Substituted γ-Lactones. 28.[1] 3-(Phenylmethylene)-2,4(3*H*,5*H*)-furandiones

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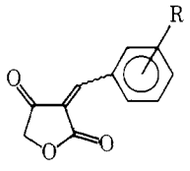
2,4(3*H*,5*H*)-Furandione (β-tetronic acid, **1**) undergoes a base-catalyzed aldol condensation with aromatic aldehydes to afford the 1:1 condensation products 3-(arylmethylene)-2,4(3*H*,5*H*)-furandiones **2**. The 1:1 condensation products **2** are also obtained when the reaction is acid catalyzed, and this constitutes a more convenient synthesis of **2**. The furandiones **2** are formed as a mixture of two geometric isomers, whose structures have been tentatively assigned on the basis of ^{1}H NMR data. Preliminary investigations dealing with condensations of **1** with aliphatic aldehydes reveal that, under all conditions employed, the products contain 2 equiv of **1** and 1 equiv of the aldehyde. Also explored are the cycloaddition reactions of **2** with triethyl phosphite, which lead to the novel furo[3,4-*d*]-1,2-oxaphospholene ring system.

The lignans constitute a group of naturally occurring substances which are currently attracting much attention because several members of this group have shown significant activity against several tumor systems in mice.[3] As a result, the development of convenient syntheses of lignans and lignan-type structures on which we published some time ago[4] again became of interest to us.

The molecule, 2,4(3*H*,5*H*)-furandione (**1**), commonly known as β-tetronic acid,[5] represents a potentially valuable building block for the preparation of these compounds. Since **1** possesses the necessary functionalities at the 3 and 4 position, it should be easily transformed into 3,4-unsymmetrically disubstituted furanones. As a logical first step toward the synthesis of lignan precursors, the preparation of 3-(phenylmethylene)-2,4(3*H*,5*H*)-furandiones, **2**, by an aldol type condensation of **1** with substituted aromatic aldehydes was explored. The resulting **2** compounds could be converted into



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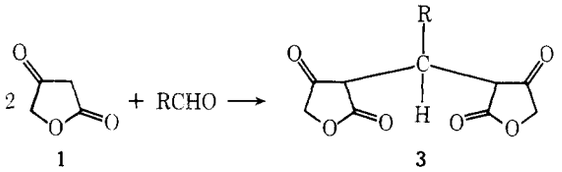
the desired lignans and lignan-type compounds via a second aldol-type condensation.

Several obstacles appeared to shed doubt on the development of a lignan synthesis based on **1** as a viable synthon. First, according to earlier reports, it is claimed that **1** does not undergo an aldol condensation reaction with aldehydes in a 1:1 ratio but rather they react in a 2:1 ratio to give compounds of general structure **3**.[6] Since there appeared to be no theo-



1 **3**

retical reason why the 1:1 aldol condensation product should not form, we decided to reinvestigate aldol condensations of **1** and substituted aromatic aldehydes.

A second obstacle in the development of a lignan synthesis based on **1** as a starting material is the lack of a reliable method for its preparation. While there exists considerable literature[7] concerned with the synthesis of **1**, the procedures which are reported and the yields which are quoted could not be repeated either by us[8] or by others.[9,10] Such attempts resulted either in complete irreproducibility or gave much lower yields than indicated in the published accounts.[7] Consequently, it was necessary to develop a reliable synthesis for **1** in order to achieve a viable lignan synthesis.

The present paper describes the results of our efforts in affecting (1) a reliable synthesis of **1** and (2) the aldol condensation of **1** with substituted aromatic aldehydes to afford the α-(phenylene)-2,4(3*H*,5*H*)-furandiones **2**. We also report on the reaction between **2** and triethyl phosphite to yield the novel furo[3,4-*d*]-1,2-oxaphospholene ring system.

