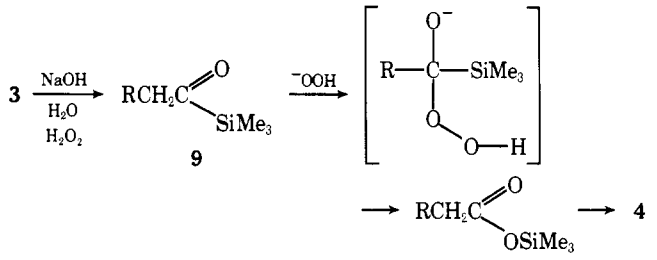


stituted acetic acids **4** can be envisioned to involve nucleophilic addition of hydroperoxide anion to **9** followed by a rearrangement of silicon to oxygen and loss of hydroxide.[15,16] This reaction scheme is consdnant with the observation that 4 equiv of hydrogen peroxide are required for complete oxidation of **3** to the acid **4** and cyclohexanol.[17] A more detailed mechanistic study of the oxidative conversion of **3** to **4** is currently in progress.

References and Notes

(1) This research was supported by the National Science Foundation through Grant CHE76-03738.
(2) T. F. Rutledge, "Acetylenic Compounds", Reinhold, New York, N.Y., 1968; H. G. Viehe, "Chemistry of Acetylenes", Marcel Dekker, New York, N.Y., 1969.
(3) Alternative methods for conversion of terminal alkynes into the corresponding carboxylic acids are: hydrolysis of chloroacetylenes with methanolic potassium hydroxide, M. Julia and J.-M. Surzur, *Bull. Soc. Chim. Fr.*, 1620 (1956); oxidation of 1,1-diborylalkanes with *m*-chloroperbenzoic acid, G. Zweifel and H. Arzoumanian, *J. Am. Chem. Soc.*, **89**, 291 (1967).
(4) R. B. Miller and T. Reichenbach, *Tetrahedron Lett.*, 543 (1974).
(5) K. Uchida, K. Utimoto, and H. Nozaki, *J. Org. Chem.*, **41**, 2941 (1976); G. Zweifel and S. J. Backlund, unpublished results.
(6) G. Zweifel, G. M. Clark, and N. L. Polston, *J. Am. Chem. Soc.*, **93**, 3395 (1971).
(7) H. C. Brown, "Organic Syntheses via Boranes", Wiley, New York, N.Y., 1975, p 210.
(8) Hydroboration of alken-1-ynyl(trimethyl)silanes containing a terminal monosubstituted double bond with an equimolar amount of a dialkylborane resulted in competing addition of boron to both the triple and double bonds.
(9) J. C. Aumiller and J. A. Whittle, *J. Org. Chem.*, **41**, 2959 (1976).
(10) Oxidation of the hydroboration product at 30–50 °C produced a 58:42 mixture of the corresponding β,γ- and α,β-unsaturated acids.
(11) It has been shown that treatment of β-trimethylsiloxy esters with aqueous ethanol produced, besides β-hydroxy esters, the corresponding isomerically pure trans-α,β-unsaturated esters: L. Birkhofer, A. Ritter, and H. Wieden, *Chem. Ber.*, **95**, 971 (1962).
(12) Applying the procedure to tertiary 3-hydroxy-1-alkynes has not yet afforded the corresponding substituted α,β-unsaturated acids in satisfactory yields.
(13) The reason for this behavior is unclear at present and is under further investigation.
(14) Through oxidation of **3** (R = *n*-C_4H_9) with 3 equiv of hydrogen peroxide it was indeed possible to isolate the acylsilane in modest yield.
(15) For rearrangements of α-hydroperoxysilanes, see: J. J. Eisch and G. R. Husk, *J. Org. Chem.*, **29**, 254 (1964).
(16) For an exceilent review on rearrangement reactions involving acylsilanes, see: A. G. Brook, *Acc. Chem. Res.*, **7**, 77 (1974).
(17) Treatment of acylsilanes with aqueous sodium hydroxide produces aldehydes.[16] Thus, it might be argued that the aldehydes are the precursors for the carboxylic acids obtained. However, treatment of *n*-hexanal with alkaline hydrogen peroxide under the experimental conditions used for the oxidation of 1-boryl-1-silyl-1-alkenes afforded only a small amount of *n*-hexanoic acid.

