
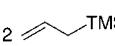
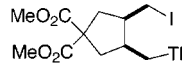
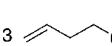
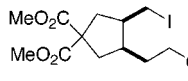
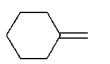
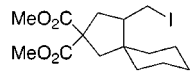
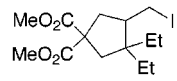
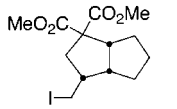
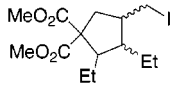


Figure 2. Additive effect of $Yb(OTf)_3$ in the reaction with **1**.

Table 3. Radical Iodine Atom Transfer [3 + 2] Cycloaddition of 1 with Various Alkyl Substituted Alkenes



Entry	Alkenes	Products		Yield (%)[a]	*cis/trans*
1			**3f**	67	6.0[b]
2			**3g**	89	5.6[b]
3			**3h**	68	10.8[b]
4			**3i**	88	—
5			**3j**	73	—
6[c]			**3k**	70	> 50
7[c]			**3l**	65	2.2[d,e]

[a] Isolated yield. [b] The ratio was determined by 75 MHz ^{13}C NMR. [c] Five equivalents of alkene was used. [d] Two stereoisomers were mainly obtained, while the sterochemistries were not determined. [e] The ratio was determined by ^1H NMR.

Radical iodine atom transfer [3 + 2] cycloaddition reactions with various alkyl-substituted alkenes using Et_3B and $Yb(OTf)_3$ are shown in Table 3. The reactions with other 1-alkenes such as vinylsilane, allylsilane, and homoallyl alcohol also proceeded with cis selectivity (**3f**,

(15) Typical reports in relation to Lewis acid mediated radical reaction: (a) Guindon, Y.; Yoakim, C.; Lemieux, R.; Boisvert, L.; Delorme, D.; Lavallee, J. F. *Tetrahedron Lett.* **1990**, *31*, 2845. (b) Yamamoto, Y.; Onuki, S.; Yamamoto, M.; Asao, N. *J. Am. Chem. Soc.* **1994**, *116*, 421. (c) Renaud, P.; Moufid, N.; Kuo, L. H.; Curran, D. P. *J. Org. Chem.* **1994**, *59*, 3259. (d) Nishida, M.; Ueyama, E.; Hayashi, H.; Ohtake, Y.; Yamamura, Y.; Yanaginuma, E.; Yonemitsu, O.; Nishida, A.; Kawahara, N. *J. Am. Chem. Soc.* **1994**, *116*, 6455. (e) Urabe, H.; Yamashita, K.; Suzuki, K.; Kobayashi, K.; Sato, F. *J. Org. Chem.* **1995**, *60*, 3576. (f) Renaud, P.; Gerster, M. *J. Am. Chem. Soc.* **1995**, *117*, 6607. (g) Wu, J.; H.; Radinov, R.; Porter, N. A. *J. Am. Chem. Soc.* **1995**, *117*, 11029. (h) Guindon, Y.; Guerin, B.; Chabot, C.; Ogilvie, W. *J. Am. Chem. Soc.* **1996**, *118*, 12528. (i) Sibi, M. P.; Ji, J.; Wu, J. H.; Gürtler, S.; Porter, N. A. *J. Am. Chem. Soc.* **1996**, *118*, 2000. (j) Murakata, M.; Jono, T.; Mizuno, Y.; Hoshino, O. *J. Am. Chem. Soc.* **1997**, *119*, 11713. For reviews: (k) Renaud, P.; Gerster, M. *Angew. Chem., Int. Ed.* **1998**, *37*, 2562. (l) Guindon, Y.; Jung, G.; Guerin, B.; Ogilvie, W. W. *Synlett* **1998**, 213.

(16) Among various Lewis acids examined ($TiCl_4$, $SnCl_4$, $ZnCl_2$, $MgBr_2$, $Sc(OTf)_3$, $Yb(OTf)_3$), the use of $Yb(OTf)_3$ gave the best result. Reports in relation to $Yb(OTf)_3$-promoted radical reaction: (a) Sibi, M. P.; Jasperse, C. P.; Ji, J. *J. Am. Chem. Soc.* **1995**, *117*, 10779. (b) Mero, C. L.; Porter, N. A. *J. Am. Chem. Soc.* **1999**, *121*, 5155. (c) Yang, D.; Ye, X.; Gu, S.; Xu, M. *J. Am. Chem. Soc.* **1999**, *121*, 5579.

