interpretation of the uv data, however, and this possible method for measuring the equilibrium constant was abandoned.

Hydration of Acetone.—The pmr spectra of 20 and 30 vol % solutions of acetone in water were determined at 60 MHz. At high amplitude a peak was observed 0.78 ppm upfield from acetone. This peak, whose size was not much larger than that of the background noise in the case of the noisier spectra, was shown, by changing the spin rate, not to be a spinning side-band. Its area and that of the nearby ^{13}C satellite of acetone were determined by counting squares. The spectra at 100 Hz were run 9–10 times and the results were averaged using a computer of average transients; then the whole process was repeated. Two other spectra were run using very slow sweep, very small response, and very large spectrum amplitude.

Addition of Methanol.—Pmr measurements at 60 MHz on solutions of acetone in methanol were made in a manner analogous to that used for the aqueous solutions. In a typical uv measurement, 0.035 ml of acetone was added to 3.0 ml of methanol and absorbance measurements were made as quickly as possible at 2760 Å using an equilibrated ketone solution with an absorbance of 1.467 in the reference cell. The observed absorbance decreased from 0.808 at 16 sec to an equilibrium value of 0.803. Extrapolation to zero time gave a value of 0.813. This change of 0.010 in a total absorbance of 2.280 corresponds to 0.44%. When small amounts of hydrochloric acid were added, much larger decreases in absorbance were observed.

Registry No.—Hydrogen peroxide, 7722-84-1; water 7732-18-5; methanol, 67-56-1; acetone, 67-64-1.

Acknowledgment.—We are indebted to Mr. Steven H. Williams for making the pmr measurements at 100 MHz, to Dr. Donald G. Kubler for valuable discussions of our results, and to the National Science Foundation for grants that aided in the purchase of the nmr spectrometers and the ultraviolet-visible spectrophotometer, whose purchase was also made possible by a generous grant from the Charles F. Kettering Foundation.

Effects of Fluorine Substitution upon Glycidyl Ether–Dibutylamine Reaction Rates

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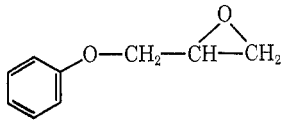
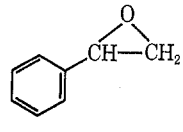
Two series of fluorine-substituted glycidyl ethers have been synthesized, and their rates of reaction with dibutylamine in *t*-amyl alcohol have been measured by means of gas chromatography. The reaction was found to be second order, with dibutylamine attacking the terminal position of the epoxide ring in all cases. Fluorinated substituents generally decreased the reaction rates within each series with one outstanding exception. Rate constants and Arrhenius parameters are presented for each of the reactions studied.

1,2-Epoxy-3-phenoxypropane (**1a**), or phenyl glycidyl ether,[1] is three to four times more reactive toward nucleophilic attack by amines in alcohol than either styrene oxide (**2**) or allylbenzene oxide (**3**).[2] It has



1a



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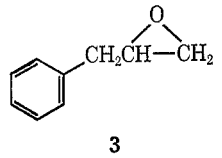

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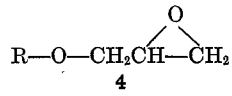
been suggested[3,4] that this increased reactivity is characteristic of all epoxides of the glycidyl ether type represented by structure **4**.



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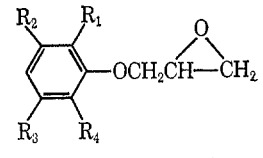
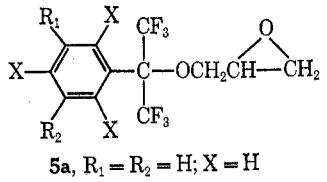
In order to determine the effects responsible for the reactivity of this type of compound, it is of interest to measure the influence of variations in the R group of **4** upon the epoxide–amine reaction rate. Although previous workers have studied the effects of solvents and the use of various nucleophiles on the rate of cleavage of the epoxide ring,[5,6] in each investigation only a single glycidyl ether was used. A comparison of the reaction rates of different glycidyl ethers under identical conditions has not to our knowledge been made.

We have prepared two series of fluorine-containing glycidyl ethers, of general structure **1** and **5**, in order to



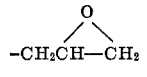
1a, $R_1 = R_2 = R_3 = R_4 = H$
b, $R_1 = R_3 = R_4 = H$; $R_2 = CF_3$
c, $R_1 = R_2 = R_3 = R_4 = F$



5a, $R_1 = R_2 = H$; $X = H$
b, $R_1 = CF_3$; $R_2 = H$; $X = H$
c, $R_1 = R_2 = CF_3$; $X = H$
d, $R_1 = R_2 = F$; $X = F$

determine the effect of increasing fluorine substitution upon the rates of ring opening of these epoxides. Compounds of type **5** represent a new class of fluoro-substituted glycidyl ethers. The present paper describes the preparation of these compounds, and presents kinetic data comparing the rates of epoxide–dibutylamine reaction, in *t*-amyl alcohol, for the glycidyl ethers above.

