A New Synthesis and Application of 1-Aryl-2,4-diones

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Abstract: Methyl ketones or ethyl acetate react with aromatic α-bromo ketones in the presence of two equivalents of *tert*-butoxy- or diethylaminomagnesium bromide in benzene (toluene) under reflux to produce 1-aryl-2,4-diones. The conversion, apparently, occurs via aldol condensation and subsequent [1,2]-sigmatropic rearrangement of the intermediate 3-bromo-2-hydroxy ketones. A number of fused aromatic and heteroaromatic phenols have been prepared by cyclodehydration of 1-aryl-2,4-diones.

Key words: α-bromo ketones, magnesium bases, aldol condensation, [1,2]-sigmatropic rearrangement, 1-aryl-2,4-diones, cyclodehydration, fused phenols

1,3-Dicarbonyl compounds are widely used as intermediates in organic synthesis for the construction of C–C bonds by alkylation,[1] condensation (Knoevenagel-type),[1] and 1,4-conjugate addition (Michael-type)[2] reactions, and also for the preparation of a great variety of five- and six-membered heterocyclic systems.[3, 4]

The main approach to the synthesis of 1,3-dicarbonyl compounds is the condensation of ketones,[5] or their derivatives such as enamines[6] and silyl ethers,[7] with esters,[5] acyl chlorides[6, 8] or anhydrides.[5] At the same time this approach is hardly applicable to the synthesis of 1-aryl-2,4-diones, mainly because of the low yields, regioselectivity, and availability of starting compounds. A few comparatively new methods for 1,3-diketone synthesis, such as the arylation of disodium salts of 1,3-diketones by diaryliodonium chlorides,[9] oxidation of the corresponding aldols,[4] condensation of diazo ketones[10] or their lithium enolates[11] with aldehydes, condensation of lithium enolates with ketenes,[12] as well as rearrangement of 3-methoxy-4-phenylthio ketones,[13] give better results in the synthesis of 1-aryl-2,4-diones. However, these methods are usually multistep procedures and preparatively complicated.

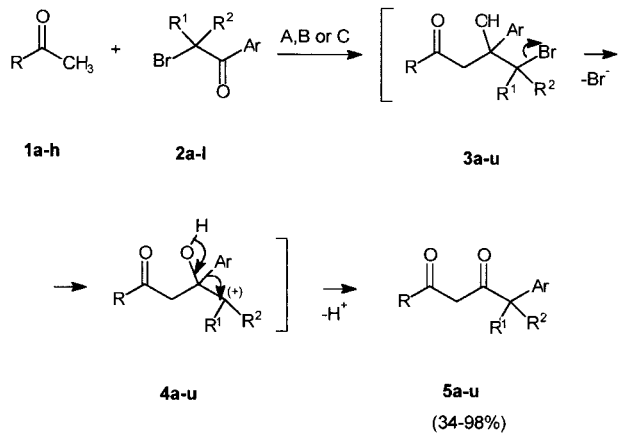
In our present research we propose a simple and efficient one-step synthesis of 1-aryl-2,4-diones based on readily available methyl ketones and aromatic α-bromo ketones. Earlier, the method of cross aldol condensation of methyl ketones with α-bromo ketones in the presence of *tert*-butoxy- or diethylaminomagnesium bromide at room temperature with formation of 3-bromo-2-hydroxy ketones has been described.[14] The latter compounds were transformed to the corresponding 1,4-diketones by treatment with triethylamine. The rearrangement, probably, occurs through intermediate hydroxycyclopropyl ketone formation.

Now we report that application of an additional equivalent of magnesium base and higher temperature for the condensation of methyl ketones **1a–g** or ethyl acetate with α-bromo ketones **2a–l** leads to the corresponding 1-aryl-2,4-diones **5a–u**. The formation of 1-aryl-2,4-diones under the action of the magnesium enolate of acetylmesitylene on α-bromo ketones was reported by Kohler and Tishler as long ago as 1935.[15] However, the authors did not propose any mechanism nor preparative variant of the transformation. Later, the rearrangement of halomagnesium derivatives of β-halohydrins to ketones with heating in benzene was found.[16] That reaction occurs through migration of an aryl or alkyl group and was ap-plied to the preparation of several cycloalkanones.[16,17] The concerted "withdrawal" (pinacol-like), or "oxide" mechanism of this transformation was discussed.[16]

In our case, we assume that the mechanism of the rearrangement of 3-bromo-2-hydroxy ketones **3a–u**, or their bromomagnesium derivatives generated as intermediates, to 1-aryl-2,4-diones **5a–u** may be concerted,[16] but with a high probability of the formation of carbenium ions **4a–u** in the transition state (at least in intimate ion pairs with the bromide anion) (see Scheme 1). Subsequent [1,2]-sigmatropic migration of the aryl group in the carbocation **4a–u** gives the corresponding 1,3-diketones **5a–u**, which produce stable magnesium chelates[8] by deprotonation with an additional equivalent of magnesium base. The fact that the reaction proceeds more smoothly (partly even at room temperature[14]) when stabilized secondary **4j–l, n–q, s** or, especially, tertiary **4m** and benzylic **4r** carbocation-like transition states occur confirms the proposed mechanism.

