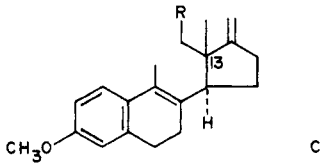
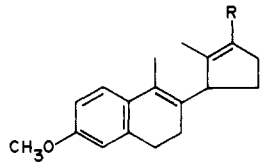
F_3CCO_2H afforded acetate **5b**, which was different from the acetate **5d** prepared in the same fashion from aldehyde **4a**. The stereochemistries of aldehydes **3a** and **4a** require the diastereomeric centers to arise during the Claisen rearrangement, preferentially having the acetaldehyde group trans to the bicyclic substituent appended to the five-membered ring. The C_8-αH stereochemistry in aldehyde **4a** was assigned by analogy. Previous studies on the tandem Cope–Claisen rearrangement have demonstrated that the lower energy Cope transition-state product is trapped by the Claisen rearrangement.[1c] Thus, **4a** would be expected to have formed by the Cope chairlike transition state followed by a Claisen rearrangement providing the cis substituents.

Occasionally, aldehydes **5a** and **5c** were obtained as minor byproducts in the tandem rearrangement. These



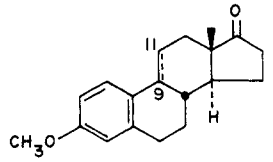
5 a, R = CHO, C_{13}-βCH_3
b, R = CH_2OAc, C_{13}-βCH_3
c, R = CHO, C_{13}-αCH_3
d, R = CH_2OAc, C_{13}-αCH_3



6 a, R = CO_2CH_3
b, R = $CH_2OCH{=}CH_2$

aldehydes could be generated as the sole products of stepwise rearrangements. Thus, thermolysis of ester **2a** (363 °C, 40 s, evacuated ampule) yielded ester **6a** in 78% yield, arising from Cope rearrangement and double bond isomerization. The initial Cope rearrangement product could never be detected, in spite of attempts to eliminate suspected fortuitous acid. Transformation of ester **6a** to vinyl ether **6b**, accomplished as described previously, followed by Claisen rearrangement (365 °C, 10 s, or 220 °C, 18 min; evacuated ampule) afforded a mixture of aldehydes **5a**/**5c** (95/5) in 95% yield, whose structures were confirmed by conversion to acetates **5b** and **5d**, respectively.

Ozonolysis of aldehyde **3a** (O_3, CH_2Cl_2, −50 °C; DMS) provided tricarbonyl compound **3b** in 70% yield. Epimerization of **3b** ($NaOCH_3$/$HOCH_3$, 25 °C) gave rise to a mixture of diketo aldehydes **3b**/**3c** (1/4), free from aldol products, from which **3c** could be isolated (69% yield). Subjection of tricarbonyl **3c** to a modified McMurry reaction[8] ($TiCl_3$, Zn/Ag, DME, no dilution, reflux) provided (±)-9,11-dehydroestrone methyl ether (**7a**) in 56% yield,



7 a, 9,11-dehydro
b, 9,11-dihydro

whose spectroscopic data was in accord with literature values.[3a] Formation of the more strained 8-iso-9,11-dehydroestrone methyl ether (from **3b**) occurred in only 15% yield. The selectivity of the olefin-forming reaction is viewed as proceeding by initial ketyl formation at the aromatic ketone, which would be expected to have the lowest reduction potential of the three carbonyl groups.

Finally, ketone **7a** was converted (K/NH_3; CrO_3)[9] to (±)-estrone methyl ether (**7b**) whose spectroscopic properties (except optical rotation) were identical with those of a sample of (+)-estrone methyl ether.[10] Estrone methyl ether has been converted to estrone.[11]

Acknowledgment. This research was supported by NIH Grant HD-14669. High-field NMR spectra were recorded at the Northeast Regional NMR Facility, Department of Chemistry, Yale University, funded by the Chemistry Division of the NSF (Grant CHE-7916210).

(8) McMurry, J. E.; Fleming, M. P.; Kees, K. L.; Krepski, L. R. *J. Org. Chem.* **1978**, *43*, 3255.