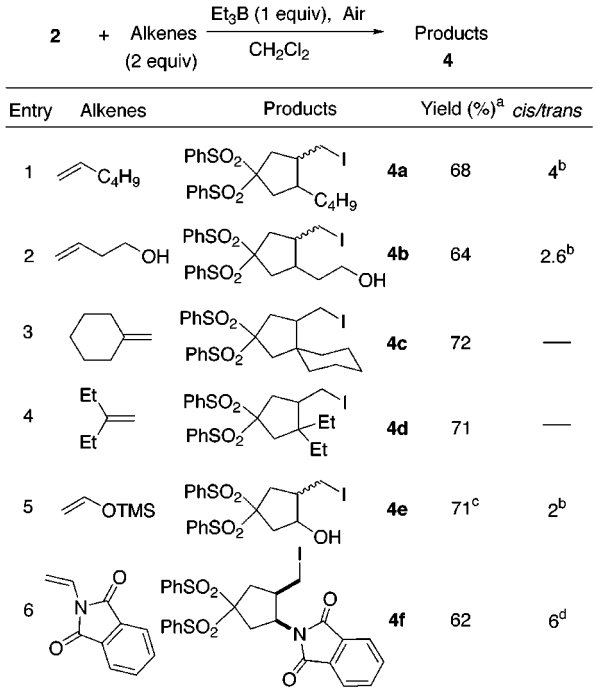
cis/trans = 6; **3g**, cis/trans = 5.6; **3h**, cis/trans = 10.8)[13] to give the products in good yields (**3f**, 67%; **3g**, 89%; **3h**, 68%) (entries 1−3). In the reactions with 1-hexene (entry 5 in Table 2), vinylsilane (entry 1 in Table 3), and allylsilane (entry 2 in Table 3), considerable increase in the chemical yields or diastereoselectivities was observed in comparison with those attained by Curran's method using allyliodomalonate (**3e**, 53%, cis/trans = 4; **3f**, 46%, cis/trans = 2; **3g**, 71%, cis/trans = 5).[2b] Similar to the case for 1-alkenes, 1,1-disubstituted alkenes also gave the cycloaddition products in good yields (**3i**, 88%; **3j**, 73%) (entries 4 and 5).

The present reaction is applicable not only to 1-alkenes and 1,1-disubstituted alkenes but also to less reactive 1,2-disubstituted alkenes; that is, the reaction with cyclopentene and *cis*-3-hexene gave the products **3k** and **3l** in good yields (70% and 65%, respectively) (entries 6 and 7). Similar to the reaction with 2,3-dihydrofuran (Table 1, entry 3), the reaction with cyclopentene also gave the isomer **3k**, having an *endo*-iodomethyl group with almost complete stereoselectivity (entry 6).[13,14] These results should be noteworthy, because it was reported that the reaction with 1,2-disubstituted alkenes hardly proceeds under Curran's conditions using allyliodomalonate as a homoallyl radical precursor.[2b]

Thus, we have found that radical iodine atom transfer [3 + 2] cycloaddition with various alkenes using dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate (**1**) efficiently proceeds to give functionalized cyclopentane derivatives in good yields. In comparison with the reaction systems previously reported by other groups, the advantages of the present reaction are as follows. (1) A large excess (15−50 equiv) of alkenes used in Oshima's and Feldman's methods is not required. That is, the [3 + 2] cycloadducts are obtained in good yields even in the presence of 2 equiv of alkenes (5 equiv in the cases of 1,2-disubstituted alkenes). (2) The present reaction can be applied not only to 1-alkenes and 1,1-disubstituted alkenes but also to less reactive 1,2-disubstituted alkenes. (3) The reaction with electron-rich alkenes is also possible because of the chemical stability of **1** in comparison with Curran's allylated iodoactive methines.

