16). Yet, given the current support for diapsid affinities of turtles but the conflicting evidence for their position within diapsids, it is likely that future discussion will shift from whether turtles are diapsids, to where exactly they fit within the Diapsida. One conclusion can safely be reached: Turtles can no longer be blithely considered a model for primitive amniote organization and physiology.

References

1. S. B. Hedges and L. L. Poling, *Science* **283**, 998 (1999).
2. J. E. Platz and J. M. Colon, *Nature* **389**, 246 (1997).
3. J. W. A. Kirsch and G. C. Mayer, *Philos. Trans. R. Soc. Lond. Ser. B* **353**, 1221 (1998).
4. R. Zardoya and A. Meyer, *Proc. Natl. Acad. Sci. U.S.A.* **95**, 14226 (1998).
5. M. deBraga and O. Rieppel, *Zool. J. Linn. Soc.* **120**, 281 (1997).
6. M. S. Y. Lee, *ibid.*, p. 197.
7. E. S. Gaffney, *Bull. Am. Mus. Nat. Hist.* **194**, 1 (1990).
8. R. Broom, *ibid.* **51**, 39 (1924).
9. E. S. Goodrich, *The Structure and Development of Vertebrates* (Macmillan, London, 1930).
10. G. R. DeBeer, *The Development of the Vertebrate Skull* (Clarendon, Oxford, 1937).
11. W. K. Gregory, *Bull. Am. Mus. Nat. Hist.* **86**, 275 (1945).
12. O. Rieppel and R. R. Reisz, *Annu. Rev. Ecol. Syst.*, in press.
13. J. Merck, *J. Vertebr. Paleontol.* **17**, 65A (1997).
14. S. Lovtrup, *The Phylogeny of Vertebrata* (Wiley, London, 1977).
15. N. V. Hofsten, *Zool. Bidr. Upps.* **20**, 501 (1941).
16. O. Rieppel, *J. Vertebr. Paleontol.* **13**, 31 (1993), A. S. Romer, *Osteology of the Reptiles* (Chicago University Press, Chicago, 1956).

PERSPECTIVES: POLYMER SYNTHESIS

Making Polymers from Carbon Dioxide

Eric J. Beckman

Green plants accomplish the task of generating monomers and then polymers from CO_2 daily on a global scale. But what seems easy for plants remains a difficult problem for polymer scientists. To be fair, the situation in nature is quite different from that in a chemical factory. An industrial plant has a fixed capacity reflecting market need, and ideally all resources are used for the generation of a pure, bulk product. In contrast, the production capacity of living plants reflects the availability of raw resources and, thus, changes continuously. A mixture of products is produced to sustain the system. Polymer production rate, reactor size, raw material cost, and energy utilization in photosynthesis have thus evolved to fit the global ecosystem rather than the global marketplace. Nevertheless, nature has developed an efficient system for extracting an abundant raw material (CO_2) from dilute solution in the atmosphere and for generating a variety of monomers and subsequently polymers from it. Can we also find ways to make use of this inexpensive, relatively benign raw material to generate synthetic polymers? And will such synthesis routes lead to desirable, economically competitive products?

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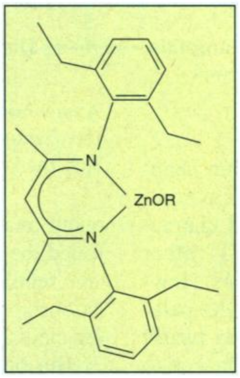
The use of CO_2 as a monomer in polymer synthesis is not new. Inoue and coworkers (*1*) reported copolymerization of CO_2 with an oxirane over a zinc catalyst in 1969. There is even earlier patent literature from the 1950s that claims the generation of polyureas from CO_2 and diamines under extreme conditions. Subsequent research, reviewed by Inoue in 1976 (*2*), Rokicki and Kuran in 1981 (*3*), and Super and Beckman in 1997 (*4*), has demonstrated that CO_2 can be copolymerized with a number of cyclic ethers, although the activity of the catalysts described was generally not high enough to warrant commercial interest. Industrial activity in the field accelerated in the 1980s, as evidenced by patent filings. However, these patents also reveal generally low catalyst activities, on the order of 50 grams of polymer per gram of metal (for comparison, activity can be well over 100,000 grams polymer per gram of metal for polyolefins). The products generated were not marketable, because of prohibitive production costs or undesirable physical properties. These results illustrate an important caveat for promoting the use of CO_2 as a raw material: Rates of reaction (at low catalyst loading) must be sufficient to support an industrial-scale process, and the materials generated must exhibit properties that provide a market advantage. Obviously, one could say this about any new synthetic polymer, and CO_2-based polymers are no exception.



