Reactions of Iodocarbenoid of Zinc. II.[1] The Iodocyclopropanation of Olefins with Diethylzinc and Iodoform[2]

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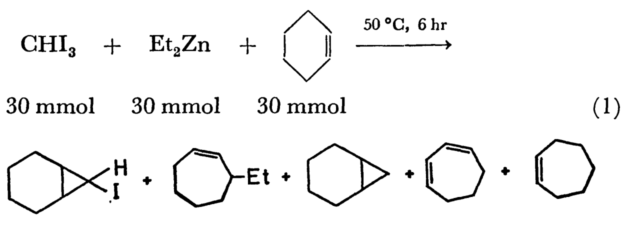
The iodocyclopropanation of olefins by the iodocarbenoid of zinc generated from diethylzinc and iodoform was investigated. When the reaction was carried out in a neat olefin, cyclohexene, 1-hexene, *cis*-2-butene, isobutene, and styrene gave the corresponding iodocyclopropanes in yields of 70, 34, 63, 55, and 44% respectively, showing that the CHI_3–Et_2Zn system is a convenient route for iodocyclopropanes. The reaction with cyclohexene was investigated in some detail. *syn*-7-Iodonorcarane easily gave 3-ethylcycloheptene upon treatment with diethyl zinc in the presence of zinc iodide.

Various carbene and carbenoid reagents are available for the cyclopropanation of olefins.[3] However, there seem to be only a few reports describing the iodocyclopropanation of olefins by iodocarbene or iodocarbenoids.[4–6] In 1971, Nishimura and Furukawa reported the formation of 7-iodonorcaranes from cyclohexene in trace amounts by a reaction with diethylzinc and iodoform in a light petroleum medium.[5] In the preceding paper,[1] we ourselves reported that, in the ring-expansion of benzene by the CHI_3–Et_2Zn system, the dilution of the substrate (benzene) with hexane caused a remarkable reduction in the yield of 7-ethyltropilidene. This was ascribed to the consumption of the iodocarbenoid reagent of zinc in the formation of propylene. These observations prompted us to examine the iodocarbenoid reaction with diethylzinc and iodoform in neat olefins; in this paper we wish to describe a convenient synthetic route for iodocyclopropanes.

Results and Discussion

Reaction of Diethylzinc and Iodoform in Neat Cyclohexene. The addition of iodoform to an equimolar quantity of diethylzinc in cyclohexene resulted in an exothermic reaction, with the precipitation of white solids. Hydrolysis with aqueous hydrogen chloride gave an organic layer which was analyzed on glc. The results are summarized in Eq. (1):



CHI_3 + Et_2Zn + 50 °C, 6 hr

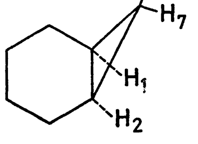
30 mmol 30 mmol 30 mmol (1)

(1) **(2)** **(3)** **(4)** **(5)**

50% 9.0% 4.8% 2.5% 1.8%

Figure 1 shows the effects of the amount of diethylzinc on the reaction. The quantitative formation of ethyl iodide and the consumption of a part of the reagents in the formation of propylene upon the treatment of diethylzinc and iodoform were reported in the previous paper.[1]

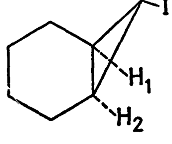
The 7-iodonorcaranes (**1**) were separated as a mixture of *syn*- and *anti*-isomer[7] after a usual work-up of the reaction mixture. The structures were confirmed by elemental analysis, by studying the NMR spectra, and by the formation of norcarane by the Na–MeOH–H_2O reduction according to the method described by Dale and Swartzentruber.[8] The *syn*- and *anti*-7-iodonorcarane were assigned on the basis of the facts that: (1) the alkylsubstituents on a cyclopropane ring would shield the *cis* H_7 more than the *trans* H_7,[9] (2) in cyclopropanes a coupling constant of vicinal-ring protons is generally $J_{cis} > J_{trans}$,[10] and (3) halocarbenoids tend to yield the more sterically-crowded *syn*-isomers.[7,11] The assignment is consistent with that for 7-bromonorcaranes reported by Seyferth *et al.*[10]



syn-**1**

H_7; $\delta = 3.05$ (triplet)

$J_{1,7}$; 7.05 Hz

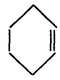


anti-**1**

H_7; $\delta = 2.05$ (triplet)

