Young, D. C. *Inorg. Synth.* **1967**, *10*, 91.
12. Edgell, W. F.; Fisher, J. W.; Asato, G.; Risen, Jr., W. M. *Inorg. Chem.* **1969**, *8*, 1103.
13. (a) Graham, W. A. G. *Inorg. Chem.* **1968**, *7*, 315. (b) Darensbourg, M. Y.; Darensbourg, D. J. *Inorg. Chem.* **1970**, *9*, 32.

A Facile Synthesis of Highly Substituted γ-Butyrolactones *via* Trans-Lactonization of the Baeyer-Villiger Products

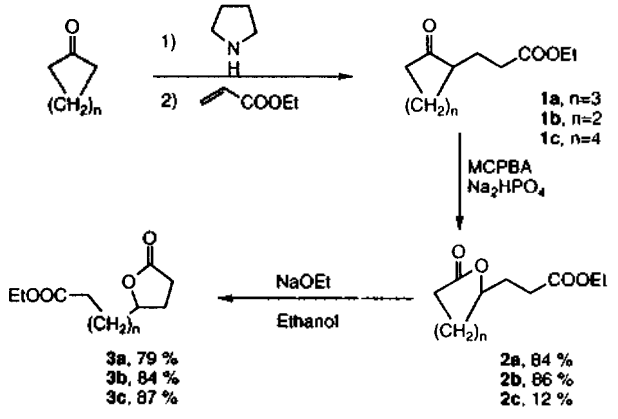
Chang Ho Oh*, Bun Seang Park, Andre Kim, and Yong Ae Park

Department of Chemistry, Inje University, Aubang 607, Kimhae 621-749, Korea

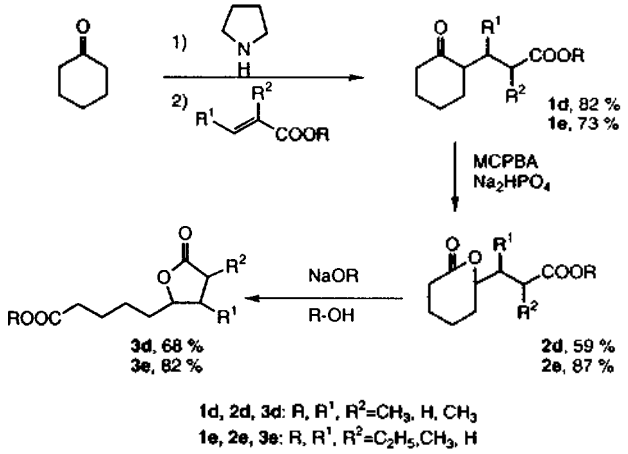
Received May 29, 1995

About 10% of all natural products and many synthetic intermediates contain a γ-butyrolactone skeleton.[1] Various synthetic methods to these γ-butyrolactones are present such as intramolecular esterification of γ-hydroxyacids or their derivatives in the presence of acid or base catalyst,[2] halolactonization of γ,δ-unsaturated acids,[3] palladium-catalyzed lactonization of γ,δ-unsaturated acids leading to the formation of γ-vinyl substituted γ-lactones[4] and an intramolecular addition of oxycarbonyl radicals to double or triple bonds.[5] Although those methods have been widely applied to the many natural products syntheses, yet γ-butyrolactones, having a labile or reactive functional group such as an ester at the γ position, are limited to access. We wish to describe an easy and convenient synthetic method to regiospecifically substituted γ-lactones. Our strategy involved three steps: alkylation of cyclic ketones,[6] Baeyer-Villiger oxidation for generating the transient γ-hydroxyacid equivalents, and followed by transesterification of the corresponding lactones (Scheme 1).[8]

The pyrrolidine enamine of cyclohexanone smoothly underwent the Michael addition with ethyl acrylate to afford ethyl



Scheme 1.

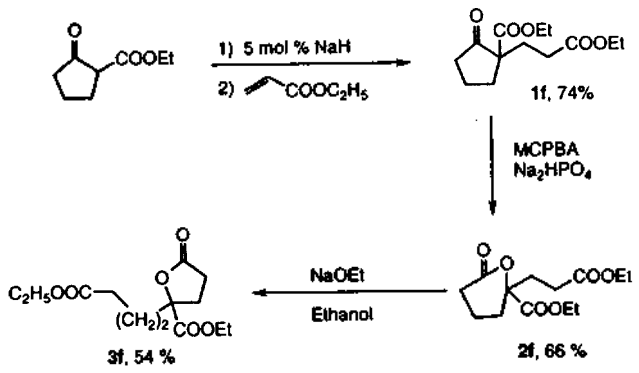


Scheme 2.

