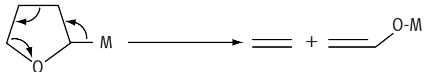
be troublesome. A typical example is the easy metalation adjacent to oxygen of cyclic ether tetrahydrofuran (THF) that invariably leads to unwanted ring-opening fragmentation (*6*):



To avoid side reactions, more elaborate reagents were introduced that combined two or more distinct components, usually a combination of organic anions and cations. Although synthetically extremely useful, their exact structures remain elusive, which made their improvement a somewhat empirical effort (*7*). The strategy of Kennedy *et al.* led to the design of a bimetallic dicationic-dianionic reagent with outstanding synthetic applications, such as the formation of an unexpectedly stable zinc-substituted THF, or THF-heterozincate, at ambient temperature that avoids ring opening or cleavage.

This transformation is quite unexpected, given previous attempts to make such compounds. Kennedy *et al.* designed a new alkali-metal–mediated zinc cationic species that forms through the co-complexation of three species (see the figure), NaTMP, bis(trimethylsilylmethyl)zinc, and TMEDA in hexane solution (*8*); TMP and TMEDA are organic compounds that contain nitrogen atoms that form bonds to the metals. The reagent that forms can directly metalate THF because it traps the fragment that would otherwise undergo deprotonation. It does so by creating a fused ring, O–Na–N–Zn–C, that increases the overall stability of the complex (see the figure). The carbon atom in the ring formed by metalation of cyclic ethers has also become a stereogenic center.

A preliminary reactivity study shows that the trapping reaction of zinc-activated THF with benzoyl chloride leads to the desired coupled product in an isolated 70% yield. This reaction also works with the larger homolog of THF, tetrahydropyran. The metalation of ethylene at 50°C with the potassium analog of the sodium-zinc reagent created a vinyl anion trapped by chelation to two metals. Zinc forms a single σ bond to the deprotonated carbon atom, and potassium interacts with the π orbital of the unsaturated ethylene unit.

This remarkable preparation of stable zinc derivatives of cyclic ethers opens new horizons in organometallic chemistry and raises many questions. One immediate question concerns the effect of the Na-O chelation in the stability of the product. Does it really stabilize the species toward elimination reactions (and, in such case, why is the five-element ring so effective), or is it only needed for the permutational exchange processes? In other words, will monometallic zincated THF, if it can be prepared, be stable toward fragmentation?

The past decade has witnessed a remarkable reassessment of metalation chemistry. The work of Kennedy *et al.* changes the perceived wisdom that low polarity metals were too slow to react. It also pinpoints a specific combination of bimetallic ligands that execute zinc metalation that is facilitated by entrapping fragments before they undergo unwanted reactions. The presence of a stereogenic center in the reagents formed could be exploited by using an enantiomerically pure base. Numerous applications could then be envisioned in the field of natural product chemistry, such as the synthesis of polyketides.

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10.1126/science.1181863

CLIMATE CHANGE

Clean Air for Megacities

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Air pollution in megacities has severe health impacts, but its control could provide opportunities for climate change mitigation.

As of 2008, over half of humanity lives in cities. The number of megacities (with populations over 10 million) grew from 3 in 1975 to 19 in 2007, and is projected to increase to 27 in 2025 (*1*). These megacities are the engines of growing economies, but are also very large sources of air pollutants and climate-forcing agents. The growth of megacities greatly aggravates the health impacts of polluted air, yet it may also provide an opportunity to mitigate climate change, if implemented air quality policies are designed to also reduce global warming.

Exposure to airborne particles and ozone raises mortality and hospital admissions due to respiratory and cardiovascular disease (*2*, *3*). These health impacts increase very rapidly with the population size of a city [(*4*, *5*) and see the figure, panel A]. All the world's megacities exceed the World Health Organization (WHO) guideline for particulate matter (see the figure, panel B).

Yet, greater population density could act to mitigate climate change because it might allow for more efficient energy use (*4*, *6*), and hence lower per capita CO_2 emission. Further, air quality control strategies that reduce total energy use—such as fast and convenient public transport, improved vehicle mileage standards, and more energy-efficient buildings—also reduce CO_2 emissions. Many such strategies are more effectively implemented as urban populations grow (*7*).

Furthermore, given that megacities are economic engines, they are better able to generate the wealth needed to address air quality and climate change issues, and to build the infrastructure required for more efficient energy use. Efforts to optimize the co-benefits of air quality and climate change policies will pay dividends for all countries. An important example is the reduction of ozone formation and soot emissions; these species have pronounced health effects (*8*, *9*), are key climate-forcing agents (*10*–*12*), and—given their short atmospheric lifetimes—allow a rapid climate response to emission reductions.

