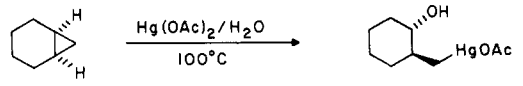
Mercury(II)-Mediated Opening of Cyclopropanes. Effects of Proximate Internal Nucleophiles on Stereo- and Regioselectivity

David B. Collum,* Fariborz Mohamadi, and John S. Hallock

Contribution from the Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, New York 14853. *Received March 25, 1983*

Abstract: The effects of internal ester and carboxylic acid moieties on the inherent regio- and stereoselectivities of mercury(II)-induced cleavage of unactivated cyclopropanes are investigated. Although the cyclizations provide lactones routinely in high stereoselectivity, surprising losses in selectivity are occasionally observed. The cyclizations also exhibit unanticipated preferences for the formation of the larger of two possible lactones. Possible origins of these anomalous stereo- and regioselectivities are considered.

Since the middle of the 19th century[1] chemists have denoted the nucleophilicity[2] of the carbon–carbon bond of cyclopropanes.[3,4] As an example, Russian workers reported the facile, stereoselective cleavage of norcarane (**1**) illustrated below.[5] Although studies have failed to differentiate mechanisms involving corner vs. edge complexation of the electrophile, in all but a few cases the observed stereo- and regioselectivities are congruent with mechanisms involving backside attack of the nucleophile at the cyclopropane carbon best able to stabilize a developing positive charge with consequent inversion of configuration.



1 85% yield

Neighboring group assisted[6] openings of cyclopropanes activated by electron deficient cyclopropyl carbinyl carbons,[4d,6f,7] as well as anchimerically assisted electrocyclic openings of dihalocyclopropanes,[8] are fully documented. However, the limited information available on internally assisted openings of *unactivated* cyclopropanes pertains to protic acid mediated cleavages and indicates that such processes are unfavorable.[9]

Table I.[a] Lactonization Selectivities for **4a-c** at 25 °C

entry	HgX_2 X =	solvent	R	yield (6a and 7a)	stereoselectivity[b] (6a:7a)
1	NO_3	DME	H	86	3:1
2	CF_3COO	DME	H	63	4:1
3	$OClO_3$	DME	H	53	10:1
4	NO_3	$CHCl_3$	Na	54	6:1
5	CF_3COO	$CHCl_3$	Na	73	4:1
6	$OClO_3$	$CHCl_3$	Na	63	16:1
7	$OClO_3$	CH_3OH	Na	78	10:1
8	$OClO_3$	CH_3NO_2	H	78	5:1
9	$OClO_3$	DME	CH_3	70	6:1
10	$OClO_3$	CH_2Cl_2	H	60	15:1
11	$OClO_3$	CH_2Cl_2	CH_3	64	11:1
12	$OClO_3$	CCl_4	H	35	52:1
13	$OClO_3$	CCl_4	CH_3	36	50:1
14	$OClO_3$	CCl_4	Na	79	27:1
15	$OClO_3$	hexane	H	44	45:1
16	$OClO_3$	hexane	CH_3	54	38:1
17	$OClO_3$	hexane	Na	83	100:1

[a] See ref 16. [b] HPLC integrations corrected for molar absorbtivities.

We report herein studies pertaining to mercury-mediated lactonizations of cyclopropyl acid derivatives. The factors affecting the regio- and stereochemical outcomes of these processes are addressed. Several surprising stereo- and regioselectivities place these cyclizations in a novel context with respect to the literature of solvomercuration of olefins,[10] electrophile-mediated cleavage of cyclopropanes,[2a-g] and kinetically controlled ring formation.[6] Overall, the process complements epoxide openings with carbon nucleophiles[11] in that both effect the addition of oxygen- and carbon-containing units across a carbon–carbon double bond. The present reaction offers additional stereo- and regiochemical control

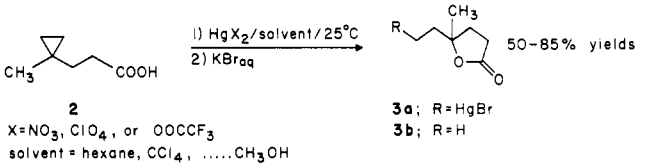
(1) Baeyer, A. *Chem. Ber.* **1855**, *18*, 2277.
(2) (a) Lukina, M. Y. *Russ. Chem. Rev.* **1962**, 419. (b) DePuy, C. H. *Top. Curr. Chem.* **1973**, *40*, 73. (c) Lee, C. C. *Prog. Phys. Org. Chem.* **1970**, *7*, 129. (d) Collins, C. J. *Chem. Rev.* **1969**, *69*, 543. (e) McAuliffe, C. A. "The Chemistry of Mercury"; McMillan: London 1977. (f) DePuy, C. H. *Acc. Chem. Res.* **1968**, *1*, 33. (g) Gibson, D. H.; Depuy, C. H. *Chem. Rev.* **1974**, *74*, 605.
(3) Moss, R. A. "Selective Organic Transformations"; Thyagarajan, B. S., Ed.; Wiley-Interscience: New York, 1972. Simmons, H. E.; Cairns, T. L.; Vladuchick, S. A.; Hoiness, C. M. *Org. React.* **1973**, *20*, 1. Bartlett, P. A. *Tetrahedron* **1980**, *36*, 3.
(4) Reviews on the chemistry of cyclopropanes and their application to synthesis: (a) Stevens, R. V. *Acc. Chem. Res.* **1977**, *10*, 193. (b) de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 809. (c) Wenkert, E. *Heterocycles* **1980**, *14*, 1703. (d) Danishefsky, S. *Acc. Chem. Res.* **1979**, *12*, 66. (e) Aksenov, V. S.; Terent'eva, G. A.; Savinykh, Y. V. *Russ. Chem. Rev.* **1980**, *49*, 549. (f) see ref 2a-g.
(5) Lukina, R. Y.; Gladshtein, M. *Dokl. Akad. Nauk SSSR* **1950**, *71*, 65.
(6) (a) McManus, S. P.; Capon, B. "Neighboring Group Participation"; Plenum Press: New York, 1976; Vol. 1. (b) Staninets, V. I.; Shilov, E. A. *Russ. Chem. Rev.* **1971**, *40*, 272. (c) Capon, B. *Q. Rev., Chem. Ser.* **1964**, *18*, 45. (d) Page, M. I. *Chem. Soc. Rev.* **1973**, *2*, 295. (e) Goodman, L. *Adv. Carbohydr. Chem.* **1967**, *22*, 109. (f) Stirling, C. J. M. *Chem. Rev.* **1981**, *78*, 517. (g) Kirby, A. J. *Adv. Phys. Org. Chem.* **1980**, *17*, 183. (h) Preston, P. M.; Tennant, G. *Chem. Rev.* **1972**, *72*, 627.
(7) For some recent examples, see: Danishefsky, S.; Regan, J.; Doehner, R. *J. Org. Chem.* **1981**, *46*, 5255. Winterfeldt, E.; Hammer, H. *Tetrahedron* **1981**, *37*, 3609. Murphy, W. S.; Wattanasin, S. *J. Chem. Soc., Perkin Trans. 1* **1982**, 271.
(8) Danheiser, R. L.; Morin, J. M., Jr.; Yu, M.; Basak, A. *Tetrahedron Lett.* **1981**, *22*, 4205.
(9) (a) Product distributions resulting from protic acid opening of simple cyclopropane substrates indicate minimal intervention of proximate, internal oxygen nucleophiles in the cleavage: Paquette, L. A.; Scott, M. K. *J. Am. Chem. Soc.* **1972**, *94*, 6751. Cliche, L.; Christol, H.; Coste, J.; Plenat, F. *Can. J. Chem.* **1981**, *59*, 2373. Peterson, P. E.; Thompson, G. *J. Org. Chem.* **1968**, *33*, 968. For an additional example we note that lactonization of acid **9a** with protic acid ($HCl/CHCl_3$/50 °C) affords an approximately even distribution of lactones **11b–14b**. (b) An intramolecular hydroperoxide-assisted mercury-mediated opening of a bicyclo[3.1.0]hexane was mentioned as a possible route to prostaglandin endoperoxides. Apparently, discouraging *intermolecular* openings precluded the testing of this hypothesis: Salomon, R. G.; Gleim, R. D. *J. Org. Chem.* **1976**, *41*, 1529.
(10) (a) Chatt, J. *Chem. Rev.* 1951, *48*, 1. (b) Kitching, W. *Organomet. Chem. Rev.* **1968**, *3*, 61. (c) Zefirov, N. S. *Russ. Chem. Rev.* **1965**, *34*, 527. (d) Fahey, R. C. *Top. Stereochem.* **1968**, *3*, 237. (e) See references cited in ref 17.
(11) Posner, G. H. "Organic Reactions"; John-Wiley and Sons, Inc.: New York, 1975; Vol. 22, pp 253–400.

0002-7863/83/1505-6882$01.50/0

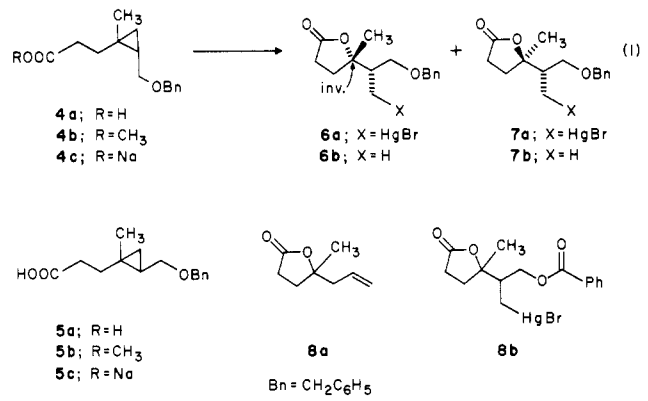
similar to that found in cyclofunctionalizations of unsaturated acids.[12]

Results and Discussion[13,14]

Treatment of acid **2** with 2.2 equiv of $Hg(NO_3)_2$, $Hg(OOCCF_3)_2$, or $Hg(OClO_3)_2 \cdot XH_2O$ [hereafter referred to as simply $Hg(OClO_3)_2$] at 25 °C for 2–20 h in a variety of solvents ranging in polarity from hexane to methanol affords lactone **3a** (after aqueous KBr workup) as the sole observable product in chromatographed yields of 50–85%. Reduction of **3a** ($NaBH_4$/0 °C/NaOH;[15] 65% yield) provides lactone **3b**.[14] Although the highest yields are obtained when lactonization is effected in polar solvents, the reaction is marginally faster in nonpolar solvents. This may reflect competitive ligation of the mercury by the cyclopropyl moiety and the solvent.[16] Also, we find that both the methyl ester and the sodium salt of **2** cyclize analogously.



