The E2C Mechanism in Elimination Reactions. The Absence of an Extreme Form of Merged Mechanism for Elimination and Substitution. A Comparison of Saytzeff *vs.* Hofmann Tendencies and of *anti vs. syn* Eliminations[1]

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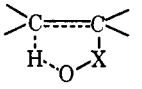
Abstract: Some bimolecular eliminations induced by halide ions in acetone, which have been classified as E2C-like reactions, have a >99.9% preference for *anti* elimination and a strong tendency to give the thermodynamically more stable olefin. Reactions of sodium thiophenoxide in 87% ethanol show similar tendencies. SN2 and E2C-like reactions do not go through a common intermediate or transition state, as required by an earlier extreme form of merged mechanism. Transition states for *anti*-diaxial and *anti*-diequatorial E2C-like eliminations have comparable free energies, in accord with loose transition states, very like products and with well-developed double bonds.

We have recently proposed that bimolecular β-elimination (E2) reactions proceed through a spectrum of transition states between the extreme structures E2H and E2C.[3,4] In this paper we examine some of the "classical" questions of E2 reactions,[5-9] insofar as they apply to E2C-like processes. These questions are as

follows. Is a *syn* or an *anti* arrangement of leaving group, X, and β-hydrogen preferred in the E2C-like transition state? Is the major olefinic product that which is most stable (*e.g.*, Saytzeff product) or can a less stable olefin (*e.g.*, Hofmann product) be formed in high yield? Does a *trans*-diaxial arrangement, in the most stable conformation of a cyclic reactant, lead to a faster elimination than a *trans*-diequatorial arrangement of H_β and X? We also examine in more detail the suggestion[10] that E2C-like and SN2 reactions proceed through a common intermediate; *i.e.*, is there an extreme form of merged mechanism of substitution and elimination?[10-12]

E2C-like transition states are utilized by strong carbon but weak hydrogen bases, B (*e.g.*, Br^-, Cl^-, RS^-), in their reactions with very weakly acidic compounds containing good leaving groups.[3,4] Such transition states are loose,[4] the double bond is thought to be well developed, and the base B is bound to both β-hydrogen and α-carbon. The products must, of course, be those from an *anti* elimination and such products, from the substrates studied in this work, are shown in Scheme I. If the double bond is well developed in the E2C-like transition state, as postulated, then the major kinetic product will be the more stable olefin, *e.g.*, the Saytzeff product.[13] *syn* eliminations would lead to different products from those shown in Scheme I. *syn* eliminations have been observed in some strongly E2H-like reactions of potassium *t*-butoxide with rather acidic compounds.[5,6,14-18] Unimolecular *syn* eliminations, through the E_i transition state,[5] are well established for pyrolysis of esters, of xanthates, and of N-oxides. The Cope elimination in DMSO[19] and the Wittig reaction in DMF[20] are of this type. In the E_i transition state, the leaving group at C_α, rather than the attacking base as in the E2C-like reaction, is bonding to hydrogen at C_β.



E_i, XO = RCO_2, R_3PO, R_2NO, xanthate

Results

Rate data are in Table I. Rate constants, k^{E+S} for the total reaction, k^S for substitution, and k^E for elimination, were calculated from observed rates of base consumed (both as RB and HB) and of acid produced.

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(2) (a) Australian-American Educational Foundation Fellow 1965-1966; (b) author to whom inquiries should be addressed.

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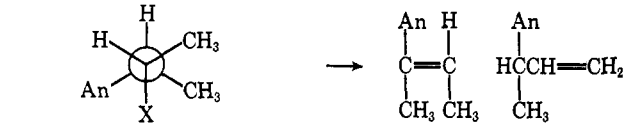
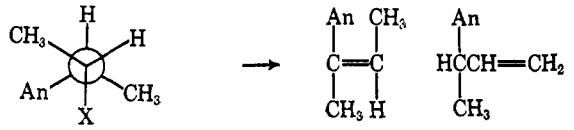
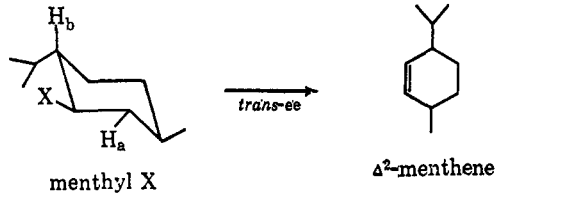
Scheme I. Products of *anti*-β-Elimination of HX



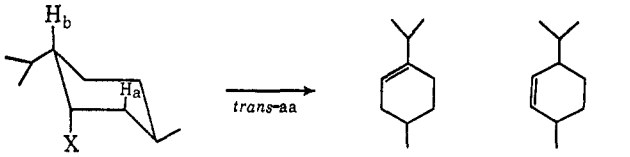
erythro-3-*p*-anisyl-2-butyl X — Saytzeff — Hofmann



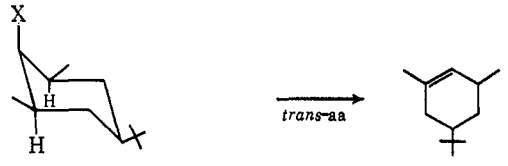
threo-3-*p*-anisyl-2-butyl X — Saytzeff — Hofmann



menthyl X — Δ²-menthene



neomenthyl X — Δ³-menthene Saytzeff — Δ²-menthene Hofmann



cis, cis-2, 6-dimethyl-*cis*-4-*t*-butylcyclohexyl X

→ no olefin

trans, trans-2, 6-dimethyl-*trans*-4-*t*-butylcyclohexyl X

Fractions of elimination F_E were calculated from acid produced and base consumed, as well as from vpc measurements. First-order solvolyses were found to be very much slower than these bimolecular reactions in acetone. No allowance has been made for incomplete dissociation of electrolytes, which usually were at 0.037 ± 0.005 *M*. Results of product analyses, by vpc, are summarized in Tables II and III.

