uum. The product weighed 1.2 g. (84%). The material can be successfully crystallized from warm nitromethane if the operation is carried out rapidly and in an inert atmosphere; ultraviolet spectrum: max. (log ϵ) 226 (4.51), 400 (4.67); min. 308 (2.67). There also occurs a shoulder at 378 mμ (4.21) and the spectrum "tails off" very slowly; the log ϵ value is still 2.56 at 540 mμ (in which area the curve also appears to have a broad shoulder).

Anal. Calcd. for $C_{13}H_9ClO_4$: ClO_4, 37.6. Found: ClO_4, 37.3, 38.0.

Deep green solutions were also formed when IX was treated with aluminum trichloride in nitrobenzene and with boron trifluoride in ether. Although the development of color probably indicated presence of the perinaphthenylium cation, only intractable materials could be isolated from these reactions.

The perchlorate salt was insoluble in all non-polar solvents; it dissolved in 60% aqueous perchloric acid, and in 35% hydrochloric acid, though the latter solutions became turbid on standing and both did so on dilution.

Reaction of Perinaphthenylium Perchlorate with: (a) **Water.**—The salt (0.47 g.) was added with stirring to a mixture of water (20 ml.) and ethanol (20 ml.). After 10 minutes the mixture was extracted with ether, the ethereal solution then washed and dried. After evaporation of the ether the residue was chromatographed over alumina, eluting first with petroleum ether followed by benzene. The colorless first fraction on evaporation yielded perinaphthene which crystallized from petroleum ether in white needles, m.p. 84°. From alcohol, the compound formed an orange-red picrate, m.p. 120° or 205° depending on the rate of heating.[14] The ultraviolet spectrum of the hydrocarbon was identical to that previously reported.[15]

(14) G. Lock and G. Gergely (*Ber.*, **77**, 461 (1944)) report a value of approximately 110° for the m.p. of this picrate, while V. Boekelheide and C. E. Larrabee (see ref. 4) report a value of 205–207°.

(15) See ref. 7, p. 429.

The yellow benzene eluate gave yellow needles of perinaphthenone (0.17 g.) on evaporation, m.p. 156°. This material dissolved in concentrated hydrochloric acid and could be recovered unchanged on dilution.

Anal. Calcd. for $C_{13}H_8O$: C, 86.7; H, 4.4. Found: C, 86.7; H, 4.2.

(b) **Zinc Dust.**—A freshly prepared sample of the salt (approx. 0.50 g.) was stirred in ether (50 ml.) with zinc dust (5.0 g.) for 20 hours. The ether was evaporated and the residue extracted with boiling benzene (3 × 50 ml.). Evaporation of the benzene afforded crude peropyrene (0.14 g.). The compound was purified by sublimation followed by recrystallization from toluene. The substance dissolved in concd. sulfuric acid to give blue-green solutions. The ultraviolet spectrum in alcohol showed peaks at 230, 264, 277, 310, 324, 366, 388, 410 and 437 mμ, in agreement with the reported values.[18]

Attempted Hunsdiecker Reaction on the Acid IV, R = COOH.—Bromine (3.1 g.) in dry benzene (30 ml.) was added dropwise to a stirred suspension of the silver salt of the acid (6.3 g.) in dry benzene (200 ml.). The mixture was stirred and refluxed for 3 hours. The silver bromide was collected. The residue after evaporation of the benzene was almost completely soluble in sodium hydroxide. It crystallized from ethanol in white prisms, m.p. 220°.

Anal. Calcd. for $C_{14}H_9BrO_2$: C, 58.1; H, 3.1; Br, 27.7. Found: C, 57.9; H, 3.3; Br, 27.2.

The same compound was formed when the acid was treated with bromine in acetic acid. The material would thus appear to be the 5-bromo derivative of the acid IV (R = COOH) though no further work was done on this compound.

Only polymeric material was formed when iodine was substituted for bromine in the above reaction.

(16) See ref. 7, p. 362.

AUSTIN, TEXAS

The Reaction of o-Phenylenediamines with Ketones. V. Further Studies with Dibenzyl Ketones[1,2]

BY ROBERT C. ELDERFIELD AND KENNETH L. BURGESS[3]

RECEIVED JULY 6, 1959

The thermal decomposition of a series of 2-benzyl-2-substituted benzylbenzimidazolines has been investigated. Analysis of the products by vapor phase chromatography or mass spectroscopy with the aid of C^{13} has shown conclusively that the decomposition is not subject to the Hammett equation as previously indicated on the basis of preliminary evidence. A definitive comparison of the accuracy of vapor phase chromatography *versus* use of C^{13} as a tracer in the analysis of mixtures of toluenes has been made. A critical study of optimum methods for the synthesis of a series of substituted phenylacetic acids and of a series of 1,3-diphenyl-2-propanones has been made.

In the preceding paper of this series[4] a study of the thermal cleavage of certain 2,2-dibenzylbenzimidazolines was reported. In particular, attention was devoted to the decomposition of products resulting from condensation of o-phenylenediamine with unsymmetrical dibenzyl ketones as typified by I–IV or I–V.[5]

(1) The material presented in this paper is taken from a dissertation submitted by Kenneth L. Burgess in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the University of Michigan, June, 1957.

(2) This investigation was supported in part by a contribution from Parke, Davis and Co., Inc., to the Michigan Memorial Pheonix Project.

(3) Procter and Gamble Fellow, 1955–1956.

(4) R. C. Elderfield and V. B. Meyer, THIS JOURNAL, **76**, 1887 (1954).

