

Complete Retention of Z Geometry in Allylic Substitution Catalyzed by an Iridium Complex

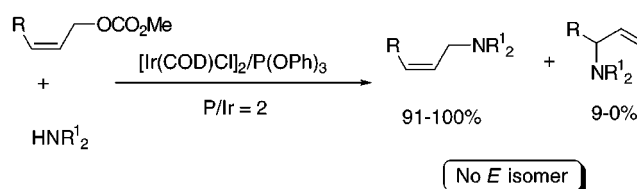
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ABSTRACT



The Z geometry of methyl (Z)-3-monosubstituted-2-alkenyl carbonate was completely retained in iridium complex-catalyzed allylic amination. The reaction of methyl (Z)-2-nonenyl carbonate with piperidine in the presence of a catalytic amount of $[\text{Ir}(\text{COD})\text{Cl}]_2$ and $\text{P}(\text{OPh})_3$ at 50 °C for 2 h gave a 98:2 mixture of (Z)-1-(2-nonenyl)piperidine and 1-(1-*n*-hexyl-2-propenyl)piperidine in 86% yield. No E isomer was obtained. Various (Z)-allylic amines were obtained in 91–100% selectivity by allylic amination of methyl (Z)-3-monosubstituted-2-alkenyl carbonate.

The chemistry of (π -allyl)metal complexes is central in organic synthesis.¹ The reaction of a (π -allyl)metal complex with a nucleophile provides various synthetically useful processes. One of the important aspects of the chemistry of (π -allyl)metal complexes is syn–anti isomerization² via a π – σ – π process which greatly affects the regio- and stereoselectivity of allylic substitution. Nucleophilic attack at the unsubstituted allylic terminus of a terminally monosubstituted syn π -allyl complex gives an (*E*)-alkene, while that of an anti π -allyl complex gives a (*Z*)-alkene.

A wide variety of transition-metal complexes are reported to be a catalyst for allylic substitution. Of the metal complexes studied, palladium is the most general and versatile catalyst.³ It is well-known that a syn (π -allyl)-

palladium complex is thermodynamically more stable than an anti complex.⁴ (π -Allyl)palladium complexes undergo a rapid syn–anti isomerization prior to the nucleophilic attack. Thus, palladium complex catalyzed allylic substitution of (Z)-3-monosubstituted-2-alkenyl esters resulted in the loss of Z geometry.⁵ A mixture of (*E*)- and (*Z*)-alkenes is obtained. A limited example of the retention of Z geometry has been reported.⁶ Åkermarck found that 2,9-disubstituted-1,10-phenanthroline could induce a preference for the anti configuration and reported Z-selective allylic alkylation of (Z)-2-hexenyl acetate.⁷ (Z)-Alkene was obtained in moderate

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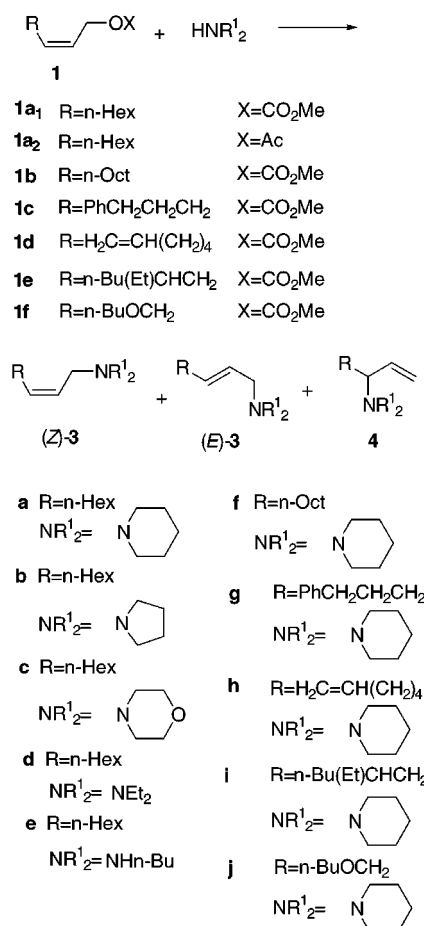
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to good selectivity, but the formation of (*E*)-alkene could not be suppressed completely.

We reported that an iridium complex is a new and efficient catalyst for allylic alkylation.⁸ The regioselectivity of iridium complex catalyzed allylic alkylation depends on the geometry of the allylic system, i.e., the regioselectivity of alkylation of a syn (π -allyl)iridium intermediate is different from that of an anti (π -allyl)iridium intermediate. The alkylation occurred prior to syn–anti isomerization. This result prompted us to investigate *Z*-selective allylic substitution. We first succeeded with the complete retention of *Z* geometry in the allylic amination^{5a,c,9} of (*Z*)-3-monosubstituted-2-alkenyl carbonate (Scheme 1).

