2,3,6-trimethylglucose diethyl mercaptal **4,5**-dibenzoate and the product was crystallized in the same manner; yield 2.2 g. Pure material was obtained on crystallization from methanol by the addition of water; m. p. 64–65°; $[\alpha]^{21}$ +33° (*c*, 3.7; $CHCl_3$).

Anal. Calcd. for $C_6H_7O(OCH_3)_4(COC_6H_5)(SC_2H_5)_2$: S, 14.4; C_6H_5CO, 23.5. Found: S (Carius), 14.2; C_6H_5CO,[14] 23.2.

We wish to acknowledge our indebtedness to the E. I. du Pont de Nemours and Co., Inc., for the fellowship grant which has made this research possible.

Summary

1. 2,3,6-Trimethyl-*d*-glucose diethyl mercaptal, its dibenzoate and the monobenzoate of 2,3,4,6-tetramethyl-*d*-glucose diethyl mercaptal have been synthesized in crystalline condition.

2. 2,3,6-Trimethyl-*d*-glucose may be prepared readily by the hydrolysis of methylated cellulose with fuming hydrochloric acid, isolation of the sugar as its diethyl mercaptal and subsequent removal of the ethylmercapto groups.

COLUMBUS, OHIO RECEIVED JANUARY 18, 1937

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

The Cleavage of Diphenyl Ethers by Sodium in Liquid Ammonia. I. Ortho and Para Substituted Diphenyl Ethers

BY PAUL A. SARTORETTO AND FRANK J. SOWA

It has been found that a solution of sodium in liquid ammonia reacts vigorously and quantitatively with diphenyl ether. The reaction is complete when two atom equivalents of sodium is added to one mole equivalent of the ether. The products are mole equivalents of sodium phenate and benzene.

Conductivity experiments by Kraus[1] have shown that sodium is ionized in the medium of liquid ammonia, the metal being in equilibrium with sodium cations and electron anions. If reactivity involves sodium cations, a compound such as sodamide which is also ionized in liquid ammonia should cleave diphenyl ether; but it does not. Cleavage, therefore, involves either atomic sodium or the electron anions. Although there is no experimental proof favoring either, in a reduction of this type the electron anions are commonly thought of[2] as being the effective reagent. The mechanism of the reaction may be expressed as

$$ROR + 2Na^+ + 2e^- \longrightarrow Re^- + ROe^- + 2Na^+$$
$$Re^- + NH_3 + Na^+ \longrightarrow RH + NH_2^- + Na^+$$

where (R) represents a phenyl group, and (e^-) an electron anion.

The purpose of this investigation was to use the above quantitative method to evaluate the effect of various substituents in the ortho and para positions. It was also employed to evaluate the effect of the ortho against the para position using the same substituent.

Experimental

For the preparation and physical properties of the substituted diphenyl ethers listed in Table I and used in this work the authors are indebted to John J. Verbanc for his assistance.

TABLE I

PHYSICAL PROPERTIES OF SOME DIPHENYL ETHERS

No.	Diphenyl ether	Yield, %	B. p., °C.	B. p., Mm.	M. p., °C.	Sp. gr., (25°C.)	$n^{25}D$
1	*p*-Nitro-	80	200	15	56–58		
2	*o*-Nitro-	70	185	8			
3	*p*-Amino-	99	188	14	83.5		
4	*o*-Amino-	99	170	18	44		
5	*o*-Methoxy-	60	288	745	76		
6	*p*-Methoxy-	55	125	5		1.1133	1.5762
7	*o,p'*-Dimethoxy-	55	203	20	77		
8	*o*-Methyl-	58	101	5		1.0468	1.5695
9	*p*-Methyl-	67	114	6		1.0450	1.5697
10	*o,p'*-Dimethyl-	54	121	7		1.0299	1.5640
11	*o*-Carboxy-	58			112–114		
12	*p*-Carboxy-	45			141		