Stereo- and Regioselectivity.[13,14] Stereochemically homogeneous substrates **4a–c** and **5a–c** were prepared from nerol and geraniol, respectively, and submitted to the gamut of reaction conditions. Since these substrates react analogously (producing complementary stereochemical results) only the data for the lactonizations of **4a–c** (eq 1) are presented (Table I). The inversion-to-retention



ratios depicted in Table I refer to the formation of γ-lactones **6a** and **7a**, the products of inversion and retention of configuration at the electrophilic quaternary carbon, respectively. The structural assignments for resulting mercurated lactones **6a** and **7a** are supported by reduction ($NaBH_4$/NaOH/0 °C) to lactones **6b** and **7b**, respectively, and comparison of these spectroscopically and

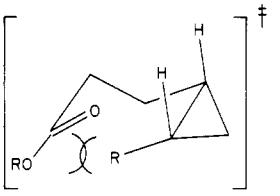
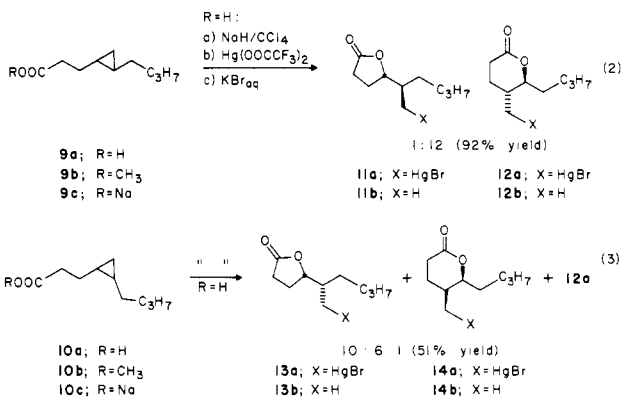


Figure 1.

chromatographically with authentic samples.[14] In most instances lactones **6a** and **7a** are the only products observed. However, in a few cases lactone **8a**,[18] the product of cyclopropyl carbinyl cationic solvolysis (e.g., entry 10; 36% yield), and benzoate **8b**,[18] the product resulting from benzylic oxidation[19] (e.g., entry 7; 6.6% yield), are isolated. These typically minor components are unique to the substrate chosen and thus are of minimal concern. It should also be noted that the reaction times required to cyclize sodium salt **4c** (generated in situ) are variable by virtue of its insolubility; extended reaction times are necessary to ensure complete conversions.

Surprisingly, in direct contrast with the mercury(II) acetate mediated cyclopropane hydrolyses reported to proceed largely (>90%) with inversion of configuration at the electrophilic carbon,[2b,20] cyclizations of **4a–c** using $Hg(NO_3)_2$ and $Hg(OOCCF_3)_2$ are effected with poor stereoselectivity under optimum conditions. Although the cyclizations using $Hg(OClO_3)_2$ in polar, aprotic solvents also proceed with very little stereocontrol, we find that mercury(II) perchlorate induced cyclizations in nonpolar solvents give lactone **6a** in >98% stereoisomeric purity (entry 17; Table I). Varying the reaction times for **4a–c** or **5a–c** effects no appreciable losses in the observed stereoselectivities, indicating the process to be under kinetic control. When the cyclizations are run at 50% conversion the starting substrates are recovered unchanged. Although the solvent dependency might be indicative of competing backside-assisted and unassisted (carbocationic) mechanisms, we favor alternative explanations as outlined subsequently.

To obtain additional information on the stereo- and regioselectivity exerted in the cyclization process, we turned to the electronically less-biased substrates **9a–c** and **10a–c**; some typical results are depicted in eq 2 and 3. As before, the structural



assignments for lactones **11a–14a** are supported by reduction (n-Bu_3SnH/AIBN/THF/25 °C)[21] and comparison of resulting

(12) (a) Kano, S.; Shibuya, S.; Ebata, T. *Heterocycles* **1980**, *14*, 661. (b) Ansell, M. F.; Palmer, M. H. *Q. Rev., Chem. Ser.* **1964**, *18*, 211. (c) Dowle, M. D.; Davies, D. I. *Chem. Soc. Rev.* **1979**, *8*, 171. (d) Clive, D. L. J. *Tetrahedron* **1978**, *34*, 1049. (e) Semple, J. E.; Joullie, M. *Heterocycles* **1980**, *14*, 1825. (f) Ganter, C. *Top. Curr. Chem.* **1976**, *67*, 15. (g) See ref 6b.

(13) A number of methods to introduce methylene units to alkenes have proven useful in this work (ref 14): Makosza, M.; Wawrzyniewicz, M. *Tetrahedron Lett.* **1969**, 4659. Suda, M. *Synthesis* **1981**, 714. Seyferth, D.; Yamazaki, H.; Alleston, D. L. *J. Org. Chem.* **1963**, *28*, 703. Pienta, M. J.; Kropp, P. J. *J. Am. Chem. Soc.* **1978**, *100*, 655. Furukawa, J.; Kawabata, N.; Nishimura, J. *Tetrahedron* **1968**, *24*, 53. Miyano, S.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1971**, *1418*. Chan, J. H.-H.; Rickborn, B. *J. Am. Chem. Soc.* **1968**, *90*, 6406.

(14) Supplementary material includes schematics for the preparation of all starting materials and authentic samples of **3b**, **6b**, **7b**, **11b–15b**, **18b**, **19b**, **22–25**, **31**, **32**, **43b**, and **44b**. Lactones **19b** and **18b** are naturally occurring (Quercus Lactones A and B, respectively): Masuda, M.; Nishimura, K. *Chem. Lett.* **1981**, 1333 and references cited therein.

(15) Bordwell, F. G.; Douglass, M. L. *J. Am. Chem. Soc.* **1966**, *88*, 993. For other methods of reductive demercuration see ref 2e.

(16) Dean, P. A. W. *Prog. Inorg. Chem.* **1978**, *24*, 109. However, the rate of oxy-metalation is more likely to depend on complex solvent, electronic, and steric effects (ref 17).

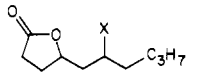
(17) Fukuzumi, S.; Kochi, J. K. *J. Am. Chem. Soc.* **1981**, *103*, 2783.

(18) (a) **8a**: 80 MHz ^1H NMR ($CDCl_3$) δ 8.10–7.98 (m, 2 H), 7.63–7.28 (m, 3 H), 4.68 (dd, J_1 = 4 Hz, J_2 = 8 Hz, 1 H), 4.33–4.05 (m, 1 H), 2.79–2.45 (m, 2 H), 2.45–1.75 (m, 4 H), 1.55 and 1.50 (2 s, 3 H), 1.35–1.20 (m, 1 H). MS (CI) m/z 473 (M + 1), 105 (100%). **8b**: 90 MHz ^1H NMR ($CDCl_3$) δ 7.40 (s, benzyl alcohol contaminant), 5.25 (s, benzyl alcohol), 5.18–5.03 (m, 1 H), 4.70 (d, J = 6 Hz, 1 H), 4.47 (s, benzyl alcohol), 2.73–2.30 (m, 4 H), 2.30–2.63 (m, 2 H), 1.4 (s, 3 H); IR (film) 3350 (benzyl alcohol), 1780, 1650 cm^{-1}. (b) Lactone **8a** becomes a serious side product during the cyclization of acids **4a** and **5a** using $Hg(OClO_3)_2$. Although this is probably due to the mole equivalent of $HClO_4$ liberated during the course of the reaction, the Lewis acidity of mercury(II) salts has been noted. For example, see: McKillop, A.; Ford, M. E. *Tetrahedron* **1974**, *30*, 2467.

(19) Barter, R. M.; Littler, J. S. *J. Chem. Soc. B* **1967**, 205.

(20) Depuy, C. H.; McGirk, R. H. *J. Am. Chem. Soc.* **1974**, *96*, 1121.

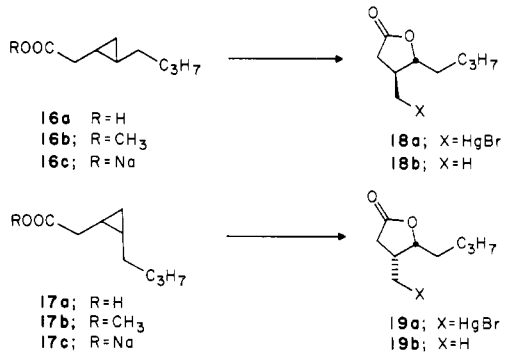
lactones **11b–14b** with authentic samples.[14] The stereo- and regioselectivities are determined by using high-pressure liquid chromatographic analysis on the reduced products. Also, we fail to detect the presence of γ-lactone **15a** (or **15b**[14] after reduction), the product derived from cleavage of the most highly substituted cyclopropane bond.



15a; X = HgBr
15b; X = H

Several aspects of our data are notable. On the basis of the well-documented kinetic preference for 5- versus 6-membered ring formation,[6] it is surprising to find significant quantities of δ-lactone **12a** upon cyclization of **9a–c** (falling in the range of δ/γ = 8–12:1 under a wide variety of conditions). Cyclizations of **10a–c** also produce anomalously large proportions of a δ-lactone (**14a**) when one accounts for the serious van der Waals interaction in the transition state leading to **14a** (Figure 1).[22] The stereochemical results are equally surprising. δ-Lactone **12a** and γ-lactones **11a** and **13a** are formed in at least[23] 20:1 selectively for inversion of configuration at the electrophilic carbon. In contrast, δ-lactone **14a** is formed in only 2–8:1 inversion selectivity.

