TABLE I

5-(1-METHOXYPROPYL)-5-ALKYL (OR 5-PHENYL) HYDANTOINS

—R	M. p., °C.	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
CH_3	234–235 (dec.)	44	51.60	51.59	7.58	7.80	15.05	15.08
C_2H_5	216.0–216.5	90	53.98	53.99	8.05	8.33	13.99	14.12
C_3H_7	188–189	52	56.05	56.09	8.47	8.55	13.08	13.33
$CH(CH_3)_2$	206–208	66	56.05	56.13	8.47	8.53	13.08	13.08
C_4H_9	197–198	48	57.86	58.07	8.83	8.95	12.27	12.39
$CH(CH_3)C_2H_5$	221–222	28	57.86	57.86	8.83	8.98	12.27	12.39
$CH_2CH(CH_3)_2$	241–242	36	57.86	57.99	8.83	8.73	12.27	12.06
C_5H_{11}	171.0–171.5	74	59.50	59.64	9.15	9.47	11.56	11.63
$CH(CH_3)C_3H_7$	154–155	62	59.50	59.98	9.15	9.29	11.56	11.46
$CH_2CH(CH_3)C_2H_5$	221–222	12	59.50	59.75	9.15	8.97	11.56	11.74
$CH_2CH_2CH(CH_3)_2$	216–218	87	59.50	59.58	9.15	9.35	11.56	11.44
$CH(C_2H_5)_2$	213.0–213.5	33	59.50	59.58	9.15	9.41	11.56	11.69
C_6H_{13}	147–148	87	60.91	60.85	9.44	9.65	10.93	11.17
Cyclo-C_6H_{11}	243–245	32	61.39	61.57	8.72	8.85	11.03	11.19
C_6H_5	210–212	92	62.88	62.82	6.50	6.76	11.28	11.39

Summary

Thirteen 5-alkyl-5-(1-methoxypropyl) hydantoins, and the analogous 5-cyclohexyl and 5-phenyl derivatives have been prepared from the corresponding ketones.
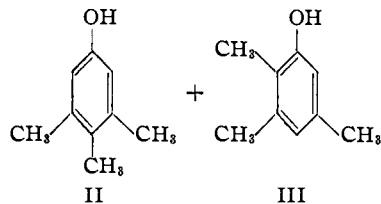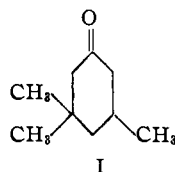
AUSTIN, TEXAS   RECEIVED FEBRUARY 21, 1949

[CONTRIBUTION FROM CHANDLER LABORATORY, COLUMBIA UNIVERSITY]

Sulfonic Acids in the Rearrangement and Aromatization of Some Cyclic Ketones[1]

BY W. VON E. DOERING AND F. MARSHALL BERINGER[2]

Unexpectedly, the reaction of dihydroisophorone (3,3,5-trimethylcyclohexanone, I) with 30% oleum[3] for one week followed by steam distillation produces small amounts of 3,4,5-trimethylphenol[4,5,6] (sym-hemimellitenol, II) and 2,3,5-trimethylphenol[7,8,9,10] (isopseudocumenol,

III). Under essentially identical conditions isophorone (3,3,5-trimethylcyclohexenone, IV) is aromatized smoothly (54% yield) and exclusively to II.[11] When treated with 5% oleum in acetic anhydride, IV is transformed (38%) into 3,4,5-trimethylphenyl acetate. In all reactions large amounts of sulfur dioxide are evolved.

While it is clear that IV may be an intermediate in that part of the aromatization of I which leads to II, further examination suggests the involve-

(1) This work, taken from a dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science of Columbia University, was presented in part at the 112th meeting of the American Chemical Society, September 16, 1947, New York, N. Y.

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(3) The experiment was vainly designed to realize an additional acid-catalyzed fission of β-trisubstituted ketones, as exemplified by the cleavage of camphor to carvenone [Bredt, Rochussen and Monheim, Ann., 314, 376 (1901)].

(4) Horning has surveyed alicyclic–aromatic conversions in Chem. Rev., 33, 89 (1943).

(5) Auwers and Saurwein, Ber., 55, 2372 (1922).

(6) Auwers and Wieners, ibid., 58, 2815 (1925).

(7) Edler, ibid., 18, 630 (1885); Smith, Hoehn and Ungnade, J. Org. Chem., 4, 351 (1939); Horning, et al., ibid., 9, 552 (1944).

(8) Kruber and Schmidt, Ber., 64, 2274 (1931).

(9) Caldwell and Thompson, THIS JOURNAL, 61, 2354 (1939); Baddeley, J. Chem. Soc., 330 (1944).

(10) While our material melts (66–66.5°) much lower than that reported[7,8,9] (93° to 96°), the coincidences of melting point of the dibromo derivative (147–148°; variously reported[5,7,8] from 147° to 152°) and the phenylurethan (169.5–170.5°; reported,[8] 174°) leave little doubt that our material is either a low-melting allotrope of III or a eutectic mixture of II and III, the latter alternative being

indicated by the grossly impure character of the crude phenylurethan.