(5) The structure of the condensation products of o-phenylenediamine and the dibenzyl ketones is arbitrarily represented by III for convenience. This is probably an oversimplification. For a detailed discussion of the tautomerism involved see ref. 4.
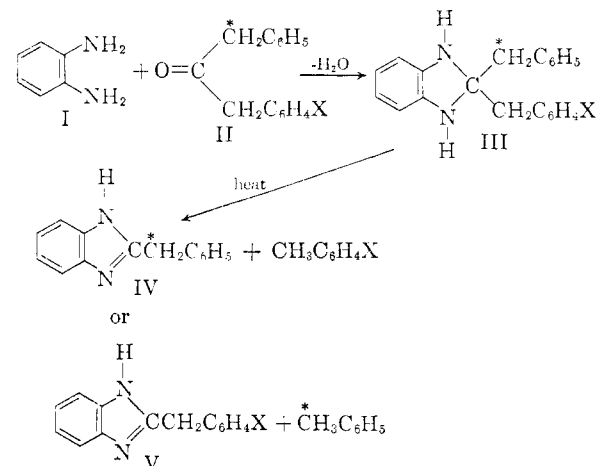
Preliminary evidence was presented that decomposition of III when X was chlorine or methoxyl in the *p*-position was governed by the Hammett σ–ρ equation[6] insofar as the relative amounts of IV and V formed were concerned. In the earlier work analytical methods for the determination of IV and V were admittedly crude and the results reported were strictly tentative. In view of the uncertainty surrounding the mechanism of this interesting reaction which involves rupture of a carbon–carbon bond under relatively mild conditions, it was felt that confirmation of the applicability of the Hammett equation was of vital importance.

We now wish to report a more detailed study of the thermal decomposition of a number of products of the condensation of *o*-phenylenediamine with a series of unsymmetrically substituted 1,3-diphenyl-2-propanones.[7]

For the purpose at hand a series of twelve unsymmetrically substituted 1,3-diphenyl-2-propanones with as wide a range of σ-values as could reasonably be hoped for was selected. These ketones all carried an unsubstituted phenyl group and a phenyl group carrying a single substituent in the *m*- or *p*-position. The six substituents originally chosen were chloro, methoxyl, methyl, methylmercapto, fluoro and carboxamido. During the course of the work it was found that the carboxamido group underwent amide exchange with *o*-phenylenediamine and that reaction of *o*-phenylenediamine with 1-(*m*-mercaptophenyl)-3-phenyl-2-propanone was accompanied by cleavage of the sulfide group. Therefore these three ketones were eliminated from the study, leaving a series of nine.

At the outset it was planned to label the ketones with isotopic carbon at the position indicated by the asterisk in II. Decomposition of the intermediate condensation product in an enclosed system, collection of the mixture of toluenes evolved and determination of the isotope content of the mixture should give an accurate measure of the ratio of toluene to substituted toluene in the mixture. Since it has been shown in the case of the similar reaction with aliphatic ketones that the reaction is first order with respect to the intermediate benzimidazoline,[8] and since it is reasonable to assume that the ratio of the products reflects the relative rates of rupture of the two carbon–carbon bonds undergoing cleavage, it was felt that these data would provide evidence for or against adherence to the Hammett equation. Since a high precision mass spectrometer was available,[9] C^{13} was chosen as the label. About this time the technique of vapor phase chromatography also became practical and this analytical method was used in most runs. However, it was of interest to compare results, using mass spectrographic meth-

ods with those using vapor phase chromatography in a few instances in order to evaluate the relative precision of the two methods.

Materials.—In view of the fact that isotopically labeled ketones were to be used, a detailed study of the synthesis of the 1,3-diphenyl-2-propanones was undertaken. It was concluded that the procedure involving interaction of an appropriately substituted phenylacetyl chloride with benzylcadmium chloride as used by Elderfield and Meyer[4] offered considerable advantages over the procedure of Coan and Becker[10] which involved condensation of benzyl cyanide with a substituted ethyl phenylacetate followed by hydrolysis and decarboxylation.

Considerable difficulty was encountered in obtaining analytically pure samples of certain of the 1,3-diphenyl-2-propanones carrying a *m*-substituent. In contrast to their *p*-isomers, the *m*-substituted ketones are liquids. Repeated distillation gave analytically pure 1-(*m*-fluorophenyl)-3-phenyl-2-propanone and 1-(*m*-methylmercaptophenyl)-3-phenyl-2-propanone. However, distillation, chromatography, conversion to derivatives and regeneration therefrom or washing with acid and base failed to give analytically pure 1-(*m*-chlorophenyl)-3-phenyl-2-propanone, 1-(*m*-methoxyphenyl)-3-phenyl-2-propanone and 1-(*m*-methylphenyl)-3-phenyl-2-propanone. Repeated distillation of these ketones gave fractions with constant refractive indices. Infrared spectra of the ketones in either thick or thin films showed no peaks that could not be attributed to the pure ketone. The molar refractivities were very close to the calculated values. Derivatives prepared from each ketone were analytically pure. It was felt that any trace of impurity not removed by the above methods would have little, if any, effect on the decomposition reaction and they were therefore used.

The unsymmetrically substituted 1,3-diphenyl-2-propanones were characterized in several instances by conversion to the corresponding tetraphenylcyclopentadienones (tetracyclones) by condensation with benzil.[11] However, the *m*-substituted 1,3-diphenyl-2-propanones reacted with benzil with difficulty and the derivatives with 1-(*m*-methylphenyl)- and 1-(*m*-methylmercaptophenyl)-3-phenyl-2-propanone could not be prepared. These refractory ketones were characterized as the semicarbazones or *p*-nitrophenylhydrazones.

The requisite phenylacetic acids were prepared by halogenation of the appropriately substituted toluene to the benzyl halide followed by conversion to the phenylacetonitrile and subsequent hydrolysis, or by application of the Willgerodt reaction.

The intermediate benzimidazolines, in general, were not isolated. These were prepared by reaction of *o*-phenylenediamine with the appropriate 1,3-diphenyl-2-propanone in refluxing benzene which served to remove the water formed by azeotropic distillation. A trace of *p*-toluenesulfonic acid served as catalyst, although this was not essential. Removal of the benzene under reduced pressure left the benzimidazoline as an unstable oil which decomposed on exposure to air or on at-

(6) L. P. Hammett, "Physical Organic Chemistry," McGraw–Hill Book Co., Inc., New York, N. Y., 1940, p. 188.

