ammonia was soon noted, and after the mixture was heated for 30 minutes, water (150 cc.) was added. The excess base was neutralized with 5 N acetic acid. The hydrolysis product was precipitated by the addition of methanol, washed repeatedly with absolute methanol, ground to a fine white product and dried in a vacuum desiccator. Analysis showed only 0.2% nitrogen.

In order to determine the degree of substitution of the resultant 2-carboxethyl ether derivative, the above crude product was treated as follows: A portion of the hydrolysis product (4 g.) was dissolved in water (75 cc.), and acetic acid was added gradually with stirring. The continuous addition of the acid caused a white fibrous product to precipitate. This product was collected, washed with methanol, and dissolved in water (50 cc.). The treatment with acetic acid (mineral acids could also be used) was repeated in a Waring Blendor. The precipitated product was collected, washed repeatedly with absolute methanol, ground, washed with ether and dried in a vacuum desiccator. The dry product was dissolved in an excess of 0.1 N sodium hydroxide and after complete solution, the excess alkali was titrated with 0.1 N hydrochloric acid. The degree of substitution was 0.17 (the usual range was 0.1–0.2).

Oxidation by Periodate of 2-Cyanoethyl Ethers.—The ether derivative (0.5 g., dry basis) was mixed with 0.05 M buffered periodate[1] (350 cc.), and reaction temperature was maintained at 17°. The consumption of oxidant at 24-, 48- and 144-hour intervals was determined by removing aliquots as previously detailed.[2] The experimental results are given in Table I.

Preparation of Carboxymethyl Ethers of Galactomannans.—A typical procedure for the preparation of the carboxymethyl ethers is as follows: The carbohydrate from guar seed (30 g.) was mixed with aqueous sodium hydroxide solution (60 g. of 20%) until a completely smooth and homogeneous mass resulted. Sodium chloroacetate (30 g. in 50 cc. water) was added with thorough mixing. The temperature of the reaction mixture was gradually increased to 80° and water (100 cc.) was added. Heating at 80° was continued for approximately two hours and water (100 cc.) was added. The reaction mixture was cooled to room temperature, and the excess alkali was neutralized with 5 N acetic acid. The reaction product was precipitated by the addition of alcohol, washed with alcohol, ground and dried *in vacuo*. The degree of substitution (0.53), which may be varied at will, was determined as previously described.

Gel Formation with Certain Polyvalent Metallic Salts.—All of the 2-carboxyethyl and carboxymethyl ethers prepared in the current study displayed the characteristic gel formation with certain water-soluble metallic salts. Accordingly, the addition with stirring of 1–5 cc. of 20% aqueous solutions of aluminum sulfate, ferrous sulfate, aluminum chloride and ferric chloride to aqueous sols (1–4%) of the carbohydrate ethers resulted in gels. The addition of either aluminum sulfate or ferrous sulfate to a 3% aqueous sol of the above-described carboxymethyl ether resulted in extremely firm gels which showed no tendency to undergo syneresis over a 72-hour period.

MINNEAPOLIS, MINNESOTA RECEIVED JULY 30, 1951

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, RUTGERS UNIVERSITY]

1-(2',3'-Dimethoxyphenyl)-1-cyclohexen-6-one

BY RODERICK A. BARNES AND DONALD F. REINHOLD[1]

2,3-Dimethoxyphenyllithium was treated with 1,2-cyclohexanedione to produce a ketol. Although the free ketol could not be dehydrated, its 2,4-dinitrophenylhydrazone lost the elements of water readily. By this procedure 1-(2',3'-dimethoxyphenyl)-1-cyclohexen-6-one was prepared in an over-all yield of 28%. The Michael addition of ethyl malonate to this ketone has been carried out.

2-Arylcyclohexanones have been used for the preparation of substituted phenanthrenes[2] and compounds related to morphine.[3,4] Similarly in recent publications which appeared while our work was in progress it has been suggested that 2-arylcyclohexenones also might be used to construct compounds having the morphine ring system.[5,6,7]

The present work was independently initiated to develop a convenient procedure for the preparation of the 2-arylcyclohexenone VII.[8] This has been accomplished by using a three-step process starting from 1,2-cyclohexanedione. An alternative procedure for the synthesis of VII has recently been reported by Pappo and Ginsberg.[6]

The reaction of 2,3-dimethoxyphenyllithium with 1,2-cyclohexanedione was carried out by adding the diketone to two equivalents of the lithium compound. The first equivalent apparently reacted to form the lithium enolate of one carbonyl group. The second carbonyl group then reacted in the normal manner. No higher molecular weight products were formed, indicating that there was little tendency to form a glycol by addition of the aryllithium to both carbonyl groups.

