[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MISSOURI]

Acylations of Aromatic Hydrocarbons with Diphenoyl Chloride

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The space relationships of the carboxyl groups of 2,2′-diphenic acid suggested the possibility of both a symmetrical and an unsymmetrical structure for its diacid chloride analogous to the two forms of the diacid chloride of 1,8-naphthalic acid established by French and Kircher.[3]

The only reported use of 2,2′-diphenoyl chloride in a Friedel–Crafts reaction is its reaction with *p*-xylene and anisole to yield 2,2′-bis-(2,5-dimethylbenzoyl)-biphenyl and 2,2′-dianisoylbiphenyl, respectively.[4] The latter compound is identical with the product of an Ullmann coupling of two molecules of 2-bromo-4′-methoxybenzophenone.[5]

In the present study of the reactions of diphenoyl chloride with aromatic hydrocarbons in the presence of aluminum chloride, different types of compounds were isolated when nitrobenzene was used as solvent rather than excess of the hydrocarbon. The results are summarized in Table I.

TABLE I

ACYLATIONS OF AROMATIC HYDROCARBONS WITH DIPHENOYL CHLORIDE

Hydrocarbon	Procedure	Product	M. p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Benzene	A	4-Benzoylfluorenone[a]	98.5–99[b]					
	B	Fluorenone-4-carboxylic acid	225–227[c]					
Toluene	A	2,2′-Bis-(4-methylbenzoyl)-biphenyl (I)	136.5–137[d]					
		I-A	122.5–123	$C_{28}H_{22}O_2$	86.13	86.41	5.68	5.77
	B	4-(4-Methylbenzoyl)-fluorenone	128–129[e]					
		Fluorenone-4-carboxylic acid	225–227					
o-Xylene	A	2,2′-Bis-(3,4-dimethylbenzoyl)-biphenyl (II)	123.5–124	$C_{30}H_{26}O_2$	86.09	86.03	6.26	6.55
		II-A	143–143.5	$C_{30}H_{26}O_2$	86.09	86.19	6.26	6.51
	B	4-(3,4-Dimethylbenzoyl)-fluorenone	145–145.5[f]					
m-Xylene	A	2,2′-Bis-(2,4-dimethylbenzoyl)-biphenyl	126.5–127	$C_{30}H_{26}O_2$	86.09	86.71	6.26	6.39
	B	4-(2,4-Dimethylbenzoyl)-fluorenone	110–111	$C_{22}H_{16}O_2$	84.59	84.30	5.16	5.43
p-Xylene	A	2,2′-Bis-(2,5-dimethylbenzoyl)-biphenyl	148–149[f]					
		4-(2,5-Dimethylbenzoyl)-fluorenone	143–144[f]					
	B	4-(2,5-Dimethylbenzoyl)-fluorenone	143–144					
Mesitylene	A	2,2′-Bis-(2,4,6-trimethylbenzoyl)-biphenyl	219–220	$C_{32}H_{30}O_2$	86.06	85.84	6.77	6.92
	B	4-(2,4,6-Trimethylbenzoyl)-fluorenone	162–162.5	$C_{23}H_{18}O_2$	84.63	84.51	5.56	5.43
Anisole	A	2,2′-Dianisoylbiphenyl	150–150.5[f]					
	B	Fluorenone-4-carboxylic acid	225–227					

[a] This benzoylfluorenone formed a monoxime, m. p. 148–145.5° (literature 146°, Goetz, *Monatsh.*, **23**, 27 (1902), and was reduced with hydrogen and copper chromium oxide catalyst in methanol solution to yield 4-benzylfluorene, m. p. 76.5–77°, the melting point recorded by Goetz. [b] Goetz reports 95°. [c] Ref. 12. [d] Ref. 5a. [e] Ref. 13. [f] Ref. 4.

Benzene was unique in that only 4-benzoylfluorenone was obtained from it in 80% yield in benzene solution. The reaction is a convenient method for the preparation of this fluorenone ketone.

