molar excess of maleic anhydride at 100°, and were shown to vary from $< 1\%$ (for naphthalene) to 45% (for 2,3-dimethylnaphthalene).

The adduct from 2,3-dimethylnaphthalene and maleic anhydride was shown to be 2,3-dimethyl-1,4-dihydronaphthalene-1,4-endo-α,β-succinic anhydride.

LOS ANGELES, CALIFORNIA RECEIVED OCTOBER 14, 1949

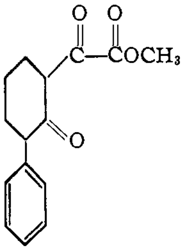
[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

Reactions of 2-Arylcyclohexanones. I. Unsaturated Lactones Formed by Glyoxalation[1]

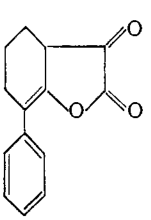
BY W. E. BACHMANN, G. I. FUJIMOTO[2] AND L. B. WICK[3]

An arylcyclohexane structure can be traced in such diverse structures as estrone and other steroids, morphine, and certain resin acids. An investigation of the chemistry of 2-arylcyclohexanones was initiated in order to determine their properties and their application to the synthesis of natural compounds or of useful analogs. At the time this study was begun little work had been done in this field. In the meantime a number of papers by other investigators on derivatives of these compounds have appeared.

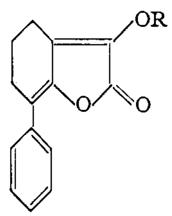
From the reaction between 2-phenylcyclohexanone and dimethyl oxalate in the presence of sodium methoxide, a crystalline product was obtained which was not the expected glyoxalate I but a cyclic compound, the analysis of which corresponded to a structure formed from the glyoxalate by loss of the elements of methanol. The same product was obtained when diethyl oxalate was employed. The structure proposed for the product is the γ-lactone of 2-hydroxy-3-phenyl-2-cyclohexeneglyoxalic acid (II), which can also exist in the enolic form IIIa. Indeed, the enolic properties of the compound, solubility in aqueous alkali, production of a deep color with ferric chloride, and formation of ethers (IIIb and IIIc) and an ester (IIId), suggested the structure (II $\rightleftarrows$ IIIa) and excluded from consideration structures IV (an enolic structure would violate Bredt's rule[4]) and V (for which no enolic structure can be written).



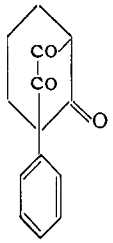
I



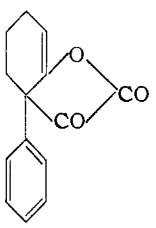
II



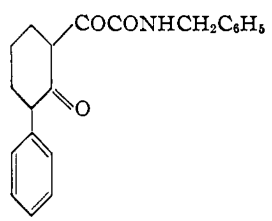
IIIa, R = H
IIIb, R = CH_3
IIIc, R = C_2H_5
IIId, R = $COCH_3$



IV



V



VI

The enol methyl ether (IIIb) was formed by reaction of the unsaturated lactone with diazomethane or with methanol in the presence of hydrogen chloride; the enol ethyl ether (IIIc) was obtained with ethanol and hydrogen chloride. The enol acetate (IIId) was produced when the lactone was treated with acetic anhydride. The enol ethers and ester gave no color with ferric chloride. Attempts to obtain the glyoxalic acid by opening the lactone ring with alkali were unsuccessful. Mild alkaline treatment simply gave the sodium enolate, a slightly soluble salt; more drastic treatment clipped off the oxalyl grouping and yielded 2-phenylcyclohexanone in 80% yield. The enol methyl ether IIIb also was cleaved by hot strong alkali to 2-phenylcyclohexanone in high yield; this result indicated that the compound was not a C-methyl derivative of IV. Benzylamine apparently opened the lactone ring, for it gave a compound which agreed with the benzylamide of the glyoxalic acid (VI) in analysis, was soluble in alkali, and gave an intense color with ferric chloride.

2-(p-Anisyl)-cyclohexanone, 2-(m-anisyl)-cyclohexanone and 2-(p-isopropyl)-cyclohexanone likewise yielded unsaturated lactones (VII) on gly-

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(1) Presented in part at the Chicago meeting of the American Chemical Society, April, 1948. The material is from the Ph.D. dissertations of G. I. Fujimoto and L. B. Wick.

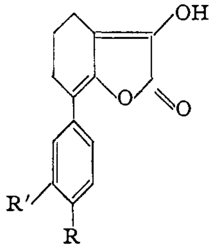
(2) Present address: Chemistry Department, University of Utah, Salt Lake City, Utah.

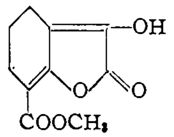
(3) Present address: Chemistry Department, Coe College, Cedar Rapids, Iowa.

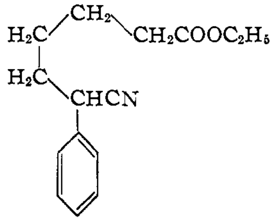
(4) Compare Bartlett and Woods, THIS JOURNAL, **62**, 2933 (1940).

