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

Acylations with the Acid Chlorides of 2,5-Diphenylfuran-3,4-dicarboxylic Acid and 2,5-Dimethylfuran-3,4-dicarboxylic Acid and Related Compounds

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Received August 18, 1958

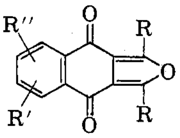
The acylation of six aromatic hydrocarbons with 2,5-diphenylfuran-3,4-dicarbonyl chloride and with 2,5-dimethylfuran-3,4-dicarbonyl chloride yielded mainly cyclic diketones and/or open diketones, occasionally accompanied by small amounts of keto acids.

2,5-Diphenylfuran-3,5-dicarboxylic acid anhydride reacted with these hydrocarbons in the presence of aluminum chloride to form keto acids. Phenyl lithium reacted with this anhydride to form a phthalide type of compound.

Since little or no work has been done with Friedel-Crafts reactions of 5-membered heterocyclic dicarboxylic acid chlorides having the carboxyl groups on adjacent carbons, 2,5-diphenylfuran-3,4-dicarbonyl chloride III and 2,5-dimethylfuran-3,4-dicarbonyl chloride IV were selected for study. These acid chlorides had not previously been reported in the literature.

The acylation of benzene, toluene, and the three xylenes with III and IV yielded mainly yellow cyclic diketones (9,10-dihydro-4,9-dioxo-1,3-di-R-naphtho[2,3c]furans) and/or colorless 2,5-di-R-3,4-diaroylfurans, occasionally accompanied by small amounts of 2,5-di-R-4-aroylfuran-3-carboxylic acid. No compounds of the phthalide type were isolated. Mesitylene formed only the 2,5-di-R-3,4-dimesitoylfuran as might be expected, in view of the fact that the acylation of this hydrocarbon with phthalyl chloride yielded only *o*-dimesitoylbenzene.[3]

The products of the acylations are summarized in Tables I and II. The preferential formation of cyclic diketones, Series I and II, by intramolecular acylation was surprising, since *o*-phthalyl chloride reacts with benzene and toluene in the presence of aluminum chloride to form mainly diaryl phthalides and only small amounts of anthraquinone.[4] For the most part, the total yield of carbonyl compounds was less in carbon disulfide than in excess hydrocarbon, but the ratio of cyclic diketone to diaroylfuran varied with the hydrocarbon being acylated. It is assumed that toluene and the xylenes acylate and cyclize in the positions usual for these types of reactions.



Series I. R = C_6H_5
Ia. R′ = R″ = H
Ib. R′ = 6-CH_3; R″ = H
Ic. R′ = 6-CH_3; R″ = 7-CH_3
Id. R′ = 6-CH_3; R″ = 8-CH_3
Ie. R′ = 5-CH_3; R″ = 8-CH_3

Series II. R = CH_3
IIa. R′ = R″ = H
IIb. R′ = 6-CH_3; R″ = H
IIc. R′ = 6-CH_3; R″ = 7-CH_3
IId. R′ = 6-CH_3; R″ = 8-CH_3
IIe. R′ = 5-CH_3; R″ = 8-CH_3

Benzene and *m*-xylene were also acylated with III in nitrobenzene and in *sym*-tetrachloroethane. The total yield of carbonyl compounds was higher in the latter solvent than in nitrobenzene or in carbon disulfide, but the product distribution was similar to that in excess hydrocarbon as solvent for the reaction.

In the Grignard machine, the cyclic diketones not only added two moles of methylmagnesium

TABLE I

ACYLATIONS WITH 2,5-DIPHENYLFURAN-3,4-DICARBONYL CHLORIDE[a]

Hydrocarbon	Hydrocarbon Solvent	Yield, %	Carbon Disulfide	Yield, %
Benzene	Cdk Ia	71	Cdk Ia	22
Toluene	Cdk Ib	36	Cdk Ib	61
	Dk	40	Dk	1
o-Xylene	Cdk Ic	78	Cdk Ic	82
m-Xylene	Cdk Id	10	Cdk Id	13
	Dk	75	Dk	43
p-Xylene	Cdk Ie	76	Cdk Ie	42
Mesitylene	Dk	74	Dk	58

