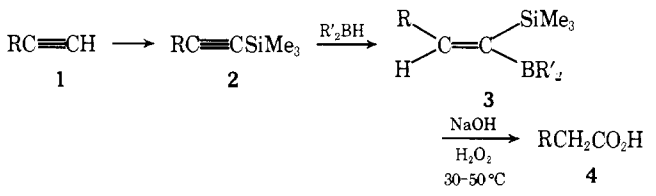
Novel Syntheses of Monosubstituted Acetic, α,β-Unsaturated, and β,γ-Unsaturated Acids via Silylation, Hydroboration, and Oxidation of the Ethynyl Group of 1-Alkynes and Functionally Substituted 1-Alkynes[1]

Sir:

The ethynyl moiety is an exceedingly versatile group for numerous chemical transformations. Thus, it is readily introduced onto a variety of organic substrates via ethynylation or coupling reactions,[2] and provides a reactive site for manifold further modifications. We now wish to disclose that the ethynyl group of 1-alkynes, alk-3-en-1-ynes, and 3-hydroxy-1-alkynes embodies the carboxyl group, which can be unmasked via the transformations **1** → **4** to afford substituted acetic acids, β,γ-unsaturated acids, and α,β-unsaturated acids, respectively.[3]

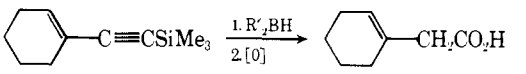


1 2 3 4

The monohydroboration of 1-alkynyl(trimethyl)silanes (**2**) with dicyclohexylborane proceeds in a stereo-[4] and regioselective[5] manner, placing the boron nearly exclusively at the silicon bearing carbon regardless of the steric requirements of the alkyl substituent attached at the β-carbon. Oxidation of the resultant 1-boryl-1-silylalkenes (**3**) with aqueous sodium hydroxide and 5 equiv of 30% hydrogen peroxide (1 equiv excess) produces the carboxylic acids **4** in greater than 80% yields along with the easily separable by-product cyclohexanol. Thus, the hydroboration-oxidation of **2** provides an operationally simple, high-yield procedure for preparing alkanoic acids.

It is important to note that the alkynylsilane precursors **2** do not need to be isolated prior to hydroboration. For example, 1-hexyne (20 mmol) in tetrahydrofuran (10 mL) was treated successively at −70 °C with butyllithium (20 mmol) in *n*-hexane and chlorotrimethylsilane (20 mmol). The reaction mixture was stirred at 25 °C for 1 h, and the resultant 1-hexynyl(trimethyl)silane was transferred into a second flask containing a suspension of dicyclohexylborane (22 mmol)[6] in tetrahydrofuran by means of the double-ended needle technique.[7] The temperature during the addition was maintained at 0–5 °C. The reaction mixture was allowed to exotherm to room temperature, where it was stirred for an additional hour. The homogeneous mixture formed was diluted with methanol (10 mL), then oxidized at 30–50 °C with 3 N sodium hydroxide (10 mL) and 30% hydrogen peroxide (10 mL). After stirring the mixture at ambient temperature for 30 min, an additional 10 mL of 3 N sodium hydroxide was added. The cyclohexanol formed was separated from the sodium hexanoate by extraction with ether. Acidification of the aqueous phase with hydrochloric acid followed by extraction with ether yielded 83% of *n*-hexanoic acid.

An important feature of the present method for conversion of the ethynyl group into an acetic acid derivative is the fact that it also can be applied to a variety of 3-alken-1-ynes to produce β,γ-unsaturated acids. This occurs as a result of the high selectivity of dialkylboranes for addition to the ethynylsilyl moiety without affecting the enyne double bond,[8] and is exemplified by the conversion of **5** into the corresponding β,γ-unsaturated acid **6** in 83% yield. Also, under the proper oxi-



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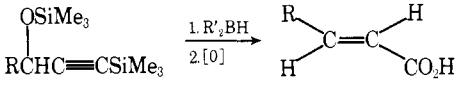
dation conditions, the method does not suffer from a major problem encountered in the preparation of γ-unsubstituted β,γ-unsaturated acids of equilibration of their salts to give mixtures of the α,β- and β,γ-unsaturated isomers.[9] Thus, monohydroboration of 3-methylbut-3-en-1-ynyl(trimethyl) silane followed by oxidation with alkaline hydrogen peroxide at 0 °C for 30 min afforded 3-methyl-3-butenoic acid containing only 6% of the α,β-unsaturated acid.[10]

