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

Polyalkylbenzenes. XXXV.[1] Action of Senecioic Acid, and of Senecioyl Chloride, upon the Tetramethylbenzenes and upon Pentamethylbenzene

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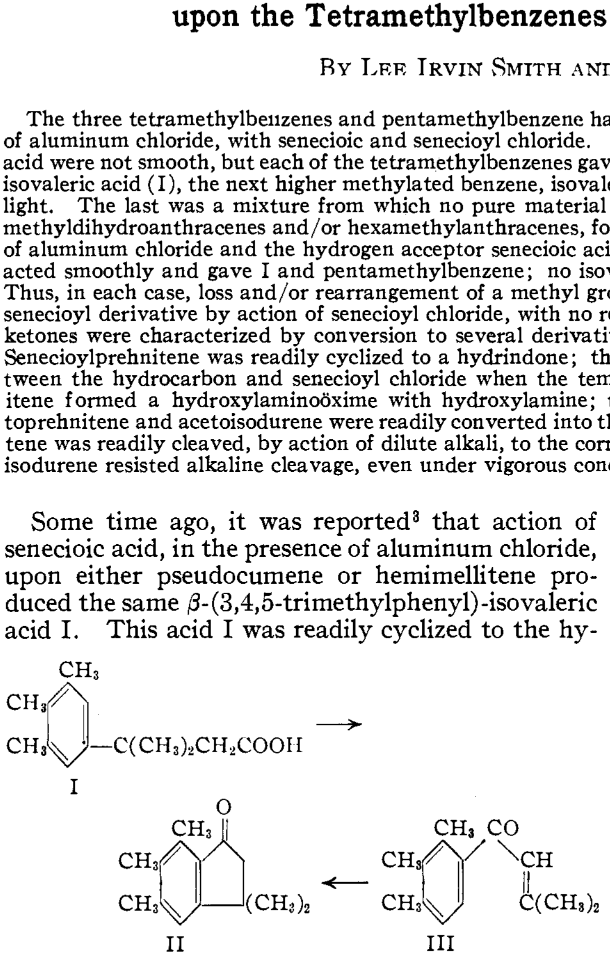
The three tetramethylbenzenes and pentamethylbenzene have been studied with regard to their reactions, in the presence of aluminum chloride, with senecioic and senecioyl chloride. Except for the case of prehnitene, the reactions with senecioic acid were not smooth, but each of the tetramethylbenzenes gave a product from which was isolated β-(3,4,5)-trimethylphenylisovaleric acid (I), the next higher methylated benzene, isovaleric acid and a yellow solid highly fluorescent under ultraviolet light. The last was a mixture from which no pure material could be obtained, but it appeared to be a mixture of hexamethyldihydroanthracenes and/or hexamethylanthracenes, formed by dehydrogenation of the hydrocarbons in the presence of aluminum chloride and the hydrogen acceptor senecioic acid. Some durene was formed from isodurene. Prehnitene reacted smoothly and gave I and pentamethylbenzene; no isovaleric acid, and very little of the yellow solid, was produced. Thus, in each case, loss and/or rearrangement of a methyl group occurred. All four hydrocarbons were converted into the senecioyl derivative by action of senecioyl chloride, with no rearrangement or loss of methyl groups. The α,β-unsaturated ketones were characterized by conversion to several derivatives; each gave the appropriate benzoic acid upon oxidation. Senecioylprehnitene was readily cyclized to a hydrindone; this hydrindone was obtained as the product of the reaction between the hydrocarbon and senecioyl chloride when the temperature was allowed to exceed 13°. The ketone from prehnitene formed a hydroxylaminoöxime with hydroxylamine; the other ketones gave hydroxylamino compounds only. Acetoprehnitene and acetoisodurene were readily converted into the respective pyridinium iodides; this derivative of acetoprehnitene was readily cleaved, by action of dilute alkali, to the corresponding benzoic acid, but the pyridinium iodide from acetoisodurene resisted alkaline cleavage, even under vigorous conditions.

Some time ago, it was reported[3] that action of senecioic acid, in the presence of aluminum chloride, upon either pseudocumene or hemimellitene produced the same β-(3,4,5-trimethylphenyl)-isovaleric acid I. This acid I was readily cyclized to the hydrindone II, which was also obtained by cyclization of 4-senecioylhemimellitene (III). Hence, in the reaction involving pseudocumene, a methyl group migrated. Later, it was reported[4] that mesitylene and *m*-xylene gave the same products in this reaction; in this case, a methyl group was eliminated from mesitylene. Recently it has been reported[5] that the β-phenylpropionic acids and γ-phenylbutyric acids derived from the tetramethylbenzenes, when cyclized by action of anhydrous hydrogen fluoride, undergo migration and/or elimination of a methyl group. In order to explore further this reaction, the action of senecioic acid, and of senecioyl chloride, upon the three tetramethylbenzenes and upon pentamethylbenzene in the presence of aluminum chloride, has been studied.



