

An extensive study of copper-chromium oxide catalysts has failed to reveal any modification of the catalyst which would bring about the production of more alcohol and less hydrocarbon in the hydrogenation of ethyl phenylacetate, than does the standard type of catalyst.

MADISON, WISCONSIN

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The Jacobsen Reaction. III. The Monobromo Derivatives of the Three Tetramethylbenzenes¹

BY LEE IRVIN SMITH AND CLARENCE L. MOYLE

In the previous papers of this series² it has been shown that when the polymethylbenzenes containing four or five methyl groups are allowed to stand in contact with concd. sulfuric acid, they first sulfonate, and then the sulfonic acids rearrange. These rearrangements are of at least two types: the first, shown by pentamethylbenzene, involves the migration of a methyl group from one molecule to another, while the second, shown by the tetramethylbenzenes, is merely a rearrangement of the methyl groups within the molecule. It was therefore of interest to investigate the monobromo derivatives of the tetramethylbenzenes, because these are pentasubstituted benzenes in which the substituents differ in nature as well as in position, and, consequently, if they were to rearrange in a manner similar to pentamethylbenzene, either a bromine atom or a methyl group could migrate and so lead to different products. There are several references in the literature to migrations of halogens among the benzene derivatives, but only two concern the bromotetramethylbenzenes. Jacobsen³ reported that a mixture of bromodurene and concd. sulfuric acid gradually became dark and evolved considerable sulfur dioxide, and from this mixture he isolated and identified five products: *viz.*, dibromodurene, prehnitene sulfonic acid, two isomeric pseudocumene sulfonic acids, and small amounts of hexamethylbenzene. In addition to these five products, Jacobsen reported a small amount of brown amorphous material, and stated that no brominated sulfonic acids were formed. Tohl⁴ investigated the action of sulfuric acid on bromoprehnitene, and reported dibromoprehnitene and prehnitene sulfonic acid as the products.

In the present work, it has been found that bromodurene, in the presence of sulfuric acid under various conditions of time, temperature and strength

(1) Abstracted from a thesis by Clarence L. Moyle, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the degree of Master of Science, June, 1932. Presented at the 84th meeting of the American Chemical Society, Denver, Colo., August, 1932. Paper VIII on the Polymethylbenzenes; VII, *THIS JOURNAL*, **54**, 1614 (1932).

(2) Smith and Lux, *ibid.*, **51**, 2994 (1929); Smith and Cass, *ibid.*, **54**, 1614 (1932).

(3) Jacobsen, *Ber.*, **20**, 2837 (1887).

(4) Tohl, *ibid.*, **25**, 1527 (1892).

of acid, rearranged to dibromodurene and prehnitene sulfonic acid. Based upon the equation: $2\text{C}_6\text{H}(\text{CH}_3)_4\text{Br} + \text{H}_2\text{SO}_4 \longrightarrow \text{C}_6\text{Br}_2(\text{CH}_3)_4 + \text{C}_6\text{H}(\text{CH}_3)_4\text{SO}_3\text{H} + \text{H}_2\text{O}$, the yields of dibromodurene were from 92 to 99%. The highest yield of prehnitene sulfonic acid obtained was 25%, but the reaction mixture evolved much sulfur dioxide, and 25 to 30% of the product consisted of brown or black amorphous materials. In no case was any hexamethylbenzene detected, and only traces of pseudocumene sulfonic acids were obtained. Bromoisodurene similarly gave dibromoisodurene (80% yield), prehnitene sulfonic acid (35–40% yield), and much sulfur dioxide, the dark amorphous material in this case amounting to 10–20% of the total product. No hexamethylbenzene was found, and only a trace of pseudocumene. Bromoprehnitene rearranged quickly and easily to dibromoprehnitene (99% yield) and prehnitene sulfonic acid (81% yield), the reaction requiring only about fifteen minutes, and giving rise to much less sulfur dioxide and amorphous materials than the other two bromo compounds.

