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. II

Dorothy V. Nightingale and Howard L. Needles (1,2)

The Friedel-Crafts acylation of six phenol ethers with 2,5-diphenylfuran-3,4-dicarbonyl chloride and with 2,5-dimethylfuran-3,4-dicarbonyl chloride yielded 2,5-di-R-3,4-diaroylfurans or cyclic diketones. 2,5-Diphenylfuran-3,4-dicarboxylic acid anhydride reacted with these ethers to form keto acids.

It has previously been shown (3) that the acylation of some alkylbenzenes with 2,5-diphenylfuran-3,4-dicarbonyl chloride (I) and with 2,5-dimethylfuran-3,4-dicarbonyl chloride (II) yielded cyclic diketones (4,9-dihydro-4,9-dioxo-1,3-di-R-naphtho[2,3c]furans) and/or 2,5-di-R-3,4-diaroylfurans rather than compounds of the phthalide type.

The study of the reaction of the acid chlorides I and II was extended to include the acylation of some phenol ethers with the thought that the strong activating effect of the methoxyl group would lead to some notable differences in product distribution as compared with alkylbenzenes of similar orientation. A few additional hydrocarbons were included for comparison purposes. Typical reactions are shown in Chart I. The data relative to yields and product distribution are shown in Tables I, II, and III.

It is assumed that the acylation of the phenol ethers takes place in the position which corresponds to the stronger directive effect of the methoxyl group (4,5), followed by cyclization in the least hindered position on the benzene ring *ortho* to the aroyl group. Naphthalene could acylate in the 1-position followed by cyclization in the 2-position or it could acylate in the 2-position followed by cyclization in the 1-position to form the same cyclic diketone.

It will be noted that from ten successful acylations with the five phenol ethers, the colorless diaroylfurans were obtained from seven of them while only three of the reactions yielded the yellow cyclic diketones and those were from I. Only one compound was isolated from each acylation of a phenol ether, whereas both cyclic diketone and diketone were often obtained from the mono and dialkylbenzenes with the cyclic diketones predominating. *m*-Cresol methyl ether yielded only amorphous material.

As in the previous studies, no compounds of the phthalide type were isolated, and the reactions of the acid chlorides with ethanol yielded only the normal esters which were identical with those obtained by the cyclization of diethyl α,α'-diacetosuccinate and diethyl α,α'-dibenzoylsuccinate.

It is of interest that cyclohexane-1,2-dicarbonyl chloride reacts with benzene to form 1,2-dibenzoylcyclohexane in good yield (6), but phthaloyl chloride forms phthalides. The behavior of the furan dicarbonyl chlorides I and II is thus more nearly comparable to that of the alicyclic acid dicarbonyl chloride than to the aromatic acid chloride, even though the heterocyclic ring system has a degree of aromatic character.

The acylation of the phenol ethers, including *m*-cresol methyl ether, with 2,5-diphenylfuran-3,4-dicarboxylic acid anhydride III in *s*-tetrachloroethane at room temperature formed the corresponding 2,5-diphenylfuran-4-aroyl-3-carboxylic acids. Attempts to acylate *p*-cresol methyl ether, *p*-xylene and naphthalene with III were unsuccessful.

The infrared spectra of the cyclic diketones all contained a single strong carbonyl band in the 1650-1660 cm^{-1} region and also a strong band at 770-735 cm^{-1}. These bands are in the expected locations for an $\alpha,\beta,\alpha'\beta'$-unsaturated ketone and for an *o*-disubstituted benzene ring which is part of a fused system (7).

The infrared spectra of the diaroylfurans all have a single strong band at 1660-1650 cm^{-1}. The region for a carbonyl group with two attached aryl groups (8) is 1670-1660 cm^{-1}.

Both the diaroylfurans and the cyclic diketones added two moles of methylmagnesium iodide in the Tschugaeff-Zerewitinoff determination of carbonyl groups.

The reduction of I with lithium tri-*t*-butoxyaluminohydride at -78° formed the lactone in variable yields rather than the dialdehyde. The infrared spectrum of this compound has a single strong band at 1750 cm^{-1}, the region for the α,β-unsaturated γ-lactones (9). The compound did not react with any of the usual carbonyl reagents.

Attempts to acylate toluene with pyridine-2,3-dicarbonyl chloride IV and with pyridine-3,4-dicarbonyl chloride V yielded only dark, intractable oils.

