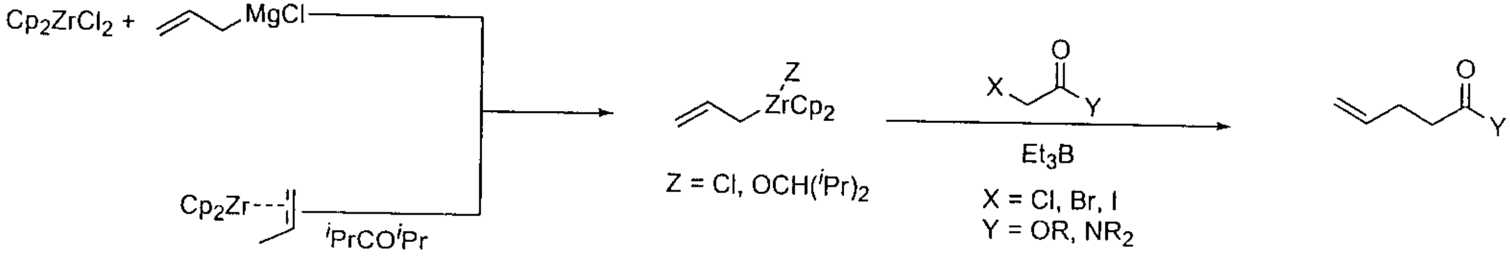
Triethylborane-Induced Radical Allylation Reaction with Zirconocene-Olefin Complex

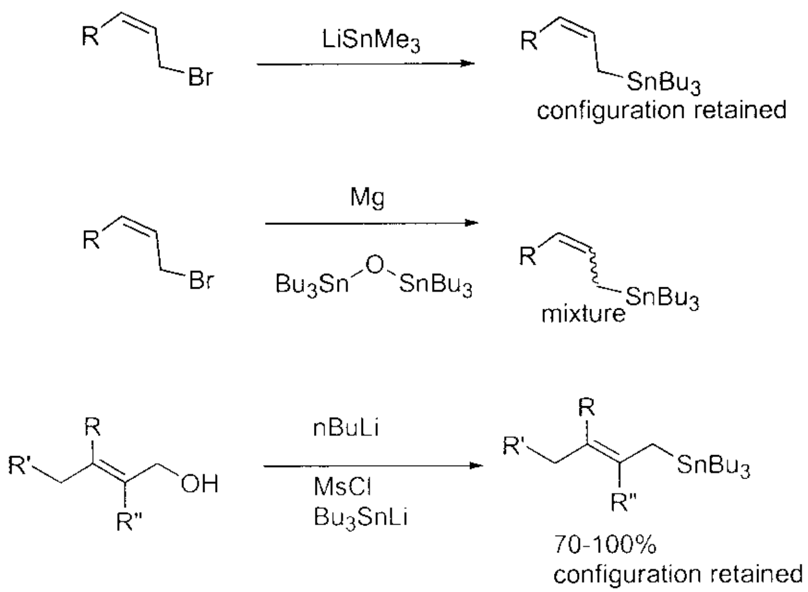
Hirano, K.; Fujita, K.; Shiokubo, H.; Oshima, K. *Org. Lett.* **2004**, 6(4), 593.



Allylstannanes

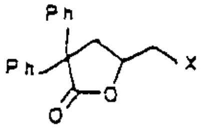
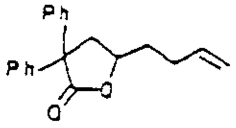
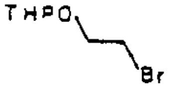
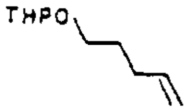
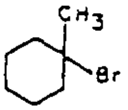
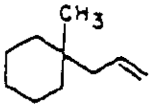
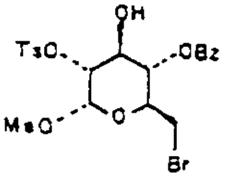
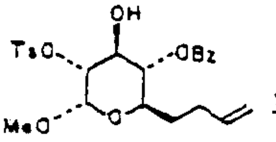
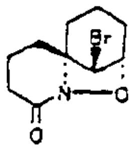
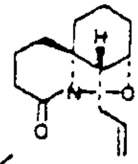
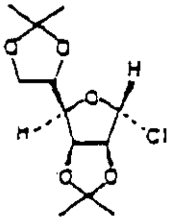
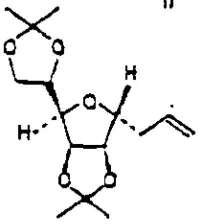
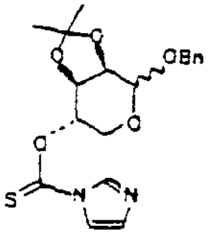
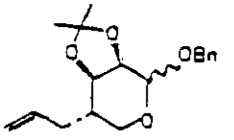
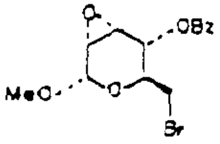
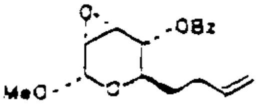
-tin reagents dominate free radical chemistry
-toxic
-problems with removing tin from product

Preparation:



Weigand, S.; Bruckner, R. *Synthesis* **1996**, 475.

