gether and the substance filtered after cooling. It weighed 5.5 g., and still gave reactions for double bonds. It melted at 222°.

Anal. Calcd. for $C_{11}H_{14}O_3N_2$: N, 12.6. Found: N, 12.5.

N-Benzyl-*dl*-asparagine (VII).—Five grams of VI was heated under reflux in 50 ml. of xylene for one hour. The resulting material did no longer show reactions for double bonds. It melted at 216° on recrystallization from water. The over-all yield from V was about 70%.

Anal. Calcd. for $C_{11}H_{14}O_3N_2$: C, 59.5; H, 6.3; N, 12.6. Found: C, 59.6; H, 6.4; N, 12.0.

dl-**Asparagine**.—Four grams of VII was dissolved in a mixture of 50 ml. of glacial acetic acid and 20 ml. of water and 0.3 g. of $PdCl_2$ on carbon catalyst (30%) added. The reduction was carried out similarly to that of N-benzyl-*dl*-aspartic acid (see above). After about three hours the reduction was complete and on filtration and evaporation of the solvent the practically theoretical amount of *dl*-asparagine was recovered.

Anal. Calcd. for $C_4H_8O_3N_2 + H_2O$: N, 18.7. Found: N, 18.4.

JERUSALEM, ISRAEL

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

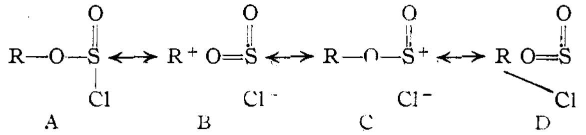
Studies in Stereochemistry. XVI. Ionic Intermediates in the Decomposition of Certain Alkyl Chlorosulfites

BY DONALD J. CRAM

RECEIVED MAY 24, 1952

The reaction of thionyl chloride with the stereoisomers of 3-phenyl-2-butanol, 2-phenyl-3-pentanol and 3-phenyl-2-pentanol has been studied. Decomposition of the initially formed chlorosulfite derivatives of these secondary alcohols in thionyl chloride, dioxane or formic acid produced phenylalkyl chloride products which were subsequently reduced to the corresponding alkylbenzenes. The structures and configurations of the individual components as well as the distributions of products in these alkylbenzene mixtures were determined through polarimetric and spectral techniques. From the stereochemical and structural relationships between the starting alcohols and the final hydrocarbon products, the following conclusions regarding the mechanism of the reaction are reached. (1) Bridged ion-pairs (phenonium chlorosulfite, phenonium chloride or both) occur as discrete intermediates in these reactions. (2) These ion-pairs collapse to give both rearranged and unrearranged products. (3) The reactions are highly stereospecific in the 3-phenyl-2-butyl and *threo*-2-phenyl-3-pentyl and *threo*-3-phenyl-2-pentyl systems, but in the *erythro*-2-phenyl-3-pentyl and *erythro*-3-phenyl-2-pentyl systems about one third of the product arises through a simple substitution reaction. The general mechanism of the S_Ni reaction is discussed in the light of these results.

The reactions of thionyl chloride,[1] phosgene,[2] phosphorus pentachloride in liquid SO_2[3] or dry hydrogen bromide (at −80°)[4] with certain secondary alcohols to give halides whose configurations are the same as those of the starting materials have been classified as examples of the S_Ni reaction.[5] Hughes, Ingold and co-workers[6] suggested that the reactions involving thionyl chloride occurred by the internal decomposition of an intermediate chlorosulfite, and although not stated explicitly, these authors imply that only one transition state intervenes between the alkyl chlorosulfite and the alkyl chloride product. This reaction has been studied kinetically by Lewis and Boozer[1c] who state that if the decomposition of the chlorosulfite intermediate does occur by the concerted mechanism, then structures A–D should all be considered as contributing to the transition state. In a study more similar to that at hand, Lucas and Gould[6] demonstrated that optically active *erythro*-3-chloro-2-butanol reacts with thionyl chloride to give a 16% yield of *meso*-2,3-dichlorobutane, whereas optically active *threo*-3-chloro-2-butanol with the same reagent produces a 20% yield of racemic *d,l*-2,3-dichlorobutane. The authors interpreted these steric results in terms of ethylene chloronium ion intermediates.



$$\underset{\text{A}}{R{-}O{-}\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle Cl}{|}}{S}}} \longleftrightarrow \underset{\text{B}}{R^+\ O{=}\overset{\overset{\displaystyle O}{\|}}{S}\ \ Cl^-} \longleftrightarrow \underset{\text{C}}{R{-}O{-}\overset{\overset{\displaystyle O}{\|}}{S}{}^+\ \ Cl^-} \longleftrightarrow \underset{\text{D}}{R\ O{=}\overset{\overset{\displaystyle O}{\|}}{S}\ \ Cl}$$

The present paper reports the results of a study of the mechanism of the decomposition of the chlorosulfites of the 3-phenyl-2-butyl, 2-phenyl-3-pentyl and 3-phenyl-2-pentyl systems. The symmetry properties associated with the first of these systems and the structural relationships between the two latter systems have already proved of value in studies of the mechanisms of the solvolytic Wagner–Meerwein rearrangement reaction,[7] the E_1 reaction,[8] and the reaction of the *p*-toluenesulfonate esters with lithium aluminum hydride.[9] A similar approach has been used in the current study in which the stereochemical relationships between the products and reactants are used to define the mechanistic requirements for the reaction.

Methods

The reactions were carried out utilizing the optically pure diastereomers of 3-phenyl-2-butanol[7a,c] (I), 2-phenyl-3-pentanol[7b,8b] (III) and 3-phenyl-2-pentanol[7b,8b] (IV) and thionyl chloride as starting materials, and excess thionyl chloride, dioxane or formic acid (the chlorosulfite was preformed) as solvents. The phenylalkyl chloride products

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(1) (a) P. A. Levene and L. A. Mikeska, *J. Biol. Chem.*, **75**, 587 (1927); (b) J. Kenyon, A. G. Lipscomb and H. Phillips, *J. Chem. Soc.*, 415 (1930); (c) J. Kenyon, H. Phillips and F. Taylor, *ibid.*, 382 (1932); (d) E. S. Lewis and C. E. Boozer, THIS JOURNAL, **74**, 308 (1952).

