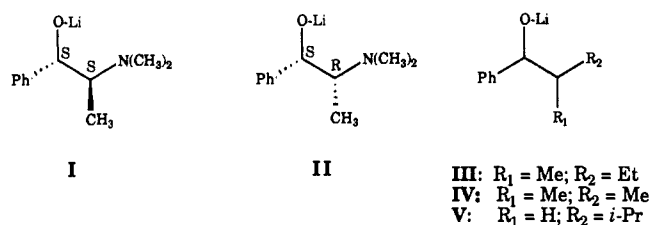


of related compounds as a testing ground for the chelation hypothesis.⁹ Figure 1 presents an ORTEP diagram of the structure of lithium (+)-*N*-methylpseudoephedrate (I) determined from



crystals obtained by precipitation from a 95:5 *p*-dioxane-THF solution.^{10,11} In the solid state, the lithium atoms are chelated between oxygen and nitrogen and the alkoxy is tetrameric.¹² That the solution structure (which is more relevant to synthetic processes) is tetrameric in benzene was demonstrated by vapor pressure osmometry (VPO, 37 °C) and cryoscopy (5.5 °C).^{5d,13-17} (Table I). A strong argument for chelation in solution can be made upon examination of the vicinal coupling constant (8.62 ± 0.60 Hz) between protons b and c, which is consistent with the conformation of an intramolecularly chelated alkoxy.^{18,19} A ⁶Li-¹H NOE NMR spectrum of [⁶Li]I in benzene-*d*₆ at 25 °C was obtained and is also consistent with intramolecular chelation. We have submitted this spectrum as supplementary material.

The foregoing structural information supports the proposal⁴ that intramolecular lithium chelation occurs in some asymmetric syntheses and also provides permissive evidence for transition structures where attack occurs on an edge of an aggregated species.²⁰ However, the more familiar monomeric transition structures cannot be ruled out entirely.⁴

We have estimated the chelation energy by comparing the heats of deprotonation (ΔH_{dep} , determined calorimetrically^{5d}) for chelatable 2-substituted-1-phenyl-1-propanols with appropriate analogues that are incapable of chelation. Data for the present case are provided in Table II, where the ΔH_{dep} of *N*-methylpseudoephedrine and *N*-methylephedrine by lithium bis(tri-

methylsilyl)amide (LHMDS) are compared to the corresponding values for deprotonation of 2-methyl-1-phenyl-1-butanol (III),²¹ 2-methyl-1-phenyl-1-butanol (IV), and 3-methyl-1-phenyl-1-butanol (V).²² The enthalpies of stabilization due to chelation (ΔH_{stab}) can be calculated from these ΔH_{dep} data by using eq 1.

$$\Delta H_{\text{stab}} = \Delta H_{\text{dep}}(\text{chelatable}) - \Delta H_{\text{dep}}(\text{nonchelatable}) \quad (1)$$

These values were found to range from 6.4 to 8.4 kcal/mol, which are in agreement with previous thermodynamic measurements of Klumpp (3.59-9.80 kcal/mol)^{4j} and Beak (8.3 kcal/mol),⁷ and the calculated values of Schleyer (10.2-13.1 kcal/mol).²³

Further explorations of the chelation question using the above techniques for a variety of other compounds have been completed and will be reported in a future publication.

Acknowledgment. This work was supported by NSF Grant CHE-8709249 to E.M.A., for which we are most appreciative. We wish to acknowledge Dr. Anthony A. Ribeiro of the Duke NMR Center for his assistance in the implementation of the ⁶Li-¹H NOE NMR experiment and Dr. Franklin J. Fisher for initial thermochemical experiments.

Supplementary Material Available: Atomic numbering scheme and tables of crystallographic data, atomic positional and thermal parameters, bond lengths and angles, and selected torsion angles for the solid-state tetramer (I)₄ and a ⁶Li-¹H NOE NMR spectrum of [⁶Li]I (16 pages); a listing of observed and calculated structure amplitudes for (I)₄ (13 pages). Ordering information is given on any current masthead.

(21) A 59:41 (±)-*RR/RS* mixture of diastereomers was used: Gonzalez, F.; Perez-Ossorio, R.; Plumet, J. *An. Quim.* **1975**, *71*, 208-212.

(22) While the aggregation states of III-V were not determined, lithium *sec*-phenethanolate was found to be hexameric and tetrameric in benzene and dioxane, respectively.

(23) See: Reference 4j, p 19.