Allylstannanes

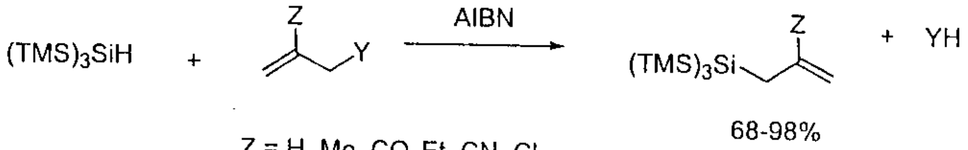
SUBSTRATE	METHOD^{a}	PRODUCT	YIELD^{b}
		 2	
1 X = Br	A B		88 82
3 X = SePh	A B		84 75
 4	A	 5	(98)
 6	A	 7	(90)
 8	A B	 9	74 60
 10	A B	 11	93 88
 12	A B	 13	79 68
 14	A B	 15	27 68
 16	A	 17	76

Yates, J.; Keck, G. *J. Am. Chem. Soc.* **1982**, 104(21), 5829.

Allylsilanes

-$(Me_3Si)_3SiH$-most widely used alternative to tin
- -less toxic
- -produces fewer byproducts
- Si-H bond is 5 kcal/mol stronger than Sn-H bond
- -high cost

Preparation:



Z = H, Me, CO_2Et, CN, Cl

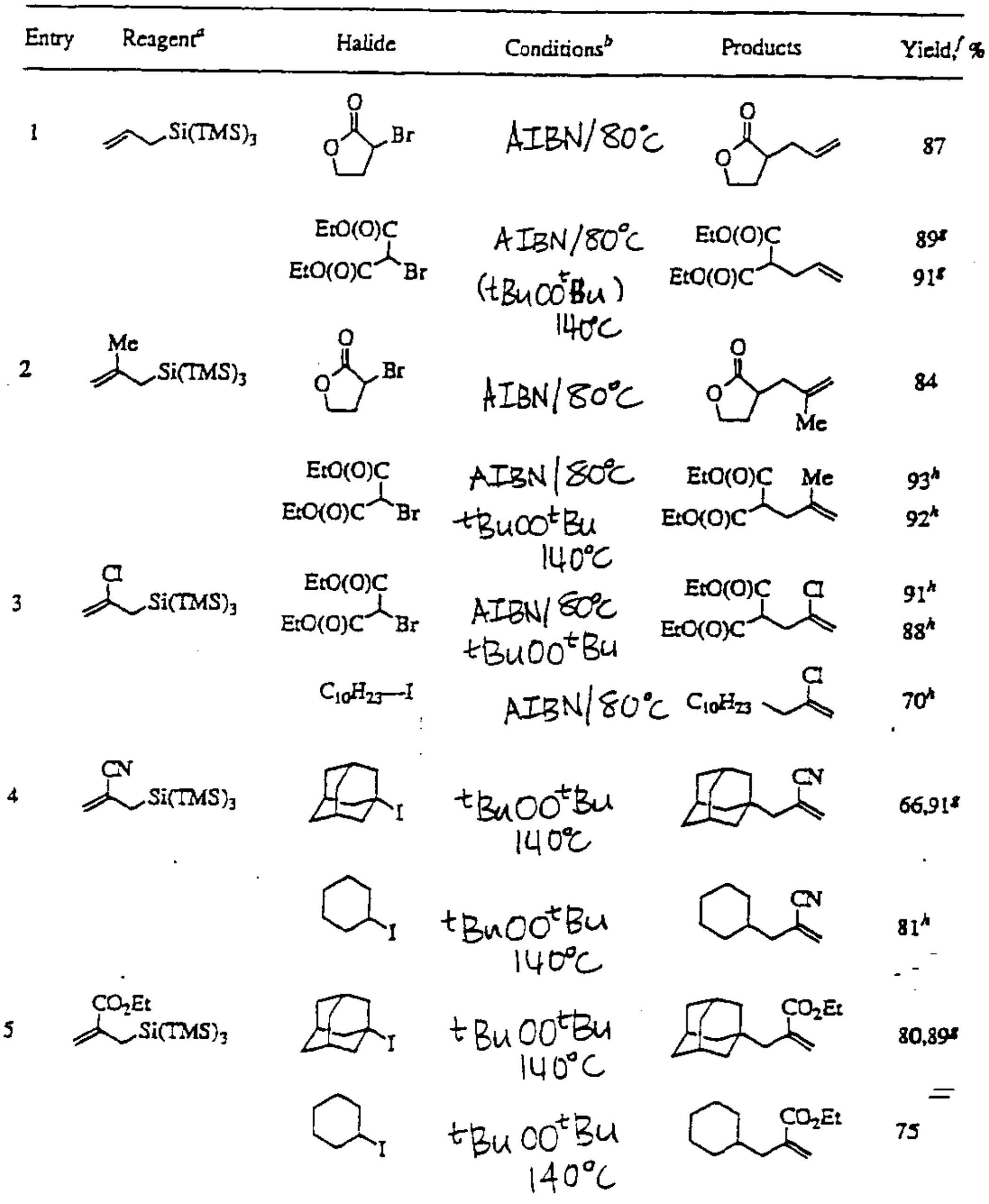
Y = PhS, $PhSO_2$

-used b/c of rapid β-elimination

Ballestri, M.; Vecchi, D.; Chatgilialoglu, C.; Curran, D.P. *Tetrahedron Letters* **1996,** 37(35), 6383.

