Michael Addition of Cyanide to Cyclohex-1-enyliodonium Salts

Morifumi Fujita,* Wan Hyeok Kim, and Tadashi Okuyama*
Graduate School of Science, Himeji Institute of Technology, Kamigori, Hyogo 678-1297

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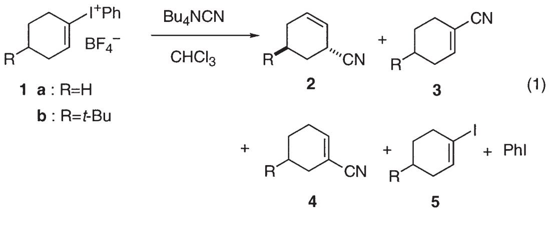
Reaction of 4-substituted cyclohex-1-enyliodonium salt with cyanide in chloroform produces three isomeric cyanocyclohexenes, *ipso* and two *cine* products. Deuterium labeling experiments showed that the allylic *cine* product is formed via the Michael addition of cyanide, followed by elimination of the iodonio group and a 1,2-H shift.

Alkenyl(phenyl)iodonium salts are highly electron-deficient vinyl compounds and afford various modes of reactions depending on the structure of the iodonium itself and on the reaction conditions.[1] Vinylic nucleophilic substitutions readily occur owing to the excellent nucleofugality of the iodonio group.[2] The substitution proceeds via S_N1 or S_N2 mechanism depending on both the stability of the vinyl cations generated by S_N1 and types of nucleophiles. The substitution product is also obtained by ligand coupling on hypervalent iodine (III).[3] The iodonio group also enhances the acidity of the α- and β-hydrogens of the vinyliodonium salts, and a mild base causes α- and β-eliminations to yield alkylidenecarbenes and alkynes, respectively.[4] For the alkynyliodonium salts,[1a-f] the Michael addition at the β-position often occurs to yield alkylidenecarbene as an intermediate and constitutes a key step in the cyclopentene annulations[5] and alkynylations.[5a] However, few examples have been reported for the Michael addition to alkenyliodonium salt:[6] Ochiai and coworkers[6a,b] found that 2-haloalk-1-enyliodonium salts react with benzenesulfinate at the 2-position. The addition step is followed by elimination of the halide, but not by elimination of the iodonio group as observed in the case of the alkynyliodonium salts. We now report that the reaction of cyclohex-1-enyl(phenyl)iodonium salts with cyanide proceeds via the Michael addition, followed by elimination of the iodonio group.

The reaction of 4-substituted cyclohex-1-enyl(phenyl)iodonium tetrafluoroborate (**1**)[7] with tetrabutylammonium cyanide was carried out in chloroform at 60 °C. The products include three cyanocyclohexenes, **2**-**4**,[8–10] as well as iodocyclohexene **5**[7] and iodobenzene (Eq 1).[11]



The products are fully characterized using NMR and MS and/or by comparison with authentic samples. The *trans* configuration of **2b** was confirmed by the coupling constants and NOE observed in the ^{1}H NMR. The product yields were affected by the added methanol as summarized in Table 1. Methanol decreased the yields of **2** and **5**, but increased the yields of **3** and **4**.

Table 1. Reaction of **1** in chloroform containing tetrabutylammonium cyanide (0.01 mol dm^{-3}) at 60 °C for 1 h[a]

		Yield/%				
Substrate	Additive	**2**	**3**	**4**	**5**	PhI
1a		12	18	b	25	64
1b		18	5	12	25	64
1a-d_3		15	7	b	18	47
1b-d_3		16	2	5	19	52
1a	MeOH[c]	3	64	b	2	85
1b	MeOH[c]	8	17	49	3	91
1a-d_3	MeOH[c]	13	40	b	4	68
1b-d_3	MeOH[c]	12	6	24	7	67

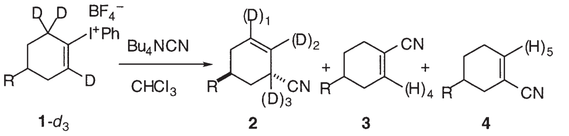
[a] [**1**] = 3 × 10^{-3} mol dm^{-3}. [b] **4a** is identical with **3a**. [c] [MeOH] = 0.25 mol dm^{-3}.

