The nature of the tube wall resulting from the staggered graphitic layers of either a scroll or a cone structure would provide a continuous path between the layers through which Ar may diffuse into the cavity. Nolan *et al.* (*26*) have pointed out that cone type tubes and fibers would have unsaturated valences at their edges. Mordkovich *et al.* (*29*) have also proposed a model for K intercalation into multi-walled nanotubes in which the nanotubes are assumed to have a scroll structure, allowing the K atoms to pass inward by attack of the helicoid on the outside edge of the scroll. In our case, amorphization as a result of the HIPing process may be responsible for sealing the gas within the tube. If a tube contains Ar, its ends must be effectively sealed. The HIPing temperature was too low to melt any of the Fe- or Zn-based materials (assuming no Zn metal was present after reaction with CO_2), which suggests that the ends of the Ar-containing tubes were sealed before HIPing. If this requirement is not met, Ar will not be retained in the tube. A similar HIPing experiment performed at the lower temperature of 400°C showed no evidence of tubes with Ar trapped in them, nor was any amorphization of the outer wall observed under these conditions. Brunaer-Emmett-Teller measurements on tubes of this type by Tibbetts *et al.* (*25*) gave a value of 9.91 m^2 for nitrogen gas absorption at room temperature. This is about half the actual physical value calculated geometrically and indicates that the tubes have little porosity. The Ar-filled tubes imply that the porosity must increase greatly at higher temperatures, that gas is more freely able to pass between the slanting graphitic layers and the inside of the tube, and that at the higher temperature, the amorphous crust formation prevents the gas from leaving.

A second C sample containing catalytically grown tubes prepared by the same synthesis route was HIPed under the same conditions as before to confirm our results. A further TEM study was carried out on the second HIPed sample, and we indiscriminately selected 30 tubes with an outer diameter in the range of 20 to 150 nm (Table 1). We found that a total of 11 tubes had Ar trapped in them at high pressures. In the majority of these filled tubes, we were able to find at least one of the ends of the tube, which was, as expected, sealed. We also found that out of the 19 empty tubes, 9 clearly had an open end. A couple of the tubes appeared to be sealed at both ends but contained no gas. It appears that the number of filled tubes is dictated largely by how many tubes have both ends sealed; there is no indication that tube diameter is an important factor in the diameter range studied.

The filled tubes were found to retain their Ar content with little change over several months at room temperature. Carbon tubes of the structure shown in this paper and those of other authors (*25*) thus show possibilities for gas storage. It is clear that if the tubes have a scroll structure (*29*) and are sealed at both ends, then it should also be possible to fill nanotubes of smaller dimensions with gases, whereas conventional nanotubes with a parallel wall structure may need to be filled through an open end before the end is sealed.

