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Palladium-catalyzed asymmetric intermolecular arylation of cyclic or acyclic alkenes using phosphinite-oxazoline ligands derived from D-glucosamine

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Abstract

Chiral phosphinite-oxazolines, 2-alkyl- or 2-aryl-4,5-(4,6-*O*-benzylidene-3-*O*-(diphenylphosphino)-1,2-di-deoxy-α-D-glucopyranosyl)-[2,1-*d*]-2-oxazolines **1a**–**f** derived from D-glucosamine hydrochloride, are revealed to work as effective *P*,*N*-bidentate ligands in the palladium-catalyzed enantioselective arylation of 2,3-dihydrofuran to give 2-aryl-2,5-dihydrofuran selectively in high yield with up to 96% ee. The first asymmetric phenylation reaction of *trans*- and *cis*-crotyl alcohols as acyclic alkenes with iodobenzene is also carried out to afford 3-phenylbutanal in moderate chemical yield with up to 17% ee. The complex [$PdCl_2$(**1b**)] is newly prepared and its structure is characterized by X-ray crystallography. Structures of the new complex [(*p*-$MeO_2CC_6H_4$)PdI(**1a**)] (**8**) and its cationic complex [(*p*-$MeO_2CC_6H_4$)Pd(**1a**)]$^+OTf^-$ (**9**) are also elucidated on the basis of ^{1}H-, ^{13}C-, and ^{31}P-NMR spectra, *p*-$MeO_2CC_6H_4$ moiety on the palladium being located *trans* to the nitrogen of **1a**. This configuration might be responsible for an enantiofacial discrimination of 2,3-dihydrofuran to produce (*R*) isomer predominantly. The stoichiometric reaction of [PhPd(**1f**)]$^+OTf^-$ (**11**) with 2,3-dihydrofuran has provided the mechanistic aspect for the arylation using *P*,*N*-ligands, in which the base-promoted deprotonation at β-position leading to an alkene(2-aryl-2,5-dihydrofuran)–palladium(0) complex has been shown to be an important step for the selective formation of the product.

Keywords: Asymmetric catalysis; Intermolecular arylation; D-Glucosamine; Phosphinite-oxazoline ligand

1. Introduction

The palladium-catalyzed arylation and vinylation of alkenes which have been known as Mizoroki–Heck-type reaction are versatile synthetic methods for carbon–carbon bond formation [1]. This methodology has found extensive applications in asymmetric synthesis [2]. Shibasaki [3] and Overman [4] have independently developed asymmetric intramolecular Mizoroki–Heck-type reactions and have convincingly demonstrated the value of such transformation in the synthesis of complex natural molecules. In 1991, Ozawa and Hayashi reported the first example of the intermolecular version of this reaction using 2,3-dihydrofuran and phenyl triflate (Scheme 1a) [5f]. Since then, this chemistry has been extensively studied using various chiral bidentate ligands [5,6]. Pfaltz et al. have demonstrated that chiral phosphine-oxazolines are effective ligands for highly regioselective and enantioselective arylation of cyclic alkenes with aryl or vinyl triflate (Scheme 1b) [6h–j]. The reaction of phenyl triflate with 2,3-dihydrofuran in the presence of (*R*)-BINAP-Pd catalyst gave optically active (*R*)-2-phenyl-2,3-dihydrofuran as a major product together with (*S*)-2-phenyl-2,5-dihydrofuran, while a similar Pd-catalyzed reaction involving the phosphine-oxazoline ligand afforded (*S*)-2-phenyl-2,5-dihydrofuran predominantly. This strikingly different catalysis in arylation of cyclic substrates is becoming one of the major concerns in the asymmetric Mizoroki–Heck-type reactions [5a,7].

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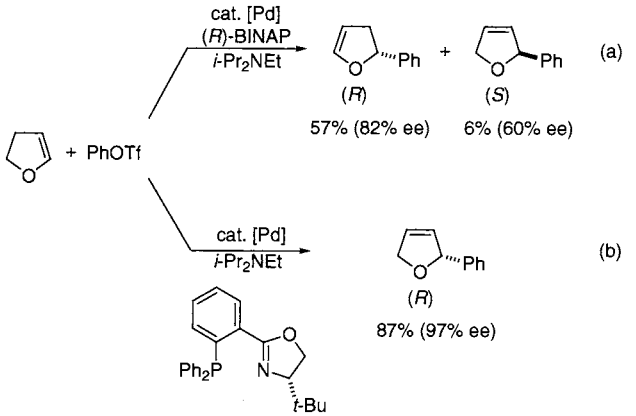
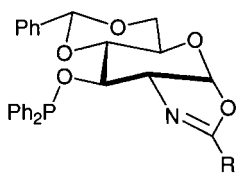


Scheme 1.



R = Me (**1a**), *i*-Pr (**1b**), *i*-Bu (**1c**), *t*-Bu (**1d**)
Ph (**1e**), Bn (**1f**)

Fig. 1. Phosphinite-oxazoline chiral ligands derived from D-glucosamine hydrochloride.

Recently, we were successful in the preparation of the novel chiral phosphinite-oxazolines, 2-alkyl- or 2-aryl-4,5-(4,6-*O*-benzylidene-3-*O*-(diphenylphosphino)-1,2-di-deoxy-α-D-glucopyranosyl)-[2,1-*d*]-2-oxazolines (**1a**–**f**), from a natural D-glucosamine hydrochloride (Fig. 1). These compounds were revealed to work effectively as chiral ligands in the enantioselective palladium-catalyzed allylic substitution reactions (up to 96% ee) [8]. These findings prompted us to investigate the intermolecular Mizoroki–Heck-type reaction using these ligands. We report herein the palladium-catalyzed asymmetric arylation of 2,3-dihydrofuran and crotyl alcohol in the presence of ligands **1**. The reaction of crotyl alcohol represents the first example of the asymmetric intermolecular Mizoroki–Heck-type reaction using a prochiral acyclic substrate. The structural elucidation of newly prepared complexes, such as [$PdCl_2$(**1b**)], [(*p*-$MeO_2CC_6H_4$)PdI(**1a**)], and [PhPdI(**1f**)], as well as the result of the stoichiometric reaction of a new complex [PhPd(**1f**)]$^+OTf^-$ with an excess of 2,3-dihydrofuran are also described, both giving some information on the reaction pathway.

