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# 1,3,4,6-TETRACARBONYL COMPOUNDS. 3.* SYNTHESIS, STRUCTURAL FEATURES, AND ANTIMICROBIAL ACTIVITY OF 1,6-DIARYL-3,4-DIHYDROXY-2,4-HEXADIENE-1,6-DIONES

**N. M. Igidov, E. N. Koz'minykh, O. A. Sof'ina, T. M. Shironina, and V. O. Koz'minykh**

*The Wittig reaction of 5-aryl-2,3-dihydro-2,3-furandiones with aroylmethylenetriphenylphosphoranes is regioselective and leads to the formation of 5-aryl-2-aroylmethylene-2,3-dihydro-3-furanones. In the presence of acid the products react with water, giving satisfactory yields of 1,6-diaryl-3,4-dihydroxy-2,4-hexadiene-1,6-diones. The latter were also obtained by the reaction of 2,3-furandiones with alkylnitroamines. The base-catalyzed condensation of 2,3-furandiones with acetophenones led to 1,6-diaryl-3,4-dihydroxy-2,4-hexadiene-1,6-diones, which exist in DMSO solution in equilibrium with the cyclic oxo tautomers – substituted 2-hydroxy-2,3-dihydro-3-furanones. Some of the synthesized compounds exhibit antimicrobial activity toward standard strains of* Staphylococcus aureus *and* Escherichia coli.

1,3,4,6-Tetracarbonyl compounds and their ring oxo tautomers 2-hydroxy-2,3-dihydro-3-furanones are finding more and more applications in organic synthesis as readily obtainable and highly reactive synthons in various nucleophilic transformations [2-8]. Among the tetraketones certain 1,6-diaryl-3,4-dihydroxy-2,4-hexadiene-1,6-diones [9-11] have weak antimicrobial activity [12] but do not exhibit inhibiting activity toward acetylcholinesterase [2]. They are used to increase the sensitivity of photoconducting compositions [13] and are intermediates in the synthesis of polymers and biologically active substances [14].

The Claisen condensation of acetophenones with diethyl oxalate (method A, see the scheme) [2, 9, 10] or with aroylpyruvic esters IV (method B) [15] is the traditional method for the synthesis of diaryl-substituted tetraketones III, the structure of which was discussed earlier [15-17]. In a continuation of research into 1,3,4,6-tetracarbonyl compounds and their cyclic tautomeric forms [1, 11, 12] in the present work we describe new simple methods for the preparation of these compounds, using 5-aryl-2,3-dihydro-2,3-furandiones (I) [18, 19] and 5-aryl-2-aroylmethylene-2,3-dihydro-3-furanones (II) [17, 19, 20] as initial reagents.

It is known that 5-aryl-2,3-dihydro-2,3-furandiones I react readily with alkoxycarbonylmethylenetriphenylphosphoranes, forming *Z*-2-alkoxycarbonylmethylene-5-aryl-2,3-dihydro-3-furanones. This Wittig reaction usually takes place both regio- and stereoselectively [12, 19-21]. In the present communication we present data on the reaction of 2,3-furandiones Ia-c,h with structurally similar aroylmethylenetriphenylphosphoranes [22], as a result of which we isolated the corresponding *Z*- and *E*-5-aryl-2-aroylmethylene-2,3-dihydro-3-furanones IIa-f (Tables 1 and 2) but not the regioisomeric 3-aroylmethylene-2,3-dihydro-2-furanones [19] (see the scheme).

It is also known that 2-*p*-halogenobenzoylmethylene-5-*p*-halogenophenyl-2,3-dihydro-3-furanones IId,e are decyclized when heated with a mixture of 70% acetic acid and pyridine for 2 h, forming the 1,6-disubstituted 3,4-dihydroxy-2,4-hexadiene-1,6-diones IIIj,m [17]. Under milder conditions (heating in acetone solution at 40-50°C in the presence of 20 % hydrochloric acid) the 2-acylmethylene-2,3-dihydro-3-furanones IIa-c,e,f undergo hydrolysis, leading satisfactory yields of the 2,4-hexadiene-1,6-diones IIIg-i,m,n (method C, Tables 4 and 5).

* For Communication 2, see [1].

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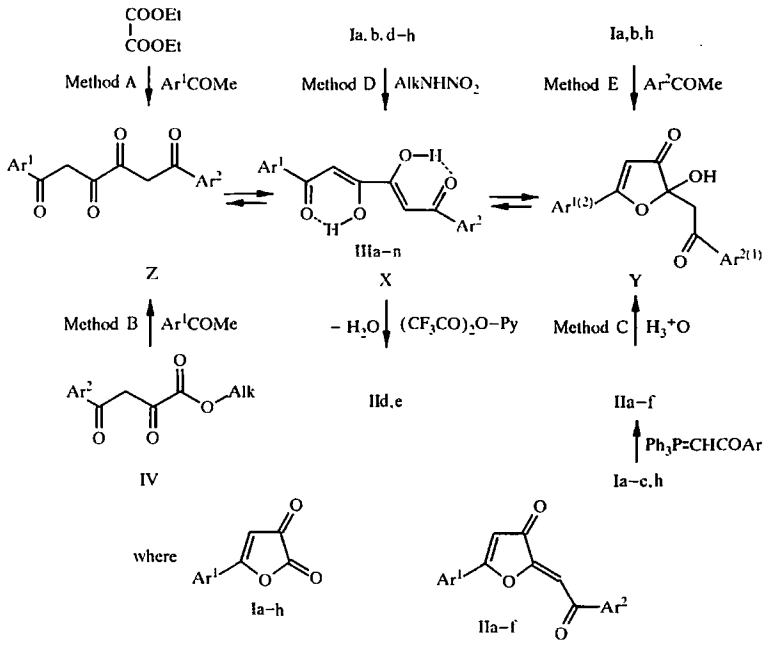