Allylsilanes

Table 1. Reactions of allyl and 2-functionalized allyl tris(trimethylsilyl)silane with alkyl halides



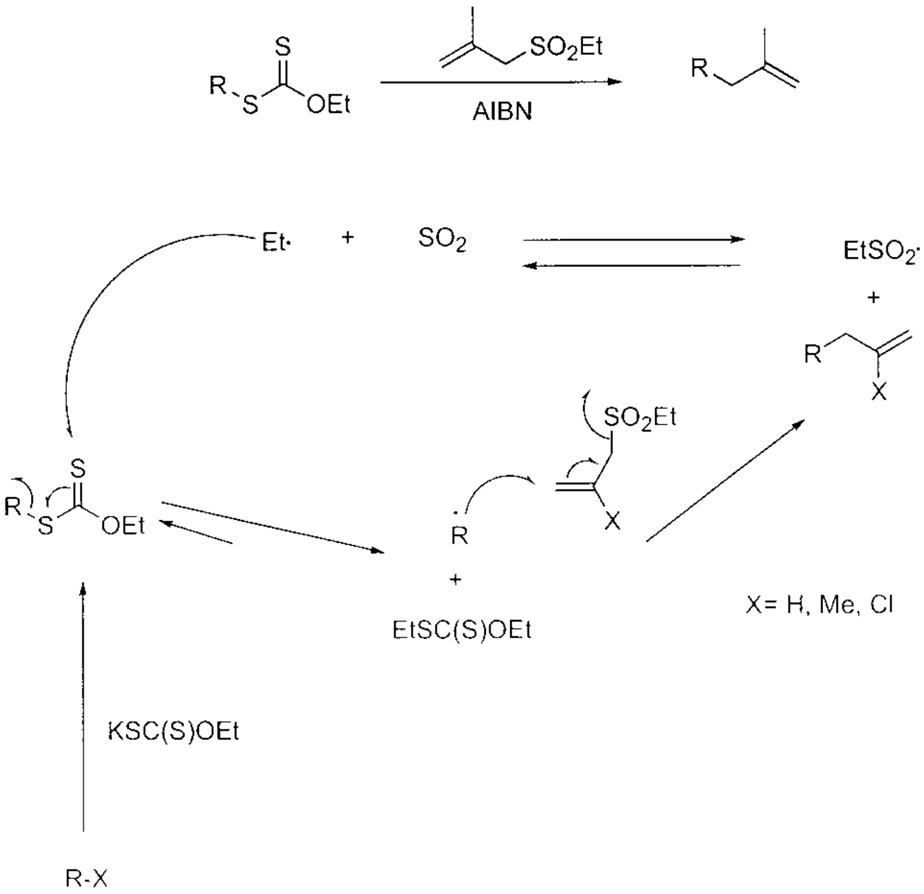
Entry	Reagent[a]	Halide	Conditions[b]	Products	Yield,[f] %
1			AIBN/80°C		87
			AIBN/80°C (tBuOO^{t}Bu) 140°C		89[g] 91[g]
2			AIBN/80°C		84
			AIBN/80°C tBuOO^{t}Bu 140°C		93[h] 92[h]
3			AIBN/80°C tBuOO^{t}Bu		91[h] 88[h]
		$C_{10}H_{23}$—I	AIBN/80°C		70[h]
4			tBuOO^{t}Bu 140°C		66,91[g]
			tBuOO^{t}Bu 140°C		81[h]
5			tBuOO^{t}Bu 140°C		80,89[g]
			tBuOO^{t}Bu 140°C		75

-In contrast to allylstannane additions, polar effects of the radical precursor (RX) and the allylsilane must be matched.

Ballestri, M.; Vecchi, D.; Chatgilialoglu, C.; Curran, D.P. *Tetrahedron Letters* **1996**, 37(35), 6387.

