1-Methyl-3-(3-oxobutyl)-4-phenylpyridinium Iodide (22). Pyridine **27** (820 mg, 3.65 mmol) was stirred at 25 °C with CH_3I (1.529 g, 10.75 mmol) in benzene (1 mL) for 8 h. Filtration provided 1.27 g (95%) of pure methiodide **22**. After recrystallization from H_2O the analytical sample had mp 176–177.5 °C.

^1H NMR (Me_2SO-d_6) δ 9.01 (1 H, br s), 8.87 (1 H, br d, J = 6 Hz), 7.95 (1 H, d, J = 6 Hz), 7.75 (5 H, s), 4.37 (3 H, s), 2.88 (4 H, br s), 2.05 (3 H, s); IR (KBr) 3100, 1710, 1670 cm^{-1}.

Anal. Calcd for $C_{16}H_{18}INO$: C, 52.33; H, 4.93; N, 3.81. Found: C, 52.37; H, 4.97; N, 3.76.

1-Methyl-4-phenyl-1,5a,8,8a-tetrahydroquinolin-7(6*H*)-one (24). The salt **22** (183 mg, 15 mmol) was treated with 4 N NaOH/Me_2SO/benzene (2 mL/1 mL/2 mL) exactly as for the preparation of **10a**, to give 116 mg (98%) of the 1,2-adduct **24** as an unstable, waxy solid, mp 80–82 °C dec.

^1H NMR ($CDCl_3$) δ 7.50–7.00 (5 H, m), 5.93 (1 H, d, J = 7 Hz), 4.65 (1 H, d, J = 7 Hz), 4.35 (1 H, br t, J = 7 Hz), 2.78 (3 H, s); IR (KBr) 1705, 1635, 1575 cm^{-1}; MS, m/z 239 (M^+), 210, 196 (100).

Anal. Calcd for $C_{16}H_{17}NO$: M_r, 239.131. Found: M_r, 239.132.

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Registry No. **5**, 5958-00-9; **6**, 86610-20-0; **7a**, 81115-41-5; **7b**, 86610-21-1; **8**, 81115-40-4; **9a**, 81115-33-5; **9b**, 81115-34-6; **10a**, 81115-38-0; **10b**, 81115-39-1; **13**, 86610-22-2; **14a**, 86610-23-3; **14b**, 81115-42-6; **15**, 86610-24-4; **19**, 86610-25-5; **20**, 86610-26-6; *anti*-**21**, 86610-27-7; *syn*-**21**, 86610-28-8; **22**, 86610-29-9; **24**, 86610-30-2; **25**, 46268-56-8; **26**, 86610-31-3; **27**, 86610-32-4; chloroacetone, 78-95-5; ethyl bromoacetate, 105-36-2; benzoyl chloride, 98-88-4; (acetylmethylene)triphenylphosphorane, 1439-36-7; 3-methyl-4-(2-methoxyphenyl)pyridine, 83463-15-4.

(±)-3-Phenylhexahydrophthalides. Synthesis and Structural Assignments

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The four racemic 3-phenylhexahydrophthalides **3a–3d** were synthesized by reducing the corresponding cis and trans γ-keto acids with a variety of metal hydride reducing agents as well as with platinum oxide catalyzed hydrogenation. The product ratio obtained by hydride reduction of an individual γ-keto acid depends on the reducing activity and the bulk of the hydride reagent. The greatest hydride reducing selectivity was observed with lithium trialkylborohydrides and lithium tri-*tert*-butoxyaluminohydride. The ratio obtained through metal–hydride reduction is reversed from that of platinum oxide catalyzed hydrogenation. The selectivity in the reduction of the corresponding methyl γ-keto esters is greatly diminished as compared to that in the reduction of the γ-keto acids.

As part of a continuation of stereochemical studies of γ-lactones,[2] we prepared the racemic 3-phenylhexahydrophthalides **3a–3d**. The synthesis, separation, and configurational assignments of these lactones, through use of ^1H and ^{13}C NMR studies, are reported.

