poured upon 300 g. of ice. The precipitate was taken up in methanol and the solution mixed with dilute sodium hydroxide; the insoluble portion was extracted with ether, which gave 7 g. of crude cinnoline. After distillation and crystallization, 5.5 g. of pure 3,4-diphenylcinnoline (XXVIII), m.p. 151–152°, was obtained (Table IV). The water-soluble portion was a sulfonated benzil hydrazone, as is evident by a comparison of the ultraviolet absorption curves (Fig. 3).

An attempt to cyclize the monophenylhydrazone of phenylglyoxal gave only sulfonation.[14]

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(14) This work was done by G. A. Reynolds, of these laboratories.

ROCHESTER 4, NEW YORK RECEIVED MAY 9, 1951

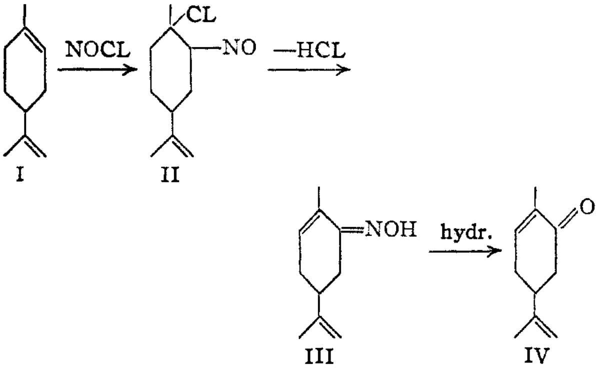
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, EMORY UNIVERSITY]

Conversion of *d*-Limonene to *l*-Carvone[1]

BY E. EARL ROYALS AND SAMUEL E. HORNE, JR.

d-Limonene has been converted into *l*-carvone in over-all yield of 56–60%. *d*-Limonene was converted to the nitrosochloride by the action of ethyl nitrite and hydrogen chloride in ethyl alcohol solution at −5°; the yield was 80%. *d*-Limonene nitrosochloride was dehydrohalogenated to *l*-carvoxime in 90–95% yield by the action of pyridine. Hydrolysis of *l*-carvoxime by refluxing with 5% aqueous oxalic acid under carefully controlled conditions gave *l*-carvone in 78–80% yield.

The conversion of *d*-limonene (I) into *l*-carvone (IV) through the intermediates of *d*-limonene nitrosochloride (II) and *l*-carvoxime (III) was of crucial importance to the determination of the structure of limonene, α-terpineol, terpin and carvone.[2] The conversion of *d*-limonene to the nitrosochloride has been effected by the action of gaseous nitrosyl chloride[3] and by the action of ethyl nitrite,[4] amyl nitrite[4] or nitrogen trioxide[5] in the presence of hydrogen chloride. We have found all of these procedures, as described in the literature, unsuited to the large scale preparation of the nitrosochloride in good yield. Alcohol,[6] alcoholic alkali,[7] sodium methoxide[8] and pyridine[9] have been used for the dehydrohalogenation of *d*-limonene nitrosochloride to *l*-carvoxime. Until quite recently[10] the hydrolysis of *l*-carvoxime to *l*-carvone has received no attention, at least from the preparative viewpoint. After completion of the present work there appeared a report[10] of the preparation of *l*-carvone in 35% over-all yield from *d*-limonene on pilot plant scale utilizing the intermediates II and III. That work differs considerably in detail from the procedures described herein.



The principal contributions of the present work are the development of satisfactory procedures for the conversions of I to II and of III to IV. Satisfactory preparative procedures for these steps, described in detail in the experimental section, have been developed permitting an over-all yield of 56–60% for the conversion of *d*-limonene to *l*-carvone. Gaseous ethyl nitrite, generated by the action of aqueous alcoholic sulfuric acid on sodium nitrite, was passed into *d*-limonene in alcohol solution at −5°; treatment of the resulting solution at −5° with moist hydrogen chloride in the presence of a small amount of water afforded *d*-limonene nitrosochloride in 80% yield. Dehydrohalogenation to *l*-carvoxime was effected by the pyridine procedure of Wallach[9] in 90–95% yield. Hydrolysis of *l*-carvoxime to *l*-carvone without racemization or isomerization was readily effected in 78–80% yield by refluxing with 5% aqueous oxalic acid. The use of dilute (5 *N*) mineral acids led to the formation of carvacrol as the major hydrolysis product. It is interesting to note that 5% oxalic acid has a *p*H of approximately 0.7, the same as the most favorable value reported[10] by Bordence, Allison and Dirstine.

