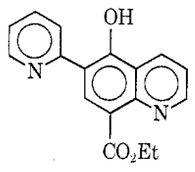
The unexpected introduction of a quinolyl group onto the acridine nucleus could have occurred in one of two ways: a second mole of quinoline 1-oxide reacts (i) with **2** to give intermediate **5** which ring closes to **4** or (ii) with **3** to yield **4**. The latter path appears unlikely in view of our failure to detect any reaction of quinoline 1-oxide with several representative phenols. Efforts to isolate either intermediate **2** or **5** have been fruitless.

Pyridine 1-oxide reacts in an analogous manner to afford 8-ethoxycarbonyl-6-(2′-pyridyl)-5-quinolinol (**6**),



6

although it could only be isolated from the reaction mixture as its fluoroborate salt and in very low yield.

Experimental Section[4]

4-Ethoxycarbonyl-2-(2′-quinolyl)-1-acridinol (**4**).—A mixture of 20 mmol of anhydrous quinoline 1-oxide, 20 mmol of diethyl glutaconate (Aldrich Chemical Co.), and 40 mmol of acetic anhydride was stirred at room temperature under nitrogen for 24 hr. The solid which formed was filtered off and recrystallized from chloroform–acetone to yield 2.37 g of very fine, orange needles, mp 204–205°. High-resolution mass spectrometry indicated the composition of the molecular ion (*m/e* 394) to be $C_{25}H_{18}N_2O_3$; ir (KBr) 3550 (OH) and 1735 cm^{-1} (C=O); nmr ($CDCl_3$) δ 1.43 (t, 3, CH_3), 4.38 (q, 2, OCH_2), 7.56–7.92 (m, 7), 8.13 (s, 1, 3-H), 8.17 (d, 1, J = 8 Hz, 3′-H), 8.55 (d, 1, J = 8 Hz, 4′-H), 8.86 (d, 1, J = 10 Hz, 5-H), 9.26 (s, 1, 9-H),[5] and 10.46 ppm (s, 1, OH); mass spectrum (60 eV) *m/e* 394 (100, M^+), 365 [96, $M^+ - (H + C_2H_4)$], and 128 (35, $C_9H_6N^+$); uv max ($CHCl_3$) 246 nm (log ϵ 4.52), 288 (4.23), and 438 (4.39).[6]

Anal. Calcd for $C_{25}H_{18}N_2O_3$: C, 76.13; H, 4.60; N, 7.10. Found: C, 76.15; H, 4.55; N, 7.04.

When the amounts of quinoline 1-oxide and acetic anhydride were doubled, the yield of **4** was increased to 4.52 g (57%).

8-Ethoxycarbonyl-6-(2′-pyridyl)-5-quinolinol (**6**).—Diethyl glutaconate (9.3 g, 0.050 mol) was added over a period of 30 min to a stirred, ice-cold solution of 9.5 g (0.10 mol) of anhydrous pyridine 1-oxide in 22.4 g (0.22 mol) of acetic anhydride under nitrogen. After the addition was complete, the mixture was allowed to warm to room temperature and stand overnight. Water (100 ml) was added and the water–acetic acid azeotrope was removed on a rotary evaporator until no acetic acid could be detected in the distillate. The reddish-black, viscous residue was triturated with water to remove any unreacted pyridine 1-oxide, taken up in 50 ml of ether, and then treated with 5% fluoroboric acid (to pH 3). The precipitate which formed was filtered off, washed successively with cold water and ether, and recrystallized twice from 80% aqueous ethanol to afford 0.72 g (4%) of yellowish-orange needles: mp 235–240° dec; ir (KBr) 3510 (OH), 1720 (C=O), and 1070 cm^{-1} (BF_4^-); nmr (DMSO-d_6) δ 1.44 (t, 3, CH_3), 4.38 (q, 2, OCH_2), 7.6–9.5 (m, 9), and 10.7 ppm (broad s, 1, OH).

Anal. Calcd for $C_{17}H_{15}BF_4N_2O_3$: C, 53.43; H, 3.96; N, 7.33. Found: C, 53.12; H, 3.59; N, 7.41.