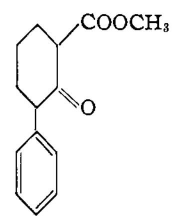
oxalation. The facile formation of these lactones in contrast to the relative stability of the glyoxalates of cyclohexanone is attributed to the activating effect of the phenyl group on the hydrogen atom at the 2-position. When the active hydrogen atom of 2-phenylcyclohexanone is replaced by a methyl group a normal glyoxalate can be prepared.[5] For comparison, the glyoxalation of 2-carbomethoxycyclohexanone was carried out. It was anticipated that an unsaturated lactone would be formed through participation of the active hydrogen atom on the carbon atom between the carbonyl and carbomethoxyl groups, and this proved to be the case. The resulting lactone (VIII) formed an enol acetate when treated with acetic anhydride; benzylamine removed the oxalyl group with the formation of the di-N-benzylamide of oxalic acid.

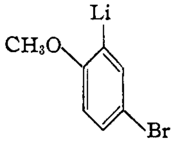
2-Phenylcyclohexanone was prepared in various ways. In one method the sodio derivative obtained from benzyl cyanide and sodamide was condensed with ethyl δ-iodovalerate, and the resulting ethyl ε-phenyl-ε-cyanocaproate (IX) was hydrolyzed to α-phenylpimelic acid. A Dieckmann cyclization of the dimethyl ester of the acid yielded crystalline 2-phenyl-6-carbomethoxycyclohexanone (X), which was hydrolyzed and decarboxylated to 2-phenylcyclohexanone. This method also provided the keto ester X, for which the usual method, decarbonylation of the glyoxalate was, of course, not available. The ketone was also prepared by chromic acid oxidation of commercial (Dow Chemical Company) 2-phenylcyclohexanol and of the alcohol obtained by the method of Cook, Hewett and Lawrence[6] by interaction of phenyllithium and cyclohexene oxide. In an attempt to prepare 2-(*p*-anisyl)-cyclohexanol by the latter procedure cyclohexene oxide was treated with the reagent prepared from *p*-bromoanisole and lithium. The only crystalline product which was isolated from the reaction mixture was a bromine-containing compound, which is undoubtedly 2-(2′-methoxy-5′-bromophenyl)-cyclohexanol (XII). This structure followed from the work of Gilman, Langham and Moore,[7] who showed that *p*-anisyllithium (which would be formed initially to some extent) is capable of metalating *p*-bromoanisole in a position *ortho* to the methoxy group to give 2-methoxy-5-bromophenyllithium (XI). The reaction of XI with cyclohexene oxide would yield the bromomethoxyphenylcyclohexanol XII.

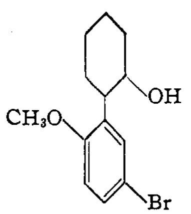

VIIa, R = OCH_3, R′ = H
VIIb, R = H, R′ = OCH_3
VIIc, R = $CH(CH_3)_2$, R′ = H

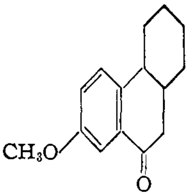

VIII

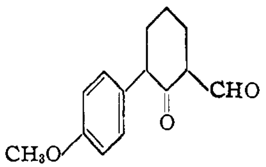

IX

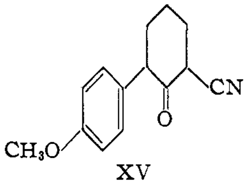

X

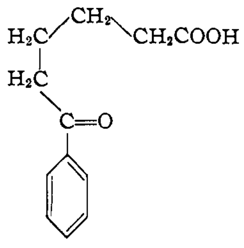

XI


XII


XIII


XIV


XV


XVI

With the appearance of the paper by Newman and Farbman[5] describing a convenient preparation of 2-phenylcyclohexanone from phenylmagnesium bromide and 2-chlorocyclohexanone, we extended the reaction to the preparation of 2-(*p*-anisyl)-cyclohexanone and other 2-arylcyclohexanones. The *m*-anisyl compound required a higher temperature and the *p*-anisyl compound a lower temperature than the phenyl compound for satisfactory results. Clemmensen reduction of 2-(*p*-anisyl)-cyclohexanone gave the known *p*-anisylcyclohexane; aluminum isopropoxide reduction of the ketone yielded crystalline 2-(*p*-anisyl)-cyclohexanol, which by a one-step dehydration and dehydrogenation process was converted into *p*-methoxybiphenyl. By the procedure employed by Cook, Hewett and Lawrence[6] on the phenyl compound, 2-(*p*-anisyl)-cyclohexanone was converted *via* the Reformatsky reaction into 7-methoxy-9-oxo-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (XIII), which after Clem-

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[5] Newman and Farbman, THIS JOURNAL, 66, 1550 (1944).

[6] Cook, Hewett and Lawrence, *J. Chem. Soc.*, 71 (1936).

[7] Gilman, Langham and Moore, THIS JOURNAL, 62, 2327 (1940).

mensen reduction and dehydrogenation yielded 2-methoxyphenanthrene. By these reactions the structure of 2-(*p*-anisyl)-cyclohexanone was established completely. Condensation of the ketone with ethyl formate in the presence of sodium ethoxide gave the 6-formyl derivative (XIV), which was converted by known methods into 6-cyano-2-(*p*-anisyl)-cyclohexanone (XV).

2-Phenylcyclohexanone is susceptible to air oxidation even in the solid state. A sample of the crystalline ketone which had been kept in a loosely-stoppered bottle for a year was found to have been converted nearly completely into crystalline δ-benzoylvaleric acid (XVI).