(11) The absence of III removes the possibility that the III formed in the aromatization of I arises by a subsequent Jacobsen-type rearrangement of II.

ment of aliphatic sulfonic acids[12] in the oxidative rearrangement. From the reaction of IV with oleum in acetic anhydride and ether,[13] two isophorone-sulfonic acids, V, m. p. 169–170°, and VI, m. p. 173–174°, are isolated in 12–16% and 45–62% of the theoretical yield, respectively. VI has been unequivocally assigned the structure of isophorone-7-sulfonic acid by comparing directly the hydrocarbon sulfonic acid (VII) derived from VI by catalytic reduction[14] with authentic 3,3-dimethylcyclohexylmethanesulfonic acid (VII) synthesized by the following series of reactions from the known 3,3 - dimethylcyclohexyl bromide (VIII).[15,16] Reaction of the Grignard reagent of VIII with formaldehyde leads to 3,3-dimethylcyclohexylcarbinol (X), from which 3,3-dimethylcyclohexylmethyl bromide (XI) is obtained by
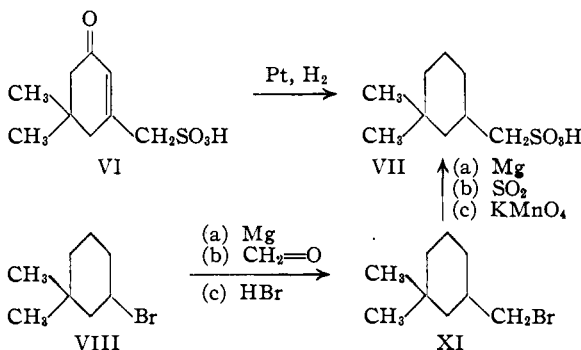
treatment with hydrogen bromide. 3,3-Dimethylcyclohexylmethanesulfinic acid (XII), obtained by the reaction of the Grignard reagent of XI with sulfur dioxide according to the general procedure of Borsche and Lange,[19] is oxidized by potassium permanganate to VII. Because the

(12) Replacement of a γ-hydrogen atom in α,β-unsaturated ketones by the sulfonic acid group is exemplified in the sulfonations of pulegone [Treibs, Ber., 70, 85 (1937)], Δ⁴-3-ketocholestene [Windaus Kuhr, Ann., 532, 52 (1937)], and Δ⁵-7-ketocholestene [Windaus and Mielke, ibid., 536, 116 (1938)].

(13) These conditions, apparently similar to those which allowed Bruson, U. S. Patent 2,301,561 (1943), to prepare a substance of low capillary activity, presumably crude sodium isophorone sulfonate, from IV, have often been used for sulfonating ketones; cf. the conversions of camphor to Reychler's acid [Bull. soc. chim., [3] 19, 120 (1898)] and of acetophenone to acetophenone-ω-sulfonic acid in the present work.

(14) In the related hydrogenation of Δ⁴-3-ketocholestene-6-sulfonic acid, Windaus and Kuhr¹² obtained only 3-hydroxycholestane-6-sulfonic acid, no desoxy material being isolated.

(15) Crossley and Renouf, J. Chem. Soc., 87, 1487 (1905).

(16) Although extensive rearrangement in the preparation of VIII from 3,3-dimethylcyclohexanol (IX) and hydrogen bromide¹⁵ is not to be expected, doubt concerning the structure of VIII is dispelled by the fact that autoxidation of the Grignard reagent from VIII, according to the general procedure of Kharasch and Reynolds,¹⁷ reforms IX, identified as its p-nitrobenzoate.¹⁸

(17) Kharasch and Reynolds, This Journal, 65, 501 (1943).

(18) Chavanne, Miller and Cornet, Bull. soc. chim. Belg., 40, 673 (1931); C. A., 26, 2712 (1932).

(19) Borsche and Lange, Ber., 40, 2220 (1907).
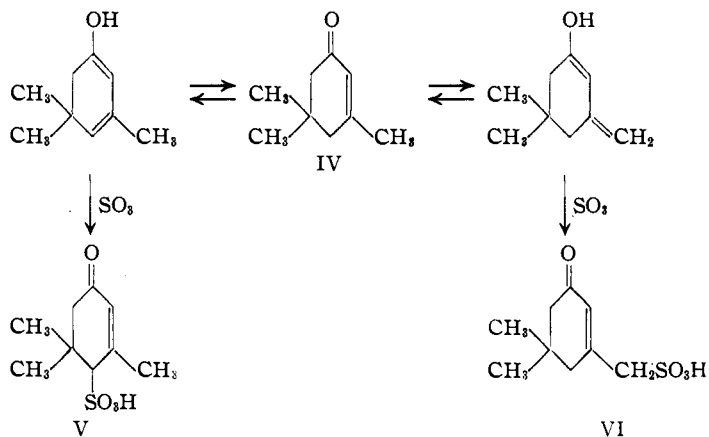
structure of VI is consistent with a mechanism of sulfonation involving electrophilic attack of an incipient positive sulfonic acid residue at the terminal carbon atom of a dienol system (possibly as the dienol acetate[20] or sulfate), V is assigned the structure of isophorone-4-sulfonic acid (V).

When the two sulfonic acids react with oleum, V gives II in 65% of the theoretical yield, while VI gives none. When boiled in acetic anhydride, both acids give II, V in 75% and VI in 24% of the theoretical yield. In the proposed mechanism the 4-sulfonic acid is transformed by sulfur trioxide or acetic anhydride to a pyrosulfate XIIIa or an acetyl sulfate XIIIb[21] in which the strong sulfur-hydroxyl bond of the sulfonic acid has been so weakened that rearrangement can be initiated. Migration of one of the gem-methyl groups may accompany departure of the bisulfate or acetate anion and sulfur dioxide leading directly to the tertiary carbonium ion XIV,[22] or it may
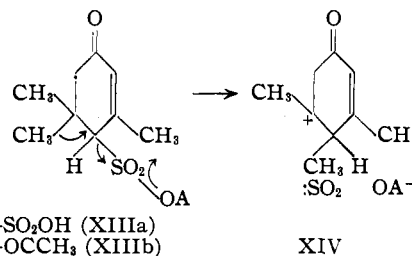
A = —SO₂OH (XIIIa)
A = —OCCH₃ (XIIIb)   XIV

involve two steps, the first of which is dissociation to the secondary carbonium ion. The subsequent prototropic changes which lead to the final product II need no explanation.[23]

In contrast to that of the 4-isomer, the decomposition of isophorone-7-sulfonic acid does not place a positive charge proximate to the quaternary carbon unless the decomposition is pre-

(20) Kuhr, ibid., 72, 929 (1939), reports the rapid sulfonation of 3-acetoxycholestadiene-3,5 to Δ⁴-3-ketocholestene-6-sulfonic acid.