***threo*- and *erythro*-3-*p*-Anisyl-2-butyl-X Compounds.** *threo*-3-*p*-Anisyl-2-butyl derivatives (*threo*-RX) react more rapidly than their *erythro* counterparts (*erythro*-RX), with tetra-*n*-butylammonium chloride in acetone. The same order has been observed for reactions of *threo*- and *erythro*-1,2-diphenyl-1-propyl derivatives with strong bases in hydroxylic solvents.[18] The relative amount of each product shown in Table II represents the actual yield of product in the reaction, except for runs 1, 4, and 5 in which an internal standard was not present, so that in these three cases, the percentages represent relative areas on the vapor phase chromatogram.

Products were all analyzed by vpc on a 1-m 3-methyl-3-nitropimelonitrile column, 25% on 40–60 mesh firebrick, at 130° column temperature. Higher temperatures were found to rearrange the olefins. The internal standard was *p*-chloroacetophenone. Components were identified with the aid of authentic samples. The authentic olefins were prepared by acetic anhydride dehydration of 2-*p*-anisyl-2-butanol.[21]

The isomeric alkyl chlorides were prepared from the pure alcohols[21] with thionyl chloride in the absence of solvent. This reaction proceeds with retention of configuration. Treatment with potassium *t*-butoxide in benzene at 75° for 40 hr gave the different products of *trans* elimination (Scheme I) from each chloride. *erythro*-ROTs, RCl, and ROBs gave identical olefins, when treated with KOBu-*t* in benzene at 75°. Six components were detected from the reaction of *erythro*-R brosylate with halide ions in acetone. Only one could not be identified by comparison with an authentic sample. This was assumed to be 3-*p*-anisyl-1-butene, on the basis of relative retention times and comparison with phenyl butenes.[22] The retention times, at a flow rate of 120 cc/min, were *trans*-2-*p*-anisyl-2-butene, 5.7 min; 3-*p*-anisyl-1-butene, 7.0 min; 2-*p*-anisyl-1-butene, 10.0 min; *cis*-2-*p*-anisyl-2-butene, 14.5 min; *threo*-RCl, 28.0 min; *erythro*-RCl, 36.0 min.

Control experiments established that 0.1% of *trans*-2-*p*-anisyl-2-butene could be easily detected in the presence of 99.9% of other olefins. In the presence of *p*-toluenesulfonic acid, 2,6-lutidine, and tetra-*n*-butylammonium chloride, there was no detectable rearrangement of olefins in acetone at 50° after 48 hr. With lutidine and tosylic acid only, *threo*-RCl slowly rearranged to *erythro*-RCl, as shown in Table IV. Under similar conditions, *erythro*-RCl is quite stable.

The relative contribution of the ionization process to the product runs of the *threo*- and *erythro*-R brosylates was estimated from the rates in Table I. It could be no more than 0.2% for Bu_4NCl with *erythro*-ROBs, 3% for Bu_4NBr with *erythro*-ROBs, and 0.5% for Bu_4NCl with *threo*-ROBs. The 2-*p*-anisyl-1-butene arises from anisyl participation in the solvolysis reaction. The acetolysis of 3-phenyl-2-butyl analogs has been discussed by Cram,[23] who observed a greater percentage of rearranged olefin from the *threo* isomer. The presence of *erythro*-RCl, in runs 2 and 3 of Table II, may arise from the ionization reaction.

We could not detect 3-*p*-anisyl-1-butene from the E2 reactions of *threo*-3-*p*-anisyl-2-butyl brosylate or chloride with a fourfold excess of chloride ion in acetone. The small amounts of this Hofmann product shown in Table II for slower E2 reactions could be from solvolysis reactions. We conclude that these E2 reactions give >99.9% of the thermodynamically more stable 2-*p*-anisyl-2-butenes.

Elimination from *erythro*-R brosylate with NBu_4Cl in acetone is 800:1 in favor of *cis*-2-*p*-anisyl-2-butene,

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Table I. Rates of Elimination (k^E) and Substitution (k^S) Reactions in Acetone

Compound[a]	Temp, °C	Salt	$10^2 M$ salt	$10^2 F_E$	$10^3 k^{E+S}$, M^{-1} sec^{-1}	$10^3 k^S$, M^{-1} sec^{-1}	$10^3 k^E$, M^{-1} sec^{-1}
erythro-ROBs	50.0	Bu_4NCl	3.893	81.0 ± 4	11.6 ± 0.1	2.2	9.4
	50.0	Bu_4NBr[f]	4.042	62.8 ± 0.4	1.94 ± 0.06	0.72	1.22
	50.0	Bu_4NBr[g]	4.022	63.8 ± 0.8	1.82 ± 0.03	0.67	1.15
	75.0						1.6[a]
threo-ROBs	50.0	Bu_4NCl	4.500	86.0 ± 1.0	17.5 ± 0.5	2.5	15.0
	25.0	Bu_4NCl	4.66	87	1.07 ± 0.04		
	25.0	Bu_4NCl	4.66		0.97 ± 0.03[e]		
	75.0	*f*					0.59[b]
	75.0	*f*			5.9[c]		
	75.0				5.1[b]		
erythro-ROTs	75.0	Bu_4NBr	3.165	64.0 ± 1.7	3.05 ± 0.1	1.10	1.95
threo-RCl	50.0	Bu_4NCl[f]	3.997				0.00175
erythro-RCl	50.0	Bu_4NCl[f]	4.130				0.00128
	75.0	Bu_4NCl[f]	3.170				0.0231
Menthyl-OBs	75.0	*f*					0.077[b]
	75.0	Bu_4NCl[f]	4.352	35.2 ± 0.6	11.1 ± 0.4	7.2	3.9
Menthyl-OTs	75.0	Bu_4NCl	3.124	33.4 ± 1.9	1.67 ± 0.5	1.12	0.55
	75.0	Bu_4NBr	2.837	42.9	0.66	0.34	0.28
Neomenthyl-OTs	75.0						0.161[b]
	75.0	Bu_4NClO_4	4.959				0.328[b]
	50.0	Bu_4NCl	3.145	100 ± 2	23.0 ± 0.6		23.0
Neomenthyl-Cl	75.0	*f*					$<10^{-3}$
	75.0	Bu_4NCl[f]	4.173				0.092
trans,trans-2,6-Dimethyl-*trans* 4-*t*-Butylcyclohexyl OTs	75.0	Bu_4NCl[f]	4.046	0.1 ± 0.01	9.27 ± 0.80	9.26	0.0093
	50.0	Bu_4NCl[f]	3.882	0.1 ±0.02	0.775 ± 0.01	0.77	0.0008
cis,cis-2,6-Dimethyl-*cis*-4-*t*-Butylcyclohexyl-OTs	50.0	Bu_4NCl[f]	5.097	99.9 ± 0.1	21.0 ± 0.2	<0.021	21.1
	50.0	Bu_4NCl[f]	3.609	100 ± 0.2	21.5 ± 0.4		21.5
Neomenthyl-OTs	25.3	$NaSC_6H_5$[d]	6.98	72 ± 1	2.41[d]	0.73[d]	1.68[d]
Menthyl-OTs	50.0	$NaSC_6H_5$[d]	10.14	0	−0.10[d]	0.10[d]	