(1) The term "glycidyl" is used to denote the following structure.



(2) N. B. Chapman, N. S. Isaacs, and R. E. Parker, *J. Chem. Soc.*, 1925 (1959).

(3) S. O. Greenlee, "Thioxyalkanoic Acids and Epoxy Curing Agents," paper presented to the American Chemical Society Division of Organic Coatings & Plastics Section, Minneaplis, Minn., April 1969.

(4) W. J. Patterson and N. Bilow, *J. Polym. Sci., Part A*, **7**, 1089 (1969).

(5) L. Shechter, J. Wynstra, and R. P. Turkjy, *Ind. Eng. Chem.*, **48**, 94 (1956).

(6) Shechter and J. Wynstra, *ibid.*, **48**, 86 (1956).

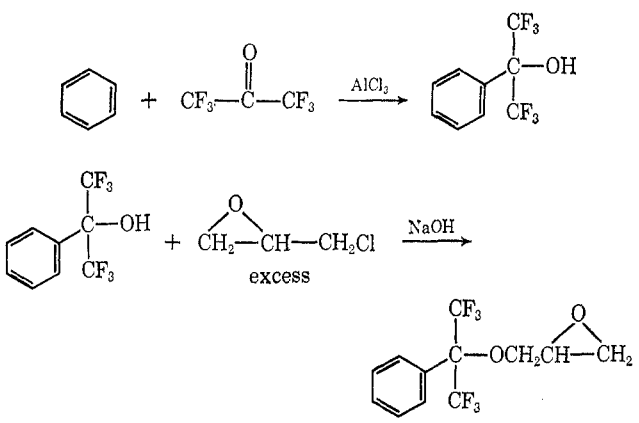
TABLE I

PHYSICAL DATA FOR FLUORO-SUBSTITUTED GLYCIDYL ETHERS[a,b]

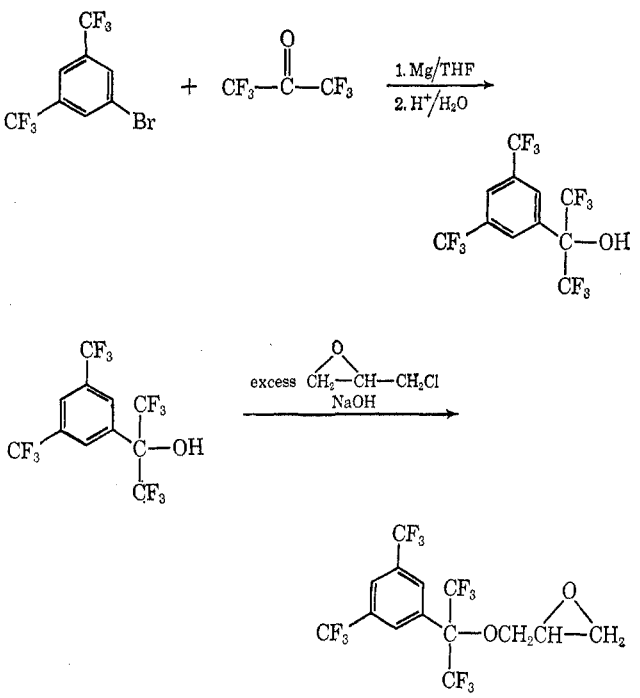
Compd	Yield, %[c]	Bp, °C (10.0 mm)	$n^{20}D$	Nmr spectrum[d,e] (R-O-CH_2-CH-CH_2) $H_{aromatic}$	H_a	H_b	H_c
1b	88	110	1.4676	7.10 (4)	4.16	3.18	2.76
					3.89		2.60
1c	67	99	1.4552	6.79 (1)	4.41	3.26	2.77
					4.09		2.59
5a	65	104	1.4371	7.56 (2)	3.82	3.15	2.75
				7.46 (3)	3.57		2.60
5b	78	108	1.4095	7.92 (1)	3.91	3.20	2.78
				7.68 (3)	3.57		2.63
5c	62	97	1.3901	8.16 (2)	3.99	3.25	2.84
				8.03 (1)	3.53		2.67
5d	38	111	1.4074		3.63	3.18	2.78
							2.51

[a] Satisfactory analytical data were obtained for all compounds in this table. [b] Epoxy equivalent weights were determined, using 1 *N* pyridine hydrochloride in pyridine, for all compounds except **5d**, and are within 1.5% of the theoretical value. [c] Per cent conversion from corresponding hydroxy compound. [d] Ppm downfield from tetramethylsilane in CCl_4 solution. [e] Listing of dual signals for H_a or H_c indicates chemical nonequivalence of the geminal protons.

