Fig. 4.—Infrared analysis: aromatics from the dehydrogenation at 240° of the destructively hydrogenated pinane.

Fig. 5.—Infrared analysis: aromatics from the dehydrogenation at 300° of the destructively hydrogenated pinane.

Summary

The fission of one of the rings in pinane, isocamphane and isobornylane was investigated.

Pinane on destructive hydrogenation in the presence of a nickel–kieselguhr catalyst yielded about 13% of 1-methyl-4-isopropyl- and 5% 1-methyl-2-isopropylcyclohexane, 65% of 1,1,2,3- and 10% of 1,1,2,5-tetramethylcyclohexane. The disubstituted cyclohexanes were se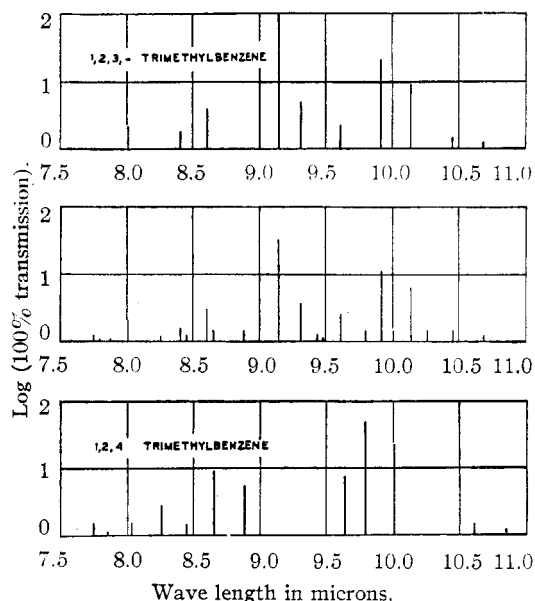parated from the polymethylated cyclohexanes by selective dehydrogenation. The dehydrogenation of the tetramethylcyclohexanes yielded the corresponding 1,2,3- and 1,2,4-trimethylbenzene. The aromatic hydrocarbons were identified by chemical means and by infrared analysis.

Isocamphane and isobornylane yielded on destructive hydrogenation a mixture of compounds which consist probably of alkylated cyclopentanes.

Hydroxyalkylation with Cyclic Alkylene Esters. I. Synthesis of Hydroxyethylapocupreine

BY WARNER W. CARLSON AND LEONARD H. CRETCHER

The hydroxyalkylation of phenolic cinchona alkaloid derivatives has been reported in previous publications[1] from this department. The reagents normally employed in such syntheses, alkylene oxides or halohydrins, were found to give low yields of the desired products, presumably because of quaternary salt formation. A two-step procedure finally was developed[1b] whereby a benzyloxyalkyl toluenesulfonate was treated with an alkali salt of the phenolic alkaloid to give a benzyloxyalkyl ether derivative; removal of the benzyl grouping by acid hydrolysis then afforded the desired hydroxyalkyl cinchona ether. The toluenesulfonate procedure, while it represented a defi-

nite improvement, in terms of yield, over methods previously employed, still was not found to be completely satisfactory. Accordingly, the search for new hydroxyalkylating agents was continued, and two such substances, the cyclic sulfite and carbonate esters of ethylene glycol, are now reported. Through the use of one of these, ethylene carbonate, the hydroxyethylation of a typical phenolic alkaloid, apocupreine, has been accomplished in good yield under mild conditions.

Only one previous instance of the use of a cyclic glycol ester as an alkylating agent has been found in the literature. By the action of silver sulfate on ethylene bromide in xylene, Baker and Field[2] prepared ethylene sulfate (I) in low yield,

(1) (a) Butler, Nelson, Renfrew and Cretcher, THIS JOURNAL, 57, 575 (1935); (b) Butler and Renfrew, ibid., 60, 1473 (1938).