(21) Russel and Cameron, This Journal, 60, 1345 (1938).

(22) It is possible to extend the hypothetical concert of the mechanism to include removal of the proton by writing the transition state as an incipient six-membered ring.

(23) In oleum the phenol is sulfonated and must be regenerated by steam distillation. Cf. Houben, "Die Methoden der organischen Chemie," Georg Thieme, Leipzig, Vol. III, 1930, p. 1298–1300.

A = —SO$_2$OH (XVa)
A = —COCH$_3$ (XVb)

XVI
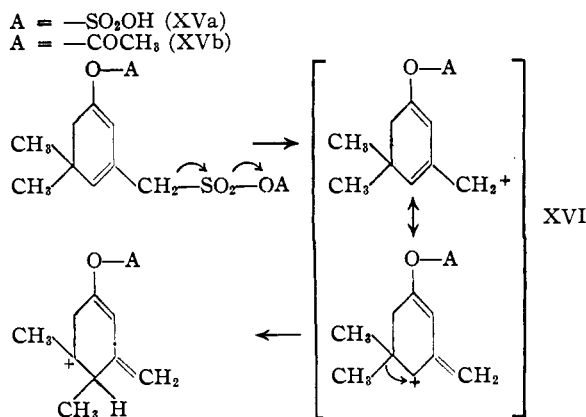
ceeded by transformation to the dienol, the dienol sulfate XVa, the dienol acetate XVb, or the $\Delta^{3,4}$-unsaturated ketone, in any one of which the transient positive charge is in allylic resonance (XVI). Possibly this additional requirement is related to the greater resistance of the 7-isomer to rearrangement.

With sulfonic acids as intermediates, the aromatizations of I (proceeding by way of the 2- and 6-sulfonic acids) and IV[24] find consistent explanation as do the transformations of fenchone and camphor to 3,4-dimethylacetophenone[25] and the oxidation of 1-methyl-4-acetylcyclohexene-1 to *p*-methylacetophenone.[26] Another example of the aromatization is the formation of 4,5-dimethylresorcinol (*o*-xylorcinol, XVIII) from dimethyldihydroresorcinol by way of 5,5-dimethyldihydroresorcinol-2-sulfonic acid (XVII), the

(24) Although IV is sulfonated in ethereal *acetic anhydride–oleum* to V in only 12–16% of the theoretical yield, an amount quite insufficient to account for the 54% yield of II obtained from IV in *oleum* (there is no inconsistency with the more directly comparable rearrangement in *acetic anhydride–oleum*), V may still be the intermediate by assuming that it is formed predominantly over the 7-isomer in *oleum*. It is, however, thinkable that the reactions in *oleum* proceed by mechanisms entirely different from those operating in *oleum–acetic anhydride*. In one alternative mechanism sulfur trioxide or a positive sulfonic acid group introduces a positive charge by abstracting a hydride ion in much the same manner as suggested by Bartlett, Condon and Schneider, THIS JOURNAL, 66, 1531 (1944), for the action of the *t*-butyl chloride–aluminum bromide complex on isopentane. Another mechanism, suggested by the remarkable transformation of isophoronoxime into 3,4,5-trimethylaniline, observed by Wolff, *Ann.*, 322, 380 (1902), proposes the decomposition of a hypothetical isophorone dienol pyrosulfate into bisulfate ion, sulfur dioxide and the same carbonium ion derivable from XIIIa.
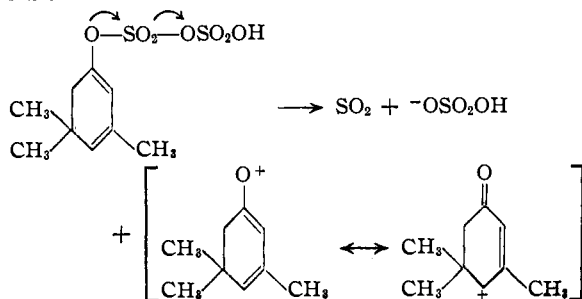
(25) Armstrong and Kipping, *J. Chem. Soc.*, 63, 81 (1893); Marsh, *ibid.*, 75, 1056 (1899); Zaugg, THIS JOURNAL, 67, 1861 (1945).
(26) Wallach, *Ann.*, 324, 91 (1902).

XVII   XVIII
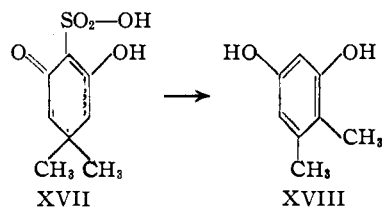
structure of which is proved by its oxidation to β,β-dimethylglutaric acid. This reaction, requiring distribution of positive charge by allylic resonance, is interpreted as is the aromatization of isophorone-7-sulfonic acid.