[a] R is 3-*p*-anisyl-2-butyl, OTs is *p*-toluenesulfonate, OBs is *p*-bromobenzenesulfonate. Substrates are at 0.015–0.025 *M*. [b] Instantaneous initial second-order rate constant for acid production by a hypothetical base at 0.030 *M*, *i.e.*, the first-order solvolysis rate, k_1 (sec^{-1}), was calculated over at least 50% reaction but is recorded here as $k_E = k_1/0.030$ (M^{-1} sec^{-1}). This enables direct comparison of solvolysis rates with bimolecular substitution and elimination. The actual first-order rate constant for solvolysis is readily calculated from $k_1 = k_E \times 0.030$. [c] Instantaneous initial second-order rate constant for racemization by a hypothetical base at 0.030 *M*, *i.e.*, $k_1(\text{rac}) = k_2 \times 0.030$ sec^{-1}. [d] Solvent 87% v/v ethanol–water. [e] Rate determined polarimetrically. [f] Acetone contains 0.02–0.03 *M* 2,6-lutidine. [g] Acetone contains 0.06 *M* 2,6-lutidine.

whereas elimination from *threo*-R brosylate is more than 1000:1 in favor of *trans*-2-*p*-anisyl-2-butene. The eliminations are therefore >99.9% *anti* (*cf.* Scheme I).

The eliminations from ROBs in the presence of the less nucleophilic base, NBu_4Br in acetone, are not quite as stereospecific as reactions of NBu_4Cl in acetone, because the ionization reaction interferes more. In the reaction of *erythro*-RCl with NBu_4Cl, the relative per cent of each olefin and the fraction of elimination change during reaction. This is due to subsequent reaction of the substitution product, *threo*-RCl, which is more reactive than *erythro*-RCl. The fraction of elimination, F_E, was extrapolated to zero time and estimated at 0.87. A plot of the per cent *cis*-olefin in the *cis–trans* mixture, *vs.* time, indicated that, at the beginning of the reaction, over 98% of the olefinic products was *cis*-2-*p*-anisyl-2-butene, *i.e.*, the product of *anti* elimination.

Menthyl–Neomenthyl System. The product runs are summarized in Table III; rate data are summarized in Table I. Neomenthyl-X has the leaving group, X, in an axial position in the stable conformation of the reactant state and is a higher energy species than menthyl X. Since X is leaving from sp^2 hybridized carbon in the E2 and SN2 transition states, neomenthyl-X is more reactive than menthyl X. In the reaction of menthyl brosylate with bromide or chloride ion, the substitution product is the highly reactive neomenthyl halide and this creates some difficulties, which were overcome by following the reaction by vpc. Products were extracted with pentane and olefins were flash distilled at 1 mm and room temperature. Starting material remained in the flask. Solvent was removed from the distillate and the olefins, with the menthyl and neomenthyl chlorides, were analyzed on a 3-m 3-menthyl-3-nitropimelonitrile column, 25% on 40–60 mesh firebrick. The internal standard was *m*-xylene. Control experiments established that 0.1% of either Δ^2- or Δ^3-menthene could be detected easily, in the presence of 99.9% of the other.

Reaction of neomenthyl chloride with NBu_4Cl in acetone gave 98% menthenes by vpc. The reaction products were monitored over 0.1–20 half-lives and their proportions remained unchanged.

Menthyl tosylate reacts with NBu_4Br in acetone to give neomenthyl bromide as the major product. This reacts further to give Δ^3-menthene. Since neomenthyl bromide eliminates about ten times faster than menthyl tosylate with bromide ion in acetone at 75°, this secondary reaction is a serious complication. The reactions of menthyl brosylate with bromide ion are less seriously affected, but there is still some contamination of the original elimination by elimination from the substitution product. Reactions of menthyl and neomenthyl brosylates with NBu_4Cl in acetone give a better picture of the stereochemistry and ratio of substitution to elim-