We are grateful to the Abbott Laboratories, the Eastman Kodak Company, and to the Horace H. Rackham School of Graduate Studies for fellowships.

Experimental

2-Phenylcyclohexanone. (a) From 2-Chlorocyclohexanone.—By following the directions of Newman and Farbman[5] 192 g. of distilled product, b. p. 150–155° at 13 mm., was obtained from 200 g. of 2-chlorocyclohexanone and the Grignard reagent from 267 g. of bromobenzene. Recrystallization from 60–75° petroleum ether gave 140 g. of 2-phenylcyclohexane with m. p. 58–60° and 15 g. with m. p. 55–58°; total yield, 60%. Further recrystallization and evaporative distillation under reduced pressure raised the m. p. of a sample to 59.5–60°.

The **2,4-dinitrophenylhydrazone** formed rapidly when 1 ml. of concentrated hydrochloric acid was added to a boiling solution of 0.5 g. of 2-phenylcyclohexanone and 0.5 g. of 2,4-dinitrophenylhydrazine in 20 ml. of ethanol. The derivative crystallized from methanol in fleecy orange needles; m. p. 138–139°.

Anal. Calcd. for $C_{18}H_{18}N_4O_4$: C, 61.0; H, 5.1; N, 15.8. Found: C, 60.8; H, 4.9; N, 15.3.

(b) **From Benzyl Cyanide.**—A solution of 5.7 g. of sodium iodide in 30 ml. of dry acetone was shaken with 7.5 g. of ethyl δ-bromovalerate[8] for two hours. After filtration the acetone solution was evaporated, a benzene solution of the product was shaken with aqueous sodium bisulfite, and the ethyl δ-iodovalerate was distilled; b. p. 119–122° at 0.3 mm.; yield, 7 g.

A stirred mixture of 1.1 g. of powdered sodamide, 2.9 ml. of benzyl cyanide and 15 ml. of toluene was refluxed for thirty minutes. After the addition of 30 ml. of ether and cooling in a dry ice-acetone bath,[5] a solution of 6.3 g. of ethyl δ-iodovalerate in 10 ml. of ether was added. After twenty minutes of refluxing, the mixture was poured onto ice, and the ethyl ε-phenyl-ε-cyanocaproate (IX) was isolated as a liquid; weight, 1.9 g.; b. p. 132–138° at 0.2 mm. A solution of 1.3 g. of the cyano ester in 20 ml. of acetic acid, 1.4 ml. of concentrated sulfuric acid and 1.6 ml. of water was refluxed under nitrogen for fifteen hours. After dilution with 5 ml. of water, removal of most of the acetic acid by distillation under reduced pressure, and further dilution with water, the solution gradually deposited 0.42 g. of α-phenylpimelic acid as colorless prisms; m. p. 89–90° (reported,[9] 92–93°). A quantitative yield of **dimethyl α-phenylpimelate** was obtained from the acid and diazomethane; b. p. 120–125° at 0.2 mm.

Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.2; H, 7.6. Found: C, 67.9; H, 7.5.

A mixture of 0.23 g. of dimethyl α-phenylpimelate, 0.19 g. of freshly prepared sodium methoxide and 15 ml. of benzene was refluxed under nitrogen for eight hours. The cooled mixture was acidified with acetic acid, washed with water and dilute sodium bicarbonate, and evaporated in a current of air. On trituration with methanol the residue solidified; weight 0.18 g.; m. p. 65–70°. The **2-phenyl-6-carbomethoxycyclohexanone** (X) crystallized from methanol in colorless rectangular prisms; m. p. 77–78°; after one year the m. p. was 99–101°. The cyclic keto ester gave a reddish-brown color with an alcoholic solution of ferric chloride.

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.4; H, 6.9. Found: C, 72.5; H, 6.7.

By refluxing a solution of 50 mg. of 2-phenyl-6-carbomethoxycyclohexanone in 4 ml. of glacial acetic acid, 2 ml. of concentrated hydrochloric acid and 0.2 ml. of water under nitrogen for fifteen hours, 30 mg. of 2-phenylcyclohexanone was obtained, which was identified by its m. p. (56–57°) and by a mixed m. p. determination.

Air Oxidation of 2-Phenylcyclohexanone.—After standing in a glass-stoppered bottle for a year, a supply of 2-phenylcyclohexanone had changed to δ-benzoylvaleric acid; m. p. 75.5–76° after recrystallization from petroleum ether. The product was soluble in aqueous sodium bicarbonate and depressed the m. p. of 2-phenylcyclohexanone. Evaporative distillation at 140–150° (0.1 mm.) followed by recrystallization from petroleum ether raised the m. p. to 76–76.3° (reported for δ-benzoylvaleric acid, 77–78°).

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.9; H, 6.8. Found: C, 69.7; H, 6.8.

When 2 g. of 2-phenylcyclohexanone in a 1-l. flask was kept in a molten state on a steam-bath for thirty-six hours and then treated with aqueous sodium hydroxide, only 1.2 g. of alkali-insoluble product remained. From the alkaline solution 0.5 g. of solid acid was isolated, which after recrystallization from petroleum ether proved to be δ-benzoylvaleric acid. Because of its susceptibility to air oxidation, 2-phenylcyclohexanone was stored under nitrogen in a refrigerator.

