CHEMISTRY OF 2-METHYLENE-2,3-DIHYDROFURAN-3-ONES.

2.* 2-ALKOXYCARBONYLMETHYLENE-5-ARYL-4-HALO-2,3-DIHYDROFURAN-3-ONES: SYNTHESIS, STRUCTURE, AND PROPERTIES

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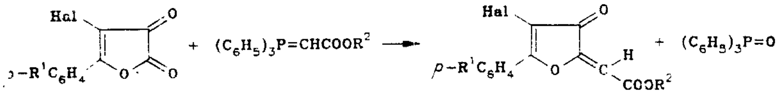
UDC 547.746'745'725'722.04:543.422.25

Reaction of 5-aryl-4-halo-2,3-dihydrofuran-2,3-diones with alkoxycarbonylmethylenetriphenylphosphoranes has given 2-alkoxycarbonylmethylene-5-aryl-4-halo-2,3-dihydrofuran-3-ones, which readily add halogens at the 2-exocyclic double bond, and on reaction with arylamines recyclize to give 2-hydroxy-2,3-dihydropyrrol-3-ones.

The presence of three reactive electrophilic centers in 2-methylene-5-aryl-2,3-dihydrofuran-3-ones enables these compounds to be used as starting materials for the synthesis of a variety of heterocyclic systems [1-3]. It has previously been shown that the introduction of a halogen into the 4-position of the ring in 5-aryl-2,3-dihydrofuran-2,3-diones markedly influences their reactivity [4]. There was therefore reason to expect that the presence of halogen in the analogous position would affect the relative electrophilicities of the reaction centers in 2-methylene-5-aryl-2,3-dihydro-3-ones, which are similar in structure to the previously-studied 5-aryl-4-halo-2,3-dihydrofuran-2,3-diones, which can be used in preparative syntheses.

With this in view, we reacted the alkoxycarbonylmethylenetriphenylphosphoranes (IIa, b) with the 5-aryl-4-halo-2,3-dihydrofuran-2,3-diones (Ia-f). On boiling equimolar amounts of the reactants in benzene for 5-10 min, the 2-alkoxycarbonylmethylene-5-aryl-4-halo-2,3-dihydrofuran-3-ones (IIIa-g) were obtained in 70-84% yields (Table 1).



Ia-f IIa,b IIIa-g

Ia, IIIa $R^1=H$; Ib,e IIIc,f $R^1=CH_3$; Ic, IIId $R^1=CH_3O$; Id IIIe $R^1=C_2H_5O$; If IIIg $R^1=Br$; Ia-d IIIa-e Hal=Cl; Ie,f IIIf,g Hal=Br; IIa IIIa,b,d,f,g $R^2=CH_3$; IIb, IIIc,e $R^2=C_2H_5$

The structures of (IIIa-g) were confirmed by their IR and PMR spectra (Table 1), which were in accordance with those of the previously-obtained 2-alkoxycarbonylmethylene-5-aryl-2,3-dihydrofuran-3-ones [5, 6].

On the basis of their PMR spectra, 2-p-phenacylidene-5-p-halophenyl-2,3-dihydrofuran-3-ones have been assigned the Z-isomer structure [7]. Since we did not have at our disposal model compounds with established positions of the groupings at the carbon atoms of the exocyclic C=C bond, in order to establish the spatial arrangement of the groups at the methylene carbon the additive method was used to calculate the chemical shifts of the exomethine proton from the screening constants of the substituents in different orientations with respect to this proton [8, p. 71]. Comparison of the experimental δ_{CH} values with the calculated values showed that in the Z-isomer these parameters are the same ($\Delta\delta_{CH}$ = 0.03-0.09 ppm). In the E-isomer, however, $\Delta\delta_{CH}$ is 0.25-0.37 ppm. Thus, calculation shows to a greater extent that (IIIa-g) possess the Z-configuration.

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*For Communication 1, see [1].

Perm State Institute of Pharmacy, Perm 614600. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1034-1038, August, 1989. Original article submitted February 15, 1988.

