other rabbit. Samples of blood for red cell counts were drawn from the same ear vein immediately before each injection of germanium, and the results are given in Table V. The first rabbit received a total of 13.2 g. of $(CH_3)_2Ge(OH)_2$, which corresponds to a total dose of 7.0 g. of germanium (or 3.8 g. germanium per kg. of body weight) in the increasing doses, but showed no toxic effects whatever.

Discussion

The fact that no local or systemic toxicity was observed in any of the animals receiving dimethylgermanium oxide indicates that the organometallic grouping remains intact, in keeping with the marked resistance of the same group to oxidation or hydrolysis *in vitro*.[5] A more decisive answer could be obtained by determining the germanium excreted as dimethylgermanium oxide and as germanium oxide over a considerable period after injection; the total germanium could be determined spectrographically, but a good method for differentiating between the inorganic and the organometallic germanium at the expected levels has not yet been developed.

While there is considerable variation between the hemoglobin levels of different control hamsters, the level for a particular animal is quite constant over the relatively short time of the tests (Table I). This is the reason for giving the results for individual animals, rather than an average for the group. Hemoglobin determinations with a Hellige hemometer are subject to an error of ±5%, however, and while the spread between the duplicate determinations usually was less than this and sometimes as little as ±1.5%, no significance can be attached to a change of less than 10% during the test. The red cell counts are subject to about the same error, and while most of the duplicate determinations checked closely, no dependence can be placed on a change of less than 10%, or about 800,000 erythrocytes per cu. mm.

With the limits defined in this way, it must be concluded that the subcutaneous injection of dimethylgermanium oxide does not markedly influence the normal hemoglobin level of the animals used, nor does it change the normal concentration of erythrocytes. It appears that there may be an initial depression of both the hemoglobin and red cell values for hamsters for a period of one to three days after injection, followed by a recovery. A similar marginal effect was noticed in the experiment with rabbits.

Summary

The subcutaneous administration of an aqueous solution of dimethylgermanium oxide to small animals, up to a level of 1 g. of germanium per kg. of body weight either in one dose or cumulatively, produces no noticeable toxic effects that might be expected to occur if the $(CH_3)_2Ge$ group underwent *in vivo* hydrolysis or oxidation. The normal hemoglobin and red cell contents of the blood are not appreciably changed by the same dose.

CAMBRIDGE, MASS. RECEIVED NOVEMBER 21, 1949

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF OREGON STATE COLLEGE]

The Exchange Reaction of Sulfur Dioxide with Concentrated Sulfuric Acid[1]

BY T. H. NORRIS

The exchange of oxygen atoms between compounds containing sulfur(IV) and sulfur(VI) was first investigated by Voge[2] using radioactive sulfur. He observed no exchange in thirty-six hours at 100° between sulfite and sulfate in either basic or 0.1 *N* acid solution. He did observe a slow exchange at 335° between sulfur dioxide and sulfur trioxide gases, which was accelerated by the presence of water, or of platinized asbestos.[3] Some experiments[4] on the exchange of sulfur dioxide with concentrated, radioactive sulfuric acid have been performed and the results, while somewhat lacking in internal consistency, indicate roughly: (1) at room temperature, negligible exchange in forty-eight hours; (2) at 100°, 5% exchange in forty-eight hours; (3) at 280°, complete exchange in less than five hours.

The last results, when compared with those for the gas phase reaction on the one hand, and the approximately neutral aqueous reaction on the other, are evidently of considerable interest. Since, unfortunately, they are rather rough and qualitative, it was felt that they would bear repetition and extension. The present report, accordingly, presents further work on the exchange: $SO_2 + H_2S^*O_4 \text{ (concd.)} \rightleftarrows S^*O_2 + H_2SO_4 \text{ (concd.)}$. It has been found that the rate is conveniently measurable in the range 160 to 210°, with a normal temperature coefficient, confirming, in a general way, Harmon's[4] results, except for his rate at 100°, which is much too high.