(2) A. H. J. Housa and H. Phillips, *J. Chem. Soc.*, **108**, 1232 (1932).

(3) E. D. Hughes, C. K. Ingold and I. C. Whitfield, *Nature*, **147**, 206 (1941). See also reference 1a.

(4) P. A. Levene and A. Rothen, *J. Biol. Chem.*, **127**, 237 (1939).

(5) This term was introduced by W. A. Cowdrey, E. D. Hughes, C. K. Ingold, S. Masterman and A. D. Scott [*J. Chem. Soc.*, 1267 (1937)] to designate those nucleophilic displacement reactions which occur with retention of configuration. This designation is limited to those reactions that do not appear to involve the participation of some neighboring group [see S. Winstein and R. E. Buckles, THIS JOURNAL, **64**, 2780 (1942)].

(6) H. J. Lucas and C. W. Gould, Jr., *ibid.*, **63**, 2541 (1941).

(7) (a) D. J. Cram, *ibid.*, **71**, 3863 (1949); (b) **71**, 3875 (1949); (c) **74**, 2129 (1952).

(8) (a) D. J. Cram, *ibid.*, **74**, 2137 (1952); (b) **74**, 2159 (1952).

(9) (a) D. J. Cram, *ibid.*, **74**, 2149 (1952); (b) **74**, 2152 (1952).

TABLE I

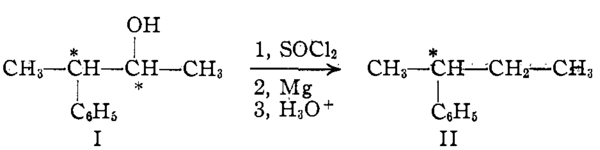
RESULTS OF THE REACTION OF THIONYL CHLORIDE WITH STEREOISOMERS OF 3-PHENYL-2-BUTANOL, 2-PHENYL-3-PENTANOL AND 3-PHENYL-2-PENTANOL

Run no.	Starting material[a]	Solvent	Temp., °C.	Time, hr.	Proc.[b]	Yield, % chl.	$n^{25}\mathrm{D}$ chl.	$\alpha^{23}\mathrm{D}$ (l 1 dm.)	Reduct. prod. (2-phenylbutane) $n^{25}\mathrm{D}$[c]	Reduct. prod. (2-phenylbutane) $\alpha^{23}\mathrm{D}$ (neat, l 1 dm.)	Reduct. prod. (2-phenylbutane) % racem.[d]
1	D-(−)-*threo*-I	$SOCl_2$	25	2	A	95	1.5184	−0.57°	1.4879	− 0.80°	97
2	L-(+)-*threo*-I	$SOCl_2$	0	3	B	95	1.5182	+0.62	1.4878	+ .83	97
3	D-(−)-*threo*-I	Diox.	100	2	C	50[e]	....	....	1.4878	− 1.20	95
4	D-(−)-*threo*-I	HCOOH	25	0.5	D	7	....	....	1.4880	− 0.06	100
4a	D-(−)-*threo*-I	HCOOH	25	4	D						
5	D-(−)-*erythro*-I	$SOCl_2$	25	2	A	90	1.5150	+8.57	1.4878	+24.0	1
6	D-(−)-*erythro*-I	Diox.	100	2	C	53[e]	....	....	1.4877	+22.8	6

Run no.	Starting material[a]	Solvent	Temp., °C.	Time, hr.	Proc.[b]	Yield, % chl.	$n^{25}\mathrm{D}$ chl.	$\alpha^{23}\mathrm{D}$ (l 1 dm.)	Mixt. 2- and 3-phenylpentane $n^{25}\mathrm{D}$[f]	Mixt. 2- and 3-phenylpentane $\alpha^{23}\mathrm{D}$ (neat, l 1 dm.)	% 2-Phenylpentane By $\alpha\mathrm{D}$[g]	% 2-Phenylpentane By infrared at λ (μ)[h] 10.15	% 2-Phenylpentane By infrared at λ (μ)[h] 11.33	% 2-Phenylpentane By infrared at λ (μ)[h] 12.02
7	L-(+)-*threo*-III	$SOCl_2$	25	2	A	93	1.5148	+6.02°	1.4861	+ 8.12°	55	53	53	53
8	L-(+)-*threo*-III	$SOCl_2$	0	3	B	96	....	+6.18	1.4862	+ 8.03	54	53	53	53
9	L(−)-*threo*-IV	$SOCl_2$	25	2	A	88	1.5148	−6.98	1.4862	− 7.44	50	51	49	49
10	L-(−)-*threo*-IV	$SOCl_2$	0	3	B	95	....	−6.80	1.4862	− 7.40	49	50	50	49
11	D-(+)-*erythro*-III	$SOCl_2$	25	2	A	93	1.5126	−9.20	1.4860	−10.82	72	72	68	68
12	L-(−)-*erythro*-III	$SOCl_2$	0	3	B	95	....	+6.32	1.4862	+10.56	70	71	72	71
13	L-(−)-*erythro*-IV	$SOCl_2$	25	2	A	93	1.5113	−4.04	1.4860	+ 5.18	35	36	36	36
13a	Alkyl chloride from run 13	HCOOH	25	4	D	90	....	−4.16	1.4860	+ 5.13	34	34	35	35
14	L-(−)-*erythro*-IV	$SOCl_2$	0	3	B	96	....	−3.42	1.4861	+ 5.61	37	39	35	38
15	DL-*threo*-3-PCl + -2-PCl[i]	......	...	..	E	...	1.5140	....	1.4861	....	..	64	64	64
16	DL-*threo*-3-PCl + -2-PCl[i]	$SOCl_2$	25	12	E	95	1.5140	....	1.4862	....	..	63	63	65
17	DL-*threo*-3-PCl + -2-PCl[i]	......	...	..	E	...	1.5151	....	1.4862	....	..	39	40	39
18	DL-*threo*-3-PCl + -2-PCl[i]	$SOCl_2$	25	12	E	96	1.5151	....	1.4862	....	..	40	40	39