3-(2-oxocyclohexyl)propanoate (**1a**) in over 80% yield. When the above 2-alkyl substituted cyclohexanone **1a** was treated with MCPBA and disodium phosphate as a base resulted in clean disappearance of the starting material on analytical TLC plate after 5-6 h at room temperature.[9] The extractive workup and separation on flash chromatography afforded the corresponding 7-membered lactone **2a** in 84% yield. The 7-membered lactone **2a** was then subjected to a catalytic amount of sodium ethoxide in refluxing ethanol and the corresponding γ-lactone **3a** was obtained after purification in 79% yield.

Structural variations from the cyclohexanone to a cyclopentanone and a cycloheptanone were highly operative. When ethyl 3-(2-oxocyclopentyl)propanoate (**1b**) was subjected to the MCPBA oxidation conditions, the corresponding δ-lactone **2b** was formed in a few hours. However, the Baeyer-Villiger reaction of ethyl 3-(2-oxocycloheptyl)propanoate (**1c**) with MCPBA was not completed, because the cycloheptanone **1c** is much less reactive than the cyclohexanone or the cyclopentanone. The synthesis of γ-butyrolactones *via* translactonization of the above 6-, 7-, and 8-membered lactones was more interesting to us. In facts, the eight membered lactone **2c** has been transformed smoothly to the corresponding γ-butyrolactone **3c** in 1 h in refluxing ethanol in the presence of a catalytic amount of sodium ethoxide, while the δ-lactone **2b** derived from ethyl 3-(2-oxocyclopentyl)propanoate (**1b**) required longer reaction time (20 h) to complete the translactonization presumably due to the stability of a 6-membered lactone **2b**. It is an important finding that the 6-membered lactone **2b** has been thermodynamically transformed to the 5-membered lactone **3b** in a very high yield. We have also concerned about the Dieckmann cyclization of the two pendant ester groups in the presence of a catalytic amount of a base. Note that no other side product was formed during this translactonization.

Further structural variations in the Michael acceptors have provided the very easy synthesis of more substituted γ-lactons (Scheme 2).[10] The substituent R_1 and R_2 in the Michael acceptors would be eventually ended in the β and α position in the final γ-lactones, respectively. Although the Michael addition of carbanions to α,β-unsaturated esters has been well-known,[11] several attempts to obtain the addition product



Scheme 3.

of the cyclohexanone enolate with substituted α,β-unsaturated esters were unsuccessful. Finally, we could find that the enamine in refluxing ethanol reacted with the substituted α,β-unsaturated esters to yield the addition products, **1d** and **1e**.

The Baeyer-Villiger oxidation of **1d** and **1e** as before underwent well to give the corresponding 7-membered lactones, **2d** and **2e**, respectively. The more substituted alkyl group was migrated to the peroxide oxygen. The substituents R_1 and R_2 did not interfere to the oxidation and translactonization.

Ethyl 2-oxocyclopentanecarboxylate was cleanly alkylated in the presence of catalytic amount of sodium ethoxide in ethanol and the resulting ketone **1f** was transformed to **3f** under the similar conditions employed above (Scheme 3). The lactone **2f**, however, was quite sluggish in the transesterification probably due to steric hindrance.

In conclusion, the present results might imply following several important features. 1) This simple method could provide an easy access to highly substituted γ-lactones in a few steps. 2) For the first time, all substituents in the α,β-unsaturated esters have been incooperated in the γ-butyrolactones **3a-f**. Therefore, the use of a properly substituted α,β-unsaturated ester could lead stereoselectively to α,β,γ-substituted-γ-lactones in high yields. 3) Dieckmann cyclization or other carbocyclization using the two pendant ester groups in the resulting γ-lactones could provide an easy access to very useful 7, 8, and 9-membered carbocycles which are rich in many natural products.[12] Further manipulation of the resulting lactones to the useful carbocycles are under study, and those results will be reported when available.

Acknowledgment. This work was financially supported by The Inje Research and Scholarship Foundation. We are also grateful to the Department of Chemistry of Pusan National University for 200 MHz FT-NMR spectrometer throughout this work.