Table II. Products of Reactions of *threo*- and *erythro*-3-*p*-Anisyl-2-butyl Systems (RX) in Acetone at 50.0°[a]

no.	Added salt	$10^2 M$ RX	$10^2 M$ salt	$10^2 M$ lut[d]	% of total reaction: *trans*-2-*p*-Anisyl-2-butene	*cis*-2-*p*-Anisyl-2-butene	2-*p*-Anisyl-1-butene	3-*p*-Anisyl-1-butene	*erythro*-RCl	*threo*-RCl	$10^2 F_E$ vpc	No. of half-lives
					erythro-ROBs							
1	—	4.14	—	6.16	10.0	50.0	4.0	26				8
2	Bu_4NCl	4.04	6.78	5.51	0.4	77.9	1.7	0.8	3.2	15.0	80.8	10, 20, 40
3	Bu_4NCl	3.04	16.64	4.96	0.1	80.0	0.1	0.3	1.2	17.8	81.0	10, 20
4	Bu_4NBr	3.44	10.50	5.10	5.0	56.8	0.8	0.4				10
					threo-ROBs							
5	—	4.14	—	6.26	33.0	46.0	7.0	14.0				8
6	Bu_4NCl	4.09	8.80	5.20	79.8	0.7	0.1	6.7	12.2	1.1	86.7	10
					82.4	0.6	0.1	3.4	12.7	0.8	86.5	20
					79.4	1.0	0.1	7.5	11.4	0.6	88.0	40
7	Bu_4NCl	3.12	13.54	5.07	86.0	—	0.5	—	13.5	—		10
					86.5	—	0.5	—	13.0	—		20
					84.1	—	0.5	—	14.4	0.6		40
					erythro-RCl							
8	Bu_4NCl	4.87	14.35	8.93	4.1	81.7	—	4.9		9.3	90.7	0.05[b]
					4.8	77.1	—	3.0		15.1	84.0	0.1
					9.2	83.5	—	—		7.2	93.0	1
					17.2	78.4	3.6	—		0.8	99.0	4
					threo-RCl							
9[c]	Bu_4NCl	2.27	6.69	3.72	79.5	20.0	—	—	0.5			10[c]
					75.0	25.0	—	—	—			20[c]

[a] A dash indicates that none of the product could be detected on the chromatogram (<0.1%). [b] The four samples analyzed correspond to calculated 1, 5, 50, and 94% reaction, respectively. [c] Run carried out at 75.0°. [d] 2,6-Lutidine.

Table III. Products of Reactions of Menthyl and Neomenthyl Systems in Acetone at 75.0°

Run no.	Added salt	$10^2 M$ RX	$10^2 M$ salt	$10^2 M$ lut	% $10^2 F_E$(±0.1): Δ^2-Menthene	Δ^3-Menthene	$10^2 F_E$ vpc	Time, half-lives
				Neomenthyl Tosylate				
1		10.05		14.80	2.3	97.7		5
					9.0	91.0		10
2	Bu_4NCl	4.10	7.71	4.79	3.2	96.8	99[a]	From 20% to 20 half-lives[b]
				Menthyl Brosylate				
3		10.00		14.50	30	70		5
4	Bu_4NCl	3.74	7.27	6.00	98.2	1.8		0.1–0.7
					96.6	3.4	32	2
					94.4	5.6		10
					93.0	7.0		20
5	Bu_4NBr	4.00	8.01	6.00	75.0	25.0		0.05[c]
					70.8	29.2	70	0.1
					59.4	40.6		0.7
					36.0	64.0		2.0
					27.0	73.0		10
				Neomenthyl Chloride				
6	Bu_4NCl	3.04	6.80	5.20	0.1	99.9	98[d]	0.1–20

[a] Menthyl chloride, 1.0 ± 0.3%. [b] The reaction was followed by vpc from *ca.* 20% to 20 half-lives. The percentage of Δ^3-menthene during the run was the following: 96.8, 96.7, 98.5, 96.8, 96.8, and 96.8. [c] The times corresponding to the five samples are the following: 2, 4, 22, 84, and 384 min, respectively. [d] Menthyl chloride, 2.0 ± 0.2%.

Table IV. Control on Isomerization of *threo*-3-*p*-Anisyl-2-butyl Chloride in Acetone, 75.0°

threo-RCl, 0.0206 *M*	2,6-Lutidine, 0.0368 *M*: Time, days 0	30	HOTs, 0.0209 *M*: Time, days 70	100
% *erythro*-RCl	1	10.5	14.5	25.5
% *threo*-RCl	99	89.5	85.5	74.5

ination in the original elimination, because the chlorides formed by substitution are much more stable and react more slowly than either brosylate.

2,6-Dimethyl-4-*t*-butylcyclohexyl System. The *trans*,*trans*,*trans*- and *cis*,*cis*,*cis*-2,6-dimethyl-4-*t*-butylcyclohexyl alcohols were prepared by alkylation of 2,6-dimethylphenol with *t*-butyl alcohol, followed by hydrogenation. Vpc analysis indicated four alcohols. The missing two probably correspond to III, having a 1,3-dimethyl–diaxial interaction[24] and being therefore less stable. The alcohols were oxidized with chromic oxide, and only two peaks (92:8), having strong carbonyl absorption in the infrared, were obtained on the vpc. Equilibration of the ketones did not change their

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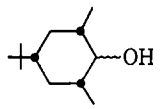
Table V. Olefins[a] from Bimolecular Elimination Reactions of *erythro*- and *threo*-3-*p*-Anisyl-2-butyl Derivatives (RX) with NBu_4Cl in Acetone[b] at 50.0°

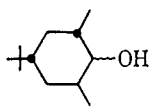
	An | $CH_3C{=}CHCH_3$[d] *cis*	 *trans*	An | $CH_3CHCH{=}CH_2$ terminal	An | $CH_2{=}CCH_2CH_3$ rearranged
erythro-ROBs	80.0	<0.1[e]	<0.3[e]	<0.1[e]
threo-ROBs	<0.1	86.0	<0.1	*Ca.* 0.3
erythro-RCl	82[c]	2[c]	<5[e]	<0.1
threo-RCl	<20[e]	>79.5	<0.1	<0.1

[a] Expressed as a percentage of total products. [b] Acetone contained 2,6-lutidine. [c] By extrapolation to zero time, see text. [d] An is *p*-methoxyphenyl. [e] The maximum values recorded here are the observed products for the sum of bimolecular elimination from initial substrate, the elimination from substitution product, and the formation of olefin by solvolysis. Thus olefins for the initial E2 reaction are less than this, as shown here (see text).

