Journal of Organometallic Chemistry
Elsevier Sequoia S.A., Lausanne
Printed in The Netherlands

THE REACTION OF OPTICALLY ACTIVE (1-METHYL-2,2-DIPHENYLCYCLOPROPYL)TRIMETHYLTIN WITH BROMINE OR IODINE

KEIITI SISIDO, TOKUO MIYANISI AND TYÛZÔ ISIDA
Department of Industrial Chemistry, Kyôto University, Kyôto (Japan)
AND SINPEI KOZIMA
Department of Liberal Arts and Sciences, Kyôto University, Kyôto (Japan)

(Received January 10th, 1970)

SUMMARY

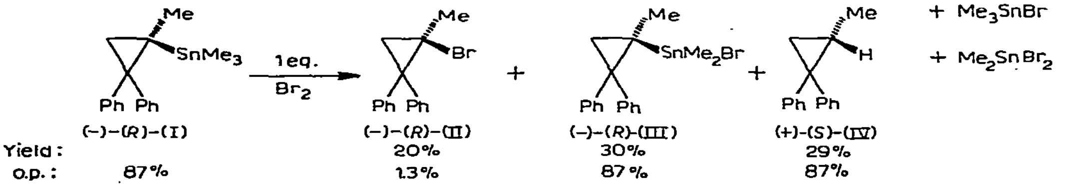
Reaction of an optically active (1-methyl-2,2-diphenylcyclopropyl)trimethyltin (I) with bromine (or iodine) afforded 1-bromo-(or iodo)-1-methyl-2,2-diphenylcyclopropane (II) with a small degree of retention of configuration. This is best interpreted in terms of radical mechanism for the cleavage of the cyclopropyl carbon–tin bond in (I) by bromine or iodine.

Attempts to synthesize optically active organotin compounds whose asymmetric center was the tin atom were not successful[1,2] and the investigation of the stereochemistry of substitution at tin has not been possible, in contrast to the situation for silicon[3].

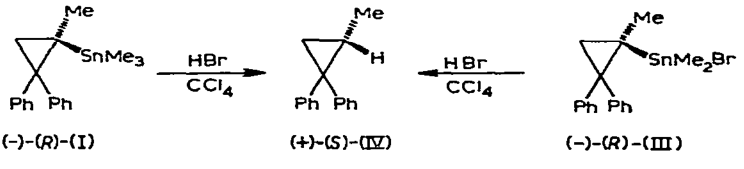
We previously[4] briefly reported the preparation of the optically active (1-methyl-2,2-diphenylcyclopropyl)trimethyltin (I) in which the asymmetric centre was the carbon atom directly attached to tin. Cleavage of the asymmetric carbon–tin bond of (I) by iodine gave the racemic cyclopropyl iodide which suggested a radical mechanism for the iodinolysis of the cyclopropyl carbon–tin bond in (I). Baekelmans, Gielen and Nasielski[5], however, reported that the *cis*-(or *trans*)-2-methylcyclopropyl carbon–tin bond is cleaved by halogen with almost complete retention ($>94\%$) of configuration, and they proposed an S_E2 mechanism for the halogenolysis of organotin compounds. Their results prompted us to reinvestigate the reaction of (I) with bromine and iodine in order to obtain more information on the reaction mechanism. The revised experiments have confirmed our previous results[4], indicating a radical mechanism.

Reaction of (–)-(*R*)-(I) [optical purity (o.p.) 87%] with an equimolar amount of bromine in carbon tetrachloride solution in the dark gave (–)-(*R*)-1-bromo-1-methyl-2,2-diphenylcyclopropane (II) (o.p. 1.3%) in which the configuration had been retained to a small extent, together with unracemized (1-methyl-2,2-diphenylcyclopropyl)dimethyltin bromide (III) (o.p. 87%), 1-methyl-2,2-diphenylcyclopropane (IV) (o.p. 87%), trimethyltin bromide and dimethyltin dibromide.

Treatment of (–)-(*R*)-(I) (o.p. 87 %) with four equivalent of bromine gave (–)-(*R*)-(II)(o.p. 1.0 %) and (+)-(*S*)-(IV) (o.p. 87 %) in 33 and 51 % yields, respectively.