The preparation of the cis γ-keto acid **1a** and its epimerization to the trans-isomer **1b** was accomplished as previously described.[3a,b] These acids were converted to the corresponding esters **1c** and **1d** with diazomethane.[4] The resulting γ-keto esters were used, as shown in Table I, in gas chromatography studies to establish the separation and purity of **1a** and **1b** and as model compounds in metal hydride reductions and catalytic hydrogenations.[3c]

Attempts to prepare the cis-fused γ-lactones **3a** and **3b** by $NaBH_4$ reduction of **1a** were frustrated by epimerization of **1a** to **1b**. Super-Hydride ($LiEt_3BH$) (Aldrich) reduction of **1a**,[5] however, proceeded with little epimerization regardless of order of addition[6a] of reactants to give cis γ-lactones **3a**/**3b** (94:6). We were unable to isolate the individual cis γ-hydroxy acids **2a** and **2b** as reduction products owing to their ease of lactonization. The ratios of products from various reductions of γ-keto acids **1a** are presented in Table II.

Table I. Reduction of Methyl γ-Keto Esters 1c and 1d

reagent	keto ester	rctn time, h	total lactone yield, %	product ratio after lactonization[a] 3a/3b	3c/3d
$Li(t\text{-}BuO)_3AlH$	1c	4	80	65:35	
$Li(t\text{-}BuO)_3AlH$	1d	4	78		54:46
PtO_2/H_2	1c	2.5	87	58:42	
PtO_2/H_2	1d	2.5	85		55:45

[a] These lactones were obtained from the corresponding methyl hydroxy esters in refluxing toluene containing 2% oxalic acid.

Reduction of **1b** with Super-Hydride and acidification at room temperature provided a mixture of trans γ-lactones **3c**/**3d** (55:45). The trans γ-hydroxy acids **2c** and

(1) Pourahmady, N. Ph.D. Thesis, Department of Chemistry, Oklahoma State University, Stillwater, OK, 1981.

(2) Eisenbraun, E. J.; Browne, C. E.; Irvin-Willis, R. L.; McGurk, D. J.; Eliel, E. L.; Harris, D. L. *J. Org. Chem.* **1980**, *45*, 3811.

(3) (a) Fieser, L. F.; Novello, C. F. *J. Am. Chem. Soc.* **1942**, *64*, 802. (b) Scribner, J. D.; Miller, J. A. *J. Chem. Soc.* **1965**, 5377. (c) GC analysis of trans ester **1d**, formed from **1b** with diazomethane, showed it to be free of cis γ-keto ester **1c** and 99.5% pure.

(4) Ruehle, P. H.; Browne, C. E.; Eisenbraun, E. J. *Chem. Ind.* **1979**, 255.

(5) Brown, H. C.; Kim, S. C.; Krishnamurthy, S. *J. Org. Chem.* **1980**, *45*, 1.

(6) (a) The ratio of products **3a**/**3b** and **3c**/**3d** is independent of the order of addition of reagents (hydride reducing agent to keto acid or the reverse mode of addition). (b) This ratio was determined by thermal lactonization at the melting point of the trans γ-hydroxy acids **2c** and **2d** and analysis by HPLC (silica column; dichloromethane/*n*-hexane, 4:1). (c) Formation of a carboxylate anion is assumed since rapid hydrogen evolution was observed upon addition of hydride reducing agent to the γ-keto acid.

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Table II. Reduction of γ-Keto Acids 1a and 1b with Various Reducing Agents

run	reagent	keto acid	rctn time,[a] h	product ratio[b] 3a/3b	product ratio[b] 3c/3d	% epimerization[b]
1	$Li(i\text{-}Bu)_3BH$	1a	4	95:5		3
2	$Li(i\text{-}Bu)_3BH$	1b	4		61:39	0
3	$LiEt_3BH$	1a	1	94:6		2
4	$LiEt_3BH$	1b	1		55:45	0
5	$Li(t\text{-}BuO)_6AlH$	1a	3	94:6		12
6	$Li(t\text{-}BuO)_3AlH$	1b	4		52:48	3
7	$NaBH_4/Al_2O_3$[c]	1a	6	79:21		8
8	$NaBH_4/Al_2O_3$[c]	1b	6		62:38	2
9	$NaBH_4$/silica[c]	1a	6	70:30		7
10	$NaBH_4$/silica[c]	1b	6		59:41	2
11	PtO_2/H_2[d]	1a	1.5	26:74		0
12	PtO_2/H_2[d]	1b	1.5		35:65	0

[a] Reactions were run at room temperature. [b] Ratios were determined by HPLC analysis. [c] Purchased from Alfa Products, Thiokol/Ventron Division. [d] In EtOAc solvent.