The Remarkable Cobalt- and Phase-Transfer-Catalyzed Carbonylation of Epoxy Alcohols: A Formal Triple Carbonylation Reaction

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Carbonylation reactions are one of the most important classes of metal-catalyzed processes.^{1,2} An attractive method for effecting a variety of carbon monoxide insertion reactions, under mild conditions, is by the use of phase-transfer catalysis. A rich chemistry has developed using cobalt carbonyl as the metal catalyst under such conditions.³⁻⁵ Of particular note are single and double carbonylation reactions, which occur by the reaction of in situ generated acylcobalt tetracarbonyl (from cobalt carbonyl, methyl iodide, and carbon monoxide) with unsaturated and strained ring compounds. Concerning the latter, vinyl epoxides undergo monocarbonylation to unsaturated hydroxy acids,⁶ while styrene oxides experience double carbonylation, affording the enol tautomer of an α -keto lactone.⁷ It was reasoned that, by the use

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(3) Petrignani, J. F. *The Chemistry of the Metal-Carbon Bond*; Hartley, F. R., Ed.; J. Wiley and Sons, Ltd.: New York, 1989, Vol. 5; pp 63-106.

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(8) The optically active alcohols were obtained from Aldrich Chemical Co.

(9) These studies will be submitted as a full paper in the future.

(10) The lithium alkoxides were prepared by addition of equimolar amounts of the alcohol and solid LHMDS (purified as described in ref 5d) in the solvent of interest.

(11) The tetramer [C₁₁H₁₆LiNO]₄, depicted in Figure 1, crystallizes in the monoclinic system, space group *P*2₁ (*C*₂^h), with *a* = 15.758 (5) Å, *b* = 12.617 (4) Å, *c* = 11.579 (4) Å, β = 90.78 (2)° (from 25 orientation reflections, 40° < θ < 47°), *V* = 2302 (2) Å³, *Z* = 2, *d*_{calcd} = 1.069 g cm⁻³, μ (Cu K α) = 4.9 cm⁻¹. Intensity data (+*h*, +*k*, \pm *l*; 4323 nonequivalent reflections; θ_{max} = 67°) were recorded on an Enraf-Nonius CAD-4 diffractometer (Cu K α radiation, λ = 1.5418 Å; graphite monochromator; ω -2 θ scans). The crystal structure was solved by direct methods (MULTAN11/82). Full-matrix least-squares refinement of atomic parameters (anisotropic C, Li, N, O; fixed H contributions) converged (maximum shift 0.02 σ) at *R* = 0.057 (*R*_w = 0.070, GOF = 1.45) over 1894 reflections with *I* > 2.0 σ (*I*). Further details are provided as supplementary material.

(12) A similar tetrameric structure was obtained for the benzene solvate of lithium (+)-*N*-methylephedrate (II) when crystallized from benzene. This structure will be reported in the future.

(13) HMDS did not interact with the alkoxy aggregate in either solvent (see ref 5d).

(14) We suspect II to be tetrameric in dioxane, although our colligative measurements failed to differentiate between the tetramer and hexamer.

(15) Variable-temperature ⁶Li NMR of [⁶Li]I and -II showed only one resonance, which was invariant to temperature.

(16) Bauer, W.; Schleyer, P. v. R. *Magn. Reson. Chem.* **1988**, *26*, 827-833, and references therein.

(17) ⁶Li metal (95.5%) was obtained from ORNL, Oak Ridge, TN. The [⁶Li]alkoxides were prepared as described in refs 10 and 5d.

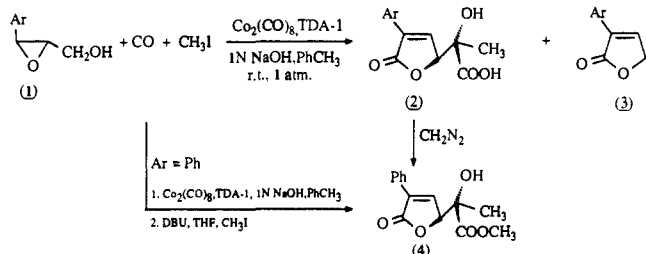
(18) Using the Karplus equation: Karplus, M. *J. Chem. Phys.* **1959**, *30*, 11; *J. Am. Chem. Soc.* **1963**, *85*, 2870. Bothner-By, A. A. *Adv. Magn. Reson.* **1965**, *1*, 195.

(19) The validity of using the vicinal coupling constant to determine the conformation of the alcohols has been shown: (a) Kanzawa, T. *Bull. Chem. Soc. Jpn.* **1956**, *29*, 398. (b) Portoghese, P. S. *J. Med. Chem.* **1967**, *10*, 1057.

(20) Aggregated transition states have been proposed for the aldol reaction: (a) Seebach, D.; Amstutz, R.; Dunitz, J. D. *Helv. Chim. Acta* **1981**, *64*, 2622. (b) Heathcock, C. H.; Lampe, J. *J. Org. Chem.* **1983**, *48*, 4330. (c) Williard, P. G.; Hintze, M. J. *J. Am. Chem. Soc.* **1987**, *109*, 5539-5541.

of β -epoxy alcohols as reactants, one could intercept the ring-opened organocobalt complex by the alkoxide ion (formed by deprotonation of the alcohol) and produce a different, unsaturated lactone. We now describe the novel phase-transfer-catalyzed conversion of epoxy alcohols to lactic hydroxy acids.