Registry No.—**4**, 34918-49-5; **6**, 34903-57-6.

Acknowledgment.—Support for part of this work by a grant from the Marshall University Foundation is gratefully acknowledged.

(4) Melting points were determined on a calibrated Mel-Temp apparatus. Infrared spectra were recorded on a Perkin-Elmer 237 spectrophotometer, nmr spectra on a Varian A-60A spectrometer, and uv spectra on a Beckman DK spectrophotometer. The mass spectrum was kindly provided by the Union Carbide Technical Center, South Charleston, West Virginia.

(5) J. P. Kokko and J. H. Goldstein, *Spectrochim. Acta*, **19**, 1119 (1963).

(6) R. M. Acheson, "Acridines," Interscience, New York, N. Y., 1956, Chapter VII.

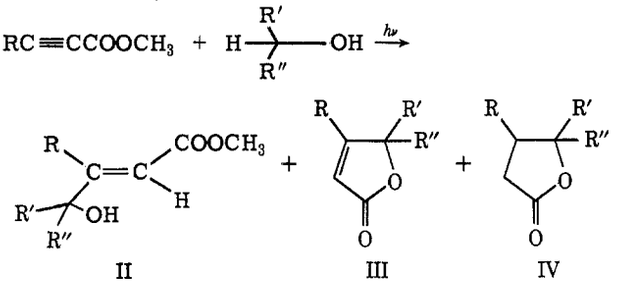
γ-Butyrolactones from the Irradiation of Unsaturated Esters in Alcohols

S. MAJETI

The Procter & Gamble Company, Miami Valley Laboratories, Cincinnati, Ohio 45239

Received November 29, 1971

In view of its intrinsic importance in natural product chemistry, γ-lactone synthesis has been a subject of several investigations. A photochemical method first explored by Schenck and coworkers[1] led to the synthesis of some γ-lactones which are not otherwise easily accessible.[2,3] It involves irradiation of an α,β-unsaturated acid in alcohol in the presence of a sensitizer. However, in many instances, particularly when primary alcohols are employed, this method gives poor yields of the lactones. More recently, direct irradiation of α,β-acetylenic esters I (R = CH_3, $COOCH_3$, or H) in alcohols has also been shown to yield γ-butyrolactones IV as secondary photolysis products, the primary products being the hydroxy esters II and the unsaturated lactones III.[4,5] The facility with which the adducts II and III are formed prompted us to investigate the possible synthesis of γ-butyrolactones by direct irradiation of olefinic esters.



Photochemical studies with olefinic esters have mainly been concerned with double bond migration *via* γ-hydrogen abstraction[6] and cycloaddition to olefins.[7] The purpose of this communication is to present some synthetic and mechanistic aspects of unsensitized addition of alcohols to olefinic esters.

Irradiation of dilute alcoholic solutions of the ester leads to disappearance of the latter and a concomitant formation of the corresponding lactone. The yields of the lactones were determined by vacuum distillation of the concentrated reaction mixtures (Table I).

The formation of γ-butyrolactones suggests that addition of the alcohol takes place across the double bond of the ester to give an open-chain γ-hydroxy ester which would readily cyclize to form the observed lactone.

(1) G. O. Schenck, G. Koltzenburg, and H. Grossman, *Angew. Chem.*, **69**, 177 (1957).

(2) R. Dulou, M. Vilkas, and M. Pfau, *C. R. Acad. Sci.*, **249**, 429 (1959).

(3) M. Pfau, R. Dulou, and M. Vilkas, *Bull. Soc. Chim. Fr.*, **34**, 3336 (1967).

(4) S. Majeti, Ph.D. Thesis, University of California, Los Angeles, 1969; *Diss. Abstr.*, **30**, 4977b (1970).

(5) B. Büchi and S. H. Feairheller, *J. Org. Chem.*, **34**, 609 (1969).

(6) R. R. Rando and W. v. E. Doering, *ibid.*, **33**, 1671 (1968); M. J. Jorgenson, *Chem. Commun.*, **137** (1965); P. J. Kropp and H. J. Krauss, *J. Org. Chem.*, **32**, 3222 (1967).