2d were not found. However, acidification at ice temperature provide a 23% yield of a mixture of trans γ-hydroxy acids **2c/2d** (4:96)[6b] and 76% of the trans-fused γ-lactones **3c/3d** (70:30). The hydroxy acids **2c** and **2d** were separated from lactones **3c** and **3d** by extraction with sodium bicarbonate solution and acidification with cold 10% HCl. When the total mixture was converted to lactones **3c** and **3d**, the ratio became 55:45. The product ratio was independent of the order of addition of reactants.[6a]

Since the ratio of cis acids **3a/3b** (94:6) was unfavorable for isolation of **3b**, we sought to change the ratio through PtO_2-catalyzed hydrogenation[7] of **1a** in ethyl acetate, which gave *cis*-**3a**/*cis*-**3b** (26:74). The preponderance of **3b** in this new ratio greatly facilitated its isolation and purification, which was accomplished by preparative high-pressure liquid chromatography (HPLC).[8] Catalytic hydrogenation of trans γ-keto acid **1b**, using PtO_2 in ethyl acetate, and subsequent thermal lactonization yielded trans γ-lactones **3c/3d** in 35:65 ratio. Again, this product ratio is reversed compared to that produced by Super-Hydride reduction.

Discussion of Results

We assumed that these reduction selectivities resulted from association of functional groups. Accordingly, we prepared the methyl γ-keto esters **1c** and **1d** for comparative studies assuming that this alteration would diminish intramolecular interaction. This was confirmed by conversion of these esters to lactone pairs as shown in Table I. Regardless of the method used for reducing the γ-keto esters, the cis γ-lactone **3a** and the trans γ-lactone **3c** predominate in their respective pairs. This is to be expected if Cram's rule[9] is obeyed for the metal hydride reductions. Also, it is to be noted that considerably less selectivity in product formation of γ-lactones from the methyl γ-keto esters is observed compared to that in the reduction of the γ-keto acids **1a** and **1b**.

Since the chiral center at C-8 of the γ-hydroxy methyl esters **2e–2h** is benzylic, we were concerned about the integrity of this center after lactonization because, in contrast to the thermal cyclization of the γ-hydroxy acids **2a–2d**, oxalic acid was used to catalyze the lactonization of the γ-hydroxy methyl esters. Accordingly, we treated a sample of γ-hydroxy acids **2c** and **2d** (4:96) with diazomethane and subsequently cyclized the mixture in refluxing toluene containing 2% oxalic acid. This experiment showed the lactone ratio was the same irrespective of lactonization procedure, i.e., **3c/3d** (4:96). We also exposed the mixture of γ-hydroxy acids **2c/2d** (4:96) to the same hydrogenation conditions used to catalytically reduce **1b** to **2c/2d** (35:65) as a test of whether the chiral center at C-8 is epimerized by reduced Adam's catalyst. The ratio of **2c/2d** remained 4:96.