$J_{1,7}$; 4.2 Hz

Diethylzinc reacts with a 2-molar amount of iodoform in the iodocyclopropanation of cyclohexene, since when the molar ratio of diethylzinc to iodoform is less than 1/2, the molar amount **1** is greater than that of the diethylzinc used (Eq. (2)):



$$+ 1/2Et_2Zn + CHI_3 \rightarrow \mathbf{1} + EtI + 1/2ZnI_2 \qquad (2)$$

3-Ethylcycloheptene (**2**), norcarane (**3**), 1,3-cycloheptadiene (**4**), and cycloheptene (**5**) were characterized by comparing their retention times on glc and on the basis of their NMR and IR spectra. Magid *et al.* reported the stereospecific formation of 7-methylnorcarane from **1** upon treatment with methyllithium.[6a] On the contrary, **1** was almost inactive toward diethylzinc in benzene. It may be concluded, however, from the effects of the amount of diethylzinc on the product composition shown in Fig. 1 and from the following results, that the **2**, **4**, and **5** were formed in the subsequent reactions of *syn*-**1** in the presence of an excess of EtZnX (X=Et or I). Diethylzinc was allowed to react with a mixture of *syn*- and *anti*-**1** in the presence of zinc iodide in benzene at 50 °C for 5 hr. Almost all of the latter was recovered unchanged, but the former was consumed to give **2**, **4**, and **5**, **2** being the major product. These results are consistent with

Table 1. Reaction of several Olefins with Et_2Zn-CHI_3

Olefin	ml	Et_2Zn mol×10	CHI_3 mol×10	Reaction temp. (°C)	Iodocyclopropane yield (%)[a]	*Syn*/*Anti* ratio
Cyclohexene	30	0.10	0.30	50	35	53/47
	30	0.30	0.30	50	50	45/55
	30	0.45	0.30	50	38	34/66
	30	0.30	0.30	0	70[b]	66/34
n-1-Hexene	100	1.0	3.0	50	34	67/33
cis-2-Butene	20	0.20	0.30	0—20	63[b]	69/31
Isobutene	20	0.25	0.30	0—20	55[b]	
Styrene	100	1.0	3.0	50	44	

a) Based on iodoform, and determined by glc. b) Diethylzinc was added to iodoform in olefin.

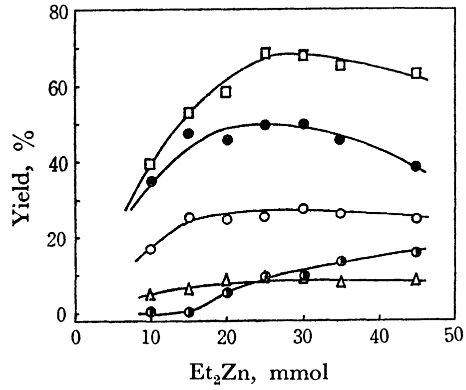
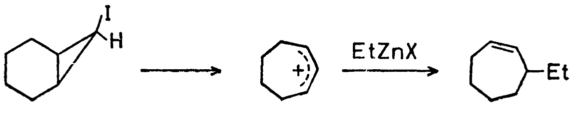
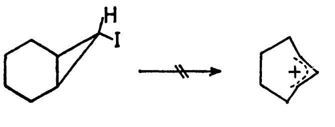


Fig. 1. Effect of the amount of Et_2Zn.
CHI_3 (30 mmol) was added over 1-hr period to a Et_2Zn in cyclohexene (30 ml) at 50 °C, and the reaction was continued for an additional 5 hr.
□: total products (**1**+**2**+**3**+**4**+**5**).
●: *syn*- and anti-7-iodonorcarane (*syn*-**1**+*anti*-**1**).
○: *anti*-7-iodonorcarane (*anti*-**1**).
◑: 3-ethylcycloheptene (**2**).
△: norcarane, 1,3-cycloheptadiene, and cycloheptene (**3**+**4**+**5**).

the assumption that, in a concerted cyclopropane ring-opening, a preferred inward rotation of *cis* groups to the leaving iodide leads to a stable allylic cation from the *syn*-**1**, as was suggested by DePuy *et al.*[12] In the *anti*-**1**, the outward rotation of the *trans* groups is prevented and a concerted ring-opening may also be forbidden (Eqs. (3) and (4)):



(3)



(4)

The *syn*-**1** was thermally less stable than the *anti*-isomer, and it easily gave **4** even during a glc analysis when a glc apparatus was operated at a high temperature. Ando *et al.* reported a similar transformation of *syn*-1-chloronorcarane into **4** upon treatment in quinoline at 200 °C.[13] The precise mechanism for the formation of the reduced products (**3** and **5**) is not yet clear.

