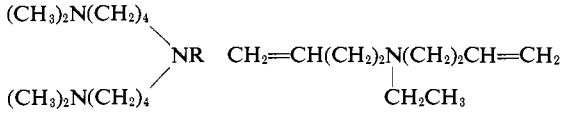
$N^+=CH_2$]. Hydrogenation (consumption, 1.3 molar equiv) furnished hydrosolapartine (λ_{max} 6.06 μ; nmr τ 6.66, 7.77, 8.73, and 9.12), with principal mass spectral peaks at *m/e* 481 ($C_{30}H_{63}N_3O$), 466 ($C_{29}H_{60}N_3O$), 453 ($C_{28}H_{59}N_3O$), and 438 ($C_{27}H_{56}N_3O$), 395, 100, 98, 84, and 58. Subsequent reduction with lithium aluminum hydride gave desoxyhydrosolapartine, nmr τ 7.77, 8.72, 9.12, and principal mass spectral peaks at *m/e* 467, 439, 353, 228, 100, 98, 84, and 58, indicative of the presence of amide and vinyl groupings in solapartine.

Acid hydrolysis of hydrosolapartine gave an amine, *solamine*, $C_{12}H_{29}N_3$ [*m/e* 251 (M^+), 129, 116, 115, 100, 98, 84, 71, and 58 (base peak); λ_{max} 2.94, 3.03, and 6.01 μ (NH); nmr τ 7.77 (NCH_3) and 8.50 (multiplet, CH_2)], and a fatty acid fraction. Mass spectrometry and glpc established that the acid fraction was a mixture of palmitic (80%) and stearic (20%) acids. These results accounted for the molecular ion peaks at *m/e* 453 (solamine + C_{16} acid) and 481 (solamine + C_{18} acid) in hydrosolapartine. Hydrolysis of solapartine gave solamine and a complex mixture of C_{16} and C_{18} acids.

Structural elucidation of solamine was accomplished *via* conversion of N-acetylsolamine (*m/e* 257 (M^+), 242 (M − 15), 213, 199, 186, 100, 98, 84, 58; λ_{max} 6.06 μ) successively to its dimethiodide and dimethohydroxide, respectively. Heating under reduced pressure gave a neutral methine (*m/e* 167 (M^+), 126, 84) and trimethylamine. Reduction of the methine with lithium aluminum hydride produced a desoxymethine [*m/e* 153 (M^+), 112 (base peak, M − 41), 84, 58, and 55], characterized as IV. Unambiguous confirmation was provided by hydrogenation of IV to its tetrahydro product [*m/e* 157 (M^+), 114, 86, and 58] and direct comparison (mass spectroscopy and mixture melting point of picrate, 85–87°, and oxalate, 92–97°) with synthetic ethyldi-*n*-butylamine. The conclusion that solamine possesses structure I was confirmed by direct comparison (infrared, nmr, mass spectra) with a sample prepared by hydrogenation of 4-dimethylaminobutyronitrile.[8]