REFERENCES AND NOTES

1. M. Endo *et al.*, *J. Phys. Chem. Solids* **54**, 1841 (1993).
2. M. Endo, *Chemtech* **18**, 568 (1988).
3. M. S. Dresselhaus, G. Dresselhaus, K. Sugihara, I. L. Spain, H. A. Goldberg, in *Graphitic Fibers and Filaments*, M. Cardonna, Ed. (Springer-Verlag, Berlin, 1995), pp. 244–286.
4. S. Iijima, *Nature* **354**, 56 (1991).
5. T. W. Ebbesen and P. M. Ajayan, *ibid.* **358**, 220 (1992).
6. T. W. Ebbesen *et al.*, *Chem. Phys. Lett.* **209**, 83 (1993).
7. M. Endo *et al.*, *Carbon* **33**, 874 (1995).
8. For a recent review, see the special issue on nanotubes, S. Iijima and M. Endo, Eds., *Carbon* **33** (no. 7) (1995).
9. P. M. Ajayan and S. Iijima, *Nature* **361**, 333 (1993).
10. C. N. R. Rao, R. Seshadri, A. Govindaraj, R. Sen, *Mater. Sci. Eng.* **R15**, 209 (1995).
11. B. C. Satishkumar, A. Govindaraj, J. Mofokeng, G. N. Subbanna, C. N. R. Rao, *J. Phys. B* **29**, 4925 (1996).
12. M. K. Karimeddini, in *New Procedures in Nuclear Medicine*, R. P. Spencer, Ed. (CRC Press, Boca Raton, FL, 1989), pp. 207–211.
13. J. S. Vogel, J. R. Southon, D. E. Earl, T. A. Brown, *Nucl. Instrum. Methods Phys. Res. Sect. B* **5**, 289 (1984).
14. J. S. Vogel, J. R. Southon, D. E. Earl, *ibid.* **29**, 50 (1987).
15. M. Audier, A. Oberlin, M. Oberlin, M. Coulon, L. Bonnetain, *Carbon* **19**, 217 (1981).
16. E. T. Turkdogan and J. V. Vinters, *Metall. Trans.* **5**, 11 (1974).
17. M. Audier, J. Guinot, M. Coulon, L. Bonnetain, *Carbon* **19**, 99 (1981).
18. M. Ishioka, T. Okada, K. Matsubara, M. Endo, *ibid.* **30**, 859 (1992).
19. ———, *ibid.*, p. 865.
20. G. A. Jablonski, F. W. Geurts, A. Sacco Jr., R. R. Biederman, *ibid.*, p. 87.
21. G. A. Jablonski, F. W. Geurts, A. Sacco Jr., *ibid.*, p. 99.
22. F. Benissad-Aissani and P. Gadelle, *ibid.* **31**, 21 (1993).
23. G. E. Gadd, M. James, S. Moricca, P. J. Evans, R. L. Davis, *Fullerene Sci. Technol.* **4**, 853 (1996).
24. T. Cabioc'h, J. P. Riviere, M. Jaouen, J. Delafond, M. F. Denanot, *Synth. Met.* **77**, 253 (1996).
25. G. G. Tibbetts *et al.*, *Carbon* **31**, 1039 (1993).
26. P. E. Nolan, M. J. Schabel, D. C. Lynch, A. H. Cutler, *ibid.* **33**, 79 (1995).
27. N. M. Rodriguez, *J. Mater. Res.* **8**, 3233 (1993).
28. R. T. Yang and L. P. Chen, *J. Catal.* **115**, 52 (1989).
29. V. Z. Mordkovich, M. Baxendale, S. Yoshimura, R. P. H. Chang, *Carbon* **34**, 1301 (1996).
30. We thank the many people at the Australian Nuclear Science and Technology Organisation who have been supportive of this work and, in particular, J. Holmes, H. Noorman, C. J. Howard, M. M. Elcombe, S. Kennedy, P. Baxter, C. Landers, M. Perry, K. Finne, and J. Bartlett and G. W. Willett, K. Fisher, and P. J. Jackson at the University of New South Wales, Randwick, for useful discussions.

Asymmetric Catalysis with Water: Efficient Kinetic Resolution of Terminal Epoxides by Means of Catalytic Hydrolysis

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Epoxides are versatile building blocks for organic synthesis. However, terminal epoxides are arguably the most important subclass of these compounds, and no general and practical method exists for their production in enantiomerically pure form. Terminal epoxides are available very inexpensively as racemic mixtures, and kinetic resolution is an attractive strategy for the production of optically active epoxides, given an economical and operationally simple method. Readily accessible synthetic catalysts (chiral cobalt-based salen complexes) have been used for the efficient asymmetric hydrolysis of terminal epoxides. This process uses water as the only reagent, no added solvent, and low loadings of a recyclable catalyst (<0.5 mole percent), and it affords highly valuable terminal epoxides and 1,2-diols in high yield with high enantiomeric enrichment.

