a limit with the introduction of three acetyl groups for each glucose residue.

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THE REACTIVITY OF ATOMS AND GROUPS IN ORGANIC COMPOUNDS. XII. THE PREPARATION AND PROPERTIES OF MIXED ALIPHATIC ETHERS WITH SPECIAL REFERENCE TO THOSE CONTAINING THE TERT.-BUTYL RADICAL

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The influence of structure on the lability of bonds in organic molecules is shown in a marked degree by compounds which contain a tertiary radical. For example, the *tert.*-butyl alcohol reacts with concentrated hydrochloric acid over 200,000 times as rapidly as does *n*-butyl alcohol. It seemed of interest, therefore, to determine whether or not the facts accumulated in connection with the study of the lability of the carbon–oxygen and of the hydrogen–oxygen bonds in alcohols[2] by means of rates of reaction could be utilized in devising improved methods for the preparation of ethers and esters. A study of these classes of compounds from the standpoint of their relative reactivities with reagents would lead to a fuller understanding of the influence of structure on the lability of atomic linkings.

Certain *tert.*-butyl alkyl ethers have been prepared by the commonly used methods, but the results, as measured by yields and purity, have been far from satisfactory. One of the methods used is based on the view that the mechanism of ether formation from alcohols involves the intermediate formation of an alkyl sulfuric acid and consequently concentrated sulfuric acid was used to bring about the reaction between *tert.*-butyl alcohol and ethyl alcohol. Since the acid rapidly converts the tertiary alcohol into polymers of isobutylene, the yields obtained were very small.

When the Williamson synthesis is used difficulties are encountered as the result of the unique behavior of compounds containing a tertiary radical. Sodium *tert.*-butylate is formed very slowly and reacts very slowly with alkyl halides. The chief reaction between tertiary alkyl halides and the sodium derivatives of normal alcohols is the removal of hydrogen halide from the alkyl halide. When these methods are used the yields are also very small.

[1] From the thesis of George Wayne Rigby submitted in partial fulfilment of the requirement for the degree of Doctor of Philosophy, 1930.

[2] (a) Norris, *Rec. trav. chim.*, **48**, 885 (1929); (b) Norris, *Z. physik. Chem.*, **130**, 662 (1927); (c) Norris and Ashdown, THIS JOURNAL, **47**, 837 (1925); (d) Norris and Cortese, *ibid.*, **49**, 2640 (1927).

It seemed probable that advantage could be taken of the great reactivity of the hydroxyl group in *tert.*-butyl alcohol and of the alcoholic hydrogen in primary alcohols in the preparation of mixed ethers through the catalytic influence of dilute acids in the way used to prepare esters.

A series of experiments showed that mixed ethers containing the *tert.*-butyl and primary alkyl radicals could be readily prepared in this way. The best yield of *tert.*-butyl ethyl ether, 95% of the theoretical, was obtained when one mole of the tertiary alcohol was added slowly to a boiling mixture of two moles of ethyl alcohol and a 15% aqueous solution of sulfuric acid, the volume of which was about 2.5 times that of the ethyl alcohol. The vapors were passed through a column at such a rate that the minimum boiling mixture of the ether and water was allowed to pass over. Other mixed *tert.*-butyl ethers containing primary radicals were prepared in a similar way.

The fact that the hydrogen of the hydroxyl group in secondary alcohols is much less reactive than the corresponding atoms in primary alcohols necessitated a change in conditions where an attempt was made to prepare *tert.*-butyl isopropyl ether. When 15% sulfuric acid was used the reaction was very slow with the resultant formation of large quantities of isobutylene. In order to increase the rate, a greater molecular ratio of the secondary alcohol was used and to decrease the decomposition of the tertiary alcohol an aqueous solution of sodium hydrogen sulfate was employed as the catalyst. The yield of the mixed ethers was 82% of the theoretical.

The formation of mixed ethers containing secondary and primary alkyl radicals was next investigated. The reactivity of the hydroxyl group in secondary alcohols is very much less than that of the same group in tertiary alcohols. The results of the study of the preparation of ethers of this class were found to be in accord with this fact. Much higher concentrations of sulfuric acid were required to bring about the reaction. The product in all cases was a mixture of the three possible ethers. The differences between the reactivities of the hydroxyl groups in primary and secondary alcohols is not sufficiently great to lead to the formation of only the mixed ether as was the case when *tert.*-butyl alcohol was used. By varying the amount and the concentration of sulfuric acid the ratio of mixed ether to simple ethers could be changed. In one experiment with *sec.*-butyl alcohol and ethyl alcohol when 50% sulfuric acid was used the total yield of the three ethers amounted to 49.5% of the theoretical of which 8% was diethyl ether and 72.5% *sec.*-butyl ethyl ether. The tendency for a larger proportion of the mixed ether to form is in accord with the differences in reactivity of the hydroxyl group and the hydrogen atoms in primary and secondary alcohols.