Attempts to dehydrate ketol I with a mixture of acetic anhydride and acetyl chloride were unsuccessful. With acetyl chloride alone some of the unsaturated ketone VII was formed but the major product was a chloroketone (II). Dehydrohalogenation of II could not be effected by heating with pyridine, lutidine or quinoline.[9]

When ketol I was treated with 2,4-dinitrophenylhydrazine and sulfuric acid in the cold the corresponding 2,4-dinitrophenylhydrazone was obtained as a yellow crystalline solid (m.p. 172–173°). However if the reaction mixture was refluxed for an hour a red 2,4-dinitrophenylhydrazone (m.p. 142–143°) separated in 90% yield. This product proved to be the derivative (IV) of the desired unsaturated ketone VII.

An alternate synthesis of VII was realized by selenium dioxide oxidation of 1-(2',3'-dimethoxy-

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[1] Abstracted from a thesis presented by D. R. Reinhold to the graduate faculty in partial fulfillment of the requirements for the Ph.D. degree, June, 1951.

[2] M. S. Newman and M. D. Farbman, THIS JOURNAL, **66**, 1550 (1944).

[3] V. Boekelheide, *ibid.*, **69**, 790 (1947).

[4] E. C. Horning, M. G. Horning and E. J. Platt, *ibid.*, **69**, 2929 (1947).

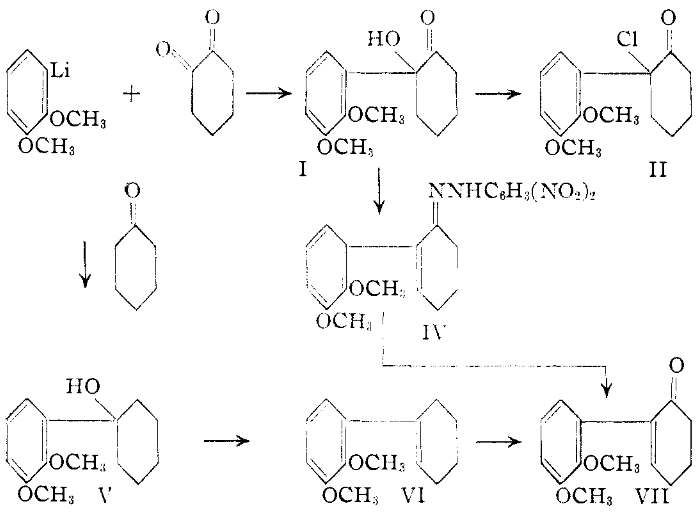
[5] W. E. Bachmann and E. J. Fornefeld, *ibid.*, **72**, 5529 (1950).

[6] R. Pappo and D. Ginsberg, *J. Chem. Soc.*, 516 (1951).

[7] C. F. Koelsch, THIS JOURNAL, **73**, 2951 (1951).

[8] The procedure reported here was devised after early experiments involving the addition of nitrosyl chloride to 1-(2',3'-dimethoxyphenyl)-1-cyclohexene were found to give poor and variable yields. R. Pappo and D. Ginsberg, ref. 6, have since reported satisfactory results from the nitrosyl chloride reaction.

[9] W. E. Bachmann and L. Wick, THIS JOURNAL, **72**, 3388 (1950), were able to eliminate hydrogen bromide from 2-bromo-2-phenylcyclohexanone by reaction with 2,6-lutidine.



phenyl)-1-cyclohexene. The ketonic products were converted to the 2,4-dinitrophenylhydrazones and after five recrystallizations some of the desired substance (IV) was obtained in pure form.

One method of converting VII to substances more closely related to morphine is by using it as the unsaturated component in a Michael reaction.[10] The reaction with diethyl malonate could be effected but attempts to bring about a reaction between ethyl acetamidomalonate and ketone VII were unsuccessful.