2. Results and discussion

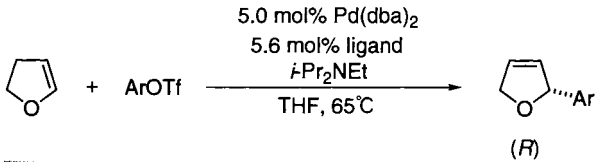
2.1. Palladium-catalyzed asymmetric intermolecular arylation of cyclic or acyclic alkenes

The applicability of chiral phosphinite-oxazolines **1a**–**f** as ligands to the palladium-catalyzed arylation of 2,3-dihydrofuran with aryl triflates was initially examined. The reactions were carried out by mixing ArOTf (0.5 mmol), 2,3-dihydrofuran (2.0 mmol), chiral compound **1** (0.028 mmol), [$Pd_2(dba)_3$]·dba (0.0125 mmol) and *i*-Pr_2NEt (1.0 mmol) in tetrahydrofuran (THF; 3 ml) and by stirring the mixture at 65°C for 1–4 days under Ar. The results are summarized in Table 1. When the compound **1a** (R = Me) was used, phenyl triflate underwent the phenylation of 2,3-dihydrofuran to give (*R*)-2-phenyl-2,5-dihydrofuran in 88% yield with high enantioselectivity (91% ee) (entry 1).

The use of the compound **1b** (R = *i*-Pr) slightly decreased both yield and enantioselectivity (84% yield and 88% ee) (entry 2). The reaction employing the compound **1c** (R = *i*-Bu) proceeded smoothly to give the product quantitatively with 93% ee (entry 3). The use of the compound **1d** having the bulkier *t*-Bu substituent resulted in a lower yield (24%) despite its high enantioselectivity (92% ee) (entry 4). With the compound **1e** (R = Ph) the almost quantitative yield and good enantioselectivity (86% ee) were obtained (entry 5). The quantitative yield and the highest selectivity (96% ee) were obtained by employing the compound **1f** (R = Bn) under the given reaction conditions (entry 6). No regioisomers such as 2-phenyl-2,3-dihydrofuran were detected in all cases. The reaction with *p*-tolyl triflate in place of phenyl triflate using either **1a** or **1f** as a ligand yielded the corresponding product quantitatively with moderate enantioselectivity (78% ee) (entries 7 and 8). The reaction with *p*-methoxyphenyl triflate gave the product in lower yield (17–34%) but with good enantioselectivity (86–90% ee) (entries 9 and 10). On the other hand, no reaction took place when *p*-(trifluoromethyl)phenyl triflate was used under the given conditions (entries 11 and 12).

Next, we attempted the phenylation of crotyl alcohols using **1** as chiral ligands. The chiral induction in this reaction was expected, since phenylation of crotyl alcohol has been known to give saturated carbonyl compound, i.e. 3-phenylbutanal [9]. The results are shown in Table 2. The reaction of *trans*-crotyl alcohol with phenyl triflate under the identical conditions for 2-aryl-2,5-dihydrofuran formation did not give any phenylated product (entry 1). On the other hand, the phenylation occurred with iodobenzene in the presence of Ag_2CO_3 using catalytic amounts of [$Pd_2(dba)_3$]·dba and **1a** to produce (*R*)-3-phenylbutanal in 54% yield with 11% ee (entry 2). The use of chiral ligand **1c** slightly improved the enantioselectivity up to 17% ee (entry 3). The phenylation of *cis*-crotyl alcohol in the presence of chiral ligand **1a** or **1c** gave 3-phenylbutanal

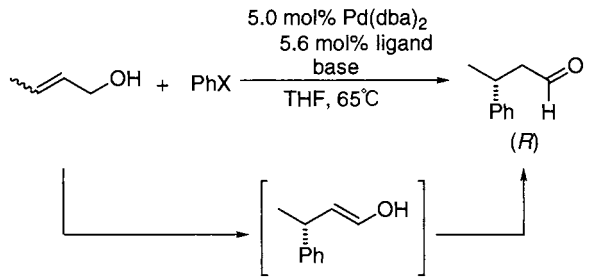
Table 1
Enantioselective arylation of 2,3-dihydrofuran with aryl triflate [a]



Entry	Aryl triflate (Ar =)	Ligand	Time (days)	Yield (%) [b]	ee (%) [c] (*R*) [d]
1	Ph	**1a**	4	88	91
2	Ph	**1b**	3	84	88
3	Ph	**1c**	3	100	93
4	Ph	**1d**	3	24	92
5	Ph	**1e**	2	96	86
6	Ph	**1f**	1	100	96
7	*p*-$CH_3C_6H_4$	**1a**	2	100	78
8	*p*-$CH_3C_6H_4$	**1f**	2	100	78
9	*p*-$CH_3OC_6H_4$	**1a**	2	34	86
10	*p*-$CH_3OC_6H_4$	**1f**	1	17	90
11	*p*-$CF_3C_6H_4$	**1a**	3	No reaction	
12	*p*-$CF_3C_6H_4$	**1f**	3	No reaction	

[a] The reaction of 2,3-dihydrofuran (2.0 mmol) with aryl triflate (0.50 mmol) was carried out in THF at 65°C in the presence of $[Pd_2(dba)_3]$·dba (1.25×10^{-2} mmol), chiral ligand (2.8×10^{-2} mmol), and *i*-Pr_2NEt (1.0 mmol).
[b] Determined by GLC with pentamethylbenzene as an internal standard.
[c] Determined by HPLC.
[d] Determined by optical rotation.

