of 0.025 mm; (4) heating one sample in a evacuated tube containing a small amount of hydroquinone.

The rearrangement product in each case was crystallized from petroleum ether. Infrared and ultraviolet spectroscopic studies showed no differences in the rearrangement product, and they were identical with the rearrangement product described earlier.

o-(α-**Methylallyl**)-*p*-**carboxyanisole**-*x*-**C**^{14} was prepared and degraded as described in the previously cited article by ozonolysis. The dimedone derivative of formaldehyde and the semicarbazone of α-(2-methoxy-5-carboxyphenyl)propionaldehyde were purified to constant activity. The analysis of the semicarbazone for carbon previously reported is in error; the found value should be 54.55 instead of 55.55.

The dimedone derivative of formaldehyde, purified to constant radioactivity, was radioassayed for a number of rearrangement products produced under different conditions. The most significant results were obtained in those rearrangements in which a long heating period (280 hr.) was used. The results in c.p.m./mmoles $\times 10^3$ are 494 (a), 483 (b), 496 (b), 493 (a,c), 497 (a,c), and 498 (b,c) where a signifies rate-of-charge method, b signifies planchet method, and c stands for 2 mole % of hydroquinone added.

Oxidation of *o*-(α-**methylallyl**)-*p*-**carboxyanisole**-*x*-**C**^{14} **to 4-methoxyisophthalic acid** was accomplished by means of potassium permanganate in the presence of potassium hydroxide. The crystalline product, m.p. 275–276° (lit.[7] m.p. 275–276°), was found to be *nonradioactive*.

Anal. Calcd. for $C_9H_8O_5$: C, 55.10; H, 4.11. Found: C, 54.91; H, 4.28.

Transformation of the Semicarbazone of α-(**2-Methoxy-5-carboxyphenyl**)**propionaldehyde to** (**2-Methoxy-5-carboxyphenyl**)**acetone, and Its Conversion to Iodoform.**—The semicarbazone (0.32 g.) and sulfuric acid (100 ml., 25%) were refluxed with stirring for 2 hr. The reaction mixture was filtered and after the addition of water, the solid material was heated under reflux. The water insoluble residue was removed (0.13 g.) and the filtrate was extracted with three 75-ml. portions of ether. The ethereal solution was evaporated to dryness and the residue was dissolved in hot water. Upon cooling, a crystalline product (89.2 mg., m.p. 143–144°) was obtained. A second crop (23.8 mg., m.p. 138–140° after sublimation) was collected. The impure semicarbazone of this ketone, 2-methoxy-5-carboxyphenylacetone, melted at 246–247°, about 20° higher than that of the starting material. The ketone (70 mg.) was dissolved in potassium hydroxide (5 ml., 5%) and a solution of iodine in aqueous potassium iodide was added dropwise until a brown color persisted. The solution was decolorized by adding a few drops of aqueous potassium hydroxide. The iodoform was collected after 30 min., dried in a desiccator under nitrogen, and then sublimed. The yield was 40 mg. The rate of charge method for radioassay was 791×10^3 c.p.m./mmole. The semicarbazone of α-(2-methoxy-5-carboxyphenyl)propionaldehyde which was used as starting material for the preparation of the iodoform was obtained by the degradation of a rearrangement product of crotyl-δ-C^{14} *p*-carbethoxyphenyl ether (988×10^3 c.p.m./mmole). The dimedone derivative of the formaldehyde which results from the ozonolysis of the methyl ether of the rearrangement product showed an activity of 210×10^3 c.p.m./mmole. Thus the remainder of the radioactivity resided in the methyl group which was assayed as iodoform.

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A Convenient Preparation of *n*-Alkyl Trityl Ethers and Bis(α-arylethyl)ethers

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In addition to the well known Williamson synthesis,[1] ethers derived from lower aliphatic alcohols are usually prepared by heating the mixture of an alcohol and sulfuric acid at an appropriate temperature. Ethyl ether can also be obtained by passing the vapor of ethanol over heated aluminum oxide.[2] Alkyl trityl ethers result when the corresponding alcohols react with trityl halides in pyridine or with triphenyl carbinol in the presence of an acid. Symmetrical ethers derived from higher and unsaturated alcohols have been reported recently. For example, *p,p′*-dichlorobenzhydrol[4] with 100% sulfuric acid and 3-hydroxycyclopentene[5] with concentrated hydrochloric acid were transformed into their corresponding symmetrical ethers in good yields. We have found that diaryl carbinols and α-phenylethanol can be converted into their corresponding symmetrical ethers by simply passing the solution of the alcohol in a nonhydroxylic solvent such as benzene through an alumina column at room temperature. Although the reaction is not a general method for ether synthesis, it provides, nevertheless, an extremely convenient tool for the preparation of bis(diarylmethyl) and bis(α-phenylethyl) ethers. For example, benzhydrol was converted to benzhydryl ether in practically quantitative yield and α-phenylethanol to bis(α-phenylethyl) ether in 75% yield, while benzyl and *p*-methoxybenzyl alcohols failed to react.

