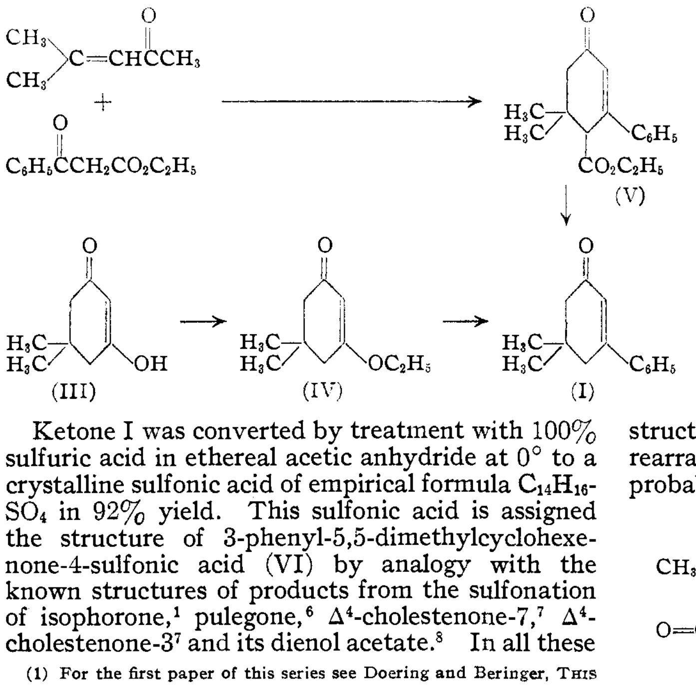
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE POLYTECHNIC INSTITUTE OF BROOKLYN]

The Aromatization and Rearrangement of Cyclic Ketones. II. 3-Phenyl-5,5-dimethylcyclohexenone[1,2]

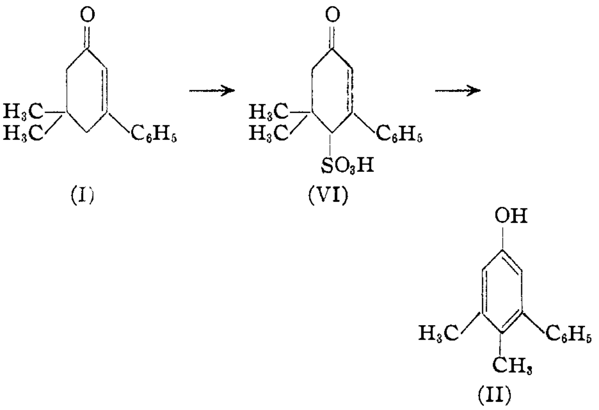
BY MARSHALL BERINGER AND IRVING KUNTZ[3]

A novel method recently developed by Doering and Beringer[1] for the aromatization and rearrangement of cyclohexenones consists in their conversion to cyclohexenonesulfonic acids with sulfuric acid in cold ethereal acetic anhydride and their subsequent decomposition to phenols with hot acetic anhydride. The present paper reports a new synthesis of 3-phenyl-5,5-dimethylcyclohexenone (I) and its conversion to 3-phenyl-4,5-dimethylphenol (II), the structure of which is confirmed by independent synthesis.

One sequence by which the ketone I was successfully prepared was that of Woods[4]: conversion of dimedone (III) to 3-ethoxy-5,5-dimethylcyclohexenone (IV), which on treatment with phenylmagnesium bromide gave 3-phenyl-5,5-dimethylcyclohexenone (I). In a second method,[5] mesityl oxide was condensed with ethyl benzoylacetate to give 3-phenyl-4-carbethoxy-5,5-dimethylcyclohexenone (V), which was hydrolyzed and decarboxylated in about 42% over-all yield from ethyl benzoylacetate to ketone I identical to that from the procedure of Woods.[4]

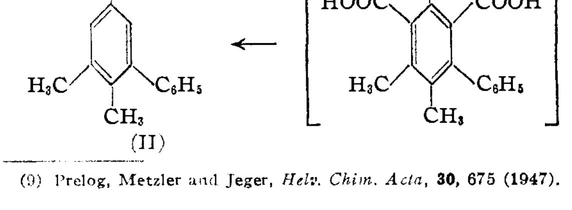


Ketone I was converted by treatment with 100% sulfuric acid in ethereal acetic anhydride at 0° to a crystalline sulfonic acid of empirical formula $C_{14}H_{16}SO_4$ in 92% yield. This sulfonic acid is assigned the structure of 3-phenyl-5,5-dimethylcyclohexenone-4-sulfonic acid (VI) by analogy with the known structures of products from the sulfonation of isophorone,[1] pulegone,[6] Δ^4-cholestenone-7,[7] Δ^4-cholestenone-3[7] and its dienol acetate.[8] In all these cases the sulfonic acid group becomes attached to the γ-carbon of the α,β-unsaturated ketone, presumably by electrophilic attack on the dienol or dienol acetate.[1,8]



