[Contribution from the Noyes Chemical Laboratory, University of Illinois]

CONJUGATE ADDITION OF GRIGNARD REAGENTS TO SORBOMESITYLENE AND SORBODURENE

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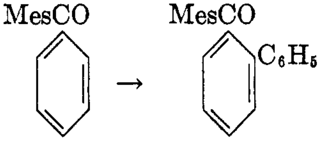
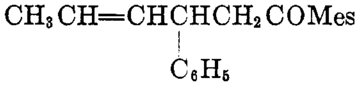
Unsaturated carbonyl compounds so constituted that reaction with Grignard reagents may involve either a 4 or 6 position, almost always are attacked at the 4 position. Attack at the 6 position has never been observed in open chain ketones. A study of conjugate addition reactions involving aromatic nuclei has shown, however, that the attack may occur at either the 4 (*ortho*) or 6 (*para*) position, depending on the reagent used. For example, mesityl phenyl ketone reacts with phenylmagnesium bromide to yield the *o*-phenyl derivative (1).[2]



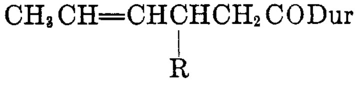
With benzyl and *tert*-butyl reagents, however, mesityl phenyl ketone undergoes *para*-alkylation (2). Attack at the *para* position occurs also when duryl phenyl ketone is treated with isopropyl, cyclohexyl, or *sec*-butyl reagents (3).

To determine whether this marked tendency of certain Grignard reagents to seek the 6 position extends to the analogous open chain ketones, we have examined the behavior of phenylmagnesium bromide with sorbomesitylene and sorbodurene and compared it with that observed with sorbodurene and benzylmagnesium chloride. No evidence was obtained to indicate that the 6 position was involved. Sorbomesitylene and phenylmagnesium bromide gave β-phenyl-β-propenylpropiomesitylene (I) in a 51% yield. Sorbodurene reacted with the phenyl and benzyl reagents to give the corresponding β-substituted ketones in yields of 73% and 88%, respectively. In none of the experiments was it possible to isolate more than one addition product.



$$CH_3CH{=}CH\underset{\displaystyle C_6H_5}{\underset{|}{C}}HCH_2COMes$$

I



$$CH_3CH{=}CH\underset{\displaystyle R}{\underset{|}{C}}HCH_2CODur$$

II R = C_6H_5
III R = $C_6H_5CH_2$

Sorbomesitylene and sorbodurene, made in 60 to 75% yields by the Friedel-Crafts method, were condensed with maleic anhydride as a means of structure confirmation. Moreover, hydrogenation of sorbomesitylene was found to produce *n*-amyl mesityl ketone, identified as its dinitro derivative. Sorbodurene underwent oxidative cleavage with permanganate, to yield durylglyoxylic acid and

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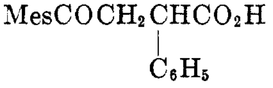
[2] Mes and Dur are used in this paper to represent mesityl and duryl, respectively.

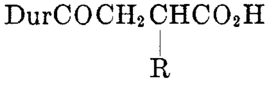
oxalic acid. No attempt was made to isolate acetic acid which, presumably, was formed also.

Oxidation of the product (I) from sorbomesitylene and the phenyl reagent yielded acetic acid and α-phenyl-β-mesitoylpropionic acid (IV).



$$\mathrm{MesCOCH_2\underset{\displaystyle C_6H_5}{\underset{|}{C}}HCO_2H}$$

IV



$$\mathrm{DurCOCH_2\underset{\displaystyle R}{\underset{|}{C}}HCO_2H}$$

V

In a similar way the duryl derivatives from the phenyl and benzyl reagents (II, III) yielded acetic acid and the corresponding α-substituted β-(2,3,5,6-tetramethylbenzoyl)propionic acids (V).

