as has been demonstrated so elegantly recently by Adams and Gebhart[7] in the benzpinacol rearrangement.

Experimental[8]

All solvents and reagents used were of ordinary quality unless otherwise noted. Details of preparation of the pinacols are given since they differ somewhat from those presented previously.[6,9]

trans-**1,2-Ditolylacenaphthenediol-1,2**, either ortho or para, was prepared by the addition of 18.2 g. (0.1 mole) of dry finely powdered acenaphthoquinone to an ice-cold solution of the Grignard reagent prepared from 7.2 g. (0.3 mole) of magnesium and 36.1 ml. (51.3 g., 0.3 mole) of the appropriate bromotoluene under nitrogen in 150 ml. of dry ether. Dry benzene, 300 ml., was added immediately, and the mixture, stirred vigorously, brought to a boil on the steam-bath. Approximately 200–250 ml. of the solvent was removed by distillation, and the mixture heated under reflux until the total period of heating was 3–4 hours. After hydrolysis of the mixture with excess dilute hydrochloric acid and ice (more ether was usually necessary), the ether layer was washed with 5% sodium hydroxide solution until no more blue solid was formed. After a short drying period, most of the solvent was removed, and replaced by isopropyl alcohol from which the products crystallize nicely. The yield of crude *o*-tolylpinacol was 22.0–24.0 g. (60–66%), which after one recrystallization gave 20.0–22.0 g. of material of m.p. 162.5–163.5°. An analytical sample had m.p. 164–165°, lit. m.p. 164°.[10] The yield of crude *p*-tolylpinacol was 25.0–27.0 g. (68–74%), which after recrystallization gave 23.0–25.0 g. of material of m.p. 185.0–185.5°, lit. m.p. 182.0–182.5°.[9]

1,8-Ditoluoylnaphthalene, either ortho or para, was prepared by the oxidation of the corresponding *trans*-pinacol, 18.3 g. (0.05 mole) in 150 ml. of boiling acetic acid with 5.0 g. (0.017 mole) of potassium dichromate added all at once (chromic oxide causes considerable rearrangement to occur). The temperature was maintained for 10–15 minutes, and 300 ml. of water added gradually while the mixture was stirred. After standing overnight, the product was collected by filtration, dried and used directly in the next step. Yields were 17.9–18.2 g. (98–99%) of crude product. Recrystallization from carbon tetrachloride gave tiny needles, m.p. 242–243°, lit. m.p. 238°,[10] of 1,8-di-*o*-toluoylnaphthalene. Recrystallization from isopropyl alcohol gave flat needles, m.p. 183–184°, lit. m.p. 181.5–182.5°,[9] of 1,8-di-*p*-toluoylnaphthalene.

cis-**1,2-Ditolylacenaphthenediol-1,2**, either ortho or para, was prepared by the addition of 18.2 g. (0.05 mole) of the corresponding 1,8-ditoluoylnaphthalene to an ice-cold mixture in 100 ml. of dry ether of magnesium plus magnesium iodide made by the addition all at once of 12.7 g. (0.05 mole) of iodine to 2.4 g. (0.1 mole) of magnesium, under nitrogen, with vigorous stirring, until the iodine color had completely disappeared. Dry benzene, 300 ml., was added, stirring resumed, the mixture heated to boiling, and 100–125 ml. of the solvent distilled. The mixture was heated under reflux until the total period of heating was 3–4 hours when the mixture was cooled and hydrolyzed in the usual manner to give 16.5 g. (90%) of the *o*-tolylpinacol, m.p. 199–203°, or 16.1 g. (88%) of the *p*-tolylpinacol, m.p. 144–148°. Recrystallization from isopropyl alcohol gave 15.2 g. of hexagonal plates, m.p. 206–207°, of *cis*-1,2-di-*o*-tolylacenaphthenediol-1,2. *Anal.*[11] Calcd. for $C_{26}H_{22}O_2$: C, 85.22; H, 6.05. Found: C, 85.43; H, 6.15. Recrystallization from carbon tetrachloride–Skellysolve B gave 14.1 g. of tiny needles, m.p. 155–156°, lit. m.p. 154.3–155.3°,[9] of *cis*-1,2-di-*p*-tolylacenaphthenediol-1,2.

