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1,4-DIOXINS FROM METHYL PHENYLCHLOROPYRUVATE. COMPETITION OF THE DARZENS, FAVORSKII, AND GABRIEL REACTIONS

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The reaction of methyl phenylchloropyruvate with potassium phthalimide and sodium imidazolide leads to isomeric 2,5-dimethoxycarbonyl-3,6-diphenyl- and 2,6-dimethoxycarbonyl-3,5-diphenyl-1,4-dioxins.

Keywords: 2,3-dihydro-1,4-dioxins, 1,4-dioxins, methyl phenylchloropyruvate, Darzens reaction, Favorskii reaction, Gabriel reaction, addition–elimination reaction. CH-π interaction, π,π-interaction, intra- and intermolecular short contacts.

We have shown that the reactions of 2-oxo-3-phenyl-3-chloropropionic (phenylchloropyruvic) acid derivatives with nucleophiles lead to different types of products depending on the nature of the nucleophiles and the reaction conditions. Esters of 3-alkoxyphenylpyruvic acid or 3-alkoxy-2,5-dialkoxycarbonyl-3,6-diphenyl-2,3-dihydro-1,4-dioxins are obtained in the reactions of the methyl and ethyl esters of phenylchloropyruvic acid with sodium alcoholates in alcoholic solutions [1-4]. O- And C-phosphonium salts are formed in the reaction of the methyl ester and dimethylamide of phenylchloropyruvic acid with triphenylphosphine [5], while the reaction with phosphites occurs only at the oxygen atom to give substituted vinyl phosphates through a Perkov reaction [6]. Functionalized 1,3-oxazoles are obtained in the reaction of the methyl and ethyl esters and diisopropylamide of phenylchloropyruvic acid with sodium azide [7].

In the present work, we studied the behavior of methyl phenylchloropyruvate (**1**) toward potassium phthalimide (**2**) and sodium imidazolide.

The reaction of α-chloro ketone **1** with phthalimide **2** under conditions of the Gabriel reaction [8] gives a compound lacking nitrogen as the major product instead of the expected N-substituted phthalimide **3**. Carrying out the reaction in formamide, DMF, acetone, and chlorobenzene leads in all cases to a crystalline product, whose ^{1}H NMR spectrum has signals only at 3.67 (s) and 7.47-7.70 ppm (m) with 3:5 integral intensity ratio. The chemical shifts and intensities of these signals correspond to the signals of the methoxycarbonyl and phenyl groups in the ^{1}H NMR spectrum of starting α-chloro ketone **1**. Thus, the product lacks phthalimide fragments as well as the methine proton of the starting chloro ketone. The elemental analysis is in accord with dimethoxycarbonyldiphenyl-1,4-dioxin. In light of the capacity of α-chloro ketone **1** to undergo condensation to give 2-alkoxy-3,5-dialkoxycarbonyl-3,6-diphenyl-2,3-dihydro-1,4-dioxins by the action of anionic nucleophiles such as MeONa and EtONa [1, 2], this most likely should be 2,5-dimethoxycarbonyl-3,6-diphenyl-1,4-dioxin (**4**). The IR spectrum of this product is in accord with this hypothesis. An X-ray diffraction suggested that the reaction of α-chloro ketone **1** with potassium phthalimide indeed proceeds to give heterocyclic derivative **4**.

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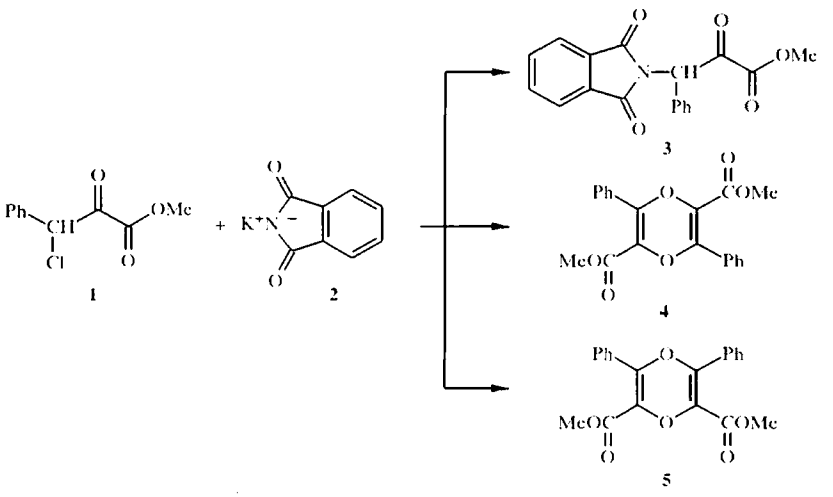
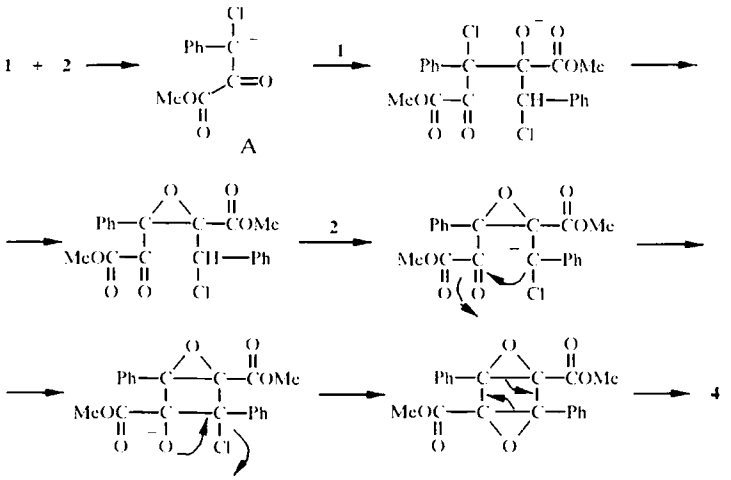


