

1650, 1700, 2500, 3150, 3300, 3420 cm^{-1} ; $\lambda_{\text{max}}^{\text{EtOH}}$ 230 $\text{m}\mu$ (ϵ 13,800).

Anal. Calcd for $\text{C}_{10}\text{H}_{17}\text{N}_3\text{O}_3$: C, 52.85; H, 7.54; N, 18.49. Found: C, 52.65; H, 7.78; N, 18.41.

trans-Octahydro-2-[2-(indol-3-yl)ethyl]-3-(2H)-isoquinolinone (5).—To a solution of 155 g of 2-formylcyclohexaneacetic acid, 380 ml of triethylamine, and 560 ml of water in 700 ml of dimethylformamide was added a solution of 135 g of tryptamine and 350 ml of water in 430 ml of dimethylformamide at -5° . After the addition had been completed, the solution was stirred for an additional 30 min at the same temperature. Then 100 g of potassium borohydride was added over a 30-min interval, after which stirring at -5° was continued for 30 min. The cooling bath was removed and stirring was continued for an additional 75 min. The mixture was diluted with 940 ml of water, pH being adjusted to 6 with acetic acid, and was heated on the steam bath for 2 hr. On standing there was deposited a solid which after recrystallization from ethanol gave 156 g (57%) of a crystalline solid, mp 240.5–241°. Further recrystallization gave an analytical sample: mp 241.5–242° (lit.¹ 244–245°); $\nu_{\text{max}}^{\text{Nujol}}$ 747, 1627, 3230 cm^{-1} ; $\nu_{\text{max}}^{\text{CHCl}_3}$ 1620, 3460 cm^{-1} ; $\lambda_{\text{max}}^{\text{EtOH}}$ 222 $\text{m}\mu$ (ϵ 37,300), 273 sh (ϵ 5700), 282 (ϵ 6200), 290 (ϵ 5400).

Anal. Calcd for $\text{C}_{19}\text{H}_{24}\text{N}_2\text{O}$: C, 76.99; H, 8.16; N, 9.45. Found: C, 76.73; H, 8.16; N, 9.56.

(\pm)-Yohimbane (6).—A mixture of 102 g of *trans*-octahydro-2-[2-(indol-3-yl)ethyl]-3(2H)-isoquinolinone, 200 ml of phosphorus oxychloride, and 2 l. of benzene was refluxed for 4 hr. Filtration of the cold reaction mixture gave, after recrystallization from ethanol-dioxane, a yellow crystalline solid (88 g). This solid was dissolved in 750 ml of ethanol and 3 g of platinum oxide added; the mixture was hydrogenated at atmospheric pressure. Uptake ceased after absorption of the theoretical amount of hydrogen. The hydrogenation mixture was treated with 2 l. of chloroform and 2000 ml of 2% sodium hydroxide solution. The chloroform layer was washed with water and dried over sodium sulfate; the solvent was removed. The residue after recrystallization from ethanol gave 61 g (64%) of a crystalline solid, mp 179–180°. Further recrystallization gave an analytical sample: mp 182.5–183.5° (lit.¹ 181.5–183°); $\nu_{\text{max}}^{\text{Nujol}}$ 740 and 3400 cm^{-1} ; $\nu_{\text{max}}^{\text{CHCl}_3}$ 2850 and 2900 cm^{-1} ; $\lambda_{\text{max}}^{\text{EtOH}}$ 225 $\text{m}\mu$ (ϵ 32,000), 273 sh (ϵ 7500), 280 (ϵ 7900), 290 sh (ϵ 6700).

Anal. Calcd for $\text{C}_{19}\text{H}_{24}\text{N}_2$: C, 81.38; H, 8.63; N, 9.99. Found: C, 81.46; H, 8.76; N, 10.09.