Experimental[27,28]

3,4,5-Trimethylphenol (II) from Isophorone (IV).—To 10 cc. of 5% oleum was added portionwise with shaking and cooling 15 cc. of IV, 100 cc. of 25% oleum (0.6 mole of sulfur trioxide), and 1 cc. of acetic anhydride. After ten days at room temperature, the mixture was poured onto 250 g. of ice and exhaustively steam-distilled.[28] The distillate was made alkaline with sodium hydroxide and again steam-distilled. The residue was acidified with hydrochloric acid, treated with sodium chloride, and steam-distilled to give 7.37 g. of ether-extractable II, m. p. 102.5–104° (54% of the theoretical yield). Crystallization from hexane gave pure II, m. p. 106–106.5°; reported,[5] m. p. 107°.

Anal. Calcd. for C$_9$H$_{12}$O: C, 79.37; H, 8.88. Found: C, 79.19; H, 8.93.

A shorter time of reaction or a lower concentration of oleum caused a reduced yield of II and an increased recovery of IV.

3,4,5-Trimethylphenyl acetate was prepared from 1.36 g. of II by boiling with 5 cc. of acetyl chloride for thirty minutes, distilling away the excess reagent, and crystallizing the residue from petroleum ether (30–60°); 1.48 g. (83%) of colorless plates, m. p. 58.5–59°; reported,[6] m. p. 59–60°.

Anal. Calcd. for C$_{11}$H$_{14}$O$_2$: C, 74.13; H, 7.92. Found: C, 73.95; H, 7.90.

To an acetic acid solution of 0.68 g. of II and excess bromine, the addition of aqueous sodium bisulfite precipitated material which was crystallized from heptane, giving 1.37 g. (93%) of lightly cream-colored needles of 2,6-dibromo-3,4,5-trimethylphenol, m. p. 144–145°. Sublimation followed by two crystallizations from hexane and from methanol, gave colorless needles, m. p. 145–145.5°; reported,[5] m. p. 142.5–143°.

Anal. Calcd. for C$_9$H$_{10}$Br$_2$O: C, 36.77; H, 3.43. Found: C, 36.84; H, 3.58.

A mixture of 1.36 g. of II and 2.2 cc. of phenyl isocyanate was heated for ten minutes and the solid product crystallized from hexane. Recrystallizations from heptane (1.87 g., 73%), m. p. 153–154°) and from benzene gave needles of the phenylurethan of II, m. p. 153.5–154°; reported,[6] m. p. 148–149°.

3,4,5-Trimethylphenyl Acetate from IV.—Fifteen minutes after the addition at 0° of 10.5 cc. of 5% oleum and 30 cc. of IV to 200 cc. of acetic anhydride crystals appeared. After eighteen hours at 0°, the mixture was heated at 100° for four hours and at reflux for four hours, and, after addition of 70 cc. of acetyl chloride, at reflux for four hours more. After removal of solvent, the residue was distilled *in vacuo*, dissolved in ether, extracted with alkali, washed with water, and dried. Crystallization of the residue from pentane gave 13.4 g. of crude product which, twice recrystallized, afforded pure 3,4,5-trimethylphenyl acetate, m. p. 58–59°.

(27) All melting points are corrected.
(28) The microanalyses have been executed by the Misses Lathrope Baker and Lois May.

3,4,5-Trimethylphenol (II) and 2,3,5-Trimethylphenol (III) from Dihydroisophorone (I).—I (b. p. 186.5–187.5°) was prepared in 69% yield from dihydroisophorol which, in turn, was prepared from IV in 70% yield, both according to Knoevenagel and Fischer.[29] To 10 cc. of 5% oleum were added successively and with cooling 15.7 cc. of I, 50 cc. of 25% oleum, and 20 cc. of 60% oleum. After a week at room temperature, the mixture was poured onto ice and steam-distilled. The ether extract of the distillate was extracted with sodium hydroxide. Ether extraction of the acidified alkaline solution gave 1.5 g. of oil from which 0.1 g. of crude II, m. p. 95–97°, crystallized. This material, after crystallization from hexane, melted at 106–107° and did not depress the m. p. of authentic II.

The remaining oil on further cooling deposited 0.5 g. of very impure III which, after two crystallizations from pentane, sublimation, and two more crystallizations from hexane, melted constantly at 66–66.5°.[10]

Anal. Calcd. for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.07; H, 8.60.

Bromination of the phenol (m. p. 66–66.5°) gave a solid from which, after two crystallizations from ethanol, sublimation, and two more crystallizations from ethanol, 4,6-dibromo-2,3,5-trimethylphenol was obtained, m. p. 147–148°; variously reported[5,7,8] 147° to 152°.

Anal. Calcd. for $C_9H_{10}Br_2O$: C, 36.77; H, 3.43. Found: C, 36.64; H, 3.37.

Treatment of 0.136 g. of the phenol (m. p. 66–66.5°) in hexane with 0.11 cc. of phenyl isocyanate gave 0.21 g. of material, m. p. *ca.* 135° after crystallization from methanol. Sublimation at 0.3 mm. and two crystallizations from methanol gave the phenylurethan of 2,3,5-trimethylphenol (III), m. p. 169.5–170.5°; reported,[8] m. p. 174°.

Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71. Found: C, 75.31; H, 6.58.

Acetophenone-ω-sulfonic Acid.—After two days at 0°, a solution of 10.5 cc. of 15% oleum and 23.2 cc. of acetophenone in 20 cc. of acetic anhydride and 80 cc. of ether was concentrated to a residue, extraction of which with hot benzene gave 15.7 g. of greenish crystals. Recrystallization from ethyl acetate or acetonitrile afforded acetophenone-ω-sulfonic acid, m. p. 77–78°, permanganate oxidation of which gave benzoic acid. Parkes and Tinsley[30] report a m. p. of 73–75° for the sulfonic acid from the reaction of phenacyl bromide with sodium sulfite.