(7) A. Cox, P. DeMayo, and R. W. Yip, *J. Amer. Chem. Soc.*, **88**, 1043 (1966); P. DeMayo, S. T. Reid, and R. W. Yip, *Can. J. Chem.*, **42**, 2828 (1966).

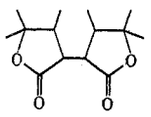
TABLE I

IRRADIATION OF UNSATURATED ESTERS IN ALCOHOLS[a]

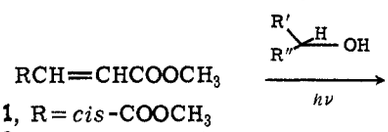
Starting ester	Alcohol	Time, hr	Unreacted ester, %	γ-Lactone, %[b]
1	2-Propanol	7	26	64
2	2-Propanol	14	38	70
3	2-Propanol	12	58	50[d]
1	Ethanol	10	40	68[c]
2	Ethanol	10	46	71[c]
3	Ethanol	15	68	59[c]

[a] No attempt was made to identify minor volatile products; however, they were taken into account in calculating yields. [b] Based on disappeared starting material. [c] Mixture of cis and trans isomers. [d] The high-boiling material obtained on irradiation of methyl crotonate in 2-propanol has been identified as a dilactone (**8**) *via* spectroscopic and analytical data.

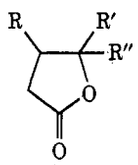
Since photolyses were carried out in the absence of a sensitizer, the addition reaction most probably took place after hydrogen abstraction from the solvent by the excited ester. Intermolecular hydrogen abstraction by



8



1, R = *cis*-$COOCH_3$
2, R = *trans*-$COOCH_3$
3, R = CH_3



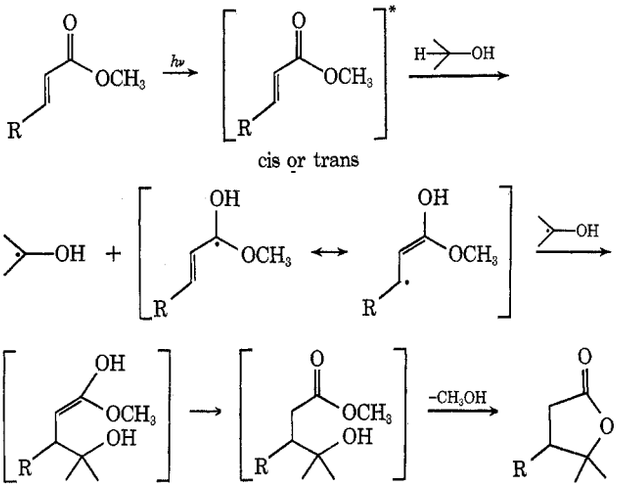
4, R = $COOCH_3$; R′ = R″ = CH_3
5, R = $COOCH_3$; R′ = CH_3; R″ = H
6, R = CH_3; R′ = R″ = CH_3
7, R = CH_3; R′ = CH_3; R″ = H

an excited olefinic ester has not yet been established, although products derived from such a reaction have been observed on several occasions.[3,7] Initial hydrogen abstraction by the excited ester carbonyl leads to α-hydroxyalkyl and allylic radicals, and coupling of the former to the β carbon of the latter followed by tautomerization gives rise to the γ-hydroxy ester, as shown in Scheme I. The hydrogen abstraction step involving the ester carbonyl group is consistent with a mechanism suggested for double bond migration to the β,γ position in the photolyses of α,β-unsaturated esters.[8,9]