ACYLATIONS WITH 2,5-DIMETHYLFURAN-3,4-DICARBONYL CHLORIDE

Hydrocarbon	Hydrocarbon Solvent	Yield, %	Carbon Disulfide	Yield, %
Benzene	Cdk IIa	73	Cdk IIa	90
Toluene	Cdk IIb	50	Cdk IIb	68
	Dk	26	Dk	1
o-Xylene	Cdk IIc	82	Cdk IIc	82
			Ka	4
m-Xylene	Cdk IId	6	Cdk IId	13
	Dk	53	Dk	67
p-Xylene	Cdk IIe	68	Cdk IIe	72
Mesitylene	Dk	54	Dk	90
	Ka	8		

[a] Cdk = cyclic diketone. Dk = 2,5-di-R-3,4-diaroylfuran. Ka = 2,5-di-R-4-aroylfuran-3-carboxylic acid.

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(1) Abstracted from the Ph.D. dissertation of Bernard Sukornick, University of Missouri, June 1957.

(2) Phillips Petroleum Company Fellow 1956–57. Present address: General Chemical Company, Morristown, N. J.

(3) R. C. Fuson, S. B. Speck, and W. R. Hatchard, *J. Org. Chem.*, 10, 55 (1945).

(4) C. Friedel and J. M. Crafts, *Ann. Chim. Physique*, (6) 1, 523 (1884).

TABLE II

ACYLATION PRODUCTS

Compound	M.P., °C.	Formula	Calcd. C	Calcd. H	Found C	Found H
Ia	225–226	$C_{24}H_{14}O_3$	82.27	4.03	82.45	4.13
Ib	204–205	$C_{25}H_{16}O_3$	82.40	4.42	82.04	4.43
Ic	270–271	$C_{26}H_{18}O_3$	82.52	4.79	82.56	4.94
Id	190–191	$C_{26}H_{18}O_3$	82.52	4.79	83.69	4.81
Ie	223–224	$C_{26}H_{18}O_3$	82.53	4.79	82.53	4.79
2,5-Diphenyl-3,4-di-p-toluoylfuran	151–153	$C_{32}H_{24}O_3$	84.19	5.30	84.32	5.54
2,5-Diphenyl-3,4-bis-(2,4-dimethylbenzoyl)furan	118–119	$C_{32}H_{28}O_3$	84.27	5.82	84.40	5.99
2,5-Diphenyl-3,4-dimesitoylfuran	171–172	$C_{36}H_{32}O_3$	84.34	6.29	84.55	6.95
IIa	171–172	$C_{14}H_{10}O_3$	74.33	4.46	74.34	4.42
IIb	190–191	$C_{15}H_{12}O_3$	74.99	5.03	74.86	5.42
IIc	273–275	$C_{16}H_{14}O_3$	75.57	5.55	75.57	5.98
IId	165–166	$C_{16}H_{14}O_3$	75.57	5.55	75.42	5.59
IIe	161–162	$C_{16}H_{14}O_3$	75.57	5.55	75.48	5.65
2,5-Dimethyl-3,4-bis-(2,4-dimethylbenzoyl)furan	85–86	$C_{24}H_{24}O_3$	79.97	6.71	79.68	6.78
2,5-Dimethyl-3,4-dimesitoylfuran	165–166	$C_{26}H_{28}O_3$	80.38	7.27	80.25	7.51

iodide, but there was also indication of a notable amount of active hydrogen from some of the compounds of Series II. These data are summarized in Table III. 2,5-Dimethylfuran does not undergo a Grignard exchange with methylmagnesium iodide,[5] but the keto groups of the cyclic diketones could activate the hydrogen on the methyl group of the furan nucleus toward the Grignard reagent. As a matter of interest, IIa was allowed to react with methylmagnesium iodide on a 0.02 mole scale. The reaction product was an intractable, very high melting black solid containing no magnesium.

