[CONTRIBUTION FROM THE CHEMISTRY DIVISION, OAK RIDGE NATIONAL LABORATORY, AND THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TENNESSEE]

A Reinvestigation of the Alkaline Cleavage of α-Arylbenzoins[1]

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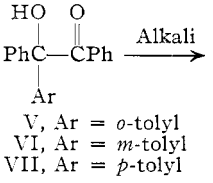
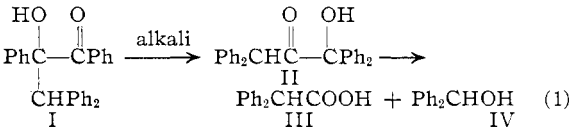
A reinvestigation of the work of Sharp and Miller (ref. 7) has disclosed that the "α-*o*-tolylbenzoin" (supposedly compound V) described by these and other investigators (ref. 10) is, in fact, α-phenyl-2-methylbenzoin (XIX). In addition to compound XIX, the addition of *o*-tolylmagnesium bromide to benzil yields authentic α-*o*-tolylbenzoin (V). The structures of XIX and V were proven by chemical means. Compound V, upon treatment with boiling, ethanolic alkali is converted to α-phenyl-2-methylbenzoin (XIX) which, in turn, is cleaved to benzhydrol and *o*-toluic acid. The additions of *m*-tolyl and of *p*-tolylmagnesium bromide to benzil have been shown also to yield both the normal and the rearranged α-arylbenzoins. Carbonyl-labeled α-phenylbenzoin undergoes alkaline cleavage to benzhydrol and benzoic acid with 3% rearrangement of the carbon-14 label; whereas under similar conditions, labeled α-anisoylanisoin (XXIXa) is incompletely cleaved and undergoes 66% rearrangement. The mechanism of the alkaline cleavage of triarylketols is discussed.

In previous papers[3] several examples of acid-catalyzed rearrangements of the carbon skeleton of the 1,1,2-triphenylethyl system have been discussed. Both single and multiple-labeling techniques with carbon-14 have been fruitful in studying the mechanisms of (a) the Wagner–Meerwein rearrangement of 1,2,2-triphenylethanol and its derivatives[3a,c,d]; (b) the semi-pinacolic dehydrobromination of 2-bromo-1,1,2-triphenylethanol[3b]; (c) the pinacol rearrangement of triphenylethylene glycol[3c]; and (d) the deamination of 1,1,2-triphenyl-2-aminoethanol.[3f] The present paper is concerned with the base-catalyzed rearrangements of 1,1,2-triphenyl-2-ketoethanol (α-phenylbenzoin, XV) and related compounds.

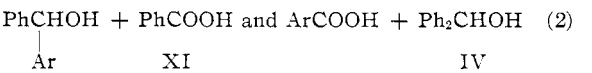


V, Ar = *o*-tolyl
VI, Ar = *m*-tolyl
VII, Ar = *p*-tolyl

Rearrangements of α-ketoalcohols (acyloins and benzoins) are known to occur in the presence of alkali.[4] Alkali is known also to cleave these systems to carbinols and acids.[5] In some cases rearrangement and cleavage reactions occur consecutively in the same medium, a phenomenon illustrated by equation 1 and first observed by Curtin and Leskowitz.[6] These workers demonstrated the rearrangement by isolation of α-hydroxydibenzhydryl ketone (II), diphenylacetic acid (III) and benzhydrol (IV) from treatment of α-benzhydrylbenzoin (I) with alkali.



Sharp and Miller have made the claim that rearrangements occur during the alkaline cleavage of other α-substituted benzoins[7] (V, VI and VII, equation 2). Our interest in these rearrangements was derived from certain anomalies in the stoichiometry[8] reported by Sharp and Miller, and from their statement[7] that "detection of rearrangement is impossible" during the alkaline cleavage of α-phenylbenzoin (XV). The extent of rearrangement during alkaline cleavage of α-phenylbenzoin



VIII, Ar = *o*-tolyl
IX, Ar = *m*-tolyl
X, Ar = *p*-tolyl

XII, Ar = *o*-tolyl
XIII, Ar = *m*-tolyl
XIV, Ar = *p*-tolyl

(XV) has now been determined by the series of reactions outlined in Chart I. By the method of Biltz,[9] benzhydryl phenyl ketone-C^{14} was converted

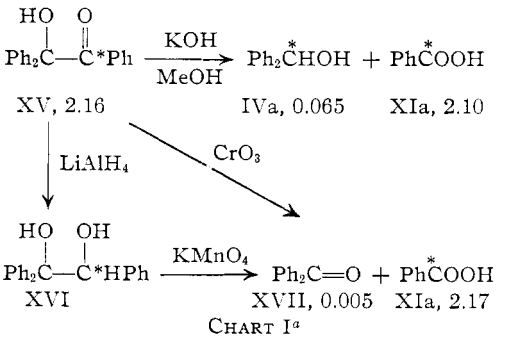


CHART I[a]

[a] Molar radioactivity of compounds expressed as millicuries.

to carbonyl-labeled α-phenylbenzoin (XV). This product XV was shown to be discretely labeled by conversion to 1,2,2-triphenylethylene-1-C^{14} glycol (XVI) followed by permanganate oxidation of the glycol to non-radioactive benzophenone (XVII) and labeled benzoic acid (XIa). Alkaline cleavage of the ketol (XV, 2.16 mc./mole) with potassium

(1) This paper is based in part upon work performed under Contract No. W-7405-eng-26 for the Atomic Energy Commission. This paper is Part VII in the Molecular Rearrangement Series Part VI, H. J. Schaeffer and C. J. Collins, THIS JOURNAL, **78**, 124 (1956), and contribution No. 149 fron the Department of Chemistry, University of Tennessee.