(7) The Geneva system of nomenclature is used rather than the more convenient dibenzyl ketone nomenclature for facility in naming the isotopically labeled ketones to be discussed.

(8) R. C. Elderfield and J. R. McCarthy, THIS JOURNAL, **73**, 975 (1951).

(9) We wish to acknowledge the coöperation of Professor R. B. Bernstein of this department in placing this instrument at our disposal.

(10) S. B. Coan and E. I. Becker, THIS JOURNAL, **76**, 501 (1954).

(11) W. Dilthey and F. Quint, *J. prakt. Chem.*, [2] **128**, 139 (1930).

tempted purification. The intermediate from 1-(p-chlorophenyl)-3-phenyl-2-propanone was obtained pure. On decomposition it gave the same mixture of toluene and p-chlorotoluene that was obtained with crude 2-(p-chlorophenyl)-2-phenyl-benzimidazoline. Use of unpurified benzimidazolines therefore appeared to be justified in the other decompositions.

Methods.—The apparatus used for the preparation of the intermediate benzimidazolines and subsequent thermal decomposition of them consisted of a 100-ml. round-bottom flask to which was sealed an outer jacket equipped with a reflux condenser. Temperature within the reaction flask was maintained by refluxing a liquid of the desired boiling point in the jacket. The reaction flask was connected to a series of two liquid air traps in a vacuum line which served to condense the volatile reaction products—toluene, substituted toluene and water.

The usual procedure was to place a mixture of equivalent amounts, usually 0.005 mole, of the 1,3-diphenyl-2-propanone and o-phenylenediamine, with or without a catalytic amount of p-toluenesulfonic acid, in the reaction flask. The flask was attached to the vacuum line and evacuated to 140 mm. Constant pressure was maintained by means of a manostat. The system was swept with dry nitrogen for 2 min. Ethylene glycol was refluxed in the heating jacket for 8 hr., during which the pressure was lowered to 0.2 mm. and maintained for one hour. The traps were then isolated from the system, allowed to come to room temperature and the contents washed out with ether when vapor phase chromatography was used for analysis of the mixture of toluenes. When mass spectroscopy was used with the isotopically labeled compounds, the contents of the traps were removed without aid of a solvent.

Some difficulty caused by sublimation of o-phenylenediamine at the start of the reaction was encountered. This was overcome to a considerable extent by carrying out the initial stage of the decomposition at atmospheric pressure. Yields of toluene plus substituted toluene ranged from 70–95% based on reacted starting material.

The apparatus for the vapor phase chromatographic analyses was built in these laboratories.[12] Helium was used as sweep gas and the column consisted of a 20 ft. length of 0.25 in. copper tubing coiled into about a 6 in. spiral. The analyzer was a Gow–Mack thermal conductivity cell. The resistance of the platinum coil in each cell was 22 ± 0.5 ohms. The sample injection system was simply a T fitting at the entrance of the column, one arm of which was closed by a Neoprene gasket through which the sample was injected by means of a hypodermic needle.

The entire apparatus—thermal conductivity cell, column, sample injection system—together with a 500-watt strip heater and thermometer was fastened to a piece of 0.25-in. Transite board and immersed in a 4-quart Dewar flask. A stirrer passed through the Transite cover. After setting

the resistance of the strip heater at a desired point, about 2 hours was required to attain thermal equilibrium.

The conductivity cells were wired as a Wheatstone bridge with a Brown recording continuous balance potentiometer, Minneapolis–Honeywell Co. model 153K17.[13]

The column was packed with partitioning agent before coiling. In all cases except one the packing was Tide. In early runs a special preparation of Tide consisting of about 50% sodium sulfate and 50% sodium dodecylbenzenesulfonate was used.[14] In later runs, it was found that Tide as obtained on the open market was entirely satisfactory. The Tide packing readily separated the mixtures of toluenes encountered, with the exception of toluene and p-fluorotoluene. However, this mixture was easily analyzed over dinonyl phthalate on crushed and screened Johns–Manville C-22 firebrick.[15]

The molar ratio of each component in a given mixture was determined from the tracings obtained from the potentiometer. The area under each peak was obtained by multiplying the height of the peak by the width at half-height. This area was divided by the sum of the areas of the peaks. Several runs were made on an approximately equimolar mixture of toluene, p-xylene and m-chlorotoluene in order to check the reproducibility of the method. The results are shown in Table I.

TABLE I

ANALYSIS OF A MIXTURE OF TOLUENE, p-XYLENE AND m-CHLOROTOLUENE

Run	Toluene	p-Xylene	m-Chlorotoluene
		Mole %	
1	33.3	31.4	35.4
2	33.5	31.4	35.1
3	33.2	31.5	35.4
4	33.2	31.6	35.3
5	33.2	31.6	35.3

Correction factors to take into account variations of thermal conductivity of the vapors with temperature were determined at approximately the temperature used in the analysis. Toluene was used as a standard with an arbitrary value of 1.000. The variations with temperature were small and within limits of experimental error over a temperature range of ±20°. The factors appear to be accurate over the entire range of concentration and for any mixture encountered. They are given in Table II.

