Yields and Stereoselectivities of Chlorinolysis of Trialkylboranes. Comparison of a Variety of Selected Methods

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Yields and stereoselectivities for chlorinolysis of a series of representative trialkylboranes R_3B (R = pentyl, hexyl, cyclohexyl, *sec*-butyl, *exo*-2-norbornyl) with a variety of chlorinolysis methods ($CuCl_2/H_2O$; $FeCl_3$; dichloramine T; NCl_3; *t*-BuOCl) are compared. Of the easily handled reagents, dichloramine T generally gives good yields and is most stereoselective (>99% *exo*-:<1% *endo*-2-norbornyl chloride). Yields and stereoselectivities of chlorinolysis with *tert*-butyl hypochlorite were higher in pentane than in tetrahydrofuran solvent.

Introduction

The use and unique of organoborane chemistry to incorporate stable and radioactive isotopes into pharmaceuticals and other biologically important molecules have been well-documented by Kabalka.[1] Iondinolysis and brominolysis of organoboranes seem particularly useful in this area.[1] Since radiochlorides are useful in studies of biosynthetic and metabolic processes such as quantitative determination of local glucose metabolism in the brain,[2] stereoselective or stereospecific chlorinolysis of organoboranes should be equally valuable. However, while the yields, stereoselectivities, and stereospecificities of several methods of iodinolysis[3] and brominolysis[4,5] of trialkylboranes have been reported, chlorinolysis reactions have not been so thoroughly studied.[5-7] Radical brominolysis[4a] of trinorbornylborane gives the exo product with a high stereoselectivity probably because of the stereochemical bias of the norbornyl group. Ionic iodinolysis[3a,c] and brominolysis[4b,g] proceed with inversion and with a higher stereoselectivity than the radical reactions. Therefore, one might expect an ionic route to be more promising for stereospecific trialkylborane chlorinolysis. Accordingly, we wished to develop an ionic chlorinolysis of trialkylboranes and to compare its stereoselectivity and stereospecificity to that of other chlorinolysis methods.[5,6]

Results

We investigated that chlorinolysis of a series of representative trialkylboranes with *tert*-butyl hypochloride (eq 1) under a variety of experimental conditions. *tert*-Butyl hypochlorite was selected as the chlorinolysis reagent to

$$R_3B \xrightarrow{t\text{-BuOCl}} RCl \qquad (1)$$

be investigated for several reasons: (1) Each reagent that effects ionic bromolysis[4] or iodinolysis[3] has a halogen atom that is polarized or polarizable with a partial positive charge. In order to favor ionic conditions, an analogous situation is desired in the selected chlorinolysis reagent and is found in *tert*-butyl hypochlorite. (2) *tert*-Butyl hypochlorite may undergo radical reactions, although an ionic reaction was desired. However, the presence of a base such as sodium methoxide or sodium acetate can change the type of reaction from radical to ionic in brominolysis[4a,b] and/or increase the reaction rate and yield in brominolysis[4] and in iodinolysis.[3] (3) There is an early report of tributylborane chlorinolysis using this reagent, in which the reaction was carried out without solvent.[6c] Also, there were extensive mechanistic studies of the reaction under conditions suitable for a radical chain process.[6f,g] However, there is no study of the reaction under conditions conducive to an ionic reaction or an investigation of the synthetic utility or stereoselectivity of the reaction.

