Free Radical Aromatic Substitution. V. The Reaction of Benzoyl Peroxide with Alkylbenzenes[1]

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The thermal decomposition of benzoyl peroxide in various alkylbenzenes has been found to give reaction both with the nucleus and side-chain of most of the compounds. The substitution in the nucleus by phenyl radicals to form biphenyl derivatives is subject to steric hindrance, for the percentages of *ortho* isomers formed from toluene, ethylbenzene and cumene are 65, 50 and 10, respectively. Reaction with the side-chains of ethylbenzene and isopropylbenzene apparently results in removal of an α-hydrogen and dimerization of the radicals thus produced. The side-chain of toluene undergoes a unique reaction to form diphenylmethane in 8% yield.

Alkylbenzenes are unique among most benzene derivatives in that not only the ring but also the side-chain may undergo reaction with a free radical. Side-chain attack has been demonstrated in the reaction of alkylbenzenes with acetyl peroxide,[2] *t*-butyl peroxide[3] and chlorine atoms.[4]

However, phenyl radicals have been reported to give only nuclear substitution with toluene.[5] Such exclusive nuclear substitution does not seem logical when contrasted with the side-chain reactions of other radicals. It has been found[6] that mesitylene and *p*-xylene do undero side-chain attack when treated with benzoyl peroxide. It therefore was decided to decompose benzoyl peroxide in toluene, ethylbenzene and cumene to determine whether: (a) the higher-order side-chain hydrogens would lead to appreciable side-chain reaction; (b) increasing size of the alkyl groups would exert a steric effect upon nuclear substitution and consequently affect the relative yields of isomeric biphenyls produced.

A similar decomposition in *t*-butylbenzene was abandoned, although partially completed, since private communications from Drs. Hey and Rondestvedt have revealed that they have completed this work.

Experimental

Benzoyl peroxide (Lucidol) and toluene (Merck reagent) were used without further purification. Ethylbenzene (Eastman Kodak Co. 719) and cumene (Eastman Kodak Co. 1481) were fractionally distilled to give materials of proper index of refraction.

o-Methylbiphenyl, *m*-Methylbiphenyl, *o*-ethylbiphenyl, *m*-ethylbiphenyl and *o*-isopropylbiphenyl of exceptional purity[7] were supplied through the generosity of Paul H. Wise and I. Goodman of the NACA Laboratories in Cleveland, Ohio.

p-Methylbiphenyl, m.p. 46–47° (lit. 48°[8]), was prepared by the method of Grieve and Hey.[5]

p-Ethylbiphenyl, m.p. 32–33° (lit.[9] 33°), was synthesized by the method of Nenitzescu and Gavat.[9]

m-Isopropylbiphenyl was prepared by low-pressure hydrogenation of 8 g. of *m*-isopropenylbiphenyl[10] in 100 ml. of absolute alcohol, using 5% palladium-on-charcoal as catalyst. Distillation of the product from sodium gave 3 g. (37% yield) of *m*-isopropylbiphenyl, b.p. 104–105° (1 mm.). The product did not decolorize Br_2–CCl_4.

Anal. Calcd. for $C_{15}H_{16}$: C, 91.7; H, 8.17. Found: C, 91.24; H, 8.17.

p-Isopropylbiphenyl was synthesized by a similar hydrogenation of 16 g. of *p*-isopropenylbiphenyl, m.p. 117–118° (lit.[10] m.p. 117–118°), to give 10 g. (62%) of *p*-isopropylbiphenyl, b.p. 125–126° (2 mm.).

Anal. Calcd. for $C_{15}H_{16}$: C, 91.7; H, 8.17. Found: C, 91.95; H, 8.18.

Methyl *o*-phenylbenzoate and methyl *m*-methylbenzoate were prepared from *o*-phenylbenzoic acid, m.p. 110–111° (lit.[11] 110–111°), and *m*-phenylbenzoic acid, m.p. 160–161° (lit.[12] 160–161°), by treatment with diazomethane.