Dithiocarbonates

- replacing halogens with a dithiocarbonate group (xanthate)
  - exhibits affinity to radicals
  - less subject to ionic degradation compared to Iodides

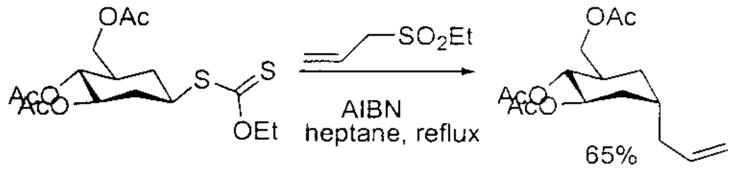


X = halide, tosylate, mesylate

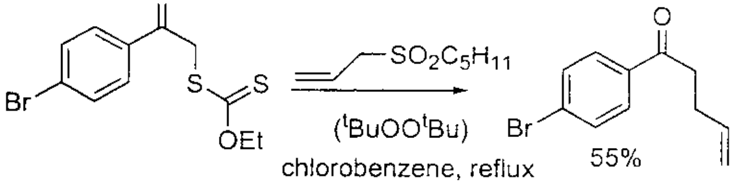
Sire, B.; Seguin, S.; Zard, S. *Angew Chem Int.Ed.* 1998, 37(20), 2864

Dithiocarbonates

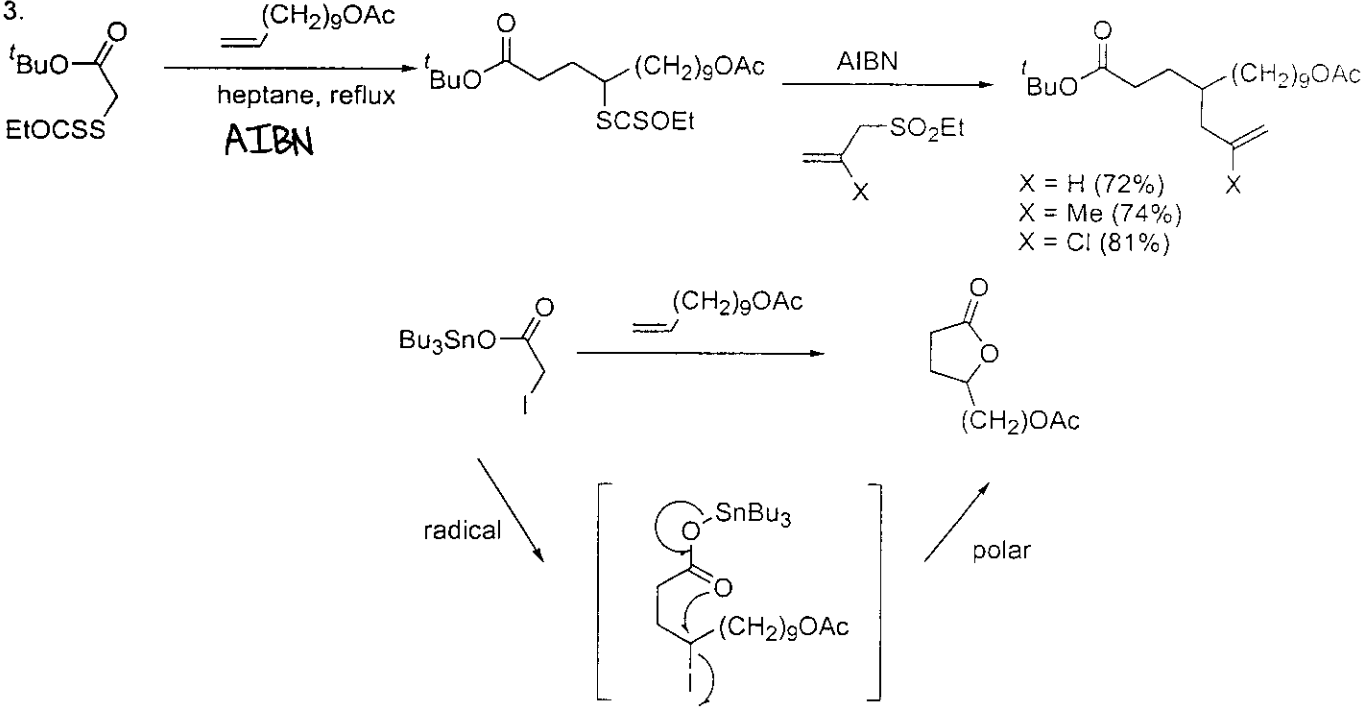
1.



2.



3.



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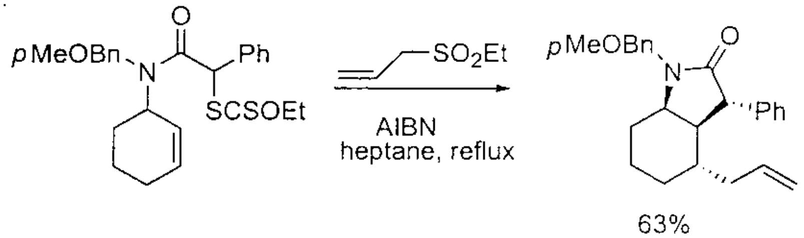
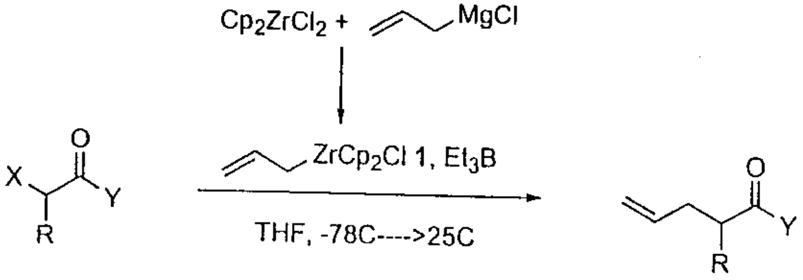


Sire, B.; Seguin, S.; Zard, S. *Angew.Chem.Int.Ed.* **1998**, 37(20), 2864.
Chang, C.-T.; Curran, D.P. *J. Org. Chem.* **1989**, 54 (13), 3141.