(9) Kuo, C. H.; Taub, D.; Wendler, N. L. *J. Org. Chem.* **1968**, *33*, 3126.
(10) We thank Dr. John Edwards (Syntex) for this sample.
(11) Johnson, W. S.; Banerjee, D. K.; Schneider, W. P.; Gutsche, C. D.; Shelberg, W. E.; Chinn, L. V. *J. Am. Chem. Soc.* **1952**, *74*, 2832.
(12) Powles, J. G.; Strange, J. H. *Mol. Phys.* **1962**, *5*, 329.
(13) The lack of visible vicinal coupling between the sp^2 aldehyde proton and the adjacent methylene protons requires comment. Powles and Strange[12] have derived the equation $J(180-\phi) = 2.54 + a_1 \cos(180-\phi) + a_2 \cos 2(180-\phi) + 0.69 \cos 3(180-\phi)$ for the vicinal coupling constant as a function of dihedral angle $(180-\phi)$. With use of $a_1 + a_2 = 5.7$ as a mean value and $J(180°) = 8.3$ Hz and $J(60°) = 0.1$ Hz as determined by Alexander and Pople[14] for acetaldehyde, the value of $a_1 = 2.3$ provides all positive coupling constants with $J(180°) = 8.9$ Hz and $J(60°) = 0.4$ Hz (reported,[12] 0.5 Hz). The average conformation has the sp^2 H bisecting the methylene protons within approximately 10° ($J(70°) = 0.1$ Hz, $J(50°) = 0.6$ Hz). These numbers are at the resolution threshold of the 500-MHz NMR spectrometer (5600 Hz/16K data points = 0.35 Hz/dp). All such coupling constants for aldehydes reported herein are in close agreement with this curve.
(14) Abraham, R. J.; Pople, J. A. *Mol. Phys.* **1960**, *3*, 609.

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Stereochemistry of Trifluoroacetolysis and Brominolysis of the Cyclohexyl–Tin Bond

Summary: (*cis*- and *trans*-4-methyl- and 4-*tert*-(butylcyclohexyl)triisopropylstannanes have been synthesized and fully characterized. Trifluoroacetolysis of these compounds proceeds stereospecifically with retention of configuration at carbon. Electrophilic bromination is characterized by a fine energetic balance between inversion and retention pathways, with the former favored for the equatorial carbon–tin bonds and the latter for axial carbon–tin bonds in these triisopropylstannanes. Bromination under free-radical conditions yields a statistical mixture of the *cis*- and *trans*-4-alkylcyclohexyl bromides, a result appropriate for bromine atom transfer to a 4-alkylcyclohexyl free radical.

Sir: The demonstration by Jensen and Davis,[1] and subsequently others,[2,3] that electrophilic bromodestannylation could have a preferred inversion pathway (e.g., I) has added a new dimension to our concepts of aliphatic electrophilic subsitution (S_E2), particularly when it is recalled that retention of configuration uniformly characterizes the favored pathway for bromo- and protiodemercuration of alkylmercurials (e.g., II and III).[4] In this latter context,

(1) Jensen, F. R.; Davis, D. D. *J. Am. Chem. Soc.* **1971** *93*, 4048. McGahey, L. F.; Jensen, F. R. *J. Am. Chem. Soc.* **1979**, *101*, 4397.
(2) Rahm, A.; Pereyre, M. *J. Am. Chem. Soc.* **1977** *99*, 1672.
(3) Gielen, M.; Fosty, R. *J. Chem. Res., Miniprint* **1977** 2373.

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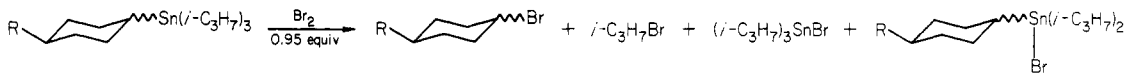
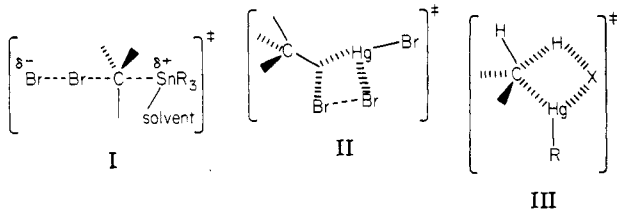
Table I. Stereochemistry of Bromodestannylation of Cyclohexylstannanes



