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MICHAEL TYPE ADDITION OF HALIDES TO ALKYNYL(PHENYL)IODONIUM TETRAFLUOROBORATES. STEREOSELECTIVE SYNTHESIS OF (Z)-β-HALOVINYL(PHENYL)IODONIUM HALIDES

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Summary: Michael type addition of halide ions (Cl^- and Br^-) to alkynyl(phenyl)iodonium tetrafluoroborates (**1**) under acidic conditions proceeds in a completely stereoselective manner and affords (Z)-β-halovinyl(phenyl)iodonium halides (**2**), potential progenitors for generating α-haloalkylidenecarbenes, in high yields.

In spite of a large number of recent studies on the reaction of alkylidenecarbenes, the available data do not shed light on the migratory aptitude of α-heteroatom substituents.[1,2] We have reported that alkylidenecarbenes with α-organosulfur substituents, generated by either a reductive α-elimination of vinyl(phenyl)iodonium tetrafluoroborates with bases or a Michael type addition of nucleophiles to alkynyl(phenyl)iodonium tetrafluoroborates (**1**), undergo either 1,2-migration of the α-organosulfur substituents or the intramolecular 1,5-carbon-hydrogen insertion yielding cyclopentenes, depending on the oxidation states of the sulfur atoms.[3] In order to gain some insight into the migratory aptitude of α-halogen atoms of alkylidenecarbenes, development of an efficient method for the generation of α-haloalkylidenecarbenes is highly desirable. β-Halovinyl(phenyl)iodonium tetrafluoroborates seem to be preferable progenitors for generating the α-haloalkylidenecarbenes by their reductive α-elimination,[3a] because of the superleaving ability of the phenyliodonio group.[4] Stereoselective Michael type addition of azido and phenylsulfonyl groups to **1** has been reported.[3b,5] We report herein an efficient method for the stereoselective synthesis of (Z)-β-halovinyl(phenyl)iodonium halides (**2**), which involves a Michael type addition of halide ions to **1**.

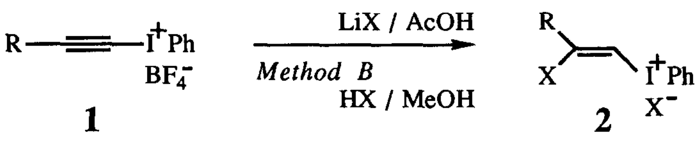
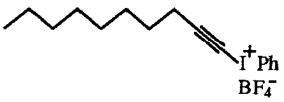
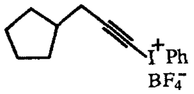
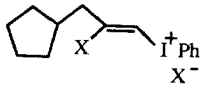
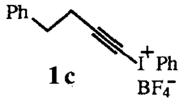
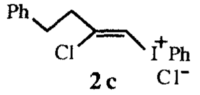
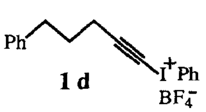
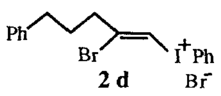
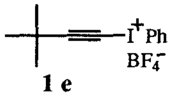
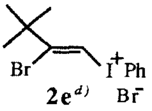


Table I. Michael type addition of halides to alkynyl(phenyl)iodonium salt (**1**)

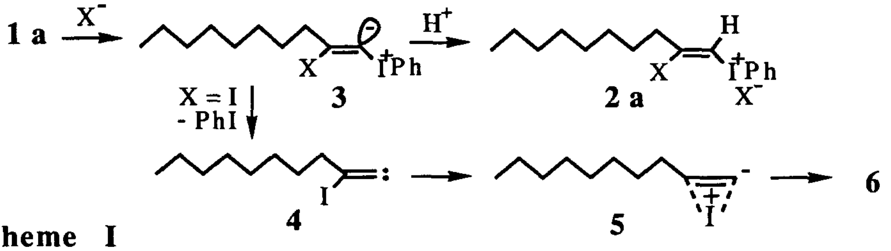
Iodonium salt **1**	Method	Halide (equiv)	Temp, °C a) (Time, h)	Product **2**	%Yield b)
					