0009-3122/89/2508-0862 $12.50

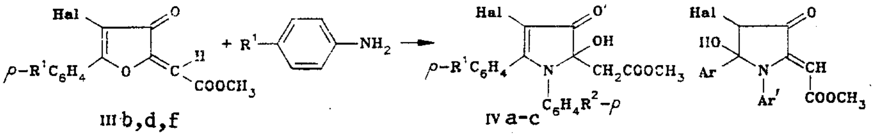
TABLE 1. Physicochemical and Spectral Properties of (IIIa-g).

Compound	Empirical formula	mp, °C	IR spectrum, ν, cm^{-1}			PMR spectrum	Yield, %
			$\underset{\text{O}}{\overset{\|}{\text{—C—OAlk}}}$	ring C=O	C=C		
IIIa	$C_{13}H_9ClO_4$	151 ... 152	1705	1698	1690	3,84 (3H, s, COOCH$_3$); 6,14 (1H, s, CH); 7,90 (5H, m, C$_6$H$_5$)	84
IIIb	$C_{14}H_{11}ClO_4$	137 ... 138	1712	1705	1690	2,46 (3H, s, CH$_3$); 3,84 (3H, s, COOCH$_3$); 6,05 (1H, s, CH); 7,33 and 8,16 (4H, 2 d C$_6$H$_4$)	73
IIIc	$C_{15}H_{13}ClO_4$	131 ... 132	1710	1702	1685	1,37 (3H, t, CH$_3$); 2,42 (3H, s, CH$_3$); 4,30 (2H, q, CH$_2$); 6,17 (1H, s, CH); 7,40 and 8,20 (4H, 2d, C$_6$H$_4$)	72
IIId	$C_{14}H_{11}ClO_5$	176 ... 178	1708	1703	1682	3,83 (3H, s, COOCH$_3$); 3,88 (3H, s CH$_3$O); 6,09 (1H, s, CH); 7,02 and 8,24 (4H, 2 d C$_6$H$_4$)	81
IIIe	$C_{16}H_{15}ClO_5$	135 ... 136	1705	1695	1672	1,38 (3H, t, CH$_3$); 4,20 (2H, q, CH$_2$); 6,10 (1H, s, CH); 7,00 and 8,25 (4H, 2 d, C$_6$H$_4$)	70
IIIf	$C_{14}H_{11}BrO_4$	152 ... 153	1708	1697	1677	2,41 (3H, s, CH$_3$); 3,83 (3H, s, COOCH$_3$); 6,17 (1H, s, CH); 7,30 and 8,25 (4H, 2 d C$_6$H$_4$)	71
IIIg	$C_{13}H_8Br_2O_4$	153 ... 154	1705	1697	1675	3,85 (3H, s, COOCH$_3$); 6,10 (1H, s, CH); 7,35 and 8,20 (4H, 2 d, C$_6$H$_4$)	78

TABLE 2. Physicochemical and Spectral Properties of (IVa-c) and (Va-c).