TABLE III

REACTIONS OF SOME OF THE CYCLIC DIKETONES WITH METHYLMAGNESIUM IODIDE

Compound	Heating Time, Min.	Carbonyl Groups per Molecule	Active H per Molecule
Ia	20	2.31	0.11
Ib	20	1.57	0.18
	120	2.42	0.18
Ic	20	1.84	0.28
IIa	20	1.62	0.33
	40	1.55	0.38
	120	1.17	0.95
IIc	20	2.22	1.53
	30	2.22	1.65
	45	2.16	1.78
	110	2.38	1.94
IId	20	2.02	1.03

The infrared absorption spectra of Ia and IIa have strong bands at 5.6 microns and 6.0 microns respectively, the expected region for a carbonyl group conjugated with an unsaturated system.[6] Strong absorption bands at 13.95 and 13.97 microns respectively indicate an *o*-disubstituted benzene ring which is part of a fused system.[7]

Ia, IIa, and IIb formed a mono 2,4-dinitrophenylhydrazone. Although forcing conditions were used, the other cyclic diketones apparently did not react with this reagent, and attempts to prepare other ketone derivatives were unsuccessful.

Acetic anhydride was used to convert acid I to its anhydride V in nearly quantitative yield, but all efforts to convert acid II to an anhydride were unsuccessful. This was surprising in view of the fact that 1-*n*-butyl-2,5-dimethylpyrrole-3,4-dicarboxylic acid formed an anhydride readily.[8] The reaction of I with thionyl chloride yielded V.

The aromatic hydrocarbons reacted with V in the presence of aluminum chloride to form 2,5-diphenyl-4-aroylfuran-3-carboxylic acids in yields of 73–97%. These data are summarized in Table IV.

Efforts to prepare the acid chloride of 2,5-diphenyl-4-benzoylfuran-3-carboxylic acid by means of phosphorus pentachloride or thionyl chloride yielded only the cyclic diketone Ia. 2,5-Diphenyl-4-mesitoylfuran-3-carbonyl chloride was obtained from the keto acid by means of thionyl chloride, and reacted with di-*n*-butylcadmium and with diphenylcadmium to form respectively a glassy product and an intractable oil.

The anhydride V did not react with phenylmagnesium bromide but with phenyllithium it

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(5) C. D. Hurd and K. Wilkinson, *J. Am. Chem. Soc.*, **70**, 738 (1948).

(6) L. F. Bellamy, *The Infra-red Spectra of Complex Molecules*, Methuen and Co., Ltd., London, 1954, pp. 119, 129.

(7) Ref. 6, p. 54.

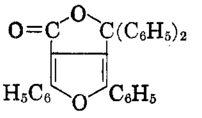
(8) D. V. Nightingale and J. A. Gallagher, *J. Org. Chem.*, **24**, 501 (1959).

TABLE IV

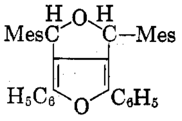
2,5-DIPHENYL-4-AROYL-3-CARBOXYLIC ACIDS

Hydrocarbon	M.P., °C.	Formula	Neut. Equiv. Calcd.	Neut. Equiv. Found	Calcd. C	Calcd. H	Found C	Found H
Benzene	149–150	$C_{24}H_{16}O_4$	368.4	367.5	78.25	4.38	78.23	4.34
Toluene	214–216	$C_{25}H_{18}O_4$	382.4	379.8	78.52	4.99	78.70	4.74
o-Xylene	207–208	$C_{26}H_{20}O_4$	396.4	397.2	78.77	5.09	78.79	5.27
m-Xylene	177–178	$C_{26}H_{20}O_4$	396.4	394.0	78.77	5.09	78.68	5.02
Mesitylene	171–172	$C_{27}H_{22}O_4$	410.5	404.9	79.00	5.69	79.18	5.40

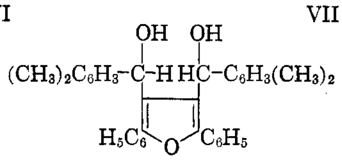
formed the lactone VI of the phthalide type. In the Grignard machine, VI added one mole of methylmagnesium iodide and there was no indication of active hydrogen. In ultraviolet light, VI had a blue fluorescence similar to that of other phthalide types of compounds synthesized in this laboratory. The infrared absorption spectrum of VI showed a strong absorption band at 5.7 microns which is characteristic of the γ-lactone structure.[9]



VI



VII



VIII

2,5-Diphenyl-3,4-dimesitoylfuran reacted with zinc in alcoholic potassium hydroxide solution to form a compound, the carbon and hydrogen percentages of which agreed with those calculated for the substituted tetrahydrofuranofuran VII, but 2,5-diphenyl-3,4-bis(2,4-dimethylbenzoyl)furan apparently formed a bis-sec-carbinol VIII.

