(3) E. A. Robbins and P. D. Boyer, *J. Biol. Chem.*, **244**, 121 (1957).
(4) The free energy of hydrolysis of phosphate esters to phosphate is taken as a measure of their phosphorylating ability. Pertinent values are ($-\Delta G°$, pH 7, kcal/mol): phosphoenol pyruvate, 14.8; carbamylphosphate, 12.3; AcP, 10.3; CP, 10.3; pyrophosphate, 8.0; ATP, 7.3; glucose 6-phosphate, 3.3 (W. P. Jencks, p J181 in ref 5).
(5) G. D. Fasman, Ed., "Handbook of Biochemistry and Molecular Biology", Chemical Rubber Publishing Co., Cleveland, Ohio, 1976.
(6) The potential of several of the systems proposed for ATP regeneration in driving thermodynamically unfavorable equilibria is discussed by R. S. Langer, B. K. Hamilton, C. R. Gardner, M. C. Archer, and C. K. Colton, *AIChE J.*, **22**, 1079 (1976).
(7) S. A. Kurdy and E. A. Noltman in "The Enzymes", 3rd ed, Vol. VIII, P. Boyer, Ed., Academic Press, New York, N.Y., 1970, pp 412–431.
(8) R. S. Langer, C. R. Gardner, B. K. Hamilton, and C. K. Colton, *AIChE J.*, **23**, 1 (1977) and references cited therein.
(9) No correction was made for the influence of ethylene glycol on the measured pH: cf, P. Maurel, G. Hui Bon Hoa, and P. Douzou, *J. Biol. Chem.*, **250**, 1376 (1975).
(10) The limiting solubility of C·H_2O in water is ~13 g L^{-1} = 110 mM: R. M. C. Dawson et al., Ed., "Data for Biochemical Research", Oxford University Press, London 1969, p 16. The presence of an excess of suspended creatine in the mixture assured that the solution was saturated, and had no apparent ill effects on the reaction. The Michaelis constants for CK are (mM) = 0.4 (MgATP), 0.14 (MgADP), 110 (C), and 3.3 (CP).[7]
(11) Enzymes, obtained from Sigma and used without purification, had specific activities (μmol min^{-1} mg^{-1}): AcK 300 U (following treatment with DTT); CK 2.5 U (defined for C → CP, pH 9.0, 25 °C). Immobilization yields were 48% for CK, and 55% for AcK. Enzyme immobilization was carried out as described by A. Pollak, R. L. Baughn, O. Adalsteinsson, and G. M. Whitesides, *J. Am. Chem. Soc.*, in press.
(12) G. M. Whitesides, M. Siegel, and P. Garrett, *J. Org. Chem.*, **40**, 2516 (1975). The AcP used was 70–80% pure, with NH_4Ac, $(NH_4)_3PO_4$, and CH_3CONH_2 as the principal impurities. The solution was maintained at 0 °C before addition to minimize hydrolysis.
(13) H. U. Bergmeyer, Ed., "Methods of Enzymatic Analysis", 2nd ed, Academic Press, New York, N.Y., 1974, p 1777.
(14) Qualitative examination indicated hydrolysis rates of ~4% h^{-1} for AcP and 0.17% h^{-1} for CP under the conditions used for the enzymatic synthesis.

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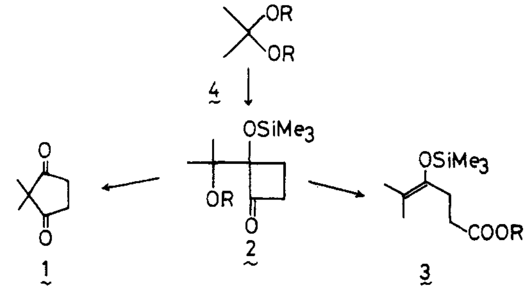
A Novel Ring-Opening Reaction. An Improved Method for Reductive Succinoylation