A number of ethers were prepared by the methods outlined above and by the application of the Williamson synthesis, which gave satisfactory

results when primary and secondary alcohols were used. Especial care was taken to obtain the ethers in a very pure condition since the physical constants recorded in the literature are not concordant. The boiling points, densities and indices of refraction were determined and are recorded in the experimental part of this paper.

One of the chief objects of this research was the study of ethers containing two different alkyl radicals to determine if their reactions are in accord with the relative reactivities of the carbon–oxygen bonds present as determined by a study of the rates at which these bonds react when present in the corresponding alcohols. It was expected that the ethers containing the *tert.*-butyl radical would show unusual reactivity, and the results proved to be in accord with the expectation. The reactions studied were those with hydrochloric acid, sulfuric acid, acetic acid, acetyl chloride, benzoyl chloride and acetic anhydride.

The aliphatic ethers are more or less soluble in solutions of hydrochloric acid. It has been shown that certain ethers form molecular compounds with hydrogen chloride at low temperatures.[3] It is highly probable that these addition products are oxonium compounds. It is possible that such compounds are formed when ethers dissolve in aqueous solutions of hydrochloric acid. It is to be expected that the tendency of the oxygen atom in ethers to form oxonium compounds would vary with the radicals which they contain. A quantitative study of the solubilities of the isomeric butyl ethyl esters was accordingly made. The solubility of an ether is determined by the concentration of the acid and the temperature. The results are shown in Figure 1. The relative solubilities of the butyl ethyl ethers in the same concentration of acid and at a definite temperature vary markedly with the structure of the butyl radicals. The solubilities show a striking relationship with the labilities of the bond linking the butyl radicals to the oxygen atom, the more labile the bond the greater the solubility. If oxonium compounds are present in the solution, it follows that the tendency for oxygen to exhibit oxonium valencies is determined by the lability of the bond linking the oxygen atom to carbon—the more reactive this bond, as measured by the rate at which it is broken by hydrochloric or hydrobromic acid, the greater the tendency to form oxonium compounds with hydrochloric acid.

It is a striking fact that with decreasing temperature the molecular ratio of the ether to hydrogen chloride in the solution approaches one to one.

The isomeric butyl ethyl ethers react extremely slowly at room temperature with concentrated hydrochloric acid, with the exception of the *tert.*-butyl compound. When *tert.*-butyl ethyl ether and concentrated hydrochloric acid in the molecular ratio of one of the former to five of the latter are mixed the ether dissolves, but is rapidly converted into *tert.*-butyl

³ Maass and McIntosh, THIS JOURNAL, **34**, 1274–1290 (1912).

chloride, which separates.   When such a mixture was allowed to stand overnight 99% of the theoretical quantity of the chloride was obtained.

In order to get a definite idea of the effect of the structure of the butyl radical on the lability of the carbon–oxygen linkage in these ethers, the rates of the reactions with hydrochloric acid at 25° were measured.   The ethers were dissolved in the acid in a vessel so constructed that the volume of the chloride formed could be measured.   The tubes were sealed, placed in a thermostat and the volume of chloride noted from time to time. Density determinations of the products showed that they were the pure butyl chloride corresponding to the ether used.
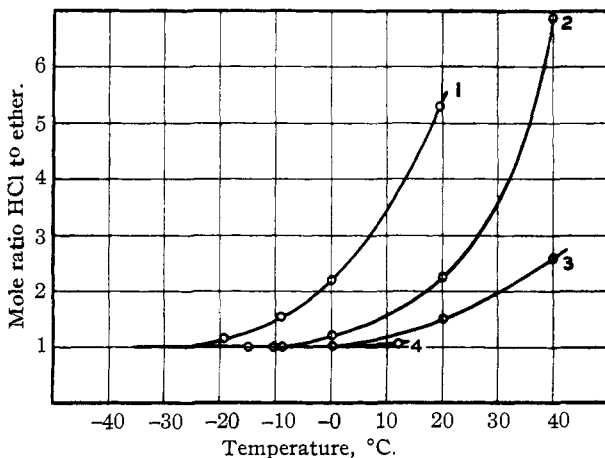
(1) *Iso*-butyl ethyl ether, (2) *n*-butyl ethyl ether, (3) *sec.*-butyl ethyl ether, (4) *tert.*-butyl ethyl ether.

Fig. 1.—Solubilities of isomeric butyl ethyl ethers in 35.21% hydrochloric acid.

There was an induction time before the chlorides separated.   In order to have the results comparable zero time was taken when a measurable amount of chloride had separated—1 to 3% of the theoretical amount. When velocity constants were calculated on the assumption that the reaction was one either of the first or second order, the values of the constants obtained dropped off rapidly after 50% of the calculated amount of chloride had separated.   In order to avoid postulation in regard to the order of the reaction as the cause of the change in the value of the constant, the results are represented in Table I as time required for the several reactions to proceed to the extent of 25%.   These values serve to compare the relative reactivities of the bonds involved.