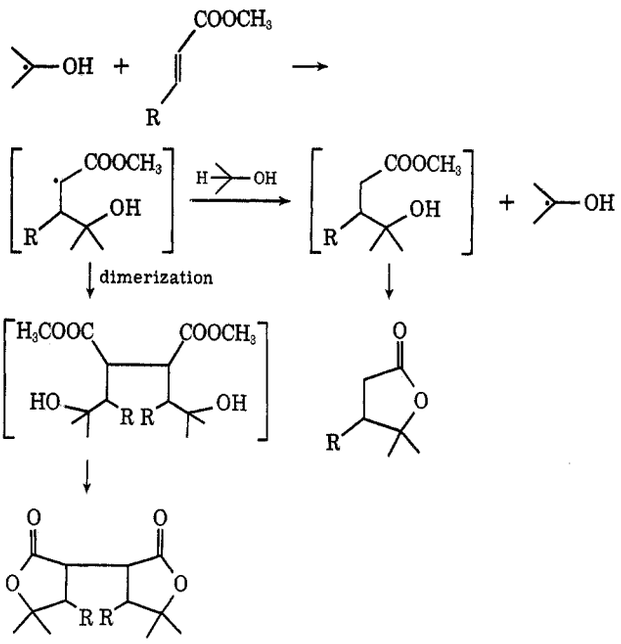
Alternatively, the α-hydroxyalkyl radical could add to the ester in its ground state, and H abstraction by the resulting radical would yield the product and simultaneously initiate chain reaction, as in the case of the benzophenone-sensitized reaction.[3] The isolation of dilactone **8** from the irradiation of methyl

(8) J. A. Barltrop and J. Wills, *Tetrahedron Lett.*, 4987 (1968).
(9) M. J. Jorgenson, *ibid.*, 4991 (1968).

SCHEME I



crotonate in 2-propanol provides support for the proposed radical sequence. However, in the absence of additional evidence it is not possible to ascertain the importance of the radical chain mechanism.



Experimental Section

General Irradiation Procedure.—Irradiations were conducted with 475-ml alcoholic solutions containing 30–50 mmol (5.0 g) of ester using a 450-W Hanovia medium-pressure mercury arc and a water-cooled Vycor immersion well. The solutions were stirred vigorously with a magnet and with a stream of argon introduced through a tube containing an opening at the bottom of the outer jacket. The irradiation mixtures were concentrated and vacuum distilled prior to glpc analysis and spectral characterization of individual components.

Methyl 2-(1-Hydroxy-1-methylethyl)succinate γ-Lactone (Methyl Terebate) (4).—Irradiation of 5.0 g of dimethyl maleate in 2-propanol gave 5.7 g of a pale yellow residue which upon distillation yielded 1.2 g of the starting ester, 3.3 g of the lactone **4**, bp 111–112° (0.2 mm), and 1.2 g of an undistilled dark residue. Similar irradiation of 5.0 g of dimethyl fumarate in 2-propanol provided after distillation 1.9 g of the starting ester, 2.8 g of lactone **4**, and 1.3 g of an undistilled residue. The lactone was

identified from its spectral data[10] and was confirmed by comparison with an authentic sample prepared by a known procedure:[1] ir 1790 (lactone C=O), 1750 (ester C=O), 1380 and 1370 cm^{-1} [$C(CH_3)_2$]; nmr δ 3.71 (s, 3, OCH_3), 2.71 (m, 3, CH_2 and CH), 1.55 (s, 3, γ-CH_3), and 1.25 (s, 3, γ-CH_3); mass spectrum *m/e* (rel intensity) 172 (1.7), 157 (48.0), 141 (9.0), 129 (32), 116 (13), 115 (39), 69 (20.5), and 55 (100.0).