| I | $Ar^1$ | Ref. |
|---|---|---|
| a | Ph | [18] |
| b | 4-$MeC_6H_4$ | [18] |
| c | 2,4-$Me_2C_6H_3$ | |
| d | 4-$EtC_6H_4$ | |
| e | 4-$MeOC_6H_4$ | [18] |
| f | 4-$EtOC_6H_4$ | |
| g | 4-$BrC_6H_4$ | [18] |
| h | 4-$ClC_6H_4$ | [18] |

| II | $Ar^1$ | $Ar^2$ | Ref. |
|---|---|---|---|
| a | Ph | 4-$BrC_6H_4$ | |
| b | 4-$MeC_6H_4$ | 4-$BrC_6H_4$ | |
| c | 2,4-$Me_2C_6H_3$ | 4-$BrC_6H_4$ | |
| d | 4-$BrC_6H_4$ | 4-$BrC_6H_4$ | [17] |
| e | 4-$ClC_6H_4$ | 4-$ClC_6H_4$ | [17] |
| f | Ph | 4-$NO_2C_6H_4$ | |

| III | $Ar^1$ | $Ar^2$ | Ref. |
|---|---|---|---|
| a | Ph | Ph | [10, 17] |
| b | Ph | 4-$MeC_6H_4$ | [15] |
| c | 4-$MeC_6H_4$ | 4-$MeC_6H_4$ | [9] |
| d | 4-$EtC_6H_4$ | 4-$EtC_6H_4$ | |
| e | 4-$MeOC_6H_4$ | 4-$MeOC_6H_4$ | [9] |
| f | 4-$EtOC_6H_4$ | 4-$EtOC_6H_4$ | |
| g | Ph | 4-$BrC_6H_4$ | [15] |

| III | $Ar^1$ | $Ar^2$ | Ref. |
|---|---|---|---|
| h | 4-$MeC_6H_4$ | 4-$BrC_6H_4$ | |
| i | 2,4-$Me_2C_6H_3$ | 4-$BrC_6H_4$ | |
| j | 4-$BrC_6H_4$ | 4-$BrC_6H_4$ | [9, 17] |
| k | Ph | 4-$ClC_6H_4$ | [15] |
| l | 4-$MeC_6H_4$ | 4-$ClC_6H_4$ | [15] |
| m | 4-$ClC_6H_4$ | 4-$ClC_6H_4$ | [9,17] |
| n | Ph | 4-$NO_2C_6H_4$ | |

It was established that there was a tautomeric ring-chain equilibrium in the solutions of the various 1,3,4,6-tetraketones in DMSO [17]. By PMR spectroscopy we detected two types of oxo tautomers in the solutions: 1,6-diaryl-3,4-dihydroxy-2,4-hexadiene-1,6-diones (X) and 5-aryl-2-aroylmethyl-2-hydroxy-2,3-dihydro-3-furanones (Y) (see the scheme), but in no case was the tetraoxo chain component observed (Table 5).

The structure of the bis-H-chelate tautomer X ($Ar^1 = Ar^2 = Ph$), detected in the chloroform solution, agrees with the data from the $^{13}C$ NMR spectrum. Thus, the difference between the experimental and calculated [23] values of the chemical shifts of the $^{13}C$ carbon atoms ($C_{(1)}C_{(7)}$ amounts to not more than 3.5 ppm, and these values are close to the values for the model methyl pyruvate [24] (Table 3). As was established [24, 25], the formation of the structure with a chelate ring close to quasisymmetrical was due to tunnel migration of a proton between the two barriers with minimum potential energy in the enolic forms of the β-dicarbonyl compounds.

TABLE 1. 5-Aryl-2-aroylmethylene-2,3-dihydro-3-furanones (IIa-f)