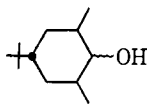
relative proportions. Equilibration of the related isomers of 2,6-dimethylcyclohexanone gives 90% *cis* and 10% *trans* isomers,[25] so the ketone obtained here in higher yield is assumed to be the *cis* isomer. The mixture was reduced with lithium aluminum hydride to give three peaks on vpc in the ratio 26:48:16. The first two components were assumed to have the stereochemistry of alkyl groups as in structure I. A fourth small peak was also present. The 26% component was separated by chromatography on silica gel with 2.5% ether–pentane as eluent. This alcohol was pure (mp 57.8–58.3°) and had the characteristic axial C–O stretching band in the infrared spectrum. It was assigned structure Ib. The 48% component was separated by preparative vpc and appeared to be a pure equatorial



Ia, OH equatorial
b. OH axial



II



III

alcohol (mp 90.8–91.2°). It was assigned structure Ia. The *p*-toluenesulfonate esters were then prepared. The equatorial *trans,trans,trans*-tosylate of Ia analyzed correctly, reacted with good second-order kinetics, and gave expected infinities. The axial *cis,cis,cis*-tosylate of Ib hydrolyzed to only 86.2% of the expected infinity. Insufficient amounts were available for further purification, so reactions were performed on the basis of 86.2% purity. In view of the uncertainty as to purity of the tosylate of Ib, the results for this compound should be treated cautiously, but the data on the tosylate of Ia are reliable, in our opinion.

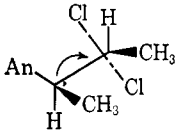
Discussion

***threo*- and *erythro*-3-*p*-Anisyl-2-butyl System.** The polarimetric rate and the titrimetric rate for acid production plus chloride consumption (Table I) are effectively the same for each of the isomers, *erythro*- and *threo*-3-*p*-anisyl-2-butyl brosylate (ROBs). Thus side reactions do not interfere with the elimination and substitution. NBu_4Cl reacts faster than NBu_4Br in acetone and gives a higher fraction of elimination.

The products of bimolecular elimination from the initial substrate, with due allowance for elimination from the substitution product and formation of olefin from solvolysis, are summarized in Table V. No terminal olefin (Hofmann product) and a negligible amount of rearranged olefin were detected from bimolecular reaction of NBu_4Cl with *threo*- and *erythro*-ROBs in acetone. The olefins from halide-induced elimination are >99.9% Saytzeff olefins. The E2 reactions must be >99.9% *anti* because *erythro*-ROBs gives this proportion of *cis*-2-*p*-anisyl-2-butene, whereas the *threo*-ROBs gives *trans*-2-*p*-anisyl-2-butene (*cf.* Scheme I). Tetra-*n*-butylammonium chloride in acetone containing 2,6-lutidine is clearly an excellent reagent for rapidly obtaining clean, stereospecific olefins from suitable substrates.

The reaction of *erythro*-RCl with NBu_4Cl in acetone is >98% *anti* and the reaction of *threo*-RCl is >80% *anti*. Precise figures are difficult to obtain because of elimination from inverted substitution products, but minimum tendencies for *syn* elimination are quite clear. The E2C-like transition state, for elimination from *erythro*-RCl, is stereochemically distinct from that for elimination from *threo*-RCl. The SN2 transition states for chloride exchange are generally accepted[26] as being one and the same species for *threo*- and *erythro*-RCl.

This is strong evidence against our original concept of the merged mechanism.[10] If the elimination proceeded through a symmetrical intermediate, IV, resembling the SN2 transition state,[26] this would be the same intermediate from either *threo*- or *erythro*-RCl and would therefore give the same mixture of olefins. Since quite different mixtures of olefins are obtained in reaction of *threo*- and *erythro*-RCl with NBu_4Cl in acetone, there cannot be a symmetrical intermediate, IV, for this E2C-like elimination. The attacking chloride ion must be bound to the substrate in a different way from the departing chloride. For example, the attacking chloride could be attached only to the β-hydrogen, as in the classical E2H transition state, or it could be bound to both β-hydrogen and C_α in an *anti* arrangement of H_β and leaving chloride, as in the E2C-like transition state.[3]



IV

Menthyl and Neomenthyl System. The steric requirements of the methyl and isopropyl groups constrain them to occupy equatorial positions[5,8] in the more stable conformation of these isomers. Thus the tosylate group is equatorial in menthyl tosylate whereas it

(25) R. Trave and L. Garanti, *Rend. Ist. Lombardo Sci. Lettere*, **94**, 405 (1960).

(26) Reference 7, Chapter 7.

is axial in neomenthyl tosylate (*cf.* Scheme I). The axial tosylate is lost more readily than the equatorial tosylate in solvolysis[5,27] and the same situation is found here for the bimolecular substitution and elimination (Table I). Tetra-*n*-butylammonium chloride reacts more rapidly with menthyl and neomenthyl compounds than does NBu_4Br in acetone. Sodium thiophenoxide in 87% ethanol appears to be as reactive or more so than halide salts in acetone, but F_E is lower.

The products of reaction with a number of reagents in different solvents are summarized in Table VI. Neomenthyl compounds give a much higher fraction of elimination than menthyl (*cf.* Table I). The reactions of sodium ethoxide in ethanol[5] and NBu_4Cl in acetone are both *anti* eliminations because menthyl tosylate gives only Δ^2-menthene (*cf.* Scheme I). However, a high percentage of the thermodynamically more stable Δ^3-menthene[28] is produced in solvolysis reactions,[5] which probably proceed *via* carbonium ions (E1 reactions).