(+)-Yohimbane.—A solution of 70.8 g of (\pm)-yohimbane and 91.5 g of O,O'-dibenzoyl-L-tartaric acid in 1.2 l. of ethanol was refluxed for 30 min. On standing there was deposited 92.0 g of a solid, mp 193–195°. Four recrystallizations from methanol gave 23.3 g of a solid, mp 178° dec. The salt was shaken with chloroform and 10% sodium hydroxide solution. The chloroform layer was washed with water and dried over sodium sulfate; the solvent was removed. Recrystallization of the residue from ethanol gave 10.0 g (28%) of a solid, mp 203–204°, $[\alpha]_D^{25} +81^\circ$ (c 0.50, ethanol).³

Diiodocarbene and the Synthesis of Monoiodocyclopropane Derivatives¹

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Diiodocarbene was reportedly generated in the basic decomposition of iodoform³ and appeared to add to cyclohexene⁴ but the product was not fully characterized. Hine⁵ pointed out that it would be of interest to establish the existence of this species and determine

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(2) Taken in part from the Ph.D. Dissertation of U. V. Rao, submitted to Wayne State University, Detroit, Mich., 1965.

(3) J. Hine and S. J. Ehrenson, *J. Am. Chem. Soc.*, **80**, 824 (1958).

(4) W. Von E. Doering and A. K. Hoffmann, *ibid.*, **76**, 6162 (1954).

(5) J. Hine, "Divalent Carbon," the Ronald Press, New York, N. Y., 1964 p 46.

the stereochemistry of its addition to olefins because of its increased steric requirements and lower stability. For this reason and for use in our studies on the electronegativity effects of substituents on the proton coupling constants of trisubstituted cyclopropane derivatives,⁶ it was found desirable to synthesize 1-iodo-2,2-dimethylcyclopropane *via* the carbene route. Hart⁷ and Applequist⁸ have synthesized iodocyclopropane derivatives by methods other than those involving carbene intermediates.

Reaction of isobutylene with iodoform in the presence of base gave rise to a high boiling fraction which could not be readily purified owing to its rapid decomposition. Evidence that this product contained 1,1-diiodo-2,2-dimethylcyclopropane (1) was obtained from its mass spectrum (see Table I) which indicated the pres-

TABLE I
THE MASS SPECTRA OF ISOMERIC
DIIODODIMETHYLCYCLOPROPANE DERIVATIVES

$\text{C}_5\text{H}_9\text{I}_2^+$	89.5 ^a	44.6	96.6
$\text{C}_5\text{H}_8\text{I}^+$	98.3	100.0	100.0
C_5H_8^+	96.8	57.0	50.2
C_5H_7^+	100.0	96.8	94.6

^a Relative abundances of the ions with an ionizing potential of 70 v.

ence of the molecular ion $\text{C}_5\text{H}_9\text{I}_2^+$. This in itself is sufficient to show the formation of the diiododerivative. However, the formation of the monoiodide, which can be more readily characterized, adds additional proof for the formation of the diiodide.

The 1-iodo-2,2-dimethylcyclopropane (2) was obtained by reduction of (1) with tri-*n*-butyltinhydride⁹ and was characterized by its infrared, nmr, and mass spectra and by chemical analysis. The infrared and nmr spectra were consistent with that of similar cyclopropane derivatives. The nmr spectrum of the ring protons analyzed as an ABC system gave $\delta_A = 6.758$, $\delta_B = 6.427$, and $\delta_C = 5.008$ ppm from the benzene with $J_{AB} = -5.64$, $J_{AC} = 4.85$, and $J_{BC} = 8.06$ cps. Details of this analysis will be given elsewhere.⁶ Additional evidence was also obtained from its mass spec-

TABLE II
THE MASS SPECTRA OF ISOMERIC
MONOIODOCYCLOPROPANE DERIVATIVES

$\text{C}_5\text{H}_9\text{I}^+$	5.7 ^a	12.6	21.5	7.6
C_5H_8^+	95.2	85.0	81.5	114.5
C_5H_7^+	100.0	100.0	100.0	100.0

^a The relative abundances of all ions have been adjusted to $\text{C}_5\text{H}_7^+ = 100$ and were obtained with a 70-v ionizing potential.