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[1] Published with the approval of the Oregon State College Monographs Committee. Research Paper No. 144, Department of Chemistry, School of Science.

[2] Voge, THIS JOURNAL, **61**, 1032 (1939).

[3] The kinetics of the gas phase exchange, $SO_2 + S^*O_3 \rightleftarrows S^*O_2 + SO_3$, have since been investigated in detail (J. L. Huston and T. H. Norris, to be published). The rate, for intensively dried gases, in Pyrex, is conveniently measurable in the range 400–440° and has a normal temperature coefficient. The reaction is heterogeneous and strongly catalyzed by water (as Voge indicated), but the data are irreproducible and involved. Contrary to Voge's postulate, the rate-determining step seems not to be $SO_3 \rightleftarrows SO_2 + {}^1/_2O_2$.

[4] K. M. Harmon, Master's Thesis, University of California, Berkeley, 1944.

Experimental

Radioactivity Procedure.—Radioactive sulfur was obtained from the Atomic Energy Commission. This was furnished, carrier free, in irradiated potassium chloride which contained, besides S^{35}, T = 87.1 days: K^{42}, T = 12.4 hr.; P^{32}, T = 14.3 days; and Cl^{36}, T = 2 × 10^6 yr. After the potassium had decayed to a low level, the material was dissolved in potassium hydroxide solution, and the sulfur oxidized to sulfate by the addition of bromine water. The solution was then acidified with hydrochloric acid, a small amount of potassium sulfate carrier added, and radioactive barium sulfate was precipitated. This was filtered off and Cl^{36} was salvaged by recrystallization of potassium chloride. Possible coprecipitation of P^{32} with the barium sulfate was not a cause for concern, since the ensuing experiments were not performed until about ten months after this purification. By this time, at any rate, the sulfur was radioactively pure, as shown by its decay rate and its self-absorption curve.

Measurements were made with an end-window counter (Tracerlab, TGC-2; 1.95 mg./sq. cm. mica). The samples were counted as barium sulfate mounted in thin layers (3-10 mg./sq. cm.) on Tracerlab "cupped planchets." Corrections were applied for decay and self-absorption, the latter on the basis of a curve empirically prepared. This curve differed slightly from data in the literature,[5] but the variation was such as to produce in the range of measurements, at the most a 6% error (usually much less); this is well within the present experimental accuracy.

Preparation of Reactants.—Sulfur dioxide from a commercial cylinder was purified of sulfur trioxide and moisture by passage through two concentrated sulfuric acid bubblers and a phosphorus pentoxide tube. It was frozen with liquid air and permanent gases were removed by pumping to a high vacuum.

Concentrated sulfuric acid containing radiosulfur was made by dissolving 91 mg. of barium sulfate of high specific activity in 5 ml. of C. P. sulfuric acid (96%), to give a clear solution. The barium sulfate was then reprecipitated by adding 5 ml. of water; the bulk of the S^{35} remained in solution. The solution was cleared by centrifugation, decanted and then brought up to strength by the addition of the calculated amount of fuming sulfuric acid. The resulting concentration, determined by duplicate titrations and density measurement (the latter is rather insensitive in this concentration range), was 97.2 ± 0.1%. The specific activity of the acid was determined, after precipitation of a portion of barium sulfate for counting, as 100 counts/min./mg. barium sulfate (sample thickness 1.2 mg./sq. cm.) at the beginning of the experiments. All other activities were corrected to this time and thickness as a matter of convenience.