| Compound | $Ar^1$ | $Ar^2$ | Empirical formula (molecular mass)*[2] | mp, °C (solvent) | Yield, %* (isomer) |
|---|---|---|---|---|---|
| IIa | Ph | $4\text{-}BrC_6H_4$ | $C_{18}H_{11}BrO_3$ (355.2) | 169-170 (ethyl acetate) | 62*[3] *E*-isomer |
| | | | | 193-195 (ethyl acetate) | 27*[3] *Z*-isomer |
| IIb | $4\text{-}MeC_6H_4$ | $4\text{-}BrC_6H_4$ | $C_{19}H_{13}BrO_3$ (369.2) | 160-161 (ethanol) | 53*[3] |
| IIc | $2,4\text{-}Me_2C_6H_3$ | $4\text{-}BrC_6H_4$ | $C_{20}H_{15}BrO_3$ (383.3) | 145-146 (acetonitrile) | 45*[3] |
| IId | $4\text{-}BrC_6H_4$ | $4\text{-}BrC_6H_4$ | $C_{18}H_{10}Br_2O_3$ (434.1) | 194-195 (decomp. (toluene*[6]) | 74*[3], 88*[4], (91*[5]) |
| IIe | $4\text{-}ClC_6H_4$ | $4\text{-}ClC_6H_4$ | $C_{18}H_{10}Cl_2O_3$ (345.2) | 184-185 (decomp. (toluene*[7]) | 87*[3], 76*[4], (89*[5]) |
| IIf | Ph | $4\text{-}NO_2C_6H_4$ | $C_{18}H_{11}NO_5$ (321.3) | 212-213 (acetone) | 47*[3] |

* Published data are given in parentheses.

*[2] The data from microanalysis agree satisfactorily with the calculated values, %: C ±0.25; H ±0.17; Hal ±0.29; N ±0.19.

*[3] In the reaction of the 2,3-furandiones with the corresponding phosphorane.

*[4] Obtained from the corresponding hexadienedione by the action of a mixture of trifluoroacetic acid and pyridine (for a modified procedure, see the experimental section).

*[5] Obtained from the corresponding hexadienedione by the action of a mixture of 70% acetic acid and pyridine [17].

*[6] Published data: mp 194-195°C (decomp.) [17].

*[7] Published data: mp 188°C (decomp.) [17].

Treatment of the 1,6-bis-*p*-halogenophenyl-3,4-dihydroxy-2,4-hexadiene-1,6-diones IIIj, m with trifluoroacetic anhydride in the presence of pyridine, as also in the case of the reaction with acetic anhydride [17], led to the corresponding 2-*p*-halogenobenzoylmethylene-5-*p*-halogenophenyl-2,3-dihydro-3-furanones IId,e (scheme, Table 1). However, in contrast to the reaction with acetic anhydride (the yields given in [17] were too high) the conditions for the reaction with trifluoroacetic anhydride are more suitable for the preparative synthesis of 2-acylmethylene-2,3-dihydro-3-furanones II. Unfortunately, we were unable to realize the dehydration of 3,4-dihydroxy-1,6-diphenyl-2,4-hexadiene-1,6-dione (IIIa) under analogous conditions – resinification of the reaction mixture was observed.

We obtained various symmetrical tetraketones IIIa,c-f,j, m as a result of the reaction between the respective 5-aryl-2,3-dihydro-2,3-furandiones Ia,b,d-h and alkylnitroamines [methylnitroamine or 1,2-bis(nitroamino)ethane] by boiling in the dioxane solution (method D, scheme and Table 4). The intermediates in the thermolysis of the 2,3-furandiones I (carbon monoxide is readily released here), i.e., the highly reactive aroylketenes, undergo reductive dimerization more rapidly than they enter in to known cycloaddition with the formation of 2,4-pyrandione derivatives [26] or the N-aroylacylation of the nitroamines. Such unusual behavior of the nitroamines was probably unknown before [27], and this process may be determined by the enhanced acidity of the amine under the influence of the neighboring nitro group.

TABLE 2. The Data from the IR and PMR Spectra of 5-Aryl-2-aroylmethylene-2,3-dihydro-3-furanones (IIa-f)

| Compound | IR spectra, ($cm^{-1}$) | PMR spectra (δ, ppm, $CDCl_3$/HMDS) |
|---|---|---|
| IIa* | 1698 ($C_{(3)}$=O ), 1668 (C=$C_{exo}$), 1642 ($Ar^2$CO) | 6.30 (1H, s, $CH_{exo}$), 6.95 (1H, s, 4-H), 7.57-8.00 (9H, m, 2 Ar); 6.57 (1H, s, $CH_{exo}$), 7.21 (1H, s, 4-H), 7.56-8.05 (9H, m, 2 Ar)*[3]; 6.95 (1H, s, $CH_{exo}$), 7.05 (1H, s, 4-H), 7.55-8.20 (9H, m, 2 Ar)*[4] |
| IIa*[2] | 1686 ($C_{(3)}$=O ), 1676 (C=$C_{exo}$), 1656 ($Ar^2$CO) | 6.17 (1H, s, $CH_{exo}$), 6.54 (1H, s, 4-H), 7.45-8.00 (9H, m, 2 Ar); 6.51 (1H, s, $CH_{exo}$), 7.15 (1H, s, 4-H), 7.60-8.04 (9H, m, 2 Ar)*[3]; 6.78 (1H, s, $CH_{exo}$), 7.18 (1H, s, 4-H), 7.55-8.20 (9H, m, 2 Ar)*[4] |
| IIb*[2] | 1689 ($C_{(3)}$=O ), 1660 (C=$C_{exo}$), 1635 ($Ar^2$CO) | 2.37 (3H, s, Me), 6.18 (1H, s, $CH_{exo}$), 6.80 (1H, s, 4-H), 7.20-7.93 (8H, m, 2 Ar); 2.37 (3H, s, Me), 6.35 (1H, s, $CH_{exo}$), 6.99 (1H, s, 4-H), 7.40-8.10 (8H, m, 2 Ar)*[3] |
| IIc*[2] | 1692 ($C_{(3)}$=O ), 1670 (C=$C_{exo}$), 1645 ($Ar^2$CO) | 2.34 (3H, s, Me), 2.48 (3H, s, Me), 6.13 (1H, s, $CH_{exo}$), 6.86 (1H, s, 4-H), 7.08-7.88 (7H, m, 2 Ar) |
| IId* | 1701 ($C_{(3)}$=O ), 1677 (C=$C_{exo}$), 1658 ($Ar^2$CO) | 6.86 (1H, s, $CH_{exo}$), 6.98 (1H, s, 4-H), 7.55-8.00 (8H, m, 2 Ar)*[4] |
| IIe* | 1692 ($C_{(3)}$=O ), 1673 (C=$C_{exo}$), 1632 ($Ar^2$CO) | 6.32 (1H, s, $CH_{exo}$), 6.98 (1H, s, 4-H), 7.50-7.95 (9H, m, 2 Ar) |
| IIf* | 1685 ($C_{(3)}$=O ), 1657 (C=$C_{exo}$), 1625 ($Ar^2$CO) | 6.55 (1H, s, $CH_{exo}$), 7.23 (1H, s, 4-H), 7.65-8.35 (9H, m, 2 Ar)*[3] |

