The Steric Course of the Reaction of Ethylene Oxide with Hydrogen Halides in the Gas Phase

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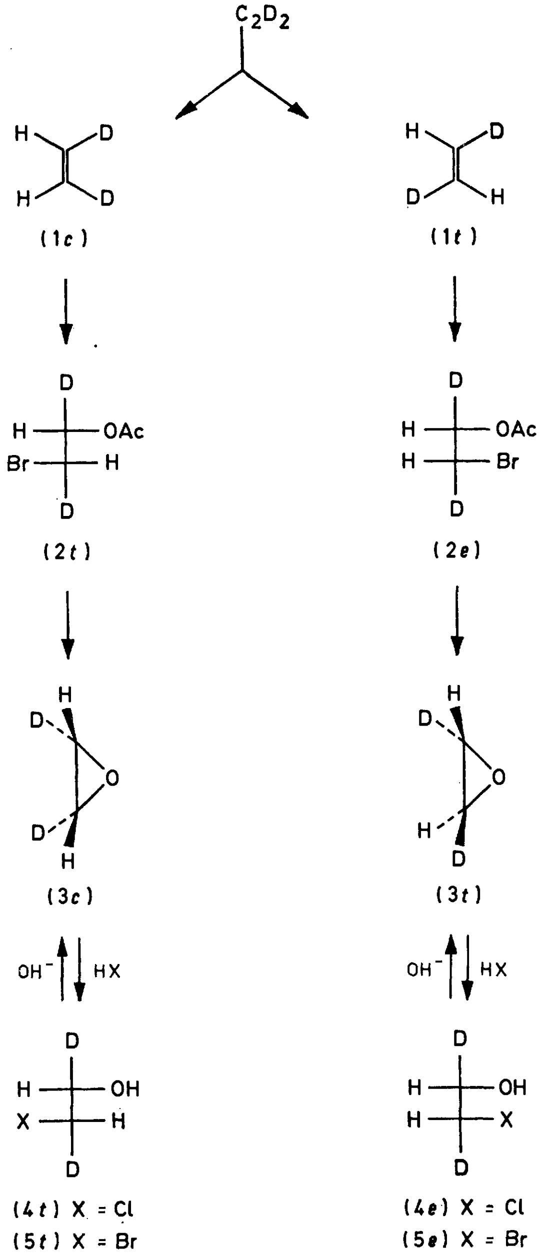
The steric course of the gas-phase reaction of *trans*-[$^2H_2$]ethylene oxide with HF, HCl, and HBr was investigated in order to test experimentally a mechanistic proposal based on *ab initio* calculations involving a concerted *syn*-opening mechanism. In contrast with this proposal the reactions with HCl and HBr take place entirely with *anti*-opening of the ring to give *erythro*-2-chloro- and 2-bromo[1,2-$^2H_2$]ethanol. The reaction of ethylene oxide with gaseous HF yields only 5% 2-fluoroethanol, 37% dioxan, oligomers and polymers being the main products. An improved method for the conversion of *cis*- and *trans*-[$^2H_2$]ethylene into the corresponding epoxides is described.

THE opening of epoxide rings under acidic conditions is usually assumed to take place exclusively in an *anti*-fashion,[1] unless substituents (such as alkenyl and aryl groups) capable of stabilizing a developing positive charge on carbon are present on the oxiran ring. Experimental evidence for this assumption is plentiful, but all of it involves reactions of substituted epoxides conducted in the liquid phase. A recent paper,[2] reporting on *ab initio* calculations for the formation of 2-fluoroethanol from oxiran and HF as isolated single molecules, suggested that a mechanism involving a hydrogen-bonded complex between the epoxide and HF, which evolves into the fluorohydrin in a concerted fashion without the intermediate formation of an ionic species, should be energetically much favoured over the usually assumed A_1, A_2, or borderline A_2 mechanisms of epoxide ring opening.[1] The proposed mechanism should occur with *syn*-opening of the ring. In view of the novelty of this suggestion and of the lack of any information on the steric course of the opening of the unsubstituted oxiran ring, we thought it worthwhile to try to subject the above proposal to a test. We therefore investigated the reaction of ethylene oxide with hydrogen halides in the gas phase although we were aware of the difficulty in reproducing experimentally ideal theoretical models.