The results of our investigations of chlorinolysis of representative trialkylboranes with *t*-BuOCl are presented in Table I. Yields are based on conversion of one alkyl group. Thus, if the trialkylborane contains three identical alkyl substituents on boron, a theoretical yield of 300% is possible. For all trialkylboranes studied, under all conditions with *t*-BuOCl, incomplete conversion of one alkyl group is obtained. As expected, use of 3 equiv of this chlorinolysis reagent usually gives a much higher yield than use of 1 equiv. Also, the yields for chlorinolysis of trialkylboranes in THF (3.7% to 53.7%) are usually less than half of those in pentane solvent (11.2% to 79.5%). Yields similar to those in pentane solvent are obtained with CCl_4 solvent. In either solvent, the range of yields of trialkylboranes with primary alkyls (16.2% to 33.4% in THF; 39.0% to 81.6% in pentane) is generally higher than that with secondary alkyls (3.7% to 26.2% in THF; 11.2% to 79.5% in pentane). However, the reaction of trinorbornylborane in pentane is exceptional in all cases, being higher than expected. Lowering the temperature from 0 °C to −78 °C generally increased the yield by a factor of about 1.5 to 3. The effect is about the same whether the reactions are run in pentane or in THF. Very little effect is observed upon changing the nucleophile from acetate to methoxide or water in the reactions of *t*-BuOCl with trihexylborane[8] or with tri-*exo*-2-norbornylborane (Table III) in pentane or in THF.

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Table I. Yields and Stereoselectivities[a] for Chlorinolysis of Representative Trialkylboranes at 0 °C with Chlorinolysis Reagents in Specified Solvents

		reagent						
		t-BuOCl[b]/aq. NaOAc						
			solvent					
entry	trialkylborane	molar equiv	pentane[g]	THF	$CuCl_2 \cdot H_2O$[c] THF	$FeCl_3$[d] THF	DCT[e] CCl_4	NCl_3[f] CCl_4
1	tripentylborane	3	66.5	26.0		177		
		1	39.0	16.20				
2	trihexylborane	3	81.6	33.4	186	180	90	
		1	51.0	32.6				
3	tricyclohexylborane	3	30.6	11.91	186	219	73	
		1	11.18	3.70				
4	*sec*-butyldiisopinocampheylborane	3	<1	<1	<1[b]	<1[b]	<1[b]	
5	tri-*exo*-2-norbornylborane	3	79.5	26.2	55.4[b]	160[b]	69.1[b]	~100
			(91:9)	(91:9)	(92:8)	(93:7)	(>99:<1)	(77:23)
		1	40.8	19.18				
			(91:9)	(66:34)				

[a] Exo/endo ratios are below yields for R = *exo*-2-norbornyl. [b] This work; an average of three runs is reported. [c] With 6 molar equiv of $CuCl_2$, ref 6e. [d] With 6 molar equiv of $FeCl_3$, ref 6e. [e] With 1 molar equiv of DCT; ref 6d. [f] With 1 equiv of NCl_3; ref 6a. [g] Similar yields and stereoselectivities are obtained in CCl_4 solvent.

Table II. Effect of Solvent and Temperature upon Yield[a] and Stereoselectivity of the Chlorinolysis of Trialkylboranes R_3B with 1 Equiv of *tert*-Butyl Hypochlorite and Sodium Acetate

	solvent			
	pentane		THF	
R	0 °C	−78 °C	0 °C	−78 °C
Pent	39.0	65.4	16.20	34.0
Hex	51.0	65.6	32.6	43.3
Chx	11.18	32.0	3.7	23.7
exo-2-Nor	40.8	63.2	19.18	22.3
	(91:9)[b]	(94:6)[b]	(66:34)[b]	(85:15)[b]

[a] Yields are based upon the conversion of one R group per molecule of R_3B. [b] Exo/endo ratio.