* *E*-isomer.

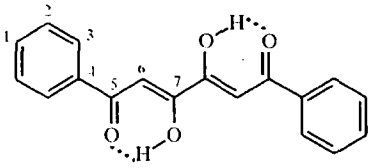
*[2] *Z*-isomer. The structure was confirmed by X-ray crystallographic analysis of compound IIc (unpublished data). The more downfield signal of the olefinic proton $CH_\alpha$ of this isomer compared with the close *E*-isomer looks unusual. According to published data, different values of the chemical shifts for the $CH_\alpha$ proton are given for 3-methoxycarbonylmethylenetetrahydro-2-furanone: 6.80 ppm (*Z*) and 6.19 ppm (*E*) [30]. The same was observed for the regio analog – substituted 2-ethoxycarbonylmethylenethietane – chemical shift 6.00 and 5.54 ppm respectively [31].

*[4] The spectrum was recorded in a 10:1 mixture of $CDCl_3$ and $CF_3COOH$.

*[5] The spectrum was recorded in DMSO-$d_6$ solution.

During the search for other methods for the synthesis of 2,3-dihydro-3-furanones and 1,3,4,6-tetraketones we unexpectedly found that the 5-aryl-2,3-dihydro-2,3-furandiones I readily react with methylene-active carbonyl compounds in the presence of bases, leading to various products. In the present work we propose a simple method for the preparation of 3,4-dihydroxy-2,4-hexadiene-1,6-diones III with aryl substituents (which can also differ from each other) by the aldol-type condensation of 2,3-furandiones Ia,b,h with aryl methyl ketones in the presence of potassium hydroxide, potassium carbonate, or its mixture with benzyltrimethylammonium chloride as phase-transfer catalyst. This takes place regioselectively with the formation of 1,6-diaryl-3,4-dihydroxy-2,4-hexadiene-1,6-diones IIIa,b,k,l (method E, scheme, and Table 4). The reaction was monitored by TLC, and the formation of the possible ring tautomers (3-hydroxy-2,3-dihydro-2-furanones or the products of the Knoevenagel reaction, i.e., 2-acylmethylene-2,3-dihydro-3-furanones II) was not observed. In the reaction mixture after treatment with water or keeping in the open air only aroylpyruvic acids easily separated and identified by a mixed melting test were detected as impurity. The 2,3-furandiones I do not give compounds III with acetone under these conditions – different products were isolated. (Their structure will be described in another paper.) The azobenzo analogs of the

TABLE 3. The $C_{(1)}$–$C_{(6)}$ Chemical Shifts in the $^{13}C$ NMR Spectra of 3,4-Dihydroxy-1,6-diphenyl-2,4-hexadiene-1,6-dione IIIa (δ, ppm, $CDCl_3$/TMS)



IIIa

| Carbon atom | Experimental* | Calculated | $\Delta\delta\ ^{13}C$ |
|---|---|---|---|
| 1 | 133.5 (133.3) | 132.4 | 1.1 |
| 2 | 127.9 (127.9) | 128.4 | 0.5 |
| 3 | 128.8 (128.7) | 129.4 | 0.6 |
| 4 | 135.7 (135.0) | 137.7 | 2.0 |
| 5 | 191.2 (190.2) | — | — |
| 6 | 95.5 (97.6) | 92.0 | 3.5 |
| 7 | 174.2 (169.4) | 172.6 | 1.6 |

* Published data on the chemical shifts of the carbon atoms in the model methyl benzoylpyruvate [24] are given in parentheses.