(2) Baker and Field, J. Chem. Soc., 86 (1932).

$$H_2C\!-\!CH_2 \quad\quad H_2C\!-\!CH_2 \quad\quad H_2C\!-\!CH_2$$

I	II	III
Ethylene sulfate	Ethylene sulfite	Ethylene carbonate
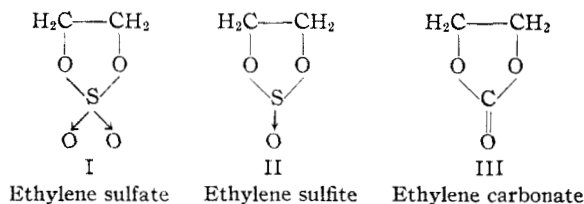
and found that it reacted with catechol to yield the cyclic ethylene ether; apparently neither mono- nor di-hydroxyethyl ether derivatives were formed. Because of the apparent lack of ability to act as a hydroxyethylating agent, we did not consider ethylene sulfate as worthy of further investigation, and our attention was turned to the more readily available compounds, ethylene sulfite (II) and ethylene carbonate (III).

The usefulness of the dialkyl sulfites as alkylating agents is known, and has been discussed by Voss and Blanke.[3] The ability of cyclic alkylene sulfites to function in this manner has not been investigated previously. Ethylene sulfite (II) was prepared in 1926 by Majima and Simanuki[4] through the action of thionyl chloride on glycol, but no study of its chemical properties was reported.

In our preliminary work with ethylene sulfite, β-naphthol was used as the phenolic substrate. Hydroxyethylation of this substance was not successful in aqueous alkaline solution, due to the readiness with which II is hydrolyzed under these conditions. Similarly, alkylation in alcoholic solutions of the alkali phenate was only partially successful, although by use of an excess of ethylene sulfite satisfactory yields of hydroxyethyl-β-naphthyl ether were obtained. Reaction with the alkali phenate suspended in an indifferent solvent such as toluene, or with the free phenol dissolved in toluene containing suspended potassium carbonate, proceeded readily at 90 to 100°, and gave the desired product in high yield.

Ethylene sulfite was also found to react with β-naphthol under neutral or acidic conditions, although in these cases much higher reaction temperatures were required. Heated with β-naphthol in the temperature range of 170 to 200°, ethylene sulfite reacted slowly with evolution of sulfur dioxide. Considerable decomposition occurred, however, and the yield of the hydroxyethyl ether was low. With the addition of a small amount of an acidic condensing agent such as concentrated sulfuric acid or, better, benzene- or toluenesulfonic acid, the reaction proceeded at a satisfactory rate in the temperature range 135 to 165°. By noting the weight loss due to evolution of sulfur dioxide, the progress of the reaction could be followed readily. Even under the most favorable conditions, however, hydroxyethylation in the presence of an acidic agent failed to approach the yields obtainable by carrying out the reaction with the al-

kali phenate, or with the phenol in the presence of an alkali carbonate. Furthermore, reaction in the presence of an acidic agent yielded a mixture of products; under such conditions either one or both alkyl-oxygen links in the ester apparently can be broken, since both hydroxyethyl β-naphthyl ether and 1,2-di-β-naphthoxyethane were identified in the reaction mixture.

Numerous attempts were made to adapt ethylene sulfite to the use for which the investigation was initiated, the synthesis of hydroxyethylapocupreine, but it was found to have only limited value for this purpose. In the absence of a condensing agent, or in the presence of an acidic condensing agent, the reaction of apocupreine with II resulted in extensive decomposition. Alkaline conditions of reaction were more favorable, but yields of the desired product rarely exceeded 15% of the theoretical, tarry substances again predominating. Similar results were obtained with a simpler nitrogenous phenol, 8-hydroxyquinoline. The reaction resulting in tar formation evidently involves the ring nitrogen atoms, for ethylene sulfite was found to react readily at 60°, and violently at 110°, with either pyridine or quinoline, tarry products being formed. Ethylene sulfite, in common with most esters of inorganic acids, apparently has little value as an alkylating agent for phenols containing basic groupings.

The search for a satisfactory hydroxyethylating agent for phenolic alkaloids such as apocupreine appeared to involve the discovery of an ester in which alkyl-oxygen[5] fission occurred readily at the demand of a reagent containing a phenolic group, but in which there was little or no tendency toward such bond rupture when the reagent was of the nature of a tertiary amine. In general, alkyl-oxygen fission occurs readily only in esters of strong inorganic acids,[6,7] and in these compounds experience indicates that such fission is brought about as readily, or even more so, by a tertiary nitrogen grouping as by the phenolic hydroxyl radical. Ease of quaternary salt formation appears to be a function of the relative strength, in the free state, of the acidic portion of the ester; this likewise is the case with those esters of organic acids which have been found[6] to form quaternary ammonium salts. In view of these facts, and because of the data accumulated on the closely related sulfite ester, it was deemed worthwhile to investigate the ethylene ester (III) of the very weak acid, carbonic acid. Because of the instability of quaternary ammonium carbonates, it was thought likely that the formation of such compounds would not be a complication in the use of III.