I, R = H
II, R = $CO(CH_2)_{14}CH_3$
III, R = *trans*-$COCH{=}CH(CH_2)_{12}CH_3$

IV

A detailed examination of the highest mass peaks for solapartine and its reduced derivatives indicated that the unsaturation corresponding to the nmr signal at τ 4.63 was present in amides with C_{18}-acyl residues. The principal components in the solapartine mixture, however, were the α,β-unsaturated C_{16}-acyl amide (mol wt 451) and the corresponding saturated C_{16}-acyl amide (mol wt 453). Separation of these two major components from the solapartine mixture was accomplished by the procedure which follows. Treatment of solapartine with peroxyacetic acid and recovery of unchanged starting material by alumina chromatography gave a mixture which showed molecular ion peaks at *m/e* 451 and 453, but no peaks at *m/e* 473–479 or at τ 4.63 in the nmr spectrum. This material was treated with bromine to yield two compounds, separable by alumina chromatography. Solapalmitine, $C_{28}H_{59}N_3O$, *m/e* 453 (M^+), 438 (M − Me), 409, 395, 381, 367, 270, 227, 214, 199, 100, 98, 84, 71, 58 (base peak), showed λ_{max} 6.06 μ (amide CO); nmr τ 6.67 (4 H, CH_2NCOR), 7.78, 8.73, 9.13. The mass spectrum of solapalmitine was identical (apart from very minor signals attributable to residual solapalmitenine) with that of II prepared by acylation of solamine with palmitoyl chloride and triethylamine. The second product was a dibromo compound, $C_{28}H_{57}Br_2N_3O$, *m/e* 531, 529 (M − HBr), 451 (M − Br_2), 450 (M − HBr − Br); λ_{max} 6.01 μ (amide CO); nmr τ 4.80–5.30 (2 H, multiplet, $-CHBrCHBr-$), 6.60 (4 H, multiplet, CH_2NCOR), 7.53 (NCH_3), 7.67 (NCH_3), 8.72, and 9.12. Debromination with zinc in acetone gave solapalmitenine, $C_{28}H_{57}N_3O$, *m/e* 451 (M^+), 436 (M − Me), 407, 393, 379, 365, 268, 225, 214, 211, 197, 100, 98, 84, 71, and 58 (base peak); λ_{max} 6.02 (amide CO), 6.16, and 10.20 μ ($-CH{=}CH-$); nmr τ 3.12 (1 H, sextet, J = 15 and 7 cps, $NCOCH{=}CHCH_2-$), 3.89 (1 H, doublet, J = 15 cps, $NCOCH{=}CH-$), 6.68, 7.77, 8.74, and 9.14. The infrared, nmr, and mass spectra of solapalmitenine were identical with those of III prepared by acylation of solamine with *trans*-hexadec-2-enoyl chloride[9] in the presence of triethylamine.

Further synthetic investigations are in progress which are aimed at determination of the structural requirements for activity among these novel tumor inhibitors.

Acknowledgment. The authors thank Drs. A. Morrison, P. C. Harries, M. T. A. Evans, and H. Preston, Unilever Ltd., England, for preliminary mass spectral and glpc data.

(8) M. Freifelder, *J. Am. Chem. Soc.*, **82**, 2386 (1960).

(9) D. Shapiro, H. Segal, and H. M. Flowers, *ibid.*, **80**, 1194 (1958).

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Reduction of *gem*-Halofluorocyclopropanes with Tri-*n*-butyltin Hydride

Sir:

The geometry of the cyclopropyl radical has long been a subject of investigations, and a number of unsuccessful attempts at intercepting the nonplanar radical have been reported.[1-3] Here we wish to report on the stereospecificity observed in the reductions of some *gem*-halofluorocyclopropanes with tri-*n*-butyltin hydride, which strongly suggests a pyramidal structure for the fluorocyclopropyl radical.

The *gem*-halofluorocyclopropanes employed in the present work were 7-chloro-7-fluoronorcarane (Ia and Ib),[4] 6-chloro-6-fluorobicyclo[3.1.0]hexane (IIIa

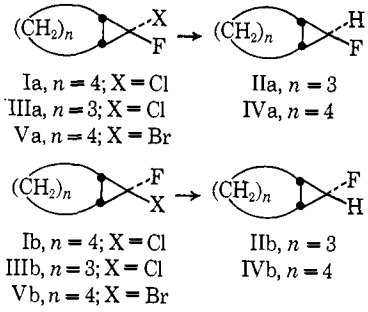
(1) D. E. Applequist and A. H. Peterson, *J. Am. Chem. Soc.*, **82**, 2372 (1960).

(2) H. M. Walborsky, C. Chen, and J. L. Webb, *Tetrahedron Letters*, 3551 (1964).

(3) K. Sisido, S. Kozima, and K. Takizawa, *ibid.*, 33 (1967).

(4) T. Ando, H. Yamanaka, S. Terabe, A. Horike, and W. Funasaka, *ibid.*, 1123 (1967).

and IIIb),[5] and 7-bromo-7-fluoronorcarane (Va and Vb).[6]



Ia, $n = 4$; X = Cl — IIa, $n = 3$
IIIa, $n = 3$; X = Cl — IVa, $n = 4$
Va, $n = 4$; X = Br

Ib, $n = 4$; X = Cl — IIb, $n = 3$
IIIb, $n = 3$; X = Cl — IVb, $n = 4$
Vb, $n = 4$; X = Br

The isomers Ia and Ib were separated by vpc, and each was reduced separately with tri-*n*-butyltin hydride (130°, 10 hr, neat, in the presence of di-*t*-butyl peroxide). The gas chromatograms and the nmr spectra[4] of the products proved that only one isomer (IIa) of 7-fluoronorcarane was formed from Ia, and the other isomer (IIb), from Ib.