2,3-furandiones (isatins) enter into condensation with acetophenones at the $C_{(3)}$=O carbonyl, leading to 3-phenacyldihydroxyindole derivatives [28, 29]. (The latter can be dehydrated by the action of acid with the formation of 3-phenacylidenehydroxyindoles.) The different behavior of 2,3-furandiones in this reaction is somewhat unusual, and the method E that we present for the first time is the first example of the condensation of a CH acid with highly reactive unsaturated monocyclic α-ketolactones, leading to the formation of stable products from addition at the lactone carbonyl.

Earlier it was discovered that substituted 2,3-dihydro-3-furanones have antimicrobial activity [12, 19]. According to our preliminary data, the structurally similar noncyclic 1,6-diaryl-3,4-dihydroxy-2,4-hexadiene-1,6-diones III have weak antimicrobial properties [12]. For further screening *in vitro* trials were carried out on the antimicrobial activity of the obtained 2,4-hexadiene-1,6-diones III against strains of Gram-positive bacteria *Staphylococcus aureus* P-209 and Gram-negative microbes *Escherichia coli* M 17. The lowest inhibiting concentration (μg/ml) at which the investigated compounds suppress the development of the test microbes was determined. It was found that certain hexadienediones III have low antimicrobial activity (LIC 125-1000 μg/ml), while compound IIIi exhibits significant antistaphylococcal activity against *S. aureus* (LIC 7.8 μg/liter).

## EXPERIMENTAL

The melting points of the compounds were determined without correction on a PTP TU 25-11-1146-76 instrument. The IR spectra were recorded on a Specord M-80 spectrometer for pastes in Vaseline oil. The UV spectra were obtained on a Specord UV-vis spectrometer at a concentration of $10^{-4}$M. The NMR spectra were recorded on a Bruker HX-90 spectrometer for solutions in deuterochloroform, carbon tetrachloride, hexadeuterodimethyl sulfoxide, a 10:1 mixture of deuterochloroform and trifluoroacetic acid, and a 10:1 mixture of hexadeuterodimethyl sulfoxide and trifluoroacetic acid with HMDS (PMR) and TMS ($^{13}C$ NMR) as internal standards on a pulse spectrometer at 77 K. The mass spectra were obtained at 70 eV on a MAT-311 instrument. The reactions and the purity of the products were monitored by TLC on Silufol UV-254 plates with 3:2 benzene–ether or 10:9:1 benzene–ether–acetone mixtures as eluants and development with iodine or UV light. Before use the benzene, ether, and dioxane were distilled over metallic sodium, and the chloroform and ethyl acetate were distilled over phosphorus pentoxide. The acetic acid was purified by freezing out.

TABLE 4. 1,6-Diaryl-3,4-dihydroxy-2,4-hexadiene-1,6-diones (IIIa-n)

| Compound | $Ar^1$ | $Ar^2$ | Empirical formula* | mp, °C (solvent) | Yield, %*[2] (method of synthesis) |
|---|---|---|---|---|---|
| IIIa | Ph | Ph | $C_{18}H_{14}O_4$ | 184-185, (177-179 [10], 180 [17]) (chloroform or toluene) | 40 (A), 95 (D), 32 (E), (62-74 [10]) (A) |
| IIIb | Ph | 4-$MeC_6H_4$ | $C_{19}H_{16}O_4$ | 181-182, (178-180 [15]) (acetonitrile) | 28 or 36 (E)*[3], (40-50 [15])(B) |
| IIIc | 4-$MeC_6H_4$ | 4-$MeC_6H_4$ | $C_{20}H_{18}O_4$ | 207-208, (194 [9]) (chloroform) | 44 (D), (92 [9]) (A) |
| IIId | 4-$EtC_6H_4$ | 4-$EtC_6H_4$ | $C_{22}H_{22}O_4$ | 212-213 (chloroform) | 52 (D) |
| IIIe | 4-$MeOC_6H_4$ | 4-$MeOC_6H_4$ | $C_{20}H_{18}O_6$ | 198-199, (198-200 [9]) (chloroform) | 43 (D) |
| IIIf | 4-$EtOC_6H_4$ | 4-$EtOC_6H_4$ | $C_{22}H_{22}O_6$ | 188-189 (chloroform) | 45 (D) |
| IIIg | Ph | 4-$BrC_6H_4$ | $C_{18}H_{13}BrO_4$ | 194-195, (177-180 [15]) (chloroform–hexane, 3:1) | 93 (C), (40-50 [15]) (B) |
| IIIh | 4-$MeC_6H_4$ | 4-$BrC_6H_4$ | $C_{19}H_{15}BrO_4$ | 230-231 (chloroform–hexane, 3:1) | 88 (C) |
| IIIi | 2,4-$Me_2C_6H_3$ | 4-$BrC_6H_4$ | $C_{20}H_{17}BrO_4$ | 165-166 (chloroform–hexane, 3:1) | 69 (C) |
| IIIj | 4-$BrC_6H_4$ | 4-$BrC_6H_4$ | $C_{18}H_{12}Br_2O_4$ | 216-217, (217-218 [9, 17]) (chloroform) | 36 (A), 55 (D); (89 [9] (A), 82 [18] (C)) |
| IIIk | Ph | 4-$ClC_6H_4$ | $C_{18}H_{13}ClO_4$ | 185-186, (176-179 [15]) (chloroform–hexane, 3:1) | 54 (B), 31 (E); (40-50 [15]) (B) |
| IIIl | 4-$MeC_6H_4$ | 4-$ClC_6H_4$ | $C_{19}H_{15}ClO_4$ | 220-222, (208-210 [15]) (ethanol) | 17 or 29 (E)*[4]; (40-50 [15]) (B) |
| IIIm | 4-$ClC_6H_4$ | 4-$ClC_6H_4$ | $C_{18}H_{12}Cl_2O_4$ | 231-232, (229 [9, 17]) (chloroform) | 82 (C), 55 (D), (94 [9] (A), 80 [17] (C)) |
| IIIn | Ph | 4-$NO_2C_6H_4$ | $C_{18}H_{13}NO_6$ | 227-228 (chloroform–hexane, 3:1) | 85 (C) |