Experimental[11]

2-(2',3'-Dimethoxyphenyl)-2-hydroxycyclohexanone (I)—A solution of 2,3-dimethoxyphenyllithium was prepared from *n*-butyl chloride (69.5 g.), lithium (10.5 g.), veratrole (82.8 g.) and anhydrous ether (500 ml.) by the procedure of Gilman, Swiss and Cheney.[12] A solution of cyclohexanedione (32 g.) in anhydrous ether (150 ml.) was added with stirring at such a rate that gentle refluxing was maintained. The mixture was refluxed for an additional two hours and finally allowed to stand for 12 hours. The resulting solution was filtered through glass wool (to remove unchanged lithium particles) into ice-water (400 ml.), the ether layer was separated and the aqueous layer extracted with two portions of ether. The combined ether solutions were dried and the ether distilled. The residue was heated to 140° at 10–15 mm. to distil out excess veratrole and any unchanged cyclohexanedione. The residue crystallized on cooling and was recrystallized from a mixture of benzene and ligroin. There was obtained 26.1 g. (39%) of ketol which melted at 110–112°. The melting point was raised to 116–118° by further recrystallization from 95% ethanol.

Anal. Calcd. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.09; H, 7.19.

The 2,4-dinitrophenylhydrazone of I was prepared by mixing a cold alcoholic solution of I and 2,4-dinitrophenylhydrazine sulfate. The product was obtained in the form of yellow needles which melted at 172–173° after recrystallization from ethanol and ethyl acetate.

Anal. Calcd. for $C_{20}H_{22}O_7N_4$: C, 55.81; H, 5.15. Found: C, 56.00; H, 5.19.

2-(2',3'-Dimethoxyphenyl)-2-chlorocyclohexanone (II).—A mixture of ketol I (5 g.) and acetyl chloride (50 ml.) was refluxed for two hours. The excess acetyl chloride was distilled and the partly crystalline residue was recrystallized from aqueous ethanol. There was obtained 1.9 g. (36%) of chloroketone II which melted at 136–137°.

Anal. Calcd. for $C_{14}H_{17}O_3Cl$: C, 62.57; H, 6.38. Found: C, 62.36; H, 6.33.

When chloroketone II was refluxed with pyridine or 2,6-lutidine for 2–3 hours it was recovered unchanged. By heating with quinoline a dark oil was formed which did not react with 2,4-dinitrophenylhydrazine.

1-(2',3'-Dimethoxyphenyl)-cyclohexanol (V).—Cyclohexanone (38.6 g.) was added dropwise to a cold solution of 2,3-dimethoxyphenyllithium prepared from lithium (6.75 g.), *n*-butyl chloride (41.4 g.) and veratrole (32.5 g.). The reaction mixture was stirred for 48 hours at room temperature and then poured into ice-water. After processing and removing the ether the crude product was distilled at 135–140° (0.25 mm.). The viscous distillate slowly crystallized and after recrystallization from aqueous ethanol there was obtained 29.5 g. (55%) of product which melted at 51–51.5°.[13]

Anal. Calcd. for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.00; H, 8.55.

A sample of alcohol V was heated with palladium on charcoal at 300° until no more hydrogen was evolved. The solid product was purified by sublimation and recrystallization from ethanol to yield 2,3-dimethoxybiphenyl which melted at 40–41°.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.45; H, 6.65.

1-(2',3'-Dimethoxyphenyl)-1-cyclohexene-6-one (VII) A—The mother liquors from the recrystallization of chloroketone II were evaporated and the combined residue distilled. A small amount of material which boiled at 210–215° (23 mm.) crystallized on standing. Recrystallization of this substance from aqueous ethanol yielded 0.45 (10%) of unsaturated ketone VII which melted at 77–78°.

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.40; H, 6.95. Found: C, 72.42; H, 6.98.

Recrystallization of this sample from ligroin changed the melting point to 95–96°.[6] The lower melting form was not obtained by recrystallizing again from aqueous ethanol.

B.—A solution of 2,4-dinitrophenylhydrazine (8 g.), water (20 ml.), sulfuric acid (20 ml.) and ethanol (100 ml.) was added cautiously to a refluxing solution of 2-(2',3'-dimethoxyphenyl)-2-hydroxycyclohexanone in ethanol (300 ml.). The dark red solution was refluxed for one hour and then allowed to stand for 12 hours. There was obtained 15 g. (90%) of IV which melted at 139–141°. The melting point was raised to 142–143° by recrystallization from ethanol and ethyl acetate.

Anal. Calcd. for $C_{20}H_{20}O_6N_4$: C, 58.25; H, 4.90. Found: C, 58.23; H, 4.98.

An attempt to prepare the 2,4-dinitrophenylhydrazone of chloroketone II also resulted in the formation of IV in low yield.

