a stirred, ice-cooled, ether solution of pyromellitoyl chloride until the solution was basic. The precipitates were filtered from the ether and excess amine and were water washed until the washings were chloride free. The product was insoluble in cold but soluble in hot ethanol and methanol. It was insoluble in ether, ligroin, benzene, nitrobenzene, and chloroform. Recrystallization from ethanol yielded pure white needles of V, m.p. 280–281°.

Anal. Calcd. for $C_{18}H_{26}N_4O_4$: N, 15.4. Found: N, 15.1.

Tetrakis(N,N-diethyl)pyromellitamide (IV). Compound IV was prepared by dropping an ether solution of diethylamine into a stirred, ice-cooled, ether solution of pyromellitoyl chloride until the solution was basic. The precipitates were filtered from the ether and excess amine and were water washed until the washings were chloride free. The product was very soluble in ethanol, methanol, glacial acetic acid, and hot carbon tetrachloride. It was recrystallized from chloroform by adding ether with strong cooling to give pure white needles of IV, m.p. 190–192°.

Anal. Calcd. for $C_{26}H_{46}O_4N_4$: N, 11.7. Found: N, 11.3.

N,N'-Diethyl pyromellitimide (VI). In a three-necked flask equipped with a thermometer, stirrer, and reflux condenser were placed IV (5.0 g., 0.014 mole), phosphorus pentachloride (12.5 g., 0.06 mole), and chloroform (250 ml.). The mixture was heated slowly to reflux and maintained there for 6 hr. The cooled chloroform solution was poured into crushed ice, and the chloroform layer was separated, filtered, and washed alternately with aqueous sodium bicarbonate followed by water until the washings were no longer acid. Evaporation of the solvent left a yellow-brown powder, 3.2 g., m.p. 270–273°. The product was soluble cold in chloroform, benzene, dioxane, and glacial acetic acid and soluble hot in carbon tetrachloride, ethanol, and methanol. It was insoluble in ligroin and ether. Recrystallization from ethanol yielded 2.3 g. (61%) of VI, m.p. 273–274°.

Anal. Calcd. for $C_{14}H_{12}N_2O_4$: C, 61.8; H, 4.4; N, 10.3. Found: C, 61.6; H, 4.2; N, 10.3.

The Friedman modification of the Rosenmund-Von Braun reaction. In a 50 ml. resin kettle were placed 2,5-dibromoterephthalic acid (2.0 g., 0.0062 mole), cuprous cyanide (1.4 g., 0.015 mole), and dimethylformamide (3 ml.). The mixture was heated slowly with stirring to reflux and after an hour was poured into a solution of ferric chloride (3.0 g.), concd. hydrochloric acid (1.0 ml.) and water (4.0 ml.). The mixture was heated to 60° for 10 min. to decompose the complex, cooled, and filtered. The product was insoluble in glacial acetic acid and was recrystallized from dimethylformamide to yield pyromellitimide (1.3 g., 98%) as shown by melting point and comparison of its infrared spectrum with that of an authentic sample.

Dimethyl-2,5-dibromoterephthalate (VIII). Anhydrous hydrogen chloride was passed into a flask containing 2,5-dibromoterephthalic acid (7.0 g., 0.216 mole) dissolved in absolute methanol (80.0 ml.) until the solution was nearly saturated. After refluxing for 8 hr., the solution was cooled to room temperature to precipitate white crystalline platelets of VIII, m.p. 148.6° (7.2 g., 97%).

Anal. Calcd. for $C_{10}H_8Br_2O_4$: C, 33.6; H, 2.3. Found: C, 34.2; H, 2.3.

Dimethyl-2,5-dicyanoterephthalate (IX). The Friedman modification[9] of the Rosenmund-Von Braun reaction was repeated on 2.0 g. of VIII. The pink filter cake obtained from the ferric chloride solution weighed 1.3 g. (m.p. 197–200°). Recrystallization from ethanol gave 0.4 g. of VIII, m.p. 219°. Infrared absorption showed the presence of CN (4.5μ), and CO plus CH_3OCO (5.8–5.9μ, 7.8–8.1μ, and 8.8μ). There were no bands characteristic of NH.