Table 2
Enantioselective phenylation of *trans*- and *cis*-crotyl alcohols [a]



Entry	Substrate	X	Base	Ligand	Time (days)	Conv (%)	Yield (%) [b]	ee (%) [c] (*R*) [d]
1	*trans*	OTf	*i*-Pr_2NEt	**1a**	3	No reaction		
2	*trans*	I	Ag_2CO_3	**1a**	3	76	54	11
3	*trans*	I	Ag_2CO_3	**1c**	3	77	30	17
4	*cis*	I	Ag_2CO_3	**1a**	2	71	32	10
5	*cis*	I	Ag_2CO_3	**1c**	2	60	16	8

[a] The reaction of crotyl alcohol (6.0 mmol) with phenyl triflate or iodobenzene (1.50 mmol) was carried out in THF at 65°C in the presence of $[Pd_2(dba)_3]$·dba (3.75×10^{-2} mmol), chiral ligand (8.4×10^{-2} mmol), and *i*-Pr_2NEt (3.0 mmol) or Ag_2CO_3 (1.5 mmol).
[b] Determined by GLC with pentamethylbenzene as an internal standard.
[c] Calculated from $[\alpha]_D^{25} = -38.0$ (c 0.2, Et_2O) [18].
[d] Determined by optical rotation.

in lower yield with lower enantioselectivity (entries 4 and 5). The enantioselectivity obtained is still low, but the present phenylation of crotyl alcohols represents the first example of the enantioselective intermolecular Mizoroki–Heck-type reaction using prochiral acyclic alkenes [10].

2.2. X-ray structure of [$PdCl_2$(**1b**)] (**2**)

In order to gain insight into the asymmetric environment imposed by the chiral ligands **1**, the neutral palladium(II) complex [$PdCl_2$(**1b**)] (**2**) was prepared by treatment of [$PdCl_2$(cod)] with **1b**, and its crystal struc-

ture was examined by X-ray diffraction. It was disclosed that the crystal is consisted of two different palladium complexes (**2a** and **2b**) together with CH_2Cl_2 in a unit cell. The most remarkable difference between them is the orientation of phenyl ring of benzylidene moiety at 4,6 positions. The ORTEP drawing of **2a** is shown in Fig. 2. The geometry around the palladium is square planar with *cis*-coordination of the nitrogen and the phosphorus atoms of **1b**. Selected bond lengths and angles of **2a** are listed in Table 3. The bond length of Pd–N is 2.05 Å (**2a**), and the length of Pd–P is 2.239 Å. The P–Pd–N angle is 92.2°. They are all reasonable compared with the reported values of palladium dichloride complex bearing oxazolinylferrocenylphosphine ligand [11].

2.3. Studies on the origin of enantioselectivity and reaction mechanism

One of the most pronounced features in the present reaction as well as the earlier work by Pfaltz [6h–j] is the selective formation of 2-aryl-2,5-dihydrofuran from 2,3-dihydrofuran. The most plausible catalytic cycle for the present reaction is given in Scheme 2. First, oxidative addition of PhOTf to a palladium complex **3** having the chiral *P*,*N*-ligand **1** affords a phenylpalladium(II) complex **4**. Coordination of 2,3-dihydrofuran to the complex **4** leads to the formation of a cationic complex **5** in which alkene insertion into the Pd–Ph bond occurs to give an alkyl complex **6**. The added base promotes the elimination of the proton β to palladium with OTf^- to give an alkene(2-phenyl-2,5-dihydrofuran)-palladium(0) complex **7**. The release of the product from **7** followed by oxidative addition of PhOTf affords the palladium complex **4** again.

The selectivity using *P*,*N*-ligands led us to examine more closely the mechanism of the arylation of 2,3-dihydrofuran. With the aim of elucidating the origin of enantioselectivity we prepared separately a new compound $[(p\text{-}MeO_2CC_6H_4)Pd(\mathbf{1a})]^+OTf^-$ (**9**) as illustrated