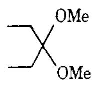
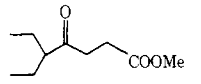
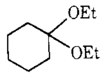
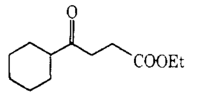
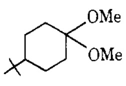
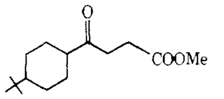
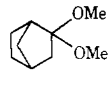
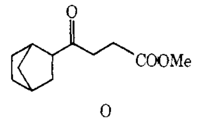
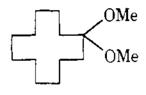
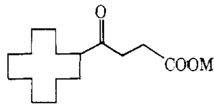
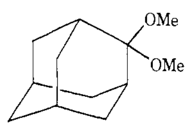
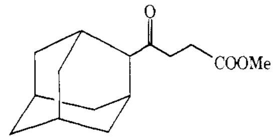
Summary: In the presence of stannic chloride, 1,2-bis(trimethylsiloxy)-1-cyclobutene and a ketal undergo two successive reactions, aldol and a new ring cleavage reaction, to give an enol silyl ether of γ-keto ester: the overall reaction represents a new, single-pot reductive succinoylation method.

Sir: We recently reported a synthetic method for the construction of five-membered ring **1** onto carbonyl groupings: the reaction consists of treating pinacol **2** with protic acid to induce ring enlargement.[1] We have now found that certain Lewis acids bring about a novel and quantitative cleavage of the cyclobutanone ring of **2** to form **3**. The primary purpose of this communication is to show the synthetic utility of this reaction, which constitutes a new approach to reductive succinoylation of a ketone function.[1]



1,2-Bis(trimethylsiloxy)-1-cyclobutene (**4**) undergoes aldol-type addition with ketals under the influence of BF_3·Et_2O to afford **2** in excellent yields,[1] yet in the presence of some Lewis acids ($AlCl_3$, $TiCl_4$, $SnCl_4$, $SbCl_5$) **2** is reactive enough to transform into **3**. Subsequently, $SnCl_4$ proved especially effectual, realizing both the initial aldol reaction of **4** and the ring cleavage of **2** in a single step. For instance, 50 mol % of $SnCl_4$ effected the reaction with cyclohexanone diethyl acetal, affording pure **5** in 86% yield after distillation.

Table I. Reductive Succinoylation Method[a]

Ketal	Product	% yield[b]
		87
	 8	93
		92
		90[c]
		91
		68[d]

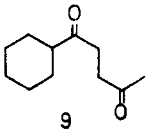
[a] Reactions (1.5–30 mmol) were carried out with a reactant ratio: ketal/4/$SnCl_4$ = 1:1:0.3–1. Reaction conditions are essentially the same as those of the typical example. [b] Yield of the pure isolated product. [c] 1.24 equiv of 4 was used. [d] An appreciable amount of adamantanone was recovered.

5 R = H, R' = Et
6 R = t-Bu, R' = Me
7

It is essential for the isolation of pure enol silyl ether to treat the reaction mixture with triethylamine followed by hexane (for dilution) before aqueous workup. Preparation of **6** and **7** was similarly accomplished in 84 and 80% yield, respectively.[2] The experimental procedure for **5** is illustrative. To a solution of $SnCl_4$ (0.3 mL, ~3 mmol) in 3 mL of methylene chloride at −78 °C was added during 10 s a mixture of cyclohexanone diethyl acetal (864 mg, 5.02 mmol) and **4** (1.163 g, 5.06 mmol) in 2 mL of methylene chloride. After 5 min, the pale yellow solution was warmed to −40 °C and stirred for an additional 10 min. Triethylamine (2.5 mL) and then 20 mL of hexane were added. The organic layer was separated from tarry material and washed successively with 1 N HCl, saturated NaCl, saturated $NaHCO_3$, and finally with saturated NaCl. The crude product (1.256 g) was distilled to give 1.215 g of silyl ether **5** (86%).[3]