Isophorone-4-sulfonic Acid (V) and Isophorone-7-sulfonic acid (VI).—To a mixture of 150 cc. of distilled IV,[31] 100 cc. of acetic anhydride, and 400 cc. of ether cooled in a Dry-Ice bath there was added 51.3 cc. of 5% oleum in five portions with stirring. From the precipitate deposited by the reaction mixture overnight and from the mother liquor there was obtained 189 g. (0.87 mole) of a crystalline mixture of V and VI. Repeated fractional crystallization from acetonitrile separated the less soluble isophorone-7-sulfonic acid (VI, 135 g., 0.62 mole) from the more soluble isophorone-4-sulfonic acid (V, 26.5 g., 0.12 mole).

In a similar experiment in which IV was in 0.1 mole excess, 13% oleum was used, and the cooling bath was ice-concentrated hydrochloric acid, VI was obtained in smaller amount (95 g., 0.45 mole) and V in slightly larger amount (35 g., 0.16 mole). The reaction of chlorosulfonic acid and IV also gave V and VI but in a more difficultly purifiable condition.

Pure VI crystallized from acetonitrile in colorless elongated prisms, which after drying *in vacuo* melted at 173–174° (dec.).

Anal. Calcd. for $C_9H_{14}O_4S$: C, 49.52; H, 6.46. Found: C, 49.24; H, 6.62.

(29) Knoevenagel and Fischer, *Ann.*, **297**, 194 (1897).

(30) Parkes and Tinsley, *J. Chem. Soc.*, 1861 (1934).

(31) When commercial isophorone, b. p. 205–220°, is distilled in a thirty-plate column at atmospheric pressure and a high reflux ratio, material of b. p. 184–186°, $n^{20}D$ 1.4635, is obtained which is probably one of the β,γ-isomers.

Pure V crystallized from acetonitrile in large yellow prisms, m. p. 169–170° (dec.) after drying *in vacuo*.

Anal. Calcd. for $C_9H_{14}O_4S$: C, 49.52; H, 6.46; S, 14.69. Found: C, 49.82; H, 6.49; S, 14.94.

A mixture of V and VI melted at 152–154° (dec.). Very soluble in water and ethanol, sparingly soluble in ether, both sulfonic acids may be crystallized from acetonitrile, dioxane, butyl acetate, and nitromethane.

On addition of an aqueous solution of 2.18 g. of VI, neutralized with sodium hydroxide, to an aqueous solution of 2.03 g. of S-benzylthiuronium chloride[32] crystals precipitated which upon crystallization from dioxane and from acetonitrile gave 3.02 g. of S-benzylthiuronium isophorone-7-sulfonate, m. p. 155–155.5°.

Anal. Calcd. for $C_{17}H_{24}N_2O_4S_2$: C, 53.10; H, 6.29. Found: C, 53.29; H, 6.39.

In an identical procedure, V yielded 2.10 g. of colorless plates of S-benzylthiuronium isophorone-4-sulfonate, m. p. 139.5–140° after crystallization from ethyl acetate and from chloroform.

Anal. Calcd. for $C_{17}H_{24}N_2O_4S_2$: C, 53.10; H, 6.29. Found: C, 53.17; H, 6.34.

A solution of 4.36 g. of VI and 1.61 cc. of pyridine in 10 cc. of acetonitrile deposited 5.24 g. of the pyridine salt of isophorone-7-sulfonic acid, m. p. 122.5–124°, which after two crystallizations from acetonitrile and drying *in vacuo* melted at 123–124°.

Anal. Calcd. for $C_{14}H_{19}NO_4S$: C, 56.54; H, 6.44. Found: C, 56.35; H, 6.27.

A solution of 2.18 g. of V and 0.81 cc. of pyridine in 10 cc. of ethyl acetate deposited 2.73 g. of the pyridine salt of isophorone-4-sulfonic acid, m. p. 119.5–120.5°. A mixture of the two pyridine salts melted at 92.4–96°.

Anal. Calcd. for $C_{14}H_{19}NO_4S$: C, 56.54; H, 6.44. Found: C, 56.29; H, 6.36.

Rearrangement of Isophorone Sulfonic Acids, V and VI. (a) In Oleum.—After standing for four days at room temperature, 2.00 g. of V in 5 cc. of 33% oleum was poured onto 25 g. of ice, and steam distilled to give 0.81 g. of II. A similar experiment with VI gave no II.

(b) In Acetic Anhydride.—A solution of V (4.36 g.) in acetic anhydride (20 cc.) was refluxed for four hours, evolution of sulfur dioxide being copious at first. After removal of solvent the residue was refluxed with 10 g. of potassium hydroxide in 30 cc. of water for several hours, acidified with hydrochloric acid, and extracted with ether to yield 2.04 g. (75%) of II. A similar experiment with VI gave II in 24% of the theoretical yield.

Preliminary attempts to isolate 3,4,5-trimethylphenyl acetate directly from the reaction mixture were successful, although the yields were only about 40% as great as when II was isolated.

3,3-Dimethyl-5-hydroxycyclohexylmethanesulfonic Acid and 3,3-Dimethylcyclohexylmethanesulfonic Acid (VII).—A suspension of 43.6 g. of VI in 200 cc. of purified acetic acid absorbed 2.67 equivalents of hydrogen when shaken for four hours in a Parr apparatus with hydrogen at 30–40 lb. pressure and 2.0 g. of Adams platinum oxide. A solution in methanol (200 cc.) of the viscous liquid remaining after removal of the catalyst and solvent (*in vacuo*) was added to a hot methanolic solution (500 cc.) of benzidine (36.8 g.). Fractional crystallization from methanol separated the resulting salt into a smaller fraction, 13.7 g., m. p. 217–219° (dec.), and a larger fraction, 38.1 g. of flat plates, m. p. 301–303° (dec., bath at 290°) which was the benzidine salt of 3,3-dimethylcyclohexylmethanesulfonic acid (VII) and which showed no depression of m. p. on mixing with synthetic material (*vide infra*).

