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SOME ARYLATED BENZOFURANS

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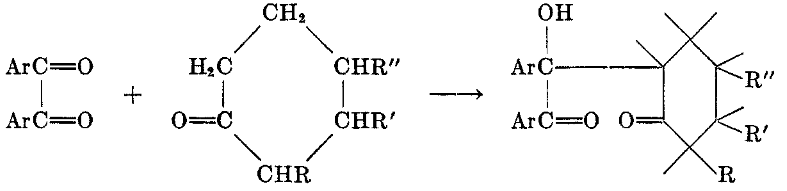
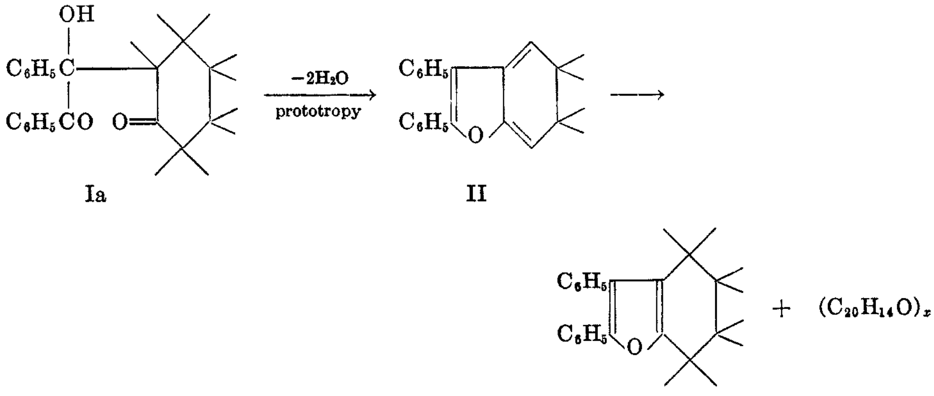
It was shown twenty years ago that cyclohexanone added to benzil in the absence of a solvent to give a 1,4-diketone (I: Ar = C_6H_5; R, R′, R″ = H), in which the components were combined in a 1:1 ratio (1).



I

It has since been found that other cyclohexanones add in this same way; twelve addition products are given in Table I. It was previously (2, 3) shown that *o*-anisil did not enter into this type of reaction; it has now been shown that *p*-anisil, 4,4′-dibromobenzil, and 4-dimethylaminobenzil likewise fail to react, but *m*-anisil gives a 1,4-diketone readily. Such behavior is to be expected and is in accord with modern electronic theories (4). Apparently, strongly electron-donating groups (CH_3O, $(CH_3)_2N$, Br) in the 4-position of the benzil so disturb the polarity of its carbonyl group that it can no longer function as an acceptor to the carbanion. The difference in reactivity between the *meta*-anisil and its *ortho* and *para* isomers is attributed to its location; *meta* substituents do not hybridize with a carbonyl group.

When the addition product (Ia) was treated with acidic dehydrating agents, a dihydrobenzofuran (II) was formed, which, upon distillation, underwent disproportionation, giving a tetrahydrobenzofuran (III) and polymeric material.



Ia

II

III

The known 2,3-diphenylbenzofuran (5, 6) is obtained by dehydrogenation of the dihydro derivative (II) using palladium on charcoal. Upon long standing, solutions of the latter slowly deposit a dimer, the structure of which has not been determined.

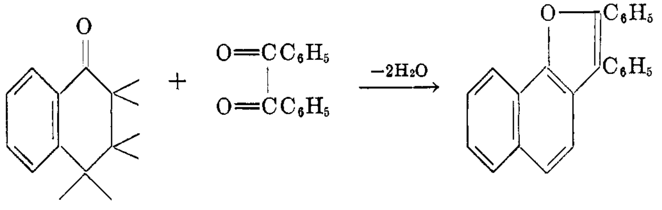
It is obvious that use of a cyclohexenone should give a single product of furan type, upon dehydration. Such a behavior was shown by the fused-ring cyclohexenones, α-tetralone and 4-keto-1,2,3,4-tetrahydrophenanthrene. These substances form addition products with benzil which, upon dehydration, give 2,3-diphenylnaphtho[1,2-*b*]furan (IV) and 2,3-diphenylphenanthro[4,3-*b*]furan (V), respectively.

