SCIENCE

Published by the **American Association for the Advancement of Science (AAAS),** *Science* serves its readers as a forum for the presentation and discussion of important issues related to the advancement of science, including the presentation of minority or conflicting points of view, rather than by publishing only material on which a consensus has been reached. Accordingly, all articles published in *Science*—including editorials, news and comment, and book reviews—are signed and reflect the individual views of the authors and not official points of view adopted by the AAAS or the institutions with which the authors are affiliated.

■

Information for Contributors appears on pages 40–42 of the 1 January 1993 issue. Editorial correspondence, including requests for permission to reprint and reprint orders, should be sent to 1333 H Street, NW, Washington, DC 20005. ***Science* Telephone:** 202-326-6500, TDD 202-408-7770. **Other AAAS Programs:** 202-326-6400.

LETTERS

Audit at Woods Hole

The 29 January ScienceScope item "WHOI slips into $14 million hole" (p. 587) says that auditors told the Office of Naval Research (ONR) that "WHOI . . . paid staff for time when records show they weren't actually working." This is not true. While the Woods Hole Oceanographic Institution has been under the same increased audit scrutiny experienced by other academic research institutions, there has been no charge that its employees were paid for time not worked. Our overhead structure, which differs from that of most universities, requires the use of timecards by all staff. What we are discussing with ONR is how to appropriately assign scientists' time to individual projects when the staff does not work the 9 a.m. to 5 p.m. time periods generally found in industry. By the very nature of scientific research, our staff works evenings, weekends, and in the early hours of the morning and routinely puts in many hours more than the traditional 40-hour work week.

I am proud of the dedication and hard work of our employees and students and their contributions to knowledge of the Earth's oceans. The U.S. taxpayer gets full measure—and more—from federal funds awarded to our institution.

Craig E. Dorman
Director,
Woods Hole Oceanographic Institution,
Woods Hole, MA 02543

■

Drugs from Third World Plants: Creative Approaches

Thomas Eisner and Ignacio Chapela (Letters, 15 Jan., p. 294) suggest that Carl Djerassi (Letters, 9 Oct., p. 203) and I (Letters, 14 Aug., p. 860) focused only on "whether the pharmaceutical industry is retroactively indebted for its successful development of natural products" and not on "whether, as a matter of self-interest," we should have some economic custodial relationship with nature. I thought we both also spoke to other issues.

The relationship between drug companies and drug sources should be based, at least in part, on logic and contribution. I said (14 Aug., p. 860) that a special case should be made for "an ethnobotanist working with a shaman in a rain forest. . . ." Shaman Pharmaceuticals, a young Californian company, is a case in point. Its team includes a physician who confirms the pathological conditions being treated. Shaman Pharmaceuticals has pledged to pass up endangered plants and is committed to furnishing royalties from drug revenues to the government and to the native communities where the plant was originally harvested. I support this approach as well as the Merck-INBio agreement in Costa Rica.

The pharmaceutical industry alone will not be able to save the biosphere. Enlightened, imaginative, and cooperative approaches at a variety of institutional, governmental, and societal levels may have a chance of fulfilling the spirit of the biodiversity treaty.

Irving S. Johnson*
4601 Rue Belle Mer,
Sanibel Island, FL 33957

---

*Former vice president of research, Eli Lilly and Co.

■

No Lack of NO Activity

We are delighted that one of our favorite molecules has hit the big time ("Molecule of the Year," 18 Dec., p. 1862). We agree with Jonathan S. Stamler *et al.* (Articles, 18 Dec., p. 1898) that the nitric oxide (NO) chemistry relevant to physiological function necessarily includes the properties of redox-related species as well as NO itself, particularly (but not exclusively) those in the neighboring +1 and +3 oxidation states. Among the potentially most significant of these is the reactive anion NO^-, conjugate to the molecule nitrosyl hydride (HNO).

More needs to be learned about this species, but a considerable body of recent literature exists on "the chemistry of NO^- in aqueous solution." Only one reference is given by Stamler *et al.* to the frequent accounts of HNO/NO^- formation in the literature of radiation chemistry (*1*). The remarkable reaction of NO^- with two molecules of NO to form N_2O and NO_2^-, first reported by Grätzel *et al.* (*1*) and seen at thermal reaction energies (*2*), is not mentioned. A reaction between NO^- and NO_2^- has been demonstrated in the reversibility of the trioxodinitrate decomposition reaction (*3*, *4*), and a similar reversibility has been found for the case of NO^- produced in *N*-hydroxybenzenesulfonamide decomposition (*5*). Reduction of NO^- to N_2 by hydroxylamine, in pH- and concentration-dependent competition with dehydrative dimerization, has been shown (*6*), and NO^-

can nitrosylate $Ni(CN)_4^{2-}$ in a direct insertion reaction (*7*).

The intermediacy of NO^- in nitric oxide reduction by hydroxylamine has been explored in considerable detail (*6*, *8*). The reactivity of NO^- formed in this source reaction is orders of magnitude less than that of trioxodinitrate-generated NO^- (*6*–*8*). This indicates occurrence of NO^- in singlet and triplet electronic states, as expected by analogy to the isoelectronic molecule O_2 and as substantiated by the production of the triplet anion on photolysis of the dianion $N_2O_3^{2-}$ (*9*).