Chlorinolysis of trialkylboranes has been reported with several other reagents: copper(II) chloride,[5,6e] iron(III) chloride,[6e] dichloramine T (DCT),[6d] and nitrogen trichloride.[6a] However, the stereochemistry has been given in only one chlorinolysis reaction; treatment of tri-*exo*-2-norbornylborane with nitrogen trichloride gives 77% *exo*- and 23% *endo*-2-chloronorbornane.[6a] Since there is no highly stereospecific method of converting trialkylboranes to alkylchlorides and the only chlorinolysis reagent for which stereoselectivity data are reported is a highly explosive one,[9] the stereoselectivities of various chlorinolysis reagents seemed of interest. Therefore, we investigated and compared the stereoselectivity of chlorinolysis of tri-*exo*-2-norbornylborane with the remaining chlorinolysis reagents. Exo/endo ratios are given in parentheses below yields in Table I. All chlorinolysis reactions with tri-*exo*-2-norbornylborane studied give predominantly the exo product, unlike the base-catalyzed brominolysis.[4b] Dichloramine T effects chlorinolysis of tri-*exo*-2-norbornylborane with the highest stereoselectivity (exo/endo = >99:<1), but with only a good yield (69.1%). Iron trichloride gives near complete conversion of two alkyls (160%) with good (93:7) stereoselectivity. The solvent effect upon stereoselectivity of chlorinolysis of tri-*exo*-2-norbornylborane using *t*-BuOCl is dramatic; switching from THF to pentane (or CCl_4) increases the exo/endo ratio from 66:34 to 91:9 (or 90:10). Lowering the reaction temperature from 0 °C to −78 °C slightly increases the selectivity for the exo isomers in pentane (91:9 → 94:6) and in THF (66:34 → 85:15) (see Table II).

(9) Bretherick, L. *Handbook of Reactive Chemical Hazards*; Butterworths: London, 1985; p 993.

Table III. Yields of Reactions of *tert*-Butyl Hypochlorite with Tri-*exo*-2-norbornylborane Run in the Presence and in the Absence of Galvinoxyl

			yield, %	
solvent	temp, °C	nucleophile	without galvinoxyl	with galvinoxyl
pentane	−78	H_2O	78.4 (92:8)	18.54 (91:9)
	0	H_2O	70.5 (91:9)	19.03 (92:8)
	0	NaOAc	79.5 (91:9)	40.6[a] (93:7)
THF	−78	H_2O	53.7 (85:15)	12.90 (87:13)
	0	H_2O	15.68 (90:10)	10.20 (90:10)
	0	NaOAc	26.2 (91:9)	13.42 (88:12)

[a] Increasing galvinoxyl to 0.1 equiv gave 62.8% (97.4:2.6).

Since the stereospecificities of the chlorinolysis reactions would also be of interest, we studied the reactions of *sec*-butyldiisopinocampheylborane with *tert*-butyl hypochlorite, with cupric chloride, with ferric chloride, and with dichloramine T. It was planned to use the stereochemical configuration of the *sec*-butyl group in order to determine the stereospecificity of each conversion. The small (<1%) yields of *sec*-butyl chloride (Table I) precluded making a stereochemical determination. The presence of isopinocampheyl chloride was obvious by ^1H NMR and by GC/MS. Several syntheses were explored in order to obtain a pure sample,[10] but difficulty in obtaining this prevented a quantitative yield approximation (see Experimental Section). Nevertheless, it was obvious that in each case considerably more isopinocampheyl chloride was obtained than *sec*-butyl chloride.

In order to investigate the radical vs ionic nature of the chlorinolysis using *tert*-butyl hypochlorite, we compared the yields of several reactions in the presence and absence of 0.01 equiv of galvinoxyl, an efficient radical scavenger.[11] The results of these reactions are displayed in Table III. In either solvent, galvinoxyl reduces the yields of reactions run in the presence of NaOAc by a factor of about 2 and in the absence of NaOAc by a factor of about 4. This

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(11) Bartlet, P. D.; Gontarev, B. A.; Sakurai, H. *J. Am. Chem. Soc.* **1962**, *84*, 3101 and references cited therein.

suggests at least some participation by a radical mechanism. Increasing the galvinoxyl to 0.1 equiv did not decrease the yield further. The stereoselectivities of these reactions are not affected significantly by the presence of galvinoxyl.

Discussion

The generally lower yields for chlorinolysis with *tert*-butyl hypochlorite of trialkylboranes with secondary alkyls (except norbornyl) than with primary alkyls is observed with all of the chlorinolysis methods studied[5,6] and is presumably a steric effect. This general trend is also observed in iodinolysis[3] and in brominolysis[4,5] under similar conditions.