Compound	Empirical formula	mp, °C (decomp.)	IR spectrum, ν, cm^{-1}			PMR spectrum	Yield, %
			OH	COOCH$_3$	CO		
IVa	$C_{21}H_{20}ClNO_4$	192 ... 193	3240 ... 3220	1727	1652	2,22 (3H, s, CH$_3$); 2,26 (3H, s, CH$_3$); 2,72 (2H, q., $J=14,0$ Hz, CH$_2$); 3,48 (3H, s, COOCH$_3$); 7,15 (8H, m, 2C$_6$H$_4$)	62
IVb	$C_{21}H_{20}ClNO_6$	184 ... 185	3225 ... 3205	1724	1650	2,82 (2H, q., $J=12,0$ Hz, CH$_2$); 3,13 (3H, s, CH$_3$O); 3,43 (3H, s, COOCH$_3$); 3,62 (3H, s, CH$_3$O); 7,05 (8H, m, 2C$_6$H$_4$)	63
IVc	$C_{21}H_{20}BrNO_5$	228 ... 229	3250 ... 3230	1732	1675	2,26 (3H, s, CH$_3$); 2,76 (2H, q, $J=13,0$ Hz, CH$_2$); 3,47 (3H, s, COOCH$_3$); 3,66 (3H, s CH$_3$O); 5,55 (1H, br.s, OH); 6,90 (8H, m, 2C$_6$H$_4$)	54
Va	$C_{13}H_9Cl_3O_4$	90 ... 92	—	1727	1710	3,70 (3H, s, COOCH$_3$); 4,98 (1H, s, CH); 7,74 (5H, m, C$_6$H$_5$)	74
Vb	$C_{14}H_{11}Cl_3O_4$	127 ... 128	—	1728	1708	2,40 (3H, s, CH$_3$); 3,67 (3H, s, COOCH$_3$); 4,95 (1H, s, CH); 7,32 and 8,03 (4H, 2 d C$_6$H$_4$)	89
Vc	$C_{14}H_{11}Br_3O_4$	126 ... 127	—	1722		2,44 (3H, s, CH$_3$); 3,72 (3H, s, COOCH$_3$); 5,06 (1H, s, CH); 7,37 and 8,17 (4H, 2 d C$_6$H$_4$)	67

Compounds (IIIa-g) undergo recyclization on reaction with aromatic amines. On heating equimolar amounts of (IIIb, d, f) with p-toluidine or p-anisidine for 3-5 min in ethanol, there are obtained the 2-methoxycarbonylmethyl-2-hydroxy-4-halo-1,5-diaryl-2,3-dihydropyrrol-3-ones (IVa-c) (Table 2).

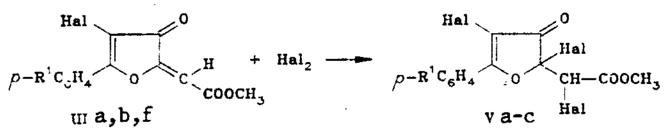


IIIb,f IVa,c $R^1=CH_3$ IIId IVb $R^1=CH_3O$; IIIb,d IVa,b Hal=Cl, IIIf, IVc Hal=Br; IVa $R^2=CH_3$,b,c $R^2=CH_3O$

The IR spectra of (IVa-c), obtained in vaseline grease, show the following absorptions: a broad band at 3250-3205 cm^{-1} due to hydroxyl group vibrations, a band at 1732-1724 cm^{-1} due to stretching vibrations of the ester carbonyl group, and a band at 1657-1650 cm^{-1}, corresponding to stretching vibrations of the carbonyl group in the 3-position of the ring. The spectral properties of (IVa-c) were in good agreement with those of the previously-described 1,5-diaryl-2-alkoxycarbonylmethyl-2-hydroxy-2,3-dihydrofuran-3-ones [1].

Compounds (IVa-c) cannot be the isomeric 2-methoxycarbonylmethylene-4-halo-5-hydroxy-1,5-diaryltetrahydropyrrol-3-ones (VI), since the PMR spectra show quadruplets for the two interacting protons of the diastereotopic CH_2 group of the methoxycarbonylmethyl group at 2.72-2.82 ppm (J_{gem} = 12-14 Hz). Compounds (IVa-c) are formed by nucleophilic attack on the reaction center in position 2 or 5, followed by recyclization of the initially formed 2- or 5-amino-3-furanone. No bands for the open-chain oxo-isomers were seen in the IR and PMR spectra of the cyclic isomers (IVa-c). This shows either that no cyclo-oxo tautomerism occurs in (IVa-c), or that the tautomeric equilibrium is shifted towards the predominant cyclic form.

Chlorine and bromine add at the exo-ethylene bond in (IIIa, b, f) at room temperature to give the 2-methoxycarbonylhalomethyl-2,4-dihalo-5-aryl-2,3-dihydrofuran-3-ones (Va-c) (Table 2).



