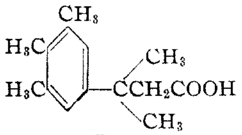
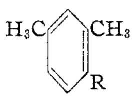
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

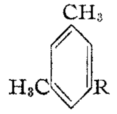
Polyalkylbenzenes. XXXII. The Reaction between Dimethylacrylic Acid and *m*-Xylene[1]

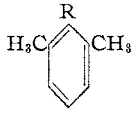
BY LEE IRVIN SMITH AND LEO J. SPILLANE[2]

In a previous paper[3] it was shown that β,β-dimethylacrylic acid reacted with either 1,2,3- or 1,2,4-trimethylbenzene in the presence of aluminum chloride to produce β-(3,4,5-trimethylphenyl)-isovaleric acid, I. The reaction with pseudocumene, therefore, involved a rearrangement, with the production of a tetrasubstituted benzene having the 1,2,3,5-orientation. In order to determine the limits of this rearrangement reaction, a detailed investigation of the action of various alkylated hydrocarbons upon β,β-dimethylacrylic acid has been undertaken, and this paper contains a report of the results obtained when the hydrocarbon is *m*-xylene.


I

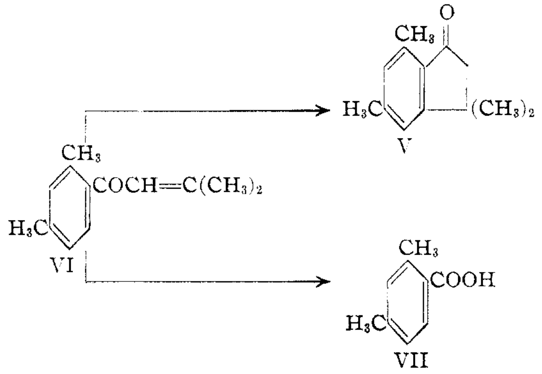

II


III


IV

R = $-C(CH_3)_2CH_2COOH$

m-Xylene and β,β-dimethylacrylic acid reacted in the presence of aluminum chloride to produce an excellent yield of a β-(dimethylphenyl)-isovaleric acid, formed by addition of one molecule of the hydrocarbon to one of the acid. Although application of the ordinary rules of orientation would lead to prediction of II, the 2,4-dimethyl isomer, as the structure of this product, it is well known that *alkylation* of *m*-xylene in the presence of aluminum chloride almost invariably leads mainly to the 1,3,5-trialkyl derivative[4]; if the 1,2,4-trialkyl derivative is desired, it is usually necessary to alkylate *m*-xylene in the absence of aluminum chloride.[5] Hence, although structures II and IV had also to be considered, it appeared most probable that the dimethylphenylisovaleric acid would prove to be the 3,5-isomer, III. This dimethylphenylisovaleric acid, in contact with sulfuric acid at room temperature, gave a quantitative yield of a tetramethylhydrindone V by loss of water. This reaction eliminated structure IV for the acid since in IV there is no vacant position in the benzene ring ortho to the acid group. In order to decide between structures II and III, the hydrindone V was synthesized by an independent method which could lead only to 3,3,5,7-tetramethylhydrindone, V. Dimethylacrylyl chloride was condensed with *m*-xylene in the presence of aluminum chloride to give 2,4,β-trimethylbenzalacetone, VI. No rearrangement was expected in this reaction, for there are many instances recorded in the literature in which normally oriented products have resulted in the Friedel–Crafts reaction between acid chlorides and alkylated benzenes.[6] That the ketone VI actually had the 1,2,4-orientation was proved by its conversion, by ozonolysis or by action of permanganate, into the known 2,4-dimethylbenzoic acid VII.



Cyclization of VI by action of hydrogen chloride and aluminum chloride gave the hydrindone V, which was identical with the hydrindone prepared by cyclization of the dimethylphenylisovaleric acid. Since, of compounds II and III, only the latter could give V on cyclization, it followed that the product formed by reaction between *m*-xylene and β,β-dimethylacrylic acid was β-(3,5-dimethylphenyl)-isovaleric acid III.

---

(1) XXXI, THIS JOURNAL, **62**, 2639 (1940).

(2) Abstracted from a thesis by L. J. Spillane, presented to the Graduate Faculty of the University of Minnesota, in partial fulfilment of the requirements for the Ph.D. degree, July, 1942.

(3) Smith and Prichard, THIS JOURNAL, **62**, 771 (1940).

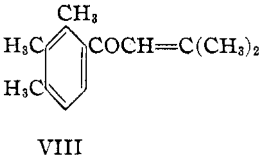
(4) Nightingale, *Chem. Rev.*, **25**, 329 (1939).