(2) (a) Research Participant at Oak Ridge National Laboratory, June-September, 1954 and 1955; (b) University of Tennessee; (c) Oak Ridge National Laboratory.

(3) (a) W. A. Bonner and C. J. Collins, THIS JOURNAL, **75**, 5372 (1953); (b) C. J. Collins and W. A. Bonner, *ibid.*, **75**, 5379 (1953); (c) C. J. Collins and W. A. Bonner, *ibid.*, **77**, 92, 6725 (1955); (d) W. A. Bonner and C. J. Collins, *ibid.*, **77**, 99 (1955); (e) C. J. Collins, *ibid.*, **77**, 5517 (1955); (f) H. J. Schaeffer and C. J. Collins, 6th Annual Southeastern Regional Meeting of the American Chemical Society, Birmingham, Alabama, 1954.

(4) The acyloin rearrangement has been extensively applied with steroids. For several examples see C. W. Shoppee and E. Shoppee in Rodd's "Chemistry of Carbon Compounds," Vol. IIB, Elsevier Publishing Co., London, 1953, p. 925.

(5) S. F. Acree, *Am. Chem. J.*, **29**, 588 (1903).

(6) D. Y. Curtin and S. Leskowitz, THIS JOURNAL, **73**, 2633 (1951); *cf.* also D. Y. Curtin and A. Bradley, *ibid.*, **76**, 5778 (1954).

(7) D. B. Sharp and E. L. Miller, *ibid.*, **74**, 5643 (1952).

(8) For example, alkaline cleavage of 28.3 moles of benzoin itself was reported to yield 32.3 moles of acids, benzoic and formic. This is a yield of 113%.

(9) H. Biltz, *Ber.*, **32**, 655 (1899).

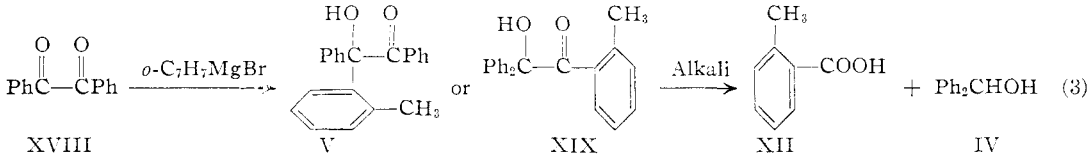
hydroxide in methanol produced benzhydrol (IVa, 0.07 mc./mole) and benzoic acid (XI, 2.10 mc./mole). From these data it can be seen that rearrangement during the alkaline cleavage of α-phenylbenzoin occurs to the extent of only a few per cent.

In two of the cases reported by Sharp and Miller (the rearrangements of VI and VII)[7] uncharacterized oils were used as starting materials. A third α-arylbenzoin, however, was a crystalline material of m.p. 116–117°, presumed from its mode of formation to be α-*o*-tolybenzoin (V). This material had been prepared by the addition of *o*-tolylmagnesium bromide to benzil by Roger and McGregor,[10] who cleaved the product with alkali (equation 3) to obtain *o*-toluic acid (XII) and benzhydrol (IV), rather than the expected phenyl-*o*-tolylcarbinol and benzoic acid. Sharp and Miller repeated the Grignard preparation and cleavage reaction with the same results as Roger and McGregor (*cf.* ref. 6). The foregoing facts led us to the conclusion that the material of m.p. 116–117° is not α-*o*-tolylbenzoin (V) but is instead an isomer, α-phenyl-2-methylbenzoin (XIX).[11] We have now repeated the addition of *o*-tolylmagnesium bromide to benzil, and have confirmed this conclusion. In several experiments we obtained yields (30% or less) of the previously isolated compound[7,10] of m.p. 116–117° which has now been shown to possess structure XIX. However the major portion of the reaction product, not previously isolated, is an isomer of m.p. 82–83°, and possessing structure V.[12] The structure XIX of the isomer of m.p. 116–117° follows from the reactions outlined in Chart II. Thus, this minor reaction product XIX from (a) addition of *o*-tolylmagnesium bromide to benzil, is the same as the product from (b) addition of *o*-tolylmagnesium bromide to methyl benzilate and (c) addition of phenylmagnesium bromide to 2-methylbenzil. This product XIX has been reduced to a known glycol (XXII)[13] and oxidized to benzophenone (XVII)[7] and *o*-toluic acid (XII). The ultraviolet spectrum of this product XIX, α-phenyl-2-methylbenzoin, compared with that of phenylbenzoin (Fig. 1) shows the steric inhibition of resonance expected for the 2-methyl group.[14]

The structure V of the isomer of m.p. 82–83° follows from the reactions outlined in Chart III. This product V has been reduced to a glycol (XXXIII) which in turn has been oxidized to 2-methylbenzophenone (XXIV) and benzoic acid (XI). The ultraviolet spectrum (Fig. 1) of this product V, α-*o*-tolylbenzoin, is quite distinct from that of its isomer XIX, α-phenyl-2-methylbenzoin, but similar to that of phenylbenzoin. Upon treatment with alkali, α-*o*-tolylbenzoin undergoes rearrangement to α-phenyl-2-methylbenzoin (XIX), which is cleaved to benzhydrol (IV) and to *o*-toluic acid (XII) without further rearrangement.

From the foregoing results it seems likely that the additions[7] of *m*-tolylmagnesium bromide and of *p*-tolylmagnesium bromide to benzil proceed with some rearrangement, and that the product in each case is a mixture of the two possible isomeric α-arylbenzoins (equation 4). This would explain earlier observations[7,10] that these two products are non-crystalline and that each is cleaved by alkali to four products (two carbinols, two acids).