Toluene yielded 2,2′-bis-(4-methylbenzoyl)-biphenyl in two polymorphic forms, I, m. p. 136–137°, the recorded value,[4] and I-A, m. p. 122–122.5°. The structure of the diketone I was established by its synthesis through an Ullmann reaction and it added phenyllithium to form the expected di-tertiary carbinol.

Analysis of I-A and a molecular weight determination agreed with the formula $C_{28}H_{22}O_2$, isomeric with I. Compound I-A added two moles of phenyllithium to form the same di-tertiary carbinol obtained from I. This fact, in addition to the similarity of their infrared absorption spectra and the melting point data indicated that I and I-A were polymorphic forms.[6]

o-Xylene yielded 2,2′-bis-(3,4-dimethylbenzoyl)-biphenyl II and compound II-A. The structure of II was established as the diketone by its synthesis from 2-bromo-3′,4′-dimethylbenzophenone by the Ullmann reaction. It added two molecules of phenyllithium to form the expected di-tertiary carbinol.

Analysis of II-A agreed with the formula $C_{30}H_{26}O_2$, isomeric with the diketone II. Melting point data suggested that II and II-A were poly-

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[1] Abstract of the Ph.D. dissertation of Sister Henrietta Eileen, June, 1949. The problem was begun under the direction of the late Prof. Herbert E. French. During his illness and after his death the research was directed by the senior author.

[2] Present address: College of St. Teresa, Kansas City, Mo.

[3] French and Kircher, THIS JOURNAL, **63**, 3270 (1941).

[4] Bell and Briggs, *J. Chem. Soc.*, 1661 (1938).

[5] (a) Bachmann, THIS JOURNAL, **54**, 1972 (1932); (b) Huntress and Moos, *ibid.*, **61**, 526 (1939).

[6] Bachmann did not mention a multiple melting point for this diketone which he synthesized by an Ullmann reaction, but he did report two melting points for 2,2′-dianisoylbiphenyl.

morphic forms, but II-A would not add phenyllithium.

The pale lavender fluorescence of an acetone solution of II-A in ultraviolet light was similar to that of 7,7′-diphenyldiphenide and suggested the possibility that II-A could be a diphenide. Sergeev[7] cleaved 7,7-diphenyldiphenide with 37% hydrobromic acid in glacial acetic acid to form 9,9-diphenylfluorenone, but II-A was recovered unchanged from a hydrobromic acid–acetic acid solution even after it had been warmed.

The infrared absorption specta of II, II-A, and 7,7-diphenyl diphenide were obtained in a Nujol mull, but it was the opinion of Dr. E. E. Pickett, spectroscopist at the University of Missouri, that these spectra did not furnish conclusive evidence for a diphenide structure for II-A nor for II and II-A as polymorphic forms of the diketone.

m-Xylene and mesitylene yielded the corresponding 2,2′-diaroylbiphenyls. Their structures were established by cleavage with concentrated sulfuric acid[4] to yield fluorenone-4-carboxylic acid. *p*-Xylene yielded 2,2′-bis-(2,5-dimethylbenzoyl)-biphenyl and some 4-(2,5-dimethylbenzoyl)-fluorenone, both known compounds.[4]

Anisole yielded only 2,2′-dianisoylbiphenyl, of established structure.[5b]

When the acylations were carried out in nitrobenzene solution, the principal products were 4-aroylfluorenones and traces of fluorenone-4-carboxylic acid except in the case of benzene and anisole. The only product isolated from the reaction of diphenoyl chloride with benzene or anisole in nitrobenzene solution was fluorenone-4-carboxylic acid.

There was no indication of the formation of the 2′-aroyl-2-carboxybiphenyls in any of these acylations, analogous to the 1-aroyl-8-naphthoic acids which French and Kircher[3] obtained from 1,8-naphthaloyl dichloride.