Radical Iodine Atom Transfer [3 + 2] Cycloaddition Reaction using 1,1-Bis(phenylsulfonyl)-2-(iodomethyl)cyclopropane (2). The radical iodine atom transfer [3 + 2] cycloaddition reaction with 1,1-bis(phenylsulfonyl)-2-(iodomethyl)cyclopropane (**2**) as another homoallyl radical precursor was investigated. In the presence of Et_3B (1 equiv), the reaction of **2** with 1-hexene (2 equiv) gave cycloadduct **4a** in a moderate yield (46%). Although the addition of $Yb(OTf)_3$, which worked well in the reactions of **1** (see Table 2), was attempted, improvement of the chemical yield was not observed. This result may indicate that the formation of the chelate complex between **2** and $Yb(OTf)_3$ does not efficiently occur. On the other hand, the reaction under high concentration was found to lead to improvement of the chemical yield. That is, when the concentration of **2** in CH_2Cl_2 was changed to 1.0 M from 0.13 M (concentration of 1-hexene: 2.0 M from 0.26 M), the chemical yield of **4a** increased to 68% from 46% (Table 4, entry 1). Under the same high concentration conditions, the reaction of homoallyl alcohol also gave the cycloadduct **4b** in good yield (64%) (entry 2). With these 1-alkenes, moderate cis selectivities were observed (**4a**, cis/trans = 4; **4b**, cis/trans = 2.6).[13]

Table 4. Radical Iodine Atom Transfer [3 + 2] Cycloaddition of 2 with Various Alkenes



[a] Isolated yield. [b] The ratio was determined by 75 MHz ^{13}C NMR. [c] The hydroxycyclopentane **4e** was obtained after desilylation by treatment with 5% HCl. [d] The ratio was determined by ^1H NMR.

Similar to the case for 1-alkenes, the reaction with 1,1-disubstituted alkenes such as methylenecyclohexane and 2-ethyl-1-butene also proceeded to give the products **4c** and **4d** in good yields (**4c**, 72%; **4d**, 71%) (entries 3 and 4). Electron-rich alkenes such as silyl enol ether and enamide could be also used (entries 5 and 6). In the reaction with enamide having a bulky imide group, higher cis selectivity in comparison with that of the reaction with silyl enol ether was observed (**4f**, cis/trans = 6) (entry 6).

Unfortunately, in contrast to the case for **1**, the reaction of **2** with 1,2-disubstituted alkenes such as cyclopentene and 2,3-dihydrofuran hardly proceeded, resulting in the quantitative recovery of **2**.

In conclusion, we have succeeded in the development of radical iodine atom transfer [3 + 2] cycloaddition with various alkenes using 2-(iodomethyl)cyclopropane-1,1-dicarboxylate (**1**) and 1,1-bis(phenylsulfonyl)-2-(iodomethyl)cyclopropane (**2**) as new homoallyl radical precursors. The present reaction should provide an efficient and practical synthetic methodology of functionalized cyclopentane skeletons from simple substrates.

Experimental Section

Melting points were uncorrected. ^1H and ^{13}C NMR spectra were recorded on a 300 MHz spectrometer. In ^1H and ^{13}C NMR spectra, chemical shifts were expressed in δ (ppm) downfield from $CHCl_3$ (7.26 ppm) and $CDCl_3$ (77.0 ppm), respectively. Mass spectra were recorded by electron impact or chemical ionization. Column chromatography was performed on silica gel (75−150 μm). Medium-pressure liquid chromatography (MPLC) was performed on a 30 × 4 cm i.d. prepacked column (silica gel, 50 μm) with a UV detector.

Starting Materials: Dimethyl 2-(Iodomethyl)cyclopropane-1,1-dicarboxylate (1).[17] **1** was prepared in accordance

with our method ($Ti(OR)_4$-mediated iodocarbocyclization[9]) or Beckwith's method.[10]