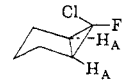
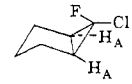
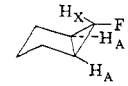
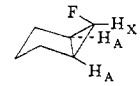
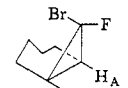
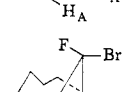
A similar stereospecificity was observed in the reduction (80°, 10 hr, neat, in the presence of azobisisobutyronitrile) of III: a mixture of IIIa and IIIb (IIIa:IIIb = 2.3) gave a mixture of the two isomers of 6-fluorobicyclo[3.1.0]hexane (IVa:IVb = 2.5, bp 55–56° (166 mm)) in 30% yield, while IIIb[7] was converted exclusively to IVb in 31% yield, with no sign of IVa being formed.

The reduction of V also proceeded with complete retention of configuration; a mixture of Va and Vb (Va:Vb = 1.7) was reduced (58°, 0.5 hr, neat, with no catalysts added) to a mixture of IIa and IIb (IIa:IIb = 1.8) in 80% yield, while Vb[8] gave only IIb under similar conditions.

The structures of IIIa, IIIb, IVa, IVb, Va, and Vb were elucidated by their proton and fluorine nmr spectra, based on the generalization that in fluorocyclopropanes $J_{HF,cis}$ is larger than $J_{HF,trans}$.[4,9] The parameters of the spectra are listed in Table I.[10]

The reduction of organic halides with organotin hydrides have been rationalized either as a free-radical chain reaction[11-13] or as a four-center type reaction,[14] and the intermediacy of a free radical has been postulated also in the reduction of some 7,7-dihalonorcaranes[15] and of 7-chloro-7-phenylnorcarane[16] with organotin hydride. In view of the catalytic action of

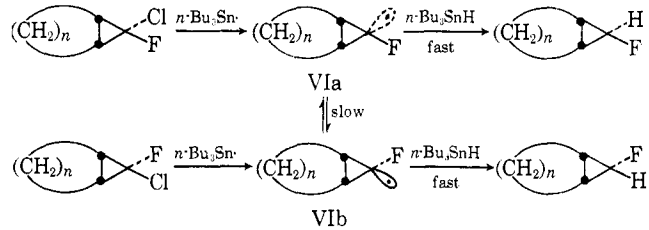
Table I. Parameters of Nmr Spectra of III, IV, and V

Structure	Compd	δ_F[a]	δ_{HX}[b]	$J_{HAF,vic}$	$J_{HXF,gem}$	$J_{HAHX,vic}$
	IIIa	48		19		
	IIIb	83		8		
	IVa	137	4.23	21	64.3	1.0
	lVb	158	4.62	10	66.3	6.5
	Va	41		40		
	Vb	76		13		

[a] Upfield from trifluoroacetic acid as external reference (at 56.4 Mc, CCl_4, 40%). [b] Downfield from TMS as internal reference (at 60 Mc, $CDCl_3$, 20%).

di-*t*-butyl peroxide and azobisisobutyronitrile,[17] it is of little doubt that the reduction of I and III, and probably of V as well, is a radical chain reaction which involves intermediate formation of a fluorocyclopropyl radical as one of the chain-propagating steps.

Provided the above interpretation is valid, it necessarily follows from the experimental facts that the fluorocyclopropyl radical thus formed (VIa and VIb) is pyramidal[18] and must abstract hydrogen from tri-*n*-butyltin hydride much more rapidly than it inverts its configuration; if it is planar, or if the inversion occurs before hydrogen abstraction, a mixture of two isomeric fluorocyclopropanes must be formed from either of the starting materials.



The hypothesis advanced above may seem to be inconsistent with the experimental data reported so far,

(5) W. Funasaka, T. Ando, H. Hosaka, and H. Yamanaka, Abstracts of the 20th Annual Meeting of the Chemical Society of Japan, Part III, 1967, p 390.

(6) Prepared from cyclohexene and bromofluorocarbene in 44% yield; bp 44–47° (6 mm); Va:Vb = 1.7.

(7) Isolated pure by treating a mixture of IIIa and IIIb with quinoline at 110° for 3 hr, followed by vacuum distillation.

(8) Isolated in a similar manner as described in ref 7.

(9) K. L. Williamson, Y. Li, F. H. Hall, and S. Swager, *J. Am. Chem. Soc.*, **88**, 5678 (1966).