4-Hydroxy-3,4-dimethylpentanoic Acid γ-Lactone (6).—Irradiation of 5.0 g of *trans*-methyl crotonate in 2-propanol provided 2.9 g of a mixture of methyl 3-butenoate and cis and trans crotonates, 1.1 g of the lactone **6**, bp 74–75° (0.8 mm), and 0.8 g of residue. Lactone **6** was identified from its spectral data and was confirmed by comparison with an authentic sample:[2] ir 1783 (C=O) and 1380 and 1370 cm^{-1} [$C(CH_3)_2$]; nmr δ 2.35 (m, 2, α-CH_2), 1.39 (s, 3, γ-CH_3), 1.21 (s, 3, γ-CH_3), and 1.05 (d, 3, β-CH_3, J = 7 Hz). The methine proton resonance was presumed to be submerged under the methyl resonances as a multiplet; mass spectrum *m/e* (rel intensity) 128 (51), 113 (60), 95 (13), 84 (17), 70 (17), 69 (37), and 59 (100). Crystallization of the residue from ether–petroleum ether (bp 30–60°) gave rise to 0.6 g of dilactone **8**, mp 161–162°, identified on the basis of its spectral data and mechanistic reasoning:[2] ir 1776 (C=O) and 1380 and 1370 cm^{-1} [$C(CH_3)_2$]; nmr δ 2.0–3.0 (m, 2, α and β-CH) 1.5 (s, 3, γ-CH_3), 1.28 (s, 3, γ-CH_3), and 1.02 (d, 3, β-CH_3, J = 6.5 Hz); mass spectrum *m/e* (rel intensity) 254 (12), 239 (55), 221 (7), 193 (5), 128 (32), 127 (12), 113 (55), 109 (17), 95 (20), 74 (17), 70 (32), 69 (30), and 59 (100).

Anal. Calcd for $C_{14}H_{22}O_4$: C, 66.11; H, 8.72. Found: C, 65.89; H, 8.62.

Methyl 2-(1-Hydroxyethyl)succinate γ-Lactone (γ-Methylparaconic Acid Methyl Ester) (5).—Dimethyl maleate (5.0 g) when irradiated in ethanol gave rise to 2.0 g of the starting material, 2.1 g of a mixture of cis and trans lactones (**5**) in 34:66 ratio, bp 94–98° (0.2 mm), and 1.0 g of residue. Similar irradiation of dimethyl fumarate yielded 2.3 g of the starting ester, 2.0 g of a mixture of cis and trans lactones **5** in 46:54 ratio, and 0.8 g of residue. The isomeric lactones were separated by glpc analysis and characterized *via* their spectral properties. Stereochemical assignment is only tentative as it is based on glpc retention times and nmr data: ir 1792 (lactone C=O) and 1754 cm^{-1} (ester C=O); nmr δ (cis) 4.6 (m, 1, OCH), 3.8 (s, 3, OCH_3), 2.3–3.0 (m, 3, CH and CH_2), and 1.5 (d, 3, γ-CH_3, J = 7 Hz), (trans) 4.8 (m, 1, OCH), 3.8 (s, 3, OCH_3), 2.3–3.0 (m, 3, CH and CH_2), 1.25 (d, 3, γ-CH_3, J = 7 Hz); mass spectrum *m/e* (rel intensity) 158 (3.8), 143 (10), 130 (19), 127 (22), 116 (32), 115 (26), 114 (49), 111 (6.0), 99 (27), 87 (27), 83 (25), 59 (23), and 55 (100); high-resolution mass data, parent ion, calcd, 158.0579; obsd, 158.0572; (M − 15) ion, calcd, 143.0344; obsd, 143.0343.

4-Hydroxy-3-methylpentanoic Acid γ-Lactone (7).—Irradiation of methyl crotonate (5.0 g) in ethanol gave 2.6 g of a mixture of methyl 3-butenoate and cis and trans crotonates, 0.8 g of a mixture of cis and trans γ-lactones in 50:50 ratio, bp 80–86° (5 mm), and 0.6 g of residue. The lactones were identified from their spectral data and from a comparison of nmr data with reported values:[11] ir 1783 cm^{-1} (C=O); nmr δ (cis) 4.15 (m, 1, OCH), 2–2.9 (m, 3, CH and CH_2), 1.4 (d, 3, γ-CH_3, J = 7 Hz), and 1.15 (d, 3, β-CH_3, J = 7 Hz); (trans) 4.6 (m, 1, OCH), 3.0–2.0 (m, 3, CH and CH_2), 1.25 (d, 3, γ-CH_3 J = 7 Hz), and 1.03 (d, 3, β-CH_3, J = 7 Hz); mass spectrum *m/e* (rel intensity) 114 (69), 99 (88), 86 (18), 71 (92), 70 (100), 56 (35), and 55 (95).

Registry No.—**4**, 6934-77-6; **5**, 35096-31-2; **6**, 2981-96-6; **7**, 6971-63-7; **8**, 35096-34-5.