These results show that, in the case of the bromotetramethylbenzenes, the bromine migrates in preference to a methyl group. Since the dibromo compound obtained is always the one corresponding to the monobromo compound used as the starting material, it is probable that the first step in the rearrangement consists of the formation of the dibromo compound and the corresponding tetramethylbenzene sulfonic acid. The latter then rearranges to the stable system prehnitene, accompanied by very small amounts of pseudocumene and hexamethylbenzene. In all these rearrangements, the first step is a sulfonation, for the bromo compounds themselves are stable in contact with phosphorus pentoxide at 80°, or when kept in a desiccator over sulfuric acid, while the sulfonic acids rearrange under these same conditions.

The gases evolved during the reactions were determined using the method already described,^{2b} and the results were practically the same as those obtained in the case of the hydrocarbons. The gas is practically entirely sulfur dioxide, with only a little carbon dioxide, and the total amount of gas is about 0.38 mole per mole of bromo compound. There is no visual evidence of free bromine, and no bromide ions are present in the absorption tube. At room temperature the rate at which this gas is evolved from a 5-g. sample is very slow during the first fifteen to twenty hours (sulfonation), then fairly constant for about one hundred-sixty hours, after which it was very slow. For a 10-g. sample, the evolution of sulfur dioxide continues for about 360 hours, and then falls off. A great deal of this sulfur dioxide may come from secondary reactions, for the rearrangement of the bromo compounds to the dibromo compounds is complete at room temperature in one or two days, while the evolution of sulfur dioxide continues for two or three weeks, and it is significant that while the brown

amorphous by-product does not contain sulfur, yet, when placed in contact with sulfuric acid, much sulfur dioxide is evolved.

The velocity and direction of the reaction of the bromo compounds with sulfuric acid is affected to a great degree by the temperature, for there appear to be upper and lower limits, outside of which the sulfonic acid merely hydrolyzes to the hydrocarbon, no rearrangements taking place. Thus bromodurene and concd. sulfuric acid gave little or no reaction in twenty-five hours at 10–15°, while at 25° complete rearrangement occurred. Using bromodurene sulfonic acid and sulfuric acid at 10–15°, about 85% of the sulfonic acid was hydrolyzed to bromodurene in twenty-five hours, while at 25–30° the *rearrangement* was complete in the same time; at 60–80°, the *rearrangement* required about thirty minutes; while at higher temperatures (130–150°), hydrolysis again became the chief reaction. The most favorable temperatures for the rearrangement are from 25 to 30°, for although somewhat higher temperatures increase the speed of the rearrangement, they also increase the amounts of amorphous by-products formed.

Experimental Part

The Jacobsen Reaction.—One experiment will be described, and the results of others given in tabular form. Bromodurene (0.1 mole, m. p. 60.5°) was mixed with eight times its weight of concd. sulfuric acid in a loosely stoppered 250-cc. flask, and set aside at room temperature (25–30°) with occasional shaking. After one hour, the mixture became pink, after twelve hours it became brown, and then slowly changed to dark brown-black. During the first twelve hours, small amounts of sulfur dioxide were evolved, which increased in rate, reaching a maximum and fairly constant rate after the second day, and continuing so for 5 days, after which the sulfur dioxide evolved decreased very much. At the end of ten days the mixture was poured onto 300 g. of ice, the lumps broken up, and then filtered. The insoluble material was dried on a porous plate and extracted thoroughly with petroleum ether, followed by chloroform. A black, insoluble carbon-like residue remained; wt., 0.6 g. The chloroform extractions were evaporated, yielding 4.8 g. of a brown, amorphous powder. The petroleum ether extractions were decolorized with norite and set aside to crystallize, yielding 13.4 g. (91.8%) dibromodurene, white needles, m. p. crude, 184–191°. This contained a little monobromodurene which was removed by repeated crystallization, after which the dibromo compound weighed 11.2 g. and melted at 200°. The dibromo compound was identified by its melting point and mixed melting point; by reducing it with hydriodic acid and red phosphorus at 225°, it gave a 90% yield of durene, m. p. 79.5–80.0°. No traces of hexamethylbenzene were detected in the water-insoluble chloroform-soluble products.