Cyclizations of *trans*-**16a–c** and *cis*-**17a–c** provide further insight. Although **16a**, **16c**, **17a**, and **17c** lactonize very slowly



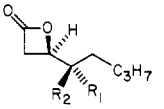
16a R = H
16b; R = CH_3
16c; R = Na

18a; X = HgBr
18b; X = H

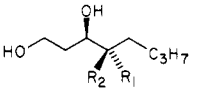
17a; R = H
17b; R = CH_3
17c; R = Na

19a; X = HgBr
19b; X = H

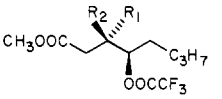
(several days at 25 °C affords low percent conversions), methyl esters **16b** and **17b** cyclize rapidly [$Hg(OOCCF_3)_2/CCl_4$/25 °C/8–12 h] to provide γ-lactones **18a** (86% yield) and **19a** (56% yield), respectively. Demercuration (Bu_3SnH) to lactones **18b** and **19b**[14] and gas chromatographic analysis show the cyclizations to be >100:1 stereoselective; the corresponding mercury perchlorate induced cyclizations, on the other hand, are essentially stereorandom. Furthermore, we are unable to detect β-lactones **20** and **21**, or their corresponding hydroxy acids resulting from hydrolytic cleavage.[24] This is shown by reduction of the crude cyclization products (LAH) and comparison of the resulting diols with authentic samples of diols **22–25**.[14] However, we do isolate stereo- and regioisomerically pure (>20:1) trifluoroacetates **26** (9% yield from **16b**) and **27** (26% yield from **17b**), the products of mercury counterion participation.[25] Our structural assignments are supported by reduction to the corresponding diols **24** and **25**,[14] respectively.



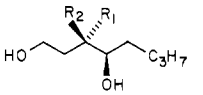
20; $R_1 = CH_2HgBr$, $R_2 = H$
21; $R_1 = H$, $R_2 = CH_2HgBr$



22; $R_1 = CH_3$, $R_2 = H$
23; $R_1 = H$, $R_2 = CH_3$



26; $R_1 = CH_2HgBr$, $R_2 = H$
27; $R_1 = H$, $R_2 = CH_2HgBr$



24; $R_1 = CH_3$, $R_2 = H$
25; $R_1 = H$, $R_2 = CH_3$

In order to determine the extent to which stereoelectronic factors[26,28] affect the regioselectivity of the cyclization, we submit acid **28a** (and its sodium salt **28b**) to the usual reaction conditions (CCl_4/25 °C/15 h) with use of $Hg(OOCCF_3)_2$. Spectroscopic [IR (film) 1775, 1730 cm^{-1}] and thin-layer chromatographic analysis of the crude product indicate the probable presence of lactones **29** and **30**. However, all attempts to effect a flash chromatographic separation of the individual components afford only γ-lactone **29** (IR 1775 cm^{-1}). Reduction of **29** (LAH/Et_2O/0 °C; 76% yield) gives diol **31** characterized in the usual manner.[14] Alternatively, reduction of the crude reaction product with $LiAlH_4$ produces a readily separable mixture of diols **31** and **32** (1.5:1, 63% overall yield from **28a**).[14] Yields and product distributions for this cyclization–reduction sequence are relatively insensitive to changes in solvent and participating group nucleophilicity; maximum regioselectivities are obtained in polar media (DME; **31**:**32** = 6:1). Cyclizations using $Hg(NO_3)_2$ and $Hg(OClO_3)_2$ produce inexplicably complex product distributions. Overall we may be observing competition between biases favoring a trans diaxial transition state leading to γ-lactone **29** and the ill-defined factors noted previously that favor the formation of the larger of two possible lactones (**30**).

Origin of Stereo- and Regioselectivity. We have depicted below the presumed major mechanistic pathway involving a direct, nucleophile-assisted cyclopropane ring cleavage (Mechanism I), along with five other intermediates representing pathways

(21) Burke, S. D.; Fobare, W. F.; Armistead, D. M. *J. Org. Chem.* **1982**, *47*, 3348 and references cited therein.

(22) The resistance of related cis-disubstituted systems to cyclize has been noted previously (ref 40).

(23) Our starting cyclopropanes *trans*-**9a–c** and *cis*-**10a–c** are prepared in 97.7% (44:1) and 94.4% (17:1) stereoisomeric purity, respectively (ref 14). We observe γ-lactone stereoselectivities in the range of 20–30:1 under all conditions studied. By virtue of the differing stereo- and regioselectivities for the cyclizations of the two cyclopropane isomers, we are unable to precisely factor out selectivity losses due to the stereoisomeric impurities. However, the loss in stereoselectivity in the conversion of *cis*-**10a–c** to δ-**14a** is unquestionably real. Furthermore, we observe the following curious kinetic effect. *trans*-**9** and *cis*-**10** react at qualitatively the same rate. However, *in the presence of trans*-**9**, *cis*-**10** fails to react until all of the *trans* isomer is consumed (shown by following the disappearance of methyl esters **9b** and **10b** by gas chromatography). Accordingly, at 95–98% conversion, stereoselectivities as high as 99.8% (>500:1) can be observed; extensive reaction times (100% conversion) cause the selectivities to decrease to 98%. We felt that these results are *consistent* with the following scenario:

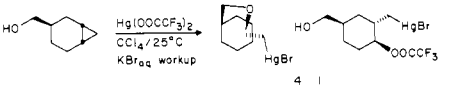
$$\textit{trans}\text{-}\mathbf{9} \underset{}{\overset{k_{eq} \gg 1}{\rightleftharpoons}} [\mathbf{9}\cdot HgX_2] \rightarrow \text{product}$$

$$\textit{cis}\text{-}\mathbf{10} \underset{}{\overset{k_{eq} > 1}{\rightleftharpoons}} [\mathbf{10}\cdot HgX_2] \rightarrow \text{product}$$

(The deficiency of mercury salt required for the competitive inhibition of the *cis*-**10** binding may result from the marginal solubility of the mercury salts.) We note that our scenario is *inconsistent* with the scenario proposed for the hydroxy-metalation of cyclopropanes (ref 30). Ouellette et al., based on similarly indirect evidence, proposed that trans-disubstituted cyclopropanes react *slower* due to a sterically encumbered, *rate-determining* complexation.

(24) A referee points out that loss of carbon dioxide from **20** or **21** would preclude their detection. Although decarboxylations of β-lactones typically require elevated temperatures [see references cited in: Trost, B. M.; Fortunak, J. M. *J. Am. Chem. Soc.* **1980**, *102*, 2841.], we have not considered the effects of mercury(II) salts. We appreciate this criticism.

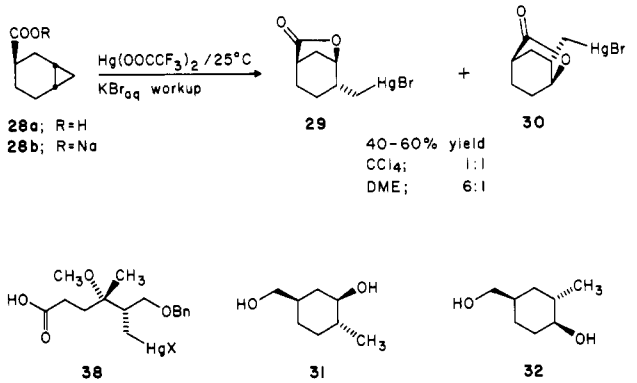
(25) Mercury counterion incorporation during the cleavage of phenylcyclopropane has been observed: Bloodworth, A. J.; Courtneidge, J. L. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1807. We also observe the following reaction:



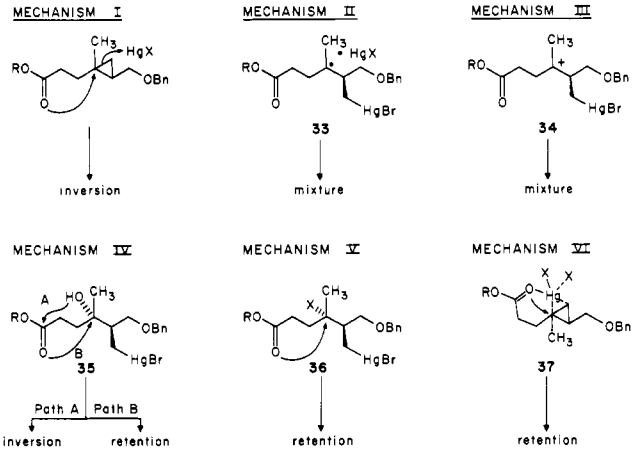
(26) Furst, A.; Plattner, P. A. "Abstracts of Papers of the 12th Congress on Pure and Applied Chemistry"; New York, 1951; p 409.

(27) Buchanan, J. G.; Sable, H. Z. "Selective Organic Transformations"; Thyagarajan, B. S., Ed.; John-Wiley and Sons: New York, 1972; Vol. 2, pp 81–95.

(28) Modest stereoelectronic control is exhibited in protic acid mediated openings of cyclopropanes: LaLonde, R. T.; Tobias, M. A. *J. Am. Chem. Soc.* **1963**, *85*, 3771.

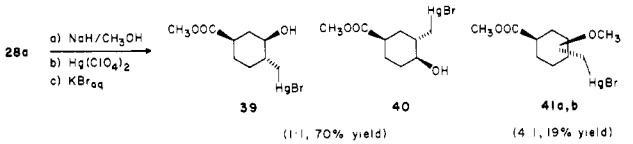


(Mechanisms II-VI) that might be invoked to account for products containing net *retention* of configuration at the electrophilic carbon centers. (Substrate **5** has been chosen for illustrative purposes.) Inspection of these intermediates underscores the additional concern that initial attack by an external nucleophile precludes the stereo- and regiocontrol adduced from neighboring group-assisted cyclopropane cleavage. Thus, we deem it important to elucidate, at least in a qualitative fashion, the relative contributions from each of these six mechanistic routes.