[a] The rotations of the starting alcohols are as follows (in each case, l 1 dm., neat): D-(−)-*threo*-I, $[\alpha]^{23}\mathrm{D}$ −31.8°; L-(+)-*threo*-I, $[\alpha]^{23}\mathrm{D}$ +32.1°; D-(−)-*erythro*-I, $[\alpha]^{23}\mathrm{D}$ −0.51° (acetate, $\alpha^{24}\mathrm{D}$ −32.8°); L-(+)-*threo*-III, $\alpha^{25}\mathrm{D}$ +12.1; L-(−)-*threo*-IV, $\alpha^{25}\mathrm{D}$ −16.8°; D-(+)-*erythro*-III, $\alpha^{25}\mathrm{D}$ −7.34°; L-(−)-*erythro*-III, $\alpha^{25}\mathrm{D}$ −7.25°; L-(−)-*erythro*-IV, $\alpha^{25}\mathrm{D}$ −20.2°. [b] See Experimental part. [c] Pure 2-phenylbutane, $n^{25}\mathrm{D}$ 1.4878 (ref. 8a). [d] Based on $\alpha^{23}\mathrm{D}$ 24.3° (neat, l 1 dm.) for optically pure material (ref. 8a). [e] A large amount of higher boiling material (probably dialkyl sulfite) was formed in this reaction and therefore the yield was diminished. [f] Pure 2-phenylpentane, $n^{25}\mathrm{D}$ 1.4858; pure 3-phenylpentane, $n^{25}\mathrm{D}$ 1.4861 (ref. 9b). [g] Optically pure 2-phenylpentane, $\alpha^{23}\mathrm{D}$ 15.0° (neat, l 1 dm.) (ref. 9b). [h] A Beckman infrared spectrophotometer (Model IR2T) with NaCl prism and NaCl cells was used. Homogeneous films of 0.03-mm. thickness were employed. Slit widths at the three wave lengths were 0.490, 0.639 and 0.755 mm., respectively. The complete spectra of these hydrocarbons have been previously reported (ref. 9b). [i] 2-P = 2-phenyl-3-pentyl and 3-P = 3-phenyl-2-pentyl.

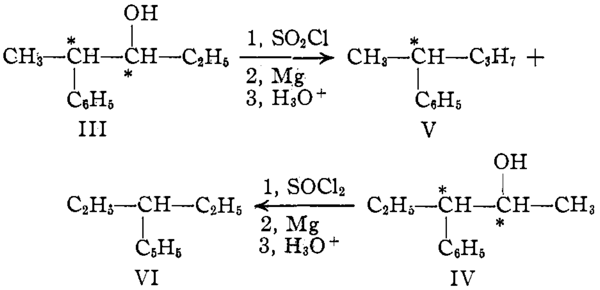
were converted through their Grignard reagents to the corresponding alkylbenzenes, which were analyzed. When the starting materials possessed structure I, the degree of racemization of the 2-phenylbutane (II) ultimately obtained[10] was measured utilizing the rotation of optically pure 2-phenylbutane[8a,9a] (II) as a standard. When the starting



$$CH_3-\overset{*}{C}H(C_6H_5)-\overset{*}{C}H(OH)-CH_3 \xrightarrow[2,\ Mg;\ 3,\ H_3O^+]{1,\ SOCl_2} CH_3-\overset{*}{C}H(C_6H_5)-CH_2-CH_3$$

$\alpha^{23}\mathrm{D}$ 24.3°
(neat, l 1 dm.)

materials possessed structures III and IV, the mixtures of 2-phenylpentane (V) and 3-phenylpentane (VI) produced were analyzed polarimetrically utilizing the plot made previously of the rotation *versus* composition of known mixtures of VI and optically pure V.[9b] The infrared spectral analytical scheme developed in paper VIII of this series[9b] for mixtures of V and VI was also applied,[11] and Table I records the results.



$$CH_3-\overset{*}{C}H(C_6H_5)-\overset{*}{C}H(OH)-C_2H_5 \xrightarrow[2,\ Mg;\ 3,\ H_3O^+]{1,\ SO_2Cl} CH_3-\overset{*}{C}H(C_6H_5)-C_3H_7 +$$

$$C_2H_5-CH(C_6H_5)-C_2H_5 \xleftarrow[2,\ Mg;\ 3,\ H_3O^+]{1,\ SOCl_2} C_2H_5-\overset{*}{C}H(C_6H_5)-\overset{*}{C}H(OH)-CH_3$$

The rearrangements noted in the various runs could theoretically have occurred during the decomposition of the chlorosulfite, or after the chloride was formed, or during the preparation of the Grignard reagent. The last possibility is highly improbable since no molecular rearrangements have ever been noted during the formation of ordinary Gri-