Iodocyclopropanation of Several Olefins. Table 1 shows the results of the iodocyclopropanation of several olefins. Cyclohexene gave **1** in the yield of as much as 70% when diethylzinc was allowed to react with iodoform in cyclohexene at 0 °C. The reaction temperature is one of the important reaction variables; Nishimura and Furukawa reported that the yield of **1** was 10% when the reaction was carried out in refluxing cyclohexene.[5] On the other hand, when the reaction temperature was kept at −5—0 °C; 1-hexene gave the 1-iodo-2-*n*-butylcyclopropanes in only a 9.8% yield, and methylene iodide was obtained as the major product. It seems to be formed by the hydrolysis of the iodocarbenoid of zinc (Eq. (5)):

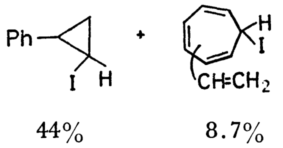
$$\mathrm{EtZnX} + \mathrm{CHI_3} \xrightarrow{-\mathrm{EtI}} \mathrm{I_2CHZnX} \xrightarrow{\mathrm{H_2O}} \mathrm{CH_2I_2} \qquad (5)$$

cis-2-Butene afforded the corresponding epimeric pair of 1-iodo-*cis*,*cis*- and 1-iodo-*trans*,*trans*-2,3-dimethylcyclopropane, and no 1-iodo-*cis*,*trans*-dimethyl isomer was detected in the reaction mixture, showing a stereospecific[14] CHI addition to *cis*-2-butene.

n-Butyl vinyl ether was polymerized vigorously upon treatment with diethylzinc and iodoform at room temperature,[15] and it failed to produce the cyclopropanated products.

When styrene was subjected to a reaction, the iodocyclopropanation of ethylene linkage preceded the ring-expansion of the benzene nucleus,[1] but it was accompanied by the formation of a large amount of polystyrene (Eq. (6)):

$CHI_3 + Et_2Zn + PhCH{=}CH_2 \longrightarrow$



(6)

The isolated iodocyclopropanated product[16] seemed to be a mixture of *syn*- and *anti*-1-iodo-2-phenylcyclopropane, but the two isomers were not differentiated from each other because of their complex NMR spectrum.

We proposed a free-radical-chain mechanism involving the homolytic abstraction of the iodo radical from CH_2IX for the formation of a zinc-carbenoid reagent from diethylzinc and CH_2IX (X=I, Cl).[9] It may be concluded that a similar mechanism is also applicable to the CHI_3–Et_2Zn system for the formation of iodocarbenoid of zinc, in view of the facts that the system is known to catalyze the radical polymerization of vinyl monomers, such as styrene and methyl methacrylate,[15] and that the iodide in CHI_3 seems to be more easily abstracted homolytically than that in CH_2IX.

Several methods have been reported to afford iodocycloproanes,[4–6,18–20] but where sufficient amounts of the starting olefins are available the CHI_3–Et_2Zn system is the preferred method in view of the simplicity of its reaction procedure and the easiness of the isolation of the products.

Experimental

The glc analysis was carried out on a Shimadzu GC 3AF apparatus equipped with hydrogen-flame detectors and two 3 m×3 mm stainless steel columns packed with Diasolid M coated with Silicone DC 550 and Silicone DC 410 respectively. The infrared spectra were obtained with a JASCO Model IR-E spectrophotometer. The NMR data were obtained with a Varian Associates Model A-60D instrument. All the chemical shifts are relative to an internal TMS or benzene reference (*ca.* 5 wt% solution in CCl_4 or benzene). Elemental analysis was performed at the Elemental Analysis Center, Chemical Research Institute of Nonaqueous Solutions, Tohoku University.

Materials. The diethylzinc and iodoform were purified as has been reported before.[1] The 1,3-cycloheptadiene (bp 69.3—70.2 °C/140 mmHg, lit,[21] 121—122 °C/760 mmHg), phenylcyclopropane,[9] and norcarane[9] were prepared according to the methods in the literature. Reagent-grade commercial olefins were purified by the usual methods before use. The materials were stored under nitrogen.