1,1-Bis(phenylsulfonyl)-2-(iodomethyl)cyclopropane (2). To allylbis(phenylsulfonyl)methane (4.7 g, 14 mmol) in CH_2Cl_2 were added Et_3N (2.9 mL, 21 mmol) and $TiCl_4$ (2.8 mL, 25.2 mmol) under an Ar atmosphere at room temperature. After the mixture was stirred for 10 min, I_2 (5.3 g, 21 mmol) was added, and then the reaction mixture was stirred for 30 min at room temperature. The mixture was poured into 2% HCl and extracted with Et_2O. The Et_2O extracts were washed with aqueous $Na_2S_2O_3$ solution, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (12/1 hexane/AcOEt) gave **2** (3.5 g, 54%). **2**: white solid; mp 111−113 °C; IR (KBr) 1321, 1147 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.00−8.06 (2H, m), 7.91−7.97 (2H, m), 7.65−7.74 (2H, m), 7.53−7.62 (4H, m), 3.74 (1H, t, J = 10.0 Hz), 3.53 (1H, dd, J = 5.9, 10.0 Hz), 2.99 (1H, ddt, J = 5.9, 8.9, 10.0 Hz), 2.28 (1H, dd, J = 6.3, 9.9 Hz), 2.12 (1H, dd, J = 6.3, 8.9 Hz); ^{13}C NMR ($CDCl_3$) δ 139.9, 138.2, 134.4, 129.6, 129.3, 128.9, 67.0, 33.8, 23.1, −1.4; MS (m/z) 462 (M^+). Anal. Calcd for $C_{16}H_{15}IO_4S$: C, 41.57; H, 3.27. Found: C, 41.69; H, 3.37. The lack of two aromatic carbon resonances in the ^{13}C NMR of **2** is due to overlap of signals.

General Procedure of Radical Iodine Atom Transfer [3 + 2] Cycloaddition Reactions of 1 with Electron-Rich Alkenes. Under an Ar atmosphere, to a solution of dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate (**1**; 149 mg, 0.5 mmol) and butyl vinyl ether (0.12 mL, 1 mmol) in CH_2Cl_2 (3 mL) was added Et_3B (0.5 mL, 1 M hexane solution). A 20 mL amount of dry air was subsequently introduced with a syringe. After being stirred for 5.5 h at room temperature, the mixture was poured into aqueous NH_4Cl solution and extracted with Et_2O. The Et_2O extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (20/1 hexane/AcOEt) gave a mixture of *cis*-**3a** and *trans*-**3a**. Further purification of the mixture by MPLC (6/1 hexane/AcOEt) gave *cis*-**3a** (less polar, 71 mg, 36%) and *trans*-**3a** (more polar, 61 mg, 30%), respectively.

***cis*- and *trans*-Dimethyl 4-*n*-butoxy-3-(iodomethyl)-cyclopentane-1,1-dicarboxylate (*cis*-3a and *trans*-3a).** *cis*-**3a**: colorless oil; IR (neat) 1737 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.84 (1H, m), 3.72 (3H, s), 3.71 (3H, s), 3.49 (1H, td, J = 6.3, 9.1 Hz), 3.33 (1H, t, J = 9.0 Hz), 3.24 (1H, td, J = 6.3, 9.1 Hz), 3.17 (1H, dd, J = 5.5, 9.0 Hz), 2.74 (1H, dd, J = 0.9, 14.5 Hz), 2.36−2.48 (2H, m), 2.14−2.28 (2H, m), 1.42−1.54 (2H, m), 1.26−1.40 (2H, m), 0.90 (3H, t, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$) δ 173.0, 171.9, 80.6, 68.3, 59.1, 52.9, 52.7, 48.1, 38.6, 37.8, 31.8, 19.3, 13.8, 4.2; MS (m/z) 399 ($M^+ + 1$). Anal. Calcd for $C_{14}H_{23}IO_5$: C, 42.22; H, 5.82. Found: C, 42.34; H, 5.75. *trans*-**3a**: colorless oil; IR (neat) 1736 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.73 (3H, S), 3.72 (3H, s), 3.57 (1H, q, J = 6.3 Hz), 3.46 (1H, td, J = 6.5, 9.2 Hz), 3.36 (1H, td, J = 6.5, 9.2 Hz), 3.32 (1H, dd, J = 4.9, 10.0 Hz), 3.23 (1H, dd, J = 7.0, 10.0 Hz), 2.69 (1H, dd, J = 7.4, 13.8 Hz), 2.67 (1H, dd, J = 6.4, 13.8 Hz), 2.21 (1H, dd, J = 6.3, 13.8 Hz), 2.14 (1H, m), 1.77 (1H, dd, J = 9.5, 13.8 Hz), 1.44−1.56 (2H, m), 1.26−1.40 (2H, m), 0.90 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 172.3, 171.9, 83.2, 69.4, 56.8, 52.8, 52.7, 46.5, 39.0, 38.0, 31.9, 19.2, 13.8, 9.7; MS (m/z) 399 ($M^+ + 1$). Anal. Calcd for $C_{14}H_{23}IO_5$: C, 42.22; H, 5.82. Found: C, 42.55; H, 5.89.

