Synthesis of Heterocyclic Compounds by the Organotin Alkoxide Promoted Cleavage of γ-Bromo β-Lactones

Ikuya Shibata,* Mitsuki Toyota, Akio Baba, and Haruo Matsuda

Department of Applied Chemistry, Faculty of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565, Japan

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A variety of 2-oxazolidinones are prepared in good to excellent yields by the organotin alkoxide promoted ring cleavage of γ-bromo β-lactones. This reaction proceeds via the key organotin haloalkoxide intermediate, which reacts with an isocyanate followed by cyclization. Stereoisomerically pure products are obtained by combination with the stereoselective bromolactonization reaction. Moreover, other heterocumulenes such as RN=C=NR, RN=C=S, CO_2, and γ-bromo β-lactam are used as substrates.

Introduction

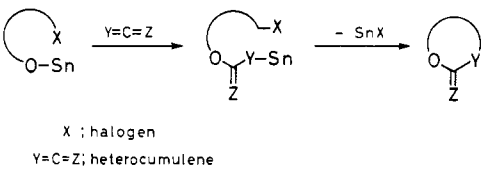
Many organotin reagents have found widespread use in organic synthesis.[1] Some important reactions of tin alkoxides include facile insertion of heterocumulenes such as isocyanates (RN=C=O), isothiocyanates (RN=C=S), carbodiimides (RN=C=NR'), and carbon dioxide (O=C=O) into the Sn—O bond,[2] and great affinity for halogen atoms.[3] In exploring these features we recently developed the preparation of five- and six-membered heterocyclic compounds by using the adduct of an organotin ω-haloalkoxide with a heterocumulene as a key intermediate (Scheme I).[4]

Halo lactones are easily prepared by cyclofunctionalization of terminally unsaturated carboxylic acids through treatment with halogen under basic conditions (Scheme II).[5]

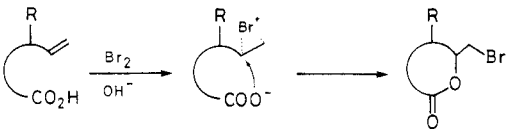
This halolactonization has proven to be a useful tool in organic synthesis, as a result of both its operational convenience and high stereoselectivity, and is often applied to the synthesis of naturally occurring compounds. The halogen group is a versatile functionality and might be used for further manipulations. Thus, expanding the synthetic utility of halo lactones is an area of significant interest.

Organotin alkoxides were employed successfully in the facile cleavage of a β-lactone ring at the acyl–oxygen bond.[6] We report herein a novel synthesis of five-membered heterocyclic compounds such as 2-oxazolidinones via the regioselective ring cleavage of γ-bromo β-lactones with organotin alkoxides. 2-Oxazolidinones are an important class of heterocyclic compounds which find many biological applications.[7] Moreover, we describe the stereoselective halolactonization and the conversion of the β-lactones to stereoisomerically pure 2-oxazolidinones. The present reaction enhances not only the synthetic utility of organotin compounds but also of halolactonization reactions.

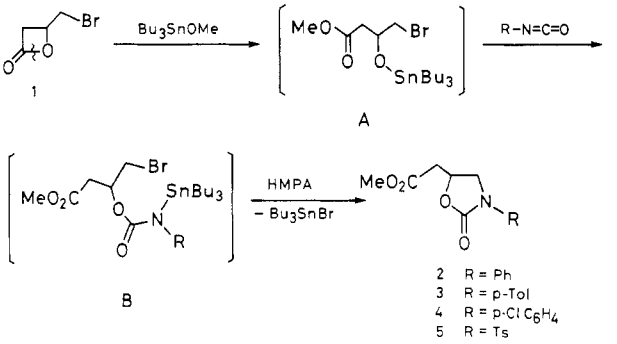
Scheme I



Scheme II



Scheme III



Results and Discussion

As shown in Scheme III, β-lactone 1, prepared from the bromolactonization of vinyl acetic acid under basic conditions,[8] was cleaved at the acyl–oxygen bond regioselectively by reaction with tributyltin methoxide (Bu_3SnOMe) at 80 °C for 4 h. The IR absorption band of the lactone carbonyl group at 1825 cm^{-1} completely shifted to 1720 cm^{-1}. Subsequently, the resulting organotin β-bromoalkoxide A reacted with phenyl isocyanate (PhNCO) spontaneously to afford B. The IR band due to N=C=O at

(1) For examples, see: (a) Pereyre, M.; Quintard, P. J.; Rahm, A. *Tin in Organic Synthesis*; Butterworth, London, 1987. (b) Omae, I. *Organotin Chemistry*; *J. Organomet. Chem. Lib. 21*; Elsevier: New York, 1989.

(2) (a) Bloodworth, A. J.; Davies, A. G. *J. Chem. Soc.* **1965**, 5238. (b) Bloodworth, A. J.; Davies, A. G.; Vasishtha, S. C. *J. Chem. Soc. C* **1967**, 1309.

(3) (a) Delmond, B.; Pommier, J. C.; Valade, J. *J. Organomet. Chem.* **1972**, *35*, 91. (b) Delmond, B.; Pommier, J. C.; Valade, J. *J. Organomet. Chem.* **973**, *47*, 337.

(4) (a) Baba, A.; Kishiki, H.; Shibata, I.; Matsuda, H. *Organometallics* **1985**, *4*, 1329. (b) Shibata, I.; Baba, A.; Iwasaki, H.; Matsuda, H. *J. Org. Chem.* **1986**, *51*, 2177. (c) Baba, A.; Shibata, I.; Kashiwagi, H.; Matsuda, H. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 341. (d) Shibata, I.; Nakamura, K.; Baba, A.; Matsuda, H. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 853.