SCHEME 1

RESULTS

In order to obtain the required stereochemical information the reactions had to be conducted on a pure diastereoisomer of [1,2-$^2H_2$]ethylene oxide. The method of Price and Spector [3] for the synthesis of these compounds (addition of bromine to the 1,2-dideuteriated ethylenes in water followed by cyclization of the bromohydrin) gives yields not higher than 10—15%, mostly because of the low recovery of 2-bromoethanol from the aqueous solution. We therefore modified this method by converting *cis*- and *trans*-[1,2-$^2H_2$]ethylene (1*c* and *t*) into the corresponding *threo*- and *erythro*-1-acetoxy-2-bromo[1,2-$^2H_2$]ethanes (2*t* and *e*) with acetyl hypobromite in CCl_4. Isolated yields of up to 80% were thus obtained when concentrations not higher than 0.1M in hypobromite were used; higher concentrations gave more side-products and lower yields. The difficulty in avoiding the presence of some free bromine in the reagent did not affect the purity of the product significantly, since the reaction of ethylene with Br_2 is much slower than that with AcOBr; thus, latter reagent reacted completely before significant amounts of 1,2-dibromoethane appeared in the product. The conversion of (2*t* and *c*) into the dideuteriated ethylene oxides (3*c* and *t*) was performed with aqueous Na-

OH, the isolated yields being as high as 70%. Previous experience had shown that the hydrolysis of the ester grouping is much faster than the replacement of the bromine by hydroxy.[4] Although no particular effort was made to optimize yields, the overall yield of *ca.* 55% in the conversion of the dideuteriated ethylenes into the corresponding ethylene oxides compares very favourably with that of the previous method.[3]

The isotopic purity of the epoxides was determined by mass spectrometry: the *trans*-isomer (3*t*) contained *ca.* 95% of dideuteriated, 5% of monodeuteriated, and <0.5% of non-deuteriated species. The configurational purity was determined by microwave spectrometry, which confirmed the presence of 5% of monodeuterioethylene oxide and of a trace of non-deuteriated ethylene oxide, and showed that the dideuteriated compound was 98.5% *trans* and 1.5% *cis*. We therefore used this *trans*-isomer, since similar checks on (3*c*) had shown that its isotopic enrichment was lower, owing to the much less satisfactory method of preparation [5] of (1*c*), involving a very slow reaction of [$^2H_2$]acetylene in an acidic medium probably favouring some D–H exchange.

The reaction of the *trans*-epoxide (3*t*) with HCl was carried out in a flask filled with the epoxide at pressures ranging from 0.1 to 0.5 atm. in which the equivalent amount of dry HCl was let in from a reservoir. The reaction was very fast, as shown by the drop in pressure and by the immediate appearance of a fog. 2-Chloro[$^2H_2$]ethanol (4) thus obtained contained only small amounts of less volatile impurities (g.l.c.) and was purified by preparative g.l.c. A sample of (4) was similarly obtained by reacting a sample of the impure *cis*-epoxide (3*c*) with HCl.

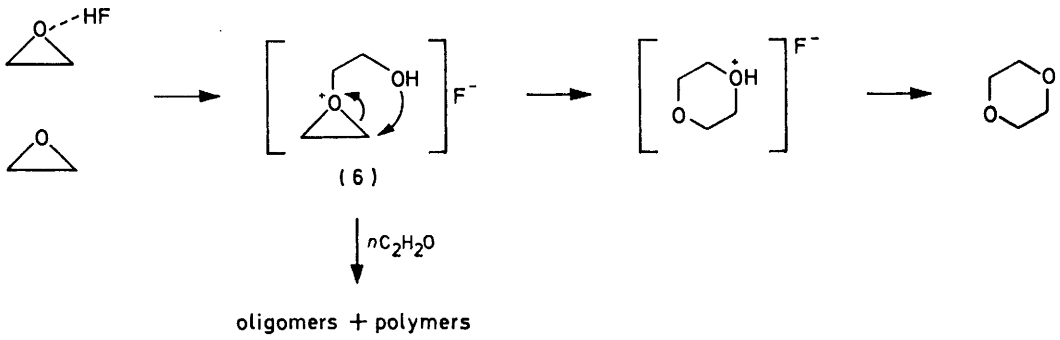
It was not possible to distinguish between the *erythro*- and *threo*-forms of (4) on the basis of their n.m.r. spectra, because the signals for the vicinal protons were poorly resolved multiplets, the expected AB system being broadened by the proximity of the deuterium atoms. Furthermore, in the corresponding bromo-acetates (2*t* and *e*) also, in which the separation of the signals for the two protons was greater and $^3J_{1,2}$ could be roughly evaluated, no significant difference was observed between the coupling constants for the two diastereoisomers. The chlorohydrin obtained from (3*t*) was therefore reconverted into the epoxide by NaOH, a reaction certainly involving inversion on the chlorine-carrying carbon.[6] Examination of the recyclized epoxide by microwave spectroscopy showed that it had exactly the same stereoisomeric composition as the epoxide used in the reaction with HCl. It was therefore deduced, on the basis of the sensitivity of the microwave analytical method, that not more than 0.5% *syn*-opening of the epoxide ring could have occurred in the reaction with HCl. Identical results were obtained both with a glass and with a polypropylene reaction apparatus. No *syn*-opening was observed in the reaction of (3*t*) with gaseous HBr giving (5*e*).