Anal. Calcd. for $C_{21}H_{30}N_2O_3S$: C, 64.58; H, 7.74; N, 7.18. Found: C, 64.50; H, 7.73; N, 7.24.

Treatment of a hot aqueous solution of the 303° benzi-

(32) Prepared according to the procedure of Chambers and Watt, *J. Org. Chem.*, **6**, 376 (1941).

dine salt with one equivalent of barium hydroxide, followed by removal of the precipitated benzidine and evaporation to cloudiness, yielded the **barium salt of VII** as a fine precipitate. The salt, which is very soluble in methanol and sparingly soluble in ethanol, crystallizes from a mixture of the two in small prisms.

Anal. Calcd. for $C_{18}H_{34}BaO_6S_2$: C, 39.46; H, 6.25; Ba, 25.07. Found: C, 39.34; H, 6.60; Ba, 25.01.

The precipitate of **S-benzylthiuronium 3,3-dimethylcyclohexylmethane sulfonate** obtained by mixing aqueous solutions of the barium salt of VII and S-benzylthiuronium chloride was crystallized twice from methanol, m. p. 181–181.5°. Mixed with the S-benzylthiuronium salt of synthetic VII (*vide infra*), this salt gave no depression of m. p.

Anal. Calcd. for $C_{17}H_{28}N_2O_3S_2$: C, 54.81; H, 7.58. Found: C, 54.80; H, 7.66.

The 219° benzidine salt, more soluble in methanol and ethanol, could not be obtained nicely crystalline and is probably a mixture of the stereoisomeric 3,3-dimethyl-5-hydroxycyclohexylmethanesulfonic acid benzidine salts.

Anal. Calcd. for $C_{21}H_{30}N_2O_4S$: C, 62.04; H, 7.44; N, 6.89. Found: C, 62.50; H, 7.68; N, 6.58.

3,3-Dimethylcyclohexanol (IX).—Dimethyldihydroresorcinol (140 g.) is reduced most satisfactorily by adding in three portions at one-hour intervals to purified acetic acid (100 cc.) in a Parr apparatus and hydrogenating at 30–40 lb. pressure with 1.5 g. of Adams platinum oxide.[33] The reaction mixture was treated with 100 g. of sodium hydroxide in 500 cc. of water and the extracted product was distilled giving 24.3 g. of 1,1-dimethylcyclohexane, b. p. 119–121° (reported,[15] b. p. 120°) and 86 g. of IX, b. p. 74–76° (8 mm.) [reported,[15,34] b. p. 73–74° (8 mm.)] and m. p. 6–8° (reported,[34] m. p. 10–11°).

3,3-Dimethylcyclohexyl *p*-nitrobenzoate, prepared in 80% yield by warming 2.56 g. of IX and 3.71 g. of *p*-nitrobenzoyl chloride in 15 cc. of pyridine, pouring into water, and crystallizing from hexane, melted at 83–83.5° in agreement with Chavanne, Miller and Cornet.[18]

Anal. Calcd. for $C_{15}H_{19}NO_4$: C, 64.96; H, 6.91. Found: C, 64.86; H, 6.60.

3,3-Dimethylcyclohexyl Bromide (VIII).—The original preparation[18] has been advantageously modified according to the general procedure of Reid, Ruhoff and Burnett.[35] A stream of hydrogen bromide was passed into 51.2 g. of IX for thirty minutes at 0–5°, for fifteen minutes at 100°, and for two hours at 130°. The organic layer was then washed with sulfuric acid, with 50% methanol, with ammonium hydroxide, and again with 50% methanol. Distillation of the dried product gave 59.0 g. (77%) of VIII, b. p. 80–82° (8 mm.).

According to the general procedure of Gilman and Furry,[36] the Grignard reagent from 3.82 g. of VII was treated with 1.69 g. of α-naphthyl isocyanate to give after several crystallizations from ethanol, **N-1-naphthyl-3,3-dimethylcyclohexanecarboxamide,** m. p. 204–204.5°.

Oxygen was bubbled into the Grignard reagent[17] from 19.1 g. of VIII for ninety minutes. The ether solution was washed with hydrochloric acid, dried, and concentrated giving an oil which was converted to the *p*-nitrobenzoate of IX as above (11.81 g., m. p. 73–78°). Further recrystallized material, m. p. 83–83.5°, showed no depression on admixture with authentic *p*-nitrobenzoate of IX.[16]

3,3-Dimethylcyclohexylcarbinol (X).—Formaldehyde (from 50 g. of paraformaldehyde) was passed for one hour into the Grignard reagent prepared from 20 g. of magne-

sium, 143.3 g. of VIII and 600 cc. of ether. After reacting two hours more, the mixture was extracted with 50 cc. of sulfuric acid and 300 g. of ice to give an ethereal solution which was concentrated. The residue was refluxed for five hours with 250 cc. of 95% ethanol and 10 cc. of concentrated hydrochloric acid, freed of ethanol by distillation, and dissolved in ether. The ethereal solution was washed with dilute sodium hydroxide and water, dried, and concentrated. Distillation of the residue gave 67 g. of X, b. p. 89–92° (8 mm.). An additional 4 g. obtained by retreating the distillation residue with hydrochloric acid brought the yield to 67% of the theoretical.