With certain recently discovered exceptions,[8]

(3) Voss and Blanke, *Ann.*, **485**, 258 (1931).

(4) Majima and Simanuki, *Proc. Imp. Acad.* (*Tokyo*), **2**, 544 (1926).

(5) The terms "acyl-oxygen" and "alkyl-oxygen," to denote the two alternative types of bond fission in carboxylic esters, were introduced by Day and Ingold, *Trans. Faraday Soc.*, **37**, 686 (1941).

(6) Hammett and Pfluger, THIS JOURNAL, **55**, 4079 (1933).

(7) Ferns and Lapworth, *J. Chem. Soc.*, **101**, 273 (1912).

(8) For a review of the different types, see (a) Kenyon, *Nature*, **148**, 196 (1941); and (b) Balfe, Hills, Kenyon, Phillips and Platt, *J. Chem. Soc.*, 556 (1942).

acyl-oxygen rather than alkyl-oxygen fission is the rule in esters of organic acids reacting in solution; as a result, such compounds usually are of no value as alkylating agents toward phenols. Rather slight basis existed for expecting alkyl-oxygen fission to occur in ethylene carbonate, for Noller and Dutton[9] reported that alkyl carbonates were inert as alkylating agents for phenols; the work of Tronov and Sibgatullin,[10] however, suggested that glycol esters might react in this way. These latter authors determined the reaction rate constants for the conversion by treatment with hydrobromic acid in glacial acetic acid, of various alkyl acetates into the corresponding bromides, a reaction which clearly involves alkyl-oxygen fission in the esters. The relative reaction rates for the different acetates were determined to be: isobutyl, 1; isoamyl, 5; butyl, 6; hexyl, 7; propyl, 9; s-butyl, 10; isopropyl, 11; ethyl, 11.25; methyl, 65; allyl, 391.6; ethylene (glycol), 1.01×10^3; t-butyl, 1.96×10^6. This glycol ester thus was shown to have an enhanced tendency toward rupture of the alkyl-oxygen bond, though its activity in this respect still was less than that of the ester containing the t-butyl radical, a grouping definitely known[11] to favor alkyl–oxygen fission. As developed more fully in the experimental section, ethylene carbonate was in fact found capable of hydroxyethylating apocupreine in good yield, and with an almost total absence of the tars commonly resulting from use of the usual alkylating agents.

Preliminary work with β-naphthol demonstrated that in its reactions ethylene carbonate (III) did not resemble organic esters in general or the dialkyl carbonates, but behaved similarly to ethylene sulfite. Alkylation of β-naphthol in aqueous alkali was not successful, the ester being lost rapidly through hydrolysis. Moderate yields could be obtained in alcoholic alkaline solution, provided that only a limited amount of solvent was employed; in the presence of excess alcohol, loss of III through ester interchange was so rapid that no alkylation was observed. Reaction of III with the alkali phenate, or with the free phenol and an alkali carbonate, either in the absence of a solvent or in the presence of an indifferent solvent, gave hydroxyethyl-β-naphthyl ether in high yield. A modification employing excess ethylene carbonate as solvent, in the presence of an alkali carbonate, was highly satisfactory. In the absence of a condensing agent, or in the presence of an acidic condensing agent, ethylene carbonate reacted with the phenol at higher temperatures, with evolution of carbon dioxide, to yield the hydroxyethyl ether. As before, this method of reaction was not as satisfactory, in terms of yield, as that involving either the alkali phenate, or the phenol in the presence of an alkali carbonate. The carbonate ester varied from its sulfite ana-

log in not showing rupture of both alkyl-oxygen bonds under neutral or acidic conditions, no 1,2-di-β-naphthoxyethane being found in the reaction products.