Chlorinolysis with cupric chloride,[6e] iron trichloride,[6e] or nitrogen trichloride (3 equiv)[6a] proceeds beyond the first alkyl group extensively. While data for chlorinolysis of trihexyl-, tripentyl-, or tricyclohexylborane with nitrogen trichloride have not been reported, Brown has mentioned that the reaction is applicable to such compounds.[6a] Nitrogen trichloride is the most efficient chlorinolysis reagent; since 3 equiv converts all three alkyl groups to the alkyl chloride and 1 equiv converts one alkyl. However, it could be hazardous to handle.[9] Lower yields are obtained in chlorinolysis with $FeCl_3$ (160–219%) or $CuCl_2$ (143–186%). Dichloramine T (1 molar equiv) does not give complete conversion of one alkyl group (69–90% yield) nor does *tert*-butyl hypochlorite (up to 82%).

The effects of changing reaction conditions (stoichiometry, solvent, and temperature) upon the yield of chlorinolysis with *t*-BuOCl were studied. Chlorinolysis with 3 molar equiv gives beter yields than using 1 molar equiv, similar to the findings using 6 molar equiv[5] versus 3 molar equiv[6a] of $CuCl_2$. Also, the yields in pentane (31–82%) are higher than those in THF (4–33%) and are close to those for dichloramine T (69–90%). The higher yields for chlorinolysis with *t*-BuOCl in pentane (or in CCl_4) than in THF are not surprising; they are consonant with our previous findings that THF can retard the rate[12] or change the course[13] of some organoborane reactions. Lowering the temperature from 0 °C to −78 °C approximately doubles the yield. This suggests suppression of a competing reaction that gives products other than the desired alkyl chloride.

Unfortunately, as might have been anticipated, the chlorinolysis reagent that produces the highest yields also gives the lowest stereoselectivity; nitrogen trichloride, exo/endo = 77:23. Iron trichloride (exo/endo = 93:7), cupric chloride (97:3), and *tert*-butyl hypochlorite in pentane (91:9) give good yields and good stereoselectivities. The best stereoselectivity (exo/endo = >99:<1) is provided by dichloramine T.

THF does not significantly affect the stereoselectivity of the reaction when 3 molar equiv of *t*-BuOCl are used. However, when 1 molar equiv is used, THF reduces the stereoselectivity remarkably, with results similar to those in other systems.[14] The preference for the exo product is increased slightly at lower temperatures (Table II). This suggests that norbornyl chloride is generated by two competing mechanisms; the temperature decrease changes somewhat the degree of participation by the two mechanisms.

Chlorinolysis of trialkylboranes with most of the above reagents has been reported to involve the alkyl radical.[5,6a,d-f] Therefore, the variation in product exo/endo ratio with respect to chlorinolysis reagent in the reaction of tri-*exo*-2-norbornylborane probably reflects the selectivities of the norbornyl radical toward those reagents. Thus, the most reactive chlorinolysis reagent (NCl_3) gives the highest yields and lowest selectivity, and the least reactive reagent (DCT) gives the lowest yields and highest selectivity. The bromination of tri-*exo*-2-norbornylborane with 3 molar equiv of cupric bromide, which also proceeds via norbornyl radical, is higher than chlorinolysis with cupric chloride in yield (77%) and lower in stereoselectivity (exo/endo of ~4).[5] The effects influencing stereoselective formation of *exo*-2-halonorbornane in these reactions are probably quite similar to those responsible for the predominance of exo product in radical halogenations of norbornane.[15a] While there are multiple properties of the chlorine atom donors that affect exo/endo selectivities,[15b] the steric factor seems to provide a nice correlation in this instance: the 2-norbornyl radical with a near planar configuration at the unsaturated center is formed, accessibility from the more sterically shielded endo side is less than from the exo direction, and the degree of exo/endo selectivity depends upon the steric bulk of the halogen donor. Thus, the most bulky chlorinolysis agent (DCT) gives highest preference for the less-hindered exo approach (>99:<1) and the least bulky (NCl_3) gives the least exo preference (77:23) of those reagents studied (Table I).