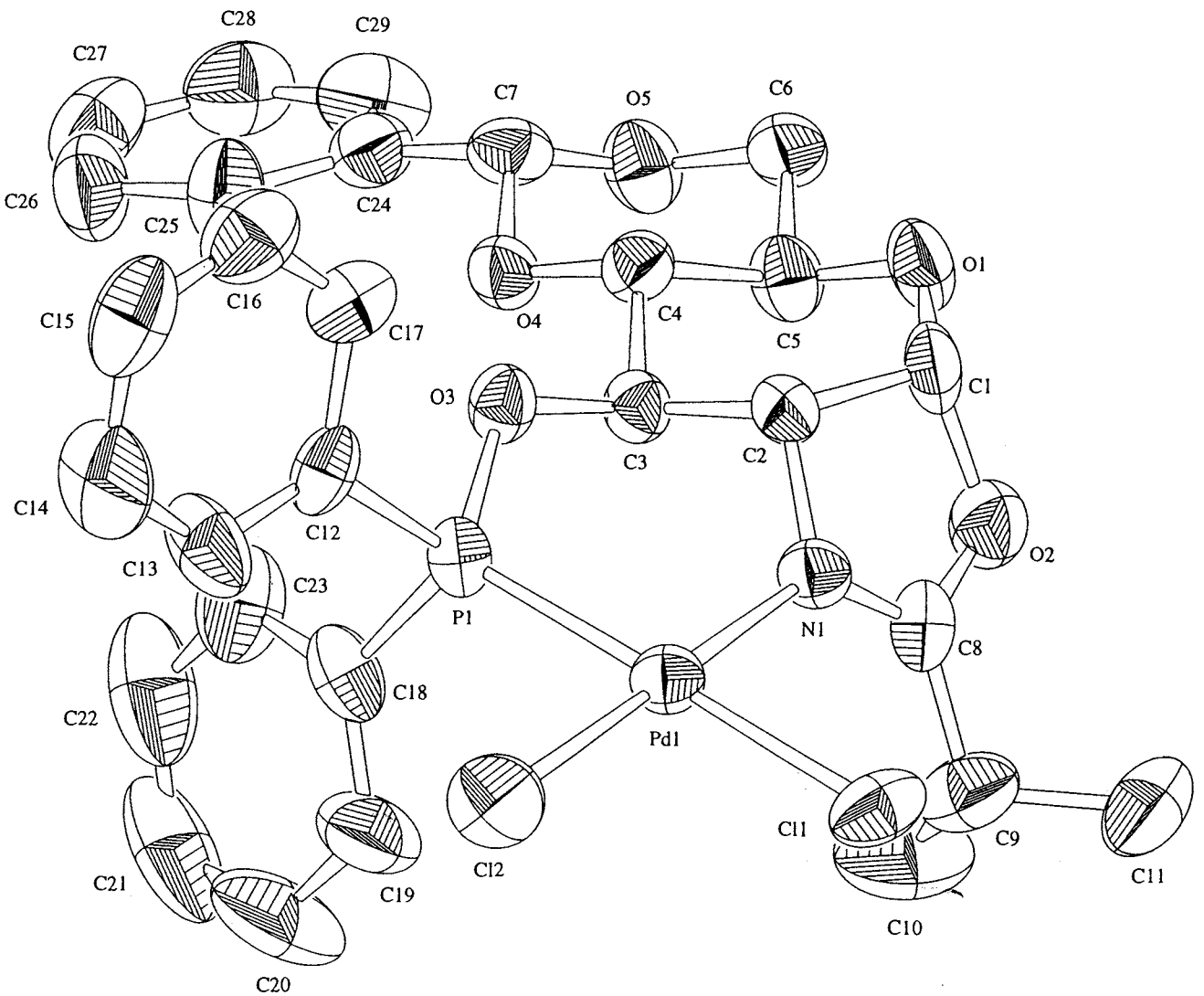
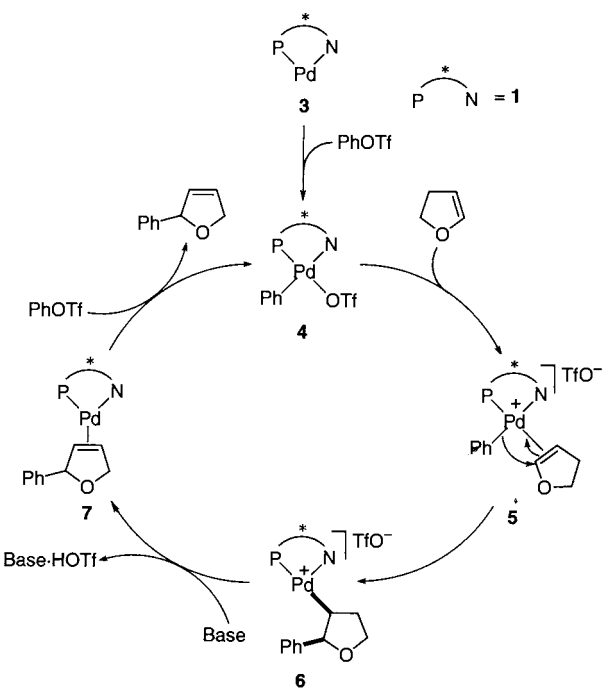


Fig. 2. Crystal structure of **2a**, showing 50% probability thermal ellipsoids. The hydrogen atoms and CH_2Cl_2 molecule are omitted for clarity.

Table 3
Selected bond distances (Å) and angles (°) for **2a**

Bond length			
Pd(1)–Cl(1)	2.373(4)	O(4)–C(4)	1.43(2)
Pd(1)–Cl(2)	2.287(4)	O(4)–C(7)	1.42(1)
Pd(1)–N(1)	2.05(1)	O(5)–C(6)	1.47(2)
Pd(1)–P(1)	2.239(5)	O(5)–C(7)	1.42(2)
N(1)–C(2)	1.49(2)	C(1)–C(2)	1.52(2)
N(1)–C(8)	1.28(2)	C(2)–C(3)	1.52(2)
P(1)–C(12)	1.78(1)	C(3)–C(4)	1.50(2)
P(1)–C(18)	1.78(1)	C(4)–C(5)	1.53(2)
P(1)–O(3)	1.606(10)	C(5)–C(6)	1.51(2)
O(1)–C(1)	1.36(2)	C(7)–C(24)	1.46(2)
O(1)–C(5)	1.39(2)	C(8)–C(9)	1.49(2)
O(2)–C(8)	1.31(2)	C(9)–C(10)	1.50(3)
O(3)–C(3)	1.45(1)	C(9)–C(11)	1.55(3)
Bond angles			
Cl(1)–Pd(1)–Cl(2)	89.9(2)	O(2)–C(1)–C(2)	118(1)
N(1)–Pd(1)–Cl(1)	91.7(3)	O(2)–C(8)–C(9)	116(1)
P(1)–Pd(1)–Cl(2)	86.3(2)	O(3)–P(1)–Pd(1)	113.5(4)
N(1)–Pd(1)–P(1)	92.2(3)	O(3)–P(1)–C(12)	97.9(6)
Pd(1)–P(1)–C(12)	118.2(4)	O(3)–P(1)–C(18)	104.8(6)
Pd(1)–P(1)–C(18)	114.2(6)	O(3)–C(3)–C(2)	109(1)
N(1)–C(2)–C(1)	102(1)	C(1)–O(2)–C(8)	107(1)
N(1)–C(2)–C(3)	107.5(10)	C(2)–N(1)–Pd(1)	119.5(8)
N(1)–C(8)–O(2)	116(1)	C(2)–N(1)–C(8)	106(1)
N(1)–C(8)–C(9)	126(1)	C(3)–O(3)–P(1)	119.2(8)



Scheme 2.