In the experiments in which the ratio of toluene to substituted toluene eliminated was followed by the aid of C^{13} mass spectrometrically, the contents of the traps were removed without the aid of a solvent and oxidized by the Van Slyke–Folch method.[16] The carbon dioxide evolved was passed

TABLE II

CORRECTION FACTORS FOR THERMAL CONDUCTIVITY OF VARIOUS SUBSTITUTED TOLUENES

Toluene	Factor	Temp., °C.
Unsubstituted	1.000	
p-Fluoro-	0.927	115
m-Fluoro-	.927	115
p-Methyl-	.863	115
m-Methyl-	.855	115
p-Chloro-	.837	150
m-Chloro-	.836	150
p-Methoxy-	.807	150
m-Methoxy-	.807	150
p-Methylmercapto-	.733	150
m-Methylmercapto-	.731	150

through barium hydroxide solution, protected by an Ascarite trap, by means of a stream of nitrogen. Barium carbonate was collected under nitrogen and dried at 120° for at least 10 hours. Yields of barium carbonate were consistently in the range of 92 to 98%.

TABLE III

PRODUCTS OF THE THERMAL DECOMPOSITION OF THE PRODUCTS FORMED BY CONDENSATION OF UNSYMMETRICALLY SUBSTITUTED 1,3-DIPHENYL-2-PROPANONES WITH o-PHENYLENEDIAMINE

Propanone substituent	p-Toluenesulfacid monohydrate, mole %	Reacn. time, hr.	Temp., °C.	Products, mole % Substd. toluene	Toluene
p-Chloro	2	8.5	190	60.1	39.9
p-Chloro	2	19	190	60.2	39.8
p-Chloro	2	1.5	190	58.8	41.2
p-Chloro	2	1.5	190	59.2	40.8
p-Chloro	2	9	151	59.0	41.0
p-Chloro	0	9	190	59.3	40.7
p-Chloro[a]	0	8	190	60.0	40.0
p-Methyl	2	9	190	55.1	44.9
p-Methyl	2	18	190	55.2	44.8
p-Methyl	2	4.5	190	55.0	45.0
p-Methyl	2	9	151	55.0	45.0
p-Methyl	0	8	190	55.1	44.9
p-Methoxy	2	9	190	68.4	31.6
p-Methoxy	2	8.5	190	68.2	31.8
p-Methoxy	0	8	190	56.5	43.5
p-Methoxy	0	8	190	58.3	41.7
p-Methoxy	20	8	190	68.3	31.7
p-Fluoro	2	8	190	50.7	49.3
p-Fluoro	0	8	190	49.7	50.3
p-Methylmercapto	2	8	190	72.6	27.4
p-Methylmercapto	2	8	190	72.5	27.5
p-Methylmercapto	0	8	190	65.8	34.4
m-Fluoro	2	8	190	56.7	43.3
m-Methoxy	2	8	190	56.5	43.5
m-Methoxy	2	8	190	56.9	43.1
m-Methoxy	0	8	190	56.7	43.3
m-Chloro	2	8	190	67.8	32.2
m-Chloro	2	8	190	67.2	32.8
m-Methyl	2	8	190	57.0	43.0
m-Methyl	2	8	190	57.2	42.8

[a] This analysis is for the decomposition products of pure 2-(p-chlorobenzyl)-2-benzylbenzimidazoline.

Carbon dioxide samples were prepared from the barium carbonate by adding 8–10 ml. of concentrated sulfuric acid to about 50 mg. of the carbonate in an evacuated system. The evolved gas was distilled through a Dry Ice–acetone cooled trap into a trap cooled by liquid air. The frozen carbon dioxide was degassed and submitted to mass spectrometric analysis for 45:44 mass ratios. Details of the method used to check the accuracy of the analytical method can be found in the dissertation.[1]

Results.—Analytical data obtained by vapor phase chromatography on the mixtures of toluene and substituted toluenes evolved on thermal decomposition of the products of the reaction of o-phenylenediamine with a series of unsymmetrically substituted 1,3-diphenyl-2-propanones are given in Table III.

Analytical data obtained mass spectrometrically with the C^{13} labeled 1,3-diphenyl-2-propanones are given in Table IV.

TABLE IV

RATIO OF C^{13}-ENRICHMENT OF CO_2 FROM COMBUSTION TO C^{13}-ENRICHMENT OF TANK CO_2

Compound	Ratio
1-(p-Chlorophenyl)-3-phenyl-2-propanone	1.0118
1-(p-Chlorophenyl)-3-phenyl-2-propanone-3-C^{13} (I)	1.1752
Toluenes from reaction of I with o-phenylenediamine	1.1557, 1.1567, 1.1563
1-(p-Methylphenyl)-3-phenyl-2-propanone-3-C^{13} (II)	1.1642, 1.1651
Toluenes from reaction of II with o-phenylenediamine	1.2098, 1.2057, 1.2068

TABLE V

COMPARATIVE ANALYSES OF MIXTURES OF TOLUENES FROM DECOMPOSITION OF PRODUCTS OF REACTION OF o-PHENYLENEDIAMINE WITH UNSYMMETRICAL 1,3-DIPHENYL-2-PROPANONES

Ketone substituent	Method	Substd. toluene, mole %	Toluene, mole %
p-Chloro	Chromatog.	60.1	39.9
p-Chloro	Mass spect.	59	41
p-Methyl	Chromatog.	41	59
p-Methyl	Mass spect.	40	60

Comparison of the results of analysis of the evolved toluenes by the two methods is given in Table V. These data were obtained by analysis of the labeled mixture itself by the two methods. Whereas the ratio of toluene to p-chlorotoluene obtained with the labeled ketone agrees well with that obtained with the unlabeled ketone (Table III), the agreement is not good with the ratio of toluene to p-xylene in the two instances. This discrepancy is undoubtedly due to faulty sampling technique in the run using labeled ketone. However, agreement between the two analytical methods is, nevertheless, excellent for this particular mixture.

Discussion.—It has been conclusively demonstrated that analysis of mixtures of the type here under consideration can be done at least as accurately, if not more so, by vapor phase chromatography than by use of isotopic labels. This represents a considerable advantage from the standpoint of cost of materials and ease of manipulation.