Low yields of *sec*-butyl chloride for the reactions of *sec*-butyldiisopinocampheylborane are not surprising considering the results of relative reactivity studies of various groups in chlorinolysis of mixed trialylboranes with $CuCl_2$ (3 molar equiv),[5] NCl_3,[6a] and DCT.[6d] In each of these, the more highly substituted carbon is the one that undergoes reaction. This suggests involvement of a reactive intermediate that is stabilized by increasing substitution. The previously discussed results and similarities of chlorinolysis with *t*-BuOCl to the other chlorinolysis methods leads one to postulate a radical mechanism. However, in the case of *sec*-butyldiisopinocampheylborane chlorinolysis, radical stability probably is not playing a very large part since all three alkyls are secondary. Statistically, formation of isopinocampheyl chloride is favored over that of *sec*-butyl chloride, but this still would not fully account for such a low yield of the latter. Perhaps the greater steric bulk of the isopinocampheyl group would cause its B–C bond to rupture preferentially.

Our attempts to attain a chlorinolysis reaction proceeding totally via an ionic mechanism were not successful. In analogy with ionic brominolysis, one would expect inversion of stereochemistry at the carbon undergoing reaction. A high preference for the exo product (retention) was observed in almost all chlorinolyses of tri-*exo*-2-norbornylborane with *tert*-butyl hypochlorite (Table I). The exception, carried out in THF in the presence of NaOAc with 1 equiv of *t*-BuOCl, gave an exo/endo ratio of 66:34, suggesting that an ionic reaction could be playing a more important role here than in the other reactions and increasing the proportion of endo (inversion) product. The stereoselectivity of the chlorinolysis with *t*-BuOCl could be explained by a radical mechanism, an S_E2 (front attack) mechanism, or an S_Ei reaction going through a four-center transition state structure involving boron.[4b,16] However,

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(14) (a) Midland, M. M.; Zolopa, A. R.; Halterman, R. L. *J. Am. Chem. Soc.* **1979**, *101*, 248. (b) Similar findings are observed in brominolysis of tri-*exo*-norbornylborane using the chloramine T procedure described in ref 4f above. Nelson, D. J.; Soundararajan, R., unpublished results.

(15) (a) Kooyman, E. C.; Vegter, G. C. *Tetrahedron* **1958**, *4*, 382–92. (b) Bartlett, P. D. *Acc. Chem. Res.* **1970**, *3*, 177.

the yield reduction upon addition of a small amount of galvinoxyl suggests at least some involvement of a radical pathway. A radical mechanism similar to that involved in brominolysis[4f,17] cannot be involved, since products resulting from alkyl transfer to the α-carbon, which would be expected from such a radical reaction carried out in the presence of a nucleophile,[4f,17] are not obtained. On the other hand, at least some participation by a mechanism involving the norbornyl radical would account for the yield reduction with galvinoxyl, the stereoselectivities similar to those of the other reactions involving norbornyl radical,[5,6a,d-f] and the small effect observed upon changing the nucleophile.[8]

Conclusion

Chlorinolysis of trialkylboranes to yield alkyl chlorides can be effected by a variety of reagents, the choice of which depends upon the relative importance of a variety of factors, including yield, stereoselectivity, and convenience. Chlorinolysis with iron(III) chloride gives very good yields (conversion of two alkyl groups) and good stereoselectivity (93% *exo*-:7% *endo*-2-norbornyl chloride from tri-*exo*-2-norbornylborane). The use of dichloramine T gives much lower yields (near conversion of one alkyl) but excellent stereoselectivity (>99% exo:<1% endo). All of the methods studied give a predominance of *exo*-2-norbornylborane; the degree of predominance is probably related to the steric bulk of the halogen donor and its realtive accessibility from the exo and endo sites of the norbornyl radical intermediate.