Anal. Calcd. for $C_{12}H_8N_2O_4$: N, 11.5. Found: N, 11.3.

Another fraction from the ethanol mother liquid melted at 195–198°. A mixed melting point with dimethyl-2,5-dicyanoterephthalate was 205–212°. The intermediate temperature but wider range makes it appear that this second fraction was another compound. Its infrared spectrum showed the presence of NH but was otherwise quite similar to that of the first fraction. It is possible that this material was a mixture of some dimethyl-2,5-dicyanoterephthalate with a substantial amount of 4-cyano-5-carbomethoxyphthalimide. Neither fraction contained halogen. The identity of the second fraction was not established.

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COLUMBUS, OHIO

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CINCINNATI]

Substituted γ-Lactones. I. Preparation of α-Substituted γ-Butyrolactones by Condensation of γ-Butyrolactone with Aldehydes. Hydrogenation of the Condensation Products

HANS ZIMMER AND JOHANNES ROTHE[1]

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The base-catalyzed condensation of γ-butyrolactone with various aldehydes is described. These condensation products can be hydrogenated to the corresponding saturated α-substituted γ-butyrolactones.

The γ-lactone ring occurs in a large variety of natural products, many of which exhibit considerable pharmacological interest.[2] As examples, the digitalis-glycosides, santonin, lignans like podophyllotoxin, and antibiotic substances like patulin may be cited. Among the more recent findings, only the antibiotic PA-147[3] and acetomycin[4] shall be mentioned.

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(2) *Cf.* L. J. Haynes, *Quart. Rev.*, **2**, 46 (1948).

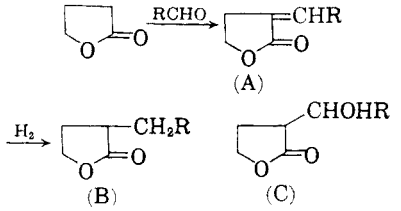
(3) H. Els, B. A. Sobin, and W. D. Celmer, *J. Am. Chem. Soc.*, **80**, 878 (1958).

(4) L. Ettlinger, E. Gäumann, R. Hütter, W. Keller-Schierlein, F. Kradolfer, L. Neipp, V. Prelog, and H. Zahner, *Helv. Chim. Acta*, **41**, 216 (1958).

We were interested in preparing certain α- and/or β-substituted butyrolactones in order to investigate some of their physiological activities. Some of the compounds were also wanted as model compounds or as intermediates in further synthetic work in the γ-lactone field. In this paper the preparation of a number of α-substituted products is described.

Various methods are described in the literature for the preparation of α-substituted lactones containing neither β- nor γ-substituents. Besides lactonization of appropriate γ-hydroxy- or γ-halo acids, the most versatile approach seems to be the condensation of malonic[5] or acetoacetic esters[6] with ethylene oxide or ethylene chlorohydrin followed by hydrolysis and decarboxylation or ketonic cleavage, respectively.

Another method which was adopted in the present investigation is the condensation of butyrolactone with carbonyl compounds, especially with aldehydes. Reactions of this kind have been performed[7] with unsaturated lactones of the type of Δ^2-angelicalactone; the condensation proceeds smoothly by heating the reactants with a catalytic amount of an organic base like diethylamine. γ-Valerolactone was the first saturated lactone which was condensed with benzaldehyde, piperonal and heptaldehyde by Losanitsch.[8] α-Benzalbutyrolactone (A, R = C_6H_5) was prepared by Pinder[9] and by Reppe[10] who also condensed butyrolactone with *o*-chlorobenzaldehyde, furfural, nonaldehyde, and cyclohexanone and obtained the corresponding saturated compounds (B) by hydrogenation.



With saturated lactones, stronger bases must be employed as condensing agents. We adopted the method of Reppe[10] (sodium methoxide in benzene at room temperature) and extended it to a number of other aldehydes, mostly aromatic ones; isovaleraldehyde was the only aliphatic representative being included in our investigation. The inexpensive lactone was always applied in excess. Generally the reaction gives reasonable yields; sometimes, it was found advantageous to heat the reaction mixture. In one case (R = *o*-ethoxyphenyl), a small amount of a compound was isolated which is believed to be the primary product C of the aldolic condensation.

