Regio- and Stereo-Controlled Alkoxyiodination of 1,3-Diene Using Iodine-Cerium(IV) Ammonium Nitrate

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(Received September 9, 1994)

Reaction of 1,3-cycloalkadienes (cyclopentadiene, cyclohexadiene, and cycloheptadiene) with iodine-cerium(IV) ammonium nitrate in alcohols, gave the corresponding regiospecific *trans*-2-alkoxy-1-iodo compounds as major products accompanied with 1,4-dialkoxy compounds as by-products. In the case of CH_3CN-H_2O as solvent, *trans*-iodohydrins were obtained. Thus the reaction of cyclic and acyclic 1,3-diene derivatives using this synthetic method afforded the 1,2-addition alkoxyiodo compounds preferentially.

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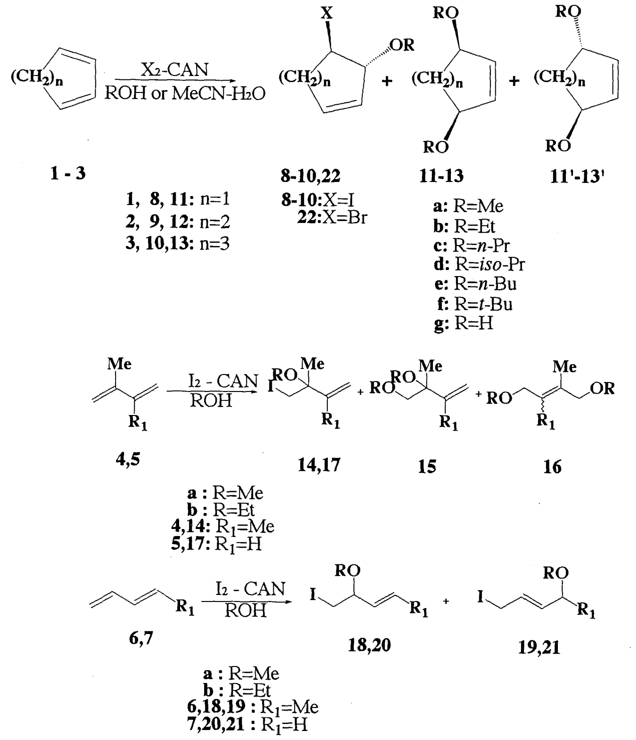
trans-2-Alkoxy-1-iodo derivatives are important synthetic intermediates. We have been investigating the syntheses of steroidal *trans*-iodo acetates and more hindered *cis*-diol using iodine-copper(II) acetate in acetic acid.[1,2] In previous papers, we reported a new alkoxyiodination of simple olefins;[3] and of α,β-unsaturated ketones and esters,[4] with iodine-cerium(IV) ammonium nitrate (CAN) in alcohol.

Several cases are known generally in which the addition reaction of 1,3-diene derivatives yielded the 1,4-addition compounds.[5] However, Barluenga *et al.* reported that the reaction of 1,3-dienes with $I(py)_2BF_4$ allows the regiospecific 1,2-addition of iodine and a nucleophile, and the 1,4-addition to internal 1,3-dienes.[6] In addition, this method is not applicable to 1,2-addition of 1,3-cycloalkadienes. Recently, Shono *et al.* reported that the electrode-oxidation of the 1,3-diene derivatives with NaX in methanol gave the regioselective 1-halo-2-methoxy derivatives.[7] However, there has been only a few report concerning the alkoxyiodo derivatives due to their unstable properties. In this paper, we would like to report that the reaction of 1,3-diene derivatives, namely, cyclopentadiene (**1**), cyclohexadiene (**2**), cycloheptadiene (**3**), 2-methyl-1,3-butadiene (**4**), 2,3-dimethyl-1,3-butadiene (**5**), 1,3-pentadiene (**6**), and 1,3-hexadiene (**7**) with iodine-CAN gave the corresponding *trans*-2-alkoxy-1-iodo compounds as major products.

Table 1 . Reaction of 1,3-Diene with Iodine - Cerium(IV) Ammonium Nitrate in Alcohol or Acetonitrile - Water