Refluxing the sulfonic acid (VI) with acetic anhydride and hydrolysis of the crude product with hydrochloric acid gave in 60% yield a phenol of empirical formula $C_{14}H_{14}O$, which was characterized by formation of an α-naphthylurethan, a *p*-nitrobenzoate and a dibromo derivative. That this phenol has the structure of 3-phenyl-4,5-dimethylphenol (2,3-dimethyl-5-hydroxybiphenyl, II) is shown by its independent synthesis according to the general procedure of Prelog, Metzler and Jeger.[9]

Ethyl acetonedicarboxylate was condensed with 3-benzoylbutanone-2 to give diester VII (ethyl 3-phenyl-4,5-dimethylphenol-2,6-dicarboxylate) in 90% yield. Hydrolysis of the diester and decarboxylation of the free acid in quinoline gave the desired 3-phenyl-4,5-dimethylphenol (II) in 23% yield. The structural identity of the phenols prepared by rearrangement and by decarboxylation is highly probable as shown by the fact that they had the



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(1) For the first paper of this series see Doering and Beringer, THIS JOURNAL, **71**, 2221 (1949).

(2) This paper is based on a thesis submitted by Irving Kuntz in partial fulfillment of the requirements for the degree of Master of Science in Chemistry in the Graduate School of the Polytechnic Institute of Brooklyn in May, 1950.

(3) Research Laboratory, Sprague Electric Company, North Adams, Mass.

(4) Woods, THIS JOURNAL, **69**, 2549 (1947).

(5) *Cf.* the preparation of isophorone by Knoevenagel and Fisher, *Ann.*, **297**, 185 (1897).

(6) Treibs, *Ber.*, **70**, 85 (1937).

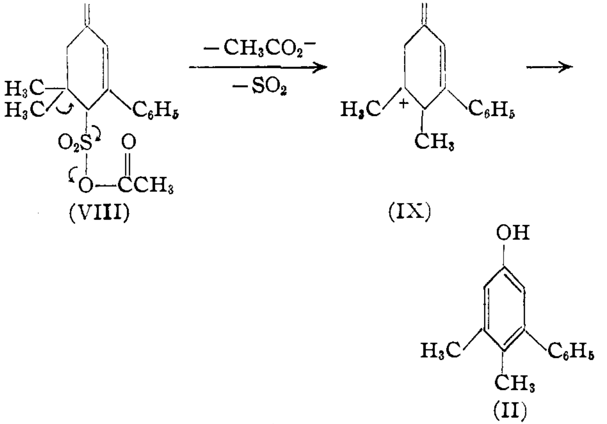
(7) Windaus and Kuhr, *Ann.*, **532**, 52 (1937); Windaus and Mielke, *ibid.*, **536**, 116 (1938).

(8) Kuhr, *Ber.*, **72**, 929 (1939).

(9) Prelog, Metzler and Jeger, *Helv. Chim. Acta*, **30**, 675 (1947).

same melting point and mixed melting point (as did also their α-naphthylurethans) and by the superposability of their ultraviolet absorption spectra.

Application of the reaction scheme tentatively proposed for 4-isophoronesulfonic acid[1] to the conversion of VI to II suggests the possible formation of an anhydride (VIII) between the sulfonic acid and acetic acid. Decomposition of this mixed anhydride at an elevated temperature to give acetate ion and sulfur dioxide would leave a secondary carbonium with an electron deficiency at the 4-position. Migration of one of the *gem* methyl groups to the 4-position would leave a new tertiary carbonium ion (IX), which by loss of a proton and a prototropic shift would give the observed phenol. The possibility that the decomposition of the mixed anhydride occurs in concert with the migration of a methyl group to give directly the tertiary carbonium ion is not excluded and seems attractive.