Efforts to obtain acid hydrazides, cyclic hydrazides, or hydroxamic acids from the acid chlorides I and II, the diethyl esters of the acids, or the anhydride III led to sparingly soluble, high melting products. Elemental analyses of these materials did not agree with those of any of the plausible products of the reactions.

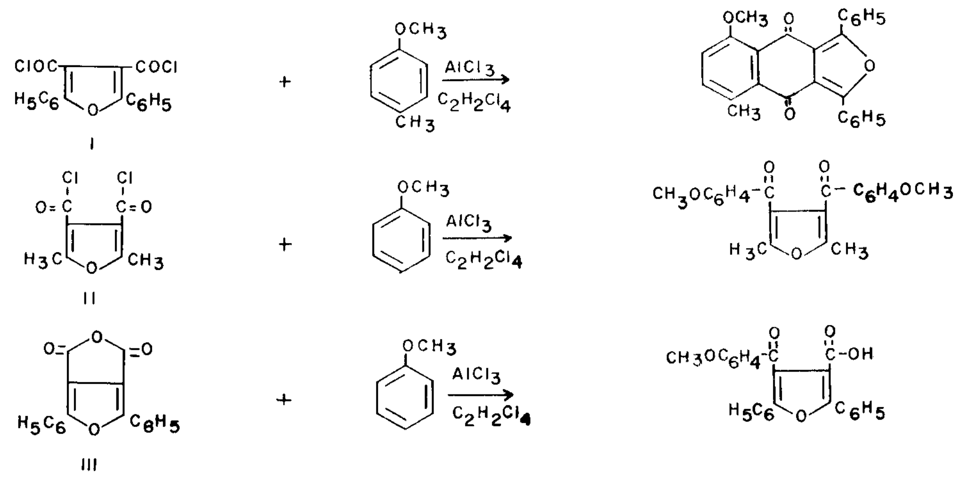

TABLE I

Acylations with 2, 5-Diphenylfuran-3, 4-dicarbonyl Chloride (I)

Compound Acylated	Product (a)	M.p. °C	Yield %		Calculated %C	Calculated %H	Found %C	Found %H
Anisole	DK	151-152	57	$C_{32}H_{24}O_5$	78.67	4.95	79.04	4.95
Veratrole	CDK	284-285	74	$C_{26}H_{18}O_5$	76.09	4.42	75.84	4.46
Resorcinol Dimethyl Ether	DK	207-208	60	$C_{34}H_{28}O_7$	74.44	5.15	74.17	5.04
o-Cresol Methyl Ether	CDK	219-220	68	$C_{26}H_{18}O_4$	79.17	4.60	79.13	4.80
p-Cresol Methyl Ether	CDK	184-185	70	$C_{26}H_{18}O_4$	79.17	4.60	79.18	4.41
Cumene	CDK	125-126	36	$C_{27}H_{20}O_3$	82.63	5.14	82.83	5.12
Pseudocumene	CDK	175-176	59	$C_{27}H_{20}O_3$	82.63	5.14	82.85	5.08
Durene	DK	198-199	74	$C_{38}H_{36}O_3$	84.41	6.71	84.53	6.71
Naphthalene	CDK	179-180	38	$C_{28}H_{16}O_3$	83.98	4.03	83.88	3.98

(a) DK = Diketone; CDK = Cyclic Diketone.

TABLE II

Acylations with 2, 5-Dimethylfuran-3, 4-dicarbonyl Chloride (II)

Compound	Product (a)	M.p. °C	Yield %		Calculated %C	Calculated %H	Found %C	Found %H
Anisole	DK	85-86	69	$C_{22}H_{20}O_5$	72.51	5.53	72.29	5.52
Resorcinol Dimethyl Ether	DK	129-130	28	$C_{24}H_{24}O_7$	67.91	5.70	68.24	5.86
o-Cresol Methyl Ether	DK	146-147	56	$C_{24}H_{24}O_5$	73.45	6.16	73.30	6.38
p-Cresol Methyl Ether	DK	136-137	46	$C_{24}H_{24}O_5$	73.45	6.16	73.26	6.10
Cumene	CDK	117-118	60	$C_{17}H_{16}O_3$	76.10	6.01	75.89	5.81
Pseudocumene	CDK	142-143	45	$C_{17}H_{16}O_3$	76.10	6.01	76.24	5.89
Durene	DK	227-228	89	$C_{28}H_{32}O_3$	80.73	7.74	80.72	7.95
Naphthalene	CDK	180-181	51	$C_{18}H_{12}O_3$	78.25	4.38	78.32	4.60

(a) DK = Diketone; CDK = Cyclic Diketone.