The additions of the *m*- and *p*-tolyl Grignard reagents to benzil (equation 4, Ar = *m*- and *p*-tolyl) have been repeated and each of these two non-crystalline products has been oxidized with chromic acid. From the neutral fraction from each



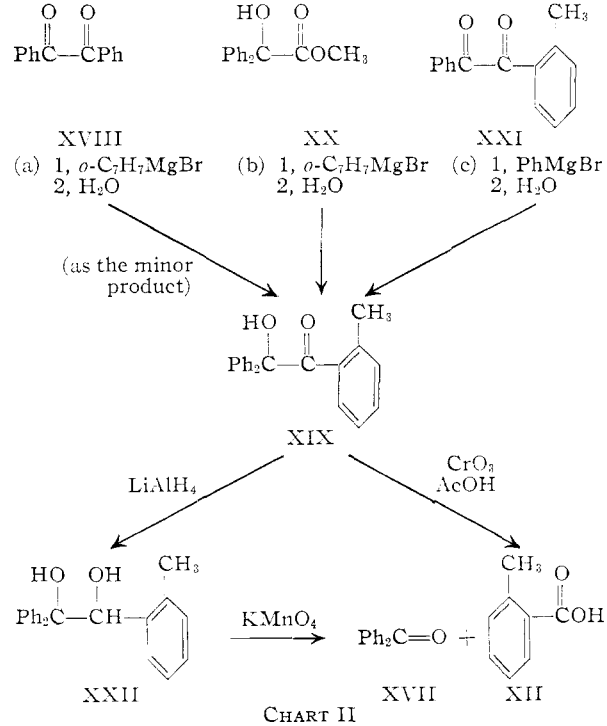


CHART II

(10) R. Roger and A. McGregor, *J. Chem. Soc.*, 442 (1934).

(11) W. E. Bachmann, THIS JOURNAL, **54**, 2112 (1932).

(12) The yields of the normal addition product V and the abnormal addition product XIX may vary considerably. In one experiment, for example, V was formed in 66% yield, whereas there was no significant amount (less than 1%) of the abnormal product XIX, as demonstrated by the carbon-14 dilution technique [R. H. Mayor and C. J. Collins, *ibid.*, **73**, 471 (1951)]. This experience was repeated in several other cases of the addition of phenyl or substituted phenyl Grignard reagents to benzil or to substituted benzils. For example, in the addition of phenyl-C^{14}-magnesium bromide to benzil, one experiment yielded α-phenylbenzoin which possessed a statistical distribution of the label among the three phenyl groups; another experiment yielded α-phenylbenzoin which had been formed without rearrangement. It is not possible to state at present how these rearrangements are controlled, or whether they occur during the Grignard addition, or in the subsequent work up. This rearrangement reaction is being investigated and will be the subject of a forthcoming paper.

(13) R. Roger and F. C. Harper, *Rec. trav. chim.*, **56**, 202 (1937).

(14) *Cf.* G. D. Heddon and W. G. Brown, THIS JOURNAL, **75**, 3744 (1953).

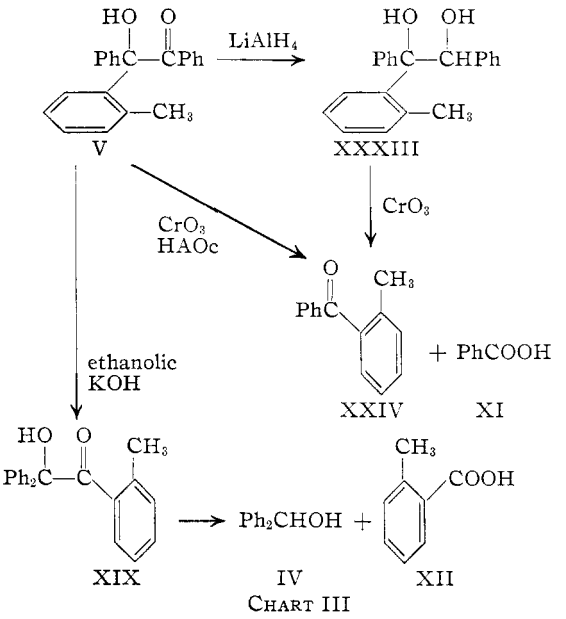
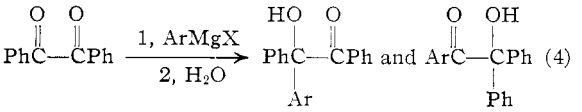


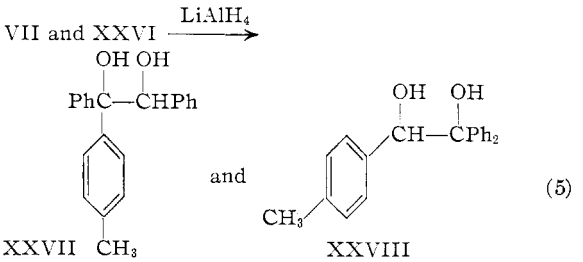
CHART III

oxidation the 2,4-dinitrophenylhydrazone of benzophenone was prepared.[15] The Grignard reactions



XVIII VI, Ar = *m*-tolyl XXV, Ar = *m*-tolyl
VII, Ar = *p*-tolyl XXVI, Ar = *p*-tolyl

of equation 4 must therefore have proceeded with some rearrangement. The yield of benzophenone derivative was less than 10% in each case. An exact measure of the extent of rearrangement in the addition of *p*-tolylmagnesium bromide to benzil was obtained by reduction of the crude product to a mixture of glycols, equation 5. The unrearranged glycol XXVII could be isolated from the



mixture by crystallization. The rearranged glycol XXVIII was shown by the isotopic dilution technique[12] to constitute 7.5% of the mixture.

One more example of the alkaline rearrangement–cleavage reaction has been studied, that of α-anisylanisoin XXIX. It seemed likely that the decreased reactivity of the carbonyl group in this case would slow the cleavage reaction (6) and allow the rearrangement reaction (7) to proceed to a greater extent. Labeled anisylanisoin (XXIXa) was prepared as shown in Chart IV and a sample treated with methanolic alkali for six hours.