(VIII) (IX) (II)

Experimental[10,11]

Synthesis of 3-Phenyl-5,5-dimethylcyclohexenone (I). (a) **From Dimedone (III).**—According to the procedure of Woods[12] a mixture of 100 g. of dimedone,[15] 500 cc. of absolute alcohol, and 10 cc. of concentrated sulfuric acid was refluxed for 6 hours, concentrated by distillation of 200 cc. of alcohol, then poured into a cold *solution* of 100 g. of potassium carbonate dihydrate in 300 cc. of a water–ice mixture. After removal by filtration and pressing between filter papers, the wet product was dried *in vacuo*, then crystallized from petroleum ether (28–39°) to give 89 g. of **3-ethoxy-5,5-dimethylcyclohexenone (IV)** of m.p. 58.5–59.5°. Distilled material (70–72° (0.3 mm.)) had a m.p. of 60–61°; reported m.p.'s 57–58°,[14] 58–60°[13] and 60°.[4]

Treatment of IV with excess phenylmagnesium bromide according to the procedure of Woods[4] gave in 66% yield **3-phenyl-5,5-dimethylcyclohexenone (I)** of m.p. 53.8–54.8° (reported[4] m.p. 54–54.5°); oxime, m.p. 160–161.3° (reported[4] 156–157°); **2,4-dinitrophenylhydrazone**, m.p. 171.5–172° (reported[4] 171–172°).

(b) **From Ethyl Benzoylacetate.**—A solution of 23.5 g. of sodium in 400 cc. of absolute ethanol, 192 g. of ethyl benzoylacetate and 100 g. of mesityl oxide (freshly distilled) was refluxed under nitrogen for 6 hours and then stood overnight. After addition of 500 cc. of 10% sulfuric acid and refluxing for 8 hours, 460 cc. of ethanol–water was removed by distillation. The oily layer was combined with the ether extracts of the water layer, washed with 5% sodium bicarbonate solution[16] and with water, and dried with anhydrous magnesium sulfate. After removal of the ether, distillation at reduced pressure gave a forerun of acetophenone[17] (48 g., 50%) and 119 g. (44%) of **3-phenyl-4-carbethoxy-5,5-dimethylcyclohexenone (V)**, a yellow oil, b.p. 152–154° (0.7 mm.); n^{25}D 1.5553. *Anal.* Calcd. for $C_{17}H_{20}O_3$: C, 74.98; H, 7.40. Found: C, 75.18; H, 7.75.

The keto-ester V gave by the usual procedure a crystalline **2,4-dinitrophenylhydrazone**, red needles from ethanol, m.p. 165–166°. *Anal.* Calcd. for $C_{23}H_{24}N_4O_6$: N, 12.38. Found: N, 12.66.

Two grams of the keto-ester V in 30 cc. of 15% ethanolic potassium hydroxide was stirred under reflux for 9 hours. The resulting solution was cooled, poured into water and neutralized. The yellow precipitate was filtered and dried *in vacuo* to give 1.42 g. (95%) of crude **3-phenyl-5,5-dimethylcyclohexenone (I)**, m.p. 47–50°. Crystallization from petroleum ether (28–39°) with charcoal treatment gave colorless needles, m.p. 53.6–54.6°, and a mixed m.p. with 3-phenyl-5,5-dimethylcyclohexenone prepared by the Grignard reaction showed no depression.

Synthesis of 3-Phenyl-4,5-dimethylphenol (II). (a) **By Aromatization of 3-Phenyl-5,5-dimethylcyclohexenone (I).**—To a solution of 28.3 g. of I and 14.5 cc. of acetic anhydride in 120 cc. of anhydrous ether cooled in a bath of cracked ice–concd. hydrochloric acid was added slowly with stirring 7.5 cc. of 100% sulfuric acid. Shortly after the first addition of acid the deposition of a yellow solid commenced. After refrigeration of the mixture overnight the sulfonic acid was filtered by suction on a sintered glass funnel, washed quickly with cold dry ether and dried *in vacuo*. With additional product from concentration of the mother liquor and the ether washings the total yield of crude **3-phenyl-5,5-dimethylcyclohexenone-4-sulfonic acid (VI)** was 35.2 g. (92%). Repeated crystallization of a small sample from dry acetonitrile gave yellow needles, which after drying at 100° *in vacuo* for an hour had a m.p. 170–171.2° (into bath at 150° with temperature rise 2° a minute). The sulfonic acid had a neutralization equivalent of 277; calcd., 280.3. *Anal.* Calcd. for $C_{14}H_{16}SO_4$: C, 59.98; H, 5.75; S, 11.44. Found: C, 60.30; H, 5.55; S, 11.29.

The dried crude sulfonic acid (VI, 28.8 g.) was added to 120 cc. of acetic anhydride (solution exothermic) and heated under reflux for 4 hours. Removal of the acetic anhydride and hydrolysis of the residue with hot hydrochloric acid gave a tarry mixture which was extracted portionwise with 500 cc. of benzene. After charcoal treatment of the extract the benzene was replaced with heptane (another charcoal treatment), and from the cooled solution there was obtained 14.1 g. (69%) of fine needles of **3-phenyl-4,5-dimethylphenol (II)**, m.p. 105–106°. Several further crystallizations from heptane and drying *in vacuo* gave colorless needles of m.p. 107.8–108.2°.