EXPERIMENTAL[3]

Sorbomesitylene. The method of preparing this ketone was patterned after that employed earlier (4) in the synthesis of mesityl propenyl ketone. Sorbyl chloride, prepared in 87% yield by the method of Doebner and Wolff (5), was allowed to react with mesitylene in the presence of aluminum chloride, all three compounds being taken in equimolecular proportions. A solution of the sorbyl chloride (27.2 g.) and mesitylene (25 g.) in 25 ml. of carbon disulfide was added dropwise over a period of 1½ hours to a mixture of 30.6 g. of aluminum chloride and 100 ml. of carbon disulfide. The reaction vessel was kept in an ice-salt bath during the mixing, which was accompanied by vigorous stirring of the reaction mixture. The sorbomesitylene, isolated by usual procedures, was a viscous, yellow liquid; b.p. 133–134°/0.9 mm.; n_D^{20} 1.5750; yield 32.7 g. (74%).

Anal. Calc'd for $C_{15}H_{18}O$: C, 84.07; H, 8.47.
Found: C, 84.19; H, 8.65.

In one preparation of sorbomesitylene by this method a large amount of an orange solid was obtained when the crude product was subjected to distillation. After being recrystallized five times from ethanol, it formed white needles, m.p. 149–149.5°. The compound had the composition of the hydrochloride of sorbomesitylene.

Anal. Calc'd for $C_{15}H_{19}ClO$: C, 71.84; H, 7.64; Cl, 14.14.
Found: C, 71.94; H, 7.65; Cl, 14.10.

Hydrogenation of sorbomesitylene. Sorbomesitylene (2 g.) dissolved in 25 ml. of absolute ethanol was hydrogenated over a Raney nickel catalyst at room temperature. Approximately two equivalents of hydrogen were consumed in the reaction. The catalyst was removed and the resulting solution distilled. The portion boiling at 102–110° at 0.9 mm. was *n*-amyl mesityl ketone.

A solid dinitro derivative was prepared by adding dropwise 0.4 g. of this yellow liquid to a mixture of 6 ml. of concentrated nitric acid and 6 ml. of concentrated sulfuric acid which had been cooled to below 10° in an ice-bath. The temperature was maintained at or below that value during the addition and for a period of 20 minutes thereafter; then the reaction mixture was poured over crushed ice. The yellow precipitate, after several crystallizations from ethanol, gave *n*-amyl 3,5-dinitromesityl ketone as a white solid, m.p. 120.5–121.5°.

Anal. Calc'd for $C_{15}H_{20}N_2O_5$: C, 58.45; H, 6.54; N, 9.09.
Found: C, 58.33; H, 6.43; N, 9.32.

n-Amyl 3,5-dinitromesityl ketone was prepared also by nitration of a sample of *n*-amyl mesityl ketone produced by condensing mesitylene with *n*-caproyl chloride. A solution of the chloride (30.8 g.), mesitylene (28 g.), and carbon disulfide (50 ml.) was added dropwise, with stirring, to a mixture of 40 g. of anhydrous aluminum chloride and 150 ml. of carbon

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[3] The microanalyses were carried out by Miss Emily Davis and Miss Rachel Kopel.

disulfide. The reaction vessel was kept in an ice-salt bath during the mixing and for 4 hours afterward, with continuous stirring. The ketone, isolated by usual procedures boiled at 120–124°/1.7 mm.; yield 27.5 g. (55%). A portion of the product was redistilled; b.p. 118.5–119° (1.0 mm.).

Anal. Calc'd for $C_{15}H_{22}O$: C, 82.51; H, 10.16.
Found: C, 82.72; H, 10.33.

A dinitro derivative was prepared from 1.0 g. of this sample of *n*-amyl mesityl ketone by the nitration procedure used above. Nearly white needles were obtained after several crystallizations from ethanol; m.p. 121–121.5°. A mixture melting point determination showed this product and that obtained above to be identical.

Anal. Calc'd for $C_{15}H_{20}N_2O_5$: C, 58.45; N, 6.54; N, 9.09.
Found: C, 58.51; H, 6.73; N, 9.23.