This mechanism is also in agreement with the fact that analogous transformation with 1-bromo-2-hydroxy ketone **6** (see Scheme 2) under the same conditions does not occur. In this case, a carbocation-like transition state ought to be destabilized by the carbonyl group. A prolonged refluxing of *erythro*-2-bromo-3-hydroxy-1,3-diphenylpropan-1-one (**6**) with excess *tert*-butoxymagnesium bromide–diethyl ether complex in benzene gave only traces of 1,3-dicarbonyl compounds (see experimental part), a small quantity of dehydration (crotonization-type) product,[18] and unreacted starting compound. The configuration of bromohydrin **6** has been established by its transformation to the known *trans*-epoxy ketone **7**[19] by treatment with triethylamine. The fact that epoxy ketone **7** and the product of its rearrangement, the corresponding 1,2-diketone,[20] do not appear in the reaction of bromohydrin **6** with *tert*-butoxymagnesium bromide, in our opinion, excludes the formation of 1-aryl-2,4-diones **5a–u** via the epoxides ("oxide" mechanism[16]).

The condensation of alkyl methyl ketones **1b,c** with α-bromo ketones **2a–l** in the presence of *tert*-butoxymagnesium bromide occurs strictly regioselectively at the meth-



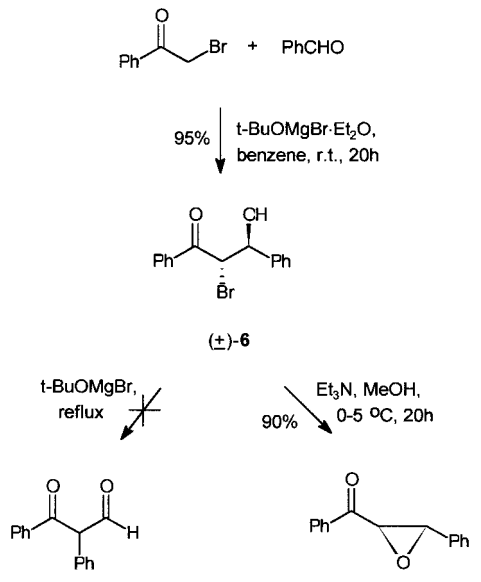
A,B: 2 *t*-BuOMgBr·Et_2O, benzene (toluene), reflux

C: 2 $Et_2NMgBr·Et_2O$, benzene, reflux

1	R	2	R^1	R^2	Ar
a	Me	**a**	H	H	Ph
b	Et	**b**	H	H	4-MeC_6H_4
c	n-Pr	**c**	H	H	4-$MeOC_6H_4$
d	Ph	**d**	H	H	2-thienyl
e	PhCH=CH	**e**	H	H	4-ethoxycarbonyl-3,5-dimethyl-2-furyl
f	Me_2C=CH	**f**	H	Me	Ph
g	4-methylchloro-2-thienyl	**g**	H	i-Pr	Ph
h	EtO	**h**	Me	Me	Ph
		i	H	Me	4-$MeOC_6H_4$
		j	H	Me	2-thienyl
		k	H	Ph	2-thienyl
		l	H	$(CH_2)_7CO_2Et$	2-thienyl