The aqueous filtrate, containing the water-soluble products of the reaction, was decolorized by boiling for five minutes with 2 g. of norite. It was then filtered and the filtrate evaporated until the temperature rose to 110°. On cooling to 0° there resulted 3.2 g. of a sulfonic acid (m. p. 89–92°) which after three crystallizations melted at 101°. It was prehnitene sulfonic acid (m. p. 103°) identified by mixed m. p., and by conversion to the sulfonamide melting at 186° (m. p., and mixed m. p.).

The filtrate from the sulfonic acid was hydrolyzed by passing steam through it at 145°. About 0.2 cc. of oil came over into the distillate. This oil gave a nitro compound melting at 182.5–183.5° which was identified as trinitropseudocumene by its mixed melting point with an authentic specimen (m. p. 184°).

TABLE I
 PRODUCTS OF THE JACOBSEN REACTION UPON THE BROMOTETRAMETHYLBENZENES

Expt.	Subs.	Wt., g.	Time	Temp., °C.	Dibromo cpd., g.	Prehnitene sulfonic acid, g.	Pseudo-cumene from hydrolysis of S. A. filtrates	Total amorphous materials, g.	Remarks
1	Bromodurene	21.3	10 days	25-30	13.4	3.2	0.2 cc.	5.4	
2	Bromodurene	5.0	7.5 days	25-30	3.8	0.1	None	1.6	
3	Bromodurene	10.0	16.5 days	25-30	6.6	.9	None	2.6	
4	Bromodurene	15.0	4 hours	80	9.3	.1	None	4.0	
5	Bromodurene ^a	10.0	5 minutes	75 ^b	6.1	.5	None	2.4	
6	Bromodurene ^c	10.0	100 days	25-30	6.8	None	None	2.5	
8	Bromodurene	5.0	5 hours	75	
10	Bromodurene sulfonic acid	5.0	1 day	30	1.5	0.3	..	1.2	
11	Bromodurene S. A. ^d	5.0	6 weeks	25-30	1.1	.1	..	0.8	
12	Bromoisodurene ^e	10.0	10 hours	25-30	5.5	2.1	..	1.0	
13	Bromoisodurene ^e	20.0	30 min.	60	8.3	3.6	0.1 cc.	3.7	5.6 g. recovered monobromo cpd.
15	Bromoprehnitene ^e	10.0	15 min.	25-30	3.4	2.4	..	0.1	5.0 g. recovered monobromo cpd.
16	Bromoprehnitene	10.0	15 min.	25-30	3.3	2.4	..	.2	4.8 g. recovered monobromo cpd.

^{a, b} With 20 cc. of a mixture of 2 parts of concd. sulfuric acid and 1 part of 60% fuming sulfuric acid. Started at room temp.; temp. rose to 75°. ^c Bromo compound dissolved in chloroform and shaken with sulfuric acid. All the bromodurene was recovered unchanged.

^d Merely stood in a desiccator over sulfuric acid for six weeks. ^e With 4 parts (by vol.) of a mixture consisting of 35 cc. of concd. sulfuric acid and 5 cc. of 60% fuming sulfuric acid.

Blank experiments on the monobromotetramethylbenzenes showed them to be perfectly stable in contact with phosphorus pentoxide or in desiccators *over* sulfuric acid. Similar experiments showed the dibromotetramethylbenzenes to be stable when *in contact* with sulfuric acid for two months; beyond a slight darkening, and evolution of a little sulfur dioxide, there was no change and 95% of the material was recovered pure.

In identifying the dibromo compounds, it was found that the mixed melting points with authentic specimens were of little use, because the depressions are so small that direct identification by this means becomes very uncertain. However, it was found that the dibromo compounds could be converted to the corresponding hydrocarbons in 90% yields by heating them to 225° with hydriodic acid and red phosphorus for a few hours. Durene was identified directly in this way, since it is a solid, while prehnitene and isodurene were identified by converting them to the dinitro compounds and comparing these with authentic specimens. While the two dinitro compounds melt fairly close together, all the possible binary mixtures of the three dinitro compounds show melting point depressions of 15° or more, against depressions of only about 2° for the mixtures of the dibromo compounds. These results are shown in Table II.