Asymmetric catalysis provides access to optically active epoxides either by oxygen-atom transfer to alkenes (*1*) or by carbene addition to carbonyl compounds (*2*). Both strategies have been developed to varying degrees, but significant gaps still exist in the scope of these methodologies. For example, there are still no effective enantioselective epoxidation methods known for the synthe-

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sis of terminal epoxides such as propylene oxide (3). Such epoxides are readily available as racemic mixtures, so the possibility of using a kinetic resolution strategy to access the enantiomerically pure materials is attractive (4). For kinetic resolutions in which recovery of unreacted substrate is targeted, a cheap and easily handled reagent is obviously desirable for effecting the resolution. Ideally, the product of reaction might also be of synthetic value. To these ends, water is an extremely appealing reagent for epoxide resolutions. Not only is it cost-effective, safe, and environmentally benign, but the 1,2-diols generated by epoxide hydrolysis are valuable chiral building blocks of demonstrated utility for organic synthesis (5). We describe a practical route to enantiomerically enriched terminal epoxides by way of a hydrolytic kinetic resolution (HKR) using simple chiral catalysts (Scheme 1; R, alkyl) (6). This process provides direct access to both unreacted epoxide and 1,2-diol products in high enantiomeric excess (ee) and yield.

The HKR was discovered unexpectedly during investigations of the reactions of epoxides with carboxylic acids. We had found previously that the (salen)Co(II) complex 1 is oxidized by air in the presence of benzoic acid, generating the corresponding (salen)Co(III)(benzoate) complex 2a, and that complex 2a catalyzes the ring-opening of meso epoxides with benzoic acid with moderate-to-good enantioselectivity (7). In efforts to extend this methodology to the kinetic resolution of racemic epoxides (8), we observed that a significant level of epoxide hydrolysis competed with ring-opening by benzoic acid (Scheme 2; Ph, phenyl; Et, ethyl; i-Pr, isopropyl; Bz, benzoyl). The fact that diol was being generated in very high ee suggested the participation of a highly enantioselective HKR involving adventitious water in the reaction medium.

Indeed, terminal epoxides reacted readily with water alone in the presence of (salen)Co catalysts. The solvent-free reaction of racemic propylene oxide (1.0 mol) with 0.55 equivalent of water in the presence of 0.2 mol % of (salen)Co(III)(OAc) complex 2b (9) proceeded within 12 hours at room temperature to afford a mixture of unreacted epoxide and propylene glycol (10). Fractional distillation provided both compounds in high chemical and enantiomeric purity (≥98% ee) and in nearly quantitative yield (11, 12). The nonvolatile residue obtained after distillation contained reduced complex 1; active catalyst 2b was regenerated from this material by treatment with acetic acid in air, such that the catalyst could be recycled with no
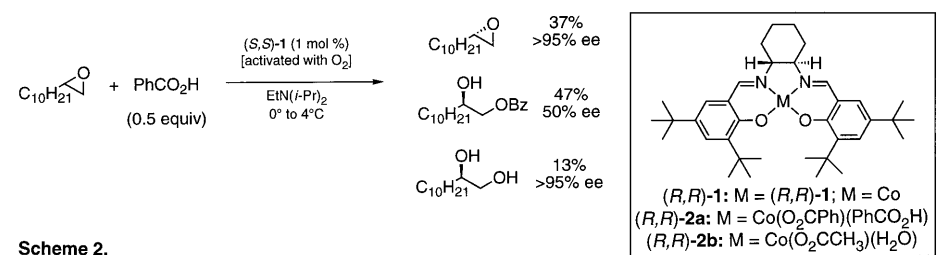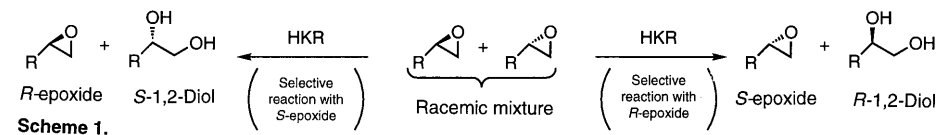
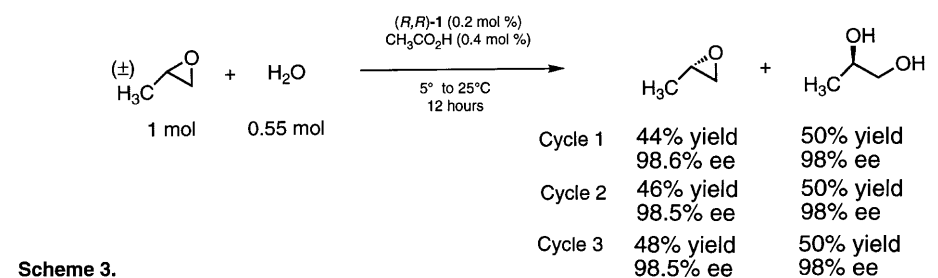observable loss in activity or selectivity (Scheme 3).