Scheme 1



The reaction of methyl (*Z*)-2-nonenyl carbonate (**1a₁**) with piperidine in the presence of a catalytic amount of [Ir(COD)-Cl]₂ and P(OPh)₃ gave a mixture of (*Z*)-**3a** and **4a**. The reaction using piperidine as a solvent at 50 °C for 2 h gave a 98:2 mixture of (*Z*)-**3a** and **4a** in 86% yield (Table 1; entry 1).¹⁰ No *E* isomer was obtained. A large excess of piperidine

Table 1. Reaction of **1a** with Piperidine^a

entry no.	substrate	catalyst ^b	P/Ir	time/h	yield/% ^c	(<i>Z</i>)- 3a / (<i>E</i>)- 3a / 4a ^d
1	1a₁	A/P(OPh) ₃	2	2	86	98/0/2
2 ^e	1a₁	A/P(OPh) ₃	2	24	14	92/0/8
3	1a₁	A/P(OEt) ₃	2	24	7	96/0/4
4	1a₁	A/PPh ₃	2	24	31	8/78/14
5	1a₁	A	0	23	15	100/0/0
6	1a₁	A/P(OPh) ₃	1	2	88	98/0/2
7	1a₁	A/P(OPh) ₃	3	4	69	97/0/3
8	1a₂	A/P(OPh) ₃	2	24	43	97/0/3
9 ^f	1a₁	B/P(OPh) ₃	2	2	90	97/0/3
10 ^g	1a₁	C/P(OPh) ₃	2	3	83	97/0/3

^a A mixture of **1a** (2 mmol), [Ir(COD)Cl]₂ (0.04 mmol), ligand, and piperidine (5 mL) was stirred under argon at 50 °C. ^b Catalyst legend: A, [Ir(COD)Cl]₂; B, [Ir(COD)₂]BF₄; C, [Ir(COD)OMe]₂. ^c Isolated yield. ^d Determined by GLC. ^e Piperidine (10 mmol) in refluxing THF (5 mL). ^f Catalyst 0.04 mmol. ^g Catalyst 0.04 mmol.

was necessary for high yield. The reaction of 5 equiv of piperidine with **1a₁** at reflux in THF for 24 h gave products in 14% yield (entry 2). The starting material was recovered in 80% yield. P(OPh)₃ was the most efficient ligand. The use of P(OEt)₃ and PPh₃ decreased the yield of products (entries 3 and 4). The ratio of P to Ir was also important. The reaction of 1 or 2 equiv of P(OPh)₃ with Ir gave products in good yield (entries 1 and 6), while that of 3 equiv of P(OPh)₃ with Ir resulted in a slight decrease of the yield (entry 7). [Ir(COD)₂]BF₄/P(OPh)₃ and [Ir(COD)OMe]₂/P(OPh)₃ showed comparable catalytic activities and selectivities (entries 9 and 10). Carbonate was more reactive than acetate. The reaction of (*Z*)-2-nonenyl acetate (**1a₂**) with piperidine gave a decrease in the yield of products at prolonged reaction time (entry 8).

The reactions of **1a₁** with various amines were examined (Table 2). Amines were used as a solvent. Allylic amines

Table 2. Reaction of **1a₁** with Amines^a

entry no.	amine	product	yield/% ^b	(<i>Z</i>)- 3 /(<i>E</i>)- 3 / 4 ^c
1 ^d	pyrrolidine	3b , 4b	71	94/0/6
2 ^e	morpholine	3c , 4c	83	95/0/5
3 ^f	diethylamine	3d , 4d	62	98/0/2
4 ^g	<i>n</i> -butylamine	3e , 4e	23	96/0/4

^a A mixture of **1a₁** (2 mmol), [Ir(COD)Cl]₂ (0.04 mmol), P(OPh)₃ (0.16 mmol), and amine (5 mL) was stirred under argon at 50 °C. ^b Isolated yield. ^c Determined by GLC. ^d Reacted for 3 h. ^e Reacted for 24 h. ^f [Ir(COD)Cl]₂ (0.08 mmol) and P(OPh)₃ (0.32 mmol). Reacted for 4 h. ^g Reacted for 3 h.

(*Z*)-**3b–e** were obtained in 94–98% selectivity. No *E* isomer was obtained. The structure of the amine had a substantial

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(10) **General Procedure for Allylic Amination of Allylic Esters.** A typical procedure is described for the reaction of **1a₁** with piperidine. A mixture of methyl (*Z*)-2-nonenyl carbonate (**1a₁**; 400 mg, 2.0 mmol), triphenyl phosphite (49.6 mg, 0.16 mmol), [Ir(COD)Cl]₂ (26.9 mg, 0.04

effect on the yield of products. The reactions of **1a₁** with secondary amines gave the corresponding products in good yield (entries 1–3). In contrast to results obtained in the reactions with secondary amines, the reaction of **1a₁** with *n*-butylamine decreased the yield considerably (entry 4). Bulky amines are therefore necessary for high yields of (*Z*)-**3**.¹¹

As shown in Table 3, (*Z*)-**1b–f** were successfully reacted with piperidine to give (*Z*)-**3f–j** with high selectivities. No *E* isomer was obtained. Terminal alkene was tolerated in