Acknowledgment.—The author wishes to acknowledge stimulating discussions with Professor Christopher S. Foote of the University of California at Los Angeles, under whose guidance the initial work was performed.

(10) Infrared spectra were obtained in chloroform solution with a Perkin-Elmer infracord spectrophotometer. Nmr spectra were determined in $CDCl_3$ solution with a Varian HA-100 or T-60 spectrometer using tetramethylsilane as an internal standard. Gas chromatographic analyses were performed on an Aerograph 200 instrument using a 10 × 0.25 in. column packed with 20% SE-30 on 60/80 mesh Chromosorb W. Mass spectra were obtained on an Atlas CH-4 instrument.

(11) J. F. Laporte and R. Rambaud, *C. R. Acad. Sci., Ser. C*, 262, 1095 (1966).

Catalytic Reduction of Azlactones in Alkaline Media. Synthesis of Amino Acids

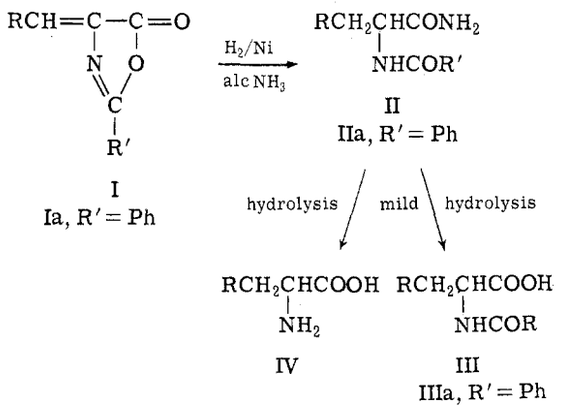
A. BADSHAH, NASEEM H. KHAN,* AND A. R. KIDWAI

Department of Chemistry, Aligarh Muslim University, Aligarh, India

Received June 23, 1971

There are three general methods, employing reduction and hydrolysis, for the conversion of azlactones to the corresponding acylamino acids or amino acids. Reduction can be effected with sodium or sodium amalgam in water or ethanol, with hydriodic acid and red phosphorus in acetic acid or acetic anhydride, or catalytically over Pt or Pd in the presence of hydrogen. Though most amino acids, excepting tryptophane, have been synthesized by treatment with hydriodic acid and red phosphorus, the method using sodium or amalgam is not of wide applicability.[1-3] Catalytic reduction has been less favored[4-7] owing, perhaps, to the high cost of Pt and Pd, which becomes a factor in large-scale laboratory preparations, and resistance of azlactones to hydrogenation, which required their initial hydrolysis to the unsaturated acylamino acids.

The present investigations in this direction were undertaken in order to devise a method which combines high yields with few experimental operations. Since catalytic hydrogenation has not received sufficient attention, an attempt has been made to improve this method and make it more economical for large-scale preparations by substituting nickel for the noble metal catalysts which, apart from being expensive, are sensitive to impurities. The sequence of reactions leading to the amino acids generally involves hydrolysis of azlactone to acylaminoacrylic acids, followed by catalytic reduction and finally hydrolysis to the amino acids. It was found that the first two steps could be combined by reductive hydrolysis of a suspension of azlactone (I) in alcoholic ammonia over Raney nickel at elevated hydrogen pressure and room temperature.



(1) H. Fischer and W. Zerweck, *Ber.*, **56**, 519 (1923).
(2) A. Sonn, E. Miller, W. Bulow, and W. Meyer, *ibid.*, **58**, 1103 (1925).
(3) F. Schaaf and A. Labouchers, *Helv. Chim. Acta*, **7**, 357 (1924).
(4) M. Bergmann, F. Stern, and C. Witte, *Justus Liebigs Ann. Chem.*, **449**, 277 (1926).
(5) H. E. Carter, P. Handler, and D. B. Melville, *J. Biol. Chem.*, **129**, 359 (1939).
(6) H. J. Harwood and T. B. Johnson, *J. Amer. Chem. Soc.*, **56**, 468 (1934).
(7) R. N. Herbst and D. Shemin, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 491.