(10) The assignment is supported by the chemical shifts of the H_X's of IVa and IVb, as a cyclopropyl hydrogen *cis* to an alkyl group is known to be more shielded than the one *trans*.

(11) (a) H. G. Kuivila, L. W. Menapace, and C. R. Warner, *J. Am. Chem. Soc.*, **84**, 3584 (1962); (b) L. W. Menapace and H. G. Kuivila, *ibid.*, **86**, 3047 (1964).

(12) (a) E. J. Kupchik and R. J. Kiesel, *J. Org. Chem.*, **29**, 764 (1964); (b) E. J. Kupchik and R. J. Kiesel, *ibid.*, **29**, 3960 (1964).

(13) F. D. Greene and N. N. Lowry, *ibid.*, **32**, 882 (1967).

(14) D. H. Lorenz, P. Shapiro, A. Stern, and E. I. Becker, *ibid.*, **28**, 2332 (1963).

(15) D. Seyferth, H. Yamazaki, and D. L. Alleston, *ibid.*, **28**, 703 (1963).

(16) F. R. Jensen and D. E. Patterson, *Tetrahedron Letters*, 3837 (1966).

(17) At 80°, the reduction of I and III was strongly catalyzed by azobisisobutyronitrile but not by di-*t*-butyl peroxide, which was very effective at 120–135°. Since the half-life of azobisisobutyronitrile is about 1.5 hr at 80° and nearly zero at 130°, and that of di-*t*-butyl peroxide is over 1000 hr at 80° and about 10 hr at 130°, it is evident that the effectiveness of a catalyst is closely related to its ability to produce a radical initiator at the reaction temperature employed. That the reduction of V needs no catalysts may be accounted for as being due to the lower energy required to cleave the C–Br, compared with the C–Cl, bond.

(18) There is good esr and infrared spectroscopic evidence that a fluorine substituent can force a normally planar radical to become preferentially pyramidal; see ref 19.

(19) (a) R. W. Fessenden and R. H. Schuler, *J. Chem. Phys.*, 43, 2704 (1965); (b) G. A. Carlson and G. C. Pimentel, *ibid.*, 44, 4053 (1966); (c) D. E. Milligan, M. E. Jacox, and J. J. Comeford, *ibid.*, 44, 4058 (1966).

particularly with the finding by Kuivila, *et al.*,[11a] and by Sisido, *et al.*,[3] that optically active halides lose their activity when reduced with organotin hydride. This apparent discrepancy can be explained, however, by the *gem*-dihalo structure of the substrates; the halogen atom which remains intact in the reaction, *i.e.*, the fluorine, might form a complex with tin compounds, to restrict the radical from inverting its configuration before it reacts with tri-*n*-butyltin hydride. The extremely high reactivity of organotin hydride with radicals and their potential use to trap configurationally labile radicals have already been pointed out by Kaplan,[20] who found that 2,2,2-triphenylethyl radical, which normally possesses a great tendency to rearrange to 1,2,2-triphenylethyl radical, can react with triphenyltin hydride before rearrangement occurs.

Further studies on these and the related reactions are now in progress.

Acknowledgment. We are indebted to the Hitachi Seisakusho Co., Ltd., for measurements of the fluorine nmr spectra.

(20) L. Kaplan, *J. Am. Chem. Soc.*, **88**, 4531 (1966).

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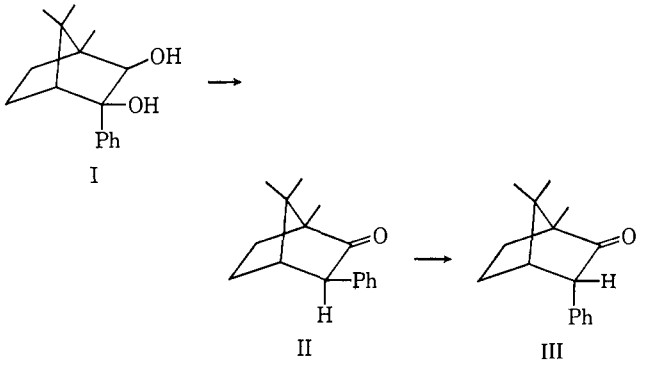
The Pinacol Rearrangement of 3-*endo*-Phenyl-2,3-*exo*,*cis*-bornanediol. An *endo*–*endo* Hydride Migration

Sir:

Recent studies[1-3] of the pinacol rearrangement of 3-*endo*-phenyl-2,3-*exo*,*cis*-norbornanediol prompted us to investigate the corresponding bornanediols as a possible synthetic route to alkyl- and aryl-substituted bornanones of known stereochemistry.