(5) For example (a) Dowle, M. D.; Davies, D. I. *Chem. Soc. Rev.* **1979**, 171. (b) Chamberlin, A. R.; Mulholland, R. L., Jr.; Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 672. (c) Bartlett, P. A.; Myerson, J. *J. Am. Chem. Soc.* **1978**, *100*, 3950.

(6) (a) Itoh, K.; Kobayashi, S.; Sakai, S.; Ishii, Y. *J. Organomet. Chem.* **1967**, *10*, 451. (b) Sakai, S.; Furusawa, S.; Matsunaga, H.; Fujinami, T. *J. Chem. Soc., Chem. Commun.* **1975**, 265. (c) Shanzer, A.; Libman, J.; Frolow, F. *J. Am. Chem. Soc.* **1981**, *103*, 7339. (d) Shanzer, A.; Libman, J. *J. Chem. Soc., Chem. Commun.* **1983**, 846.

(7) For Reviews see (a) Dyen, M. E.; Swern, D. *Chem. Rev.* **1967**, *67*, 197. (b) Pankrotov, V. A.; Frenkel, T. M.; Fainleib, A. M. *Usp. Khim. Zh. (Russ. Ed.)* **1983**, *52*, 1018.

(8) For the synthesis of β-lactones: (a) Barnett, W. E.; Mckenna, J. *Tetrahedron Lett.* **1971**, 2595. (b) Barnett, W. E.; Sohn, W. H. *J. Chem. Soc., Chem. Commun.* **1972**, 472. (c) Barnett, W. E.; Sohn, W. H. *Tetrahedron Lett.* **1972**, 1777.

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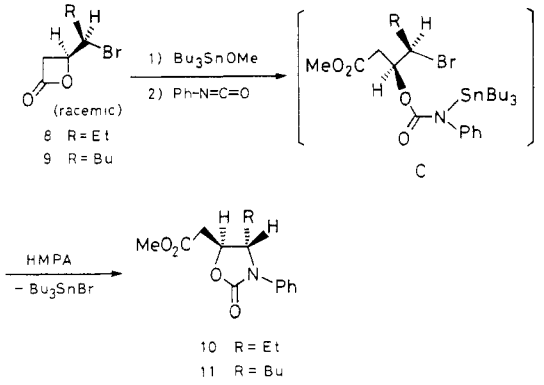
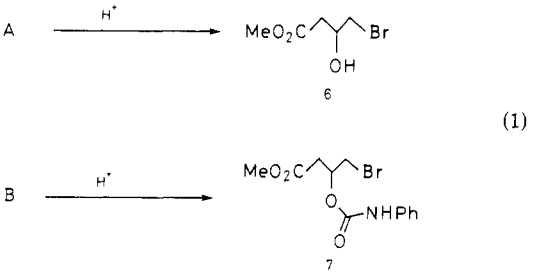
Scheme IV



about 2100 cm^{-1} disappeared immediately. Next, 1 equiv of HMPA was added to effect the cyclization. Heating at 60 °C for 1 h induced the cyclization, accompanied by formation of Bu_3SnBr, yielding 2-oxazolidinone **2** in quantitative yield from **1** by a one-pot procedure.

Scheme III outlines the general reaction sequence using several isocyanates. Oxazolidinones **3**, **4**, and **5** were obtained in 99%, 99%, and 100% yields, respectively.

The above reaction path was confirmed in each case by hydrolysis of the intermediate. Quenching the heated mixture of A with MeOH gave the bromohydrin **6**. Similarly, intermediate B gave **7** quantitatively (eq 1).



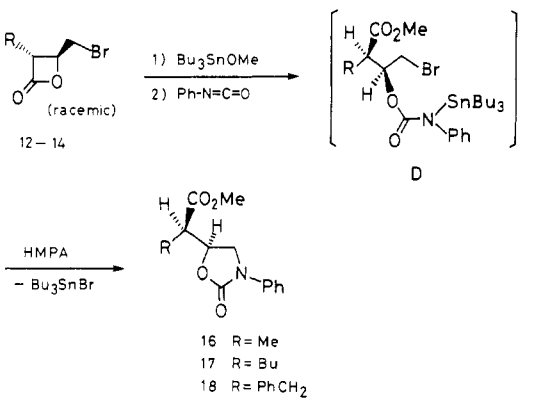
(1)

Two points should be emphasized: one concerns the use of benzene as solvent. It has been reported that a nonpolar solvent is most effective for selective ring cleavage at the acyl–oxygen bond, whereas reaction using a polar solvent or in the absence of solvent induces partial cleavage of the alkyl–oxygen bond.[6] In fact, without solvent, the yield of **2** was not as good (77%) as in the case using benzene. Secondly, the addition of 1 equiv of HMPA plays a very important role at the cyclization step. Our recent study on the intramolecular cyclization of adducts of an organotin ω-haloalkoxide with heterocumulenes revealed that addition of HMPA dramatically accelerates the cyclization, since HMPA (which can coordinate the tin atom) enhances the nucleophilicity of the nitrogen atom adjacent to the tin atom.[4]

The neutral conditions of the present method are advantageous, because similar 2-oxazolidinones bearing a (methoxycarbonyl)methyl group on the side chain are reported to decompose easily in alkaline media.[9] In fact, treatment of **2** with aqueous NaOH initiated decomposition to give a complex mixture.

Next, we were interested in the stereoselective synthesis of heterocycles. One feature of halolactonizations is that the reaction proceeds in a stereospecific manner because of the backside attack of the carboxylate anion on the terminal bromonium ion.[5] For example, from the bromolactonization of terminally trans-substituted hexenoic

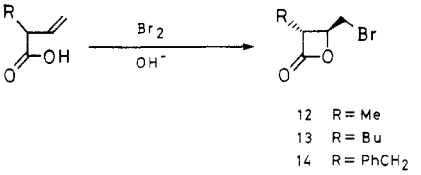
Scheme V



and octenoic acids, stereoisomerically pure β-lactones **8** and **9**, respectively, can be prepared.[10] With these β-lactones, 2-oxazolidinone derivatives could be prepared as single stereoisomers by our present method (Scheme IV).