George Zweifel,* Stephen J. Backlund

Department of Chemistry, University of California, Davis
Davis, California 95616

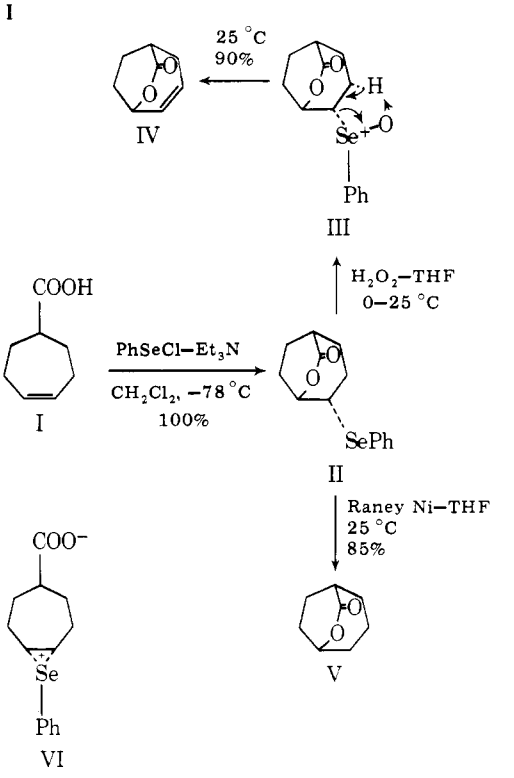
Received November 24, 1976

Phenylselenolactonization. An Extremely Mild and Synthetically Useful Cyclization Process

Sir:

The halolactonization reaction is a powerful process in synthetic organic chemistry for regio- and stereoselective functionalization of olefinic bonds.[1] Its application in the construction of natural and unnatural products has been amply demonstrated.[2] However, the usual requirement for aqueous, basic media and the rather drastic conditions required to convert the halolactones to useful synthetic intermediates impose severe limitations on this method. In addition, the incompatibility of a rather large number of important functionalities and protecting groups with halogens decreases the area of applicability of this conventional procedure. The necessity for a milder lactonization method for unsaturated carboxylic acids, coupled with the recent successful applications of selenium reagents in organic synthesis initiated by Sharpless[3] and Reich,[4] prompted us to investigate these reagents in connection with the above problem. Herein, we describe a new method for internal lactonization of unsaturated carboxylic acids employing phenylselenenyl halides[5] (PhSeCl, PhSeBr) which appears to be highly effective and can be carried out in organic media under very mild conditions and low temperatures.[6] This discovery represents one of the most facile and mild lactonization procedures that introduces, at the same time, into the molecule the phenylselenenyl moiety, a highly desirable group, on account of its recent and synthetically fertile chemistry.[3,4] This is the first of several important synthetic applications we have discovered for this mild cyclization procedure.

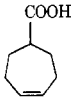
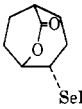
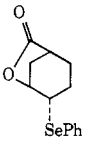
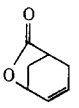
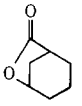
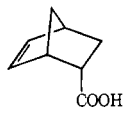
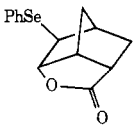
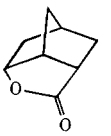
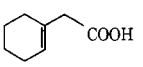
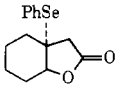
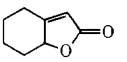
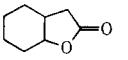
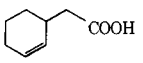
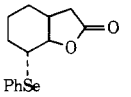
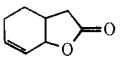
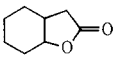
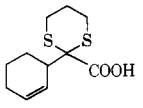
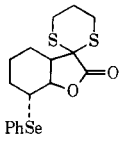
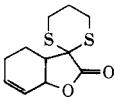
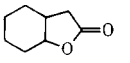
Scheme I