TABLE I

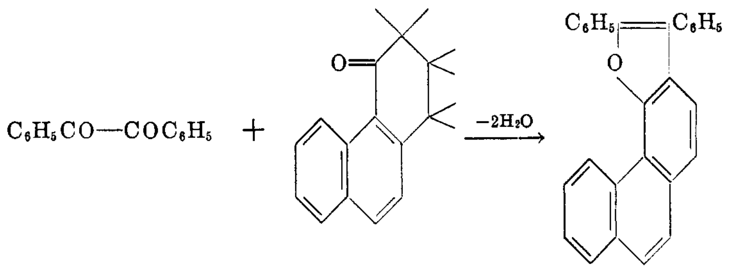
PROPERTIES OF 1,4-DIKETONES

BENZIL USED	KETONE USED	NUMBER	M.P., °C.	EMPIRICAL FORMULA	ANALYSES			
					Calc'd		Found	
					C	H	C	H
Benzil	Cyclohexanone	Ia	139					
Benzil	2-Methylcyclohexanone	I; R = CH_3 R′, R″ = H	121	$C_{21}H_{20}O_3$	78.8	6.3	78.7	6.7
Benzil	3-Methylcyclohexanone	I; R′ = CH_3 R, R″ = H	119	$C_{21}H_{20}O_3$	78.8	6.3	78.2	6.9
Benzil	4-Methylcyclohexanone	I; R″ = CH_3 R, R′ = H	139	$C_{21}H_{20}O_3$	78.8	6.3	79.1	7.0
Benzil	4-Isopropylcyclohexanone	I; R″ = *i*-C_3H_7 R, R′ = H	139	$C_{23}H_{26}O_3$	79.2	7.2	78.7	7.7
Benzil	4-*sec*-Butylcyclohexanone	I; R″ = *s*-C_4H_9 R, R′ = H	146	$C_{24}H_{28}O_3$	79.2	7.7	79.4	8.0
Benzil	4-*tert*-Butylcyclohexanone	I; R″ = *t*-C_4H_9 R, R′ = H	171	$C_{24}H_{28}O_3$	79.2	7.7	79.6	7.8
Benzil	4-Cyclohexylcyclohexanone	I; R″ = C_6H_{11} R, R′ = H	178	$C_{26}H_{29}O_3$	80.2	7.5	80.1	8.0
m-Anisil	Cyclohexanone	I; Ar = C_7H_7O R, R′, R″ = H	163	$C_{22}H_{24}O_5$	71.7	6.5	71.3	6.6
o-Tolil	Cyclohexanone	I; Ar = C_7H_7 R, R′, R″ = H	153	$C_{20}H_{24}O_3$	77.0	7.7	77.2	7.3
p-Tolil	Cyclohexanone	I; Ar = C_7H_7 R, R′, R″ = H	185	$C_{20}H_{24}O_3$	77.0	7.7	77.4	7.3
Benzil	α-Tetralone		173	$C_{24}H_{19}O_3$	85.0	5.4	84.8	5.4
Benzil	4-Keto-1,2,3,4-tetrahydrophenanthrene		221	$C_{28}H_{21}O_3$	83.0	5.2	83.2	5.6
Furil	Cyclohexanone		160	$C_{16}H_{16}O_5$	66.6	5.5	66.7	5.2

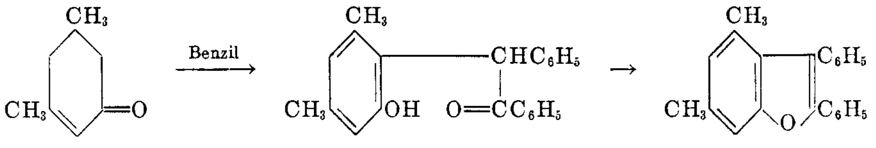
It should be noted that in these cyclohexenones the unsaturation is a part of a stable aromatic system. If this conjugation is not present, dehydration and aromatization occur simultaneously with the addition reaction, as is shown with 3,5-dimethylcyclohexenone. This substance gives rise to the phenolic ketone (VI) which forms a 2,4-dinitrophenylhydrazone and, when treated quantitatively with methylmagnesium iodide, shows one active hydrogen and one addition. It is smoothly converted to 2,3-diphenyl-4,6-dimethylbenzofuran (VII) by distillation under reduced pressure.