Run Procedure.—Runs were made in sealed Pyrex tubes, of uniform shape and volume (10 ± 1 ml.). If, as is highly probable, the reaction occurs in the liquid phase, the apparent rate (as calculated for Table I) would, for constant p_{SO_2}, vary inversely with the total volume (a large volume of inactive sulfur dioxide dilutes that sulfur dioxide which is being radioactivated by the sulfuric acid): hence the necessity for uniform tube volume. In every case 1 ml. of radioactive sulfuric acid was measured, with a volumetric pipet, into a tube, which was then attached by a ground joint to the vacuum line, exhausted ($<10^{-3}$ mm.) and filled with sulfur dioxide to ~430 mm. (395 ± 5 mm. at 0°). The tube was then sealed off before the gas had dissolved to any extent in the acid, the latter being a fairly slow process. Calculation from solubility data[10] shows the equilibrium amount of gas dissolved in the acid to be ~67% at 25°, decreasing to ~5% at 211°. Room temperature runs were literally just that; all others were made in conventional laboratory ovens, which left something to be desired in the way of temperature control. This was undoubtedly the largest source of experimental error. Nonetheless, an inspection of Fig. 1 will show that reasonably self-consistent results were obtained.

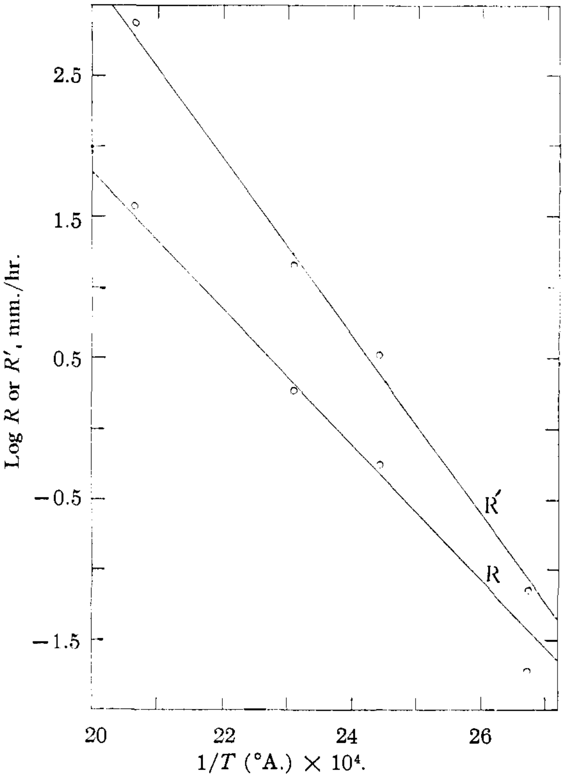

Fig. 1.—Temperature dependence of exchange rate.

The room temperature runs were agitated during most or all of their course. In the other runs, the tubes lay undisturbed, on their sides in order to give the maximum surface exposure. However, since the high temperature coefficient (Fig. 1) indicates that this is not a diffusion controlled process, considerations of this sort seem of little importance.

At the completion of a run, the reaction tube (equipped with a break-off tip) was broken *in vacuo* and the sulfur

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(5) Henriques, Kistiakowsky, Margnetti and Schneider, *Ind. Eng. Chem., Anal. Ed.*, **18**, 349 (1946). These authors' Geiger counter data are best fitted by a self-absorption coefficient, α, of 0.27 sq. cm./mg. in their expression

$$I = I_0\left(\frac{1 - e^{-\alpha d}}{\alpha d}\right)$$

(d = sample thickness in mg./sq. cm.). The present data yield, over the same range (0–12 mg./sq. cm.), α ~ 0.235, and, over the entire range of measurement (0–50 mg./sq. cm.), α ~ 0.215. These data lack the nicety of the earlier work, so are not to be overly stressed; on the other hand, the geometry, etc., differed somewhat for the two cases. The present samples were counted as barium sulfate mounted on metal and placed 1.0 cm. from the counter window, whereas, in the former case, benzidine sulfate was used, mounted on paper, placed ~2 mm. from the window. Incidentally, Huston,[6] using geometry described elsewhere,[7] has counted barium sulfate on metal and obtained, on the basis of data much less extensive than Henriques and co-workers, α ≐ 0.23 (0–18 mg./sq. cm.). It is gratifying to find that the present data, when plotted as a "saturation" curve,[7,8] "saturate" at a thickness of 26–29 mg./sq. cm. This compares favorably with an expected value of 28.3 mg./sq. cm., obtained by subtracting from the absorption limit (in aluminum) of S^{35}, 31.4 mg./sq. cm.,[9] the effective thickness of air and counter window that the sulfur betas must penetrate.