Experiments 1, 2 and 3 show the effect of change in structure of the butyl radical on the rate at which the carbon–oxygen bond is broken by concentrated hydrochloric acid with the consequent formation of the

TABLE I

FORMATION OF BUTYL CHLORIDES FROM THE ISOMERIC BUTYL ETHYL ETHERS

No.	Compound	Temp., °C.	Mol. ratio compd. to HCl	Concn. of HCl, %	Time in hours to 25% conversion
1	n-Butyl ethyl ether	25.0	1:18.8	35.21	768
2	Sec.-butyl ethyl ether	25.0	1:18.8	35.21	105
3	Iso-butyl ethyl ether	25.0	1:18.8	35.21	1250
4	Tert.-butyl alcohol	0.0	1:10	26.75	1.6
5	Tert.-butyl methyl ether	.0	1:10	26.75	3.5
6	Tert.-butyl ethyl ether	.0	1:10	26.75	0.83

butyl chlorides. The order of reactivity is the same as that previously obtained in the study of the rates at which the corresponding butyl alcohols react with aqueous solutions of hydrobromic acid, with the formation of the butyl bromides.

The tertiary butyl ethers react so rapidly with concentrated hydrochloric acid at 25° that it was necessary to study them under different conditions. Experiments 4, 5 and 6 show the effect of the change from H to CH_3 and to C_2H_5 on the lability of the bond linking the carbon atom of the butyl radical to oxygen. The results bring out an important point. When the alcoholic hydrogen atom in methyl alcohol and that in ethyl alcohol are replaced by a p-nitrobenzoyl radical, the former reacts about twice as rapidly as the latter.[2c] The results in the table show that when similar ethers of these alcohols are converted into the respective alcohols the ethyl ether reacts almost five times as rapidly as the methyl ether. When RO—H is converted into RO—R' the reaction is more rapid when R is CH_3 than when it is C_2H_5. When RO—R' is converted into RO—H the reverse is true. These results bring out the important fact, often overlooked, that the relative lability of a bond, as measured by rates of reactions, is not a fixed property of the radical but is determined both by the nature of the radical itself and the nature of the group with which it is brought into combination in the reactions studied. It has been shown, for example, that tert.-butyl chloride reacts much more rapidly with water than does n-butyl chloride, but that the tertiary chloride reacts more slowly with potassium iodide than does the normal chloride.[4] The relative lability of the carbon–chlorine bonds in the two chlorides is different when measured by different reagents. In one case chlorine is replaced by hydroxyl and in the other by iodine. It should be noted in this connection that tert.-butyl alcohol reacts rapidly with hydrochloric acid, whereas it reacts much more slowly with hydriodic acid. These facts and those of a similar nature must be considered in comparing the relative activating effects of radicals on atomic linkings.

The action of sulfuric acid with the ethers was studied. One mole

[4] Conant and Hussey, THIS JOURNAL, **47**, 476 (1925).

of normal or isobutyl ethyl ether dissolves in one mole of concentrated sulfuric acid. When ice is added to the mixture the ethers are recovered unchanged. All the *tert.*-butyl ethers are quickly decomposed by concentrated sulfuric acid. If the temperature of the mixture is allowed to rise the higher polymers of isobutylene are obtained. If the reactants are cooled to 0° and mixed so that the temperature does not rise, the polymer formed is almost entirely tri-isobutylene. When heated with dilute sulfuric acid (10%) the tertiary ethers are slowly hydrolyzed; at the same time some isobutylene is formed.

All the butyl ethyl ethers react at room temperature with acetyl chloride in the presence of zinc chloride. Two reactions occur: the one yielding *n*-butyl chloride and ethyl acetate takes place to the extent of 34%, and the one yielding ethyl chloride and *n*-butyl acetate, 58%. Both the ethyl–oxygen and the *n*-butyl–oxygen bonds are broken. At 60° the chief products are ethyl chloride and butyl acetate. The effect of increase in temperature on the relative labilities of the two bonds is marked in the case of the two normal radicals.

At room temperature isobutyl ethyl ether gives chiefly isobutyl acetate and ethyl chloride. At 80° the reaction produced a number of products among which were *tert.*-butyl chloride and isobutylene. The bond broken in the ethers containing secondary and tertiary radicals is the one between these radicals and oxygen. *Sec.*-butyl ethyl ether at room temperature in the presence of zinc chloride gave only *sec.*-butyl chloride and ethyl acetate. *Tert.*-butyl ethyl ether under these conditions reacted rapidly and gave a theoretical yield of *tert.*-butyl chloride and ethyl acetate.

Acetic anhydride did not react with the ethers at room temperature or at 100° in the absence of a catalyst. Reaction did take place slowly at room temperature in the presence of zinc chloride. In all cases the pure acetates containing the two radicals were formed.