(15) Conditions for oxidation were those used by Sharp and Miller[7] on the mixed products of alkaline cleavage of these oils. *p*-Benzoylbenzoic acid subjected to these conditions did not undergo decarboxylation.

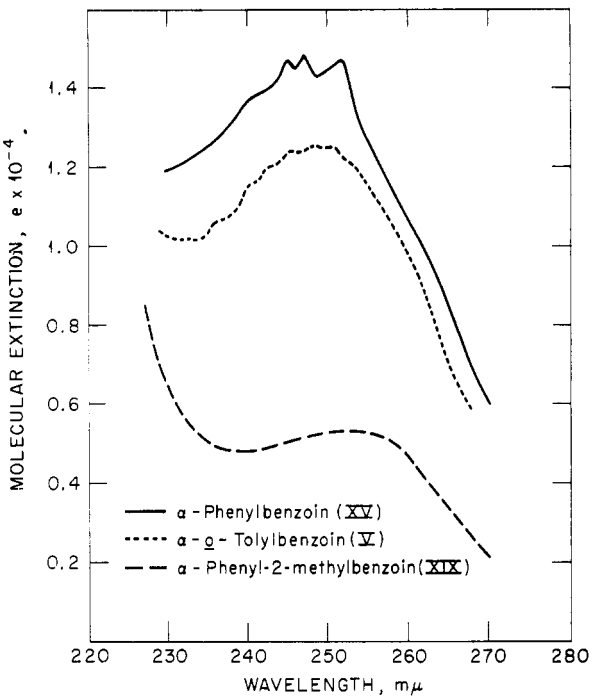


Fig. 1.

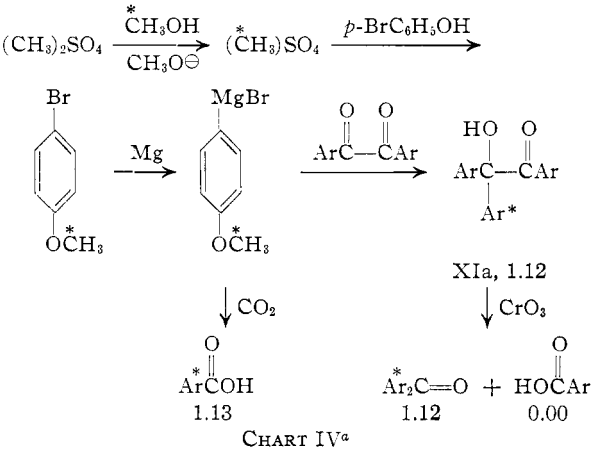
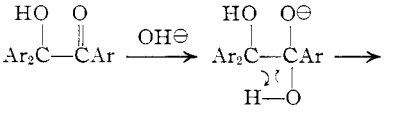
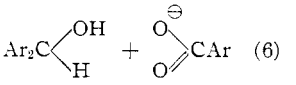


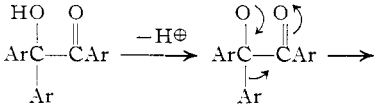
CHART IV[a]

[a] Molar radioactivity expressed as millicuries.

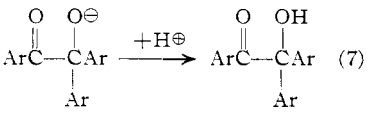


XXIX, Ar = *p*-anisyl XXX

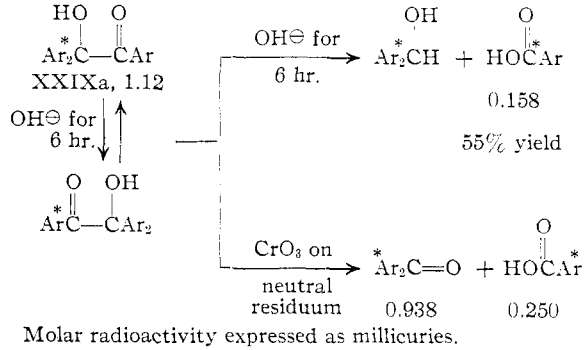




XXIX, Ar = *p*-anisyl XXXI



The amount of anisic acid produced during this time was taken as a measure of the extent of cleavage. The neutral residuum, consisting of the cleavage-produced carbinol and uncleaved ketol, was oxidized with chromium trioxide. The activity of the anisic acid produced by oxidation was taken as a measure of the rearrangement in the ketol. The results are summarized in Chart V. Under con-



Molar radioactivity expressed as millicuries.

CHART V

ditions which caused the complete cleavage of the triphenyl ketol in two hours, the trianisyl ketol was only 55% cleaved after six hours. During this time the uncleaved material had approached complete rearrangement (statistical redistribution of the anisyl groups) 66% of the way. Rearrangement in the cleaved material had, of course, proceeded to a lesser extent, about 47%.[16]

To explain the difference between α-phenylbenzoin (XV) and its tri-*p*-methoxy derivative XXIX it seems useful to compare the rearrangement reaction with the pinacol rearrangement and the cleavage reaction with the benzilic acid rearrangement. Cleavage (equation 6) involves hydroxide attack on the carbonyl group, as in the benzilic acid rearrangement. From its large negative sigma value (Hammett function) a *p*-methoxy group would be expected to slow such nucleophilic attack, as it does in the benzilic acid rearrangement.[17] Rearrangement (equation 7) involves migration of an aryl group with its bonding electrons; introduction of a *p*-methoxy group should facilitate this migration as it does in the pinacol rearrangement.[18,19]

To explain the difference between α-phenylbenzoin and its two *o*-methyl derivatives (V and XIX) the mechanisms shown in equations 6 and 7 are similarly useful. As stated (Chart III), the cleavage products from treatment of α-*o*-tolylbenzoin (V) with alkali are toluic acid and benzophenone, rearrangement products. Rearrangement of this arylbenzoin in base obviously occurs much more rapidly than does cleavage. The latter reaction (6) with α-*o*-tolylbenzoin (V) should logically be slowed by steric compression developed by the *o*-methyl group in the intermediate needed (*cf.* XXX); the rearrangement reaction (7) on the other hand should be facilitated by the steric effect, since migration of a phenyl group (*cf.* XXXI) would leave the *o*-tolyl group on a trigonal carbon atom relieving considerable compression. The cleavage[7,10] of the isomeric α-phenyl-2-methylbenzoin (XIX) without rearrangement follows consistently with this reasoning.