Preparation of Other 2-Arylcyclohexanones.—It was found necessary to modify the Newman and Farbman procedure employed for 2-phenylcyclohexanone in order to obtain certain 2-arylcyclohexanones in satisfactory yields.

(a) **2-(*p*-Anisyl)-cyclohexanone.**—To an ice cold solution of the Grignard reagent prepared from 32.8 g. of *p*-bromoanisole and 4.5 g. of magnesium in 150 ml. of ether a solution of 23 g. of 2-chlorocyclohexanone in 100 ml. of ether was added slowly with stirring. After standing for fifteen hours at room temperature the mixture was poured into a cold saturated solution of ammonium chloride. The organic layer was washed with water and dried over magnesium sulfate, and the ether was removed. The ketone which distilled at 134–140° and 0.2 mm. solidified to a colorless mass; weight, 18.2 g.; m. p. 80–85°. After several recrystallizations from 60–75° petroleum ether the **2-(*p*-anisyl)-cyclohexanone** formed clusters of fine colorless needles; m. p. 89–89.2°. The crystalline ketone was unchanged after exposure to air for three years.

Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.4; H, 7.9. Found: C, 76.1; H, 7.7.

The **oxime**, formed in quantitative yield by refluxing a mixture of 0.3 g. of 2-(*p*-anisyl)-cyclohexanone, 0.3 g. of hydroxylamine hydrochloride, 5 ml. of pyridine and 5 ml. of absolute alcohol for two hours, crystallized from methanol in colorless needles; m. p. 166–167°.

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.2; H, 7.8; N, 6.4. Found: C, 71.6; H, 7.8; N, 6.2.

The **2,4-dinitrophenylhydrazone** of 2-(*p*-anisyl)-cyclohexanone, which formed rapidly when prepared by the procedure described for 2-phenylcyclohexanone, crystallized from methanol in orange, fleecy needles, m. p. 144–145°.

Anal. Calcd. for $C_{19}H_{20}N_4O_5$: C, 59.4; H, 5.25; N, 14.55. Found: C, 59.2; H, 5.2; N, 14.7.

(b) **2-(*m*-Anisyl)-cyclohexanone.**—To the Grignard reagent prepared from 15 g. of *m*-bromoanisole in 50 ml. of

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[8] Prepared by the procedure of Allen and Wilson, *Org. Syntheses*, **26**, 52 (1946), from bromine and silver ethyl adipate.

[9] Case, THIS JOURNAL, **55**, 2927 (1933).

ether was added a solution of 14 g. of 2-chlorocyclohexanone in 50 ml. of ether at such a rate that the solution boiled gently.[5] The ether was removed, 50 ml. of toluene was added, and the mixture was refluxed for twenty-four hours. The 2-(*m*-anisyl)-cyclohexanone was obtained as a colorless liquid which was not analytically pure; weight, 4.8; b. p. 150–158° at 0.2 mm.

A mixture of 1 g. of the ketone and 1 g. of hydroxylamine hydrochloride in pyridine and absolute alcohol was refluxed for twenty-four hours, the solvents were removed, the residue was taken up in water and benzene, and the oxime was extracted from the benzene solution with cold concentrated hydrochloric acid. Neutralization of the chilled diluted acidic solution with sodium hydroxide gave 0.7 g. of slightly oily solid. By one recrystallization from methanol 0.55 g. of the oxime with m. p. 125–127° was obtained. After a second recrystallization the **oxime** formed clusters of tiny colorless needles; m. p. 129.5–130°.

Anal. Calcd. for $C_{13}H_{17}NO_2$: C, 71.2; H, 7.8; N, 6.4. Found: C, 71.2; H, 7.9; N, 6.5.

One-half gram of the ketone was added to about 10 ml. of a cold solution of 1 g. of 2,4-dinitrophenylhydrazine in 2 ml. of concentrated sulfuric acid, 15 ml. of methanol and 3 ml. of water. The viscous oil which precipitated at room temperature solidified to an orange-yellow mass on standing overnight; weight 0.6 g.; m. p. 115–120°. After two recrystallizations from ethanol the **2,4-dinitrophenylhydrazone** formed long orange needles; m. p. 124–125°.

Anal. Calcd. for $C_{19}H_{20}N_4O_5$: C, 59.4; H, 5.3; N, 14.6. Found: C, 59.6; H, 5.4; N, 15.0.

(c) 2-(*p*-Isopropylphenyl)-cyclohexanone.—To a solution of the Grignard reagent prepared from 40 g. of *p*-bromocumene in 250 ml. of ether, cooled in an ice-salt-bath, a solution of 27 g. of 2-chlorocyclohexanone in 100 ml. of ether was added with stirring. After about one-half of the ether had been removed by distillation, 100 ml. of benzene was added and the mixture was refluxed for two hours and then hydrolyzed with an ice cold solution of ammonium chloride. The ketone (21.5 g.) distilling at 140–145° and 0.1 mm. solidified when triturated with petroleum ether and crystallized from petroleum ether in colorless plates; m. p. 68–69°.

Anal. Calcd. for $C_{15}H_{20}O$: C, 83.3; H, 9.3. Found: C, 83.5; H, 9.4.

The **oxime** of 2-(*p*-isopropylphenyl)-cyclohexanone crystallized from ethanol in colorless needles; m. p. 154–155°.