The **pinacolones** were obtained as described previously.[6,9] Curiously, both 2,2-di-*o*-tolylacenaphthenone and 2,2-di-*p*-tolylacenaphthenone have the same m.p., 135.5–136.5° (lit. m.p. for the latter 128.5–129.5°).[9] The *o*-pinacolone, 1.0 g., was cleaved to **8-(di-*o*-tolylmethyl)-1-naphthoic acid** by boiling with 2.0 g. of potassium hydroxide in 20 ml. of ethanol for 3 hours. Then 50 ml. of water was added, the alcohol removed by distillation, and the acid precipitated from the cooled solution by the addition of 20 ml. of 3 *N* hydrochloric acid. Crystallization from benzene, and recrystallization from ethanol gave 0.4 g. of colorless needles, m.p. 247–248°. *Anal.*[11] Calcd. for $C_{26}H_{22}O_2$: C, 85.22; H, 6.05. Found: C, 84.98; H, 5.92.

The reactions in methanol were carried out as described previously.[2] The dimethyl acetal of the *p*-tolylpinacolone, **2,2-di-*p*-tolyl-1,1-dimethoxyacenaphthene**, colorless prisms from isopropyl alcohol, m.p. 172–173°. *Anal.*[11] Calcd. for $C_{28}H_{26}O_2$: C, 85.24; H, 6.64; CH_3O, 15.73. Found: C, 85.43; H, 6.34; CH_3O, 15.39.

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[7] K. H. Adams and H. J. Gebhart, Jr., Organic Division, American Chemical Society Meeting, Atlantic City, New Jersey, September 14–19, 1952.

[8] All melting points are uncorrected.

[9] W. E. Bachmann and E. J. Chu, THIS JOURNAL, **58**, 1118 (1936).

[10] E. Clar, H. Wallenstein and R. Avenarius, *Ber.*, **62**, 950 (1929).

[11] Analysis by Mr. Joseph Pirie.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MISSOURI]

Substituted Long Chain Fatty Acid Hydrazones of 5-Nitrofurfural

BY NORMAN RABJOHN AND M. S. COHEN[1]

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Methods have been developed for a generalized procedure of preparation of derivatives of branched, long chain acid hydrazides which contain a substituted quaternary ammonium group.

Bacteriological tests[2] on certain members of a series of 5-nitrofurfurylidene derivatives of quaternary ammonium acethydrazones[3] indicated that these compounds have about the same level of antibacterial activity, *in vitro*, against a spectrum of selected organisms as does Furacin (5-nitrofurfural semicarbazone). It was thought that lengthening and branching of the acid chain might enhance the desired type of action.

In a previous study[4] of quaternary ammonium salts of branched chain fatty acid hydrazides, the preparative procedure employed permitted substitution of an alkyl group in the position beta to the carboxyl function. The present investigation was undertaken to develop methods whereby it would be possible to obtain a branched alkyl grouping at other places along the chain, as well as to incorporate the 5-nitrofurfurylidene radical into the compound.

The synthetic scheme employed should lead to structures of the general formula

$$[R_3N(CH_2)_x\ CHR'(CH_2)_y\ CONHN{=}CHR'']^+Br^-$$

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[1] Abstracted in part from a thesis submitted by M. S. Cohen to the Graduate College of the University of Missouri, 1952, in partial fulfillment of the requirements for the Ph.D. degree.

[2] E. C. Heath, H. S. Goldberg and M. N. Green, *Bact. Proc.*, 142 (1950).

[3] Norman Rabjohn and M. S. Cohen, unpublished work.