New methods of preparing *tert.*-butyl acetate which yielded the compound in a state of high purity are described in the experimental part of this paper. The ester was converted rapidly by concentrated hydrochloric acid into *tert.*-butyl chloride and acetic acid. The preparation and properties of *tert.*-butyl benzoate, prepared for the first time, also are given.

The work shows clearly the practical value from the standpoint of the synthesis of organic compounds of the results obtained from the study of the reactivity of bonds as measured by rates of reactions. They also give additional information in regard to the mechanism of ether formation under the influence of sulfuric acid. The older view of Williamson that an alkyl sulfuric acid is formed as an intermediate product does not appear to apply in the case, at least, of the ethers containing the *tert.*-butyl radical. Experiments showed that there was no evidence of the formation of an

alkyl sulfuric acid when ethyl alcohol alone, or mixed with *tert.*-butyl alcohol, was heated at 70° with 15% sulfuric acid. The solutions when cooled and carefully titrated showed the presence of the amount of sulfuric acid used. The fact that primary, secondary, and tertiary alcohols required different strengths of acid to bring about the formation of ethers is in accord with the relative stabilities toward water of the addition products of the alcohols and sulfuric acid.

Even in the case of a primary alcohol it is doubtful whether or not the mechanism involves the intermediate formation of an alkyl sulfuric acid. It has been shown by Barbet[5] that diethyl ether is best prepared, with a yield of 95% or better, when alcohol is passed through concentrated sulfuric acid heated to 140°. When alcohol vapor was passed into ethyl sulfuric acid at the same temperature the yield was 70% and much sulfur dioxide was evolved.

Experimental Details

Materials Used.—The most convenient way to purify the four butyl alcohols is to fractionate their constant boiling mixtures with water. The products obtained in this way, which boiled within 0.5°, were dried, first with potassium carbonate and then with lime, and were fractionated. The alcohols obtained boiled within 0.1°.

In some of the larger scale preparations involving the use of *tert.*-butyl alcohol, a commercial sample of the alcohol was used, which was found to contain 10% of water but was otherwise quite pure.

The acetic anhydride when distilled in an all-glass apparatus boiled at 137°. The acetyl chloride was obtained from a so-called "practical" sample. Seven distillations with precautions against superheating were necessary to obtain a product that boiled constantly at 50.9° (corr.) at 760 mm. and had the density d_4^{25} 1.0922. The chloride reacted very slowly when added to a large volume of cold water. A sample remained in contact with bright sodium chips for nine months at room temperature without apparent action. Care was used in the preparation because the constants given in the literature are not concordant and because it was found that the presence of impurities in the chloride affected its behavior with the ethers studied. The boiling point obtained agrees with that given by Thorpe.[6]

The benzoyl chloride used boiled at 198° at 760 mm. and at 77° at 2 mm. pressure.

The alkyl halides were prepared from the alcohols and aqueous solutions of the acids and gave constants in agreement with the literature.

Determination of Boiling Points.—Distillations were carried out through columns of the Vigreux type fitted with condensing heads and covered with insulating material. In the final purifications and the determinations of boiling points vacuum jacketed spiral columns of the Davis[7] type were used.

In the distillations heat was supplied from an electric heater connected in series with a slide-wire rheostat. Attention was paid to the heat furnished and the amount of reflux. Under the conditions used the flat portion of a distillation curve of the pure compound included almost the entire sample, with a variation in temperature of less than 0.05°.

5 Barbet, British Patent 100,406 (1915) and 101,724 (1916).
6 T. E. Thorpe, *J. Chem. Soc.*, **37**, 188 (1880).
7 Davis, *Ind. Eng. Chem., Anal. Ed.*, **1**, 61 (1929).

The distillation curve of a sample of *tert.*-butyl ethyl ether serves to detect the presence of a trace of *tert.*-butyl alcohol, which can be separated only with great difficulty.   The shape of the curve makes it possible to detect as little as 0.05% of the alcohol and a smaller quantity of water.

The physical constants of the *tert.*-butyl ethers reported in the literature show that the compounds have not been hitherto prepared in a state of purity.   Samples prepared by the published methods gave the constants reported, but when distillation curves were made the presence of impurities was evident.   The behavior of the ethers with certain reagents is affected by the presence of these impurities.

The careful study of the problem leads to the conclusion that accurate distillation curves made with an efficient column are a better criterion of purity than density determinations.   Bennett and Philip,[8] who worked with *tert.*-butyl methyl ether, have expressed the opinion that density is a better criterion of purity than boiling point.

All accurate boiling points were determined with short range "normal glas" Anschütz thermometers, graduated to 0.2°.   They were compared with thermometers calibrated by the Reichsanstalt and by the United States Bureau of Standards.   Corrections were made for atmospheric pressure.

Determinations of Density.—These determinations were made with a glass-stoppered Sprengel tube having a capacity of about 13.5 cc.   The temperature was 25 ± 0.005°.   The weights were checked against a set calibrated by the United States Bureau of Standards.   Densities are reported to the fourth decimal place and appear to be accurate to 2 in this place.

