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Reduction of Some 7-Halonorcaranes with Tri-*n*-butyltin Hydride

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It has been found that the reduction of 1-chloro-(or -bromo-)1-fluorocyclopropanes with tri-*n*-butyltin hydride at 0—135°C generally proceeds stereospecifically, *i.e.*, with a complete retention of the configuration.[1,2] Thus, 7-*exo*-chloro-7-*endo*-fluoronorcarane gives 7-*endo*-fluoronorcarane exclusively, and 7-*endo*-chloro-7-*exo*-fluoronorcarane gives 7-*exo*-fluoronorcarane exclusively. Since the reduction of organic halides with organotin hydrides is known to be a radical process,[3] this result must be interpreted as being due to the pyramidal structure of the intermediately-formed 7-fluoro-7-norcaryl radical and the slow rate of its inversion of configuration relative to its hydrogen abstraction.

As was mentioned in the previous paper,[2] the reduction of 7-bromo-7-chloronorcarane shows a lower degree of stereospecificity; one of its geometrical isomers, 7-*exo*-bromo-7-*endo*-chloronorcarane, gives a 76: 24 mixture of 7-*endo*- and -*exo*-chloronorcarane when reduced with tri-*n*-butyltin hydride at 0°C. Analogous results have very recently been reported by Altman and Baldwin.[4] Obviously, the inversion of the 7-chloro-7-norcaryl radical can compete with hydrogen abstraction even at 0°C, resulting in the decrease of stereospecificity.

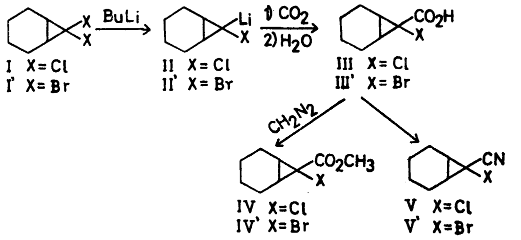
In contrast, the reduction of the geometrical isomers of 1-bromo-1-trifluoromethyl-2-phenylcyclopropane with triphenyltin hydride has been reported to give a mixture of the two possible geometrical isomers of the same composition, irrespective of the geometry of the starting material.[5]

These experimental facts suggest that the configurational stability of cyclopropyl radicals is strongly affected by the nature of the substituent at the 1-position.

The present paper will deal with studies of the reduction of 7-methoxycarbonyl- and 7-cyano-substituted 7-chloro-(or -bromo-)norcarane with tri-*n*-butyltin hydride, carried out in order to ascertain the effect of substituents at the 7-position upon the configurational stability of 7-norcaryl radicals.

Results and Discussion

The norcarane derivatives employed for the present study, *i.e.*, methyl 7-chloro-(or -bromo-)norcarane-7-carboxylate (IV or IV′) and 7-chloro-(or -bromo-)-norcarane-7-nitrile (V or V′), were prepared from the corresponding carboxylic acids (III and III′), which had been synthesized by applying the method of Köbrich and Goyert[6] to 7,7-dichloro-(and -dibromo-)-norcarane (I and I′):



It was found that, although 7,7-dichloronorcarane (I) gave a mixture of the two geometrical isomers of the chloro acid (III), 7,7-dibromonorcarane (I′) gave little, if any, of the *endo*-bromo isomer of 7-bromonorcarane-7-carboxylic acid (III′), even when the reaction (treatment with *n*-butyllithium followed by

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[1] T. Ando, F. Namigata, H. Yamanaka, and W. Funasaka, *J. Amer. Chem. Soc.*, **89**, 5719 (1967).

[2] T. Ando, H. Yamanaka, F. Namigata, and W. Funasaka, *J. Org. Chem.*, **35**, 33 (1970).

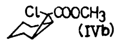
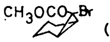
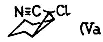
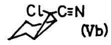
[3] L. W. Menapace and H. G. Kuivila, *J. Amer. Chem. Soc.*, **86**, 3047 (1964).

[4] L. J. Altman and R. C. Baldwin, *Tetrahedron Lett.*, **1971**, 2531.

[5] L. J. Altman and J. C. Vederas, *Chem. Commun.*, **1969**, 895.

[6] G. Kobrich and W. Goyert, *Tetrahedron*, **24**, 4327 (1968).

Table 1. Properties of 7-substituted 7-halonorcaranes

Structure	Bp, °C/mmHg (Mp, °C)	n_D (°C)	$\nu_{C=O}$, cm^{-1} ($\nu_{C\equiv N}$, cm^{-1})	δ_{OCH_3}, ppm (δ_{OH}, ppm)	C % Found	C % Calcd	H % Found	H % Calcd	N % Found	N % Calcd
 (III'a)	(110—111)	—	1705	(11.76)	44.09	43.85	5.31	5.07	—	—
 (IVa)	123—126/22	1.4892 (18)	1745	3.77	57.43	57.29	6.96	6.96	—	—
 (IVb)	123—126/22	1.5009 (18)	1730	3.73	57.23	57.29	6.90	6.96	—	—
 (IV'a)	70—72/3	1.5080 (19)	1730	3.78	46.35	46.37	5.67	5.63	—	—
 (Va)	118—120/20	1.4940 (22)	(2250)	—	61.60	61.34	6.55	6.45	8.70	8.94
 (Vb)	118—120/20	1.5007 (22)	(2250)	—	61.54	61.34	6.56	6.45	8.67	8.94
 (V'a)	119/13	1.5249 (16)	(2230)	—	47.76	48.02	5.05	4.73	6.72	7.00

carbonation) was conducted at −150 to −140°C. The assignment of the *exo*-bromo configuration to the isolated product was based on the methanolysis of the reaction mixture at the same temperature, which gave predominantly the *exo*-bromo isomer of 7-bromonorcarane.[7,8] Probably the *endo*-bromo lithium carbenoid (II', X=*endo*-Br), if formed, had reacted with the tetrahydrofuran solvent to form 7-*exo*-(2-tetrahydrofuryl)norcarane[6] before carbon dioxide was added to the reaction mixture. The possibility cannot be excluded, however, that the *endo*-bromo carbenoid isomerizes to the *exo*-bromo carbenoid under the reaction conditions.