Diene reaction between sorbomesitylene and maleic anhydride. A mixture of 20.0 g. of sorbomesitylene and 9.2 g. of maleic anhydride was heated under reflux in xylene for 90 hours. When the resulting solution was cooled, a white, crystalline solid separated. After five crystallizations from xylene, the adduct melted at 168–169.5°.

Anal. Calc'd for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45; Neut. equiv., 156.18.
Found: C, 73.13; H, 6.31; Neut. equiv., 160.91.

Sorbodurene. This substance was prepared by a procedure similar to that described for sorbomesitylene. From 173 g. of durene and 168.3 g. of sorbyl chloride was obtained 175.1 g. of an orange liquid, b.p. 150–159° (0.7–3.0 mm.), which solidified completely; the yield was 59%. The unsaturated ketone was obtained as yellow plates after six crystallizations from petroleum ether (40–60°); m.p. 88–89°.

Anal. Calc'd for $C_{16}H_{20}O$: C, 84.16; H, 8.83.
Found: C, 84.00; H, 8.81.

Oxidative degradation of sorbodurene. A suspension of 0.4 g. of sodium bicarbonate in a solution of 2.0 g. of sorbodurene in 20 ml. of acetone was cooled in a salt-ice bath. While this mixture was stirred vigorously, finely-ground potassium permanganate was added in small portions until a faint pink color persisted. Removal of the acetone left a dark-brown mass which was extracted with three portions of a hot, dilute sodium hydroxide solution. The insoluble manganese dioxide was removed and the filtrate allowed to cool. The alkaline solution was extracted with ether, then acidified with dilute hydrochloric acid. A brown oil separated from the acidic solution; extraction with ether and evaporation of the ether extract produced 0.5 g. of solid which, after three crystallizations from petroleum ether (90–110°), melted at 122–124° and had the composition of durylglyoxylic acid.

Anal. Calc'd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84; Neut. equiv., 296.23.
Found: C, 69.62; H, 7.03; Neut. equiv., 217.55.

The aqueous layer was made just alkaline with a 10% sodium hydroxide solution and evaporated to dryness. The resulting crystalline mass was heated with absolute ethanol and removed on a filter. Evaporation of the ethanol solution left a small amount of solid material. A *p*-bromoanilide was prepared from this substance which, after crystallization from water, melted at 301-306°. The reported melting point of the di-*p*-bromoanilide of oxalic acid is "above 300°".

Diene reaction between sorbodurene and maleic anhydride. To 5.0 g. (0.022 mole) of sorbodurene dissolved in a mixture of xylenes was added 2.2 g. (0.022 mole) of maleic anhydride. The maleic anhydride was dissolved on heating and the reaction mixture was heated under reflux for 24 hours. When the mixture was cooled the solid, yellow adduct separated in a yield of 0.9 g. (12.6%); m.p. 196–197°, after three crystallizations from nitromethane.

Anal. Calc'd for $C_{20}H_{22}O_4$: C, 73.59; H, 6.80.
Found: C, 73.42; H, 6.98.

Reaction of sorbomesitylene and phenylmagnesium bromide. A solution of 46.5 g. of sorbomesitylene in anhydrous ether was added dropwise (at a rate to promote gentle reflux) to a Grignard reagent prepared from 39.3 g. of bromobenzene and 6.1 g. of magnesium turnings. The mixture was heated under reflux for an hour after the addition was completed, then decomposed by pouring into a saturated ammonium chloride solution. The ether layer was separated, washed twice with a 10% sodium hydroxide solution, twice with water, and dried over magnesium sulfate. After the solvent had been removed, the residue was distilled and the portion boiling at 183–185° (0.7 mm.), was collected; n_D^{20} 1.5581. Yield of β-phenyl-β-propenylpropiomesitylene was 51.3 g. (81%).

Anal. Calc'd for $C_{21}H_{24}O$: C, 86.25; H, 8.27.
Found: C, 86.47; H, 8.33.