Experimental Section

General Data. The general procedures for manipulation of boron reagents are given elsewhere.[18] The alkenes were purchased from Aldrich Chemical Co., distilled under nitrogen from a small amount of calcium hydride, and then stored under nitrogen. The *cis*-2-butene was used as received. *n*-Pentane was pretreated by stirring over concentrated H_2SO_4 overnight, washing with water, and drying over anhydrous calcium chloride. It was then distilled over calcium hydride and under nitrogen. THF was distilled under nitrogen from a small amount of LAH and stored under nitrogen. The alkanes used as internal standards were obtained from the Humphrey Chemical Co. and were used as received. Cupric chloride was obtained from Mallinckrodt Inc., ferric chloride from J. T. Baker Chemical Co., and dichloramine T from CTC Organics. *tert*-Butyl hypochlorite was made according to the literature procedure.[19] Galvinoxyl, isopinocampheol, benzonitrile, and palladium(II) chloride were purchased from Aldrich Chemical Co.

Instruments. The GC analyses were carried out on a Hewlett-Packard 5890 gas chromatograph equipped with a flame ionization detector and using 3.2 mm o.d. columns. The chromatograph was connected to a Hewlett-Packard 3390A integrator for determining peak areas. The following GC columns were used: 4 m of 10% SE-30 on 100/200-mesh Chromosorb W and 6 m of 15% Zonyl E-7 on 80/100-mesh Chromosorb W. Mass spectral data were obtained on a Hewlett-Packard 5985 gas chromatograph/mass spectrometer data system equipped with a 4 mm × 2 m column packed with 3% SE-30 on 100/120-mesh Chromosorb W. Optical rotations were measured on a Perkin-Elmer 241 polarimeter using a 1-cm microcell.

Procedures. Preparation of Trialkylboranes (R_3B). The trialkylboranes were prepared according to literature procedures.[18,20] In those reactions carried out in pentane or in CCl_4, the trialkylborane was prepared as above in THF, the THF was removed under vacuum, and pentane or CCl_4 was added.

Chlorinolysis of Trialkylboranes. The typical procedure for chlorinolysis of trialkylboranes with *tert*-butyl hypochlorite is as follows: 5 mmol of the trialkylborane was added to 10 mL of a suitable solvent in a 50-mL round-bottom flask. The solution was cooled to 0 °C. Then, a known amount of an internal standard (*n*-undecane) was added, followed by 1.68 mL (15 mmol) of *t*-BuOCl and 5.01 mL of 3 N NaOAc. After 6 h of stirring at 0 °C, the solution was extracted with ether. The ether layer was washed with water and dried over anhydrous $MgSO_4$. The alkyl chloride products were identified by GC coinjection with authentic samples and by mass spectral fragmentation patterns. The products were then analyzed by GC for the amount of alkyl halide present.

Stereoselectivity: Chlorinolysis of Tri-*exo*-2-norbornylborane. Chlorinolyses of tri-*exo*-2-norbornylborane with $CuCl_2 \cdot 2H_2O$,[6e] $FeCl_3$,[6e] and DCT[6d] were carried out according to the literature procedures. *exo*-2-Norbornyl chloride was identified by GC coinjection with an authentic sample (Aldrich) and by its mass spectral fragmentation pattern. For each chlorinolysis method, the yield and exo/endo ratio were determined by GC analysis. The exo and endo isomers were assumed to have equal GC response factors.