* The data from microanalysis agree satisfactorily with the calculated values, %: C ±0.35; H ±0.23; Hal ±0.39; N ±0.25.

*[3] Methods of synthesis A–D. Method D: The yields are given only for the reaction with 1,2-bis(nitroamino)ethane. Method E: The yields are indicated for the above-mentioned reaction with potassium carbonate as the most effective catalyst.

*[3] The yield was 28% in the reaction of 5-phenyl-2,3-dihydro-2,3-furandione Ia with *p*-methylacetophenone and 36% in the reaction of 5-*p*-tolyl-2,3-dihydro-2,3-furandione Ib with acetophenone.

*4 The yield was 17% in the reaction of 5-*p*-tolyl-2,3-dihydro-2,3-furandione Ib with *p*-chloroacetophenone and 29% in the reaction of 5-*p*-chlorophenyl-2,3-dihydro-2,3-furandione Ih with *p*-methylacetophenone.

TABLE 5. The Data from the IR and PMR Spectra of 1,6-Diaryl-3,4-dihydroxy-2,4-hexadiene-1,6-diones (IIIa-i,k,m,n)

| Compound | IR spectra, $cm^{-1}$ | PMR spectra, δ, ppm $CDCl_3$ (X-Y tautomers) |
|---|---|---|
| IIIa | 1585-1605 ($CO_{chelate}$, C=C) | 7.07 (2H, s, 2CH-X*); 7.25-8.08 (10H, m, 2Ph); 15.27 (2H, b, 2OH)*[2]; 3.48, 3.95 (2H, two d, $CH_2$, $J$ = 14.0 Hz, $CH_2$-Y (53%); 6.35 (1H, s, CH-Y); 7.15-8.05 (12H, m, 2CH-X, 2Ph-X+Y)*[2] |
| IIIb | 1605-1612 ($CO_{chelate}$, C=C) | 2.33 (3H, s, Me-X + Y); 3.42, 3.84 (2H, two d, $CH_2$, $J$ = 15.5 Hz, $CH_2$-Y (20%)); 6.30 (1H, s, CH-Y); 7.24-7.89 (11H, m, 2CH-X, 2Ar-X + Y)*[3]; 2.38 (3H, s, Me-X + Y); 3.42, 3.52 (2H, two d, $CH_2$, $J$ = 16.0 Hz, $CH_2$-Y(27%)); 6.29 (1H, s, CH-Y); 7.10-7.91 (11H, m, 2CH-X, 2Ar-X + Y)*[4] |
| IIIc | 1585-1605 ($CO_{chelate}$, C=C) | 2.38 (6H, s, 2Me); 7.05 (2H, s, 2CH-X); 7.20-8.05 (8H, m, 2Ar)*[2]; 2.35 (6H, s, 2Me); 3.35, 3.78 (2H, two d, $CH_2$, $J$ = 16.0 Hz, $CH_2$-Y); 6.15 (1H, s, CH-Y); 7.05-8.10 (10H, m, 2CH-X, 2Ar-X + Y); 15.40 (2H, b, 2OH-X)*[3] |
| IIId | 1570-1595 ($CO_{chelate}$, C=C) | 1.25 (6H, t, 2Me); 3.65 (4H, q, $2CH_2$); 7.08 (2H, s, 2CH-X); 7.15-8.08 (8H, m, 2Ar); 15.55 (2H, broad, 2OH-X)*[2] |
| IIIe | 1568-1595 ($CO_{chelate}$, C=C) | 3.88 (6H, s, 2MeO); 6.98 (2H, s, 2 CH-X); 7.05-8.15 (8H, m, 2Ar)*[5] |
| IIIf | 1570-1590 ($CO_{chelate}$, C=C) | 1.38 (6H, t, 2Me); 4.05 (4H, q, $2CH_2$); 6.85 (2H, s, 2CH-X); 7.10-7.95 (8H, m, 2Ar)*[2] |
| IIIg | 1585-1597 ($CO_{chelate}$, C=C) | 3.74 (2H, m, $CH_2$-Y); 7.27 (2H, s, 2CH-X); 7.53-8.22 (9H, m, 2Ar-X + Y)*[4] |
| IIIh | 1580-1590 ($CO_{chelate}$, C=C) | 2.39 (3H, s, Me-X + Y); 3.69 (2H, , $CH_2$-Y); 7.15-7.80 (10H, m, 2CH-X, 2Ar-X + Y)*[4] |
| IIIi | 1584-1590 ($CO_{chelate}$, C=C) | 2.33 (3H, s, Me); 2.52 (3H, s, Me); 6.92 (1H, s, CH-X); 7.17 (1H, s, CH-X); 7.20-8.15 (7H, m, 2Ar)*[2] |
| IIIk | 1590-1605 ($CO_{chelate}$, C=C) | 7.17 (2H, s, 2CH-X); 7.45-8.13 (9H, m, 2Ar-X + Y)*[4] |
| IIIm | 1582-1593 ($CO_{chelate}$, C=C) | 3.41, 3.98 (2H, two d, $CH_2$, $J$ = 16.0 Hz, $CH_2$-Y(80%)); 6.31 (1H, s, CH-Y); 7.15-8.05 (10H, m, 2CH-X, 2Ar-X + Y)*[3] |
| IIIn | 1578-1590 ($CO_{chelate}$, C=C) | 3.82 (2H, m, $CH_2$-Y); 6.45 (1H, s, CH*[6]); 6.70 (1H, s, CH*[7]); 7.60-8.33 (9H, m, 2Ar-Y(100%)*[4] |