We were not interested in elaborating the optimal conditions in every single case. With several aldehydes, only one experiment was run; thus, some of the yields given might not represent the maximal ones obtainable. Nevertheless, a certain trend in the yields is evident which apparently is dependent on the electronegative character of the aldehydes. The condensation did not proceed well with negatively substituted benzaldehydes (*o*-, *m*-, *p*-nitro-, *p*-cyano-, *p*-acetamido) and with pyridine carboxaldehydes. Low yields were obtained together with tars and unidentified noncrystalline side-products. Assuming the mechanism of the common aldol condensation, these findings are rather unexpected.[11] One should expect that the electron-withdrawing effect of the negative substituent makes the carbonyl carbon of the aldehyde particularly susceptible to condensation with the anionoid α-position of the butyrolactone. This influence on the yields has been clearly observed in related reactions of the aldol type; *e.g.*, in the Perkin reaction,[12] the nitrobenzaldehydes give yields from 75 to 82% of the corresponding cinnamic acids while the unsubstituted benzaldehyde furnishes only 45–50%. Parallel to our findings, however, is the behavior of the nitrobenzaldehydes in the Stobbe condensation[13] with diethyl succinate; under the classical conditions[14] (sodium ethoxide in ether in the cold, thus similar to the conditions in the present investigation) only resinous products were obtained.

Assuming that the higher reactivity of the nitrobenzaldehydes might have led to excessive secondary reactions, we attempted to counteract this reactivity to get better results by use of short reaction periods and low temperatures. However, the results remained the same.

On the other hand, compounds with electron-releasing substituents such as *p*-dimethylaminobenzaldehyde gave fairly good yields. This aldehyde fails completely in the Perkin reaction. Alkyl- and alkoxybenzaldehydes which give low yields in the Perkin reaction worked well in our condensation experiments. At present we do not have any reasonable explanation for these findings. However, several authors report that in certain aldol-type condensations of aldehydes with compounds con-

(5) *e.g.*, R. Fittig, *Ann.*, **226**, 322 (1884); I. L. Knunyantz, G. W. Chelintzev, and E. D. Osetrova, *Chem. Abstr.*, **28**, 4383[2] (1934).

(6) *e.g.*, W. Traube and E. Lehmann, *Ber.*, **34**, 1971 (1901); B. Rothstein, *Bull. soc. chim. France*, (5) **2**, 80 (1935); K. Wiesner, Z. Valenta, A. J. Manson, and F. W. Stonner, *J. Am. Chem. Soc.*, **77**, 675 (1955).

(7) *e.g.*, J. Thiele and F. Straus, *Ann.*, **319**, 155 (1901); J. Thiele, R. Tischbein, and E. Lossow, *Ann.*, **319**, 180 (1901); W. F. v. Oettingen, *J. Am. Chem. Soc.*, **52**, 2024 (1930); D. H. Marrian, P. B. Russell, and A. R. Todd, *Biochem. J.*, **45**, 533 (1949).

(8) M. S. Losanitsch, *Monatsh.*, **35**, 311 (1914).

(9) A. R. Pinder, *J. Chem. Soc.*, 2236 (1952).

(10) W. Reppe *et al.*, *Ann.*, **596**, 158 (1955).

(11) E. R. Alexander, *Principles of Ionic Organic Reactions*, John Wiley & Sons, Inc., New York, 1950, p. 176.

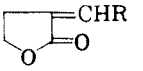
(12) J. R. Johnson, *Org. Reactions*, **1**, 210 (1942).

(13) W. S. Johnson and G. H. Daub, *Org. Reactions*, **6**, 1 (1951).

(14) H. Stobbe, *Ann.*, **380**, 49 (1911).