References

1. (a) Devon, T. K.; Scott, A. I. *In* Handbook of Naturally Occurring Compounds, Academic Press: New York, 1975, vol. 1. (b) Trost, B. M., Fleming, I., Eds.; In *Comprehensive Organic Synthesis*; Pergamon Press: Oxford; Vol. 6, p 350-380. (c) Grieco, P. A.; Oguri, T.; Gilman, S. *J. Am. Chem. Soc.* **1980**, *102*, 5886-5891. (d) Mulzer, J.; Salimi, N.; Hartle, H. *Tetrahedron: Asymmetry* **1993**, *4*, 457-471.
2. (a) Mulzer, J.; deLasalle, P.; Chucholowski, A.; Blaschek, U.; Bruntrup, G.; Jibril, I.; Huttner, G. *Tetrahedron* **1984**, *40*, 2211. (b) Kunz, T. A.; Reissig, H.-U. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 268. (c) Reissig, H.-U.; Angert, H. *J. Org. Chem.* **1993**, *58*, 6280-6285. (d) Creger, P. L. *J. Org. Chem.* **1972**, *37*, 1907.
3. Corey, E. J.; Weinshenker, N. M.; Schaaf, T. K.; Huber, W. *J. Am. Chem. Soc.* **1969**, *91*, 5675.
4. (a) Larock, R. C.; Hightower, T. R. *J. Org. Chem.* **1993**, *58*, 5298-5300. (b) Backvall, J.-E.; Granberg, K. L.; Andersson, P. G.; Gatti, R.; Gogoll, A. *J. Org. Chem.* **1993**, *58*, 5445-5451.
5. Bachi, M. D.; Bosch, E. *J. Org. Chem.* **1992**, *17*, 4696-4705.
6. Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkovicz, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207-222.
7. Trost, B. M., Fleming, I., Eds.; In *Comprehensive Organic Synthesis*; Pergamon Press: Oxford; Vol. 5, p 671-688.
8. For a typical transesterification, *See*: Seebach, D.; Hungerbuhler, E.; Naef, R.; Schnurrenberger, P.; Weidmann, B.; Zuger, M. *Synthesis* **1982**, 138-141.
9. (a) Kim, S.; Hong, C. Y.; Moon, Y. C. *J. Org. Chem.* **1982**, *47*, 4350-4351. (b) Kaneda, K.; Ueno, S.; Imanaka, T.; Shimotsuma, E.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1994**, *59*, 2915-2917.
10. IR and ^{1}H NMR data of typical compounds are given. **2a**: IR (neat) 1720 cm^{-1} (two C=O); ^{1}H NMR (200 MHz) δ 4.33 (m, 1H), 4.11 (q, J=7.2 Hz, 2H), 2.69-2.57 (m, 2H), 2.52-2.43 (m, 2H), 1.93-1.88 (m, 6H), 1.64-1.52 (m, 2H), 1.24 (t, J=7.2 Hz, 3H). **2c**: ^{1}H NMR (200 MHz) δ 4.70 (m, 1H), 4.14 (q, J=7.2 Hz, 2H), 2.45 (m, 2H), 1.98-1.40 (m, 10H), 1.26 (t, J=7.2 Hz, 3H). **2d**: IR (neat) 1720 cm^{-1} (two C=O); ^{1}H NMR (200 MHz) δ 4.28 (m, 1H), 3.66 (s, 3H), 2.85-2.45 (m, 3H), 2.25-2.10 (m, 1H), 1.92-1.48 (m, 7H), 1.16 (d, J=7.0 Hz, 3H). **2e**: IR (neat) 1720 cm^{-1} (two C=O); 1H NMR (200 MHz) δ 4.36-4.20 (m, 1H), 4.13 (q, J=7.2 Hz, 2H), 2.70-2.58 (m, 2H), 2.58-2.40 (m, 2H), 2.03-1.80 (m, 3H), 1.70-1.47 (m, 4H), 1.25 (t, J=7.1 Hz, 3H), 1.04 and 1.01 (d, J=6.4 Hz, 3H). **2f**: IR (neat) 1720 cm^{-1} (two C=O); ^{1}H NMR (200 MHz) δ 4.22 (q, J=7.0 Hz, 2H), 4.08 (q, J=7.0 Hz, 2H), 2.70-2.08 (m, 7H), 1.95-1.55 (m, 3H), 1.26 (t, J=7.1 Hz, 3H), 1.19 (t, J=7.1 Hz, 3H). **3a**: IR (neat) 1800, 1760 cm^{-1} (two C=O); ^{1}H NMR (200 MHz) δ 4.43 (m, 1H), 4.04 (q, J=7.2 Hz, 2H), 2.39-2.30 (m, 2H), 2.30-2.20 (m, 3H), 1.85-1.25 (m, 7H), 1.17 (t, J=7.2 Hz, 3H). **3b**: IR (neat) 1775, 1725 cm^{-1} (two C=O); ^{1}H NMR (200 MHz) δ 4.51(m, 1H), 4.14 (q, J=7.8 Hz, 2H), 2.55 (m, 2H), 2.38 (m, 3H), 1.95-1.87 (m, 1H), 1.84-1.66 (m, 4H), 1.26 (t, J=7.9 Hz, 3H). **3c**: ^{1}H NMR (200 MHz) δ 4.50 (m, 1H), 4.13 (q, J=7.4 Hz, 2H), 2.58-2.26 (m, 5H), 1.95-1.36 (m, 9H), 1.26 (t, J=7.1 Hz, 3H). **3d**: IR (neat) 1750, 1720 cm^{-1} (C=O); ^{1}H NMR (200 MHz) δ 4.52-4.20 (m, 1H), 3.62 (s, 3H), 2.70-2.37 (m, 3H), 2.28 (t, J=6.8 Hz, 2H), 2.07-1.90 (m, 1H), 1.75-1.32 (m, 6H), 1.23 (d, J=7.0 Hz, 3H). **3e**: IR (neat) 1760, 1720 cm^{-1} (two C=O); ^{1}H NMR (200 MHz) δ 4.40 and 3.99 (m, 1H), 4.07 (q, J=7.2 Hz, 2H), 2.75-2.48 (m, 1H), 2.32-2.10 (m, 3H), 1.80-1.10 (m, 7H), 1.22(t, J=7.2 Hz, 3H), 1.11 and 0.98 (d, J=6.1, 7.2 Hz, 3H). **3f**: IR (neat) 1740, 1720 cm^{-1} (two C=O); ^{1}H NMR (200 MHz) δ 4.24 (q, J=7.2 Hz, 2H), 4.10 (q, J=7.2 Hz, 2H), 2.52-1.97 (m, 6H), 1.82-1.40 (m, 4H), 1.30 (t, J=7.2 Hz, 3H), 1.23 (t,

