Hydrogenation of 3.5 g. of pure X in ethyl acetate using a Parr apparatus and Adams catalyst resulted in the uptake of one equivalent of hydrogen. Distillation afforded 3.0 g. of a liquid, b.p. 172–174°, $n^{25}\text{D}$ 1.4682. The infrared spectrum of this compound was identical with that of an authentic sample of *cis*-3-oxabicyclo[4.3.0]nonane prepared as described below.

To 3 g. of *cis*-1,2-cyclohexenedimethanol, m.p. 40–42°, in 25 ml. of boiling water was added slowly 1.0 ml. of concentrated sulfuric acid. The resulting distillate was collected and the organic layer separated. The aqueous layer was extracted with ether. The ether layer was combined with the organic material and this in turn was washed with water and sodium carbonate solution. Distillation afforded 1.0 g. of a liquid, of characteristic camphor-like odor, b.p. 168–170°, $n^{25}\text{D}$ 1.4680.

ITHACA, NEW YORK

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Duryl 2,6-Disubstituted Phenyl Ketones[1]

BY REYNOLD C. FUSON AND BRUNO VITTIMBERGA

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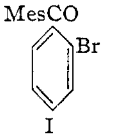
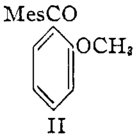
Duryl 2,6-dimethoxyphenyl ketone (IV) has been found to suffer displacement of both methoxyl groups by the action of phenylmagnesium bromide. The resulting duryl 2,6-diphenylphenyl ketone (VI) reacted with the *t*-butyl Grignard reagent to give duryl 4-*t*-butyl-2,6-diphenylphenyl ketone (XI). This same ketone was prepared from the dimethoxy ketone by an alternative route; *t*-butylation at the 4-position was followed by displacement of the methoxyl groups by use of the phenyl reagent.

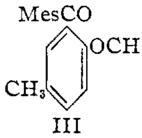
Diphenylated products have been obtained by the action of phenylmagnesium bromide on mesityl 2-bromophenyl (I), mesityl 2-methoxyphenyl (II) and mesityl 2-methoxy-5-methylphenyl (III) ketones.[2] It seems safe to conclude that a radical that replaces the bromine atom or one of the methoxyl groups enters the position occupied by the substituent which is replaced. That the second radical occupies the remaining *o*-position might be questioned. If the products are indeed 2,6-diphenylated ketones, the further question arises as to whether the crowding at these positions might deactivate the ring to such a degree that attack by the *t*-butyl reagent at the 4-position would become difficult or impossible. From this point of view, it would be even more interesting to see what effect *t*-butyl groups would exert if they could be introduced into the 2- and 6-positions. The present study was undertaken with the hope of finding answers to these questions.



I

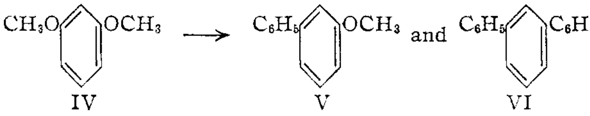


II



III

A logical starting point seemed to be duryl 2,6-dimethoxyphenyl ketone (IV), a compound readily obtainable from duroyl chloride and the lithium derivative of the dimethyl ether of resorcinol. It was found to react with the phenyl reagent to give a mixture of the mono-(V) and diphenylated (VI) ketones.



IV V VI

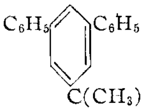
The diphenyl compound was formed also from duryl 2-methoxyphenyl ketone (VII) along with duryl 2-biphenylyl ketone (VIII), which was identified by comparison with an authentic sample.[3]

From these results it is apparent that the phenyl radicals in all cases occupy positions *ortho* to the ketone function. Moreover, no example is known of phenylation of a ketone in the *p*-position by the action of a Grignard reagent.

The possibility of introducing a *t*-butyl group into an *o*-position in a similar manner was explored with duryl 2-methoxyphenyl ketone (VII), which was found to undergo *t*-butylation in the *p*-position. The structure of the product (IX) was established by cleavage to the known duryl 4-*t*-butyl-2-hydroxyphenyl ketone. Duryl 2,6-dimethoxyphenyl ketone (IV) likewise was attacked only at the *p*-position; the product was duryl 4-*t*-butyl-2,6-dimethoxyphenyl ketone (X).

The effect of the phenyl groups in the 2- and 6-positions on the reactivity of duryl phenyl ketone was studied by the use of *t*-butylmagnesium chloride, which had shown itself to be especially effective in substitution at the *p*-position. Alkylation occurred at that position to give duryl 4-*t*-butyl-2,6-diphenylphenyl ketone (XI).