SCHEME I



SCHEME II



Discussion and Results

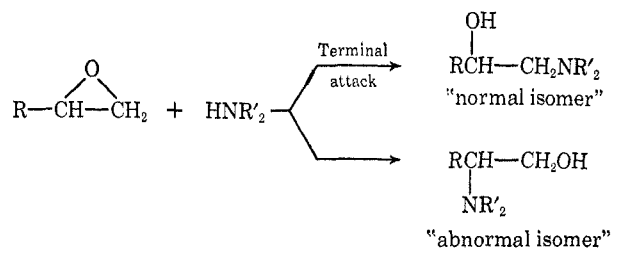
Synthesis of Glycidyl Ethers.—We have found that arylbis(trifluoromethyl)carbinols react with excess epichlorohydrin in much the same manner as do phenols.[7] This reaction is a convenient new means for obtaining 2,3-epoxy-1-propoxy compounds, or glycidyl ethers, which contain fluorocarbon. The acidic carbinol intermediates may be obtained *via* direct, $AlCl_3$-catalyzed condensation of aromatic hydrocarbons with hexafluoroacetone[8] (Scheme I), or by means of aromatic Grignard reagents (Scheme II). We have found fluoroalkyl-substituted aromatics to be unreactive toward hexafluoroacetone in the presence of $AlCl_3$, presumably owing to ring deactivation by electronegative substituents. Therefore, the alternate synthesis *via* the Grignard reagent was employed for compounds **5b–d**.

Table I contains physical properties and yields for the four new glycidyl ethers of type **5** prepared by this method. Also included are compounds **1b** and **1c**, which were prepared from the corresponding phenols and epichlorohydrin by the method of Kelly, *et al.*[7]

(7) P. B. Kelly, A. J. Landau, and C. D. Marshall, *J. Appl. Polym. Sci.*, **6**, 431 (1962).

(8) B. S. Farah, E. E. Gilbert, and J. P. Sibilia, *J. Org. Chem.*, **30**, 998 (1965).

Nature of the Reaction.—The reaction between a secondary amine and an unsymmetrical epoxide compound may proceed *via* two different pathways, depending upon which of the epoxide-ring carbons is attacked.



Terminal attack, leading to the formation of a secondary alcohol, is the exclusive or predominant pathway

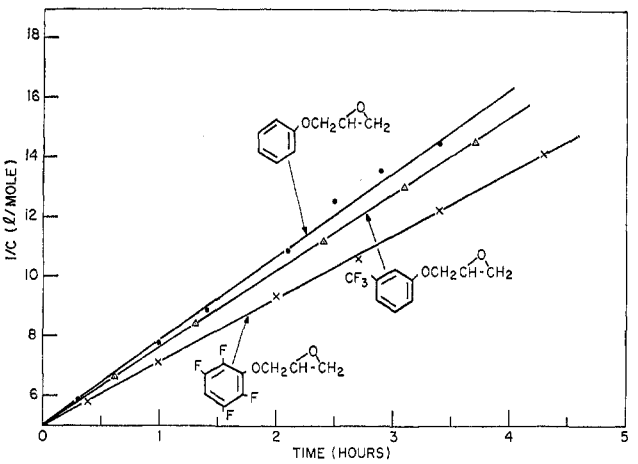


Figure 1.—Reaction of dibutylamine with glycidyl ethers of type 1 in *t*-amyl alcohol (T = 60°), using equimolar amounts of reactants. Reciprocal concentration of the glycidyl ether is plotted as a function of time.

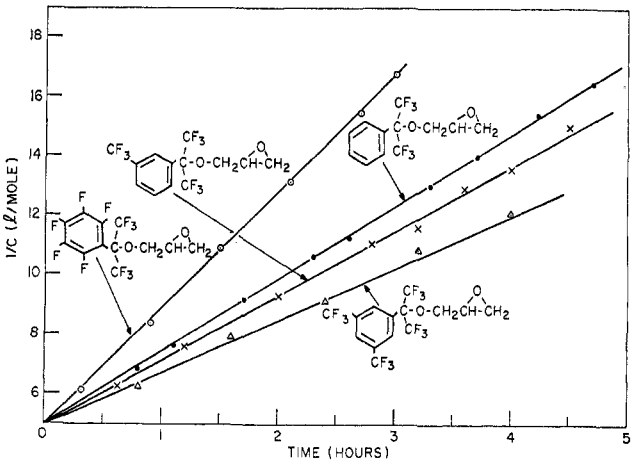


Figure 2.—Reaction of dibutylamine with glycidyl ethers of type 5 in *t*-amyl alcohol (T = 60°), using equimolar amounts of reactants. Reciprocal concentration of the glycidyl ether is plotted as a function of time.

followed by nearly all nucleophiles under neutral or basic conditions.[9-11] This is due primarily to the steric hindrance exerted by the R group on the more substituted ring carbon atom. The product corresponding to terminal attack is commonly labeled the "normal isomer," because of the overwhelming tendency for this mode of reaction. Previous workers[2] have shown that phenyl glycidyl ether and piperidine conform to the trend, reacting in ethanol to give greater than 99% normal isomer.