The surprising capacity of NO to convert to HNO/NO^- by hydrogen atom abstraction is seen in reactions with $H_2N_2O_2$ (*10*), and with hydroxylamine and with its alkyl derivatives (*6*, *8*, *11*). Finally, there has been a kinetic demonstration of direct nitrosylation by NO^- of the Fe(II) site in membrane-bound cytochrome *d* (*12*).

This incomplete recital shows that there is a rich and diverse aqueous solution chemistry of NO^-, much more so than in the gas phase. It seem likely that one or more of these features may help unravel the physiological function pathways for the Molecule of the Year, and for that reason they should be called to the attention of investigators who may be about to enter the thickets of nitrogen redox chemistry for the first time.

Francis T. Bonner
Department of Chemistry,
State University of New York,
Stony Brook, NY 11794–3400
Martin N. Hughes
Department of Chemistry,
King's College London, The Strand,
London WC2R 2LS, United Kingdom

References

1. M. Grätzel, S. Taniguchi, A. Henglein, *Ber. Bunsenges. Phys. Chem.* **74**, 1003 (1970).
2. D. A. Bazylinski and T. C. Hollocher, *Inorg. Chem.* **24**, 4285 (1985); Y. Ko and F. T. Bonner, unpublished results.
3. M. N. Hughes and P. E. Wimbledon, *J. Chem. Soc. Dalton Trans.* 703 (1976); *ibid.* 1650 (1977).
4. M. J. Akhtar, C. A. Lutz, F. T. Bonner, *Inorg. Chem.* **18**, 2369 (1979).
5. F. T. Bonner and Y. Ko, *ibid.* **31**, 2514 (1992).
6. F. T. Bonner, L. S. Dzelzkalns, J. A. Bonucci, *ibid.* **17**, 2487 (1978).
7. F. T. Bonner and M. J. Akhtar, *ibid.* **20**, 3155 (1981).
8. F. T. Bonner and N. Y. Wang, *ibid.* **25**, 1858 (1986).
9. C. E. Donald, M. N. Hughes, J. M. Thompson, F. T. Bonner, *ibid.*, p. 2676.
10. M. J. Akhtar, F. T. Bonner, M. N. Hughes, *ibid.* **24**, 1934 (1985).
11. N. Y. Wang and F. T. Bonner, *ibid.* **25**, 1863 (1986).
12. F. T. Bonner, M. N. Hughes, R. K. Poole, R. I. Scott, *Biochim. Biophys. Acta* **1056**, 133 (1991).

The "Molecule of the Year" review by Elizabeth Culotta and Daniel E. Koshland, Jr. (p. 1862), does not discuss the therapeutic use of NO in its chemical form as glyceryl trinitrate, more commonly (though incorrectly) known as nitroglycerin. Readers might think that NO only recently emerged as a subject for study in humans. The discovery of organic nitrates, principally nitroglycerin, as an effective treatment for angina pectoris dates back to the late 19th century (*1*), and the properties of nitroglycerin and its metabolites have been intensely studied over the past several decades. In the 1970s, several research groups found that nitroglycerin is metabolized in the body to form NO (*2*). The pharmacological effects of nitroglycerin—in the relief of angina, lowering of blood pressure, and relaxation of smooth muscle in many organ systems—all derive from its metabolism to form NO.

The therapeutic use of opiate alkaloids from the opium poppy anticipated the discovery of the endogenous pathways of endorphins and enkephalins. In similar fashion, the clinical uses of nitroglycerin antedated by more than a century the discovery of endogenous NO signaling systems and of a family of related NO synthase genes (*3*). Improvements in drug design and therapeutics of this venerable compound will likely emerge from recent findings about the molecular mechanisms of NO synthesis and metabolism.

Thomas Michel
Brigham and Women's Hospital,
Harvard Medical School, Boston, MA 02115

References

1. T. L. Brunton, *Lancet* ii, 97 (1867).
2. H. Kimura, C. K. Mittal, F. Murad, *J. Biol. Chem.* **250**, 8016 (1975); P. A. Craven and F. R. DeRubertis, *ibid.* **253**, 8433 (1978); L. J. Ignarro *et al.*, *J. Pharmacol. Exp. Ther.* **218**, 739 (1981).
3. S. Lamas, P. A. Marsden, G. K. Li, P. Tempst, T. Michel, *Proc. Natl. Acad. Sci. U.S.A.* **89**, 6348 (1992).

■

Tyrolean Paraphernalia

Horst Seidler suggests (Letters, 18 Dec., p. 1868) that the ice-bound prehistoric Tyrolean man (*1*) may have been using the fungus *Piptoporus betulinus* as an antibiotic but not necessarily as a hallucinogen. In Europe this opportunistic bracket fungus infects senile birch trees and, together with the related *Polyporus squamous*, is known as the razor strop fungus. For this function, strips of it were glued to a leather strap, a practice known to the barbers of Cesalpinus' day (*2*). Entomologists use it to make