3-5: R, R^1, R^2, Ar, see Table 1

Scheme 1



Scheme 2

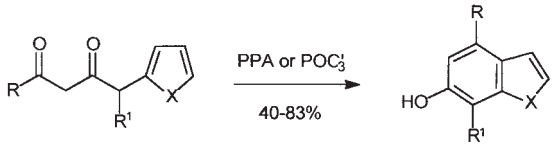
yl group. In all cases isomeric products of the reaction at the methylene group of ethyl methyl ketone (**1b**) have not been found. The reaction is sensitive to steric hindrance. Thus, refluxing acetophenone with 1-bromo-2-methylpropyl phenyl ketone (**2g**) and excess *tert*-butoxymagnesium bromide in toluene for ten hours produced the corresponding 1,3-diketone **5l** in low yield (40%). An attempt to involve 2-bromo-1-tetralone in this reaction in order to cause ring contraction failed fully. Primary alkyl groups and hydride ion do not migrate under these conditions. The reaction of 2-bromopentan-3-one and 2-bromobutanal with acetophenone in the presence of excess *tert*-butoxymagnesium bromide gave complicated mixtures of products and only traces of 1,3-dicarbonyl compounds. Ester groups (i.e. **5i,s**) and activated double bonds (i.e. **5g,q**) remained unchanged under the reaction conditions, but in the latter case the yield of 1,3-diketone **5g** was lower. The (chloromethyl)aryl group in **1g** is completely converted to the (bromomethyl)aryl group in **5o**, apparently due to an exchange reaction with magnesium bromide.

We have elaborated three variants of the condensation procedure. In the first (Method A), all components were mixed at once and refluxed; this was applied to α-bromo ketones **2f–l** containing secondary or tertiary α-carbon atoms. Formation of the least stabilized primary carbocations **4a–i** in the transition state is hampered, and in this case the competitive process is the rearrangement of the intermediate 3-bromo-2-hydroxy ketones **3a–i** into the corresponding 1,4-diketones.[14] In addition, a substantial quantity of byproducts, a result of the self-condensation[14] of primary α-bromo ketones **2a–e**, is formed. To prevent the self-condensation of bromo ketones **2a–e**, we utilized their dropwise addition to a refluxing mixture of methyl ketones **1a–e** and *tert*-butoxymagnesium bromide in benzene or toluene (Method B). The yields of 1-aryl-2,4-diones **5a–i** increase with increasing nucleophilicity of the migrating aryl group. This becomes apparent especially when passing from the phenyl (**5a**) to the 4-methyl- (**5b,c**) and 4-methoxyphenyl (**5d–f**) group and may be explained in terms of transition state stabilization by the electron-donating migrating ring. Ethyl acetate did not react with α-bromo ketones in the presence of *tert*-butoxymagnesium bromide. At the same time, 3-oxo esters **5t,u** were obtained from ethyl acetate when diethylaminomagnesium bromide was used as the condensation agent (Method C). Unfortunately, only α-bromo ketones **2c,i** containing aromatic rings activated by an electron-donating substituent gave acceptable yields of the corresponding 3-oxo esters **5t,u**.

Three methods for the isolation of 1-aryl-2,4-diones were used. The yields of products in the reaction of methyl ketones **1a–g** with α-bromo ketones **2f–l** containing a secondary or tertiary α-carbon atom were close to quantitative (except **5l**). The reaction product, after decomposition of the magnesium complex, was purified by flash chromatography on a short column of silica gel (Method A), or by distillation (Method B). A convenient

method for the isolation of pure 1-aryl-2,4-diones **5a–i**, in cases where moderate yields are obtained, is treatment of the reaction mixture with an aqueous solution of copper(II) acetate, followed by filtration and decomposition of the copper(II) complex[5] (Method C).

In this paper we also propose the synthetic application of 1-aryl-2,4-diones for the preparation of fused aromatic ring systems (see Scheme 3). Cyclodehydration of polyketides[21] or products of self-condensation of 1,3-diketones[22] under acidic, basic or fluoride catalysis with formation of aromatic compounds has been described. It is also thought that the biosynthesis of aromatic rings proceeds in a similar manner.[21] We have found that the cyclodehydration of 1-phenyl-2,4-diones **5a,k** may be achieved by heating with polyphosphoric acid. The analogous transformation of 1-(2-thienyl)-2,4-diones **5p,r,s** occurs under much milder conditions and was accomplished by refluxing with phosphoryl chloride in carbon tetrachloride. To prevent the oxidation of the 6-hydroxybenzo[*b*]thiophenes **8p,r,s** obtained, they were converted to the corresponding acetates.



5a,k,p,r,s **8a,k,p,r,s**

R, R1 and X see Table 2

Scheme 3

In conclusion, the method described gives very good results in the synthesis of 1-aryl-2,4-diones containing electron-donating substituents or without substituents in the aromatic ring. At the same time, the method is not applicable for the preparation of 1-aryl-2,4-diones with electron-poor aromatic rings. 1-Aryl-2,4-diones appear to be promising substrates for the synthesis of fused aromatic and heteroaromatic systems.

