[Contribution from the Chemical Laboratories of the University of Notre Dame]

THE ORIENTATION OF ISOPROPYL AND *tert*-BUTYL GROUPS IN BENZENE DIALKYLATION[1]

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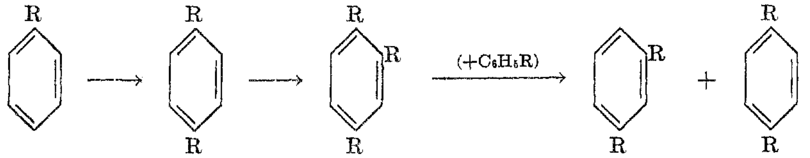
Received February 1, 1952

It has long been known that alkylation of monoalkylbenzenes by Friedel-Crafts procedures produces unusually large amounts of the *meta* product along with the expected *ortho* and *para* isomers. The amount of *meta* product is commonly one-third or even one-half of the total dialkylbenzene formed. Electrophilic substitutions in monoalkylbenzenes ordinarily give some *meta* by-product, to be sure, but the amount is relatively small. An interesting case in point concerns the nitration of *tert*-butylbenzene, recently shown (1) to produce 11.5% of the *meta* isomer. The *para/meta* ratio, however, did not differ much from the value for toluene (8.45 and 6.32, respectively). The anomalous situation almost always found in alkylation has never been explained satisfactorily. Price and Ciskowski (2) proposed that some of the initially formed *ortho* or *para* compound further alkylates to the 1,2,4-trisubstituted derivative which subsequently dealkylates (as by a transalkylation reaction) in the 1-position.



This explanation, though entirely valid in many cases, can hardly be fitted to the observation that *tert*-butylation of toluene (3, 4) produces typical *meta-para* mixtures. The antecedent of *m-tert*-butyltoluene would need to possess two *tert*-butyl groups *ortho* to each other, a situation very unfavorable from steric considerations. Condon (5) has shown in other cases, that *meta* products form in large amount by direct substitution rather than by isomerization or alkylation-dealkylation mechanisms.

If it is accepted that *meta* alkylations may occur directly, in serious competition with reactions in the *ortho* and *para* positions, it may be concluded that the free energies of formation of the three isomeric ionic intermediates differ very little. A rather distinctive feature of the intermediate $(RC_6H_5R)^+$, or transition state corresponding to it, is that the ring bears only electron-releasing groups.[2] We may imagine that the charge distribution in such situations is not much less favorable in the *meta* structure than in the *para*. If *meta* and *para* products form in equal amount, it would appear that the rate of the *para* reaction is twice that of one of the *meta* reactions and we may calculate readily that the free energies of

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[1] This paper is based on the M.S. Dissertations of Rev. Albert J. Driesch, T.O.R., and Mr. Paul L. Dee, University of Notre Dame, 1951.

[2] In other electrophilic substitutions in alkylbenzenes, *e.g.*, nitration, sulfonation, halogenation, etc., the attaching group is electron-attracting in every case.

activation at 25° thus differ by only 0.4 kcal. ($\Delta F^{\ddagger}_{meta} - \Delta F^{\ddagger}_{para}$). A difference of 1.7 kcal. corresponds to 90% *para* substitution and 10% *meta*.

Attention has been called repeatedly to the great differences in the extent of *ortho* substitution in alkylbenzenes and it is generally accepted that this is due to steric factors (1, 5). How steric hindrance can affect the *p/m* ratio in alkylations is certainly less clear. Activation of the ring by the inductive effect of the initially present group is $m > p$. Contrary results are usually ascribed to hyperconjugation where $p \gg m$. Should the hyperconjugative effect be largely counterbalanced by induction, substitution in these two positions may be seriously competitive, except in special cases where steric considerations indicate otherwise.