Our kinetic data were obtained by treating various glycidyl ethers with dibutylamine, using *t*-amyl alcohol as a solvent. Because dibutylamine is even more hindered than is piperidine, a negligible yield of abnormal isomers is expected under the reaction conditions employed. Investigation of the products of each of the glycidyl ether–dibutylamine reactions supported this prediction. Glpc analysis of the reaction mixtures at various column temperatures indicated only a single, sharp product peak in each case. These products were identified by their nmr spectra as the corresponding normal isomers (see Experimental Section). No evidence of formation of the abnormal isomer could be detected, using these techniques, for any of the systems. For this reason, and in light of the above discussion, we have considered terminal attack to be the exclusive reaction pathway for the kinetic studies reported. The formation of trace amounts of abnormal isomer, although not rigorously excluded, would have a negligible effect on our rate measurements.

The possibility of alcoholysis of the epoxide ring by solvent molecules has been ruled out by previous studies. It has been shown[2] that ethanol does not attack phenyl glycidyl ether in neutral solution, and even refluxing in the presence of phenoxide anion led to only 2% reaction between ethanol and phenyl glycidyl ether.[11] Our work was carried out using hindered *t*-amyl alcohol at 60° or less; so it is not surprising that no sign of alcoholysis was found.

Order of the Reaction.—As anticipated by various studies, which show that nucleophilic attack on an epoxide ring in neutral or basic media proceeds according to second-order kineiics,[12,13] all of the glycidyl ethers, **1a-c** and **5a-d**, follow a second-order rate law in their reactions with dibutylamine. Using equal initial concentrations of amine and glycidyl ether in *t*-amyl alcohol, and plotting the reciprocal of the glycidyl ether concentration as a function of time, we obtained good straight lines for each system at three different reaction temperatures (Figures 1 and 2). This linear behavior is characteristic of second-order reactions. Concentrations were determined as a function of time by analyzing aliquots of the reaction solution in the gas chromatograph, and measuring integrated peak areas as percentages of initial areas. This technique allows for determination of the amounts of each reactant remaining at any time. However, rate measurements were based only upon the glycidyl ether concentrations, which could be determined more accurately owing to complete isolation of the gas chromatographic peak. It was clear from the simultaneous measurement of the amine concentration that a 1:1 reaction was taking place.

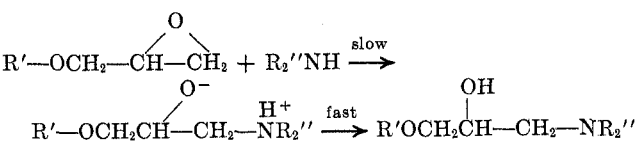
$$\frac{dC_A}{dt} = -k_2 C_A C_B$$

$$\text{for } C_A = C_B$$

$$\frac{dC_A}{dt} = -k_2 C_A^2$$

$$\frac{1}{C_A} = -k_2 t + C_A^0$$

Predicted Effect of Fluorinated Substituents.—Because of the second-order appearance of these reactions, it seems clear that the mechanism is SN2, with dibutylamine attacking the terminal carbon of the epoxy ring in the rate-determining step. This slow step may then be followed by rapid proton transfer, probably *via* the hydroxylic solvent.[5]



(9) E. L. Eliel, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, pp 106–114.

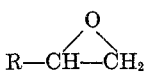
(10) S. Winstein and R. B. Henderson, *Heterocycl. Compounds*, **1**, 22 (1950).

(11) G. L. Brode and J. Wynstra, *J. Polym. Sci., Part A*, **4**, 1045 (1966).

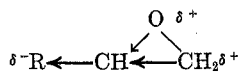
(12) R. E. Parker and N. S. Isaacs, *Chem. Rev.*, **59**, 737 (1959).

(13) N. S. Isaacs and R. E. Parker, *J. Chem. Soc.*, 3497 (1959).

It has been inferred[2] from this mechanism that the sharp increase in reactivity of phenyl glycidyl ether (**1a**) compared with styrene oxide (**2**) or 1,2-epoxy-3 phenylpropane (**3**) in ethanol is due to polarization of the bonds in structure **6a** as in **6b**. The overall effect of



6a



6b

polarizing the epoxy ring in this fashion is to facilitate the reaction by enhancing the approach of the nucleophilic amine.[2,14] It was felt that the greater electronegativity of phenoxymethyl *vs.* phenyl or benzyl activated the epoxide ring, thereby causing its increased reactivity. If we extend this reasoning to the introduction of fluorine into the aromatic nucleus of **1a**, the subsequent increase in electronegativity of that part of the molecule is expected to produce an epoxide even more reactive than **1a** itself. Tetrafluorophenoxy, for example, being more electron withdrawing than phenoxy, should cause tetrafluorophenyl glycidyl ether (**1c**) to react with nucleophiles faster than does phenyl glycidyl ether (**1a**). This argument also pertains to compounds of type **5**, in which increased fluorine substitution on the aromatic nucleus should coincide with increasing rate constants.