^{1}H NMR spectra were recorded on a "Tesla-BS 467A" (60 MHz) spectrometer. Samples were examined in CCl_4 containing 5% by volume of HMDS. IR spectra of products as 0.01 M solns in CCl_4 were obtained on a Specord IR-75 spectrophotometer. MS were recorded on a "Class-5000" chromato-mass spectrometer at 70 eV. Methyl ketones **1a–f**, and α-bromo ketones **2a–c,f,h** were commercially available. 2-Acetyl-4-(chloromethyl)thiophene (**1g**) was obtained by chloromethylation of 2-acetylthiophene.[23] α-Bromo ketones were synthesized by bromination of the corresponding ketones with dioxane dibromide.[24] All ketones were commercially available, except ethyl 5-acetyl-2,4-dimethylfuran-3-carboxylate (obtained by condensation of acetoacetic ester with tribromopropane, followed by acylation[25]) and the 2-thienyl ketones (synthesized by acylation of thiophene with the corresponding acyl chlorides[26]). The solvents, *t*-BuOH and Et_2NH were dried by distillation from Na before use.

1-Aryl-2,4-diones 5a–u; General Procedure:
Preparation:
Mg (0.58 g, 24 mmol), Et_2O (3.10 mL), and EtBr (0.20 mL) were placed in a one-neck, round-bottom, 25-mL flask fitted with a magnetic stirrer and reflux condenser. After the reaction had started, a solution of EtBr (1.76 mL, 24 mmol) in benzene (toluene, see Table 1) (10 mL) was added dropwise through the reflux condenser at such a rate that the mixture was not hot (35–40 °C). When the reaction was complete, subsequent procedure was carried out by one of the following methods:

Method A: The resulting solution of EtMgBr•Et_2O in benzene (toluene) was cooled to 0 °C, and a solution of *t*-BuOH (2.30 mL, 24 mmol) in benzene (toluene) (1 mL) was added slowly, dropwise through the reflux condenser. The cooling bath was removed, and methyl ketone **1a–g** (13 mmol), and α-bromo ketone **2a,f–l** (10 mmol) were added successively. The mixture was stirred under reflux for the time given in Table 1, cooled, quenched with cold 5% aq H_2SO_4 (15 mL), washed 5% aq NaCl (2×10 mL), and dried (Na_2SO_4). 1,3-Diketones **5a,j–s** were isolated by one of the methods (see Table 1) given below.

Method B: A solution of the α-bromo ketone **2b–e** (10 mmol) in benzene (toluene) (5–7 mL) was added dropwise through the reflux condenser over 40–60 min to a refluxing and stirred mixture of *t*-BuOMgBr•Et_2O in benzene (toluene), prepared as above (Method A), and methyl ketone **1a–e** (13 mmol). The mixture was stirred under reflux for 30–40 min, cooled, and quenched as above (Method A). 1,3-Diketones were isolated by Method C given below.

Method C: Et_2NH (2.48 mL, 24 mmol) was added to the solution of EtMgBr•Et_2O in benzene, prepared as described above, and the mixture was stirred for 15 min and cooled to 0 °C. A solution of EtOAc (3.00 mL, 30 mmol) and α-bromo ketone **2c,i** (10 mmol) in benzene (5 mL) was added dropwise over 20–30 min to the resulting solution of Et_2NMgBr•Et_2O under stirring and cooling (0 °C). The cooling bath was removed, the mixture was heated under reflux for 0.5 h, cooled, and treated as described above. For the isolation of 3-oxo esters **5t,u**, see Table 1.

Isolation:
Method A: The solvent was evaporated under vacuum, and the residue was mixed with benzene (7 mL), and chromatographed over a short column of silica gel (approximately 6 g) with benzene as eluent.

Method B: The product was purified by distillation of the residue under vacuum (1 Torr): bp 102–104 °C (**5j**); 165–170 °C (**5k**); 97–99 °C (**5m**).

Method C: To the mixture, after the evaporation of approximately two-thirds of the solvent volume, hexane (5 mL) and sat. aq $Cu(OAc)_2$ (30 mL) were added. The mixture was stirred vigorously for 1–2 h, allowed to stand ovemight at 0–5 °C, and filtered. The copper(II) complex was washed thoroughly with cold benzene/hexane (1:2) (for compounds **5a,i,q** 1:4) (10 mL), placed in a separating funnel and decomposed by shaking with 10% aq HCl (10 mL) and benzene (7 mL). The organic layer was separated, washed with 5% aq NaCl (2 ×) and chromatographed over a short column with a layer of silica gel (approximately 3 g) below, and anhyd Na_2SO_4 above, using benzene as eluent to afford 1,3-diketones **5a–i,o–q** of high purity.