The negative results with HCl and HBr did not prove that a mechanism involving *syn*-opening of the oxiran ring did not operate when HF was the reagent, since the calculations mentioned in the Introduction [2] referred to this acid, which often behaves differently from the other halogen halides. When ethylene oxide was reacted with HF in the gas phase in a polypropylene apparatus rather different behaviour was observed, the reaction being much slower than with HCl and HBr; not more than 5% 2-fluoroethanol was present in the product. The main volatile product (*ca.* 37%) was 1,4-dioxan, identified by its mass spectrum. Small amounts of other unidentified compounds were also present (g.l.c.), and the rest was polymeric material. We therefore gave up this line, in view of the very low yield of the fluorohydrin and of the difficulty in separating sufficient amounts of it for stereochemical characterization.

DISCUSSION

The results obtained with HCl and HBr provided no evidence at all for a *syn*-addition mechanism as postulated [2] for the reaction with HF; *anti*-opening of the ring of the protonated oxiran (A_2 mechanism) [1] appears to take place with ethylene oxide as usually assumed for other aliphatic epoxides. The shorter bond length and higher dissociation energy of HF could on the other hand favour a different mechanism, but unfortunately we were not able to check this experimentally owing to the different course of this reaction. We also want to stress the fact that our operating conditions, as usual, were quite different from the theoretical model which involves isolated molecules on which calculations were based. Even if surface effects are not too important for the runs conducted in polypropylene vessels, intermolecular bonding between hydrogen halide molecules was probably present at the pressures at which the reactions were carried out.

The fact that dimerization and polymerization is by far the main course of the reaction of ethylene oxide with HF in the gas phase agrees with what is known about the same reaction when conducted in low polarity aprotic solvents:[7] polymers were mostly obtained, even if the formation of dioxan was not reported previously. Substantial amounts of dioxan were, however, formed in the



SCHEME 2

treatment of ethylene oxide with different acids in solution and with BF_3 in the gas phase.[8] This difference in behaviour towards ethylene oxide between HF and the other hydrogen halides, points to particularly unfavourable energetics for the A_2 or borderline A_2 mechanisms when the former reagent is involved, in accord with the *ab initio* calculations; however, the alternative concerted *syn*-opening mechanism appears not to be very favourable either, an alternative route involving attack by a second molecule of oxiran on the oxiran–HF complex * becoming competitive and leading to (2-hydroxyethyl)oxiranium ion (6) that can either cyclize to monoprotonated 1,4-dioxan, or undergo further attack by oxiran to yield cyclo-oligomers and polymers (Scheme 2). A somewhat similar explanation for the concurrent formation of dioxan in the $SnCl_4$-promoted polymerization of oxiran was proposed by Worsfold and Eastham,[10] who, however, assumed the unlikely intermediacy of primary carbenium ions. Ions of type (6) were also proposed by Vandenberg [11] and by Price and Spector [3] as intermediates of the cationic polymerization of epoxides, and evidence was provided for their formation with inversion during nucleophilic attack by the epoxide oxygen on an epoxide–acid complex.

