therefore provides a rationale for the nucleophilic ring opening reactions of the arylcyclopropane cation radicals described earlier.[1] The model makes a further general prediction that *the stereochemical course of nucleophilic displacements on σ one-electron bonds will be governed by the σ* (LUMO) orbital of the one-electron bond and will therefore proceed with inversion of configuration at the site of attack.*[10,11] We should caution, however, that when overlap binding ceases to be the dominant factor, as in metallic or higher row elements, the stereoselection rule will accordingly be weakened and stereoretention may become competitive with stereoinversion.

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(10) It is worth pointing out an isoelectronic analogy of the nucleophilic cleavages of one-electron σ bonds, namely, the cleavages of two-electron σ bonds by radicals. This isoelectronic analogy implies isostereospecificity. Indeed, although the analysis is less straightforward,[8,12] it is still possible to identify the σ*(LUMO) orbital of the two-electron bond as the main stereoelectronic component which controls the reaction stereochemistry. Thus, much the same as in the nucleophilic cleavages of one-electron σ bonds, the radical cleavages of two-electron σ bonds are also predicted to proceed with stereoinversion. In fact, they do.[13]

(11) In principle, the valence-bond model can also be used to analyze the *regiochemistry* of nucleophilic additions to cation radicals. In practice, this problem is more complicated, however, because it requires consideration of both the thermochemistries of the various regiochemical pathways and the orbital interaction terms. This problem is discussed in detail in a forthcoming paper on the isoelectronic reaction of radical additions to olefins. See: Shaik, S. S.; Canadell, E. *J. Am. Chem. Soc.* **1990**, *112*, 1446.

(12) See discussion on p 197 of ref 8 using a classical valence bond treatment. By analyzing the problem in fragment MO's, as done in the present paper, and by using the mixing rules in ref 8, it is possible to show that the resonance interaction in the radical cleavage of two-electron σ bonds will be proportional to the *product* of overlaps between the orbital of the radical and both the σ and σ* orbitals of the R-X bond, $(\phi_{rad}-\sigma_{CX})(\phi_{rad}-\sigma^*_{CX})$, and that this product virtually vanishes for front-side attack, prefering the backside cleavage.

(13) (a) Incremona, J. H.; Upton, C. J. *J. Am. Chem. Soc.* **1972**, *94*, 301. (b) Incremona, J. H.; Upton, C. J. *J. Org. Chem.* **1976**, *41*, 523. (c) Maynes, G. G.; Applequist, D. E. *J. Am. Chem. Soc.* **1973**, *95*, 856. (d) Shea, K. J.; Skell, P. S. *J. Am. Chem. Soc.* **1973**, *95*, 6728. (e) Poutsma, M. L. *J. Am. Chem. Soc.* **1965**, *87*, 4293. (f) Jarvis, B. *J. Org. Chem.* **1970**, *35*, 924.

The Synthesis of Substituted Lactones by Intramolecular Chirality Transfer with Stereodifferentiating Chiral α-Ester Radical Intermediates

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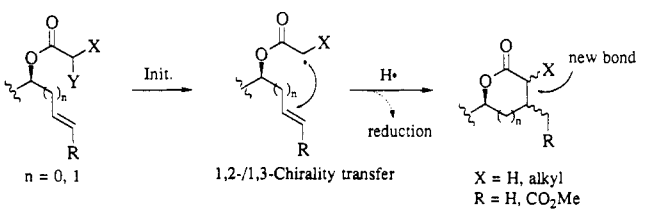
Summary: Carbon radicals generated from α-halo acetate, propionate, and related allylic and homoallylic esters can cyclize onto activated and unactivated olefins to give α,-β-substituted lactones with good to excellent stereochemical control in yields ranging from 52 to 90%.