TABLE I

CONDENSATION PRODUCTS OF γ-BUTYROLACTONE WITH VARIOUS ALDEHYDES



No.	R	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	M.P., °C.	[a]	Reaction Time, Hr. Cold	Reaction Time, Hr. Heating	Yields b	Yields c
I	Isobutyl	$C_9H_{12}O_3$	70.10	70.22	9.15	9.21	[d]	...	2	0.5	78	..[e]
II	4-Methylphenyl	$C_{12}H_{12}O_2$	76.57	76.56	6.43	6.43	63 - 64	Et	3	..	46	..
III	4-Isopropylphenyl	$C_{14}H_{16}O_2$	77.74	76.63	7.46	7.67	65 - 66	Et-P	4.5	..	62	..
IV	2-Hydroxyphenyl	$C_{11}H_{10}O_3$	69.46	69.44	5.30	5.51	184 -185	M	3	0.75	63	93[f]
V	3-Hydroxyphenyl	$C_{11}H_{10}O_3$	69.46	69.55	5.30	5.33	196 -197	M	4.5	1	69	..[g]
VI	4-Hydroxyphenyl	$C_{11}H_{10}O_3$	69.46	69.05	5.30	5.38	181 -182	W	15	1	44	70[h]
VII	4-Methoxyphenyl	$C_{12}H_{12}O_3$	70.57	70.35	5.92	5.95	126 -127	E	2	1	48	..[e]
VIII	2-Ethoxyphenyl	$C_{13}H_{14}O_3$	71.54	71.45	6.47	6.45	105 -105.5	M	2.5	..	79	..[i]
IX	3,4-Dimethoxyphenyl	$C_{13}H_{14}O_4$	66.66	66.81	6.02	6.16	116 -116.5	M	Short	0.5	53	..
X	3,4-Diethoxyphenyl	$C_{15}H_{18}O_4$	68.68	68.85	6.92	6.92	116	M	4.5	0.5	63	..
XI	3,4,5-Trimethoxyphenyl	$C_{14}H_{16}O_5$	63.63	63.59	6.10	6.10	152 -152.5	M	1	0.5	58	..[e]
XII	3,4-Methylenedioxyphenyl	$C_{12}H_{10}O_4$	66.05	65.90	4.62	4.64	178 -178.5	D	3.5	..	82	..
XIII	4-Benzyloxyphenyl	$C_{18}H_{16}O_3$	77.12	76.60	5.75	6.04	166 -166.5	A	1	0.5	71	..
XIV	3-Methoxy-4-benzyloxyphenyl	$C_{19}H_{18}O_4$	73.53	73.23	5.85	5.98	151 -152	D	1.5	1	74	..
XV	4-Isopropoxyphenyl	$C_{14}H_{14}O_3$	72.39	72.26	6.94	7.05	115 -115.5	M	1	2.5	79	98
XVI	4-(2-Butoxy)-phenyl	$C_{15}H_{16}O_3$	73.75	73.42	6.60	7.40	54 - 55.5	M	2	0.5	24	..[e,i]
XVII	3-Methoxy-4-hydroxyphenyl	$C_{12}H_{12}O_4$	65.45	65.20	5.49	5.45	153.5-154	W	4	1	6	..[k]
XVIII	4-Chlorophenyl	$C_{11}H_9ClO_2$	63.32	63.46	4.35	4.50	142 -144	E	2	..	79	..
XIX	3-Nitrophenyl	$C_{11}H_9NO_4$	60.27	60.70	4.14	4.23	147 -148	M	1	1	15	..[l]
XX	4-Nitrophenyl	$C_{11}H_9NO_4$	60.27	60.17	4.14	4.22	202 -203	Mc	1	1	1	..[m]
XXI	4-Dimethylaminophenyl	$C_{13}H_{15}NO_2$	...	...	..	..	195 -196	D	1	0.5	59	87[n]
XXII	4-Diethylaminophenyl	$C_{15}H_{19}NO_2$	...	...	..	..	126 -128	E	2	0.5	56	..[o]
XXIII	4-Acetamidophenyl	$C_{13}H_{13}NO_3$	...	...	..	..	199 -200	M	Short	1	2	..[p]
XXIV	Phenylvinyl	$C_{13}H_{12}O_2$	77.98	77.73	6.04	6.26	133.5-135	M	0.5	..	67	..
XXV	*p*-Dimethylaminophenylvinyl	$C_{15}H_{17}NO_2$	...	...	..	..	181 -182	D	2	..	54	..[e,q]
XXVI	1-Naphthyl	$C_{15}H_{12}O_2$	80.33	80.25	5.39	5.50	104 -105	M	1	..	23	..
XVII	2-Furylvinyl	$C_{11}H_{10}O_3$	60.46	69.33	5.30	5.36	98 - 99	E	1	1	62	..