Durene did not react well with senecioic acid; after many experiments leading only to acidic gums in poor yield, it was found that when durene in carbon bisulfide was added to a mixture of senecioic acid and aluminum chloride in the same solvent, and the mixture was allowed to stand for ten hours at room temperature, a product resulted which could be separated into two parts by steam distillation. From the volatile part of the product, there was isolated isovaleric acid (corresponding to reduction of 42% of the senecioic acid), durene and pentamethylbenzene. One equivalent of durene, based upon the senecioic acid initially used, disappeared. From the non-volatile part of the product, there was isolated a gummy acidic component, and a neutral yellow solid with a wide (135–160°) melting point range. The acidic gum was esterified with methanol and the mixture of esters was fractionated; the middle, constant boiling fraction, when hydrolyzed, gave a solid acid which after many crystallizations melted at 106–110° alone or when mixed with I. The total yield of crude I did not exceed 15%, however. The yellow solid could not be separated into any pure components by fractional crystallization.

Isodurene underwent the reaction with senecioic acid much more smoothly than did durene; although the same sorts of products were obtained. The acid I was obtained in 53% yield, along with a neutral yellow solid. The volatile part of the reaction consisted of pentamethylbenzene (51%) equivalent to I, durene, unchanged isodurene and isovaleric acid (corresponding to reduction of 23% of the senecioic acid). The yellow neutral solid was chromatographed from petroleum ether onto alumina, and the column, which fluoresced brightly throughout under ultraviolet light, was developed continuously with the same solvent. Each portion of the eluate contained a small (0.01–0.04 g.) amount of material, but no real separation could be effected; all the solids melted over 15–25° ranges, although the melting points of the materials from successive fractions steadily increased. The solid obtained from one of the later (twenty-first) portions melted at 192–205°; several recrystallizations of this yielded small, yellow needles melting at 207–210°. Analysis indicated a hydrocarbon $(C_{10}H_{11})_x$ or $(C_{10}H_{12})_x$. The substance exhibited brilliant fluorescence under ultraviolet light, and was not the octamethylbiphenyl (m.p. 121–122°) derived from

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[1] Paper XXXIV, Smith and Schubert, THIS JOURNAL, **70**, 2656 (1948).

[2] Abstracted from a thesis by J. J. Rosenbaum, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, January, 1951.

[3] L. I. Smith and W. W. Prichard, THIS JOURNAL, **66**, 771 (1940).

[4] L. I. Smith and L. J. Spillane, *ibid.*, **65**, 202 (1943).

[5] Aitkin, Badger and Cook, *J. Chem. Soc.*, 331 (1950).

isodurene. The analytical values agree fairly well with $C_{20}H_{24}$, a hexamethyldihydroanthracene, or with $C_{20}H_{22}$, a hexamethylanthracene. Formation of either of these from isodurene involves loss of one methyl group and release of four or six hydrogen atoms—quite enough to account for the reduction of considerable senecioic acid to isovaleric acid.[6]

Prehnitene reacted smoothly with senecioic acid; the non-volatile product consisted of I (51%) and a very small amount of gummy material. The volatile product contained a small amount of senecioic acid and a neutral oil which consisted of unchanged prehnitene and pentamethylbenzene.

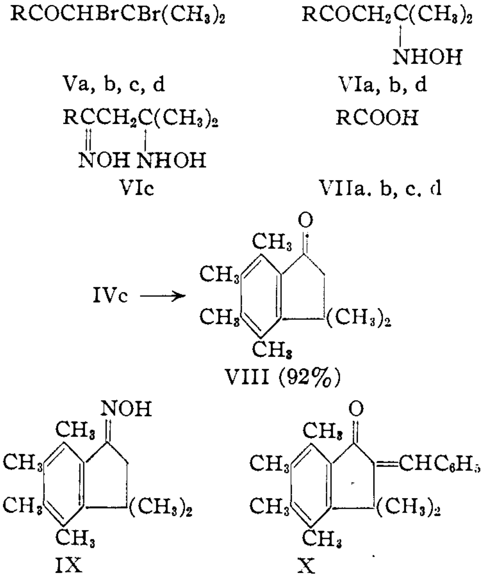
Pentamethylbenzene reacted with senecioic acid with difficulty, and the product was a complete mixture. The non-volatile portion consisted of an acidic gum (20%) and a high melting, fluorescent yellow solid. The acidic part was esterified with methanol, and the mixture of esters was fractionated; each fraction yielded a gum on hydrolysis. These gums were subjected to action of sulfuric acid in the hope of obtaining a mixture of hydrindones more readily purified; each fraction gave a solid melting at 111–112° but which was still not pure. Analytical values indicated the composition $C_{15}H_{20}O$ or $C_{16}H_{22}O$ for this substance; it was not, however, VIII ($C_{15}H_{20}O$) which melts at 76–76.5°. The volatile portion of the original product consisted of isovaleric acid (corresponding to 25% of the senecioic acid) pentamethylbenzene and hexamethylbenzene.