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 257 spectrometer, a 10-cm cell being used for gaseous samples. N.m.r. spectra were recorded with a Varian CFT 20 spectrometer. Microwave spectra were taken on a Hewlett–Packard 8460C M.R.R. instrument. Mass spectra were obtained with a Varian CH 7 spectrometer with 70-eV ionization energy. G.l.c. analyses were performed with a Carlo Erba Fractovap 2300 instrument and preparative separations with a Perkin-Elmer F 20 instrument.

$[^2H_2]$Acetylene, obtained from calcium carbide with 99% D_2O, was converted into *cis*- and *trans*-$[^2H_2]$ethylene according to the method of Nicholas and Carroll.[5] The formation of the *trans*-isomer by reduction with chromium(II) chloride gave a product of satisfactory isotopic purity (*ca.* 95%) and high stereochemical purity (*ca.* 98%, as indicated by the intense band at 987 cm^{-1} of *trans*-$[^2H_2]$ethylene and by the absence of any appreciable band at 843 cm^{-1} characteristic of the *cis*-isomer).[12] The reduction to the *cis*-isomer with zinc–copper catalyst gave poorer and less reproducible results: the very long reaction times and the concurrent formation of hydrogen in the reaction vessel which had to be eliminated in order to avoid an excessive build-up of pressure and slowing down of hydrogenation, caused low yields and loss in isotopic enrichment, probably because of D–H exchange at the acetylene or ethylene stage.

erythro-1-*Acetoxy*-2-*bromo*$[^2H_2]$*ethane* (2*e*).—A solution of acetyl hypobromite was prepared according to Levine and Wall [13] by a very slow addition at 0 °C of bromine (0.12 mol) in CCl_4 (100 ml) to a stirred suspension of silver acetate (0.14 mol) in CCl_4 (900 ml). The filtered solution was approximately 0.1M (iodometric titration). The flask containing the solution was evacuated with a water pump and connected to a gas burette (2 l) filled with *trans*-$[^2H_2]$ethylene. Absorption of the gas occurred rapidly into the magnetically stirred solution and the reaction was stopped when, most of the gas having been absorbed, the colour changed from greenish yellow to light yellow-brown due to the free bromine. At this point iodometric titration indicated that only 2.7 mmol of bromine was still present. The solution was washed twice with 10% $NaHSO_3$, dried ($MgSO_4$), evaporated, and the residue was distilled to give (2*e*) (12 g, 80% with respect to the ethylene), b.p. 60 °C at 30 mmHg (lit.,[14] 159—164 °C for the non-deuteriated compound). G.l.c. (10% polyethylene glycol succinate on silanized Chromosorb W, 80—100 mesh) showed that the only impurity (*ca.* 1%) was 1,2-dibromoethane.

threo-1-Acetoxy-2-bromo$[^2H_2]$ethane, (2*t*) was similarly prepared from (1*c*). In this case, since, owing to the method of preparation, the corresponding ethylene contained much hydrogen and absorption was much slower, it was found more convenient to bubble the gas slowly into the acetyl hypobromite solution contained in a series of three gas washing bottles.

The n.m.r. spectra of the two diastereoisomeric compounds were very similar, both exhibiting the expected AM system, the doublets at δ 3.7 and 4.4 being further split by small couplings with deuterium. The value of J_{AM} was *ca.* 6 Hz for both diastereoisomers and was therefore not useful for differentiating them.

trans- *and* cis-$[^2H_2]$*Ethylene Oxide* (3*t and c*).—Compound (2*e* or *t*) (10 g, 59 mmol) was placed in a flask (50 ml) provided with a dropping funnel, a gas inlet tube, and a vertical condenser containing 3 Å molecular sieves in the two upper bulbs and connected at the top to a liquid nitrogen trap protected by a $CaCl_2$ drying tube. A slow nitrogen stream was bubbled through the liquid while a solution of 25% aqueous NaOH (25 ml) was added dropwise with magnetic stirring. The contents of the flask were slowly heated to 100 °C until complete solution ensued and kept at this temperature for a further 10 min. The product which condensed in the cold trap was distilled into a graduated test tube which was cooled at −80 °C. Pure ethylene oxide was thus obtained in yields ranging from 60 to 70%. I.r. spectra (gas) of the two stereoisomers were consistent with the literature data,[15] but the spectrum of the *cis*-isomer clearly indicated the presence of some $[^2H]$ethylene oxide.