***erythro*-2-Bromo-3-hydroxy-1,3-diphenylpropan-1-one (6):**
To a solution of *t*-BuOMgBr•Et_2O in benzene, prepared as described above from Mg (0.29 g, 12 mmol), EtBr (1.05 mL, 14 mmol), Et_2O (1.80 mL), benzene (20 mL), and *t*-BuOH (1.20 mL, 12 mmol), α-bromoacetophenone (1.99 g, 10 mmol) and PhCHO (1.02 mL, 10 mmol) were added. The mixture was stirred for 5 h, allowed to stand overnight, treated with 5% aq H_2SO_4 (15 mL), washed with 5% aq NaCl (2 × 10 mL), and dried (Na_2SO_4). Chromatography of the mixture over a short column of silica gel (6 g) with benzene as eluent gave bromohydrin **6** as a slightly yellow, viscous oil (3.00 g, 95%).
IR: ν = 3573, 3060, 3027, 1680, 1453, 1280, 680 cm^{-1}.
^{1}H NMR: δ = 3.47 (s, 1H), 4.87 (d, 1H, J = 9 Hz), 5.07 (d, 1H, J = 9 Hz), 7.0–7.5 (m, 8H), 7.7–8.0 (m, 2H).

Table 1. 1-Aryl-2,4-diones **5a–u** Prepared

Product[a]	R	R^1	R^2	Ar	Preparation	Time[b] (h)	Isolation	Yield[c] (%)	n_D^{20} or mp (°C) (Solvent)
5a	n-Pr	H	H	Ph	A	2	C[d]	36	1.5346
5b	Me	H	H	4-MeC_6H_4	B[e]	1.5	C	50	1.5515
5c	Et	H	H	4-MeC_6H_4	B[e]	1.5	C	65	1.5364
5d	Me	H	H	4-$MeOC_6H_4$	B	1.5	C	77	1.5525
5e	Et	H	H	4-$MeOC_6H_4$	B	1.5	C	78	1.5440
5f	Ph	H	H	4-$MeOC_6H_4$	B	1.5	C	81	55–56 (pentane/Et_2O 2:1)
5g	PhCH=CH	H	H	4-$MeOC_6H_4$	B	1.5	C	41	78–79 (hexane/CCl_4 1:1)
5h	Et	H	H	2-thienyl	B[e]	1.5	C	58	1.5540
5i	n-Pr	H	H	4-ethoxycarbonyl-3,5-dimethyl-2-furyl	B	1.5	C	67	1.5097
5j	Et	H	Me	Ph	A	2	B	84	1.5343
5k	Ph	H	Me	Ph	A	1.5	B	86	1.6157
5l	Ph	H	i-Pr	Ph	A[e]	10	–[f]	41	91–92 (pentane/Et_2O 35:1)
5m	Et	Me	Me	Ph	A	3	B	83	1.5302
5n	Me	H	Me	4-$MeOC_6H_4$	A	1	A	98	1.5463
5o	4-(bromomethyl)-2-thienyl[g]	H	Me	4-$MeOC_6H_4$	A	1	C	81	1.6409
5p	Ph	H	Me	2-thienyl	A	1	C	82	34–35 (pentane/Et_2O 3:1)
5q	Me_2C=CH	H	Me	2-thienyl	A	1.5	C	80	1.5902
5r	Me	H	Ph	2-thienyl	A	1	A	96	1.6113
5s	Me	H	$(CH_2)_7CO_2Et$	2-thienyl	A	2	A	90	1.5162
5t	EtO	H	H	4-$MeOC_6H_4$	C	0.5	–[h]	34	1.5234
5u	EtO	H	Me	4-$MeOC_6H_4$	C	0.5	A	80	34–35 (pentane/Et_2O 2:1)

[a] For all compounds satisfactory microanalyses were obtained: C ± 0.38, H ± 0.35.
[b] Reaction time included the time of α-bromo ketone **2b–e** addition, when Method B was applied.
[c] Yield of isolated product based on **2**.
[d] Mp of copper(II) complex of **5a** 148–150 °C (lit.[9] mp 149–151 °C); bp of **5a** 116–118 °C/1 Torr (lit.[9] bp 145–l48 °C/7 Torr).
[e] The condensation was carried out in toluene.
[f] The product **5l** was isolated by crystallization.
[g] The starting compound was 2-acetyl-4-(chloromethyl)thiophene (**1g**). The fact of chloro–bromine exchange was established by elemental analysis and the mass spectrum of the product **5o**. MS: *m/z* (%) = 382 (M^+, 1.40), 380 (M^+, 1.35), 301 (M^+-Br, 5.10), 135 (4-$MeOC_6H_4C^+HCH_3$, 100).
[h] The product **5t** was isolated by column chromatography (silica gel, benzene).