The many attributes of carbon–carbon bond formation through free-radical processes have been lauded in recent years,[1] primarily as a result of a number of elegant studies on the mechanism and preparative aspects of these reactions. Because of their stabilized nature, ester α-radical species have been considered unsuitable[2,3] for C–C bond formation in the presence of tin hydrides, as exemplified by the synthesis of lactones[4] from such radicals and olefins (Scheme I). This prompted Ueno[5] and Stork[6] to develop

Scheme I



the α-bromo acetal method as an indirect yet efficient route to γ- and δ-lactones. Another practical solution to this problem has been devised by Curran and Chang[2] based on the halogen atom transfer method. The prospects of a direct formation of lactones by intramolecular capture of an ester radical as shown in Scheme I has a number of redeeming features. Moreover, the potential for stereochemical control at the newly formed sterogenic centers presents additional amenities and obvious challenges in free-radical processes.[2,6,7]

We report herein that primary and secondary radicals generated from α-halo esters with triphenyltin (or tributyltin) hydride at low concentrations (0.02–0.012 M

(1) (a) Curran, D. P. *Synthesis* **1988**, 417, 489. (b) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (c) Giese, B. Radicals in *Organic Synthesis; Formation of Carbon–Carbon Bonds*; Pergamon Press: Oxford, 1986. (d) Hart, D. J. *Science* **1984**, *223*, 883. (e) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073. (f) Surzur, J.-M. In *Reactive Intermediates*; Abramovitch, R. A., Ed.; Plenum Press, New York, 1982; Vol. 2, p 121.

(2) (a) Curran, D. P.; Chang, C.-T. *J. Org. Chem.* **1989**, *54*, 3140 and references cited therein. (b) See also: Stork, G.; Mah, R. *Heterocycles* **1989**, *28*, 723.

(3) Surzur, J.-M.; Bertrand, M. P. *Pure Appl. Chem.* **1988**, *60*, 1659.

(4) Direct butyrolactone production by a radical process in yields ranging from 19 to 50% has been recently demonstrated. (a) Belletire, J. L.; Mahmoodi, N. O. *Tetrahedron Lett.* **1989**, *30*, 4363. (b) For radical cyclizations of propargyl bromoesters, see: Clough, J. M.; Pattenden, G.; Wight, P. G. *Tetrahedron Lett* **1989**, *30*, 7469.

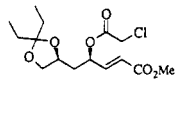
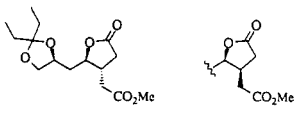
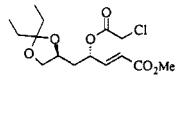
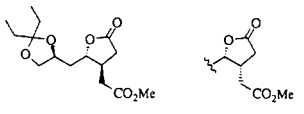
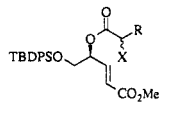
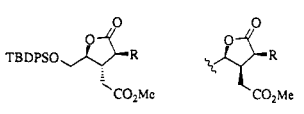
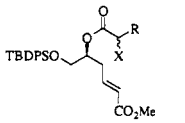
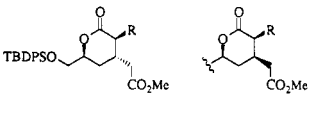
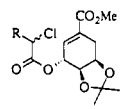
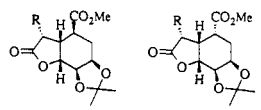
(5) Ueno, Y.; Chino, K.; Watanabe, M.; Moriya, O.; Okawara, M. *J. Am. Chem. Soc.* **1982**, *104*, 5564; *J. Chem. Soc., Perkin Trans 1* **1986**, 1351.

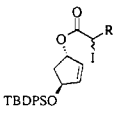
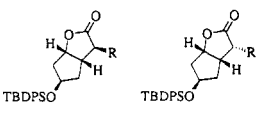
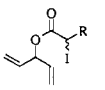
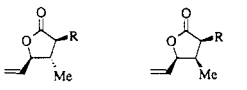
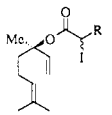
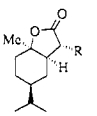
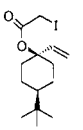
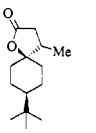
(6) Stork, G.; Mook, R., Jr.; Biller, S. A.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **1983**, *105*, 3741. Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1983**, *105*, 6765. Stork, G.; Sher, P. M.; Chen, H.-L. *J. Am. Chem. Soc.* **1986**, *108*, 6384. Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 303. Stork, G. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 149 and references cited therein.