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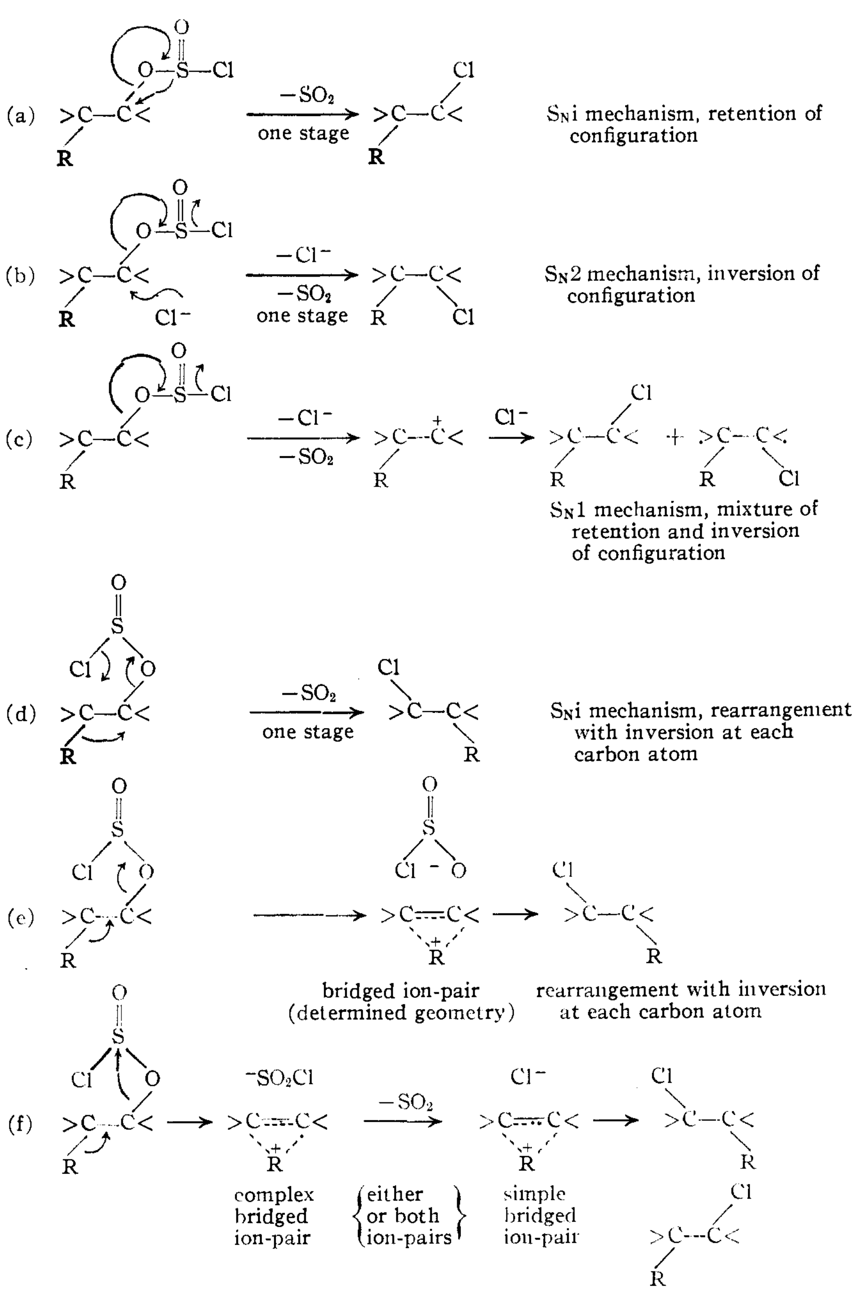
(10) The small amount of olefin produced in both the decomposition of the chlorosulfite as well as in the Grignard reduction reaction was removed through the use of the 2,4-dinitrobenzenesulfenyl chloride reagent (see ref. 8). The small amount of coupled product from the Grignard reaction was removed by distillation.

(11) In the present study three wave lengths were used, and for each wave length a plot of optical density *vs.* composition of known mixtures was used as a standard. The deviations from Beer's law were small (see ref. 9b).

gnard reagents of this type.[12] The possibility that the chlorides once formed underwent rearrangement was disposed of in runs 15 through 18 in Table I. A relatively large amount of racemic *threo*-3-phenyl-2-pentanol was converted to a mixture of 3-phenyl-2-pentyl chloride and 2-phenyl-3-pentyl chloride (the ratio should be the same as that found in runs 7-10). This mixture was submitted to careful fractional distillation, and two fractions, one rich in 2-phenyl-3-pentyl chloride and the other rich in 3-phenyl-2-pentyl chloride, were reduced directly to hydrocarbon. A second portion of each fraction was first submitted to the conditions of the formation and decomposition of the chlorosulfites (see Experimental part), and was then recovered and converted to hydrocarbon. The analyses of each fraction before and after such treatment were identical (compare runs 15 and 16, and runs 17 and 18). Therefore, the molecular rearrangements observed in the reaction sequence of runs 1, 2, 5 and 7-14 must have occurred during the decompositions of the chlorosulfites. Since the reaction conditions of runs 3 and 6 were much milder from the point of view of the ionizing power of the solvent (dioxane), it is highly probable that in these runs also the observed rearrangements occurred only during the decomposition of the chlorosulfites.

To demonstrate that the chloride once formed in run 4 (formic acid) did not further react, a portion of the alkyl chloride mixture (non-equilibrated) formed in run 13 was submitted to the reaction conditions of run 4 (run 13a). The material was unaltered by this treatment. To demonstrate that the configuration of the formate once formed in run 4 was virtually preserved, half of the reaction mixture was allowed to stand in formic acid seven times (run 4a) as long as the other half (run 4). The alcohol ultimately obtained in run 4a was only 4% more racemized than the alcohol from run 4.



Since the configurations of the starting alcohols and hydrocarbon products have all been related to one another (and to D-glyceraldehyde) through a number of different reaction sequences,[8,9,13] the configurational and structural transformations that occurred during the decomposition of the starting chlorosulfites can be inferred.

Discussion

Bridged Ion-pairs as Intermediates in the Chlorosulfite Decomposition Reaction.—A number of possible mechanisms for the decomposition of chlorosulfite intermediates in these reactions presented themselves at the outset of this investigation, these paths being based on analogies to observations or speculations made previously. The possibilities are outlined in the reaction sequences a through e.[14] Reaction sequence f could be either two or three stage; the products would be the same. The results at hand allow a partial assignment of mechanism to the decomposition of the chlorosulfites of I, III and IV.

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(12) For instance, neophyl chloride readily forms a Grignard reagent which carbonates in the ordinary way to give β,β-dimethylhydrocinnamic acid [F. C. Whitmore, C. A. Weisgerber and A. C. Shabica, THIS JOURNAL, **65**, 1469 (1943)]. Likewise, P. A. Levene and R. E. Marker [*J. Biol. Chem.*, **100**, 685 (1933)] prepared 3-phenylbutyric acid from 3-phenylpropyl bromide.