Observed Effect of Fluorinated Substituents.—For both series of analogous compounds the surprising finding of our kinetic studies is that increased fluorine substitution on the aromatic ring slows the rate of epoxide ring opening in all cases but one. The actual decrease in reactivity is substantial, in view of the fact that the substituents are quite distant from the site of attack.

As seen in Figures 1 and 2, and in Table II, rate constants tend to decrease rather than increase as fluorinated substituents are added to **1a** and **5a**. Only compound **5d** exhibits the predicted acceleration in its reaction with dibutylamine. For all other compounds, there is a decrease in reactivity within each series which is roughly proportional to the degree of fluorine substitution. Arrhenius parameters for the reactions studied are given in Table III. As can be seen, activation energies and entropies are quite similar in all cases.

TABLE II

MEASURED RATE CONSTANTS

Compd	$10^4 k_2$[a] (T = 41°)	$10^4 k_2$ (T = 51°)	$10^4 k_2$ (T = 60°)
1a	2.96	5.28	8.15
1b	2.72	4.87	7.59
1c	2.41	3.83	6.00
5a	2.68	4.88	7.03
5b	2.24	3.81	6.17
5c	1.78	3.27	5.12
5d	4.78	7.71	11.14

[a] k_2 in l. mol^{-1} sec^{-1}.

TABLE III

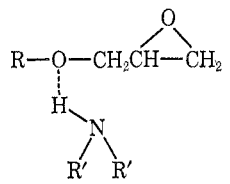
ARRHENIUS PARAMETERS

Compd	E_a, kcal/mol	Log A	$\Delta S^{\ddagger}$,[a] eu
1a	11.0 ± 1	4.2 ± 0.5	−42 ± 3
1b	11.2 ± 1	4.3 ± 0.5	−41 ± 3
1c	10.4 ± 1	3.6 ± 0.5	−44 ± 3
5a	10.5 ± 1	3.7 ± 0.5	−44 ± 3
5b	10.9 ± 0.6	3.9 ± 0.3	−43 ± 2
5c	11.4 ± 1	4.2 ± 0.5	−42 ± 3
5d	9.3 ± 1	3.2 ± 0.5	−46 ± 3

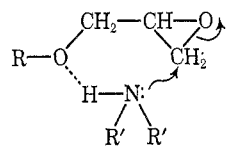
[a] Activation parameter, calculated at 300°K according to J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," Wiley, New York, N. Y., 1963, p 71.

The steric situation in the vicinity of the epoxide ring is identical for each of the compounds of type **1**, as it is for those of type **5**. Therefore, differences in reactivity within the two groups of compounds must be attributed to electronic effects caused by substituents on the aromatic ring, or to steric considerations involving the glycidyl ether oxygen, rather than the epoxide ring itself.

The unexpected behavior of fluorine-substituted compounds led us to consider an alternative to the simple inductive explanation for the highly reactive nature of glycidyl ethers in the SN2 reactions discussed. The assumption of activation of the epoxide ring *via* a simple inductive effect is inconsistent with the observed deactivating influence of fluorinated substituents in compounds **1a–c** and **5a–c**. Therefore, we suggest that at least part of the activation caused by the glycidyl ether oxygen may be due to its ability to hydrogen bond with the attacking amine as in **7**.[15]



7



8

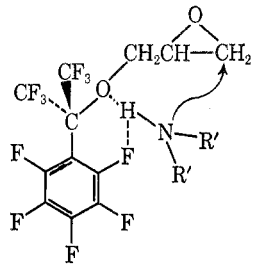
Association of this type between the amino hydrogen and the ether oxygen would enhance the approach of the amine, and place it in a favorable position for attacking the epoxide ring. In the six-membered-ring intermediate (**8**) which results from terminal attack the ether oxygen might also stabilize the transition state by delocalizing the positive charge on the nitrogen during formation of the C–N bond. This mechanism is consistent with the absence of the abnormal isomer, which would require a five- rather than six-membered-ring intermediate for its formation. Fluorine or fluorocarbon substituents on the R group of **8** are expected to decrease the electron density around the glycidyl ether oxygen, and consequently reduce its ability to associate with the amino hydrogen. Formation of a complex such as **8** should, therefore, be less favored. If this effect outweighs the activation of the epoxide ring due to polarization (as in **6b**), it would account for the decreasing rate constants corresponding to increasing fluorine content in compounds **1a–c** and **5a–c**.

Compound **5d**, our most heavily fluorinated epoxide, is anomalous to the trend of deactivation by fluorine substitution, and in fact is the most reactive of all the glycidyl ethers studied. Only this compound, of the seven tested, reacts faster than phenyl glycidyl ether. It seems unlikely that the inductive effect of the fluo-

(14) C. N. Hinshelwood, K. J. Laidler, and E. W. Timm, *J. Chem. Soc.*, 848 (1938).