This process, termed *phenylselenolactonization,* is exemplified *in Scheme I.* Reaction of 4-cycloheptene-1-carboxylic acid (I)[11a] with PhSeCl[7] at −78 °C in dry methylene chloride in the presence of triethylamine proceeds rapidly and quantitatively to afford the phenylselenolactone II.[8] The reaction proceeds equally well in the presence of pyridine, *or even in the absence of a base.*[9] The selenolactone II is cleanly converted to the saturated lactone V (85%) by Raney nickel[10] in tetrahydrofuran (THF) at 25 °C or to the unsaturated lactone IV (90%) by exposure to hydrogen peroxide (THF, 0–25 °C) via the selenoxide III.[3,4] The exclusive syn elimination away from the lactone oxygen in III is in accord with previous observations[3] and provides an excellent route to these important synthons.

A series of unsaturated carboxylic acids[11a-f] was utilized for the lactonization studies as shown in Table I. These sub-

Table I. Phenylselenolactonization and Useful Transformations of Phenylselenolactones

Entry	Unsaturated acid	Ref	Phenylseleno-lactone	Yield (%)	Unsaturated lactone	Yield (%)	Saturated lactone	Yield (%)
1		11a		100		90		85
2		11b		90		81		80
3		11c		95	a			83
4		11d		91		87		84
5		11e		93		92		76
6		11f		98		82		73

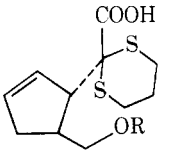
[a] The elimination of the corresponding selenoxide has not been studied in detail yet.

stances were subjected to the phenylselenolactonization reaction to produce a series of phenylselenolactones which were transformed smoothly to the saturated and unsaturated lactones shown, by reduction and oxidation–elimination, respectively. As indicated in Table I, good to excellent yields were obtained for this series of intermediates.[8]

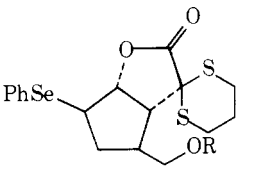
The cyclization presumably proceeds via a dipolar intermediate such as VI (Scheme I) or a closely related equivalent,[12] which ring-closes by an internal nucleophilic attack to the phenylselenolactone. The ring closure is expected to proceed at the carbon able to sustain the most stable carbonium ion, although isomerization of the initial product to the thermodynamically most stable lactone could occur, in principle, during the reaction or during the isolation of the product.[13] Stereochemistry is tentatively assigned on mechanistic grounds.

The following experimental procedure illustrates the ease by which the transformations referred to in Table I are carried out. Triethylamine (1.01 g; 10 mmol) was added to a solution of 4-cycloheptene-1-carboxylic acid (I)[11a] (1.40 g; 10 mmol) in dry methylene chloride (100 mL) at 25 °C and the mixture stirred for 30 min, cooled to −78 °C, and treated slowly with PhSeCl (2.11 g; 11 mmol) (30 min addition time and 30 min further stirring) under argon. Warming to room temperature followed by column chromatography (silica gel; methylene chloride; R_f 0.14) afforded pure selenolactone II (2.95 g; 100%) as a colorless crystalline solid, mp 71–71.5 °C (hexane): IR (KBr) ν_{max} 1735 cm^{-1} (δ-lactone); NMR (220 MHz, $CDCl_3$) τ 2.35 (m, 2 H, aromatic), 2.55 (m, 3 H, aromatic), 5.33 (m, 1 H, proton adjacent to oxygen), 6.37 (m, 1 H, proton adjacent to selenium), 7.14 (m, 1 H, proton adjacent to carbonyl) 7.66–8.24 (m, 8 H, CH_2); mass spectrum *m/e* 298, 296 (base peak), 294, 293, 292, 290 (ratio, 11:57:27:9:10:1; parent, characteristic family of peaks for Se due to natural isotopic abundance). Treatment of selenolactone II (1.475 g; 5 mmol) in THF (25 mL) with 30% hydrogen peroxide (0.70 mL; 7.5 mmol) initially at 0 °C (1 h) and subsequently at 25 °C (15 h) under argon, afforded after the usual workup[3,4] and chromatography, the unsaturated lactone IV[8] (640 mg; 90%). Reduction of II (1.475 g; 5 mmol) with Raney nickel[10] (5 g) in THF (50 mL) was complete in 1 h at 25 °C to furnish, after removal of the catalyst and chromatography, the saturated lactone V[8] (595 mg; 85%).