Experimental[8]

Materials.—The 2,2′-diphenic acid was made according to the directions of Atkinson and Lawler.[9] The 2,2′-dibenzoylbiphenyl was obtained by the procedure of Werner and Grob.[10]

The diphenoyl chloride was prepared essentially according to the method of Bell and Robinson,[11] from 45 ml. of thionyl chloride and 20 g. of diphenic acid. When the temperature of the water-bath was maintained at 35–40° the yield of pure acid chloride was 80%.

The hydrocarbons were acylated with excess hydrocarbon as solvent (method A) and with nitrobenzene as solvent (method B). The acylations of toluene and *o*-xylene and the identification of their reaction products are typical. None of the diketones would form any of the usual ketone derivatives. Table I lists all of the acylation products, their physical constants and analyses.

Acylation of Toluene, Method A.—Anhydrous analytical reagent aluminum chloride (3.5 g.) was added slowly during fifteen minutes to a well-stirred mixture of 25 ml. of toluene and 2.7 g. of pure diphenoyl chloride at room temperature. The mixture was stirred for at least an hour after the addition of the aluminum chloride, or until hydrogen chloride was no longer evolved. The complex was decomposed with iced hydrochloric acid and allowed to stand overnight. The solid (1 g.) which separated was removed by filtration and the toluene layer was dried over calcium chloride. The toluene was removed under reduced pressure to yield about 1 g. of solid. Fractional crystallization of these solids usually yielded two main fractions, one melting at 123–127°, the other at 135–137°. Sometimes further recrystallization yielded two products, I, m. p. 136–137° and I-A, m. p. 122–123°, but as a rule I was the only compound isolated. Occasionally I-A was the only one obtained. A mixture of I and I-A melted at 123–136°, and on standing in a stoppered vial the melting point of I-A increased slowly over a period of several months.

A mixture of I and an authentic sample of 2,2′-bis-(4-methylbenzoyl)-biphenyl (m. p. 136–137°) synthesized by an Ullmann reaction[4] melted at 136–137°.

Addition of Phenyllithium to I and I-A.—The diketone I (0.4 g., 0.001 mole) was added to 0.006 mole of phenyllithium in 50 ml. of dry ether. The mixture was stirred and refluxed for several hours, then decomposed with iced hydrochloric acid. The solid which separated was recrystallized from aqueous dioxane and melted at 234–236°.

Anal. Calcd. for $C_{40}H_{34}O_2$: C, 87.8; H, 6.27. Found: C, 87.68; H, 6.58.

The reaction was repeated with 0.4 g. of I-A. The product melted at 233.5–235° and did not depress the melting point of the di-tertiary carbinol obtained from I.

Acylation of Toluene. Method B.—Aluminum chloride (8.4 g., 0.063 mole) was added to a solution of 6 g. (0.021 mole) of pure diphenoyl chloride in 15 ml. of nitrobenzene. The reaction was slightly exothermic. The solution was stirred two hours at room temperature and then 15 ml. of toluene was added. Stirring was continued for an additional hour and a half. The complex was decomposed with iced hydrochloric acid, the yellow solid (0.5 g.) was removed by filtration and extracted with sodium carbonate solution. The clear extract was acidified and the yellow solid which separated was washed and dried. It melted at 225–227° and did not depress the melting point of an authentic sample of fluorenone-4-carboxylic acid.[12]

The nitrobenzene layer was steam distilled to leave a solid residue (4.5 g.) which was extracted with sodium carbonate solution and recrystallized from alcohol to yield the bright yellow 4-(4-methylbenzoyl)-fluorenone, m. p. 128–129°, which did not depress the melting point of an authentic sample of 4-(4-methylbenzoyl)-fluorenone prepared by the method of Pick.[13]

Acylation of *o*-Xylene by Method A.—*o*-Xylene (35 ml.) was acylated with 2.5 g. of diphenoyl chloride and 3.5 g. of aluminum chloride as described above. Fractional crystallization of the product sometimes yielded two colorless compounds, the diketone II, m. p. 123.5–124°, and II-A, m. p. 143–143.5°. Generally II was the only compound isolated.