Methyl *p*-phenylbenzoate, m.p. 116–117° (lit.[13] 117–118°), was obtained from Dr. Curtis B. Coleman.[14]

Reaction of Benzoyl Peroxide with Toluene.—To 660 g. (7.2 moles) of toluene kept at 75 ± 2° was added 98.7 g. (0.4 mole) of benzoyl peroxide of 99.2% purity.[15] After completion of the addition of the peroxide, the temperature of 75° was maintained for 4 days, and then the system was swept with CO_2-free air. The total CO_2 evolved, measured by the increase in weight of an attached ascarite train, was 21.5 g. (0.49 mole).

The reaction mixture was extracted four times with 250-ml. portions of 10% sodium hydroxide, and acidification of this aqueous layer precipitated a mixture of benzoic and phenylbenzoic acids. Extraction of this mixture of acids with hot water gave 39.1 g. (0.32 mole) of benzoic acid, m.p. 122°, and 0.3 g. (0.002 mole) of phenylbenzoic acids, neutralization equivalent 195 (theoretical 198).

The reaction mixture remaining after extraction of the organic acids was distilled at atmospheric pressure to give 2.9 g. (0.037 mole) of benzene, $n^{20}D$ 1.5010 (identified as dinitrobenzene, m.p. 89–90°) and 625 g. of toluene. Vacuum distillation of the distilland gave 28.1 g. of unidentified residual tar and 36.8 g. of a mixture of methylbiphenyls and diphenylmethane. Oxidation of a 2-g. sample of the fraction containing diphenylmethane with a slight excess of chromic acid, and steam distillation of the products, yielded a mixture of phenylbenzoic acids and benzophenone. An ether solution of these products was extracted with sodium hydroxide to remove the acids, the ether layer evaporated, and treatment of a methanol solution of the residue with 2,4-dinitrophenylhydrazine gave a few milligrams of benzophenone 2,4-dinitrophenylhydrazone, m.p. 229° (lit.[16] 229°). Comparison of the infrared spectrum of the original fraction to the infrared spectra of known mixtures of diphenylmeth-

(1) From the thesis submitted by Baruch Zaremsky to the Graduate School, Western Reserve University, in partial fulfillment of the requirements for the doctor's degree. Presented at the Chicago Meeting of the American Chemical Society, September, 1953.

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(5) W. S. M. Grieve and D. H. Hey, *ibid.*, 1798 (1934).

(6) D. R. Augood, D. H. Hey, A. Nechtvatal, T. S. Robinson and G. H. Williams, *Research*, 4, 386 (1951).

(7) P. H. Wise and I. Goodman, THIS JOURNAL, 72, 3076 (1950).

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(13) W. Schlenk and T. Weickel, *Ann.*, 368, 304 (1909).

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ane and o-, m- and p-methylbiphenyl[17] proved the composition to be 15% diphenylmethane and 85% methylbiphenyls (65% ortho-, 19% meta- and 16% para-).

Reaction of Benzoyl Peroxide with Ethylbenzene.—To 672.4 g. (6.33 moles) of ethylbenzene kept at 75 ± 2° was added 96.8 g. (0.4 mole) of benzoyl peroxide (99.2% pure). The weight of carbon dioxide evolved was found to be 20.0 g. Extraction of the reaction mixture with four 250-ml. portions of 10% sodium hydroxide and acidification of the alkaline extracts precipitated 43.5 g. of crude benzoic acids. The mixture of crude acids in ethereal solution was treated with excess diazomethane, the ether removed, and the esters vacuum distilled to give 44.5 g. (0.32 mole) of methyl benzoate (b.p. 65–85° at 25 mm.) and 3.4 g. (0.016 mole) of methyl phenylbenzoates (b.p. 110–130° at 3 mm.). Comparison of the infrared absorption spectra of known mixtures of the methyl esters of o-, m- and p-phenylbenzoic acids to that of the methyl phenylbenzoate fraction proved the composition to be 50% ortho, 20% meta and 30% para isomer.