Table 2. Fused Phenols **8** Prepared

Product[a]		R	R^1	X	Reagent	Time (h)	Yield[b] (%)	mp (°C) (Solvent)
8a	4-propyl-2-naphthol	n-Pr	H	CH=CH	PPA	2	40	33–34 (pentane)
8k	1-methyl-4-phenyl-2-naphthol	Ph	Me	CH=CH	PPA	4	73	104–l05 (hexane)
8p	6-hydroxy-7-methyl-4-phenylbenzo[*b*]thiophene	Ph	Me	S	$POCl_3$	3	74	72–73[c] (pentane/ Et_2O 1:1)
8r	6-hydroxy-4-methyl-7-phenylbenzo[*b*]thiophene	Me	Ph	S	$POCl_3$	1	83	94–95[c] (pentane/Et_2O 1:2)
8s	7-(7-ethoxycarbonylheptyl)-6-hydroxy-4-methylbenzo[*b*]thiophene	Me	$(CH_2)_7CO_2Et$	S	$POCl_3$	3	55	oil

[a] For all compounds satisfactory microanalyses were obtained: C ± 0.33, H ± 0.30.
[b] Yield of isolated phenols **8a–s**.
[c] Mp of the corresponding acetate.

Table 3. ^{1}H NMR Spectra of 1-Aryl-2,4-diones **5a–u**

Product[a]	^{1}H NMR (Major Form)[b] δ, J (Hz)	δ (3-H) of Minor Form[c]	Ratio[d] Enol/Ketone
5a	0.77 (t, 3H, J = 7), 1.45 (sextet, 2H, J = 7), 2.04 (t, 2H, J = 7), 3.43 (s, 2H), 5.21 (s, 1H), 7.13 (s, 5H)	3.61	95:5
5b	1.80 (s, 3H), 2.20 (s, 3H), 3.30 (s, 2H), 5.17 (s, 1H), 6.93 (s, 4H)	3.47	94:6
5c	1.00 (t, 3H, J = 7), 2.13 (q, 2H, J = 7), 2.27 (s, 3H), 3.37 (s, 2H), 5.20 (s, 1H), 6.97 (s, 4H)	3.53	94:6
5d	1.73 (s, 3H), 3.20 (s, 2H), 3.53 (s, 3H), 5.07 (s, 1H), 6.53 (d, 2H, J = 8), 6.87 (d, 2H, J = 8)	3.37	85:15
5e	0.90 (t, 3H, J = 7), 2.03 (q, 2H, J = 7), 3.07 (s, 2H), 3.37 (s, 3H), 5.07 (s, 1H), 6.53 (d, 2H, J = 8), 6.87 (d, 2H, J = 8)	3.40	85:15
5f	3.42 (s, 2H), 3.60 (s, 3H), 5.87 (s, 1H), 6.63 (d, 2H, J = 8), 7.00 (d, 2H, J = 8), 7.1–7.3 (m, 3H), 7.5–7.7 (m, 2H)	–	> 97:3
5g	3.38 (s, 2H), 3.60 (s, 3H), 5.30 (s, 1H), 6.17 (d, 1H, J = 16), 6.63 (d, 2H, J = 8), 6.6–7.5 (m, 8H)	–	> 97:3
5h	0.75 (t, 3H, J = 7), 2.10 (q, 2H, J = 7), 3.57 (s, 2H), 5.27 (s, 1H), 6.6–6.9 (m, 2H), 6.9–7.2 (m, 1H)	3.73	85:15