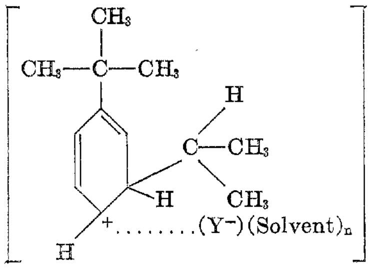
Consider the alkylations

$$RC_6H_5 + R'Y \rightarrow [(RC_6H_5R')^+Y^-] \rightarrow RC_6H_4R' + HY$$

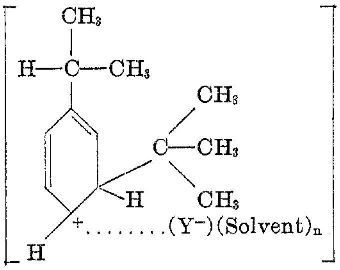
$$\text{and}\quad R'C_6H_5 + RY \rightarrow [(R'C_6H_5R)^+Y^-] \rightarrow R'C_6H_4R + HY.$$

While the end-products (*o*-, *m*-, and *p*-) are identical by either method, we are concerned with six reactions of the same kinetic order and mechanism and for each of these the velocity constant is a function of the work ($-\Delta F^{\ddagger}$) necessary to get the reactants into a transition state. If R and R′ are moderately large (and of course different) we may expect that one method will involve more steric hindrance in the formation of the *meta* transition state than the other. The *p/m* ratio of products would therefore *not* be the same for the two modes of dialkylation.

It was expected, for example, that I (obtained by isopropylation of *tert*-butylbenzene) would have greater formation tendency than II (obtained by *tert*-butylation of cumene).



(I; 3 resonance forms)



(II; 3 resonance forms)

In I the bulky *tert*-butyl group is attached to a trigonal carbon atom and is coaxial with the ring. Steric interference with the angular isopropyl group is not serious. If the two groups are exchanged (II) the angular *tert*-butyl group occupies a less favorable position and steric interference with the isopropyl group is more likely. Thus II may be expected to have higher free energy than I and hence decreased formation tendency. In *para* substitution, on the other hand, there is no steric interference of the two groups, irrespective of the order of introduction; therefore the free energies of substitution should differ relatively little.

Considerations such as these led us to study the dialkylation of benzene with *tert*-butyl and isopropyl compounds, introducing first one group, then the other and *vice-versa*. Significant results were obtained only when the alcohols were used as alkylating agents, employing 85% sulfuric acid as the reaction medium. When such reactions were carried out at 25° the results of the two modes of dialkylation were very different and in complete harmony with the notions expressed above. Either way the yield of dialkylbenzene amounted to about 45–50% of the theoretical. Isopropylation of *tert*-butylbenzene gave a product containing the *meta* and *para* isomers in about equal amounts. By *tert*-butylation of isopropylbenzene (alkylation steps reversed) the product was about nine-tenths *para* and one-tenth *meta*. Each isomer could be isolated, purified, and identified. Examination of the infrared spectra of various fractions indicated the presence of *ortho* isomer in the mid-fractions, particularly from isopropylations, but the compound could not be isolated or converted to an isolable derivative. Fortunately *m*- and *p*-*tert*-butylisopropylbenzene boil about 10° apart at atmospheric pressure so that separation was not difficult. Alkylations as described above were clean and no indication of isomerizations or alkylation-dealkylation side reactions was observed. In every case, however, there was an appreciable still residue, indicating some polyalkylation. When the reactions were carried out at 25° by standard Friedel-Crafts procedures, using alkyl chlorides as alkylating agents and aluminum bromide or ferric chloride as a catalyst, the reaction product was usually a complex mixture; toward the end of the fractional distillation the column head always froze up with solid *p*-di-*tert*-butylbenzene (m.p. 77°). The lower-boiling fractions contained diisopropylbenzenes as well as *tert*-butylisopropylbenzenes. Hence no worthwhile conclusions regarding orientation by direct substitution could be drawn from such reactions.

To test the hypothesis that *m*-*tert*-butylisopropylbenzene does not originate *via* an isomerization or dealkylation reaction in the alcohol-sulfuric acid method, a sample of purified *p*-*tert*-butylisopropylbenzene was stirred in 85% sulfuric acid with a little isopropyl alcohol as in the alkylation procedure. The compound was recovered in 90% yield without evidence of formation of the *meta* isomer.

The *m*- and *p*-*tert*-butylisopropylbenzenes were first reported by Barbier (6). His descriptions of these compounds, however, are very inadequate. The *para* isomer was much better characterized by Corbett (7) and our physical constants are in very good agreement with his. Unfortunately, a similar comparison of our *meta* compound cannot be made. Samples from the present study gave infrared spectra[3] as expected (8); oxidation with dilute nitric acid produced *m*-*tert*-butylbenzoic acid having the correct melting point (4) and neutral equivalent. Nitration produced a dinitro derivative which had the correct analysis and melted at 122°. Barbier (6) claimed that the dinitro derivative melted at 149°. We cannot explain the discrepancy.

