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Convenient synthesis of furo[2,3-*c*][1,2]dioxoles from 1-aryl-2-allylalkane-1,3-diones

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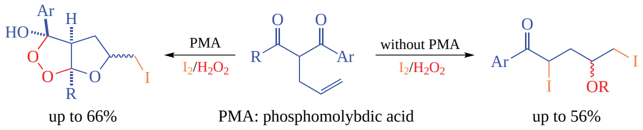
Treatment of 1-aryl-2-allylalkane-1,3-diones with I_2/H_2O_2 system in the presence of catalytic amount of phosphomolybdic acid affords furo[2,3-*c*][1,2]dioxole derivatives. With other acidic catalysts such as $BF_3\cdot Et_2O$, $SnCl_4$, H_2SO_4 or TsOH, mixtures with linear 4-acyloxy-2,5-diiodoalkan-1-ones are formed.



Keywords: furo[2,3-*c*][1,2]dioxoles, iodination, peroxides, cyclization, hydrogen peroxide, iodine, acetals, phosphomolybdic acid, catalysis.

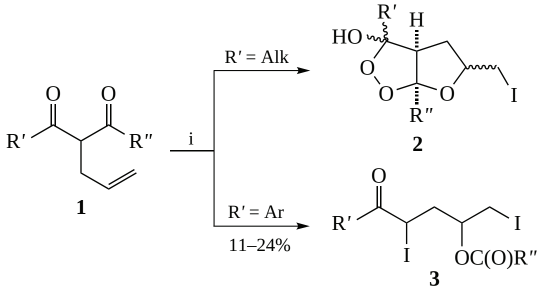
Peroxides are widely used as initiators of radical polymerization and thermosets in curing processes.[1] Nowadays, these compounds attract more attention due to their antihelmintic[2] and anticancer[3] activities.

It is known that I_2/H_2O_2 system can react with C=C double bonds giving α,β-iodo peroxides[4,5] being valuable precursors in the synthesis of complex organic molecules containing –O–O– fragment. This system showed catalytic activity for peroxide groups insertion into carbonyl compounds.[6,7] A combination of I_2 and H_2O_2 was also applied for a number of transformations including alkene iodoalkoxylation,[8] iodinations of arenes,[9] ketones[10] and alkynes.[11] Oxidation properties of this system provided its successful application for Baeyer–Villiger oxidation of ketones,[12] ring shrinking of 1,2-quinones,[13] oxidative C–N[14] and C–O[15] coupling, synthesis of heterocyclic compounds.[16]

Selectivity of peroxidation can be usually improved by the application of various catalysts such as H_2WO_4,[17] phosphomolybdic (PMA) and phosphotungstic (PTA) acids,[18] $MeReO_3/CF_3CH_2OH$,[19] trifluoroacetic acid with cinchona alkaloids,[20] Re_2O_7,[21] $BF_3\cdot Et_2O$,[22] cerium ammonium nitrate,[23] silicon-supported sodium hydrogen sulfate,[24] camphorsulfonic acid,[25] $SnCl_2\cdot 6H_2O$,[26] and ruthenium,[27] copper,[28] cobalt,[29] and iron salts[30,31] as well as metalloporphyrin systems.[32]

Previously, the reaction of aliphatic 2-allylalkane-1,3-diones **1** (Scheme 1, R′ = R″ = Alk) with I_2/H_2O_2 system leading to furo[2,3-*c*][1,2]dioxole derivatives **2** was documented.[33] In the case of 1-aryl-2-allylalkane-1,3-diones (R′ = Ar), keto esters **3** were formed.

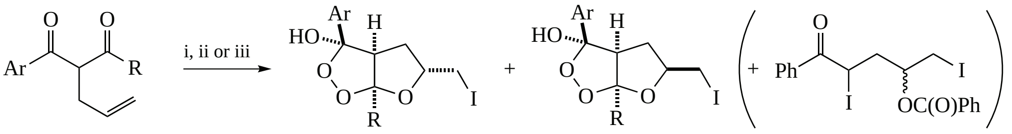
Herein, we present a successful transformation of 1-aryl-2-allylalkane-1,3-diones **1a**–**c** into furodioxole derivatives **2a**–**c** upon treatment with I_2/H_2O_2 system in the presence of catalytic amounts of PMA (Scheme 2). Optimization was carried out with diketone **1a** (Table 1) using fivefold amount of H_2O_2 and twofold amount of I_2 in CH_2Cl_2 at ambient temperature.



Scheme 1 *Reagents and conditions*: i, I_2 (2 equiv.), H_2O_2 (5 equiv.), CH_2Cl_2, ambient temperature, 1 h.

In fact, treatment of diketone **1a** with I_2/H_2O_2 results in compound **3** as a single product (see Table 1, entry 1). Application of 5–20 mol% of PMA was enough to suppress oxidation of **1a** into **3** resulting in a formation of **2a** as the sole product (entries 2–4). Yield of **2a** is dropping from 66 to 52% when amount of PMA is decreased from 20 to 5 mol%. Further decrease in PMA amount results in the mixture of products **2a** and **3** (entry 6). Phosphotungstic acid (PTA) shows lower catalytic effect in comparison with PMA, as products **2a** and **3** were formed approximately in equal amounts (entry 5). Other Brønsted and Lewis acids such as H_2SO_4, TsOH, $SnCl_4$ and $BF_3\cdot Et_2O$ are not effective (entries 7–10).

Diketones **1b**,**c** were transformed into bicyclic products **2b**,**c** under optimized reaction conditions (see Scheme 2). Compounds **2a**–**c** are unstable and turn dark brown even if stored at –20 °C. Thus, low yield of **2b**,**c** may be due to degradation of these compounds on SiO_2 during purification process.