Each of the geometrical isomers of 7-chloronorcarane-7-carboxylic acid (III), as well as 7-*exo*-bromonorcarane-7-*endo*-carboxylic acid (III'a), was converted to the corresponding methyl ester or nitrile by the usual methods. The assignment of configuration to the products is straightforward, since no configurational change should occur during these transformations.

The properties of the hitherto-unknown 7-substituted 7-chloro-(or -bromo-)norcaranes thus prepared are shown in Table 1.

The reduction of the chloro (or bromo) esters and nitriles was performed by treating them with a slight excess of tri-*n*-butyltin hydride under the variety of conditions shown in Table 2. The yields of the reduction product were about 90% for the esters and about 70% for the nitriles. The isomer distributions in the product, which were determined by vpc before distillation, are also listed in Table 2.

As is evident from Table 2, the isomer ratios in the product were nearly identical in all experimental runs. This implies that the 7-methoxycarbonyl- or -cyano-7-norcaryl radical, which would be intermediately formed in the process of the reduction, is either pyramidal but inverts its configuration so rapidly that it behaves as if it were planar, or is in fact planar. Very probably the *p*-*π* conjugation between the *π*-electrons in the methoxycarbonyl or the cyano group and the *p*-electron at the radical center lowers the energy barrier for the inversion of the configuration of these radicals.

Table 2. Reduction of 7-substituted 7-halonorcaranes

Compound reduced	Reaction condition Catalyst	Temp., (°C)	Time, (hr)	Isomer ratio in product (*endo*-: *exo*-)
IVa	AIBN	80	8	93:7
	DTBP	140	4	92:8
IVb	AIBN	80	8	94:6
	DTBP	140	4	93:7
IV'a	None	0	2	95:5
	None	110	2	93:7
	None	170	2	90:10
Va	AIBN	80	8	93:7
	DTBP	140	4	92:8
Vb	AIBN	80	8	94:6
	DTBP	140	4	92:8
V'a	None	0	2	97:3
	None	110	2	94:6
	None	170	2	91:9

The predominant formation of the *endo*-substituted isomers in these reductions must be due to the greater steric repulsion in the hydrogen transfer from the tin hydride to the *endo* side of the radical than to the *exo* side. The increase in the relative amount of the *exo*-substituted product with the increase in the reaction temperature may be explained on the same ground.

Experimental

The proton NMR spectra were recorded on a JEOL C-60H spectrometer in carbon tetrachloride with tetramethylsilane (TMS) as the internal reference. The chemical shifts (δ) are expressed in ppm downfield from TMS. In vapor-phase chromatography (vpc), a Golay column of 0.5 mm × 45 m (BDS 45) was used for analytical purposes, and a column of 10 mm × 0.8 m (30% Silicone Grease on 60—80 mesh Celite 550), for preparative purposes. The isomer distributions in the products were determined from the peak areas in vpc before distillation.

*Reduction of 7-Substituted 7-Halonorcaranes with Tri-*n*-butyltin Hydride.* The reduction of chloro derivatives was effected by heating a mixture of an isomerically-pure substrate (IVa, IVb, Va, or Vb) and a slight excess of tri-*n*-butyltin hydride under nitrogen with stirring in the presence of a small amount

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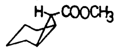
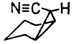
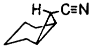
[7] D. Seyferth, H. Yamazaki, and D. L. Alleston, *J. Org. Chem.*, **28**, 703 (1963).

[8] C. L. Osborn, T. C. Shields, B. A. Shoulders, C. G. Cardenas, and P. D. Gardner, *Chem. Ind.* (London), **1965**, 766.

Table 3. Properties of the products

Structure	Bp, °C/mmHg	n_D (°C)	$\nu_{C=O}$, cm^{-1} ($\nu_{C\equiv N}$, cm^{-1})	δ_{OCH_3}, ppm	C %		H %		N %	
					Found	Calcd	Found	Calcd	Found	Calcd
	93—95/18	1.4786 (18)	1735	6.93	69.78	69.65	9.20	9.09	—	—
	93—95/18	1.4729 (26)	1720	6.43	69.51	69.65	8.95	9.09	—	—
	125—130/55	1.4930 (19)	(2250)	—	79.31	79.29	8.93	9.15	11.44	11.56
	109—111/22	1.4857 (25)	(2250)	—	79.56	79.29	9.30	9.15	11.75	11.56

of azobisisobutyronitrile (AIBN) or di-*t*-butyl peroxide (DTBP). For bromo derivatives (IV′a or V′a), tri-*n*-butyltin hydride was gradually added to a substrate kept at a constant temperature. The reaction conditions and the isomer distributions in the products are shown in Table 2. The identification of the products was made by preparing authentic samples of norcarane-7-*endo*- or -*exo*-carboxylic acid by the method of Skell and Etter,[9] converting them to the corresponding methyl esters or nitriles in the usual way and then comparing their physical properties (IR, NMR, and mass spectra as well as retention times in vpc) with those of the products. Generally, the *endo* esters or nitriles had a shorter retention time than the *exo* isomers. The properties of the products are summarized in Table 3, together with the results of elemental analyses.

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[9] P. S. Skell and R. M. Etter, *Proc. Chem. Soc.*, **1961**, 443.