Preparation of *Tert.*-butyl Ethers.—*Tert.*-butyl methyl ether was made by the methods described in the literature.   The preparation from sodium *tert.*-butylate and methyl iodide[9] gave a yield of 60% of a product which boiled at 53–55°, and was difficult to purify.   The yield, by similar methods, of the ethyl ether was 50%, of the *n*-propyl ether 25% and the *n*-butyl ether 65%.

Tert.-butyl ethyl ether was also prepared by the action of a small amount of concentrated sulfuric acid on the two alcohols.[10]   The yield of the crude ether was 48%.

Since these methods were not entirely satisfactory, the effect of other catalysts was studied.   Potassium hydrogen sulfate gave good results.   When a mixture of 10 cc. of commercial 90% *tert.*-butyl alcohol, 6 cc. of ethyl alcohol (95%) and 1.3 g. of powdered potassium hydrogen sulfate was distilled very slowly, the yield of crude ether (b. p. 64 to 70°) was 91% of the theoretical.

The best practical method of preparation was found to involve the use of dilute sulfuric acid as a catalyst.   In this way the methyl, ethyl, *n*-propyl and *n*-butyl ethers derived from *tert.*-butyl alcohol were prepared.   The details of the preparation of one ether by this process, which is new, are given below.

Preparation of *Tert.*-butyl Ethyl Ether.—In a 3-liter flask are mixed 988 cc. of distilled water and 98 cc. of pure sulfuric acid (sp. gr. 1.84).   When the solution has cooled, 0.5 g. of powdered silicic acid to ensure regular boiling and 450 cc. of 95% ethyl alcohol are added.   The flask is attached to a 2-bulb Wurtz column by means of a stopper which carries a 100-cc. separatory funnel and a thermometer.   A thermometer is inserted in the column, which is connected with a condenser and heat is applied.   When the temperature in the flask reaches 70°, 100 cc. of *tert.*-butyl alcohol (90%) is added from the funnel.   The product is distilled slowly, care being taken by the regulation of the supply of heat to keep the temperature of the issuing vapors at 64°, which is the boiling point of the minimum boiling mixture of the ether and water.   From 0.5 to 0.75

[8] Bennett and Philip, *J. Chem. Soc.*, 1930 (1928).

[9] Henry, *Rec. trav. chim.*, **23**, 329 (1904).

[10] Mamontroff, *J. Russ. Phys.-Chem. Soc.*, **29**, 230 (1897).

cc. of distillate collects per minute. From time to time 25 cc. of the butyl alcohol is added until the total amount is 350 cc. The final distillate measures about 460 cc.

The product is washed in a separatory funnel repeatedly with 25 cc. of water. From ten to fifteen treatments are necessary to remove the last traces of *tert.*-butyl alcohol. When all the alcohol has been removed, the two layers separate instantly and completely, leaving the ether layer absolutely clear. The product is shaken with potassium carbonate and finally dried by refluxing over sodium for one hour. The pure ether boils at 73.1°. The yield is 95% of the theoretical calculated from the *tert.*-butyl alcohol used.

In the above directions the alcohols are in ratio of approximately one of butyl alcohol to two of ethyl alcohol. The excess of the latter serves to hasten the reaction and diminishes the formation of isobutylene. An efficient column is not advisable during the preparation as it holds back the ether and partial decomposition takes place in the flask. The distillation should not be stopped and the mixture left overnight because 15% sulfuric acid in the presence of ethyl alcohol slowly converts *tert.*-butyl alcohol, on standing, into isobutylene and its polymers.

If larger quantities of the crude ether are to be separated from *tert.*-butyl alcohol, it is preferable to redistil the product with a large amount of water and collect a second time the minimum boiling mixture of the ether.

A saturated aqueous solution of *tert.*-butyl ethyl ether contains at 25° 1.3% and at 0° 3.4% of the ether.

According to Henry[9] *tert.*-butyl methyl ether reacts slowly with sodium. This observation was no doubt due to the fact that the sample studied contained some of the butyl alcohol from which it was prepared. A sample of the highly purified ether was heated with sodium in a sealed tube at 90° for six weeks; only slight superficial action on the metal was observable.

The preparations of the following mixed ethers containing the *tert.*-butyl radical were made according to the directions just given, using the alcohols in the molecular ratio of one of the tertiary to two of the primary alcohol: methyl, *n*-propyl, and *n*-butyl. On account of the boiling points, the tertiary alcohol must be added very slowly in the preparation of the *n*-butyl ether. The yields of the purified ethers were CH_3, 95%; C_2H_5, 95%; n-C_3H_7, 68%; n-C_4H_9, 51.5%.