Primary alkyl trityl ethers can also be prepared in good yield by passing a solution of trityl alcohol in a desired primary alcohol through alumina. Methanol and ethanol with triphenyl carbinol each furnished the corresponding ether in approximately 75% yield where isopropyl alcohol failed to furnish either the trityl isopropyl ether or the ditrityl ether. When diphenyl carbinol was treated with alumina in methanol, it yielded neither dibenzhydryl nor benzhydryl methyl ether. The different behavior of triphenyl carbinol and diphenyl carbinol with primary alcohols may be attributed at least partially to the difference of their basicity[6] that, when the acidity of the column toward the carbinol is diminished in the presence of a hydroxylic solvent such as methanol instead of benzene, the concentration of benzhydryl carbonium ion from the less basic diphenyl carbinol becomes too low to effect the formation of any ether.

Experimental

Dibenzhydryl Ether.—A solution of 1 g. of benzhydrol (Eastman, m.p. 68–69°) in 50 ml. of benzene was passed through a column packed with 20 g. of alumina (M. Woelm-Eschwege, acid, activity grade 1) previously wet with petroleum ether (40–60°). The flow was approximately 2 drops per second. Upon concentration, the eluent furnished 0.88 g. of benzhydryl ether, m.p. 90–105°. Crystallization from ethanol raised the m.p. to 110° (lit.[7] m.p. 109–111°). A mixture melting point with an authentic sample was not depressed. The infrared spectrum was obtained in chloroform: 3.4 (w), 3.55 (w), 5.1 (w), 5.2 (w), 5.5 (w), 6.2 (s), 6.7 (s), 6.88 (s), 7.5–7.8 (b), 8.5 (s), 9.2 (s), 9.5 (s), 9.81 (s), 10.9 (m), 11.7 (w).

Bis(α-**phenylethyl**)**Ether.**—A solution of 10 g. of *dl*-α-methylbenzyl alcohol (Eastman, b.p. 204–206°) in 100 ml. of benzene

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was passed through a column packed with 100 g. of alumina as in the previous experiment. Fractionation of the eluent afforded 6.8 g. of bis(α-phenylethyl) ether, b.p. 335–338° (lit.[8] m.p. 335–340°). The infrared spectrum in chloroform showed: 3.2 (w), 3.4 (w), 5.1 (w), 5.2 (w), 5.5 (w), 5.9 (w), 6.2 (s), 6.7 (s), 6.9 (s), 7.3 (s), 7.65 (s), 7.8 (s), 9.2 (s), 9.45 (s), 9.8 (s), 10.5 (s), 10.9 (w), 11.7 (w). Due to the limited information available concerning the assignment of C–O–C bands in aralkyl ethers, we tentatively suggest that 9.2-, 9.5-, 9.8-μ peaks are responsible for such ether linkages.

Methyl Trityl Ether.—Triphenyl carbinol 0.5 g. (m.p. 160°, Matheson Coleman and Bell) dissolved in excess methanol (reagent grade, Baker's) was passed through a column packed with 5 g. of alumina. Evaporation of the eluent led to the isolation of 0.35 g. of pure methyl trityl ether, m.p. 82–83° (lit.[9] m.p. 82°). Mixture melting point with an authentic sample showed no depression.

Ethyl trityl ether was obtained in the same manner in comparable yield, m.p. 81–82° (lit.[10] m.p. and m.m.p. 82–83°).

Attempted Preparation of Dibenzyl Ether.—Benzyl alcohol (5 g.) (Eastman, b.p. 204–206°) dissolved in 50 ml. of benzene was passed through a column packed with 50 g. of alumina as in the previous experiments. Fractionation of the eluent led to the recovery of the starting material in 90% yield, b.p. 205–206°, and no higher boiling fraction was obtained.