TABLE II

MIXED MELTING POINTS OF THE DIBROMO- AND DINITROTETRAMETHYLBENZENES	
Dibromo compounds	Dinitro compounds
Isodurene (199) + prehnitene (208), 198-201°	Isodurene (181) + prehnitene (176), 155-165°
Isodurene (199) + durene (200), 198-199°	Isodurene (181) + durene (206-207), 165-178°
Prehnitene (208) + durene (200), 203-204°	Prehnitene (176) + durene (206-207), 162-169°
	Isodurene (181) + trinitropseudocumene (184), 161-167°

Gaseous Products of the Reaction.—Experiments 2 and 3 were carried out in closed systems, sweeping a slow current of nitrogen through the apparatus and collecting the gaseous products in a suitable absorption train.² Experiment 2 was run for 180 hours, and experiment 3 for 360 hours. The weight of the gaseous products was very small during the first twenty-four hours, then it increased quite rapidly during the next 125 (experiment 2) or 250 hours (experiment 3), after which the hourly production of gas became very small again. The results are given in the table below.

TABLE III

RESULTS OF ANALYSES OF THE GASEOUS PRODUCTS					
Expt.	Total gas evolved (Gain in wt. of KOH bulb)	SO ₂ as sulfite	SO ₂ as sulfate	CO ₂	Mole ratio, bromo cpd. to av. SO ₂
2	0.5560	0.5284	0.5381	0.0261	0.356
3	1.1505	...	1.0920	.0599	.363

The liquid in the absorption bulbs contained no sulfides, and only faint traces of halides.

Preparation of Materials

Bromodurene.⁵—Durene (50 g.) was dissolved in carbon tetrachloride (100 g.) in a 500-cc. 3-necked flask provided with separatory funnel, stirrer and exit tube. A crystal of iodine was added, the flask cooled in an ice-bath and then a solution of 62.7 g. of

(5) Jacobsen, *Ber.*, **20**, 2837 (1887).

bromine (5% excess) in 60-cc. of carbon tetrachloride was slowly added. The flask was kept out of direct sunlight during the bromination. The bromine was added during one and one-half hours, after which the mixture was stirred at room temperature for one hour longer. The product was washed with 200 cc. of 5% sodium hydroxide, then thoroughly with water. The carbon tetrachloride was removed by distillation through a short column, the residue boiled for thirty minutes with a solution of 4 g. sodium in 100 cc. ethyl alcohol, and then allowed to stand overnight. Water (900 cc.) was added, the precipitated solid filtered and dried; wt. 77.5 g. (calcd. 79.5). It was purified by steam distilling it for five hours to remove small amounts of dibromo compound. The monobromo compound was removed from the distillate by filtration, and then crystallized from 95% ethyl alcohol. It was pure white, weighed 62.8 g., and melted at 60.5°.

Bromoprehnitene and Bromoisodurene.—The hydrocarbon (50 g.) was dissolved in glacial acetic acid (100 cc.) containing a crystal of iodine, and brominated with a solution of 62.7 g. of bromine in 62 cc. of acetic acid, using the same apparatus and conditions given above for bromodurene. The reaction product was poured into water at 0°, whereupon a solid separated out. The water was decanted off, and the solid washed thoroughly with alkali followed by water (all washings at 0°). The solid was crystallized from alcohol at -15° and was then fractionated through a short packed column. Bromoisodurene, b. p., 140–142° (22 mm.), n_D^{25} 1.5614, m. p. 7.5–8.5°; yield 34.8 g. from 25 g. of isodurene (calcd. 39.7 g.). Bromoprehnitene, b. p. 140–141° (30 mm.), n_D^{25} 1.5650, m. p. 29–30°; yield 59.8 g. from 50 g. of prehnitene (calcd. 79.4 g.).

Dibromo Compounds.—The hydrocarbon (10 g.) was dissolved in 30 cc. of glacial acetic acid, a crystal of iodine added, and then brominated, with stirring, by adding a solution of 25 g. of bromine in 20 cc. of acetic acid. The bromine was added during ten minutes, after which the reaction mixture stood for one hour. The resulting mass of liquid and solid was diluted with water, the liquid decanted, and the residual solid washed with alkali followed by water, after which it was filtered and dried. The solid obtained in this way was white and weighed 19–21 g. (calcd. 21.8). The dibromo compounds were purified by repeated crystallization from chloroform–alcohol, by dissolving them in hot chloroform, adding hot alcohol and boiling until crystallization began. The melting points are given in Table II.