(6) U. V. Rao, M. T. Emerson, and J. P. Oliver, to be published.

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(8) D. Applequist and D. F. O'Brien, *J. Am. Chem. Soc.*, **85**, 743 (1963).

(9) H. G. Kuivila and L. W. Menapace, *J. Org. Chem.*, **28**, 2165 (1963).

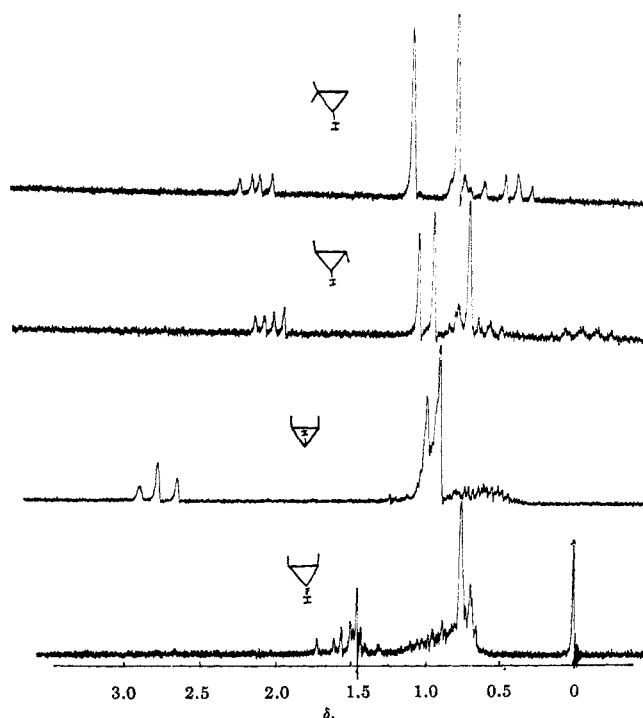


Figure 1.—The nmr spectra of isomeric iododimethylcyclopropanes taken at 60 Mc relative to tetramethylsilane.

trum which is given in Table II and is consistent with the structure.

The stereochemistry for the addition of diiodocarbene was established by reacting it with *cis*- and *trans*-butene-2 which gave the corresponding 1,1-diiodo-2,3-*cis*-dimethylcyclopropane (3) and 1,1-diiodo-2,3-*trans*-dimethylcyclopropane (4). Evidence for the formation of these products was obtained from their infrared spectra which showed the presence of the cyclopropyl ring and from their mass spectra as seen in Table I. The latter also suggested that the three diiodides differed because of the differences observed in the relative abundances of the ions, a result which would be expected if on isomerization occurred. Other indirect evidence for the stereospecificity of the reaction was obtained by examination of the infrared spectra of the unreacted olefins recovered from the reaction mixture which indicated no isomerization had taken place.

Both 3 and 4 were subsequently reduced by the same procedure used for the preparation of 2. From 4 a single isomer, 1-iodo-*cis,trans*-2,3-dimethylcyclopropane (5),¹⁰ was obtained and was identified by its infrared spectrum and mass spectrum as seen in Table II. Its structure was confirmed by a comparison of its nmr spectrum with that of 1-bromo-*cis,trans*-2,3-dimethylcyclopropane⁶ and by a comparison with the other isomeric monoiodocyclopropane derivatives as seen in Figure 1.