Anal. Calcd. for $C_{15}H_{21}NO$: C, 77.9; H, 9.1; N, 6.0. Found: C, 77.6; H, 8.7; N, 5.9.

The **2,4-dinitrophenylhydrazone** crystallized from ethanol in yellow-orange needles; m. p. 155.5–156.5°.

Anal. Calcd. for $C_{21}H_{24}N_4O_4$: C, 63.6; H, 6.1. Found: C, 63.9; H, 6.2.

2-(2′-Methoxy-5′-bromophenyl)-cyclohexanol (XII).—A mixture of 2.8 g. of lithium wire and 30 g. of *p*-bromoanisole in 200 ml. of ether was refluxed under nitrogen for four hours. The lithium did not react completely; titration of an aliquot of the solution with standard acid indicated 56% reaction. To the cooled solution 12.6 g. of cyclohexene oxide was added slowly. Hydrolysis after two hours of refluxing and fractional distillation of the isolated product yielded a fraction (8.6 g., b. p. 120–135° at 0.05 mm.) which deposited 2 g. of a solid with m. p. 80–88°. After recrystallization from petroleum ether and then from dilute methanol the product (XII) formed colorless needles; m. p. 99–100°.

Anal. Calcd. for $C_{13}H_{17}BrO_2$: C, 54.7; H, 6.0; Br, 28.1. Found: C, 54.7; H, 5.9; Br, 28.1.

Reactions of 2-(*p*-Anisyl)-cyclohexanone. (a) Reduction.—To a mixture of 12 g. of amalgamated zinc, 20 ml. of acetic acid and 20 ml. of concentrated hydrochloric acid was added a solution of 1.3 g. of the ketone in 12 ml. of toluene. After four days of refluxing with one addition of 10 ml. and three of 5 ml. of hydrochloric acid during this time, 1.1 g. (92%) of *p*-anisylcyclohexane with m. p. 47–50° was isolated. After evaporative distillation under reduced pressure and recrystallization from methanol it melted at 56.4–57.5° (reported,[10] 56.8–57.5° for the compound prepared from cyclohexene and anisole).

Reduction of 1.55 g. of 2-(*p*-anisyl)-cyclohexanone by aluminum isopropoxide gave a liquid which yielded 0.5 g. of solid (m. p. 45–47.5°) when triturated with methanol. The **2-(*p*-anisyl)-cyclohexanol** crystallized from methanol in colorless rhombic prisms; m. p. 51.5–52.5°.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.7; H, 8.8. Found: C, 75.6; H, 8.6.

Heating a mixture of 0.2 g. of 2-(*p*-anisyl)-cyclohexanol and 0.03 g. of 10% palladium–charcoal catalyst at 300–310° for one-half hour gave 0.12 g. of solid (m. p. 75–80°) after recrystallization from petroleum ether. Further recrystallization and evaporative distillation under reduced pressure gave pure *p*-methoxybiphenyl; m. p. 86.8–87.3° alone and when mixed with an authentic specimen.

(b) Synthesis of 7-Methoxy-9-oxo-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (XIII).—To 10 g. of freshly cleaned, granulated zinc and a few crystals of iodine in 100 ml. of dry benzene and 100 ml. of anhydrous ether, 4 g. of 2-(*p*-anisyl)-cyclohexanone and 3 ml. of methyl bromoacetate were added; the reaction started after a few minutes of refluxing. Four additions of zinc and iodine and one of the bromoester were made in the course of four hours. The greenish-yellow complex was dissolved with a little acetic acid and methanol, and the solution was poured into dilute acetic acid. After being washed with water and dilute aqueous ammonia, the solution was evaporated; the residue crystallized when scratched; yield, 5.04 g. (92%); m. p. 88–92°. The **methyl 1-hydroxy-2-(*p*-anisyl)-cyclohexaneacetate** crystallized from methanol in short colorless needles; m. p. 96–96.5°.

Anal. Calcd. for $C_{16}H_{22}O_4$: C, 69.1; H, 7.9. Found: C, 69.0; H, 8.0.

To a cold mixture of 5 ml. of benzene, 1.5 ml. of pyridine and 3 ml. of thionyl chloride (mixed in that order) was added 2.15 g. of the Reformatsky ester. After three hours at room temperature, the solution was washed with ice water and the benzene solution was refluxed with 50 ml. of 10% methanolic potassium hydroxide for one-half hour; 12 ml. of 45% aqueous potassium hydroxide was added and the refluxing was continued for one hour. After the addition of 50 ml. of water, removal of the benzene and two hours of refluxing the solution was cooled and acidified; weight of solid acid, 1.8 g. (94%); m. p. 95–103°. The unsaturated acid, probably **2-(*p*-anisyl)-1-cyclohexeneacetic acid**, formed colorless needles after several recrystallizations from dilute acetic acid; m. p. 116–117°.

Anal. Calcd. for $C_{15}H_{18}O_3$: C, 73.2; H, 7.3. Found: C, 72.9; H, 7.3.