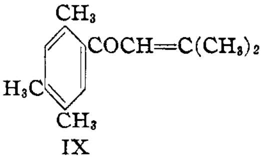
(5) (a) Meyer and Bernhauer, *Monatsh.*, **53**, 721 (1928); (b) Kirrmann and Graves, *Bull. soc. chim.*, [5] **1**, 1494 (1934).

(6) Thomas, "Anhydrous Aluminum Chloride in Organic Chemistry," Reinhold Publishing Corp., New York, N. Y., 1941, p. 219.

In the previous work[7] it was found that mesitylene condensed with β,β-dimethylacrylic acid to give a dimethylphenylisovaleric acid with loss of one of the methyl groups of the hydrocarbon. This acid melted at 110–111°, and it gave a hydrindone by action of sulfuric acid. The acid obtained from mesitylene is identical with III obtained from *m*-xylene; both acids melt at the same temperature and there is no depression in melting point when the two are mixed. There was not enough of the hydrindone (m. p. 62–63°) left from the previous work for a determination of a mixed melting point with V (m. p. 57.5–58°) but there can be little doubt about the identity of the two hydrindones.

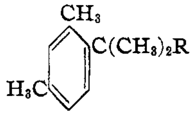
The ketone VI was rather resistant toward ring closure, and, in order to bring about cyclization, it was necessary to saturate the solution of the ketone in carbon bisulfide with hydrogen chloride and then to remove the solvent on the water-bath in the presence of a large excess of aluminum chloride. Under these drastic conditions, the yield of V was only 48%, and the product was accompanied by a great deal of tarry material. Less drastic conditions, or the use of other cyclizing agents such as sulfuric acid or stannic chloride, produced little or no hydrindone from VI. These observations agree well with the generalization of v. Auwers and Risse,[8] who studied a number of reactions of this type and found that in α,β-unsaturated ketones of the type of VI, cyclization to hydrindones by action of aluminum chloride was greatly hindered when a methyl group was present in the meta position to the ring hydrogen atom involved in the reaction, and was promoted when a methyl group was in the ortho or para position. However, in case of the ketones VIII and IX, cyclization was found to be particularly smooth and easy.[3]


VIII

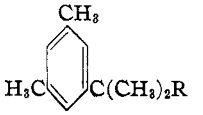

IX

It was considered unlikely that a rearrangement might have occurred during the cyclization of the acid III to the hydrindone V, and that the acid was in reality II, because of the very mild conditions under which the cyclization occurred. The conditions under which a Jacobsen rearrangement would occur are much more drastic than the conditions used for cyclization of III to V; moreover, no case has been observed so far in which a trialkylbenzene undergoes this rearrangement with sulfuric acid.[9] Although the evidence for absence of a rearrangement during the cyclization was considered good, it was not absolutely conclusive, and to make certain that structure III was correct, attempts were made to obtain confirmatory evidence either by an independent synthesis of II or III, or by degradation of III to some compound which could, in turn, be synthesized independently. Although none of these experiments could be carried to a successful conclusion, they served to emphasize more fully the extreme ease with which the acid III and its derivatives underwent cyclization.

The first synthetic experiments involved the sequence X–XIII and paralleled that previously found to be successful in another series of compounds.[10]



X, R = OH
XI, R = Br
XII, R = —CH(COOC$_2$H$_5$)$_2$
XIII, R = —CH(COOH)$_2$
II, R = —CH$_2$COOH
XIV, R = Cl
XV, R = OCH$_3$
XVI, R = K
XVII, R = COOH



XVIII, R = K
XIX, R = CN
XX, R = CONH$_2$
XXI, R = COOH
XXII, R = COCl
XXIII, R = CON$_3$
III, R = —CH$_2$COOH
XXIV, R = —CH$_2$COOCH$_3$
XXV, R = —CH$_2$C(OH)(CH$_3$)$_2$
XXVI, R = —CH=C(CH$_3$)$_2$
XXIX, R = H

But this synthesis of II failed when the action of sodiomalonic ester upon XI produced, not the malonic ester XII, but the unsaturated hydrocarbon formed by elimination of hydrobromic acid from XI. A second synthesis, involving the sequence XIV–XVII also failed, because carbonation of the organo potassium compound XVI gave only small amounts of oils which could not be crystallized. In a third synthesis, 3,5-dimethylisopropylbenzene was metalated with benzylpotassium, in the hope of obtaining XVIII, but again carbonation of the organo potassium com-

---

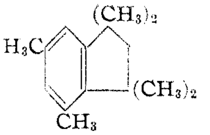
(7) Ref. 3, p. 774.

(8) v. Auwers and Risse, *Ann.*, **502**, 282 (1933).

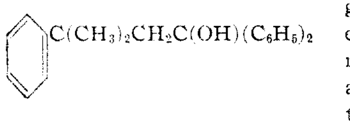
(9) (a) Smith and Guss, THIS JOURNAL, **62**, 2625, 2631 (1940); (b) Smith and Kiess, *ibid.*, **61**, 989 (1939); (c) Smith and Cass, *ibid.*, **54**, 1614 (1932); (d) Moyle and Smith, *J. Org. Chem.*, **2**, 112 (1932).