If, on the other hand, preparation of isomerically pure α,β-unsaturated acids is desired, this can be accomplished using the sequence **1** → **4** starting with the silyl derivatives **7** derived from 3-hydroxy-1-alkynes. These yielded, after hydroboration-oxidation, trans-α,β-unsaturated acids **8**.[11] Hence, this procedure, which uses readily available precursors, provides an alternative to the Reformatsky and phosphonate syntheses of these acids.[12] However, it should be pointed out that isolation of **7** prior to hydroboration is necessary for achieving high yields of the unsaturated acids.[13]



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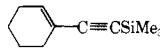
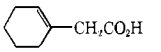
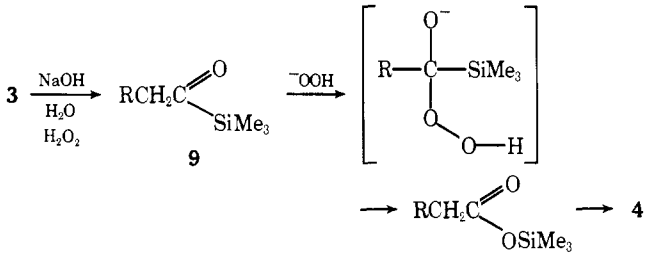
A summary of the yields of carboxylic acids obtained from 1-alkynes and functionally substituted 1-alkynes using our procedure is presented in Table I.

Finally, although our primary aim in the present work was to explore the synthetic aspects of this novel reaction sequence, the results obtained are also of considerable interest in that they indicate that oxidation of the 1-boryl-1-silyl-1-alkenes **3** with alkaline hydrogen peroxide proceeds first via formation of acylsilane intermediates **9**.[14] The conversion of these to sub-

Table I. Yields of Carboxylic Acids Derived from Alkynylsilanes

Alkynylsilane	Method[a]	Carboxylic acid product[b]	Isolated yield, %
n-$C_4H_9C{\equiv}CSiMe_3$	A	n-$C_4H_9CH_2CO_2H$	89
	B		83
t-$C_4H_9C{\equiv}CSiMe_3$	A	t-$C_4H_9CH_2CO_2H$	84
$C_6H_5C{\equiv}CSiMe_3$	A	$C_6H_5CH_2CO_2H$	91
	A		83
	B		84
$CH_2{=}C(CH_3)C{\equiv}CSiMe_3$	B	$H_2C{=}C(CH_3)CH_2CO_2H$	64[c,d]
n-$C_3H_7CH{=}CHC{\equiv}CSiMe_3$[e]	B	n-$C_3H_7CH{=}CHCH_2CO_2H$	68[c,f]
$CH_3(CH_2)_2CH(OSiMe_3)C{\equiv}CSiMe_3$	A	(E)-$CH_3(CH_2)_2CH{=}CHCO_2H$	70[g]
$CH_3(CH_2)_3CH(OSiMe_3)C{\equiv}CSiMe_3$	A	(E)-$CH_3(CH_2)_3CH{=}CHCO_2H$	82[g]

[a] A = Utilization of pure alkynylsilanes. B = Utilization of in situ prepared alkynylsilanes. [b] The physical constants of the acids agreed with those reported in the literature. Also, the NMR spectra were consistent with the proposed structures. [c] Utilization of a stoichiometric amount of dicyclohexylborane. [d] The oxidation was carried out at 0 °C. The product contained 6% of the α,β-unsaturated isomer. [e] A cis–trans mixture of the enyne was used. [f] The product contained 4% of the corresponding α,β-unsaturated acid. [g] The oxidation was carried out at 25 °C.



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 consonant 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 excellent 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.

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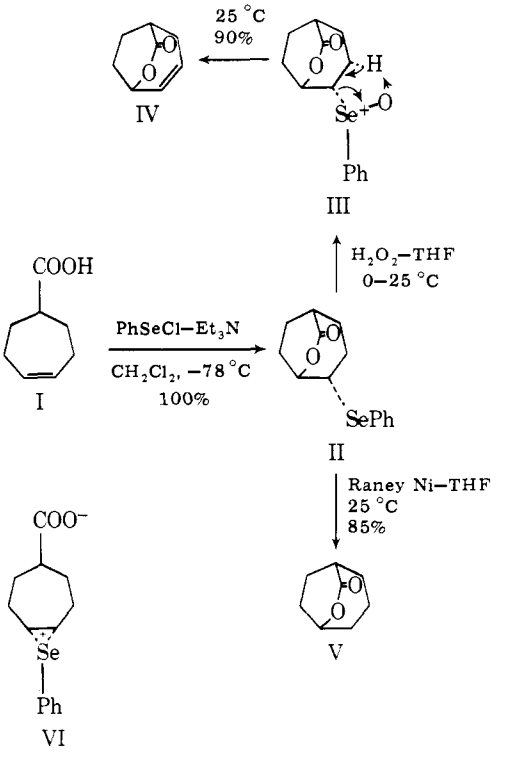
Received November 24, 1976

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-