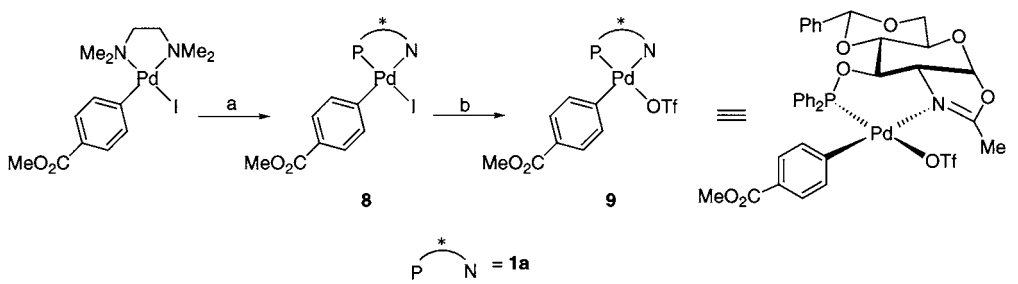
in Scheme 3. The treatment of [(*p*-$MeO_2CC_6H_4$)-PdI(TMEDA)] [6d,12] (TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine) and **1a** in dry degassed benzene at room temperature (r.t.) for 30 min gave the pale yellow complex [(*p*-$MeO_2CC_6H_4$)PdI(**1a**)] (**8**) [13] in 71% isolated yield. The addition of AgOTf to the solution of **8** in $CDCl_3$ at r.t. and filtration of the precipitated AgI gave the yellow supernatant solution of **9** in $CDCl_3$. ^{1}H- and ^{31}P-NMR spectra of the solution indicated the formation of a single stereoisomer at various temperatures through $-78 \sim 50$°C. The structure of the complex **9** was clarified from the NMR analyses, particularly on the basis of NOE experiments. Thus, we could not observe any significant increase of the integrals of aryl protons and methyl protons of *p*-carbomethoxy group on irradiation at methyl protons of the oxazoline ring. Also, no coupling was observed between a phosphorus nucleus and an *ipso*-carbon of *p*-$MeO_2CC_6H_4$ moiety bound to Pd [14]. These experimental results show that the *p*-$MeO_2CC_6H_4$ moiety on the palladium is located *cis* to the phosphorus. This is probably due to the electronic effect rather than steric effect. In the light of these results, the phenyl group is considered to be located *cis* to the phosphorus in the complex **4** as well. The next alkene coordination to the palladium to give the complex **5** which may be regarded as an enantiofacial discrimination step is expected to occur at the *trans* position of the coordinated phosphorus atom as illustrated in Scheme 2. In the step giving the complex **5**, two possible coordination modes might be postulated as shown in Scheme 4. The coordination through *si*-face of 2,3-dihydrofuran in the complex **5A** followed by alkene-insertion leads to the formation of the complex **6A**. The subsequent β-hydrogen elimination from **6A** occurs to give (*R*)-2-phenyl-2,5-dihydrofuran. In contrast, the alkene complex **5B** followed by the coordination through *re*-face of 2,3-dihydrofuran leads to the opposite (*S*) product. As suggested from the molecular structure shown in Fig. 2, the complex **5A** is apparently preferable to **5B**, because of a significant steric repulsion between 2,3-dihydrofuran and the substituent R of oxazoline in the latter complex. Hence, the (*R*) isomer is predominantly produced in the catalytic reaction. However, surprisingly, 3-phenylbutanal with the (*R*) configuration was obtained from both *cis*- and *trans*-crotyl alcohols in the analogous reactions. Although this enantioselection could not be rationalized at present, a hydroxyl group might play some roles in its coordination to palladium [9b].

On the other hand, the exclusive formation of 2-phenyl-2,5-dihydrofuran in the present catalytic reaction in contrast to the case using BINAP is one of other concerns. To clarify this point we attempted to perform the stoichiometric reaction of some palladium-complexes with an excess of 2,3-dihydrofuran. First, we prepared the complex [PhPdI(**1f**)] (**10**) [13] by the reaction between [PhPdI(TMEDA)] [12] and **1f** in 45% yield. To a solution of **10** in d_8-THF was added silver triflate at r.t. to give a [PhPd(**1f**)]$^+$OTf$^-$ (**11**) [15] solution which corresponds to the complex **4** bearing the ligand **1f** in Scheme 2. Four molar equivalents of

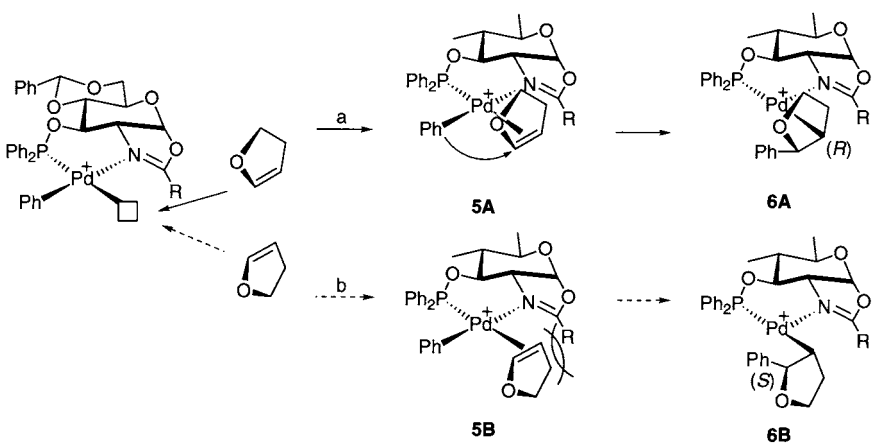
2,3-dihydrofuran were added to the above solution at −78°C and ^{1}H-NMR spectra of the solution were measured at various temperatures through −78 ∼ 50°C. However, the formation of both 2-phenyl-2,5-dihydrofuran and hydridopalladium species was not observed during the NMR analysis [16]. We could detect the formation of 2-phenyl-2,5-dihydrofuran only by allowing the solution of **11** and 2,3-dihydrofuran to stand in the *presence* of *i*-Pr_2NEt for prolonged reaction time at 50°C, although no evidence of the formation of both the corresponding alkylpalladium intermediate and hydridopalladium species was obtained. This is in a sharp contrast to the result using a BINAP–Pd as a catalyst. Brown et al. reported that the formation of 2-phenyl-2,3-dihydrofuran was observed with the concomitant formation of an alkylpalladium complex resulting from the insertion of 2,3-dihydrofuran into Pd–H bond in the stoichiometric reaction between [PhPd(BINAP)(THF)]$^+$OTf$^-$ and 2,3-dihydrofuran in the *absence* of base at −30°C [7b]. The fact that we could not detect both the product and a hydridopalladium species in the stoichiometric reaction, the latter of which might allow the insertion and isomerization to give an isomerized 2-phenyl-2,3-dihydrofuran, indicates that β-hydrogen elimination from the complex **6** under the thermal conditions is an unlikely process in the *absence* of base. Recently, Deeth and co-workers suggested that the agostic hydrogen β to palladium is kinetically more acidic than non-agostic hydrogen in their theoretical study of a model alkyl complex [$(CH_3CH_2CH_2)Pd(H_2NCH_2NH_2)]^+$, since the former is preferentially abstracted as a proton with a base to give [$Pd(CH_3CH{=}CH_2)(H_2NCH_2NH_2)]^+$ and H^+·base [17]. Although the possibility of the presence of the hydridopalladium species is not excluded at present, we believe that the exclusive formation of 2-aryl-2,5-dihydrofuran in our case is ascribed to the fast elimination pathway of a proton at β-position with a base, as proposed by Deeth [17] (Scheme 2).