A mixture of IV (12 g.), pyruvic acid (85 ml.), glacial acetic acid (50 ml.), chloroform (50 ml.), water (10 ml.) and concentrated hydrochloric acid (2 ml.) was heated at 70° for three hours and then allowed to stand at 45° for 24 hours. Ether (250 ml.) was added to the cold reaction mixture and the solution washed with saturated sodium carbonate solution until the washings were colorless. Evaporation of the ether and sublimation of the residue results in 5.3 g. (80%) of light yellow product. Recrystallization of this substance from ligroin produced colorless needles (5.0 g.) which melted at 95.5–96°. This product was identical with that obtained in part A.

C.—1-(2',3'-Dimethoxyphenyl)-cyclohexanol (25.5 g. was heated at 50° with a 2:1 mixture of acetic anhydride and acetyl chloride (425 ml.) for six hours. The solvents were removed at reduced pressure and the residue dissolved in ether. The ether solution was washed with sodium bicarbonate solution, dried and concentrated. Distillation of the residue produced 19.1 g. (82%) of **1-(2',3'-dimethoxyphenyl)-cyclohexene** (VI) which boiled at 167–169° (23 mm.), $n^{18}{}_{\mathrm{D}}$ 1.5465.[14] Olefin VI (4.5 g.), selenium dioxide

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[10] D. Ginsberg and R. Pappo, *J. Chem. Soc.*, 938 (1951), have reported the successful addition of ethyl malonate and ethyl cyanoacetate to VII.

[11] Analyses by W. Manser, Zurich, Switzerland.

[12] H. Gilman, J. Swiss and L. C. Cheney, This Journal, **62**, 1965 (1940).

[13] R. Bergmann, R. Pappo and D. Ginsberg, *J. Chem. Soc.*, 1369 (1950), also report the melting point of V as 51–51.5°.

[14] R. Bergmann, R. Pappo and D. Ginsberg, ref. 13, have reported the boiling point of this olefin to be 145–150° at 0.01 mm.; this is surprising since it is ten degrees higher than the alcohol from which it was prepared.

(2.96 g.) and water (5 ml.) were heated on the steam-bath with stirring for six hours. The reaction mixture was processed and distilled at reduced pressure to yield 3 g. of starting material and 0.75 g. of a ketonic fraction, b.p. 170–200° (20 mm.). This fraction was treated with 2,4-dinitrophenylhydrazine and after five recrystallizations from ethanol–ethyl acetate the product melted at 142–143° alone or when mixed with a sample of IV obtained in part B.

Michael Additions to VII.—The procedure of Bachmann and Fornefeld[5] was followed using ethyl malonate (5 g.), unsaturated ketone VII (0.928 g.) and a solution of sodium (0.138 g.) in absolute ethanol (10 ml.). After processing there was obtained 0.825 g. (53%) of product which boiled at 188–190° (0.58 mm.).[10] This product formed a semicarbazone which melted at 164–165°.

Anal. Calcd. for $C_{22}H_{31}O_7N_3$: C, 58.5; H, 6.9. Found: C, 59.38; H, 7.14.

Four experiments using different temperatures, reaction times and ratios of sodium ethoxide were carried out in attempts to cause the addition of ethyl acetamidomalonate to VII. In all cases the starting materials were recovered unchanged.

NEW BRUNSWICK, NEW JERSEY RECEIVED AUGUST 2, 1951

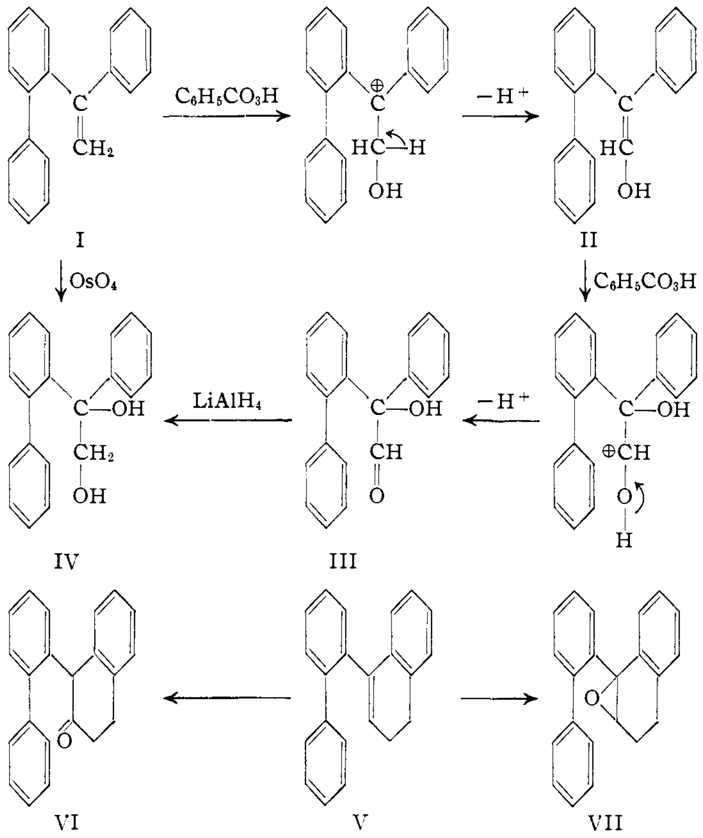
[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