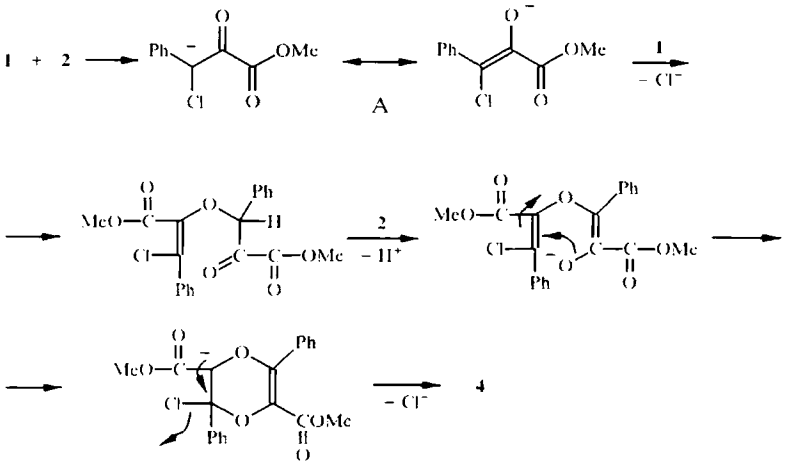
Dioxin **4** is also obtained when sodium imidazolide is used instead of potassium phthalimide. Fractional distillation gave a minor product in addition to dioxin **4** obtained in good yield. Elemental analysis as well as the ^{1}H NMR and IR spectra of this minor product, which hardly differed from the corresponding spectra of the major product, suggested an isomer, namely, dioxin **5**. This conclusion was also confirmed by X-ray analysis.

The expected Gabriel reaction product was found in this reaction mixture in small amounts not exceeding 5%. This product could not be isolated but its presence was indicated in the ^{1}H NMR spectrum of the mixture by singlets for the carbomethoxy group at 3.84 ppm and methine proton at 4.75 ppm, phthalimide multiplets at 7.15-7.20 and 7.25-7.30 ppm (a somewhat distorted AA'BB' system), and phenyl multiplet at 7.50 ppm with integral intensity ratio 3:1:(2+2):5.

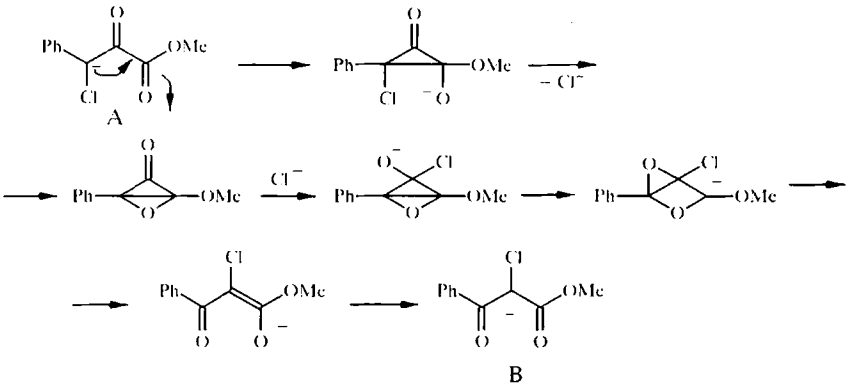
Several pathways could lead to the formation of dioxin **4**. One pathway involves double self-condensation of α-chloro ketone **1** through a Darzens reaction. In the first step, a chloro ketone molecule provides for the generation of anion A and then another such molecule reacts with this anion at its ketone group. The 1-α-chlorobenzyl and 2-methoxycarbonylformyl substituents play the same roles in the resultant oxirane intermediate.



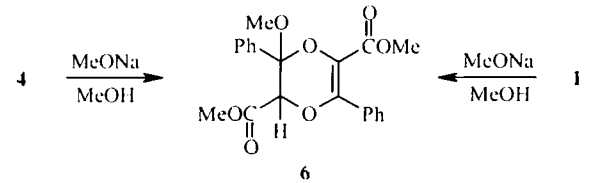
Another possibility entails the replacement of the chlorine atom in α-chloro ketone **1** by mesomeric anion A in the first step and the loss of HCl as the result of an intramolecular addition–elimination reaction in the second step.



The mechanism for the formation of 3,5-diphenyldioxin **5**, similar to the mechanism for the formation of dioxin **4**, may be represented by two pathways (see above) with the difference that the anion of methyl 3-oxo-3-phenyl-2-chloropropionate (B) rather than anion A is a starting species for dioxin **5**. The formation of anion B as a side-intermediate under the basic conditions of the Gabriel reaction may be explained by the rearrangement of anion A according to a mechanism generally adopted for the Favorskii rearrangement [9-12].



Treating dioxin **4** with sodium methylate in methanol leads to the addition of MeOH at a double bond to give 3-methoxy-2,5-dimethoxycarbonyl-3,6-diphenyl-2,3-dihydro-1,4-dioxin (**6**), identical to the compound obtained directly from α-chloro ketone **1** upon analogous treatment [3].



We note that prolonging the reaction or raising the base concentration does not affect the final result and addition of a second methanol molecule was not observed. This failure may be attributed to steric and electronic factors. The addition of one methanol molecule leads to transformation of the planar molecule of dioxin **4** (available to attack from both sides) to molecule **6**, whose heterocycle has half-chair conformation and the approach of a second methanol molecule to the 2,3-dihydrodioxin double bond is sterically blocked.

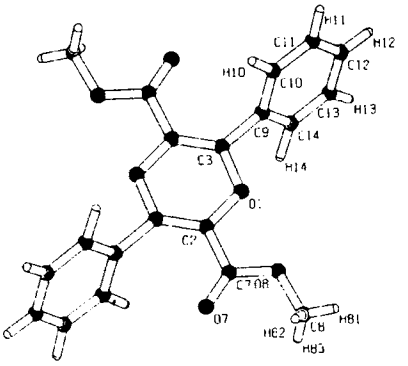


Fig. 1. Geometry of compound **4** in the crystal.

Let us examine the three-dimensional structures of dioxins **4** and **5** relative to the X-ray diffraction data obtained for their crystals.

The molecule of dioxin **4** is found in a special position at a center of symmetry. Thus, the symmetrically independent part of the crystalline cell is one-half of this molecule (Fig. 1).