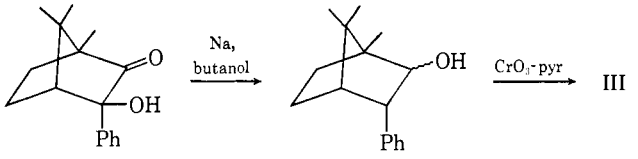
We have treated 3-*endo*-phenyl-2,3-*exo*,*cis*-bornanediol (I) with 1:100 $HClO_4$–HOAc for 4 hr at room temperature and have obtained results which are highly significant in terms of their theoretical implications. The product, obtained in approximately 80% yield, is 3-*exo*-phenylcamphor (II) (*Anal.* Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 84.04; H, 8.86), whose structure has been unambiguously established by its nmr spectrum and its rearrangement to 3-*endo*-phenylcamphor (III). *Anal.* Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83. Found: C, 84.25; H, 8.74. The *exo*-phenyl ketone exhibits a one-proton singlet at 3.22 ppm as well as three methyl singlets at 0.59, 0.92, and 0.95 ppm. The signal at 0.59 ppm has been assigned to the *syn*-7-methyl which, as models clearly show, is shielded by the *exo*-phenyl group.



I II III

When the reaction is continued beyond the 4-hr period, the ketone formed initially undergoes slow epimerization to the *endo*-phenyl ketone III, whose nmr spectrum exhibits a one-proton doublet ($J_{3,4}$ = 4.5 cps) at 3.79 ppm, the methyl at 0.59 ppm having merged with the other methyl signals at approximately 1.0 ppm. Complete epimerization can be effected by stirring II with dilute NaOH for a few hours. It is significant that ketone III is thermodynamically more stable than ketone II while 2-*exo*-phenylnorbornanone, on the other hand, is clearly more stable than the 2-*endo*-phenyl epimer.[1,4] This observation undoubtedly is a result of the spatial requirement of the *syn*-7-methyl which makes the *exo* side of the bornanone more encumbered than the *endo*.

Ketone III has been independently synthesized from 3-*endo*-phenyl-3-*exo*-hydroxycamphor[5] (IV) by reaction with sodium in butanol[6] and oxidation of the epimeric alcohols with CrO_3–pyridine complex.



IV

3-*endo*-Phenyl-2,3-*exo*,*cis*-bornanediol (*Anal.* Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.94; H, 8.96) was prepared from hydroxy ketone IV by reduction with lithium aluminum hydride. The *cis* structure of the diol was established by its infrared trace and its acid-catalyzed reaction with acetone to form an acetonide. *Anal.* Calcd for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.89; H, 9.23. The infrared spectrum of the diol showed bands at 3527 and 3632 cm^{-1} ($\Delta\nu$ = 105 cm) indicative of strongly intramolecularly bonded hydroxyl.

Our results indicate that rearrangement takes place *via* an *endo*–*endo* *2,3-hydride shift*. We have confirmed this hypothesis by subjecting the deuterated diol V to the same conditions that effected rearrangement of diol I. The product ketone, VI, contained more than 90% of the deuterium at the 3-*endo* position. Its nmr spectrum in deuteriochloroform was identical with the protonated form except for the signal at 3.22 ppm. When the deuterated ketone was heated for several hours at 70°, a doublet at 3.79 ppm appeared representing conversion to ketone III through enolization and exchange. We believe that these observations represent the first case of an *endo*–*endo* migration in the bicyclo[2.2.1]heptyl series.[1,4,7]

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(2) B. M. Benjamin and C. J. Collins, *ibid.*, **88**, 1556 (1966).
(3) D. C. Kleinfelter and T. E. Dye, *ibid.*, **88**, 3174 (1966).
(4) D. C. Kleinfelter and P. von R. Schleyer, *ibid.*, **83**, 2329 (1961).
(5) J. Gripenberg, *Suomen Kemistilehti*, **18B**, 53 (1945); *Chem. Abstr.*, **41**, 739e (1947).
(6) H Rupe and A. Wirz, *Verhandl. Naturforsch. Ges.* (Basel), **38**, 164 (1927); *Chem. Abstr.*, **23**, 1405 (1929).
(7) J. Berson in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, Chapter 3, p 159.