EXPERIMENTAL

Reagents. Isopropylbenzene, purchased from Eastman Kodak Company, and *tert-butylbenzene*, prepared from benzene and *tert*-butyl chloride, were carefully fractionated from sodium before use. *Isopropyl alcohol* and *tert*-butyl alcohol were freshly distilled and only materials of correct boiling point and refractive index were used.

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[3] We are indebted to Professor C. L. Wilson, Ohio State University, for determination of the infrared absorption spectra.

Fractionating column. The reaction products described below were fractionally distilled through an electrically heated, total condensation, partial take-off column whose packed section measured 1.2 × 90 cm. The column was filled with "Heli-Pak" No. 2917, a precision spaced, rectangular section, nichrome wire column filler supplied by Podbelniak, Inc., Chicago. The manufacturer claims a very high fractionating efficiency for this material.

Alkylation of isopropylbenzene with tert-butyl alcohol. The reactor consisted of a one-liter, three-necked flask equipped with a stirrer, dropping-funnel, and air-condenser. One mole (120 g.) of isopropylbenzene and three-fourths mole (55.5 g.) of *tert*-butyl alcohol were placed in the flask and the mixture was cooled in an ice-bath. The stirrer was started and 500 g. of cold 85% sulfuric acid was added from the dropping-funnel over a period of 1½ hours. The ice-bath was removed, the dropping-funnel replaced by a thermometer, and the mixture allowed to warm to 25° (two hours). Stirring was then continued for 8½ hours, maintaining an inside temperature of 25° with occasional cooling as required. The reaction product was then transferred to a separatory-funnel and the lower acid layer removed as quickly as possible. The hydrocarbon layer was washed three times with 100 ml. of brine, once with 100 ml. of 10% sodium hydroxide solution, and finally with 100 ml. of brine. The crude product (156 g.) was dried over calcium chloride, filtered, and carefully fractionated from metallic sodium at 30 mm. The distillate was collected in small fractions whose total weight was 125.6 g. Of this amount 61 g. was recovered isopropylbenzene, nearly all of which came over at 59–60° at 30 mm., n_{D}^{25} 1.4875. There was a short but distinct plateau in the distillation curve at 110–112° (30 mm.) and a 3.42-g. fraction, n_{D}^{25} 1.4879, was collected at this point. This material was subsequently shown to be chiefly *m-tert*-butylisopropylbenzene. Then followed a long plateau at 119° (30 mm.) affording four constant-boiling fractions weighing more than 11 g. each, n_{D}^{25} 1.4885, which proved to be the *para* isomer. There were ten dialkylbenzene fractions weighing a total of 63.2 g., corresponding to a yield of 47.9% (based on *tert*-butyl alcohol). The distillation curve indicated that about 10% of the material was *meta* and about 90% *para*. Fractions of nearly the same boiling point, density, and refractive index were combined and refractionated to obtain pure compounds.

Alkylation of tert-butylbenzene with isopropyl alcohol. The procedure described above was used with repetition of every detail, except that one mole (134 g.) of *tert*-butylbenzene was reacted with three-fourths mole (45 g.) of isopropyl alcohol. The crude product weighed 152 g. (compare with 156 g. above) and the total distillate weighed 139 g. Of this amount 77.4 g. was recovered *tert*-butylbenzene, b.p. 73° at 30 mm., n_{D}^{25} 1.4900, and 62.2 g. represented *tert*-butylisopropylbenzenes (47% yield based on isopropyl alcohol). The *tert*-butylisopropylbenzene fractions, of which there were ten, corresponded to two plateaus on the distillation curve. These were of nearly equal length. The mid-point of the first occurred at 111° (30 mm.) and of the second at 118° (30 mm.). The indices of refraction at the mid-points were 1.4868 and 1.4908, respectively, at 25°. Redistillations of fractions of narrow boiling range proved that the products corresponding to the plateaus described above were *m*- and *p-tert*-butylisopropylbenzene, respectively, formed in nearly equal amount.