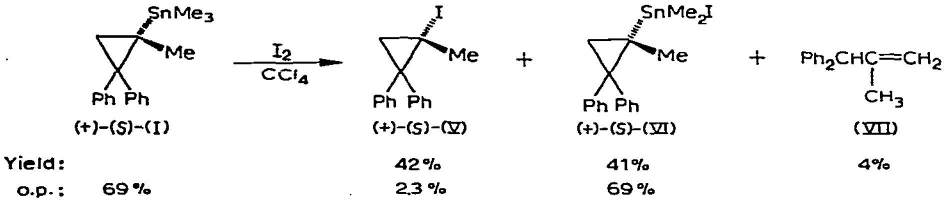


The tin-free cyclopropane derivative (IV) in which there has been over-all retention of configuration might have been produced from (I) and/or (III) by the reaction with hydrogen bromide generated in the system, and we confirmed that, when anhydrous hydrogen bromide was bubbled into a carbon tetrachloride solution of (I) under the same reaction condition the cyclopropane (IV) was obtained with the complete retention of the configuration. The reaction of the organotin monobromide (III) with anhydrous hydrogen bromide gave a similar result. The reaction with anhydrous hydrogen bromide in carbon tetrachloride possibly proceeds via an ionic mechanism, analogous to the reaction of (I) with concentrated hydrochloric acid in carbon tetrachloride[4].



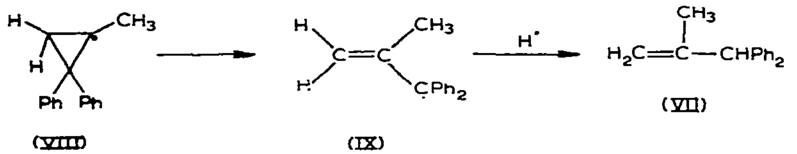
Since the brominolysis was carried out under the anhydrous condition, there was no source of hydrogen for the hydrogen bromide except the three methyl and/or 1-methyl-2,2-diphenylcyclopropyl groups. A small amount of an unidentified tarry material containing bromine and phenyl group was obtained from the reaction mixture and probably represented at least a part of the brominated fragments which had supplied hydrogen.

The reaction of (+)-(*S*)-(I) (o.p. 69 %) with four equimolar amounts of iodine in carbon tetrachloride afforded almost fully racemized (+)-(*S*)-1-iodo-1-methyl-2,2-diphenylcyclopropane (V) (o.p. 2.3 %), together with unracemized (1-methyl-2,2-diphenylcyclopropyl)dimethyltin iodide (VI) and 2-methyl-3,3-diphenylpropene (VII).

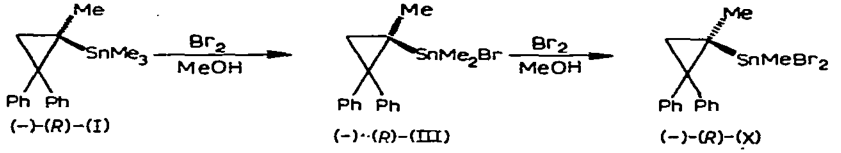


It was checked that optically active (II) and (V) did not lose optical activity during the separation on a silica gel column. The possibility that (II) or (V) is racemized in the presence of halogen and the methyltin halides is unlikely, since optically active (II) or (V) does not lose its optical activity under such condition. The racemization must therefore occur during the actual halogenolysis of (I).

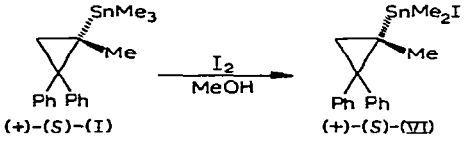
An electrophilic mechanism is improbable for the racemization because complete stereospecificity was established in the halogenolysis of optically-active 1-methyl-2,2-diphenylcyclopropyllithium[6,7]. Thus the formation of the almost fully racemized (II) and (V) could be best interpreted in terms of a radical mechanism, since the 1-methyl-2,2-diphenylcyclopropyl radical (VIII) is known to be incapable of maintaining the configuration[8]. The slight retention of the optical activities of (II) and (V) produced by the halogenolyses of the optically active (I) might be attributable to the relatively rapid front-side trapping of the radical (VIII) by halogen before complete configurational equilibration could be attained, as in a case as discussed by Jacobus and Pensak[9]. Correspondingly, the slight inversion found in the reduction of (II) with triphenyltin hydride to give (VI) was attributed to front-side blocking by the triphenyltin group[10]. The propylene derivative (VII) might be produced by the hydrogen abstraction of a radical (IX) formed by the radical migration from the cyclopropyl radical (VIII).