Va R^1=H,b,c $R^1=CH_3$; a,b Hal=Cl, c Hal=Br

The IR spectra of (Va-c), obtained as a mull in vaseline grease, show strong absorption at 1728-1722 cm^{-1}, due to stretching vibrations of the alkoxycarbonyl carbonyl group. Thus, addition of halogen at the exo-ethylene bond results in a shift in the ester carbonyl absorption to higher frequencies by approximately 10 cm^{-1}.

The PMR spectra of (Va-c), obtained in deuterochloroform, show singlets for the methoxy group in the ester grouping at 3.67-3.72 ppm, singlets for the proton of the CH group of the methoxycarbonylhalomethyl grouping at 4.95-5.06 ppm, and signals for the benzene ring protons. The mass spectrum of (Vc) shows four peaks for the molecular ion differing the mass number by two units, and with an intensity ratio of 1:2.8:2.8:1, showing the presence of three atoms of bromine. Breakdown of M^+ takes place mainly with successive loss of two atoms of bromine, followed by elimination of a methoxy or methoxycarbonyl group, in good agreement with the structure proposed for (Vc).

EXPERIMENTAL

IR spectra were obtained on a UR-20 spectrophotometer (as a mull in vaseline grease). PMR spectra were recorded on a PC-60 spectrometer (60 MHz) in $CDCl_3$, internal standard HMDS. Mass spectra were obtained on a Varian MAT-311 at an ionizing voltage of 70 eV, chamber temperature 130°C, with direct introduction of the sample into the ion source.

The properties of the compounds obtained are shown in Tables 1 and 2. The elemental analyses were in agreement with the calculated values.

Z-2-Alkoxycarbonylmethylene-5-aryl-4-halo-2,3-dihydrofuran-3-ones (IIIa-g). A mixture of equimolar amounts (0.01 mole of each) of the 5-aryl-4-halo-2,3-dihydrofuran-2,3-dione (Ia-f) and the alkoxycarbonylmethylenetriphenylphosphorane (IIa, b) in 200 ml of benzene was boiled for 5-10 min. The solvent was evaporated, and the product washed with acetonitrile and recrystallized from ethanol or toluene to give (IIIa-g).

2-Methoxycarbonylmethyl-2-hydroxy-4-halo-1,5-diaryl-2,3-dihydropyrrol-3-ones (IVa-c). A mixture of equimolar amounts (0.01 mole of each) of (IIIb, d, f) and p-toluidine or p-anisidine in 150 ml of 96% ethanol was boiled for 3-5 min. The solvent was removed, and the product recrystallized from ethanol or acetone to give (IVa-c).

2-Methoxycarbonylhalomethyl-2,4-dihalo-5-aryl-2,3-dihydrofuran-3-ones (Va-c). To a suspension of 0.01 mole of (IIIa, b, f) in 200 ml of carbon tetrachloride was added dropwise with stirring at room temperature a small excess (0.012 mole) of bromine, or a stream of chlorine was passed in until the solid dissolved. The solvent was removed under a water pump vacuum, and the residue triturated with ether and recrystallized from ethanol to give (Va-c). Mass spectrum of (Vc), m/z* (% of maximum peak): 480 (24) [M], 401 (29) [M − Br], 373 (6) [M − Br − CO], 342 (7) [M − Br − $COOCH_3$], 322 (98) [M − 2Br], 291 (32) [M − 2Br − OCH_3], 263 (5) [M − 2Br − $COOCH_3$], 194 (65) [p-$CH_3C_6H_4C{\equiv}CBr$], 143 (99) [p-$CH_3C_6H_4C{\equiv}C{-}C{\equiv}O$], 119 (91) [p-$CH_3C_6H_4C{\equiv}O$], 115 (100) [p-$CH_3C_6H_4C{\equiv}C$], 91 (71) [p-$CH_3C_6H_4$], 80 (100) [HBr], 79 (79) [Br].

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*Values for ions containing ^{79}Br shown.