(10) Smith and Prichard, THIS JOURNAL, **62**, 772 (1940).

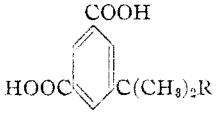
pound produced no definite products. Finally, mesitylene was converted into 3,5-dimethylbenzyl cyanide via 3,5-dimethylbenzyl bromide,[11] and starting with the cyanide, the sequence XIX–XXIII was undertaken. The synthesis was successful through compound XXII, but the Arndt–Eistert reaction failed and the product of the reaction between sodium azide and XXII could not be converted into III. Having synthesized XXI, the lower homolog of III, an attempt was made to convert III into XXI by the degradative method of Barbier–Wieland.[12] The methyl ester of III (XXIV) was converted into the carbinol XXV by action of methylmagnesium iodide. Since the carbinol was a liquid, no attempts were made to purify it completely but, instead, the crude carbinol was dehydrated by refluxing it with acetic anhydride containing a drop of sulfuric acid. Although the product gave the proper analytical values for the hydrocarbon XXVI, it showed no unsaturation toward bromine, alkaline permanganate or ozone. This substance was not investigated further, but since it was a saturated isomer of XXVI, it doubtless was 1,1,3,3,4,6-hexamethylindane, XXVII. This easy cyclodehydration of the carbinol XXV to a hydrindene was somewhat surprising, inasmuch as a very similar carbinol, XXVIII, had been found to give the corresponding olefin on distillation under reduced pressure.[13]



XXVII



XXVIII



XXX, R = —CH_2COOH
XXXI, R = COOH

Attempts were next made to decarboxylate the acid III and so convert it into 1,3-dimethyl-5-*t*-butylbenzene, XXIX, which could then be identified as the trinitro derivative. But a mixture of products resulted when the sodium salt of III was heated with soda lime, and it was not possible to obtain a solid by nitration of the low-boiling portion of this product. A Hoffmann degradation of III via the amide could not be tried because the amide could not be prepared. The ammonium salt of III, when heated, simply lost ammonia and reverted to III, and all attempts to convert III to the acid chloride by action of thionyl chloride in the presence or absence of pyridine, or by action of phosphorus trichloride, gave large amounts of the hydrindone V and no amide could be isolated by pouring the mixture into ammonia.

Oxidative degradation of III to XXI was likewise unsuccessful. The acid I, as well as an isomer of I with a different orientation of the substituents, had been found to undergo oxidative degradation to the lower homologs, the trimethylphenylbutyric acids, by prolonged action of permanganate.[3] But this procedure, when applied to III, either destroyed it completely or else converted it into the tribasic acid XXX. Action of dilute nitric acid at 200° upon III likewise produced XXX. In a similar fashion, these oxidizing agents converted the isobutyric acid XXI into the tribasic acid XXXI, but no method was found whereby either XXX or XXXI could be oxidized to trimesic acid.

Experimental Part[14]

β-(3,5-Dimethylphenyl)-isovaleric Acid (III).—β,β-Dimethylacrylic acid[15] (19.5 g., 0.2 mole) and *m*-xylene (80.5 g., 0.76 mole) were placed in a 200-cc. three-necked flask equipped with an exit tube, thermometer and stirrer. The mixture was stirred and cooled (−8°), and powdered aluminum chloride (29.3 g., 0.22 mole) was added in portions over a period of fifteen minutes while the temperature was maintained below 5°. When nearly all the catalyst had been added, a brisk evolution of hydrogen chloride began. The reaction mixture was cooled and stirred for twenty minutes longer, then the cooling bath was removed and the mixture was vigorously stirred and allowed to attain room temperature slowly (five and one-half hours). The product was poured over a large quantity of ice containing some hydrochloric acid, and the excess *m*-xylene was removed by steam distillation. The pale yellow oil remaining in the distillation flask solidified on cooling to a nearly white solid. The solid was filtered, washed thoroughly with water and dried in the air. It weighed 40 g. (97%) and melted at 103–111.5°. After crystallization from aqueous alcohol or dilute acetic acid, the product melted at 111–112°. For best results, the reaction mixture must be allowed to come to room temperature, and must be stirred for some time, after adding all the aluminum chloride, which must be present in slight excess over the dimethylacrylic acid.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.67; H, 8.80. Found: C, 75.63; H, 8.80.

---

[11] Robinet, *Compt. rend.*, **96**, 501 (1883); *Ber.*, **16**, 965 (1883).

[12] (a) Barbier and Locquin, *Compt. rend.*, **156**, 1443 (1913); (b) Wieland, Schlichting and Jacobi, *Z. physiol. Chem.*, **161**, 80 (1926).