The condensation of ethylene carbonate with apocupreine or 8-hydroxyquinoline was not successful under neutral or acidic conditions, extensive decomposition occurring. This probably was due to the fact that ethylene carbonate, like its sulfite analog, reacts at elevated temperatures with pyridine or quinoline with evolution of carbon dioxide, forming tarry substances. However, condensation with apocupreine or 8-hydroxyquinoline under alkaline conditions, as described for β-naphthol, proceeded smoothly at temperatures well below those causing this side-reaction, and the hydroxyethyl ether derivatives were formed in good yield. The variation involving the use of excess ethylene carbonate as solvent was especially satisfactory and is the favored mode of reaction for the preparation of hydroxyethylapocupreine.

The investigation has been extended to include the cyclic sulfite and carbonate esters of a variety of glycols, e. g., trimethylene, 2,3-butylene and propylene glycol. The preparation of these various compounds, and their use, along with II and III, in the hydroxyalkylation of phenols, amines and mercaptans will be discussed in subsequent publications.

Experimental

Ethylene Sulfite (II).—Majima and Simanuki[4] prepared II in moderate yield by heating an excess of thionyl chloride with ethylene glycol; much better yields were obtained here when conditions similar to those used by Suter and Gerhart[12] for the synthesis of dibutyl sulfite were employed. Ethylene glycol (83.7 g., 1.35 mole) was added to a flask equipped with a stirrer, thermometer, gas outlet tube, and dropping funnel. An equimolar quantity of thionyl chloride (160 g.) was divided into two portions of 40 and 120 g. Preliminary trials indicated that during addition of the first quarter of the thionyl chloride, no gas evolution occurred and considerable heat was evolved; during addition of the remainder of the acid chloride, copious evolution of hydrogen chloride took place, and heat was absorbed. The 40-g. portion was therefore added slowly with sufficient cooling to maintain the reaction mixture in the range 35 to 40°. During addition of the 120 g., heat was applied as necessary to maintain the same reaction temperature. After addition of the thionyl chloride was complete, the mixture was heated at 70° for fifteen minutes, then distilled through an 18-inch Vigreux column; yield of fraction b. p. 86–88° (38 mm.), 131 g., 90%.

Anal. Calcd. for $C_2H_4O_3S$: S, 29.65. Found: S, 29.52.

Ethylene Carbonate (III).—A number of different methods for the preparation of ethylene carbonate have been reported in the literature: (a) the reaction of glycol with phosgene[13]; (b) condensation of glycol with ethyl chlorocarbonate[14] in the presence of pyridine; (c) the action of ethylene chlorohydrin on concentrated aqueous sodium bicarbonate[15]; (d) ester interchange[16] between glycol and

(9) Noller and Dutton, THIS JOURNAL, **55**, 424 (1935).

(10) Tronov and Sibgatullin, *Ber.*, **62**, 2850 (1929).

(11) Cohen and Schneider, THIS JOURNAL, **63**, 3383 (1941).

(12) Suter and Gerhart, "Organic Syntheses," Coll. Vol. II, 112 (1943).

(13) Nemirowsky, *J. prakt. Chem.*, **28** [ii], 439 (1883).

(14) Allpress and Maw, *J. Chem. Soc.*, **125**, 2259 (1924).

(15) Steimmig and Wittmer, German Patent 516,281, November 15, 1928.

(16) Morgan and Cretcher, THIS JOURNAL, **68**, 781 (1946).

diethyl carbonate; and (e) condensation of ethylene oxide with carbon dioxide.[17] With the exception of process (e) all the various preparations were tested, but method (d) was found to be the most convenient for synthesis of the compound on a laboratory scale. As carried out here, the process has been described by Morgan and Cretcher.[16]

Hydroxyethylation of β-Naphthol. 1. Under Neutral or Acidic Conditions. A. With Ethylene Sulfite.— Ethylene sulfite and β-naphthol, heated together in equimolar quantities to 190–200°, reacted slowly with evolution of sulfur dioxide. Considerable decomposition occurred, however, and β-hydroxyethyl naphthyl ether could be isolated from the tarry products only in low yield. The reaction proceeded much more readily in the presence of an acidic condensing agent such as concentrated sulfuric or benzenesulfonic acid, and a typical example is given below.