***cis*- and *trans*-Dimethyl 3-Hydroxy-4-(iodomethyl)-cyclopentane-1,1-dicarboxylate (*cis*-3b and *trans*-3b).** Under an Ar atmosphere, to a solution of dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate (**1**; 447 mg, 1.5 mmol) and silyl enol ether (0.45 mL, 3 mmol) in CH_2Cl_2 (7 mL) was added Et_3B (1.5 mL, 1 M hexane solution). A 20 mL amount of dry air was subsequently introduced with a syringe. After the mixture was stirred for 2 h at room temperature, 5% HCl (8 mL) and MeOH (15 mL) was added and then the mixture was stirred for 15 min. After removal of MeOH by evaporation, the residue was extracted with Et_2O. The Et_2O extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (4/1 hexane/AcOEt) gave *cis*-**3b** (less polar, 146 mg, 28%) and *trans*-**3b** (more polar, 262 mg, 51%). *cis*-**3b**: colorless oil; IR (neat) 3527, 1731 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.32 (1H, q, J = 4.2 Hz), 3.76 (3H, s), 3.73 (3H, s), 3.29 (1H, t, J = 9.6 Hz), 3.21 (1H, dd, J = 6.3, 9.6 Hz), 2.50−2.68 (2H, m), 2.40 (1H, dd, J = 4.4, 15.0 Hz), 2.38 (1H, m), 2.00−2.16 (2H, m); ^{13}C NMR ($CDCl_3$) δ 173.7, 172.5, 74.2, 59.2, 53.2, 53.0, 48.8, 42.9, 37.8, 3.7; MS (m/z) 342 ($M^+ + 1$). Anal. Calcd for $C_{10}H_{15}IO_5$: C, 35.11; H, 4.42. Found: C, 35.44; H, 4.63. *trans*-**3b**: colorless oil; IR (neat) 3502, 1732 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.99 (1H, m), 3.76 (3H, s), 3.74 (3H, s), 3.31 (1H, dd, J = 6.1, 10.0 Hz), 3.23 (1H, dd, J = 6.8, 10.0 Hz), 2.62 (2H, m), 2.28 (1H, dd, J = 5.5, 13.7 Hz), 2.14 (1H, dd, J = 6.2, 13.7 Hz), 1.93 (1H, dd, J = 9.4, 13.8 Hz); ^{13}C NMR ($CDCl_3$) δ 172.9, 172.1, 57.1, 53.1, 53.0, 49.1, 42.6, 38.9, 17.5, 8.8; MS (m/z) 342 ($M^+ + 1$). Anal. Calcd for $C_{10}H_{15}IO_5$: C, 35.11; H, 4.42. Found: C, 35.40; H, 4.57.

General Procedure of Radical Iodine Atom Transfer [3 + 2] Cycloaddition Reaction of 1 with Simple Alkyl-Substituted Alkenes. Under an Ar atmosphere, to a solution of dimethyl 2-(iodomethyl)cyclopropane-1,1-dicarboxylate (**1**; 149 mg, 0.5 mmol), 1-hexene (0.13 mL, 1 mmol), and $Yb(OTf)_3$ (310 mg, 0.5 mmol) in CH_2Cl_2 (4 mL) was added Et_3B (0.5 mL, 1 M hexane solution) at 0 °C. A 20 mL of dry air was subsequently introduced with a syringe. After being stirred for 5 h at 0 °C, the mixture was poured into aqueous NH_4Cl solution and extracted with Et_2O. The Et_2O extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (20/1 hexane/AcOEt) gave an inseparatable mixture of *cis*-**3e** and *trans*-**3e** (157 mg, 82%, cis/trans = 11.2). ^1H NMR data of **3e** coincided with those reported in the literature.[2b]