After completion of the extraction with alkali, the reaction mixture was distilled at atmospheric pressure to remove 18 g. (0.23 mole) of benzene (identified as in the toluene experiment) and about 90% of the ethylbenzene. On cooling of the residual ethylbenzene solution, white crystals formed. These were removed, additional ethylbenzene distilled, and the solution chilled to give more of the crystalline material. This operation was repeated until all of the ethylbenzene was removed. The crystalline material, 7.5 g., after recrystallization from 95% ethanol, had a m.p. of 128–129° (meso-2,3-diphenylbutane, m.p. 127–128°[18]). Oxidation of a sample of the material with an aqueous mixture of chromic acid and potassium acid sulfate gave acetophenone, identified as its 2,4-dinitrophenylhydrazone, m.p. 237°.

After complete removal of the ethylbenzene, the residual material was vacuum distilled from lithium aluminum hydride (to remove any traces of carbonyl compounds) to give 22.4 g. of distillate, b.p. 110–115° at 1 mm., and 26.4 g. of unidentified residual tar. The infrared absorption spectrum of the distillate was found to correspond to that of a mixture of molar composition, 10.5% meso- and 42% rac-2,3-diphenylbutanes together with 23.8% o-, 11.9% m- and 11.9% p-ethylbiphenyl.

Reaction of Benzoyl Peroxide with Cumene.—By the methods previously described, the decomposition of 77.7 g. (0.315 mole) of benzoyl peroxide (98.2% pure) in 606 g. (5.04 moles) of cumene produced 15.35 g. (0.35 mole) of carbon dioxide and 30 g. (0.25 mole) of benzoic acid. Treatment of the benzoic acid fraction with diazomethane, etc., showed the phenylbenzoic acid content to be negligible.

Distillation of the reaction mixture at atmospheric pressure gave 8.0 g. (0.10 mole) of benzene and 585 g. of cumene. Distillation at 2 mm. pressure of the remainder of the material gave 17.2 g. of a mixture of isopropylbiphenyls and sym-tetramethyldiphenylethane as well as 24 g. of unidentified residual tar. A sample of the distillate, on chilling, gave a precipitate of sym-tetramethyldiphenylethane, m.p. 119–120° from ethanol (lit.[19] 119–120°). Comparison of the infrared spectra of known mixtures showed the molar composition to be 31% sym-tetramethyldiphenylethane and 6.9% o-, 41.5% m- and 20.7% p-isopropylbiphenyl.

Results and Conclusions.—As all of the experiments were run in duplicate, the values listed in Table I are averages of two separate determinations, and the deviations are those experimentally observed.

Several conclusions are obvious from these data: (a) In all of the experiments, the sum of the CO_2 and C_6H_5COOH yields accounts for practically all of the peroxide carbonyl units, but only about 50%

(17) The spectra of many of these compounds have not been reported and all of the spectra have been deposited as Document number 4403 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the document number and by remitting to advance $1.25 for photoprints or $1.25 for 35 mm. microfilm by check or money order payable to: Chief, Photoduplication Service, Library of Congress.

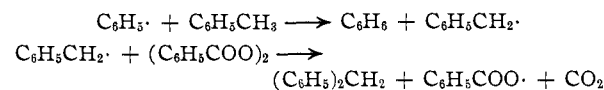(18) E. Ellingboe and R. C. Fuson, THIS JOURNAL, **55**, 2960 (1933).

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TABLE I

MOLES/MOLE OF PEROXIDE

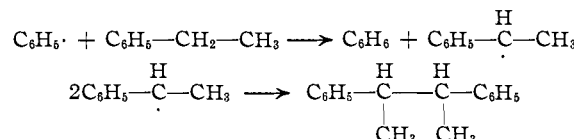| Product	Toluene	Ethylbenzene	Cumene
CO_2	1.2	1.12 ± 0.01	1.11 ± 0.01
C_6H_5COOH	0.79 ± 0.01	0.81 ± 0.01	0.78
$C_6H_5C_6H_4COOH$	.004	.04	0
C_6H_6	.1 ± 0.01	.57	.34 ± 0.01
$R\cdot C_6H_4\cdot C_6H_5$	.46	.14	.18
Side-chain dvt.	.08	.24	.08
Grams residue per mole peroxide	67	67 ± 1	76

of products from the phenyl radicals were isolated. Therefore, the residues must consist of phenylated materials and not esters.