[4] Norman Rabjohn and P. D. Strickler, THIS JOURNAL, **75**, 3852 (1953).

where $x = 3$ or greater and $y = 1$ or more. Specifically, the following sequence of reactions was carried out.

$$\mathrm{Br(CH_2)_{10}COCl\ (I)} \xrightarrow{\mathrm{(CH_3)_2Cd}} \mathrm{Br(CH_2)_{10}COCH_3\ (II)}$$

$$\mathrm{II + C_2H_5O(CH_2)_3MgBr} \xrightarrow[\text{hydrolysis}]{\text{after}} \underset{\mathrm{III}}{\mathrm{Br(CH_2)_{10}C(CH_3)(OH)(CH_2)_3OC_2H_5}}$$

$$\mathrm{III} \xrightarrow{-\mathrm{H_2O}} \text{mixture of olefins (IV)}$$

$$\mathrm{IV} \xrightarrow[\text{and hydrolysis}]{\text{Mg; then } \mathrm{CO_2}} \text{mixture of unsaturated acids (V), or}$$

$$\mathrm{IV} \xrightarrow{\mathrm{KCN}} \text{mixture of unsaturated nitriles (VI)} \xrightarrow{\mathrm{H_2O}} \mathrm{V}$$

$$\mathrm{V} \xrightarrow{\mathrm{H_2,\ Ni}} \mathrm{C_2H_5O(CH_2)_3CH(CH_3)(CH_2)_{10}CO_2H\ (VII)}$$

$$\mathrm{VII} \xrightarrow{\mathrm{HBr}} \mathrm{Br(CH_2)_3CH(CH_3)(CH_2)_{10}CO_2H\ (VIII)}$$

$$\mathrm{VIII} \xrightarrow{\mathrm{C_2H_5OH,\ H^+}} \mathrm{Br(CH_2)_3CH(CH_3)(CH_2)_{10}CO_2C_2H_5\ (IX)}$$

$$\mathrm{IX} \xrightarrow{\mathrm{(CH_3)_3N}} \mathrm{[(CH_3)_3N(CH_2)_3CH(CH_3)(CH_2)_{10}CO_2C_2H_5]^+Br^-\ (X)}$$

$$\mathrm{X} \xrightarrow{\mathrm{H_2NNH_2}} \mathrm{[(CH_3)_3N(CH_2)_3CH(CH_3)(CH_2)_{10}CONHNH_2]^+Br^-\ (XI)}$$

$$\mathrm{XI + NO_2C_4H_2OCHO} \longrightarrow \mathrm{[(CH_3)_3N(CH_2)_3CH(CH_3)(CH_2)_{10}CONHN{=}C_5H_3O_3N]^+Br^-\ (XII)}$$

The carbinol III was prepared by the route shown after it was found[5] that an attempted condensation of the bromo acid chloride I with a supposed γ-phenoxy- or ethoxycadmium reagent led to anomalous results. The bromo ketone II was obtained satisfactorily; however, when a 6:1 ratio of dimethylcadmium (prepared from methylmagnesium iodide) to acid chloride was used in an attempt to improve the yield of II, the main product was not the ketone, but a mixture of compounds. It appeared to consist of the tertiary alcohol, which would result from the normal Grignard type of addition, olefins from the dehydration of the carbinol and a high boiling product. Although no special effort was made to identify any of these compounds, analytical data suggest that the latter might be an unsaturated dibromide, $C_{24}H_{44}Br_2$. It is conceivable that some of the methyl 10-bromodecyl ketone might have undergone a bimolecular condensation in the presence of the inorganic salts, and the diol subsequently suffered dehydration.

In trial experiments, ethyl 10-bromodecyl ketone and phenyl 10-bromodecyl ketone were synthesized in relatively high yields from 11-bromohendecanoyl chloride and the appropriate organocadmium reagent.

The ketone II was converted to the ethoxy acid VII by the two routes shown without isolation of the intermediates III, IV or V. The preparation of the acid VII by carbonation of the Grignard reagent from IV and reduction of the mixture of acids V gave a lower yield than the alternative procedure in which the mixture of nitriles VI was taken to the ester IX without isolation of the intermediate compounds.