(6) J. L. Huston, private communication.

(7) Yankwich, Rollefson and Norris, *J. Chem. Phys.*, **14**, 131 (1946).

(8) Libby, *Ind. Eng. Chem., Anal. Ed.*, **19**, 2 (1947).

(9) Solomon, Gould and Anfinsen, *Phys. Rev.*, **72**, 1097 (1947).

(10) Milbauer, *Bull. soc. chim. (France)*, [5] **3**, 221 (1936).

dioxide was separated from the acid by exhaustive pumping with a Töpler pump. The room temperature results (Table I) showed this procedure to be satisfactory. The sulfur dioxide was then absorbed in 1 *N* sodium hydroxide, oxidized with bromine water, acidified and precipitated as barium sulfate for counting. Since the sulfuric acid concentration was much greater than that of the sulfur dioxide in the experiments, the specific activity of the former remained constant and equal to 100 c./m./mg. Therefore, in a given run, the final specific activity of the sulfur dioxide gave a direct measure of the per cent. attainment of exchange equilibrium.

Results and Discussion

The experimental results are summarized in Table I.

TABLE I

EXCHANGE BETWEEN SULFUR DIOXIDE AND CONCD. SULFURIC ACID

T, °C.	Time, hr.	Sp. act. SO_2[a] c./m./mg., or % exchg.	Rate, mm./min.	Rate'[b] mm./min.	Half-time
~25	21	−0.1 ± 0.1[c]	Unobservable		
~25	1367	<0.4[d] ± 0.1	<0.001	<0.002	>27 yr.
101	332	1.6 ± 0.2	0.020	0.073	1.6 yr.
137	154	19.0 ± 0.3	0.543	3.19	20.5 da.
135	251	30.6 ± 0.4	0.585	3.44	
160	7.0	3.8 ± 0.2	2.1	17.1	6.2 da.
160	52.3	18.8 ± 0.3	1.53	12.2	
211	1.50	14.2 ± 0.2	40.6	811	7.5 hr.
211	3.00	22.5 ± 0.3	33.5	670	

[a] Counted as barium sulfate and corrected for decay and self-absorption. For complete exchange the specific activity in every case would have been 100, hence the identity of specific activity and per cent. of exchange equilibrium. [b] Rate' = 100 rate/% SO_2 in liquid. See Discussion. [c] Calculated standard deviation. [d] Actual activity of sample counted was 3 c./min.

All runs are directly comparable, being nearly identical in every respect except temperature and time. An exchange reaction must follow a first order course[11,12] and since in the present experiments there was always a large excess concentration of sulfuric acid, the rate of exchange, *R*, in mm./hr. (mm. at 0°), is given by

$$R = -(2.3\, p_{SO_2}/t) \log (1 - F)$$

where $F = \%$ exchange/100 and t is the run time in hours. Values of per cent. exchange and of *R* are given in the third and fourth columns, respectively, of Table I. For a given temperature, *R* should be constant; it may be seen that the experimental error is not inconsiderable. The half-times for exchange are shown in the last column as averages for each temperature.

These data may be compared with Harmon's[4] since conditions were rather similar, except that his sulfur dioxide pressures were approximately twice as great and he used 96% acid. It seems unlikely that these factors would *greatly* influence the rate. Harmon's result at 280° seems to be corroborated, but the rate at 100° is slower than he indicated (1.6% exchange in fourteen days as against 5% in two days). The 100° rate is particularly interesting in that, as compared with Voge's[2] results in approximately neutral solution (no exchange in thirty-six hours), an acceleration of the reaction by concentrated acid is no longer necessarily indicated and, though plausible, still remains to be demonstrated.