The Reaction of Perbenzoic Acid with Certain Olefins

BY FRANK L. WEISENBORN[1] AND DAVID TAUB[2]

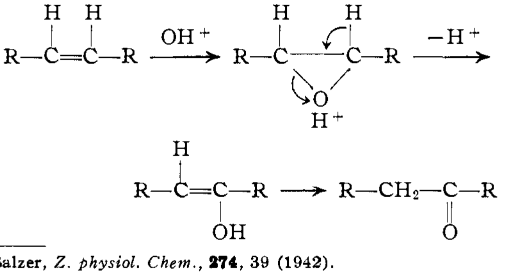
The product of the reaction of perbenzoic acid with 1-phenyl-1-(2-biphenylyl)-ethylene has been shown to be phenyl-(2-biphenylyl)-glyoxal and a mechanism for its formation is suggested. 1-(2-Biphenyl)-3,4-dihydronaphthalene has been shown to give the normal oxide by reaction with monoperphthalic acid to give 1-(2-biphenylyl)-2-tetralone by reaction with perbenzoic acid.

In the course of studying methods of synthesis of substituted phenanthrene derivatives Bradsher[3] reported the formation of a neutral "dioxide," $C_{20}H_{16}O_2$, by the reaction of perbenzoic acid with 1-phenyl-1-(2-biphenylyl)-ethylene (I). In connection with another investigation of the reactions of peracids it was of interest to us to determine the structure of this compound.



A number of reactions have previously been reported in which the action of perbenzoic acid on systems similar to I has given rise to a ketone rather than an oxide. Thus from 3,4-dihydro-6-methoxynaphthalene Salzer[4] obtained 6-methoxy-β-tetralone. Newbold and Spring[5] have also recorded the formation of diphenylacetaldehyde in 35% yield by treatment of 1,1-diphenylethylene with perbenzoic acid. Zaugg, Freifelder and Horrom[6] have obtained 1-phenyl-2-tetralone from 1-phenyl-3,4-dihydronaphthalene by perbenzoic acid oxidation followed by treatment with sulfuric acid.[7] In addition, we have found that 1-(2-biphenylyl)-3,4-dihydronaphthalene (V) reacts with perbenzoic acid in chloroform to give 1-(2-biphenylyl)-2-tetralone (VI), m.p. 165–166°. Evidence for the presence of a carbonyl group is given by the infrared spectrum (Fig. 1C). Bradsher and Rapoport,[8] on the other hand, have reported that monoperphthalic acid in ether reacts with this same olefin (V) to give a different substance, m.p. 99°. Actually, this latter compound is the normal oxide (VII) as shown by the absence of any carbonyl absorption in the infrared spectrum (Fig. 1B).

The mechanism of formation of these ketones by reaction with perbenzoic acid may be formulated



$$R-\overset{H}{C}=\overset{H}{C}-R \xrightarrow{OH^+} R-\overset{H}{C}-\underset{\underset{H^+}{O}}{\ }-\overset{H}{C}-R \xrightarrow{-H^+}$$

$$R-\overset{H}{C}=\underset{OH}{C}-R \longrightarrow R-CH_2-\underset{\underset{O}{\|}}{C}-R$$

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[1] Public Health Service Postdoctoral Fellow, 1950–1951; Riker Laboratories, Inc., Los Angeles, California.

[2] Public Health Service Postdoctoral Fellow, 1950–1951.

[3] C. K. Bradsher, THIS JOURNAL, **66**, 45 (1944).

[4] W. Salzer, *Z. physiol. Chem.*, **274**, 39 (1942).

[5] G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 247 (1945).

[6] H. E. Zaugg, M. Freifelder and B. W. Horrom, *J. Org. Chem.*, **15**, 1197 (1950).

[7] Although the character of the product obtained before treatment with sulfuric acid was not investigated by these authors it was probably the ketone.

[8] C. K. Bradsher and Lorence Rapoport, THIS JOURNAL, **65**, 1646 (1943).