Anal. Calcd. for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 84.64; H, 6.98.

The absorption spectrum of II in 95% ethanol was taken with a Beckman model DU quartz spectrophotometer with a one-cm. cell. The absorption spectra of this phenol and of the phenol prepared by condensation and decarboxylation as discussed below were superposable ($\lambda_{max.}$ 2880 Å., log ϵ 3.45; $\lambda_{min.}$ 2685 Å., log ϵ 3.13) and were qualitatively similar to that reported for 3-hydroxybiphenyl.[9]

A mixture of one gram each of II and α-naphthyl isocyanate and three drops of anhydrous pyridine was warmed to 100° for five minutes, cooled and scratched to give a solid. The solid was transferred to the cup of a rubber extractor and extracted with 50 cc. of petroleum ether (90–100°) for one-half hour. From the cooled solution there was obtained 1.3 g. (70%) of fine needles of the α-naphthylurethan of 3-phenyl-4,5-dimethylphenol, m.p. 170–170.8°. Recrystallization raised the m.p. to 171–172°. *Anal.* Calcd. for $C_{25}H_{21}O_2N$: C, 81.71; H, 5.76. Found: C, 81.83; H, 6.00.

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[10] Boiling points are not corrected. Melting points were taken with a modified Hershberg apparatus with calibrated Anschütz thermometers.

[11] Analyses were performed by H. Biletch, K. Ritter, F. Schwarzkopf and the Clark Microanalytical Laboratory.

[12] We gratefully acknowledge the private communication of Dr. G. F. Woods, as previously described procedures [4,13] gave in our hands unsatisfactory yields of the enol ether. Recently[14] *p*-toluenesulfonic acid has been used as a catalyst in the etherification.

[13] Crossley and Renouf, *J. Chem. Soc.*, **93**, 640 (1908).

[14] Frank and Hall, THIS JOURNAL, **72**, 1645 (1950).

[15] Blatt, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 200.

[16] Acidification gave benzoic acid, as determined by m. p. and mixed m. p. with an authentic sample.

[17] Identified as the 2,4-dinitrophenylhydrazone, m.p. 240–242° (uncor.), with no depression on mixed m.p. with an authentic sample. *Anal.* Calcd. for $C_{14}H_{12}N_4O_4$: N, 18.66. Found: N, 18.46.

From the reaction of 1.5 g. of II with 1.0 g. of *p*-nitrobenzoyl chloride in 6 cc. of anhydrous pyridine there was obtained by the usual procedures 2.1 g. (80%) of **3-phenyl-4,5-dimethylphenyl *p*-nitrobenzoate**, needles from ethanol, m.p. 97.2–98°. *Anal.* Calcd. for $C_{21}H_{17}O_4N$: C, 72.61; H, 4.93. Found: C, 72.93; H, 4.79.

Bromination of II in ethanol gave by the usual procedures **2,6-dibromo-3-phenyl-4,5-dimethylphenol** as colorless needles from ethanol–water, m.p. 116–116.5°. *Anal.* Calcd. for $C_{14}H_{12}Br_2O$: C, 47.22; H, 3.40; Br, 44.89. Found: C, 47.38; H, 3.33; Br, 44.65.

(b) **By Condensation and Decarboxylation.**—Acetophenone was condensed with ethyl acetate by the action of sodium in ether to give in 50% yield benzoylacetone of m.p. 57–58.8°; reported[18] m.p. 59–60°. Benzoylacetone was methylated in 76% yield to 3-benzoylbutanone-2, b.p. 139–140° at 12 mm., $n^{22}\text{D}$ 1.5312, by the general procedure of Sprague, Beckham and Adkins[11]; reported[19] b.p. 150–152° at 20 mm.

A solution of 2.83 g. of sodium in 40 cc. of absolute ethanol, 21.27 g. of 3-benzoylbutanone-2 and 24.26 g. of ethyl acetonedicarboxylate stood at room temperature for 2 days, after which the ethanol was removed under reduced pressure. The residue was poured into water, acidified and extracted with ether. The combined ether extracts were washed with 5% sodium bicarbonate solution, then with water until the washings were neutral to litmus, and finally dried over anhydrous magnesium sulfate. After removal of the ether, distillation of the residue gave a forerun of unchanged reactants and a very pale yellow oil, b.p. 181–183° at 0.08 mm., which in the receiver set to a colorless solid of m.p. 84–86°. The solid (7.99 g., 19.2%) was recrystallized from petroleum ether (30–60°) or ethanol and sublimed *in vacuo* to give colorless crystals of diester VII (**ethyl 3-phenyl-4,5-dimethylphenol-2,6-dicarboxylate**) of m.p. 88.4–89.6°.