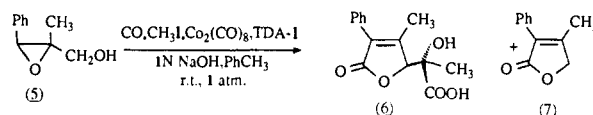
Treatment of 3-(hydroxymethyl)-2-phenyloxirane (**1**, Ar = Ph) with carbon monoxide and methyl iodide, using toluene as the organic phase, 1 N NaOH as the aqueous medium, $\text{Co}_2(\text{CO})_8$ as



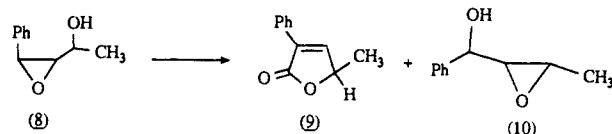
the metal catalyst [10:1 ratio of $1/\text{Co}_2(\text{CO})_8$], and tris(poly-oxaheptyl)amine (TDA-1)⁶⁻⁸ as the phase-transfer agent, for 8–12 h at room temperature afforded 2-C-(2,5-dihydro-2-oxo-3-phenylfur-5-yl)lactic acid, (**2**, Ar = Ph), in 42% yield of pure material, with 10% 2,5-dihydro-2-oxo-3-phenylfuran (**3**, Ar = Ph)⁹ formed as a byproduct. Lower yields of **2** were attained with cetyltrimethylammonium bromide (25% yield of **2**) as the phase-transfer catalyst, or at higher concentrations of base (16% with 5 N NaOH). Compound **2** (Ar = Ph) was characterized as such¹⁰ or as its methyl ester **4**. The latter was obtained either by reaction of **2** with diazomethane (96% yield), or in 44% yield from **1** by a two-step process, the first being the carbonylation reaction, followed by exposure to 1,5-diazabicyclo[5.4.0]undec-5-ene and methyl iodide in tetrahydrofuran (THF). Excellent quality crystals of **4** were obtained and an X-ray structure determination (to be published separately)¹¹ provided conclusive evidence for the assigned structure. The process is diastereospecific, as X-ray and NMR analyses reveal that only the anti diastereomer is present in the solid state and in solution. Repetition of the phase-transfer reaction of **1** using ^{13}C O resulted in incorporation of the label at the lactone carbonyl, carboxylic acid carbon, as well as at the carbon bearing the hydroxyl group (^{13}C NMR: $J_{\text{C}^{13}-\text{C}^{13}} = 59.2$ Hz for the hydroxy and acid carbons).¹²

This remarkable triple carbonylation reaction occurs with other epoxy alcohols related to **1**, including those with a 1-naphthyl (46% yield of **2**) or *p*-tolyl (50% yield) instead of a phenyl substituent

ring. In addition, use of the trisubstituted oxirane **5** as the reactant



affords approximately equal amounts of the triple (**6**, 33%)¹² and single (**7**, 36%)¹³ carbonylation products. Only monocarbonylation to **9**¹⁴ and rearrangement (**10**) occurs with the secondary alcohol **8** as the reactant [**10** is also formed in the absence of $\text{Co}_2(\text{CO})_8$].



Analysis of the above results suggested that the product of triple carbonylation may arise via **3**. Indeed, exposure of **3** to the reaction conditions described for **1** [i.e., $\text{Co}_2(\text{CO})_8$, CH_3I , CO , 1 N NaOH, PhCH_3 , TDA-1, room temperature, 16 h] gave **2** in 78% yield. Note that **3** does not react with 1 N NaOH, CH_3I , and TDA-1 in the absence of CO and $\text{Co}_2(\text{CO})_8$. Similarly, **7** afforded **6** in 58% yield. A possible pathway for the double carbonylation of butenolides may involve the participation of enol cobalt intermediates (steric factors are evident in the failure of **9** to undergo double carbonylation).

In conclusion, cobalt carbonyl and TDA-1 catalyze the unique conversion of epoxy alcohols to 2-C-(2,5-dihydro-2-oxofur-5-yl)lactic acids in moderate yields, and under exceptionally mild conditions. The products can be considered as unusual lactic acid systems. This transformation constitutes the first example, to our knowledge, of a net triple carbonylation reaction. Furthermore, these are the first cases of double carbonylation of butenolides.

Acknowledgment. We are grateful to British Petroleum, and to the Natural Sciences and Engineering Research Council of Canada, for support of this research.