J=7.2 Hz, 3H).
11. (a) For asymmetric reaction, Pfau, M.; Revial, G.; Guingant, A.; d'Angelo, J. *J. Am. Chem. Soc.* **1985**, *107*, 273-274. (b) *For a review*, Trost, B. M., Fleming, I., Eds.; In *Comprehensive Organic Synthesis*; Pergamon Press: Oxford; Vol. 4, p 1-67.
12. Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1995**, *117*, 3705-3716.

Electrostatic Potential Maps of Silacyclohexane: The Origin of the "Gauche Effect" on Silicon Compounds

Soo Gyeong Cho

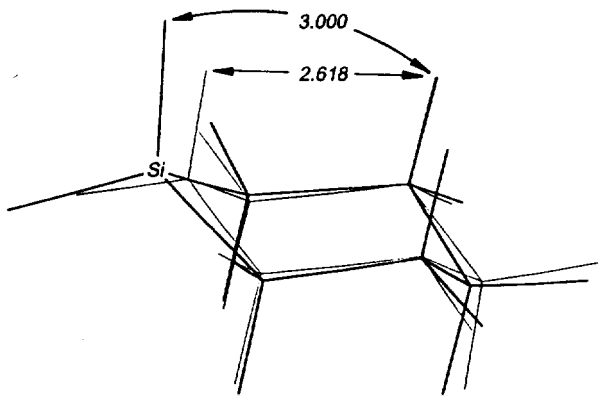
Agency for Defense Development, P.O. Box 35-1, Yuseong, Taejon 305-600, Korea

Received July 14, 1995

The incorporation of heteroatom to hydrocarbon molecules changes the conformational preference dramatically. One of the interesting features is a phenomenon known as the "gauche effect".[1] Many molecules containing N, O, S, P, F, or Cl atom show the preference to adopt the gaucheconformation.[1,2] The "gauche effect" in these molecules has been interpreted on the basis of electronic natures such as lonepairs, electron/nuclear charge distributions, and polar bonds.