In summary, the data collected show that α-phenylbenzoin (XV) itself rearranges less during alkaline cleavage than either its tri-*p*-methoxy derivative XXIX or its α-*o*-methyl derivative V, but more than its 2-*o*-methyl derivative XIX. These data on the alkaline treatment of the four α-arylbenzoins (V, XV, XIX, XXIX) can be correlated by comparison of their cleavage (equation 6) with the benzilic acid rearrangement and their rearrangement (equation 7) with the pinacol rearrangement.

Experimental[20]

α-Phenylbenzoin, Carbonyl-labeled (XV).—To a hot solution of 8.00 g. of phenyl benzhydryl ketone-C^{14} (2.161 mc./mole)[21] in 36 ml. of glacial acetic acid in an open erlenmeyer flask there was added 10.1 ml. of concentrated nitric acid in one portion. The solution was gently boiled in the open flask for 30 minutes during which time considerable nitrogen oxide escaped. The cooled solution was poured onto ice and the resulting mixture was extracted with ether. The ether solution was washed with dilute aqueous base, dried over sodium sulfate and evaporated to leave a yellow oil. The desired product could be leached from this oil with hot hexane leaving an uncharacterized amorphous yellow solid. Dilution of the hot hexane with benzene and slow cooling yielded 6.1 g. of pale yellow crystals, m.p. 84–86°. Recrystallization gave colorless α-phenylbenzoin-*carbonyl*-C^{14} (XV), m.p. 87.5–89° (reported[22] 87–88°), 2.163 mc./mole. Procedure was adapted from that of Biltz.[9]

1,1,2-Triphenylethylene-1-C^{14} Glycol (XVI).—A solution of 0.20 g. of arylbenzoin XV (carbonyl-labeled, 2.163 mc./mole) and 0.1 g. of lithium aluminum hydride in 20 ml. of ether was refluxed for one hour, to yield 1,2,2-triphenylethylene-1-C^{14}-glycol (XVI). The recrystallized yield was 0.18 g., m.p. 166.5–167.5°, undepressed by authentic material prepared by addition of phenylmagnesium bromide to benzoin.

Oxidation of α-Phenylbenzoin.—A 0.20-g. sample of the phenylbenzoin (XV, carbonyl-labeled, 2.163 mc./mole) was dissolved in five ml. of acetic acid and treated with 0.090 g. of chromium trioxide in a few drops of water. The resulting solution was kept at 15° for one hour, diluted with 20 ml. of water and extracted with ether. The ether solution was washed with water, extracted with alkali, dried and evaporated. The residual benzophenone was characterized as its 2,4-dinitrophenylhydrazone, m.p. 239–239.5° (radioactivity assay, *ca.* 0.005 mc./mole). The aqueous alkaline extract from the oxidation was made acidic with sulfuric acid and extracted with ether. Washing, drying and evaporating the ether left crude crystalline benzoic acid. Recrystallization from water and sublimation gave 48 mg. of the pure acid, m.p. 121–123°, 2.176 mc./mole.

Oxidation of 1,1,2-Triphenylethylene-1-C^{14} Glycol.—This oxidation was carried out with permanganate as described

(16) Cleavage or oxidation of a triaryl ketol of activity *m* randomly distributed in the aryl groups would yield an aromatic acid of activity *m*/3.

(17) J. H. Blanksma and W. H. Zaaiger, *Rec. trav. chim.*, **57**, 883 (1938); J. D. Roberts, D. R. Smith and C. Lee, THIS JOURNAL, **73**, 619 (1951); M. T. Clark, E. C. Hendley and O. K. Neville, *ibid.*, **77**, 3280 (1955).

(18) G. W. Wheland, "Advanced Organic Chemistry," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1949, p. 515.

(19) The decreased reactivity in the anisoyl type carbonyl need not profoundly affect the rearrangement reaction since all energy lost by interruption of the original carbonyl's conjugation is regained by formation of an identical new conjugated carbonyl. This is not true in the cleavage reaction.

(20) Melting points are reported uncorrected. Radioactivity determinations were performed in the usual manner [C. J. Collins, THIS JOURNAL, **70**, 2419 (1948)] using the vibrating-reed electrometer. Assays of individual compounds were reproducible to approximately ±0.5%.

(21) W. A. Bonner and C. J. Collins, *ibid.*, **75**, 5372 (1953).

(22) S. F. Acree, *Ber.*, **37**, 2753 (1904).

previously.[3c,d,e] From the alkali-insoluble residue was prepared the 2,4-dinitrophenylhydrazone of benzophenone, m.p. 238–239° (undepressed by an authentic sample), <0.01 mc./mole.[23]

Alkaline Cleavage of α-Phenylbenzoin (XV).—A solution of 0.400 g. of α-phenylbenzoin (XV, carbonyl-labeled, 2.163 mc./mole), 0.8 g. of potassium hydroxide and 12 ml. of water in 16 ml. of methyl alcohol was refluxed for two hours. The solution was concentrated under reduced pressure, diluted with water, and extracted with ether. (For work up of the basic aqueous solution, see next paragraph.) The ether solution was washed with dilute acid and with brine, filtered and evaporated to leave 0.233 g. of crude, crystalline benzhydrol. Vacuum sublimation gave pure benzhydrol, m.p. 66–68°, 0.0661 mc./mole. A portion of the benzhydrol was oxidized with chromium trioxide in acetic acid to benzophenone which was characterized as its 2,4-dinitrophenylhydrazone, m.p. 238–239°, 0.0648 mc./mole.