Thus in each of these reactions, loss and rearrangement of a methyl group occurred; the three tetramethylbenzenes were each converted into I; the next higher methylated benzene was formed in each case—never any lower homologs. Prehnitene reacted most readily, followed in order by isodurene, durene and pentamethylbenzene, the last two reacting poorly and with difficulty.

Each of the four hydrocarbons was acylated by action of senecioyl chloride and aluminum chloride; the reactions proceeded smoothly and with good yields except in the case of isodurene, and no rearrangement or elimination of methyl groups occurred. The products were unsaturated ketones, the corresponding senecioyl derivatives (IV) of the hydrocarbons. Each ketone formed a dibromide (V); each ketone, when oxidized, gave the corresponding benzoic acid (VII). Action of hydroxylamine upon the ketones IVa, b, d produced not oximes, but the hydroxylamino compound VIa, b, d, respectively. In the case of ketone Vc, action of hydroxylamine produced the hydroxylaminoöxime VIc. The ketone IVc, when subjected to the action of sulfuric acid at room temperature, was cyclized smoothly to the hexamethylbenzhydrindone VIII. This hydrindone VIII could be obtained also directly as a product of the reaction between prehnitene and senecioyl chloride: when the reaction was conducted at 0–5° and then allowed to warm to 13°, the product was the ketone IVc, but when the reaction mixture was allowed to warm to 28°, the product was the hydrindone VIII. This hydrindone VIII was characterized by conversion to an oxime (IX) and a benzal derivative (X). The hydrindone VIII was stable in the presence of aluminum chloride; it was recovered unchanged after a solution of it in benzene or pseudocumene was refluxed with aluminum chloride.

$RCOCH{=}C(CH_3)_2$

IVa, R = duryl (65–72%)
b, R = isoduryl (29%)
c, R = 2,3,4,5-tetramethylphenyl (68%)
d, R = pentamethylphenyl (84%)



The benzoic acid VIIc was synthesized from acetoprehnitene *via* the pyridinium iodide[7]; the iodide was readily cleaved to VIIc by action of dilute alkali. Acetoisodurene, however, gave a highly hindered pyridinium iodide which resisted cleavage to VIIb, even under drastic conditions. This result is in agreement with the observations of King[8] and of Babcock, Nakamura and Fuson[9] who found that the pyridinium halides of acetomesitylene were not cleaved by action of alkali.

Experimental Part[10]

Senecioic acid (50–60%) was prepared from mesityl oxide.[11] For purposes of identification, the *p*-bromophenacyl and *p*-phenylphenacyl esters of senecioic acid were prepared. They are new compounds.

***p*-Bromophenacyl ester of senecioic acid**, m.p. 100.5–101.3°. *Anal.* Calcd. for $C_{13}H_{13}O_3Br$: C, 52.54; H, 4.41. Found: C, 52.74; H, 4.62.

***p*-Phenylphenacyl ester of senecioic acid**, m.p. 143–144°. *Anal.* Calcd. for $C_{19}H_{18}O_3$: C, 77.53; H, 6.16. Found: C, 77.41; H, 6.48.

Reaction with Durene.—Aluminum chloride (30 g., 0.23 mole) was added (20 minutes) to a cooled (ice-bath) and vigorously stirred solution of senecioic acid (10 g., 0.1 mole) in carbon bisulfide. To the resulting suspension of the complex salt durene (40 g., 0.3 mole) in carbon bisulfide (150 cc.) was added (90 minutes) with stirring. Stirring was continued while the temperature was allowed to come to that of the room (four hours); the mixture was then heated to 30–35° for 4.5 hours. The mixture was poured over ice (400 g.) and hydrochloric acid (30 cc.) and the solvent was removed by steam distillation. The residue was then steam distilled

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[6] V. N. Ipatieff, *et al.*, THIS JOURNAL, **70**, 2123, 3859 (1948); *ibid.*, **71**, 3534 (1949); *J. Org. Chem.*, **5**, 253 (1940), have reported several such "hydrogen transfers."

[7] L. C. King, THIS JOURNAL, **66**, 895 (1944).

[8] L. C. King, *ibid.*, **70**, 239 (1948).

[9] S. H. Babcock, Jr., F. I. Nakamura and R. C. Fuson, *ibid.*, **54**, 4407 (1932).

[10] Microanalyses by J. Buckley, W. Cummings, L. Errede, R. Kelly, H. Turner and E. Wheeler.