No hydrogen was absorbed at room temperature and one atmosphere pressure by a mixture of 1.3 g. of the unsaturated acid and 0.1 g. of Adams catalyst in 40 ml. of methanol until eight drops of concentrated hydrochloric acid was added; then 160 ml. (theoretical, 150 ml.) of hydrogen was absorbed in eight hours. Removal of the solvent gave 1.3 g. of colorless solid; m. p. 120–134°. One recrystallization from ethyl acetate raised the m. p. to 146–147°. The analytical sample of **2-(*p*-anisyl)-cyclohexaneacetic acid** crystallized from dilute methanol in clusters of tiny needles; m. p. 147–147.5°.

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.6; H, 8.1. Found: C, 72.6; H, 8.2.

After a mixture of 0.92 g. of 2-(*p*-anisyl)-cyclohexaneacetic acid and 0.9 g. of phosphorus pentachloride had been heated on a steam-bath until the vigorous reaction subsided, volatile products were removed under reduced pressure. To a solution of the residual acid chloride in 100 ml. of benzene, which was chilled to the freezing point, 0.56 g. of anhydrous aluminum chloride was added in por-

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(10) Price, THIS JOURNAL, **66**, 629 (1944).

tions with stirring over a ten-minute period. After four hours at room temperature the solution was hydrolyzed and acidic material was removed with 2% aqueous sodium hydroxide. Evaporative distillation of the product at 170–195° under reduced pressure gave 0.67 g. of the ketone; m. p. 77–81°. After several recrystallizations from dilute methanol the **7-methoxy-9-oxo-1,2,3,4,4a,9,10,10a-octahydrophenanthrene** (XIII) formed clusters of colorless needles; m. p. 95–96°.

Anal. Calcd. for $C_{15}H_{18}O_2$: C, 78.2; H, 7.9. Found: C, 77.9; H, 7.9.

The **2,4-dinitrophenylhydrazone** crystallized from acetone in orange needles which contained a molecule of acetone of crystallization. The needles softened and partially melted at 110°; solidification set in and melting occurred at 205–206°.

Anal. Calcd. for $C_{21}H_{22}N_4O_5 \cdot CH_3COCH_3$: C, 61.7; H, 6.0; N, 12.1. Found: C, 62.1; H, 5.9; N, 12.4.

A mixture of 3 g. of amalgamated zinc, 5 ml. of acetic acid, 5 ml. of concentrated hydrochloric acid and a solution of 0.5 g. of the ketone (XIII) in 3 ml. of toluene was refluxed for thirty hours; during this time 3 ml. of hydrochloric acid was added. The liquid 7-methoxyoctahydrophenanthrene (0.4 g.), after evaporative distillation, was dehydrogenated without further purification. A mixture of 0.15 g. of the octahydro compound and 0.03 g. of 10% palladium–charcoal catalyst was heated at 280–310° until the evolution of hydrogen ceased. The evaporatively distilled 2-methoxyphenanthrene (0.1 g., m. p. 81–90°) after two recrystallizations from alcohol melted at 97.5–98°, and its picrate melted at 123–124°, in agreement with reported values.

(c) **Formylation.**—To a chilled mixture of dry powdered sodium methoxide (from 1 g. of sodium) and 3.2 g. of ethyl formate in 25 ml. of benzene was added with swirling 4.4 g. of 2-(*p*-anisyl)-cyclohexanone in 25 ml. of benzene. After four hours the mixture was hydrolyzed with ice and water, and the organic layer was separated and washed with 2% aqueous sodium hydroxide. The combined aqueous solutions were extracted with ether, cooled and acidified. The precipitated **6-formyl-2-(*p*-anisyl)-cyclohexanone** (XIV), isolated by means of ether, crystallized on standing in a refrigerator; yield, 4 g. (80%); m. p. 63–66°. One recrystallization from benzene raised the m. p. to 66–68°. From methanol the compound crystallized in colorless prisms; m. p. 68–69°. It gave a dark purple color with an alcoholic solution of ferric chloride.

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.4; H, 6.95. Found: C, 72.6; H, 6.8.

From 3 g. of the formyl compound (XIV) 1.2 g. of cyanoketone was obtained *via* the isoxazoles[11]; m. p. 93–97°. From methanol the **6-cyano-2-(*p*-anisyl)-cyclohexanone** (XV) crystallized in colorless needles; m. p. 109.5–110.5°.

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.3; H, 6.6; N, 6.1. Found: C, 73.2; H, 6.7; N, 5.8.

Preparation of the Lactones. (a) **From 2-Phenylcyclohexanone.**—A solution prepared from 0.5 g. of sodium and 5 ml. of anhydrous methanol was evaporated at 100° under reduced pressure, the sodium methoxide was powdered, 2.4 g. of dimethyl oxalate was added, and the flask and condenser were evacuated and filled with nitrogen. After the addition of 10 ml. of benzene, the mixture was refluxed for ten minutes with shaking and then cooled. A solution of 1.74 g. of 2-phenylcyclohexanone in 15 ml. of benzene was added, and the mixture was shaken for fifteen minutes. After four hours at room temperature the mixture was poured onto ice and water. The pale-yellow, water-insoluble sodium enolate remained suspended in the benzene layer. The sodium salt was collected on a filter, washed with benzene, and dissolved in methanol; concentrated hydrochloric acid was added slowly to the chilled, stirred solution, water was added, and the precipitated lactone was collected. Alternately, the benzene suspension of the sodium salt was shaken with water and 5 ml. of concentrated hydrochloric acid, and the water layer, which now contained the lactone in suspension, was drawn off and filtered; weight, 0.9 g.; m. p. 169–172°. From the benzene solution an additional 0.8 g. of the lactone (m. p. 165–172°) was isolated; total yield, 74%. After several recrystallizations from dilute methanol the **γ-lactone of 2-hydroxy-3-phenyl-2-cyclohexeneglyoxalic acid** (II) formed fine pale-yellow needles; m. p. 178–179°. When diethyl oxalate was substituted for the dimethyl ester, a 79% yield of the same lactone was obtained. The lactone gives an immediate deep black color with an alcoholic solution of ferric chloride; it reacts with 2% sodium hydroxide and with warm 5% sodium bicarbonate to give the sparingly soluble sodium enolate, from which the lactone can be recovered upon acidification.