substrate, R	entry	conditions	trans	cis	i-C_3H_7Br	preferred stereochemistry[c]
trans-4-methyl	1	MeOH/0 °C/dark	11[a] (10	14[a] 17	75[a] 73)[b]	inversion (56%)
cis-4-methyl	2	MeOH/0 °C/dark	10 (13	16 17	74 70)	retention (61%)
cis-4-methyl	3	MeOH/0 °C/dark/NaBr (2 equiv)	10	20	70	retention (66%)
trans-4-*tert*-butyl	4	MeOH/0 °C/dark	15 (14	25 19	60 67)	inversion (63%)
cis-4-*tert*-butyl	5	MeOH/0 °C/dark	10 (12	15 16	75 72)	retention (60%)
cis-4-*tert*-butyl	6	CH_3CN/20 °C/dark	3.0	3.5	93.5	retention (54%)
trans-4-methyl	7	C_6H_5Cl/light/20 °C	17.5 (15.0	16.5 15.0	66 70)	none
cis-4-methyl	8	C_6H_5Cl/light/20 °C	16.6 (15	16.4 15	67 70)	none
trans-4-*tert*-butyl	9	C_6H_5Cl/light/20 °C	19.5 (18	20.5 18	60 64)	none
cis-4-*tert*-butyl	10	C_6H_5Cl/light/20 °C	14 (13	15 13	71 74)	none
cis-4-*tert*-butyl	11	C_6H_5Cl/hydroquinone/dark	14.8	15.2	70	none

[a] Bromide distributions (±2%) based on capillary VPC examination and comparison with authentic samples.[7c] Corrected for response factors. [b] Values in parentheses for each entry are based on comparisons of like-signal intensities in the ^{13}C NMR spectrum. These latter values must be regarded as less precise but serve as confirmation. Distributions of alkyl bromides are in general agreement withthe proportions of the two product trialkyltin bromides on the basis of ^{119}Sn NMR intensities. [c] There was always a small amount of unreacted cyclohexylstannane, whose ^{119}Sn signal demonstrated its unchanged nature.

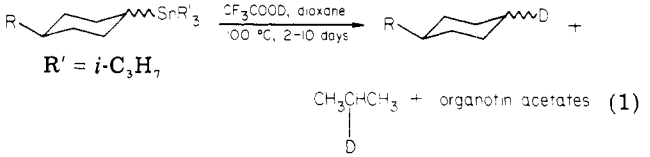
cyclohexylmercurials featured prominently,[5] and in view of the necessity to provide much additional data on destannylation,[1] comparative studies of cyclohexylstannanes and -mercurials would appear to be especially instructive. With respect to protonolysis, retention is the preferred course for alkylmercurials (e.g., III below) when highly competitive radical isomerization can be controlled,[5] but the stereocourse for protolytic destannylation is unknown.



I II III

(*cis*- and *trans*-4-methyl- and 4-*tert*-butylcyclohexyl)-triisopropylstannanes were obtained isomerically pure and fully characterized by elemental analyses and ^1H, ^{13}C, and ^{119}Sn NMR spectra. The cis isomers were obtained by reaction of the pure *trans*-4-alkylcyclohexyl tosylates with (triisopropyltin)lithium,[6] such displacement proceeding with strict inversion of configuration at carbon.[7] The trans stannanes resulted from a sequence of protolytic dephenylation and isopropylation of the pure (*cis*- and *trans*-4-alkylcyclohexyl)triphenylstannanes.[7c]

Trifluoroacetolysis (eq 1) resulted when the stannanes



$R' = i\text{-}C_3H_7$ (1)