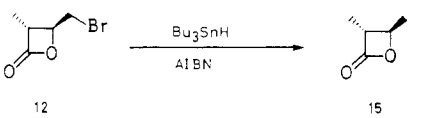
The stannylcarbamate moiety of C attacks the secondary alkyl bromide in an S_N2 process.[11] Thus 4,5-trans-substituted 2-oxazolidinones, **10** and **11**, were obtained in 97% and 98% yields, respectively. Spectral data indicated that these products were single stereoisomers. The coupling constant between methine protons on the ring was 3.6–3.9 Hz.

We next examined the use of α-substituted γ-bromo β-lactones as substrates, which can be prepared from the bromolactonization of α-substituted β,γ-unsaturated carboxylic acids. Earlier work[8] has never discussed the stereochemical consequences of this type of halolactonization, although the highly stereoselective synthesis of functionalized five- and six-membered lactones by halocyclization has been especially notable.[5] Interestingly, we found in our case that completely stereoselective cyclization took place by the bromolactonization of α-substituted β,γ-unsaturated carboxylic acids under basic conditions ($NaHCO_3$). Thus, α,β-trans-substituted β-lactones, **12**, **13**, and **14**, were obtained in 58, 72, and 82% yields, respectively (eq 2).[12]



(2)

The stereochemistry of the β-lactones was confirmed by the halogen reduction of **12** with tri-*n*-butyltin hydride (Bu_3SnH) in the presence of AIBN, affording *trans*-α,β-dimethyl β-lactone (**15**) in 89% yield (Scheme V). The coupling constant between methine protons on the ring was 3.9 Hz, and the spectral data (IR, NMR) were consistent with those of authentic samples reported previously.[13] No cis isomer was detected at all (eq 3).



(3)

(9) Bongini, A.; Cardillo, G.; Orena, M.; Porzi, G.; Sandri, S. *Tetrahedron* **1987**, *43*, 4377.

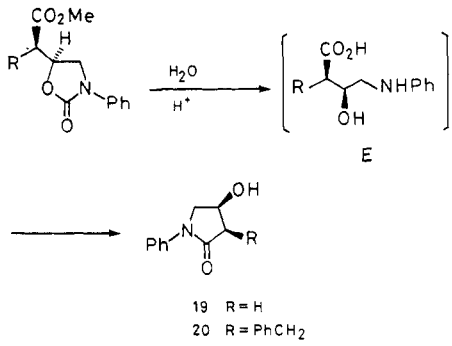
(10) Cook, C. H.; Cho, Y. S.; Jew, S. S.; Suh, Y. G.; Kang, E. K. *Arch. Pharmacal. Res.* **1983**, *6*, 45; *Chem. Abstr.* **1983**, *99*, 175494*k*.

(11) An Sn–O or Sn–N bond attacks secondary alkyl halides in an S_N2 type reaction.[3,4d]

(12) This stereoselective bromolactonization was reported as a communication: Shibata, I.; Toyota, M.; Baba, A.; Matsuda, H. *Chem. Express.* **1989**, *4*, 241.

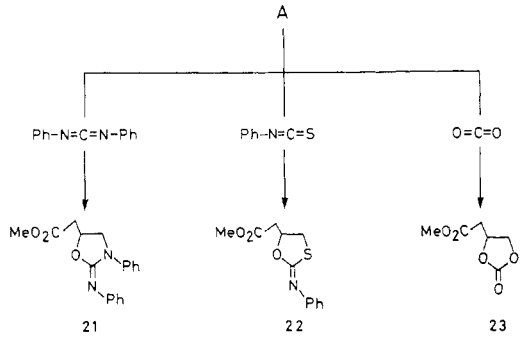
(13) Griesbeck, A.; Seebach, D. *Helv. Chim. Acta* **1987**, *70*, 1320.

Scheme VI



19 R = H
20 R = $PhCH_2$

Scheme VII



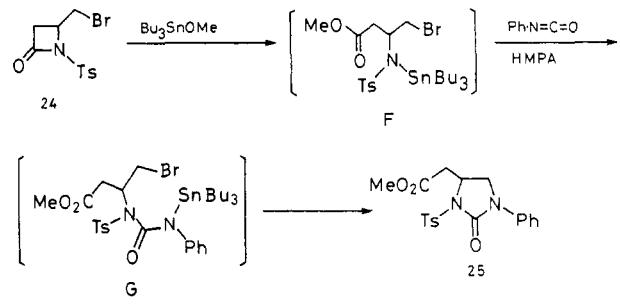
The completely stereoselective formation of the β-lactones is noteworthy, because the configuration of the β-lactone ring can be transformed to 2-oxazolidinones completely. As shown in Scheme V, the ring cleavage by Bu_3SnOMe and the cyclization of D provided the expected 2-oxazolidinones bearing methyl, butyl, and benzyl groups on the side chain to give **16**, **17**, and **18** in 71, 98, and 95% yields, respectively. The configuration of each product was confirmed by ^1H NMR spectroscopy.

In an extension of the above reaction, we examined the transformation of the products (Scheme VI). The products prepared herein possess desirable structural features for further reactions, since the oxazolidinone moiety is an acid-sensitive protected amino alcohol[7] and is easily hydrolyzed to an amino alcohol under acidic conditions.[9] Moreover, the methoxycarbonyl group on the side chain is also useful in this regard. In fact, **2** was readily converted to 4-hydroxy γ-lactam[14] (**19**) in 77% yield by hydrolysis (aqueous HCl). This γ-lactam appears to be formed by the intramolecular condensation of carboxy amino alcohol intermediate E, which was formed by the hydrolysis of the methoxycarbonyl group and the 2-oxazolidinone ring of the starting material. Similarly, from diastereomerically pure 2-oxazolidinone **18**, 3,4-cis-substituted γ-lactam (**20**) was obtained in 90% yield.