Preparation of Tert.-butyl Isopropyl Ether.—Isopropyl alcohol reacts with *tert.*-butyl alcohol more slowly than does *n*-propyl alcohol. When the ether is prepared under the conditions used in making the *n*-propyl compound, the yield is reduced as the result of the formation of isobutylene by the long continued action of the dilute sulfuric acid. It was found that an aqueous solution of sodium hydrogen sulfate gave excellent results. The ether was prepared as follows.

In a 500-cc. flask with three necks were placed 120 cc. of water, 22 g. of sodium hydrogen sulfate, 70 cc. of isopropyl alcohol and 0.5 g. of silicic acid. In one neck of the flask was placed a 2-bulb Wurtz column, in the second a dropping funnel and in the third a thermometer which extended into the liquid. Heat was applied and 50 cc. of *tert.*-butyl alcohol (90%) allowed to drop in slowly during ten hours. The distillate boiling at 70–71° was collected. The yield of the crude ether was 82% of the theoretical. The product was purified in the way described above. The ether boiled at 87.6° and had the density 0.7365_4^{25}.

Henry[11] reports that this ether boils at 75–76° and has the density 0.7734^{20}. We obtained a product that boiled constantly at 77.2° and had the density 0.7543_4^{25}. It reacted rapidly with sodium, however. After repeated treatment with the metal the ether had the boiling point and density recorded above. It was not affected by sodium.

[11] Henry, *Rec. trav. chim.*, **23**, 329 (1904).

n-Butyl Ethyl Ether.—This ether was prepared from sodium butylate and ethyl bromide. It was purified by shaking with a mixture of one volume of sulfuric acid and one volume of water and by fractional distillation. Its physical properties are given in Table II.

Preparation of Sec.-butyl Ethyl Ether.—This compound has not been described. It was prepared as follows: to 1 liter of anhydrous *sec.*-butyl alcohol (b. p. 99.5°) was added 8.5 g. of sodium. When the metal had dissolved, 25 cc. of pure ethyl bromide was added and the mixture allowed to stand for two days. Ten grams of sodium was added and later 25 cc. of ethyl bromide and the mixture allowed to stand for two days. The process was repeated until 175.5 cc. of ethyl bromide had been used. The product was distilled and the part boiling between 80 and 85° collected. This was mixed with 1 liter of water, distilled, and the portion boiling at 67–72° collected. This was re-distilled with water and the portion boiling at 71–72° collected. The ether was sepa-rated, dried, refluxed with sodium and fractionated. The physical properties are given in Table II.

Preparation of Sec.-butyl Ethyl Ether with Sulfuric Acid as Catalyst.—The forma-tion of an ether from a secondary and a primary alcohol requires a much higher con-centration of sulfuric acid than is needed when one of the reactants is tertiary alcohol. A series of experiments was made with 25 cc. of *sec.*-butyl alcohol and 25 cc. of ethyl alcohol. When 100 cc. of 25% sulfuric acid was used, no ether was formed. With 400 cc. of 40% acid the yield was 5.5%. With 300 cc. of 50% acid the yield of the three ethers was 49.5% calculated as the secondary ether formed. When 150 cc. of 75% acid was used the crude ethyl ether in the product amounted to 38%. No ethers were formed when a 15% solution of sodium hydrogen sulfate was used. The products in all cases contained the three possible ethers, the mixed ether predominating. This fact is in accord with the labilities of the bonds involved.

Isobutyl Ethyl Ether.—This ether was prepared from isobutyl alcohol (b. p. 107.9), sodium and ethyl bromide. The yield of purified ether was 66%.

Preparation of Isopropyl Ethyl Ether.—In the study of the formation of this ether from the alcohols and sulfuric acid the following results were obtained.

When 200 cc. of isopropyl alcohol, 300 cc. of ethyl alcohol and 534 cc. of sulfuric acid (75%) were used the yield of ethers formed was 77.5% calculated as isopropyl ethyl ether. The mixture on fractionation was shown to contain 34% diethyl ether and 61% isopropyl ethyl ether. A series of experiments showed that the yield of ethers decreased with decrease in the strength of the acid, but that the proportion of mixed ether increased.

When 25 cc. of each alcohol was slowly distilled with 200 cc. of 50% acid, the yield of the product, which was shown to be chiefly the mixed ether, was 33.8%.

The isopropyl ethyl ether boiled at 53–54° and had the density 0.720_4^{25}.

In all the preparations the reaction was very slow. Fourteen hours were required to complete the experiments noted above.

Preparation of *Tert.*-butyl Acetate.—This compound was prepared by a number of different methods. The method described in the literature[12] furnishes a yield of impure ester of 45% of the theoretical.

When 10 cc. of *tert.*-butyl alcohol, 14 cc. of acetic acid and 10 cc. of 15% sulfuric acid were used, the yield of ester was 24%.

When 100 cc. of the alcohol, 78.5 cc. of acetic acid and 100 cc. of an aqueous solution of sodium hydrogen sulfate were used, the yield of ester before purification was 65%.