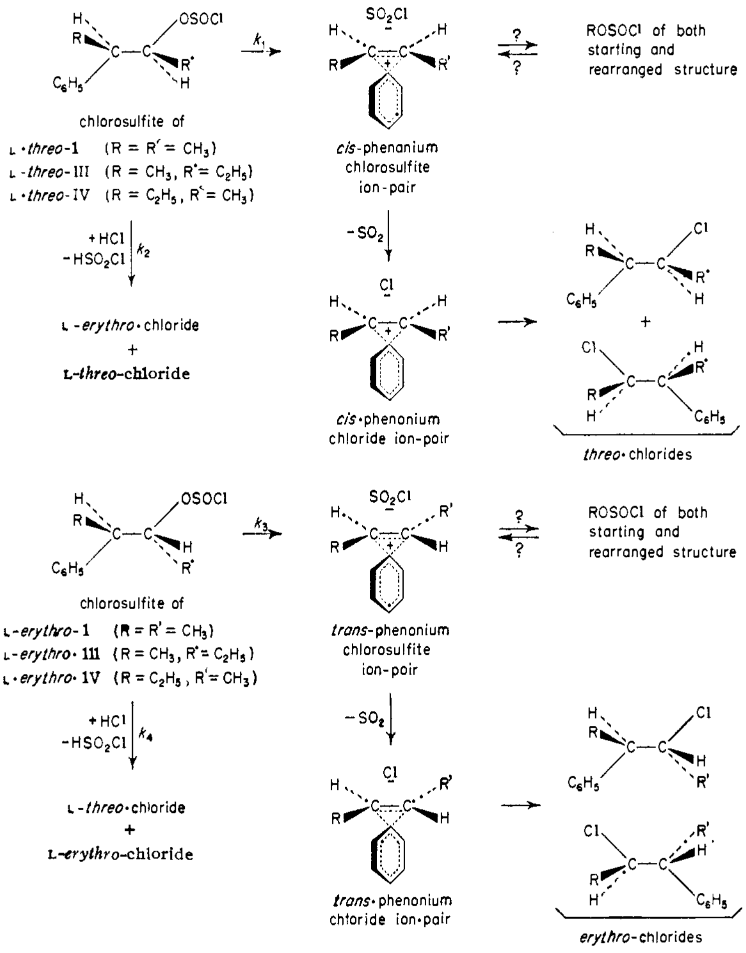
(13) D. J. Cram, THIS JOURNAL, **71**, 3883 (1949).

(14) Formulations a, b and c represent the classical SNi, SN2 and SN1 mechanisms, respectively, of Hughes and Ingold [see series of papers starting with *J. Chem. Soc.*, 1177 (1937)]. Reaction sequence d, termed the SNi mechanism, is essentially that suggested by E. S. Wallis and P. I. Bowman (*J. Org. Chem.*, **1**, 383 (1936)) to explain the production of optically active 1-phenyl-2-methyl-2-chlorobutane by the action of thionyl chloride on 2-methyl-2-phenyl-1-butanol. S. Winstein, *et al.*, [THIS JOURNAL, **74**, 1113 (1952)] also suggested that the SNi mechanism is potentially operative in systems of this type; J. D. Roberts, W. G. Young and S. Winstein [*ibid.*, **64**, 2157 (1942)] presented evidence that the SNi mechanism is operative in allylic systems. Mechanism e is the two stage equivalent of d, whereas f is analogous to the mechanism demonstrated for the solvolysis of 3-phenyl-2-butyl tosylate (ref. 7).

In those runs in which the starting materials possessed the *threo*-configuration and which were carried out in excess thionyl chloride as solvent (runs 1, 2 and 7–10), reaction sequence f or its steric equivalent would appear to account for at least 97% of the alkyl chloride produced. The other 3% must have arisen by mechanism a, b or c. The results do not allow a choice to be made between these latter possibilities. In reaction sequence f, either or both of the ion-pairs shown could exist as discrete intermediates. If only the *complex* bridged ion-pair was the intermediate, then it must have had a long enough life and an indeterminate enough geometry to allow the two oxygens and the chlorine (the three groups upon which a negative charge can be distributed) to become shuffled before collapse occurs. Otherwise the product predicted by reaction sequences d and e would have been isolated. On the other hand, these results do not differentiate between mechanism f and its steric equivalent in which the ion-pairs become completely dissociated.

Practically all of the product in run 5 in which D-(−)-*erythro*-3-phenyl-2-butanol was the starting material ($SOCl_2$ as solvent) would also appear to have arisen by a reaction sequence such as f. On the other hand, with starting materials of the *erythro* configuration in the two pentanol systems (runs 11–14, $SOCl_2$ solvent), the results indicate that such a reaction path accounts for only about two-thirds of the products whereas the other third must have come into being by mechanisms a, b or c (or their steric equivalents). This marked difference in the reaction course of the *erythro* and *threo* starting materials correlates with the differences in rates with which the *erythro*- and *threo*-1,2-diphenyl-1-propyl brosylates underwent the S_N2 reaction with halide ions.[15] In this benzyl system, that diastereomer which in solvolysis gave *trans* phenonium ions was found to undergo the S_N2 reaction faster than that diastereomer which under solvolytic conditions gave *cis* phenonium ions.[15] A similar relationship exists in runs 11–14 if one assumes that the part of the starting material that did not go to *trans* phenonium ions became involved in an S_N2-like substitution reaction with the HCl produced in the formation of the chlorosulfite. If this interpretation is correct, greater differences in reactivity between diastereomers would appear to be associated with the simple substitution than with the solvolytic–rearrangement reaction. In other words, in Chart I, $k_4/k_3 > k_2/k_1$.

The stereochemical relationships between reactants and products indicate that mechanisms d and e do not operate, but these results do not allow a decision to be made as to whether one or two bridged ion-pairs exist in sequence f. A further possibility exists in which sequence f could be further complicated by the collapse of the first (complex) ion-pair to either starting or rearranged chlorosulfite. The fact that similarly constituted phenonium tosylate ion-pairs can collapse in this manner has been demonstrated to occur in these same systems.[7c,8b] On the other hand, the instability of the chlorosulfite ion as compared to the tosylate ion would tend to militate against such a possibility. An attempt was made to settle the question of whether rearranged chlorosulfite was formed under the conditions of run 8 by determining if rearranged olefin was produced as a product of the reaction. The total amount of olefin formed was so small that the attempt failed.