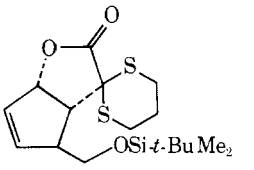
To demonstrate the value of this novel cyclization process in sensitive cases and its potential applicability in the construction of complex natural products, the highly functionalized cyclopentene carboxylic acids VII and VIII were synthesized[14] and subjected to the phenylselenolactonization reaction, affording the phenylselenolactones IX[8] and X[8] in 92 and 90% yield, respectively. These examples clearly illustrate



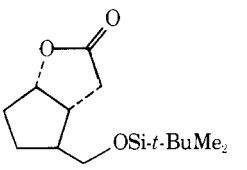
VII, R = Si-*t*-$BuMe_2$
VIII, R = THP



IX, R = Si-*t*-$BuMe_2$
X, R = THP



XI



XII

the compatibility of our reaction with very important protecting groups (i.e., dithiane,[15] tetrahydropyran, and silyl ethers[16]) commonly used in organic synthesis. Selective oxidation of the phenylselenenyl group followed by syn elimination to the olefin XI[8] was achieved (86%) using hydrogen peroxide (1.5 equiv) in THF, whereas, reduction with Raney nickel[10] (THF, 25 °C) removed both the phenylselenenyl and

the dithiane moieties, furnishing the γ-lactone XII[8] (70%). Compounds IX–XII represent excellent synthetic intermediates for construction of important, biologically active molecules, namely, prostaglandin A_2 and brefeldin A,[17] and investigations directed toward these goals are currently in progress in our laboratories.

The introduction of selenium reagents as initiators to induce ring closures offers promising avenues for forming heterocycles of various sizes. We are currently engaged in examining the mechanistic and stereochemical aspects of this reaction as well as exploring the synthetic utility of this process in the construction of β-lactones[13,18] and macrocyclic lactones.[19,20]

Acknowledgments. We wish to express our deep gratitude and appreciation to Professor Madeleine M. Joullié for helpful discussions and support during this investigation. We are indebted to Dr. Fred L. De Roos for mass spectra. This research was supported by the University of Pennsylvania.

References and Notes

(1) For a discussion of this reaction see: (a) H. O. House, "Modern Synthetic Reactions", 2nd ed., W. A. Benjamin, Calif., 1972, p 441, and references cited therein; (b) W. E. Barnett and L. L. Needham, *J. Org. Chem.*, **40,** 2843 (1975).

(2) (a) For a number of elegant applications of the halolactonization reaction in the synthesis of prostaglandins see: E. J. Corey, T. K. Schaaf, W. Huber, U. Koelliker, and N. M. Weinshenker, *J. Am. Chem. Soc.*, **92,** 397 (1970); E. J. Corey, U. Koelliker, and J. Neuffer, *ibid.*, **93,** 1489 (1971); E. J. Corey, T. Ravindranathan, and S. Terashima, *ibid.*, **93,** 4326 (1971); E. J. Corey and G. Moinet, *ibid.*, **95,** 6831 (1973); E. J. Corey and J. Mann, *ibid.*, **95,** 6832 (1973); (b) for another type of related lactonizations see T. Tokoroyama, K. Matsuo, R. Kanazawa, H. Kotsuki, and T. Kubota, *Tetrahedron Lett.*, 3093 (1974).