Other heterocumulenes can also be used in place of RN=C=O. A variety of heterocyclic compounds could be prepared by the present method. The use of diphenylcarbodiimide (PhN=C=NPh) gave 1,3-oxazolidin-2-imine **21** in 95% yield. With phenyl isothiocyanate (PhN=C=S), the addition took place at the C=S group of the isothiocyanate regioselectively, affording 1,3-oxathiolan-2-imine **22** in 56% yield. The reaction with carbon dioxide provided the corresponding cyclic carbonate **23** in 40% yield (Scheme VII).

We were interested in seeing whether a similar reaction might be accomplished in the case where β-lactam (**24**) was used in place of a β-lactone. The preparation of **24** was recently reported from the halocyclization of *N*-tosyl β,γ-unsaturated amide.[15]

Scheme VIII



As shown in Scheme VIII, the β-lactam ring of **24** was cleaved selectively by Bu_3SnOMe at the acyl–nitrogen bond. The intermediate tin amide F, however, did not react with PhN=C=O even at elevated temperature (80 °C), in contrast to the tin alkoxide intermediate A (Scheme III). The reason for this initial failure appears to be the steric bulkiness at the Sn–N bond of tin amide. However, this problem was solved by the addition of HMPA at this step. The coordination of HMPA to the Sn atom increases the nucleophilicity of the tin amide toward the isocyanate, and the intermediate undergoes cyclization. As a result, 1,3-imidazolidin-2-one (**25**) was obtained in 64% yield.

By employing these methods, various types of heterocyclic compounds can be obtained very easily. Our method provides several advantages in terms of mild and neutral conditions, high yields of products, and operational convenience.

Experimental Section

Melting points were taken on a Yanaco melting point apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra (tetramethylsilane as an internal standard) were recorded on a HITACHI R-90H (90 MHz) or a JEOL JNM-GSX-400 (400 MHz) spectrometer. Infrared spectra were recorded with a HITACHI 260-30 instrument. Mass spectra were obtained with a JEOL JMS-DS303 spectrometer. Analytical GLC was performed on a SHIMADZU GC-3B with TCD using a 2 m × 3 mm glass column packed with Silicone OV-17 on Uniport HP (5%, 60–80 mesh) or a SHIMADZU GC-14A with FID using a 25 m × 0.3 mm capillary column packed with CBP-10. Column chromatography was performed on silica gel (Wakogel C-200 or C-300).

Tri-*n*-butyltin methoxide (Bu_3snOMe) was synthesized from Bu_3SnCl and NaOMe.[16] α-Alkyl β,γ-unsaturated acids were prepared by the double deprotonated carboxylic acids with LDA and subsequent alkylation.[17] Isocyanates (RN=C=O) and phenyl isothiocyanate were commercial products used without further purification. Diphenylcarbodiimide (PhN=C=NPh) was prepared according to the published method.[18] γ-Bromo β-lactam (**24**) was prepared by the method described by Ganem et al.[15]

General Procedure for the Preparation of γ-Bromo β-Lactones. γ-Bromo β-lactones were prepared by the standard procedure for β-lactones 1[8a] as described below. β,γ-Unsaturated acid (10 mmol) was dissolved in a saturated sodium bicarbonate ($NaHCO_3$) solution (40 mL) to produce a homogeneous aqueous solution. The solution was added dropwise over 10 min at 0 °C with stirring to a solution of bromine (10 mmol) in ether (100 mL). The mixture was stirred for 1 h and washed with $Na_2S_2O_3$ solution and with water. The organic layer was dried over $MgSO_4$ and filtered. Removal of the solvent under reduced pressure gave a β-lactone, which was purified by column chromatography. In the

(14) Tabei, K.; Itoh, H.; Tanaka, T. *Heterocycles* **1980**, *14*, 1779.

(15) Biloski, A. J.; Wood, R. D.; Ganem, B. *J. Am. Chem. Soc.* **1982**, *104*, 3233.
(16) Alleston, D. L.; Davies, A. G. *J. Chem. Soc.* **1962**, 2050.
(17) Rajendra, G.; Miller, M. J. *J. Org. Chem.* **1987**, *52*, 4471.
(18) Monagle, J. J. *J. Org. Chem.* **1962**, *27*, 3851.

formation of **8** and **9** the halolactonization produced a mixture with the five-membered ring compound.[10] However, the β-lactone was easily separated by column chromatography (hexane–AcOEt, 3:1). Compounds **1**, **12**, **13**, and **14** formed with no accompanying γ-lactone. The spectral data of the β-lactones are shown below.

4-(1-Bromopropyl)oxetan-2-one (8): wax; IR (neat) 1825 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.11 (t, 3 H, J = 7.1 Hz, CH_3), 1.60–2.20 (m, 2 H, CH_2Me), 3.20–3.80 (m, 2 H, CH_2C=O), 4.00 (td, 1 H, J = 3.9 and 8.6 Hz, CHBr), 4.40–4.61 (m, 1 H, OCH); ^{13}C NMR ($CDCl_3$) δ 11.4, 27.7, 43.4, 56.8, 71.1, 166.6; MS m/z 193 (M^+).

4-(1-Bromopentyl)oxetan-2-one (9): wax; IR (neat) 1825 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80–2.10 (m, 9 H, Bu), 3.20–3.80 (m, 2 H, CH_2C=O), 4.01 (td, 1 H, J = 3.7 and 8.6 Hz, CHBr), 4.39–4.60 (m, 1 H, OCH); ^{13}C NMR ($CDCl_3$) δ 14.0, 20.2, 29.2, 34.5, 43.9, 55.2, 71.7, 166.6; MS m/z 221 (M^+).