[11] L. I. Smith, W. W. Prichard and L. J. Spillane, *Org. Syntheses*, **23**, 27 (1943).

until 2 l. of distillate (B) was collected. The residue (C, 10 g.), a red sticky oil, was dissolved in ether (100 cc.) and the solution was extracted with six 25-cc. portions of aqueous sodium hydroxide (10%). The red aqueous extracts (D) were combined, extracted with ether, and the ether extracts were combined with C. Dissolved ether was removed from D, which was then filtered and acidified with hydrochloric acid (1:1). The reddish gum was removed by ether extraction and after evaporation of the solvent, was refluxed for 24 hours in methanol (200 cc.) containing sulfuric acid (15 cc.) and benzene (20 cc.). After removal of most of the solvents, the residue was poured into water and extracted with ether (aqueous layer discarded). The ethereal solution was washed successively with aqueous sodium bicarbonate (10%) and water, and was dried (potassium carbonate). The solvent was removed and the residue was distilled under 4 mm. through a short column. Three fractions were collected: (1) 3 g., b.p. 125–139.5°; (2) 1.5 g., b.p. 139.5°; (3) 1.5 g., b.p. 140–150°. The nearly colorless middle fraction was saponified by action of aqueous ethanolic sodium hydroxide. The resulting gummy acid (0.65 g.) was removed and dried. After two crystallizations from aqueous ethanol, and two from aqueous acetic acid, this acid melted at 106–110°. When mixed with an authentic specimen of I (m.p. 109–110°), the substance melted at 107–110°. The ether solution C, when evaporated, left a yellow solid (0.5 g.), which after crystallization from methanol (violet fluorescence) melted at 200–220°. The steam distillate B was extracted five times with ether; the aqueous layer was discarded, and the ether solution was extracted with four 15-cc. portions of aqueous sodium hydroxide (10%). Evaporation of the ether layer left a residue of durene (24.1 g.) melting at 60–70°; mixed m.p. with durene (80°), 72–78°; mixed m.p. with pentamethylbenzene (53°), 40°. A little pentamethylbenzene was separated from this durene by fractional distillation. The aqueous alkaline solution was evaporated to 30 cc., cooled, acidified with hydrochloric acid (1:1) and extracted with ether. The ether was removed, and the residual oil was distilled. The distillate (4.18 g.) boiled at 172–172.5° and was identified as isovaleric acid by conversion to the *p*-bromophenacyl ester, m.p. and mixed m.p. 80–82°. The reaction between durene and senecioic acid 67–69°, and to the *p*-phenylphenacyl ester, m.p. and mixed m.p. was carried out many times and under a variety of conditions, but the conditions outlined above were the only ones which led to isolation of identifiable materials in any quantity.

Reaction with Isodurene.—Aluminum chloride (54 g., 0.4 mole) was added (25 minutes) to a cooled (0°) and vigorously stirred solution of senecioic acid (19.6 g., 0.2 mole) in isodurene (77.3 g., 0.41 mole). The mixture was stirred at room temperature for 4.5 hours, then heated to 45° for 45 minutes and decomposed by pouring it over ice (250 g.) and hydrochloric acid (40 cc.). It was then steam distilled until 2 l. of distillate was collected. The residue in the distilling flask (31.8 g.) was separated into an acid (22.8 g., 53%) identified as I (portion crystallized from aqueous ethanol, with Norit, m.p. and mixed m.p., 108–110°, converted to hydrindone II, m.p. and mixed m.p. 103–105°) and a yellow neutral fluorescent solid (2.95 g.). The steam distillate was separated into isovaleric acid (4.72 g.), I (1.32 g.) and a neutral oil. The latter gave a distillate boiling at 192–210° (13.4 g.) consisting of durene (1 g.) and isodurene and a residue (14.9 g.) of pentamethylbenzene. The yellow fluorescent solid (1 g.) was dissolved in benzene (20 cc.) and the solution was poured through a column (2 × 31 cm.) packed with alumina (Alcoa F-20). The chromatogram was developed with benzene; twenty-five portions (each 20 cc.) of eluate were collected. The first six portions contained 0.86 g. of material; each residue was highly fluorescent, the colors ranging from blue-green to blue and violet. This 0.86 g. of material was dissolved in petroleum ether (15 cc., b.p. 77–115°) and chromatographed as above under ultraviolet light and using petroleum ether as the developing solvent. Twenty-five eluates (100 cc. each) were collected; evaporation of the solvent from these left residues of 0.01–0.07 g., melting over wide ranges from 115 to 200°. The residue from the twenty-first eluate was greatest in amount (0.07 g.) and had the highest melting point (192–205°). It was recrystallized twice from acetic acid, washed with methanol and dried under reduced pressure, when it melted at 207–210°.

Anal. Calcd. for $C_{20}H_{24}$ (hexamethyldihydroanthracene): C, 90.85; H, 9.15. Calcd. for $C_{20}H_{22}$ (hexamethylanthracene): C, 91.54; H, 8.45. Found: C, 91.05; H, 8.74.

