Structural Effects in Solvolytic Reactions. VII. Solvolysis of Optically Active *threo*-4-Phenyl-3-hexyl Tosylate. A Need for a Revision of Previous Results

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Abstract: The acetolysis and formolysis of optically active *threo*-4-phenyl-3-hexyl tosylate have been reexamined. It was previously reported that the solvolysis of this compound proceeds with high stereospecificity (predominant retention), similar to that observed in the *threo*-3-phenyl-2-butyl system. However, in contrast to the largely racemic nature of the retained product from the 3-phenyl-2-butyl derivative, the retained product obtained in the acetolysis or formolysis of the active hexyl derivative was reported to contain 6–8% of the optically active isomer. As the polarimetric to titrimetric rate ratio is 3.3 in the acetolysis of this compound, a major amount of active retained product (*ca.* 21%) is indicated in the absence of racemization arising from internal return. As a part of our investigation in the nature of the reaction pathways involved in solvolysis of secondary β-arylalkyl derivatives, we undertook to reexamine this system in detail with a hope of clarifying the nature of the pathway leading to this active retained product. This study revealed that the acetolysis gives retained product with only approximately 1% of the active form and that the formolysis proceeds to yield completely racemic *threo*-formate. Consequently, these results remove the reported discrepancy between the solvolytic behavior of the 3-phenyl-2-butyl and the 4-phenyl-3-hexyl systems.

In 1953, Cram and Abd Elhafez reported that the acetolysis of L(+)-*threo*-4-phenyl-3-hexyl tosylate (L-I-OTs) produced a 50% yield of secondary acetate (96% threo and 4% erythro) and that 6.4% of the threo product was optically active.[2] Similarly, the formolysis of L-I-OTs, conducted at 25°, was reported to give a 80% yield of secondary formate (>99.5% threo), 6.8% of this ester being found to be active.[2] As the internal return process, which causes racemization of the starting material, is important in acetolysis ($k_\alpha/k_t = 3.3$),[2] the reaction in acetic acid is expected to yield a major amount of the active retained product (*ca.* $21\% = 6.4 \times 3.3$) in the absence of the return process.[2]

These results are in marked contrast to those obtained in the homologous 3-phenyl-2-butyl system; *i.e.*, the retained product from the acetolysis or formolysis of active *threo*-3-phenyl-2-butyl tosylate (II-OTs) was found to be nearly completely racemic.[3] Cram postulated that in the acetolysis or formolysis of L-I-OTs the simple substitution reaction, which was characterized to involve rate-determining ionization to an open cation, gives predominantly retained product.[4]

We were intrigued by these results and explanations. Recent developments now suggest that the solvolysis of secondary β-arylalkyl derivatives proceeds *via* two discrete pathways, the aryl assisted (k_Δ) and the aryl unassisted (k_s).[5–10] The k_s pathway is considered to be assisted significantly by nucleophilic solvent participation, the stereochemical result being expected to be net inversion, while the k_Δ process is generally believed to occur with retention and also with complete racemization when the system is symmetric. For obvious reasons, the origin of the observed large amount of retained yet optically active product reported to form in the solvolysis of I-OTs is of great interest for the understanding of the mechanism of such solvolytic processes. If this product arises from the k_s pathway, we would have a unique example of an anchimerically unassisted process in acetolysis or formolysis of secondary acyclic derivatives which proceeds with preferential retention. On the other hand, if this active retained product is formed *via* the k_Δ pathway, we can no longer consider a symmetrically bridged phenonium ion as the only intermediate involved in the k_Δ pathway. Accordingly, as a part of a project designed to investigate the nature of the reaction pathways involved in solvolysis of secondary β-arylalkyl derivatives, we undertook to reexamine the *threo*-4-phenyl-3-hexyl system with the better analytical tools available today.

Results

The L(+)- and D(−)-*threo*-4-phenyl-3-hexyl tosylates were prepared according to the reported procedure.[11] The rotational values of the materials obtained in this study are in good agreement with the reported values (Table III). The optical purity of the L(+) alcohol was examined by the method of Raban and Mislow,[12] and the result showed that this alcohol is essentially optically pure.