The search for analogous structures [13] revealed only one compound of this type, namely, 2,5-dibenzoyl-3,5-bis(4'-methoxyphenyl)-1,4-dioxin studied in our earlier work [14]. As in the latter molecule, the dioxin ring in **4** is planar (the deviation of the atoms from the ring plane does not exceed 0.006(2) Å). The $C_{(2)}=C_{(3')}$ (1-x, -y, -z) double bonds are somewhat elongated (1.341(3) Å) in comparison with these bonds in the 2,5-dibenzoyl analog (1.327(5) Å) [14] and cyclohexene (1.326 Å) [15]. The C–O bonds (1.396(3) and 1.386(3) Å) are also longer than $C_{(sp2)}$–$O_{(2)}$ bonds in six-membered heterocycles (the average for analogous cyclic systems according to the Cambridge Structural Database System is 1.368 Å [13]) but coincide within experimental error to the values found for the dibenzoyl analog (1.394(4) Å). The planes of the phenyl substituent and methoxycarbonyl group form dihedral angles of 70.2(1)° and 3.5(3)°, respectively, with the dioxin ring plane. No short intramolecular contacts are found in **4**. We should note the C–H···O intermolecular hydrogen bonds. $H_{(14)}$ in the *ortho* position of the phenyl fragment interacts with $O_{(7'')}$ (1-x, 1-y, -z) of the ester group: $C_{(14)}\cdots O_{(7'')}$, 3.500(3) Å; $H_{(14)}\cdots O_{(7'')}$, 2.48(3) Å; $\angle C_{(14)}$–$H_{(14)}$–$O_{(7'')}$, 176(2)°. Also $H_{(83)}$ of the methyl group interacts with O(1''') (x, 1+y, z) of the dioxin ring: $C_{(8)}\cdots O_{(1''')}$, 3.607(3) Å; $H_{(83)}\cdots O_{(1''')}$, 2.44(5) Å; $\angle C_{(8)}$–$H_{(83)}$–$O_{(1''')}$, 156(4)° (Fig. 2).

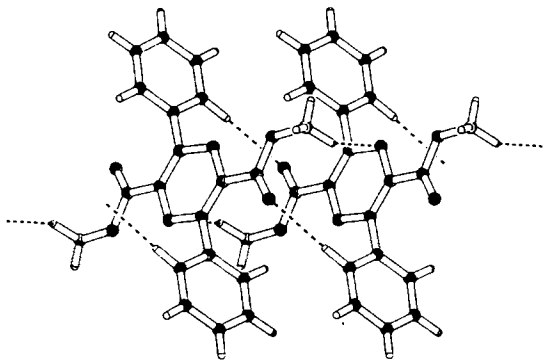


Fig. 2. Hydrogen bond system in the crystal of compound **4** (hydrogen bonds shown by dashed lines).

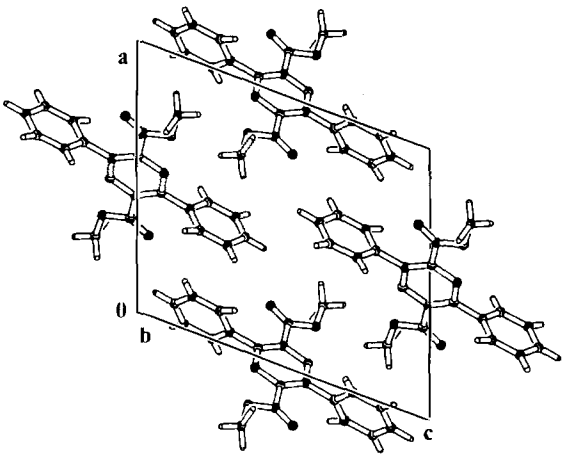


Fig. 3. The packing of molecules **4** along the *0Y* axis in the crystal.

The packing of the molecules in the unit cell (Fig. 3) features π,π-interactions between the dioxin rings of molecules related by a center of symmetry with the following parameters: the dihedral angle between the ring planes is 0.2(2)° and the distance between the ring planes is 3.436(3) Å. Each dioxin ring participates in two such interaction. It is also interesting to note the CH···π interaction between $H_{(13)}$ of the phenyl group and the π-system of the phenyl group of the molecule related to it by the symmetry operation (1/2-*x*, 1/2+*y*, 1/2-*z*) (the distance from $H_{(13)}$ to the center of the phenyl ring (Cg2) is 3.144 Å, angle $C_{(13)}$–$H_{(13)}$···Cg1 is 129.5°) and between the methoxyl group proton both with the dioxin (Cg1) and phenyl rings (Cg2) of the adjacent molecules with the following characteristics:

Bond	Symmetry operation	*d* (H...Cg), Å	∠D-H...Cg, deg.
$C_{(8)}H_{(82)}$...Cg2	(3/2-*x*, 1/2+*y*, 1/2-*z*)	2.74	146.2
$C_{(8)}H_{(83)}$...Cg1	(*x*, 1+*y*, *z*)	2.48	158.2

The heterocycle of dioxin **5** has a proper (noncrystallographic) symmetry plane traversing the oxygen atoms of the dioxin ring (Fig. 4). However, the molecule loses this symmetry element in the unit cell. The most significant difference in conformation relative to dioxin **4** is the nonplanar dioxin ring in boat form (the dihedral angle between the $O_{(1)}$–$C_{(6)}$–$C_{(5)}$–$C_{(4)}$ and $O_{(1)}$–$C_{(2)}$–$C_{(3)}$–$C_{(4)}$ planes is 32.2(1)°). The base of the ring (the $C_{(2)}C_{(3)}C_{(5)}C_{(6)}$ fragment) is planar within ±0.004(2) Å. The deviations of $O_{(1)}$ and $O_{(4)}$ from this plane are 0.384(1) and 0.293(1) Å to the same side but at different distances. The dihedral angles between this plane and the $C_{(6)}$–$O_{(1)}$–$C_{(2)}$ and $C_{(3)}$–$O_{(4)}$–$C_{(5)}$ planes are 29.7(2) and 23.2(2)°, respectively. The planes of the phenyl substituents $C_{(15)}$–$C_{(20)}$ and $C_{(9)}$–$C_{(14)}$ form dihedral angles with the plane of the dioxin base equal to 36.9(1)° and 55.7(1)°, respectively, while the methoxycarbonyl groups $C_{(21)}O_{(21)}O_{(22)}C_{(22)}$ and $C_{(7)}O_{(7)}O_{(8)}C_{(8)}$ form dihedral angles with this plane equal to 26.6(2)° and 21.4(2)°, respectively. The methoxycarbonyl groups are twisted in different way relative to the heterocycle. The C=O and ring C–O bonds are eclipsed in one such group, while the methoxy group C–O bond is eclipsed by the endocyclic bond in the other (torsion angles: $O_{(1)}$–$C_{(2)}$–$C_{(7)}$–$O_{(7)}$, 6.8(2)°; $O_{(1)}$–$C_{(6)}$–$C_{(21)}$–$O_{(22)}$, 10.6(2)°). Thus, the rotation of the methoxycarbonyl groups at the ring atoms leads to the reduction in the proper symmetry of the molecule.