An examination of the molecular model of the diphenylated ketone VI reveals that the phenyl groups can lie in positions perpendicular to the plane of the middle ring of the terphenyl system (Fig. 1).



XI

In this perpendicular position, the *o*-substituents offer little if any resistance to the coplanarity of the carbonyl group with the central benzene ring. Indeed, the electronegativity of the phenyl rings in the 2,6-positions might even render the middle ring more sensitive to attack by nucleophilic agents.

It is interesting to consider the possibility that large *o*-substituents such as *t*-butyl groups might

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(1) This investigation was supported in part by a grant from the Office of Ordnance Research, U. S. Army (Contract No. DA-11-022-ORD-874).

(2) R. C. Fuson and S. B. Speck, THIS JOURNAL, **64**, 2446 (1942).

(3) R. C. Fuson and W. S. Friedlander, *ibid.*, **76**, 5782 (1954).

cause inhibition of resonance. Even in such a situation a residual activation of the benzene ring might still exist by virtue of a charge separation induced in the ring by a highly polarized carbonyl group (Fig. 2).

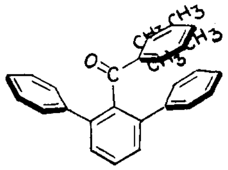

Fig. 1.

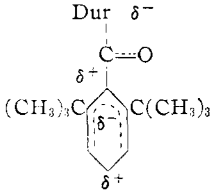

Fig. 2.

The structure of duryl 4-*t*-butyl-2,6-diphenylphenyl ketone (XI) was established by comparison with the product obtained from the treatment of duryl 4-*t*-butyl-2,6-dimethoxyphenyl ketone (X) with phenylmagnesium bromide; the two samples proved to be identical. Since a 2,4-di-*t*-butylphenyl ketone could be obtained by the displacement of the acetoxyl group of duryl 2-acetoxy-4-*t*-butylphenyl ketone by the action of *t*-butylmagnesium chloride,[4] it seemed logical to assume that a similar behavior might be expected with duryl 4-*t*-butyl-2-methoxyphenyl ketone (IX). However, when this ketone was treated with *t*-butylmagnesium chloride, only starting material could be isolated. Moreover, when duryl 4-*t*-butyl-2,6-dimethoxyphenyl ketone (X) was treated with this reagent under forcing conditions, the principal solid isolated was shown to be merely a crystalline modification of the starting material.

In all these reactions involving methoxyl compounds, it is noteworthy that phenolic by-products were isolated only from those reactions which could possibly pass through a dihydro intermediate. It is probable that ether cleavage takes place at this dihydro stage when the ether is of the vinyl type and is thus highly susceptible to cleavage by the Lewis acids that are invariably present in these reaction mixtures.

Experimental[5]

Duryl 2,6-Dimethoxyphenyl Ketone (IV).—This ketone, prepared according to a method described earlier,[6] was recrystallized from an ether-alcohol solution; yield 70%, m.p. 147.5–148.5°.

Treatment of Duryl 2,6-Dimethoxyphenyl Ketone with Phenylmagnesium Bromide.—To a Grignard reagent[7] prepared from 0.96 g. (0.039 g. atom) of magnesium, 6.3 g. (0.040 mole) of bromobenzene and 60 ml. of anhydrous ether was added over a period of 5 minutes, a solution of 4 g. (0.013 mole) of duryl 2,6-dimethoxyphenyl ketone dissolved in 50 ml. of anhydrous benzene. During the course of the reaction, the mixture became purple. Heating under reflux was continued for 1.5 hr., and hydrolysis was then effected with ammonium chloride. The organic layer was washed several times with water and dried over anhydrous sodium sulfate. The drying agent was removed by filtration and the solvent by distillation. The light-yellow oil that remained was induced to crystallize by the addition of absolute ethanol. This crude material was subjected to chromatography. The first of two solids obtained as major products appeared in the early fractions. Recrystallization from ethanol furnished a total of 1.96 g. (37%) of duryl 2,6-diphenylphenyl ketone (VI) in the form of small colorless needles, m.p. 142–143°.

Anal.[8] Calcd. for $C_{29}H_{26}O$: C, 89.19; H, 6.71. Found: C, 89.37; H, 6.72.

The infrared spectrum[9] exhibits a band at 1664 cm.$^{-1}$ assignable to a conjugated hindered ketone group. Bands attributed to monosubstitution of the benzene ring appear at 671 and 678 cm.$^{-1}$.

The second solid obtained from the chromatogram was recrystallized from ethanol; yield 1.04 g. (22%), m.p. 157–159°. Two further recrystallizations from the same solvent furnished pure duryl 6-methoxy-2-phenylphenyl ketone (V) melting at 158–159°.