3. Summary

Chiral phosphinite-oxazolines **1a**–**f** derived from D-glucosamine hydrochloride were revealed to be effective ligands in the Pd-catalyzed enantioselective arylation of 2,3-dihydrofuran to give 2-aryl-2,5-dihydrofuran (up to 96% ee). The enantioselective phenylation of crotyl alcohols also occurred to give 3-phenylbutanal with up to 17% ee, representing the first example of the enan-



Scheme 3. (a) Chiral ligand **1a**, benzene, r.t., 30 min, 71%. (b) AgOTf, $CDCl_3$, r.t., 10 min.



Scheme 4.

tioselective intermolecular arylation of prochiral alkenes. We prepared the palladium(II) complex [$PdCl_2$(**1b**)] and characterized its structure by X-ray diffraction. We newly isolated the arylpalladium complex [(*p*-$MeO_2CC_6H_4$)PdI(**1a**)] (**8**) and also prepared in situ its cationic complex **9** which corresponds to the expected reaction intermediate. In these complexes an aryl group was coordinated *trans* to the nitrogen of its oxazoline. From the configuration of these complexes, we could disclose the origin of enantioselectivitiy using the chiral ligands **1a**–**f**. The stoichiometric reactions of the complex [PhPd(**1f**)]$^+OTf^-$ (**11**) with 2,3-dihydrofuran at various temperatures have provided the mechanistic aspect for Mizoroki–Heck-type reaction using *P*,*N*-ligands, in which the deprotonation at β-position with a base leading to an alkene(2-phenyl-2,5-dihydrofuran)–palladium(0) complex **7** is responsible for the selective formation of the product.

4. Experimental

4.1. General

Tetrahydrofuran (THF) and diethyl ether were distilled from sodium benzophenone ketyl under argon. Benzene, *N*,*N*-diisopropylethylamine, and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) were distilled from calcium hydride. Hexane was distilled from sodium. Analytical thin-layer chromatographies (TLC) were performed with silica gel 60 Merck F-254 plates. Column chromatographies were performed with Merck silica gel 60. NMR spectra were measured on JEOL EX-400, JEOL JNM-AL300, and JEOL JNM-GSX270 spectrometers for solutions in $CDCl_3$ or d_8-THF with Me_4Si as an internal standard (^1H and ^{13}C) or with $P(OMe)_3$ as an external standard (^{31}P). Optical rotations were measured on JASCO DIP-1000. GLC analyses were performed using 25 m HiCap-CBP-10-S25 column. HPLC analyses were performed using Daicel Chiralcel® OB column (4.6 × 250 mm) at 40°C. Melting points are uncorrected. Chiral phosphinite-oxazolines **1a**–**f** were prepared according to the reported procedure [8].

4.2. A typical procedure for the asymmetric intermolecular arylation of 2,3-dihydrofuran

A mixture of [$Pd_2(dba)_3$]·dba (12 mg, 1.25×10^{-2} mmol) and the chiral ligand **1f** (15 mg, 2.8×10^{-2} mmol) in dry degassed THF (3.0 ml) was stirred under Ar at r.t. for 15 min. Phenyl triflate (0.12 g, 0.50 mmol), *N*,*N*-diisopropylethylamine (0.17 ml, 1.0 mmol), and 2,3-dihydrofuran (0.14 g, 2.0 mmol) were added to the catalyst solution. The solution was stirred at 65°C for 1 day under Ar (GLC yield 100%). The reaction mixture was cooled, diluted with pentane (3.0 ml) and filtered through Celite pad to remove solid materials. The solvent was removed under reduced pressure, and the residue was subjected to column chromatography on SiO_2 with hexane–Et_2O 1:1 (v/v) as an eluent to give (*R*)-2-phenyl-2,5-dihydrofuran. The ee (96%) was determined by HPLC using Daicel Chiralcel® OB column at 40°C (0.5 ml min^{-1}, 10% 2-PrOH–hexane, 210 nm, (*S*): $t_1 = 13.0$ min; (*R*): $t_2 = 15.9$ min). The separation of racemic mixtures under HPLC conditions is as follows: (*R*)-2-*p*-tolyl-2,5-dihydrofuran (OB, 0.5 ml min^{-1}, 10% 2-PrOH–hexane, 210 nm), (*S*): $t_1 = 13.5$ min; (*R*): $t_2 = 17.3$ min; (*R*)-2-*p*-methoxyphenyl-2,5-dihydrofuran (OB, 0.5 ml min^{-1}, 10% 2-PrOH–hexane, 230 nm), (*S*): $t_1 = 23.1$ min; (*R*): $t_2 = 36.7$ min.