The scientific and engineering knowledge accumulated as earlier developing megacities dealt with air quality problems is a crucial resource for developing megacities. The pronounced air pollutant levels that accompanied past development can perhaps be avoided. For example, ozone reached very high concentrations in Los Angeles (*13*) before responding to control strategies over the past three decades (see the figure, panel C). In Mexico City (*14*, *15*), high ozone concentrations appeared later, peaked in the early 1990s, apparently

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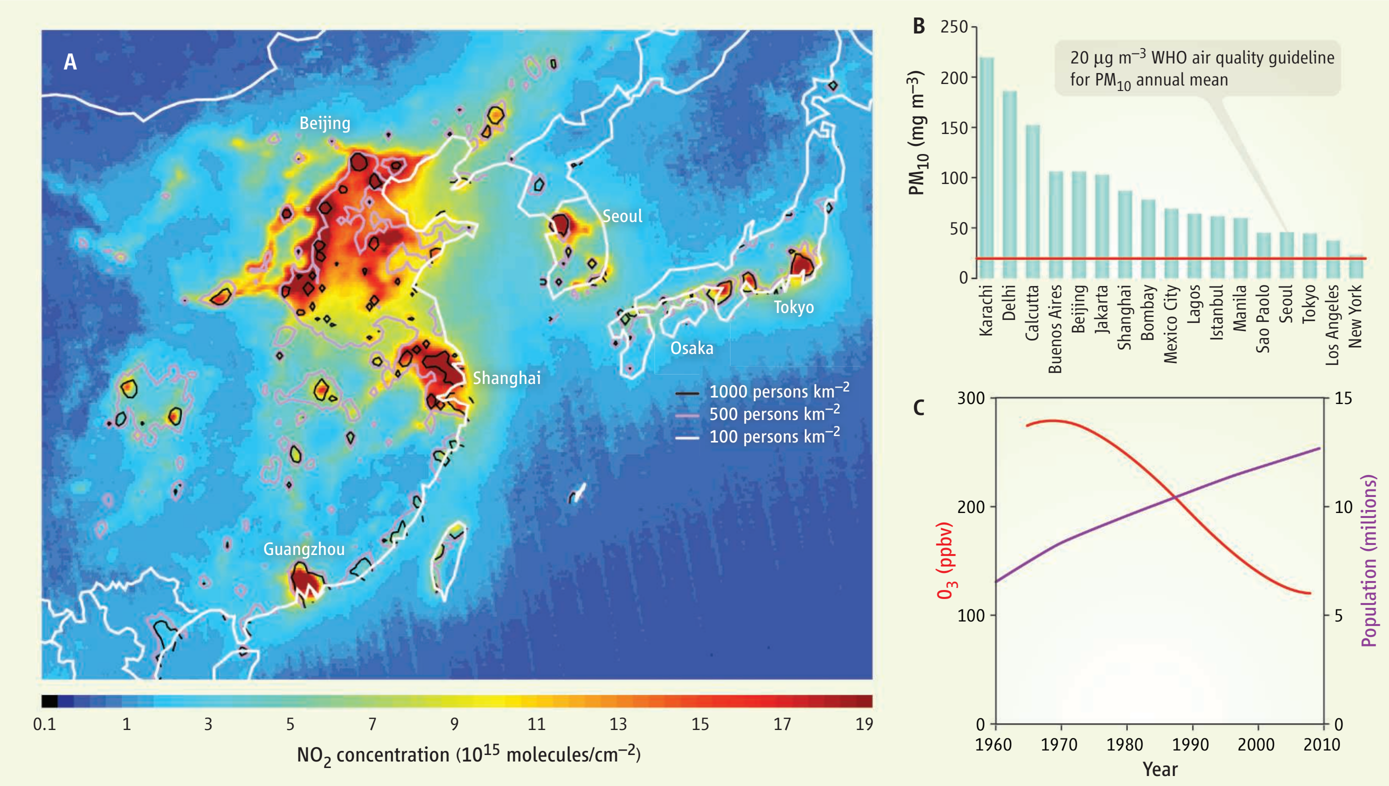

Centers of pollution. (**A**) Satellite image (*22*) of NO_2 concentrations over Asia. NO_2 is a short-lived pollutant released from combustion processes and is a precursor to ozone pollution. NO_2 concentrations are elevated in urban areas. (**B**) Annual mean concentrations of particles with diameters of less than 10 µm (PM_{10}) in the world's megacities (*23*). (**C**) Population and evolution of maximum ozone concentration in Los Angeles. Red line, polynomial fit to observed annual maximum ozone concentrations (*13*). Purple line, population of Los Angeles from (*24*). ppbv, parts per billion by volume.

never reaching the peak Los Angeles concentrations, and have since declined more rapidly there than in Los Angeles. The limited research data sets available from Beijing (*16*) suggest that ozone concentrations, although low in the 1980s, are increasing rapidly there, with concentrations measured during preparations for the 2008 Olympics Games (*17*) comparable to those in Los Angeles and Mexico City. However, Beijing has already implemented aggressive emission controls on automobiles and limits heavy truck traffic in the city to nighttime to mitigate traffic congestion (*18*). Motorized vehicles are the main emitters of ozone precursors in these three (and likely all) megacities, because growing vehicle fleets generally accompany megacity development. Past experience suggests that it is efficient and ultimately cost-effective for megacities to introduce vehicular emission controls before the expensive and lengthy development of locally tailored control programs (*19*).

Major scientific challenges lie in understanding the dual role of particulate matter as the air pollutant with the greatest health impacts, and as both a cooling and a warming agent for climate (*20*, *21*). On balance, particulate matter in the atmosphere is believed to presently compensate for a large fraction of the warming effects of greenhouse gases, but there is large uncertainty in our understanding of its net climate effects and on the different time and space scales on which particulate matter affects climate. Whereas CO_2 is mixed nearly uniformly throughout the globe, the shorter-lived particulate matter has strong regional differences in its effect on temperature and precipitation patterns (*21*).

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