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Substituted γ-Lactones XVIII (1). Preparation of Substituted *Alpha*-Benzylidene-*Gamma*-Butyrolactones by the Wittig Reaction

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Certain mono- substituted α-[2-nitrobenzylidene]-γ-butyrolactones (A) and mono- substituted α-[2-hydroxybenzylidene]-γ-butyrolactones were desired for further synthesis in the field of linearly condensed heterocyclic systems. Previously, it was shown that direct aldol-type condensations proceeded poorly or not at all between γ-butyrolactone and aromatic aldehydes which were substituted by strong electron withdrawing groups such as nitro- or cyano-group (3).

An alternate route to obtain the desired type-A compounds, by nitration of the corresponding α-benzylidene-γ-butyrolactones, did not prove too successful (4) (5). Though the nitration did succeed, the site of substitution often was not at the desired 2- or 6-position. Consequently, it was necessary to find a new synthetic route to compounds of type A.

In this communication we wish to report a new and general way to synthesize these compounds by the Wittig reaction. α-[γ-Butyrolactonylidene]triphenylphosphorane, which was recently described (6) when our studies were underway, was allowed to react with the appropriately substituted aldehydes to yield the olefins in high yields. The results of these condensations are enumerated in Table I.

Table I Page 96

The yields obtained by this procedure were very good, *e.g.*, α-[2-nitrobenzylidene]-γ-butyrolactone, which could not be obtained at all by the direct condensation method (3) was synthesized in 77% yield utilizing the Wittig reaction. Also α-[4-acetamidobenzylidene]-γ-butyrolactone was prepared in 89% yield by this method, whereas by direct condensation, the yield was only 2% (3).

The application of this procedure to the dialdehyde, terephthaldehyde, proved especially fruitful. Most of the product crystallized out of the refluxing solution and could be filtered off. In contrast, this bis-condensation product could not be obtained at all by direct condensation (2), terephthalic acid being the only characterized product.

EXPERIMENTAL

Melting points are uncorrected. Microanalyses by A. Bernhardt, Mikroanalytisches Laboratorium im Max-Planck-Institut, Mülheim (Ruhr), Germany. Generally Eastman White Label or comparable grade reagents by other suppliers were employed directly.

General Procedure for the Wittig-Reaction.

In 200 ml. of reagent grade tetrahydrofuran, 2 g. of α-[γ-butyrolactonylidene]triphenylphosphorane and a slight excess of the appropriate aldehyde were refluxed for 10 hours. (Except for compound XV, where exactly two moles of α-[γ-butyrolactonylidene]triphenylphosphorane to one mole of dialdehyde were used.) After evaporating the solvent, the remaining residue was recrystallized. In all cases, methanol could be used, except for compound XV, which required acetone. The reported yields are based on recrystallized product.

The following aldehydes were obtained by standard procedures (7).

3-Nitro-4-bromobenzaldehyde.

Chromic acid oxidation of 3-nitro-4-bromotoluene yielded the diacetate, m.p. 97-98°.

Anal. Calcd. for $C_{11}H_{10}BrNO_6$: C, 39.76; H, 3.01; Br, 24.10; N, 4.22. Found: C, 39.66; H, 2.98; Br, 24.28; N, 4.21.

Acid hydrolysis of the diacetate produced the aldehyde.

2-Nitro-4-chlorobenzaldehyde.

Chromic acid oxidation of 2-nitro-4-chlorotoluene yielded the diacetate, m.p. 119-120°.

Anal. Calcd. for $C_{11}H_{10}ClNO_6$: C, 45.91; H, 3.48; Cl, 12.35; N, 4.87. Found: C, 45.70; H, 3.69; Cl, 12.53; N, 4.74.

Acid hydrolysis of the diacetate produced the aldehyde. These two aldehydes were used in condensations without further purification.

Compounds I, II, III, IV, and XI were reduced by a procedure using stannous chloride as reported earlier (5). The expected amines were obtained; pertinent data are compiled in Table I.