Ethylene sulfite (5.4 g.), β-naphthol (7.2 g.) and benzenesulfonic acid (0.75 g.) were mixed in a small flask and heated under a reflux condenser in an oil-bath at 150° until evolution of sulfur dioxide had ceased (thirty minutes). The reaction mixture, which had become semisolid during the heating period, was diluted with 40 cc. of ethanol, refluxed for fifteen minutes, chilled, and filtered. The precipitate, 1,2-di-β-naphthoxyethane, was recrystallized from hot ethanol. The silver-gray platelets weighed 4.3 g. (50% yield) and had m. p. 218°. Koelle[18] gives m. p. 217°. The melting point was not depressed on mixture with a sample prepared by the method of Koelle.[18] The filtrate from above was poured with stirring into 200 cc. of cold 2 N alkali, precipitating hydroxyethyl β-naphthyl ether. The product was filtered, washed with water, and dried; wt., 4.5 g. (45.5% yield). Recrystallized from aqueous alcohol, m. p., 77°; Rindfusz, Ginnings and Harnack[19] give m. p., 77–77.5°. The melting point was not depressed on mixture with a sample prepared[19] by the use of ethylene chlorohydrin.

In the example given, 45.5% of the β-naphthol appeared as the hydroxyethyl ether and 50% as the diaryloxyethane compound, for an over-all yield of 95.5%. It was found that the ratio of the two products could be altered by variations in the molar quantities of reactants used, and in reaction temperatures employed.

B. With Ethylene Carbonate.—The reaction of ethylene carbonate with β-naphthol is not influenced as greatly by acidic condensing agents as is the case with ethylene sulfite. A typical reaction under neutral conditions is given below.

Ethylene carbonate (35.2 g., 0.4 mole) and β-naphthol (28.8 g., 0.2 mole) were mixed in a tared flask and heated under a reflux condenser in an oil-bath at 195° for one and one-half hours. At the end of this time the weight loss, due to evolution of carbon dioxide, was 9.5 g. Theoretical loss, based on 0.2 mole, was 8.8 g. The reaction mixture was cooled, diluted with 75 cc. ethanol, and chilled. Since no precipitate of 1,2-di-β-naphthoxyethane was formed, the solution was poured into 300 cc. of cold 3 N alkali. The precipitate of β-hydroxyethyl naphthyl ether was filtered off and washed with cold water. Carbon dioxide was passed into the filtrate until the solution was colorless to phenolphthalein, but no unused β-naphthol was recovered. The precipitate of the hydroxyethyl ether was dissolved in benzene, the solution partially distilled to remove water, and filtered from a small amount of inorganic material. Benzene was removed by vacuum distillation, the residue solidifying on cooling; wt., 38.5 g.; theoretical yield, 37.6 g. The product had a m. p. 72–73°. It was highly soluble in ethanol, again indicating the absence of 1,2-di-β-naphthoxyethane. By repeated crystallizations from aqueous ethanol, β-hydroxyethyl naphthyl ether of m. p. 77° was obtained. A sample of the hydroxyethyl ether, heated at 195° with ethylene carbonate, slowly gave off carbon dioxide, indicating the possible formation of a

polyglycol ether. The synthesis of a small amount of a polyglycol ether is suggested as the explanation for the formation of both carbon dioxide and hydroxyalkyl ether in quantities greater than the theoretical.

2. Under Alkaline Conditions. A. With Ethylene Sulfite.—Sodium hydroxide (4.0 g., 0.1 mole) and β-naphthol (14.4 g., 0.1 mole) were dissolved in 50 cc. of methanol. The solution was evaporated to dryness under reduced pressure, and the residue powdered under 75 cc. of toluene. Two-tenths mole (21.6 g.) of ethylene sulfite was added, and the mixture heated on the steam-bath, with stirring, for one and one-half hours. Fifty cc. of 3 N alkali were added, the mixture transferred to a separatory funnel, shaken, and the aqueous layer removed. The toluene layer was washed with water, dried over sodium sulfate, and the solution taken to dryness under reduced pressure. The residue, β-hydroxyethyl naphthyl ether, crystallized on cooling; weight, 18.5 g., 98% yield. A sample had m. p. 75°, which was raised on recrystallization to 77.5°.

In addition to the above method, the reaction may be carried out in alcoholic solution, provided an excess (two to three molar) of ethylene sulfite is employed. A method employing the free phenol and ethylene sulfite, heated together in toluene in the presence of a molar proportion of potassium carbonate, also gave yields of the hydroxyethyl ether in excess of 90%. In none of these methods was the formation of any 1,2-di-β-naphthoxyethane observed.