Anal. Calcd. for $C_9H_{18}O$: C, 76.00; H, 12.75. Found: C, 76.03; H, 12.67.

Upon heating a mixture of 1.42 g. of X, 1.48 g. of phthalic anhydride and 3 cc. of pyridine at 100° for ninety minutes, and extracting the ethereal solution with hydrochloric acid there was obtained, after two crystallizations from benzene, 2.05 g. of the **acid phthalate of X,** m. p. 122.5–123.5°.

Anal. Calcd. for $C_{17}H_{22}O_4$: C, 70.32; H, 7.64. Found: C, 70.48; H, 7.75.

Using the procedure of Lennartz,[37] there was prepared the **3-nitrophthalate of X,** crystallizing from benzene (3.93 g. from 200 cc.) as small plates, m. p. 200.5–202.5°; m. p. 204.5–206° when recrystallized from aqueous methanol.

Anal. Calcd. for $C_{17}H_{21}NO_6$: C, 60.88; H, 6.31. Found: C, 61.10; H, 6.57.

When 28.5 g. of X was treated with hydrogen bromide as described above, 29.75 g. of **3,3-dimethylcyclohexylmethyl bromide (XI)** was obtained, b. p. 92–94° (8 mm.).

Anal. Calcd. for $C_9H_{17}Br$: C, 52.69; H, 8.35. Found: C, 52.30; H, 8.27.

3,3-Dimethylcyclohexylmethanesulfonic Acid (VII).—For one hour at −40° sulfur dioxide was bubbled into a solution of the Grignard reagent prepared from 10.25 g. of XI, 1.34 g. of magnesium and 300 cc. of ether. After evaporation of the ether, addition of 200 cc. of cold 20% sulfuric acid, and repeated extraction with ether, the intermediate sulfinic acid was extracted with aqueous sodium carbonate and oxidized with 6.0 g. of potassium permanganate in 300 cc. of water. After one hour the excess permanganate was destroyed with methanol, and the filtered solution was evaporated to dryness. A hot 95% ethanolic extract of the solid residue deposited 4.55 g. of the **sodium salt of 3,3-dimethylcyclohexylmethanesulfonic acid (VII)** in glistening plates.

Anal. Calcd. for $C_9H_{17}NaO_3S$: Na, 10.07. Found: Na, 10.38.

Treatment of 0.228 g. of the sodium salt in 5 cc. of water with 0.203 g. of S-benzylthiuronium chloride in 3 cc. of water gave a precipitate from which pure **S-benzylthiuronium 3,3-dimethylcyclohexylmethanesulfonate** (0.29 g.), m. p. 181–181.5°, was obtained after two crystallizations from methanol.

Anal. Calcd. for $C_{17}H_{28}N_2O_3S_2$: C, 54.81; H, 7.58. Found: C, 54.86; H, 7.43.

On cooling a solution of 0.37 g. of benzidine, 0.46 g. of VII sodium salt, and 0.2 cc. of concentrated hydrochloric acid, a mixture of salts precipitated which was separated by repeated crystallization from methanol into benzidine hydrochloride and the **benzidine salt of 3,3-dimethylcyclohexylmethanesulfonic acid,** m. p. 299–303° (dec.).

5,5-Dimethyldihydroresorcinol-2-sulfonic Acid (XVII).—A few minutes after 20.5 cc. of 5% oleum had been added to a cooled suspension of 56 g. of powdered dimethyldihydroresorcinol in 50 cc. of acetic anhydride and 300 cc. of ether, the mixture became almost solid. After being stirred for an hour, the precipitate was filtered and separated by fractional crystallization from ethyl acetate and from acetonitrile into 16 g. of recovered dimethyldihydroresorcinol and 49 g. of 5,5-dimethyldihydroresorcinol-2-sulfonic acid (XVII), m. p. 119–121°.

(33) With variations in solvent and catalyst, the hydrogenation has been effected by Zelinsky, Packendorf and Chochlowa [*Ber.,* **68**, 98 (1935)], Wibaut and Gitsels [*Rec. trav. chim.,* **60**, 577 (1941)], Chavanne, Miller and Cornet[18] and Henshall [*J. Chem. Soc. Ind.,* **62**, 127 (1943)].

(34) Auwers and Lange, *Ann.,* **401**, 324 (1913).

(35) Reid, Ruhoff and Burnett, "Organic Syntheses," John Wiley and Sons, New York, N. Y., 1943, Coll. Vol. II, p. 246.

(36) Gilman and Furry, THIS JOURNAL, **50**, 1214 (1928).

(37) Lennartz, *Ber.,* **76**, 248 (1943).

Anal. Calcd. for $C_8H_{12}SO_5$: C, 43.63; H, 5.49. Found: C, 43.64; H, 5.48.

Oxidation of XVII with aqueous potassium permanganate or with nitric acid gave β,β-dimethylglutaric acid, m. p. 98–99° (variously reported,[38] 100° to 104°); neutral equivalent: calcd., 80.1; found, 79.2. The β,β-dimethylglutaric acid was identified further by conversion to the anil, N-phenyl-β,β-dimethylglutarimide, of m. p. 156–157°; reported,[39] 157°.

S-Benzylthiuronium 5,5-dimethyldihydroresorcinol-2-sulfonate, at first quite soluble in methanol, changed on scratching to a much less soluble form, m. p. 157.5–158.5°.

Anal. Calcd. for $C_{16}H_{22}N_2S_2O_5$: C, 49.72; H, 5.74. Found: C, 49.41; H, 5.90.