Reaction with Prehnitene.—The reaction was conducted as described for isodurene, using senecioic acid (10 g.), prehnitene (28 g.) and aluminum chloride (16 g.). The residue after steam distillation (11.2 g., 51%) melted at 87–103°; it was separated into 0.2 g. of a neutral gum, and about 11 g. of I, which, after crystallization from aqueous ethanol several times melted at 110–111° alone or when mixed with I; it was converted to the hydrindone II, m.p. and mixed m.p. 102–103.5°, oxime, m.p. and mixed m.p. 192–194°. The steam distillate was extracted with ether, and the residue, after removal of the ether, was separated into senecioic acid (2.2 g., m.p. and mixed m.p. 67–69°), prehnitene (6.4 g., b.p. 197–205°, dinitro compound, m.p. and mixed m.p. 173–174.5°), and pentamethylbenzene (2.3 g., m.p. and mixed m.p. 48–52°).

Reaction with Pentamethylbenzene.—The reaction was conducted as described above for durene using senecioic acid (10 g.) and aluminum chloride (30.8 g.) in carbon bisulfide (100 cc.), and pentamethylbenzene (44.4 g.) in carbon bisulfide (100 cc.). During the steam distillation, hexamethylbenzene (m.p. and mixed m.p., 160–162°) deposited in the condenser. The residue after steam distillation was separated into an acidic gum and a neutral fluorescent yellow solid (4.76 g.) which was largely hexamethylbenzene. The acidic gum was converted into methyl esters (5.45 g.), but fractionations of these gave no pure materials. Each fraction, on saponification, gave a gum. In the hope of converting these acids into hydrindones more easily separated, the gums were dissolved in sulfuric acid and the solutions were allowed to stand for some time. The products were largely gummy acids, but small amounts of neutral solid were isolated. This melted at 111–114° after two crystallizations from aqueous ethanol.

Anal. Calcd. for $C_{15}H_{20}O$ (II or isomer): C, 83.28; H, 9.32. Calcd. for $C_{16}H_{22}O$ (VIII or isomer): C, 83.41; H, 9.63. Found: C, 83.37; H, 9.56.

The steam distillate, containing a white solid, was extracted with ether, and the residue, after removal of the ether, was separated into isovaleric acid (2.5 g.), pentamethylbenzene (24.8 g., b.p. 214–232°, m.p. and mixed m.p. 48–52°), and hexamethylbenzene (1.4 g.). The total hexamethylbenzene obtained from this residue and from the deposit in the condenser was 2.8 g.

Senecioyldurene (IVa).—Aluminum chloride (13 g.) was rapidly (15 minutes) added to a cooled (5–10°) and vigorously stirred solution of durene (13.4 g.) and senecioyl chloride (11.9 g.)[12] in carbon bisulfide (100 cc.). The cooling bath was removed and the temperature was allowed to rise to 15° (20 minutes), when the mixture was poured over ice (350 g.) and hydrochloric acid (30 cc.). Carbon bisulfide was removed by steam distillation, the residue was extracted with ether, and the ether solution was extracted with aqueous sodium carbonate (10%). The carbonate extracts, on acidification, gave 0.7 g. of senecioic acid. The ether solution was steam distilled; ether was collected separately, and discarded, and then 2 l. of distillate was collected. This, when cooled, yielded 4 g. of durene, m.p. and mixed m.p. 75–78°. The residue from the steam distillation solidified when cooled; the solid (15.6 g., 72%) was removed, dissolved in methanol (200 cc.), the solution was decolorized (Norit) and the hot filtrate was diluted with water to faint turbidity, and cooled. The product (13.6 g.) melted at 72–75°; the analytical sample, crystallized three times from aqueous methanol, formed creamy white needles melting at 74–74.5°.

Anal. Calcd. for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.26; H, 9.50.

Dibromide (Va).—Bromine (1.1 g.) was added dropwise to a cold (0°) solution of IVa (1.5 g.) in ether (15 cc.). Removal of the solvent left an oil (2.1 g., 100%) which solidified on cooling and then melted at 90–93°. The material was recrystallized from methanol (Norit) when it was white and melted at 95–96.5°.

Anal. Calcd. for $C_{15}H_{20}OBr_2$: C, 47.89; H, 5.36. Found: C, 47.98; H, 5.53.

Hydroxylamino Compound (VIa).—This substance (3.6 g., 88%) was prepared from the ketone IVa (4 g.) and hy-

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[12] L. I. Smith and V. A. Engelhardt, THIS JOURNAL, **71**, 2672 (1949).

droxylamine hydrochloride (10 g.). After two crystallizations from ethanol it melted at 180–181°.

Anal. Calcd. for $C_{15}H_{21}ON$ (oxime): C, 77.87; H, 9.15. Calcd. for $C_{16}H_{23}O_2N$ (VIa): C, 72.25; H, 9.30. Found: C, 72.53; H, 9.46.

2,3,5,6-Tetramethylbenzoic Acid (VIIa).—Oxidation of IVa (4.3 g.) in acetone (85 cc.) by action of potassium permanganate (6 g.) at 5–15° yielded 0.65 g. of recovered IVa and 2.4 g. (71%) of acid VIIa melting at 173–175.5° after crystallization from petroleum ether (F).[13] The methyl ester, prepared from the acid and diazomethane, melted at 59–60°; Jacobsen, ref. 13b, gives the m.p. as 59°.