Reaction of Cyclohexene with Diethylzinc and Iodoform. The reaction procedure was almost analogous to that reported for the reaction of benzene with diethylzinc and iodoform.[1] For the identification of the reaction products, a controlled reaction was carried out as follows. Iodoform (40.0 g, 0.102 mol) was added, portion by portion, to a diethylzinc (10 ml, 0.10 mol) solution in cyclohexene (100 ml) over a 2-hr period at 50 °C. The reaction mixture was stirred at 50 °C for another 4 hr, and was then hydrolyzed in an ice-water bath with a dilute aqueous hydrogen chloride solution. After the usual work-up, the distillation of the organic layer gave three fractions: (1) 0.16 g, boiling range 55—56 °C/78 mmHg, (2) 0.71 g, bp 68—68.5 °C/28 mmHg, (3) 6.3 g, 65.5—71 °C/3 mmHg. Glc analysis showed that Fraction 1 was composed of almost equal amounts of cycloheptene (**5**) (NMR: δ 5.85—5.65 (m) for olefinic protons, 2.3—1.9 (br) for allylic protons, IR: 3020 cm^{-1} ($\rangle$C=CH–), 1650 cm^{-1} ($\rangle$C=C$\langle$)) and norcarane (**3**) (characteristic absorptions of the cyclopropane ring, IR: 3060, 1020 cm^{-1}, NMR: δ 0.8—−0.2), plus a trace amount of 1,3-cycloheptadiene (**4**). The retention times of these three substances in glc increased in this order: $\mathbf{5}<\mathbf{3}<\mathbf{4}$ (Silicone DC 550, 110 °C). Fraction 2 was 3-ethylcycloheptene contaminated with a small amount of an unidetified material. NMR: δ 5.7—5.5 (2H, m), 2.3—1.8 (4H, br), 1.8—1.1 (7H, m), 1.1—0.3 (3H, t). IR (liq. film): 3020 cm^{-1} ($\rangle$C=CH–), 1645 cm^{-1} ($\rangle$C=C$\langle$).

Fraction 3 was essentially pure 7-iodonorcaranes (**1**), and redistillation gave 4.0 g of an analytical sample of a 46 : 54 mixture of *syn*- and *anti*-**1** boiling at 68.5—69.5 °C/3 mmHg. Found: C, 38.04; H, 4.90%. Calcd for $C_7H_{11}I$: C, 37.86; H, 4.99; I, 57.15%. IR (liq. film, cm^{-1}): 3000(m, sh), 2900 (s), 2850(s), 1460(m, sh), 1445 (s), 1355 (m), 1340 (m), 1270(m), 1240(s), 1205(s), 1180(w), 1155(w, sh), 1140(m), 1080(w, sh), 1070(w), 1005(m), 960(w), 950(w), 920(w), 895(w), 830(w), 765(w), 725(w). The *syn*- and *anti*-isomer ratio was determined on the basis of the NMR spectrum and the peak areas on glc (Silicone DC 410 column, 110 °C), the former giving a longer retention time than the latter. When a glc analysis was carried out on a Silicone DC 550 column operated at 170 °C, the *syn*-isomer completely disappeared, giving a new peak the retention time of which coincided with that of 1,3-cycloheptadiene.

*Reduction of **1** with Na-MeOH-H_2O.* A 46 : 54 mixture of *syn*- and *anti*-**1** (1.30 mmol) in wet methanol (0.5 ml of water to 10 ml of methanol) was treated with 1.0 g of sodium metal. The reaction mixture was then neutralized with hydrogen chloride and extracted with ether. Glc analysis showed the presence of 0.82 mmol of norcarane (63% based on **1**), 0.17 mmol of unchanged *syn*-**1**, and 0.25 mmol of *anti*-**1**.

*The Reaction of **1** with Diethylzinc in the Presence of Zinc Iodide.* To a 43 : 57 mixture of *syn*- and *anti*-**1** (2.06 mmol) and 1.03 mmol of zinc iodide in 10 ml of benzene, we added 0.50 ml of diethylzinc (5.0 mmol). The reaction mixture was then stirred at 50 °C for 5 hr. Glc analysis showed that 98.4% of the *anti*-**1** was recovered unchanged, but 50% of the *syn*-**1** reacted to leave a 27 : 73 mixture of *syn*- and *anti*-**1**, and 0.40 mmol of **2**, 0.064 mmol of **5**, and 0.022 mmol of **4** were detected in the reaction mixture. Upon the similar treatment of **1** with diethylzinc in the absence of zinc iodide, the **1** was recovered almost unchanged and trace amounts of **5** and **4** were detected after the reaction.