B. With Ethylene Carbonate.—The reaction of the dry sodium salt of β-naphthol with ethylene carbonate in the presence of toluene, carried out exactly as described under 2A for the sulfite analog, gave a 94% yield of the hydroxyethyl ether derivative. The modification employing the free phenol, ethylene carbonate and potassium carbonate in the presence of toluene, also was found to be satisfactory, although at least a one-molar excess of the alkylating agent was found to be necessary.

Reaction in the presence of absolute ethanol was found to be partially successful so long as only a limited amount of alcohol was employed as solvent. One-tenth molar quantities of ethylene carbonate and β-naphthol were mixed with 0.2 mole hot ethanol containing 0.1 mole potassium carbonate in suspension. The mixture was heated on the steam-bath, with stirring and under reflux, for one hour. On working up the reaction mixture a 23% yield of the hydroxyethyl ether was obtained, 74% of unchanged β-naphthol being recovered. Under the above conditions, alkyl-oxygen fission in the carbonate ester, resulting in the hydroxyethylation of the phenol, proceeded at a rate sufficiently fast to allow it to compete with destruction of the alkylating agent through ester interchange. A reaction carried out as described, but with one mole of ethanol as solvent, resulted in a practically quantitative recovery of unchanged β-naphthol. In this case, removal of the ethylene carbonate through ester interchange was sufficiently rapid and complete as to prevent alkylation.

Hydroxyethylation of Apocupreine and 8-Hydroxyquinoline. 1. Under Neutral or Acidic Conditions. A. With Ethylene Sulfite.—Ethylene sulfite (10.8 g., 0.1 mole) and apocupreine (3.1 g., 0.01 mole) were mixed in a small flask and heated at 100° for fifteen minutes. Sulfur dioxide was evolved vigorously, the mixture becoming very dark. From the tarry products no hydroxyethylapocupreine could be isolated, although some impure apocupreine was recovered. A similar result was obtained with 8-hydroxyquinoline. An attempt was made to use the sulfate salts of the nitrogenous phenols, but these would not dissolve in ethylene sulfite, even at relatively high temperatures.

The side reaction resulting in tar formation evidently involves the ring nitrogen atoms. Ethylene sulfite (10.8 g.) and pyridine (7.9 g., 0.1 mole) were mixed in a small flask equipped with a reflux condenser, and heated to 110°. A violent reaction occurred, part of the materials being forced out through the condenser by the sudden evolution of sulfur dioxide. The same quantities of these

(17) Vierling, German Patent 740,366, September 2, 1943.

(18) Koelle, Ber., 13, 1954 (1880).

(19) Rindfusz, Ginnings and Harnack, THIS JOURNAL, 42, 157 (1920).

compounds reacted vigorously, with evolution of sulfur dioxide, even when·heated at 60°; the reaction mixture turned blue, then red, and finally deposited a dark-colored oil. No reaction products were isolated.

B. With Ethylene Carbonate.—Apocupreine (3.1 g., 0.01 mole) and ethylene carbonate (13.2 g., 0.15 mole) were mixed in a small flask and heated. The apocupreine dissolved readily, and slow evolution of carbon dioxide began at 110°. At 115° carbon dioxide formation was quite rapid, and the mixture was held at this temperature for twenty-five minutes. On pouring the reaction mixture into cold 3 N alkali, a black gum was deposited, but hydroxyethylapocupreine could not be isolated from this material. On passing carbon dioxide into the alkaline supernatant, some crude apocupreine was recovered. An attempt was made to use apocupreine acid sulfate, but this material would not dissolve in ethylene carbonate until the temperature was raised so high (ca. 140°) that extensive decomposition occurred.

Heating ethylene carbonate with pyridine or quinoline gave results similar to those reported for ethylene sulfite. At 115–120° carbon dioxide evolution was quite rapid, a black, tarry reaction product being formed.

2. Under Alkaline Conditions. A. With Ethylene Sulfite.—Apocupreine (15.5 g., 0.05 mole) and sodium hydroxide (2.0 g., 0.005 mole) were dissolved in 40 cc. of hot absolute ethanol, and 0.2 mole (21.6 g.) of ethylene sulfite added. The mixture was heated under reflux on the steam-bath, with stirring, for two hours. The reaction mixture was poured into 300 cc. of cold 3 N alkali, a red gum being deposited. The product was purified by repeated solution in absolute ethanol, followed by partial precipitation with absolute ether. The final alcohol–ether solution was taken to dryness, the residue dissolved in ethanol, and concentrated hydrochloric acid added to a congo red end-point. The solution was taken to dryness on the steam-bath under reduced·pressure, and the residue crystallized from three volumes of absolute ethanol. There was obtained 1.9 g. (9%) of hydroxyethylapocupreine dihydrochloride. The material, from which it was impossible to remove entirely a pink discoloration, had $[\alpha]_D$ −212.3°.