Senecioylisodurene (IVb).—This compound was prepared as described for IVa, using isodurene (13.4 g.) and the same amounts of other materials specified above. The products were recovered senecioic acid (4.73 g.), recovered isodurene (5.2 g.) and the ketone IVb (4.2 g., 20%). The ketone, a liquid, boiled at 161° (9 mm.).

Anal. Calcd. for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 82.72; H, 9.30.

Dibromide (Vb) (2.4 g.) prepared from the ketone (1.37 g.) as described above and crystallized from aqueous methanol, melted at 95–97°. This substance was somewhat unstable; when dried at 78° in a pistol, it became green and the melting point fell.

Anal. Calcd. for $C_{15}H_{20}OBr_2$: C, 47.89; H, 5.36. Found: C, 47.98; H, 5.75.

Hydroxylamino compound (VIb) (0.56 g.) prepared from IVb as described above and crystallized from aqueous ethanol, melted at 139–140° (dec.).

Anal. Calcd. for $C_{15}H_{23}O_2N$: C, 72.25; H, 9.30. Found: C, 72.22; H, 9.44.

2,3,4,6-Tetramethylbenzoic acid (VIIb) (1 g.) was prepared from IVb (2 g.) as described above. The acid, after two crystallizations from petroleum ether (B), melted at 161–164°; when mixed with acid VIIa, it melted at 135–155°.[14]

Pyridinium Iodide of Acetoisodurene.—The ketone (8.8 g.), iodine (12.7 g., powdered) and pyridine (45 cc.) were heated on the steam-bath for 50 minutes and then allowed to stand overnight at room temperature. The black crystalline solid was removed, washed with cold ether (20 cc.) and water, and dried in the air. It weighed 6.69 g. (35%) and melted at 270° (dec.). Two recrystallizations from water gave nearly colorless needles melting sharply at 228° (dec).

Anal. Calcd. for $C_{17}H_{20}ONI$: C, 53.56; H, 5.29. Found: C, 53.97; H, 5.44.

Aqueous sodium hydroxide (5 cc., 10%) was added to a suspension of the crude pyridinium iodide (1.9 g.) in aqueous ethanol (80 cc., 50%), and the mixture was heated on the steam-bath for one hour. Acidification of a small portion of the mixture gave a solid containing halogen and melting at about 290°. More sodium hydroxide (10 cc.), then solid potassium hydroxide (1 g.) were added, and the mixture was heated again for one hour, with the same result. No cleavage occurred when the iodide was subjected to the action of potassium hydroxide (50%) in boiling aqueous glycerol (b.p., 155°); the product in this case was a tar, and contained none of the benzoic acid VIIb.

Senecioylprehnitene (IVc) was prepared as described above, using prehnitene (26.8 g.), senecioyl chloride (23.8 g.), aluminum chloride (26.2 g.) and carbon bisulfide (120 cc.). The reaction mixture was kept at or below 13° throughout. The products were a small amount of unchanged prehnitene and IVc, an oil (29 g., 67%), which was fractionated through a column (2 × 20 cm.) packed with glass helices. The main fraction (21.1 g.) boiled at 129–131° (1.5 mm.), and had $n^{26}D$ 1.5553.

Anal. Calcd. for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.40; H, 9.56.

3,3,4,5,6,7-Hexamethyl-1-hydrindone (VIII).—When the above experiment was duplicated except that, after addition of the aluminum chloride (20 minutes), the reaction mixture was brought to 28° for 40 minutes and then decomposed, the product was a solid (39.5 g., 91%). This was dissolved in methanol (Norit) and the hot filtrate was diluted with water to faint turbidity and cooled. The solid was removed and crystallized twice (Norit) from aqueous methanol, when it melted at 76.5–77°. The hydrindone was inert toward permanganate, and reacted by substitution with bromine in carbon tetrachloride.

Anal. Calcd. for $C_{15}H_{20}O$: C, 83.28; H, 9.32. Found: C, 83.00; H, 9.00.

The hydrindone VIII (2 g.) in benzene (20 cc.) was refluxed for 40 minutes with aluminum chloride (2 g.). The reaction mixture was poured over ice, and steam distilled. The residue in the distilling flask (1.8 g.) melted at 70–76°, alone or when mixed with VIII. The same result was obtained when the experiment was duplicated but using pseudocumene as the solvent.

Dibromide (Vc) (1.7 g.) was prepared from the ketone (1 g.) as described above and crystallized from methanol (Darco A). The white solid melted at 74–75°.

Anal. Calcd. for $C_{15}H_{20}OBr_2$: C, 47.87; H, 5.36. Found: C, 47.83; H, 5.26.

Hydroxylaminoöxime (VIc) (0.7 g., 58%) was prepared from IVc (1 g.) as described above, and crystallized three times from 1:1 benzene–petroleum ether (B). It was white and melted at 139.5–141°.