[13] Bergmann, Taubadel and Weiss, *Ber.*, **64**, 1493 (1931).

[14] Microanalyses by E. E. Renfrew and Stanley Rolfson.

[15] Barbier and Leser, *Bull. soc. chim.*, [3] **33**, 815 (1905).

Methyl Ester.—The acid III (25 g.) was esterified by refluxing it for two hours in methanol (118 cc.) containing sulfuric acid (4 cc.). The mixture was poured into water and the ester was extracted with benzene. The benzene solution was washed with bicarbonate (two 25-cc. portions), then with water, and the benzene was removed by distillation under reduced pressure. The residual oil was fractionated under reduced pressure through a 6-inch packed column. The fraction boiling at 134–137° (11 mm.) weighed 24.5 g. (94%), and a specimen removed at the mid-point of the distillation of this fraction had $n_D^{28.5}$ 1.4998.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.31; H, 9.15. Found: C, 76.31; H, 8.97.

3,3,5,7-Tetramethylhydrindone (V).—The acid III (4.07 g.) was dissolved in sulfuric acid (30 cc.) and the solution was allowed to stand at room temperature for seven hours. The mixture was poured over ice and the solid was removed, washed with water and dried. It weighed 3.6 g. (100%) and melted at 52–56°. After two crystallizations from aqueous alcohol, the substance melted at 57.5–58°.[15a]

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.93, 82.95; H, 8.71, 8.57.

Oxime.—Prepared in the usual way, and crystallized from aqueous alcohol, the oxime melted at 154.5–155°.

Anal. Calcd. for $C_{13}H_{17}ON$: C, 76.83; H, 8.43. Found: C, 76.84; H, 8.21.

2,4,β-Trimethylbenzalacetone (VI).—*m*-Xylene (19.0 g., 0.18 mole) and β,β-dimethylacrylyl chloride (16.4 g., 0.14 mole) were dissolved in carbon disulfide (45 cc.). The solution was stirred vigorously and cooled (below 0°) while aluminum chloride (0.2 mole) was added portionwise. The mixture was slowly (thirty-five minutes) warmed to 35° and then poured over iced hydrochloric acid. The organic layer was removed, and the aqueous layer was extracted with six 20-cc. portions of ether. The combined organic solutions were washed successively three times with water, once with bicarbonate (10%) and again three times with water. The solvents were removed by steam distillation and the residue was extracted with four 20-cc. portions of ether. The combined ethereal solutions were dried (sodium sulfate), the solvent was removed, and the residual oil was fractionated under reduced pressure. The ketone VI (15.9 g., 61%) boiled at 137–139° (15 mm.). It was a pale yellow liquid with a pleasant odor.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 83.25; H, 8.36.

The ketone VI (1.44 g.) was dissolved in acetone (20 cc.) and powdered potassium permanganate (1.08 g.) was added in small portions while the mixture was shaken and kept slightly below room temperature. The reaction was very rapid. The product, isolated in the usual way and crystallized successively from aqueous alcohol and from petroleum ether (b. p. 60–68°), weighed 0.7 g. and melted at 127.5–128°. This is the recorded melting point of 2,4-dimethylbenzoic acid, VII.[16] Ozonolysis of the ketone VI (1.44 g.) in acetic acid (60 cc.), followed by hydrolysis of the ozonide, likewise yielded 2,4-dimethylbenzoic acid VII, m. p. 125.5–127°.

Cyclization to 3,3,5,7-Tetramethylhydrindone (V).—The ketone VI (0.69 g.) was dissolved in carbon disulfide (5 cc.) and the solution was cooled and shaken while aluminum chloride (1.0 g.) was added. The mixture was saturated, at room temperature, with hydrogen chloride and then was stirred and refluxed for fifty minutes, after which it was again saturated with hydrogen chloride at room temperature. The solvent was evaporated on the steam-bath and the residue was poured into iced hydrochloric acid. The yellow solid was removed, dissolved in alcohol (1 cc.) and the solution was decolorized with Norite. The hydrindone V, after recrystallization from aqueous alcohol, melted at 57–58.5°, alone or when mixed with a specimen prepared by cyclization of the acid III. Less drastic conditions led to recovery of much unchanged ketone VI; likewise, use of a less powerful catalyst, such as stannic chloride, resulted in recovery of the ketone. Action of sulfuric acid at room temperature had little effect upon VI, but at 100°, a reaction occurred and the product was 2,4-dimethylbenzoic acid VII, m. p. 126–127°.