The "gauche effect" is also ubiquitous in various silicon compounds.[3,6] Various butane-like silicon compounds such as ethylmethylsilane ($CH_3CH_2SiH_2CH_3$),[3a,b,4,6b] ethylchlorosilane ($CH_3CH_2SiH_2Cl$),[6b,c] 1,2-dimethyldisilane ($CH_3SiH_2SiH_2CH_3$),[5a,b,6a] and (chloromethyl)methylsilane ($ClCH_2SiH_2CH_3$)[6c,d] are more stable in the gauche conformation than in the anti conformation. Cyclic 6-membered ring systems also provide valuable information about the "gauche effect". The A value, the free energy difference between the axial and equatorial conformations, is largely attributed to the gauche/anti energy difference of the torsional frame which is composed of the substituent and 3 ring atoms. 1-Methylsilacyclohexane and 1-chlorosilacyclohexane are more stable in the axial conformation than in the equatorial conformation by 0.13 kcal/mol,[3b] and 0.81 kcal/mol,[6c] respectively. In contrast to other heteroatoms, the "gauche effect" of silicon compounds has been explained mostly by steric reasons due to the longer Si-C bond length.[3b,4,6a,b,c]

In connection with the conformational analyses of various monosubstituted silacyclohexanes (SCHs), we have been interested in the structure and electronic nature of SCH. Understanding the exact structural and electronic natures of SCH is important, because SCH serves as the reference molecule in quantifying the A values of various monosubstituted SCHs. Especially, it is our intention to analyze electronic natures including the electrostatic potential (ESP), which is generally accepted to furnish useful information about the charge distribution around the molecule.[7]



Figures 1. MP2/6-31G* optimized chair conformation of CH (−) and SCH (—); least-square fit using 4 ring carbons (2α-carbons and 2β-carbons in SCH).

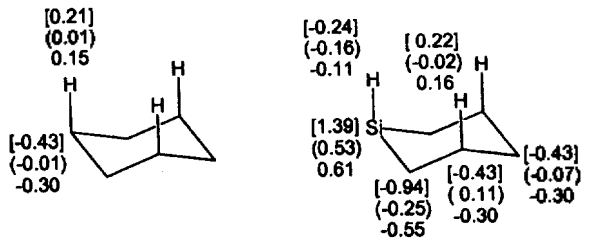


Figure 2. [NP], (CHELPG), and MP charges of ring atoms and axial hydrogens in CH and SCH calculated by MP2/6-31G*.

Ab initio molecular orbital calculations have been performed using the GAUSSIAN-92 series of programs,[8] on a Cray Y-MP computer. The geometries of cyclohexane (CH) and SCH have been optimized at the MP2/6-31G* level of theory.[9] Only the chair conformation has been considered by imposing D_{3d} symmetry on CH and C_s symmetry on SCH.

The MP2/6-31G* calculated structures of SCH and CH are compared in Figure 1. An interesting structural modification in SCH is that the axial hydrogen attached to Si moves away from the ring. According to our MP2/6-31G* calculations, the torsional angles of ring carbons in CH are 55.6° In SCH, the torsional angle of C-Si-C-C is only 45.8° which shows the Si tip of the ring quite flattened. The torsional angle of C_2-C_3-C_4-C_5 in SCH is 65.8° which indicates the puckering degree of γ-carbon greater (See Figure 1). Consequently, the change of ring skeleton forces the geometric parameters including hydrogens to be altered substantially. The distances from the axial hydrogen of Si to the axial hydrogens of β-Cs in SCH are 3.00 Å, while the distances between 1,3-diaxial hydrogens in CH are 2.62 Å. This implies that most axial substituents at Si atom of SCH may relieve unfavorable 1,3-diaxial interactions due to (1) the longer Si-bonds, i.e. Si-C ring bonds and exocyclic Si bonds to substituents, and (2) flattening of Si tip. However, the subtle increase of the distance between 1,3-diaxial hydrogens by 0.4 Å may not be accounted for the "gauche effect" of silicon compounds entirely.

The nonbonded interactions between neutral atoms usually contribute small energy differences with respect to electro-