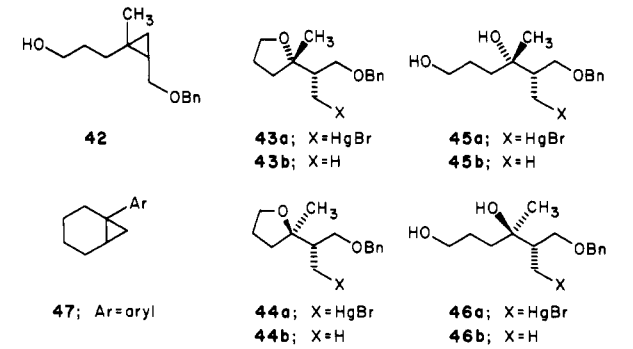


Although the possible intermediacy of carbon-centered radicals (cf. **33**, Mechanism II) acquires some support from the well-documented free radical chemistry of organomercury compounds,[29] we are confident that a radical process is not causing loss of stereospecificity in these cyclizations. All reactions are run at ambient temperatures with exclusion of light. Addition of free radical inhibitors (oxygen or duroquinone) shows no discernible effects on the reaction rates or product distributions. The large negative ρ value (−3.2) found for mercury-mediated cyclopropylbenzene hydroxymercurations further supports an ionic mechanism,[30] as does the insignificant role that radicals play in the chemistry of alkene solvomercuration.[10]

A more immediate concern is the possibility that the observed solvent dependencies (Table I) are indicative of the intervention of configurationally ill-defined cationic intermediates (e.g., **34**, Mechanism III), although such an explanation seems unpalatable for the cyclizations effected in the nonpolar solvents. When substrates **4b**, **5b**, and **9b** are submitted to the usual reaction conditions in neat (approximately 40 M) anhydrous methanol, we observe no products (≤5%) resulting from methanol incorporation. (Substrates **10b**, **16b**, and **17b** fail to react under these conditions.) If significant amounts of methanol incorporation occur,[31] giving rise to solvolytically labile ethereal intermediates (e.g., **38**), predominant net *retention* of configuration (if methanol effects a backside-assisted displacement) or a total randomization of configuration will result. *This is not observed* (cf. Table I, entry 7). However, when **28a** is cyclized in neat methanol with $Hg(OClO_3)_2$ we obtain hydroxy esters **39** and **40** (derived from methanolysis of lactones **29** and **30**, respectively) in a ratio of 1:1 (70% yield), along with a 19% yield of an inseparable 4:1 mixture of ethereal products **41a,b** (80 MHz ^{1}H NMR exhibits singlets at 3.34 and 3.39 ppm).[32] Although methyl ethers **41a,b** may arise from a resistance of **28b** to cyclize due to conformational biases disfavoring axial disposition of the carboxyl group, the geometric constraints preventing internally assisted solvolytic displacement of the methoxy moiety are notable. Additional experiments shed some light on this point.



Alcohol **42** was prepared in order to factor out the processes involving hydration followed by a Fisher esterification (e.g., Mechanism IV, path a). We anticipated that intramolecular and intermolecular delivery of the entering nucleophile would produce cyclic (e.g., **43a** or **44a**) and acyclic (e.g., **45a** or **46a**) products, respectively. When **42** is treated with 4.0 equiv of $Hg(OClO_3)_2$ in hexane containing solid $NaHCO_3$ at 25 °C (10 min) we isolate exclusively tetrahydrofuran-containing material (79% yield after flash chromatography) to the complete exclusion (≤2%) of diol. Reduction (Bu_3SnH/AIBN) and correlation with authentic material[14] shows that **43a** is formed in only 92% inversion of configuration (**43b**:**44b** = 12:1). When an analogous cyclization is effected in DME (8.0 h/25 °C), tetrahydrofurans **43a** and **44a** (3:1, 60% yield) are isolated along with an 11% yield of diol. By reduction of the diol (Bu_3SnH) and conversion to the corresponding tetrahydrofuran we find that diol **45a** is formed in >98% inversion of configuration (**45b**:**46b** = 62:1). *In contrast to the poorly stereoselective cyclization, the hydration reaction proceeds with an exceptionally high degree of inversion of configuration.*

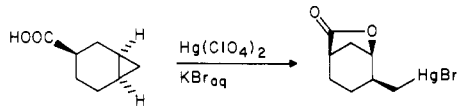


All attempts to cyclize the intermediate diol through extensive reaction times, or by resubmission of diol **45a** to the reaction conditions, fail. Thus, we conclude that the hydration processes depicted in Mechanism IV cannot be invoked to explain the anomalous stereochemical results. Furthermore, the solvolytic stability of diol **45a** along with the stereochemical results found in our attempts to capture cationic intermediates with methanol allow us to cautiously note that incipient cations (Mechanism III) are unlikely intermediates.

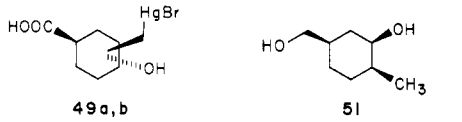
Remaining Mechanisms V and VI cannot readily be distinguished at this time. Although trifluoroacetate esters appear not to be viable reaction intermediates en route to lactones (Mechanism V) since trifluoroacetates **26** and **27** fail to cyclize even during extensive reaction times, intermediate perchlorate esters cannot be ruled out.[33-35]

(29) Jensen, F. R.; Rickborn, B. "Electrophilic Substitution of Organomercurials"; McGraw-Hill: New York, 1968.
(30) Ouellette, R. J.; Robins, R. D.; South, A., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 1619.
(31) In the absence of an internal nucleophile, methanol incorporation is readily observed. For example, see: Giese, B.; Heuck, K.; Luning, U. *Tetrahedron Lett.* **1981**, *22*, 2155.
(32) Thin-layer chromatographic analysis shows the methyl ester function in **41a,b** (3 H singlet at δ 3.67) to arise *prior* to cyclization, presumably by mercury-mediated esterification.

Support for Mechanism VI derives from close parallels with the chemistry of norbornene solvomercuration.[10b,d,36] Recently, Macchia and DePuy noted anomalously large amounts of retention products (predominate retention in some instances) in the mercury-mediated hydrolyses of arylcyclopropanes of type **47**.[37] A mechanism analogous to Mechanism VI was invoked. We can



48 **50**



49a,b **51**

also show that participation with retention can compete with intermolecular water participation. Mercury perchlorate mediated cyclization of **48** provides a γ-lactone believed to be **50** to the exclusion (<5%) of acidic materials. Reduction of **50** (LAH) affords diol **51** (32% overall yield from **48**) along with traces (7% by gas chromatographic integration) of isomeric material [GC-MS; m/z 144 (M^+), m/z 126 ($M^+ - H_2O$)].

The cyclizations described herein are curious in that, with the exception of the electronically biased substrates **4** and **5**, they proceed to unexpectedly large extents through "fused" mode transition states.[38] Although fused mode closures providing 5-,[39] 6-,[40] and 7-membered[41] rings, as well as bicyclo [2.2.2] ring systems analogous to **30**,[42] have been documented, they surely are out of the ordinary.[6] Our working hypotheses are that either the internal nucleophilic carboxyl functionality and mercury salt are intimately associated *prior to cyclization*[43] or an abnormal nucleophile trajectory[44] is an important determinant of the regioselectivity. However, we would like to emphasize that the literature pertaining to kinetic cyclizations by participation on to cyclopropanoid functionalities (including 3-membered cyclic onium ions) is *not* free of ambiguities. The regioselectivities of intramolecular epoxide openings are often condition and substrate dependent. The literature on electrophile-mediated cyclizations of unsaturated acids[12] is laced with ambiguities; regiochemical equilibrations via dyotropic rearrangements or facile ring fissions have been detected,[45,46] while many reports fail to address the possibility.

Summary

We have investigated the regio- and stereochemical control exerted in hitherto unknown mercury-mediated lactonizations of cyclopropane acid derivatives. For the most part, the products derive from apparent backside entry of the internal nucleophile with good to excellent stereocontrol at the electrophilic cyclopropane carbon. Anomalous stereo- and regiochemical results occassionally arise from what appear to be several competing *intramolecular* pathways; the possibility of initial participation by the poorly nucleophilic mercury counterions, however, cannot be rigorously excluded. Overall, the cyclization process represents an operational equivalent of a carbon electrophile based cyclofunctionalization of unsaturated acids.

Experimental Section[47]

Lactonization Method A. Sodium bicarbonate (10 mg, 0.12 mmol), the appropriate carboxylic acid substrate (0.10 mmol, vide infra), mercury salt (0.22 mmol), and solvent (1.0 mL) are combined and stirred at room temperature with complete exclusion of light. In most instances the poor solubilities of the sodium carboxylate and mercury salt lead to highly variable reaction times and make monitoring the course of the reaction by TLC difficult. Accordingly, although termination of the reactions within 10 h occasionally affords respectable yields of mercurated lactones, the reactions are routinely stirred at 25 °C for 3–5 days to ensure high percent conversions. The reactions are quenched and worked up as follows. Saturated aqueous potassium bromide (2.0 mL) is added and the two-phase system is vigorously stirred for 0.5 h. Fol-

(33) Kevill, D. N.; Shen, B. W. *J. Am. Chem. Soc.* **1981**, *103*, 4515 and references cited therein.

(34) Hudson, R. F. "Chemical Reactivity and Reaction Paths"; Klopman, Ed.; Wiley-Interscience: New York, 1974; Chapter 5.

(35) A surprising nucleophilicity of perchlorate ion has been reported: Zefirov, M. S.; Koz'min, A. S.; Zhdankin, V. V. *Tetrahedron* **1982**, *38*, 291. Zefirov, M. S.; Koz'min, A. S.; Zhdankin, V. V.; Nikulin, A. V.; Zyk, N. V. *J. Org. Chem.* **1982**, *47*, 3679.

(36) Traylor, T. G.; Baker, A. W. *Tetrahedron Lett.* **1959**, *14*; *J. Am. Chem. Soc.* **1963**, *85*, 2746. Bach, R. D.; Richter, R. F. *Ibid.* **1972**, *94*, 4747.

(37) Battistini, C.; Crotti, P.; Macchia, B.; Macchia, F.; Depuy, C. H. *J. Org. Chem.* **1978**, *43*, 1400.