The following compounds are colored: XIII, XIV, XIX, XX, XXIV, yellowish; XXVII, brownish; XXII, yellow; XXI, yellow-greenish; XXV, orange-red. The following give a coloration with $FeCl_3$ in dioxane or ethanol: IV, yellowish green; VI and XVII, green. The following give a coloration with H_2SO_4 in the cold: IV, V, VII–XI, yellow; XIII, XXV, orange; VI, XIV, red; XXVII, brown; XXVI, yellowish brown; XII, brownish. [a] Solvents for recrystallization: E = Ethyl alcohol, Et = diethyl ether, P = petroleum ether b.p. 40–60°, M = methanol, W = water, D = dioxane, A = acetic acid, Mc = methylene chloride. [b] Based on applied aldehyde. [c] Based on consumed aldehyde. [d] B.p. 99–100°/3 mm; n_D^{20} 1.4751. [e] Only one experiment; yield can possibly be improved. [f] *Acetyl deriv.*, m.p. 122–123° (from methanol). *Anal.:* Calcd. for $C_{13}H_{12}O_4$: C, 67.23; H, 5.21. Found: C, 66.84; H, 5.34. [g] *Acetyl deriv.*, m.p. 108.5–110° (from methanol). *Anal.:* Found: C, 67.08; H, 5.41. [h] *Acetyl deriv.*, m.p. 142.5–143.5° (from benzene). Anal.: Found: C, 67.13; H, 5.25. [i] In this experiment, a 5% yield of a *compound* $C_{13}H_{16}O_4$, m.p. 134.5–136° (from methanol) was isolated from the sulfuric acid layer; the properties of this substance (Calcd.: C, 66.13; H, 6.83. Found: C, 65.93; H, 6.96. Infrared spectrum in nujol: bands at 2.93 [OH] and 5.68μ [lactone], no band between 6.0 and 6.2μ. Insoluble in cold dilute sodium carbonate solution) correspond best to the primary aldolic product (C, R = *o*-ethoxyphenyl). The compound was not investigated further. [j] Low yield probably due to small amount of starting material. [k] *Acetyl deriv.*, m.p. 151.5–152.5° (from methanol). Anal.: Calcd. for $C_{14}H_{14}O_5$: C, 64.11; H, 5.38. Found: C, 64.11; H, 5.39. [l] Calcd.: N, 6.39. Found: N, 6.45. [m] Calcd.: H, 6.39. Found: N, 6.32. [n] Calcd.: N, 6.45. Found: N, 6.33. *Hydrochloride*, m.p. 178° (dec.; from methanolic HCl), is white, but turns yellow-greenish in the open air or in a desiccator ($CaCl_2$); stable in HCl-atmosphere; not analyzed. [o] Calcd.: N, 5.71. Found: N, 5.61. *Hydrochloride*, m.p. 203–204° (dec.; from 7% aq. HCl), White, not quite as unstable as the preceding hydrochloride. Anal.: Calcd. for $C_{15}H_{20}ClNO_2$: Cl, 12.58. Found: Cl, 12.72. [q] Calcd.: N, 5.76. Found: N, 5.82.

taining active methyl groups (substituted toluenes,[15] picoline methiodide[16]), *p*-dimethylaminobenzaldehyde gives better results than the unsubstituted benzaldehyde. A mechanism proposed for the latter reaction[16] seems not to be applicable in the present case.

In spite of several attempts, and unexpectedly after the good yields with other hydroxy or methoxy substituted aldehydes, the condensation did not proceed well with vanillin. Haworth[17] reported a failure in an attempted Stobbe condensation with this compound and circumvented the difficulties by application of benzylvanillin. We did likewise

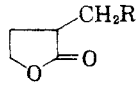
(15) L. Chardonnens and W. J. Kramer, *J. Am. Chem. Soc.*, **79**, 4955 (1957).

(16) A. P. Phillips, *J. Org. Chem.*, **12**, 337 (1947).

(17) R. D. Haworth and F. H. Slinger, *J. Chem. Soc.*, 1098 (1940).