3-Methyl-4-(bromomethyl)oxetan-2-one (12): wax; IR (neat) 1820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.46 (d, 3 H, J = 9.2 Hz, CH_3), 3.48–3.55 (m, 2 H, one of CH_2Br and MeC*H*C=O), 3.71 (dd, 1 H, J = 4.9 and 10.7 Hz, one of CH_2Br), 4.35–4.41 (m, 1 H, OCH); ^{13}C NMR ($CDCl_3$) δ 12.2, 31.4, 51.1, 75.8, 170.0; MS m/z 179 (M^+).

3-Butyl-4-(bromomethyl)oxetan-2-one (13): wax; IR (neat) 1820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90–1.90 (m, 9 H, Bu), 3.40–3.47 (m, 1 H, CHC=O), 3.52 (dd, 1 H, J = 7.8 and 10.7 Hz, one of CH_2Br), 3.70 (dd, 1 H, J = 4.9 and 10.7 Hz, one of CH_2Br), 4.40–4.46 (m, 1 H, OCH); ^{13}C NMR ($CDCl_3$), δ 13.7, 22.3, 27.3, 28.9, 31.5, 56.5, 74.5, 169.5; MS m/z 221 (M^+).

3-Benzyl-4-(bromomethyl)oxetan-2-one (14): mp 37–38 °C; IR (neat) 1825 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.13 (d, 2 H, J = 7.0 Hz, PhCH_2), 3.45–3.65 (m, 2 H, CH_2Br), 3.63–3.81 (m, 1 H, CHC=O), 4.34–4.56 (m, 5 H, OCH); ^{13}C NMR ($CDCl_3$) δ 31.4, 33.1, 57.3, 73.4, 127.1, 128.8 (2 C), 136.2, 168.7; MS m/z 255 (M^+).

3,4-*trans*-Dimethyloxetan-2-one (15). A mixture of β-lactone **12** (0.90 g, 5 mmol), tri-*n*-butyltin hydride (Bu_3SnH) (1.45 g, 5 mmol), and 0.05 equiv of AIBN in 10 mL of dry benzene was refluxed for 2 h. After evaporation of the solvent, the residue was chromatographed (benzene): wax; IR (neat) 1820 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (d, 3 H, J = 7.7 Hz, 3C-CH_3), 1.55 (d, 3 H, J = 5.9 Hz, 4C-CH_3), 3.21 (dq, 1 H, J = 3.9 and 7.6 Hz, CHC=O), 4.33 (dq, 1 H, J = 3.9 and 6.0 Hz, OCH). These spectral data were consistent with those reported previously.[13]

General Procedure for the Preparation of 2-Oxazolidinone. Bu_3SnOMe (1.60 g, 5 mmol) was added to **1** (0.83 g, 5 mmol) in benzene (5 mL) under nitrogen atmosphere. This mixture was stirred at 80 °C for 4 h to give intermediate A. The solution of A was cooled to room temperature, and PhN=C=O (0.60 g, 5 mmol) was added. After 10 min, the IR absorption band of the NCO group had disappeared. HMPA (0.90 g, 5 mmol) was added, and the reaction was heated at 60 °C for 1 h. After evaporation of the solvent, the reaction mixture was chromatographed on silica gel. The byproduct, Bu_3SnBr, was removed easily by using hexane as an eluent, and with benzene, 2-oxazolidinone **2** was obtained as white needles and was purified by recrystallization from benzene–hexane.

3-Phenyl-5-[(methoxycarbonyl)methyl]-1,3-oxazolidin-2-one (2): mp 69–70 °C; IR (KBr) 1745 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.80 (dd, 1 H, J = 7.8 and 16.6 Hz, one of OC=OCH_2), 3.00 (dd, 1 H, J = 5.9 and 16.6 Hz, one of OC=OCH_2), 3.75 (s, 3 H, OCH_3), 3.80 (dd, 1 H, J = 9.3 and 6.3 Hz, one of NCH_2), 4.26 (dd, 1 H, J = 8.8 and 9.3 Hz, one of NCH_2), 4.90–5.10 (m, 1 H, OCH), 7.10–7.60 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 39.3, 50.5, 52.2, 68.9, 118.3, 124.2, 129.1, 138.1, 153.6, 169.6; MS m/z 235 (M^+). Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95. Found: C, 61.07; H, 5.58; N, 5.74.

3-*p*-Tolyl-5-[(methoxycarbonyl)methyl]-1,3-oxazolidin-2-one (3): mp 123–124 °C; IR (KBr) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.33 (s, 3 H, ArCH_3), 2.79 (dd, 1 H, J = 7.8 and 16.6 Hz, one of OC=OCH_2), 3.00 (dd, 1 H, J = 5.4 and 16.6 Hz one of OC=OCH_2), 3.74 (s, 3 H, OCH_3), 3.77 (dd, 1 H, J = 6.9 and 9.3 Hz, one of NCH_2), 4.22 (t, 1 H, J = 9.3 Hz, one of NCH_2), 4.90–5.10 (m, 1 H, OCH), 7.10–7.50 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$) δ 20.9, 39.3, 50.7, 52.2, 68.9, 118.5, 129.6, 133.9, 135.6, 154.3, 169.6; MS m/z 249 (M^+). Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.06; N, 5.62. Found: C, 62.74; H, 6.02; N, 5.57.