B. With Ethylene Carbonate.—As has been indicated, the usefulness of ethylene carbonate as an alkylating agent in the presence of hydroxylic solvents is limited due to loss of the material through ester interchange. The low solubility of apocupreine in inert substances such as toluene limited the use of these solvents. Heating and stirring a suspension of the dry sodium or potassium salt of apocupreine in benzene or toluene containing ethylene carbonate was found to give acceptable yields of the hydroxyethyl ether derivative, but the method was not considered satisfactory, especially in that it involved preliminary preparation of the dry alkali salt of the phenol. The observation that ethylene carbonate possesses excellent solvent properties for a wide variety of substances led to the development of the method outlined below.

Apocupreine (31.0 g., 0.1 mole) and ethylene carbonate (176 g., 2 moles) were mixed in a three-necked flask equipped with a mercury-sealed stirrer and thermometer, the other outlet being closed with a "drierite" tube. With continuous stirring the mixture was heated in an oil-bath until the inside temperature was 95°. Potassium carbonate (27.6 g., 0.2 mole) was then added, and heating and stirring continued for one hour, care being taken that

the inside temperature never exceeded 100°. Above this temperature a side reaction resulting in the formation of tarry products begins to be observed. At the end of the reaction period the mixture was cooled to about 50°, diluted with 200 cc. of chloroform and filtered. The chloroform filtrate was transferred to a separatory funnel and extracted with three 30-cc. portions of 5 N hydrochloric acid. The three acidic solutions were united, and extracted twice with 100-cc. portions of chloroform. The chloroform solutions were united, dried, and the solvent removed at reduced pressure. The residue, which crystallized on cooling, consisted of 117 g. of unchanged ethylene carbonate, a 70% recovery of the excess ester used as solvent in the reaction.

The aqueous acidic solution was transferred to a separatory funnel containing 150 cc. of chloroform and some cracked ice. With constant swirling, cold 10 N sodium hydroxide was added until the aqueous layer was distinctly alkaline to phenolphthalein. The aqueous layer was drawn off, and the chloroform solution washed, dried and evaporated to dryness at reduced pressure. The residue was dissolved in ethanol, 20 cc. of concentrated hydrochloric acid added, and the solution taken to dryness under reduced pressure. The product, hydroxyethylapocupreine dihydrochloride, weighed 39.6 g. (93%). It had $[\alpha]_D$ −216.8°.

Twice-repeated digestion of the product with three volumes of absolute ethanol yielded 33.2 g. (78%) of the compound with $[\alpha]_D$ −230.7°.

Isolation of the compound is simpler if recovery of unused ethylene carbonate is not desired. In that case the reaction mixture is poured with stirring into one liter of ice-cold 5 N alkali, the hydroxyethylapocupreine filtered off, washed, dried, dissolved in ethanol and isolated as the dihydrochloride salt.

Tertiary alcohols, which are not very active in ester interchange, may be used to replace 50 to 75% of the excess ethylene carbonate. Dimethylethylcarbinol ("isoamyl alcohol," U. S. I.) was found to be satisfactory.

A number of condensing agents other than sodium or potassium carbonate, e. g., alkaline earth oxides and carbonates, and tertiary amines, were tried, but none was found to be as efficient as the alkali carbonates.

The hydroxyethylation of 8-hydroxyquinoline (88% yield) was accomplished by a method essentially as published[16] for 6-hydroxy-8-nitroquinoline; yield 89%; m. p. 84°; Butler and Renfrew[20] give m. p., 83–84°.

Summary

1. Two new hydroxyethylating agents for phenols, ethylene sulfite, and ethylene carbonate, have been prepared.

2. The reactions of these compounds with β-naphthol under neutral, acidic, and alkaline conditions have been described.

3. The hydroxyethylation of apocupreine in good yield, free from tarry by-products, has been accomplished through use of ethylene carbonate.

(20) Butler and Renfrew, THIS JOURNAL, 60, 1582 (1938).