The lengths of the C=C bonds in dioxin **5** (1.331(2) and 1.326(2) Å) are slightly less than in dioxin **4**. Some differences are found in the lengths of the endocyclic O–C bonds: the $O_{(1)}$–$C_{(6)}$ bond length (1.394(2) Å) coincides with the lengths of the bonds at $O_{(4)}$ and bond lengths in dioxin **4**, while the $O_{(1)}$–$C_{(2)}$ bond is elongated (1.403(2) Å). There is probably conjugation of the endocyclic double bonds, methoxycarbonyl C=O bonds, and oxygen nonbonded electron pairs in the planar heterocycle of dioxin **4**. Conjugation is less likely in the nonplanar heterocycle of dioxin **5** and the bonds are localized.

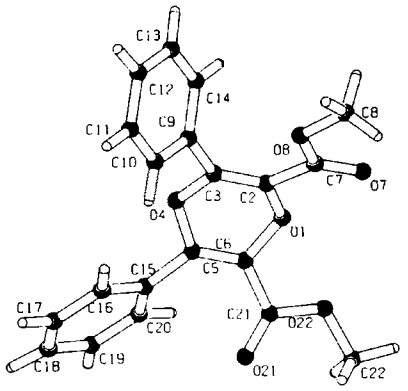


Fig. 4. Geometry of compound **5** in the crystal.

The following intra- and intermolecular short contacts are found in the crystal of dioxin **5**:

Bond	Symmetry element of related molecule	*d* (D-H), Å	*d* (H...A), Å	*d* (D...A), Å	∠D-H...A, deg.
$C_{(10)}H_{(10)}...O_{(21)}$	1−*x*, 1−*y*, −*z*	0.96(2)	2.54(1)	3.257(2)	131.3(1)
$C_{(14)}H_{(14)}...O_{(1)}$	*x*, 1−*y*, −*z*	0.99(2)	2.41(2)	3.372(2)	164.7(2)
$C_{(20)}H_{(20)}...O_{(21)}$	Intramolec.	1.00(2)	2.58(2)	2.961(2)	102.4(1)

The packing of the molecules in the crystal of **5** (Fig. 6), in contrast to **4**, features parallel arrangement of the phenyl substituents $C_{(9)}$–$C_{(14)}$ (Cg2) and $C_{(5)}$–$C_{(20)}$ (Cg3) in adjacent molecules and the following π,π-interactions (Cg–Cg is the distance between the ring centers, α is the angle between the ring planes, β is the angle between the normal to the ring plane and line connecting their centers, and *L* is the distance between the ring planes):

Cg Cg	Symmetry operation	*d*(Cg Cg), Å	α, deg.	β, deg.	*L*, Å
Cg2 Cg2	−*x*, 2−*y*, −*z*	5.74	0.0	57.4	3.09
Cg3 Cg3	1−*x*, −*y*, −*z*	5.72	0.2	59.6	2.91

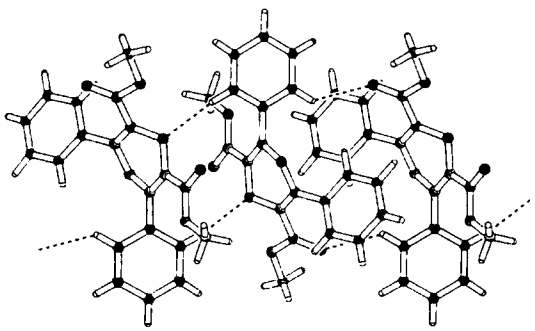


Fig. 5. Intramolecular hydrogen bonds in the crystal of dioxin **5** (hydrogen bonds shown by dashed lines).

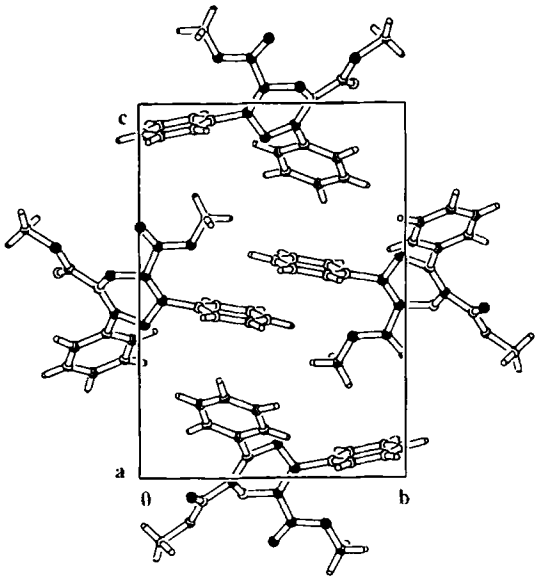


Fig. 6. View along the *OX* axis in the unit cell of **5**.

Furthermore, short intermolecular CH···π contacts are found in the crystal of dioxin **5**:

C–H...Cg	Symmetry	*d*(H...Cg), Å	∠C–H...Cg, deg.
$C_{(10)}$–$H_{(10)}$...Cg3	1–*x*, 1–*y*, –*z*	3.14	130.2
$C_{(18)}$–$H_{(18)}$...Cg2	1–*x*, *y*–1/2, 1–*z*	2.77	140.9
$C_{(22)}$–$H_{(22)}$...Cg3	*x*, *y*–1/2, *z*–1/2	3.28	156.9

MNDO calculations of the nonperturbed conformation of the dioxin ring showed that the major reason for the distortion from the planar conformation of the ring in dioxin **5** is the effect of the crystal field involving both optimization of the molecular packing in the unit cell and the fullest realization of all the intermolecular interactions noted. This is indicated by the somewhat reduced calculated density of the crystal of dioxin **5** in comparison with the density of the crystal of dioxin **4**. Mastryukov [16] and Borbulevych [17] carried out theoretical analyses of the conformations for non-aromatic heterocycles and came to a similar conclusion.

