

Department of Chemistry, University of Cincinnati

Substituted γ -Lactones. XX (1). Reactions of α -Benzylidene- γ -Butyrolactones with Bromine and Some Chemical Properties of the Resulting Products

Hans Zimmer and Roderich Walter (2)

In previous papers from this laboratory the sulfochlorination and nitration of α -benzylidene- γ -butyrolactones are described (3,4). In the present communication we wish to report the reaction of substituted α -nitrobenzylidene- γ -butyrolactones with one mole of bromine (Scheme A; Table I, compounds I-IV) and of a substituted α -benzylidene- γ -butyro-

lactone with two moles of bromine (Scheme B; Table I, compound V).

Furthermore, the behavior of these brominated compounds under treatment with certain nucleophilic reagents is presented. Interestingly enough, an elimination of bromine rather than of hydrogen bromide occurs when compounds I-IV react with

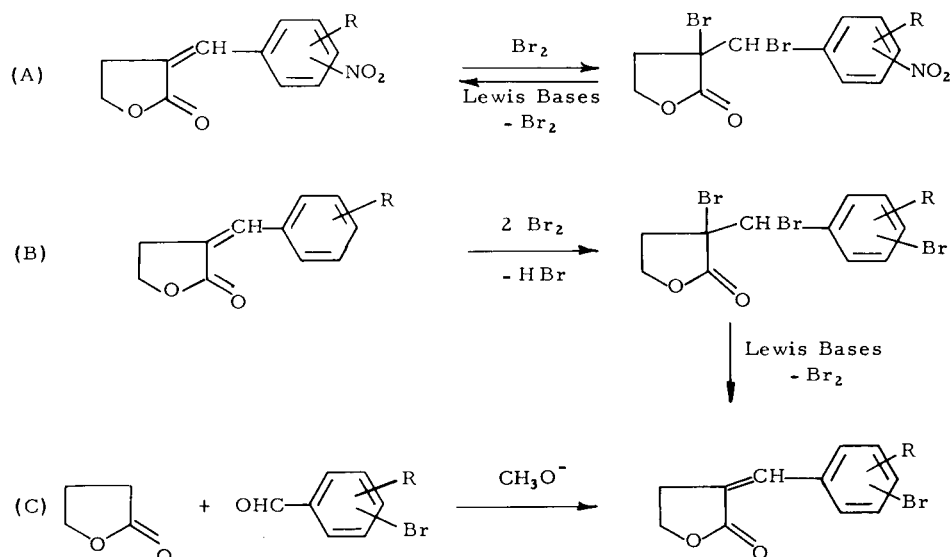
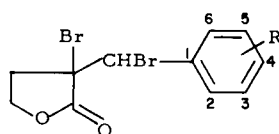


TABLE I



No.	Position of -NO ₂ Group	Position of Substituents				Formula	Carbon, % Calcd. Found		Hydrogen, % Calcd. Found		Nitrogen, % Calcd. Found		Bromine, % Calcd. Found		M. P. °C	Yield %
		2	3	4	5											
I	2			-O-CH ₂ -O-		C ₁₂ H ₉ Br ₂ NO ₆	34.06	34.33	2.14	1.92	3.31	3.34	37.78	37.63	186	78
II	4	OCH ₃			OCH ₃	C ₁₃ H ₁₃ Br ₂ NO ₆	35.57	35.39	2.98	2.91	3.19	3.17	36.41	36.39	184	62
III	5	OCH ₃	OCH ₃			C ₁₃ H ₁₃ Br ₂ NO ₆	35.57	35.55	2.98	3.02	3.19	3.25	36.41	36.54	132	58
IV	2			OC ₂ H ₅	OC ₂ H ₅	C ₁₅ H ₁₇ Br ₂ NO ₆	38.58	38.97	3.67	3.41	3.00	3.16	34.22	33.91	169	81
V	-	Br		-O-CH ₂ -O-		C ₁₂ H ₉ Br ₃ O ₄	31.51	31.67	1.98	1.82	-	-	52.47	52.35	195	40

various Lewis bases, *e.g.*, quinoline, thiocarbonyl anilide in ethanol, triphenylphosphine in dimethylformamide (5), *t*-butyltriphenylphosphinimine in *p*-dioxane (6), thiourea in methanol, and trimethylphosphite (7). Moreover, under the above reaction conditions α -(2-bromo-4,5-methylenedioxybenzylidene)- γ -butyrolactone results from compound V, exhibiting an analogous loss of one mole of bromine. The unambiguous synthesis of α -(2-bromo-4,5-methylenedioxybenzylidene)- γ -butyrolactone by the condensation of γ -butyrolactone with 2-bromopiperonal served as a structural confirmation (Scheme C). This shows also that α -benzylidene- γ -butyrolactones which are substituted by activating groups are easily susceptible towards nuclear bromination.

EXPERIMENTAL

Melting points are uncorrected. Microanalyses by A. Bernhardt, Mikroanalytisches Laboratorium im Max-Planck-Institut, Mülheim, Germany. Compounds described previously (4) served as starting materials.

Reaction of α -Nitrobenzylidene- γ -butyrolactones with One Equivalent of Bromine.

One-fiftieth mole of the substituted α -nitrobenzylidenelactone was dissolved in 60 ml. of warm glacial acetic acid. The mixture was cooled to room temperature and one equivalent of bromine was added in a continuous stream by means of a burette. After a few minutes an exergonic reaction occurred as the solution decolorized. During the next twelve hours the brominated compound crystallized in long yellow needles which were filtered off and quickly washed with methanol followed by ethyl ether. The material was recrystallized from glacial acetic acid, methanol, or ethanol. The reported yields are based on recrystallized product. The ultraviolet absorption spectra of compounds I-IV displayed a maximum centered around 335 m μ (solvent 95% ethanol), while their infrared absorption spectra exhibited a typical carbonyl absorption band for saturated lactones at 5.62-6.64 μ (KBr pellet).