It is obvious from the data obtained that the decomposition under discussion does not follow the Hammett equation as suggested by the earlier tentative observations.[4] In every instance except one, the molar amount of substituted toluene evolved is greater than that of toluene. From the reaction with 1-(p-fluorophenyl)-3-phenyl-2-propanone, approximately equal molar amounts of toluene and p-fluorotoluene were obtained. The σ-values of the various substituents ranged from −0.268 for p-methoxyl to +0.373 for m-chloro. If the provisional ρ-value of +1.24 proposed by Elderfield and Meyer[4] is valid, the ratio of substituted toluene to toluene evolved should vary from 0.46 to 2.7. Actually, the ratio varies from 1 to 2.64 and the observed variations have no relationship to the σ-values.

Another interesting observation is the effect of acid in promoting elimination of substituted toluene at the expense of toluene when the substituent is p-methoxyl or p-methylmercapto. No such effect of acid was noted with any of the other substituents nor was it present when these two substituents were in the m-position. Earlier observations[8] have shown that in the corresponding decomposition of benzimidazolines carrying two alkyl substituents in the 2-position acid catalysis is not noted. Apparently, protonation of the oxygen or sulfur in the two compounds subject to acid-catalyzed decomposition must play a role, which is presently obscure, in the decomposition.

At present it is not possible to write a completely satisfactory mechanism which takes into account all of the factors known to be operative in this reaction. From the results presented here a radical elimination would seem to be involved. On the other hand, the powerful base catalysis noted previously[8] and the acid catalysis noted in certain well defined instances in the present work point to an ionic mechanism for some stage of the decomposition. If the departing substituent does indeed leave as a radical, it is remarkable that no hydrocarbon derivatives arising from union of two such radicals have been found among the reaction products. Further discussion of the mechanism of the reaction is given in the succeeding paper.[17]

Experimental[18,19]

The Substituted Phenylacetic Acids.—A representative procedure for each of the methods used will be cited with deviations therefrom noted as necessary.

Method A.—p-Chlorobenzyl chloride was prepared by the general method of Kharasch and Brown[20] and converted to p-chlorophenylacetonitrile by refluxing with sodium cyanide in 50% alcohol for 4 hr. The yield of material, b.p. 140° (13 mm.), was 82%; reported[21] b.p. for the nitrile prepared by another method 137–139° (12 mm.),

Acid hydrolysis of the nitrile gave much higher yields than basic hydrolysis as previously reported. A mixture of 220 g.

(17) R. C. Elderfield and E. C. McClenachan, THIS JOURNAL, **82**, 1982 (1960).

(18) All melting and boiling points are corrected for stem exposure.

(19) Microanalyses were done by Spang Microanalytical Laboratory, Ann Arbor, Mich., or by Mrs. Anna Griffin of the University of Michigan.

(20) M. S. Kharasch and H. C. Brown, THIS JOURNAL, **61**, 2142 (1939). In our experience the details as given are insufficient to enable successful consistent duplication. Explicit details are given in ref. 1.

(21) N. Campbell and J. E. McKail, J. Chem. Soc., 1251 (1948).

of the nitrile, 220 ml. of concd. sulfuric acid, 220 ml. of glacial acetic acid and 220 ml. of water was refluxed for 2 hr. After cooling to 0°, the solid was collected, washed with three 50-ml. portions of water and dried. The yield was 225 g. (90%). After recrystallization from ligroin and then from water, the acid melted at 106–106.5°; reported[21] m.p. 104–106°.

Method B.—When chlorination of m-chlorotoluene was attempted by the above procedure, large amounts of starting material together with intractable tars were obtained. Bromination according to Jenkins[22] was therefore used to give m-chlorobenzyl bromide in 31% yield.

m-Chlorobenzyl bromide (25.2 g.) was added slowly to a refluxing solution of 12 g. of sodium cyanide in 15 ml. of water and 20 ml. of ethanol over 15 min. If an alcoholic solution of the bromide was used the major product was m-chlorobenzyl ethyl ether. The yield of material, b.p. 145° (18 mm.), was 15.2 g. (74%); reported[22] b.p. 137–139° (12 mm.).

Hydrolysis of the nitrile as in method A gave 47% of the acid, m.p. 77–77.5°; reported[23] m.p. 76°.

Method C.—Methods A and B both gave discouragingly poor yields when applied to the preparation of p-methoxyphenylacetic acid. It was therefore prepared in 45% yield by the Willgerodt reaction as modified by Schwenk and Papa.[24] The acid melted at 88–89°; reported[25] m.p. 84–86°.

m-Methylmercaptophenylacetic acid was prepared by two routes, the first of which gave slightly better yields, but is somewhat more difficult.

m-Nitrobenzyl bromide, b.p. 115–117° (0.8 mm.), was prepared in 40% yield according to Bent, et al.[26] Conversion to the nitrile, b.p. 155–165° (2–2.5 mm.), m.p.61–61.5°, was accomplished in 61.5% yield by method B; reported[27] m.p. 61–62°.

m-Aminophenylacetonitrile was prepared by adding 165 g. of the nitro compound to a stirred solution of 690 g. of stannous chloride in 790 ml. of concentrated hydrochloric acid. The temperature of the mixture was allowed to rise to 60° and held at that point by external cooling while a second 165-g. portion of the nitrile was added. When the exothermic reaction had subsided, cooling was discontinued and the mixture was stirred 2 hr. at room temperature. The mixture was poured into 1 kg. of ice and 2 l. of 40% sodium hydroxide solution. The temperature was held below 35° during the neutralization. The oil was separated and the aqueous solution was extracted with ether. The ether extracts were combined with the original oil, dried and the residue, after removal of the solvent, was distilled to give material, b.p. 148–154° (1.4 mm.); reported[28] b.p. 183–187° (13 mm.).

The above nitrile was hydrolyzed by refluxing it in 1 liter of 10% sodium hydroxide solution until no more ammonia was evolved. The filtered solution was brought to pH 7 and the m-aminophenylacetic acid, m.p. 146–147°, was collected; reported[29] m.p. 146–147°. The yield was 42% from m-nitrobenzyl bromide.