(b) Toluene is unique in that the side-chain undergoes substitution by phenyl radicals. The similarity of yields of diphenylmethane and benzene suggests that they are related in some way. For example, the following equations may represent the mechanism of this reaction

$$C_6H_5\cdot + C_6H_5CH_3 \longrightarrow C_6H_6 + C_6H_5CH_2\cdot$$

$$C_6H_5CH_2\cdot + (C_6H_5COO)_2 \longrightarrow$$
$$(C_6H_5)_2CH_2 + C_6H_5COO\cdot + CO_2$$

This is in accord with the report that the rate of decomposition of benzoyl peroxide in toluene is higher than first order.[20]

(c) In the ethylbenzene reaction, the yield of benzene is twice that of the side-chain product. This suggests that the following equations probably account for the formation of these products

$$C_6H_5\cdot + C_6H_5-CH_2-CH_3 \longrightarrow C_6H_6 + C_6H_5-\overset{H}{\underset{\cdot}{C}}-CH_3$$

$$2C_6H_5-\overset{H}{\underset{\cdot}{C}}-CH_3 \longrightarrow C_6H_5-\overset{H}{\underset{\underset{CH_3}{|}}{C}}-\overset{H}{\underset{\underset{CH_3}{|}}{C}}-C_6H_5$$

In the cumene reaction there is no simple relationship of the yields of benzene and side-chain product. In this instance the radical obtained by extraction of a hydrogen atom from the side-chain apparently undergoes another reaction (e.g., reaction with the peroxide) instead of dimerization.

The lower yield of benzene in the cumene run as compared to the ethylbenzene experiment is surprising in that cumene has a higher-order side-chain hydrogen. The benzene must be obtained principally by reaction of phenyl radicals with the alkyl side-chains, for other aromatic compounds (e.g., nitrobenzene) give negligible quantities of benzene when treated with benzoyl peroxide. The lower yield of benzene may be due to steric hindrance to approach of the phenyl group to the tertiary hydrogen.

In Table II are listed the relative yields of isomeric alkyl-biphenyls produced.

TABLE II

COMPOSITIONS OF ALKYLBIPHENYL FRACTIONS

Parent hydrocarbon	% ortho	% meta	% para
Toluene	65	19	16
Ethylbenzene	50	25	25
Cumene	10	60	30

(20) K. Nozaki and P. D. Bartlett, THIS JOURNAL, **68**, 1686 (1946).

It is obvious that aromatic substitution suffers steric hindrance, for as the size of the substituent increases, the amount of *ortho* substitution decreases. In addition, the so-called law of invariable *ortho–para* substitution is not adhered to. When *ortho* substitution (in the cumene run) is substantially prevented, *meta* and *para* substitution are statistical in quantity.

Acknowledgment.—We would like to express our deepest appreciation to Irving Goodman and Paul Wise of the Lewis Flight Propulsion Laboratory of the National Advisory Committee for Aeronautics in Cleveland, Ohio, for supplying us with pure samples of *o*-methyl-, *m*-methyl-, *o*-ethyl-, *m*-ethyl- and *o*-isopropylbiphenyl. We also wish to thank Ernest Yeager for his advice in the performance of the infrared work described.

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The Effect of Ring Formation on Optical Rotatory Power. A Comparison of the Optical Rotations of 2-Phenylcyclopentanone and of Some Acyclic α-Phenyl Ketones

By Kurt Mislow and Charles L. Hamermesh

2-Phenylcyclopentanone has been resolved *via* its tartramazone. The extraordinarily high value of the specific rotation of this ketone, $[\alpha]^{28}$D $+4190°$ (cyclohexane), is five to ten times larger than that of any of ten acyclic analogs, whose maximum rotations have been established in this work. A convincing demonstration has thus been provided that ring formation results in an enhancement of optical activity.