EXPERIMENTAL[10]

The preparation of 2,5-dimethylfuran-3,4-dicarboxylic acid. The procedure for the preparation of 2,5-dimethyl-3,4-dicarbethoxyfuran is an adaptation of the method of Nowlin[11] for the furanization of 1,4-diketones. This method gave a better quality of ester than the cyclization with sulfuric acid.[12] In a liter three-necked flask equipped with a stirrer and thermometer was placed 200 g. of polyphosphoric acid. The flask was heated to 50° and 42 g. (0.16 mole) of the solid β-form of α,α'-diacetoethylsuccinate[13] (m.p. 84–86°) was added in small portions with stirring. The temperature rose to 70° and was maintained at 70–75° for another 20 min. The separated brown complex was decomposed with ice and the mixture was extracted with several 100 ml. portions of ether. The ether solution was dried over magnesium sulfate and distilled to yield 34.8 g. (90%) of the furan ester as a red oil which distilled at 128–148° (1 mm.). Without further purification, this crude ester was saponified by means of 25% alcoholic potassium hydroxide[9] to form the acid II in nearly quantitative yield.

When crude, oily α,α'-diacetosuccinate was cyclized in this manner or with sulfuric acid, the yield of furan ester was only 19%.

Preparation of 2,5-dimethylfuran-3,4-dicarbonyl chloride. In a 500 ml. three-necked flask fitted with a stirrer, thermometer, and a gas outlet was placed 42 g. (0.23 mole) of 2,5-dimethylfuran-3,4-dicarboxylic acid I. To this was added 332 g. (2.8 moles) of thionyl chloride with stirring. After the vigorous evolution of gas had subsided, the mixture was heated at 60–70° for 1 hr. The excess thionyl chloride was removed with an aspirator and the product was distilled under further reduced pressure. Yield, 41 g. (80%), b.p. 117–120° (1 mm.). Efforts to obtain an analytical sample of this acid chloride resulted in a product contaminated with acid.

This acid chloride reacted with aniline in benzene solution to form a *dianilide*, m.p. 203–205°, in 80% yield.

Anal. Calcd. for $C_{20}H_{18}N_2O_3$: C, 71.84; H, 5.43. Found: C, 71.77; H, 5.21.

Preparation of 2,5-diphenylfuran-3,4-dicarboxylic acid. The procedure was identical with that described for the preparation of 2,5-dimethylfuran-3,4-dicarboxylic acid, except that the polyphosphoric acid was heated to 60° prior to the addition of dibenzoylethylsuccinate. From 50 g. (0.13 mole) of solid dibenzoylethylsuccinate and 250 g. of polyphosphoric acid there was obtained 45 g. (95%) of 2,5-diphenyl-3,4-dicarbethoxyfuran, m.p. 84–86°.

An 85% yield of the acid I, m.p. 235–237°, literature value,[14] 238°, was obtained from this ester.

Preparation of 2,5-diphenylfuran-3,4-dicarbonyl chloride. The procedure was essentially that of Hofman and Bridgewater.[15]

To a solution of 11 g. (0.036 mole) of I in 200 ml. of dioxan and 175 g. of chloroform was added 30 g. (0.145 mole) of phosphorus pentachloride. The mixture was shaken vigorously for 20 min. and then filtered. After the solvent had been removed with an aspirator, the residue was dissolved in boiling anhydrous ether. The ether was evaporated and the acid chloride was recrystallized from petroleum ether (b.p. 60–70°); yield 9.3 g. (75%), m.p. 119–120°.

Anal. Calcd. for $C_{18}H_{10}O_3Cl_2$: C, 62.63; H, 2.92. Found: C, 62.89; H, 3.13.