Anal. Calcd. for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 70.41; H, 6.41.

Diester VII (2.5 g.) was saponified by refluxing with 30 cc. of 15% methanolic potassium hydroxide for 12 hours. By the usual procedures there was obtained a dry ether solution of a fraction insoluble in water but soluble in 5% sodium bicarbonate solution. The residue from removal of the ether was decarboxylated by heating at 190–210° in 5 cc. of quinoline until carbon dioxide evolution ceased. The cooled reaction mixture was taken up in ether, washed thoroughly with 5% hydrochloric acid and with water, and dried over anhydrous magnesium sulfate. The residue from removal of the ether was crystallized twice from heptane, then sublimed to give 0.34 g. (23.5%) of colorless crystals of **3-phenyl-4,5-dimethylphenol** (II), of m.p. 107.8–108.2°.

Anal. Calcd. for $C_{14}H_{14}O$: C, 84.81; H, 7.12. Found: C, 84.89; H, 7.09.

This phenol on mixing with the phenol from the sulfonic acid rearrangement gave no depression of the m.p.

The ultraviolet absorption spectrum of this phenol was superposable on that of the phenol from rearrangement of the sulfonic acid (see above).

An α-naphthylurethan prepared as described above melted at 171.3–172.5° and showed no depression of m.p. on mixing with the previously described sample prepared from the phenol obtained by rearrangement of VI.

Summary

A previous synthesis of 3-phenyl-5,5-dimethylcyclohexenone has been confirmed and a new synthesis developed. The conversion of this ketone by way of its sulfonic acid to 3-phenyl-4,5-dimethylphenol, the structure of which is proved by its independent synthesis, exemplifies the synthetic possibilities of a recently reported method of aromatization and rearrangement.

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[18] Sprague, Beckham and Adkins, THIS JOURNAL, **56**, 2665 (1934).

[19] Dieckmann, *Ber.*, **45**, 2685 (1912).

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Effect of Structure on the Fiber Properties of Linear Polymers. I. The Orientation of Side Chains[1]

BY JAMES H. BREWSTER[2]

It would be expected that the size, distribution and steric orientation of side-chains attached to the backbone of a linear polymer would affect those properties of the polymer which are a function of its crystallinity, *i.e.*, melting point, solubility and especially ability to form oriented fibers. The present study concerns the effect of the stereochemical configuration of the side chains on polymer properties.

Side chains on polymer molecules appear to interfere with the formation of strong oriented fibers.[3] There is some evidence that polymers whose side chains are distributed according to a regular and recurrent pattern are more crystalline than isomeric polymers having irregularly distributed side chains. Polymers with regularly spaced side chains may be prepared from symmetrical bifunctional reactants or from pure unsymmetrical monomers which must condense in a head to tail fashion (*e.g.*, ω-amino acids).

A polymer having *n* unpaired side chains attached to the polymer chain has *n* asymmetric carbon atoms. If the steric configuration of these asymmetric atoms is not uniform (as in polymers made from symmetrical bifunctional reactants or from racemic α-amino acids), the number of molecular species theoretically possible is 2^n (assuming that all polymer chains are of the same length). The disorder produced by lack of stereochemical uniformity of side chain orientation might well interfere with polymer crystallinity and cause modifications in polymer properties. That such is, indeed, the case is indicated by the work of Astbury and co-workers,[4] who noted that polymers of *dl*-alanine are water soluble, while those of *l*-alanine are not. It is further suggestive that silk, wool and other proteins[5] form strong oriented fibers despite the fact that numerous side chains are attached to the polypeptide backbone of a protein. This may well be due, at least in part, to the uniform steric configuration of the naturally-occurring amino acids.[6]

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[1] This work was supported by a grant from the Samuel S. Fels Fund.

[2] Chemistry Department, Purdue University, Lafayette, Ind.

[3] Hill and Walker, *J. Polymer Sci.*, **3**, 609 (1948).

[4] Astbury, Dalgleish, Darmon and Sutherland, *Nature*, **162**, 596 (1948).

[5] Lundgren, in "Advances in Protein Chemistry," V. Interscience Publishers, New York, N. Y., 1949, p. 305.

[6] Neuberger, *ibid.*, IV, 1948, p. 297.