2,4-Dimethylphenyl-2-propanol (X).—2,4-Dimethylacetophenone (21.96 g., 0.148 mole) in ether (30 cc.) was added dropwise and with stirring to a solution of methylmagnesium bromide (prepared from 4.5 g., 0.164 mole, of magnesium, 110 cc. of ether, and excess gaseous methyl bromide). The mixture was refluxed for forty minutes and then poured into iced ammonium chloride solution. The ether layer was removed, and the aqueous layer was extracted several times with ether. The combined ethereal solutions were washed and dried (sodium sulfate) and the solvent was removed by distillation. The residue was fractionated under reduced pressure through a 6-inch packed column. The fraction boiling at 88–90° (2 mm.) was colorless, weighed 20.5 g. (88%) and had $n^{20}D$ 1.5247.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.46; H, 9.82. Found: C, 80.58; H, 9.94.

2-[2,4-Dimethylphenyl]-2-bromopropane (XI).—The carbinol X (18.1 g., 0.11 mole) was dissolved in ether (100 cc.) and phosphorus tribromide (10.25 g., 0.038 mole) was slowly added to the cooled solution. After the mixture was allowed to stand for forty minutes at room temperature, it was poured into water. The ether layer was removed, the aqueous layer was extracted several times with ether, and the combined ethereal solutions were washed successively with water, dilute bicarbonate, and again with water. The solution was dried (magnesium sulfate) and the solvent was removed at room temperature under reduced pressure. The residual light yellow oil was not purified further.

The above bromo compound was dissolved in dry benzene (120 cc.) and the cooled solution was added to a solution of sodiomalonic ester in alcohol (prepared from 12 g., 0.52 mole, of sodium, 350 cc. of dry alcohol, and 65.4 g., 0.41 mole, of ethyl malonate). The reaction mixture was kept at 0° for forty-eight hours, then at room temperature for twenty-eight hours, and was finally refluxed for ten hours. The solvents were removed by distillation and the residual esters were hydrolyzed by refluxing them with potassium hydroxide (250 cc., 40%). The solution was diluted with water (250 cc.) and extracted with ether. A

[15a] The melting point of a hydrindone probably identical with V was previously reported (ref. 7) as 62–63°. This material was available only in very small amounts, and the specimen was probably contaminated with a high melting impurity (probably the acid) for the analytical value (ref. 7, p. 776) for carbon was quite low.

[16] Böeseken, *Rec. trav. chim.*, **26**, 287 (1907).

small amount of a yellow oil was isolated from the ether extract; this boiled at 82–82.5° (18 mm.) and gave a colorless distillate (1.74 g.) which had $n^{20}\mathrm{D}$ 1.5145 and was unsaturated toward bromine. This was considered to be 2,4-dimethylisopropenylbenzene, but it was not investigated further. No other products could be isolated; the alkaline solution, on acidification and extraction with ether, gave only a small amount of a red oil.

2-[2,4-Dimethylphenyl]-2-methoxypropane (XV).—The carbinol X (17.85 g., 0.109 mole) was converted into the chloride by dissolving it in petroleum ether (25 cc., b. p. 33–38°) and subjecting the solution to the action of dry hydrogen chloride at 0° for one and one-half hours. The reaction mixture was processed as described above for the bromide; the chloride was a colorless oil. It was dissolved in methanol (70 cc.) and anhydrous potassium carbonate (60 g.) was added to the solution. After the vigorous reaction subsided, the mixture was cooled and allowed to stand at room temperature for two days. The mixture was poured into water, extracted with ether, and the ether solution was dried (Drierite). The solvent was removed by distillation and the residual oil was fractionated through a short packed column. The ether (10.0 g., 51%) boiled at 62.5–65° (2 mm.) and was colorless.

Anal. Calcd. for $C_{12}H_{18}O$: C, 80.83; H, 10.18. Found: C, 80.98; H, 10.48.

The above ether XV (2.17 g.) was dissolved in dry ether (200 cc.) and the solution was added to sodium–potassium alloy (sodium, 0.4 g., potassium, 2.0 g.). The mixture was then shaken for sixty hours, after which a stream of dry carbon dioxide was passed through the dark red suspension. The red color faded at once but, when the mixture was processed in the usual way, only a small amount of alkali-soluble oil was obtained.

Potassium sand[17] (4.3 g., 0.11 mole) was suspended in dry toluene (75 cc.), 1,3-dimethyl-5-isopropylbenzene[18] (7.5 g., 0.05 mole) was added, followed by a solution of chlorobenzene (5.6 g., 0.05 mole) in toluene (10 cc.). All operations were conducted under a stream of pure, dry nitrogen, and the mixture was vigorously stirred while the reagents were combined. The black mixture was refluxed for four hours, then cooled and poured over Dry-Ice. Alcohol was added to destroy excess potassium, and then the mixture was extracted with water. From the alkaline solution there was obtained, on acidification, a brown oil (about 1 cc.) which solidified when cooled. This product melted at 48–92° and resisted all attempts to separate it into pure materials.

