UNSATURATED BENZO-1,4-DIOXANE DERIVATIVES

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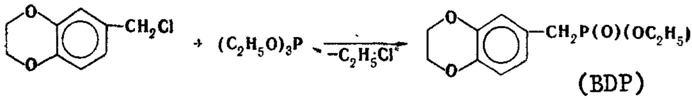
UDC 547.841.07

Reaction of 6-chloromethylbenzo-1,4-dioxane with triethyl phosphite gives a phosphonate, the condensation of which with aldehyde gives unsaturated compounds containing a benzo-1,4-dioxane ring.

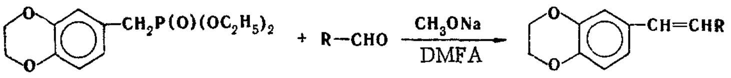
Benzo-1,4-dioxane derivatives are of interest owing to their diversified biological activity. We studied the previously undescribed reaction of triethyl phosphite with 6-chloromethylbenzo-1,4-dioxane. It was found that the latter in the absence of a solvent and on brief heating readily undergoes the Arbuzov reaction to give diethyl (benzo-1,4-dioxan-6-yl)methylphosphonate (BDP), which is a colorless viscous high-boiling liquid, in excellent yield.



(BDP)

The IR spectrum of the phosphonate contains an intense absorption band at 1260 cm^{-1}, which is characteristic for the PO group, and an intense band at 1040 cm^{-1}, which is affiliated with P—O—Alk groups [1]. Two equivalents of methane are evolved on reaction of BDP with methylmagnesium iodide, and on the basis of this it may be concluded that both hydrogen atoms of the methylene group of the phosphonate have completely clearly expressed lability.

It is known that organophosphorus compounds containing the $P(O)-CH_2$ group react with carbonyl compounds to give olefins and various derivatives on the olefins (the PO-olefination reaction) [2]. In order to obtain unsaturated compounds containing a benzo-1,4-dioxane ring, we used BDP, subjecting it to condensation with a number of aldehydes. Sodium metal, sodium hydride, and sodium methoxide in varous solvents were tested as the condensing agents. The metallation of the phosphonate proceeds most smoothly in anhydrous dimethylformamide (DMFA) with sodium methoxide. A solution of the aldehyde was added to the metallated derivative without isolating it from the reaction mixture; brief heating is required for the reaction.

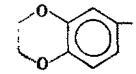


As a result, we obtained a number of unsaturated compounds (I-IX) containing a benzo-1,4-dioxane ring, data for which are presented in Table 1.

In order to prove the structures of the compounds obtained we carried out the alternative synthesis of II and VII. In the reaction of diazotized 6-aminobenzo-1,4-dioxane and styrene in the presence of cupric chloride under the conditions of the haloarylation reaction [3] styrene is arylated to give the benzo-1,4-dioxane analog of stilbene in good yield.

Chernovitskii State University. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 469-472, April, 1975. Original article submitted May 14, 1974.

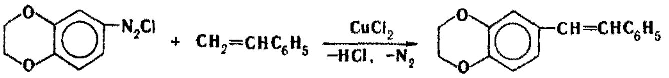
TABLE 1. 1-(Benzo-1,4-dioxan-6-yl)-2-aryl(alkyl)ethylenes

Compound	R	bp, °C (mm) or mp (crystallization solvent)	Empirical formula	Found, %		Calc., %		Yield, %
				C	H	C	H	
I	$(CH_2)_6CH_3$	184—186 (3)	$C_{17}H_{24}O_2$	78,2 78,2	8,9 9,5	78,5	9,2	34
II	C_6H_5	81—82 (alcohol)	$C_{16}H_{14}O_2$	80,3 80,5	5,8 6,2	80,7	5,9	68
III	p-$CH_3OC_6H_4$	112—113 (hexane)	$C_{17}H_{16}O_3$	76,4 76,3	5,9 5,6	76,1	6,0	67
IV	3,4-$(CH_3O)_2C_6H_3$	113—114 (alcohol-water 2 : 1)	$C_{18}H_{18}O_4$	72,3 72,1	5,8 5,7	72,5	6,0	61
V	p-ClC_6H_4	114—115 (hexane)	$C_{16}H_{13}ClO_2$[a]	70,8 70,6	5,1 5,2	70,5	4,8	79
VI	p-$N(CH_3)_2C_6H_4$	174—175 (hexane-benzene 2 : 1)	$C_{18}H_{19}NO_2$[b]	76,8 76,6	6,6 6,4	76,9	6,8	42
VII	p-$NO_2C_6H_4$	186—186,5 (hexane-benzene 1 : 1)	$C_{16}H_{13}NO_4$[c]	67,5 67,7	4,9 4,8	67,8	4,6	73
VIII		129—130 (alcohol)	$C_{18}H_{16}O_4$	72,7 72,4	5,0 5,1	73,0	5,4	90
IX	Furyl	183—185 (4)	$C_{14}H_{12}O_3$	73,4 73,3	5,1 4,9	73,8	5,3	62

[a] Found: Cl 13.2, 12.9%. Calculated: Cl 13.0%

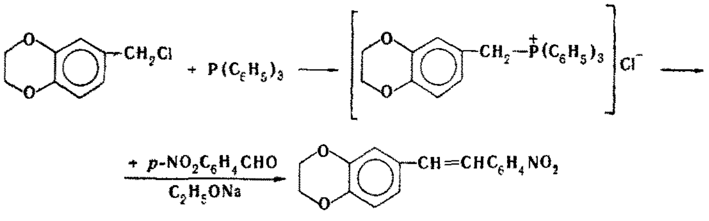
[b] Found: N 4.8, 4.7%. Calculated: N 5.0%.