* X and Y are tautomers of (III).

*[2] The linear form X (100%) in solution in $CDCl_3$.

*[3] The linear form X (%) and the ring tautomer (Y) (%) in DMSO-$d_6$ solution.

*[4] The spectrum was recorded in a 10:1 mixture of DMSO-$d_6$ and trifluoroacetic acid.

*[5] The linear form X (100%) in $CCl_4$ solution.

*[6] 57% of the tautomer $Y^1$ ($Ar^1$ = 4-$NO_2C_6H_4$, $Ar^2$ = Ph).

*[7] 43% of the tautomer $Y^2$ ($Ar^1$ = 4-$NO_2C_6H_4$, $Ar^2$ = Ph).

**5-Aryl-2,3-dihydro-2,3-furandiones (Ia-h). Modified General Procedure [19].** A mixture of 10 mmol of the respective aroylpyruvic acid and 30-40 ml of acetic anhydride was heated at 60-70°C with stirring until it had dissolved (2-5 min). After cooling to room temperature the yellow-orange precipitate was filtered off, washed with dry ether, and recrystallized from chloroform or tetrachloromethane. The pure compounds I were obtained.

**5-Phenyl-2,3-dihydro-2,3-furandione (Ia).** Yield 78%; mp 137-138°C (decomp.). Published data: 131-132°C [18]. IR spectrum (NaCl): 1848, 1824 (lactone CO), 1722 (C=O), 1600, 1566, 1452, 1332 $cm^{-1}$. PMR spectrum (DMSO-$d_6$), ppm: 6.92 (1H, s, CH); 7.57-8.05 (5H, m, $C_6H_5$).

**5-*p*-Tolyl-2,3-dihydro-2,3-furandione (Ib).** Yield 71%; mp 136-137°C (decomp.). Published data: 130-131°C [18]. IR spectrum (NaCl): 1850, 1826 (lactone CO), 1716 ($C_{(3)}$=O), 1588, 1560, 1504, 1462, 1332 $cm^{-1}$. PMR spectrum (DMSO-$d_6$), ppm: 2.40 (3H, s, Me); 6.92 (1H, s, CH); 7.38-8.04 (4H, m, $C_6H_4$).

**5-(2,4-Dimethylphenyl)-2,3-dihydro-2,3-furandione (Ic).** Yield 64%; mp 108-109°C (decomp.). IR spectrum (NaCl): 1816 (broad peak, lactone CO), 1718 ($C_{(3)}$=O), 1636, 1608, 1582, 1552 $cm^{-1}$. PMR spectrum ($CDCl_3$), ppm: 2.30 (3H, s, Me); 2.46 (3H, s, Me); 6.28 (1H, s, CH); 6.95-7.90 (3H, m, $C_6H_3$). Found, %: C 71.5; H 4.8. $C_{12}H_{10}O_3$. Calculated, %: C 71.3; H 4.9.

Compounds Id-h were obtained similarly. Yields and melting points (°C, decomp.): 65, 133-134 Id; 72, 134-135 (published data 133-134 [18]) Ie; 57, 131-132 If; 80, 138-139 (published data 138-139 [18]) Ig; 66, 139-140 (published data 136-137 [18]) Ih.

***Z*- and *E*-Aryl-2-aroylmethylene-2,3-dihydro-3-furanones (IIa-f). General Procedure.** A mixture of 10 mmol of the respective 5-aryl-2,3-dihydro-2,3-furandione Ia-c,h and 10 mmol of the aroylmethylene-triphenylphosphorane [22] was boiled in 100 ml of dry benzene for 5-10 min. After evaporation of the solvent the residue was washed with 30-50 ml of acetonitrile to remove the triphenylphosphine oxide and recrystallized from ethyl acetate for IIa (the *E* isomer), ethanol for IIb, acetonitrile for IIc, toluene for IId,e, or acetone (for IIf), and this led to the pure compounds II.