Stereospecificity: Chlorinolysis of *sec*-Butyldiisopinocampheylborane. Reaction of the title compound (50 mmol) with *t*-BuOCl was carried out as described earlier except *n*-tridecane was used as the solvent instead of *n*-pentane. The chlorinolysis of *sec*-butyldiisopinocampheylborane (50 mmol) with $CuCl_2 \cdot 2H_2O$[6e] and $FeCl_3$[6e] were carried out as reported earlier. Chlorinolysis of *sec*-butyldiisopinocampheylborane with DCT[6d] was carried out as in the literature procedure except that *n*-tridecane was used as solvent instead of carbon tetrachloride. Attempts were made to ascertain the optical purity of the *sec*-butyl chloride produced in these reactions, but difficulties due to the low yields proved insurmountable. Yields were determined by GC as described earlier.

Attempted Synthesis of Isopinocampheyl Chloride.[10] One method did enable GC/MS identification of the peaks corresponding to isopinocampheyl chloride in the chlorinolysis of *sec*-butyldiisopinocampheylborane. Isopinocampheol (0.68 g) was added to a solution of freshly prepared[19] Pd $(PhCN)_2Cl_2$ (1.68 g) in 15 mL of dry benzene. The solution was stirred at 60 °C for 6 h, cooled, and washed with water. A black precipitate was observed; the $PdCl_2$ (Aldrich) needed to synthesize $Pd(PhCN)_2Cl_2$ could be regenerated from the black precipitate as described earlier.[21] The organic layer was dried and concentrated under a vacuum. The product was purified by column chromatography on silica gel (80–200 mesh) with petroleum ether as eluent. The fraction corresponding to R_f = 0.6 (developed on Eastman Chromagram TLC plates using petroleum ether) was isolated, and the solvent was evaporated at 0 °C under vacuum. This product (250 mg) showed a single spot on TLC, but the GC and HPLC analyses showed the presence of more than three components.

Nevertheless, an NMR (300 MHz, $CDCl_3$) spectrum of the mixture revealed a signal (δ = 4.20 ppm, br) for the proton α to the exo chlorine; this is downfield from the signal (δ = 4.05 ppm) for the α-H in isopinocampheol[22] by the same amount (0.15 ppm) that the α-H signal (δ = 3.85 ppm, br) in norbornyl chloride[23] is downfield from that (δ = 3.70 ppm) in norborneol.[24]

The mass spectra (GC/MS) of isopinocampheol and isopinocampheyl chloride show similar fragmentation patterns: isopinocampheyl chloride, *m/z* (relative intensity) 137 $[M - Cl]^+$ (1.1), 136 $[C_{12}H_{16}]^+$ (4.0), 121 $[C_{12}H_{16}]^+$ (9.4), 119, (100); isopinocampheol,[25] *m/z* (relative intensity) 137 $[M - OH]^+$ (2.9), 136

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$[C_{12}H_{16}]^+$ (3.1), 121 $[C_{12}H_{16} - Me]^+$ (5.8), 41, (100). The spectra also display similar hydrocarbon fragmentation patterns with strong peaks that are characteristic of alkyl groups (43, 57, 71, 85), alkenyl groups (41, 55, 69, 83), pinane (77, 79, 93, 121), and α-pinene (79, 81, 95, 119, 121).

A similarity in mass spectra is also apparent between *exo*-2-norborneol (*m/z* (relative intensity) 95 $[M - OH]^+$ (82.4), 93 $[C_7H_9]^+$ (21.1), 67 $[C_5H_7]^+$ (98.9), along with strong alkyl (43, 57, 71, 85) and alkenyl (41, 55, 69, 83) peaks) and the corresponding chloride.[20b]

Radical Quenching Reactions. Five millimoles of trihexylborane was added to 10 mL of pentane or THF in a 50-mL round-bottom flask. The solution was cooled to 0 °C, and a known amount of an internal standard (*n*-undecane) was added, followed by addition of 0.021 g (0.01 eq) or 0.21 g (0.10 equiv) of galvinoxyl (Aldrich). Then, 1.68 mL of *t*-BuOCl and 5.01 mL of 3 N NaOAc were added. The solution was allowed to stir at 0 °C for 6 h, and then it was extracted with ether. The ether layer was washed with water, dried over anhydrous $MgSO_4$, and analyzed by GC.