1a	A	LiF (10)	RT (4)	—— c)	
1a	A	LiCl (10)	RT (20)	**2a** (X = Cl)	100
1a	B	HCl (10)	0 (0.5)	**2a** (X = Cl)	65
1a	A	LiBr (10)	RT (20)	**2a** (X = Br)	86
1a	B	HBr (1.5)	0 (0.5)	**2a** (X = Br)	85
					
1b	A	LiCl (10)	RT (20)	**2b** (X = Cl)	95
1b	A	LiBr (10)	RT (20)	**2b** (X = Br)	81
 **1c**	B	HCl (5)	0 (0.5)	 **2c**	95
 **1d**	A	LiBr (10)	RT (20)	 **2d**	74
 **1e**	A	LiBr (10)	RT (20)	 **2e** d)	66

a) RT: room temperature. *b)* Isolated yields. *c)* **1a** was recovered unchanged. *d)* Stereochemistry of **2e** was tentatively assigned.

Reaction of **1**[6] with halide ions under neutral conditions gave a complex mixture of products; however, under acidic conditions clean Michael type addition of halide ions (Cl^- and Br^-) to **1**, with concomitant ligand exchange on the trivalent iodine atoms, was observed. Exposure of 1-decynyl(phenyl)iodonium tetrafluoroborate (**1a**) to 10 equiv of lithium chloride in acetic acid[6] at room temperature (Method A)[8] quantitatively gave (*Z*)-2-chloro-1-decenyl(phenyl)iodonium chloride (**2a**) (X = Cl).[9,10] With the use of lithium bromide in acetic acid, (*Z*)-β-bromovinyliodonium bromide (**2a**) (X = Br) was prepared in an 86% yield (Table I). The addition reactions were completely stereoselective to the limits of NMR detection at 270 MHz. The (Z)-stereochemistry of these vinyliodonium halides (**2a**) (X = Cl and Br) was established by observation of a nuclear Overhauser effect (NOE) enhancement between the vinylic and allylic protons. The conjugate addition takes place even in the presence of a sterically demanding *tert*-butyl group at the β-acetylenic carbon of **1** and thus 3,3-dimethyl-1-butynyliodonium salt (**1e**) afforded **2e** (X = Br) by the reaction with lithium bromide in acetic acid in a 66% yield. However, no desired product was obtained by the reaction of trimethylsilylethynyliodonium tetrafluoroborate with lithium bromide.

Furthermore, exposure of **1** to hydrogen halides in a protic solvent (Method B)[11] also undergoes the stereoselective Michael type addition of halides. Reaction of **1a** with 1.5 equiv of hydrogen bromide in methanol at 0°C for 30 min afforded (Z)-isomer **2a** (X = Br) in an 85% yield. Conjugate addition of hydrogen chloride in methanol gave **2a** (X = Cl).

The attempted addition of fluoride ion to **1a** utilizing Method A and B gave poor results because of the low nucleophilicity of fluoride ion and **1a** was recovered unchanged (Table I). Prolonged treatment (2 days) of **1a** with lithium fluoride in acetic acid at room temperature led to the formation of 1-acetoxy-2-decanone, produced by conjugate addition of the solvent acetic acid instead of fluoride ion to **1a**.[12] On the other hand, addition of iodide ion to **1a** is very rapid; however, under standard conditions of Method A (room temperature, 20 h), the reaction gave a complex mixture of products presumably due to the facile decomposition of an addition product. ^{1}H NMR experiments indicated the immediate formation of 1-iodo-1-decyne **6** in good yield (79%) along with a small amount of 1-decyne (21%) in the reaction of **1a** with lithium iodide (1 equiv) in CD_3CO_2D at room temperature. Similarly, when a solution of **1a** in dichloromethane was shaken with an aqueous solution of potassium iodide (3 equiv) using a separatory funnel, the alkyne **6** was produced in an essentially quantitative yield.



Scheme I

Scheme I illustrates a possible reaction process leading to the formation of **6**, which involves Michael type addition of iodide ion, as well as chloride and bromide ions, to **1a** and produces β-iodovinyliodonium ylide **3** (X = I). The β-chloro- and β-bromoiodonium ylides **3** (X = Cl and Br) will be trapped stereoselectively by a proton under acidic conditions to give (Z)-iodonium salts **2a**, while the β-iodoiodonium ylide **3** (X = I) probably undergoes a rapid reductive elimination of iodobenzene, which may be assisted by the β-iodine atom, and affords the alkyne **6**. Thus, the formation of **6** may suggest the *in situ* generation of α-iodoalkylidenecarbene **4** in the reaction.

