

Other Natural Bromo Compounds

In their interesting article about the remarkable occurrence of such a large amount of 2,6-dibromophenol in the marine organism *Balanoglossus biminensis*, Ashworth and Cormier (1) point out that the reported instances of natural products containing bromine are rare. The number of such compounds is indeed small, but not quite so small as one might conclude from the two examples cited in their paper. There are, in fact, at least eight other natural bromo compounds reported in the literature.

The classical one is Tyrian purple, used by the ancients and identified as 6,6'-dibromoindigo by Friedländer in 1911 (2). The following were reported more recently: aplysin and aplysinol (3), laurencin (4), laurinterol (5), and 2,3,4-tribromo-5-(3,5-dibromo-2-hydroxyphenyl)pyrrole (6). It is probably significant that these compounds, as well as those referred to by Ashworth and Cormier, are derived from marine sources. In addition, as summarized by Petty (7), three classes of bromine-containing natural products of nonmarine origin have been reported: the bromo analogs of chloramphenicol (8), the bromotetracyclines (9), and bromodechlorogriseofulvin (10).

Note added in proof: Two more natural compounds have been reported. One of these, 3,5-dibromo-1-hydroxy-4-oxo-2,5-cyclohexadiene-1-acetamide (11), is from a marine source, whereas the other, the bromo analog of caldariomycin, is a forced mold metabolite (12).

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References and Notes

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2. See L. Fieser and M. Fieser, *Organic Chemistry* (Reinhold, New York, ed. 3, 1956), p. 908.
3. S. Yamamura and Y. Hirata, *Tetrahedron* **19**, 1485 (1963).
4. T. Irie, M. Suzuki, T. Masamune, *Tetrahedron Letters* **1965**, 1091 (1965).
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LSD: Effects on Offspring

In a study on pregnant rats (1), the claim was made that LSD produced abnormalities. The effect of a single subcutaneous injection of LSD before the time of implantation and differentiation produced normal, small, or still-born offspring, and pregnancies which resulted in "presumed" abortions. Interruption of pregnancy would have facilitated conclusions concerning missing embryos. A potential teratogenic effect should also have been determined in animals given LSD at different periods during gestation, including the time of maximum differentiation, which for the rat embryo is from about the 9th to 12th day. Oral treatment might have been attempted, especially since dosage was selected to correspond to the human hallucinogenic dose.

The relevance of chromosomal abnormalities (2) would be difficult to assess even if they had been dealt with as part of this study. Under the circumstances, extrapolation from cultured human lymphocytes—from an in vitro to an in vivo system—is just as dangerous as extrapolation from one species to another.

The concern over drug abuses and the thalidomide tragedy of the past few years should not be taken as justification for reporting incomplete studies. This discussion is in no way intended to minimize the potential hazards of LSD but is to suggest that well-designed studies should be made.

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2. M. M. Cohen, M. J. Marinello, N. Back, *ibid.* **155**, 1417 (1967).

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DiPaolo has made some interesting suggestions for the design of experiments directed at elucidation of the specific mechanism of the LSD effect on pregnancy. Whether his approach, or others that could be suggested, would be more likely to yield the desired information is a matter beyond the scope of this reply. Two points, however, require further comment.

DiPaolo's reference to drug abuses and the thalidomide affair exemplifies an attitude with which we do not agree. We were, of course, aware of all the pertinent factors mentioned in his let-

ter. We considered them carefully before deciding to submit our report for publication, and concluded that, if there ever was a time when publication of preliminary results was called for, this was the time. We felt that we had no right to keep silent while in possession of these data.

Our purpose was to report upon only one phase of a detailed study of LSD, namely the damage to offspring of rats given subcutaneous injections of the drug early in pregnancy. In this limited sense, our paper, although preliminary, contained observations which were conclusive as well as reproducible. Additional work, in progress at the time, on the effect of administration of LSD by various routes, generally appeared to confirm our results. These new findings will be presented upon completion of the comprehensive study now under way.

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The Supernova of 1572

Through a slip in translation, Botley (1) has drawn an unwarranted conclusion with respect to the sighting of the supernova on 7 November 1572 by Bernhard Lindauer (2). The relevant passage reads:

"A. 1572 den 7. Nov. ist am himmel ein neuer grosser heiterer stern gesehen worden zu Winterthur, gleich ob dem haubt Cassiopeæ. . . ."

Botley concludes that the magnitude of the supernova sighted by Lindauer was equal to that of α Cassiopeiae, whereas a more accurate translation is:

"On November 7, 1572 a new large bright star has been seen in the sky at Winterthur, just above the head [star] of Cassiopeia."

Thus Lindauer clearly refers to the position of the supernova, and not its magnitude. The expression in question is similar to one still in current usage in the Swiss-German dialect.

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