3-(*p*-Chlorophenyl)-5-[(methoxycarbonyl)methyl]-1,3-oxazolidin-2-one (4): mp 116–117 °C; IR (KBr) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.80 (dd, 1 H, J = 8.3 and 16.6 Hz, one of OC=OCH_2), 3.00 (dd, 1 H, J = 5.4 and 16.6 Hz, one of OC=OCH_2), 3.75 (s, 3 H, OCH_3), 3.78 (dd, 1 H, J = 6.3 and 8.8 Hz, one of NCH_2), 4.23 (t, 1 H, J = 8.8 Hz, one of NCH_2), 4.90–5.10 (m, 1 H, OCH), 7.20–7.60 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$) δ 39.1, 50.3, 52.2, 68.9, 119.4, 129.0, 129.3, 136.7, 154.0, 169.5; MS m/z 270 (M^+). Anal. Calcd for $C_{12}H_{12}NO_4Cl$: C, 53.44; H, 4.48; N, 5.19. Found: C, 53.43; H, 4.50; N: 5.21.

3-Tosyl-5-[(methoxycarbonyl)methyl]-1,3-oxazolidin-2-one (5): mp 63–64 °C; IR (KBr) 1735, 1780 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.45 (s, 3 H, ArCH_3), 2.71 (dd, 1 H, J = 7.8 and 16.6 Hz, one of OC=OCH_2), 2.87 (dd, 1 H, J = 5.9 and 16.6 Hz, one of OC=OCH_2), 3.70 (s, 3 H, OCH_3), 3.79 (dd, 1 H, J = 6.9 and 9.8 Hz, one of NCH_2), 4.24 (dd, 1 H, J = 8.3 and 9.8 Hz, one of NCH_2), 4.80–5.10 (m, 1 H, OCH), 7.10–8.10 (m, 4 H, Ar); ^{13}C NMR ($CDCl_3$) δ 21.7, 38.2, 49.3, 52.1, 70.2, 128.1, 129.8, 133.8, 145.7, 151.0, 168.8; MS m/e 313 (M^+). Anal. Calcd for $C_{13}H_{15}NO_6S$: C, 49.83; H, 4.83; N, 4.47. Found: C, 49.71; H, 4.89; N, 4.43.

3-Phenyl-*trans*-4-ethyl-5-[(methoxycarbonyl)methyl]-1,3-oxazolidin-2-one (10): wax; IR (neat) 1730, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.91 (t, 3 H, J = 7.3 Hz, CH_3), 1.70–1.80 (m, 2 H, MeCH_2), 2.79 (dd, 1 H, J = 6.8 and 16.1 Hz, one of OC=OCH_2), 2.89 (dd, 1 H, J = 5.9 and 16.1 Hz, one of OC=OCH_2), 3.74 (s, 3 H, OCH_3), 4.16 (td, 1 H, J = 3.9 and 5.9 Hz, NCH), 4.69 (ddd, 1 H, J = 3.9, 5.9, and 6.9 Hz, OCH), 7.15–7.50 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 7.7, 24.3, 39.4, 52.1, 61.9, 73.4, 121.6, 125.2, 129.1, 136.5, 154.4, 169.5; MS m/z 263 (M^+). Anal. Calcd for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.50; N, 5.32. Found: C, 63.57; H, 6.42; N, 5.35.

3-Phenyl-*trans*-4-butyl-5-[(methoxycarbonyl)methyl]-1,3-oxazolidin-2-one (11): wax; IR (neat) 1740, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80–1.80 (m, 9 H, Bu), 2.78 (dd, 1 H, J = 6.8 and 16.1 Hz, one of OC=OCH_2), 2.88 (dd, 1 H, J = 5.9 and 16.1 Hz, one of OC=OCH_2), 3.74 (s, 3 H, OCH_3), 4.16 (td, 1 H, J = 3.6 and 6.8 Hz, NCH), 4.69 (ddd, 1 H, J = 3.6, 5.9, and 6.8 Hz, OCH), 7.10–7.50 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.5, 25.8, 31.4, 39.5, 52.1, 61.2, 74.0, 121.7, 125.2, 129.1, 136.6, 154.5, 169.5; MS m/z 291 (M^+). Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found: C, 66.18; H, 7.22; N, 4.58.

3-Phenyl-5(*S*')-[1'(*S*')-(methoxycarbonyl)ethyl]-1,3-oxazolidin-2-one (16): mp 113–114 °C; IR (KBr) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (d, 3 H, J = 7.3 Hz, CH_3), 3.00 (qd, 1 H, J = 6.6 and 7.3 Hz, MeC*H*C=OO), 3.74 (s, 3 H, OCH_3), 3.85 (dd, 1 H, J = 6.8 and 9.3 Hz, one of NCH_2), 4.13 (t, 1 H, J = 9.3 Hz, one of NCH_2), 4.90–5.00 (m, 1 H, OCH), 7.10–7.60 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 11.2, 43.1, 47.6, 52.3, 72.6, 118.4, 124.2, 129.1, 138.0, 154.3, 172.8; MS m/z 249 (M^+). Anal. Calcd for $C_{13}H_{15}NO_4$: C; 62.64; H, 6.07; N, 5.62. Found: C, 62.58; H, 6.11; N, 5.55.

3-Phenyl-5(*S*')-[1'(*S*')-(methoxycarbonyl)pentyl]-1,3-oxazolidin-2-one (17): wax; IR (neat) 1740, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.80–1.80 (m, 9 H, Bu), 2.75–2.85 (m, 1 H, OC=OCH), 3.74 (s, 3 H, OCH_3), 3.86 (dd, 1 H, J = 7.3 and 9.3 Hz, one of NCH_2), 4.10 (t, 1 H, J = 9.3 Hz, one of NCH_2), 4.83 (td, 1 H, J = 7.3 and 9.3 Hz, OCH), 7.10–7.55 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 13.7, 22.4, 26.7, 29.2, 48.1, 49.5, 51.9, 72.7, 118.0, 123.8, 128.8, 137.9, 154.0, 172.3; MS m/z 291 (M^+). Anal. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.26; N, 4.81. Found: C, 65.72; H, 7.26; N, 4.38.