TABLE II

HYDROGENATION PRODUCTS



R	Formula	Analytical Values C Calcd.	C Found	H Calcd.	H Found	M.P. or B.P., °C.	Solvent for Recrystallization or n_D^{20}	Yield
4-Methylphenyl	$C_{12}H_{14}O_2$	75.75	75.83	7.43	7.89	135/4 mm.	1.5272	99
4-Isopropylphenyl	$C_{14}H_{18}O_2$	77.03	76.69	8.31	8.48	138–140/5 mm.	1.5219	92
2-Hydroxyphenyl	$C_{11}H_{12}O_3$	68.73	68.12	6.29	6.20	174–175/5 mm.	1.5485	76
3-Hydroxyphenyl	$C_{11}H_{12}O_3$	68.73	68.74	6.29	6.51	120–121	W-M[a]	85[a]
4-Hydroxyphenyl	$C_{11}H_{12}O_3$	68.73	68.04	6.29	6.26	192–193/4 mm.	1.5546	83
4-Methoxyphenyl	$C_{12}H_{14}O_3$	69.88	69.98	6.84	6.86	44	Et-P	76
2-Ethoxyphenyl	$C_{13}H_{16}O_3$	70.88	70.86	7.32	7.43	154–156/5 mm.	1.5421	95[a]
3,4-Dimethoxyphenyl	$C_{13}H_{16}O_4$	66.08	66.13	6.83	6.94	105.5–106.5	M	81
3,4-Diethoxyphenyl	$C_{15}H_{20}O_4$	68.16	68.31	7.63	7.66	68–69	M	80
3,4,5-Trimethoxyphenyl	$C_{14}H_{18}O_5$	63.14	62.86	6.82	6.97	72	M	83
3,4-Methylenedioxyphenyl	$C_{12}H_{12}O_4$	65.44	65.25	5.49	5.50	52-52.5	M	83
3-Methoxy-4-benzyloxyphenyl	$C_{19}H_{20}O_4$	73.06	72.12	6.45	6.52	232/4 mm.	1.5819	60[b,c]
3-Methoxy-4-hydroxyphenyl	$C_{12}H_{14}O_4$	64.85	64.62	6.35	6.43	183–184/4 mm.	1.5515	78
p-Chlorophenyl	$C_{11}H_{11}ClO_2$	62.71	62.97	5.26	5.30	159–161/4 mm.	1.5471	69
p-Dimethylaminophenyl	$C_{13}H_{17}NO_2$	71.20	71.08	7.81	7.72	92	M	95[c]
p-Diethylaminophenyl	$C_{15}H_{21}NO_2$	...	...	...	...	173–174/4 mm.	1.5534	52[c,d]
2-Phenylethyl	$C_{13}H_{16}O_2$	76.44	76.15	7.90	8.04	145–146/4 mm.	1.5224	91
2-(*p*-Dimethylaminophenyl)-ethyl	$C_{15}H_{21}NO_2$	...	...	...	...	187/4 mm.		81[e]
1-Naphthyl	$C_{15}H_{14}O_2$	79.62	78.99	6.24	6.80	205–207/6 mm.	1.5838	90
2-Furylethyl	$C_{11}H_{14}O_3$	66.64	66.35	9.15	8.98	150–152/5 mm.	1.4797	89
Isobutyl	$C_9H_{14}O_3$	...	...	...	...	83–84/5 mm.	1.4477	69[f]
p-Isopropoxyphenyl	$C_{14}H_{18}O_3$	71.77	71.66	7.74	8.68	136–141/4 mm.	1.4957	80

[a] W = water; M = methanol; Et = ether; P = petrol ether. [b] The analytical values seem to indicate that during the hydrogenation (neutral medium) the benzyl group is split off partly. This is confirmed by a weak $FeCl_3$-reaction (green) of the distilled product. [c] Hydrogenation was performed in tetrahydrofuran. [d] Calcd.: N, 5.66. Found: N, 5.34. [e] Calcd.: N, 5.66. Found: N, 5.68. The product solidified after three distillations (m.p. 34–38.5°); no attempt of recrystallization was made. [f] B. Rothstein, *Bull. soc. chim. France*, *5*, 2, (1935), gives b.p. 129°/15 mm.; n_D^{23} 1.4455.

and obtained an excellent yield of α-[3-methoxy-4-hydroxybenzylidene]-γ-butyrolactone (XVII) by hydrolyzing the benzylvanillin condensation product. (XIV). In an analogous manner, α-[*p*-hydroxybenzylidene]-γ-butyrolactone (VII) was produced from its benzyl ether (XIII).