(1) and (2) prepared according to the method of Brewster and Groening, "Organic Syntheses," John Wiley and Sons, New York, Vol. XIV, p. 67. (3) and (4) by the reduction of the corresponding nitro compounds employing the method of Suter, THIS JOURNAL, **51**, 2583 (1929). (5) and (6) prepared by heating 252 g. of guaiacol, 56 g. of potassium hydroxide and 2 g. of copper catalyst to 150° until all of potassium hydroxide dissolved. The water was distilled, any guaiacol that steam distilled was replaced. After adding 137 g. of bromobenzene the mixture was heated on an oil-bath for two and one-half hours at 220–230°. *p*-Methoxydiphenyl ether prepared by same procedure except phenol was used in place of guaiacol and *p*-bromoanisole in place of bromobenzene. (7) Similar to preparation (5) using guaiacol and *p*-bromoanisole and heated on an oil-bath for three hours. (8),

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[1] Kraus, THIS JOURNAL, **30**, 1323 (1908).

[2] Franklin, "The Nitrogen System of Compounds," Am. Chem. Soc. Monograph, 1935, p. 50.

(9) and (10) the procedure was the same as described under method (5) using the reagents phenol and *o*-bromotoluene for (8), phenol and *p*-bromotoluene for (9) and *o*-cresol and *p*-bromotoluene for (10). (11) Described by Brewster and Strain, THIS JOURNAL, **56**, 117 (1934). (12) *p*-Carboxydiphenyl ether was prepared from the *p*-methyldiphenyl ether by oxidation. Twenty-five grams of *p*-methyldiphenyl ether was stirred with 1300 cc. of water and 60 g. of potassium permanganate was added in 20-g. portions. The mixture was refluxed and stirred for eight hours. After treatment with dilute potassium hydroxide solution and extraction with ether, the mixture was acidified by adding sulfur dioxide. The *p*-carboxydiphenyl ether separated as white fluffy crystals. The compounds *p*-methoxydiphenyl ether, *o,p'*-dimethyldiphenyl ether were new compounds. The carbon and hydrogen analyses checked well with the calculated values.

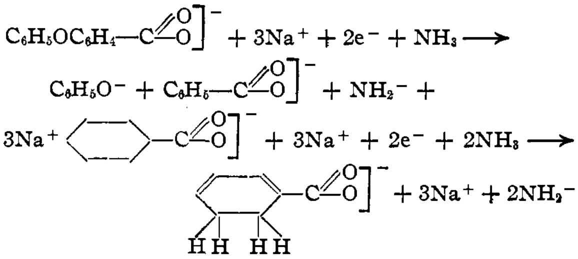
A standard method of cleavage, described below, was followed throughout this work.

Cleavage of Diphenyl Ethers.—A 2-liter 3-necked flask was fitted with a mercury-sealed mechanical stirrer, liquid ammonia reflux condenser and a large spout dropping funnel. About 200 cc. of liquid ammonia was added to the flask and a solution of 0.25 mole of the diphenyl ether in 25 cc. of dry ethyl ether was introduced slowly. About 200 cc. of dry liquid ammonia was added to the dropping funnel, and to this was added 0.25 gram atomic weight of sodium. After a sufficient time was allowed for the sodium to dissolve, the solution was introduced into the reaction flask with constant stirring. Another 0.25 gram atomic weight of sodium was made to react in a similar manner. Completion of the reaction was indicated by the appearance of a permanent blue sodium–liquid ammonia coloration. The mixture was evaporated to dryness with the aid of a cold water-bath, hydrolyzed with water and acidified with dilute hydrochloric acid, substituting an ice-bath for the last two processes. The cleavage products were extracted with ether and analyzed, each according to a method thought most suitable.

In Table II the cleavage products and methods of analysis are listed for each cleavage. For brevity, the groups attached to oxygen of the ether are designated as (R) and (R'). In every case the yield was based upon the phenolic products, for it was found that products such as benzene and toluene were short of theoretical recovery, due to loss in entrainment with ammonia gas evolving from heat of reaction.

Discussion of Experimental Results

The cleavage of the above diphenyl ethers requires two atom equivalents of sodium with the exception of the carboxydiphenyl ethers. 4-Carboxydiphenyl ether reacts with approximately 5 atom equivalents of sodium, the last two atom equivalents reacting slowly. The mechanism for the reaction, based on the supposition that sodium reacts slowly with sodium benzoate in liquid ammonia,[3] and also that the sodium salt of the carboxydiphenyl ether reacts with 4 atom equivalents of sodium to form hydrogenated benzoic acid and phenol, is as follows



The second reaction is to be investigated further.