(38) See ref 4d. An alternative nomenclature [Baldwin, J. E.; Cutting, J.; DuPont, W.; Kruse, L.; Silberman, L.; Thomas, R. C. *J. Chem. Soc., Chem. Commun.* **1976**, 736] proves to be inappropriate by virtue of its implication of the degree of hybridization at the electrophilic center of the cyclopropanoid.

(39) (a) Henbest, H. B.; Nicholls, B. *J. Chem. Soc.* **1959**, 227. (b) Gunstone, F. D.; Inglis, R. P. *J. Chem. Soc., Chem. Commun.* **1970**, 877. (c) Takahashi, T.; Kimihiko, H.; Tsuji, J. *Chem. Lett.* **1981**, 1189. (d) Cruickshank, P. A.; Fishman, M. *J. Org. Chem.* **1969**, *34*, 4060. (e) Hanessian, S.; Dixit, D. M.; Liak, T. J. *Pure Appl. Chem.* **1981**, *53*, 129. (f) Kende, A. S.; Toder, B. H. *J. Org. Chem.* **1982**, *47*, 163. (g) Biloski, A. J.; Wood, R. D.; Ganem, B. *J. Am. Chem. Soc.* **1982**, *104*, 3233. (h) Murai, A.; Ono, M.; Masamune, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 1226. (i) Demole, E.; Enggist, P. *Helv. Chim. Acta* **1968**, *51*, 481.

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(46) For evidence of facile regiochemical equilibrations occurring during electrophile-mediated cyclofunctionalizations, see: Current, S.; Sharpless, K. B. *Tetrahedron Lett.* **1975**, 5075. Barnett, W. E.; Sohn, W. H. *Ibid.* **1972**, 1777. Garratt, D.; Ryan, M.; Beauliene, P. L. *J. Org. Chem.* **1980**, *45*, 839. Clive, D. L. J.; Chittattu, G.; Curtis, N. J.; Kiel, W. A.; Wong, C. K. *J. Chem. Soc., Chem. Commun.* **1977**, 725. Nicolaou, K. C.; Lysenko, Z. *J. Am. Chem. Soc.* **1977**, *99*, 3185. Haufe, G.; Kleinpeter, E. *Tetrahedron Lett.* **1982**, *23*, 3555. Toshimitsu, A.; Aoai, T.; Uemura, S.; Okano, M. *J. Org. Chem.* **1981**, *46*, 3021. Clive D. L. J.; Russell, C. G.; Chittattu, G.; Singh, A. *Tetrahedron* **1980**, *36*, 1399.

(47) Microanalysis are performed by Galbraith Laboratories, Knoxville, Tenn. ^{1}H NMR spectra are taken on Varian EM-390 (90 MHz) or a CFT-20 (80 MHz) spectrometer and ^{13}C NMR spectra are taken on a JEOL-FX-90Q instrument. Gas chromatography is performed on a Varian 3700 instrument equipped with digital integration. Solvents are purified and dried by using standard protocol, and the mercury salts are used as received.

lowing separation of the layers and three 2.0 mL chloroform extractions of the aqueous phase, the combined organic layers are dried (Na_2SO_4) and concentrated in vacuo. Purifications and analyses are effected as described for each specific substrate (vide infra).

Lactonization Method B. The appropriate carboxylic acid substrate (0.10 mmol) and mercury salt (0.22 mmol) are added to 1.0 mL of solvent. Although ill-defined aggregation effects occasionally cause the reaction times to be only marginally reproducible, TLC analysis usually indicates the reactions are complete within 2–10 h at 25 °C. The reaction mixture is dealt with as described in lactonization Method A.

Lactonization Method C. The methyl esters are prepared from the corresponding carboxylic acids using a standard ethereal diazomethane-based procedure and are reacted as follows. To 1.0 mL of moist solvent is added the appropriate ester (0.10 mmol) and mercury salt (0.22 mmol). TLC analysis indicates that the starting ester is usually consumed within 2–20 h at 25 °C. The reaction mixture is dealt with as described in lactonization Method A.

Reduction Method D.[15] To the mercurated lactone (0.05–0.10 mmol) dissolved in 0.50 mL of methanol at 0 °C under nitrogen is added a solution of sodium borohydride (11 mg, 0.30 mmol) dissolved in 0.48 mL of 3.5 M aqueous sodium hydroxide. The mixture is stirred for 60 s and then acidified to pH 2 using 5% aqueous hydrochloric acid. The resulting gray solution is washed with three 2-mL portions of dichloromethane. The organic extracts are combined, dried (Na_2SO_4), and concentrated in vacuo. The residue is purified and analyzed as described (vide infra).

Reduction Method E.[21] To a solution of mercurated lactone (0.05–0.10 mmol) in anhydrous tetrahydrofuran (1.0 mL) are added sequentially azobisisobutylnitrile (1.0 mg) and tri-*n*-butyltin hydride (54 μl, 0.20 mmol) under nitrogen. After 30 min at 25 °C 1.0 mL of 15% aqueous potassium fluoride is added.[48] The resulting white suspension is extracted with three 2-mL portions of hexane. The combined organic extracts are dried (Na_2SO_4) and concentrated in vacuo. Purifications and analyses are effected as reported (vide infra).

Reduction Method F. Lithium aluminum hydride (9.1 mg, 0.24 mmol) suspended in anhydrous tetrahydrofuran under nitrogen atmosphere is cooled to 0 °C and treated with the mercurated lactone (0.05–0.10 mmol) in anhydrous tetrahydrofuran (1.0 mL). The reaction contents are stirred at 0 °C for 2.0 h, diluted with 2.0 mL of tetrahydrofuran, and then quenched sequentially with (a) H_2O (9 μL, caution; foaming), (b) 15% aqueous sodium hydroxide (9 μL), and (c) H_2O (27 μL).[49] The resulting flocculant precipitate is stirred for 0.5 h and then filtered through Celite with copious hot ethyl acetate rinsing. The filtrate is concentrated in vacuo, affording a residue that is purified and analyzed as described (vide infra).

Lactonization of 1-Methylcyclopropanepropanoic Acid (2). Acid **2** is prepared as depicted in the Supplementary Material: ^{1}H NMR (90 MHz, CCl_4) δ 2.37 (t, J = 8 Hz, 2 H), 1.53 (t, J = 8 Hz, 2 H), 1.02 (s, 3 H), 0.32–0.22 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 180.8, 34.5, 32.1, 22.3, 15.0, 13.1; MS (EI) m/z 128 (M^+), 55 (100%); IR (film) 3000, 1730 cm^{-1}. Anal. Calcd for $C_7H_{12}O_2$: C, 65.63; H, 9.38. Found C, 65.84; H, 9.50.

Lactonization of **2** using methods A, B, or C followed by flash chromatographic purification[50] of the crude product (50% ethyl acetate in hexane) affords **3a** as an oil (50–80% yield): ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.57 (t, J = 9 Hz, 2 H), 2.23–1.77 (m, 6 H), 1.33 (s, 3 H); IR (film) 1780 cm^{-1}. Reductive demercuration of lactone **3a** using method D followed by flash chromatography (30% ethyl acetate in hexane) affords pure lactone **3b** in 70% yield. This compound is identical with an authentic sample prepared as depicted in the Supplementary Material: ^{1}H NMR (90 MHz, CCl_4) δ 2.73–2.53 (m, 2 H), 2.27–1.90 (m, 2 H)8 1.87–1.60 (m, 2 H), 1.37 (s, 3 H), 0.97 (t, J = 8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 176.4, 86.7, 33.2, 31.9, 28.8, 24.2, 7.8; IR (film) 1770 cm^{-1}. Exact mass calcd for $C_7H_{12}O_2$: 128.0837. Found: 128.0842.

Lactonization of *trans*-2-(Benzyloxymethyl)-1-methylcyclopropanepanoic Acid (4a). Preparation of stereoisomerically pure acid **4a** (>99.5%) is depicted in schematic form in the Supplementary Material: ^{1}H NMR (90 MHz, CCl_4) δ 7.25 (s, 5 H), 4.46 (s, 2 H), 3.64 (dd, J_1 = 5 Hz, J_2 = 8 Hz, 1 H), 3.24 (dd, J_1 = J_2 = 9 Hz, 1 H), 2.73–2.17 (m, 2 H), 1.70 (t, J = 6 Hz, 2 H), 1.12 (s, 3 H), 1.00–0.70 (m, 1 H), 0.51 (dd, J_1 = 4 Hz, J_2 = 9 Hz, 1 H), 0.21 (dd, J_1 = J_2 = 6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 180.1, 138.3, 128.4, 127.9, 127.6, 72.8, 70.7, 32.0, 29.2, 24.4, 23.9, 19.7, 17.6; MS (EI) m/z 142 ($M^+ - C_7H_6O$), 91 (100%); IR (film) 3000, 1720 cm^{-1}. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.58; H, 8.06. Found: C, 72.38; H, 8.16.