TABLE 1. Atomic Coordinate for Dioxin **4**, Equivalent Isotropic Temperature Parameters of the Non-hydrogen Atoms ($B = 4/3 \cdot \sum_{i=1}^{3}\sum_{j=1}^{3}(\mathbf{a}_i \cdot \mathbf{a}_j)B(i,j)$, Å^2) and Isotropic Temperature Parameters of the Hydrogen Atoms

Atom	*x*	*y*	*z*	*B*
1	2	3	4	5
$C_{(2)}$	0.5758(2)	0.1862(4)	1.0058(1)	2.53(4)
$O_{(1)}$	0.5458(2)	0.1303(3)	1.0926(1)	3.76(3)
$O_{(5)}$	0.7056(2)	0.4561(4)	0.9609(1)	4.98(4)
$O_{(8)}$	0.6925(2)	0.4774(3)	1.1178(1)	3.18(3)
$C_{(3)}$	0.5306(2)	0.0632(4)	0.9167(2)	2.41(4)
$C_{(7)}$	0.6652(2)	0.3854(4)	1.0232(2)	2.58(4)
$C_{(8)}$	0.7786(2)	0.6748(5)	1.1422(2)	3.66(6)
$C_{(9)}$	0.5520(2)	0.1052(4)	0.8187(1)	2.33(4)

TABLE 1 (continued)

1	2	3	4	5
$C_{(10)}$	0.5016(2)	0.3073(5)	0.7574(2)	3.18(5)
$C_{(11)}$	0.5167(3)	0.3331(5)	0.6630(2)	3.75(5)
$C_{(12)}$	0.5798(2)	0.1636(5)	0.6288(2)	3.59(5)
$C_{(13)}$	0.6315(2)	-0.0329(5)	0.6899(2)	3.58(5)
$C_{(14)}$	0.6159(2)	-0.0639(5)	0.7841(2)	3.01(4)
$H_{(10)}$	0.462(2)	0.432(5)	0.782(2)	3.4(5)*
$H_{(11)}$	0.492(3)	0.477(6)	0.621(3)	7.0(9)*
$H_{(12)}$	0.594(2)	0.178(5)	0.563(2)	4.4(6)*
$H_{(13)}$	0.676(2)	-0.143(4)	0.665(2)	2.8(5)*
$H_{(14)}$	0.638(2)	-0.209(6)	0.834(2)	5.4(7)*
$H_{(81)}$	0.809(3)	0.705(6)	1.210(2)	6.3(8)*
$H_{(82)}$	0.856(3)	0.618(7)	1.135(3)	8(1)*
$H_{(83)}$	0.701(4)	0.831(9)	1.101(4)	12(1)*

* Refined isotropically.

TABLE 2. Atomic Coordinates for Dioxin **5**, Equivalent Isotropic Temperature Parameters of the Non-Hydrogen Atoms ($B = 4/3 \cdot \sum_{i=1}^{3}\sum_{j=1}^{3}(\mathbf{a}_i \cdot \mathbf{a}_j)B(i,j)$, Å^2) and Isotropic Temperature Parameters of the Hydrogen Atoms

Atom	x	y	z	B
1	2	3	4	5
$O_{(1)}$	0.85233(9)	-0.1084(1)	0.54307(8)	3.98(2)
$O_{(4)}$	0.7272(1)	0.0217(1)	0.41068(7)	3.69(2)
$O_{(7)}$	0.9912(2)	0.0058(1)	0.6717(1)	6.33(3)
$O_{(8)}$	0.9354(1)	0.1978(1)	0.62373(8)	5.09(3)
$O_{(21)}$	0.5971(1)	-0.3046(1)	0.5514(1)	5.29(3)
$O_{(22)}$	0.7809(1)	-0.3123(1)	0.61834(9)	4.82(3)
$C_{(2)}$	0.8599(1)	0.0237(1)	0.5412(1)	3.24(3)
$C_{(3)}$	0.8009(1)	0.0881(1)	0.4743(1)	3.19(3)
$C_{(5)}$	0.6804(1)	-0.0915(1)	0.4421(1)	3.26(3)
$C_{(6)}$	0.7402(1)	-0.1531(1)	0.5104(1)	3.31(3)
$C_{(7)}$	0.9354(1)	0.0728(2)	0.6196(1)	3.55(3)
$C_{(8)}$	1.0098(2)	0.2553(2)	0.6955(1)	6.50(5)
$C_{(9)}$	0.7983(1)	0.2255(1)	0.45610(9)	3.11(3)
$C_{(10)}$	0.6925(1)	0.2920(2)	0.4608(1)	3.70(3)
$C_{(11)}$	0.6891(2)	0.4205(2)	0.4435(1)	4.39(4)
$C_{(12)}$	0.7907(2)	0.4839(2)	0.4210(1)	4.55(4)
$C_{(13)}$	0.8957(2)	0.4176(2)	0.4149(1)	4.57(4)
$C_{(14)}$	0.9004(1)	0.2890(2)	0.4319(1)	3.97(3)
$C_{(15)}$	0.5679(1)	-0.1235(2)	0.3903(1)	3.40(3)
$C_{(16)}$	0.4841(2)	-0.0289(2)	0.3711(1)	3.98(3)
$C_{(17)}$	0.3802(2)	-0.0558(2)	0.3192(1)	4.87(4)
$C_{(18)}$	0.3592(2)	-0.1762(2)	0.2853(1)	5.31(4)
$C_{(19)}$	0.4423(2)	-0.2701(2)	0.3026(1)	5.38(4)
$C_{(20)}$	0.5466(2)	-0.2449(2)	0.3547(1)	4.49(4)
$C_{(21)}$	0.6969(1)	-0.2633(2)	0.5613(1)	3.53(3)
$C_{(22)}$	0.7456(2)	-0.4222(2)	0.6701(1)	5.99(5)
$H_{(10)}$	0.622(1)	0.247(2)	0.474(1)	4.4(4)*
$H_{(11)}$	0.616(2)	0.465(2)	0.448(1)	6.9(5)*
$H_{(12)}$	0.786(2)	0.575(2)	0.405(1)	6.2(5)*
$H_{(13)}$	0.960(2)	0.464(2)	0.399(2)	6.7(5)*
$H_{(14)}$	0.977(2)	0.243(2)	0.428(1)	5.3(4)*

TABLE 2 (continued)

1	2	3	4	5
$H_{(16)}$	0.500(2)	0.058(2)	0.393(1)	5.3(4)*
$H_{(17)}$	0.321(2)	0.018(2)	0.309(1)	6.6(5)*
$H_{(18)}$	0.290(2)	-0.196(2)	0.241(2)	6.9(5)*
$H_{(19)}$	0.428(2)	-0.354(2)	0.280(1)	5.7(5)*
$H_{(20)}$	0.606(2)	-0.311(2)	0.375(1)	4.7(4)*
$H_{(21)}$	1.009(2)	0.214(3)	0.754(2)	9.5(7)*
$H_{(22)}$	0.981(2)	0.344(2)	0.694(2)	9.0(7)*
$H_{(23)}$	1.091(3)	0.274(4)	0.677(3)	14(1)*
$H_{(221)}$	0.721(2)	-0.486(2)	0.628(2)	7.9(6)*
$H_{(222)}$	0.817(2)	-0.439(2)	0.716(2)	7.6(6)*
$H_{(223)}$	0.679(3)	-0.381(3)	0.698(2)	12.1(9)*

* Refined isotropically.