Reaction of (I) with an equimolar amount of bromine was carried out in methanol under the similar conditions, and resulted in a distinctively selective cleavage of the methyl carbon–tin bond to give (III) in 97% yield. Treatment of (I) with two equivalents of bromine brought about cleavage of an additional methyl carbon–tin bond and afforded (1-methyl-2,2-diphenylcyclopropyl)methyltin dibromide (X) in 74% yield. The dibromide (X) did not react further to give either 1-methyl-2,2-diphenylcyclopropyltin tribromide or (II) even under more vigorous reaction condition, *i.e.*, heating at 65° in the presence of more than two equivalents of bromine.



When compound (I) was treated with an equimolar amount of iodine in methanol, (VI) was produced in 93% yield. Treatment of (I) with more than an equivalent of iodine, however, did not give diiodide. The observation that methyl groups in (I) are more easily cleaved from tin by bromine or iodine than the 1-methyl-2,2-diphenylcyclopropyl group is consistent with the observations of Nasielski and his



co-workers[11] that the methyl groups of cyclohexyltrimethyltin are cleaved by bromine with high selectivity.

Since the secondary cyclopropyl can be expected to invert more readily than a tertiary radical[12-14], the contrast between our results and those obtained with the 2-methylcyclopropyl group by Nasielski and collaborators[5] cannot be attributed simply to the configurational difference, and further investigations are in progress.

EXPERIMENTAL

All reactions were carried out under dry nitrogen at room temperature in the dark. Solvents were of ultraviolet spectrum grade unless otherwise stated. The bromine was dried over phosphorus pentoxide and distilled immediately before use.

Reaction products were analyzed by gas chromatography using a Shimazu GC-2C instrument, and preparative scale separations were carried out by elution chromatography on silica gel.

The NMR spectra were measured in deuterochloroform on the Japan Electron Optics C-60-H Spectrometer operating at 60 MHz, and were enlarged where necessary. Chemical shifts are given in ppm downfield from internal tetramethylsilane. Optical rotations were measured within 0.5° on a Yanagimoto OR-20 Direct Reading Polarimeter.

(−)-(*R*)-(I), b.p. 145–146°/2 mm, $[\alpha]_D$ −35.5° (*c* 1.12 in $CHCl_3$), was obtained by treating (−)-(*R*)-(II), $[\alpha]_D$ −99.2° (*c* 1.34 in $CHCl_3$, o.p. 87%) with trimethylstannyllithium in dry tetrahydrofuran, as described previously[4]. The same treatment of (+)-(*S*)-(II), $[\alpha]_D$ +76.7° (*c* 1.31 in $CHCl_3$, o.p. 69%) gave (+)-(*S*)-(I), $[\alpha]_D$ +27.5° (*c* 1.14 in $CHCl_3$).

Reaction of (−)-(R)-(I) with bromine in carbon tetrachloride

To a stirred solution of 1.10 g (0.0030 mole) of (−)-(*R*)-(I) in 30 ml of carbon tetrachloride 0.48 g (0.0030 mole) of freshly distilled bromine in 30 ml of carbon tetrachloride was added dropwise during 30 min. The solution became colourless after 3 h stirring and white fumes of hydrogen bromide appeared when the solution was exposed to air. The solvent was removed *in vacuo* to give 1.30 g of a dark green liquid which was separated by column chromatography on silica gel (20 × 700 mm) and eluted as follows. (*i*). n-Hexane (300 ml) eluted 0.17 g (29%) of (+)-(*S*)-(IV), $[\alpha]_D$ +111.1° (*c* 1.14 in $CHCl_3$, o.p. 87%), b.p. 111–113°/3 mm (lit.[7] b.p. 77–80°/0.05 mm), together with 0.06 g of the recovered (−)-(*R*)-(I). (*ii*). With additional 500 ml of n-hexane there was eluted 0.16 g (20%) of (−)-(*R*)-(II), $[\alpha]_D$ −1.5° (*c* 1.04 in $CHCl_3$, o.p. 1.3%), m.p. 82–83° (lit.[7] m.p. 81–82°), which was identified by NMR spectrum and elemental analysis. (*iii*). Benzene (500 ml) yielded 0.37 g (30%) of (−)-(*R*)-(III), $[\alpha]_D$ −39.9° (*c* 1.21 in $CHCl_3$), m.p. 112–113° (methanol). (Found: C, 49.57, H, 4.78. $C_{18}H_{21}BrSn$ calcd.: C, 49.82, H, 4.88%) The NMR spectrum of (III) had a multiplet at 7.13–7.61 (10 H, phenyl protons), a multiplet at 1.41–1.76 (2 H, ring protons), a singlet at 1.32 (3 H, carbon-methyl protons) and two singlets, at 0.61 and −0.13 ppm (6 H, tin-methyl protons) accompanied by small satellite peaks [$J(^{117}Sn{-}CH_3)$ 53.4, $J(^{119}Sn{-}CH_3)$ 55.5 Hz]. The difference in the chemical shifts for the two tin-methyl protons can be explained in terms of the dissimilar environments for the methyl groups arised from diastereotopic shielding by neighbouring asymmetric carbon center[15]. (*iv*). A mixture of ether (180 ml) and benzene (120 ml), and an additional 300 ml of ether gave 0.11 g of a dark, tarry mixture which could not be identified. The infrared spectrum of the mixture exhibited phenyl absorption and the Beilstein test showed the existence of bromine. (*v*). Elution with methanol (400 ml) gave 0.11 g of stannic oxide. The presence of trimethyltin bromide and dimethyltin dibromide in the reaction mixture was affirmed by the GLC analysis involving comparison with authentic samples.