Allylation Reactions with Allylzirconium Reagent



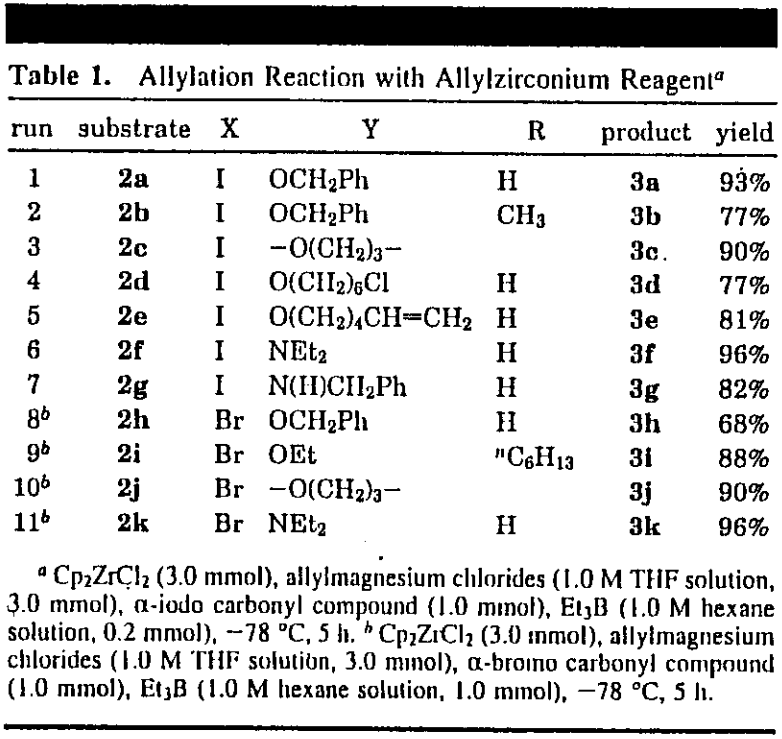


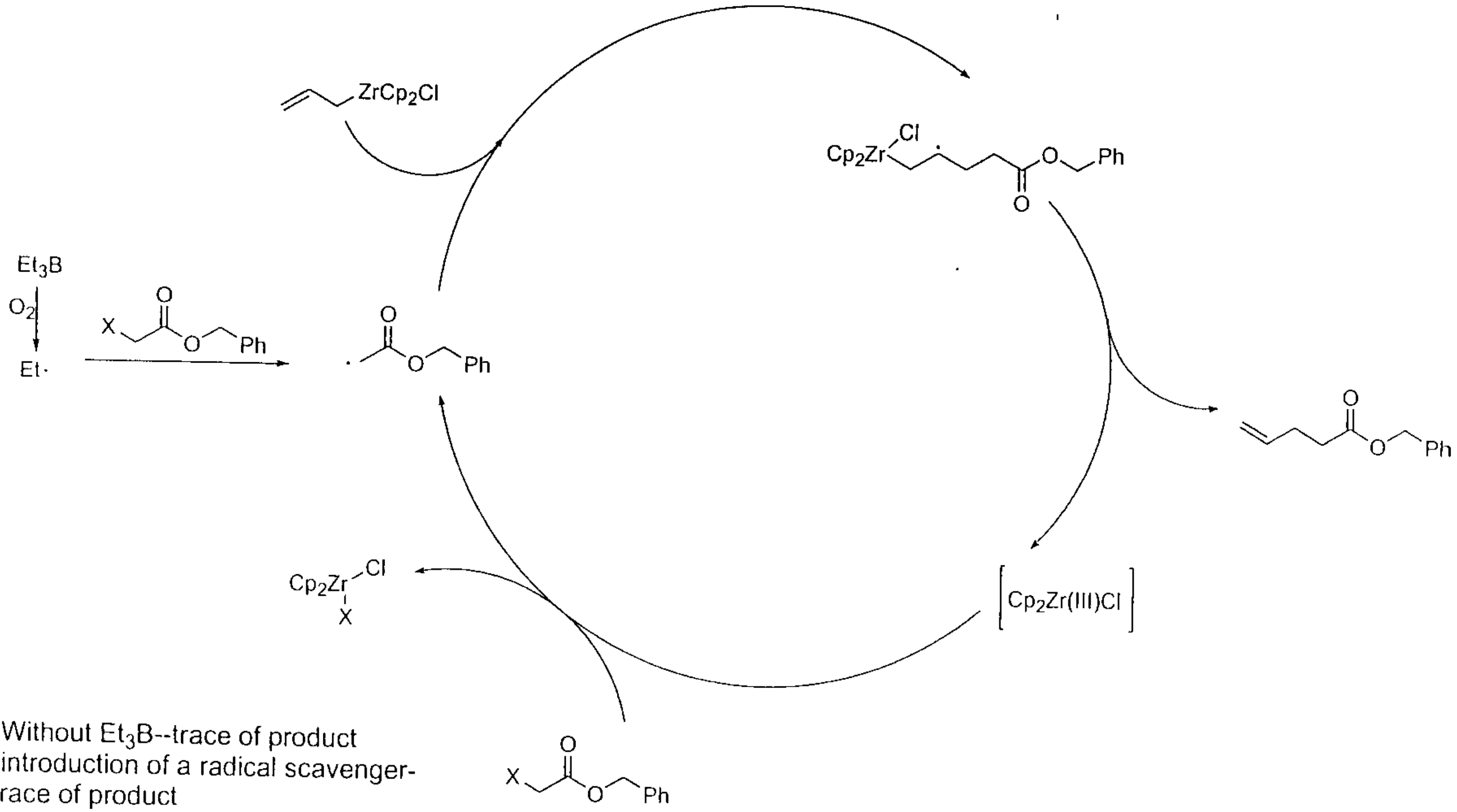
Table 1. Allylation Reaction with Allylzirconium Reagent[a]