The HKR was also found to be applicable to a series of other terminal epoxides. The substrates shown in Table 1 are representative of epoxides that are inexpensive as racemates and previously have not been readily accessible in optically pure form. Unbranched alkyl-substituted epoxides (13) such as 1-hexene oxide and 1-octene oxide (entries 3 and 4) were superb substrates for the HKR (relative rate constant $k_{rel} > 250$). Epichlorohydrin (entry 2) also underwent efficient resolution, although the diol product was formed with lower ee

(86%). Conjugated epoxides such as styrene oxide and butadiene monoepoxide (entries 5 to 7) were resolved with lower selectivity, but highly enantiomerically enriched epoxide or diol could still be obtained in useful yield by simply adjusting the amount of water used in the reaction (such as entries 6 and 7).

Preliminary kinetic studies were carried out on the HKR of 1-octene oxide. Although this epoxide is immiscible with water, the reaction mixture was rendered homogeneous by addition of 20 mol % (±)-1,2-hexanediol. This additive had no measurable effect on the enantioselectivi-

Table 1. Hydrolytic kinetic resolution of terminal epoxides with water catalyzed by **2b**. The values for k_{rel} were calculated using the equation $k_{rel} = \ln[(1 - c)(1 - ee)]/\ln[(1 - c)(1 + ee)]$, where ee is the enantiomeric excess of the epoxide and c is the fraction of epoxide remaining in the final reaction mixture (4).

| Entry | R | Concentration | | Time (hours) | Epoxide | | Diol | | k_{rel} |
		2b (mol %)	Water (equiv)		ee (%)	Isolated yield (%)	ee (%)	Isolated yield (%)	
1	CH₃	0.2	0.55	12	>98	44	98	50	>400
2	CH₂Cl	0.3	0.55	8	98	44	86	38	50
3	(CH₂)₃CH₃	0.42	0.55	5	98	46	98	48	290
4	(CH₂)₅CH₃	0.42	0.55	6	99	45	97	47	260
5	Ph	0.8	0.70	44	98	38	98*	39*	20
6	CH=CH₂	0.64	0.50	20	84	44	94	49	30
7	CH=CH₂	0.85	0.70	68	99	29	88	64	30

*After recrystallization.

Scheme 1.

Scheme 2.

Scheme 3.

ty of the reaction but did allow the acquisition of reproducible data for the rate constant. The reaction followed a second-order dependence on the concentration of **2b**, consistent with a mechanism wherein two discrete catalyst molecules cooperate to activate both the electrophile (epoxide) and the nucleophile (water). Compelling evidence for a similar bimetallic mechanism has been obtained in the asymmetric ring-opening of epoxides by azide nucleophiles catalyzed by related chromium-containing catalysts (*14*). It is noteworthy that bimetallic catalysis is apparently operative with such distinct classes of reactions, and it hints at the possible generality of such a mechanism.

The HKR is an attractive procedure for the preparation of optically enriched terminal epoxides and 1,2-diols. The criteria for evaluating the practicality of chemical processes such as this one have become increasingly stringent. High standards of yield and selectivity in product formation must be met, but additional issues such as reagent cost, volumetric productivity, waste generation, reagent toxicity, and handling risks weigh more heavily than ever before. With these criteria positively met, the HKR appears to hold significant potential for large-scale application (*15*).