TABLE 3. Bond Lengths (d) in the Structures of **4** and **5**

Structure **4**		Structure **5**			
Bond	d, Å	Bond	d, Å	Bond	d, Å
$O_{(1)}$–$C_{(2)}$	1.396(3)	$O_{(1)}$–$C_{(2)}$	1.394(2)	$C_{(11)}$–$C_{(12)}$	1.383(3)
$O_{(1)}$–$C_{(3)}$	1.373(3)	$O_{(1)}$–$C_{(10)}$	1.403(2)	$C_{(12)}$–$C_{(13)}$	1.381(3)
$C_{(2)}$–$C_{(3)}$	1.341(3)	$O_{(4)}$–$C_{(4)}$	1.394(2)	$C_{(13)}$–$C_{(14)}$	1.378(2)
$C_{(2)}$–$C_{(7)}$	1.482(3)	$O_{(4)}$–$C_{(5)}$	1.394(2)	$C_{(5)}$–$C_{(15)}$	1.472(2)
$O_{(8)}$–$C_{(7)}$	1.183(3)	$C_{(2)}$–$C_{(3)}$	1.331(2)	$C_{(15)}$–$C_{(16)}$	1.388(2)
$O_{(7)}$–$C_{(7)}$	1.330(2)	$C_{(5)}$–$C_{(6)}$	1.336(2)	$C_{(15)}$–$C_{(20)}$	1.395(2)
$O_{(8)}$–$C_{(8)}$	1.447(3)	$C_{(2)}$–$C_{(7)}$	1.475(2)	$C_{(16)}$–$C_{(17)}$	1.382(2)
$C_{(3)}$–$C_{(9)}$	1.476(3)	$O_{(7)}$–$C_{(7)}$	1.188(2)	$C_{(17)}$–$C_{(18)}$	1.377(3)
$C_{(9)}$–$C_{(10)}$	1.399(3)	$O_{(8)}$–$C_{(7)}$	1.318(2)	$C_{(18)}$–$C_{(19)}$	1.373(3)
$C_{(9)}$–$C_{(14)}$	1.382(3)	$O_{(8)}$–$C_{(8)}$	1.434(2)	$C_{(19)}$–$C_{(20)}$	1.383(3)
$C_{(10)}$–$C_{(11)}$	1.380(3)	$C_{(3)}$–$C_{(9)}$	1.472(2)	$C_{(6)}$–$C_{(21)}$	1.478(2)
$C_{(11)}$–$C_{(12)}$	1.375(4)	$C_{(9)}$–$C_{(10)}$	1.387(2)	$O_{(21)}$–$C_{(21)}$	1.206(2)
$C_{(12)}$–$C_{(13)}$	1.377(4)	$C_{(9)}$–$C_{(14)}$	1.396(2)	$O_{(22)}$–$C_{(21)}$	1.324(2)
$C_{(13)}$–$C_{(14)}$	1.384(3)	$C_{(10)}$–$C_{(11)}$	1.377(2)	$O_{(22)}$–$C_{(22)}$	1.452(3)

TABLE 4. Major Bond Angles (ω) in the Structure of Dioxin **4**

Bond angle	ω, deg.	Bond angle	ω, deg.
$C_{(2)}$–$O_{(1)}$–$C_{(3)}$	116.4(2)	$O_{(7)}$–$C_{(7)}$–$O_{(8)}$	124.4(2)
$C_{(7)}$–$O_{(8)}$–$C_{(8)}$	115.3(2)	$C_{(3)}$–$C_{(9)}$–$C_{(10)}$	120.4(2)
$O_{(1)}$–$C_{(2)}$–$C_{(3)}$	122.4(2)	$C_{(3)}$–$C_{(9)}$–$C_{(14)}$	119.8(2)
$O_{(1)}$–$C_{(2)}$–$C_{(7)}$	113.7(2)	$C_{(10)}$–$C_{(9)}$–$C_{(14)}$	119.7(2)
$C_{(3)}$–$C_{(2)}$–$C_{(7)}$	123.9(2)	$C_{(9)}$–$C_{(10)}$–$C_{(11)}$	119.0(2)
$O_{(1)}$–$C_{(3)}$–$C_{(2)}$	121.2(2)	$C_{(10)}$–$C_{(11)}$–$C_{(12)}$	121.0(2)
$O_{(1)}$–$C_{(3)}$–$C_{(9)}$	110.5(2)	$C_{(11)}$–$C_{(12)}$–$C_{(13)}$	120.0(2)
$C_{(2)}$–$C_{(3)}$–$C_{(9)}$	128.3(2)	$C_{(12)}$–$C_{(13)}$–$C_{(14)}$	119.8(3)
$C_{(2)}$–$C_{(7)}$–$O_{(7)}$	124.6(2)	$C_{(9)}$–$C_{(14)}$–$C_{(13)}$	120.4(2)
$C_{(2)}$–$C_{(7)}$–$O_{(8)}$	110.9(2)		