5i	0.80 (t, 3H, J = 7), 1.20 (t, 3H, J = 7), 1.2–1.8 (m, 2H), 1.93 (s, 3H), 1.9–2.3 (m, 2H), 2.33 (s, 3H), 3.27 (s, 2H), 4.03 (q, 2H, J = 7), 5.07 (s, 1H)	3.22	75:25
5j	0.87 (t, 3H, J = 7), 1.27 (d, 3H, J = 7), 2.00 (q, 2H, J = 7), 3.40 (q, 1H, J = 7), 5.20 (s, 1H), 7.17 (s, 5H)	3.17	87:13
5k	1.50 (d, 3H, J = 7), 3.70 (q, 1H, J = 7), 6.03 (s, 1H), 7.0–7.4 (m, 8H), 7.5–7.8 (m, 2H)	3.83	97:3[e]
5l	0.63 (d, 3H, J = 7), 0.93 (d, 3H, J = 7), 2.1–2.7 (m, 1H), 2.97 (d, 1H, J = 11), 6.03 (s, 1H), 7.0–7.8 (m, 8H), 7.6–7.9 (m, 2H)	–	> 97:3
5m	0.88 (t, 3H, J = 7), 1.33 (s, 6H), 2.03 (q, 2H, J = 7), 5.13 (s, 1H), 7.30 (s, 5H)	3.10	91:9
5n	1.23 (d, 3H, J = 7), 1.73 (s, 3H), 3.38 (q, 1H, J = 7), 3.63 (s, 3H), 5.23 (s, 1H), 6.73 (d, 2H, J = 8), 7.30 (d, 2H, J = 8)	3.20	80:20
5o	1.38 (d, 3H, J = 7), 3.48 (q, 1H, J = 7), 3.62 (s, 3H), 4.20 (s, 2H), 5.75 (s, 1H), 6.67 (d, 2H, J = 8), 6.9–7.5 (m, 4H)	–	> 97:3
5p	1.48 (d, 3H, J = 7), 3.83 (q, 1H, J = 7), 5.97 (s, 1H), 6.76 (d, 2H, J = 3), 7.00 (t, 1H, J = 3), 7.1–7.4 (m, 3H), 7.5–7.8 (m, 2H)	–	> 97:3
5q	1.43 (d, 3H, J = 7), 1.77 (s, 3H), 2.05 (s, 3H), 3.73 (q, 1H, J = 7), 5.20 (s, 1H), 5.47 (s, 1H), 6.77 (d, 2H, J = 4), 6.9–7.1 (m, 1H)	3.33	97:3
5r	1.80 (s, 3H), 4.90 (s, 1H), 5.37 (s, 1H), 6.7–6.9 (m, 2H), 7.0–7.1 (m, 1H), 7.17 (s, 5H)	3.33	93:7
5s	1.0–1.7 (m, 15H), 1.88 (s, 3H), 1.9–2.3 (m, 2H), 3.53 (t, 1H, J = 7), 3.95 (q, 2H, J = 7), 5.33 (s, 1H), 6.7–6.9 (m, 2H), 6.9–7.1 (m, 1H)	3.33	90:10
5t	1.17 (t, 3H, J = 7), 3.20 (s, 2H), 3.57 (s, 2H), 3.67 (s, 3H), 4.03 (q, 2H, J = 7), 6.67 (d, 2H, J = 8), 7.00 (d, 2H, J = 8)	4.70	25:75
5u	1.10 (t, 3H, J = 7), 1.23 (d, 3H, J = 7), 3.10 (d, 2H, J = 2), 3.63 (s, 3H), 3.70 (q, 1H, J = 7), 3.93 (q, 2H, J = 7), 6.67 (d, 2H, J = 8), 6.97 (d, 2H, J = 8)	4.73	10:90