Results and Discussion

Synthesis of 2,4(3*H*,5*H*)-Furandione (β-Tetronic Acid, 1). Experiments in our laboratories have indicated that with certain modifications the method of Kumler[11] offered the best preparation for **1**. The synthesis starts with the bromination of ethyl acetoacetate, followed by pyrolysis of the crude dibromination product to yield 3-bromo-2,4(3*H*,5*H*)-furandione. These steps can be done on a fairly large scale. The next step involves a catalytic debromination with PtO_2. With this catalyst, only anhydrotetronic acid was obtained.[2b,8] While it is known that platinum and its compounds are rather poor dehydrohalogenation catalysts, palladium is usually the better catalyst for this reaction.[12] Use of palladium on carbon (5–10%), under approximately 40 lbs of hydrogen pressure, results in good yields (80%) of **1**. This method is now being continuously used in our laboratories and represents a reliable method to obtain **1** in a convenient manner.

Acid-Catalyzed Aldol Condensations of 1 with Aromatic Aldehydes. Since it is known that the protons in the 3 position of **1** are fairly acidic (pK_a = 3.76),[11] the acid-catalyzed aldol condensation of **1** with aromatic aldehydes, affording the 1:1 condensation products, should be possible. It was found that the reaction of **1** with 3 equiv of a substituted aromatic aldehyde, in the absence of solvent and introducing hydrogen chloride gas, results in the formation of the desired 1:1 condensation product. In the case of solid aldehydes, the reaction was performed in a melt of the aldehyde to which **1** and the HCl was added. The mixture would solidify after a few minutes. For workup the solid was broken up and then washed with a suitable solvent to remove the excess aldehyde. The resulting type **2** compounds were easily purified by recrystallization. These acid-catalyzed condensations proceed equally well with both electron-donating and electron-withdrawing groups on the aromatic ring of the aldehydes. The 3-(arylmethylene)-2,4(3*H*,5*H*)-furandiones, **2**, are highly colored substances and they are easily characterized by their spectral data (IR, NMR, and UV). The results of the acid-catalyzed aldol condensations of **1** and substituted aromatic aldehydes are summarized in Table I.

Acid-Catalyzed Aldol Condensations of 1 with Aliphatic Aldehydes. Preliminary experiments with aliphatic

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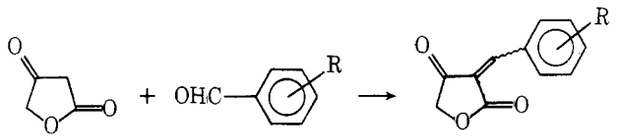
Table I. 3-(Phenylmethylene)-2,4(3*H*,5*H*)-furandiones



Compd	R	Formula	Mp, °C	C, % Calcd	C, % Found	H, % Calcd	H, % Found	% yield
2a	2-Chloro	$C_{11}H_7ClO_3$	117–118	59.34	59.20	3.17	3.32	43
2b	4-Chloro	$C_{11}H_7ClO_3$	110–111	59.34	59.15	3.17	3.22	40
2c	2-Nitro	$C_{11}H_7NO_5$	159–160	56.63	56.57	3.03	3.31[b]	25
2d	H	$C_{11}H_8O_3$	154.5–155.5	70.21	70.71	4.25	4.29	30
2e	2-Hydroxy	$C_{11}H_8O_4$	Dec >178	64.70	64.75	3.95	4.21	15
2f	3,4-Methylenedioxy	$C_{12}H_8O_5$	198.5–200	62.07	62.34	3.47	3.31	55
2g	*a*	$C_{13}H_{10}O_3$	204–205	72.89	72.96	4.71	4.86	41
2h	3,4-Dimethoxy	$C_{13}H_{12}O_5$	197–198	62.90	62.61	4.82	4.68	45
2i	4-Dimethylamino	$C_{13}H_{13}NO_3$	223–225	67.52	67.76	5.67	5.87[c]	42
2j	3,4,5-Trimethoxy	$C_{14}H_{14}O_6$	187	60.43	60.56	5.07	5.21	50