Run	Substrare	Solvent	Temp / ℃	Time / h	Product (Yield %)^a
1	**1**	MeOH	0 ℃	2	**8a** (35) + **11a+11'a** (29) [**11a/11'a**=1.2]^c
2	**1**	EtOH	0 ℃	3	**8b** (42) + **11b+11'b** (45) [**11b/11'b**=1.0]^c
3	**1**	*n*-PrOH	0 ℃	4	**8c** (27) + **11c+11'c** (30) [**11c/11'c**=0.9]^c
4	**1**	MeCN-H$_2$O	0 ℃	4	**8g** (35)
5	**2**	MeOH	RT	8	**9a** (60) + **12a+12'a** (21) [**12a/12'a**=2.9]^c
6	**2**	EtOH	RT	8	**9b** (66) + **12b+12'b** (19) [**12b/12'b**=3.5]^c
7	**2**	*n*-PrOH	RT	8	**9c** (66) + **12c+12'c** (11) [**12c/12'c**=3.5]^c
8	**2**	*iso*-PrOH	RT	8	**9d** (60) + **12d+12'd** (19) [**12d/12'd**=8.0]^c
9	**2**	*n*-BuOH^b	RT	8	**9e** (60) + **12e+12'e** (12) [**12e/12'e**=5.2]^c
10	**2**	*t*-BuOH^b	RT	8	**9f** (40) + **12f** (11)
11	**2**	MeCN-H$_2$O	0 ℃	4	**9g** (42)
12	**3**	MeOH	RT	4	**10a** (25) + **13a+13'a** (39) [**13a/13'a**=2.5]^c
13	**3**	EtOH	RT	3	**10b** (23) + **13b** (15)
14	**4**	MeOH	RT	2	**14a** (77) + **15a** (13) + **16a** (4)
15	**4**	EtOH	RT	2	**14b** (53) + **15b** (18) + **16b** (7)
16	**5**	MeOH	RT	2	**17a** (57)
17	**5**	EtOH	RT	2	**17b** (48)
18	**6**	MeOH	RT	2	**18a** + **19a** (88) [**18a/19a**=2.6]^c
19	**6**	EtOH	RT	2	**18b** + **19b** (81) [**18b/19b**=2.0]^c
20	**7**	MeOH	RT	2	**20a** + **21a** (85) [**20a/21a**=2.5]^c
21	**7**	EtOH	RT	2	**20b** + **21b** (95) [**20b/21b**=2.2]^c

^{a}Isolated yields. ^{b}BuOH (10ml)-MeCN (10ml) was employed. ^{c}Ratio determined from the peak area of ^{1}H-NMR spectrum.



A typical procedure is as follows. A mixture of 1,3-cyclohexadiene (**2**)(6.24 mmol), iodine (6.24 mmol), CAN (3.12 mmol), and methanol (20 ml) was stirred at room temperature for 8 h. The reaction mixture was extracted with ether. The ethereal solution was washed with aqueous sodium hydrogen carbonate and water, dried, and concentrated. The resulting oil was chromatographed on silica gel. Elution with benzene-ethyl acetate (3:1)(120 ml) gave *trans*-2-alkoxy-1-iodo-3-cyclohexene (**9a**) (61%) and 3,6-dialkoxy-1-cyclohexene (**11**)(21%). These results are summarized in Table 1.

As can be seen in the Table 1, the reaction proved to have general applicability in the synthesis of the 1,2-*trans*-alkoxyiodo adducts of 1,3-diene derivatives. Some of the products in the Table 1 have not been reported previously. The synthesis described in this paper is certainly the most convenient procedure for preparing 1,2-alkoxy iodides from this type of 1,3-diene derivatives and affords a considerable potentiality to organic syntheses. This success for 1,2-addition of cyclic 1,3-diene is no doubt attributable to the special properties of the iodine / CAN system.

In the case of cyclopentadiene (**1**) or cyclohexadiene (**2**) with iodine-CAN in CH_3CN-H_2O (10:1) at 0 ℃, 1-iodo-3-cyclopenten-2-ol (**8 g**) or 1-iodo-3-cyclohexen-2-ol (**9 g**) was obtained. These iodohydrin compounds are very unstable and sensitive to light. Moreover, the reaction of acyclic 1,3-alkadiene derivative with iodine-CAN gave 1,2-addition alkoxyiodo compounds which are similar to 1,3-cycloalkadiene as described above.

Table 2. Reaction of 1,3-Cyclohexadiene (**2**) with Bromine - Cerium (IV) Ammonium Nitrate in Alcohol[a]

Run	Alcohol	Temp	Time / h	Product (Yield%)[b]
1	MeOH	RT	1	**22a** (49) + **23** (10)
2	EtOH	RT	2.5	**22b** (26) + **23** (29)
3	*n*-PrOH	RT	2.5	**22c** (15) + **23** (17)
4	*iso*-PrOH	RT	2.5	**22d** (15) + **23** (30)

[a] Substrate (3.19 mmol), bromine (3.19 mmol), CAN (1.60 mmol), and solvent (15 ml) were employed. [b] Isolated yields.

Moreover, the reaction of **1** with bromine-CAN in methanol at room temperature yielded 4-bromo-3-methoxy-1-cyclohexene (**22a**)(49%) and 3,6-dibromo-1-cyclohexene (**23**)(10%). These results are summarized in Table 2. In the case of ethanol, 1-propanol, or 2-propanol, the ratio of 1,4-dibromo compound was increased.

The authors wish to express their thanks to Dr. Takashi Sugiyama, Institute for Chemical Research, Kyoto University, for his valuable suggestions, to Dr. Mitsuo Hayashi and Mr. Tamotsu Yamamoto, Research Laboratories of Asahi Kasei Kogyo Co., Ltd. for their measurement of the high resolution mass spectra, and SEIMI Chemical Co., Ltd. for providing cerium(IV) ammonium nitrate. This work was supported by Rikkyo University Grant for the Promotion of Research.

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