It is apparent from the high temperature coefficient (~1.8 per 10° in the range 160–170°, from Fig. 1) that the reaction rate is not limited by diffusion, since such rates increase approximately as $\sqrt{T}$. Rather a chemical process is rate-determining. Figure 1 gives a plot of log *R* *vs.* $1/T$, °A. (lower curve), the points being averages for each temperature from Table I. From this, one may calculate an apparent activation energy of 22.0 kcal./mole. The experimental data for the three highest temperatures give a reasonable approximation to a straight line; the fourth point (101°) is less satisfactory, but this represents only one run, and that, necessarily since the reaction was here so slow, of considerably lower presumptive accuracy than the other runs. The activity of the sample on which this point is based amounted to only 50% above background. It would appear that, over the range of measurement, but one reaction mechanism is involved.

Table I includes an approximately two-months-long room temperature run. Since in this case the actual measured activity amounted to only about 10% over background (*i. e.*, ~3 c./min.!) little weight can be placed on the numerical value of *R*, except as an upper limit. The value expected from an extrapolation of Fig. 1 is lower by a factor of fifty-two.

If, as seems probable, the reaction occurs in the liquid phase, the data at different temperatures are not strictly comparable, since, while the total concentration of the gas remains constant, the fraction dissolved in the liquid decreases rapidly with temperature. On the assumption that the rate is proportional to the sulfur dioxide concentration in the liquid, a correction has been made by dividing *R* by this fraction, to obtain *R'*, given in the fifth column of Table I. This fraction was estimated approximately on the basis of published solubility data for 90.8% sulfuric acid.[10] The solubility in 98% acid at 20° is only ~30% different. The upper line in Fig. 1 is a plot of log *R'* *vs.* $1/T$. As may be seen, the fit of the data is improved; this may, of course, be fortuitous. The corrected activation energy becomes 28.8 kcal./mole.

Since the exchange is essentially an oxidation of sulfur dioxide by sulfuric acid and since hot concentrated sulfuric acid is normally considered a good oxidizing agent, it is surprising that the reaction is so slow. It is, however, tremendously faster than the sulfur dioxide–sulfur trioxide gas phase exchange.[2,3] The latter, though, is a surface reaction, so further comparison of the two cases is difficult. Whether the catalysis by water vapor of the gas reaction is to be correlated with

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[11] McKay, *Nature*, **142**, 997 (1938).

[12] Duffield and Calvin, THIS JOURNAL, **68**, 557 (1946).

the higher rate of the exchange in liquid sulfuric acid is not yet entirely apparent.

Speculation on the mechanism of the reaction is tempting, but this must await a more detailed kinetic study; it is planned that such will be undertaken in the near future.

Acknowledgment.—This work was supported by a grant-in-aid from General Research funds administered by the Graduate Council of Oregon State College, for which the author wishes to express his appreciation.

Summary

Using radioactive S^{35} the exchange reaction between sulfur dioxide and sulfuric acid (97.2%) has been investigated over the range from room temperature to 211°. The observed half-times for exchange are: at room temperature, > 27 yr.; at 101°, ~1.6 yr.; at 211°, ~7.5 hr. The temperature coefficient of the rate is, at 165°, ~1.8 per 10°, corresponding to an apparent activation energy of 22.0 kcal./mole.

CORVALLIS, OREGON RECEIVED AUGUST 23, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

Chemical Effects of Steric Strains. II. The Effect of Structure on Olefin Formation in the Hydrolysis of Tertiary Aliphatic Chlorides

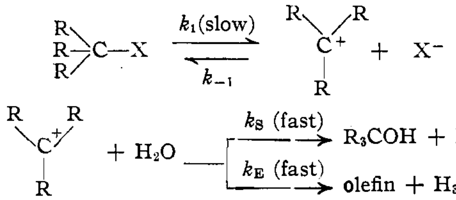
BY HERBERT C. BROWN[1] AND ROSLYN SILBER FLETCHER[1,2]

It has been suggested that the accumulation of three or four alkyl groups on a single carbon atom may constitute a center of strain and that such strain (B-strain) could be an important factor in the reactions of highly branched carbon compounds.[3] To test this hypothesis, a study was made of the rates of hydrolysis of twelve tertiary aliphatic chlorides in 80% aqueous alcohol.[4] The effect of structure on the rates of hydrolysis would be difficult to understand without the assistance of the B-strain concept. The present investigation was undertaken to learn whether the steric strain concept could contribute to an understanding of the effect of structure on olefin formation in the hydrolysis of tertiary chlorides.