The quaternary ammonium salt X was found to be too deliquescent to handle readily, so analytical data on it were not obtained. It was converted by conventional procedures to the hydrazide XI and then to the 5-nitrofurfurylidene derivative XII. The latter is a mustard-yellow colored solid, soluble in water.

The synthesis of an unbranched 5-nitrofurfurylidene derivative of a long chain hydrazide of a quaternary ammonium bromide, *i.e.*, the hydrazide of trimethyl-10-carbethoxydecylammonium bromide, was carried out in preliminary experiments. Its method of synthesis is described in the Experimental section. Pharmacological tests have not been carried out on these compounds.

Experimental[6]

Methyl 10-Bromodecyl Ketone (II).—The dimethylcadmium reagent was prepared in the usual manner from 5.8 g. (0.24 gram-atom) of magnesium turnings, excess gaseous methyl bromide, 23.8 g. (0.13 mole) of anhydrous cadmium chloride and 125 ml. of anhydrous ether. To this well stirred mixture was added slowly 50 g. (0.18 mole) of 11-bromohendecanoyl chloride (b.p. 130–132° (1 mm.), n^{19}D 1.4800; lit.[7] b.p. 174–175° (10 mm.)) dissolved in 40 ml. of dry benzene. After heating under reflux for 40 minutes, the reaction mixture was decomposed in the customary fashion. The organic layer was washed, dried over anhydrous sodium sulfate and the solvent was removed under diminished pressure. The residual oil was distilled *in vacuo* and there was obtained 28.5 g. (60%) of material; b.p. 130–132° (1 mm.), n^{18}D 1.4701.

Anal. Calcd. for $C_{12}H_{23}OBr$: C, 54.75; H, 8.81. Found: C, 54.67; H, 9.04.

A semicarbazone was prepared from a sample of the ketone. It was recrystallized from methanol and obtained in the form of white prisms, m.p. 118–119°.

Anal. Calcd. for $C_{13}H_{26}ON_3Br$: C, 48.75; H, 8.18. Found: C, 48.63; H, 8.42.

Phenyl 10-bromodecyl ketone, m.p. 49–50° (from methanol), and ethyl 10-bromodecyl ketone, m.p. 30–31° (from petroleum ether b.p. 28–38°) were prepared in a similar fashion.

Anal. Calcd. for $C_{17}H_{25}OBr$: C, 62.76; H, 7.78. Found: C, 62.91; H, 7.97. Calcd. for $C_{13}H_{25}OBr$: C, 56.31; H, 9.09. Found: C, 56.03; H, 9.14.

Their 2,4-dinitrophenylhydrazones melted at 95–96° (from cyclohexane) and 49–50° (from petroleum ether b.p. 28–38°), respectively.

Anal. Calcd. for $C_{23}H_{29}O_4N_4Br$: C, 54.65; H, 5.78. Found: C, 54.58; H, 6.03. Calcd. for $C_{19}H_{29}O_4N_4Br$: C, 49.89; H, 6.39. Found: C, 50.10; H, 6.62.

15-Ethoxy-12-methylpentadecanoic Acid (VII).—γ-Ethoxypropylmagnesium bromide, prepared from 3.5 g. (0.14 gram-atom) of magnesium, 23 g. (0.14 mole) of γ-ethoxypropyl bromide and 60 ml. of anhydrous ether, was caused to react with 38 g. (0.14 mole) of methyl 10-bromodecyl ketone dissolved in 30 ml. of dry ether. The reaction mixture was decomposed by means of a saturated solution of ammonium chloride. The organic layer was separated, and the ether was removed to leave a light yellow oil which was dehydrated to a mixture of olefins by heating at 170–180° in the presence of a crystal of iodine. The product was subjected to vacuum distillation and there was collected 35 g. (73%) of a colorless oil, b.p. 169–170° (1 mm.), n^{16}D 1.4745. A micro-hydrogenation was performed on a sample

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(5) Norman Rabjohn and M. S. Cohen, THIS JOURNAL, **74**, 6290 (1952).