Table VI. Olefins from Elimination by Menthyl and Neomenthyl Tosylates

Reagent	Menthyl tosylate		Neomenthyl tosylate	
	% Δ^3-menthene (Saytzeff)	% Δ^2-menthene (Hofmann)	% Δ^3-menthene (Saytzeff)	% Δ^2-menthene (Hofmann)
E1 solvolyses[a]	70	30	99	1
E2 reactions[a]	0	100	76	24
NaOEt–EtOH[b]	0	100	78	22
Me_2CO, lut[c]	70	30	98	2
Me_2CO, NBu_4Br			97	3
Me_2CO,NBu_4Cl	<1.8	>98.2	97	3

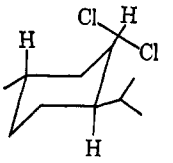
[a] Banthorpe[5] has reviewed these types of reactions with different bases and solvents and arrives at these representative figures. Solvolyses in ethanol, acetic acid, DMSO, and DMF (S. Winstein and J. Schwartz, unpublished work) also roughly give these values. [b] For reaction of menthyl and neomenthyl chloride, ref 8. [c] Lut = 2,6-lutidine.

Neomenthyl tosylate can eliminate in an *anti* process either by losing H_a or H_b (*cf.* Scheme I). In practice the product is almost exclusively the Saytzeff product, Δ^3-menthene, in reaction with NBu_4Cl in acetone, showing that H_b is eliminated in preference to H_a. This is an illustration of the tendency of E2C-like reactions to give the more stable[28] olefin. The Saytzeff obedience is much better (97:3 *vs.* 4:1) for reaction with NBu_4Cl in acetone than with NaOEt in ethanol or with other "classical" (*i.e.*, more E2H-like) E2 reactions.[5] The E1 solvolysis of neomenthyl tosylate in acetone is also strongly Saytzeff.

The tendency for *anti* elimination is stronger than the tendency to give the more stable olefin in E2C-like reactions. Thus menthyl tosylate with NBu_4Cl in acetone gives almost exclusively the Hofmann product, Δ^2-menthene. Menthyl tosylate cannot give Δ^3-menthene by an *anti* elimination (*cf.* Scheme I) and it strongly prefers the *anti* elimination of H_a to *syn* elimination of H_b, even though the former gives the less stable olefin.

(27) S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan, and H. Marshall, *J. Am. Chem. Soc.*, 74, 1127 (1952).
(28) H. Pines and L. A. Schaap, "Advances in Catalysis," Academic Press, New York, N. Y., 1960, Chapter XII.

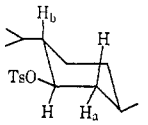
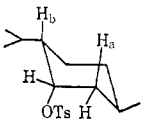
The reaction of neomenthyl chloride with NBu_4Cl in acetone gives >98% Δ^3-menthene, which is the product of *anti* elimination, whereas menthyl chloride with NBu_4Cl in acetone, by analogy with all E2C-like reactions of menthyl compounds,[5] *e.g.*, of menthyl tosylate, almost certainly gives very high yields of Δ^2-menthene. Thus menthyl chloride and neomenthyl chloride do not eliminate *via* a common symmetrical transition state (or intermediate) V, which is modeled on the generally accepted transition state for the SN2 exchange of chloride.[26] These observations show further that the extreme form of merged mechanism, as earlier envisaged,[10] is not operating in E2C-like reactions, and that substitution and elimination proceed *via* different transition states.



V

The relative rates of substitution and of elimination of the secondary hydrogen, H_a, and the tertiary hydrogen, H_b, in reactions of menthyl and neomenthyl tosylate with NBu_4Cl in acetone (*cf.* Scheme I) are shown in Table VII. These rates were calculated from the

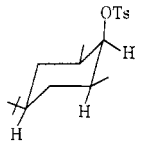
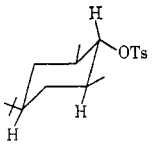
Table VII. Rates of Substitution and Elimination in Reactions of Menthyl and Neomenthyl Tosylates with NBu_4Cl in Acetone at 75.0°

	10^5k_S,[a] M^{-1} sec^{-1}	10^5k_E,[b] M^{-1} sec^{-1}	10^5k_E,[c] M^{-1} sec^{-1}
 Menthyl tosylate	109	54 *anti*-ee	<1 *syn*-ae
 Neomenthyl tosylate	<234	700 *anti*-aa	22,500 *anti*-aa

[a] Rate of substitution. [b] Rate of formation of Δ^2-menthene (H_a eliminated). [c] Rate of formation of Δ^3-menthene (H_b eliminated).

over-all rate, on the reasonable assumption that the olefinic and substitution products were kinetically controlled, *i.e.*, that the rate-determining and product-determining steps were the same. Elimination of H_aOTs (*cf.* Table VII) from menthyl tosylate is an *anti*-diequatorial process, elimination of H_bOTs is a *syn*-axial–equatorial process. Eliminations of H_bOTs and H_aOTs from neomenthyl tosylate are both *anti*-diaxial processes (*cf.* Table VII) but the tertiary hydrogen, H_b, is eliminated preferentially to give Δ^3-menthene. The *anti*-diaxial elimination from neomenthyl tosylate to give Δ^2-menthene is only 13 times as fast as the *anti*-diequatorial elimination from menthyl tosylate to give the same olefin. Taking into account the ground-state free-energy difference of the two isomers, where the neo-

Table VIII. Rates of Substitution and Elimination in Reactions of 0.04 *M* Bu_4NCl with 2,6-Dimethyl-4-*t*-butylcyclohexyl Tosylate in Acetone at 50.0°

	10^5k^{E+S}, M^{-1} sec^{-1}	$100F_E$	10^5k^E, M^{-1} sec^{-1}	10^5k^S, M^{-1} sec^{-1}
 *cis,cis*-2,6-Dimethyl-*cis*-4-*t*-butylcyclohexyl tosylate	2130	99.9 ± 0.1	2128 (*anti*-aa)	<10[a]
 *trans,trans*-2,6-Dimethyl-*trans*-4-*t*-butylcyclohexyl tosylate	77.5	0.1 ± 0.2	0.1 ± 0.02 (*syn*-ae)	77.4

[a] Rate data for this compound should be treated with caution (see text) when small effects are interpreted (*e.g.*, if F_E were 98%, 10^5k^S would be 40).

menthyl tosylate is of *ca.* 1 kcal higher energy,[5] this means that these E2C-like transition states have almost the same free energy. If the E2C-like transition states I are very like products (*i.e.*, Δ^2-menthene + HCl + OTs^-), then of course they will be much the same, no matter whether they are formed from menthyl or neomenthyl tosylate as reactants.