The acylations. The general procedure[3] for all the acylations was as follows: In a 200 ml. three-necked round bottom flask fitted with the usual equipment was placed 30 ml. of aromatic hydrocarbon and 3 g. (0.023 mole) of aluminum chloride. The flask was cooled in an ice bath and the solid acid chloride (3.5 g., 0.01 mole) of I was added slowly from a 60-ml. Erlenmeyer flask connected to the reaction flask by

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(9) Ref. 6, p. 153.

(10) The carbon and hydrogen analyses were performed by Mr. Y. C. Lee, Mr. R. Elliot, and Mr. A. Mendel at the University of Missouri, and by the Weiler-Strauss Laboratories, Oxford, England. The melting points and boiling points are uncorrected.

(11) G. Nowlin, *J. Am. Chem. Soc.*, **72**, 5754 (1950).

(12) L. Knorr, *Ann.*, **306**, 332 (1899).

(13) G. H. U. Harrow, *J. Chem. Soc.*, **33**, 425 (1878).

(14) W. H. Perkin and A. Schloesser, *J. Chem. Soc.*, **57**, 944 (1890).

(15) K. Hofman and A. Bridgewater, *J. Am. Chem. Soc.*, **67**, 738 (1945).

rubber tubing. When the addition was complete, the ice bath was removed and the material stirred overnight at room temperature.

The complex was decomposed with iced hydrochloric acid and the mixture steam distilled to remove unreacted hydrocarbon. The separated solid reaction product was triturated with warm 10% aqueous potassium hydroxide solution and the insoluble material collected on a filter and recrystallized from ethanol. When the product consisted of two neutral compounds, they were separated by fractional recrystallization from ethanol. The alkaline filtrate was acidified to precipitate any keto acid if present.

When the hydrocarbons were acylated in carbon disulfide, nitro benzene or *sym*-tetrachloroethane, the amounts of reactants were usually 0.08 mole of hydrocarbon, 15 ml. of solvent, 4.4 g. (0.02 mole) of acid chloride and 6 g. (0.045 mole) of aluminum chloride. The liquid acid chloride of II was added through a separatory funnel.

Yields, physical constants and analyses of the acylation products are summarized in Tables I and II.

Preparation of the anhydride (V) *of 2,5-diphenylfuran-3,4-dicarboxylic acid.* A mixture of 25 g. of I and 200 ml. of acetic anhydride was refluxed for 2 hr. The acetic anhydride was hydrolyzed by the addition of cold water. Recrystallization of the yellow solid from glacial acetic acid gave 23.5 g. of V, m.p. 260–262°, lit.[16] 254–255°.

Acylations with V. The general procedure was as follows: In a 200 ml. round bottom flask fitted with the usual equipment was placed 100 ml. of hydrocarbon and 6 g. (0.045 mole) of aluminum chloride. The flask was cooled in an ice bath and 5.8 g. of V was added during 5 min. with stirring. The ice bath was removed, the mixture stirred at room temperature for 9 hr., and then allowed to stand an additional 15 hr.

The complex was decomposed in the usual manner and excess hydrocarbon removed by steam distillation. The solid residue was triturated with hot 10% aqueous sodium hydroxide solution and the insoluble sodium salt of the keto acid was collected on a filter and extracted with ether to remove any neutral compounds. The sodium salt was suspended in dilute ethanol, hydrochloric acid was added, and the separated keto acid was collected on a filter. Yields were 73% to 97%. Physical constants and analyses of the keto acids are summarized in Table IV.

Reaction of V *with phenyllithium.* A solution of phenyllithium prepared from 6.28 g. (0.04 mole) of bromobenzene was added dropwise with stirring to a slurry of 5.8 g. (0.02 mole) of V in 100 ml. of ether in the conventional apparatus. When the addition was complete, the mixture was stirred at room temperature for 3 hr. and then allowed to stand overnight. The complex was decomposed with 150 ml. of water.

The hydrolyzate was filtered and 0.55 g. of a solid was obtained. The aqueous layer was separated from the ether layer, washed twice with ether, and the ether layers were combined. These combined ether solutions were extracted with 5% sodium carbonate solution and the basic extract added to the original separated aqueous layer.