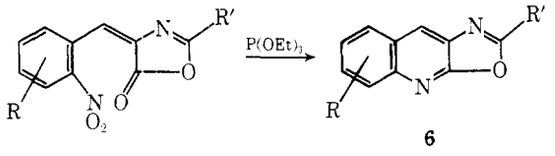
[a] Cinnamaldehyde was used as the reacting aldehyde. [b] Anal. Calcd: N, 6.01. Found: N, 5.91. [c] Anal. Calcd: N, 6.06. Found: N, 6.26.

aldehydes and **1** indicate that, under acid conditions, the aldol condensation does not occur, permitting the self-condensation of the reacting aldehyde exemplified by the formation of the 1,3,5-trioxane when pivalaldehyde is the reacting species. Under basic conditions aliphatic aldehydes react with **1** to form only the bis-condensation product of type **3.** Consequently, a more detailed investigation is presently underway to determine the parameters needed for 1:1 aldol condensation between **1** and aliphatic aldehydes.

^{1}H NMR Spectra of 1 and 2a–j. The ^{1}H NMR spectrum of **1** exhibits peaks in three areas; the peak due to the enolic OH group is extremely broad and not visible. Only the appearance of a HOD peak after exchange of a solution of **1** with D_2O reveals the presence of an enol form. The proton at the vinyl position of the enol form gives rise to a peak at δ 5 and the peak due to the methylene group appears at δ 4.75. The areas covered by the peaks are in a ratio of 1:2, thus indicating the compound to exist completely in the enolic form.

All type **2** compounds show two characteristic singlets between δ 4.7 and 4.85 which are not exchangeable with D_2O. This implies that type **2** compounds are not involved in a keto–enol equilibrium. A likely explanation for these two peaks, attributed to the methylene protons, is to assume that all type **2** compounds occur as two geometric isomers, A (*E* isomer) and B (*Z* isomer). The differences in the chemical shift of their respective methylene protons are thought to be caused by a long-range shielding effect due to the phenyl ring. Examination of Dreiding models points out that, in both isomers, the phenyl ring and the furanone ring are essentially coplanar. Furthermore, the models reveal that in isomer A the phenyl group is closer to the methylene protons than in isomer B. Using isoshielding lines according to Johnson and Bovey[13] the difference in the chemical shifts for these two protons in structures A and B was calculated to be 0.11 ppm, which is in accord with the observed value of 0.1 ppm. Integration of these two methylene peaks attributed to the *Z* and *E* isomers of **2** (specifically shown in the case of **2b**) permits us to estimate the ratio of A and B to be 2:3.

Reactions of 2 with Triethyl Phosphite. It has been shown that 2-nitrobenzylidene azlactones are cyclized under the influence of triethyl phosphite to oxazoloquinolines.[14a]



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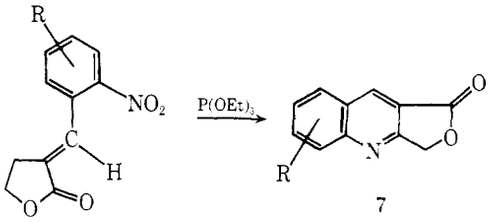
Similarly, α-(2-nitrobenzylidene)-γ-butyrolactones undergo a cyclization where the geometry of the double bond is maintained, and nitrene insertion, followed by oxidative dehydration, occurs to afford a furo[3,4-*b*]quinolin-1(3*H*)-one[8,14b,15] such as **7.**

It was anticipated that, in the case of **2b,** treatment of it with triethyl phosphite might also afford the quinoline derivative **7.**



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When an isomeric mixture of **2b** was treated with triethyl phosphite, the anticipated reductive cyclization did not take place, but rather a white precipitate was formed instantly. It was shown by elemental analysis and spectroscopic data to have structure **8.** The reaction is general and the isolation of the crystalline oxaphospholenes, **8,** is straightforward since they are insoluble in ether, whereas the starting materials are soluble. Table II summarizes the results.

