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Substituted γ -Lactones. XVI. (1)

Condensation of 2(3H)-Benzofuranone with Aromatic Aldehydes

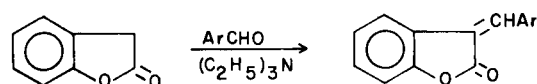
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In the course of investigating the scope of a new method for the synthesis of heterocyclic compounds starting with certain *ortho* substituted α -benzylidene- γ -lactones (2a, b), we became interested in the preparation of 3-benzylidene-2-(3H)-benzofuranones. Three fundamentally different methods for their synthesis are described in the literature. First, the sodium metal-catalyzed condensation of *o*-hydroxyphenylacetic acid with benzaldehyde results in 2-(2-hydroxyphenyl)cinnamic acid, which dehydrates upon heating to yield 3-benzylidene-2-(3H)benzofuranone (3). A second method is represented by the base catalyzed rearrangement of 3-hydroxyflavanones (4). Finally, the von Pechmann condensation of polyphenols or methylated polyphenols with phenylpyruvic acid yields 3-benzylidene-2-(3H)benzofuranones (5).

We should like to describe as a fourth method the direct condensation of the γ -lactone, 2-(3H)benzofuranone, with a large number of different aromatic aldehydes.

Chatterjea attempted the synthesis of 3-benzoyl-2-(3H)benzofuranone by reacting ethyl benzoate with 2-(3H)benzofuranone (6). In the presence of strong bases such as sodium ethoxide or sodium hydride, only the self-condensation product, 3-(*o*-hydroxyphenylacetyl)-2-(3H)benzofuranone, was isolated.

This dimerization reaction is suppressed if a stronger electrophile, *e.g.*, an aromatic aldehyde, is present. Thus when the condensation of 2-(3H)benzofuranone with piperonal is catalyzed by sodium methoxide, 3-(3,4-methylenedioxybenzylidene)-2-(3H)benzofuranone is obtained in 50% yield. However, the condensation reaction proceeds more smoothly in the presence of a catalytic amount of an organic base such as triethylamine. Saturated γ or δ -lactones condense with aromatic or aliphatic aldehydes only in the presence of very strong bases, *e.g.*, sodium methoxide, yielding the desired α -benzylidene derivatives (7). However, β,γ -unsaturated- γ -lactones often undergo this condensation in a rather exothermic reaction even in the presence of relatively weak bases, such as piperidine or triethylamine (8). This deviation in behavior results from the greater resonance stabilization of the anion of the β,γ -unsaturated γ -lactones in comparison with that of the saturated γ -lactones.

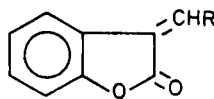


The condensation proceeds best with negatively substituted aldehydes (*o*-, *m*-, *p*-nitrobenzaldehyde) and with pyridine carboxyaldehydes. These findings are in agreement with related aldol type reactions, *e.g.*, the Perkin reactions (9). However, they are at variance with results obtained during the aldol type condensation of saturated γ -lactones with aromatic aldehydes (7). Some of the yields may not represent maximal ones as our interest was not in elaborating the optimal conditions in every single instance. Only one experiment was run with most of the aldehydes.

In this study 2-(3H)benzofuranone was condensed with benzaldehydes substituted with methoxy, ethoxy, halogen, alkyl, alkoxy, dimethylamino and nitro groups. In addition, the reaction was performed with cinnamic aldehyde, furfural and naphthoic aldehyde. The normal reaction path is not followed in the case of *o*-hydroxy- and *o*-aminobenzaldehydes. Instead, a rearrangement reaction analogous to the one in the α -(2-amino- and 2-hydroxybenzylidene)- γ -butyrolactone series was observed (2). This subject will be treated in a forthcoming communication. Table I summarizes the compounds synthesized during this work.

The structure assignment of the compounds is based upon elementary analysis and infrared spectra. The lactone carbonyl absorption was observed at 5.64 - 5.70 μ for all reported compounds.

Table I
Condensation Products of 2-(3H)Benzofuranone with Various Aromatic Aldehydes