(15) It has been suggested that the reactions of epoxy resins of the glycidyl ether type with amine curing agents are accelerated by this mechanism. [A. L. Cupples, H. Lee, and D. G. Stoffey, *Advan. Chem. Ser.*, **92**, 173 (1970)].

rine in this case should suddenly activate the epoxide ring, since the trend established in all other cases is toward deactivation. A study of the molecular model of compound **5d** suggests one possible explanation for its anomalous behavior. Owing to the steric hindrance of the two *ortho* fluorine atoms, the *gem*-trifluoromethyl groups in this molecule appear to be somewhat constrained perpendicular to the aromatic ring. The preferred orientation appears to be that shown, in which the glycidyl ether oxygen is found to be very close to one of the *ortho* fluorine atoms. It appears that a



9

complex such as **8** could be formed not only through association of the amino hydrogen with the glycidyl ether oxygen, but also with the *ortho* fluorine atoms as in **9**. Of the compounds studied, then, **5d** seems to be unique for two reasons: (1) the rotation of the *gem*-trifluoromethyl groups may be hindered by adjacent fluorine substituents, and (2) fluorine atoms (on the benzene ring) are positioned such that association with the amino hydrogen might lead to a favorable geometry for attack on the epoxide ring. One or both of these factors may be responsible for the anomalous behavior of this compound. Synthesis of compounds closely related to **5d** is in progress, in order to determine the basic requirements for enhanced reactivity in fluoro-substituted glycidyl ethers.

Experimental Section

Nuclear magnetic resonance spectra were obtained at 24° as 10–20% solutions in CCl_4 on a Varian HA-100 spectrometer, using tetramethylsilane as an internal standard. Infrared spectra were run as smears of the neat liquids between salt plates on a Perkin-Elmer Model 457 grating spectrophotometer. All glycidyl ethers were fractionated on a Nester–Faust auto annular Teflon spinning-band still (10.0 mm) prior to use in kinetic experiments. Analytical samples of the glycidyl ethers were used for all kinetic runs. Elemental analyses were performed at the Schwarzkopf Laboratories, N. Y.

Materials.—Phenyl glycidyl ether was purchased from the Shell Chemical Company, and purified by distillation through the column described above. Starting materials including 2,3,5,6-tetrafluorophenol, 3-trifluoromethylphenol, 3-bromobenzotrifluoride, 3,5-di(trifluoromethyl)bromobenzene, hexafluoroacetone, and pentafluorophenyl bromide were obtained from Peninsular ChemResearch Co., and used as received. 2-Phenyl-2-hydroxyhexafluoropropane was prepared from benzene and hexafluoroacetone according to published procedure.[8]

The dibutylamine used for kinetic studies was purified by careful distillation through a 3-ft, helices-packed column. A single fraction, bp 158–159° (760 mm), was used for all runs. Distillation of the *t*-amyl alcohol was carried out on the same column, and the central fractions, bp 101.0–101.5° (760 mm), were combined for use. After purification, neither the amine nor the alcohol solvent showed any traces of impurity in the gas chromatograph. All runs were made using materials from the same batch of amine, and from the same batch of solvent, to ensure further against variations in the relative reaction rates due to trace impurities. The glycidyl ethers used showed no traces of impurity by glpc analysis on the columns described below.

2-(3-Trifluoromethylphenyl)hexafluoro-2-propanol.—3-Bromobenzotrifluoride, 41 g (0.18 mol), magnesium turnings, 4.5 g (0.19 g-atom), precleaned with dilute hydrochloric acid and dried, and 100 ml of anhydrous ether were placed into a 100-ml, four-necked resin kettle equipped with a magnetic stirrer, gas inlet tube and a Dry Ice–acetone reflux condenser protected from the atmosphere by a drying tube. Prior to reactant addition, the kettle was heated with a heat lamp and purged with dry nitrogen. When the flask contents were gently heated, the reaction started and proceeded smoothly for 0.5 hr to yield a dark brown solution. Hexafluoroacetone, 22 ml (0.19 mol), was condensed into a trap from a cylinder, and then allowed to distil over into the resin kettle above the liquid surface at such a rate to maintain gentle reflux at the Dry Ice condenser. The addition required 1.5 hr during which the Grignard solution was stirred vigorously. Excess 2 *N* hydrochloric acid was used to decompose the magnesium salt after the reactant solution had stirred overnight. Additional ether was added, and the ethereal solution was separated, washed twice with water and once with saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure, and the residue was fractionated through a 6-in., vacuum-jacketed Vigreux column. The fraction boiling at 89° (44 mm) was collected as a clear, colorless liquid, 36 g (63% overall yield based on starting bromide). The product was alkali soluble, and the nmr spectrum in carbon tetrachloride displayed signals at δ 8.02 (s, 1, Ar–H), 7.70 (m, 3, Ar–H), and 3.40 (s, 1, O–H). The infrared spectrum had a sharp hydroxyl peak at 3600 cm^{-1} and a broad one between 3500 and 3200 cm^{-1}.