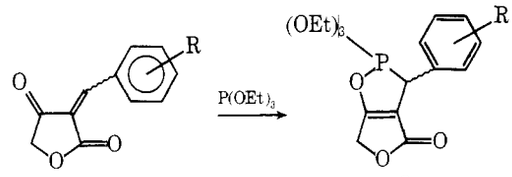
The result of these reactions is reminiscent of the chelatropic cycloaddition of trimethyl phosphites to α,β-unsaturated ketones as reported by Ramirez.[16]

These novel furo[3,4-*d*]-1,2-oxaphosphol-4(6*H*)-ones were characterized by their spectroscopic (IR and NMR) properties. In the ^{1}H NMR, the protons at the 6 position of these furanones **8** exhibit a doublet (J = 4 Hz) which is attributed to long-range three-bond ^{31}P–^{1}H coupling. The pattern for the benzylic proton coupled to phosphorus overlaps the quartet of doublets of the ethyl (CH_2) protons. However, integration of the different regions of the NMR spectrum is in agreement with the proposed structure. The lactone carbonyl group can be easily recognized in the IR spectrum by the peak in the range between 1730 and 1760 cm^{-1}.

Experimental Section

Melting points were determined with a Fischer-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded using a Beckman IR-18A infrared spectrophotometer. Nuclear magnetic resonance spectra were recorded on Varian T-60 spectrometer with tetramethylsilane as internal standard. Mass spectra were obtained on a Perkin-Elmer RMU-7 instrument. Microanalysis were performed by either Chemalytics, Inc., of Tempe, Ariz., or Integral Microanalytical Laboratories, Inc., of Raleigh, N.C.

Table II. 2,2,2-Triethoxy-2,5-dihydro-3-(substituted phenyl)furo[3,4-*d*]-1,2-oxaphosphol-4(6*H*)-ones



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Compd	Registry no.	R	Formula	Mp, °C	C, % Calcd	C, % Found	H, % Calcd	H, % Found	% yield
8a	65276-42-8	4-Chloro	$C_{17}H_{22}ClO_6P$	108–108.5	52.52	52.44	5.70	5.53[a]	40.5
8b	65276-43-9	2-Nitro	$C_{17}H_{22}NO_8P$	138–139	51.13	51.32	5.55	5.65[b]	69
8c	65276-44-0	4-Nitro	$C_{17}H_{22}NO_8P$	123–124	51.13	50.76	5.55	5.34[c]	71
8d	65276-45-1	3,4-Methylenedioxy	$C_{18}H_{23}O_8P$	123	54.27	54.05	5.82	5.75[d]	69
8e	65276-46-2	3,4-Dimethoxy	$C_{19}H_{27}O_8P$	128–129	55.07	54.73	6.57	6.53[e]	68
8f	65276-47-3	3,4,5-Trimethoxy	$C_{20}H_{29}O_9P$	130–132	54.05	53.89	6.58	6.29[f]	22

[a] Anal. Calcd: Cl, 9.12. Found: Cl, 9.61. [b] Anal. Calcd: N, 3.51. Found: N, 3.24. [c] Anal. Calcd: N, 3.51. Found N, 3.19. [d] Anal. Calcd: P, 7.78. Found P, 7.78. [e] Anal. Calcd: P, 7.47. Found P, 7.32. [f] Anal. Calcd: P, 6.97. Found: P, 7.03.

α-Bromotetronic Acid. This compound was prepared by pyrolysis of ethyl α,γ-dibromoacetoacetate according to the procedure of Kumler.[11] The resulting solids were triturated with several portions of benzene to remove colored impurities and dried at room temperature. The slightly tan product was used without further purification: mp 183 °C dec (lit.[11] 183 °C dec). Protected from moisture and light the product could be stored for several months.