The aqueous alkaline solution, remaining from the above removal of benzhydrol, was made acidic with sulfuric acid and extracted with ether. The ether solution was washed, dried, and evaporated to leave 180 mg. of crude crystalline benzoic acid. Purification by recrystallization from water and vacuum sublimation gave pure benzoic acid, m.p. 122–124°, 2.097 mc./mole.

Grignard Preparations of α-Phenyl-2-methylbenzoin (XIX)

(a) Addition of *o*-Tolylmagnesium Bromide to Benzil.—The procedure of Roger and McGregor[10] was followed as closely as possible. The crude product was distilled and from the fraction distilling at 200–225° (*ca.* 1 mm.) α-phenyl-2-methylbenzoin (VI) crystallized. Residual oil in the fraction was removed by trituration with benzene–hexane (1:10) and the product was recrystallized from benzene–hexane to give material with m.p. 116–117° as reported.[10] By this process yields of 30% or less of the α-phenyl-2-methylbenzoin were obtained. Isolation of α-*o*-tolylbenzoin (I) from the same reaction is described below.

(b) Addition of *o*-Tolylmagnesium Bromide to Methyl Benzilate.—This preparation differed from that of Bachmann[11] only in the inverse mixing of ester and Grignard reagent, which apparently results in a better yield of ketol. From 4.8 g. of methyl benzilate and 3.5 g. of *o*-bromotoluene there was obtained 3.9 g. of recrystallized α-phenyl-2-methylbenzoin, m.p. 116–117°, undepressed by material prepared by method (a) above.

(c) Addition of Phenylmagnesium Bromide to 2-Methylbenzil.—To a stirred solution of 0.9 g. of 2-methylbenzil[24] in ether there was added dropwise a filtered ethereal solution of 4.4 moles of phenylmagnesium bromide. The reaction mixture was poured onto an ice–ammonium chloride mixture and the ether layer worked up in the usual manner. The crude product was crystallized from benzene–hexane to give 0.5 g. of material whose m.p. was 115–116.5°, undepressed by α-phenyl-2-methylbenzoin prepared by either of the above methods.

α-*o*-Tolylbenzoin (V).—An ether solution of *o*-tolylmagnesium bromide prepared from 73 g. of bromotoluene and 12.2 g. of magnesium turnings was added slowly to 105 g. of benzil dissolved in ether. The addition product was cooled in an ice-bath and decomposed with dilute HCl and ice. The semi-crystalline residue obtained from the ether layer was crystallized twice from methanol to yield 76 g. of pale yellow crystals, m.p. 60–70°. The crude product (40 g.) was distilled through a 10-inch Vigreux column; 30 g. distilled 187–190° (*ca.* 0.5 mm.). Seven grams of the distillate was recrystallized five times from hexane to yield colorless α-*o*-tolylbenzoin (V), m.p. 82–83°. The yield of V in this particular run, as determined by the isotopic dilution method, was 66% based on unrecovered benzil. The yield of XIX by the same method was negligible (1.1%).[25]

Calcd. for $C_{21}H_{18}O_2$: C, 83.42; H, 6.00. Found: C, 83.54; H, 6.06.

Oxidation of α-*o*-Tolylbenzoin (V).—A solution of 5.00 g. of V in 40 ml. of acetic acid was heated on the steam-bath during the addition of 10.0 g. of chromium trioxide in a little water. One ml. of 70% sulfuric acid was added and the mixture was kept at steam-bath temperature for an additional hour. The solution was poured onto 100 g. of ice and worked up in the usual manner. The ethereal solution remaining after the extraction of benzoic acid was evaporated and the residual 2-methylbenzophenone was converted to its 2,4-dinitrophenylhydrazone. The crude hydrazone, 1.97 g., was recrystallized three times from a tetrahydrofuran–ethanol mixture to yield the pure 2,4-dinitrophenylhydrazone, m.p. 183–184°, undepressed by admixture with an authentic sample.

Reduction of α-*o*-Tolylbenzoin (V).—An ether solution of 1.00 g. of the ketol V was reduced with lithium aluminum hydride. The reduction product, isolated in the usual manner, weighed 1.00 g., m.p. 120–130°. The crude glycol was recrystallized five times from benzene–hexane to yield 1,2-diphenyl-1-*o*-tolylethylene glycol, m.p. 144–145°. This melting point was depressed by the addition of the diastereomeric 1,2-diphenyl-1-*o*-tolylethylene glycol, m.p. 157–158°, prepared by adding *o*-tolylmagnesium bromide to benzoin.[26]

Calcd. for $C_{21}H_{20}O_2$: C, 82.85; H, 6.62. Found: C, 82.55; H, 6.64.

Oxidation of 1,2-Diphenyl-1-*o*-tolylethylene Glycol (XXIII).—A 0.838-g. sample of glycol XXIII and 0.260 g. chromium trioxide in 12 ml. of acetic acid was heated for one hour on the steam-bath; the acid and neutral fractions were recovered as described for other chromic acid oxidations reported in this paper. The yield of crude benzoic acid was 0.100 g., m.p. 110–115°. Purification by vacuum sublimation gave pure benzoic acid, m.p. 122–123°. The 2-methylbenzophenone fraction was converted to 0.653 g. of its 2,4-dinitrophenylhydrazone. Three recrystallizations from ethyl acetate–ethanol gave 0.2 g. of the 2,4-dinitrophenylhydrazone, m.p. 183–186°, undepressed by admixture with an authentic sample.