4.3. A typical procedure for the asymmetric intermolecular phenylation of trans- or cis-crotyl alcohol

A mixture of [$Pd_2(dba)_3$]·dba (35 mg, 3.75×10^{-2} mmol) and the chiral ligand **1a** (39 mg, 8.4×10^{-2} mmol) in dry degassed THF (10 ml) was stirred under Ar at r.t. for 15 min. Iodobenzene (0.31 g, 1.50 mmol), Ag_2CO_3 (0.20 g, 1.5 mmol), and *trans*- or *cis*-crotyl alcohol (0.43 g, 6.0 mmol) were added to the above solution. The solution was stirred under Ar at 65°C for 2 ~ 3 days (GLC yield: up to 54%). The reaction mixture was cooled, diluted with pentane (10 ml), and filtered through a Celite pad to remove solid materials. The solvent was removed under reduced pressure, and the residue was subjected to column chromatography on SiO_2 with hexane–AcOEt 1:1 (v/v) followed by benzene–CH_2Cl_2 1:1 (v/v) as an eluent to give (*R*)-3-phenylbutanal. The ee (up to 17%) was determined by optical rotation [18].

4.4. Synthesis of [$PdCl_2$(**1b**)] (**2**)

A solution of [$PdCl_2$(cod)] (20 mg, 0.1 mmol) and the chiral ligand **1b** (50 mg, 0.1 mmol) in dry degassed THF (1 ml) was stirred under Ar at r.t. for 30 min. By the addition of dry degassed diethyl ether (10 ml) the yellow solid **2** precipitated, which was collected on a sintered glass filter and subsequently washed with degassed dry hexane (5 ml × 2). **2** (33 mg, 4.8×10^{-2} mmol, 48%): m.p. 176.2–177.0°C (dec.). ^1H-NMR (400 MHz, $CDCl_3$): δ 1.17 (d, $J = 6.8$ Hz, 3H), 1.25 (d, $J = 6.8$ Hz, 3H), 3.53–3.69 (m, 2H), 3.83 (t, $J = 10.0$ Hz, 1H), 3.93 (t, $J = 10.0$ Hz, 1H), 4.16 (m, 1H), 4.27 (t, $J = 7.1$ Hz, 1H), 4.35 (dd, $J = 4.9$, 10.0 Hz, 1H), 5.58 (s, 1H), 6.20 (d, $J = 7.1$ Hz, 1H), 7.35–8.35 (m, 15H) ppm. ^{13}C-NMR (100 MHz, $CDCl_3$) δ 18.4, 19.5, 28.0, 30.2, 63.6, 66.3, 67.6, 80.7, 101.5, 104.0, 126.0–136.3

(12 carbons), 181.8 ppm. ^{31}P-NMR (161.9 MHz, $CDCl_3$) δ 103.6 ppm. Anal. Calc. for $C_{29}H_{30}Cl_2NO_5$-PPd: C, 51.16; H, 4.44; N, 2.06. Found: C, 51.47; H, 4.54; N, 1.73%.

4.5. Synthesis of [(p-$MeO_2CC_6H_4$)PdI(**1a**)] (**8**)

A solution of [(*p*-$MeO_2CC_6H_4$)PdI(TMEDA)] [6d, 12] (72 mg, 0.15 mmol) and the chiral ligand **1a** (86 mg, 0.18 mmol) in dry degassed benzene (8.0 ml) was stirred under Ar at r.t. for 30 min. By the addition of dry degassed diethyl ether (10 ml) the white solid **8** precipitated, which was collected on a sintered glass filter and subsequently washed with diethyl ether (5 ml × 2). **8** (90 mg, 0.11 mmol, 71%): m.p. 178.2–181.0°C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.49 (s, 3H), 3.56–3.76 (m, 4H), 3.66 (s, 3H), 4.21 (dd, $J = 4.9$, 10.7 Hz, 1H), 4.23 (t, $J = 7.2$ Hz, 1H), 5.43 (s, 1H), 5.99 (d, $J = 7.2$ Hz, 1H), 6.79–7.96 (m, 19H) ppm. ^{13}C-NMR (100 MHz, $CDCl_3$): δ 18.1, 51.5, 65.5, 65.8, 67.7, 74.8 (d, $J = 7.3$ Hz), 79.7, 101.1, 103.7, 124.3–137.7 (15 carbons), 151.5, 168.0, 172.7 ppm. ^{31}P-NMR (161.9 MHz, $CDCl_3$): δ 109.3 ppm. Anal. Calc. for $C_{35}H_{33}INO_7PPd$: C, 49.81; H, 3.94; N, 1.66 (Calc. for $C_{35}H_{33}INO_7PPd \cdot 1/4\ I_2$: C, 46.33; H, 3.67; N, 1.54). Found: C, 46.17; H, 3.69; N, 1.33%.

4.6. Synthesis of [(p-$MeO_2CC_6H_4$)Pd(**1a**)]$^+$ OTf^- (**9**)

Silver triflate (10 mg, 4.0×10^{-2} mmol) was added to a vigorously stirred solution of the complex **8** (25 mg, 3.0×10^{-2} mmol) in $CDCl_3$ at r.t. Stirring was continued for 10 min, during which period a white precipitate was formed. The supernatant was rapidly transferred by a syringe into an NMR tube and the formation of the complex **9** was confirmed by NMR spectroscopies. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 2.06 (s, 3H), 3.60–3.79 (m, 4H), 3.68 (s, 3H), 4.22 (dd, $J = 4.9$, 10.7 Hz, 1H), 4.39 (br s, 1H), 5.44 (s, 1H), 6.20 (d, $J = 7.5$ Hz, 1H), 6.97–7.84 (m, 19H) ppm. ^{13}C-NMR (75 MHz, $CDCl_3$): δ 15.3, 51.8, 65.2, 65.7, 67.8, 74.5 (d, $J = 8.1$ Hz), 80.9, 101.2, 104.3, 125.3–136.5 (15 carbons), 146.2, 167.6, 173.3 ppm. ^{31}P-NMR (161.9 MHz, $CDCl_3$): δ 117.9 ppm.