The hydrogenation of the α-exo double bond proceeded readily at room temperature with platinum oxide under 50 lb in the Parr-apparatus. Reppe[10] had used Raney nickel under high pressure (200 atm.) at 100°.

Some of the pharmacological properties of the compounds prepared are to be reported elsewhere.

EXPERIMENTAL

Melting points are uncorrected. Microanalyses by A. Bernhardt, Mikroanalytisches Laboratorium im Max-Planck-Institut, Mülheim/Ruhr, Germany.

Materials. Generally, Eastman White Label products or comparable grades were employed without further purification.

Benzene was U.S.P. grade and was not specially dried before use. In a number of experiments, recovered benzene, dried over calcium chloride, was used, apparently without any decrease of the yields.

Sodium methoxide, from Matheson Coleman and Bell or Harshaw Chemical Co. was used. It was found that the quality of the sodium methoxide is a very decisive factor in the success of the condensations. The use of aged material that might have been partially contaminated by moisture resulted in markedly lowered yields; sometimes the reaction failed completely when sodium methoxide of a low quality was applied.

The following compounds were prepared according to standard procedures given in the literature: *Benzylvanillin*,[18] m.p. 64°. *p-Benzyloxybenzaldehyde*, m.p. 68–71°. *p-Isopropoxybenzaldehyde*,[19] b.p.$_{18}$ 120°. *p-2-Butoxybenzaldehyde*,[19] b.p.$_{19}$ 153–155°. *p*-Cyanobenzaldehyde,[20] m.p. 100°.

Condensations. (Table I). The condensations were generally run as follows: The aldehyde (0.1 mole) and 0.2 mole of butyrolactone were dissolved in 50–200 cc. of benzene. Sodium methoxide (0.15 mole) was gradually added and the mixture was continuously stirred for the periods given in Table I; for hydroxyaldehydes, 0.25 mole of CH_3ONa were used. In most cases, initial cooling (ice salt) was applied. The reactions with the more sensitive aldehydes were carried out under a stream of dry nitrogen. In a number of experiments, the mixture eventually was heated on a water bath.

The reaction mixtures were then decomposed with 10% sulfuric acid, and stirring continued for about 1 hr. to effect relactonization. In several instances, the products precipitated and could be filtered off. The filtrate was separated and the layer was discarded except in the cases of basic compounds. The benzene layer was washed with dilute

(18) R. Dickinson, I. M. Heilbron, and F. Irving, *J. Chem. Soc.*, 1888 (1927).

(19) M. Zimmer, unpublished experiments.

(20) L. Weisler, *Org. Syntheses*, **Coll. Vol. II**, 443 (1943).

sodium bicarbonate solution, then with water, and the benzene distilled off without previous drying (the small amount of water still being present distils azeotropically with the benzene). The residue was recrystallized or distilled, respectively, as indicated in Table I.

Example: α-[*o-hydroxybenzylidene*]-γ-*butyrolactone* (IV). The apparatus consisted of a 500-cc. three-neck flask fitted with a stirrer, a reflux condenser, a thermometer, and a nitrogen-inlet tube. 12.2 g (0.1 mole) of salicylaldehyde and 17.2 g. (0.2 moles) of butyrolactone were dissolved in 100 cc. of benzene. The mixture was cooled down to +3° by means of an ice salt bath. During the whole reaction the mixture was well stirred. A slow stream of nitrogen was passed over the mixture. Within 15 min., 13.5 g. (0.25 mole) of sodium methoxide were added in portions. The temperature rose to 27° and the mixture turned to a brownish jelly which was then diluted with 100 cc. of benzene. Stirring was continued for 3 more hr., then the mixture was heated on a water bath for 45 min. (temperature 60–65°).