Anal. Calcd. for $C_{15}H_{24}O_2N_2$: C, 68.14; H, 9.15; N, 10.60. Found: C, 67.98; H, 9.18; N, 10.81.

2,3,4,5-Tetramethylbenzoic acid (VIIc) (2.88 g., 81%) was prepared from IVc by permanganate oxidation as described above, and crystallized twice from 1:1 benzene–petroleum ether (F). It melted at 167–168.5° and had a neutral equivalent of 178.6 (calcd., 178.2); Meyer, ref. 13a, gives the m.p. of this acid as 168–169°. The methyl ester, prepared from the acid by action of diazomethane and crystallized from chloroform, melted at 34–36°; Meyer, ref. 13a, gives 36°.

Pyridinium Iodide of Acetoprehnitene.—The ketone (8.8 g.), iodine (12.7 g.) and pyridine (45 cc.) were brought into reaction as described above for acetoisodurene. The product (1.8 g., 9%), after crystallization twice from water, formed small orange cubes melting at 220.5–221.5° (dec.).

Anal. Calcd. for $C_{17}H_{20}ONI$: C, 53.56; H, 5.29. Found: C, 53.15; H, 5.72.

The pyridinium iodide (1 g.) was readily cleaved by action of sodium hydroxide (2 g.) in aqueous ethanol (55 cc., 50%) for one hour on the steam-bath. The mixture, after standing overnight at room temperature, was processed as described above. The solid (0.37 g., 39%) after crystallization twice from 1:1 benzene–petroleum ether (B) melted at 166–168°, alone or when mixed with VIIc prepared by oxidation of IVc.

Senecioylprehnitene (IVc) (0.5 g.) was dissolved, with shaking, in sulfuric acid (15 cc.) at room temperature. After five minutes, the solution was poured over ice (20 g.) and the solid (0.5 g.) was removed and crystallized from aqueous methanol (Norit). It melted at 76.5–77°, alone or when mixed with hydrindone VIII prepared directly from prehnitene.

Oxime IX (3.49 g., 82%) prepared from VIII (4 g.) and hydroxylamine hydrochloride, and crystallized twice from aqueous ethanol, melted at 168–169°.

Anal. Calcd. for $C_{15}H_{21}ON$: C, 77.87; H, 9.15; N, 6.06. Found: C, 78.11; H, 9.36; N, 6.14.

Benzal Derivative (X).—The hydrindone VIII (2.16 g.) was dissolved in ethanolic potassium hydroxide (35 cc.), benzaldehyde (1.1 g.) was added, and the solution was allowed to stand at room temperature for three hours. The solid (1.85 g., 61%) was removed and crystallized once from aqueous ethanol and once from aqueous methanol, when it formed small yellow needles melting at 155.5–157.5°.

Anal. Calcd. for $C_{22}H_{24}O$: C, 86.80; H, 7.95. Found: C, 86.60; H, 8.16.

Senecioylpentamethylbenzene (IVd) was prepared as described above, using pentamethylbenzene (14.82 g.), senecioyl chloride (11.85 g.), aluminum chloride (13 g.) and carbon bisulfide (150 cc.). The products were a trace of recovered pentamethylbenzene and the ketone IVd (19.3 g., 84%) which, after three crystallizations from aqueous methanol, melted at 88.5–90°.

Anal. Calcd. for $C_{16}H_{22}O$: C, 83.41: H, 9.63. Found: C, 82.67, 82.90: H, 9.58, 9.82.

Dibromide (Vd) (3.85 g., 98 %) was prepared from ketone

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[13] (a) V. Meyer, *Ber.*, **29**, 2570 (1896), gives the m.p. as 176.5°; (b) Jacobsen, *ibid.*, **22**, 1223 (1889), gives 179°.

[14] L. Gattermann, *Ber.*, **32**, 1118 (1899), gives the m.p. of VIIb as 164–165°.

IVd (2.3 g.) as described above, but with chloroform (15 cc.) as the solvent. The product was recrystallized from methanol (Norit) when it melted at 133.5° (dec.).

Anal. Calcd. for $C_{16}H_{22}OBr_2$: C, 49.25; H, 5.68. Found: C, 49.60; H, 5.85.

Hydroxylamino compound (VId) (1.16 g., 88%) was prepared from IVd (1.15 g.) and hydroxylamine hydrochloride as described above, and crystallized twice from methanol. It melted at 181.5–182.5°.

Anal. Calcd. for $C_{16}H_{25}O_2N$: C, 72.95; H, 9.57. Found: C, 73.36; H, 9.86.