Alkaline Cleavage of α-*o*-Tolylbenzoin (V).—A solution of 5.000 g. of α-*o*-tolylbenzoin, 150 ml. of methyl alcohol, 10.0 g. of potassium hydroxide and 150 ml. of water was refluxed gently for three hours. The solution was concentrated under reduced pressure, diluted with water and extracted with ether and worked up as described in the next paragraph. Evaporation of the ether extract left 3.626 g. of neutral residue which was partially sublimed *in vacuo* to yield a small amount of crude, crystalline benzhydrol, m.p. 58–60°. After four crystallizations from light petroleum ether this material had an m.p. of 67–68°, undepressed on mixing with an authentic sample of benzhydrol. The residual oil from the partial sublimation of benzhydrol was crystallized four times from hexane to yield 0.55 g. of the rearranged benzoin (XIX), m.p. 114–115°, undepressed on mixing with an authentic sample of α-phenyl-2-methylbenzoin.

The aqueous alkaline solution remaining after removal of the neutral fraction was acidified with hydrochloric acid and extracted with ether. Upon evaporation of the ether there remained 1.628 g. of pale yellow crystals, m.p. 86–90°. *o*-Toluic acid was found to be present therein to the extent of 86% as determined by the isotopic dilution method.[25]

Oxidation of α-Phenyl-2-methylbenzoin (XIX).—This was oxidized in the same way as compound XV. Thus a solution of 0.339 g. of ketol XIX in 4 ml. of acetic acid was treated with a solution of 0.074 g. of chromium trioxide in a few drops of water. The benzophenone was characterized as its 2,4-dinitrophenylhydrazone, twice recrystallized yield 0.221 g., m.p. 238–239° alone or admixed with an authentic sample. After recrystallization and sublimation the yield of *o*-toluic acid was 0.082 g., m.p. 104–105°, undepressed by an authentic sample.

Reduction of α-Phenyl-2-methylbenzoin (XIX).—A solution of 0.51 g. of the ketol VI in 10 ml. of ether was reduced with 0.4 g. of lithium aluminum hydride in 20 ml. of ether to yield 0.38 g. of glycol XXII, m.p. 126–127° (lit.[13] 125.6°).

Oxidation of Glycol XIX.—A solution of 0.25 g. of glycol XIX, 0.18 g. of potassium permanganate, five ml. of water and six drops of acetic acid in 20 ml. of acetone was allowed to stand at room temperature for four days. Work up in

(23) In accordance with our previous experience with permanganate oxidation, the acid fraction in this experiment assayed lower in activity than the starting ketol, presumably because of some oxidation of benzophenone to benzoic acid. An interesting finding in this connection was that α-phenylbenzoin was quite stable to the permanganate oxidation conditions which cleaved the glycol (1,1,2-triphenylethylene glycol). Chromium trioxide in acetic acid readily cleaves either compound.

(24) A. McKenzie and A. L. Kelman, *J. Chem. Soc.*, 412 (1934).

(25) For the sake of brevity the details of the isotopic dilution technique employed[12] are given only in the Experimental section dealing with 1,1-diphenyl-2-*p*-tolylethylene glycol (XXVIII). The details in other applications are similar.

(26) R. Roger and W. B. McKay, *J. Chem. Soc.*, 2229 (1934).

the usual manner gave a neutral fraction; benzophenone was characterized as its 2,4-dinitrophenylhydrazone, yield 0.13 g., m.p. 238–239°, undepressed by an authentic sample. Recrystallization of the acid fraction gave 0.053 g. of pure *o*-toluic acid, m.p. 104–105°, undepressed by an authentic sample.

Addition of *m*- and *p*-Tolylmagnesium Bromides to Benzil.—The experimental procedure previously reported[7,9] was followed as closely as possible, except that the initial Grignard addition product, which precipitated and was separated from the supernatant ether solvent, was decomposed with cold ammonium chloride solution. After the run starting with *p*-tolylmagnesium bromide, some starting benzil was removed by vacuum distillation of the oily product, b.p. 195–200° at 0.2 mm. The same procedure was followed for the *m*-isomer, b.p. 175–180° at 0.1 mm.

Oxidation of Product from *p*-Tolylmagnesium Bromide Addition to Benzil.—To a solution of 7.4 g. of the above oily product, obtained from the addition of *p*-tolylmagnesium bromide to benzil, in 29 ml. acetic acid there was added a solution of 14.8 g. of chromium trioxide in 6.5 ml. of acetic acid containing a few drops of water. The mixture was heated two hours on the steam-bath, then diluted with water and extracted with ether. The ether extracts were washed with water and dilute hydrochloric acid and extracted with aqueous sodium carbonate until the aqueous layer was alkaline. After the ether solution was dried and evaporated, there remained approximately 1.2 g. of neutral material. From this there was prepared a 2,4-dinitrophenylhydrazone, m.p. 238–239° with or without admixture of the authentic 2,4-dinitrophenylhydrazone of benzophenone. The weight of sharp melting 2,4-dinitrophenylhydrazone obtained was 0.4 g., which is equivalent to 0.2 g. of benzophenone in the neutral fraction.

A sample of *p*-benzoylbenzoic acid was treated under the conditions described above and worked up in the same manner. No neutral portion was obtained.

Oxidation of Product from *m*-Tolylmagnesium Bromide Addition to Benzil.—A 1.5-g. sample of the oily product obtained from the addition of *m*-tolylmagnesium bromide to benzil was oxidized in the manner described above. Work up yielded a neutral fraction from which 0.21 g. of the 2,4-dinitrophenylhydrazone of benzophenone was prepared.