[c] Found: N 5.3, 5.1%. Calculated: N 4.9%



No melting-point depression was observed for a mixture of II and the product obtained via the chloroarylation of styrene. The identical character of these substances is also confirmed by the IR spectra.

A phosphonium salt --(benzo-1,4-dioxan-6-yl)methylenetriphenylphosphonium chloride —was obtained by reaction of 6-chloromethylbenzo-1,4-dioxane with triphenyl phosphite. A phosphorane was obtained from it by means of sodium ethoxide, and the phosphorane was subjected to the Wittig reaction [4] with p-nitrobenzaldehyde:



The product of this reaction proved to be identical to the compound that we previously obtained in [3] and also in VII.

The IR spectra of II and VII were recorded, and an intense absorption band at 1250 cm^{-1}, which is characteristic for benzo-1,4-dioxane derivatives [5] and corresponds to the stretching vibrations of the C—O—C group of the dioxane ring, is observed in them. In addition, bands at 970 cm^{-1}, ascribable to the out-of-plane deformation vibrations of C—H groups in substituted trans-ethylene systems, are present in the spectra. Bands at 1590 cm^{-1}, which are characteristic for the stretching vibrations of conjugated C═C bonds, are also observed. Consequently, on the basis of the IR spectra it can be concluded that I-IX apparently have trans structures.

EXPERIMENTAL METHOD

The IR spectra of mineral-oil suspensions of the compounds were recorded with an IKS-14A spectrometer. 6-Chloromethylbenzo-1,4-dioxane, with bp 125-127° (3 mm) and n_D^{20} 1.5710, was obtained by the method in [6].

Diethyl (Benzo-1,4-dioxan-6-yl)methylphosphonate. A 28-g (0.15 mole) sample of 6-chloromethylbenzo-1,4-dioxane was heated to 150°, and 29 g (0.17 mole) of triethyl phosphite was added dropwise with stirring in the course of 1.5 h while maintaining the temperature at 150-155°. Ethyl chloride evolution was observed during the reaction. At the end of the addition of the triethyl phosphite, the temperature was gradually raised to 170°, and the mixture was stirred for 1 h, after which it was allowed to stand overnight. It was then vacuum-distilled to give 41.5 g (93%) of the phosphonate as a colorless viscous liquid with bp 187° (3 mm) and n_D^{20} 1.5186. Found %: P 10.6. $C_{13}H_{19}O_5P$. Calculated %: P 10.8. n_D^{20} 1.5186.

1-(Benzo-1,4-dioxan-6-yl)-2-arylethylenes (I-IX). A solution of 0.02 mole of the appropriate aldehyde in 20 ml of DMFA was added dropwise with stirring to a mixture of 0.02 mole of the phosphonate and 0.022 mole of CH_3ONa in 20 ml of DMFA dried over KOH. The temperature of the mixture rose spontaneously 5-10°. After the aldehyde had been added, the mixture was heated with stirring at 60-70° for 3 h and allowed to stand overnight. In the preparation of I, the mixture was heated at 80-90° for 10 h, whereas in the preparation of VI the mixture was heated at 100° for 6 h. The mixture was poured into 300 ml of water, and the resulting precipitate was removed by filtration, dried, and crystallized from a suitable solvent. It was extracted with ether, the ether solution was dried with magnesium sulfate, the solvent was removed by distillation, and the residue was vacuum-distilled.

1-(Benzo-1,4-dioxan-6-yl)-2-(4-nitrophenyl)ethylene (VII). A solution of 1.85 g (0.01 mole) of 6-chloromethylbenzo-1,4-dioxane and 2.62 g (0.01 mole) of triphenylphosphine in 30 ml of dry o-xylene was refluxed for 10 h, after which it was cooled, and the precipitated salt was removed by filtration and washed with benzene to give 3 g (67%) of white crystals of (benzo-1,4-dioxan-6-yl)methyltriphenylphosphonium chloride as white crystals with mp 217-218°. Found %: Cl (ionic) 8.6. $C_{27}H_{24}ClO_2P$. Calculated % Cl: (ionic) 8.0.

A solution of 2.25 g (5 mmole) of the phosphonium salt and 0.75 g (5 mmole) of p-nitrobenzaldehyde in 30 ml of alcohol—DMFA (2:1) was added with vigorous stirring in the course of an hour to sodium ethoxide obtained from 0.13 g of sodium and 20 ml of absolute alcohol, after which the mixture was stirred at room temperature for another 2 h. The resulting precipitate was removed by filtration, and water (one third of the volume of the filtrate) was added to the filtrate. The addition of water precipitated another small amount of the product, whereas triphenylphosphine oxide remained in solution. Workup of the mixture gave 0.46 g (33%) of olefin VII as yellow crystals with mp 185-186° (from alcohol). Found %: N 5.1. $C_{16}H_{13}NO_4$. Calculated %: N 5.0.

1-(Benzo-1,4-dioxan-6-yl)-2-phenylethylene (II). A cold (0°) solution of a diazonium salt obtained from 7.5 g (0.05 mole) of 6-aminobenzo-1,4-dioxane, 10 ml of concentrated HCl, and 3.5 g of $NaNO_2$ was added dropwise with stirring at 20° in the course of 45 min to a mixture of 5.2 g (0.05 mole) of styrene, 50 ml of acetone, and 2 g of $CuCl_2 \cdot 2H_2O$. At the end of the addition of the diazonium compound, the mixture was stirred at room temperature for another 6 h and allowed to stand overnight. It was then diluted with 250 ml of water, and the resulting oil began to crystallize on cooling to 0° to give 8.4 g (70%) of II with mp 81-82° (from alcohol). Found %: C 80.8; H 6.2. $C_{16}H_{14}O_2$. Calculated %: C 80.7; H 5.9.

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