Experimental

Preparation of *d*-Limonene Nitrosochloride.—The method of Wallach[4] was found to be quite suitable for the preparation of *d*-limonene nitrosochloride on a small scale. In our hands, the yields on 0.06 molar scale ranged from 32 to 60% depending upon the temperature of reaction. In general, the yield increased with lower reaction temperature. Quite small yields were obtained when attempt was made to scale up this procedure. Similarly, the procedures of Tilden[3] and of Rupe[5] gave quite low yields of *d*-limonene nitrosochloride on 0.5 molar scale (8–11 and 16%, respectively).

The following procedure was found quite suitable to the preparation of *d*-limonene nitrosochloride on 0.5 molar scale. A mixture of 68.1 g. (0.5 mole) of *d*-limonene and 85 ml. of ethyl alcohol was placed in a 500-ml., three-necked flask equipped with a mechanical stirrer, a thermometer and a gas inlet tube. The flask was surrounded by an ice–salt freezing mixture, and the contents were cooled to −10°. Gaseous ethyl nitrite was passed into the limonene solution while maintaining a temperature of −8 to −10°. The ethyl nitrite was generated by dropping a mixture of 32.2

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(1) This paper is taken from a thesis presented by Samuel E. Horne, Jr., to the Graduate Faculty of Emory University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, August 30, 1950.

(2) H. Goldschmidt and R. Zurrer, *Ber.*, **18**, 1729 (1885); G. Wagner, *ibid.*, **27**, 2270 (1894).

(3) W. A. Tilden and W. A. Shenstone, *J. Chem. Soc.*, **31**, 554 (1877).

(4) O. Wallach, *Ann.*, **245**, 255 (1888); *ibid.*, **252**, 109 (1889).

(5) H. Rupe, *Helv. Chim. Acta*, **4**, 149 (1921).

(6) H. Goldschmidt and R. Zurrer, *Ber.*, **18**, 2220 (1885).

(7) O. Wallach, *Ann.*, **246**, 227 (1888); *ibid.*, **270**, 175 (1892).

(8) A. Hahn, *ibid.*, **369**, 60 (1909).

(9) O. Wallach, *ibid.*, **414**, 257 (1918).

(10) C. Bordence, R. K. Allison and P. H. Dirstine, *Ind. Eng. Chem.*, **43**, 1196 (1951).

g. (0.70 mole) of ethyl alcohol, 39 ml. of sulfuric acid, and sufficient water to make 390 ml. into a mixture of 95 g. (1.38 moles) of sodium nitrite, 32.2 g. (0.70 mole) of ethyl alcohol and sufficient water to make 390 ml. The generator flask was warmed slightly with a warm water-bath from time to time to ensure a steady evolution of ethyl nitrite. After all of the ethyl nitrite had been passed into the alcoholic limonene solution, 10 ml. of water was added, and moist hydrogen chloride was passed into the solution. The reaction was quite exothermic, but the introduction of hydrogen chloride could be so regulated as to maintain a reaction temperature of 0 to −10°, preferably −5°. The moist hydrogen chloride was generated by dropping 114 ml. of concentrated hydrochloric acid (1.5 moles of HCl) into sulfuric acid and passing the evolved hydrogen chloride through concentrated hydrochloric acid. After addition of the hydrogen chloride was complete, the reaction mixture was stirred for about thirty minutes to permit the reaction temperature to drop to −10°. The precipitated *d*-limonene nitrosochloride, 80 g. (80% yield), was filtered with suction and washed with cold ethyl alcohol. The addition of 10 ml. of water to the reaction mixture prior to introduction of hydrogen chloride was found to be absolutely necessary to the isolation of a good yield of product. When anhydrous conditions were maintained, yields of only 9–11% were realized.

A similar procedure using methyl nitrite gave yields of *d*-limonene nitrosochloride of the order of 70%.

Preparation of *l*-Carvoxime.—*d*-Limonene nitrosochloride was dehydrohalogenated by the pyridine procedure of Wallach[9] to afford *l*-carvoxime in 90–95% yield; m.p. 74° (reported[11] m.p. 72°).

Hydrolysis of Carvoxime.—The following procedures were found satisfactory for the hydrolysis of *l*-carvoxime to *l*-carvone:

Procedure A: A mixture of 10 g. (0.06 mole) of *l*-carvoxime and 100 ml. of 5% aqueous oxalic acid was heated to reflux for two hours. At the end of this time, the reaction mixture was steam distilled, and the distillate was extracted with ether. The ethereal solution was dried over sodium sulfate and fractionally distilled to give 7.1 g. (78%) of *l*-carvone.

Procedure B: A mixture of 37 g. (0.22 mole) of carvoxime and 500 ml. of 5% oxalic acid was steam distilled without previous reflux. The distillate was treated as described above to give 20.5 g. of *l*-carvone. Nine grams of carvoxime was recovered from the residue from steam distillation. The yield of *l*-carvone was 80% based on the unrecovered *l*-carvoxime.