TABLE III

2, 5-Diphenyl-4-aroylfuran-3-carboxylic Acids

Compound Acylated	M.p. °C	Yield %	Formula	Calculated %C	Calculated %H	Found %C	Found %H	Neut. eq. Calc'd.	Neut. eq. Found
Anisole	213-215	78	$C_{25}H_{18}O_5$	75.37	4.55	75.22	4.65	394.4	396.3
Veratrole	175-176	70	$C_{26}H_{20}O_6$	72.89	4.71	72.77	4.79	428.4	429.6
Resorcinol Dimethyl Ether	172-173	75	$C_{26}H_{20}O_6$	72.89	4.71	72.60	4.64	428.4	427.5
o-Cresol Methyl Ether	193-194	68	$C_{26}H_{20}O_5$	75.71	4.89	75.48	4.90	412.4	412.2
m-Cresol Methyl Ether	163-164	61	$C_{26}H_{20}O_5$	75.71	4.89	75.51	4.92	412.4	412.5
Cumene	185-186	83	$C_{27}H_{22}O_4$	79.00	5.40	79.11	5.57	410.4	411.5
Pseudocumene	189-190	93	$C_{27}H_{22}O_4$	79.00	5.40	79.04	5.22	410.4	410.9
Durene	186-187	66	$C_{28}H_{24}O_4$	79.22	5.70	79.20	5.78	424.5	424.9

EXPERIMENTAL (10)

The Acylations.

The general procedure for all of the acylations with I, II, and III are the same as those described in the previous publication (3) except that 15 ml. of *s*-tetrachloroethane was used as solvent for all of the reactions. The reaction product was extracted with sodium hydroxide solution to remove any phenolic products formed by cleavage of the ethers.

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

The Reaction of I with Lithium Tri-*t*-butoxyaluminohydride.

The procedure is that of Brown and Rao (11). In a flask equipped with a nitrogen inlet and outlet, separatory funnel and stirrer, were placed 3.45 g. (0.01 mole) of acid chloride I and 10 ml. of dry tetrahydrofuran. The mixture was cooled to dry ice temperature and 4.75 g. (0.02 mole) of lithium tri-*t*-butoxyaluminohydride with sufficient tetrahydrofuran to wash it down was added over a period of 1 hr. After the addition, the flask was slowly warmed to room temperature and the contents then poured into crushed ice, giving a solid which was removed by filtration. This solid was recrystallized from 95% ethanol to yield 0.5 g. (36%) of the lactone, m.p. 194-195°.

Anal. Calcd. for $C_{18}H_{12}O_3$: C, 78.25; H, 4.38. Found: C, 77.93; H, 4.53.

The same procedure for the reaction of II yielded only 2, 5-dimethylfuran-3, 4-dicarboxylic acid.

The Preparation of Pyridine-2, 3-dicarbonyl Chloride IV and Pyridine-3, 4-Dicarbonyl Chloride V.

The procedure was that of Scheiber and Knothe (12) for IV.

To 8.4 g. (0.05 mole) of pyridine-3, 4-dicarboxylic acid (or pyridine-2, 3-dicarboxylic acid) was added 20.8 g. (0.1 mole) of phosphorus pentachloride at ice bath temperature. Almost immediately the reactants liquified and the reaction was completed by heating the mixture on a steam bath. The phosphorus oxychloride was removed at aspirator pressure and then the acid chloride V was distilled at 2 mm. Efforts to obtain analytical samples of IV and V resulted in a product contaminated with the acid.

The acid chloride IV, b.p. 135-137° (2mm.), reported 159° (19 mm.), was obtained in yields of 69-76%.

Aniline reacted with IV in dry benzene to form a dianilide, m.p. 233-234°.

Anal. Calcd. for $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.75; N, 13.24. Found: C, 72.06; H, 4.76; N, 13.00.

Acid chloride V, not previously described in the literature, b.p. 100-101° (2 mm.), was obtained in yields of 78-85%.

The dianilide of V melted at 229-230°.

Anal. Calcd. for $C_{19}H_{15}N_3O_2$: C, 71.91; H, 4.76; N, 13.24. Found: C, 71.99; H, 4.77; N, 13.20.

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Received January 13, 1964

Columbia, Missouri