(25) CI mass spectral values for *exo*-2-norborneol have been given earlier (*m/z* (relative intensities) $[C_7H_9]^+$ (1.3), 95 $[M - OH]^+$ (83.4); 111 $[M - H]^+$ (2.6)). Jelus, B. L.; Dalrymple, D. L.; Michnowicz, J.; Munson, B. *Org. Mass Spectrom.* **1978**, *13*, 163-6.

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Solvent and Temperature Dependence of the Anomeric Effect in 2-[(4-Methoxyphenyl)seleno]-1,3-dithianes. Dominance of the Orbital Interaction Component

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The conformational equilibrium of 2-[(4-methoxyphenyl)seleno]-1,3-dithiane in three solvents at low temperature has been studied by ^{77}Se NMR spectroscopy. The equilibrium of the configurational isomers, *r*-2-[(4-methoxyphenyl)seleno]-*cis*-4,*cis*-6- and -*trans*-4,*trans*-6-dimethyl-1,3-dithiane, in the same solvents at higher temperatures has been studied by acid-catalyzed equilibration experiments. Plots of ln *K* vs $1/T$ using points from both types of experiments are linear, permitting evaluation of the enthalpic and entropic contributions to the S-C-Se anomeric effect in these derivatives. $\Delta H°_{eq-ax}$ values of -1.43 ± 0.24, -0.98 ± 0.21, and -1.59 ± 0.16 kcal mol^{-1}, and $\Delta S°_{eq-ax}$ values of -3.4 ± 1.0, -2.1 ± 1.0, and -4.8 ± 0.6 cal mol^{-1} K^{-1} in toluene, methylene chloride, and acetone, respectively, are obtained. Uncertainties in the parameters are at the 95% confidence level. The preferential stabilization in enthalpy terms of the axial isomer in acetone vs methylene chloride and its destabilization in entropy terms is interpreted in terms of the dominance of $n_s \rightarrow \sigma^*_{C-Se}$ orbital interactions over dipolar interactions, leading to a polar "double-bond no-bond" structure. Interestingly, the equilibrium in chloroform is almost isoenthalpic, $\Delta H°_{eq-ax} = +0.04$ kcal mol^{-1} and $\Delta S°_{eq-ax}$ is positive (+1.5 cal mol^{-1} K^{-1}). The latter results are attributed to specific hydrogen bonding effects, which favor the equatorial isomer enthalpically and the axial isomer entropically.

Introduction

We have recently reported[1,2] the effects of substitution on the conformational equilibria of 2-[(4-substituted-phenyl)seleno]-1,3-dithianes. The results constituted systematic experimental evidence for stabilizing orbital interactions operating in S-C-Se fragments and for the existence of the S-C-Se anomeric effect. However, our preliminary attempt[2] to evaluate the relative importance of orbital-interaction effects and electrostatic effects by studying the effect of solvent on the conformational free energies was unsuccessful because it yielded anomalous results. For example, an increase in the proportion of the less polar axial conformer was observed in the more polar solvent, acetone, relative to that in methylene chloride. The result was surprising, considering that the more polar medium is predicted[3] to minimize dipolar interactions and to increase the proportion of the more polar equatorial conformer. Two tentative explanations were proposed[2] to account for this behavior: (1) that the conformer with the smaller molar volume (the axial conformer) should increase in the more polar solvent owing to higher internal pressure exerted by the solvent[4] and (2) that the more polar double-bond no-bond structure, resulting from a dominance of orbital interactions in the axial conformer, will be stabilized in the more polar solvent.[5] Although it is tempting to accept the latter explanation, detailed arguments based on conformational free energies and not conformational free enthalpies must be made with caution since it is the latter values that are most readily correlated with electronic effects of this type.[6a] Indeed Booth et al.[6a] in their recent investigation of the enthalpic and entropic contributions to the endo and exo anomeric effect in 2-sub-

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