run	substrate	X	Y	R	product	yield
1	**2a**	I	OCH_2Ph	H	**3a**	93%
2	**2b**	I	OCH_2Ph	CH_3	**3b**	77%
3	**2c**	I	$-O(CH_2)_3-$		**3c**	90%
4	**2d**	I	$O(CH_2)_6Cl$	H	**3d**	77%
5	**2e**	I	$O(CH_2)_4CH{=}CH_2$	H	**3e**	81%
6	**2f**	I	NEt_2	H	**3f**	96%
7	**2g**	I	$N(H)CH_2Ph$	H	**3g**	82%
8[b]	**2h**	Br	OCH_2Ph	H	**3h**	68%
9[b]	**2i**	Br	OEt	$^nC_6H_{13}$	**3i**	88%
10[b]	**2j**	Br	$-O(CH_2)_3-$		**3j**	90%
11[b]	**2k**	Br	NEt_2	H	**3k**	96%

[a] Cp_2ZrCl_2 (3.0 mmol), allylmagnesium chlorides (1.0 M THF solution, 3.0 mmol), α-iodo carbonyl compound (1.0 mmol), Et_3B (1.0 M hexane solution, 0.2 mmol), −78 °C, 5 h. [b] Cp_2ZrCl_2 (3.0 mmol), allylmagnesium chlorides (1.0 M THF solution, 3.0 mmol), α-bromo carbonyl compound (1.0 mmol), Et_3B (1.0 M hexane solution, 1.0 mmol), −78 °C, 5 h.

Org. Lett. 2004, 6(4), 593.

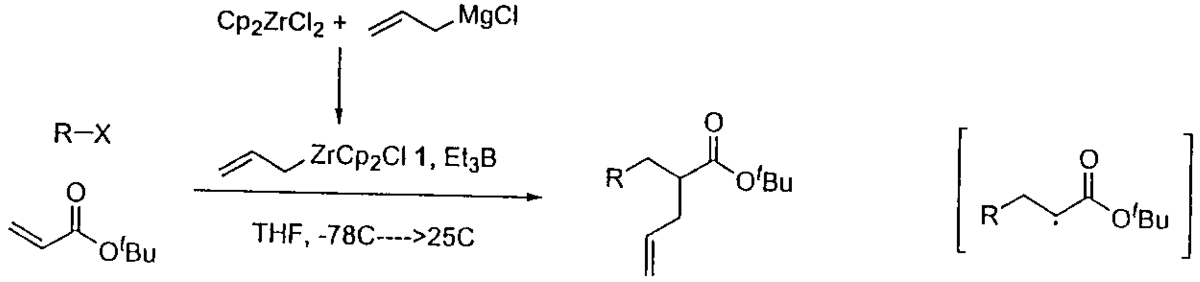
Proposed Mechanism



-Without Et$_3$B--trace of product
-introduction of a radical scavenger-
trace of product

Org. Lett. **2004**, 6(4), 593.