TABLE 5. Major Bond Angles (ω) in the Structure of Dioxin **5**

Bond angle	ω, deg.	Bond angle	ω, deg.
$C_{(2)}$-$O_{(1)}$-$C_{(6)}$	112.6(1)	$O_{(1)}$-$C_{(6)}$-$C_{(2)}$	114.4(1)
$C_{(3)}$-$O_{(4)}$-$C_{(5)}$	115.6(1)	$C_{(5)}$-$C_{(6)}$-$C_{(2)}$	126.2(1)
$C_{(7)}$-$O_{(8)}$-$C_{(8)}$	117.0(1)	$O_{(7)}$-$C_{(7)}$-$O_{(8)}$	124.4(1)
$C_{(2)}$-$O_{(22)}$-$C_{(22)}$	115.5(1)	$O_{(7)}$-$C_{(7)}$-$C_{(2)}$	122.9(1)
$O_{(1)}$-$C_{(2)}$-$C_{(3)}$	119.6(1)	$O_{(8)}$-$C_{(7)}$-$C_{(2)}$	112.7(1)
$O_{(1)}$-$C_{(2)}$-$C_{(7)}$	111.6(1)	$C_{(3)}$-$C_{(9)}$-$C_{(10)}$	119.6(1)
$C_{(3)}$-$C_{(2)}$-$C_{(7)}$	128.8(1)	$C_{(3)}$-$C_{(9)}$-$C_{(14)}$	120.7(1)
$O_{(4)}$-$C_{(3)}$-$C_{(2)}$	118.8(1)	$C_{(10)}$-$C_{(9)}$-$C_{(14)}$	119.7(1)
$O_{(4)}$-$C_{(3)}$-$C_{(9)}$	111.7(1)	$C_{(15)}$-$C_{(15)}$-$C_{(16)}$	119.3(1)
$C_{(2)}$-$C_{(3)}$-$C_{(9)}$	129.5(1)	$C_{(15)}$-$C_{(15)}$-$C_{(20)}$	121.6(1)
$O_{(4)}$-$C_{(5)}$-$C_{(6)}$	118.6(1)	$C_{(16)}$-$C_{(15)}$-$C_{(20)}$	118.9(1)
$O_{(4)}$-$C_{(5)}$-$C_{(15)}$	111.1(1)	$O_{(21)}$-$C_{(21)}$-$O_{(22)}$	123.8(2)
$C_{(6)}$-$C_{(5)}$-$C_{(15)}$	130.4(1)	$O_{(21)}$-$C_{(21)}$-$C_{(6)}$	124.0(1)
$O_{(1)}$-$C_{(6)}$-$C_{(5)}$	119.3(1)	$O_{(22)}$-$C_{(21)}$-$C_{(6)}$	112.2(1)

TABLE 6. Major Torsion Angles (τ) in the Structure of Dioxin **4**

Angle	τ, deg.	Angle	τ, deg.
$O_{(1)}$-$C_{(2)}$-$C_{(3)}$-$O_{(12)}$	-1.8(3)	$O_{(12)}$-$C_{(2)}$-$C_{(3)}$-$O_{(1)}$	1.8(3)
$C_{(2)}$-$C_{(3)}$-$O_{(12)}$-$C_{(2')}$	1.7(3)	$C_{(2')}$-$C_{(3)}$-$O_{(1)}$-$C_{(2)}$	-1.7(3)
$C_{(3)}$-$O_{(12)}$-$C_{(2')}$-$C_{(3')}$	-1.7(3)	$C_{(3)}$-$O_{(1)}$-$C_{(2)}$-$C_{(7)}$	1.7(3)
$C_{(7)}$-$C_{(2)}$-$C_{(3)}$-$C_{(9)}$	-4.0(3)	$C_{(8)}$-$O_{(8)}$-$C_{(7)}$-$C_{(2)}$	-179.6(2)
$O_{(1)}$-$C_{(2)}$-$C_{(7)}$-$O_{(7)}$	177.6(2)	$C_{(8)}$-$O_{(8)}$-$C_{(7)}$-$O_{(7)}$	-0.7(3)
$O_{(1)}$-$C_{(2)}$-$C_{(7)}$-$O_{(8)}$	-3.4(2)	$O_{(1)}$-$C_{(3)}$-$C_{(9)}$-$C_{(10)}$	-108.3(2)
$C_{(3)}$-$C_{(2)}$-$C_{(7)}$-$O_{(7)}$	0.0(4)	$C_{(2')}$-$C_{(3)}$-$C_{(9)}$-$C_{(10)}$	72.0(3)
$C_{(3)}$-$C_{(2)}$-$C_{(7)}$-$O_{(8)}$	178.9(2)		

TABLE 7. Major Torsion Angles (τ) in the Structure of Dioxin **5**

Angle	τ, deg.	Angle	τ, deg.
$C_{(6)}$-$O_{(1)}$-$C_{(2)}$-$C_{(3)}$	-34.3(2)	$C_{(3)}$-$C_{(2)}$-$C_{(7)}$-$O_{(7)}$	-174.2(2)
$C_{(6)}$-$O_{(1)}$-$C_{(2)}$-$C_{(7)}$	144.8(1)	$C_{(3)}$-$C_{(2)}$-$C_{(7)}$-$O_{(8)}$	4.6(2)
$C_{(2)}$-$O_{(1)}$-$C_{(6)}$-$C_{(5)}$	35.1(2)	$O_{(4)}$-$C_{(3)}$-$C_{(9)}$-$C_{(10)}$	62.5(2)
$C_{(2)}$-$O_{(1)}$-$C_{(6)}$-$C_{(21)}$	-141.4(1)	$O_{(4)}$-$C_{(3)}$-$C_{(9)}$-$C_{(13)}$	-115.8(1)
$C_{(5)}$-$O_{(4)}$-$C_{(3)}$-$C_{(2)}$	27.1(2)	$C_{(2)}$-$C_{(3)}$-$C_{(9)}$-$C_{(10)}$	-116.2(2)
$C_{(5)}$-$O_{(4)}$-$C_{(3)}$-$C_{(9)}$	-151.7(1)	$C_{(2)}$-$C_{(3)}$-$C_{(9)}$-$C_{(13)}$	65.5(2)
$C_{(3)}$-$O_{(4)}$-$C_{(5)}$-$C_{(6)}$	-26.2(2)	$O_{(4)}$-$C_{(5)}$-$C_{(6)}$-$O_{(1)}$	-5.3(2)
$C_{(3)}$-$O_{(4)}$-$C_{(5)}$-$C_{(15)}$	154.3(1)	$O_{(4)}$-$C_{(5)}$-$C_{(6)}$-$C_{(21)}$	170.7(1)
$C_{(8)}$-$O_{(8)}$-$C_{(7)}$-$O_{(7)}$	1.2(3)	$C_{(15)}$-$C_{(5)}$-$C_{(6)}$-$O_{(1)}$	174.1(1)
$C_{(8)}$-$O_{(8)}$-$C_{(7)}$-$C_{(2)}$	-177.6(1)	$C_{(15)}$-$C_{(5)}$-$C_{(6)}$-$C_{(21)}$	-9.9(3)
$C_{(22)}$-$O_{(22)}$-$C_{(21)}$-$O_{(21)}$	0.1(2)	$O_{(4)}$-$C_{(5)}$-$C_{(15)}$-$C_{(16)}$	-43.6(2)
$C_{(22)}$-$O_{(22)}$-$C_{(21)}$-$C_{(6)}$	-179.3(1)	$O_{(4)}$-$C_{(5)}$-$C_{(15)}$-$C_{(20)}$	132.1(2)
$O_{(1)}$-$C_{(2)}$-$C_{(3)}$-$O_{(4)}$	3.8(2)	$C_{(6)}$-$C_{(5)}$-$C_{(15)}$-$C_{(16)}$	136.9(2)
$O_{(1)}$-$C_{(2)}$-$C_{(3)}$-$C_{(9)}$	-177.6(1)	$C_{(6)}$-$C_{(5)}$-$C_{(15)}$-$C_{(20)}$	-47.4(2)
$C_{(7)}$-$C_{(2)}$-$C_{(3)}$-$O_{(4)}$	-175.2(1)	$O_{(1)}$-$C_{(6)}$-$C_{(21)}$-$O_{(21)}$	170.0(1)
$C_{(7)}$-$C_{(2)}$-$C_{(3)}$-$C_{(9)}$	3.5(3)	$O_{(1)}$-$C_{(6)}$-$C_{(21)}$-$O_{(22)}$	-10.6(2)
$O_{(1)}$-$C_{(2)}$-$C_{(7)}$-$O_{(7)}$	6.8(2)	$C_{(5)}$-$C_{(6)}$-$C_{(21)}$-$O_{(21)}$	-6.2(3)
$O_{(1)}$-$C_{(2)}$-$C_{(7)}$-$O_{(8)}$	-174.4(1)	$C_{(5)}$-$C_{(6)}$-$C_{(21)}$-$O_{(22)}$	173.1(1)