Anal. Calcd. for $C_{24}H_{24}O_2$: C, 83.69; H, 7.02. Found: C, 83.77; H, 7.19.

The infrared spectrum contains absorption bands assignable to the carbonyl group of a conjugated hindered ketone (1669 cm.$^{-1}$) and to the C–O stretching vibrations of an aromatic methoxyl group (1261 cm.$^{-1}$). Other bands appear at 761 and 698 cm.$^{-1}$ assignable to monosubstitution and at 762 cm.$^{-1}$ to 1,2,3-trisubstitution of the benzene ring. In a subsequent reaction, in which a 6-hr. reaction time was employed, the yield of duryl 2,6-diphenylphenyl ketone (VI) was 79%.

Treatment of Duryl 2-Methoxyphenyl Ketone with Phenylmagnesium Bromide.—Phenylmagnesium bromide was prepared from 1.44 g. (0.060 g. atom) of magnesium, 9.42 g. (0.060 mole) of bromobenzene and 40 ml. of anhydrous ether. To this reaction mixture was added, rapidly with vigorous stirring, a solution of 4 g. (0.015 mole) of duryl 2-methoxyphenyl ketone in 40 ml. of anhydrous benzene. The addition of the ketone immediately produced an orange-red color which changed to shades of yellow, green, blue and finally to deep purple-black. The reaction was allowed to continue for 8 hr. under reflux. Dry air was passed into the cold mixture for 30 minutes, during which time the color changed from blue to yellow-orange. The reaction mixture was then treated with ammonium chloride solution. The organic layer was washed several times with water, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The green oil which remained was subjected to chromatography directly. Three solid ketones were isolated. Recrystallization of the first of these from ethanol afforded 1.61 g. (28%) of the pure ketone, m.p. 141.5–142.5°. A mixture melting point with a previously prepared sample of duryl 2,6-diphenylphenyl ketone (VI) showed no depression.

The second solid, recrystallized from ethanol, separated in the form of small plates with a yellow-green tint; yield 0.32 g. (6.8%), m.p. 129–130.5°. The infrared spectrum of this compound was found to be the same as that of duryl 2-biphenylyl ketone (VIII).

The third ketone, after recrystallization from ethanol, melted at 254–255.5°, yield 0.13 g. (1.8%). A mixture melting point with a known sample of 2,2′-diduroylbiphenyl[10] showed no depression.

Treatment of Duryl 2-Methoxyphenyl Ketone with *t*-Butylmagnesium Chloride.—*t*-Butylmagnesium chloride was prepared from 7.0 g. (0.291 g. atom) of magnesium, 27.7 g. (0.299 mole) of *t*-butyl chloride and 160 ml. of absolute ether. To the refluxing reaction mixture was added a solution of 13.4 g. (0.050 mole) of duryl 2-methoxyphenyl ketone in 100 ml. of anhydrous benzene. The addition was made over a 10-minute interval with vigorous stirring. A murky, pink suspension was produced immediately upon addition of the ketone. The reaction mixture was heated under reflux for 2 hr. longer. Decomposition was effected with 4 *N* sulfuric acid solution, and the products were isolated by usual procedures including chromatography.

The major product, duryl 4-*t*-butyl-2-methoxyphenyl ketone (IX), was recrystallized from ethanol to yield 5.73 g. (35%) of colorless prisms, m.p. 122.5–124.5°.

Anal. Calcd. for $C_{24}H_{24}O_2$: C, 81.44; H, 8.70. Found: C, 81.15; H, 8.95.

Under certain conditions this ketone was obtained in a form which melted at 116–117°. The infrared spectra

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[4] R. C. Fuson and F. T. Fang, THIS JOURNAL, **77**, 3781 (1955).

[5] All melting points are corrected.

[6] R. C. Fuson and R. Tull, THIS JOURNAL, **71**, 2543 (1949).

[7] Precautions were taken to avoid an excess of magnesium.

[8] The microanalyses were performed by Mr. Rollo Nesset, Mrs. Ruby Ju, Mrs. Alice Terra and Miss Claire Higham.

[9] The infrared spectra were determined by Mr. James Brader, Mrs. Louise Griffing and Mr. Sy Portnow. The spectra were obtained from a Perkin-Elmer model 21 spectrophotometer and were measured in carbon disulfide solution unless otherwise indicated.

[10] R. C. Fuson and R. O. Kerr, *J. Org. Chem.*, **19**, 373 (1954).