***Z*-2-*p*-Bromobenzoylmethyl-5-phenyl-2,3-dihydro-3-furanone (IIa).** After the reaction of 5-phenyl-2,3-dihydro-2,3-furandione Ia (1.74 g, 10 mmol) with *p*-bromobenzoylmethylenetriphenylphosphorane (4.95 g, 10 mmol) according to the general procedure (see above) and treatment of the residue with 50 ml of acetonitrile the filtrate was evaporated to dryness, and the residue was recrystallized from ethyl acetate. The *Z*-isomer of compound IIa was isolated. After the addition of 20 ml of hexane to the remaining solution triphenylphosphine oxide was isolated; mp 155-156°C.

***E*-2-*p*-Halogenobenzoylmethylene-5-*p*-halogenophenyl-2,3-dihydro-3-furanones (IId,e). Modified General Procedure.** To a vigorously stirred suspension of the respective 1,6-bis-*p*-halogenophenyl-3,4-dihydroxy-2,4-hexadiene-1,6-dione IIIj,m [9, 17] (5 mmol) in chloroform (100 ml) 3 ml of trifluoroacetic anhydride and 1 ml of pyridine were added. The mixture was stirred for 2 h and left overnight. The next day the orange precipitate was filtered off and recrystallized from toluene, and compounds IId,e were isolated. The reaction was monitored by TLC. The obtained 2,3-dihydro-3-furanones II were identified by the appearance of a bright color ranging from dark-red to brown during the action of a 10% solution of sodium hydroxide in ethanol.

**1,6-Diaryl-3,4-dihydroxy-2,4-hexadiene-1,6-diones (IIIa-n). General Methods. A, B.** The following compounds were obtained by the known methods: IIIa (method A) [10], IIIj (method A) [9], IIIk (method B) [15].

**3,4-Dihydroxy-1,6-diphenyl-2,4-hexadiene-1,6-dione (IIIa).** UV spectrum, [ethanol, $\lambda_{max}$(log ε), nm]: 211 (4.31), 247 (4.20), 264 (4.27).

**C.** The hexadienediones IIIg-i,m,n were obtained by this method. To a solution of the respective 2-aroylmethylene-5-aryl-2,3-dihydro-3-furanone IIa-c,e,f (5 mmol) in 100-150 ml of acetone while stirring at 40-50°C 20% hydrochloric acid (2 ml) was added. The stirring was continued at room temperature for 2 h, and the colorless precipitate was filtered off and recrystallized from chloroform (compound IIIn) or a 3:1 mixture of chloroform and hexane (compounds IIIg-i,m). The pure hexadienediones were isolated. With a solution of iron III chloride in ethanol the compounds III give a color ranging from dark-red to brown, due to the presence of the bischelate form.

**1,6-Bis-*p*-chlorophenyl-3,4-dihydroxy-2,4-hexadiene-1,6-dione (IIIi).** UV spectrum [ethanol, $\lambda_{max}$ (log ε), nm]: 211 (4.05), 260 (4.07), 323 (4.25). The last short-wave band is probably due to the preponderance of the cyclic tautomer 2,3-dihydro-3-furanone Y in the solution. We were unable to prove this suggestion because this

compound does not dissolve in ethanol to a sufficient degree to record an informative PMR spectrum. NQR spectrum ($\nu_{Cl}$crystals): 35.035 MHz.

**D**. The hexadienediones IIIa, c-f, j, m were obtained by this method. A mixture of the respective 5-aryl-2,3-dihydro-2,3-furandione Ia,b,d-h (6 mmol) and alkylnitroamines [methylnitroamine or 1,2-bis(nitroamino)ethane] [27] in 20-30 ml of dioxane was boiled with a reflux condenser for 2-3 h. The solvent was then removed, and the residue was washed with 30 ml of ethanol. The crude product was recrystallized from chloroform or toluene, and the pure hexadienediones III were obtained.

**E**. The hexadienediones IIIa,b,k,l were obtained by this method. To a solution of the respective 5-aryl-2,3-dihydro-2,3-furandione Ia,b,h (10 mmol) in 30-40 ml of ethyl acetate while stirring acetophenone, *p*-methylacetophenone, or *p*-chloroacetophenone (10 ml) and a catalyst for the aldol condensation, i.e., potassium carbonate (0.2-0.3 g) or a mixture of potassium carbonate (0.1 g) and benzyltrimethylammonium chloride (0.14 g) or potassium hydroxide 0.3-0.4 g) were added. The mixture was boiled with a reflux condenser and stirred for 10-15 min. The next day the precipitate was filtered off and washed at room temperature with 3-5 ml of 10% hydrochloric acid in ethanol to remove the inorganic impurities. It was then purified by fractional crystallization from chloroform (compound IIIa), acetonitrile (compound IIIb), a 3:1 mixture of chloroform and hexane (compound IIIk), or ethanol (compound IIIl). Compounds III and the accompanying aroylpyruvic acids were obtained. The remaining filtrate was evaporated, and the dry residue was recrystallized from the above-mentioned solvents, giving additional quantities of compounds III. The highest yields of the hexadienediones were obtained with potassium carbonate as catalyst (Table 3). As a result of some of the investigated reactions we isolated small amounts of colorless products, the structure of which is being determined.

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