Determination of the Isotopic Purity of (3*t*) *by Mass Spectroscopy*.—This determination was complicated by the fact that ethylene oxide has rather abundant fragmentation peaks at $M - 1$ and $M - 2$ [16] so that the diagnostically useful peak at *m/e* 45 can be due either to $C_2H_3DO^{+\bullet}$ or to $C_2HD_2O^{+\bullet}$. Furthermore, since the fragmentation pattern of ethylene oxide is very similar to that of acetaldehyde,[17] one can assume that the molecular ion rearranges at least in part to the $CH_3CHO^{+\bullet}$ ion, and in the case of (3*t*) this could give either $CHD_2CHO^{+\bullet}$ or $CH_2DCDO^{+\bullet}$. The data were analysed on the basis of the simplifying assumptions that isotopic effect in the loss or rearrangement of hydrogen can be neglected; this should not lead to a very significant error, as shown for instance by the fact that abundances of the ions at *m/e* 29 (CHO^+) and 30 (CDO^+) are similar. The Table shows the relative abundances of the peaks at *m/e* 41—48 for the non-deuteriated and deuteriated compounds. If one assumes an equal probability for the loss of H or D from the molecular radical cation the contributions of ions $C_2D_2HO^+$ and $C_2DH_2O^+$, respectively, to the *m/e* 45 and 44 peaks should be one-half of the relative

* Recent work [9] has provided evidence for the particular and peculiar stability of the $H_3O^+\cdot F^-$ proton-transfer complex in aqueous hydrofluoric acid and for the existence of related species from anhydrous HF and organic bases such as ethers.

abundances of the $M - 1$ peak in the spectrum of the non-deuteriated species. By subtracting this value (13.2%) from the abundance of the *m/e* 45 peak one obtains 5.5% as the contribution of the $C_2H_3DO^{+\bullet}$ ion. The *m/e* 44 peak in the deuteriated compound can correspond to the $C_2D_2O^+$, $C_2H_2DO^+$, and $C_2H_4O^+$ ions. A contribution of 2.1% from $C_2D_2O^+$, equal to the relative abundance of the *m/e* 42 ion ($C_2H_2O^+$) can be assumed on the basis of the above hypothesis. The ion $C_2H_2DO^+$ is derived either from loss of deuterium from $C_2H_2D_2O^+$ (13.2% contribution) or from loss of protium from $C_2H_3DO^{+\bullet}$; the latter process should contribute *ca.* 3/4 of that for the same fragmentation of the non-deuteriated compound, *i.e.* $0.75 \times 5.5 \times 0.263 = 1.1\%$. Subtraction of $2.1 + 13.2 + 1.1$ from the total abundance of the *m/e* 44 ion gives *ca.* 0.3% for the relative abundance of the $C_2H_4O^{+\bullet}$ ion. Our *trans*-[$^2H_2$]ethylene oxide therefore contained *ca.* 95% dideuteriated, 5% monodeuteriated, and <0.5% non-deuteriated species.

Mass spectral data for non-deuteriated and dideuteriated ethylene oxide

m/e	Relative abundance (%)	
	Ethylene oxide [a]	*trans*-[$^2H_2$]Ethylene oxide [b]
41	2.1	1.4
42	15.3	2.1
43	26.3	12.5
44	100	16.7
45	2.6	18.7
46	0.2	100
47		2.0
48		0.6

[a] Relative to the molecular ion; the base peak is at *m/e* 29. [b] The base peak is coincident with the molecular peak. Other relevant peaks at *m/e* (relative abundance %) 30 (75), 29 (65), 28 (12), 17 (30), 16 (29), 15 (17), and 14 (15).

Determination of Stereochemical Purity by Microwave Spectroscopy.—This analysis was based on the rotational transitions given below (in MHz):[18]

Transition	*trans*-$C_2H_2D_2O$	*cis*-$C_2H_2D_2O$	C_2H_3DO	C_2H_4O
$3_{21} \longleftarrow 3_{12}$	19 742.8	—	—	—
$4_{31} \longleftarrow 4_{22}$	25 859.6	24 408.0	25 443.5	24 834.3

It was thus found that the *trans*-oxide contained *ca.* 1.5% of the *cis*-isomer, and that 5.0% of the monodeuteriated species and *ca.* 0.1% of the non-deuteriated species were also present. The *cis*-oxide was found to be much less pure; different preparations contained variable amounts of *trans*-oxide (up to 3%), monodeuteriated oxide (up to 20%), and the non-deuteriated species (up to 10%).