While the problem of optical rotatory power may be regarded, in principle, as solved,[1,2] very few simple empirical generalizations are known which make possible predictions of rotatory power from an *a priori* inspection of over-all structural features. One of the most consistently successful such rules had already been noted by van't Hoff,[3] who remarked that "the interaction of the several groups, r_1, r_2, r_3 and r_4 attached to the asymmetric carbon atom which may be accompanied by ring formation, appears to have quite an extraordinary influence on the magnitude of the sign of the rotation." This effect on rotatory power of ring formation has been noted in miscellaneous instances, such as in comparisons of hydroxy acids with their lactones,[4] of diesters with cyclic ketoesters derived therefrom,[5] of acyclic with cyclic amino acids,[6] of alkylsuccinic and alkylglutaric acids with their anhydrides,[7] of polyols with (cyclic) aldohexoses and aldopentoses[2] and of 3-methylpentanal with 3-methylcyclopentanone.[2] Unfortunately, in none of the cited cases are comparisons entirely satisfactory: either new asymmetric atoms are introduced, or the functional groups are considerably different in the compared systems. Nevertheless the trend is unescapable, and it is a generally accepted dictum, based on firm theoretical grounds, that ring formation enhances the rotatory power approximately tenfold.[2]

The present investigation was initiated with a view toward subjecting this generalization to a somewhat more systematic experimental scrutiny. The choice of the system to be studied, the α-phenyl ketones, was motivated by the convenience entailed in determining the maximum rotations of the acyclic members of the series (*vide infra*), while the selection of a five-membered ring for the cyclic ketone was principally governed by the consideration that an observed effect might be more pronounced in the cyclopentane than in the cyclohexane system: the rotation of 3-methylcyclopentanone[8] considerably exceeds that of 3-methylcyclohexanone.[9]

Ten unbranched acyclic α-phenyl ketones (I), containing a total of four to seven atoms in the straight-chain portion of the molecule, were studied for purposes of comparison of optical rotatory power with 2-phenylcyclopentanone. These ketones, prepared by the reaction of partially resolved acids II and alkyllithium III frequently were contaminated with tertiary carbinols, formed by further reaction of I and III.[10] Purification of the ketones involving negligible racemization could be effected through hydrolysis of the recrystallized semicarbazones in a refluxing ligroin–dilute hydrochloric acid mixture. The physical and optical properties of the ten ketones thus prepared are listed in Table I.

$$RCH(C_6H_5)COOH + R'Li \longrightarrow RCH(C_6H_5)COR'$$

$$\text{II} \qquad\qquad \text{III} \qquad\qquad \text{I}$$
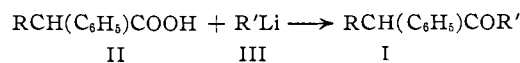
Since partial racemization accompanies the preparation of I,[11] the optical purity of I was judged by comparison with that of V, obtained by the stereospecific[11] perbenzoic acid oxidation of I to ester IV, followed by hydrolysis to V. Results of the oxidation–hydrolysis are reported in Table II, while cal-

(1) E.g., J. G. Kirkwood, J. Chem. Phys., **5**, 479 (1937); E. U. Condon, Rev. Modern Phys., **9**, 432 (1937); E. Hückel, Z. Elektrochem., **50**, 13 (1944); W. Kuhn, ibid., **56**, 506 (1952); G. W. van Vloten, Chem. Weekblad, **48**, 977 (1952); T. R. Thomson, This Journal, **75**, 6070 (1953).

(2) W. J. Kauzman, J. E. Walter and H. Eyring, Chem. Revs., **26**, 339 (1940); cf. especially p. 376 ff.

(3) J. H. van't Hoff, "The Arrangement of Atoms in Space," 2nd ed. (translated by A. Eiloart), Longmans, Green and Co., London, 1898, p. 146.

(4) I. I. Kutyukov, Bull. Siberian Inst. Tech., **50**, no. 2 (1929); C. A., **24**, 2978 (1930); D. M. Bovey and E. E. Turner, J. Chem. Soc., 3223 (1951); J. A. Reid and E. E. Turner, ibid., 3219 (1951).

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