2-[3,5-Dimethylphenyl]-2-cyanopropane (XIX).—3,5-Dimethylbenzyl cyanide (40.2 g., 0.277 mole, m. p. 42–44°) was dissolved in dry ether (300 cc.). To this solution there was added freshly prepared sodamide (13.0 g., 0.33 mole)[19] which had been finely ground under dry benzene. After the initial, vigorous reaction subsided, the mixture was refluxed for eighteen hours, and evolution of ammonia ceased. Methyl iodide (47.0 g., 0.33 mole) was added dropwise (twenty minutes) and after the reaction subsided, the mixture was refluxed for two hours. A small amount of alcohol was added, and the ethereal layer was decanted and washed three times with water. The water washings were added to the sludge of sodium iodide and the solution was extracted with one 100-cc. portion and three 25-cc. portions of ether. The combined ether solutions were washed with water and dried (sodium sulfate). The solvent was removed, and the residual orange oil was dissolved in benzene (375 cc.). About 75 cc. of benzene was removed by distillation, and to the residual solution there was added powdered sodamide (15.5 g., 0.4 mole). From this point, the procedure followed that described above for the introduction of the first methyl group; 57.1 g. (0.4 mole) of methyl iodide was used in the second step. The final product, an oil, was fractionated and the fraction boiling at 126–128° (15 mm.) was collected. This weighed 20.2 g. (42%).

Anal. Calcd. for $C_{12}H_{15}N$: C, 83.18; H, 8.73. Found: C, 81.55; H, 8.53.

The material was redistilled, and a narrow fraction (b. p. 131° (25 mm.)) was collected, but this did not give better analytical values. When the methylation of the cyanide (10 g.) was carried out in liquid ammonia, a relatively large amount (4.5 g.) of mesitylene (trinitro derivative, m. p. and mixed m. p. 234–235°) was formed. This cleavage of a nitrile to a hydrocarbon by action of sodium in liquid ammonia is an interesting example of a reductive cleavage of a carbon–carbon bond.

α-[3,5-Dimethylphenyl]-isobutyramide (XX).—The cyanide XIX (13.3 g., 0.77 mole) was heated with sulfuric acid (85%, 73 cc.) at 100° for ten and one-half hours. The black solution was poured over ice, and extracted exhaustively with ether. The ether solution was washed with bicarbonate (10%) and dried (sodium sulfate). Removal of the ether left a dark residue, which was crystallized from petroleum ether (b. p. 60–68°). The brown crystals were dissolved in alcohol and the solution was decolorized by repeated treatment with Norite. The white solid (4.9 g., 33%) melted at 109.5–110.5°.

Anal. Calcd. for $C_{12}H_{17}ON$: C, 75.34; H, 8.96. Found: C, 75.57; H, 8.72.

α-[3,5-Dimethylphenyl]-isobutyric Acid (XXI).—The amide XX (4.7 g., 0.025 mole) was refluxed for five and one-half hours with sulfuric acid (25%, 90 cc.). The product was isolated by ether extraction; the ether solution was extracted with sodium hydroxide solution (10%) and the acid was precipitated by cooling the acidified aqueous solution. The tan product (2.84 g., 59%, m. p. 115–117°) was purified by repeated treatment of the solution in methanol with Norite, followed by crystallization from dilute acetic acid. It then melted at 116.5–117.5°. From the ether solutions, 1.17 g. of unchanged amide XX was recovered.

Anal. Calcd. for $C_{12}H_{16}O_2$: C, 74.96; H, 8.39; N.E., 192. Found: C, 75.09; H, 8.44; N.E., 193.

The acid XXI (0.17 g.) was converted into the acid chloride by action of thionyl chloride (1.5 cc.) and pyridine (1 drop). Benzene (1 cc.) was added and the mixture was evaporated to dryness under reduced pressure; addition of benzene and evaporation was repeated twice more. The residual yellow oil was dissolved in benzene (3 cc.) and this

---

(17) *Organic Syntheses*, **18**, 25 (1938).

(18) Nightingale and Carton, This Journal, **62**, 280 (1940). The yield of this product may be increased to 70% by stirring and heating the reaction mixture at 50–55° for three hours.

(19) Vaughn, Vogt and Nieuwland, This Journal, **56**, 2120 (1934).

solution was added to a solution of excess diazomethane in ether (4 cc.). After the mixture was allowed to stand at 0° for six hours, the solvents were removed under reduced pressure and the residual oil was dissolved in methanol (15 cc.) and added to a suspension of silver oxide (0.3 g.) in methanol (15 cc.). The mixture was refluxed for eleven hours, the solvent was then removed, and the residue was refluxed for two hours with sodium hydroxide (1 *N*, 10 cc.) and methanol (4 cc.). Only a small amount of alkali soluble material could be isolated.