(measured in carbon tetrachloride) of the two forms are identical. Bands are present at 1408 and 1368 cm.$^{-1}$ assignable to a *t*-butyl group, at 1240 cm.$^{-1}$ assignable to an aromatic methoxyl group and at 1670 cm.$^{-1}$ attributed to the carbonyl absorption of a conjugated hindered ketone.

The other solids were isolated in low yield. The first of these melted at approximately 168°; yield 0.54 g. (3.45%). On the basis of the infrared spectrum (CCl_4) the compound is thought to be duryl 4-*t*-butyl-5,6-dihydro-2-hydroxyphenyl ketone. Bands are present which are assignable to a conjugated diene system (1635 cm.$^{-1}$), to a *t*-butyl group (1375 and 1395 cm.$^{-1}$) and to a chelated carbonyl function (1590 cm.$^{-1}$).

The second compound was recrystallized from ethanol–water; yield 0.04 g. (0.26%), m.p. 180–181.0°. The infrared spectrum (CCl_4) of this ketone was superimposable on that of duryl 4-*t*-butyl-2-hydroxyphenyl ketone. An authentic sample (m.p. 183–184°) of the latter compound was prepared in 75% yield by cleavage of the methoxy compound according to a procedure previously described.[11]

Treatment of Duryl 2,6-Dimethoxyphenyl Ketone with *t*-Butylmagnesium Chloride.—A Grignard reagent prepared from 0.94 g. (0.039 g. atom) of magnesium, 3.7 g. (0.040 mole) of *t*-butyl chloride and 55 ml. of absolute ether was heated under reflux for 2.5 hr., and a solution of 4 g. (0.013 mole) of duryl 2,6-dimethoxyphenyl ketone in 30 ml. of anhydrous benzene was added. The addition, which required 10 minutes, produced a white precipitate, and the mixture acquired a pink color. Heating under reflux was continued for 1 hr. longer, at the end of which time the color had changed to dark violet-purple. Dry air was then passed into the cool reaction mixture for 30 minutes and 200 ml. of cold 4 *N* sulfuric acid solution was added. The organic layer was washed several times with water, dried over anhydrous sodium sulfate and concentrated. The residual reddish-yellow oil was subjected to chromatography. By combination and recrystallization of fractions, one crystalline product, duryl 4-*t*-butyl-2,6-dimethoxyphenyl ketone (X), was isolated as colorless needles; yield 1.78 g. (37%), m.p. 125.5–127°. A purified sample melted at 126–127°.

Anal. Calcd. for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53. Found: C, 78.02; H, 8.28.

The infrared spectrum contains bands at 1670, 870, 1137, 833, 1607 and 1570 cm.$^{-1}$ which are consistent with the assigned structure.

The alcohol fractions of the chromatogram were shown by infrared analysis to contain, in approximately 10% yield, *t*-butylated phenols, formed presumably by the cleavage of the corresponding methyl ethers. In a previous run, in which a longer reaction time was used, a higher yield of phenols was obtained.

Treatment of Duryl 4-*t*-Butyl-2-methoxyphenyl Ketone with *t*-Butylmagnesium Chloride.—One gram of duryl 4-*t*-butyl-2-methoxyphenyl ketone (IX) (0.0031 mole) dissolved in 25 ml. of anhydrous benzene was added rapidly to a Grignard reagent prepared from 0.50 g. (0.020 g. atom) of magnesium, 2.50 g. (0.027 mole) of *t*-butyl chloride and 55 ml. of absolute ether. The color changed quickly to orange, violet-purple and then slowly became milky. The reaction mixture was heated under reflux for 16 hr. and then it was treated in a manner similar to that described for the purification of the dimethoxy compound X. The residual reddish-yellow oil was induced to crystallize by the addition of methanol. Purification by recrystallization from this solvent gave colorless crystals; 0.86 g., m.p. 114.5–115.5°; they showed no mixture melting point depression with the starting material (86% recovery). In a previous run, in which a 1-to-1 ratio of ether to benzene and a 1 hr. reaction time were employed, 86% of starting material was isolated.

Treatment of 4-*t*-Butyl-2,6-dimethoxyphenyl Ketone with Phenylmagnesium Bromide.—To a Grignard reagent prepared from 0.26 g. (0.011 g. atom) of magnesium, 1.80 g. (0.012 mole) of bromobenzene and 35 ml. of anhydrous ether was added, over a 15-minute period, a solution of 1 g. (0.0028 mole) of duryl 4-*t*-butyl-2,6-dimethoxyphenyl ketone (X) in 35 ml. of anhydrous benzene. The color turned pink immediately when the ketone was added, then changed slowly to a reddish-purple. The mixture was heated under reflux for 8 hr., cooled and treated with 150 ml. of a saturated solution of ammonium chloride. The yellow organic layer was washed several times with water, dried over anhydrous sodium sulfate and concentrated under reduced pressure. The residual, partially crystallized oil was dissolved in cyclohexane and subjected to chromatography. Combination of fractions and two recrystallizations from ethanol gave the duryl 4-*t*-butyl-2,6-diphenylphenyl ketone (XI) in the form of small clear prisms; yield 0.94 g. (74%), m.p. 173–174°.