3-Component Coupling Reactions



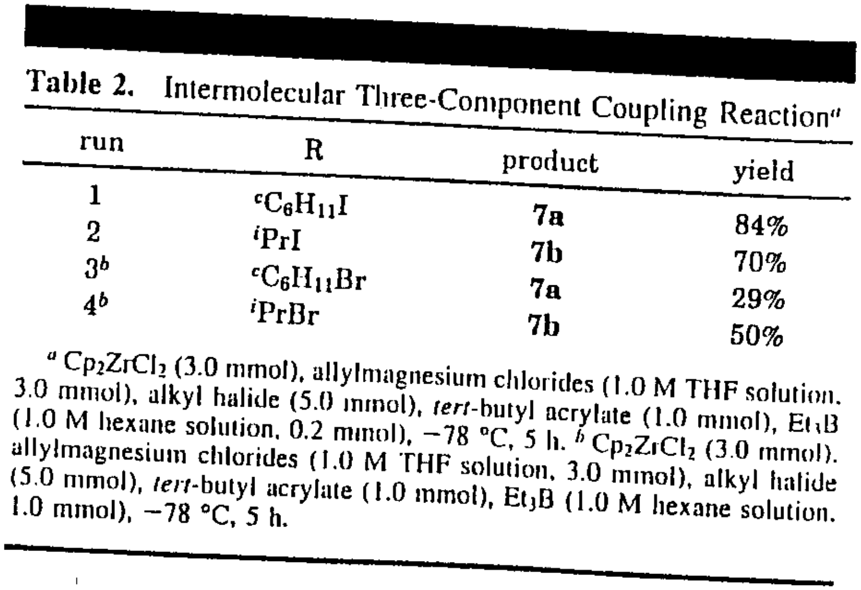


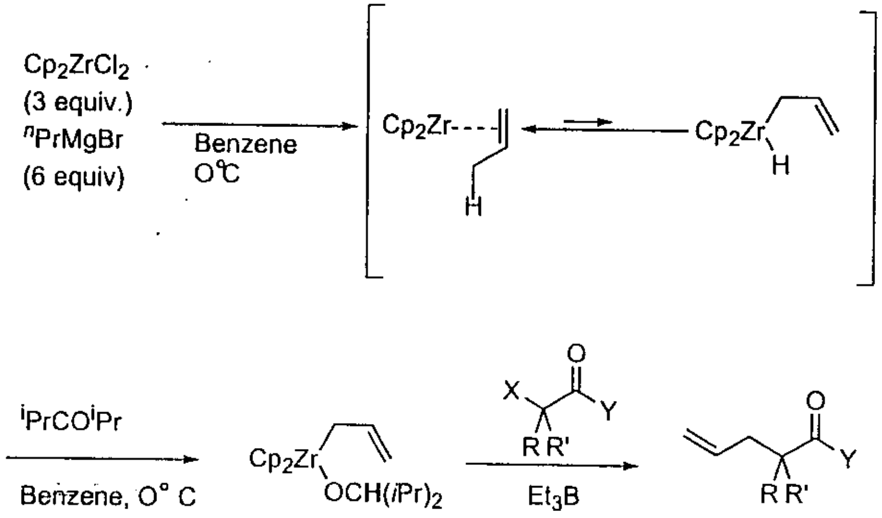
Table 2. Intermolecular Three-Component Coupling Reaction[a]

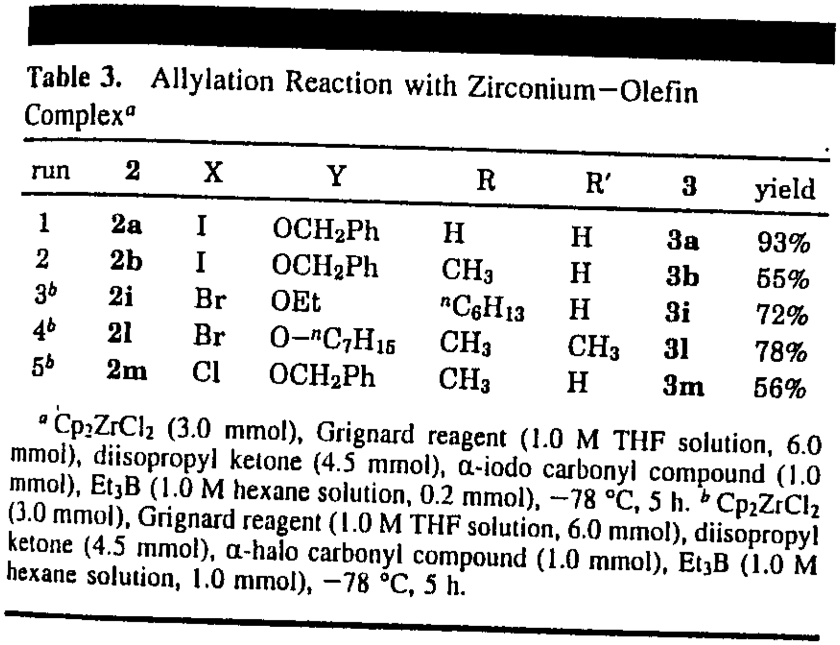
run	R	product	yield
1	$^cC_6H_{11}I$	**7a**	84%
2	^iPrI	**7b**	70%
3[b]	$^cC_6H_{11}Br$	**7a**	29%
4[b]	^iPrBr	**7b**	50%

[a] Cp_2ZrCl_2 (3.0 mmol), allylmagnesium chlorides (1.0 M THF solution, 3.0 mmol), alkyl halide (5.0 mmol), *tert*-butyl acrylate (1.0 mmol), Et_3B (1.0 M hexane solution, 0.2 mmol), −78 °C, 5 h. [b] Cp_2ZrCl_2 (3.0 mmol), allylmagnesium chlorides (1.0 M THF solution, 3.0 mmol), alkyl halide (5.0 mmol), *tert*-butyl acrylate (1.0 mmol), Et_3B (1.0 M hexane solution, 1.0 mmol), −78 °C, 5 h.