1,1,3,3,4,6-Hexamethylindane (XXVII).—The methyl ester of III (5.0 g., 0.023 mole) in dry ether (10 cc.) was added to a solution of methylmagnesium iodide (0.51 mole) in ether (25 cc.). The mixture was stirred and refluxed for one and one-half hours, and was then poured over iced hydrochloric acid and processed in the usual way. The viscous red oil (about 5 cc.) remaining after removal of the ether was refluxed for one and one-half hours with acetic acid (20 cc.) containing a drop of sulfuric acid. The mixture was poured into water, extracted repeatedly with ether, and the ethereal solution was washed with saturated bicarbonate, then with water, and dried (Drierite). The solvent was removed and the residual oil was distilled through a short packed column. The product (2.2 g.) was a mobile liquid which boiled at 114–117° (13 mm.) and had the following constants: d_{31}^{31} 0.905; d_4^{31} 0.901; $n^{28.5}\text{D}$ 1.5100.

Anal. Calcd. for $C_{15}H_{22}$: C, 89.05; H, 10.96. Found: C, 88.65; H, 10.90.

This material was indifferent to alkaline permanganate in the cold, and decolorized bromine in chloroform only slowly. Ozonolysis of the material (0.5 g.) in ethyl bromide (60 cc.) was unsuccessful, and no ozone was absorbed. This product, therefore, was not XXVI and must have been the isomeric substance XXVII.

Attempted Decarboxylation of III.—The dried sodium salt of III (3.42 g.) was mixed thoroughly with powdered soda lime (12 g.) and the mixture was heated in a bath under 48 mm. The bath temperature was gradually raised to 470° over a period of two hours. Distillation began at 420° and was fairly rapid at 468° (bath temperatures). The distillate (3.05 g.) was redistilled under reduced pressure. No definite fractionation was observed, but the lower boiling portion of the material (0.3 g., b. p. 103–140° (20 mm.)) was nitrated with a mixture of sulfuric and fuming nitric acids. No solid nitro compound was obtained.

The acid III was converted into the chloride (an oil) by several methods: action of thionyl chloride alone or with pyridine, or of both reagents in ether, or by action of phosphorus trichloride. The chloride was then subjected to the action of ammonia in aqueous or ethereal solution, or to the action of dry ammonium carbonate, but in no case could any solid product be isolated. The ammonium salt of III was prepared; when it was heated on the steam-bath, it decomposed to ammonia and the acid III.

α-[3,5-Dicarboxyphenyl]-isobutyric Acid (XXXI).—The isobutyric acid XXI (1.0 g., 0.0052 mole) was dissolved in water (75 cc.) containing sodium hydroxide (5 cc., 20%). Potassium permanganate (3.6 g., 0.023 mole) was added and the mixture was refluxed and stirred for four hours. Excess permanganate was destroyed by addition of alcohol, the hot solution was filtered, and the filtrate was acidified to congo red with hydrochloric acid. The cooled solution deposited 1.0 g. of the white, crystalline tribasic acid XXXI. It melted at 298–300° to a brown liquid.

Anal. Calcd. for $C_9H_9(COOH)_3$: N. E., 84.0. Found: N. E., 84.5.

The methyl ester, prepared by action of diazomethane upon the acid and recrystallized from petroleum ether, melted at 73.5–76.5°.

β-[3,5-Dicarboxyphenyl]-isovaleric Acid (XXX).—The isovaleric acid III (0.51 g.) was dissolved in water (55 cc.) containing sodium hydroxide (4 cc., 20%) and oxidized with permanganate (2.6 g.) for five hours according to the procedure described above. The white crystalline solid (0.38 g.) melted at 247–250°. Prolonged action (thirty hours) of permanganate upon III produced no XXX, nor any material which could be precipitated by barium chloride (absence of trimesic acid). The acid XXX also resulted when III (0.46 g.) was heated in a sealed tube at 190–200° for seventeen hours with nitric acid (1 cc.) and water (2 cc.).

Anal. Calcd. for $C_{10}H_{11}(COOH)_3$: N. E., 88.7. Found: N. E., 88.8.

The trimethyl ester, prepared by action of diazomethane upon the acid and recrystallized successively once from aqueous methanol and twice from petroleum ether (b. p. 60–68°), melted at 68.5–69.5°.

Anal. Calcd. for $C_{16}H_{20}O_6$: C, 62.30; H, 6.55. Found: C, 62.52; H, 6.30.

Summary

1. *m*-Xylene condenses with β,β-dimethylacrylic acid in the presence of aluminum chloride to form β-[3,5-dimethylphenyl]-isovaleric acid, III. This is also the product that results when mesitylene is used in place of *m*-xylene. The acid III is converted into 3,3,5,7-tetramethylhydrindone, V, by action of cold sulfuric acid.

2. *m*-Xylene condenses with β,β-dimethylacrylyl chloride in the presence of aluminum chloride to give 2,4,β-trimethylbenzalacetone, VI. The orientation of this ketone was proved by its conversion, on oxidation, to the known 2,4-dimethylbenzoic acid, VII. The ketone VI is converted into the hydrindone V by action of hydrogen chloride and aluminum chloride, and this fact establishes the orientation of the groups in the acid III.