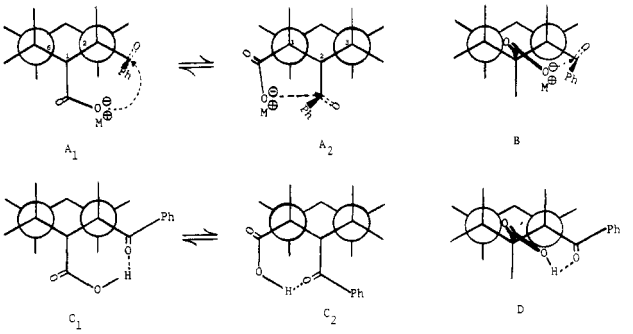


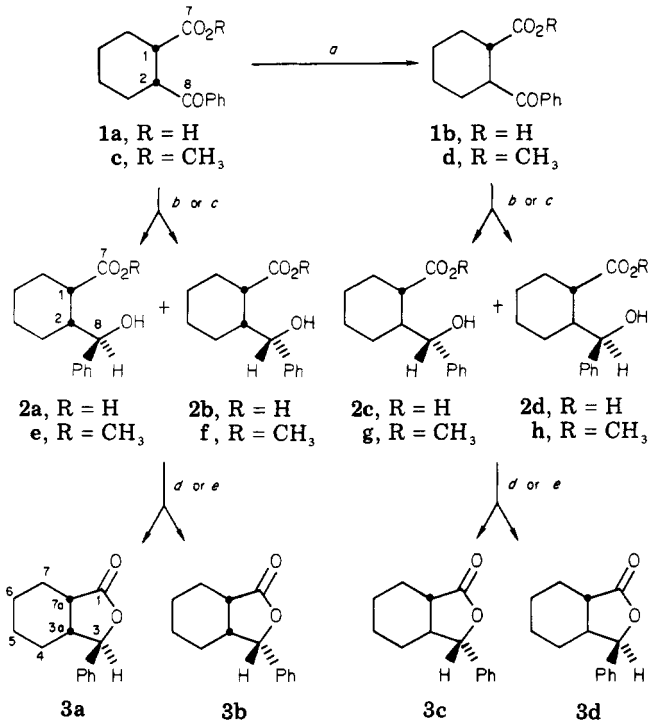
Figure 1. Proposed intramolecular interactions during reduction of γ-keto acids.

A representation of the proposed intramolecular association of carboxylate anion[6c] and γ-ketone carbonyl carbon is shown in forms A_1, A_2 for **1a** and form B for **1b** in Figure 1. Also shown in Figure 1 is the intramolecular hydrogen bonding represented by forms C_1 and C_2 for **1a** and form D for **1b**.

We suggest that these intramolecular associations are responsible for the selectivity observed in the reduction of γ-keto acid **1a** and to a lesser extent **1b**. A Dreiding model of **1a** (form A_1, Figure 1) with an equatorial benzoyl group shows there is clear access on one side of the ketone carbonyl group for approach of hydride reducing agent to provide γ-hydroxy acid **2a**. Approach to the other side, in form A_1, is blocked by carboxylate anion and its counterion. Consideration of form A_2 of **1a** with an axial benzoyl group shows that approach of hydride reducing agent to produce γ-hydroxy acid **2b** is hindered by two axial hydrogens located at C-4 and C-6 (axial protons on carbons, γ to ketone carbonyl). Thus the preferential formation of **2a** and **3a** is favored by both conformations (forms A_1 and A_2). From these conformational considerations, we assumed that selectivity to favor **3a** should increase with increased bulkiness of metal hydride reducing agent. This assumption is supported by the metal hydride reduction data shown in Table II. The highest selectivity is achieved with monohydrides (runs 1, 3, 5). Reduction with $NaBH_4$ (runs 7–10) is less selective and we assume this is the result of competing hydride donation from hydride-containing counterion. In contrast, catalytic hydrogenation of cis γ-keto acid **1a** with PtO_2 catalyst pro-

(7) Pd/C catalyst was not suitable since hydrogenolysis to desoxy acid occurred.
(8) HPLC (Waters Prep LC/System 500) using silica gel columns and eluting with dichloromethane/*n*-hexane (4:1).
(9) Cram, D. J.; Abd Elhafez, F. A. *J. Am. Chem. Soc.* **1952**, *74*, 5828.

Scheme I



[a] OH^-, H_3O^+. [b] $LiEt_3BH$. [c] H_2, PtO_2, EtOAc. [d] Spontaneous lactonization. [e] Δ.

vides **3b** as the major product as shown by run 11 in Table II. This reversal of the product ratio may be attributed to the rotation of the ketone carbonyl group in response to intramolecular hydrogen bonding as shown for forms C_1 and C_2 of Figure 1. These conformational forms suggest that attack from the side leading to **2b** and ultimately to **3b** (anti-Cram product) is favored.

Consideration of the most stable chair form of the anion of trans γ-keto acid **1b** (form B, Figure 1) during metal hydride reduction suggests that preferential approach of hydride reducing agent is absent during its reduction and hence a decreased product selectivity is to be expected as compared to that in metal hydride reduction of **1a**.

The selectivity observed for PtO_2-catalyzed hydrogenation of **1b** (Table II, run 12; **3c** < **3d**) may be rationalized by using the same argument that was used for catalytic hydrogenation of **1a** and referring to form D of Figure 1, in which the underside of form D is considered to be preferentially exposed to catalyst.