The *anti*-diaxial elimination to give Δ^3-menthene is at least 10^4 times as fast as the *syn*-a,e elimination (Table VII). This emphasizes the advantage of a *trans* arrangement of β-hydrogen and leaving group in the ground state in E2C-like reactions.

2,6-Dimethyl-4-*t*-butyl System. Results for SN2 and E2C-like reactions of isomeric 2,6-dimethyl-4-*t*-butylcyclohexyl tosylates with NBu_4Cl in acetone are summarized in Table VIII. The 4-*t*-butyl group is equatorial and acts as a conformational control;[29] the methyl groups are also equatorial, in the pair of isomers used here. In the axial isomer, *cis,cis*-2,6-dimethyl-*cis*-4-*t*-butylcyclohexyl tosylate, the tosylate group is axial and *trans* to the hydrogens at C_2 and C_6, which are axial (*cf.* Scheme I).

In the equatorial isomer, *trans,trans*-2,6-dimethyl-*trans*-4-*t*-butylcyclohexyl tosylate, the tosylate group is equatorial and *cis* to the hydrogens at C_2 and C_6 which are axial. The axial isomer gives exclusively elimination; the equatorial isomer gives exclusively substitution. The rate difference between an *anti*-diaxial elimination from the axial isomer and a *syn*-a,e elimination from the equatorial isomer is $>10^4$, *i.e.*, at least as large as is observed in the menthyl–neomenthyl series for a *trans*-a,a *vs. cis*-a,e conformation of β-hydrogen and leaving group in the ground state.

In this work we have shown that the transition state for a type of E2 reaction, which we have classified as E2C-like, is not the same as that for an SN2 reaction. The SN2 and E2C-like reactions do not share a common intermediate. The E2C-like transition state appears to be very like the products and may have a well-developed double bond. The reactions have a very strong preference for *anti* elimination and this is consistent with the E2C-like transition state. However, an E2C-like transition state is not the only structure required by the results reported here; stronger evidence for the E2C-like transition state has been presented.[3]

Experimental Section

Kinetic Measurements and Product Analysis. Acid was estimated by pouring aliquots into cold acetone and titrating with sodium methoxide in methanol. Brom phenol blue and *p*-hydroxyazobenzene were used as indicators. A second aliquot was poured into pentane and extracted three times with water; the aqueous extracts were titrated with silver nitrate by the Volhard method.

Olefins were analyzed in the following general way. The reaction mixtures, containing an internal standard, were extracted with pentane, and the pentane washed with water, dilute acid, and sodium bicarbonate. The pentane layer was dried over potassium carbonate, filtered, and flash distilled at 1 mm (or less) into a trap cooled in acetone–Dry Ice. The pentane solution of olefins was then analyzed by vpc. The *threo*- and *erythro*-3-*p*-anisyl-2-butanols were available.[21] *dl-erythro*-3-*p*-Anisyl-2-butyl *p*-bromobenzenesulfonate, mp 67–68° (lit.[30] mp 67–68°), was prepared from the alcohol in the usual way,[30] and crystallized from ether–pentane. The *dl-threo*-3-*p*-anisyl-2-butyl *p*-bromobenzenesulfonate, mp 97.5° (lit.[30] mp 97.5–98.5°), was available.[30] *dl-erythro*-3-*p*-Anisyl-2-butyl *p*-toluenesulfonate, mp 51.0–52.0°, was prepared from the alcohol using the usual tosylation procedure.[30] *Anal.* Calcd for $C_{18}H_{22}O_4S$: C, 64.64; H, 6.63. Found: C, 64.85; H, 6.69.

***dl-erythro*-3-*p*-Anisyl-2-butyl Chloride.** The pure *erythro*-alcohol[21] (2.1 g) was placed in a round-bottomed flask and cooled with the aid of an ice–salt bath. Thionyl chloride (Eastman White Label) was added in excess (2:1) to dissolve all the alcohol. Hydrogen chloride came off immediately and it subsided gradually. After standing at room temperature for about 1 hr, the mixture was transferred to a distilling flask with the aid of a little benzene. Distillation at reduced pressure gave 1.9 g of a substance, containing chlorine and boiling at 96° (1.8 mm), $n^{25}D$ 1.5228. The yield of product was 81.5%. *Anal.* Calcd for $C_{11}H_{15}OCl$: C, 66.49; H, 7.61. Found: C, 66.69; H, 7.49. The alkyl chloride (0.3 g) was treated with 5 ml of 1 *M* potassium *t*-butoxide in benzene at 75.0° for 40 hr. The olefin *cis*-2-*p*-anisyl-2-butene was produced in over 96% yield by vpc. The remaining 4% of product was made up by 3-*p*-anisyl-1-butene. The olefins, *trans*-2-*p*-anisyl-2-butene and 2-*p*-anisyl-1-butene, were present in less than 0.1%.

***dl-threo*-3-*p*-Anisyl-2-butyl Chloride.** A sample (3.8 g) of pure alcohol[21] was treated with thionyl chloride as described for the case

(29) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, 77, 5562 (1955).

(30) S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck, and G. C. Robinson, *ibid.*, 78, 328 (1956).

of the *erythro* isomer. The product was pure by vpc: bp 97.5° (2.0 mm), $n^{25}D$ 1.5254. The *threo*- and *erythro*-RCl's have quite different retention times on vpc columns.

