

TABLE I

	M. p., °C.	Nitrogen, %	
		Calcd.	Found
<i>m</i> -C ₂ H ₅ SC ₆ H ₄ NHCOOCH ₂ - CH ₂ N(C ₂ H ₅) ₂ ·HCl	148	8.43	8.31
<i>m</i> -C ₂ H ₅ SC ₆ H ₄ NHCOOCH ₂ CH ₂ - CH ₂ N(C ₂ H ₅) ₂ ·HCl	113	8.09	7.90
<i>m</i> -C ₄ H ₉ SC ₆ H ₄ NHCOOCH ₂ - CH ₂ N(C ₂ H ₅) ₂ ·HCl	94	7.78	7.77
<i>m</i> -C ₄ H ₉ SC ₆ H ₄ NHCOOCH ₂ CH ₂ - CH ₂ N(C ₂ H ₅) ₂ ·HCl	158	7.48	7.35

Alkamine Esters of Alkylthiophenylcarbamic Acids.—
These compounds were prepared from the above iso-

cyanates by mixing them in dry ether solution with the desired amino alcohol and refluxing the solutions to complete the reaction. The free bases were not isolated but the hydrochlorides were precipitated by passing a stream of dry hydrogen chloride into the reaction mixture. These hydrochlorides were purified by recrystallization from dry acetone. The compounds prepared are listed in Table I.

Summary

Four alkamine esters of *m*-alkylthiophenyl carbamic acids have been prepared and found to be active local anesthetics.

NEW HAVEN, CONN.

RECEIVED JULY 20, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

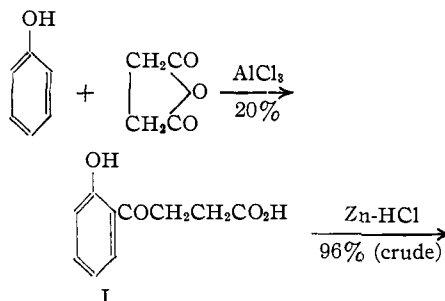
Quinonyl Derivatives of Fatty Acids

BY LOUIS F. FIESER, MARSHALL D. GATES, JR., AND GLEN W. KILMER¹

Various considerations suggest that, in the series of compounds characterized by having a quinone nucleus in combination with a fatty acid side chain, substances may be encountered possessing interesting biological actions. The association of a biological function with the isolated quinone structure itself is illustrated by the pronounced bactericidal² and spermicidal³ potency of quinone and toluquinone, and by the anti-hemorrhagic activity of certain naphthoquinones possessing a long, branched-chain hydrocarbon residue (vitamin K type). The importance of the second structural feature mentioned is well set forth in Robinson's stimulating survey⁴ of the role of branched-chain fatty acids associated with leprosy and with tuberculosis. Certain acids meeting this general specification exert a leprocidal action and are at least weakly germicidal to the similarly acid-fast bacteria of tuberculosis, while others, isolated from the tubercle bacillus, are capable of causing the formation of typical tubercular lesions at the point of injection. A fatty acid having an attached group capable of functioning as an oxido-reduction catalyst might possess enhanced or significantly modified actions. Furthermore, if such an acid were to occur as a constituent of a natural fat, the quinone group would almost certainly be destroyed in the saponification step of the usual isolation procedure. Thus the quinone group of vitamin K₁ is severed

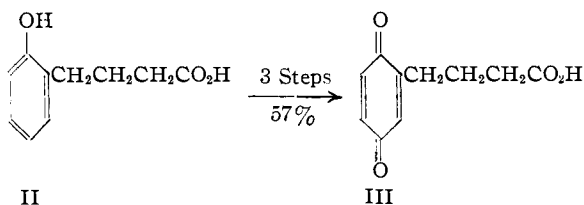
from the hydrocarbon chain by gentle treatment with alkali.⁵ Another point of interest is that the simplest member of the quinone-fatty acid series is excreted in the reduced form (homogentisic acid) in huge amounts in the urine of persons suffering from alkaptonuria.