Except for trans γ-hydroxy acid **2d**, we were unsuccessful in obtaining pure samples of the γ-hydroxy acids of Scheme I. Although we were able to obtain the cis γ-hydroxy acids **2a** and **2b** as a mixture, attempts to separate them invariably caused lactonization. The trans γ-hydroxy acid **2c** was obtained only as a mixture with **2d**. The latter, mp 150–151 °C, is probably the acid described by Fieser and Novello.[3a]

Discussion of ^1H and ^{13}C NMR Data

The structural assignments for lactones **3a–3d** were made through use of the selected ^{13}C and ^1H NMR data presented in Tables III and IV. The data from Table III were used to establish the stereochemistry of the ring junctions of the lactone pairs. Similarly, the ^{13}C NMR data verified the logic of the earlier structure assignments[3b] to **1a** and **1b**.

The ^{13}C chemical shift assignments for the tertiary carbons of the cyclohexane ring of γ-keto acids **1a** and **1b** were made readily through use of SFORD experiments and

Table III. ^{13}C NMR Chemical Shifts for γ-Lactones 3a-3d[a]

C	3a	3b	3c	3d
1	178.0	177.9	176.3	177.5
3	83.0	86.0	85.4	82.0
3a	37.9	37.8	46.6[b]	40.2[b]
4	26.8	27.8	27.1	27.6
5	22.9	(22.7)[c]	(24.8)[c]	(25.0)[c]
6	22.9	(22.9)[c]	(25.0)[c]	(25.1)[c]
7	23.0	23.6	25.2	25.3
7a	42.9[b]	42.2[b]	51.8	46.7

[a] Spectra were recorded as 0.5 M solutions in $CDCl_3$; chemical shifts are reported in ppm downfield from internal Me_4Si. [b] Assignments confirmed through deuterium exchange. [c] Parentheses indicate interchangeable assignments.

Table IV. Experimental and Theoretical $^3J_{HH}$ Coupling for Benzylic Protons of Lactones 3a-3d

lactone	φ[a], deg	$^3J_{HH}$ calcd[b]	$^3J_{HH}$ obsd[b]
3a	110–135	1.1–5.0	3.0
3b	40–15	5.9–9.3	6.0
3c	150–160	7.5–8.8	9.0
3d	40–35	5.9–6.7	6.0

[a] Measured from extremes of possible conformations in Dreiding models. [b] In hertz.

substituent shift parameters[10] with ^{13}C signals appearing at 42.7 (C-1) and 44.1 (C-2) ppm for **1a** and 44.2 (C-1) and 46.6 (C-2) ppm for **1b**. These assignments were confirmed through deuterium exchange (NaOD in D_2O) of the tertiary proton adjacent to the ketone carbonyl group of **1b**. From the above data and the premise that an equatorial substituent produces a chemical shift downfield from that of a corresponding axial substituent[11] and assuming that a chair conformation with diequatorial substituents for **1b** would prevail, we assigned cis configuration to **1a** and trans configuration to **1b**.

The deuterium exchange in **1b** and its subsequent reduction provided trans-fused γ-lactones **3c** and **3d** with label at position C-3a. This permitted unequivocal chemical shift assignment of ^{13}C signal appearing at 46.6 ppm for **3c** and 40.2 ppm for **3d**.

An earlier NMR experiment involving selective proton decoupling at C-1 of γ-hydroxy acid **2d** and observation of which ^{13}C signals were affected gave a result consistent with the assignments from the preceding deuterium-exchange studies. Since deuterium exchange could not be carried out on **1a** without epimerization to **1b**, we subjected the cis γ-lactone mixture **3a**/**3b** (94:6) to deuterium exchange (CD_3O^-, CD_3OD) and obtained a deuterated mixture of **3a**, **3b**, **3c**, and **3d** with **3a** predominating. The expected deuterium exchange took place at position C-7a and permitted assignment of the ^{13}C signal at 42.9 ppm for **3a** and 42.2 ppm for **3b**.

As shown in Scheme I, it can be assumed that the γ-lactones **3a** and **3b** would have cis ring fusion and that of **3c** and **3d** would be trans. The ^{13}C chemical shifts of the tertiary C-3a and C-7a in each case are in agreement with the assigned structure. As shown in Table III, the ^{13}C chemical shift values for these carbons are as follows: **3a**,

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(11) (a) Dalling, D. K.; Grant, D. M. *J. Am. Chem. Soc.* **1967**, *89*, 6612. (b) Perlin, A. S.; Koch, H. J. *Can. J. Chem.* **1970**, *48*, 2639.