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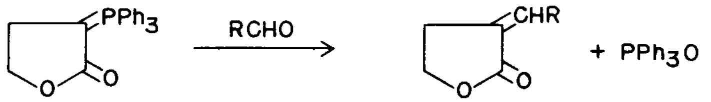
TABLE I

Wittig Reactions with α-[γ-Butyrolactonylidene]Triphenylphosphorane



No.	R		Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	m.p. (°C)	% Yield
I	3-nitro-4-bromophenyl	$C_{11}H_8BrNO_4$	44.30	44.22	2.68	2.76	4.70	4.67	188-189	82 (a)
II	2-nitro-4-chlorophenyl	$C_{11}H_8ClNO_4$	52.07	52.51	3.16	3.22	5.52	5.45	143-145	78 (b)
III	2-nitro-5-chlorophenyl	$C_{11}H_8ClNO_4$	52.07	52.00	3.16	3.36	5.52	5.41	164-165	80 (c)
IV	2,4-dinitrophenyl	$C_{11}H_8N_2O_6$	50.01	50.45	3.05	3.30	10.60	10.77	137-138	82 (d)
V	2-nitrophenyl	$C_{11}H_9NO_4$							96-97	77 (e)
VI	3-nitrophenyl	$C_{11}H_9NO_4$							147-148	81 (f)
VII	4-nitrophenyl	$C_{11}H_9NO_4$							202-203	88 (f)
VIII	2-hydroxy-5-nitrophenyl	$C_{11}H_9NO_5$	56.17	56.13	3.86	3.84	5.96	6.11	265-267	81
IX	4-cyanophenyl	$C_{12}H_9NO_2$	72.35	72.19	4.55	4.33	7.03	7.10	157-159	82
X	4-methoxyphenyl	$C_{12}H_{12}O_3$							126-127	83 (f)
XI	2-nitrophenylvinyl	$C_{13}H_{11}NO_4$	63.67	63.43	4.52	4.49	5.71	5.79	158-159	87 (g)
XII	4-acetamidophenyl	$C_{13}H_{13}NO_3$							199-200	89 (f)
XIII	2-nitro-4,5-dimethoxyphenyl	$C_{13}H_{13}NO_6$							165-166	81 (h)
XIV	3,4,5-trimethoxyphenyl	$C_{14}H_{16}O_5$							152-153	80 (f)
XV	4-[α-methylidenyl-γ-butyrolactone]phenyl	$C_{16}H_{14}O_4$	71.10	70.77	5.22	5.23			293-295	84 (i)

(a) Calcd.: Br, 26.85. Found: Br, 26.91. α-[3-Amino-4-bromobenzylidene]-γ-butyrolactone obtained by $SnCl_2$-reduction of I; m.p. 186-187°. *Anal.* Calcd. for $C_{11}H_{10}BrNO_2$: C, 49.25; H, 3.73; N, 5.22. Found: C, 49.23; H, 3.95; N, 5.40. (b) Calcd.: Cl, 14.00. Found: Cl, 13.64. α-[2-Amino-4-chlorobenzylidene]-γ-butyrolactone obtained analogously from II; m.p. 147-148°. *Anal.* Calcd. for $C_{11}H_{10}ClNO_2$: C, 59.06; H, 4.47; Cl, 15.88; N, 6.26. Found: C, 58.75; H, 4.77; Cl, 15.66; N, 6.40. (c) Calcd.: Cl, 14.00. Found: Cl, 14.14. α-[2-Amino-5-chlorobenzylidene]-γ-butyrolactone obtained analogously from III; m.p. 112-113°. *Anal.* Calcd. for $C_{11}H_{10}ClNO_2$: C, 59.06; H, 4.47; Cl, 15.88; N, 6.26. Found: C, 58.89; H, 4.44; Cl, 16.26; N, 6.36. (d) Identical with α-[x,y-dinitrobenzylidene]-γ-butyrolactone as obtained earlier by direct nitration (5); diacetyl derivative of α-[2,4-diaminobenzylidene]-γ-butyrolactone obtained by $SnCl_2$-reduction of IV; m.p. 219-221°. *Anal.* Calcd. for $C_{15}H_{16}N_2O_4$: C, 62.49; H, 5.59; N, 9.72. Found: C, 62.33; H, 5.49; N, 9.52. (e) Identical with authentic sample (5). (f) Identical with authentic sample (3). (g) α-[2-Aminophenylvinyl]-γ-butyrolactone obtained by $SnCl_2$-reduction from XI; m.p. 193-194°. *Anal.* Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.09; H, 5.98; N, 6.50. (h) Identical with authentic sample (4). (i) Mononitro deriv.; m.p. 235-237°. *Anal.* Calcd. for $C_{16}H_{13}NO_6$: C, 60.95; H, 4.16; N, 4.44. Found: C, 60.58; H, 4.23; N, 4.62.