As a first step in a study of quinone-acids, we have synthesized for exploratory tests four acids of the general type indicated. Attempts to obtain the butyric acid derivative of quinone starting with the succinylation of hydroquinone or its dimethyl ether appeared unpromising. The known β -(2,5-dimethoxybenzoyl)-propionic acid⁶ was reduced successfully, if in poor yield, but the demethylation presented difficulties. A better route was found starting with the succinylation of phenol at a high temperature as described in the literature,^{7,8} although under the conditions employed by us the reaction afforded the desired ortho isomer (I) in only about 20% yield.



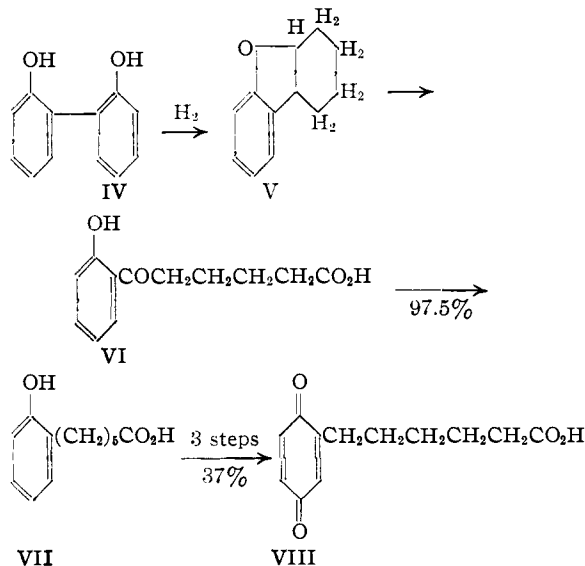
(1) Du Pont Research Fellow.
(2) Morgan and Cooper, *Biochem. J.*, **15**, 587 (1921); *J. Soc. Chem. Ind.*, **43**, 532T (1924).
(3) Gulland, *Biochem. J.*, **26**, 32 (1932).
(4) R. Robinson, *J. Chem. Soc.*, 505 (1940).

(5) Fieser, *THIS JOURNAL*, **61**, 3467 (1939).
(6) Dalal and Nargund, *J. Indian Chem. Soc.*, **14**, 406 (1937).
(7) Raval, Bokil and Nargund, *J. Univ. Bombay*, **7**, 184 (1938).
(8) Mitter and De, *J. Indian Chem. Soc.*, **16**, 35 (1939).



In agreement with the observations of Mitter and De,⁸ Clemmensen reduction of the keto acid I was found to proceed very smoothly. The reduction product II was readily converted by coupling with diazotized sulfanilic acid, reduction, and oxidation of the aminophenol, into γ -quinonylbutyric acid, III.

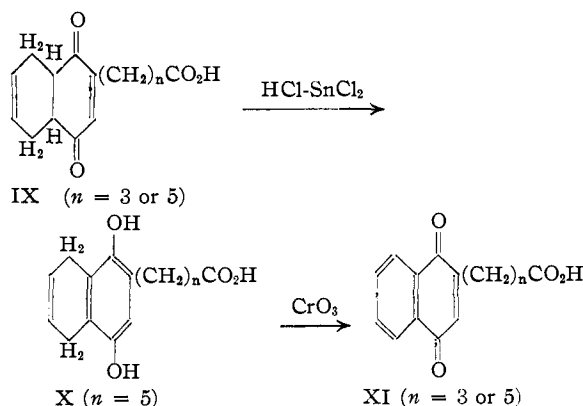
A novel reaction discovered by von Braun⁹ provided a convenient source of starting material for the synthesis of a caproic acid derivative. This consists in converting *o*-diphenol (IV) by hydrogenation into the reduced oxide V and opening the ring by oxidation. Although the yields are low, δ -salicyloylvaleric acid, VI, is obtainable readily by this method. The reduction again



proceeded nearly quantitatively, and the reduced acid was converted without difficulty to ϵ -quinonylcaproic acid (VIII) and the corresponding hydroquinone. Quinones III and VIII melt at 105° and at 102°, while the hydroquinones melt at 132° and 97°, respectively.