Deuterium labeling provides useful information about the mechanism for cyanide substitution. 2,6,6-Trideuterated iodonium salts **1**-d_3 of ca. 90% D purity[12] were subjected to a reaction with Bu_4NCN under the same conditions. The protium contents of the products were determined by ^{1}H NMR, and are summarized in Table 2. The total content of the deuteriums is essentially maintained in the allylic product **2**, but one of the deuterium atoms is shifted to produce the 1,2,3-trideuterio product. In contrast, the vinylic deuterium in both vinylic products **3** and **4** was mostly lost.

The pair of vinylic *ipso* and *cine* substitution products, **3** and **4**, are similar to that of the acetate products, which are concluded to be formed from the intermediate cyclohexyne.[13] The product ratio of **4b**/**3b** = 3-4 is also compatible with the observed selectivity of the acetate addition to the cyclohexyne.

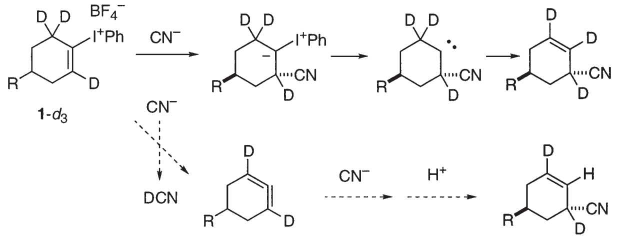
The formation of the trideuterated allylic cyanide product can be rationalized by the reaction pathways involving the Michael addition-elimination illustrated in Scheme 1. An alternative possibility that **2** formed via the elimination-addition pathway with the cyclohexa-1,2-diene intermediate can be disregarded. If

Table 2. Protium contents of product from **1**-d_3



		Protium Content/%				
Substrate	Additive	$(H)_1$	$(H)_2$	$(H)_3$	$(H)_4$	$(H)_5$
1a-d_3[a]		6	7	1	91	c
1b-d_3[b]		9	10	9	85	100
1a-d_3[a]	MeOH[d]	6	16	5	100	c
1b-d_3[b]	MeOH[d]	8	16	6	100	100

[a] Protium contents at 2- and 6-positions of **1a**-d_3 are 4 and 9%, respectively. [b] Protium contents at 2- and 6-positions of **1b**-d_3 are 9 and 13%, respectively. [c] The protium content values at $(H)_4$ and $(H)_5$ are shown together. [d] [MeOH] = 0.25 mol dm^{-3}.



Scheme 1.

this pathway had taken place, the protium should have been incorporated at the 2-position of **2**. Highly nucleophilic cyanide attacks the β-carbon of **1**, and then elimination of the iodonio group occurs to give a carbene, which is finally transformed to the allylic product **2** by a 1,2-hydride shift. The iodonium ylide formation followed by elimination to yield the carbene has been reported in the Michael addition to alkynyliodonium salts.[1,5] Hydrogen has a high migratory aptitude in the 1,2-shift of carbenes.[14]

Deuterium labeling also affects the product distributions; the ratio of allylic to vinylic cyanides, **2**/(**3**+**4**), obtained from **1**-d_3 is greater than that from the normal **1**, both in the presence and absence of methanol. These results are consistent with the mechanisms proposed for the formation of the allylic and vinylic products. Primary deuterium isotope effects retard the deprotonation from **1** in the rate-determining steps of the elimination-addition mechanism to lead to the vinylic product, while the isotope effects are only secondary in the initial step of the addition-elimination mechanism to afford the allylic product. Cyanide works as a base for the elimination of **1** to generate cyclohexyne but as a nucleophile for the Michael addition. Methanol also affects the relative nucleophilic and basic reactivity of cyanide and thus the distribution of the allylic and vinylic products.

The Michael addition is a new type for reaction of vinyliodonium salts to provide a route to a ylide-carbene intermediate, and extends the scopes of the iodonium and carbene chemistries.

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9 Selective formation of **3b** has been reported in the reaction of **1b** with KCu(CN)$_2$.[7]

10 Products **3a** and **4a** are identical, but the labeled substrate reveals the difference.

11 a) Benzene was also detected in a corresponding amount of **5**, but benzonitrile was not detected. The benzene formation has been proposed to occur via hydrogen atom abstraction by the phenyl radical, which is generated by the one-electron reduction of phenyliodonium salts.[11b] b) M. Ochiai, T. Shu, T. Nagaoka, and Y. Kitagawa, *J. Org. Chem.*, **62**, 2130 (1997).

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