(ca. 1 M) were treated with CF_3COOD (ca. 2 M) in dioxane at 100 °C (sealed ampule). The reaction progress was monitored directly by ^2H, ^{119}Sn, and ^{13}C NMR spectra of the reaction mixture, and it was established that isomerization of starting materials or products was not a problem. By comparison with the ^2H NMR shifts of authentic propane-2-*d* and mixtures of *cis*- and *trans*-4-*tert*-butyl and *cis*- and *trans*-4-methylcyclohexane-1-*d* (^2H_2O quench of the corresponding Grignard reagents), and "spiking" of the reaction mixture with these authentic samples, the ^2H signals of the product mixture could be assigned with certainty.[8] Trifluoroacetolysis of *trans*-4-methyl-, *trans*-4-*tert*-butyl-, and *cis*-4-methylcyclohexyl-substituted stannanes led to propane (65–70%) and the 4-alkylcyclohexane-1-*d* (ca. 35–30%), whereas with (*cis*-4-*tert*-butylcyclohexyl)stannane, the proportion of propane was now much higher (ca. 92%). ^2H NMR shift comparisons[8] established that in all cases the 4-alkylcyclohexane-1-*d* produced was the geometric isomer corresponding to the

(4) See, for example, Sayre, L. M.; Jensen, F. R. *J. Am. Chem. Soc.* **1979**, *101*, 6001 and references therein, especially ref 3.

(5) For this aspect, see Jensen F. R.; Rickborn, B. "Electrophilic Substitution of Organomercurials"; McGraw-Hill: New York, 1968.

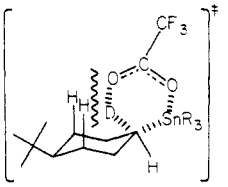
(6) Kitching, W.; Olszowy, H. A.; Drew, G. M. *Organometallics* **1982**, *1*, 1244.

(7) (a) Kitching, W.; Olszowy, H. A.; Waugh, J.; Doddrell, D. *J. Org. Chem.* **1978**, *43*, 898. (b) San Fillipo, J.; Silberman, J.; Fagan, P. J. *J. Am. Chem. Soc.* **1978**, *100*, 4834. (c) Kitching, W.; Olszowy, H. A.; Harvey, K. *J. Org. Chem.* **1982**, *47*, 1893 and references therein.

(8) See Kitching, W.; Atkins, A. A.; Wickham, G.; Alberts, V. *J. Org. Chem.* **1981**, *46*, 563, for another study of ^2H-substituted cyclohexanes. The procedure for obtaining the ^2H NMR spectra was as follows: the reaction mixture (ca. 0.4 mL) was added to chloroform (1.5 mL) containing one drop of deuteriochloroform for referencing. The shift of C^2HCl_3 was set at δ 7.24. Under these conditions the ^2H shifts were as follows: *trans*-4-methylcyclohexane-1-*d*, δ 1.44; *cis*-4-methylcyclohexane-1-*d*, δ 0.93; *trans*-4-*tert*-butylcyclohexane-1-*d*, δ 1.38; *cis*-4-*tert*-butylcyclohexane-1-*d*, δ 0.84; propane-2-*d*, δ 1.09.

starting stannane. *Trifluoroacetolysis of cyclohexyltriisopropylstannanes thus proceeds stereospecifically with retention of configuration.* (We estimate that <2% of the deuterated cyclohexane of opposite configuration would have been detected easily under our accumulation conditions.)

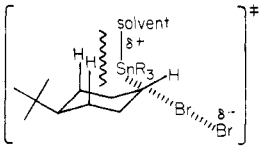
The *cis*-4-*tert*-butylcyclohexylstannane would adopt to an overwhelmingly extent a conformation with an axial $Sn(i\text{-}C_3H_7)_3$ group,[9] and although the retention course is essentially exclusive, axial approach of the electrophile is apparently impeded, as judged by the greater proportion of isopropyl group cleavage. This would suggest that the conformationally "mobile" (*cis*-4-methylcyclohexyl)stannane[9] would react very largely via the conformer with an equatorial $Sn(i\text{-}C_3H_7)_3$ group. The significant steric requirement of the axial transition state for trifluoroacetolysis (e.g., IV) has a counterpart in protolytic demercuration.[5]



IV

Bromination of these stannanes was examined under varying conditions[1-5] (Table I) and product distributions were established by capillary VPC and ^{13}C and ^{119}Sn NMR examination of the reaction mixtures. Isomerization of starting stannanes or product bromides was not a complication. The results are in Table I.