(3) (a) K. B. Sharpless and R. F. Lauer, *J. Am. Chem. Soc.*, **95,** 2697 (1973); (b) K. B. Sharpless, R. F. Lauer, and A. Y. Teranishi, *ibid.*, **95,** 6137 (1973); (c) K. B. Sharpless, and K. M. Gordon, R. F. Lauer, D. W. Patrick, S. P. Singer, M. W. Young, *Chem. Scr.*, **8A,** 9 (1975), and references cited therein.

(4) (a) H. J. Reich, I. L. Reich, and J. M. Renga, *J. Am. Chem. Soc.*, **95,** 5813 (1973); (b) H. J. Reich and S. K. Shah, *ibid.*, **97,** 3250 (1975); (c) H. J. Reich, J. M. Renga, and I. L. Reich, *ibid.*, **97,** 5437 (1975), and references cited therein.

(5) Phenylsulfenyl chloride also reacts with certain unsaturated carboxylic acids in a similar manner: K. C. Nicolaou and Z. Lysenko, *J. Chem. Soc., Chem. Commun.*, in press.

(6) (a) For related ring closures effected by arylselenenyl bromides under synthetically unattractive conditions (refluxing acetic acid) see M. D. M. Campos and N. Petragnani, *Chem. Ber.*, **93,** 317 (1960). (b) Electrophilic additions of phenylselenenyl derivatives to olefins have been reported: H. Reich, *J. Org. Chem.*, **39,** 428 (1974); K. B. Sharpless and R. F. Lauer, *ibid.*, **39,** 429 (1974); D. L. J. Clive, *J. Chem. Soc. Chem. Commun.*, 695 (1973); 100 (1974).

(7) The commercially available PhSeCl is the preferred reagent. PhSeBr, which can be prepared from PhSeSePh and Br_2, reacts similarly.

(8) All new compounds were characterized by full spectroscopic and analytical data. The properties of known compounds were also in agreement with their structures and compared well with the literature data.

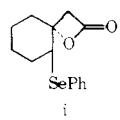
(9) Triethylamine was routinely used to neutralize the liberated hydrogen chloride. However, it is important to preform the salt of the acid before adding the PhSeCl, since this reagent reacts with free triethylamine, see N. Petragnani and M. D. M. Campos, *Tetrahedron*, **21,** 13 (1965).

(10) This catalyst was prepared at 75 °C according to L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, Wiley, New York, N.Y., 1967, p 729.

(11) (a) G. Stork and H. D. Landesman, *J. Am. Chem. Soc.*, **78,** 5129 (1956). (b) Prepared from 3-cyclohexene-1-carboxaldehyde by Jones oxidation. (c) Prepared from an endo–exo mixture by iodolactonization followed by regeneration of the endo acid from the pure iodolactone with zinc in acetic acid. (d) J. Klein, *J. Am. Chem. Soc.*, **81,** 3611 (1959). We are indebted to Professor A. B. Smith, III, for a generous gift of this compound. (e) H. O. House, R. G. Carlson, and H. Babad, *J. Org. Chem.*, **28,** 3359 (1963). (f) Prepared from 3-bromocyclohexene by new methodology which will be reported shortly.

(12) See (a) W. H. Mueller and P. E. Butler, *J. Am. Chem. Soc.*, **90,** 2079 (1968); (b) G. H. Schmid and D. G. Garratt, *Tetrahedron Lett.*, 3991 (1975); (c) ref 1 and 2.

(13) Preliminary observations indicate that the initial product in entry 4 is the spiro β-lactone i (IR, ν_{max} 1820 cm^{-1}) which subsequently rearranges to the γ-lactone (IR, ν_{max} 1765 cm^{-1}).



i

(14) Efficient syntheses of these cyclopentene acids have been developed from cyclopentadiene. These steps will be reported together with the complete sequences leading to the final products in due course.