REFERENCES AND NOTES

1. E. N. Jacobsen, in *Comprehensive Organometallic Chemistry II*, G. Wilkinson, F. G. A. Stone, E. W. Abel, L. S. Hegedus, Eds. (Pergamon, New York, 1995), vol. 12, chap. 11.1.
2. V. K. Aggarwal, J. G. Ford, A. Thompson, R. V. H. Jones, M. Standen, *J. Am. Chem. Soc.* **118**, 7004 (1996).
3. The highest enantioselectivity reported to date for the epoxidation of propylene is 41% [R. Sinigalia, R. A. Michelin, F. Pinna, G. Strukul, *Organometallics* **6**, 728 (1987)].
4. For leading references on kinetic resolution, see E. L. Eliel, S. H. Wilen, L. M. Mander, *Stereochemistry of Organic Compounds* (Wiley-Interscience, New York, 1994), pp. 395–415; H. B. Kagan and J. C. Fiaud, in *Topics in Stereochemistry*, N. L. Allinger and E. L. Eliel, Eds. (Interscience, New York, 1987), vol. 14, p. 249.
5. H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **94**, 2483 (1994).
6. Enantioselective hydrolysis of epoxides with the use of biocatalysts has received considerable attention [K. Faber, *Biotransformations in Organic Chemistry* (Springer-Verlag, New York, 1992), chap. 2.1.5; C. A. G. M. Weijers, *Tetrahedron: Asymmetry* **8**, 639 (1997), and references therein].
7. E. N. Jacobsen, F. Kakiuchi, R. G. Konsler, J. F. Larrow, M. Tokunaga, *Tetrahedron Lett.* **38**, 773 (1997).
8. The kinetic resolution of epoxides with (CH$_3$)$_3$SiN$_3$ with (salen)Cr complexes has been documented [J. F. Larrow, S. E. Schaus, E. N. Jacobsen, *J. Am. Chem. Soc.* **118**, 7420 (1996)]. Despite the high selectivity observed in these kinetic resolutions, this method is impractical for the recovery of enantiomerically enriched epoxide because it requires consumption of azide, a relatively precious reagent.
9. Complex **2b** can be generated in situ from **1** (*7*) by treatment with acetic acid (2 equiv) in toluene under air, followed by evaporation of solvent. ^{1}H nuclear magnetic resonance (NMR) (400 MHz, dry acetone-d_6) δ (ppm) relative to tetramethylsilane: −1.95 (br s, 2 H, H$_2$O), 1.21 (s, 9 H, *t*-Bu), 1.28 (s, 9 H, *t*-Bu), 1.33 (s, 9 H, *t*-Bu), 1.53 (s, 9 H, *t*-Bu), 1.58 [s, 3 H, CH$_3$C(O)], 1.6 (m, 2 H, CH$_2$), 1.9 to 2.0 (m, 2 H, CH$_2$), 2.23 (br q, *J* = 9.8 Hz, 1 H, C*H*H), 2.79 (d, *J* = 11.8 Hz, 1 H, CH*H*), 2.88 (br d, 2 H, CH$_2$), 3.27 (brt, 1 H, CHN), 4.35 (brt, 1 H, CHN), 7.17 (d, *J* = 2.4 Hz, 1 H, ArH), 7.22 (s, 1 H, CH=N), 7.29 (d, *J* = 2.4 Hz, 1 H, ArH), 7.35 (d, *J* = 2.4 Hz, 1 H, ArH), 7.46 (d, *J* = 2.4 Hz, 1 H, ArH), 7.59 (s, 1 H, CH=N). Infrared (KBr) 1719 w, 1638 s, 1611 s, 1545 s, 1540 s, 1526 s, 1461 s, 1436 s, 1408 s, 1390 s, 1361 s, 1339 s, 1323 s, 1270 s, 1255 s, 1235 m, 1202 m, 1169 s, 834 m, 783 m; melting point (open capillary) 108°C (decomposes).
10. The hydrolysis reactions were mildly exothermic on a laboratory scale. For the kinetic resolution of propylene oxide (boiling point, 34°C), the reaction vessel was cooled in an ice bath during the addition of water to limit substrate loss as a result of evaporation.
11. A mixture of (*S*,*S*)-**1** (1.208 g, 2.0 mmol, 0.2 mol %), toluene (10 ml), and acetic acid (0.23 ml, 4.0 mmol, 2 equiv to catalyst) was stirred while open to the air for 1 hour at room temperature. The solvent was removed by rotary evaporation, and the brown residue was dried under vacuum. Propylene oxide (58.7 g, 1.0 mol) was added in one portion, and the stirred mixture was cooled in an ice-water bath. Water (9.9 ml, 0.55 mol, 0.55 equiv) was slowly added until the temperature of the reaction mixture began to rise. The temperature rose to ~25°C before dropping to 15°C, at which point water addition was continued at a rate that maintained the reaction temperature near 20°C. After 1 hour, addition was complete; the ice bath was removed, and the reaction was stirred at room temperature for 11 hours. The flask was then affixed with a distillation head equipped with a receiver cooled to −78°C, and the unreacted epoxide was distilled under N$_2$ until no more material came over with gentle heating. The system was then placed in a mild vacuum to collect any residual epoxide [yield: 26.05 g, >99% pure by gas chromatography (GC), 0.444 mol, 44% yield]. The receiver was changed, and the system was carefully placed in a full vacuum (<65 Pa). The diol was then distilled under vacuum into an ice-cooled receiver and isolated as a colorless, viscous liquid (yield: 38.66 g, >99% pure by GC, 0.503 mol, 50% recovery).
12. It is significant that propylene glycol is isolated in high enantiomeric purity and yield. Even though excellent methods exist for the asymmetric dihydroxylation (AD) of most olefins (*5*), the highest enantioselectivity obtained to date in the AD of propylene is only 49% [K. P. M. Vanhessche and K. B. Sharpless, *Chem. Eur. J.* **3**, 517 (1997)].
13. For a practical method for the epoxidation of α-olefins, see K. Sato, M. Aoki, M. Ogawa, T. Hashimoto, R. Noyori, *J. Org. Chem.* **61**, 8310 (1996).
14. K. B. Hansen, J. L. Leighton, E. N. Jacobsen, *J. Am. Chem. Soc.* **118**, 10924 (1996).
15. The HKR of propylene oxide has been carried out successfully on a 10-kg scale at a pilot plant at Chirex, Inc. (Dudley, UK) (J. Cummins and G. Thorpe, private communication).
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Protein Transport by Purified Yeast Sec Complex and Kar2p Without Membranes