Dimethyl 3-*n*-Butyl-4-(iodomethyl)cyclopentane-1,1-dicarboxylate (3e). ^1H NMR data of **3e** coincided with those reported in the literature.[2b] *cis*-**3e**: ^{13}C NMR ($CDCl_3$) δ 173.1, 173.0, 58.5, 52.9 ($OCH_3 \times 2$), 45.5, 42.6, 40.1, 38.4, 30.2, 28.3, 22.8, 14.0, 7.8 (CH_2I). trans-**3e**: ^{13}C NMR ($CDCl_3$) δ 11.0 (CH_2I).

(3*S,3a*S**,6a*R**)-Dimethyl 3-(Iodomethyl)hexahydro-1,1-(2*H*)-pentalenedicarboxylate (3k). 3k** was prepared from **1** (149 mg, 0.5 mmol) and cyclopentene (0.22 mL, 2.5 mmol) in accordance with the general procedure for the reaction with simple alkyl-substituted alkenes. Purification of the residue by column chlomatography (20/1 hexane/AcOEt) gave **3k** (129 mg, 70%) as a single stereoisomer. **3k**: colorless oil; IR (neat) 1728 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.74 (3H, s), 3.69 (3H, s), 3.30 (1H, q, J = 9.0 Hz), 3.19 (1H, dd, J = 6.5, 9.6 Hz), 3.07 (1H, t, J = 9.6 Hz), 2.64 (1H, m), 2.25 (1H, m), 2.21 (1H, dd, J = 5.0, 12.4 Hz), 1.99 (1H, dd, J = 12.4, 13.5 Hz), 1.73−1.87 (2H, m), 1.71 (1H, m), 1.32 (1H, m), 1.11 (1H, m), 0.94 (1H, m); ^{13}C NMR ($CDCl_3$) δ 172.4, 170.7, 63.5, 52.9, 52.3, 47.8, 45.7, 42.9, 37.4, 30.6, 27.2, 26.9, 5.4; MS (m/z) 367 ($M^+ + 1$). Anal. Calcd for $C_{13}H_{19}IO_4$: C, 42.64; H, 5.23. Found: C, 43.01; H, 5.23.

General Procedure of Radical Iodine Atom Transfer [3 + 2] Cycloaddition Reaction of 2 with Alkenes. Under an Ar atmosphere, to a solution of 1,1-bis(phenylsulfonyl)-2-(iodomethyl)cyclopropane (**2**; 231 mg, 0.5 mmol) and methylenecyclohexane (0.13 mL, 1 mmol) in CH_2Cl_2 (0.5 mL) was added Et_3B (0.5 mL, 1 M hexane solution). A 20 mL portion of dry air was subsequently introduced with a syringe. After being stirred for 2 h at room temperature, the mixture was poured into aqueous NH_4Cl solution and extracted with Et_2O. The Et_2O extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (12/1 hexane/AcOEt) gave **4c**, including impurity. Further purification of the mixture by MPLC (5/1 hexane/AcOEt) gave **4c** (201 mg, 72%).

2,2-Bis(phenylsulfonyl) 4-(Iodomethyl)spiro[4.5]decane-2,2-dicarboxylate (4c). 4c: white solid; mp 166−168 °C; IR (KBr) 1316, 1146 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.04−8.10 (4H, m), 7.69−7.76 (2H, m), 7.57−7.65 (4H, m), 3.22 (1H, dd, J = 3.0, 9.6 Hz), 2.75−2.93 (3H, m), 2.44−2.61 (2H, m), 2.15 (1H, m),

(17) Kitagawa, O.; Inoue, T.; Hirano, K.; Taguchi, T. *J. Org. Chem.* **1993**, *58*, 3106.

0.90−1.70 (10H, m); ^{13}C NMR ($CDCl_3$) δ 136.8, 135.7, 134.7, 134.6, 131.5, 131.3, 128.9, 128.7, 91.3, 52.7, 46.0, 40.1, 38.1, 37.5, 28.4, 25.8, 23.8, 22.0, 4.5; MS (*m*/*z*) 431 ($M^+ - I$); HRMS calcd for $C_{23}H_{27}O_4S_2$ ($M^+ - I$) 431.1350, found 431.1348.