Acetic anhydride gave better results. The ester can be prepared conveniently from commercial 90% *tert.*-butyl alcohol as follows: 100 cc. of the alcohol, 100 cc. of acetic anhydride and 1 g. of zinc dust are refluxed for two hours. The product is dis-

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[12] Kondakow, *Bull. soc. chim.*, [3] **7**, 583 (1892).

tilled and the portion boiling below 98° is refluxed with 50 cc. of acetic anhydride. The yield (94%) was 114 cc. of the ester which boiled at 97.8°. Equally good results were obtained when zinc was replaced by magnesium.

Significant results using anhydrous tert.-butyl alcohol were as follows: 10 cc. of the alcohol and 10 cc. of the anhydride reacted under the influence of 0.004 g. of anhydrous zinc chloride. On standing for twelve hours at room temperature, or by refluxing for one hour, the yield of crude ester was the theoretical.

The preparation of the ester from the alcohol and acetyl chloride furnished an explanation of the behavior of tertiary alcohols with acyl chlorides. It has been concluded in the past that tertiary alcohols behave abnormally in their reactions with acyl chlorides in that tertiary halides and acetic acid are formed instead of an ester and hydrochloric acid.

In the presence of a molecular quantity of dimethylaniline, a 98% yield of the ester was obtained. In the absence of the amine and when heated to boiling for ten minutes, 50% ester and 50% chloride were formed. When the temperature was kept below 20°, a quantitative yield of the chloride was formed.

These facts show that the primary reaction between the alcohol and the acyl chloride is the formation of the ester. The latter subsequently reacts with the hydrochloric acid and is converted into the butyl chloride. The ester is rapidly converted into the chloride by concentrated hydrochloric acid.

When tert.-butyl acetate (5 cc.) was refluxed with methyl alcohol (1 cc.) and 2 drops of concentrated sulfuric acid, the chief product was methyl acetate.

Preparation of Tert.-butyl Benzoate.—Twenty cc. of anhydrous tert.-butyl alcohol, 24.4 cc. of pyridine and 16.8 cc. of benzoyl chloride were mixed. Heat was evolved and white crystals separated. The next day the mixture was treated with water and the oil dried and distilled at 2 mm. pressure. The yield of the ester was 80%. Its physical properties are given in Table II.

The compound decomposed completely into isobutylene and benzoic acid when distilled at atmospheric pressure. Dilute sulfuric and hydrochloric acids hydrolyze it rapidly; it appears to be quite stable toward a solution of sodium hydroxide.

TABLE II

PROPERTIES OF CERTAIN MIXED ETHERS AND COMPOUNDS CONTAINING THE Tert.-BUTYL RADICAL

The compounds marked with an asterisk, some of the indexes of refraction, and the minimum boiling mixtures with water are reported for the first time.

Compound	Boiling point, °C., at 760 mm. (corr.)	Minimum b. p. with water, °C., at 760 mm. (corr.)	d_4^{25}	n_D^{25}
Tert.-$C_4H_9OCH_3$	55.2	51	0.7354	1.3667
Tert.-$C_4H_9OC_2H_5$	73.1	64	.7364	1.3728
*Tert.-C_4H_9O-n-C_3H_7	97.4	81	.7472	1.3830
Tert.-C_4H_9O-n-C_4H_9	124	88	.758	1.3928
Tert.-C_4H_9O-iso-C_3H_7	87.6	71	.7365	1.3773
*Tert.-$C_4H_9OC_2H_4OC_2H_5(\beta)$	147	94	.829	1.4170
*Sec.-$C_4H_9OC_2H_5$	81.2	71	.7377	1.3753
Iso-$C_4H_9OC_2H_5$	81.1	69	.7323	1.3739
n-$C_4H_9OC_2H_5$	92.3	75	.7447	1.3798
Tert.-C_4H_9Cl	50.7	49	.8370	1.3828
Tert.-$C_4H_9OOCCH_3$	97.8	76	.8593	1.3838
*Tert.-$C_4H_9OOCC_6H_5$	96 (2 mm.)	..	.9928	1.4896

Chemical Reactions of the Mixed Ethers with Acetic Acid.—None of the highly purified ethers reacted with glacial acetic acid at room temperature or when heated at 100° for forty-eight hours. The reported formation of the acetate from *tert.*-butyl ethyl ether was no doubt due to the presence of the alcohol in the ether used. In the presence of a trace of sulfuric acid this ether was converted almost quantitatively by acetic acid into ethyl acetate and *tert.*-butyl alcohol. The latter may not have been the primary products of the reaction since it was shown, as stated above, that *tert.*-butyl acetate is converted by methyl alcohol in the presence of sulfuric acid into methyl acetate and the tertiary alcohol.

At room temperature there was no reaction between any of the ethers and acetic acid in the presence of zinc chloride.

With Acetyl Chloride.—There was no reaction between the ethers and acetyl chloride in the absence of a catalyst. All the mixed ethers reacted slowly with acetyl chloride at room temperature in the presence of anhydrous zinc chloride.