(7) For some recent examples, see: Stork, G.; Kahn, M. *J. Am. Chem. Soc.* **1985**, *107*, 500. Koreeda, M.; George, I. A. *J. Am. Chem. Soc.* **1986**, *108*, 8098. Rajanbabu, T. V.; Fukunaga, T.; Reddy, G. S. *J. Am. Chem. Soc.* **1988**, *111*, 1759.

0022-3263/90/1955-3436$02.50/0

Table I

entry	substrate[a]	products, yield,[b] %	ratio[c,d]
A		 77% (18%)	96 : 4
B		 74% (10%)	92 : 8
C	 7 R = H X = Cl,I 8	 81% (17%) 9	88 : 12
D	10 R = Me X = Cl 11	81% (15%) 12	80 : 20[d,e]
E	13 R = i-C_3H_7 X = Br 14	91% (1.5%) 15	91 : 9[d,f]
F	 16 R = H; X = I	 17 51% (35%) 18	23 : 77
G	19 R = Me; X = Cl	20 63% (23%) 21[g]	78 : 22[d]
H	 22 R = H	 23[g] 81% (14%) 24[g]	86 : 14[d]
I	25 R = Me	26[g] 79% (14%) 27[g]	47 : 53[d]

entry	substrate[a]	products, yield,[b] %	ratio[c,d]
J	 28 R = H	 29 54% (42%)	
K	30 R = Me	31 37% (48%) 32	82 : 18
L	 33 R = H	 34 74% 35	81 : 19[d]
M	36 R = Me	37 86% 38	78 : 22[h]
N	 39 R = H	 40 53%[d,i]	
O	41 R = Me	42 52%[d]	
P	 43	 44 90%[d]	

[a] Except for entries J–P, all starting materials were optically pure and homogeneous; TBDPS = *tert*-butyldiphenylsilyl. [b] Cyclizations were carried out by slow addition of triphenyltin hydride using a syringe pump, at the reflux temperature of benzene (0.02–0.012 M solution); for details, see ref 18 and supplementary material. Yields are for isolated chromatographically homogeneous lactones as single isomers or mixtures; numbers in parenthesis refer to yields of isolated reduction byproducts. [c] Ratio determined by ^1H and/or ^{13}C NMR in addition to weight of lactones. [d] Ratio determined by weight of individual isolated isomers. [e] Minor isomer in the ratio of 10 (for **12**):7:3, isolated by preparative HPLC. [f] Minor isomers in ratio of 4 (for **15**):5 another cis/trans isomer. [g] X-ray single-crystal structure. [h] Balance consists of a mixture of the other three isomers in a ratio of 9:8:5. [i] Total yield of cyclization, 83%.

syringe-driven pump) undergo smooth intramolecular cyclization with *activated and unactivated* olefins to give γ- and δ-lactones with good to excellent stereochemical control in the majority of the cases studied. Table I shows the results with allylic and homallylic α-halo esters. Of importance is the fact that an anti stereochemical preference is maintained in relation to the ester bearing carbon atom in the formation of all the monocyclic as well as bicyclic lactones. It is also possible to generate two new contiguous stereogenic centers with excellent anti selectivity *even when the α-halopropionate segment originates from a racemic 2-halopropionic acid* (entries D, E, G, I, M, O). Whereas the nature of the halogen seems to be unimportant in the case of activated olefins (entry C), α-iodo esters are preferred when cyclization involves unactivated olefins. In all cases studied so far cyclization takes place in the exo mode,[8] and the byproducts are the reduced esters which can be recycled if necessary. Cyclization is more favored in the case of allylic esters giving γ-lactones, compared to the 6-exo cyclization[9] of the homoallylic esters where reduction is proportionately a more competitive process. The successful γ-lactone formation from tertiary alcohols (entries N, O, P) further demonstrates the potential utility of the α-halo ester radical cyclization technology. In addition to the obvious preparative utility, a number of fundamentally important issues regarding the mechanism and the stereochemical course of these reactions can be addressed. Even though the tin hydride concentrations are very low in our protocol,[10] the stabilized radical must, in addition to escaping its inevitable reduction, overcome geometric constraints associated with the ester function.[2b,11] It must also contend with unfavorable orbital interactions,[12] particularly in the case of electron-deficient olefins. In such cases, the transition state for radical ring closure[2,12,13] probably occurs *later* on the reaction coordinate, compared to those for the more nucleophilic radicals. All the secondary radicals generated from the racemic α-halopropionate tethers undergo stereocontrolled cyclizations to give γ- and δ-lactones in which *the newly formed stereogenic center bearing the original propionate methyl group is of high stereochemical purity*. Clearly, this must be the consequence of a preferred orientation of the radical specie in the chiral intermediate ("chirad") in the transition state, just prior to