2-[3,5-Di(trifluoromethyl)phenyl]hexafluoro-2-propanol.—This compound was prepared *via* the Grignard reaction in essentially the same manner as the preceding intermediate, except that a mixture of ether and tetrahydrofuran was required as solvent. Magnesium could not easily be induced to react with 3,5-di(trifluoromethyl)bromobenzene in dry ether alone. A 60-g (0.205 mol) sample of the bromide gave an overall yield of 54.6 g (70%) of the desired product: bp 85–90° (40 mm); nmr δ 8.20 (s, 2, Ar–H), 8.03 (s, 1, Ar–H), 3.79 (s, 1, O–H). The infrared spectrum contained a sharp hydroxyl peak at 3610 cm^{-1}.

2-(Pentafluorophenyl)hexafluoro-2-propanol.—This perfluorinated alcohol was synthesized *via* the readily produced Grignard reagent of pentafluorophenyl bromide in dry ether. In this case, the reaction between the Grignard reagent and hexafluoroacetone appeared to be unusually sluggish, and it was necessary to heat the ethereal solution nearly to boiling in order to achieve a moderately rapid reaction. From 50 g (0.20 mol) of bromide was obtained 45 g (64% overall yield) of the alcohol, bp 167–170° (760 mm). The infrared spectrum had a sharp hydroxyl band at 3620 cm^{-1}.

Preparation of Glycidyl Ethers.—All of the glycidyl ethers were prepared in essentially the same manner. The procedure for preparation of the glycidyl ether of 2-(3-trifluoromethylphenyl)-hexafluoro-2-propanol (**5b**) is typical.

Into a 2-l., three-necked, round-bottom flask equipped with a reflux condenser, dropping funnel and stirrer were placed 195 g (0.65 mol) of 2-(3-trifluoromethylphenyl)hexafluoro-2-propanol, 500 g epichlorohydrin (5.4 mol), 600 ml acetone and 70 ml water. Into the dropping funnel was placed a 20% aqueous solution of sodium hydroxide containing 28.0 g (0.70 mol) of the alkali. The flask contents were stirred and heated to reflux. One-sixth of the sodium hydroxide solution was added slowly, and reflux was continued 15 min before another one-sixth portion was added. This was repeated until five-sixths of the alkali had been added, and, after the fifth reflux period, the aqueous layer was drawn off and discarded. Then, reflux was resumed and the remaining alkali solution was added. After 15 min, the aqueous layer was again withdrawn. Most of the acetone and epichlorohydrin was distilled at atmospheric pressure, and the remaining solution was decanted from a residual precipitate of sodium chloride. The solution was then diluted with 300 ml of ether. This ethereal solution was washed once with water and twice with saturated aqueous sodium chloride. After it was dried over anhydrous sodium sulfate, the solution was filtered, and the ether was removed on a rotary evaporator. The resulting product solution was vacuum distilled through a 6-in. Vigreux column and a fraction boiling at 120° (13 mm) was collected; 180 g (78%) of 2-(3-trifluoromethylphenyl)hexafluoro-2-propyl glycidyl ether were obtained. This was redistilled through the Nester–

Faust spinning-band column to yield 151 g of analytically pure product (Table I).

Rate Measurements.—Gas chromatographic analyses were performed using a Beckman GC-2A gas chromatograph, equipped with a 10-in. recorder and Disc integrator, and containing a 2 ft × 0.25 in. column of 30% silicone 550 on 42–60 mesh firebrick. Concentrations were obtained as a function of time by comparing the integrated area of a reactant peak at time t with the area of that peak at time t_0. Since the t_0 peak corresponded to a known initial concentration, the actual concentration at time t was found from the ratio of peak areas.

In a typical run, 2.00×10^{-4} mol of glycidyl ether and 2.00×10^{-4} mol of dibutylamine were weighed into a 10-ml volumetric flask, and enough *t*-amyl alcohol was added to bring the total volume to exactly 10 ml.[16,17] The solution was then immediately transferred to a round-bottom flask equipped with a magnetic stirrer and a self-sealing rubber septum cap. The flask was capped and placed in a constant temperature bath, which was maintained at the reaction temperature ±0.05°. The t_0 reading was then taken by piercing the septum cap with a syringe and withdrawing a 10.0-μl aliquot, which was injected directly into the gas chromatograph for analysis. Subsequent 10.0-μl samples were withdrawn at various times and analyzed in an identical manner. Variation in the height of the sharp *t*-amyl alcohol peak, which served as an internal standard, was generally less than 1% during a run, and never more than 2.5%. All reactions were followed to at least 60% completion.

Each of the reactions was run at three different temperatures (41.0, 51.0, and 60.0°) using initial concentrations of 0.200 *M* in *t*-amyl alcohol for each reactant. All of the 60° reactions were run in duplicate. Rate constants were reproducible to within 1% in most cases, and to within 3% in the least favorable case.