The titrimetric and polarimetric rates of acetolysis of I-OTs were determined at 75.05° without added salt; $k_t = 1.39 \times 10^{-4}$ sec^{-1}, $k_\alpha = 4.5 \times 10^{-4}$ sec^{-1}. The k_α/k_t ratio becomes 3.2, which agrees well with the

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[1] Research assistant on a grant (GP 6492X) supported by the National Science Foundation.

[2] D. J. Cram and F. A. Abd Elhafez, *J. Amer. Chem. Soc.*, **75**, 3189 (1953).

[3] D. J. Cram, *ibid.*, **74**, 2129 (1952).

[4] It was estimated that this process occurs with as much as 80% retention in the acetolysis and with greater than 90% retention in the formolysis.[2] For discussions on the mechanism, see ref 2 and D. J. Cram, H. L. Nyquist, and F. A. Abd Elhafez, *ibid.*, **79**, 2876 (1957).

[5] For current discussions on the problems that exist in this area, see footnotes 6–10 and references cited therein.

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[12] M. Raban and K. Mislow, *Tetrahedron Lett.*, 4249 (1965); *Top. Stereochem.*, **2**, 216 (1967).

Table I. Products of Acetolysis of Optically Active *threo*-4-Phenyl-3-hexyl Tosylate, 75°

Isomer	[I-OTs], *M*	[KOAc], *M*	Products, %: Secondary alcohols	Products, %: Olefins	Alcohol configuration: Threo	Alcohol configuration: Erythro	% threo optically active
L(+)[a]	0.20[b]	0.24	50	40	96	4	6.4
D(−)[a]	0.09[b]	0.105	48	39	96	4	8.2
L(+)	0.10[c]	0.20	54[d]	46	97	3	0.9 ± 0.2[e]
L(+)	0.10[c]	None	52[d]	48	97	3	1.0 ± 0.2[e]
D(−)	0.20[b]	0.24	51[d]	49	97	3	0.9 ± 0.2[e]
D(−)	0.20[c]	0.24	53[d]	47	96	4	0.8 ± 0.2[e]

[a] Reference 2. [b] Solvolysis conducted for 57 half-lives. [c] Solvolysis conducted for 10 half-lives. [d] Relative yields determined by glpc, uncorrected for detector response. [e] Determined polarimetrically.

Table II. Products of Formolysis of Optically Active *threo*-4-Phenyl-3-hexyl Tosylate, 25°

Isomer	[I-OTs], *M*	[NaO$_2$CH], *M*	Products, %: Secondary alcohols	Products, %: Olefins	Alcohol configuration: Threo	Alcohol configuration: Erythro	% threo optically active
L(+)[a]	0.20[b]	0.24	80	11	100	0	6.8
D(−)	0.10[c]	0.20	89	11	99.5	0.5	0[d]

[a] Reference 2. [b] Solvolysis conducted for 135 half-lives. [c] Present study; solvolysis conducted for 15 half-lives. [d] Under the conditions of measurement as much as 0.1–0.2% activity could have gone undetected.

Table III. Summary of Physical Data

Compound[a]	Mp, °C: Obsd	Mp, °C: Lit.[c]	Bp, °C (mm): Obsd	Bp, °C (mm): Lit.[c]	n^{20}D: Obsd	n^{20}D: Lit.[c]	[α]D (*c*, temp)[b]: Obsd	[α]D (*c*, temp)[b]: Lit.[c]
4-Phenyl-3-hexanone			67–70 (0.6)	83–84 (2)	1.5048			
4-Phenyl-3-hexanol[d]			80–82 (1.3)	83–85 (1–2)	1.5110	1.5080[e]		
(±)-I-OPhTh[f]	124–125	125–126						
(±)-I-OH			71–72 (0.7)	83 (1)	1.5102	1.5072[e]		
(±)-I-OTs	76.5–77.5	73.5–74.5						
L(+)-I-ODNB[g]	60–61	61–62					−9.0 (5, 24)	−9.2 (5, 28)
L(+)-I-OH			70–71 (0.6)				+20.8 (3, 25)	+20.9 (3, 25)
L(+)-I-OTs	92–93	93–94					+21.9 (3, 25)	+21.6 (5, 28)
Strychnine salt of D(−)-I-OPhTh[f,h]							−67.9 (6, 27)	−55 (6, 24)
D(−)-I-ODNB[g]	61.5–62.5	61–62					+8.9 (6, 26)	+9.2 (6, 29)
D(−)-I-OH			70–71 (0.6)				−21.1 (3, 25)	−21.2 (5, 28)
D(−)-I-OTs	94.5–95.5	94–95					−22.5 (3, 25)	−22.1 (5, 28)