***cis*- and *trans*-1,1-Bis(phenylsulfonyl)-3-hydroxy-4-(iodomethyl)cyclopentane (*cis*-4e and *trans*-4e).** Under anAr atmosphere, to a solution of 1,1-bis(phenylsulfonyl)-2-(iodomethyl)cyclopropane (**2**; 231 mg, 0.5 mmol) and silyl enol ether (0.15 mL, 1 mmol) in CH_2Cl_2 (0.5 mL) was added Et_3B (0.5 mL, 1 M hexane solution). A 20 mL portion of dry air was subsequently introduced with a syringe. After being stirred for 2 h at room temperature, 5% HCl (2.5 mL) and MeOH (2.5 mL) was added and then the mixture was stirred for 30 min at room temperature. The mixture was extracted with AcOEt. The AcOEt extracts were washed with brine, dried over $MgSO_4$, and evaporated to dryness. Purification of the residue by column chromatography (5/1 hexane/AcOEt) gave a mixture of *cis*-**4e** and *trans*-**4e**. Further purification of the mixture by MPLC (2/1 hexane/AcOEt) gave *cis*-**4e** (less polar, 119 mg, 47%) and *trans*-**4e** (more polar, 61 mg, 24%), respectively. *cis*-**4e**: white solid; mp 161−163 °C; IR (KBr) 3510, 1307, 1143 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.10 (2H, d, J = 8.0 Hz), 8.03 (2H, d, J = 7.8 Hz), 7.72−7.81 (2H, m), 7.58−7.70 (4H, m), 4.33 (1H, m), 3.12−3.34 (3H, m), 2.69−2.92 (3H, m), 2.23−2.46 (2H, m); ^{13}C NMR ($CDCl_3$) δ 135.3, 135.2, 135.1, 135.0, 131.5, 131.3, 129.0, 128.9, 93.0, 73.3, 49.5, 40.3, 35.9, 1.9; MS (*m*/*z*) 379 ($M^+ - I$). Anal. Calcd for $C_{18}H_{19}IO_5S_2$: C, 42.69; H, 3.78. Found: C, 42.73; H, 4.16. *trans*-**4e**: white solid; mp 84−88 °C; IR (KBr) 3526, 1317, 1146 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.10 (2H, d, J = 7.5 Hz), 8.08 (2H, d, J = 7.5 Hz), 7.74 (2H, t, J = 7.5 Hz), 7.62 (4H, t, J = 7.5 Hz), 3.95 (1H, m), 3.36 (1H, dd, J = 4.0, 10.3 Hz), 3.29 (1H, dd, J = 6.2, 10.3 Hz), 2.92 (1H, dd, J = 7.1, 15.1 Hz), 2.64 (1H, dd, J = 7.7, 15.4 Hz), 2.52 (1H, dd, J = 8.8, 15.1 Hz), 2.44 (1H, brd, J = 6.3 Hz), 2.29 (1H, dd, J = 11.4, 15.4 Hz), 1.94 (1H, m); ^{13}C NMR ($CDCl_3$) δ 135.5, 134.9, 131.5, 131.4, 128.9, 89.0, 75.3, 47.2, 39.2, 35.6, 8.0; MS (*m*/*z*) 506 (M^+); HRMS calcd for $C_{18}H_{19}O_5S_2$ ($M^+ - I$) 379.0674, found 379.0643. The lack of three aromatic carbon resonances in the ^{13}C NMR of *trans*-**4e** is due to overlap of signals.

Supporting Information Available: Text giving experimental procedures for the preparation and characterization data of products **3c** (**3c′**), **3d**, **3f**−**3j**, **3l** (**5l**), **4a**, **4b**, **4d**, and **4f** and figures giving ^{1}H and ^{13}C NMR spectra of new compounds (**4a** (cis/trans mixture), **4b** (cis/trans mixture), **4c**, *trans*-**4**e, *cis*-**4f**) lacking elemental analysis. This material is available free of charge via the Internet at http://pubs.acs.org.

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