The **pyridinium 5,5-dimethyldihydroresorcinol-2-sulfonate**, formed in good yield from the components in acetonitrile, crystallizes as large colorless prisms, m. p. 141–141.5°.

4,5-Dimethylresorcinol (XVIII).—A solution of 44.0 g. of XVII in 100 cc. of acetic anhydride was refluxed for four hours, the initial evolution of sulfur dioxide being copious, and then evaporated to dryness *in vacuo*. The residue was refluxed two hours with aqueous (200 cc.) sodium hydroxide (80 g.). An ethereal extract of the cooled, acidified solution was concentrated to a residue, crystallization of which from benzene gave 6.70 g. (2.13 g. from second crop) of orange crystals. Sublimation and recrystallization from benzene gave pure colorless XVIII, m. p. 135.5–136° (reported,[40] m. p. 133–134.5° and 134–135°).

Anal. Calcd. for $C_8H_{10}O_2$: C, 69.54; H, 7.30. Found: C, 69.45; H, 7.30.

The reaction of XVIII with benzoyl chloride in the presence of sodium carbonate gave the sodium hydroxide-soluble, heptane-crystallizable *o*-xylorcinol monobenzoate, m. p. 121–121.5°.

(38) Beilstein, "Handbuch der organische Chemie," Julius Springer, Berlin, 1920, Hauptwerke, 4th ed., Vol. II, p. 684.

(39) Perkin, *J. Chem. Soc.*, **69**, 1457 (1896).

(40) Backer and Strating, *Rec. trav. chim.*, **62**, 66 (1943); Karrer and Schick, *Helv. Chim. Acta*, **26**, 800 (1943).

Anal. Calcd. for $C_{15}H_{14}O_3$: C, 74.36; H, 5.82. Found: C, 74.55; H, 5.71.

When, instead of sodium carbonate, 2 N sodium hydroxide (15 cc. at first and 15 cc. more in three portions) and benzoyl chloride (2.32 cc. at first and then 2.32 cc. in three portions) reacted with XVIII (1.38 g.), an ethereal extract was obtained which after washing with alkali and water and evaporating yielded a crude neutral oil. On crystallization from 5 cc. of ethanol, 3.18 g. (92%) of *o*-xylorcinol dibenzoate was obtained. Recrystallization from ethanol, sublimation, and recrystallization gave pure material, m. p. 102–103° (reported,[41] m. p. 100–102°).

Anal. Calcd. for $C_{22}H_{18}O_4$: C, 76.28; H, 5.24. Found: C, 76.34; H, 5.52.

Summary

A novel oxidative rearrangement of isophorone (IV) to 3,4,5-trimethylphenol (II) and of dihydroisophorone (I) to II and 2,3,5-trimethylphenol (III) by treatment with sulfur trioxide–sulfuric acid plausibly involves sulfonic acid intermediates, of which isophorone-4-sulfonic acid (V) and isophorone-7-sulfonic acid (VI) have been prepared and rearranged under related conditions. The structure of VI has been proved by the synthesis of its hydrogenation product. A mechanism for the rearrangement and aromatization of the sulfonic acids involving a new method of forming carbonium ions is proposed. 4,5-Dimethylresorcinol (XVIII) has been prepared from dimethyldihydroresorcinol by rearrangement of the intermediate 5,5-dimethyldihydroresorcinol-2-sulfonic acid (XVII).

(41) Simon, *Ann.*, **329**, 306 (1903).

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[Contribution from the Chemical Laboratory, Harvard University]

"α"-Spinasterol

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"α"-Spinasterol[1] is a doubly unsaturated sterol found by Larsen and Heyl[2] to yield a hydrogenation-resistant dihydride that could be isomerized with acid to a Δ^{14}-stenol capable of being hydrogenated to stigmastanol. Fernholz and Ruigh[3] established that the more readily hydrogenable double bond is at the 22,23-position in the side chain, and by hydrogenation of 7-dehydrostigmasterol (I) with palladium catalyst they prepared the $\Delta^{8(14)}$-stenol III and found it identical with the hydrogenation-resistant dihydride from "α"-spinasterol. Fernholz and Ruigh reasoned that the nuclear double bond of "α"-spinasterol is also at the 8,14-position on the basis of their observation that no bond migration occurred when

a solution of "α"-spinasterol was shaken with platinum catalyst in the absence of hydrogen (which would attack the side chain). Stavely and Bollenback,[4] however, showed that this evidence is not valid because the characteristic migrations of double bonds from C_7-C_8 or C_8-C_9 to C_8-C_{14} occur only if the catalyst is saturated with hydrogen, an observation confirmed by Barton and Cox.[5] Stavely and Bollenback found that "α"-spinasterol is converted by chromic acid oxidation of the acetate into products analogous to those derived from "α"-dihydroergosterol, and since the latter compound was at the time thought to contain an 8,9-double bond they concluded that "α"-spinasterol is similarly constituted. At about the same time, however, Wieland and

(1) Hart and Heyl, *J. Biol. Chem.*, **95**, 311 (1932); Simpson, *J. Chem. Soc.*, 730 (1937); Dam and co-workers, *Helv. Chim. Acta*, **22**, 313 (1939); Fernholz and M. L. Moore, This Journal, **61**, 2467 (1939).

(2) Larsen and Heyl, *ibid.*, **56**, 2663 (1934).

(3) Fernholz and Ruigh, *ibid.*, **67**, 2341 (1945).

(4) Stavely and Bollenback, *ibid.*, **65**, 1600 (1943).

(5) Barton and Cox, *J. Chem. Soc.*, 1354 (1948); we are greatly indebted to Dr. D. H. R. Barton for kindly sending us a copy of the manuscript.