4.7. Synthesis of [PhPdI(**1f**)] (**10**)

A solution of [PhPdI(TMEDA)] [12] (64 mg, 0.15 mmol) and the chiral ligand **1f** (83 mg, 0.15 mmol) in dry degassed benzene (5.0 ml) was stirred at r.t. for 30 min. By the addition of dry degassed diethyl ether (15 ml) the white solid **10** precipitated, which was collected on a sintered glass filter and subsequently washed with diethyl ether (10 ml × 2). **10** (58 mg, 6.8×10^{-2} mmol, 45%): m.p. 191.5–192.0°C. ^{1}H-NMR (400 MHz, d_8-THF); δ 3.50–3.60 (m, 2H), 3.74 (t, $J = 10.3$ Hz, 1H), 3.91 (t, $J = 9.6$ Hz, 1H), 4.21 (dd, $J = 5.1$, 10.3 Hz, 1H), 4.27 (d, $J = 14.4$ Hz, 1H), 4.53 (t, $J = 6.8$ Hz, 1H), 4.82 (d, $J = 14.4$ Hz, 1H), 5.56 (s, 1H), 6.25 (d, $J = 6.8$ Hz, 1H), 6.44–7.89 (m, 25H) ppm. ^{13}C-NMR (100 MHz, d_8-THF): δ 36.7, 66.4, 66.7, 68.4, 75.7 (d, $J = 9.1$ Hz), 80.2, 101.5, 105.4, 122.2–141.6 (19 carbons), 144.4, 174.0 ppm. ^{31}P-NMR (161.9 MHz, d_8-THF): δ 108.5 ppm. Anal. Calc. for $C_{39}H_{35}INO_5PPd$: C, 54.34; H, 4.09; N, 1.62 (Calc. for $C_{39}H_{35}INO_5PPd \cdot I_2$: C, 41.98; H, 3.16; N, 1.26). Found: C, 41.87; H, 3.22; N, 1.07%.

4.8. Synthesis of [PhPd(**1f**)]$^+$ OTf^- (**11**)

Silver triflate (12 mg, 4.0×10^{-2} mmol) was added to a vigorously stirred solution of the complex **10** (18 mg, 2.0×10^{-2} mmol) in d_8-THF at r.t. Stirring was continued for 10 min, during which period a white precipitate was formed. The supernatant was rapidly transferred by a syringe into an NMR tube and the formation of the complex **11** was confirmed by NMR spectroscopies. ^{1}H-NMR (400 MHz, d_8-THF): δ 3.52–3.80 (m, 3H), 3.93 (d, $J = 12.5$ Hz, 1H), 4.02 (t, $J = 9.7$ Hz, 1H), 4.18 (dd, $J = 4.4$, 10.9 Hz, 1H), 4.19 (d, $J = 12.5$ Hz, 1H),

Table 4
Crystallographic data for **2**

Empirical formula	$C_{58}H_{60}Cl_4N_2O_{10}P_2Pd_2 \cdot CH_2Cl_2$
Formula weight	1446.61
Crystal system	Monoclinic
Space group	$P2_1$
Crystal color	Yellow
Unit cell dimensions	
a (Å)	12.373(7)
b (Å)	11.009(7)
c (Å)	23.694(7)
β (°)	92.29(4)
V (Å^3)	3224(2)
Z	2
D_{calc} (g cm^{-3})	1.490
$F(000)$	1468
μ_{cal} (cm^{-1})	9.11
Max. 2θ (°)	55
No. of reflections	7967
No. of independent reflections	7785
No. of data used ($I > 3\sigma(I)$)	5580
No. of parameters refined	793
Reflection/parameter ratio	7.04
R	0.062
R_w	0.067
Goodness of fit	1.47
Max shift/error in final cycle	0.13
Maximum peak in final difference map (e Å^{-3})	0.94
Minimum peak in final difference map (e Å^{-3})	−1.25

4.79 (t, $J = 7.2$ Hz, 1H), 5.58 (s, 1H), 6.48 (d, $J = 7.2$ Hz, 1H), 6.65–7.84 (m, 25H) ppm. ^{13}C-NMR (100 MHz, d_8-THF): δ 35.5, 66.3, 66.8, 68.4, 75.6 (d, $J = 7.4$ Hz), 81.3, 101.5, 106.3, 124.8–138.5 (19 carbons), 146.2 (d, $J = 2.0$ Hz), 175.1 ppm. ^{31}P-NMR (161.9 MHz, d_8-THF): δ 119.2 ppm.

4.9. Crystallography

Single crystal ($C_{58}H_{60}Cl_4N_2O_{10}P_2Pd_2 \cdot CH_2Cl_2$: **2a**·**2b**·$CH_2Cl_2$) suitable for X-ray analysis was prepared by recrystallization from CH_2Cl_2–Et_2O. Diffraction data was collected on a Rigaku AFC-7R four-circle automated diffractometer with Mo–K_α ($\lambda = 0.7109$ Å) radiation and a graphite monochromator at 23°C using the ω–2θ scan technique. Details of the X-ray diffraction study are summarized in Table 4.

For a structure analysis and refinement, computations were performed using TEXSAN [19] crystallographic software package of molecular structure. Neutral atom scattering factors were taken from Ref. [20]. Anomalous dispersion effects were included in F_{calc} [21]; the values of $\Delta f'$ and $\Delta f''$ were those of Ref. [22]. The structure was solved by the direct methods. Full-matrix least squares refinement (on F) was employed with anisotropic thermal parameters for all non-hydrogen atoms. Hydrogen atoms were included but not refined. The weighing scheme $\omega = 1/\sigma^2(F_o)$ with $\sigma(F_o)$ from counting statistics gave satisfactory agreement analyses.

5. Supplementary material

Crystallographic data for the structural analysis has been deposited with the Cambridge Crystallographic Data Centre, CCDC no. 136731. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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[13] Combustion analytical data of the new complexes **8** and **10** did not fit to the expected structure even after several recrystallization of the compounds obtained in several runs. However, these fit well if it was assumed that these complexes have some I_2 in their molecules as shown in experimental section.

[14] No coupling ($J = 0$ Hz) was observed between the phosphorus and *ipso*-carbon in both complexes **8** and **9**. The larger coupling constants over 100 Hz between a phosphorus nucleus and trans *ipso*-carbon of related complexes have been reported [6d].

[15] ^{13}C-NMR spectrum of **11** showed the coupling constant ($J = 2.0$ Hz) between a phosphorus and an *ipso*-carbon.

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