(6) All melting points are uncorrected. The authors are indebted to Mr. P. D. Strickler and Mr. Y. N. Lee for the semi-micro analyses.

(7) F. J. Buckle, F. L. M. Pattison and B. C. Saunders, *J. Chem. Soc.*, 1471 (1949).

of this material and the hydrogen uptake corresponded to 0.99 mole of hydrogen/mole of olefin.

A solution of 35 g. (0.1 mole) of the mixed olefins, 14.2 g. (0.1 mole) of methyl iodide and 175 ml. of anhydrous ether was added slowly to 5.3 g. (0.22 gram-atom) of magnesium. After the addition had been completed, the reaction mixture was heated to gentle reflux for 90 minutes after which time only a small quantity of magnesium remained. The Grignard solution was forced into a 250-ml. separatory funnel under the pressure of an atmosphere of dry nitrogen. It was then dropped slowly onto a slurry of 100 g. of Dry Ice and 100 ml. of anhydrous ether. The reaction mixture was decomposed in the usual way, and the ethereal solution was extracted with three 120-ml. portions of 10% sodium bicarbonate solution. The combined alkaline extracts were acidified and the oil which separated was taken up in ether. The ether solution was dried and concentrated to give 25 g. of a light yellow oil which was not distilled, but was hydrogenated directly.

A mixture of the oil (25 g.), 125 ml. of ethanol and 4 g. of Raney nickel catalyst was heated at 65° and 2,300 lb. pressure of hydrogen. After removing the catalyst and solvent, the residue was distilled *in vacuo*. There was obtained 14 g. (44.5%) of an acid which boiled at 150–153° (0.01 mm.), n^{21}D 1.4519.

Anal. Calcd. for $C_{18}H_{36}O_3$: C, 71.95; H, 12.08. Found: C, 71.58; H, 12.40.

An amide was prepared from the above acid; repeated crystallizations from *n*-hexane gave white crystals, m.p. 70–71°.

Anal. Calcd. for $C_{18}H_{37}O_2N$: C, 72.19; H, 12.45. Found: C, 72.02; H, 12.24.

15-Bromo-12-methylpentadecanoic Acid (VIII).—A mixture of 12.5 g. (0.04 mole) of 15-ethoxy-12-methylpentadecanoic acid, 30 ml. of glacial acetic acid and 9.5 g. (0.12 mole) of dry hydrogen bromide was sealed in a 100-ml. pressure bottle. The contents of the bottle were maintained at approximately 90° for 45 hours and then allowed to cool to room temperature. The solvent and excess hydrogen bromide were removed under slightly reduced pressure and the dark, oily residue was distilled *in vacuo*. There was obtained 9.7 g. (69%) of material which boiled at 181–182° (0.1 mm.) and solidified in the receiver. After two crystallizations from aqueous methanol, 8.6 g. of white platelets was obtained which melted at 44–45°.

Anal. Calcd. for $C_{16}H_{31}O_2Br$: C, 57.31; H, 9.32; neut. equiv., 335. Found: C, 57.52; H, 9.53; neut. equiv., 339.

Ethyl 15-Bromo-12-methylpentadecanoate (IX).—A solution of 8.6 g. (0.03 mole) of 15-bromo-12-methylpentadecanoic acid, 1.0 g. of *p*-toluenesulfonic acid and 100 ml. (1.7 moles) of absolute ethanol was refluxed in a flask equipped with a Soxhlet extractor which contained 25 g. of calcium carbide. After the esterification had been completed, the excess alcohol was removed on a steam-bath and the residue was taken up in 30 ml. of petroleum ether (b.p. 28–38°). The latter solution was washed with water, 10% sodium bicarbonate solution, water and then dried over anhydrous sodium sulfate. The petroleum ether was evaporated and the residue was distilled under reduced pressure to give 7.2 g. (80%) of product, b.p. 138–140° (0.5 mm.), n^{19}D 1.4600.

Anal. Calcd. for $C_{18}H_{35}O_2Br$: C, 59.49; H, 9.71. Found: C, 59.69; H, 10.05.