IV

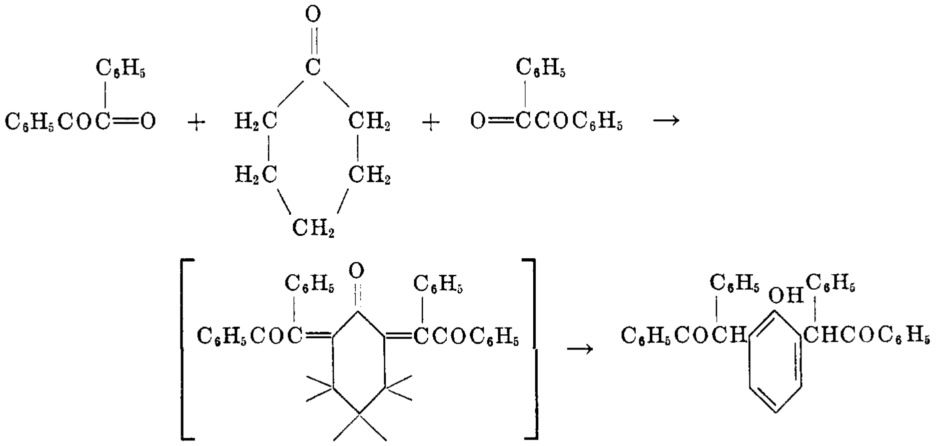


V



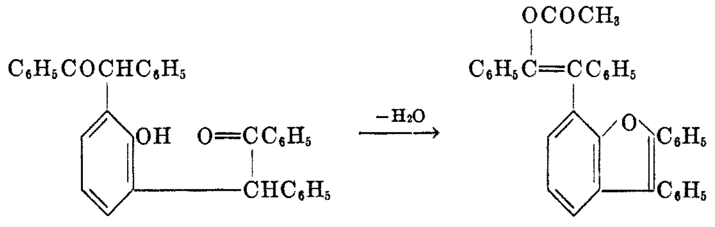
VI VII

The catalyst used to bring about the addition of cyclohexanone to benzil was sodium methoxide in considerable amount; it was further emphasized that the absence of water was essential (1). It has now been found that if the reaction is carried out in "absolute alcohol" with only a small amount of potassium hydroxide, 2,6-bidesylphenol (VIII) only is obtained.



VIII

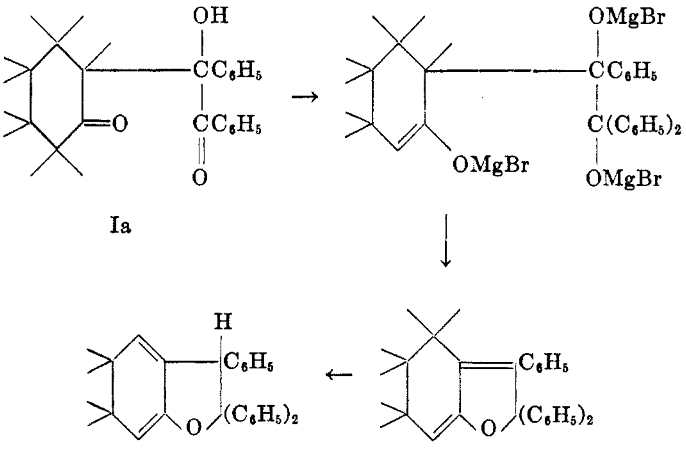
The bidesylphenol is cyclized to the benzofuran (IX) by acetic anhydride, as would be expected.