The reduction of 3 gave rise to two products in a ratio of 3:1 corresponding to 1-iodo-*cis,cis*-2,3-dimethylcyclopropane (6) and 1-iodo-*trans,trans*-2,3-dimethylcyclopropane (7). These products were identified by their mass spectra as seen in Table II and by their nmr spectra as seen in Figure 1. In this case the structural assignment was again made on the basis of the

nmr spectra with the details of this discussion given elsewhere.⁶

The ratio of 6:7 was somewhat unexpected since the thermodynamic stability of these products would be expected to be in the opposite order; thus it is suggested that the reduction of 3 is a kinetically controlled process with the iodide in the more exposed position being removed preferentially. From the above discussion it is evident that diiodocarbene is generated in the basic decomposition of iodoform and adds *cis* to double bonds to give the corresponding iodocyclopropanes with the retention of original stereochemical configuration. This reaction proceeds in good yield to give a convenient route for the synthesis of simple iodocyclopropane derivatives.

Experimental Section

1-Iodo-2,2-dimethylcyclopropane (2).—Iodoform (0.25 mole, 100 g, Eastman Kodak) and 56 g (1.0 mole) of isobutylene (Matheson C.P. grade) were placed in a three-necked flask equipped with a pressure equalizing addition funnel, Hirschberg stirrer, and a Dry Ice condenser. The flask was externally cooled to -30° prior to the addition of isobutylene to the well-stirred mixture, and 0.25 mole of potassium *t*-butoxide dissolved in 250 ml of freshly distilled *t*-butyl alcohol was added dropwise. The addition was complete in 1–2 hr with the reaction temperature maintained between -30 and -10° by external cooling. After the addition was complete, the reaction mixture was allowed to stir for an additional 2 hr and worked up with the addition of *n*-pentane followed by water and separation of the two layers. The *n*-pentane layer was washed three or four times with water and later dried over anhydrous magnesium sulfate for 12 hr. The *n*-pentane layer was purple, probably owing to iodine formed in the decomposition of the 1,1-diiodo-2,2-dimethylcyclopropane (1). The *n*-pentane was removed by distillation and a dark brown residue remained. Attempts to purify this material resulted in the formation of free iodine indicating decomposition.

Compound 2 was then prepared by reduction of 1 with tri-*n*-butyltinhydride at room temperature in 65% yield: bp 40 – 41° (20 mm); n_D^{20} 1.5065.

Anal. Calcd for C_5H_9I : C, 30.64; H, 4.63; I, 64.74. Found:¹¹ C, 30.54; H, 4.67; I, 64.89.

1-Iodo-*cis,trans*-2,3-dimethylcyclopropane (5) was prepared from 1,1-diiodo-2,3-*trans*-dimethylcyclopropane (4) which was obtained in 65% yield from *trans*-butene-2 in a manner similar to that used for 1. Compound 4 was then reduced with tri-*n*-butyltin hydride as 2 in 60% yield: bp 44 – 45° (19 mm); n_D^{20} 1.5067.

Anal. Calcd for C_5H_9I : C, 30.64; H, 4.62; I, 64.74. Found:^{11,12} C, 30.89; H, 4.66; I, 67.56.

1-Iodo-*cis,cis*-2,3-dimethylcyclopropane (6) and **1-iodo-*trans,trans*-2,3-dimethylcyclopropane (7)** were obtained by the reduction of 1,1-diiodo-2,3-*cis*-dimethylcyclopropane (3) which was obtained from *cis*-butene-2 in 80% yield by the same procedure used for the preparation of 1. The reduction gave 70% yield of a mixture of 6 and 7 with bp 50 – 52° (40 mm). Gas chromatographic analysis indicated the ratio of products was 3:1 and this technique was used to separate sufficient material for nmr and mass spectral studies.

All nmr spectra were obtained with a Varian DP-60 spectrometer in 20% benzene solution with benzene used as an internal standard or on a Varian A-60 spectrometer with the same samples. The mass spectra were obtained on an Atlas CH-4 mass spectrometer with 70-v ionizing potential.

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(11) Analysis was carried out by Midwest Micro Lab, Inc., Indianapolis, Ind.

(12) The compound underwent some decomposition prior to analysis for iodine.

(10) *cis* and *trans* refer to the position of the methyl group relative to the halogen atom in the monohalo derivatives.