The topic of elimination reactions has recently been the subject of an extensive discussion by Hughes and Ingold.[5] These authors conclude that steric effects are "seldom important in unimolecular reactions" and the dominating factor in unimolecular eliminations involves electromeric effects. Unfortunately, Hughes and Ingold base their conclusions on the study of eliminations involving but two different tertiary alkyl radicals, *t*-butyl and *t*-amyl. The present study of structural effects of some twelve different tertiary alkyl radicals permits a more detailed analysis of influence of structure on the course of the elimination reaction.

Results

Hughes and Ingold have offered convincing evidence that the hydrolysis of tertiary chlorides in aqueous solvents proceeds through the mechanism[6]



Therefore, determination of the quantity of olefin and of hydrogen ion formed in a given period of time yields the fraction of olefin present in the product. This quantity is identical with the ratio $k_E/(k_E + k_S)$, where k_E is the unknown rate constant for the elimination reaction and k_S is the unknown rate constant for the substitution reaction. The results are summarized in Table I.

TABLE I

OLEFIN FORMATION IN THE HYDROLYSIS OF TERTIARY ALKYL CHLORIDES AT 25° IN "80%" AQUEOUS ETHANOL[a]

	Alkyl chloride, R′R″R‴CCl	R′	R″	R‴	$k_E/(k_E + k_S)$
1	*t*-Butyl[b]	Me	Me	Me	0.16
2	*t*-Amyl[c]	Me	Me	Et	.34
3	Dimethyl-*n*-propylcarbinyl	Me	Me	*n*-Pr	.33
4	Dimethylisopropylcarbinyl	Me	Me	*i*-Pr	.62
5	Dimethyl-*n*-butylcarbinyl	Me	Me	*n*-Bu	.35
6	Dimethyl-*t*-butylcarbinyl	Me	Me	*t*-Bu	.61
7	Dimethylneopentylcarbinyl	Me	Me	neo-C_5	.65
8	Methyldiethylcarbinyl	Me	Et	Et	.41
9	Triethylcarbinyl	Et	Et	Et	.40
10	Diethylisopropylcarbinyl	Et	Et	*i*-Pr	.80
11	Diethyl-*t*-butylcarbinyl	Et	Et	*t*-Bu	.90
12	Methyldiisopropylcarbinyl	Me	*i*-Pr	*i*-Pr	.78

[a] Density d^{25}_4 0.8496. [b] Cooper, Hughes and Ingold, *J. Chem. Soc.*, 1280 (1937), report 17% olefin. [c] Hughes and McNulty, *ibid.*, 1283 (1937), report 33% olefin.

Discussion

The Steric Factor in the Elimination Reaction.—According to the steric strain hypothesis, an increase in the size and bulk of the three alkyl groups, R, of a tertiary halide, R_3CX, should result in an increase in the strain at the tertiary carbon atom. Since such strain would be mark-

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[1] Present address: Department of Chemistry, Purdue University.

[2] Parke, Davis and Company Fellow at Wayne University, 1945–1947.

[3] Brown, *Science*, **103**, 385 (1946).

[4] Brown and Fletcher, THIS JOURNAL, **71**, 1845 (1949).

[5] Hughes, Ingold, *et al.*, *J. Chem. Soc.*, 2038–2119 (1948).

[6] Hughes and Ingold, *Trans. Faraday Soc.*, **37**, 657 (1941).