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.6; H, 5.3. Found: C, 73.6; H, 5.2.

When a mixture of 0.1 g. of the lactone (II), 4 ml. of 20% sodium hydroxide and 3 ml. of water was heated on a steam-bath, the lactone went into solution. After three minutes 2-phenylcyclohexanone began to precipitate as a liquid; after forty-five minutes the mixture was cooled and 60 mg. (80%) of crystalline 2-phenylcyclohexane was isolated; m. p. 55–57° alone and when mixed with an authentic specimen.

The **enol methyl ether** (IIIb) was formed immediately in quantitative yield when diazomethane was added to an ether solution of 0.2 g. of the lactone at 0°; m. p. 112–115°. It was also obtained by passing dry hydrogen chloride into a hot solution of 0.3 g. of the lactone in 10 ml. of methanol for thirty minutes. On cooling the solution deposited 0.2 g. of colorless needles (m. p. 115–116.5°); from the filtrate an additional 0.09 g. (m. p. 105–108°) was isolated. By recrystallization from methanol the enol ether was obtained in colorless needles; m. p. 117–118.5°. It is insoluble in alkali and gives no color with alcoholic ferric chloride.

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.4; H, 5.8. Found: C, 74.4; H, 5.9.

Cleavage of 0.1 g. of the enol methyl ether by aqueous sodium hydroxide was carried out as described for the lactone. Twenty minutes was required for complete solution and one and one-half hours was given for the complete reaction; yield of 2-phenylcyclohexanone, 55 mg.

The **enol ethyl ether** (IIIc), prepared with alcoholic hydrogen chloride, crystallized from dilute ethanol in colorless needles; m. p. 85.2–89.5°.

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.9; H, 6.3. Found: C, 74.8; H, 6.2.

The **enol acetate** (IIId) was prepared by adding 5 ml. of acetic anhydride to a solution of 0.5 g. of the lactone in 8 ml. of pyridine, refluxing three minutes, and pouring the mixture onto ice and water; weight, 0.52 g.; m. p. 105–107°.

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.2; H, 5.2. Found: C, 71.1; H, 5.1.

The benzylamine derivative, presumably the **benzylamide of 3-phenyl-2-oxocyclohexane-1-glyoxalic acid** (VI), was prepared by warming a solution of 0.5 g. of the lactone and 1.2 ml. of benzylamine in 10 ml. of ethanol on a steam-bath for a few minutes and cooling. The product which precipitated (0.62 g., m. p. 138–145°) crystallized from methanol in colorless fleecy needles; m. p. 132–133.5° dec. when introduced at room temperature and 143–145° dec. when put in the bath at 135°. It gave a deep black color with ferric chloride and was soluble in aqueous alkali.

Anal. Calcd. for $C_{21}H_{21}O_3N$: C, 75.2; H, 6.3; N, 4.2. Found: C, 75.1; H, 6.6; N, 4.3.

(b) **From 2-(*p*-Anisyl)-cyclohexanone.**—An 80% yield of the **γ-lactone of 2-hydroxy-3-(*p*-anisyl)-2-cyclohexeneglyoxalic acid** (VIIa) with m. p. 165–170° was obtained from the ketone. After several recrystallizations from methanol it formed short cream-colored needles; m. p. 175–175.5° (mixed m. p. with II, 150–168°). It gives a

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(11) Auwers, *J. prakt. Chem.*, **134**, 89 (1932).

black color with ferric chloride and forms a sodium salt with aqueous sodium hydroxide or sodium bicarbonate.

Anal. Calcd. for $C_{15}H_{14}O_4$: C, 69.7; H, 5.5. Found: C, 69.5; H, 5.5.

The enol **acetate of VIIa** crystallized from methanol in needles; m. p. 132.5–133.5°.

Anal. Calcd. for $C_{17}H_{16}O_5$: C, 68.0; H, 5.4. Found: C, 68.0; H, 5.3.

The **benzylamide of the glyoxalic acid** obtained from VIIa and benzylamine crystallized from dilute methanol in fine needles; m. p. 151.5–152° dec. when inserted into the bath at room temperature and 155–156° dec. when introduced at 150°.

Anal. Calcd. for $C_{22}H_{23}O_4N$: C, 72.3; H, 6.4; N, 3.8. Found: C, 71.9; H, 6.5; N, 3.5.

(c) **From 2-(*m*-Anisyl)-cyclohexanone.**—The **γ-lactone of 2-hydroxy-3-(*m*-anisyl)-2-cyclohexeneglyoxalic acid** (VIIb), obtained in nearly quantitative yield, crystallized from methanol in rectangular prisms; m. p. 166–166.5°.