Reaction of sorbodurene and phenylmagnesium bromide. This reaction was carried out in a manner similar to that employed with sorbomesitylene except that the solvent was an ether-benzene mixture. During the addition the contents of the flask turned milky and a yellow solid gradually separated. Removal of the solvent by evaporation under reduced pressure (20 mm.) left a viscous, orange liquid, which solidified on standing in the icebox. This solid crystallized from an ethanol-water mixture (10:1) to yield 35.4 g. of slightly yellow crystals which, after being dried in a vacuum desiccator over calcium chloride, weighed 24.3 g. (73%): m.p. 60–63°. Further recrystallization of a small portion yielded white crystals, m.p. 69–71°.

Anal. Calc'd for $C_{22}H_{26}O$: C, 86.23; H, 8.55.
Found: C, 86.19; H, 8.79.

Reaction of sorbodurene and benzylmagnesium chloride. The procedure differed from that described for the phenyl reagent in that the period of heating was 2 hours. Removal of the solvent by evaporation under reduced pressure (20 mm.) left a white solid residue which, after three crystallizations from an ethanol-water mixture (10:1), melted at 91–92°. The yield of β-benzyl-β-propenylpropiodurene was 11.8 g. (88%).

Anal. Calc'd for $C_{23}H_{28}O$: C, 86.20; H, 8.81.
Found: C, 86.08; H, 8.74.

Oxidative degradation of Grignard adducts. This degradation was carried out in the manner of the oxidative degradation of sorbodurene (which see). The resulting ether-extracted alkaline solution was acidified to give a water-insoluble oil which was separated by ether extraction. Evaporation of the ether left a crystalline acid which was purified by crystallization from a suitable solvent.

The acid aqueous layer was made just alkaline with a dilute sodium hydroxide solution and evaporated to dryness on the steam-bath. The resulting mixed salts were boiled for several minutes with 25 ml. of absolute ethanol and collected. The cooled filtrate was evaporated to dryness. The crude sodium acetate thus obtained was converted to the *p*-bromophenacyl ester which, after crystallization from an ethanol-water mixture (10:1), melted at 84.5–86°. A mixture melting point with a known sample of *p*-bromophenacyl acetate showed no depression.

β-Phenyl-β-propenylpropiomesitylene. The water-insoluble α-phenyl-β-mesitoylpropionic acid was obtained as cream-colored plates after three crystallizations from nitromethane; m.p. 176.5–177° [Literature m.p. 172° (6)].

Anal. Calc'd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80; Neut. equiv., 296.35.
Found: C, 76.73; H, 7.02; Neut. equiv., 299.3.

β-Phenyl-β-propenylpropiodurene. The cleavage product, α-phenyl-β-(2,3,5,6-tetramethylbenzoyl)propionic acid, was purified by crystallization from an ethanol-water mixture (2:1), m.p. 184.5–186°. A specimen of this acid, prepared by a different method melted at 185–185.5° (7). A mixture melting point showed no depression.

Anal. Calc'd for $C_{20}H_{22}O_3$: C, 77.39; H, 7.15; Neut. equiv., 310.4.
Found: C, 77.47; H, 7.31; Neut. equiv., 315.5.

β-Benzyl-β-propenylpropiodurene. This oxidation was carried out entirely at room temperature since no reaction occurred at 0°. The resulting α-benzyl-β-(2,3,5,6-tetramethylbenzoyl)propionic acid was crystallized from an ethanol-water mixture (1:1); m.p. 184–186°.

Anal. Calc'd for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46; Neut. equiv., 324.4.
Found: C, 77.50; H, 7.70; Neut. equiv., 331.1.

SUMMARY

Sorbomesitylene and sorbodurene have been prepared from sorbyl chloride and the corresponding hydrocarbons by the method of Friedel and Crafts.

Both ketones have been condensed with phenylmagnesium bromide. Sorbodurene has also been treated with the benzyl Grignard reagent. In each addition reaction the hydrocarbon radical of the reagent entered the 4 position. The structure of the products was established by oxidative degradation.

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