The two benzoquinones were then employed as starting materials for the preparation of the naphthoquinones by the Diels–Alder synthesis. The butadiene addition products IX were obtained in 75–86% yield, and the lower homolog

(9) Von Braun, *Ber.*, **55**, 3761 (1922).



afforded the naphthoquinone in 64% yield when a solution of the substance in acetic acid was treated with sulfuric acid to effect isomerization and then with chromic acid. In the caproic acid series the intermediate dihydronaphthoquinone X was isolated prior to oxidation. The 2-naphthoquinonyl butyric and caproic acids melt at 152° and 147°, respectively.

Experimental Part¹⁰

Butyric Acid Series (G. W. K.)

β -(2,5-Dimethoxybenzoyl)-propionic acid⁶ was prepared by succinoylation of hydroquinone dimethyl ether (59 g.) in tetrachloroethane–nitrobenzene solution by the general procedure of Fieser and Hershberg,¹¹ using 120 g. of aluminum chloride and allowing the reaction to proceed at 5° for forty-five hours and at room temperature for four hours. After clarification of a soda solution of the acidic material with Norit, acidification gave a gray powder, m. p. 97–99°. Crystallization from 125–150 cc. of alcohol yielded 53 g. (51.9%) of almost colorless prismatic needles, m. p. 101–102°. The dark material from the mother liquor was crystallized from methanol and then the potassium salt was thrown out of a hot aqueous solution as an oil by the addition of potassium carbonate. The acid liberated from the oily salt was only slightly colored and melted at 101–102°; this crop amounted to 6.5 g. (6.3%).

γ -(2,5-Dimethoxyphenyl)-butyric Acid.—The dimethoxy keto acid (17.8 g.) was reduced by the Clemmensen–Martin¹² method and the alkaline solution of the product was submitted to remethylation according to Martin.¹² The material collected with ether was a light yellow paste. Extraction with 400 cc. of hot hexane left a tarry residue of 3.5 g., and the solution after concentration afforded 8.6 g. of a white solid, m. p. 59–66°. This was crystallized twice from hexane, small quantities of insoluble tar being removed by decantation, and yielded 7.0 g. (41.8%) of colorless, microcrystalline material, m. p. 64.5–67°. The best sample consisted of small jagged prisms, m. p. 66–66.8°.

*Anal.*¹³ Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.61; H, 7.38.

(10) All melting points are corrected.

(11) Fieser and Hershberg, *THIS JOURNAL*, **58**, 2315 (1936).

(12) Martin, *ibid.*, **58**, 1438 (1936).

(13) Microanalysis by Lyon Southworth.

Attempts were made to demethylate this acid by heating it with aluminum chloride, aluminum chloride and benzene, and hydrobromic and acetic acids but under the conditions tried the material was either converted into intractable tars or left unchanged.¹⁴ Direct oxidation of the dimethyl ether with a slight excess of chromic anhydride¹⁶ at 60° or 20° yielded as the only isolated product a very small amount of an unidentified substance which when crystallized once from acetic acid melted at 222–223° dec. The analysis of this partially purified product (found: C, 62.23; H, 4.92) agrees with that calculated for the expected quinone acid C₁₀H₁₀O₄ (C, 61.85; H, 5.19), but the melting point is much too high for such a substance.

Trial condensations of succinic anhydride with hydroquinone by the Friedel and Crafts reaction in nitrobenzene-tetrachloroethane or with hydrogen fluoride led only to tars.

β -Salicyloylpropionic Acid.^{7,8,18}—To a solution of 21 g. of freshly distilled phenol and 20 g. of pure succinic anhydride in 100 cc. of purified tetrachloroethane at 55° was added 60 g. of aluminum chloride during fifty minutes. When about three-fourths of the halide had been added, a solid began to separate from the red solution, and at the end of the addition stirring became difficult. On raising the bath temperature to 130–135°, the mixture at first became fluid and black, evolved much hydrogen chloride and then rapidly set to a solid cake. After two hours at 130–135° the mixture was cooled in ice and treated with 100 cc. of 10% hydrochloric acid, when it became somewhat fluid again. The solvent was removed with steam and after cooling in ice the black, lumpy solid was collected and taken up in 200 cc. of warm dilute sodium carbonate solution. After being filtered from considerable alumina, the solution was treated with Norit, cooled in ice and acidified under mechanical stirring. The fine yellow precipitate, m. p. 115–134°, on crystallization from boiling water (Norit) gave 8.5 g. of large blady needles, m. p. 137–139°. This was taken up in water and the solution concentrated until crystals began to separate on the surface; on ice cooling 7.9 g. (20%) of long colorless needles of the ortho isomer separated, m. p. 139–140°. Slightly yellow β -(*p*-hydroxybenzoyl)-propionic acid separated rapidly from the filtrate; 1.2 g. (3%), m. p. 154–156°. The yield of para isomer in a larger run was 5%.