3-Phenyl-5(*S*')-[1'(*S*')-(methoxycarbonyl)-2'-phenylethyl]-1,3-oxazolidin-2-one (18): mp 115–116 °C; IR (KBr) 1740, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.98–3.11 (m, 3 H, PhCH_2 and C*H*C=O), 3.74 (s, 3 H, OCH_3), 3.87 (dd, 1 H, J = 6.7 and 9.2 Hz, one of NCH_2), 4.14 (t, 1 H, J = 9.2 Hz, one of NCH_2), 4.80–4.90 (m, 1 H, OCH), 7.10–7.50 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$) δ 33.6, 48.3, 51.4, 52.4, 71.9, 118.4, 124.3, 127.0, 128.7, 128.9, 129.1, 129.3, 137.2, 154.1, 171.6; MS m/z 325 (M^+). Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.30. Found: C, 70.24; H, 5.85; N, 4.37.

1-[(Methoxycarbonyl)methyl]-2-bromoethanol (6). To the heated mixture containing the intermediate A (5-mmol scale) was added excess amounts of MeOH (10 equiv). This solution was stirred at reflux for 10 min. Removal of MeOH under reduced pressure followed by column chromatography (benzene as an eluent) yielded the product as a colorless oil: wax; IR (neat) 3400, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.67 (d, 2 H, J = 5.7 Hz, CH_2C=O), 3.10 (br, 1 H, OH), 3.49 (d, 2 H, J = 4.8 Hz, $BrCH_2$), 3.73 (s, OCH_3, 3 H), 4.09–4.33 (m, 1 H, OCH); ^{13}C NMR ($CDCl_3$) δ 37.36; 39.35, 51.88, 67.43, 171.79.

1-[(Methoxycarbonyl)methyl]-2-bromoethyl *N*-Phenylcarbamate (7). This compound was isolated by quenching the

reaction mixture of B. The product was isolated quantitatively by column chromatography (benzene): wax; IR (neat) 3300, 1710, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.84 (d, 2 H, J = 6.4 Hz, $COCH_2$) 3.66-3.77 (m, 5 H, OCH_3 and $BrCH_2$), 5.23-5.47 (m, 1 H, OCH), 6.70 (br, 1 H, NH), 7.20-7.30 (m, 5 H, Ph); ^{13}C NMR ($CDCl_3$) δ 34.0, 37.4, 52.1, 69.6, 118.8, 123.7, 129.0, 137.4, 152.1, 170.1.

1-Phenyl-4-hydroxy-2-pyrrolidinone (19). Compound **2** (0.42 g, 1.8 mmol) was dissolved in 10 mL of acetone and 20 mL of HCl solution (6 N). The mixture was heated at reflux for 24 h and then quenched by the addition of aqueous KOH (2 N). The mixture was diluted with ether (50 mL) and washed with brine, and the ether layer was dried over $MgSO_4$. Removal of ether left a colorless oil, which was chromatographed over silica gel: mp 87 °C (lit.[15] mp 88 °C); IR (KBr) 1685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.10 (br, 1 H, OH), 2.50-3.10 (m, 2 H, CH_2C=O), 3.60-4.20 (m, 2 H, NCH_2), 4.50-4.80 (m, 1 H, OCH), 7.10-7.70 (m, 5 H, Ph); MS m/z 177 (M^+).

1-Phenyl-*cis*-3-benzyl-4-hydroxy-2-pyrrolidinone (20): mp 110-111 °C; IR (KBr) 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.60 (br, 1 H, OH), 2.95-3.05 (m, 2 H, CHC=O), 3.36 (dd, 1 H, J = 2.9 and 13.2 Hz, one of $PhCH_2$), 3.72 (dd, 1 H, J = <1.0 and 11.2 Hz, one of NCH_2), 3.98 (dd, 1 H, J = 4.2 and 12.0 Hz, one of NCH_2), 4.39 (m, 1 H, OCH), 7.34-7.40 (m, 10 H, Ph); ^{13}C NMR ($CDCl_3$) δ 29.3, 50.6, 55.7, 64.0, 118.8, 123.4, 125.6, 128.0, 128.6, 128.6, 139.7, 140.3, 173.2; MS m/z 267 (M^+). Anal. Calcd for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.15; H, 6.32; N, 5.33.

***N*-Phenyl-3-phenyl-5-[(methoxycarbonyl)methyl]-1,3-oxazolidin-2-imine (21)**: Bu_3SnOMe (1.60 g, 5 mmol) was added to 1 (0.83 g, 5 mmol) in benzene (5 mL) under nitrogen atmosphere. This mixture was stirred at 80 °C for 4 h to give the intermediate A. The solution was cooled to room temperature, and diphenylcarbodiimide (PhN=C=NPh) (0.97 g, 5 mmol) was added. After 10 min, HMPA (0.9 g, 5 mmol) was added, and heated at 60 °C for 1 h. Solvent was removed under reduced pressure, and the residue was chromatographed on silica gel. The byproduct, Bu_3SnBr, was removed easily by using hexane as an eluent, and with benzene, the product **21** was obtained as white needles which was purified by recrystallization from benzene-hexane: mp 125-126 °C; IR (KBr) 1660, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.40-2.90 (m, 2 H, OC=OCH_2), 3.71 (s, 3 H, OCH_3), 3.95-4.60 (m, 2 H, NCH_2), 4.80-5.05 (m, 1 H, OCH), 6.90-7.70 (m, 10 H, Ph); MS m/z 310 (M^+).