Tetronic Acid (1). To 250 mL of methanol was added 34.2 g (0.108 mol) of barium hydroxide octahydrate and 39.0 g (0.217 mol) of α-bromotetronic acid. Only a small residue remained after vigorous stirring. The solution was stirred a few minutes with 0.5 g of decolorizing carbon at room temperature and filtered through kieselguhr. (A large stock solution of barium α-bromotetronate was often made, using proportionally larger quantities, from which aliquots were taken for hydrogenolysis. The remaining solutions was refrigerated and used within a few days.) The solution (ca. 280 mL) was added to a nitrogen-flushed Parr bottle to which had been added an additional 34.2 g of $Ba(OH)_2 \cdot 8H_2O$ followed by 1 g of 5% palladium on carbon. The bottle was flushed with hydrogen, charged to 40 psi, and shaken until additional hydrogen uptake was negligible (ca. 5 h); the theoretical pressure drop was 17.3 psi. If less than 90% of the theoretical hydrogen uptake was observed, additional palladium on carbon was added. The nearly colorless solution was filtered through kieselguhr and the methanol was evaporated at reduced pressure. The resulting aqueous slurry was diluted with water to 200 mL and adjusted carefully to pH 0.5 using concentrated hydrochloric acid (ca. 17 mL) while monitoring with a narrow range pH paper (Fisher, short range No. 1). The solution was extracted with ether, and the ether layer was dried over anhydrous sodium sulfate and concentrated to a small volume. Crystals formed on cooling which were washed with cold ether. A second crop was similarly obtained from the mother liquor and ether washings. Drying was accomplished in a vacuum dessicator over calcium sulfate (Drierite). The yield after ten 100-mL hand extractions was 14 g (65%), mp (slight sinter at 135 °C) 142–144 °C (lit.[6a] sinters at 135, 141 °C). Twenty-four-hour extraction in a liquid–liquid extractor gave 80% yields. The tetronic acid was generally used without further purification; ethyl acetate can be used for additional recrystallization if necessary. The product was stored in a freezer for several months with no apparent deterioration: NMR (Me_2SO-d_6) δ 4.65 (s, 2 H), 4.97 (s, 1 H) [lit.[9] 4.67 (s, 2 H), 4.97 (s, 1 H)].

General Procedure for Preparation of α-(Phenylmethylene)-2,4(3*H*,5*H*)-furandiones. To a 3 equiv excess of the appropriate aldehyde was added 1 equiv of tetronic acid and 1.1 equiv of concentrated hydrochloric acid. The mixture was stirred vigorously until solidification occurred. The solid was then broken up and washed with either hexane or ether (depending on the solubility of the aldehyde in the solvent). The crude condensation product was then recrystallized from abolute ethanol or ethyl acetate. Analogously, the following compounds were prepared.

2a: IR (KBr) 1765, 1710, and 1615 cm^{-1}; NMR (Me_2SO-d_6) δ 4.7 and 4.8 (2 s, 2 H), 7.65 (m, 3 H), 8.15 (d, 1 H), 8.63 (m, 1 H); mass spectra M^+ 222 (20), M + 2 224 (8).

2b: IR (KBr) 1760, 1710 cm^{-1}; NMR (Me_2SO-d_6) δ 4.72 and 4.85 (2 s, 2 H), 7.17 (d, 2 H, J = 8 Hz), 7.5 (s, 1 H), 8.2 (d, 2 H, J = 8 Hz); mass spectra M^+ 222 (42.6), M + 1 223 (6.7), M + 2 224 (16.7).

2c: IR (KBr) 1760, 1720 cm^{-1}; NMR ($CDCl_3$) δ 4.67 and 4.8 (2 s, 2 H), 7.8 and 8.33 (m, 5 H); mass spectra M^+ 233.

2d: IR (KBr) 1760, 1700 cm^{-1}; UV (EtOH) 336, 253 nm (sh); UV (EtOH + HCl) 336, 231 nm; NMR ($CDCl_3$) 4.65 and 4.78 (2 s, 2 H), 7.62 (m, 3 H), 8.05 (s, 1 H), 8.45 (M= 2 H); mass spectra M^+ 188 (63.34), M + 1 189 (8.41).