A sample of the *o*-compound when crystallized several times from dilute alcohol, alcohol, or ethyl acetate melted constantly at 140.4–140.8°, with slight previous softening.

*Anal.*¹³ Calcd. for C₁₀H₁₀O₄: C, 61.85; H, 5.19. Found: C, 62.02; H, 5.38.

γ -(*o*-Hydroxyphenyl)-butyric Acid^{9,17}—Reduction of the keto acid (14.4 g.) was conducted by Martin's procedure¹² with a refluxing time of ten hours. The product was collected in toluene and ether, and after removal of the solvents in vacuum was obtained by cooling and rubbing as a pink solid, m. p. 53–60°; yield, 12.9 g. (96%). A small sample purified by crystallization from hexane formed glistening white plates, m. p. 64–67.5°.

(14) Compare L. I. Smith, Ungnade, Opie, Prichard, Carlin and Kaiser, *J. Org. Chem.*, **4**, 323 (1939).

(15) Tishler, Fieser and Sampson, *THIS JOURNAL*, **62**, 1881 (1940).

(16) Rosenmund and Schapiro, *Arch. Pharm.*, **272**, 313 (1934).

(17) Schroeter, German Patent 562,827 (1928) [*Chem. Abstr.*, **27**, 1224 (1933)].

γ -Quinonylbutyric Acid (III).—A solution of 2.6 g. of the crude phenol-acid in 15 cc. of water containing 3 g. of sodium hydroxide was treated at 0° with the diazo reagent from 3.14 g. of sulfanilic acid.¹⁸ After fifty minutes reduction was accomplished with 6.9 g. of sodium hydrosulfite at 70° and the pale yellow solution was saturated with salt and cooled to 5°. The grayish precipitate was collected, washed with saturated brine containing hydrosulfite, and dissolved in the minimum amount of hot 4% hydrochloric acid containing a little stannous chloride. The filtered solution was treated with 3 cc. of concentrated hydrochloric acid and iced, but since the aminophenol hydrochloride failed to separate, the solution was made just alkaline with 50% sodium hydroxide containing hydrosulfite, a transient precipitate redissolving in the alkali. As saturation with salt caused no precipitation, the solution was made just acid again with a few drops of hydrochloric acid, when a heavy white precipitate separated. Washed with brine and hydrosulfite and dried, the material left a considerable residue on ignition. It was dissolved in 30 cc. of 25% sulfuric acid and the solution was filtered from a little gum and treated at 5° with 8 cc. of 4 *N* sodium dichromate solution, which gave a purple solution (oxidation procedure of Willstätter and Dorogi¹⁹). After standing at 5° for eleven hours, the dark solution containing separated solid was diluted with an equal volume of water and extracted five times with ether. The ethereal solution was washed twice with saturated brine, concentrated on the steam-bath to a volume of 250 cc. and then evaporated in vacuum to half that volume. After Norit treatment the ether was removed completely in vacuum, leaving 1.6 g. (57%) of a bright yellow powder, m. p. 99–100°. The substance crystallizes from ether-petroleum ether in yellow plates, the best sample melting at 104.9–105.3°. It gives an immediate blue-green color in the Craven test.²⁰

*Anal.*¹³ Calcd. for C₁₀H₁₀O₄: C, 61.85; H, 5.19. Found: C, 61.77; H, 5.41.

γ -Hydroquinonylbutyric acid was obtained by reduction of the quinone with aqueous sodium hydrosulfite and crystallized from ether-petroleum ether. It formed a white powder, m. p. 131.2–132°, with previous sintering.

*Anal.*¹³ Calcd. for C₁₀H₁₂O₄: C, 61.21; H, 6.17. Found: C, 61.15; H, 6.40.