Bifunctional compound **3** is a useful synthetic intermediate. First, the enol silyl ether moiety can react with various electrophiles. Hydrolysis is achieved simply by quenching the reaction mixture with water. Distillation usually gives an *analytically pure* product. Thus, the present reaction provides a simple, high-yield procedure for reductive succinoylation of the ketone functionality, which has been performed in lower yield through multiple steps.[1] In addition, the reaction conditions are definitely milder than those required in the former procedure. Results are summarized in Table I.[4]

The potential of γ-keto ester for further transformation is notable: 1,4-diketone **9** was prepared in 67% overall yield



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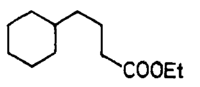

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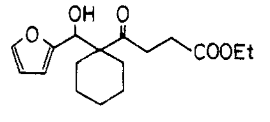
(thiacetalization, OH^-, MeLi, and $CuCl_2$/CuO), and ester **10** was obtained by hydrogenolysis of the ketone function (thioacetalization and W-2 Raney nickel) in 74% yield starting from keto ester **8**.

Carbon electrophiles also react with **3**. Of two possible approaches, one involves specific activation of enol silyl ether to form an enolate species without affecting the neighboring ester group. Quaternary ammonium fluoride allowed such reaction to occur.[5] Treatment of silyl ether **5** and furfural (1 equiv) with tetrabutylammonium fluoride[6] (30 mol %) at low temperature gave pure aldol **11** in 69% yield after chromatographic purification. We were unable to detect any regioisomer or lactone which might be formed by intramolecular O-acylation reaction of the enolate species.



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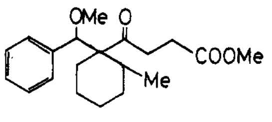
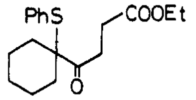


12

Another methodology is to trap the enol silyl ether by a Lewis acid activated carbonyl carbon.[7] On such occasions, further reaction of **3** may be best carried out in situ. Thus, the coupling of three components, 2-methylcyclohexanone, succinate moiety, and benzaldehyde acetal was quickly achieved without isolating any intermediates. The isolated yield of **12** was 70%. Two procedures descrbed here represent new entries to the conversion of C–O bonds of the carbonyl group to two C–C bonds, namely, geminal alkylation.[8]

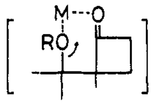
Regiospecific introduction of a heteroatom to **3** is also possible.[9] Addition of phenylsulfenyl chloride[10] to **5** prepared in situ gave **13** in 78% yield (from acetal).



13

Comparison of **2** and **3** reveals that the ketone group of the ring cleavage product is "masked"in **2**, and thereby selective functionalization with respect to the ester moiety of **3** at the stage of **2** is envisioned. Actually, such a possibility has already been demonstrated.[1] In light of these studies, the present method proved versatile for preparing substituted γ-keto esters, as well as synthetic transformations centered on the parent ketone group.

On the basis of a crossover experiment,[11] we suggest here that a complex **14**, instead of hemiacetal **15** or diketone **1**, directly breaks down to silyl ether **3**. The completely different effect of proton[1] and Lewis acid on cyclobutanone **2** is remarkable, and probably indicates that cyclobutanone **2** behaves as a bidentate ligand of the Lewis acid as in **14**.



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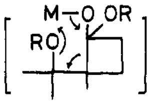
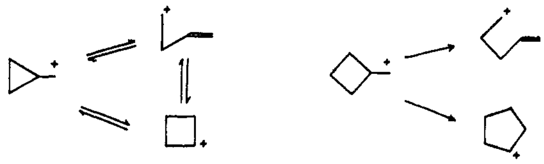


15

Cyclopropylcarbinyl cation is known to undergo both a ring enlargement and a ring cleavage reaction.[12] Nonetheless, only a ring enlargement reaction has been recorded in the reactions of cyclobutylcarbinyl cation.[12] It is interesting to note that the present reaction represents, at least in a formal sense, a ring-opening reaction of cyclobutylcarbinyl cation. We are presently investigating the generality of the ring-cleavage reaction.