Bromodurene Sulfonic Acid, $C_6Br(CH_3)_4SO_3H \cdot 1.5H_2O$.—Bromodurene (21.3 g.) was stirred for five minutes at 0° with 60 cc. of a mixture of 2 parts of concd. sulfuric acid and 1 part of 60% fuming sulfuric acid. The reaction mixture was poured onto 500 g. of ice and the resulting aqueous solution extracted once with chloroform. It was then cooled to 0° and 200 cc. of concd. sulfuric acid carefully added with stirring, keeping the temperature below 25°, but adding the acid as quickly as possible since the sulfonic acid is slowly hydrolyzed in contact with the mineral acid. The precipitated sulfonic acid was filtered through cloth, and was recrystallized twice from 20% hydrochloric acid. The dried acid weighed 16.7 g., m. p. 142–143° (dec.).

Anal. Calcd. for $C_6Br(CH_3)_4SO_3H$: Br, 25.0; S, 10.0. Found: Br, 24.8; S, 9.98. Water of hydration (loss in weight in vac. desiccator over $CaCl_2$ for twenty-four hours) 8.5%; calcd. for $1.5 H_2O$, 8.4%.

Bromodurene Sulfonyl Chloride.—The dried sodium sulfonate was treated with 1.5 times its weight of phosphorus pentachloride for one hour. The reaction mixture was treated with water, the solid filtered off and recrystallized twice from ether as white prisms, m. p. 185°.

Bromodurene Sulfonamide.—The sulfonyl chloride was heated with concd. ammonium hydroxide for fifteen minutes, the reaction mixture cooled and the solid filtered off and crystallized from alcohol; m. p. 194°.

Summary

1. The Jacobsen reaction on the bromotetramethylbenzenes consists in the migration of a bromine atom to give the corresponding dibromo compound and prehnitene sulfonic acid. The usual by-products of sulfur dioxide and a brown amorphous material are obtained.

2. The first step in the reaction is sulfonation, and the sulfonic acid is the rearranging molecule.

3. Whether the reaction consists of the rearrangement or merely hydrolysis of the sulfonic acid, depends on the temperature. At very low and very high temperatures, the main reaction is hydrolysis. The best temperature for the rearrangement is from 25 to 65°.

4. The dibromo compounds cannot be identified by their mixed melting points, as the depressions are only about 2°, but the dinitro compounds give depressions of 15° or more and the series dibromo compound, hydrocarbon, dinitro compound can be used as a method of identification.

5. The dibromo compounds do not rearrange in contact with sulfuric acid.

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Preparation of Substituted Vanillic Acids

BY L. CHAS. RAIFORD AND DWIGHT J. POTTER

Benzaldehyde¹ and anisaldehyde² are easily oxidized by air to the corresponding acids. *p*-Hydroxybenzaldehyde³ and protocatechuic aldehyde⁴ are more resistant and are not oxidized readily by potassium permanganate solution but require fusion with caustic potash to give the acids. Tiemann⁵ found that treatment of vanillin solutions with oxidizing agents caused hardly any change, or else complete decomposition, depending on conditions. Vogel⁶ prepared 5-nitrovanillic acid, and Brady and Dunn⁷ obtained the 5-bromo compound by hydrolysis with alkali of the corresponding nitriles which, in turn, had been obtained from the respective oximes. Bromovanillin could not be oxidized by acetic acid solution of chromic acid or by alkaline permanganate.

The recent syntheses in this Laboratory of all chlorine and bromine

- (1) Wöhler and Liebig, *Ann.*, **3**, 250 (1832).
- (2) Cahours, *ibid.*, **56**, 308 (1845).
- (3) Bücking, *Ber.*, **9**, 529 (1876).
- (4) Fittig and Remsen, *Ann.*, **159**, 150 (1871).
- (5) Tiemann, *Ber.*, **9**, 415 (1876).
- (6) Vogel, *Monatsh.*, **20**, 389 (1899).
- (7) Brady and Dunn, *J. Chem. Soc.*, **107**, 1860 (1915).