Addition of Butadiene to γ -Quinonylbutyric Acid.—A mixture of 3.49 g. of the quinone III, 28 g. of butadiene and 55 cc. of benzene was heated in a capped bottle for eight hours at 65–70°. After cooling overnight at 5°, the butadiene was allowed to evaporate and the crystalline yellow product which had separated was collected and washed with cold benzene; yield 3.85 g. (86%), m. p. 125.5–127.5°. Much of the yellow color was removed by washing with a small volume of ether, in which the addition product is but sparingly soluble. The sample for analysis was crystallized from alcohol-water, giving very fine needles with a slight tinge of yellow, m. p. 124.5–125.5°.

*Anal.*¹³ Calcd. for C₁₄H₁₆O₄: C, 67.72; H, 6.50. Found: C, 67.80; H, 6.75.

(18) Fieser, "Organic Syntheses," Vol. 17, 1937, p. 9.

(19) Willstätter and Dorogi, *Ber.*, **42**, 2166 (1909).

(20) Craven, *J. Chem. Soc.*, 1605 (1931).

γ -(1,4-Naphthoquinonyl-2)-butyric Acid.—In a preliminary trial the diene addition product was isomerized with acetic acid containing a little hydrochloric acid and tannous chloride and the hydroquinone was obtained in a nearly pure condition as rosets of tiny needles, m. p. 171–173°. The naphthoquinone is conveniently prepared without isolation of the isomerization product, as follows:

A solution of 753 mg. of the crude addition product in 4.5 cc. of purified acetic acid was treated with one drop of concentrated sulfuric acid and one drop of water and heated on the steam-bath for forty-five minutes. After cooling the solution to 40°, 810 mg. of chromic anhydride in 7 drops of water and 3 cc. of acetic acid was added dropwise, keeping the temperature from rising above 60°. After heating for one-half hour at 60–65°, the solution was poured onto ice and the yellow precipitate was collected; 621 mg., m. p. 143–145°. One crystallization from methanol gave 476 mg. (64%) of tan needles, m. p. 147–149°. The quinone could be crystallized from water, although sometimes decomposition seemed to occur: From methanol (Norit) the material was obtained as bright yellow needles, m. p. 151.3–152°; Craven test, slowly developing lavender color.

*Anal.*¹³ Calcd. for $C_{14}H_{12}O_4$: C, 68.84; H, 4.95. Found: C, 68.79; H, 5.24.

Caproic Acid Series (M. D. G.)

ϵ -(*o*-Hydroxyphenyl)-caproic Acid (VII).—The *o*-sali-cyloylvaleric acid⁹ used melted at 91.5–92.5°; oxime, m. p. 126–127°. The acid (4.54 g.) was reduced according to Martin,¹² using 200 cc. of 1:1 hydrochloric acid, 100 cc. of toluene and 50 g. of amalgamated zinc and refluxing the mixture vigorously for thirty-five hours, with the addition during this period of 50 g. of the zinc and 160 cc. of 3:2 hydrochloric acid. After separation of the layers and extraction with ether, the product was extracted from the toluene-ether solution with 10% sodium hydroxide in three portions. After washing the alkaline liquor with ether it was made acid to congo red and the precipitated oily acid was collected by ether extraction. After thorough pumping out to remove traces of ether, the residue solidified to a nearly colorless mass, m. p. 85–89°; yield 4.14 g. (97.5%). This crude material was used as such in the synthesis. An analytical sample purified by crystallizations from ether-petroleum ether, dilute alcohol, and benzene-hexane showed the constant melting point 89–90.5°. A mixture of this and the keto acid was depressed to 69–77°. The substance invariably crystallizes very slowly and tends to come out as an oil on rapid cooling. It forms fine loose needles from dilute alcohol and tight rosets of prismatic needles from the above non-aqueous solvents.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.20; H, 7.75. Found: C, 69.15; H, 7.89.