37.9, 42.9; **3b**, 37.8, 42.2; **3c**, 46.6, 51.8); and **3d**, 40.2, 46.7. Again C-3a and C-7a experience the greater downfield shift in trans lactones compared to those in cis lactones. This effect arises because the cis ring junction of **3a** and **3b** requires an axial–equatorial arrangement of substituents, which in turn produces a γ-gauche (1,3) interaction with C-5 and C-6. As a consequence, C-5 and C-6 in the cis-isomers **3a** and **3b** experience greater shielding compared to those of the trans-isomers **3c** and **3d**.

With the stereochemistry of the ring junctions of the cis γ-lactones **3a** and **3b** and the trans lactones **3c** and **3d** established, we sought a configuration assignment at C-3 of each lactone. This was accomplished by comparison of experimental and calculated coupling constants of proton attached to C-3 and coupled with the proton at C-3a. Application of the Abraham–Loftus equation[12] (eq 1)

$$J_{CH-CH} = 10 \cos^2 \phi \quad (1)$$

permitted calculation of the coupling constant from torsional angles between vicinal CH–CH bonds in each case. Comparison of calculated and observed coupling constants in Table IV shows there is good agreement with the respective assignment.

Experimental Section

All melting and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 681 instrument. Proton NMR spectra were determined at 100.1 MHz on a Varian XL-100A instrument using tetramethylsilane as internal standard in $CDCl_3$ or Me_2SO-d_6 solvent. The ^{13}C NMR spectra were obtained at 25.2 MHz in the FT mode on a Varian XL-100A spectrometer instrument interfaced with a 12 K Nicolet 1080 computer system. Gas chromatographic analyses were obtained with a Varian 3700 capillary gas chromatography apparatus using a SE-54 column (30 m/0.25 mm). Analytical and preparative HPLC separations were performed on a Waters Associates system.[8] Microanalyses were purchased from Galbraith Laboratories, Inc., Knoxville, TN.

Lithium Triethylborohydride (Super-Hydride) Reduction of Cis γ-Keto Acid 1a. An 11.6-g (0.05 mol) sample of acid **1a** in 250 mL of dry THF was added dropwise to a cold (ice bath) solution of Super-Hydride (150 mL, 1 M in THF). The mixture was stirred at room temperature for 1 h and then poured into 1 L of ice water. Most of the THF was removed by rotary evaporation, the product was extracted with ether, and the extract was shaken three times with saturated sodium bicarbonate solution. The bicarbonate extract was acidified with dilute hydrochloric acid and extracted with ether, and the extract was washed with water, dried ($MgSO_4$), and concentrated to 8.9 g (82%) of yellow oil, which was distilled (Kugelrohr; 140–142 °C, 0.05 mm) and shown by HPLC (silica column; dichloromethane/*n*-hexane, 4:1) to be a 94:6 mixture (isomer **3b** elutes first) of cis lactones **3a** and **3b**: ^1H NMR ($CDCl_3$) δ 7.28 (m, 5, Ar H), 5.16 (d, 1, J = 3 Hz, Ar CH), 2.60 (m, 3), 2.02–1.20 (m, 7); ^{13}C NMR ($CDCl_3$) 178.0 (CO), 138.4, 128.4 (×2), 127.8, 124.9 (×2), 83.0, 42.9, 37.9, 26.8, 23.0, 22.9 ppm (×2). Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.25; H, 7.41.

Catalytic Hydrogenation of *cis*-2-Benzoylcyclohexanecarboxylic Acid (1a). Hydrogenation of 10 g (0.04 mol) of cis acid **1a** in 250 mL of ethyl acetate was carried out in the presence of 1 g of platinum oxide catalyst, with hydrogen uptake ceasing after shaking at 40 psi for 90 min. The catalyst was removed by filtering through Dicalite. The filtrate was extracted with cold saturated bicarbonate solution. The remaining ethyl acetate solution was dried ($MgSO_4$) and concentrated to give 1.8 g (19%) of cis lactones **3a** and **3b** (26:74). The bicarbonate extract was acidified with cold 5% hydrochloric acid to yield a semisolid mixture of cis hydroxy acids **2a** and **2b** (26:74). This mixture lactonizes upon warming or spontaneously in an organic solvent (ether). Lactone **3b** was isolated from the cyclized mixture by preparative HPLC (silica column; dichloromethane/*n*-hexane; 4:1): mp 68–70 °C; ^1H NMR ($CDCl_3$) δ 7.28 (m, 5, Ar H), 5.48 (d, 1, J = 6.0 Hz, Ar CH), 2.65 (m, 2), 2.02–1.10 (m, 8); ^{13}C NMR ($CDCl_3$) 177.9 (CO), 135.8, 128.1 (×2), 127.4, 124.9 (×2), 86.0, 42.4, 37.8, 27.8, 23.6, 22.9, 22.7 ppm.