A mixture of II and an authentic sample of 2,2′-bis-(3,4-dimethylbenzoyl)-biphenyl, m. p. 122.5–123°, synthesized by an Ullmann reaction melted at 122–123°.

Addition of Phenyllithium to II and II-A.—The diketone II (1.1 g.) was added to 0.02 mole of phenyllithium in 35 ml. of dry ether as described above. The di-tertiary carbinol was recrystallized from alcohol and melted at 195–195.5°.

Anal. Calcd. for $C_{42}H_{38}O_2$: C, 88.2; H, 6.64. Found: C, 88.3; H, 6.83.

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[7] Sergeev, *J. Russ. Phys.-Chem. Soc.*, **61**, 1421 (1929); *Chem. Abstr.*, **24**, 1365 (1930).

[8] The carbon and hydrogen analyses were done by Richard A. Carpenter and Sister Henrietta Eileen.

[9] Atkinson and Lawler, "Organic Syntheses," Coll. Vol. I, 2nd Edition, John Wiley and Sons, New York, N. Y., 1941, p. 222.

[10] Werner and Grob, *Ber.*, **37**, 2899 (1904).

[11] Bell and Robinson, *J. Chem. Soc.*, 1695 (1927).

[12] Graebe and Aubin, *Ber.*, **20**, 845 (1887).

[13] Pick, *Monatsh.*, **25**, 978 (1904).

The reaction was repeated twice with 2 g. of II-A, but only unchanged starting material was recovered.

Compound II-A (0.5 g.) was added to 2.5 ml. of 47% hydrobromic acid and 10 ml. of glacial acetic acid. The mixture was warmed to 50° for fifteen minutes, then poured into iced water. The separated solid was unchanged starting material.

Acylation of *o*-Xylene. Method B.—Aluminum chloride (3.9 g., 0.03 mole) was added to 2.7 g. (0.01 mole) of diphenoyl chloride dissolved in 10 ml. of nitrobenzene, and 3.5 ml. of *o*-xylene was added, as described above. The product, 4-(3,4-dimethylbenzoyl)-fluorenone, melted at 145–145.4°, the recorded value.[4]

Preparation of 2-Bromo-3′,4′-dimethylbenzophenone.—The ketone was obtained by the usual Friedel–Crafts procedure from 20 g. of *o*-bromobenzoyl chloride, 18.3 g. of aluminum chloride and 35 ml. of *o*-xylene in 51% yield; m. p. 40–41°.

Anal. Calcd. for $C_{15}H_{13}BrO$: C, 62.28; H, 4.77. Found: C, 62.28; H, 4.89.

Preparation of II by the Ullmann Reaction.—A mixture of 2 g. of 2-bromo-3′,4′-dimethylbenzophenone and 5 g. of copper powder was heated at 250–260° for one hour. The reaction mixture was extracted with alcohol. The diketone melted at 122.5–123° after recrystallization from alcohol.

Preparation of 7,7-Diphenyldiphenide from Diphenic Anhydride and Phenyllithium.—Solid diphenic anhydride (3.5 g.) was added to 0.056 mole of phenyllithium in 100 ml. of dry ether, in an atmosphere of nitrogen. The reaction mixture was stirred and refluxed for about two hours, then decomposed with iced hydrochloric acid. The sticky yellowish solid was recrystallized from glacial acetic acid and melted at 189–190°, the recorded value.[7]

The 7,7-diphenyldiphenide was also prepared according to Sergeev's procedure,[7] from diphenic anhydride and phenylmagnesium bromide, and a mixture of the two compounds melted at 189–190°. A better yield was obtained from the phenyllithium reaction.