The cleavage of 2-carboxydiphenyl ether required approximately 4 atom equivalents of sodium, with incomplete hydrogenation of sodium benzoate.

In mono-substituted diphenyl ethers the linkage between the oxygen and the substituted phenyl group is strengthened against cleavage by sodium in liquid ammonia by the introduction of the following substituents, listed according to their increasing effectiveness: *o*-CH_3, *p*-CH_3, *p*-OCH_3, *o*-NH_2, *p*-NH_2; and the linkage is weakened toward cleavage by the following substituents, similarily listed: *o*-OCH_3, *o*-COONa, *p*-COONa. The results of cleavage of 2,4'-disubstituted diphenyl ethers, using the same substituent in each phenyl group, are in accord with those results expected from the knowledge of cleavage of mono-substituted diphenyl ethers.

In all the cleavages studied that are comparative, it has been indicated that a substituent, either hindering or facilitating cleavage of the linkage between oxygen and the substituted phenyl group, is more effective in para position than in ortho position.

Theoretical Discussion

Unequal amount of cleavage on each side of the oxygen to carbon linkage in substituted diphenyl ethers indicates that the electronic configuration of the carbon atoms directly linked to oxygen has been disturbed by the effects of the substituents. Since the electron (or sodium atom) may be considered as a nucleus seeking reagent, it will attach itself more readily to the carbon atom, linked to oxygen, which has the lowest electron density. In the mono-substituted diphenyl ethers, containing a substituent of the first series mentioned above, the electron attaches itself more readily to the phenyl group

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[3] Kraus and White, THIS JOURNAL, **45**, 768 (1923).

TABLE II

Compound ROR′		Method of analysis of cleavage products	Cleavage products as mole %	
R	R′		ROH	R′OH
Phenyl	Phenyl	Fractional distillation	100% Phenol	
Phenyl	4-Methylphenyl	Iodometric titration[a]	25.6 Phenol	74.9 *p*-Cresol
Phenyl	2-Methylphenyl	Iodometric titration	47.1 Phenol[b]	52.9 *o*-Cresol
			46 Phenol	54 *o*-Cresol
2-Methylphenyl	4-Methylphenyl	Indices of refraction[c]	39 *o*-Cresol	61 *p*-Cresol
Phenyl	4-Methoxyphenyl	Fractional distillation	19 Phenol[d]	81 *p*-Methoxyphenol
Phenyl	2-Methoxyphenyl	Fractional distillation	55 Phenol[d]	45 Guaiacol
2-Methoxyphenyl	4-Methoxyphenyl	Fractional distillation	1 Guaiacol[d,e]	99 *p*-Methoxyphenol
Phenyl	4-Aminophenyl	Fractional crystallization	....	100 *p*-Aminophenol
Phenyl	2-Aminophenyl	Fractional crystallization	1 Phenol[f]	99 *o*-Aminophenol
Phenyl	4-Carboxyphenyl	Phys. prop. of phenol; m. p. acid; amide	100 Phenol[g]	....
Phenyl	2-Carboxyphenyl	Phys. prop. of phenol; m. ps. of acids	90 Phenol[h]	

[a] Redman and Weith, Brock, *J. Ind. Eng. Chem.*, **5**, 831 (1913). [b] Two cleavages were performed. [c] Plotting indices of refraction, at constant temperature, of known composition of ortho- and para- cresol mixtures, against percentage composition, a straight line was obtained, from which the composition of the unknown mixture was obtained. Suggested by Dr. A. J. Boyle. [d] Yield of anisole served as check. [e] Just a trace of guaiacol obtained. [f] Just a trace of phenol obtained. [g] Approximately theoretical amount of dihydrobenzoic acid obtained. [h] A mixture of dihydrobenzoic and benzoic acid obtained, which was short of the theoretical yield; *p*-hydroxybenzoic acid was not isolated, consequently the analysis was based on phenol.

that does not contain the substituent. It is reasonable to assume that the electronic configuration of the carbon atom, to which the electron attaches itself more readily, has not been disturbed appreciably by the substituent in the opposite phenyl group. Therefore, the electron density of the carbon atom (of the substituted phenyl group), which is attached to oxygen, has increased by the introduction of a substituent of the first series. On the other hand, the second series of substituents decrease the electron density of the carbon atom (of the substituted phenyl group) attached to oxygen.