EXPERIMENTAL

The melting points were determined on a Boetius block. The IR spectra were taken on UR-20 and JASCO Model A-102 spectrometers in vaseline oil. The ^{1}H NMR spectra were recorded on a Bruker 250 spectrometer.

X-ray Crystallographic Study. The crystallographic data for monoclinic crystals of dioxin **4**, $C_{20}H_{16}O_6$; mp 211-212°C. At 20°C: a = 11.808(8), b = 5.4988(9), c = 13.794(6) Å, β = 110.22(4)°, V = 840.5(7) Å^3, Z = 2, d_{calc} = 1.39 g/cm^3, space group $P2_1/n$. An empirical correction for adsorption was introduced, μCu 8.2 cm^{-1}.

The crystallographic data for monoclinic crystals of dioxin **5**, $C_{20}H_{16}O_6$; mp 145-147°C. At 20°C: a = 11.264(2), b = 10.533(6), c = 14.610(6) Å, β = 93.71(3)°, V = 1729.7(9) Å^3, Z = 4, d_{calc} = 1.35 g/cm^3, space group $P2_1/c$. An empirical correction for adsorption was introduced, μCu 8.0 cm^{-1}.

The unit cell parameters and intensities of 1978 (**4**) and 7416 (**5**) reflections, of which 1380 (**4**) and 5924 (**5**) with $I > 3\sigma$, were measured on a four-circle Enraf–Nonius CAD-4 diffractometer at 20°C (λCuKα = 1.514 Å, graphite monochromator, ω/2θ scanning, θ ≤ 56°). No drop in the intensities of the three control reflections was observed over the exposure time.

The structures were determined by the direct method using the SIR program [18] and refined isotropically and, then, anisotropically. The electron difference maps revealed all the hydrogen atoms, which were refined isotropically in the final stage. The final divergence factors: R = 00582, R_w = 0.0748 for the structure of dioxin **4** using 1195 reflections with $F^2 \geq 3\sigma$; R = 0.0606, R_w = 0.0897 for the structure of dioxin **5** using 5405 reflections with $F^2 \geq 3\sigma$. All the calculations were carried out using the MolEN program package [19] on a DEC Alpha Station 200 computer. The PLATON program [20] was used to calculate the intermolecular interactions and provide a graphic representation of the molecular geometry. The atomic coordinates for dioxin **4** are given in Table 1, while the atomic coordinates for dioxin **5** are given in Table 2. The bond lengths, bond angles, and torsion angles for dioxins **4** and **5** are given in Tables 3-7.

Reaction of Methyl Phenylchloropyruvate 1 with Potassium Phthalimide. α-Chloro ketone **1** (1.60 g, 7.5 mmol) was added with stirring to a suspension of potassium phthalimide (2.80 g, 15 mmol) in chlorobenzene (20 ml) at 20°C. The reaction mixture was heated to 100°C and stirring was continued for an additional 8 h. After cooling, the solvent was distilled off. The residue was recrystallized from methanol and phthalimide (1.90 g, 86%) was separated off. The mother liquor was evaporated to dryness. Recrystallization of the residue from 2-propanol gave 2,5-dimethoxycarbonyl-3,6-diphenyl-1,4-dioxin **4** (0.95 g, 72%); mp 211-212°C (methanol). IR spectrum: 1735, 1650, 1450, 1360, 1305, 1200, 1140, 1100, 1030, 840, 770, 720 cm^{-1}. ^{1}H NMR spectrum (DMSO–acetone-d_6): 3.67 (3H, s, CH_3); 7.47-7.70 (5H, m, C_6H_5). Found, %: C 68.31; H 4.50. $C_{20}H_{16}O_6$. Calculated, %: C 68.19; H 4.54.

The mother liquor (2-propanol solution) after removal of dioxin **4** was evaporated and the residue was recrystallized from 2-propanol to give 2,6-dimethoxycarbonyl-3,5-diphenyl-1,4-dioxin **5** (65 mg, 5%); mp 145-147°C. IR spectrum: 1735, 1655, 1450, 1355, 1300, 1210, 1145, 1100, 1035, 840, 775 cm^{-1}. ^{1}H NMR spectrum ($CDCl_3$): 3.69 (3H, s, CH_3); 7.45-7.72 (5H, m, C_6H_5). Found, %: C 68.45; H 4.41. $C_{20}H_{16}O_6$. Calculated, %: C 68.19; H 4.54.

Reaction of α-Chloro Ketone 1 with Sodium Imidazolide. The same procedure using sodium imidazolide instead of potassium phthalimide gave dioxin **4** in 63% yield identical to the sample described above.

Addition of Methanol to Dioxin 4. Dioxin **4** (0.80 g) was dissolved in methanolic sodium methylate obtained by dissolving sodium (0.05 g) in methanol (15 ml) and the mixture was heated at reflux for 30 min. Cooling led to the crystallization of 3-methoxy-2,5-dimethoxycarbonyl-3,6-diphenyl-2,3-dihydro-1,4-dioxin (**6**) (0.67 g, 77%); mp 158.5-160°C (methanol), which corresponds to the melting point of a reported sample [2]. A mixed sample of this product and the authentic sample did not give a depressed melting point.

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