References and Notes

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2) For 1,2-migration of α-aryl groups and hydrogen of alkylidenecarbenes, see: (a) Newman, M. S.; Gromelski, S. J. *J. Org. Chem.* **1972**, *37*, 3220. (b) Köbrich, G.; Merkel, D.; Thiem, K.-W. *Chem. Ber.* **1972**, *105*, 1683. (c) Gilbert, J. C.; Giamalva, D. H.; Weerasooriya, U. *J. Org. Chem.* **1983**, *48*, 5251. (d) Kowalski, C. J.; Haque, M. S.; Fields, K. W. *J. Am. Chem. Soc.* **1985**, *107*, 1429. (e) Walsh, R.; Untiedt, S.; Stohlmeier, M.; Meijere, A. *Chem. Ber.* **1989**, *122*, 637. (f) McDouall, J. J. W.; Schlegel, H. B.; Francisco, J. S. *J. Am. Chem. Soc.* **1989**, *111*, 4622.
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6) For synthesis of **1**, see: (a) Ochiai, M.; Kunishima, M.; Sumi, K.; Nagao, Y.; Fujita, E. *Tetrahedron Lett.* **1985**, *26*, 4501. (b) Ochiai, M.; Kunishima, M.; Nagao, Y.; Fuji, K.; Fujita, E. *J. Chem. Soc., Chem. Commun.* **1987**, 1708.
7) Ma, S.; Lu, X. *J. Chem. Soc., Chem. Commun.* **1990**, 1643.
8) General procedure for Method A: To a solution of lithium halide (5 mmol) in acetic acid (10 ml) was added 1-alkynyliodonium tetrafluoroborate (**1**) (0.5 mmol) at room temperature and the solution was stirred for 20 h. The solvent was evaporated under reduced pressure. After addition of distilled water, the mixture was extracted with dichloromethane. The combined organic extracts were washed with an aqueous solution of lithium halide (10 mmol). Filtration and concentration under reduced pressure gave a (*Z*)-isomer **2** as crystals, which was recrystallized from dichloromethane-hexane.
9) **2a** (X = Cl): colorless needles, mp 131-131.5°C; IR (Nujol) 1595, 1570, 980, 730 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 8.1-8.0 (2 H), 7.57-7.5 (1 H), 7.48-7.36 (2 H), 6.97 (s, 1 H), 2.60 (t, J = 7.3 Hz, 2 H), 1.7-1.5 (2 H), 1.4-1.1 (10 H), 0.87 (t, J = 6.6 Hz, 3 H); ^{13}C NMR (68 MHz, $CDCl_3$) δ 152.5 (s), 134.4 (d), 130.9 (d), 130.6 (d), 120.0 (s), 105.0 (d), 39.8 (t), 31.6 (t), 28.9 (t), 28.9 (t), 28.2 (t), 27.3 (t), 22.4 (t), 13.9 (q). Anal. Calcd for $C_{16}H_{23}Cl_2I$: C, 46.51; H, 5.61. Found: C, 46.42; H, 5.48.
10) Beringer and Galton reported that the attempted ligand exchange of phenylethynyl(phenyl)iodonium chloride with sodium tetrafluoroborate led to the formation of (Z)-2-chloro-2-phenylethenyl(phenyl)iodonium tetrafluoroborate in 50% yield: Beringer, F. M.; Galton, S. A. *J. Org. Chem.* **1965**, *30*, 1930.
11) General procedure for Method B: To a solution of **1** (0.1 mmol) in methanol (1 ml) was added 1*N* methanolic hydrogen halide solution at 0°C and the mixture was stirred for 30 min. An aqueous solution of potassium halide (20 mmol) was added and the organic solvent was evaporated under reduced pressure. The mixture was extracted with dichloromethane. Filtration and concentration under reduced pressure gave a (*Z*)-isomer **2** as crystals.
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