[a] IR spectra of all 1,3-dicarbonyls **5a–u** contained broad absorption peaks in the fields of ν = 3280–2370 cm^{-1} (associated OH), and ν = 1760–1500 cm^{-1} (C=O + C=C).
[b] Enolic form of 1,3-diones **5a–s**, keto form of 3-oxo esters **5t,u**. Signal of OH proton of enolic form of 1,3-diones **5a–s** was not fixed.
[c] (3-CH_2) of keto form of 1,3-diones **5a–s**, (3-CH) of enolic form of 3-oxo esters **5t,u**.
[d] Approximate ratio for 10% solns in CCl_4, established by ^{1}H NMR spectroscopy.
[e] Lit.[12] δ (3-CH_2) ≅ 3.5, enol/ketone = 90:10.

Table 4. ^{1}H NMR and IR Spectra of Fused Phenols **8**

Product	^{1}H NMR, δ, J (Hz)	IR ν (cm^{-1})
8a	0.83 (t, 3H, J = 7), 1.55 (sextet, 2H, J = 7), 2.77 (t, 2H, J = 7), 6.77 (s, 2H), 7.0–7.5 (m, 4H), 7.7–7.9 (m, 1H)	3600, 3413, 3067, 2920, 2867, 1627, 1600, 1173, 840
8k	2.33 (s, 3H), 5.17 (s broad, 1H), 6.63 (s, 1H), 6.8–7.8 (m, 9H)	3600, 3440, 3080, 3027, 2920, 1600, 1373, 1347, 693
8p	2.27 (s, 3H), 5.17 (s broad, 1H), 6.50 (s, 1H), 6.93 (d, 1H, J = 5), 7.0–7.2 (m, 6H)	3513, 3060, 3027, 2920, 1360, 1153, 693
	acetate: 2.10 (s, 3H), 2.23 (s, 3H), 6.83 (s, 1H), 7.0–7.4 (m, 7H)	3060, 3027, 2913, 1760, 1360, 1147, 693
8r	2.40 (s, 3H), 4.83 (s, 1H), 6.67 (s, 1H), 6.93 (d, 1H, J = 6), 7.10 (d, 1H, J = 6), 7.33 (s, 5H)	3507, 3060, 3027, 2920, 1367, 693
	acetate: 1.77 (s, 3H), 2.43 (s, 3H), 6.72 (s, 1H), 7.0–7.2 (m, 2H), 7.23 (s, 5H)	3060, 3027, 2920, 1760, 1360, 1187, 693
8s	0.8–1.8 (m, 13H), 1.9–2.3 (m, 2H), 2.33 (s, 3H), 2.5–2.8 (m, 2H), 3.97 (q, 2H, J = 7), 6.03 (s, 1H), 6.47 (s, 1H), 6.97 (d, 1H, J = 5), 7.07 (d, 1H, J = 5)	3507, 2920, 2850, 1733, 1373, 677
	acetate: 0.9–1.7 (m, 13H), 1.9–2.2 (m, 2H), 2.17 (s, 3H), 2.43 (s, 3H), 2.5–2.8 (m, 2H), 3.93 (q, 2H, J = 7), 6.67 (s, 1H), 7.53 (s, 2H)	2920, 2853, 1760, 1733, 1467, 1373, 680

Anal. calcd for $C_{15}H_{13}BrO_2$: C, 59.02; H, 4.26. Found C, 58.87; H, 4.18.

Condensation of α-bromoacetophenone with PhCHO in the presence of *t*-BuOMgBr (2 equiv) at r.t. for 20 h and reflux for 6 h gave mainly the same product (according to ^{1}H NMR spectra), with traces of dibenzoylmethane, 2,3-diphenyl-3-oxopropanal, and 2-bromo-1,3-diphenylprop-2-en-1-one [according to TLC analysis (Kavalier silufol UV 254, benzene)].

***trans*-2,3-Epoxy-1,3-diphenylpropan-1-one (7):**

Et_3N (0.17 mL, 1.20 mmol) was added to a solution of bromohydrin **6** (0.30 g, 1 mmol) in MeOH (3 mL) under stirring and cooling (0 °C). The mixture was stirred at 0 °C for 1 h, and allowed to stand overnight at 0–5 °C. Epoxy ketone 7 was filtered, washed with cold aq MeOH and dried; yield: 0.20 g (90%); mp 86–87 °C (lit.[19] mp 86–87 °C).

Substituted 2-Naphthols (8a,k); General Procedure:

A mixture of PPA (3 mL) (prepared by dehydration of concd H_3PO_4 at 150 °C/15 Torr for 6 h) and the 1-phenyl-2,4-dione **5a,k** (1 mmol) was stirred at 135–140 °C for the time given in Table 2, cooled, diluted with water (10 mL), and extracted with benzene (5 mL). The organic layer was separated, dried (Na_2SO_4) and chromatographed over a column of silica gel with benzene as eluent to afford naphthols **8a,k** (Tables 2, 4).

Substituted 6-Hydroxybenzo[*b*]thiophenes (8p,r,s); General Procedure:

To a solution of the 1-(2-thienyl)-2,4-dione **5p,r,s** (1.5 mmol) in CCl_4 (4 mL) was added $POCl_3$ (0.30 mL, 3.2 mmol), and in cases **5p,s** one drop of concd H_3PO_4 (to start the reaction). The mixture was refluxed for the time given in Table 2, cooled, poured into water, and extracted with benzene/hexane (1:1) (12 mL). The organic layer was separated, washed with 20% aq NaOAc and chromatographed over a short column with a layer of silica gel (approximately 3 g) below, and anhyd Na_2SO_4 above, (benzene/hexane 1:1) to afford the pure benzothiophenes **8p,r,s** (Tables 2, 4). The products **8p,r,s** were converted to the corresponding acetates by successive treatment of the cold (0 °C) solution in benzene (2 mL) with pyridine (0.21 mL, 2.6 mmol), and AcCl (0.18 mL, 2.6 mmol). After standing overnight at r.t., the mixture was washed with water, dried (Na_2SO_4), and chromatographed over a short column of silica gel (3 g) with benzene as eluent (Tables 2, 4).

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