A superior catalyst. Catalyst developed by Cheng *et al.* (*7*) for the copolymerization of CO_2 and cyclohexene oxide. R may be a methyl or acetyl group.

In the 1990s, interest in the use of CO_2 as a raw material increased, quite possibly as a result of the mistaken notion that such technology could ultimately be used to reduce the atmospheric concentration of CO_2. Regardless of the initial motivation, increased industrial and academic research on the use of CO_2 as a raw material led to the discovery of new reactions of CO_2 with co-monomers, for example, with diynes, and to rapid improvements in catalyst activity in the copolymerization of CO_2 and cyclohexene oxide. Leading the way, Darensbourg and Holcamp developed a series of phenoxy zinc catalysts (*5*) that produce over 400 grams of polymer per gram of zinc, an order of magnitude improvement over previous catalysts. Soon afterward, Super *et al.* (*6*) developed a high-activity fluorinated (and thus soluble) zinc catalyst that was used to generate copolymers of CO_2 and cyclohexene oxide. In this approach, CO_2 was used as both monomer and solvent. Finally, in a recent paper (*7*), Coates and co-workers demonstrated the use of a zinc catalyst (see the figure below) that exhibits higher activity than any previous catalyst in the copolymerization of CO_2 and cyclohexene oxide. Importantly, this catalyst demonstrated high activity at low CO_2 pressure. Those familiar with the production of polyethylene will recall that the development of catalysts that rapidly generated polymer at low pressure improved the economics of production substantially. In fact, Cheng and co-workers used a catalyst design strategy resembling that used in the creation of metallocene catalysts for polyolefins, where the ligands are designed to allow insertion of the monomer at only a single well-defined site.

Thus, over the past 5 years, we have seen orders of magnitude improvements in the activity of catalysts in the copolymerization of CO_2 and cyclohexene oxide. Where do we go from here? Although the recent studies (*5*–*7*) are impressive, a desperate need for their resulting product, poly(cyclohexene carbonate), has yet to materialize. This polymer exhibits a relatively high softening point of 135°C, but its overall physical properties, the current price of the cyclohexene oxide monomer, and other factors combine to prevent it from competing effectively in the restrictive world of commodity polymers. The recent work has

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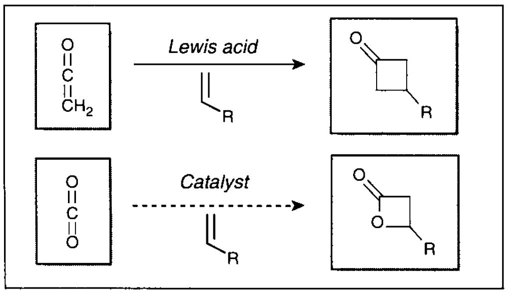

Exploiting homology? Reaction schematic showing the potential analogy between a ketene and CO_2 in reaction with olefins. The compounds are structurally homologous but whether they also react similarly remains to be shown.

clearly shown that the rate of reaction of CO_2 in a polymerization can be increased markedly, but the other half of the equation—the generation of truly competitive materials—must also be considered.

The CO/olefin copolymers recently introduced by Shell may offer a model here. These novel materials evolved from breakthroughs in catalyst design. They use new palladium-based catalysts to allow a perfectly alternating copolymerization of CO and olefins, generating poly(alkyl ketones). These materials, formed efficiently from inexpensive commodities, exhibit physical properties that may allow them to compete against existing thermoplastics used in engineering applications.

Could such scientific and commercial success also be achieved for a CO_2-based polymer? One area where scientific advances could lead to industrial breakthroughs is in the reaction of CO_2 with olefins to produce lactones and thus aliphatic polyesters. These polymers are widely used as degradable materials in medical implants and have also been promoted as environmentally degradable polymers for use in consumer packaging. Microbially generated hydroxybutyrate and hydroxyvalerate copolymers were originally developed by ICI/Zeneca. However, the high price of these microbial processes has greatly limited the marketability of the materials. A joint venture between Cargill and Dow is currently attempting to reduce the cost of production of poly(lactic acid) by optimization of a microbial process for generation of the lactic acid monomer. An efficient CO_2-based chain reaction polymerization might represent a more economical route to an aliphatic polyester than these microbial processes. An interesting possibility, but is it scientifically possible? The literature is mostly silent on this issue, although there is a brief mention (*8*) of the reaction of CO_2 with vinyl ethers and dienes to generate low molecular weight polyesters.