Org. Lett. **2004**, 6(4), 593.

Allylation: Zirconium-Olefin Complex





[redacted]

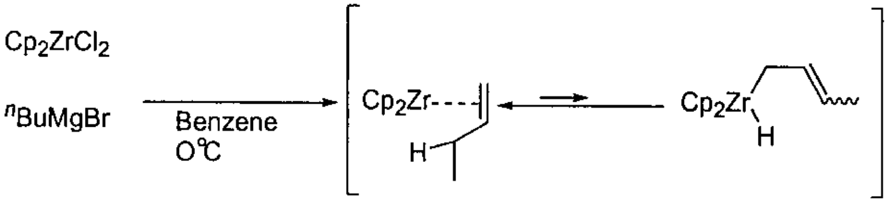
Table 3. Allylation Reaction with Zirconium–Olefin Complex[a]

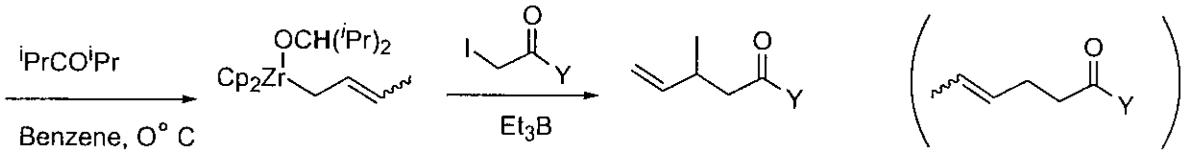
run	2	X	Y	R	R′	3	yield
1	**2a**	I	OCH_2Ph	H	H	**3a**	93%
2	**2b**	I	OCH_2Ph	CH_3	H	**3b**	55%
3[b]	**2i**	Br	OEt	${}^{n}C_6H_{13}$	H	**3i**	72%
4[b]	**2l**	Br	$O{-}{}^{n}C_7H_{15}$	CH_3	CH_3	**3l**	78%
5[b]	**2m**	Cl	OCH_2Ph	CH_3	H	**3m**	56%

[a] Cp_2ZrCl_2 (3.0 mmol), Grignard reagent (1.0 M THF solution, 6.0 mmol), diisopropyl ketone (4.5 mmol), α-iodo carbonyl compound (1.0 mmol), Et_3B (1.0 M hexane solution, 0.2 mmol), −78 °C, 5 h. [b] Cp_2ZrCl_2 (3.0 mmol), Grignard reagent (1.0 M THF solution, 6.0 mmol), diisopropyl ketone (4.5 mmol), α-halo carbonyl compound (1.0 mmol), Et_3B (1.0 M hexane solution, 1.0 mmol), −78 °C, 5 h.

Org. Lett. 2004, 6(4), 593.

Crotylation: Zirconium-Olefin Complex





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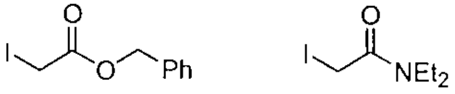

99%

65%

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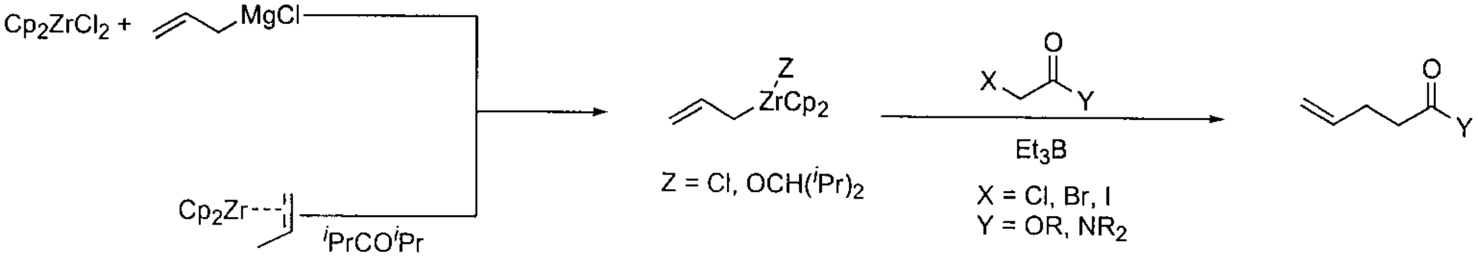
Conclusions:



- In the allylzirconium allylation reactions, the key steps are homolytic cleavage of the C-Zr bond and halogen abstraction by the $Cp_2ZrCl(III)$.

- Protocol is general while reactive Iodides as well as less reactive Bromides and Chlorides give moderate to high yields of allylated products.

- In radical allylation reactions, allylzirconium species can be a nice alternative to allylstannanes and allylsilanes.

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