Reaction with Styrene. Iodoform was allowed to react with diethylzinc in styrene according to the above procedure except that the iodoform was added over a 1-hr period, after which the reaction was continued for another 5 hr. The distillation of the reaction mixture gave a portion boiling at 74.5—76 °C/6.5 mmHg (0.5 g), which was characterized as a mixture of vinyl-7-ethyltropilidenes on the basis of its NMR and IR spectra. IR (liq. film, cm^{-1}): 985, 900 (vinyl), 1630, 1613, 1595 (polyene structure). After the distillation, 20.5 g of a viscous, dark brown residue remained; this was dissolved in 10 ml of acetone and precipitated with 300 ml of methanol. The precipitate (8.2 g) gave IR absorption spectra (KBr) identical with those of polystyrene film over the wave range from 650 to 3200 cm^{-1}. The methanol solution was distilled to give 5.3 g of 1-iodo-2-phenylcyclopropane (**6**) as a slightly pale yellow liquid boiling at 100—102 °C/3 mmHg (lit,[18] bp 80—81 °C/0.4 mmHg). Found: C, 44.23; H, 3.56%. Calcd for C_9H_9I: C, 44.29; H, 3.72; I, 52.00%. IR (liq. film, cm^{-1}): 3080 (m, sh), 3060(s), 2930(m, sh), 2850(m, sh), 1605(s), 1580(w, sh), 1505(s), 1455(s), 1440(m, sh), 1370(w), 1240(s), 1220(m), 1185(w), 1165(w), 1160—1070(m), 1045(m), 1030(m), 995(m), 960(w), 915(m), 820(m), 770(m), 735(m), 700(s). NMR: δ 7.3—7.0 (5H), 3.1—1.0 (4H, m).

6 (0.40 mmol) in wet methanol (0.5 ml of water to 10 ml of methanol) was treated with 1 g of sodium metal to give phenylcyclopropane in a yield of 77%.

*1-Iodo-2-*n*-butylcyclopropanes (**7**).* Bp 68—71 °C/7 mmHg (5.0 g). Found: C, 37.02; H, 5.96%. Calcd for $C_7H_{13}I$: C, 37.52; H, 5.85; I, 56.64%. IR (liq. film, cm^{-1}): 2950(s, sh), 2925(s), 2855(s), 1460—1440(m, br), 1380(m), 1235(s), 1192(m), 1035(m), 822(m), 735(w). NMR: δ 2.8—2.4 (m, H_1 for *syn*-**7**), 2.3—1.8 (m, H_1 for *anti*-**7**).

In a separate run, diethylzinc (15 ml) was added to iodoform (60 g) in 1-hexene (100 ml) which had been kept at −5—0 °C over a 1-hr period, after which the reaction mixture was kept at 0 °C for 5 hr with stirring. Glc analysis showed that the yield of **7** was reduced to 9.8%; 10.4 g of methylene iodide were recovered by distillation.

1-Iodo-2,3-dimethylcyclopropanes (8). *cis*-2-Butene (*ca.* 20 ml) was distilled into a sealed tube which contained 12 g of iodoform. From the side arm of the tube, 2 ml of diethylzinc were added to the mixture, drop by drop, over a 2-hr period with occasional cooling in an ice-water bath. The reaction mixture was then allowed to stand at room temperature for 1 hr with stirring. After the unchanged butene had been distilled off, the reaction mixture was diluted with ether and treated as usual. A portion boiling at 63—64 °C/29 mmHg was collected as a mixture of *syn*- and *anti*-**8** (2.0 g) (lit,[18] bp 50—52 °C/40 mmHg). Found: C, 29.50; H, 4.79%. Calcd for C_5H_9I: 30.63; H, 4.63; I, 64.74%. IR (liq. film, cm^{-1}): 3025(m, sh), 3000(s, sh), 2950(s), 2925(s), 2870(s, sh), 1455(s, br), 1390(s), 1240(s), 1220(s), 1165(m), 1115(s), 1060(m), 910(w), 750(s). The NMR spectrum was consistent with that of **8**[18]); H_1 for the *syn*-**8**, δ 2.85, $J_{1,3}=7.7$ Hz.

1-Iodo-2,2-dimethylcyclopropane (9). Bp 56—57 °C/51 mmHg (1.5 g) (lit,[18] bp 40—41 °C/20 mmHg). Found: C, 30.97; H, 4.23%. Calcd for C_5H_9I: C, 30.63; H, 4.63; I, 64.74%. IR (liq. film, cm^{-1}): 2950(s), 2840(s, sh), 1465(m, sh), 1450(s), 1440(s), 1380(m), 1280(m), 1195(s), 1123(w), 1086(w), 1035(m), 950(w), 900(m), 825(w). NMR spectrum was consistent with **9**.[18]

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