A solution of 33.8 g. of the above acid in 41 g. of concentrated hydrochloric acid and 100 g. of ice was added to a cold solution of 14.6 g. of sodium nitrite in 91 ml. of water. After stirring for one hour at 0°, the mixture was added to a warm solution of 33.8 g. of potassium ethyl xanthate and 27.1 g. of sodium carbonate in 183 ml. of water. The solution was refluxed for 2 hr., cooled and acidified with hydrochloric acid. Recrystallization of the solid which separated from 33% ethanol gave m-mercaptophenyl acetic acid, m.p. 104–105°. A large amount of insoluble high melting solid separated during the recrystallization.

The slightly impure acid (6 g.) obtained above was heated with 4.2 g. of sodium sulfide in 200 ml. of N sodium hydroxide solution until the solid completely dissolved and 10 g. of dimethyl sulfate was added. After cooling, the mixture was acidified and the solid which separated was recrystallized from 50% methanol to give 4 g. of m-methylmercapto-

(22) S. S. Jenkins, THIS JOURNAL, **55**, 2897 (1933).

(23) J. Kenner and F. Morton, J. Chem. Soc., 679 (1934).

(24) E. Schwenk and D. Papa, J. Org. Chem., **11**, 798 (1946).

(25) W. Wenner, ibid., **15**, 548 (1950).

(26) R. L. Bent, et al., THIS JOURNAL, **73**, 3100 (1951).

(27) G. Heller, Ann., **358**, 357 (1907).

(28) C. F. Koelsch, THIS JOURNAL, **65**, 437 (1943).

(29) M. W. Cronyn, J. Org. Chem., **14**, 1013 (1949).

TABLE VI

2-SUBSTITUTED BENZYLBENZIMIDAZOLES

Benzimidazole	Formula	Carbon, %		Hydrogen, %		Nitrogen, %		M.p., °C.
		Calcd.	Found	Calcd.	Found	Calcd.	Found	
2-(4-Chlorobenzyl)	C₁₄H₁₁ClN₂	69.28	69.51	4.68	4.63	11.54	11.32	197.3–198[a]
2-(4-Methoxybenzyl)	C₁₅H₁₄N₂O	75.61	75.57	5.92	6.05	11.76	11.64	171–172.5[b]
2-(4-Methylbenzyl)	C₁₆H₁₄N₂	81.06	80.96	6.35	6.31	12.60	12.49	202–203
2-(4-Methylmercaptobenzyl)	C₁₅H₁₄N₂S	70.83	71.17	5.55	5.71	11.02	11.25	208.5–209.5
2-(4-Fluorobenzyl)	C₁₄H₁₁FN₂	74.32	74.21	4.90	5.05	12.38	12.30	177.5–179.5
2-(3-Methylbenzyl)	C₁₅H₁₄N₂	81.06	81.11	6.35	6.59	12.60	12.60	152.2–153.2
2-(3-Methoxybenzyl)	C₁₅H₁₄N₂O	75.61	75.48	5.92	6.07	11.76	11.76	188–189

[a] Reported[34] m.p. 192–193°. [b] Reported[34] m.p. 165–165.5°.

phenylacetic acid, m.p. 78°. The yield was 9.9% from m-aminophenylacetic acid.

The second route to m-methylmercaptophenylacetic acid involved conversion of m-aminoacetophenone[30] to m-methylmercaptoacetophenone as described above and application of the Willgerodt reaction.[25] The acid prepared by this route melted at 77°. Repeated recrystallization from petroleum ether and final sublimation gave material, m.p. 78–78.5°.

Anal. Calcd. for C₉H₁₀O₂S: C, 59.9; H, 5.5; S, 17.6. Found: C, 59.8; H, 5.7; S, 17.6.

p-Fluorophenylacetic acid, m.p. 88–89°, was prepared from *p*-fluorotoluene by method A in 45% over-all yield; reported[23] m.p. 85°.

m-Fluorophenylacetic acid, m.p. 47.5–48° from petroleum ether, was prepared from m-fluorotoluene by method B in 30% over-all yield. It was necessary to distil the acid before it could be crystallized, b.p. 125° (2.5 mm).

Anal. Calcd. for C₈H₇FO₂: C, 62.3; H, 4.5. Found: C, 62.3; H, 4.4.

p-Methylmercaptophenylacetic Acid. *p*-Methylmercaptoacetophenone.—When acetylation of thioanisole was attempted on a large scale, a very poor yield of poor quality material was obtained. The following procedure gave reproducible results. A solution of 24.8 g. (0.2 mole) of thioanisole and 23.5 g. (0.3 mole) of acetyl chloride in 150 ml. of dry carbon bisulfide was placed in a 500-ml. three-necked flask equipped with a stirrer, thermometer and an erlenmeyer flask attached with a piece of gooch tubing. After cooling the mixture to −5°, 30 g. (0.22 mole) of aluminum chloride was added from the erlenmeyer flask over one hour with stirring. The dark green solution was stirred for an additional 4 hr. at 0°. Ice and hydrochloric acid were added and the organic layer was separated. The residue after removal of the carbon bisulfide was exhaustively extracted with warm ether. Recrystallization of the residue after evaporation of the ether from 1:1 ether–petroleum ether gave 20 g. (60%) of *p*-methylmercaptoacetophenone, m.p. 71–73°; reported[31] m.p. 72–75°.

The above ketone without further purification was converted to *p*-methylmercaptophenylacetic acid in 70% yield by the Willgerodt reaction.[24] The acid melted at 94–95°; reported[31] m.p. 94°.

p-Methylphenylacetic acid, m.p. 92°, was prepared in 57% yield from *p*-methylbenzyl chloride by method A; reported[32] m.p. 91.5°.

m-Methylphenylacetic acid was prepared in 10% yield from m-xylene by method B, except that no solvent was used in the bromination step. The acid melted at 62°; reported[33] m.p. 61°.