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(10) Properties for **2** (Ar = Ph): mp 236.0–238.8 °C; IR (KBr) ν 3426 (OH), 1748 (CO) cm^{-1} ; ^1H NMR ($\text{DMSO}-d_6$) δ 1.48 (s, 3 H, CH_3), 5.36 (d, 1 H, H5, $J_{\text{H4-H5}} = 1.9$ Hz), 7.43 (m, 3 H, Ph protons), 7.94 (dd, 2 H, Ph protons ortho), 8.20 (d, 1 H, $\text{CH}=\text{C}$) ppm; ^{13}C NMR ($\text{DMSO}-d_6$) δ 22.6 (CH_3), 73.9 (C(OH) CH_3), 84.2 (CHO), 126.6, 128.4, 128.9, 129.6, 130.8, 146.8 (Ph and olefinic carbons), 170.9 (CO-lactone), 174.4 (COOH) ppm. **2** (Ar = *p*- $\text{CH}_3\text{C}_6\text{H}_4$): mp 240.6–242.7 °C; IR (KBr) ν 3420 (OH), 1745 (CO) cm^{-1} ; ^1H NMR [$(\text{CD}_3)_2\text{CO}$] δ 1.44 (s, 3 H, CH_3), 2.31 (s, 3 H, $\text{CH}_3\text{C}_6\text{H}_4$), 5.31 (d, 1 H, H5, $J_{\text{H4-H5}} = 1.7$ Hz), 7.24 (d, 2 H, protons ortho to methyl-bearing carbon), 7.81 (d, 2 H, other aromatic protons), 8.09 (d, 1 H, $\text{CH}=\text{C}$) ppm; ^{13}C NMR ($\text{DMSO}-d_6$) δ 20.9 (CH_3), 73.9 (C(OH) CH_3), 84.1 (CHO), 126.4, 126.7, 128.9, 130.7, 138.5, 145.6 (aromatic and olefinic carbons), 171.0 (CO-lactone), 174.4 (COOH) ppm. **2** (Ar = 1- C_{10}H_7): IR (KBr) 3475 (OH), 1740 (CO) cm^{-1} ; ^1H NMR [$(\text{CD}_3)_2\text{CO}$] δ 1.55 (s, 3 H, CH_3), 5.57 (d, 1 H, H5, $J_{\text{H4-H5}} = 1.9$ Hz), 7.50–8.05 (m, 8 H aromatic and olefinic protons). **4**: mp 169.0–170.0 °C; IR (KBr) ν 3487 (OH), 1760 (CO), 1738 (CO) cm^{-1} ; ^1H NMR (CDCl_3) δ 1.57 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 5.17 (d, 1 H, H5, $J_{\text{H4-H5}} = 2.1$ Hz), 7.38 (m, 3 H, Ph protons), 7.55 (d, 1 H, $\text{CH}=\text{C}$), 7.84 (dd, 2 H, Ph protons ortho) ppm; ^{13}C NMR (CDCl_3) δ 22.8 (CH_3), 53.2 (OCH_3), 76.0 (C(OH) CH_3), 84.9 (CHO), 128.1, 129.7, 130.2, 131.2, 133.6, 146.1 (aromatic and olefinic carbons), 172.0 (CO), 174.9 (CO) ppm. **6**: mp 223.6–226.1 °C; IR (KBr) ν 3339 (OH), 1748 (CO), 1739 (CO) cm^{-1} ; ^1H NMR [$(\text{CD}_3)_2\text{CO}$] δ 1.57 (s, 3 H, CH_3COH), 2.17 (s, 3 H, $\text{CH}_3\text{C}=\text{C}$), 5.30 (s, 1 H, CHO), 7.47 (m, 5 H, Ph) ppm; ^{13}C NMR [$(\text{C}_2\text{D}_2)_2\text{CO}$] δ 14.2 (CH_3), 23.2 (CH_3), 75.5 (C(OH) CH_3), 86.2 (CHO), 128.8, 128.9, 129.9, 131.1, 159.0 (Ph and olefinic carbons), 171.9 (CO-lactone), 174.9 (COOR) ppm (Note: NMR assignments for **2**, **4**, and **6** established by COSY and HETCOR techniques).

(11) Hynes, R., unpublished results.

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Intramolecular Conversions of Acyllithium. Cyclization in the Reaction of Carbon Monoxide with [1-(Silyl)vinyl]lithium

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The use of unstable, exceedingly reactive acyl anions in synthesis represents a challenge of intense interest.¹ In order to realize selective transformations from acyl anions, Seyferth et al. have studied *intermolecular* reactions involving direct trapping with electrophiles under carefully controlled reaction conditions.² On the other hand we have devised an *intramolecular* reaction involving the conversion of [2-(silyl)acyl]lithiums to acylsilane

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