3. α-[3,5-Dimethyl]-isobutyric acid, XXI, has been synthesized from mesitylene via 3,5-dimethylbenzyl cyanide, which was methylated by action of methyl iodide and sodamide in ether. When attempts were made to methylate this cyanide in liquid ammonia, the product was mesitylene.

4. Both monobasic acids III and XXI, when

oxidized by permanganate, gave the respective tribasic acids XXX and XXXI. It was not possible to degrade III to XXI, nor to convert XXI into III, although many attempts were made. Nor was it possible to degrade the tribasic acid XXX into XXXI. Many new compounds, incidental to these investigations, have been described.

MINNEAPOLIS, MINNESOTA RECEIVED NOVEMBER 4, 1942

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, SCHOOL OF TROPICAL MEDICINE OF THE UNIVERSITY OF PUERTO RICO, UNDER THE AUSPICES OF COLUMBIA UNIVERSITY]

Puerto Rican Fatty Oils. II. The Characteristics and Composition of *Guanábana* Seed Oil

BY CONRADO F. ASENJO AND JOSÉ A. GOYCO

The Puerto Rican variety of *guanábana* (*Annona muricata* L.) is an ovoid or somewhat heart-shaped fruit, 15 to 20 cm. long and 9 to 12 cm. broad. The skin is green with isolated curved fleshy spinules; its pulp white and juicy and pleasantly subacid. Imbedded in the pulp is found a large number of seeds, dark brown in color and oblong-elliptic in shape, measuring about 1.6 cm. in length and 1 cm. in breadth. Thirty-three per cent. of the seed is husk and 67% kernel. The common English name of the fruit is soursop.

Locally, the pulp of the fruit has been used for a very long time in the preparation of a deliciously refreshing drink, which is now being canned for commercial purposes. For this reason large amounts of seeds are easily available for study. These seeds are a fairly promising source of oil and yield by acetone extraction 23.86%. The percentage obtained by hot expression (110°) is somewhat lower. This paper presents the results obtained from the study of a sample of hot expressed oil which was kindly supplied to us by the Division of Investigation and Industrial Development of the Department of Agriculture and Commerce of Puerto Rico.

With the exception of a short report from the Food Testing Laboratory of Surinam,[1] in which the iodine, saponification, and Maumené numbers were recorded for a sample of *Annona muricata* L. seed oil, no previous chemical study of this oil could be found in the literature. The present investigation is therefore concerned with the determination of the characteristics and with the isolation, identification, and quantitative estimation of the acids present in the expressed oil.

Physical and Chemical Examination.—The oil was yellowish brown in color; the sample was odorless and had a bland taste. Its chemical and physical properties were determined by the usual procedures[2] with the results given in Table I.

TABLE I

CHEMICAL AND PHYSICAL CHARACTERISTICS OF EXPRESSED *Guanábana* SEED OIL

Specific gravity 25°/25°	0.9178
Refractive index 20°	1.4709
Iodine number (Hanus)	87.79
Saponification no.	197.0
Acid value	2.29
Acetyl value	12.56
Reichert-Meissl no.	0.81
Polenske no.	.56
Unsaponifiable residue, %	1.02
Soluble acids, %	0.37
Insoluble acids, %	91.90
Saturated acids, % (corrected)	22.02
Unsaturated acids, % (corrected)	70.02
Iodine no. of unsaturated acids	105.1
Saponification no. of unsaturated acids	202.1

The iodine number shows little unsaturation and the Reichert-Meissl and Polenske numbers show small amounts of glycerides of volatile acids.

Examination of the Unsaturated Acids of the Expressed Oil.—Bromination of the unsaturated acids in the usual manner showed the absence of linolenic acid. Tetrabromostearic acid melting at 114° was obtained, showing the presence of linoleic acid. The percentages of the linoleic and oleic acids were calculated using the iodine number of the unsaturated acid.[3]

Examination of the Saturated Acids of the Expressed Oil.—The saturated acids were esterified by the Twitchell method, as modified by Hilditch,[4] and the mixed methyl esters obtained

---

(1) Anonymous, *Olien en Vetten*, No. 30, 387-389 (1920), through *Chem. Abs.*, **14**, 1230 (1920).

(2) Association of Official Agricultural Chemists, "Methods of Analysis," Washington, D. C., 4th ed., 1935, pp. 404-429.

(3) J. Lewkowitsch, "Chemical Technology and Analysis of Oils, Fats and Waxes," 6th ed., Macmillan and Co., Ltd., London, 1921, p. 574.

(4) T. P. Hilditch, "The Chemical Composition of Natural Fats," John Wiley and Sons, New York, N. Y., 1941, pp. 371-372