The same treatment of 0.46 g (0.0012 mole) of (−)-(*R*)-(I) (o.p. 87%) with four equivalents of bromine gave two main products; 0.13 g (51%) of (+)-(*S*)-(IV), $[\alpha]_D$ +111.4° (*c* 1.12 in $CHCl_3$, o.p. 87%) and 0.12 g (33%) of (−)-(*R*)-(II), $[\alpha]_D$ −1.2° (*c* 1.31 in $CHCl_3$, o.p. 1.0%).

Reaction of (+)-(*S*)-(*I*) *with iodine in carbon tetrachloride*

To a stirred solution of 0.95 g (0.0026 mole) of (+)-(*S*)-(I) in 30 ml of carbon tetrachloride was added dropwise 2.60 g (0.0104 mole) of iodine in 120 ml of carbon tetrachloride. The reaction was slower than that with bromine and the end of the reaction was determined by a gas chromatography sampling at every hour. After vigorous stirring for 65 h, the solvent was removed *in vacuo* and ether was added. The ether layer was shaken with dilute solution of sodium bisulfite, and washed with water, dried with sodium carbonate and concentrated under reduced pressure to give 1.16 g of products which were separated by column chromatography. (*i*). The mixture was eluted with 300 ml of n-hexane to give 0.07 g of amber-coloured mixtures containing a volatile product. By preparative GLC using a packing of High Vacuum Silicone Grease, 0.02 g (4%) of (VII) was separated, n_D^{20} 1.3764. (Found: C, 92.15, H, 7.87. $C_{16}H_{16}$ calcd.: C, 92.26; H, 7.74%.) The NMR spectrum showed a multiplet at 7.23 (10 H, phenyl protons), a multiplet at 5.08 (1 H, *trans*-proton of terminal olefin with respect to methyl group), a multiplet at 4.52 (1 H, *cis*-proton with respect to methyl group), a multiplet at 4.72 (1 H, allylic proton) and a singlet at 1.81 ppm (3 H, methyl protons). (*ii*). A further 400 ml of n-hexane eluted 0.36 g (42%) of (+)-(*R*)-(V), $[\alpha]_D$ +4.0° (*c* 2.00 in $CHCl_3$, o.p. 2.3%), m.p. 94–95° (lit.[7] m.p. of racemate 86.5–88.0°, m.p. of pure enantiomer 117–119°). (*iii*). A mixture of 60 ml of benzene and 180 ml of ether, and 300 ml of ether eluted 0.51 g (41%) of (+)-(*S*)-(VI), $[\alpha]_D$ +34.1° (*c* 1.01 in $CHCl_3$), m.p. 150–151° (petroleum ether). (Found: C, 44.47, H, 4.68. $C_{18}H_{21}ISn$ calcd.: C, 44.77, H, 4.38%.) The NMR spectrum consisted of a multiplet at 7.06–7.58 (10 H, phenyl protons), a multiplet at 1.35–1.74 (2 H, ring protons), a singlet at 1.30 (3 H, carbon-methyl protons) and two singlets at 0.60 and −0.06 ppm [6 H, tin-methyl protons; $J(^{117}Sn–CH_3)$ 53.5, $J(^{119}Sn–CH_3)$ 55.5 Hz]. The difference in the chemical shifts of the two tin-methyl groups can be explained as for (−)-(*R*)-(III).