Table 3. Reaction of **1** with Piperidine^a

entry no.	substrate	product	time/h	yield/% ^b	(<i>Z</i>)- 3 /(<i>E</i>)- 3 / 4 ^c
1	1b	3f, 4f	8	83	94/0/6
2	1c	3g, 4g	15	81	91/0/9
3	1d	3h, 4h	3	89	100/0/0
4 ^d	1e	3i, 4i	5	70	100/0/0
5	1f	3j, 4j	4	78	98/0/2

^a A mixture of **1** (2 mmol), [Ir(COD)Cl]₂ (0.04 mmol), P(OPh)₃ (0.16 mmol), and piperidine (5 mL) was stirred under argon at 50 °C. ^b Isolated yield. ^c Determined by GLC. ^d [Ir(COD)Cl]₂ (0.08 mmol) and P(OPh)₃ (0.32 mmol).

the allylic amination. The reaction of **1d** with piperidine was regiospecific to give (*Z*)-**3h** in 89% yield (entry 3). The steric congestion around the carbon–carbon double bond affected the reaction time and the yield of the product. The reaction

mmol), and piperidine (5.0 mL) was stirred at 50 °C for 2 h under an Ar atmosphere. The progress of the reaction was monitored by GLC. After **1a₁** was consumed, the reaction mixture was diluted with ether. The ethereal solution was extracted with 6 M HCl. The combined acidic layers were neutralized with NaOH and extracted with ether. The organic layer was dried with MgSO₄ and filtered. After evaporation of the solvent, the residue was purified by column chromatography (*n*-hexane/ethyl acetate (70/30)) to give (*Z*)-**3a** and **4a** (360 mg; yield 86%). (*Z*)-**1**-(2-Nonenyl)piperidine ((*Z*)-**3a**): ¹H NMR (400 MHz, C₆D₆) δ 1.00 (t, *J* = 7.0 Hz, 3H), 1.30–1.51 (m, 10H), 1.66 (quintet, *J* = 5.1 Hz, 4H), 2.19 (q, *J* = 7.1 Hz, 2H), 2.48 (t, *J* = 5.1 Hz, 4H), 3.09 (d, *J* = 6.7 Hz, 2H), 5.64 (dt, *J* = 11.0, 7.3, 1.6 Hz, 1H), 5.77 (dt, *J* = 11.0, 6.7, 1.5 Hz, 1H); ¹³C NMR (67.8 MHz, CDCl₃) δ 14.0, 22.6, 24.4, 26.0 (2C), 27.4, 28.9, 29.5, 31.7, 54.5 (2C), 55.9, 126.4, 132.8. Anal. Calcd for C₁₄H₂₇N: C, 80.31; H, 13.00; N, 6.69. Found: C, 80.07; H, 13.01; N, 6.65. **1**-(1-*n*-Hexyl-2-propenyl)piperidine (**4a**): Compound **4a** could not be isolated in pure form. A partial ¹H NMR spectrum was obtained from the mixture of (*Z*)-**3a**. ¹H NMR (400 MHz, C₆D₆): δ 5.12 (dd, *J* = 17.2, 2.2 Hz, 1H), 5.21 (dd, *J* = 10.3, 2.2 Hz, 1H), 5.83 (ddd, *J* = 17.2, 10.3, 6.9 Hz, 1H).

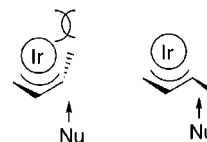
(11) Cone angles of secondary amines are larger than those of primary amines; see: Seligson, A. L.; Troglor, W. C. *J. Am. Chem. Soc.* **1991**, *113*, 2520.

(12) See reference 8a and references therein.

of **1e** with piperidine for 22 h gave (*Z*)-**3i** exclusively in 33% yield. Increasing the amount of the catalyst to 8 mol % accelerated the reaction to give (*Z*)-**3i** in 70% yield (entry 4). The alkoxy functionality was also tolerated and did not alter the regio- and stereoselectivity of the allylic amination; allylic amine (*Z*)-**3j** was obtained with 98% selectivity (entry 5).

As seen in allylic alkylations,^{8a} the selectivity of the allylic amination depends on the geometry of the allyl system. The reaction of (*E*)-**1a₁** with piperidine at 50 °C for 2 h gave a 28:1:71 mixture of (*E*)-**3a**, (*Z*)-**3a**, and **4a** in 93% yield. The *syn*-(*π*-allyl)- and *anti*-(*π*-allyl)iridium intermediates gave different results. This difference in regioselectivity is reasonably explained as follows. When the amine approaches the substituted allylic terminus of the *anti*-(*π*-allyl)iridium intermediate, the substituent and iridium moiety are close together and thereby increase steric repulsion (Scheme 2).¹²

Scheme 2



The transition state of the amination at the substituted allylic terminus of the *anti*-(*π*-allyl)iridium intermediate is therefore less stable than that of the *syn*-(*π*-allyl)iridium intermediate. Thus, amination of the *anti*-(*π*-allyl)iridium intermediate preferentially occurs at the unsubstituted allylic terminus.

In summary, we have succeeded with the complete retention of *Z* geometry in the allylic amination. This unique feature of iridium catalysis will have wide synthetic application.

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Supporting Information Available: Text giving experimental procedures and compound characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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