The stereochemical relationships between the starting chlorosulfites and the alkyl halide products as well as the preferred mechanism are set forth in Chart I (the results of Wallis and Bowman[14] can be similarly interpreted). This mechanism is similar to that set forth previously for the solvolyses of the tosylates of these systems in acetic acid. The similarity can be made even more striking if one includes in the anion of the first ion-pair a molecule of solvent as is done in Chart II, which illustrates the mechanism as applied to the tosylate of L-*threo*-I. That the anion of this

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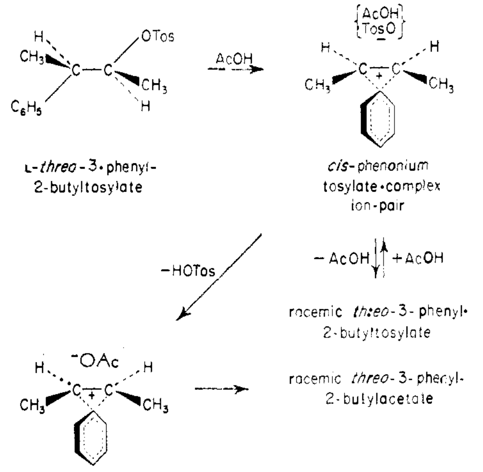
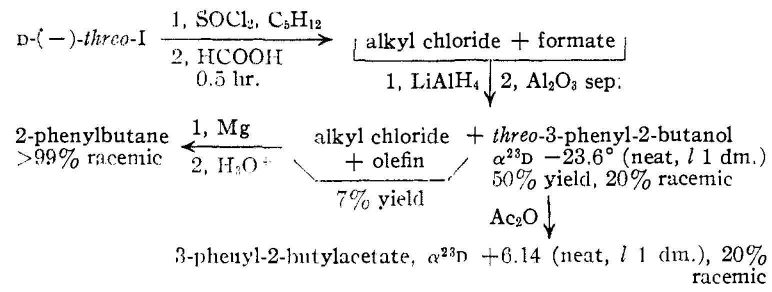
(15) D. J. Cram and F. Abd Elhafez, THIS JOURNAL, **74**, 5851 (1952).

and of analogously constituted ion-pairs are solvated is suggested by a number of observations made in earlier papers of this series. Thus, the isomerization of L-*threo*-3-phenyl-2-butyl tosylate to racemic *threo*-tosylate in acetonitrile was found to be catalyzed by *p*-toluenesulfonic acid,[7c] and similar isomerization reactions seemed to be promoted by lithium aluminum hydride in ether.[9a,9b] Furthermore, the substitution of chloride by iodide with retention of configuration (no rearrangement) in the *threo*-1,2-diphenyl-1-propyl system in benzene was found to occur only in the presence of a lithium amine salt.[15] Each of these cases suggests that the anion of the ion-pair is in reality an aggregate of molecules among which a negative charge is distributed. If a molecule of acetic acid is added to a tosylate anion, an aggregate results which is not dissimilar to that represented by the chlorosulfite anion, and the production of acetate could occur by an internal decomposition of a tosylate–acetic acid aggregate in much the same fashion as a chlorosulfite anion decomposes internally.



The same kind of solvent effects appear to operate in the decomposition of the chlorosulfites of the systems at hand as operated in the isomerization and solvolytic reactions of the tosylates of the same alcohols studied previously.[7c] Thus the more ionizing the solvent in each case, the more readily the reaction occurs, and the more highly specific appears to be the steric result. For instance, the solvolytic and (or) isomerization reactions of the tosylates became more sluggish and less stereospecific in passing from formic acid to acetic acid to acetonitrile to chloroform. A similar trend appears in the decomposition of the chlorosulfites in passing from thionyl chloride to dioxane. Lewis and Boozer[1b] noted a similar trend in the decomposition of 2-butyl and 2-octyl chlorosulfites both with regard to rate and steric result.

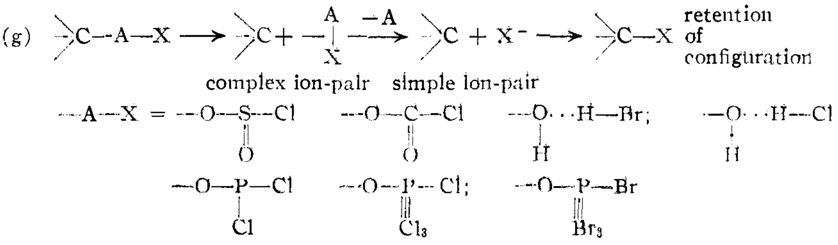
In run 4 the chlorosulfite of D-(−)-*threo*-I was shaken with a large volume of dry formic acid, and the mixture of formate and chloride was converted to a mixture of alcohol and chloride. These components were separated and analyzed, and the results are reported below.



If the alcohol and acetate produced are both assumed to be exclusively of the *threo*-configuration, then from the rotations for optically pure alcohol and acetate[7c] these materials appear to be 20% and 20% racemized, respectively. Since the magnitudes of the rotations of the optically pure diastereomers of I and their acetates differ widely,[7c] the fact that the above percentages agree is evidence that the formate originally produced possessed only the *threo* configuration. Thus the ratio of racemic alcohol to chloride (racemic) formed is at least 1.4/1 (traces of olefin mixed with the chloride would increase the value of this ratio), and the ratio of active to racemic alcohol is about 5/1.

The optically active formate initially formed in the above experiment could either have arisen by the simple cleavage of the O–S bond or by a complex S$_{\mathrm{N}}$i reaction in which a formic acid molecule solvating the chlorosulfite group formed the new bond when the C–O bond of the chlorosulfite broke. With respect to the production of racemic alcohol and racemic chloride, the most attractive explanation is analogous to that used to explain the solvolytic and isomerization reactions in formic acid of the tosylate of the same starting alcohol. One of the intermediate bridged ion-pairs in reaction sequence f (*e.g.*, the phenonium chloride ion-pair) could have exchanged its anion for formate anion and then collapsed, this process competing with the simple collapse of the phenonium chloride itself. It is interesting that the ratio of 1.4/1 which crudely measures the relative rates of these two processes (collapse and exchange) is not very different from the ratio of 3/1 found for the relative rates of collapse and exchange of phenonium tosylate ion-pairs in formic acid.[7c]

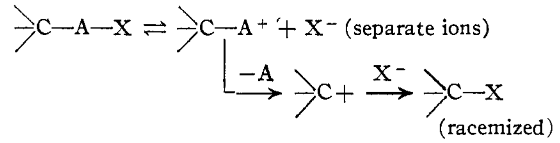
The Possibility of Open Ion-pairs as Intermediates in the S$_{\mathrm{N}}$i Reaction.—The above results suggest that at least in some solvents under some