For the generation of lactones, CO_2 should behave as a ketene analog in a 2 + 2 cycloaddition reaction (see the figure above). In my group, we have performed calculations that suggest that the reaction between certain olefins and CO_2 to form a lactone may be thermally neutral. Given that ring formation is involved, the reaction would be entropically more favorable at higher pressures, where CO_2 becomes both reactant and solvent, thus removing the need for an additional organic solvent. The key unanswered questions here involve the nature of the catalyst required to perform such a reaction and the severity of the conditions required.

Polymer science has made great strides in learning to use CO as a monomer, leading to commercial products with improved performance and price. The development of similar processes that use CO_2, an inexpensive, environmentally benign raw material, has lagged far behind. However, given the recent rapid improvement in the activity of catalysts used in copolymerization of CO_2 and cyclohexene oxide, we may be optimistic that we will one day see commercial CO_2-based polymers.

References

1. S. Inoue, H. Koinuma, T. Tsuruta, *J. Polym. Sci. Polym. Lett.* **7**, 287 (1969).
2. S. Inoue, *Chemtech* (September, 1976), p. 588.
3. A. Rokicki and W. Kuran, *J. Macromol. Sci. Rev. Macromol. Chem.* **21**, 135 (1991).
4. M. S. Super and E. J. Beckman, *Trends Polym. Sci.* **5**, 236 (1997).
5. D. J. Darensbourg and M. W. Holtcamp, *Macromolecules* **28**, 7577 (1995).
6. M. S. Super, E. Berluche, C. Costello, E. J. Beckman, *ibid.* **30**, 368 (1997).
7. M. Cheng, E. B. Lobkovsky, G. W. Coates, *J. Am. Chem. Soc.* **120**, 11018 (1998).
8. K. Soga, M. Sato, S. Hosoda, S. Ikeda, *J. Polym. Sci. Polym. Lett.* **13**, 543 (1975); K. Soga, S. Hosoda, T. Tazuke, S. Ikeda, *ibid.*, p. 265.

PERSPECTIVES: CELL PROLIFERATION

Unlimited Mileage from Telomerase?

Titia de Lange and Ronald A. DePinho

If oncogene activation is akin to a jammed gas pedal and tumor suppressor inactivation to loss of the brakes, what then is telomerase activation in this hackneyed cancer-car analogy? Telomerase, the reverse transcriptase that maintains the ends of eukaryotic chromosomes, has long been stigmatized for its association with human cancer. This judgment has grown from the observations that, although most normal cells are devoid of telomerase's enzymatic activity and lack its main protein component (human telomerase reverse transcriptase, or hTERT), nearly all human tumors express hTERT and have active telomerase (*1, 2*). New data confirm that telomerase is neither tumor suppressor nor oncogene, underscoring the unique role of telomeres in tumorigenesis.

In normal cells, insufficient telomerase activity and a finite store of telomeric DNA limit the number of divisions a cell can undergo before critical telomere shortening signals entry into replicative senescence, defined by a finite capacity for cell division (*3, 4*). As such, replicative senescence is believed to represent a prominent genetic roadblock on the way to cancer, one that can be avoided by activation of telomerase (*4, 5*) but that can also be detoured by oncogene activation (for example, Myc) or loss of tumor suppressor function (such as RB/p53) (*6–8*). However, cells that use Myc or loss of RB/p53 to circumvent senescence will eventually experience rampant genome instability due to the loss of their telomeres and require a mechanism to maintain these essential elements (*9*). Thus, no matter which road the aspiring cancer cell travels, counteracting telomere shortening appears to be a key step. On the basis of the frequent activation of telomerase in human cancer, upregulation of this enzyme is apparently the simplest way toward this end.

Thus, telomere erosion and the associated limitations in replicative life-span have been proposed as a potent tumor suppression mechanism, and telomerase was censured as a "bad" enzyme whose activity subverts our normally constrained somatic cells by providing the opportunity for boundless growth. Initial efforts to understand the mechanics underlying the telomerase-tumorigenesis connection seemed to yield more questions than answers. Is its activation essential for cancers to develop? Is telomerase really all that is needed for cellular immortalization, and will enforced somatic expression of telomerase lead to a cancer-prone condition?

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