The *l*-carvone prepared by either procedure showed the following properties: b.p. 88–90° (4 mm.); $n^{20}\text{D}$ 1.4989; d^{25}_4 0.9673; $[\alpha]^{25}\text{D}$ −54.2°. The properties reported[12] for natural *l*-carvone are: b.p. 97–98° (9 mm.); $n^{20}\text{D}$ 1.4988; d^{15}_{15} 0.9652; $[\alpha]^{20}\text{D}$ −62.46°. Our *l*-carvone gave a semicarbazone, m.p. 140–141.5°; reported[13] m.p. 141–142°.

A mixture of 20 g. (0.12 mole) of *l*-carvoxime and 100 ml. of 5 *N* hydrochloric acid was heated to reflux for 15 minutes. The mixture was steam distilled, the distillate was extracted with ether, and the ethereal solution was dried over anhydrous sodium sulfate. Removal of the ether left 13.3 g. of an oil which was completely soluble in 5% aqueous sodium hydroxide. This oil was characterized as carvacrol through the formation of 2-methyl-5-isopropylphenoxylacetic acid, m.p. 152.0–152.5°; reported[14] m.p. 150–151°. The yield of crude carvacrol was 74%. An attempt to prevent isomerization of carvone to carvacrol by steam distilling the hydrochloric acid solution without reflux led also to carvacrol in 77% yield.

An attempted oxime exchange between benzaldehyde and carvoxime in glacial acetic acid as solvent was unsuccessful; carvoxime was almost quantitatively recovered.

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[11] O. Wallach, *Ann.*, **305**, 324 (1899).

[12] J. L. Simsonsen, "The Terpenes," Second Ed., Vol. I, The University Press, Cambridge, Mass., 1947, p. 396.

[13] H. Rupe and K. Dorschky, *Ber.*, **39**, 2112, 2372 (1906).

[14] C. F. Koelsch, THIS JOURNAL, **53**, 304 (1931).

EMORY UNIVERSITY, GA. RECEIVED MAY 28, 1951

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, EMORY UNIVERSITY]

Studies in Mixed Ester Condensations. II[1]

BY E. EARL ROYALS, JOHN C. HOPPE, A. D. JORDAN, JR.,[2] AND A. G. ROBINSON, III[2]

A study has been made of the acylation of several aliphatic methyl esters with methyl benzoate, methyl furoate, methyl isobutyrate and methyl isovalerate as acylating agents. The lower aliphatic methyl esters have been benzoylated in satisfactory yields under forcing conditions with benzene as azeotropic distillation agent for removal of methyl alcohol and with sodium methoxide as catalyst; a ratio of three moles of aliphatic ester per mole of methyl benzoate was necessary for satisfactory yields. Methyl furoate is a much more active acylating agent for aliphatic esters than is methyl benzoate; yields of the order of 30% of α-furoylated esters were obtained under non-forcing conditions without the use of an excess of the aliphatic ester, while yields of 60–70% were readily obtained using a threefold excess of the aliphatic ester under forcing conditions. Acetic, propionic, *n*-valeric and *n*-caproic esters have been isobutyrylated in approximately 30% yields using a threefold excess of the aliphatic ester and forcing conditions; attempted isobutyrylation of methyl *n*-butyrate led to an inseparable mixture of mixed and self condensation products. Acetic, propionic and *n*-caproic esters were isovalerylated in 21–30% yields using a threefold excess of the aliphatic ester and forcing conditions; attempted isovalerylation of methyl *n*-butyrate and methyl *n*-valerate led to inseparable mixtures of mixed and self condensation products.

It has previously been shown[1] that satisfactory yields of methyl α-benzoylpropionate and of methyl α-benzoyl-*n*-butyrate may be obtained by direct ester condensation provided that an excess of the aliphatic ester is used. It was found that the previously reported poor yields for benzoylation of *n*-butyric esters is due to an unfavorable equilibrium rather than to a preference of the *n*-butyric ester for self condensation, and that a yield of 41% of the mixed condensation product may be obtained by using a fourfold excess of methyl *n*-butyrate and conducting the condensation under forcing conditions.

Although esters fail completely to undergo sodium alkoxide catalyzed acetoacetic ester condensation in benzene solution under non-forcing conditions, it has been found that benzene, rather than an excess of the aliphatic ester, may be used as azeotropic distillation agent for forced benzoylations of aliphatic esters. The use of benzene as azeotropic distillation agent for these forced mixed ester condensations is of considerable practical advantage, since smaller supplies of pure aliphatic ester are required. Assuming that benzoic and aliphatic esters are of comparable reactivity as

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[1] For the first paper in this series, see E. E. Royals, THIS JOURNAL, **70**, 489 (1948).

[2] Taken in part from theses presented by A. D. Jordan, Jr., and A. G. Robinson, III, to the Graduate Faculty of Emory University in partial fulfillment of the requirements for the degree of Master of Science, 1950 and 1951, respectively.