(8) Beckwith, A. L. J.; Schiesser, C. H. *Tetrahedron* **1985**, *41*, 3925.
(9) Julia, M. *Pure Appl. Chem.* **1974**, *40*, 553. See also refs 1e,f, 11.
(10) The possibility of successful cyclization with reactive halides as in α-iodo or α-bromo carbonyl compounds has been pointed out[2a] and recently shown.
(11) Beckwith, A. L. J.; Glover, S. A. *Aust. J. Chem.* **1987**, *40*, 157. Wu, L.; Fischer, H. *Helv. Chim. Acta* **1983**, *66*, 138.
(12) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959.
(13) Ghodoussi, V.; Gleicher, G. J.; Kravetz, M. *J. Org. Chem.* **1986**, *51*, 5007.

the formation of the new sp^3 bond. When the α-substituent is bulky (entry E), reduction of the corresponding radical is no longer a competing reaction.

We have shown that allylic and homoallylic ester radicals can be viable reactive species in the intramolecular reaction with suitably disposed activated and unactivated olefins.[14] The overall reaction can be formally related to the alkylation or Michael reaction of an ester enolate,[15] albeit via a free-radical intermediate (Scheme I). The resulting γ- and δ-lactones which can contain vicinal and/or alternating substituents should be valuable chirons for the synthesis of a variety of natural products derived from well-known biosynthetic routes.

Acknowledgment. We thank the NSERCC and the FCAR for generous financial assistance.

Supplementary Material Available: Physical constants, $[\alpha]_D$, ^1H NMR, ^{13}C NMR, mass, and elemental analyses, X-ray crystal structures, representative spectra, and selected experimental procedure (29 pages). Ordering information is given on any current masthead page.

(14) Reactions can be conveniently carried out on preparative scale as shown in the following example. To a magnetically stirred solution of **36** (1.3 g, 4.88 mmol) in dry benzene (245 mL, solution 0.02 M) was added AIBN (10 mg, 0.098 mmol), at room temperature, under argon atmosphere. A solution of triphenyltin hydride (2.91 g, 8.3 mmol) in dry benzene (170 mL, 0.049 M solution) was injected in four portions using a syringe pump, into the refluxing solution over 14 h. The solvent was removed by evaporation, and the residue was purified by flash chromatography (ethyl acetate/hexanes 5–13% hexanes gradient) to give a crystalline mixture of four isomers (596 mg, 86%) (ratio 9.5:1.1:1.0:0.6 by NMR), the major isomer being the anti/anti (see the supplementary material).

(15) For recent reviews, see: Heathcock, C. H. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, p 111. Evans, D. A. *Science* **1988**, *240*, 420 and references cited therein.

Platinum-Catalyzed Intramolecular Hydrosilation of Allylamines: Formation of 1-Aza-2-silacyclobutanes and Application to Stereoselective Synthesis of 2-Amino Alcohols[1]

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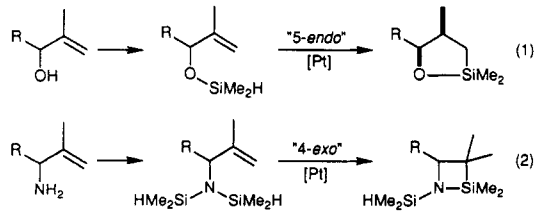
Received April 2, 1990

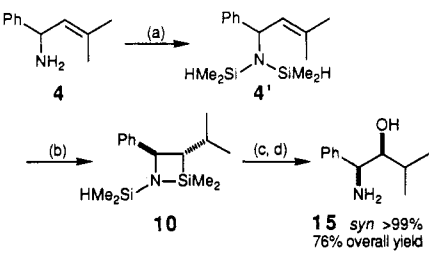
Summary: *N,N*-Bis(dimethylsilyl)allylamines undergo intramolecular hydrosilation in the presence of Pt-[{CH_2=CH)Me_2Si}$_2O$]$_2$ (0.2 mol %) to form four-membered cyclic compounds, 1-aza-2-silacyclobutane derivatives, which can be transformed into 2-amino alcohols by oxidation with 30% H_2O_2 in the presence of KF and $KHCO_3$.