(15) For the importance of this moiety in organic synthesis see D. Seebach and E. J. Corey, *J. Org. Chem.*, **40,** 231 (1975), and references cited therein.

(16) See E. J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, **94,** 6190 (1972), and references cited therein.

(17) For structure see H. P. Weber, D. Hauser, and H. P. Sigg, *Helv. Chim. Acta*, **54,** 2763 (1971); for partial synthesis see E. J. Corey, K. C. Nicolaou, and L. S. Melvin, Jr., *J. Am. Chem. Soc.*, **97,** 654 (1975). For total synthesis see E. J. Corey and R. H. Wollenberg, *Tetrahedron Lett.*, 4705 (1976).

(18) For recent reports on β-lactone synthesis and reactions see (a) S. Masamune, Y. Hayase, W. K. Chan, and R. L. Sobczak, *J. Am. Chem. Soc.*, **98,** 7874 (1976); (b) W. Adam, J. Baeza, and J-C Liu, *ibid.*, **94,** 2000 (1972); (c) G. W. Holbert, L. B. Weiss, and B. Ganem, *Tetrahedron Lett.*, 4435 (1976).

(19) For a review on the synthesis of Macrolides see K. C. Nicolaou, *Tetrahedron Report*, in press.

(20) For the use of PhSeCl is the synthesis of: (a) cyclic ethers see K. C. Nicolaou and Z. Lysenko, *Tetrahedron Lett.*, in press; (b) (4*E*)-isoprostacyclin see K. C. Nicolaou and W. Barnette, *J. Chem. Soc., Chem. Commun.*, in press.

K. C. Nicolaou,* Zenon Lysenko

Department of Chemistry, University of Pennsylvania
Philadelphia, Pennsylvania 19174

Received December 17, 1976

Excited State Proton Transfer of a Metal Complex: Determination of the Acid Dissociation Constant for a Metal-to-Ligand Charge Transfer State of a Ruthenium(II) Complex

Sir:

We wish to report the first observation of protonation of an electronic excited state of a metal complex without excited state deactivation. This allows the first direct determination of the pK_a of an electronic excited metal complex (pK_a*). Such studies have been carried out for a number of organic molecules,[1] but there is a conspicuous absence of such information for excited transition element complexes. In view of the strong current interest in the chemistry of metal-to-ligand charge transfer (MLCT) excited complexes and the availability of a number of such systems with excited state lifetimes long enough for proton transfer equilibria to be established prior to electronic deactivation,[2-8] pK_a* measurements for these systems deserve particular attention. Values of pK_a* for MLCT states have been estimated[9,10] from absorption measurements but are subject to question for reasons cited below.

One candidate for study is the complex Ru (2,2′-bipyridine)$_2$(2,2′-bipyridine-4,4′-dicarboxylic acid)$^{2+}$, whose diester derivatives have recently been reported to photoassist decomposition of water, presumably be means of photoinduced electron transfer from a MLCT excited state.[11] The parent Ru(2,2′-bpy)$_3^{2+}$ species and a variety of related Ru(II) complexes have been extensively investigated and the results indicate MLCT character for the lowest (luminescent) excited state.[2] The close similarity in the electronic absorption and emission spectra of Ru(2,2′-bpy)$_3^{2+}$, its dicarboxylic acid, and diester derivatives suggests the MLCT assignment for the lowest excited state in the latter complexes.

We have investigated[12] the excited state proton transfer equilibrium involving the carboxylic acid derivative and can now add proton transfer to the known intermolecular processes of excited Ru(II) complexes, which to date have only included electron transfer and energy transfer.[13] The equilibrium measured is indicated in eq 1. The ground state pK_a, pK_a^0, can be determined by spectrophotometric titration, i.e., by measurements of the absorption spectra as a function of pH in aqueous solution, Figure 1. The spectral changes are completely reversible. Isosbestic points are preserved over the entire pH excursion, evidencing that both –COOH groups have ap-