Reduction of Product from *p*-Tolylmagnesium Bromide Addition to Benzil. (a) Isolation of 1,2-Diphenyl-1-*p*-tolylethylene Glycol (XXVII).—A sample of 1.0 g. of the oily product obtained from the addition of *p*-tolylmagnesium bromide to benzil, 0.4 g. of lithium aluminum hydride and 50 ml. of ether were refluxed two hours. The reaction mixture was carefully treated with dilute acid and the ether layer worked up in the usual manner. When the ether was evaporated, there remained a solid which was recrystallized from ethanol three times to give 0.43 g. of 1,2-diphenyl-1-*p*-tolylethylene glycol, m.p. 184.5°, undepressed by an authentic sample.[26]

(b) Isotopic Dilution with 1,1-Diphenyl-2-*p*-tolylethylene Glycol (XXVIII).—The reduction described in (a) above was repeated and the total crude product carefully vacuum dried. A 0.0975-g. sample of this reduction product was mixed with 0.1928 g. of pure 1,1-diphenyl-2-*p*-tolylethylene glycol (XXVIII), m.p. 194–195°, 3.812 mc./mole.[27] The mixed material was recrystallized three times from ethanol to give 0.107 g. of repurified glycol XXVIII, m.p. 194–195°, 3.667 mc./mole. From these figures it can be calculated that the original sample of crude reduction product was 7.5% glycol XXVIII.[12]

α-(Anisyl-C^{14})-anisoin (XXIXa).—Approximately one millicurie of C^{14}-methanol (about 0.02 ml.) was frozen onto 5 ml. of freshly distilled dimethyl sulfate by standard vacuum line technique. After the solution had warmed to room temperature about 0.03 g. of dry sodium methoxide was added to it and the mixture was heated on the steam-bath for five minutes, then allowed to stand at room temperature for ten days. Two milliliters of the labeled dimethyl sulfate prepared in this manner was diluted to 10 g. with inactive dimethyl sulfate and added dropwise to a solution of 7 g. of sodium hydroxide, and 25 g. of *p*-bromophenol in 60 ml. of water.[28] The reaction mixture was refluxed gently during the addition and for one hour thereafter. The heavy oily product was separated from the cooled reaction mixture and the basic water layer extracted with ether. The combined ether and oily product was washed, dried and distilled to yield 14.6 g. of methyl-labeled *p*-bromoanisole, b.p. 143° (70 mm.).

By standard technique a sample of the *p*-bromoanisole was converted to the Grignard reagent[29] and carbonated to give *p*-anisic acid, m.p. 181–182°, 1.125 mc./mole.

To a refluxing stirred solution of 1.90 g. of anisil and 25 ml. of benzene in 25 ml. of ether there was added the Grignard reagent[29] prepared from 1.84 g. of labeled *p*-bromoanisole in 20 ml. of ether. Precipitation occurred during the addition. The reaction mixture was further stirred for 20 minutes, then poured into saturated aqueous ammonium chloride. The ether layer was washed with more ammonium chloride solution, dried and evaporated to leave a viscous oil which partially crystallized upon standing. The crude product was triturated with a hexane–benzene mixture and recrystallized from methanol to give 1.85 g. of labeled α-anisylanisoin (XXIXa), m.p. 116–117°,[30] 1.116 mc./mole.

Oxidation of α-Anisylanisoin (XXIXa).—A solution of 0.198 g. of XXIXa, 0.048 g. of chromium trioxide and a few drops of water in 4 ml. of acetic acid was heated on the steam-bath for 45 minutes. The reaction mixture was then diluted with ether and separated into acid and neutral fractions. Crystallization of the acid fraction from ethanol–water yielded 0.042 g. of *p*-anisic acid, m.p. 178–180°, 0.01 mc./mole. Crystallization of the neutral fraction from ethanol gave 0.052 g. of 4,4′-dimethoxybenzophenone, m.p. 140–142° (undepressed by an authentic sample), 1.114 mc./mole.

Alkaline Cleavage of α-Anisylanisoin (XXIXa).—A solution of 0.208 g. of XXIXa, 0.6 g. of potassium hydroxide and 6 ml. of water in 10 ml. of oxygen-free methanol was refluxed for six hours. The cooled reaction solution was poured into a mixture of water and ether. (The ether layer containing the neutral fraction was worked up as described in the next paragraph.) The water layer was washed with ether, acidified and extracted with ether. From the ether extractions 0.046 g. of *p*-anisic acid was obtained, recrystallized, m.p. 178–181°, 0.158 mc./mole.

The neutral fraction from the above treatment was obtained by evaporation of its ether solution. The neutral fraction was oxidized with chromium trioxide in acetic acid. After oxidation, the new acid fraction was isolated and recrystallized to give *p*-anisic acid, m.p. 178–181°, 0.250 mc./mole. Crystallization of the final neutral fraction gave 4,4′-dimethoxybenzophenone, m.p. 141–142°, 0.938 mc./mole.[31]

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(27) The authors thank B. M. Benjamin and D. J. Feeney who made available to us their unpublished preparation of 1,1-diphenyl-2-*p*-tolylethylene glycol (X).

(28) *Cf.* S. Natelson and S. P. Gottfried, THIS JOURNAL, **61**, 1001 (1939).

(29) At the completion of reaction between *p*-bromoanisole and magnesium in ether, two liquid layers are present. The lower dark oily layer apparently contains most of the organometallic compound. Although undoubtedly frequently observed, this phenomenon does not appear to have been explained, or even previously reported.

(30) C. W. Shoppee, *J. Chem. Soc.*, 506 (1936).

(31) Since the cleavage acid fraction yield was 55%, the final acid fraction must have been 45% and the total activity in the acid fractions then was (0.55)(0.158) + (0.45)(0.250) = 0.199 mc./mole. This added to the activity in the dimethoxybenzophenone, 0.938 mc./mole, gives a total activity of 1.14 mc./mole. Within experimental error, this value of 1.14 is in good agreement with the 1.12 mc./mole activity of the starting ketol.