Identification of p-tert-butylisopropylbenzene. Material prepared from the isopropylbenzene alkylation with *tert*-butyl alcohol boiled at 119° at 30 mm.; n_{D}^{25} 1.4885; d^{25} 0.8575. When distilled at atmospheric pressure the boiling point was 220° (uncorr.) at 746 mm.; n_{D}^{25} 1.4888. Corbett (7) gives the following properties: b.p. 131.5° at 50 mm., 226.4° at 760 mm.; n_{D}^{25} 1.4887; d^{25} 0.8570.

The infrared spectrum showed a very strong absorption band at 12.1 μ and medium intensity ones at 9.0, 9.4, and 9.8 μ. Bands corresponding to *ortho* and *meta* isomers were absent.

Oxidation of a 2-ml. sample (1.7 g.) by refluxing for 11 hours with 25 ml. of nitric acid in 75 ml. of water gave 1.14 g. of crude product. Several crystallizations from dilute alcohol yielded *p-tert*-butylbenzoic acid, m.p., 166–167° (4); N. E. calc'd 178.2; obs'd 174.8 and 181.4.

Identification of m-tert-butylisopropylbenzene. Material obtained from the alkylation of *tert*-butylbenzene with isopropyl alcohol was refractionated and boiled at 111° at 30 mm.; n_{D}^{25} 1.4865; d^{25} 0.8547. When redistilled at atmospheric pressure the boiling point was 209–210° (uncorr.); n_{D}^{25} 1.4870. Barbier (6) gives b.p. 216° at 729 mm. (no density or refractive index).

The infrared spectrum showed nice absorption bands at 12.65 μ and 14.25 μ and the typical fingerprint bands for *ortho* and *para* isomers were absent.

Oxidation of a 2-ml. sample with dilute nitric acid gave *m-tert*-butylbenzoic acid, m.p. 127° (4); N. E. calc'd 178.2; obs'd 178.4 and 176.8.

A 5-ml. sample (4.25 g.) was cautiously nitrated with mixed acid (34 ml. of conc'd sulfuric acid and 17 ml. of nitric acid, *d.* 1.4) in the usal way. Upon pouring over ice, the mixture deposited yellow crystals, recovered by filtration. The product was washed with cold water, 10% sodium bicarbonate solution, again with water, and dried. Crystallization from isopropyl alcohol gave 3.74 g. (58% yield) of nearly colorless, odorless crystals, m.p. 120–121°. Recrystallization raised the m.p. to 122°.

Anal. Calc'd for $C_{13}H_{18}N_2O_4$: C, 58.63; H, 6.81; N, 10.52.

Found:[4] C, 58.93; H, 7.05; N, 10.81.

Dialkylation by other methods. Using the molar proportions and quantities cited above, a number of experiments were carried out substituting alkyl chlorides for alcohols and small amounts of ferric chloride or aluminum bromide for sulfuric acid. At 25°, the temperature previously employed, transalkylations and/or isomerizations occurred in every case. The distillation curves showed short plateaus corresponding to diisopropylbenzenes and both *tert*-butylisopropylbenzenes. Finally solid *p*-di-*tert*-butylbenzene, m.p. 77° after crystallization from methanol, appeared in the column head and condenser. Good results were obtained, however, when one mole of isopropylbenzene was alkylated with three-fourths mole of *tert*-butyl chloride and 3 g. of anhydrous ferric chloride at 0°. This procedure gave 98 g. of distilled product which appeared to contain about 5 g. of *m*- and 83 g. of *p-tert*-butylisopropylbenzene, a ratio of about 1/16.5. Unfortunately, when the alkylation steps were reversed (again at 0°) only starting materials were recovered. Apparently isopropyl chloride does not alkylate the ring at the low temperature with ferric chloride.

SUMMARY

1. When *tert*-butylbenzene is isopropylated under conditions which do not provoke transalkylation or isomerization, the product is a mixture of the *meta* and *para* isomers in about equal amounts. When the alkylation steps are reversed, the product is chiefly (at least nine-tenths) *para*. In either case a little *ortho* contamination appears, particularly from isopropylations, but the amount is too small to permit isolation.

2. Some theoretical aspects of orientation in the dialkylation of benzene by electrophilic substitution are discussed. It is suggested that hyperconjugation plays only a minor role in the stabilization of ionic intermediates and that the *o-/m-/p*-ratio is profoundly affected by steric features of the transition states.

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[4] Analysis by Mr. Charles W. Beazley, Micro-Tech Laboratories, Skokie, Illinois.