[a] I stands for *threo*-4-phenyl-3-hexyl. [b] Determined in chloroform. [c] Reference 11. [d] Reduction product from the reaction of 4-phenyl-3-hexanone and lithium aluminum hydride. A glpc analysis indicated 80% threo and 20% erythro. [e] At 25°. [f] Hydrogen phthalate. [g] 3,5-Dinitrobenzoate. [h] Fractionally recrystallized using the triangular scheme described by Wiberg: K. B. Wiberg, "Laboratory Techniques in Organic Chemistry," McGraw-Hill, New York, N. Y., 1960, p 110.

reported value of 3.3 determined at 74.64° in the presence of 0.105 *M* potassium acetate.[2]

The product studies were conducted in the usual manner in both acetic acid and formic acid under various conditions. In each run the reaction mixture was treated with lithium aluminum hydride and analyzed by glpc. Isolation of pure threo alcohol was performed by preparative glpc separation, followed by optical rotation measurement. The results are summarized in Table I (acetolysis) and Table II (formolysis), which also contain the data of Cram and Abd Elhafez.[2]

Comparing the original data and those obtained in this study, one finds a satisfactory agreement in the values for the product distribution.[13] However, a serious discrepancy was found in the amount of the optically active retained product; the present study yielded a consistent value of 0.8–1.0% in the acetolysis runs and 0% in the formolysis run, whereas Cram and Abd Elhafez obtained considerably higher values in the range of 6–8% in both acetolysis and formolysis studies. As the present study was conducted under various conditions (one of which duplicates Cram's condition) with the use of a very careful isolation procedure, it is unlikely that the present results are in error. It appears, therefore, necessary to revise the original experimental data obtained by Cram and Abd Elhafez.[14]

Conclusion

The present study revealed that in the acetolysis of I-OTs the amount of optically active isomer in the retained product is approximately 1% instead of the originally reported value of 6–8%.[2] This value is not

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(13) One may appreciate the accuracy of these original values, determined as they were by the use of techniques involving extensive ir analyses.

(14) The high values of optical activity in the threo material found by Cram and Abd Elhafez could be the result of (a) small amounts of active threo alcohol in the starting tosylate or (b) as a result of contamination of the product alcohol with small amounts of optically active olefin produced during solvolysis. Professor Cram has suggested in a private communication that the difference might be due to small amounts of contamination by optically active *threo*- and *erythro*-4-phenyl-2-hexanols, produced by hydride shift from the 2 carbon. However, in glpc analysis of the solvolysis product, only about 1% of extraneous peaks that could not be identified were observed. We find explanation (a) quite probable because it has been reported[2] that both acetolysis and formolysis produce about equal amounts of active threo material (see Tables I and II).

greatly different from the corresponding value of 0.6% observed in the acetolysis of *threo*-3-phenyl-2-butyl tosylate (II-OTs).[3,15] Consequently, this result removes the reported discrepancy in solvolytic behavior of these two closely related systems,[2] and, in turn, no longer required is the theory which postulates that a process involving the formation of solvated open species could lead to predominantly retained product.[2,4] We are currently exploring the question of from which of the two pathways, the k_Δ and k_s, this small but significant amount of active retained product arises.

Experimental Section

Materials. The syntheses were carried out according to the procedure described by Cram and his coworkers.[11] The observed physical constants of the compounds are in good agreement with the reported values (Table III). The resolved alcohols are essentially optically pure, judging from the result of the following experiment. (−)-*O*-methylmandelic acid was prepared by the method of Jacobus and Raban,[16] mp 66.5–67.5°, $[\alpha]^{25}\text{D}$ −163.5 (*c* 1.5, H_2O). This was converted to the acid chloride by the action of thionyl chloride, and this acid chloride was allowed to react with L(+)-*threo*-4-phenyl-3-hexanol ($[\alpha]\text{D}$ +20.8) in pyridine–benzene for 12 hr at room temperature. The ester was purified by preparative glpc and examined by pmr. The methine and the methoxy protons of the acid moiety appear as singlets (δ 4.70 and 3.37, respectively), showing the presence of a single diastereomeric isomer.