Hydrochloride of ϵ -(2-Hydroxy-5-aminophenyl)-caproic Acid.—The hydroxy acid (1.13 g.) was coupled with sulfanilic acid and the dye reduced with hydrosulfite according to the standard procedure.¹⁸ On saturating the resulting yellow solution with salt and cooling, an easily filterable cream colored precipitate separated. This was washed with brine containing hydrosulfite and dissolved by warming in 8 cc. of water containing 0.8 cc. of concentrated hydrochloric acid and 0.2 g. of stannous chloride. After

filtering by suction to remove a small amount of residue, 1 cc. of concentrated hydrochloric acid was added to the hot, nearly colorless filtrate, when colorless needles began to separate. More acid (1 cc.) was added, and after ice cooling the product was collected and recrystallized from 9 cc. of water and 10 cc. of hydrochloric acid containing a trace of stannous chloride. This gave 0.71 g. (50%) of fine colorless needles. The sample for analysis was dried at 60° and 30 mm.; it left a slight ash in the boat.

Anal. Calcd. for $C_{12}H_{15}O_3NCl$: C, 55.50; H, 6.99. Found: C, 55.06; H, 7.14.

ϵ -Quinonylcaproic Acid (VIII).—The thick paste formed by rapid cooling of a solution of 0.67 g. of the above hydrochloride in 20 cc. of 25% sulfuric acid was treated with 1.61 cc. of 4 *N* sodium dichromate solution and the mixture was kept overnight at 5° in a stoppered flask. The dark brown solution containing suspended solid was diluted with water and extracted five or six times with ether. The solution was washed twice with saturated salt solution, shaken at room temperature with Norit, filtered through sodium sulfate, and the bright yellow filtrate was concentrated under diminished pressure until the quinone began to separate. This was brought into solution, a little petroleum ether was added, and the solution was allowed to cool. The first crop (404 mg.) consisted of tiny, bright yellow plates, m. p. 101–102°, and a second crop (56 mg.) melted at 99–100.5°; yield 83%. Recrystallization of the first crop from ether-petroleum ether gave material melting at 101.4–102°; Craven test, immediate blue-green deepening to intense blue with a greenish tinge.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.86; H, 6.35. Found: C, 64.82; H, 6.65.

ϵ -Hydroquinonylcaproic Acid.—A suspension of 52 mg. of the quinone VIII in ether was shaken with aqueous sodium hydrosulfite solution, when the yellow color was discharged immediately. The separated ethereal layer was washed with saturated salt-solution, filtered through sodium sulfate, concentrated and treated with petroleum ether. The product separated as rosets of colorless blades, m. p. 96–97.5° (31 mg.). A recrystallized sample melted at 96.8–97.6° (14 mg.).

*Anal.*¹⁸ Calcd. for $C_{12}H_{14}O_4$: C, 64.25; H, 7.19. Found: C, 64.54; H, 7.41.

Addition of Butadiene to ϵ -Quinonyl-caproic Acid.—A mixture of 750 mg. of the quinone, 4 cc. of benzene and 2–3 cc. of butadiene was heated in a sealed tube at 70° for six hours. The reaction mixture, containing much crystalline solid, was washed out with acetone, the solution was filtered and evaporated and diluted with hexane, giving a total of 793 mg. of brown or tan product, m. p. 100–103°. Treatment with Norit in ether effectively removed the tan color, leaving a very pale yellow solution; crystallization from ether-petroleum ether then gave 699 mg. (75%) of faintly yellow blades, m. p. 101.5–103°. A recrystallized sample melted at 102.8–103.6°.

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.55; H, 7.52.

ϵ -(5,8-Dihydro-1,4-naphthohydroquinonyl-2)-caproic Acid (X). (a) From the Addition Product.—A solution of 63 mg. of the addition product in the minimum amount of alcohol was treated with three drops of

concentrated hydrochloric acid and a trace of stannous chloride, boiled for three minutes, and diluted with three volumes of water. A microcrystalline product separated on cooling and this was collected by ether extraction and crystallized from ether-petroleum ether. Small colorless prismatic needles were obtained (29 mg.), and two recrystallizations brought the melting point to 154–154.8° (16 mg.).

Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.30; H, 7.55.

(b) From the Ethyl Ester.—The ester of X (603 mg.), prepared as described below, was dissolved in 10 cc. of 30% potassium hydroxide containing 0.2–0.3 g. of sodium hydrosulfite in a flask flushed with nitrogen. The solution was refluxed under a slight pressure of nitrogen for one hour, the vat liquor remaining clear yellow. The solution was cooled slightly, acidified cautiously under nitrogen with 5 cc. of acetic acid, diluted with water and allowed to cool. The solid which separated was not easily filtered and was therefore extracted with ether. The extract was washed with saturated salt solution, concentrated and diluted with petroleum ether. On crystallization under forcing conditions, 504 mg. (92%) of colorless prismatic needles was obtained, m. p. 150–152° (after drying at 60° and 30 mm. to remove traces of acetic acid).