This basic solution was allowed to stand overnight and during this time a solid precipitated. It was collected and combined with the solid from the first filtration. The combined solids were treated with warm concentrated hydrochloric acid to decompose any remaining metal complex. After recrystallization from ethanol, this solid, the lactone VI, melted at 189–190°; yield 4.1 g. (47.7%). On evaporation of the ether solution, an additional 0.2 g. of VI was obtained.

Anal. Calcd. for $C_{30}H_{20}O_3$: C, 84.09; H, 4.71. Found: C, 83.86; H, 4.76.

The lactone VI showed a strong blue fluorescence in ultraviolet light, and was insoluble in hot concentrated potassium hydroxide solution.

In the Grignard machine, VI added one mole of methylmagnesium iodide but liberated no methane, indicating the presence of one carbonyl group and no active hydrogen.

Acidification of the basic filtrate yielded 1.9 g. of the acid I.

Preparation of 2,5-diphenyl-4-mesitoylfuran-3-carbonyl chloride. In a 200 ml. flask fitted with the conventional equipment was placed 11.0 g. (0.028 mole) of 2,5-diphenyl-4-mesitoylfuran-3-carboxylic acid and 50 ml. of thionyl chloride. After the mixture was stirred for 1.5 hr., the excess thionyl chloride was removed. The residue was recrystallized twice from petroleum ether (b.p. 60–70°) to yield 11 g. (94%) of acid chloride, m.p. 135–138°. Efforts to recrystallize this product further for an analytical sample resulted in decomposition.

This partially purified acid chloride reacted with aniline in benzene solution to form an anilide in 80% yield, m.p. 161–162.5°.

Anal. Calcd. for $C_{33}H_{27}O_3N$: C, 81.62; H, 5.61. Found: C, 81.30; H, 5.95.

Preparation of the 2,4-dinitrophenylhydrazones. The procedure was that of Josten.[17] In a 250 ml. flask was placed 2.0 g. of the ketone IIa, 3.5 g. of 2,4-dinitrophenylhydrazine, 4 ml. of sulfuric acid, and 75 ml. of dioxan. The solution was refluxed for 2 hr. under a slight pressure of nitrogen, then diluted and filtered. The orange brown solid was washed with dilute hydrochloric acid and recrystallized from ethyl acetate to yield, 2.8 g. (76%) of derivative, m.p. 268–269°.

Anal. Calcd. for $C_{20}H_{14}O_6N_4$: C, 59.11; H, 3.47. Found: C, 58.82; H, 3.42.

The *2,4-dinitrophenylhydrazone* of IIb melted at 242–243°.

Anal. Calcd. for $C_{21}H_{16}O_6N_4$: C, 60.00; H, 3.84. Found: C, 59.93; H, 3.68.

The *2,4-dinitrophenylhydrazone* of Ia melted at 233–235°.

Anal. Calcd. for $C_{30}H_{18}N_6O_4$: C, 67.92; H, 3.42. Found: C, 67.92; H, 3.77.

Reaction of 2,5-diphenyl-3,4-dimesitoylfuran with zinc.[3] To 4.3 g. (0.076 mole) of potassium hydroxide dissolved in 425 ml. of 95% ethanol was added 2.0 g. (0.004 mole) of 2,5-diphenyl-3,4-dimesitoylfuran. The mixture was refluxed for 14 hr., cooled, and filtered. The yellow filtrate was poured into dilute acetic acid and the mixture extracted with ether. The ether layer was separated and washed and the solvent removed by distillation. The oily residue was triturated with a mixture of ethanol and petroleum ether and finally solidified. The product V melted at 119–120° after recrystallization from ethanol.

Anal. Calcd. for $C_{36}H_{34}O_2$: C, 86.91; H, 6.87. Found: C, 86.82; H, 7.02.

Reaction of 2,5-diphenyl-3,4-bis(2,4-dimethylbenzoyl)furan with zinc. By the procedure described above this ketone yielded VI, m.p. 156.5–158° after recrystallization from ethanol.

Anal. Calcd. for $C_{34}H_{32}O_3$: C, 83.57; H, 6.60. Found: C, 83.77; H, 6.47.

COLUMBIA, MO.

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(16) W. H. Perkin and A. Calman, *J. Chem. Soc.*, 49, 154 (1886).

(17) W. Josten, *Ber.*, 41, 2230 (1931).