2e: IR (KBr) 3310, 1740, 1690 cm^{-1}; NMR (Me_2SO-d_6) δ 4.67 and 4.78 (2 s, 2 H), 6.47 (s, 1 H, exchangeable with D_2O), 6.8–7 (m, 3 H), 8.35 (d, 1 H, J = 2.5 Hz), 10.78 (dd, 1 H, J = 8, 2.5 Hz); mass spectra M^+ 204.

2f: IR (KBr) 1740, 1685, cm^{-1}; UV (EtOH) 402, 282 (sh), 252 nm; NMR (Me_2SO-d_6) δ 4.67 and 4.78 (2 s, 2 H), 6.20 (s, 2 H), 7.13 (d, 1 H, J = 8 Hz), 7.83 (t, 1 H, $J \sim 1.4$ Hz), 8.03 (s, 1 H, J = 8, 1.4 Hz), 8.42 (t, 1 H, $J \sim 1.4$ Hz); mass spectra M^+ 232.

2g: IR (KBr) 1750, 1685 cm^{-1}; NMR (Me_2SO-d_6) δ 4.6 and 4.65 (2 s, 2 H), 7.2–8.2 (m, 8 H); mass spectra $M^{+\cdot}$ 214 (100), M + 1 215 (14.7).

2h: IR (KBr) 1770, 1705 cm^{-1}; NMR (Me_2SO-d_6) δ 3.90 and 3.97 (2 s, 6 H), 4.7 and 4.8 (2 s, 2 H), 7.1 (d, 1 H, J = 8 Hz), 7.57 (s, 1 H), 8.15 (d, 1 H, J = 8 Hz), 8.77 (s, 1 H); mass spectra M^+ 248 (100), M + 1 249 (13.4).

2i: IR 1725, 1670 cm^{-1}; NMR (Me_2SO-d_6) δ 3.20 (s, 6 H), 4.7 and 4.8 (2 s, 2 H), 7.13 (d, 2 H, J = 9 Hz), 7.85 (s, 1 H), 7.92 (d, 2 H, J = 9 Hz); mass spectra M^+ 231.

2j: IR (KBr) 1780, 1695 cm^{-1}; NMR (Me_2SO-d_6) δ 3.81 and 3.83 (2 s, 9 H), 4.65 and 4.76 (2 s, 2 H), 7.83 (s, 1 H), 8.06 (s, 2 H); mass spectra $M^{+\cdot}$ 278 (100), M + 1 279 (15.8).

General Procedure for Reactions of 3-(Phenylmethylene)-2,4(3*H*,5*H*)-furandiones with Triethyl Phosphite to Give 2,2,2-Triethoxy-2,5-dihydro-3-(substituted phenyl)furo[3,4-*d*]-1,2-oxaphosphol-4(6*H*)-ones. To a fivefold excess of triethyl phosphite was added the furandione. The mixture was stirred vigorously at room temperature. Formation of a white crystalline product occurred within 5 min in most cases. The product was filtered and washed with ether to yield analytically pure 2,2,2-triethoxy-2,3-dihydro-3-(substituted phenyl)furo[3,4-*d*]-1,2-oxaphosphol-4(6*H*)-one (**8**). Analogously, the following compounds were prepared.

8a: IR (KBr) 1740 cm^{-1}; NMR ($CDCl_3$) δ 1–1.65 (m, 9 H), 3.8–4.6 (m, 7 H), 4.7–4.8 (d, 2 H, $J_{^{31}P-^1H}$ = 4 Hz), 7.2–7.7 (m, 4 H); mass spectra M^+ 388 (25.75), M + 1 389 (5.37).