2-Substituted benzyl benzimidazoles.—The above phenylacetic acids were converted to the 2-benzylbenzimidazoles by a standard procedure.[34] These furnished convenient derivatives for characterization. They have also been submitted for evaluation as anti-cancer agents.

Equivalent amounts of the appropriate phenylacetic acid and o-phenylenediamine (commercial material recrystallized three times from benzene, m.p. 101.5–102.5°) were mixed with 0.1 equivalent of o-phenylenediamine dihydrochloride. The mixture was heated under nitrogen at 210° for one hour.

(30) H. Rupe and co-workers, *Ber.*, **33**, 3407 (1900); **34**, 3523 (1901).

(31) J. W. Corse, *et al.*, THIS JOURNAL, **70**, 2841 (1948).

(32) W. Wenner, *J. Org. Chem.*, **13**, 763 (1948).

(33) B. Radzieszewski and P. Wispeck, *Ber.*, **18**, 1282 (1885).

(34) V. B. Meyer, Ph.D. Dissertation, Columbia University, 1953.

After cooling to somewhat above room temperature, a slight excess of ammonium hydroxide was added and the mixture was stirred until crystallization ensued. Recrystallization of the crude benzimidazoles from dilute methanol with decolorization or from benzene gave pure compounds. The analytical data and melting points are given in Table VI.

The Unsymmetrically Substituted 1,3-Diphenyl-2-propanones.—After considerable experimentation, a standard procedure was adopted for the preparation of the ketones. Benzylmagnesium chloride was prepared from a solution of 0.2 mole of redistilled benzyl chloride in 100 ml. of absolute ether and a molar equivalent of magnesium.[35] The clear dark solution of the Grignard reagent was transferred from residual magnesium into a second flask by means of nitrogen through a glass wool plug. The solution was diluted with absolute ether so that the concentration of the Grignard reagent was no greater than 0.2 mole per 300 ml. and then cooled in an ice-bath. Cadmium chloride (0.8 mole per mole of benzyl chloride used) was added with vigorous stirring over 10–15 min. Stirring was continued with cooling for 2 hr. Weak positive tests for Grignard reagent with Michler's ketone could usually be obtained up to 90 min. after addition of the cadmium chloride.

TABLE VII

p-SUBSTITUTED-1,3-DIPHENYL-2-PROPANONES[a]

2-Propanone	Yield, %	M.p., °C.	B.p. °C.	Mm.
1-(*p*-Methylphenyl)-3-phenyl	60–70	31–31.5	143	0.3
1-(*p*-Chlorophenyl)-3-phenyl	60–75	40.5–41	149	.4
1-(*p*-Fluorophenyl)-3-phenyl	50	36–36.5	112–115	.3
1-(*p*-Methoxyphenyl)-3-phenyl	60–70	47.5–48	152–154	.4
1-(*p*-Methylmercaptophenyl)-3-phenyl	50	44–44.5	167–168	.4

[a] All ketones were recrystallized from 40–60° petroleum ether.

Substituted phenylacetyl chlorides were prepared by reaction of the appropriate phenylacetic acid with 2.1 molar equivalents of pure thionyl chloride for one hour at 40–50° followed by one hour on the steam-bath. The excess thionyl chloride was removed by distillation, followed by repeated distillation of benzene from the residue. After distillation under reduced pressure, the acid chlorides were used directly.

A solution of the appropriate phenylacetyl chloride in 3 volumes of absolute ether was added to the cold benzylcadmium reagent over 5 min. It was necessary to use a 2:1 molar ratio of cadmium reagent to acid chloride. If the ratio was less a considerable amount of acid was found in the product. The mixture was stirred in an ice-bath for 8 hr. and hydrolyzed with ice and 20% sulfuric acid. The ether layer was separated and the aqueous phase was extracted twice with ether. The combined ether solutions were washed successively with water and 10% sodium bicarbonate solution and allowed to stand without drying overnight. The ether solution was then extracted with four more 25-ml. portions of sodium bicarbonate solution. The combined

(35) H. Gilman and W. E. Catlin, "Organic Syntheses," Coll. Vol. I, 2nd edition, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 471.

TABLE VIII

m-SUBSTITUTED-1,3-DIPHENYL-2-PROPANONES

2-Propanone	Yield, %	B.p., °C.	Mm.	$n^{20}D$	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
1-(*m*-Fluorophenyl)-3-phenyl	35	115	0.3	1.5524	77.96	77.57	5.98	5.56
1-(*m*-Methylmercaptophenyl)-3-phenyl	42	169	.4	1.5960	74.96	74.86	6.29	6.39
1-(*m*-Methylphenyl)-3-phenyl	41	115–117	.2	1.5640^a	85.67	84.54	7.10	7.04
1-(*m*-Chlorophenyl)-3-phenyl	35–55	154	.1	1.5745^b	73.62	72.72	5.35	5.26
1-(*m*-Methoxyphenyl)-3-phenyl	55	150	.6	1.5689	79.98	79.25	6.70	6.60

^{a} $n^{25}D$ 1.5617, d_{25} 1.4060 g./ml., R_D 69.35 cc. (calcd. 68.80 cc.). ^{b} $n^{25}D$ 1.5725, d_{25} 1.1684 g./ml., R_D 68.96 cc. (calcd. 69.17 cc.).