***cis*- and *trans*-2-*p*-Anisyl-2-butene and 2-*p*-Anisylbutene.** These olefins were prepared by Allred and the assignment of structures was made by Allred, Sonnenberg, and Winstein.[21]

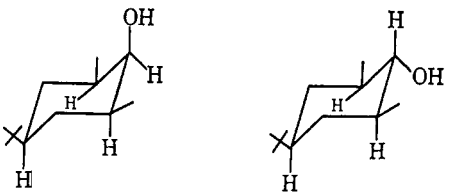
Menthyl *p*-Bromobenzenesulfonate. A 5-g quantity of *dl*-menthol (Eastman White Label) was dissolved in 20 ml of dry pyridine which was cooled and 12 g of *p*-bromobenzenesulfonyl chloride was added. The flask was left in a cold room overnight. The mixture was poured into 30 ml of ice water and the oil which formed was induced to crystallize. The washed crystals (8.4 g) were dried under reduced pressure and then recrystallized from Skelly B solvent, mp 95.5–96.5°. *Anal.* Calcd for $C_{16}H_{23}O_3SBr$: C, 51.20; H, 6.17. Found: C, 51.07; H, 6.02.

Neomenthyl *p*-toluenesulfonate, mp 64.5° (lit.[27] mp 65–65.5°), and menthyl *p*-toluenesulfonate, mp 92.4–93.6° (lit.[27] mp 93.5–94°), were prepared from the alcohols in the usual way.[27] The neomenthyl *p*-toluenesulfonate was extremely unstable; it was stored as a solution in pentane–ether. Solid samples could be stored in clean ammonia-rinsed bottles at −10°. Neomenthyl chloride was prepared as described by Hughes and Ingold.[31] The product, bp 76° (20 mm), showed *ca.* 30% impurities by vpc analysis. A sample was purified by preparative vpc and was 95.4% pure. It was contaminated with 2.5% Δ^3-menthene and 2.2% menthyl chloride, as shown by vpc of authentic mixtures. Samples of Δ^2-, Δ^3-, and Δ^4-menthene were provided by J. Schwartz.

***trans,trans*-2,6-Dimethyl-*trans*-4-*t*-butylcyclohexyl *p*-Toluenesulfonate.** 2,6-Dimethyl-4-*t*-butylphenol, mp 80.5° (lit.[32] mp 82.5°), was prepared from 2,6-dimethylphenol and *t*-butyl alcohol.[32] This was hydrogenated in ethanol at 150° at a pressure of 1500 psi with a Raney nickel catalyst[33] for 1 day. Analysis of the product by vpc on a Carbowax 4000 column (10 psi 160°) showed four components in the ratio 57:29:7:7. The 2,6-dimethyl-4-*t*-butylcyclohexanol was then oxidized to the ketone as follows.

The mixed alcohol (8.2 g) was dissolved in 150 ml of ether and 36 g of chromic oxide in 100 cc of water was slowly added, while stirring and cooling (molar ratio of alcohol to oxidizing agent = 2:16). Stirring was continued for *ca.* 2 hr. The ketone was extracted with 600 cc of pentane, washed several times, and the solvent was evaporated off. The residue was distilled and gave 7 g of product, bp 92° (5 mm). The infrared spectrum showed a strong ketone band and analysis by vpc indicated the presence of two components (93:7). Some unreacted alcohol was also present. The two ketones were equilibrated with 5 g of potassium hydroxide in 25 ml of water and 25 ml of dioxane at refluxing temperature for 20 hr. The ketones were then extracted with 500 ml of pentane, washed thoroughly, and the solution was dried over magnesium sulfate. The product recovered was 6 g, bp 92.5° (5.5 mm). Upon equilibration, the ratio of the two ketones remained unchanged (*ca.* 92:8). Comparison of the infrared spectrum at 13.50 mμ with that reported in ref 25, suggests that the major ketone has *cis*-dimethyl groups. The ketones were reduced to alcohols as follows.

A 5.7-g quantity of the ketone mixture, dissolved in 25 ml of ether, was added to 1.0 g of lithium aluminum hydride in 25 ml of ether with stirring and cooling in an ice–water bath. At the end of the addition period, 4 ml of 10% sodium hydroxide was slowly added with cooling. After 30 min, the ether layer was decanted, washed, and dried over magnesium sulfate. Distillation yielded 4 g of solid product. Vpc analysis indicated the presence of three major peaks and a shoulder (26:58:shoulder:16). Only the first two peaks were separated. The first component was separated from the other ones by chromatography on silica gel (150 g). It was the first alcohol to come off the column, using 2.5% ether–pentane as the eluent solvent. Recrystallization of this material from pentane gave 1.1 g of alcohol VI, mp 57.8–58.3°. The infrared spectrum showed an axial OH group and no carbonyl absorption. The other components were washed off the column with ether and then alcohol VII was separated by preparative vpc on a 2M Carbowax 4000 column, 25% on Chromosorb W. After recrystallization, it had mp 90.8–91.2°. The infrared spectrum showed an equatorial OH absorption; there was no carbonyl absorption. The two alcohols were assigned the structures VI and VII on the basis of the discussion already given. A mixture melting point of the two alcohols was 40–45°.



VI VII

A 1.5-g quantity of *trans,trans*-2-6-dimethyl-*trans*-4-*t*-butylcyclohexanol (alcohol VII) was treated with 3 g of tosyl chloride in 10 ml of dry pyridine. The tosylate was worked up the following day by the usual procedure.[30] The product (2.3 g) had mp 120.0–121.0°. *Anal.* Calcd for $C_{19}H_{30}SO_3$: C, 67.39; H, 8.93. Found: C, 67.44; H, 9.09.

***cis,cis*-2,6-Dimethyl-*cis*-4-*t*-butylcyclohexyl Tosylate.** Alcohol VI (1.5 g) was treated as described above and allowed to stand at room temperature for 4 days. The product (2.1 g) was not pure, mp 27–52°. Acetolysis in the presence of sodium acetate gave an experimental infinity equivalent to 86.2% of the theoretical value.

(31) E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, 3839 (1953).
(32) G. H. Stillson, D. W. Sawer, and C. K. Hunt, *J. Am. Chem. Soc.*, 67, 303 (1945).
(33) N. L. Drake, *Org. Syn.*, 21, 15 (1941).