Acid **4a** is lactonized by using lactonization Methods A, B, or C. The resulting crude residue can be purified by flash chromatography[50] (50% ethyl acetate in hexane elution), affording mercurated lactone **6a** contaminated by varying quantities of stereoisomeric lactone **7a**. The ratio of **6a** to **7a** can be determined by using analytical HPLC (30% ethyl acetate in hexane elution; the relative retention times for **6a** and **7a** are 1.3 and 1.0, respectively). The yields and stereoselectivities obtained under a variety of conditions are listed in Table I. Lactones **6a** and **7a** can be separated by MPLC (50% ethyl acetate in hexane elution). **6a**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.38 (s, 5 H), 4.56 (s, 2 H), 3.59 (dd, J_1 = 4 Hz, J_2 = 9 Hz, 1 H), 3.25 (dd, J_1 = J_2 = 8 Hz, 1 H), 2.70–2.42 (m, 2 H), 2.40–1.82 (m, 3 H), 1.32 (s, 3 H); IR (film) 1780 cm^{-1}. **7a**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.37 (s, 5 H), 4.57 (s, 2 H), 3.83 (dd, J_1 = 3 Hz, J_2 = 9 Hz, 1 H), 3.26 (dd, J_1 = J_2 = 9 Hz, 1 H), 2.73–2.40 (m, 2 H), 2.40–1.73 (m, 3 H), 1.3 (s, 3 H); IR (film) 1780 cm^{-1}. Lactones **6a** and **7a** are each reductively demercurated by using reduction Method D. Pure lactones **6b** and **7b** are obtained after flash chromatography (30% ethyl acetate in hexane; 50–60% yield). These materials are identical with authentic samples of **6b** and **7b** prepared as depicted schematically in the supplementary Material. **7b**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.35 (s, 5 H), 4.48 (s, 2 H), 3.64 (dd, J_1 = 5 Hz, J_2 = 9 Hz, 1 H), 3.42 (dd, J_1 = 7 Hz, J_2 = 10 Hz, 1 H), 2.70–2.43 (m, 2 H)8 2.40–1.80 (m, 3 H), 1.33 (s, 3 H), 1.04 (d, J = 6 Hz, 3 H); ^{13}C NMR δ 176.6, 138.3, 128.3, 127.5, 127.0, 88.4, 73.7, 71.6, 42.7, 31.9, 28.9, 23.1, 12.8; IR (film) 1780 cm^{-1}. Exact mass calculated for $C_{15}H_{20}O_3$: 248.1412. Found: 248.1402. **6b**: ^{1}H NMR (90 MHZ, $CDCl_3$) δ 7.33 (s, 5 H), 4.47 (s, 2 H), 3.43 (d, J = 5 Hz, 2 H), 2.68–1.70 (m, 5 H), 1.30 (s, 3 H), 1.05 (d, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 176.6, 138.1, 128.3, 127.4, 127.1, 88.2, 73.1, 71.6, 42.3, 32.0, 28.8, 22.8, 12.6; IR (film) 1780 cm^{-1}. Exact mass calcd for $C_{15}H_{20}O_3$: 248.1412. Found: 248.1402.

Lactonization of *cis*-2-(Benzyloxymethyl)-1-methylcyclopropanepropanoic Acid (5a). Preparation of stereoisomerically pure (>99.5%) acid **5a** is depicted schematically in the Supplementary Material: ^{1}H NMR (90 MHz, CCl_4) δ 7.18 (s, 5 H), 4.40 (s, 2 H), 3.55 (dd, J_1 = 6 Hz, J_2 = 9 Hz, 1 H), 3.17 (dd, J_1 = 8 Hz, J_2 = 10 Hz, 1 H), 2.38 (t, J = 8 Hz, 2 H), 1.75–1.38 (m, 2 H), 1.04 (s, 3 H), 0.95–0.78 (m, 1 H), 0.53 (dd, J_1 = 3 Hz, J_2 = 8 Hz, 1 H), 0.12 (dd, J_1 = J_2 = 5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 180.1, 138.6, 128.5, 127.8, 127.7, 72.7, 70.8, 36.1, 31.9, 23.4, 19.6, 17.9, 17.0; MS (EI) m/z 142 ($M^+ - C_7H_6O$), 91 (100%); IR (film) 3000, 1720 cm^{-1}. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.58; H, 8.06. Found: C, 72.39; H, 8.31.

Cyclizations of **5a** using lactonization Methods A, B, or C provide mixtures of lactones **6a** and **7a** in yields and stereoselectivities (**7a** is the major product in this case) virtually identical with those obtained from substrate **4a** described above.

Lactonization of *trans*-2-Butylcyclopropanepropanoic Acid (9a). *trans*-**9a** (97.7% stereoisomerically pure) is prepared as depicted in the Supplementary Material: ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.43 (t, J = 8 Hz, 2 H), 1.90–1.07 (m, 8 H), 0.90 (t, J = 6 Hz, 3 H), 0.73–0.14 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 180.6, 34.3, 33.8, 31.7, 29.5, 22.6, 18.9, 18.1, 14.1, 11.8; MS (EI) m/z 171 (M^+ + 1), 55 (100%); IR (film) 3000, 1720 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.58; H, 10.59. Found: C, 70.70; H, 10.65.

Following cyclization of acid **9a** via Methods A–C, flash chromatographic purification of the crude residue (60% ethyl acetate in hexane) affords inseparable lactones **11a–14a** [IR (film) 1730, 1770 cm^{-1}] in 60–90% yield under a variety of conditions (see Table I, for example). The lactones are reduced by using Method E, providing **11b–14b** as a mixture in 70–80% yield after flash chromatography (20% ethyl acetate in hexane elution). Lactones **11b–14b** could be separated by semipreparative HPLC (12% ethyl acetate in hexane elution; relative retention times of **11b–14b** are 1.00, 1.41, 1.06, and 1.53, respectively) and correlated with authentic materials (ref 14). **11b**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.22 (dd, J_1 = 6 Hz, J_2 = 13 Hz, 1 H), 2.63–2.33 (m, 2 H), 2.33–1.02 (m, 8 H), 1.02–0.80 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 178.2, 84.8, 37.7, 32.4, 29.2, 28.9, 25.4, 25.2, 22.9, 14.0; IR (film) 1775 cm^{-1}. Exact mass calcd for $C_{10}H_{18}O_2$: 170.1307. Found: 170.1305. **12b**: ^{1}H NMR (90 MHz, CCl_4) δ 3.97–3.70 (m, 1 H), 2.70–2.23 (m, 2 H), 2.23–1.10 (m, 9 H), 1.10–0.80 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 171.9, 85.9, 33.2, 32.2, 29.5, 27.8, 26.6, 22.6, 17.4, 13.9; IR (film) 1740 cm^{-1}. Exact mass calcd for $C_{10}H_{18}O_2$: 170.1307. Found: 170.1305. **13b**: ^{1}H NMR (90 MHz, CCl_4) δ 4.30–4.07 (m, 1 H), 2.53–2.30 (m, 2 H), 2.30–1.10 (m, 9 H), 1.10–0.80 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 177.0, 84.6, 37.6, 31.4, 28.9, 28.8, 25.5, 22.6, 14.7, 13.8; IR (film) 1785 cm^{-1}. Exact mass calcd for $C_{10}H_{18}O_2$: 170.1307. Found: 170.1303. **14b**: ^{1}H NMR (90 MHz, CCl_4) δ 4.27–4.14 (m, 1 H), 2.37 (t, J = 7 Hz, 2 H), 2.20–1.83 (m, 2 H), 1.83–1.10 (m, 7 H), 1.10–0.75 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 171.9, 83.0, 31.7, 29.4, 27.7, 26.8, 26.1, 22.5, 13.9, 12.5; IR (film) 1740 cm^{-1}. Exact mass calcd for $C_{10}H_{18}O_2$: 170.1307. Found: 170.1302.

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(50) When product analyses are effected subsequent to purifications, proper precautions are taken to show that product ratios are not distorted (ref 24).

Lactonization of *cis*-2-Butylcyclopropanepropanoic Acid (10a). Acid **10a** is prepared in 94.4% (17:1) stereoisomeric purity as depicted in the Supplementary Material: ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.47 (t, J = 8 Hz, 2 H), 2.13–1.17 (m, 8 H), 1.17–0.83 (m, 4 H), 0.83–0.60 (b s, 2 H), 0.00 to −0.23 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 180.6, 34.7, 32.4, 28.3, 24.2, 22.7, 16.1, 15.2, 14.1, 10.8; MS (EI) m/z 171 (M^+ + 1), 55 (100%); IR (film) 3000, 1720 cm^{-1}. Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.58; H, 10.59. Found: C, 70.36; H, 10.42.

Lactonizations of **10a** are effected and product analyses are achieved as described above for acid **9a**.

Lactonization of *trans*-2-Butylcyclopropanethanoic Acid (16a). Acid **16a** is prepared in 98.9% (87:1) stereoisomeric purity as depicted in the Supplementary Material: ^{1}H NMR (90 MHz, $CDCl_3$) δ 11.90 (b s, 1 H), 2.28 (d, J = 7 Hz, 2 H), 1.60–1.17 (m, 6 H), 0.93 (t, J = 7 Hz, 3 H), 0.96–0.30 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 180.2, 38.9, 33.5, 31.6, 22.4, 18.6, 14.0, 13.9, 11.6; MS (CI) m/z 157 (M^+ + 1, 100%); IR (film) 3000, 1720 cm^{-1}. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.39; H, 10.50.

Lactonization of **16a** by Method C (as the corresponding methyl ester) in CCl_4 with use of 2.2 equiv of mercury trifluoroacetate over 19 h affords mercurated lactone **18a** (86% yield) and trifluoroacetate ester **26** (9% yield) after flash chromatography (30% ethyl acetate in hexane elution; the R_f values of **18a** and **26** in the same solvent are 0.16 and 0.54, respectively). **18a**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.30–3.86 (m, 1 H), 3.06–2.06 (m, 3 H), 2.16 (d, J = 12 Hz, 2 H), 2.00–1.20 (m, 6 H), 1.01 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 175.8, 88.4, 40.8, 39.0, 38.0, 33.6, 27.7, 22.3, 13.8; IR (film) 1750 cm^{-1}. **26**: ^{1}H NMR[51] (90 MHz, $CDCl_3$) δ 5.21–4.94 (m, 0.3 H),[51] 3.74 (d, 2 H), 3.38 (s, 1 H), 3.31–1.57 (m, 5 H), 1.57–1.16 (m, 4 H), 0.98 (t, J = 5 Hz, 3 H); IR (film) 1775, 1730 cm^{-1}; MS (CI) m/z 451 (100%), 169 (80%).