TABLE IX

DERIVATIVES OF THE 1,3-DIPHENYL-2-PROPANONES

2-Propanone	Derivative ^{b}	M.p., °C.	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
1-(*p*-Chlorophenyl)-3-phenyl	T	191.5–192.5	83.10	83.04	4.60	4.88^a
1-(*p*-Fluorophenyl)-3-phenyl	T	215–216	86.57	86.22	4.76	4.81^a
1-(*p*-Methylphenyl)-3-phenyl	T	191–191.5	90.48	90.31	5.56	5.69^a
1-(*p*-Methoxyphenyl)-3-phenyl	T	191–192	86.93	86.82	5.35	5.61^a
1-(*p*-Methylmercaptophenyl)-3-phenyl	T	200–200.5	83.68	83.61	5.15	5.24^a
1-(*m*-Methoxyphenyl)-3-phenyl	T	210–211	86.93	87.13	5.35	5.23
1-(*m*-Fluorophenyl)-3-phenyl	T	209–209.5	86.57	86.44	4.76	4.61
1-(*m*-Chlorophenyl)-3-phenyl	T	177.2–178	83.10	83.05	4.60	4.70
1-(*m*-Chlorophenyl)-3-phenyl	S	151–152	63.47	63.69	5.33	5.12
1-(*m*-Methylmercaptophenyl)-3-phenyl	N	118.5–119.5	67.51	67.87	5.39	5.36
1-(*m*-Methylphenyl)-3-phenyl	S	86–86.5	72.59	72.55	6.81	6.58

^{a} Previously described from ketones made by another method.[36] ^{b} T = tetraphenylcyclopentadienone; S = semicarbazone; N = *p*-nitrophenylhydrazone.

bicarbonate extracts were extracted twice with ether. All the ether extracts were combined, washed with water and dried over anhydrous sodium sulfate. This rather involved procedure was found to be necessary for complete removal of phenylacetic acids, the presence of which interfered with subsequent purification of the ketones. Removal of the ether and distillation of the residue at reduced pressure gave the ketones. The yields and physical constants of the diphenylpropanones carrying a substituent in the *p*-position are given in Table VII. These have been prepared previously by another method.[10] Pertinent data on the ketones carrying a *m*-substituent, which are new, are given in Table VIII. As indicated previously, certain of these failed to give satisfactory analytical figures. However, derivatives prepared from them were satisfactory.

During the course of these studies, certain observations which may be of value in connection with the use of cadmium reagents have been made. Variation of the reagent from benzylcadmium chloride to dibenzylcadmium made little difference in the yield. Changing the solvent from ether to benzene or toluene after preparation of the Grignard reagent was advantageous in some instances, but the yield of benzylcadmium reagent appeared to depend somewhat on how much residual ether was left in the solution. If no ether was present, the time required for the formation of the benzylcadmium reagent was so long that formation of appreciable amounts of dibenzyl occurred. The thermal stability of dibenzylcadmium is so low that it is virtually impossible to change solvents after the reagent is formed. Decreasing the temperature of the reaction mixture during and after the addition of the acid chloride resulted in the formation of considerable amounts of tertiary alcohol. It appears that, at least with this cadmium reagent, at low temperatures the rate of reaction of dibenzylcadmium with acid chlorides is decreased to a greater extent than is the rate of reaction of the reagent with the ketone. These conclusions are substantiated by the following experiment.

1-(*p*-Methylphenyl)-3-phenyl-2-propanone.—The standard preparation method gave 60–70% yields based on the acid chloride. However, when benzene or toluene were the solvents at lower temperatures, large amounts of 4-methylbenzyldibenzylcarbinol, m.p. 72–73°, were formed.

Anal. Calcd. for $C_{23}H_{24}O$: C, 87.3; H, 7.6. Found: C, 87.2; H, 7.6.

Derivatives of the 1,3-Diphenyl-2-propanones.—For characterization of the ketones condensation of them with benzil

to yield the appropriately substituted 2,3,4,5-tetraphenylcyclopentadienones was attempted. To a solution of the ketone and benzil in a molar ratio of 1:1.1 in absolute ethanol (2.0 ml. per millimole of ketone) either 0.2 ml. per millimole of ketone of a 20% solution of potassium hydroxide in absolute ethanol or 0.2 ml. per millimole of ketone of a 35% solution of benzyltrimethylammonium hydroxide in methanol was added. After boiling the solution for 30 min. and cooling, the highly colored product was collected and recrystallized from 2:1 absolute ethanol–benzene. The yields of pure cyclopentadienones varied from 12% with 1-(*m*-chlorophenyl)-3-phenyl-2-propanone to 80% with 1-(*p*-chlorophenyl)-3-phenyl-2-propanone. Certain of these derivatives have been prepared previously from 2-propanones synthesized by another method.[36]

1-(*m*-Chlorophenyl)-3-phenyl-2-propanone and 1-(*m*-methylphenyl)-3-phenyl-2-propanone failed to yield well defined products by condensation with benzil. They were, therefore, characterized as the semicarbazones. Likewise, 1-(*m*-methylmercaptophenyl)-3-phenyl-2-propanone was characterized as the *p*-nitrophenylhydrazone. Pertinent data on these derivatives are given in Table IX.

Preparation of the 1,3-Diphenyl-2-propanones-3-C^{13}.—The general outline of the synthesis only will be given. Details can be found in the dissertation.[1] Benzyl alcohol-α-C^{13} was prepared by reduction of benzoic acid, C^{13}, which was in turn prepared by reaction of phenylmagnesium bromide with enriched carbon dioxide, with lithium aluminum hydride. Conversion to benzyl chloride-α-C^{13} and reaction of the labeled cadmium reagent with an appropriate phenylacetyl chloride as in the preceding cases gave the labeled 2-propanones.

Reaction of *o*-Phenylenediamine with Benzamide.—When a mixture of benzamide and *o*-phenylenediamine was refluxed for 20 hr. alone or for 2 hr. in the presence of 2% of *p*-toluenesulfonic acid monohydrate N-benzoyl-*o*-phenylenediamine was formed. Since the latter on heating yields 2-phenylbenzimidazole, no useful information obviously could be gained from further study of the carboxamido group as a substituent.

ANN ARBOR, MICH.

(36) S. B. Coan, D. E. Trucker and E. I. Becker, THIS JOURNAL, **77**, 60 (1955).