This ester was prepared in 10% greater over-all yield from the same starting materials, *i.e.*, the mixture of 4-methyl-1-ethoxy-14-bromotetradecene-3 and -4 (IV), by way of the nitrile synthesis. In this series none of the intermediates, with the exception of the nitrile, was isolated.

1-Ethoxy-4-methyl-14-cyanotetradecene-3 and -4 (VI).—To a solution of 24.0 g. (0.07 mole) of a mixture of 1-ethoxy-4-methyl-14-bromotetradecene-3 and -4 (IV) in 35 ml. of ethanol were added 6.5 g. (0.1 mole) of potassium cyanide and 7 ml. of water. The mixture was heated under reflux for 12 hours after which it was reduced to one-half its volume by distillation, and 40 ml. of water was added. The oil which separated was removed by extraction with two 15-ml. portions of ether. The extracts were combined, washed with water, dried over anhydrous sodium sulfate and concentrated on a water-bath. The residue was distilled and there was obtained 15.5 g. (78%) of a colorless oil, b.p. 183–185° (3 mm.), n^{17}D 1.4599.

Anal. Calcd. for $C_{18}H_{33}ON$: C, 77.36; H, 11.90. Found: C, 77.17; H, 11.70.

Trimethyl-(4-methyl-14-carbethoxy)-tetradecylammonium Bromide (X) and Its Derivatives XI and XII.—To a solution of 5.5 g. (0.015 mole) of ethyl 15-bromo-12-methylpentadecanoate in 30 ml. of dry benzene, contained in a 100-ml., thick-walled bottle was added a two molar excess of trimethylamine. The bottle was sealed and the temperature was maintained at 60–70° for 10 hours after which it was cooled and opened. The contents were reduced to about one-half by heating on a steam-bath. Three volumes of petroleum ether (b.p. 28–38°) was added and a white, silky solid precipitated. The clear, upper layer was removed by decantation and the solid was washed with five successive portions of petroleum ether. The last traces of solvent were removed by warming. The product melted at 200–205° with prior softening and was so deliquescent that it did not appear to be feasible to attempt to purify it for analysis. Its hydrazide XI was prepared in the conventional manner in 57% yield; m.p. 176–178° (from absolute ethanol).

Anal. Calcd. for $C_{19}H_{42}ON_3Br$: C, 55.86; H, 10.36. Found: C, 55.69; H, 10.46.

Condensation of XI with 5-nitrofurfural[8] gave the substituted hydrazone XII. It was purified by repeated precipitation from alcoholic solution by the addition of dry ether. The yellow powder (79% yield) melted at 124–126°.

Anal. Calcd. for $C_{24}H_{43}O_4N_4Br$: C, 54.23; H, 8.15. Found: C, 54.03; H, 8.44.

Reaction of 5-Nitrofurfural with the Hydrazide of Trimethyl-10-carbethoxydecylammonium Bromide.—Trimethyl-10-carbethoxydecylammonium bromide was obtained by heating ethyl 11-bromohendecanoate and trimethylamine in ether solution at 85–90° for 11 hours. The lustrous platelets (66%) were crystallized from ethyl acetate; m.p. 166–169°.

Anal. Calcd. for $C_{16}H_{34}O_2NBr$: C, 54.53; H, 9.72. Found: C, 54.25; H, 9.93.

Its hydrazide was purified by trituration with dioxane; m.p. 133–136°.

Anal. Calcd. for $C_{14}H_{32}ON_3Br$: C, 49.69; H, 9.53. Found: C, 49.40; H, 9.69.

The 5-nitrofurfurylidene derivative of the hydrazide was obtained in 79% yield after recrystallization from pyridine; m.p. 151–153°.

Anal. Calcd. for $C_{19}H_{33}O_4N_4Br$: C, 49.45; H, 7.21. Found: C, 49.70; H, 7.51.

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(8) The authors would like to thank the Eaton Laboratories for a generous sample of 5-nitrofurfural diacetate from which this material was prepared.