Anal. Calcd. for $C_{33}H_{34}O$: C, 88.74; H, 7.67. Found: C, 88.47; H, 7.62.

The infrared spectrum (CCl_4) of a purified sample contains bands assignable to a conjugated hindered ketone function (1669 cm.$^{-1}$), to a *t*-butyl group (1410 and 1378 cm.$^{-1}$) and to monosubstitution of a benzene ring (700 cm.$^{-1}$).

Treatment of Duryl 2,6-Diphenylphenyl Ketone with *t*-Butylmagnesium Chloride.—To a solution of *t*-butylmagnesium chloride prepared from 0.25 g. (0.010 g. atom) of magnesium, 1.02 g. (0.011 mole) of *t*-butyl chloride and 35 ml. of anhydrous ether was added, with stirring, a solution of 1 g. (0.0026 mole) of duryl 2,6-diphenylphenyl ketone (VI) in 30 ml. of anhydrous benzene. The addition required 5 minutes. After about 15 minutes the color began to change slowly to a reddish-brown. The reaction mixture was heated under reflux for a total of 8 hr. Dry air was then passed into the reaction mixture, which had become milky, for a period of 30 minutes, and 100 ml. of a saturated solution of ammonium chloride was added. The organic layer was washed with water and dried over anhydrous sodium sulfate. Removal of the solvent at reduced pressure left a yellow oil which could not be induced to crystallize from ethanol. The alcohol was removed and the oil was subjected to chromatography.

After combination of fractions and recrystallization from ethanol, 0.53 g. of small colorless prisms was obtained which melted at 146.5–147.5°. After one additional recrystallization from ethanol, colorless prisms melting at 173–174° were obtained in nearly quantitative yield. Further purification and combination of fractions produced 0.57 g. (49%) of duryl 4-*t*-butyl-2,6-diphenylphenyl ketone (XI), m.p. 173–174°.

The infrared spectrum of this ketone was superimposable on that of the previously prepared sample.

The alcohol fraction from the chromatogram furnished a small quantity of a colorless solid which, when recrystallized from ethanol, separated in the form of small colorless needles, m.p. 179° (approx.).

The infrared spectrum (Nujol mull) has peaks suggesting the presence of a hydroxyl group (3444 cm.$^{-1}$), a conjugated carbonyl group (1645 cm.$^{-1}$) and a monosubstituted benzene function (700 and 760 cm.$^{-1}$).

Treatment of Duryl 4-*t*-Butyl-2,6-dimethoxyphenyl Ketone with *t*-Butylmagnesium Chloride.—To a Grignard reagent prepared from 0.264 g. (0.011 g. atom) of magnesium, 1.10 g. (0.012 mole) of *t*-butyl chloride and 35 ml. of anhydrous ether, was added, rapidly with vigorous stirring, a solution of 1 g. (0.0028 mole) of duryl 4-*t*-butyl-2,6-dimethoxyphenyl ketone (X) in 60 ml. of anisole. The color changed immediately to dark purple, then rapidly to light yellow-green. The temperature of the reaction mixture was raised to 128° during 1.5 hr. and the reaction was allowed to continue at this temperature for 6.5 hr. longer. The reaction mixture was then cooled and treated with 100 ml. of a saturated solution of ammonium chloride. The organic layer was washed several times with water, dried over anhydrous sodium sulfate and freed of solvent by distillation. The residual oil was subjected to chromatography from which one major compound could be isolated. By combination of fractions and by recrystallization from ethanol–water, 0.63 g. of colorless plates melting at 141–142.5° was obtained.

An infrared spectrum of this compound was superimposable on that of the starting material X (needle form of melting point 126–127°). When the latter was stored for 7 months, its melting point changed from 126–127° to 141–143° (still needle form). A mixture melting point of the two crystalline modifications—needles, m.p. 141–143° and plates, m.p. 141–142°—showed no depression. Conversion of the needles to the plate form could be effected by seeding the solution of the crystals. The reversal of this phenomenon could not be achieved.

URBANA, ILLINOIS

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[11] R. C. Fuson, G. W. Parshall and E. H. Hess, THIS JOURNAL, **77**, 3776 (1955).