Pentamethylbenzoic acid (VIId) (1.78 g., 40%) was prepared from IVd (4.6 g.) by permanganate oxidation as described above. The oxidation was sluggish, and 1.8 g. of the ketone was recovered unchanged. The acid, crystallized twice from 1:1 benzene–petroleum ether (B), melted at 203–207° alone or when mixed with an authentic specimen (m.p. 210–211°). The methyl ester, prepared from the acid by action of diazomethane, melted at 66–67° alone or when mixed with an authentic specimen (m.p. 68–70°); Jacobsen, ref. 13b, gives 67.5°.

MINNEAPOLIS 14, MINNESOTA RECEIVED MARCH 1, 1951

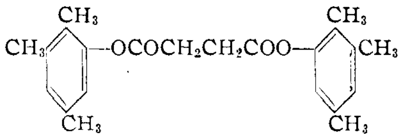
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

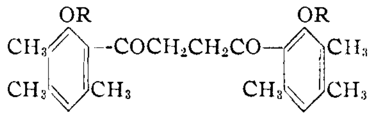
Fries Rearrangement of 2,3,5-Trimethylphenyl Succinate[1]

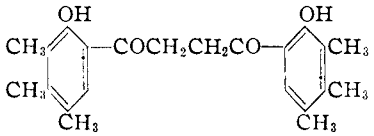
BY LEE IRVIN SMITH AND RICHARD REMSEN HOLMES

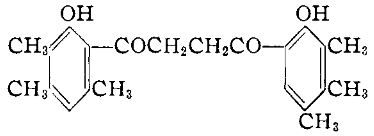
The Fries rearrangement of 2,3,5-trimethylphenyl succinate gives products resulting from a double rearrangement. These are the diorthohydroxy-1,4-diketone II, formed without rearrangement of methyl groups, and the isomeric diketone III, formed with rearrangement of one or more methyl groups. The diketone II has been converted into a diarylfuran X, and this into the bis-quinone XI.

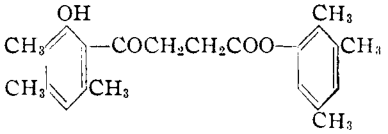
Fries rearrangements of phenolic esters of dibasic acids are considerably less satisfactory, with respect to yield and simplicity, than are the corresponding rearrangements of simple phenol esters, and few double Fries rearrangements are reported in the literature. Fries and Bartens[2] carried out such rearrangements of the succinate esters of *p*-cresol and *sym*-*m*-xylenol, but no yields were given. Schwenk and Priewe[3] carried out a double Fries rearrangement using the adipic ester of *m*-cresol; no yields were given, although the product was well characterized. Huebner and Link[4] reported that rearrangement of phenyl glutarate occurred, but the product of the double rearrangement was produced in very low yield. Recently Baddar and El-Assal[5] studied the action of aluminum chloride upon a mixture of phenol and succinic anhydride; they reported that the product was a mixture of *o*- and *p*-hydroxybenzoylpropionic acid.


I


II, R = H
VI, R = CH_3
VII, R = Ac


IIIa


IIIb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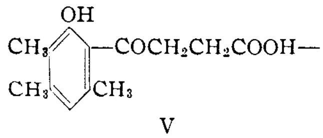
V

In connection with the studies of the reactions between quinones and metallic enolates, it was desired to prepare some bis-quinones with the two quinone nuclei joined by a chain of four carbon atoms, and as an approach to synthesis of such compounds, introduction of the four-carbon chain *via* a double Fries rearrangement of 2,3,5-trimethylphenyl succinate (I) was investigated. When the succinate I in tetrachloroethane was heated to 140° for several hours with two moles of aluminum chloride, a complex mixture resulted which could be separated—although with considerable difficulty—into the diketone II melting at 208–210°; an isomeric diketone melting at 246–248°, most likely having structure IIIa or IIIb; the keto ester IV; and the corresponding keto acid V; trimethylphenol and a considerable residue of an intractable tar. Formation of *o*-hydroxyketones by rearrangement of I at 140° is in agreement with the observations of Fries and Finck,[6] Auwers and Mauss,[7] Baddeley,[8] and others[9] who found that at temperatures above 100° meta substituted phenol esters rearrange almost exclusively to orthohydroxyketones in the

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[1] Abstracted from a thesis by Richard Remsen Holmes, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, July, 1950. American Chemical Society Predoctoral Fellow, 1946–1950.

[2] K. Fries and K. Bartens, *Ann.*, **442**, 261 (1925).

[3] E. Schwenk and H. Priewe, THIS JOURNAL, **56**, 2101 (1934).

[4] C. F. Huebner and K. P. Link, *J. Biol. Chem.*, **138**, 529 (1941).

[5] F. G. Baddar and L. S. El-Assal, *J. Chem. Soc.*, 3606 (1950).

[6] K. Fries and G. Finck, *Ber.*, **41**, 4271 (1908).

[7] K. v. Auwers and W. Mauss, *Ann.*, **460**, 240 (1928).

[8] G. Baddeley, *J. Chem. Soc.*, 273 (1943).

[9] L. I. Smith and J. W. Opie, *J. Org. Chem.*, **6**, 427 (1941).