1a–c **2a–c** (dr = 2 : 1) **2′a–c** **3** (i or ii, for **1a**)

Optimal yields (iii) for **2** + **2′**
a Ar = R = Ph (66%)
b Ar = 4-MeC_6H_4, R = Me (26%)
c Ar = Ph, R = Me (30%)

Scheme 2 *Reagents and conditions*: i, H_2O_2 (5 equiv.), I_2 (2 equiv.), CH_2Cl_2, ambient temperature; ii, conditions i with acid additive (0.2 mol%, see Table 1); iii, conditions i with PMA (0.05–0.2 mol%) as the acid.

Table 1 Reaction of diketone **1a** with I_2/H_2O_2 system.

Entry	Catalyst (mol%)	Yield^a (%)	
		2	**3**
1	–	–	24
2	PMA (0.2)	66^b	–
3	PMA (0.1)	60	–
4	PMA (0.05)	52	–
5	PTA (0.05)	60	42
6	PMA (0.01)	40	7
7	$SnCl_4$ (0.2)	18	21
8	H_2SO_4 (0.2)	4	56
9	PTSA (0.2)	18	27
10	$BF_3 \cdot Et_2O$ (0.2)	–	48

^{a}NMR yield. ^{b}Isolated yield.

All products **2a–c** are new, and are isolated as 2 : 1 diastereomer mixtures. Structure of compounds **2a–c** was studied by NMR (including 2D methods, see Online Supplementary Materials). The molecular and crystal structure of compound **2b** was also determined from single-crystal X-ray diffraction data (Figure 1).†

Possible mechanism of the reaction is presented in Scheme 3. Higher nucleophilicity of 3-positioned carbonyl oxygen in comparison with the 1-positioned one may be the reason for regio-direction of the process. Cation **A** adds PMA–peroxide complex giving intermediate **B**, which would undergo the second intramolecular cyclization into product **2**. In the absence of PMA, cation **A** adds H_2O_2 undergoing subsequent protonation and rearrangement into acyclic product **3**. Thus, the role of PMA is a formation of a complex with hydrogen peroxide molecule, which does not undergo rearrangement with furan ring cleavage.

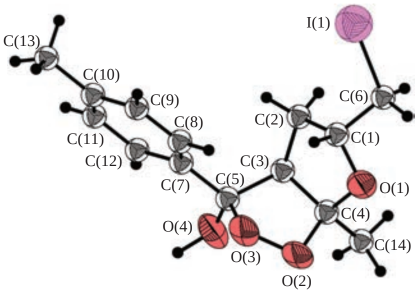
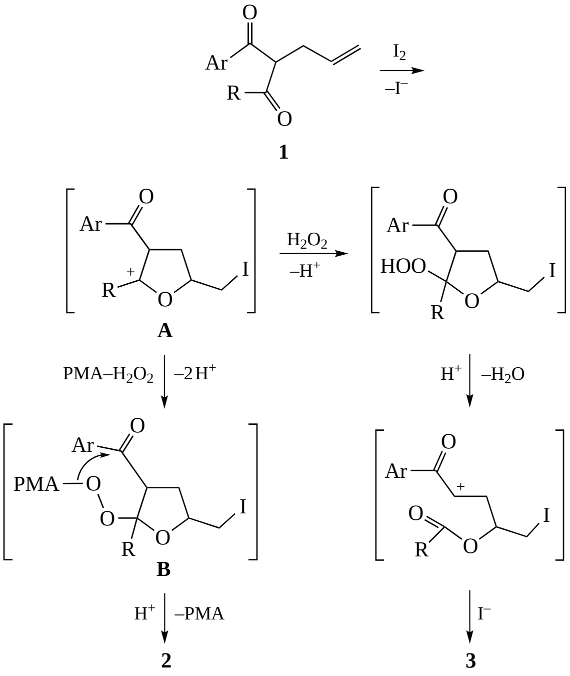


Figure 1 The molecular structure of **2b** showing the atomic numbering and 50% probability displacement ellipsoids.



Scheme 3

In summary, the synthesis of furo[2,3-*c*][1,2]dioxole derivatives **2** from 1-aryl-2-allylalkane-1,3-diones was accomplished. It was found that PMA played a key role in this reaction *via* coordination with H_2O_2 forming a stable complex. In the absence of acidic catalyst, only acyclic diiodo keto esters of type **3** were formed.

X-ray structural study was fulfilled using a STOE STADI VARI PILATUS-100K diffractometer purchased by M. V. Lomonosov Moscow State University Development Program.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2020.09.018.

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† *Crystal data for* **2b**. $C_{14}H_{17}IO_4$ (M_r = 376.17), monoclinic, space group *P*21/*c*, a = 10.890(5), b = 12.115(5) and c = 11.686(4) Å, V = 1538.9(11) Å^3, Z = 4, d_x = 1.624 Mg m^{-3}, absorption coefficient: 16.423 mm^{-1}, F(000) = 744, the final R = 0.0779, wR = 0.2416 and S = 1.045 for 2682 observed reflections with $I > 2\sigma(I)$.

The single-crystal X-ray diffraction experiment for **2b** was carried out at room temperature using monochromated CuKα radiation on a STOE STADI-VARI Pilatus-100K diffractometer. The structure was solved with SHELXS and refined with SHELXL. All hydrogen atoms were located on a difference Fourier map, then placed in idealized positions (C–H 0.93–0.98 Å), and refined as riding with U_{iso}(H) = 1.2–1.5 U_{eq}(C).

CCDC 1996372 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

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