When *n*-butyl ethyl ether was used and the reactants were allowed to stand for twenty-one days in a sealed tube, the products obtained were separated and determined. The reaction which led to the formation of ethyl acetate and normal butyl chloride took place to the extent of 33.6% when measured by the amount of the former product and 36.6% by the amount of the latter. The reaction by which *n*-butyl acetate and ethyl chloride were formed was found to be 58.3% from the former and 58.6% from the latter. At 60° the reactions by which ethyl acetate and *n*-butyl acetate were formed took place to the extent of 23 and 76%, respectively.

When isobutyl ethyl ether was allowed to stand with acetyl chloride and zinc chloride at room temperature for sixteen days, the ethyl acetate reaction took place to the extent of 22.8% (from ethyl acetate formed) and 21% (from *n*-butyl chloride) and the *n*-butyl acetate reaction 65% (from acetate) and 64% (from ethyl chloride).

When *sec.*-butyl ethyl ether was used the products, after twelve days, were as follows: 95.6% ethyl acetate and 76.5% secondary butyl chloride.

Tert.-butyl ethyl ether reacted rapidly at room temperature. After standing overnight the theoretical yield of ethyl acetate and *tert.*-butyl chloride was obtained. The same result was obtained when the mixture was heated for ten minutes.

With Benzoyl Chloride.—All the ethers reacted at room temperature with benzoyl chloride in the presence of zinc chloride. The reaction was slower than with acetyl chloride. Analogous products were obtained—*n*-butyl ethyl ether gave 86% *n*-butyl benzoate, after standing for sixty-one days; the isobutyl ether 62.5% isobutyl benzoate; the *sec.*-butyl ether 98% *sec.*-butyl chloride and the *tert.*-butyl ethyl ether, on standing for twelve hours, gave 99% of *tert.*-butyl chloride and ethyl benzoate.

With Acetic Anhydride.—The ethers did not react at room temperature. In the presence of zinc chloride the results were as follows: *n*-butyl ethyl ether in sixty-two days, 13% each of butyl acetate and ethyl acetate; the isobutyl ether in sixty-two days, 8% of the two acetates; the *sec.*-butyl ether in forty-three days, 23%; *tert.*-butyl ethyl ether, overnight, 82%. In all cases the two acetates were formed in equivalent amounts.

Zinc dust can be used instead of zinc chloride. When equivalent quantities of *tert.*-butyl ethyl ether and acetic anhydride were refluxed with zinc dust for two hours, a quantitative yield of the two esters was obtained.

Zinc Chloride as Catalyst.—Zinc chloride does not act as a true catalyst in the reaction described above. When acetic acid, acetyl chloride, or acetic anhydride was used, the chloride at first dissolved and later zinc acetate separated in crystalline form. The salt was identified by its melting point, 342.5–343° (uncorr.) and by its properties. The reactions brought about by zinc chloride took place when zinc acetate or magnesium dust was used.

At room temperature zinc chloride does not decompose the mixed ethers, but forms a compound with them. When a solution of zinc chloride in *tert.*-butyl methyl ether which had stood for eighty-one days was opened there was no evidence of the presence of an unsaturated hydrocarbon. When the excess of the ether was removed an oil was obtained which decomposed at 80° and yielded a gas which showed the properties of methyl chloride. When the evolution of gas ceased, the product was heated to 165°; at this temperature there was a second evolution of gas, which proved to be an unsaturated hydrocarbon. When some of the liquid obtained by heating the addition product to 165° was treated with concentrated hydrochloric acid, *tert.*-butyl chloride was formed.

Summary

1. The results of the previous study of the relative reactivities of the hydroxyl group and the hydrogen of this group in the three classes of alcohols have been utilized in devising new and improved methods for the preparation of certain mixed ethers.

2. Mixed ethers which contain the *tert.*-butyl radical and a methyl, ethyl, *n*-propyl, *n*-butyl or isopropyl radical can be prepared conveniently with satisfactory yields, when the two alcohols are heated with a 15% aqueous solution of sulfuric acid or of sodium hydrogen sulfate.

3. In order to prepare ethers containing a secondary and a primary radical, the strength of the acid to effect the reaction must be 50% or greater. In all cases the three possible ethers are formed, the mixed ether being produced in the largest amount.

4. The results indicate that the mechanism of the formation of ethers with the use of sulfuric acid does not involve the intermediate formation of an alkyl sulfuric acid. An addition product of an alcohol and sulfuric acid is probably the active material involved.

5. A number of mixed ethers have been prepared in a very pure condition and their physical constants determined.

6. The behavior of a number of mixed ethers with hydrochloric acid, sulfuric acid, acetic acid, acetyl choride, benzoyl chloride and acetic anhydride has been studied. The results obtained are in accord with labilities of the bonds involved, as determined by rates of reactions.

7. *Tert.*-butyl acetate and benzoate have been prepared by new and improved methods and their behavior studied.

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