After standing over night, sufficient 10% sulfuric acid was added under stirring to make the mixture acidic; stirring was continued for 1 hr. and the precipitate which had been formed was filtered by suction and washed thoroughly with water. Yield: 12.0 g. (63%), m.p. 184–185°. The analytical sample, after 3 recrystallizations from methanol, had the same melting point.

The filtrate was separated, the benzene layer was washed with dilute sodium bicarbonate solution, then with water and distilled. A brown oil remained which furnished, on distillation, 4.0 g. of salicylaldehyde, b.p. 195–200°. Yield based upon consumed aldehyde: 93%.

Tetrabromide of XXIV. 2 g. of XXIV were dissolved in 10 cc. of chloroform. By means of a buret, a solution of 6.2 g. bromine in 20 cc. of chloroform was added dropwise and the solution left over night in an open porcelain dish. White crystals (5.0 g., 96%), m.p. 182–183.5°, were formed after evaporation of the solvent. After 3 recrystallizations from methanol, the m.p. was 192.5–193° (dec.).

Anal. Calcd. for $C_{13}H_{12}Br_4O_2$: Br, 61.49. Found: Br, 61.86.

An attempt to prepare a bromide of XXVII by similar means resulted only in dark viscous oils.

α-[*3-Methoxy-4-hydroxybenzylidene*]-γ-*butyrolactone* (XVII) *from* XIV. 15.5 g. of XIV, 100 cc. of concd. hydrochloric acid, and 250 cc. of glacial acetic acid were heated under reflux for 1.5 hr. After standing over night the solvents were distilled off. The residue solidified and was recrystallized by dissolving in 100 cc. of methanol and adding 100 cc. of water. Yield 10.5 g. (95%), m.p. 151–152°.

α-[*p-Hydroxybenzylidene*]-γ-*butyrolactone* (VI) *from* XIII. 38.1 g. of XIII, 266 cc. of concd. hydrochloric acid, and 762 cc. of glacial acetic acid were boiled for 1.5 hr., then the solvents were removed. The residue was recrystallized from 1.5 liter of water furnishing 16.2 g. of product, m.p. 179–180°. By concentrating the mother liquors, an additional 1.5 g. (m.p. 173–176°) were obtained. Total yield: 17.7 g. (69%).

Hydrogenations (Table II). The hydrogenations were performed by dissolving or suspending 2–20 g. (mostly 5 g.) of the condensation products in 250 cc. of methanol (or tetrahydrofuran), adding 5–10% by weight of platinum oxide (by American Platinum Works) and shaking under 45–50 lbs. of hydrogen in a Parr apparatus until the pressure remained constant. Application of heat apparently had no influence on the yields. After 15 min. to 24 hr. (depending on the amount of starting material rather than on the particular compound), the pressure remained constant.

The catalyst was removed by filtration, the solvent distilled off and the residue worked up by crystallization or distillation.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF WAYNE STATE UNIVERSITY]

The Halodiphenacyls. III. The Structure and Reactions of the Hydrogen Bromide Adduct[1]

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The adduct formed from the reaction of β-bromodiphenacyl with hydrogen bromide was shown to be the α-hydroxy-β-bromoketone III and is interpreted in this work to involve *cis* addition to the epoxide. The reaction of III with sodium iodide gave the α-hydroxy-β-methylene ketone IV, which was stable in neutral solution but which rearranged to the diketone VI in acid solution. The two acetates, XIV and IIIa, which had previously been prepared from the reaction of acetyl bromide with I and II, respectively, proved to be diastereoisomers and showed that the opening of the α,β-epoxyketones with acetyl bromide in this instance is stereospecific and involved the same stereochemistry as the opening with hydrogen bromide.

Previous studies have resulted in the elucidation of the structure and stereochemistry of the halodiphenacyls.[3–6] Thus α-, and β-bromodiphenacyl were shown to be I and II, respectively, and the facile isomerization of the α-isomer (I) to the β-isomer (II) with base has been discussed.[4,6]

The conversion of II to I by reaction with hydrogen bromide followed by treatment of the adduct with ammonia has been reported.[6] The present re-

(1) Abstracted from the thesis of Mr. Richard G. Hiskey submitted in June 1955 to the Graduate School at Wayne State University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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