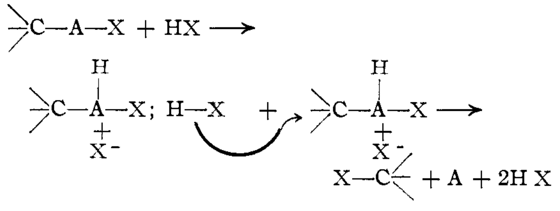
reaction conditions, the classical S$_{\mathrm{N}}$i reaction goes by a multistage mechanism in which open (nonbridged) ion-pairs intervene as discrete intermediates between the starting material and product. The reaction sequence g in which either one or two ion-pairs are involved is not incompatible with the steric requirements for, or with the circumstances under which the S_{Ni} reaction has been observed to occur. In this sequence the ion-pairs are assumed to *effectively* maintain asymmetry at the carbon atom undergoing substitution.

With regard to the circumstances under which the S_{Ni} reaction has been observed to occur, the following generalizations have been made. (1) The S_{Ni} reaction has the best chance of predominating over competing reactions when electron releasing groups (*e.g.*, phenyl) are attached to the carbon undergoing substitution.[1,3] Since sequence g contains an ionizing stage, such a reaction would be promoted by the presence of a group which would permit distribution of the positive charge created. (2) In liquid sulfur dioxide, the presence of added chloride ion appears to suppress the competing S_N1 processes when phenyl alkyl carbinols are treated with the usual halogen-substituting reagents, and an S_{Ni} reaction results.[3] Hughes and Ingold[3] have suggested that the competing S_N1 reaction occurs by a process such as h. The alternative ionizing stage of process g would be promoted both by the strongly ionizing character of the solvent as well as by the suppression of the concentration of the ionized form shown in h. (3) In the decomposition of chlorosulfites of ordinary dialkylcarbinols, the S_{Ni} reaction predominates decisively in dioxane but is not detectable in isoöctane (about half of the product is inverted and half is racemized).[1d] The poor ionizing ability of isoöctane would be far less conducive to a process such as g than would dioxane; furthermore, dioxane would form an oxonium chloride salt with the hydrogen chloride liberated as the reaction proceeded, and the chloride ion thus liberated would tend to suppress process h. On the other hand, the chlorosulfite itself in isoöctane might be a proton acceptor, and a process such as i becomes conceivable. The observation has been made that when systems such as $R\text{-}\underset{\text{OH}}{\underset{|}{\text{CH}}}\text{-}C_6H_5$ are added to thionyl chloride, the S_{Ni} reaction has its best chance of predominating when the concentration of the hydrogen chloride liberated is kept to a minimum.[16] (4) In the presence of pyridine, the reactions of secondary alcohols with the ordinary halogen-substituting reagents occur with predominant inversion of configuration, and no S_{Ni} process is detectable.[1b,17] The explanation offered[3,17] for this phenomenon is summarized in slightly modified form in j. The quite different roles played by dioxane in encouraging the S_{Ni} reaction[1d] and pyridine in promoting the competing S_N1 and S_N2 reactions probably lies in their widely differing basic strengths.

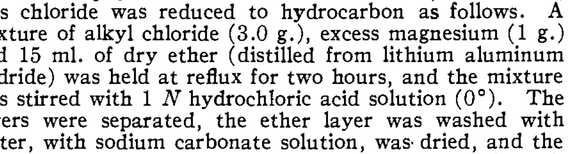
(h)



(i)



(j)



The above hypothetical mechanism for the S_{Ni} reaction coupled with the suggestion that the S_N1 reaction occurs by a mechanism involving ion-pair intermediates[7c,18] presents a unified picture of multistage substitution reactions. Thus the S_{Ni} reaction differs from the S_N1 reaction only in the sense that the departing group is complex, and that the anion of the first ion-pair can decompose internally under some conditions faster than an anion or potential anion can react at the rear of the carbon undergoing substitution.

Experimental Part

Reaction of D-(−)-*threo*-3-Phenyl-2-butanol with Excess Thionyl Chloride (Procedure A).—Optically pure alcohol (3.2 g.) was added dropwise (10 minutes) to 25 ml. of pure thionyl chloride at room temperature. After the addition was complete the mixture was allowed to stand for two hours at room temperature, and then was held at reflux for one hour. About two-thirds of the excess thionyl chloride was distilled (atmospheric pressure), and the residue was stirred with ice. The resulting chloride was extracted with *pure* pentane, the organic layer was washed with water, with sodium carbonate solution and again with water. The pentane solution was dried, the solvent was evaporated through a short column and the alkyl chloride product was flash distilled at 20 mm. pressure; wt. 3.2 g.

After the physical constants were obtained (see Table I), this chloride was reduced to hydrocarbon as follows. A mixture of alkyl chloride (3.0 g.), excess magnesium (1 g.) and 15 ml. of dry ether (distilled from lithium aluminum hydride) was held at reflux for two hours, and the mixture was stirred with 1 *N* hydrochloric acid solution (0°). The layers were separated, the ether layer was washed with water, with sodium carbonate solution, was dried, and the solvent was evaporated through a short column. The residue was mixed with 2 g. of 2,4-dinitrobenzenesulfenyl chloride[10] and 10 ml. of glacial acetic acid, and the mixture was warmed to 100° for one hour. The mixture was then shaken with pure pentane and water, the pentane layer was separated from the water layer and from the gum that appeared, and was washed with water and with a sodium carbonate solution. The solution was then dried, the solvent was evaporated through a short column, and the residue was twice flash distilled at 20 mm. of pressure to give 1.6 g. of pure 2-phenylbutane. This material was submitted directly to polarimetric analysis.

Procedure B.—This procedure was the same as A except in the following respects. The alcohol was dripped into thionyl chloride held at 0° (10 minutes). The resulting solution was allowed to stand at 0° for one hour, at 25° for three hours and was stirred with ice. The oil that separated was treated as in Procedure A.