R	Formula	Carbon, %		Hydrogen, %		Halogen or Nitrogen, %		M. P. °C	(a)	Yield %
		Calcd.	Found	Calcd.	Found	Calcd.	Found			
2-Furyl	C ₁₃ H ₈ O ₃	73.58	73.92	3.80	4.10	-	-	109-110	M	56.5
2-Pyridyl	C ₁₄ H ₈ NO ₂	75.32	75.22	4.06	4.27	6.28	6.30	137-138	Et	69
3-Pyridyl	C ₁₄ H ₈ NO ₂	75.32	75.56	4.06	4.01	6.28	6.37	147	Et	34.5
4-Pyridyl	C ₁₄ H ₈ NO ₂	75.32	75.62	4.06	4.14	6.28	6.19	148	Et	100
3,4-Dichlorophenyl	C ₁₅ H ₈ Cl ₂ O ₂	61.88	61.65	2.77	2.57	24.36	24.30	188	Et	82.5
2,4-Dinitrophenyl	C ₁₅ H ₈ N ₂ O ₆	57.70	57.13	2.58	2.65	8.97	8.95	206-207	DMF	93
2-Bromophenyl	C ₁₅ H ₈ BrO ₂	59.82	59.86	3.01	3.34	26.54	26.38	138-139	Et	79
4-Bromophenyl	C ₁₅ H ₈ BrO ₂	59.82	59.69	3.01	2.98	26.54	26.72	165-166	DMF	99.6
2-Chlorophenyl	C ₁₅ H ₈ ClO ₂	70.18	70.03	3.53	3.56	13.81	14.48	133-134	Et	99.5
3-Chlorophenyl	C ₁₅ H ₈ ClO ₂	70.18	70.07	3.53	3.53	13.81	13.80	141-142	M	78
4-Chlorophenyl	C ₁₅ H ₈ ClO ₂	70.18	70.22	3.53	3.30	13.81	14.01	152	Et	94.5
2-Fluorophenyl	C ₁₅ H ₈ FO ₂	74.99	74.64	3.78	4.07	7.91	7.79	124-126	Et	93
2-Nitrophenyl	C ₁₅ H ₈ NO ₄	67.41	67.32	3.39	3.43	5.24	5.42	164-165	DMF	75
3-Nitrophenyl	C ₁₅ H ₈ NO ₄	67.41	67.26	3.39	3.36	5.24	5.25	194-195	Et	63.5
4-Nitrophenyl	C ₁₅ H ₈ NO ₄	67.41	66.74	3.39	3.45	5.24	5.41	238	DMF	94.5
4-Methylphenyl	C ₁₆ H ₁₂ O ₂	81.34	81.65	5.12	5.12	-	-	166-167	Et	51
3,4-Methylenedioxyphenyl	C ₁₆ H ₁₀ O ₄	72.18	71.77	3.79	3.91	-	-	205	Et	77.5
2-Methoxyphenyl	C ₁₆ H ₁₂ O ₃	76.18	76.74	4.80	4.85	-	-	128-129	Et	89.5 (b)
3-Methoxyphenyl	C ₁₆ H ₁₂ O ₃	76.18	75.79	4.80	4.66	-	-	101-102	M	47.5 (c)
4-Methoxyphenyl	C ₁₆ H ₁₂ O ₃	76.18	76.14	4.80	4.73	-	-	132	M	83 (d)
2-Nitrophenylvinyl	C ₁₇ H ₁₁ NO ₄	69.62	69.70	3.78	3.88	4.78	4.81	243	DMF	99
2-Phenylvinyl	C ₁₇ H ₁₂ O ₂	82.24	81.81	4.87	4.90	-	-	171-173	DMF	92.5
2-Ethoxyphenyl	C ₁₇ H ₁₄ O ₃	76.67	76.77	5.30	5.38	-	-	96-97	Et	95
3,4-Dimethoxyphenyl	C ₁₇ H ₁₄ O ₄	72.33	72.51	5.00	5.07	-	-	99-100	Et	81.5 (e)
4-Dimethylaminophenyl	C ₁₇ H ₁₅ NO ₂	76.96	76.90	5.70	5.74	5.28	5.28	208-209	Et	72
1-Naphthyl	C ₁₉ H ₁₂ O ₂	83.80	84.27	4.44	4.83	-	-	145	DMF	66
2-Naphthyl	C ₁₉ H ₁₂ O ₂	83.80	83.74	4.44	4.65	-	-	126	DMF	88
3,4-Diethoxyphenyl	C ₁₉ H ₁₈ O ₄	73.53	73.34	5.85	5.85	-	-	129-130	Et	73

(a) Solvents for recrystallization; Et = ethyl alcohol, M = methanol, DMF = dimethylformamide. (b) Reported m.p.: 126-127°, see ref. 3. (c) Reported m.p.: 118-119°, see ref. 3. (d) Reported m.p.: 132°, see ref. 3. (e) Reported m.p.: 99-100°, see ref. 3.

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EXPERIMENTAL

Melting points were taken in an open capillary and are uncorrected; Microanalyses are by A. Bernhardt, Mikroanalytische Laboratorium, Mühlheim/Ruhr, Germany.

General Condensation Procedure.

A mixture of 2-(3H)benzofuranone (0.01 mole) and aldehyde (0.01 mole) in a 25 ml. beaker was heated on a water bath until a clear solution results. The addition of 2-10 drops of freshly distilled triethylamine brought about an exothermic reaction which was completed after several minutes. If the reaction product does not solidify by itself, crystallization was induced by addition of 3 ml. of methanol. The crude material was purified by recrystallization from an appropriate solvent (Table I).

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