***N*-Phenyl-5-[(methoxycarbonyl)methyl]-1,3-oxathiolan-2-imine (22).** To the solution of A was added phenyl isothiocyanate (PhN=C=S) (0.68 g, 5 mmol) at room temperature. After 10 min, HMPA (0.90 g, 5 mmol) was added, and the mixture was heated at 60 °C for 1 h. Solvent was removed under reduced pressure, and the residue was chromatographed on silica gel. With benzene as an eluent, **22** was isolated as a colorless oil: wax; IR (neat) 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.60-3.10 (m, 2 H, OC=OCH_2), 3.40-4.50 (m, 5 H, NCH_2 and OCH_3), 4.80-5.30 (m, 1 H, OCH), 6.90-7.70 (m, 5 H, Ph); MS m/z 251 (M^+).

5-[(Methoxycarbonyl)methyl]-1,3-dioxolan-2-one (23). Carbon dioxide was bubbled through a solution of A at room temperature. After 1 h, HMPA (0.90 g, 5 mmol) was added, and the mixture was heated at 60 °C for 1 h. Solvent was removed under reduced pressure, and the residue was chromatographed on silica gel. With benzene as an eluent, **23** was isolated as a colorless oil: wax; IR (neat) 1740, 1800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.60-3.20 (m, 2 H, OC=OCH_2), 3.74 (s, 3 H, OCH_3), 4.22 (dd, 1 H, J = 6.9, 8.7 Hz, one of OCH_2), 4.67 (t, 1 H, J = 8.7 Hz, one of OCH_2), 4.90-5.20 (m, 1 H, OCH); MS, m/z 160 (M^+).

1-Tosyl-3-phenyl-[5-(methoxycarbonyl)methyl]-1,3-imidazolidin-2-one (25). Bu_3SnOMe (1.85 g, 5 mmol) was added to β-lactam **24** (1.94 g, 5 mmol) in benzene (5 mL) under nitrogen atmosphere. This solution was stirred at 80 °C for 4 h to form F. The IR absorption at 1780 cm^{-1} due to the β-lactam ring shifted to 1710 cm^{-1}. This solution was cooled to room temperature, and PhN=C=O (0.60 g, 5 mmol) and HMPA (0.90 g, 5 mmol) were added. After heating at 60 °C for 1 h, the mixture was chromatographed on silica gel. The byproduct, Bu_3SnBr, was removed easily by using hexane as an eluent. With benzene, **25** was obtained as white needles and was purified by recrystallization from benzene-hexane: mp 148-149 °C; IR (KBr) 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.43 (s, 3 H, $ArCH_3$), 2.84 (dd, 1 H, J = 10.0 and 16.9 Hz, one of OC=OCH_2), 3.36 (dd, 1 H, J = 3.2 and 16.9 Hz, one of OC=OCH_2), 3.61 (dd, 1 H, J = 3.9 and 9.8 Hz, oen of NCH_2), 3.71 (s, 3 H, OCH_3), 4.17 (t, 1 H, J = 9.8 Hz, one of NCH_2), 4.65-4.80 (m, 1 H, NCH), 7.00-8.20 (m, 9 H, Ar); ^{13}C NMR ($CDCl_3$) δ 21.6, 39.5, 48.8, 49.7, 52.0, 118.7, 124.4, 128.3, 128.9, 129.6, 135.6, 138.1, 145.0, 151.2, 170.5; MS m/z 388 (M^+). Anal. Calcd for $C_{19}H_{20}N_2O_5S$: C, 58.75; H, 5.19; N, 7.21. Found: C, 58.63; H, 5.14; N, 7.10.

Registry No. **1**, 125762-98-3; **2**, 125762-99-4; **3**, 125763-00-0; **4**, 125763-01-1; **5**, 125780-99-6; **6**, 125827-29-4; **7**, 125763-02-2; **8**, 125763-03-3; **9**, 125763-04-4; **10**, 125763-05-5; **11**, 125763-06-6; **12**, 125763-07-7; **13**, 125763-08-8; **14**, 125763-09-9; **15**, 125827-30-7; **16**, 125763-10-2; **17**, 125763-11-3; **18**, 125763-12-4; **19**, 125763-13-5; **20**, 125763-14-6; **21**, 125763-15-7; **22**, 125763-16-8; **23**, 125763-17-9; **24**, 125780-87-2; **25**, 125763-18-0; H_2C=$CHCH(CH_3)CO_2H$, 50304-40-0; H_2C=$CHCH(Bu)CO_2H$, 125763-19-1; H_2C=$CHCH(CH_2Ph)CO_2H$, 89022-02-6; H_2C=$CHCH_2CO_2H$, 625-38-7; (*E*)-$EtCH$=$CHCH_2CO_2H$, 1577-18-0; (*E*)-$H_3C(CH_2)_3CH$=$CHCH_2CO_2H$, 5163-67-7; Bu_3SnOMe, 1067-52-3; PhNCO, 103-71-9; *p*-MeC_6H_4NCO, 622-58-2; *p*-ClC_6H_4NCO, 104-12-1; *p*-$MeC_6H_4SO_2NCO$, 4083-64-1; PhN=C=NPh, 622-16-2; PhNCS, 103-72-0.

Acetyl Chloride Promoted Cyclopropanations of Alkenes with Dibromomethane Using Zinc Dust and Copper(I) Chloride in Ether

Edwin C. Friedrich* and Eric J. Lewis

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

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Acetyl chloride strongly accelerates the cyclopropanation reactions of alkenes with dibromomethane or diiodomethane using zinc dust and copper(I) chloride in ether and results in improved yields of cyclopropane products.

We have recently reported[1] our discovery that the addition of catalytic amounts of titanium(IV) chloride strongly promotes the rates of cyclopropanation of alkenes in ether with dibromomethane or diiodomethane using zinc dust and copper(I) chloride. Satisfactory yields of cyclopropanation products, however, were only obtained when using this method with simple hydrocarbon alkenes not bearing Lewis acid sensitive functional groups.

We now disclose that the replacement of titanium(IV) chloride by as little as 1 mol % of acetyl chloride based on zinc not only strongly accelerates alkene cyclo-

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