Preparation and Decomposition of the Chlorosulfite of D-(−)-*threo*-3-Phenyl-2-butanol in Dioxane (Procedure C).

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[16] F. A. Abd Elhafez, THIS JOURNAL, **75**, 339 (1953).

[17] M. Balfe and J. Kenyon, *J. Chem. Soc.*, 463 (1940).

[18] S. Winstein, R. Grunwald and H. W. Jones, THIS JOURNAL, **73**, 2706 (1951).

—The alcohol (3.0 g.) was added dropwise to a stirred solution of 4.6 g. of thionyl chloride dissolved in 50 ml. of pure dioxane (room temperature). The resulting solution was allowed to stand at room temperature for 10 hours, was heated to 100° for two hours and cooled. The solution was shaken with a mixture of pure pentane and water, and pentane layer was washed with water (twice), with a sodium carbonate solution, and was dried. The solvent was evaporated through a short column, and the product was flash distilled at 20 mm. pressure. About one-third of the material was high-boiling and was discarded. Since the lower-boiling material was acidic, it was taken up in pure pentane, and the solution was washed with water and dilute sodium carbonate solution. The organic layer was dried, the solvent was evaporated through a short column, and the residue was flash distilled at 20 mm. of pressure. After the physical constants were recorded (Table I) the chloride was reduced by the same method outlined in Procedure A.

Control for Runs Utilizing Procedures A and B.—Racemic *threo*-3-phenyl-2-pentanol (24 g.) was converted to its chloride by Procedure B and was submitted to fractional distillation at 75 mm. pressure through a center-rod column (fifty theoretical plates). The following four fractions were taken: first, wt. 5.2 g., b.p. 149.0–149.5°, n^{25}D 1.5130; second, wt. 6.9 g., b.p. 149.5–150.0°, n^{25}D 1.5141; third, wt. 3.4 g., b.p. 150.0–152°, n^{25}D 1.5145; fourth, wt. 3.9 g., b.p. 152–154°, n^{25}D 1.5151. Fraction 1 was again submitted to fractional distillation in an attempt to isolate the trace of olefin that was probably present. No pure olefin could be isolated. Fractions 2 and 4 were each divided in half, the first halves being reduced and analyzed (runs 15 and 17) as in Procedure A, the other halves (runs 16 and 18) were each mixed with equivalent amounts of absolute ethanol and each resulting mixture was submitted to the whole of Procedure A. The analyses of the hydrocarbon products for runs 15 and 16 are virtually identical, and the same is true for runs 17 and 18.

Solvolysis of the Chlorosulfite of D-(−)-*threo*-3-Phenyl-2-butanol in Formic Acid (Procedure D).—To a mixture of 18.4 g. (0.155 equivalent) of thionyl chloride dissolved in 80 ml. of pentane was added dropwise with stirring 8 g. (0.0533 equivalent) of the above alcohol (α^{23}D −31.0°, neat, *l* 1 dm.). The resulting solution was allowed to stand at room temperature for three hours and was divided into two equal portions, 1 and 2. The pentane and thionyl chloride of portion 1 was evaporated at 20 mm. of pressure at room temperature, and finally at 1 mm. of pressure. The resulting oil was divided into two equal portions, 1a and 1b. One of these was mixed with ice, and the resulting alcohol was isolated (*via* pentane extraction and flash distillation), wt. 1.2 g., α^{23}D −30.6° (neat, *l* 1 dm.). The remainder of the starting material had apparently gone to a high boiling dialkyl sulfite which could not be distilled. An attempt was made to distil portion 1b under 20 mm. of pressure, but no product distilled under 180°. Both 3-phenyl-2-butyl chloride and 3-phenyl-2-butanol distil at about 130° at 20 mm. Apparently this oil was a mixture of alkyl chlorosulfite and dialkyl sulfite.

Portion 2 was shaken vigorously with 200 ml. of dry formic acid for half an hour. A mixture of sulfur dioxide, hydrogen chloride and pentane was evolved during this process. The resulting mixture was divided into two equal parts, 2a and 2b. Part 2a was shaken with water and pentane, the pentane layer was washed with water, with sodium carbonate solution, was dried and evaporated. The resulting oil was added dropwise to a slurry of 0.5 g. of lithium aluminum hydride and ether. The mixture produced was shaken with ice-cold 1 *N* hydrochloric acid solution, the organic layer was washed with water, dried and the solvent was evaporated. The resulting oil was placed on a column of alumina made up in pure pentane (30 cm./2 cm.), and the chloride was washed through the column with pure pentane, the alcohol with methanol. The pentane eluate was set aside. The solvent of the methanol eluate was evaporated through a short column, the residue was shaken with a mixture of pure pentane and water. The pentane solution was dried, and solvent was evaporated, and the residue was flash distilled to give 1.20 g. of 20% racemized D-(−)-*threo*-3-phenyl-2-butanol, α^{23}D −24.8° (neat, *l* 1 dm.). The acetate (20% racemized) was prepared in the usual way, α^{23}D +6.50[9] (neat, *l* 1 dm.). The rotation of optically pure L-(−)-3-phenyl-2-butylacetate is α^{23}D −8.08° (neat, *l* 1 dm.).

Part 2b was shaken for 3.5 hours longer, and was submitted to the same procedure as part 2a. Alcohol (1.16 g.) was recovered, α^{23}D −23.6° (neat, *l* 1 dm.) (24% racemized), which gave acetate, α^{23}D +6.26° (neat, *l* 1 dm.) (23% racemized).

The pentane eluates from the chromatographs used in the work-up of parts 2a and 2b were combined, and the pentane was evaporated through a short column. The residue was flash distilled to give 0.30 g. of 3-phenyl-2-butyl chloride. This material was reduced by the method outlined in Procedure A to give virtually racemic 2-phenylbutane (run 4).

Control for Run 4.—Half of the mixture of alkyl chlorides (1.6 g.) formed in run 13 was mixed with 0.54 g. of absolute ethanol. This material was subjected to Procedure D, the conditions applied to portion 2b being approximated. The alkyl halide recovered (1.45 g.) from the chromatograph was reduced as in Procedure A to give an alkylbenzene mixture (see run 13a) essentially the same as that obtained in run 13.

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