References and Notes

(1) E. Nakamura and I. Kuwajima, *J. Am. Chem. Soc.*, **99**, 961 (1977).

(2) Yields are based on spectroscopically pure products. Enol silyl ethers were characterized by IR, NMR, and mass spectra, and hydrolyzed to the corresponding keto esters, which showed correct elemental compositions. Other products in the text were characterized by IR and NMR as well as microanalysis or high-resolution mass spectroscopy.

(3) Bp 110 °C (bath temp) (0.04 mm); IR (neat) 1745 (s), 1677 (m); NMR (CCl_4) 0.12 (s), 1.26 (t, $J = 7$ Hz), 1.3–2.6 (m), 2.36 (s), 4.10 ppm (q, $J = 7$ Hz). This compound is sensitive to moisture and should be stored in a sealed ampule.

(4) Reaction rates differ greatly among substrates. The adduct of **4** and acetone dimethyl acetal rearranges slowly even at 0 °C (1 equiv of $SnCl_4$), whereas cyclohexanone acetal forms the expected rearranged product rapidly at −40 °C.

(5) I. Kuwajima and E. Nakamura, *J. Am. Chem. Soc.*, **97**, 3257 (1975); R. Noyori, K. Yokoyama, J. Sakata, I. Kuwajima, E. Nakamura, and M. Shimizu, *ibid.*, **99**, 1265 (1977).

(6) Commerical TBAF hydrate was dried at ~20 °C (0.5 mm).[5] We thank Fluka AG for the gift of this reagent.

(7) T. Mukaiyama and M. Hayashi, *Chem. Lett.*, 15 (1974); T. Mukaiyama, K. Banno, and K. Narasaka, *J. Am. Chem. Soc.*, **96**, 7503 (1974).

(8) See ref 5 of ref 1.

(9) Review: J. K. Rasmussen, *Synthesis*, 91 (1977).

(10) S. Murai, Y. Kuroki, K. Hasegawa, and S. Tsutsumi, *J. Chem. Soc., Chem. Commun.*, 946 (1972).

(11) A mixture of cyclohexanone diethyl acetal and 4-*tert*-butylcyclohexanone dimethyl acetal was treated with 2 equiv of **4** and a catalytic amount of $SnCl_4$, and the analysis of the reaction mixture revealed that little crossover occurred in the reaction. The conclusion was made on the basis of the comparison of the mass spectrum of the reaction mixture with those of the authentic samples and their mixture. The fact that trimethylchlorosilane which might trap free alkoxide anion did not prevent the rearrangement also supports intramolecular alkoxyl migration.

(12) H. G. Richey, Jr., *Carbonium Ions*, **3**, 1201–1294 (1972).

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Thallium in Organic Synthesis. 49. Oxidative Rearrangement of Chalcone Dimethyl Ketals to Methyl 2,3-Diaryl-3-methoxypropanoates with Thallium(III) Trinitrate in Trimethyl Orthoformate[1]

Summary: Treatment of chalcones (ArCH=CHCOAr′) with thallium(III) trinitrate (TTN) in acidic methanol gives 3,3-dimethoxy-1,2-diarylpropan-1-ones (**2**) by rearrangement of the Ar group. However, prior conversion of chalcones to their dimethyl ketals (which can be carried out in situ in trimethyl orthoformate as solvent), followed by reaction with TTN, yields methyl 2,3-diaryl-3-methoxypropanoates (**6**) by rearrangement of the Ar′ group.

Sir: During the past decade, thallium(III) trinitrate (TTN)