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Posttranslational protein translocation across the endoplasmic reticulum membrane of yeast requires a seven-component transmembrane complex (the Sec complex) in collaboration with the lumenal Kar2 protein (Kar2p). A translocation substrate was initially bound to the cytosolic face of the purified Sec complex in a signal-sequence–dependent but Kar2p- and nucleotide-independent manner. In a subsequent reaction, in which Kar2p interacted with the lumenal face of the Sec complex and hydrolyzed adenosine triphosphate, the substrate moved through a channel formed by the Sec complex and was released at the lumenal end. Movement through the channel occurred in detergent solution in the absence of a lipid bilayer.

Protein transport across the membrane of the endoplasmic reticulum (ER) occurs through an aqueous channel (*1*) whose major component is the Sec61p complex (*2–6*). In posttranslational protein transport in yeast, the Sec61p complex (Sec61p, Sbh1p, and Sss1p) associates with the tetrameric Sec62-63 complex (Sec62p, -63p, -71p, and -72p) to form the Sec complex (*7, 8*). A lumenal domain of Sec63p (the J domain) interacts with the

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adenosine triphosphatase (ATPase) Kar2p (BiP) (*9*). Posttranslational protein transport occurs in distinct steps (*2, 3, 10, 11*) and can be reproduced with reconstituted proteoliposomes that contain only the purified Sec complex and Kar2p (*8*). We have now developed a soluble system made up of these components that eliminates many of the problems inherent in reactions that involve membranes and allows in-depth analysis of the molecular mechanism of the translocation process.

To develop a soluble system, we first tested whether an interaction between translocation substrates and the Sec complex would be maintained in detergent