Kinetic Procedure. The titrimetric and polarimetric rates of acetolysis were determined by the previously described procedure.[17]

Product Studies. The procedure is similar to that reported previously.[6] Isolation of retained product from the reaction mixture was performed by preparative glpc separation. A controlled experiment showed that no significant amount of racemization takes place during this isolation process.

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(15) The expected amount of active retained product in the absence of internal return becomes *ca.* 3.3% (1 × 3.3) for I-OTs and *ca.* 2.6% (0.6 × 4.4) for II-OTs.

(16) J. Jacobus and M. Raban, *J. Chem. Educ.*, **46**, 351 (1969); mp 66–67°, $[\alpha]^{25}\text{D}$ −164 (*c* 1.5, H_2O).

(17) S. Winstein and D. Trifan, *J. Amer. Chem. Soc.*, **74**, 1147 (1952).

Hydroboration. XXXIII. Cyclic Hydroboration of 1,4-Pentadiene with Borane in Tetrahydrofuran. Thermal Behavior of the Organoborane Derivatives and a Simple Synthesis of Bisborinane and *B*-Alkylborinanes

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Abstract: The hydroboration of 1,4-pentadiene with borane in tetrahydrofuran in the 3:2 molar ratio produces in 72% yield a mixture of at least six 3:2 compounds. Oxidation of the product provides 1,5- and 1,4-pentanediols in a ratio of 42:58. Thermal treatment of the 3:2 product at 170°, followed by oxidation, yields 1,5- and 1,4-pentanediols and 1-pentanol in a ratio of approximately 80:10:10. The reaction of the thermally treated 3:2 product with an equimolar quantity of borane in tetrahydrofuran provides bisborinane in 80% yield. The hydroboration of olefins with bisborinane represents a simple convenient synthesis of *B*-alkylborinanes in excellent yields. The two major components of the thermally treated 3:2 product have been identified as 1,5- and 1,1-bis(1′-borinyl)pentanes by utilizing the carbonylation technique. A set of empirical rules predicting the thermal behavior of the dumbbell-shaped 3:2 compounds derived from dienes is proposed. The hydroboration of 1,4-pentadiene with borane in tetrahydrofuran in the 1:1 molar ratio followed by heating at 70–100° cleanly transforms the pentamethylene and 1-methyltetramethylene moieties into bisborinane (~45% yield) and 2,7-dimethyl-1,6-diboracyclodecane (~50% yield), respectively. Physical and chemical properties of the latter substance closely resemble those of the parent compound, 1,6-diboracyclodecane. At or below 100° both bisborinane and 2,7-dimethyl-1,6-diboracyclodecane are stable. Neither interconversion of the ring systems nor isomerization of the individual pentamethylene and 1-methyltetramethylene moieties takes place. At higher temperatures (>100°) both compounds undergo decomposition without evidence of interconversion.

Hydroboration of 1,4-pentadiene with borane in tetrahydrofuran (THF), followed by oxidation, yields 38% of 1,5- and 62% of 1,4-pentanediols.[2] Simple hydroboration–oxidation of this diene had been expected to yield predominantly the 1,5-diol. The unusual distribution which was realized led to the suggestion that in this case hydroboration must involve the formation of cyclic organoborane species.[2] However, no attempt was made to isolate and characterize these products. Until recently[3] these had been the only results available on the hydroboration of 1,4-pentadiene with borane in THF.

Recently we have developed experimental procedures for studying such cyclic organoboranes. Applied to the hydroboration of 1,3-butadiene, these methods clarified the course of the reaction and the nature of the products obtained.[4]

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(1) (a) Postdoctoral Research Associate on a research grant, DA 31-134 ARO(D) 453, supported by the U. S. Army Research Office, Durham; (b) Graduate Assistant on a research grant (GM 10937) supported by the National Institutes of Health.

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