Interpreting the experimental data in the light of electronic theories of Ingold,[4] Robinson,[5] etc., the influence of various substituents upon the carbon atoms in a phenyl group consists of two factors: an inductive effect, and a tautomeric effect. The effects observed in the case of the first series of substituents are in agreement with the application of these theories to such cleavage reactions and indicate that the tautomeric effect is the more dominating effect, and more pronounced in para than in ortho position; while the effect of the ortho substitution of OCH_3 group can be explained only by assuming that the inductive effect of the OCH_3 dominates the tautomeric effect, in this particular instance. This assumption is further substantiated by the cleavage of 2,4′-dimethoxydiphenyl ether. It is not in accord with the usual views, although it is to be expected that the inductive effect would be more pronounced in ortho than in para position.

The authors wish to express their appreciation to Dr. Andrew J. Boyle for his helpful suggestions.

Summary

Sodium in liquid ammonia cleaves diphenyl ethers rapidly and quantitatively at the carbon–oxygen linkage.

In mono-substituted diphenyl ethers, the tendency for the linkage between oxygen and the substituted phenyl group to cleave is decreased by the introduction of the following substituents, listed according to their increasing effectiveness: *o*-CH_3, *p*-CH_3, *p*-OCH_3, *o*-NH_2, *p*-NH_2. The tendency for the linkage between oxygen and the substituted phenyl group to cleave is increased by the introduction of the following substituents, similarly listed: *o*-OCH_3, *o*-COONa, *p*-COONa. The results of cleavage of 2,4′-disubstituted diphenyl ethers, using the same substituent in each phenyl group, are in accord with those results expected from the knowledge of cleavage of mono-substituted diphenyl ethers.

In all the cleavages studied that are compara-

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(4) (a) Ingold and Ingold, *J. Chem. Soc.*, 1310 (1926). (b) Ingold, *Chem. Rev.*, **15**, 225 (1934).

(5) Robinson and others, *J. Chem. Soc.*, 401 (1926).

tive, it has been indicated that a substituent, either hindering or facilitating cleavage of the linkage between oxygen and the substituted phenyl group, is more effective in para position than in ortho position.

NOTRE DAME, INDIANA RECEIVED DECEMBER 24, 1936

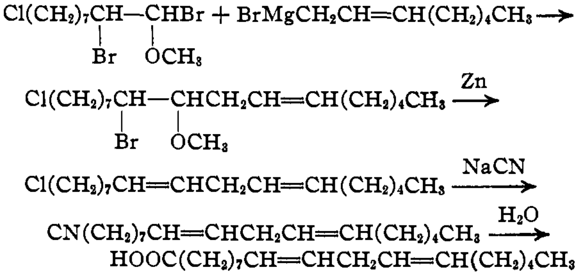
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

The Synthesis of Unsaturated Fatty Acids. II. Linoleic and 11-*n*-Amyl-9,12-tridecadienoic Acids

BY C. R. NOLLER AND M. D. GIRVIN

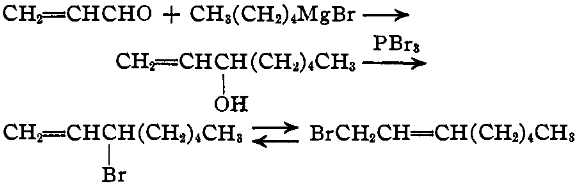
The synthesis of linoleic acid (9,12-octadecadienoic acid) is desirable not only because the commonly accepted structure is periodically questioned[1] but also because linoleic acid is apparently one of the accessory food factors, designated by Evans and his co-workers[2] as vitamin F, which is necessary for the growth and fertility of both male and female rats.