Product Analysis.—Product investigation was done by glpc analysis of the infinite-time kinetic samples. A 6 ft × 0.25 in. column packed with 30% Ucon 50 HB 2000 on 42–60 mesh firebrick was used for analytical and preparative work.

Glpc analysis of the reaction mixtures indicated a single, sharp product peak for each of the reactions. After purification by preparative glpc, these products were characterized by their nmr spectra as the "normal" isomers (products of terminal attack by the amine on the epoxide ring). No trace of the second (abnormal) isomer could be found in any of the systems. In each case, the ratio of the nmr integral of the N–C–H *vs.* O–C–H protons was 2:1, corresponding to that required for the normal isomer.

Since all products are identical on the amino side of the glycidyl ether oxygen, the features of interest in their spectra are extremely similar. These features are illustrated by the following example.

Adduct of Dibutylamine and Glycidyl Ether 1c.—The reaction product had a retention time of 2.5 min at 35 psig, T = 200°, on the column described above. Its nmr spectrum showed maxima at δ 6.73 (triplet of triplets, 1, Ar–H), 4.18 (d, 2, O–CH_2) 3.83 (m, 1, CHOH), 3.60 (s, 1, O–H), 2.52 (m, 6, N–CH_2), 1.36 (m, 8, C–CH_2), 0.93 (t, 6, CH_3).

The infrared spectrum showed absorptions at 3440 cm^{-1} (hydroxyl); 2900, 1460 (C–H): 1640, 1540, and 1490 (aromatic); 1175 (Ar–O–R); and 1100 (C–F, alcoholic C–O).

Registry No.—**1a,** 122-60-1; **1b,** 585-45-5; **1c,** 25056-10-4; **5a,** 25056-11-5; **5b,** 25056-12-6; **5c,** 25056-13-7; **5d,** 25080-58-4; 2-(3-trifluoromethylphenyl)-hexafluoro-2-propanol, 25056-14-8; 2-[3,5-di(trifluoromethyl)phenyl]hexafluoro-2-propanol, 25056-15-9; 2-(pentafluorophenyl)hexafluoro-2-propanol, 13732-52-0; adduct of dibutylamine and glycidyl ether **1c,** 25056-17-1.

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(16) In an unpublished study involving neat solutions of dibutylamine and the glycidyl ethers above, we have shown that the error introduced by allowing the reactants to be in contact during weighing is about 0.1%. This slight error has been ignored in our measurements.

(17) Initial concentrations were corrected for the expansion of the solution upon heating from room temperature to reaction temperature.

Ozonation of Amines. IV.[1] Di-*t*-butylamine

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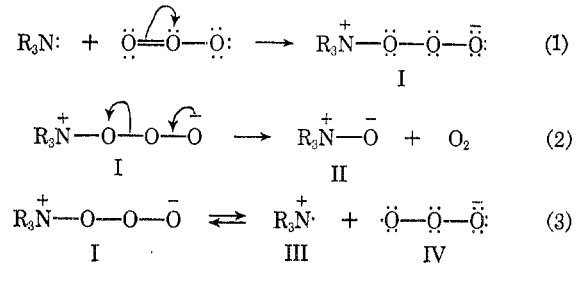
Results of a thorough study of the ozonation of a secondary amine, di-*t*-butylamine, are reported for the first time. The major final products from ozonation in chloroform are 2-methyl-2-nitropropane, di-*t*-butylammonium chloride, and various derivatives of the *t*-butyl group lost in formation of the nitro compound. In contrast to the ozonation of *t*-butylamine, the ozonate anion radical is not produced initially, but di-*t*-butyl nitroxide is. To explain these results a new (fourth) fate of the amine–ozone adduct is proposed.

The first paper of this series[2] initiated a systematic study of the ozonation of primary, secondary, and tertiary aliphatic amines in which the alkyl groups are varied as to whether they are primary, secondary, or tertiary. A working hypothesis was presented in the preceding papers[1-3] as a rationale for the reactions found both by us and others to occur during the ozonation of amines. This involved the formation of an initial amine–ozone adduct (I, eq 1) followed by three fates thereof: (a) loss of molecular oxygen with formation of an amine oxide (II, eq 2) or further reaction products thereof; (b) an intramolecular side-chain oxidation; (c) homolytic dissociation to a nitrogen cation radical (III) and the ozonate anion radical (IV, eq 3), followed by reactions of these. Paper II[3] reported the results of ozonation of tri-*n*-butylamine, a tertiary amine with primary alkyl groups, for which the major competitive fates of the amine–ozone adduct (I) were amine oxide formation (eq 2) and side-chain oxidation. Paper III[1] discussed the ozonation of *t*-butylamine, a primary amine having a tertiary alkyl group, for which the major fates of I were those of eq 2 and 3.



(1) Part III: P. S. Bailey and J. E. Keller, *J. Org. Chem.*, **33**, 2680 (1968).

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