Ethyl ϵ -(5,8-Dihydro-1,4-naphthohydroquinonyl-2)-caproate.—A solution of 653 mg. of the diene addition product in 4 cc. of warm 95% ethyl alcohol was treated with 0.5 cc. of concentrated hydrochloric acid and a crystal of stannous chloride and heated for twenty-five minutes on the steam-bath. The ester did not crystallize readily on cooling but after some manipulation it formed rosetts of colorless needles. Collected, washed with acidified water, and dried in vacuum, the substance melted at 93–95.5° and depressed the melting point of the starting material; yield 633 mg. (88%). A sample crystallized twice from ether-petroleum ether melted at 95–96°.

Anal. Calcd. for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found: C, 70.67; H, 8.10.

ϵ -(1,4-Naphthoquinonyl-2)-caproic Acid (XI, $n = 5$).—To a pasty suspension of 504 mg. of ϵ -(5,8-dihydro-1,4-

naphthohydroquinonyl-2)-caproic acid in 4 cc. of acetic acid, a solution of 0.50 g. of chromic anhydride in 0.6 cc. of water and 1.5 cc. of acetic acid was added by drops. The material largely dissolved and a brown intermediate then separated and later dissolved. After warming at 60° for one-half hour, the solution was poured onto ice and the precipitate was collected and washed with water. The light yellow solid, which is but sparingly soluble in ether, crystallized from dilute methanol in centimeter-long needles of dull appearance melting at 142–146° (356 mg.). Two recrystallizations gave 300 mg. (60.5%) of product, m. p. 145.5–146.5°, but the dull appearance persisted. Recrystallization from benzene-hexane (Norit) gave 279 mg., m. p. 146.2–147.2°, and on a further crystallization from benzene the quinone formed fairly bright yellow leaf-like blades, m. p. 146–147.5° with slight preliminary softening. In the Craven test the substance gave a light lavender blue color deepening to a beautiful blue with a trace of purple.

*Anal.*¹³ Calcd. for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.56; H, 6.20.

Summary

Certain considerations suggest that, in the series embracing quinones having a fatty acid side chain, compounds may be found possessing interesting biological actions. As a first step in a study of such substances, the known *o*-hydroxybenzoyl derivatives of propionic and valeric acid were reduced by the Clemmensen method and the products were converted through the *p*-sulfo-benzeneazo and amino derivatives into γ -quinonylbutyric acid and ϵ -quinonylcaproic acid. These benzoquinones were converted, by the addition of butadiene, isomerization and oxidation, into the corresponding naphthoquinone acids.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS RECEIVED AUGUST 17, 1940

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

The Synthesis of 3,4-Benzphenanthrene and 1-Methylpyrene

BY W. E. BACHMANN AND R. O. EDGERTON¹

As starting material for the synthesis of the carcinogenic hydrocarbon 3,4-benzphenanthrene (IV) and of 1-methylpyrene (VIII) we employed the readily available 4-keto-1,2,3,4-tetrahydrophenanthrene. In the synthesis of the first hydrocarbon, the cyclic ketone was treated with zinc and methyl bromoacetate and the product of the Reformatsky reaction was dehydrated to methyl 4-(1,2-dihydrophenanthryl)-acetate (I). The ester group of this compound was reduced to

an alcohol group by sodium and methanol, the nucleus being reduced partially at the same time. The alcohol was converted to the corresponding bromide, which was condensed with sodio-malonic ester. The methyl ester of the acid obtained by decarboxylation of the substituted malonic acid was dehydrogenated to the ester of γ -(4-phenanthryl)-butyric acid (II). Cyclization of this acid through its acid chloride yielded 1'-keto-1',-2',3',4'-tetrahydro-3,4-benzphenanthrene (III), which was reduced by the Clemmensen method to

(1) From the Ph.D. dissertation of R. O. Edgerton.