Lithium Triethylborohydride (Super-Hydride) Reduction of Trans γ-Keto Acid 1b. A sample of **1b** (4 g, 17 mol) in 75 mL of dry THF was added dropwise to a cold (ice bath) solution of Super-Hydride (50 mL, 1 M in THF). The mixture was stirred at room temperature for 1 h and then poured into 100 mL of ice water. Most of the THF was removed by rotary evaporation, the product was extracted with ether, and the ether layer was washed three times with saturated sodium bicarbonate solution. The combined bicarbonate extracts were acidified, extracted with ether, washed with water, and dried ($MgSO_4$). Concentration afforded 0.95 g (23% yield) of crystalline trans γ-hydroxy acid **2d** (ratio **2c**/**2d**, 4:96), which showed 12 peaks in the ^{13}C NMR spectrum: IR (KBr) 3590, 2930, 2860, 1690 (CO) cm^{-1}; ^1H NMR (Me_2SO-d) δ 7.26 (m, 5, Ar H), 4.72 (s, 1, OH), 2.50 (m, 2) 2.10–0.90; ^{13}C NMR (Me_2SO-d_6) 177.0, 145.1, 127.6 (×2), 126.1, 125.5 (×2), 72.1, 45.7, 45.6, 30.2, 25.4, 25.1, 22.1 ppm. Acid **2d** lactonizes at mp 150–151 °C to lactone **3d**.

The original ether layer was concentrated to 2.8 g (76%) of a yellow oil, which was proven to be a mixture of trans lactones **3c** and **3d** (70:30) by HPLC (silica column, methylene chloride/*n*-hexane, 4:1).[6a] Isomer **3d** elutes first. Preparative HPLC[8] was used to separate lactones **3c** and **3d**. After isolation, lactone **3d**, containing 3% of **3c**, melted at 82–83 °C: IR (KBr) 1770 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42–7.04 (m, 5, Ar H), 5.60 (d, 1, J = 6 Hz, Ar CH), 2.40–1.00 (m, 10); ^{13}C NMR ($CDCl_3$) 177.5 (CO), 135.5, 128.2 (×2), 127.7, 124.9 (×2), 82.0, 46.7, 40.2, 27.6, 25.3, 25.1, 25.0 ppm.

Lactone **3c** containing 5% of **3d** showed the following: mp 79–81 °C; IR (KBr) 1770 (CO) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.32 (m, 5, Ar H), 4.96–1.12 (m, 4); ^{13}C NMR ($CDCl_3$) 176.3, 137.1, 128.4 (×2), 128.2, 125.6 (×2), 85.4, 51.8, 46.6, 27.1, 25.2, 25.0, 24.8 ppm.

Catalytic Hydrogenation and Metal Hydride Reduction of Cis and Trans Methyl γ-Keto Esters 1c and 1d. The cis and trans methyl esters **1c** and **1d**, prepared by treating γ-keto acids **1a** and **1b** with diazomethane, were catalytically reduced in the presence of Adams catalyst and with $Li(t\text{-}BuO)_3AlH$ as described for the γ-keto acids **1a** and **1b**. The product ratios, as γ-lactones, were determined by gas chromatography and HPLC as described above. The results are presented in Table I.

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Registry No. (±)-**1a**, 86528-42-9; (±)-**1b**, 86528-43-0; (±)-**1c**, 86561-42-4; (±)-**1d**, 86561-43-5; (±)-**2a**, 86528-44-1; (±)-**2b**, 86561-44-6; (±)-**2c**, 86561-45-7; (±)-**2d**, 86561-46-8; (±)-**3a**, 86528-45-2; (±)-**3b**, 86528-46-3; (±)-**3c**, 86528-47-4; (±)-**3d**, 86528-48-5.

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