Reduction of lactone **18a** using Method E and GC analysis (the relative retention times of **18b** and **19b** are 1.26 and 1.0, respectively) shows that after accounting for stereoisomeric impurities in starting material **16a** the lactonization proceeds in essentially total stereoselectivity for inversion of configuration. Flash chromatography (25% ethyl acetate in hexane elution) affords quercus lactone B[14] (**18b**; 75% yield): ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.11–3.81 (m, 1 H), 2.87–1.90 (m, 3 H), 1.91–1.21 (m, 6 H), 1.13 (d, J = 6 Hz, 3 H), 0.92 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 176.5, 87.2, 36.9, 35.9, 33.5, 27.7, 22.3, 17.3, 13.7; IR (film) 1785 cm^{-1}. Exact mass calcd for $C_9H_{16}O_2$: 156.1150. Found: 156.1156. Alternatively, reduction of the crude cyclization product (including trifluoroacetate **26**) using Method F (LAH) affords diol **24** after flash chromatography. Diol **24** is shown spectroscopically to be essentially homogeneous upon comparison with authentic diols **22–25** prepared as described in the Supplementary Material. **22**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.08–3.02 (m, 5 H), 1.88–1.02 (m, 9 H), 1.10–0.60 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 75.6, 61.5, 39.0, 34.1, 31.9, 29.4, 22.9, 14.8, 14.0; IR (film) 3330 cm^{-1}; MS (EI) m/z 75 (100%), 45 (38%). **23**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.23–3.07 (m, 5 H), 2.00–1.03 (m, 9 H), 1.17–0.78 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 74.6, 61.2, 38.7, 35.4, 32.4, 29.4, 22.8, 14.0; IR (film) 3340 cm^{-1}; MS (EI) m/z 75 (100%), 45 (39%). Anal. Calcd for $C_9H_{20}O_2$: C, 67.45; H, 12.58. Found: C, 67.24; H, 12.40. **24**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 3.88–3.08 (m, 5 H), 1.95–1.15 (m, 9 H), 1.15–0.68 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 75.6, 60.1, 36.3, 35.2, 34.0,28.0, 22.7, 16.5, 14.0; IR (film) 3330 cm^{-1}; MS (EI) m/z 85 (93%), 56 (100%). Anal. Calcd for $C_9H_{20}O_2$: C, 67.45; H, 12.58. Found: C, 67.53; H, 12.69. **25**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.20–3.10 (m, 5 H), 1.96–1.20 (m, 9 H), 1.20–0.73 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 74.7, 60.2, 35.8, 33.0, 28.6, 22.7, 14.0, 13.8; IR (film) 3330 cm^{-1}; MS (EI) m/z 85 (100%), 56 (84%).

Lactonization of *cis*-2-Butylcyclopropanethanoic Acid (17a). Acid **17a** is prepared in 97.5% (39:1) stereoisomeric purity as depicted in the Supplementary Material: ^{1}H NMR (90 MHz, $CDCl_3$) δ 10.31 (b s, 1 H), 2.40 (d, J = 6 Hz, 2 H), 1.62–1.15 (m, 6 H), 0.93 (t, J = 6 Hz, 3 H), 1.11–0.64 (m, 3 H), −0.05 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 180.6, 33.7, 32.1, 28.4, 22.5, 15.4, 14.0, 11.1, 10.7; MS (CI) m/z 157 (M^+ + 1, 100%); IR (film) 3000, 1710 cm^{-1}. Anal. Calcd for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 69.35; H, 10.29.

Cyclization of **17a** by Method C (via the corresponding methyl ester) in CCl_4 using 2.2 equiv of $Hg(OOCCF_3)_2$ affords mercurated lactone **19a** (56% yield) and trifluoroacetate ester **27** (26% yield) after flash chromatography (35% ethyl acetate in hexane elution). **19a**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.66–4.33 (m, 1 H), 3.30–2.16 (m, 3 H), 2.02 (d, J = 7 Hz, 2 H), 1.93–1.20 (m, 6 H), 0.96 (t, J = 6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 176.3, 84.0, 39.3, 38.0, 34.1, 29.3, 28.0, 22.4, 13.9; IR (film) 1730 cm^{-1}. **27**: ^{1}H NMR[51] (90 MHz, $CDCl_3$) δ 5.27–4.94 (m, 0.7 H),[51] 3.70 (s, 2.4 H), 3.38 (s, 0.3 H), 3.11–1.54 (m, 6 H), 1.54–1.14 (m, 5 H), 0.94 (t, J = 6 Hz, 3 H); IR (film) 1775, 1725 cm^{-1}; MS (CI) m/z 564 (M^+ + 1), 169 (100%). Stereochemical analyses as described above for the lactonization of **16a** show the lactonization to be essentially totally stereo- and regioselective for the formation of lactone **19a**. Reduction of **19a** by Method E affords quercus lactone A[14] (**19b**) in 70–80% yield; ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.58–4.28 (m, 1 H), 2.93–1.93 (m, 3 H), 1.92–1.20 (m, 6 H), 1.20–0.83 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 176.8, 83.6, 37.5, 32.9, 29.5, 28.0, 22.4, 13.8; IR (film) 1785 cm^{-1}. Exact mass calcd for $C_9H_{16}O_2$: 156.1150. Found: 156.1146.

Lactonization of [α,β,α]-Bicyclo[4.1.0]heptane-3-carboxylic Acid (28a). Stereoisomerically pure (>98.0%) acid **28a** is synthesized as described in the Supplementary Material: mp 43.5–45.0 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.50–1.87 (b s, 4 H), 1.83–1.23 (m, 3 H), 1.20–0.87 (m, 2 H), 0.83–0.55 (m, 1 H), 0.06 (dd, J_1 = 5 Hz, J_2 = 9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 183.1, 37.7, 26.0, 25.0, 23.1, 10.9, 10.0, 8.4; MS (EI) m/z 140 (M^+), 95 (100%); IR (film) 3000, 1715 cm^{-1}. Anal. Calcd for $C_8H_{12}O_2$: C, 68.57; H, 8.57. Found: C, 68.70; H, 8.52.

Acid **28a** is cyclized with $Hg(O_2CCF_3)_2$ in carbon tetrachloride by using Method A (5 days, 25 °C) or Method B (20 h, 25 °C). The resulting crude residues exhibit infrared absorptions anticipated for γ-lactone **29** and δ-lactone **30** (film; 1775, 1730 cm^{-1}, respectively). However, all attempts at flash chromatographic separation effect destruction of the δ component. Furthermore, acidification followed by usual extractive workup of the remaining aqueous layer affords small amounts of hydroxy acid (5–7%) derived from hydrolysis of the labile lactone **30** (shown by independent reduction to diol **32**, vide infra). Accordingly, the workups and analyses are performed as follows. After addition of saturated aqueous potassium bromide (2.0 mL) and vigorous stirring for 0.5 h, the aqueous phase is acidified to pH 2 wth 48% aqueous hydrogen bromide. Following extraction with chloroform (3 × 2.0 mL), the combined organic layers are dried (Na_2SO_4) and concentrated in vacuo. The crude residue is submitted directly to reduction Method F (LAH). GC analysis of the crude mixture of diols shows **31**:**32** = 2.5:1 (the relative retention times of **31** and **32** are 1.00 and 1.11, respectively). Diols **31** and **32** can be separated by careful flash chromatography (ethyl acetate elution, 50–60% combined yield from acid **28a**) and shown to be identical with authentic samples prepared as depicted in the Supplementary Material. **31**: mp 100–101 °C; ^{1}H NMR (80 MHz, $CDCl_3$) δ 3.45 (d, J = 8 Hz, 2 H), 3.35–3.00 (m, 1 H), 2.15–1.85 (m, 2 H), 1.85–1.35 (m, 6 H), 1.30–1.13 (m, 2 H), 1.00 (d, J = 6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 76.0, 68.1, 40.3, 39.8, 38.6, 32.8, 28.8, 18.4; IR (KBr) 3350 cm^{-1}. Exact mass calcd for $C_8H_{16}O_2$: 144.1150. Found: 144.1142. **32**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 3.48 (d, J = 6 Hz, 2 H), 3.40–3.17 (m, 1 H), 2.27 (s, 2 H), 2.00–1.43 (m, 6 H), 1.43–1.13 (m, 2 H), 0.97 (d, J = 6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 74.4, 65.5, 34.7, 32.3, 29.1, 24.5, 18.2; IR (film) 3350 cm^{-1}. Exact mass calcd for $C_8H_{16}O_2$: 144.1150. Found: 144.1146.

Cyclization of *trans*-2-(Benzyloxymethyl)-1-methylcyclopropanepropanol (42). Alcohol **42** is prepared as depicted in schematic form in the Supplementary Material: ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.20 (s, 5 H), 5.37 (s, 2 H), 3.60–3.05 (m, 4 H), 1.79 (s, 1 H), 1.74–1.05 (m, 4 H), 0.94 (s, 3 H) 1.03–0.69 (m, 1 H), 0.40 (dd, J_1 = 8 Hz, J_2 = 5 Hz, 1 H), 0.01 (dd, J_1 = J_2 = 5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 138.3, 128.2, 127.8, 127.5, 72.6, 70.6, 62.8, 30.2, 29.9, 24.3, 24.1, 19.7, 17.6; IR (film) 3430 cm^{-1}; MS (CI) m/z 235 (M^+ + 1), 127 (59%).

The following cyclization procedure is representative. Cyclization of alcohol **42** by Method A with $Hg(ClO_4)_2$ in DME affords tetrahydrofurans **43a** and **44a** as a mixture (63% yield) and diols **45a** and **46a** as a mixture (11% yield) after flash chromatography (15% ethyl acetate in hexane followed by 60% ethyl acetate in hexane elution; **43a** and **44a** elute first). **43a, 44a**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.23 (s, 5 H), 4.43 (s, 2 H), 3.90–3.33 (m, 3 H), 3.16 (dd, J_1 = J_2 = 8 Hz), 2.33–1.30 (m, 5 H), 1.77 (d, J = 6 Hz, 2 H) (two methyl singlets; 1.07, 1.01; 1:3 ratio); IR (film) 1060 cm^{-1}. **45a, 46a**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.32 (s, 5 H), 4.51 (s, 2 H), 4.06–3.29 (m, 6 H), 1.93–1.73 (m, 3 H), 1.73–1.45 (m, 4 H), 1.25 (s, 3 H); IR (film) 3350 cm^{-1}. Reduction of the mixture of tetrahydrofurans **43a** and **44a** using Method E affords **43b** and **44b** in 70% yield after flash chromatography (10% ethyl acetate in hexane elution). Comparison of the mixture with authentic samples of **43b** and **44b** by HPLC (2% ethyl acetate in hexane elution; the relative retention times are 1.0 and 1.1, respectively) demonstrates that the cyclization proceeds in only 80% selectivity for inversion of configuration (**43b**:**44b** = 4:1). The spectroscopic data for authentic samples are as follows. **43b**: ^{1}H NMR (80 MHz, $CDCl_3$) δ 7.30 (s, 5 H), 4.46 (s, 2 H), 3.80–3.63 (m, 2 H), 3.63–3.10 (m, 2 H), 2.17–1.46 (m, 5 H), 1.09 (s, 3 H), 1.04 (d, J = 8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.7, 128.2, 127.4, 84.0, 73.1, 66.9, 42.7, 35.6, 26.0, 22.9, 13.3; IR (film) 1080 cm^{-1}; MS (CI) m/z 235 (M^+ + 1, 100%). **44b**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.26 (s, 5 H), 4.41

(51) The ^{1}H NMR spectra of trifluoroacetate esters **26** and **27** exhibit extraneous peaks; the assignments are reported as they appear. The reductions of **26** and **27** provide surprisingly clean diols **24** and **25**, respectively, which are correlated in the usual manner (ref 14).