Reactions of (3*t*) *with* (HCl). erythro-2-*Chloro*[1,2-$^2H_2$]-*ethanol* (4*e*).—The reaction was carried out in a three-necked round bottom glass flask (1 l), connected through a three-way stopcock to a manometer and a vacuum pump, the other two necks being used for the admission of ethylene oxide and HCl. The reaction flask was baked in an oven at 150 °C, the whole apparatus was evacuated to 0.1 mmHg,[*] and *trans*-[$^2H_2$]ethylene oxide (dried over 3 Å molecular sieves) was let into the reactor at the desired pressure (0.1—0.5 atm). Gaseous HCl from a tank was bubbled through concentrated H_2SO_4, condensed in a U tube cooled with liquid N_2, distilled into a second U tube and transferred into a flask (500 ml) that had been dried as above, the pressure of 1 atm being maintained through a mercury valve. A stopcock connecting the HCl reservoir to the reactor was slowly opened and the gas admitted through a tube reaching to the centre of the reaction flask. An immediate reaction was revealed by a drop in pressure and by the formation of a fog. Admission of HCl was stopped when the pressure had returned to the initial value. The product was collected by rinsing the flask with CH_2Cl_2 and the solution was evaporated at room temperature in a rotary evaporator. The residue was 2-chloroethanol containing only small amounts of less volatile impurities. It was purified by preparative g.l.c. (3-m × 8-mm column, 5% ethylene glycol succinate on silanized Chromosorb G, 60—80 mesh). The 100-MHz n.m.r. spectrum showed the signals for the protons on carbon at δ 3.97 and 4.23 as poorly resolved multiplets, from which it was not possible to deduce the ^3J values because of coupling with deuterium. The same reaction was also carried out in a polypropylene apparatus.

Conversion of (4*e*) *into* (3*t*).—The chlorohydrin (4*e*) was converted into the corresponding ethylene oxide with the same set-up as described above for the transformation of (2) into (3). The yield was 75—80%. The epoxide thus obtained both from the chlorohydrin prepared in the glass and in the polypropylene reactors, both at 0.1 and 0.5 atmosphere, had exactly the same i.r. spectrum as the starting *trans*-[$^2H_2$]ethylene oxide and the same ratio of *trans*- to *cis*-isomers resulted from microwave spectroscopic analysis, within a 1% error limit.

Reaction of (3*t*) *with* HBr.—This reaction was carried out in the same manner as the corresponding reaction with HCl, except that the hydrogen bromide was not bubbled through H_2SO_4. The crude *erythro*-2-bromo[$^2H_2$]ethanol was reconverted into ethylene oxide that had the same composition as the starting epoxide.

Reaction of Ethylene Oxide with HF.—A polypropylene flask (1 l) was filled with ethylene oxide at a pressure of 0.5 atm and gaseous HF was let in slowly. The reaction was much slower than those with HCl and HBr, as indicated by a rapid increase in pressure, followed by a slow decrease. When, after a few minutes the pressure remained constant at 0.5 atm, air was blown through the flask to eliminate the excess of HF, the product was taken up with ether, a known amount of 2-chloroethanol was added as an internal standard, and the solution was analysed by g.l.c. The amount of 2-fluoroethanol was estimated as 65 mg (5% yield), while a second major peak (330 mg, 37% yield) was identified as 1,4-dioxan through comparison of its fragmentation pattern obtained by g.l.c.–mass spectra, with that of an authentic sample. Irregular peaks at higher retention times were probably due to the decomposition of material of higher molecular weight.

Similar results were obtained when the initial pressure of ethylene oxide was 0.1 atm.

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[*] One referee has observed that our experimental techniques were not such that the presence of trace amounts of oxygen could be excluded. We are fully aware of this fact, but did not think it necessary to adopt high vacuum techniques, since the incursion of free radical mechanisms was definitely excluded for the reactions under discussion.

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