VIII IX

The formation of the phenol illustrates the great tendency for exocyclic double bonds to enter a ring so that an aromatic structure results. Since this tendency is now well established (7, 8, 9), the formation of the diphenyltetrahydrobenzofuran (III) by distillation of the dehydration product of 2-(hydroxydesyl)cyclohexanone (Ia) becomes explicable. The two dehydrations give rise to a dihydrobenzofuran (II) which disproportionates on heating to give the tetrahydro derivative (III) and polymeric material. Since diphenylbenzofuran is now known (5, 6) but has not been found in this work, the polymer may arise from that substance as well as by a diene synthesis involving the cyclohexadiene (II).

An additional example of the exocyclic bond shift is furnished by the formation of a tetrahydrobenzofuran (X) when 2-(hydroxydesyl)cyclohexanone (Ia) is treated with phenylmagnesium bromide. 2-(Hydroxydesyl)cyclohexanone shows two active hydrogens and one addition, when treated quantitatively with methylmagnesium iodide; to account for this, enolization of the carbonyl group on the reduced ring has been assumed. Therefore, the reaction between 2-(hydroxydesyl)cyclohexanone and phenylmagnesium bromide is written in this way.



Ia

X

EXPERIMENTAL

I. *The addition products and related substances.* These were prepared by the procedure (1) previously used in yields of 70–90%. Their properties are presented in Table I.

2-(Hydroxydesyl)cyclohexanone showed two active hydrogens and one addition with methylmagnesium iodide, when a specimen was freshly recrystallized from dry ligroin (b.p. 90–120°).

2-Desyl-3,5-dimethylphenol (VI). To a solution of 15.6 g. of benzil in 75 ml. of methanol and 9.5 ml. of 3,5-dimethylcyclohexenone (10) there was added 4 ml. of 7.5% sodium methoxide solution, and the mixture was left at room temperature for one week. The solid was recrystallized from isopropyl alcohol; yield, 19 g., 81%; m.p. 200–203°. After two recrystallizations from isopropyl alcohol, it melted at 211°. When treated with methylmagnesium iodide, it showed one active hydrogen and one addition.

The *2,4-dinitrophenylhydrazone* was prepared in the usual manner and recrystallized from xylene; it formed bright red crystals, m.p. 310°.

Anal. Calc'd for $C_{28}H_{24}N_4O_5$: C, 67.7; H, 4.9.
Found: C, 67.9; H, 5.2.

2,6-Bidesylphenol (VIII). The yellow mixture of 11 g. of cyclohexanone, 21 g. of benzil, 250 ml. of absolute ethyl alcohol, and 1 g. of potassium hydroxide gradually turned red and crystals separated; after one week, 5.1 g. was collected. The crystals were recrystallized from butyl acetate and then from xylene; yellow crystals, m.p. 210–211°, which gave an intense red color with concentrated sulfuric acid.

Anal. Calc'd for $C_{34}H_{26}O_3$: C, 84.6; H, 5.3; Mol. wt., 482; 1 act. H; 2 addn.
Found: C, 84.7; H, 5.7; Mol. wt., 486 (in boiling benzene); 1 act. H; 2 addn.

II. *The benzofurans.* The *dihydro-2,3-diphenylbenzofuran* (II) was prepared as previously described, and recrystallized from dry ligroin (b.p., 90–120°); it is a bright yellow powder, m.p. 102–105°.

Anal. Calc'd for $C_{20}H_{16}O$: C, 88.2; H, 5.9; Mol. wt., 272.
Found: C, 88.5; H, 6.2; Mol. wt., 276 (in boiling methylene chloride).

2,3-Diphenylbenzofuran was obtained by heating the dihydro derivative with 1 g. of palladium on charcoal at 350–360° for four hours. The product was distilled, and the fraction collected up to 250°/14 mm.; the distillate was recrystallized from acetic acid, followed by alcohol. It melted at 118–119°, both alone and on admixture with a specimen prepared as directed in the literature (5, 6).