Anal. Calcd. for $C_{15}H_{14}O_4$: C, 69.7; H, 5.5. Found: C, 69.7; H, 5.5.

(d) **From 2-(*p*-Isopropylphenyl)-cyclohexanone.**—The **γ-lactone of 2-hydroxy-3-(*p*-isopropylphenyl)-2-cyclohexeneglyoxalic acid** (VIIc), prepared in 57% yield, crystallized from methanol in pale-yellow rectangular plates; m. p. 158–159°.

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.5; H, 6.7. Found: C, 75.4; H, 6.8.

(e) **From 2-Carbomethoxycyclohexanone.**—From 490 g. of cyclohexanone and 590 g. of dimethyl oxalate, 330 g. (43%) of 2-carbomethoxycyclohexanone was prepared by the method employed for the ethyl ester[12]; b. p. 105–106° at 18–20 mm. To a solution of sodium methoxide prepared from 3 g. of sodium and 30 ml. of methanol under nitrogen was added 15 g. of dimethyl oxalate, followed by a solution of 10 g. of 2-carbomethoxycyclohexanone in 75 ml. of methanol. After four hours at room temperature most of the methanol was removed under reduced pressure, and the residue was added to water and benzene. The benzene contained 5 g. of unchanged keto ester; the aqueous solution contained the sodium enolate from which 3.7 g. of the **γ-lactone of 3-carbomethoxy-2-hydroxy-2-cyclohexeneglyoxalic acid** (VIII) was isolated; m. p. 195–199°. It crystallized from methanol in colorless needles; m. p. 196–197°. It gives an immediate dark green color with ferric chloride and is soluble in aqueous alkali.

Anal. Calcd. for $C_{10}H_{10}O_5$: C, 57.2; H, 4.8. Found: C, 57.3; H, 4.8.

The **enol acetate of VIII** crystallized from methanol in colorless needles; m. p. 88–89°.

Anal. Calcd. for $C_{12}H_{12}O_6$: C, 57.2; H, 4.8. Found: C, 57.2; H, 4.9.

A solution of 0.5 g. of the lactone and 1.2 ml. of benzylamine in 10 ml. of ethanol which had been warmed on a steam-bath for a few minutes deposited 0.15 g. of the di-N-benzylamide of oxalic acid; m. p. 215–216°. It crystallized from pyridine in plates; m. p. 219–220°, alone and when mixed with an authentic specimen.

Summary

The reaction of dimethyl oxalate with 2-arylcyclohexanones gave unsaturated lactones instead of the glyoxalates. A lactone was also obtained from 2-carbomethoxycyclohexanone. The enol ethers and acetate of some of the lactones were prepared.

The preparation of phenyl-, 2-(*p*-anisyl)-, 2-(*m*-anisyl)- and 2-(*p*-isopropylphenyl)-cyclohexanone and the synthesis of 7-methoxy-9-oxo-octahydrophenanthrene from 2-(*p*-anisyl)-cyclohexanone are described.

2-Phenylcyclohexanone undergoes air oxidation to δ-benzoylvaleric acid.

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[12] Snyder, Brooks and Shapiro, *Org. Syntheses*, Coll. Vol. II, 531 (1943).

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MICHIGAN]

Reactions of 2-Arylcyclohexanones. II. The Preparation of Intermediates in the Synthesis of Resin Acids

BY W. E. BACHMANN AND L. B. WICK[1]

Although the structures of dehydroabietic acid (I, R = $CH(CH_3)_2$, R′ = H) and of the resin acid podocarpic acid (I, R = H, R′ = OH) have been constructed,[2] apparently the natural stereoisomers have not yet been obtained. The 2-arylcyclohexanones appeared to offer another route to these compounds. Methylation of properly substituted 2-arylcyclohexanones would give II, from which the acid IV could probably be prepared by methods employed extensively in the synthesis of steroids and related compounds.[3] This would include glyoxalation of II, decarbonylation of the glyoxalate followed by methylation of the β-keto ester to III, and conversion of III to IV by way of the Reformatsky reaction; by obvious steps the acid IV could be converted into the resin acid structures. As a model we used the readily available 2-phenylcyclohexanone, which would yield desoxypodocarpic acid (I, R = R′ = H) if the synthesis proved successful.

After the work had been initiated, Newman and Farbman[4] reported the preparation of 2-methyl-2-phenylcyclohexanone (II, R = R′ = H) and its glyoxalate for another purpose. We found that the glyoxalate lost carbon monoxide readily when heated with powdered glass or with Cargille boiling stones and gave 2-methyl-2-phenyl-6-carbomethoxycyclohexanone, which with sodium methoxide and methyl iodide yielded the desired 2,6-dimethyl-2-phenyl-6-carbomethoxycyclohexanone (III, R = R′ = H) as a separable

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[1] From the Ph.D. dissertation of L. B. Wick.

[2] Haworth and Barker, *J. Chem. Soc.*, 1299 (1939); Haworth and Moore, *ibid.*, 633 (1946); Bhattacharaya, *J. Indian Chem. Soc.*, **22**, 165 (1945).

[3] Compare Bachmann, Cole and Wilds, THIS JOURNAL, **62**, 824 (1940).

[4] Newman and Farbman, *ibid.*, **66**, 1550 (1944).