8b: IR (KBr) 1765 cm^{-1}; NMR ($CDCl_3$) δ 1.28 (m, 9 H), 4.08 (m, 7 H), 4.75 (d, 2 H, $J_{^{31}P-^1H}$ = 3 Hz), 5.23 (d, 1 H, J = 27 Hz), 7.2–8.2 (m, 4 H); mass spectra M^+ 399.

8c: IR (KBr) 1760 cm^{-1}; NMR ($CDCl_3$) δ 1–1.7 (m, 9 H), 3.9–4.8 (pentet and singlet, 7 H), 4.9 (d, 2 H, $J_{^{31}P-^1H}$ = 4 Hz), 7.8–8.2 (AB q, 4 H, J = 8, 4 Hz); mass spectra M^+ 399, M + 1 400.

8d: IR (KBr) 1740 cm^{-1}; NMR ($CDCl_3$) δ 1.33 (m, 9 H), 4.13 (m, 7 H), 4.75 (d, 2 H, $J_{^{31}P-^1H}$ = 4 Hz), 5.92 (s, 2 H), 6.55–7.25 (m, 3 H); mass spectra M^+ 398.

8e: IR (KBr) 1750 cm^{-1}; NMR ($CDCl_3$) δ 1.1–1.7 (m, 9 H), 3.8–4.6 (m, 13 H), 4.8 (d, 2 H, $J_{^{31}P-^1H}$ = 4 Hz), 6.9–7.5 (m, 3 H); mass spectra M^+ 414 (36.6), M + 1 415 (7.4).

8f: IR (KBr) 1730 cm^{-1}; NMR ($CDCl_3$) δ 1.1–1.7 (m, 9 H), 3.8–4.6 (m, 16 H), 4.8 (d, 2 H, $J_{^{31}P-^1H}$ = 4 Hz), 6.90 (d, 2 H, $J \cong 1$ Hz); mass spectra M^+ 444 (44.4), M + 1 445 (11.1).

Base-Catalyzed Reaction of 1 with 3,4-Dimethoxybenzaldehyde. To 0.5 g of **1** and 4.15 g of 3,4-dimethoxybenzaldehyde in 250 mL of absolute ethanol was added 10 drops of pyridine. The solution was refluxed for 12 h and cooled, and the solvent was removed in

vacuo. The residue was washed with ether and crystallized from 2-propanol. The product was identical with the acid-catalyzed product **2b:** yield 60%.

3,3′-(1,1′-Octanediylidene)bis[4-hydroxy-2(5*H*)-furanone]. Following the same procedure for base catalysis, 1-octanal was reacted with tetronic acid. The white product was recrystallized at 0 °C from (1:150) ethyl acetate–cyclohexane: mp 198 °C; NMR ($CDCl_3$) δ 0.5–2.2 (m, 15 H), 3.96 (t, 1 H, J = 8 Hz), 4.72 (s, 4 H), 10.66 (s, 2 H, exchangeable with D_2O). Anal. Calcd for $C_{16}H_{22}O_6$: C, 61.92; H, 7.15. Found: C, 61.71; H, 7.09

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Registry No.—**1,** 4971-56-6; (*E*)-**2a,** 65276-56-4; (*Z*)-**2a,** 65276-57-5; (*E*)-**2b,** 65276-58-6; (*Z*)-**2b,** 65276-59-7; (*E*)-**2c,** 65276-60-0; (*Z*)-**2c,** 65276-61-1; (*E*)-**2d,** 65276-62-2; (*Z*)-**2d,** 65276-48-4; (*E*)-**2e,** 65276-49-5; (*Z*)-**2e,** 65276-50-8; (*E*)-**2f,** 65276-51-9; (*Z*)-**2f,** 65276-52-0; (*E*)-**2g,** 65276-53-1; (*Z*)-**2g,** 65276-54-2; (*E*)-**2h,** 65276-55-3; (*Z*)-**2h,** 65276-37-1; (*E*)-**2i,** 65276-38-2; (*Z*)-**2i,** 65276-39-3; (*E*)-**2j,** 65276-40-6; (*Z*)-**2j,** 65276-41-7; α-bromotetronic acid, 1192-50-3; *o*-chlorobenzaldehyde, 89-98-5; *p*-chlorobenzaldehyde, 104-88-1; *o*-nitrobenzaldehyde, 552-89-6; benzaldehyde, 100-52-7; *o*-hydroxybenzaldehyde, 90-02-8; 3,4-methylenedioxybenzaldehyde, 120-57-0; cinnamaldehyde, 104-55-2; 3,4-dimethoxybenzaldehyde, 120-14-9; 4-dimethylaminobenzaldehyde, 100-10-7; 3,4,5-trimethoxybenzaldehyde, 86-81-7; triethyl phosphate, 122-52-1; 1-octanal, 124-13-0; 3,3′-(1,1′-octanediylidene)bis[4-hydroxy-2(5*H*)-furanone], 65276-34-8.