Reaction of an α -Benzylidene- γ -butyrolactone with Two Equivalents of Bromine.

One-fiftieth mole of α -(3,4-methylenedioxybenzylidene)- γ -butyrolactone was dissolved in 60 ml. of glacial acetic acid. Two equivalents of bromine were then added by means of a burette. The solution decolorized directly as white fumes and the odor of hydrobromic acid became apparent. After a period of twelve hours at room temperature the mixture was poured into 500 ml. of water. The solvent was decanted and the yellowish gummy residue was treated with methanol, inducing crystallization. Ethanol served as the solvent for recrystallization. The product exhibited in its infrared absorption spectrum a lactone carbonyl absorption at 5.66 μ (KBr pellet).

Reaction of Compounds I-V from Table I with Lewis Bases.

The elimination of bromine by Lewis bases is delineated with compound I as an example:

A. One gram of compound I was dissolved in 15 ml. of quinoline and refluxed for two hours. The solid material which separated from the dark solution upon cooling was isolated by filtration. Recrystallization from methanol yielded 0.5 g. (72%) of yellowish crystals, which gave a negative Beilstein test for halogens. The ultraviolet absorption spectrum of this compound exhibited a maximum centered

around 345 m μ (solvent 95% ethanol), while the infrared absorption spectrum showed a lactone carbonyl absorption at 5.75 μ and a carbon-carbon double bond absorption at 6.05 μ (KBr pellet). The material melted at 182-183°. The melting point of a mixture of this material with authentic α -(2-nitro-4,5-methylenedioxybenzylidene)- γ -butyrolactone (4) was 182-183°, confirming the fact that debromination had occurred. The criteria employed in the identification of this product were applied to the following reactions as well.

B. In 150 ml. of 95% ethanol 2.1 g. of compound I and 0.76 g. of thiocarbonyl anilide were refluxed for two hours. Upon cooling, yellow crystals were obtained, m.p. 178-179°, yield 0.8 g. (55%).

C. The mixture of 8.45 g. of compound I and 5.24 g. of triphenylphosphine was stirred overnight in dimethylformamide. The next morning the solvent was removed *in vacuo* and the residue washed with water, methanol, and finally ethyl ether, m.p. 178-180°, yield 72%.

D. A mixture of 1 g. of compound I and 1.57 g. of *t*-butyltriphenylphosphinimine was refluxed for six hours in *p*-dioxane. The crystals which precipitated from the solution kept for five days at room temperature were filtered by suction and washed successively with acetone, m.p. 178-179°, yield 92%.

E. Debromination was also observed when 2 g. of compound I was treated overnight at room temperature with an equivalent amount of thiourea in 50 ml. of methanol. Following the removal of the solvent *in vacuo* 91% of α -(2-nitro-4,5-methylenedioxybenzylidene)- γ -butyrolactone was isolated.

F. Two grams of compound I were heated on a steam bath in 50 ml. of trimethylphosphite for one day. Cooling resulted in a quantitative yield of the debrominated product, m.p. 180-181°. A similar result was obtained when compound I was refluxed for two hours with a five-fold excess of trimethylphosphite in toluene.

When the last two experiments (E, F) were performed with compound V, a new product was isolated with a m.p. of 200-201°.

Anal. Calcd. for C₁₂H₉BrO₄: C, 48.51; H, 3.05; Br, 26.90. Found: C, 48.62; H, 2.78; Br, 27.10.

Synthesis of α -(2-Bromo-4,5-methylenedioxybenzylidene)- γ -butyrolactone by Aldol Condensation.

The condensation of 5 g. of 2-bromopiperonal with 3 g. of γ -butyrolactone was performed following a previously reported procedure (8). The product crystallized from methanol, forming white needles in 47% yield, m.p. 199-200°. The melting point of a mixture of this material with the above sample was 199-200°, indicating the identity of the two products. This finding was further confirmed by a comparison of their ultraviolet and infrared absorption spectra.

Acknowledgment.

The authors gratefully acknowledge the support of the U. S. Public Health Service through grant GM-08797 of the National Institutes of Health, Bethesda, Maryland.

REFERENCES

- (1) Part XIX of this series: Hans Zimmer, D. C. Armbruster and L. J. Trauth, *J. Heterocyclic Chem.*, 2, 171 (1965).
- (2) Taken in part from Ph.D. Thesis, University of Cincinnati, 1964.
- (3) Hans Zimmer and J. Rothe, *J. Org. Chem.*, 24, 100 (1959).
- (4) Hans Zimmer, R. Walter and D. Genge, *ibid.*, 29, 925 (1964).
- (5) H. Hoffman and H. J. Diehr, *Tetrahedron Letters*, 583 (1962).
- (6) Hans Zimmer and Gurdial Singh, *J. Org. Chem.*, 28, 483 (1963).
- (7) W. S. Abramow and S. Pall, *Trudy Kazan. Khim. Tekhnol. Inst. im. S. M. Kirova*, 23, 105 (1957); *Chem. Abstr.*, 52, 9949 (1958); S. Dershowitz and S. Proskauer, *J. Org. Chem.*, 26, 3595 (1961).
- (8) Hans Zimmer and J. Rothe, *ibid.*, 24, 28 (1959).

Received October 20, 1965

Cincinnati, Ohio 45221