Reaction of 2,2′-Bis-(2,4-dimethylbenzoyl)-biphenyl and 2,2′-Bis-(2,4,6-trimethylbenzoyl)-biphenyl with Concd. Sulfuric Acid.—The diketone (0.3 g.) was warmed with 1 ml. of concd. sulfuric acid at 110–120° for fifteen minutes. The cooled mixture was poured into water and the yellow solid which separated was recrystallized from alcohol. Both diketones yielded fluorenone-4-carboxylic acid, m. p. and mixed m. p. 225–227°.

Summary

2,2′-Diphenoyl chloride reacted as the symmetrical diacid chloride with toluene, the xylenes, mesitylene and anisole in the presence of aluminum chloride to form the 2,2′-diarylbiphenyls.

In nitrobenzene solution, 2,2′-diphenoyl chloride reacted with the methylbenzenes to yield 4-aroylfluorenones.

2,2′-Diphenoyl chloride and benzene reacted in benzene solution to yield 4-benzoylfluorenone. In nitrobenzene solution the fluorenone-4-carboxylic acid was the only product isolated.

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[FROM THE CHEMISTRY LABORATORY OF THE STATE UNIVERSITY OF IOWA]

The Synthesis of Substituted β-Arylglutaric Acids

BY WALTER T. SMITH, JR., AND PAUL G. KORT

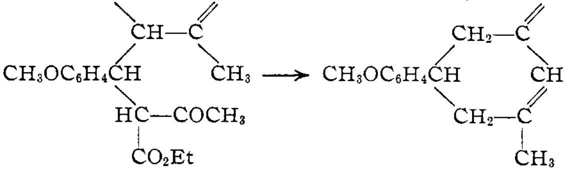
β-Arylglutaric acids have been prepared frequently by saponification and decarboxylation of the tri-ester obtained by the addition of malonic ester to cinnamic esters or to substituted cinnamic esters.[1] This method has the disadvantage of being rather long and requiring carefully dried reagents and anhydrous conditions.

Knoevenagel[2] reported that β-(*m*-nitrophenyl)- and β-(*p*-nitrophenyl)-glutaric acids were formed by cleavage of the corresponding ethyl nitrobenzal-bis-acetoacetates but no yields were given. The principal products of the reactions were the nitrophenylcyclohexenones. The substituted ethyl benzal-bis-acetoacetates are usually readily prepared by the piperidine-catalyzed condensation of an aromatic aldehyde with two moles of ethyl acetoacetate.

It was the purpose of the present work to determine if cleavage of substituted benzal-bis-acetoacetic esters might not be a convenient method for the preparation of substituted β-arylglutaric acids, and at the same time to prepare some β-arylglutaric acids in which the aryl groups are derived from vanillin. These acids are of interest because of their possible toxicity toward aerobic microörganisms which attack foods, particularly in view of the recent reports concerning the high toxicity of certain esters of vanillic acid and related compounds toward representative microörganisms.[3]

Ten aromatic aldehydes were successfully condensed with ethyl acetoacetate by means of piperidine to give the corresponding ethyl benzal-bis-acetoacetates in yields ranging from 34–80%. The data for these products are summarized in Table I.

Sodium ethoxide has been used to cleave disubstituted ethyl acetoacetates to disubstituted ethyl acetates.[4] Efforts to cleave ethyl anisal-bis-acetoacetate (I) by a similar procedure gave only the cyclic ketone, 5-anisyl-3-methyl-2-cyclohexen-1-one (II).



I II

However, cleavage of the condensation products

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(1) Michael, *Am. Chem. J.*, **9**, 114 (1887).

(2) Knoevenagel, *Ann.*, **303**, 223–257 (1898).

(3) Pearl and Beyer, THIS JOURNAL, **71**, 1066 (1949).

(4) Renfrow and Walker, *ibid.*, **70**, 3957 (1948).