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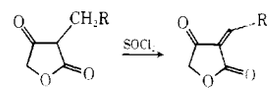
(10) Certain compounds of type **2** were recently obtained by a sequence which does not proceed via **1.** Substituted 3-benzyl-β-tetronic acids were dehydrated by thionyl chloride to give type **2** compounds. However, since the yields of this reaction were less than acceptable for a good synthetic procedure and the choice of substituents is severely limited, this pathway does not represent a generally applicable alternative pathway for the preparation of the desired furandiones **2.** See ref 6b.



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Macrocyclic Ureas as Masked Isocyanates

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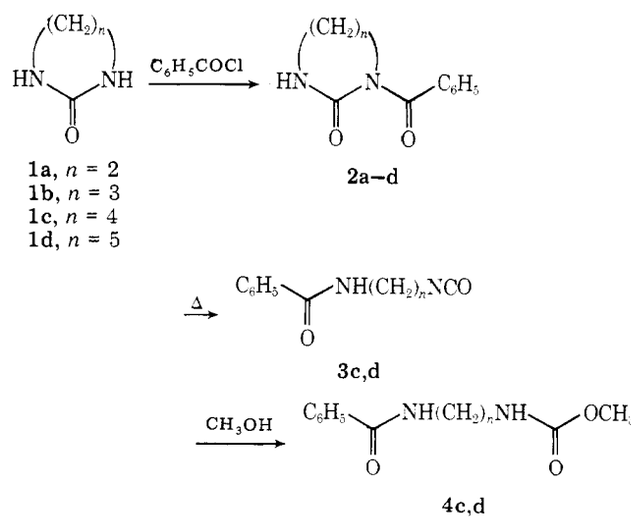
Macrocyclic *N*-aroylureas, synthesized by aroylation of macrocyclic ureas with mono- and dicarboxylic acid chlorides, undergo a facile thermal ring-opening reaction to give *N*-aroylamidoalkylene isocyanates **3.** Treatment of the crude isocyanates with methanol yields the corresponding methyl carbamates **4.**

The blocking of isocyanate groups has been attempted previously in order to formulate stable one-component polyurethane systems.[1] Heating of the blocked isocyanates generate the free isocyanates with release of the blocking agent. The ideal blocking agent should become part of the polymer backbone after release, thereby eliminating the need for well-ventilated working areas. This paper deals with the design of blocked isocyanates in which the blocking agents are incorporated into the polyurethane backbone.

The key to the design of functional blocking agents was our observation that certain 1,3-disubstituted ureas undergo facile thermal dissociation to produce isocyanate and an amine derivative.[2] If the urea group is part of a cyclic system, both fragments could conceivably be incorporated into a growing polymer chain. In order to test this hypothesis, the *N*-benzoylureas **2** were synthesized as model compounds. While the five- and six-membered ring ureas **2a** and **2b** (n = 2 and 3) did not appreciably dissociate upon heating in an inert high-boiling solvent, the seven- and eight-membered ring ureas **2c** and **2d** undergo ring opening on refluxing in *o*-dichloroben-

Scheme I



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