We recently reported intramolecular hydrosilation of allyl alcohols as well as homoallyl alcohols forms five-membered ring compounds selectively (5-endo ring closure),[2] as exemplified by eq 1; the products can be transformed into 1,3-diols by hydrogen peroxide oxidation.[3] We now find, to our surprise, that platinum-catalyzed intramolecular hydrosilation of allylamines forms four-membered ring compounds, 1-aza-2-silacyclobutane derivatives, almost exclusively (4-exo ring closure),[2] as shown in eq 2. Reported herein are the regio- and stereoselective formation of 1-aza-2-silacyclobutanes and their application to the stereoselective synthesis of 2-amino alcohols.



Representative results are listed in Table I. Scheme I illustrates transformations of allylamine **4** (entry 4).

Scheme I[a]



[a] (a) *n*-BuLi (×2.2))/$ClSiMe_2H$ (×2.2)/Et_2O; (b) Pt[{(CH_2=CH)Me_2Si}$_2O$]$_2$ (0.2 mol %)/room temperature/0.5 h; (c) EDTA·2Na/hexane/room temperature; (d) 30% H_2O_2/KF/$KHCO_3$/MeOH/THF/room temperature/18 h.

Thus, the amino group in **4** was converted into a bis(dimethysilyl)amino group by repeating *twice* a sequence of lithiation (*n*-BuLi) and silylation (HMe_2SiCl). The bis(silyl)amine **4'** was treated in dry ether with a catalytic amount (0.2 mol %) of Pt[{(CH_2=CH)Me_2Si}$_2O$]$_2$.[4] Intramolecular hydrosilation occurred exothermically at room temperature and was complete within 0.5 h, as monitored by ^1H NMR. Bulb-to-bulb distillation gave **10**[5] as a single trans isomer in 90% yield. Transformation to an amino alcohol was carried out, without isolation of **10**, as follows. After removal of the platinum catalyst by treatment with crystalline EDTA·2Na, **10** was subjected to the hydrogen peroxide oxidation under usual condition, followed by column chromatography, to afford the amino alcohol **15**[5] as a syn isomer in 76% overall yield.[6]

(1) Silafunctional Compounds in Organic Synthesis. 46. Part 45: Tamao, K.; Hayashi, T.; Ito, Y. *Tetrahedron Lett.* **1989**, *30*, 6533.

(2) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734. 5-Endo and 4-exo ring closure modes observed in the hydrosilation products may be regarded as 6-endo and 5-exo modes, respectively, in transition-metal-containing intermediates.[3]

(3) (a) Tamao, K.; Tanaka, T.; Nakajima, T.; Sumiya, R.; Arai, H.; Ito, Y. *Tetrahedron Lett.* **1986**, *27*, 3377. (b) Tamao, K.; Nakajima, T.; Sumiya, R.; Arai, H.; Higuchi, N.; Ito, Y. *J. Am. Chem Soc.* **1986**, *108*, 6090. (c) Tamao, K.; Nakagawa, Y.; Arai, H.; Higuchi, N.; Ito, Y. *J. Am. Chem. Soc.* **1988**, *110*, 3712.

(4) Readily available from chloroplatinic acid: (a) Chandra, G.; Lo, P. Y.; Hitchcock, P. B.; Lappert, M. F. *Organometallics* **1987**, *6*, 191. (b) Lewis, L. N.; Lewis, N. *J. Am. Chem. Soc.* **1986**, *108*, 7228. The intramolecular hydrosilation proceeded rather slowly with $Pt(PPh_3)_4$ as a catalyst, while H_2PtCl_6·$6H_2O$-catalyzed reaction resulted in the formation of rather complex mixture.

(5) All new compounds showed satisfactory spectral and analytical data, as shown in the supplementary material.

(6) Stereochemistry and isomer ratios of 2-amino alcohols were determined by capillary GLC analysis and ^1H NMR spectroscopy of amino alcohol themselves or of their oxazolidone derivatives.

0022-3263/90/1955-3438$02.50/0