(s, 2 H), 3.90–3.47 (m, 3 H), 3.23 (dd, $J_1 = J_2 = 9$ Hz, 1 H), 2.13–1.40 (m, 5 H), 1.04 (s, 3 H), 0.97 (d, $J = 7$ Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 138.9, 128.2, 127.5, 127.3, 84.3, 73.1, 72.8, 67.2, 42.8, 35.9, 25.9, 22.5, 13.9; IR (film) 1060 cm^{-1}; MS (CI) m/z 235 ($M^+ + 1$, 100%). Reduction of the mixture of diols **45a** and **46a** using reduction Method E affords diols **45b** and **46b** after flash chromatography (60% ethyl acetate in hexane elution; 70% yield). Comparison of the mixture spectroscopically with authentic samples of **45b** and **46b** prepared as depicted in the Supplementary Material shows that the inversion selectivity is greater than 95% (**45b**:**46b** > 20:1). By conversion of the mixture of **45b** and **46b** to their respective tetrahydrofurans **45b** and **46b** (1.1 equiv TsCl/Et_3N/CH_2Cl_2) it is shown that the selectivity for inversion of configuration in the formation of hydration products is on the order of 98% (**43b**:**44b** = 62:1). Spectroscopic data for authentic samples of diols **45b** and **46b** are as follows. **45b**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.26 (s, 5 H), 4.46 (s, 2 H), 4.10–2.50 (b, 2 H), 3.75–3.32 (m, 4 H), 2.21–1.75 (m, 1 H), 1.75–1.35 (m, 4 H), 1.15 (s, 3 H), 0.95 (d, $J = 7$ Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 137.5, 128.4, 127.8, 127.7, 74.4, 73.5, 63.5, 42.6, 34.3, 27.0, 25.4, 12.9; IR (film) 3400 cm^{-1}; MS (CI) m/z 235 (100%). **46b**: ^{1}H NMR (90 MHz, $CDCl_3$) δ 7.26 (s, 5 H), 4.46 (s, 2 H), 4.15 (b s, 1 H), 3.71–3.41 (m, 4 H), 3.35 (b s, 1 H), 2.15–1.79 (m, 1 H), 1.88–1.42 (m, 4 H), 1.07 (s, 3 H), 0.82 (d, $J = 7$ Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 137.4, 128.5, 127.8, 74.6, 73.7, 73.6, 63.4, 40.2, 38.2, 26.6, 22.3, 13.0; IR (film) 3400 cm^{-1}; MS (CI) m/z 193 ($M^+ - C_3H_7O$), 91 (100%).

Lactonization of [α,α,α]-Bicyclo[4.1.0]heptane-3-carboxylic Acid (48). Stereoisomerically pure (>98.0%) acid **48** is prepared as depicted schematically in the Supplementary Material: mp 35–36.5 °C; ^{1}H NMR (90 MHz, $CDCl_3$) δ 2.53–2.13 (m, 1 H), 2.13–1.48 (m, 4 H), 1.48–0.80 (m, 4 H), 0.80–0.43 (m, 1 H), 0.08 (dd, $J_1 = 5$ Hz, $J_2 = 10$ Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 183.1, 40.1, 27.0, 22.9, 22.7, 10.6, 9.9, 7.8; MS (EI) m/z 140 (M^+), 95 (100%); IR (film) 3000, 1710 cm^{-1}. Anal. Calcd for $C_8H_{12}O_2$: C, 68.57; H, 8.57. Found: C, 68.52; H, 8.78.

Cyclization of acid **48** using lactonization Method A (5 days/25 °C/CCl_4) affords γ-lactone **50** in only 14% yield after flash chromatography (40% ethyl acetate in hexane elution): ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.51 (d, $J = 6$ Hz, 1 H), 2.74–1.14 (m, 8 H), 2.05 (d, $J = 5$ Hz, 2 H); IR (film) 1785 cm^{-1}. Lactone **50** is reduced to diol **51** using reduction Method F (LAH) in 60–70% yield after flash chromatography (ethyl acetate): ^{1}H NMR (80 MHz, $CDCl_3$) δ 3.90–3.62 (m, 1 H), 3.52 (d, $J = 5$ Hz, 2 H), 2.24–1.07 (m, 10 H), 0.92 (d, $J = 7$ Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 71.9, 68.0, 38.4, 34.4, 32.7, 29.3, 23.5, 12.2; IR (film) 3350 cm^{-1}. Exact mass calcd for $C_8H_{16}O_2$: 144.1150. Found 114.1157.

Alternatively, direct reduction of the crude lactone product using reduction Method F (LAH) affords diol **51** and a trace amount of an isomeric diol (GC-MS m/z 144; the relative retention times of **51** and the impurity are 1.14 and 1.00, respectively; 15:1 ratio). Flash chromatography (ethyl acetate elution) affords the two diols in 35% overall yield from acid **48**.

We note that acidification (48% HBR) of the basic aqueous layer remaining after cyclization workup, followed by the usual extractive workup, affords only traces (<5%) of material corresponding to hydroxy acids **49a,b**. Also, neither **50** nor **51** are rigorously characterized by correlation with authentic samples; they are distinguishable spectroscopically and gas chromatographically from their closely related isomeric counterparts, **29** and **31**, respectively.

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Registry No. 2, 87433-66-7; **3a**, 87433-86-1; **3b**, 2865-82-9; **4a**, 87433-63-4; **4b**, 87433-64-5; **4c**, 87433-65-6; **5a**, 87433-67-8; **5b**, 87433-68-9; **5c**, 87433-69-0; **6a**, 87433-88-3; **6b**, 87433-90-7; **7a**, 87433-87-2; **7b**, 87433-89-4; **8a**, 69492-28-0; **8b**, 87434-21-7; **9a**, 87433-70-3; **9b**, 87433-71-4; **9c**, 87433-72-5; **10a**, 87433-73-6; **10b**, 87433-74-7; **10c**, 87433-75-8; **11a**, 87433-91-8; **11b**, 87433-95-2; **12a**, 87433-92-9; **12b**, 87433-96-3; **13a**, 87433-93-0; **13b**, 87433-97-4; **14a**, 87433-94-1; **14b**, 87433-98-5; **16a**, 87433-76-9; **16b**, 87433-77-0; **16c**, 87433-78-1; **17a**, 87433-79-2; **17b**, 87433-80-5; **17c**, 87433-81-6; **18a**, 87433-99-6; **18b**, 39638-67-0; **19a**, 87434-06-8; **19b**, 55013-32-6; **22**, 87434-03-5; **23**, 87434-04-6; **24**, 87434-02-4; **25**, 87434-05-7; **26**, 87434-00-2; **27**, 87434-01-3; **28a**, 87433-82-7; **28b**, 87433-83-8; **29**, 87434-07-9; **30**, 87434-08-0; **31**, 87434-09-1; **32**, 87434-10-4; **42**, 87434-22-8; **43a**, 87434-11-5; **43b**, 87434-15-9; **44a**, 87434-12-6; **44b**, 87434-16-0; **45a**, 87434-13-7; **45b**, 87434-17-1; **46a**, 87434-14-8; **46b**, 87434-18-2; **48**, 87433-85-0; **50**, 87434-19-3; **51**, 87434-20-6; $Hg(NO_3)_2$, 10045-94-0; $Hg(O_2CCF_3)_2$, 13257-51-7; $Hg(ClO_4)_2$, 7616-83-3; [α,β,α]-3-(hydroxymethyl)bicyclo[4.1.0]heptane, 87433-84-9.

Supplementary Material Available: Schematics for the preparation of all starting materials and authentic samples of **3b**, **6b**, **7b**, **11b–15b**, **18b**, **19b**, **22–25**, **31**, **32**, **43b**, and **44b** (5 pages). Ordering information is given on any current masthead page.

Methano-Bridged Compounds. 1. Correlation of the ^{13}C Nuclear Magnetic Resonance Shift Average and Shift of the Bridge Carbon with the Average π-Electron Density of Methano-Bridged and Homoaromatic Compounds

Ronald J. Hunadi[1]

Contribution from R. J. Consultants, 4524 Tobias Avenue, Sherman Oaks, California 91403.
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Abstract: It was shown that the shift of the bridge carbon and ^{13}C NMR chemical shift average of methano-bridged and homoaromatic systems correlates well with the average π-electron density. The following equations were developed from the plot of the shift of the bridge carbon vs. electron density: $\delta_{bridge} = 51.97\rho_{av} - 16.40$ with $r = 0.942$ for methano-bridged systems and $\delta_{bridge} = 81.68\rho_{av} - 34.68$ with $r = 0.931$ for homoaromatic systems. Also developed were the following equations for the ^{13}C NMR shift average vs. π-electron density: $\delta_{av} = 275.85 - 145.71\rho_{av}$ with $r = 0.90$ for methano-bridged systems and $\delta_{av} = 234.52 - 117.40\rho_{av}$ with $r = 0.948$ for homoaromatic systems. If the slopes for the ^{13}C NMR chemical shift average vs. electron density are indicative of the degree of aromaticity, then the order of aromaticity is [0]bridged > methano-bridged > homoaromatic systems (161 > 146 > 117 ppm/e$^-$) as would be expected.

Although various studies have been reported on the properties and characterization of methano-bridged systems,[2] none of these studies resulted in a correlation between the $^{13}C_{av}$ NMR chemical shift and electron density of the system and/or the ^{13}C NMR

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