Using the following series of reactions which is similar to that previously used for the synthesis of oleic and elaidic acids[3] we have succeeded in synthesizing a product which contains α-linoleic acid.



$$\mathrm{Cl(CH_2)_7\underset{\displaystyle Br}{C}H-\underset{\displaystyle OCH_3}{C}HBr + BrMgCH_2CH{=}CH(CH_2)_4CH_3 \longrightarrow}$$
$$\mathrm{Cl(CH_2)_7\underset{\displaystyle Br}{C}H-\underset{\displaystyle OCH_3}{C}HCH_2CH{=}CH(CH_2)_4CH_3 \xrightarrow{Zn}}$$
$$\mathrm{Cl(CH_2)_7CH{=}CHCH_2CH{=}CH(CH_2)_4CH_3 \xrightarrow{NaCN}}$$
$$\mathrm{CN(CH_2)_7CH{=}CHCH_2CH{=}CH(CH_2)_4CH_3 \xrightarrow{H_2O}}$$
$$\mathrm{HOOC(CH_2)_7CH{=}CHCH_2CH{=}CH(CH_2)_4CH_3}$$

The 1-bromooctadecene-2 from which the Grignard reagent was prepared was obtained by the series of reactions



$$\mathrm{CH_2{=}CHCHO + CH_3(CH_2)_4MgBr \longrightarrow}$$
$$\mathrm{CH_2{=}CH\underset{\displaystyle OH}{C}H(CH_2)_4CH_3 \xrightarrow{PBr_3}}$$
$$\mathrm{CH_2{=}CH\underset{\displaystyle Br}{C}H(CH_2)_4CH_3 \rightleftarrows BrCH_2CH{=}CH(CH_2)_4CH_3}$$

It was realized at the outset that a mixture of 1-bromooctadecene-2 and 3-bromooctadecene-1 would result but the work of Winstein and Young[4] on analogous compounds indicated that the primary bromide would be formed in larger amount. Moreover, it was expected that the products arising from the secondary bromide would be the lower boiling and would be partially removed during the purification of the intermediate products of the synthesis.

The final product of the synthesis had the correct neutralization equivalent, iodine value, and molecular refraction for linoleic acid. Bromination of the product, however, gave none of the solid tetrabromide characteristic of α-linoleic acid. Since in the synthesis of oleic and elaidic acids[3] the equilibrium mixture of the two stereoisomers was obtained, it seemed unlikely that a mixture now had been obtained in which the geometrical isomer corresponding to α-linoleic acid was missing. Nevertheless a quantity of the synthetic material was elaidinized with Poutet's reagent[5] and the product again treated with bromine. Again no solid tetrabromide was obtained.

A portion of elaidinized product was next oxidized with permanganate according to the modified Hazura procedure used by Green and Hilditch[6] when a quantity of tetrahydroxystearic acids was obtained from which both α- and β-sativic acids were isolated. This proves definitely that α-linoleic acid was present. The amount of crude tetrahydroxy acids was about seven-tenths of that obtained from a sample of elaidinized natural α-linoleic acid and this would indicate that the amount of α-linoleic acid present in the synthetic mixture was of the order of 70%. The crude hydroxy acids from the synthetic product, however, were quite gummy and the total amount of once recrystallized product was only about 28% of that obtained from the natural product.

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[1] Takahashi, *J. Chem. Soc. Japan*, **42**, 130 (1921); *C. A.*, **15**, 2273 (1921); Haworth, *J. Chem. Soc.*, 1456 (1929); Nunn and Smedley-McLean, *Biochem. J.*, **29**, 2742 (1935).

[2] Burr and Burr, *J. Biol. Chem.*, **82**, 345 (1929); **86**, 587 (1930); Burr, Burr and Miller, *ibid.*, **97**, 1 (1932); Evans and Lepkovsky, *ibid.*, **96**, 143 (1932); Evans, Lepkovsky and Murphy, **106**, 431, 441, 445 (1934).

[3] Noller and Bannerot, THIS JOURNAL, **56**, 1563 (1934).

[4] Winstein and Young, *ibid.*, **58**, 104 (1936).

[5] Griffiths and Hilditch, *J. Chem. Soc.*, 2315 (1932).

[6] Green and Hilditch, *Biochem. J.*, **29**, 1554 (1935).