Reaction of (−)-(*R*)-(*I*) *with bromine in methanol*

To a vigorously stirred solution of 1.05 g (0.0028 mole) of (−)-(*R*)-(I) in 30 ml of methanol was added dropwise 0.45 g (0.0028 mole) of bromine in 30 ml of methanol. Though the colour of bromine initially disappeared, the reaction solution became dark red as the addition proceeded. After stirring for 3 h at room temperature, methanol was evaporated under reduced pressure from the pale orange solution to leave 1.32 g (97%) of (−)-(*R*)-(III), $[\alpha]_D$ −40.1° (*c* 1.02 in $CHCl_3$).

Reaction of 1.26 g (0.0034 mole) of (−)-(*R*)-(I) in 35 ml of methanol with 2.18 g (0.0136 mole) of bromine in 140 ml of methanol was carried out as above for 10 h. The solvent was removed *in vacuo* and the resultant white solid was recrystallized from petroleum ether to give 1.25 g (74%) of (−)-(*R*)-(X), $[\alpha]_D$ −56.4° (*c* 1.11 in $CHCl_3$), m.p. 94–95°. (Found: C, 41.07, H, 3.87. $C_{17}H_{18}Br_2Sn$ calcd.: C, 40.77; H, 3.62%.) The NMR spectrum showed a multiplet at 7.10–7.74 (10 H, phenyl protons), a multiplet at 1.47–2.07 (2 H, ring protons), a singlet at 1.46 (3 H, carbon-methyl protons) and a singlet at 0.35 ppm (3 H, tin-methyl protons) accompanied by satellites [$J(^{117}Sn-CH_3)$ 64.5, $J(^{119}Sn-CH_3)$ 67.5 Hz].

Reaction of (+)-(S)-(I) with iodine in methanol

To a stirred solution of 0.89 g (0.0024 mole) of (+)-(*S*)-(I) in 25 ml of methanol was added dropwise 2.45 g (0.0096 mole) of iodide in 100 ml of the same solvent. After vigorous stirring for 65 h, the reaction solution was treated as above to give 0.93 g (93%) of (+)-(*S*)-(VI), $[\alpha]_D$ +33.9° (*c* 1.34 in $CHCl_3$).

Reaction of (−)-(R)-(I) with anhydrous hydrogen bromide

Anhydrous hydrogen bromide was bubbled into 30 ml of a carbon tetrachloride solution of (−)-(*R*)-(I) (0.24 g, 0.00065 mole, o.p. 87%) with vigorous stirring. When the starting material was consumed, the solvent was evaporated under reduced pressure to give 0.13 g (96%) of (+)-(*R*)-(IV), $[\alpha]_D$ +111.3° (*c* 1.51 in $CHCl_3$, o.p. 87%). The corresponding amount of trimethyltin bromide was trapped by a condenser cooled in a solid carbon dioxide/acetone bath.

REFERENCES

1 W. J. Pope and S. J. Peachey, *Proc. Chem. Soc.*, 16 (1900) 42, 116.
2 F. B. Kipping, *J. Chem. Soc.*, (1928) 2365.
3 L. H. Sommer, *Stereochemistry, Mechanism and Silicon*, McGraw-Hill, New York, 1965.
4 K. Sisido, S. Kozima and K. Takizawa, *Tetrahedron Lett.*, (1967) 33.
5 P. Baekelmans, M. Gielen and J. Nasielski, *Tetrahedron Lett.*, (1967) 1149.
6 J. B. Pierce and H. M. Walborsky, *J. Org. Chem.*, 33 (1968) 1962.
7 H. M. Walborsky, F. J. Impastato and A. E. Young, *J. Amer. Chem. Soc.*, 86 (1964) 3283.
8 H. M. Walborsky, Chen-Jong Chen and J. L. Webb, *Tetrahedron Lett.*, (1964) 3351; H. M. Walborsky and Chen-Jong Chen, *J. Amer. Chem. Soc.*, 89 (1967) 5499.
9 J. Jacobus and D. Pensak, *Chem. Commun.*, (1969) 400.
10. L. J. Altman and B. W. Nelson, *J. Amer. Chem. Soc.*, 91 (1969) 5163.
11 S. Boué, M. Gielen and J. Nasielski, *Tetrahedron Lett.*, (1968) 1047.
12 D. E. Applequist and A. H. Peterson, *J. Amer. Chem. Soc.*, 82 (1960) 2372.
13 H. Nozaki, T. Aratani and Y. Nakanisi, *Tetrahedron Lett.*, (1969) 1809.
14 M. J. S. Dewar and J. M. Harris, *J. Amer. Chem. Soc.*, 91 (1969) 3652.
15 M. Van Gorkom and G. E. Hall, *Quart. Rev.*, 22 (1968) 14.