Entries 1-6 are considered to represent the outcomes of electrophilic destannylations not only because of the reaction conditions that are known to favor polar processes[1-3] but because added sodium bromide, a known free-radical suppressor in these systems,[1] has a marginal effect. Additionally, given the accuracy (±2%) of our capillary VPC analyses, the results are quite different from those in entries 7-9, the conditions for which are very conductive to free-radical production. Although the results (entries 1-6) indicate that the energetics of inversion and retention pathways are finely balanced, inversion of configuration is favored for bromodestannylation of equatorial C-Sn bonds, but retention is favored for axial C-Sn bonds in these cyclohexyltriisopropylstannanes. A subtle interplay of steric and solvation effects and electronic differences[4] between axial and equatorial bonds is presumably involved. For example, inverting displacement of an axial SnR_3 group could involve significant interactions with the axial 3,5-hydrogens by the leaving tin group, but this effect, e.g., V, is not so severe that it prohibits inversion (Table



V

I). Thus the transition state for these bromodestannylations is not characterized by a large steric requirement, judged as well by the relative constancy of the alkyl group selectivity, i.e., ($k_{isopropyl}/k_{cyclohexyl}$). This would be consistent with an "earlier" transition state for brominolysis than for protonolysis. Rahm and Pereyre[2] opined that the crucial feature favoring inversion was front-side steric bulk on the basis that retention was favored for *sec*-butyltriisopropylstannane, in contrast to overall inversion for the trineopentyl derivative. Our results for the *trans*-triisopropylstannanes, i.e., predominant inversion, suggests the more cautious view[1] that other factors may be just as important as front-side steric bulk. Further work is needed to delineate these factors and their relative importance.

Entries 7-10 demonstrate a statistical mixture of *cis*- and *trans*-cyclohexyl bromides, a result appropriate for bromine atom transfer to a 4-alkylcyclohexyl free radical. Brominolysis of (4-alkylcyclohexyl)mercuric bromides in nonpolar solvents proceeds similarly.[5] We attempted to observe the result for electrophilic destannylation in a nonnucleophilic solvent[1,3] (entry 11) by suppressing the radical route by hydroquinone and air, but a statistical distribution of bromides was still obtained. While this type of result has been attributed[3] to competing inversion and retention pathways, it may simply indicate a failure[10] to suppress the radical route.

The possibility that increasing front-side steric bulk may result in more specific electrophilic bromodestannylation (inversion) is being explored for cyclohexylstannanes and full details of this work will be presented at a later date.

Acknowledgment. We are grateful to the Australian Research Grants Scheme for partial funding of this work.

(9) Consider the following *A* values[7c] (kcal/mol): $(i\text{-}C_3H_7)_3Sn$, 1.10; CH_3, 1.74; $(CH_3)_3C$, >4.5.

(10) See footnote 17 in ref 2 also.

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Substituent Effects in 1,6-Methano[10]annulene: Carbon-13 Nuclear Magnetic Resonance Spectra of 2- and 3-Substituted Derivatives

Summary: The carbon-13 nuclear magnetic resonance spectra of a series of 2(α)- and 3(β)-substituted 1,6-methano[10]annulenes have been obtained for relatively dilute (0.2 M) solutions in deuteriochloroform. The spectra have been assigned and substituent chemical shifts calculated for all ring positions. The substituent shifts at nonproximate sites have been analyzed by the dual substituent parameter treatment and appropriate comparisons have been made with the corresponding positions in the isoelectronic naphthalene systems. Blends of inductive (ρ_I) and resonance (ρ_R) effects are remarkably similar for corresponding substituent-probe dispositions in the two systems.

Sir: 1,6-Methano[10]annulene, first synthesized[1] by Vogel in 1964, satisfies the chemical and spectroscopic criteria for aromaticity, and if the 1,6 bridge is neglected, I is the second member of the $(4n + 2)\pi$ annulene series with a neutral $(4n + 2)$ carbon framework.[2,3] Fundamental to

(1) Vogel, E.; Roth, H. D. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 228.
(2) Reviews of the synthesis, chemistry, and spectra of the 1,6-methano[10]annulene system are available. For example, see: Vogel, E. In "Aromaticity: An International Symposium"; The Chemical Society: London, 1967; p 113 and references therein. Vogel, E. *Proc. Robert A. Welch Found. Conf. Chem. Res.* **1968**, *12*, 215.

0022-3263/82/1947-5232$01.25/0