Attempted Preparation of Dianisyl Ether.—A solution of 5 g. of anisyl alcohol (Eastman, m.p. 25°) in 50 ml. of benzene was treated with alumina and worked up as in the previous experiment; almost quantitative recovery of anisyl alcohol was obtained. Mixture melting point with the starting material showed no depression.

Attempted Preparation of Trityl Isopropyl Ether.—Triphenyl carbinol, 0.5 g., dissolved in excess of isopropyl alcohol, was treated with 5 g. of alumina and worked up in the same manner as in the case of methyl trityl ether. Triphenyl carbinol (0.45 g.) was recovered, m.p. and m.m.p. 160°.

Attempted Preparation of Methyl Benzhydryl Ether.—A solution of 1 g. of benzhydrol (Eastman, m.p. 68–69°) in excess of methanol was treated with alumina and worked up in the same manner, and the recovery of benzhydrol was almost quantitative.

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An Improved Method of Synthesis of Secondary Amides from Carboxylic Esters

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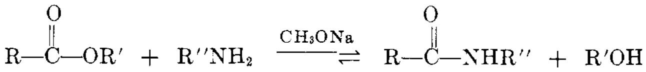
The direct synthesis of amides by the reaction of the appropriate amine and either an acid chloride or anhydride is a well known organic synthetic procedure. However, when it is desired to convert an ester of an organic acid to the corresponding secondary amide, no general direct technique is available. Unsubstituted amides, and some amides from primary aliphatic amines, can be prepared by direct aminolysis. In general, aromatic amines will not undergo this conversion.

The use of a trace of sodium methoxide as a catalyst for the ammonolysis of esters is well known.[1] Catalytic amounts of alkoxides have been used to promote the reaction between aliphatic amines and esters.[2-4] However, no example has been found in the literature in which an aromatic amine and an organic ester can be caused to react under the influence of a metal alkoxide.

The present work reports an improved procedure for the conversion of organic esters and primary aliphatic and aromatic amines to secondary amides by the action of a molar equivalent of sodium methoxide. This conversion may be represented by the following general equation.

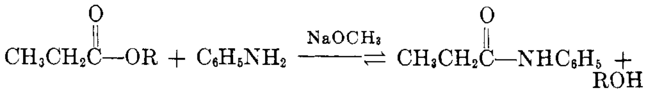


$$R-\overset{\overset{O}{\|}}{C}-OR' + R''NH_2 \overset{CH_3ONa}{\rightleftharpoons} R-\overset{\overset{O}{\|}}{C}-NHR'' + R'OH$$

The results of several experiments dealing with the preparation of N-phenylpropionamide are given in Table I. These help to define some of the variables in this reaction.

TABLE I

EFFECTS OF VARIABLES IN THE PREPARATION OF N-PHENYLPROPIONAMIDE[a]



$$CH_3CH_2\overset{\overset{O}{\|}}{C}-OR + C_6H_5NH_2 \overset{NaOCH_3}{\rightleftharpoons} CH_3CH_2\overset{\overset{O}{\|}}{C}-NHC_6H_5 + ROH$$

R	Equivalents of $NaOCH_3$ added	% Yield of N-phenylpropionamide
Methyl	1.1	69.4
Butyl	1.1	71.1
Ethyl	1.1	70.0
Ethyl	0	0.0
Ethyl	0.1	5.3
Ethyl	2.2	77.2
Ethyl	1.1	73.3[b]
Ethyl	1.1	82.4[c]

[a] All experiments involved a 7-hr. reflux period except where stated otherwise. [b] A 24-hr. reflux. [c] Methanol removed as benzene azeotrope during reaction.

It can be seen that there was no reaction between aniline and ethyl propionate upon refluxing in benzene for seven hours in the absence of sodium methoxide. The addition of a catalytic amount of sodium methoxide gave only an equivalently small yield of N-phenylpropionamide. However, the use of a slightly greater than molar equivalent of sodium methoxide gave an acceptable yield of the amide. No significant increase in yield was obtained by increasing the sodium methoxide ratio further. An appreciable yield increase was obtained by azeotropically removing the alcohol as it was formed with benzene. In the same way, use of other volatile alcohols (in the form of their esters) and of reaction solvents with which the alcohols form azeotropes, favors the formation of substituted amides. Longer heating times did not appreciably raise the yield with this simple amide.

A brief study has been made to determine some of the limitations of this reaction and the data obtained are summarized in Table II. In each reaction, equivalents of ester, amine, and sodium methoxide were refluxed for seven hours in benzene, and the amides were then isolated in a standard way.

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