Anal. Calc'd for $C_{20}H_{14}O$: C, 88.8; H, 5.2.
Found: C, 88.3; H, 5.6.

Dimerization took place when 4 g. of the dihydro derivative in 100 ml. of ethyl acetate was left for three weeks at room temperature. After two recrystallizations from dimethylformamide, 1.1 g. of a yellow, amorphous powder remained; m.p. 250–252°.

Anal. Calc'd for $(C_{20}H_{16}O)_2$: C, 88.2; H, 5.9; Mol. wt., 544.
Found: C, 87.9; H, 5.9; Mol. wt., 676, 697 (in boiling benzene).

4,6-Dimethyl-2,3-diphenylbenzofuran (VII). Five grams of 2-desyl-3,5-dimethylphenol was distilled; b.p. 200–250°/1 mm. It was taken up in benzene, ligroin added, and the furan allowed to crystallize, then recrystallized from ligroin, followed by alcohol; m.p. 158°. Yield, 3.2 g.

Anal. Calc'd for $C_{22}H_{18}O$: C, 88.5; H, 6.0.
Found: C, 88.4; H, 5.9.

2,3-Diphenylnaphtho[1,2-b]furan (IV) (6). A warm solution of 1 g. of the tetralone addition product, 7 ml. of acetic anhydride, and a drop of concentrated sulfuric acid was left overnight; the crystals that separated were crystallized from isopropyl alcohol; m.p. 100–101°.

Anal. Calc'd for $C_{24}H_{16}O$: C, 90.0; H, 5.0.
Found: C, 90.0; H, 5.0.

2,3-Diphenylphenanthro[4,3-b]furan (V) was prepared in a similar manner and crystallized from *n*-butyl alcohol; m.p. 201°.

Anal. Calc'd for $C_{28}H_{18}O$: C, 90.9; H, 4.3.
Found: C, 90.7; H, 4.9.

7-(β-Acetoxy-α-phenylstyryl)-2,3-diphenylbenzofuran (IX) was obtained by suspending 2.7 g. of bidesylphenol in 10 ml. of acetic anhydride containing one drop of concentrated sulfuric acid, and warming the orange solution. The next day the white furan that had separated was removed and crystallized from glacial acetic acid; the yield was 1.5 g., m.p. 195°.

Anal. Calc'd for $C_{36}H_{27}O_3$: C, 85.0; H, 5.3.
Found: C, 85.0; H, 5.4.

2,2,3-Triphenyl-2,3,5,6-tetrahydrofuran (X) was obtained by the interaction of phenylmagnesium bromide and 2-(hydroxydesyl)cyclohexanone, adding the latter solid to the Grignard solution with stirring. It was then refluxed for four hours, decomposed by iced ammonium chloride, and finally acidified with sulfuric acid. The yellow ether layer was removed and steam-distilled to remove biphenyl. The residual oil was taken up in benzene, and manipulated with solvents to get a pure specimen; m.p., 152°. It is very soluble in chloroform, but recrystallizes well from methanol-chloroform. The yield was very low, about 10%, because of the tedious recrystallizations.

Anal. Calc'd for $C_{26}H_{22}O$: C, 89.2; H, 6.3.
Found: C, 89.3; H, 6.3.

SUMMARY

Aromatic 1,2-diketones and cyclohexanones form 1:1 addition products in the presence of a large amount of anhydrous sodium methoxide, provided there is no strong electron-donating group in the *ortho* or *para* position of the benzil.

The same components give rise to a bidesylphenol with a low concentration of alcoholic potassium hydroxide.

Benzil and fused-ring ketones containing an aromatic ring likewise give 1:1 addition products, but use of an unsaturated cyclic ketone results in the formation of a phenolic ketone.

The latter is converted to a benzofuran, on being heated at an elevated temperature, whereas the other addition products require the use of an acidic dehydrating agent at a moderate temperature. A tetrahydrofuran was prepared by the action of phenylmagnesium bromide upon one of the adducts.

The mechanism of the various reactions is discussed.

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