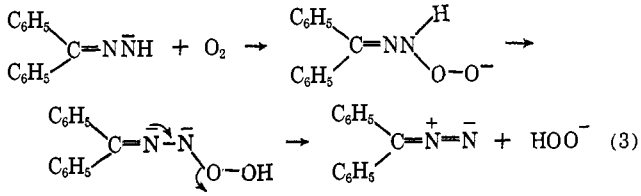
hydroperoxide anion[4] as shown in eq 3. The initial



attack is similar to that suggested for the oxidation of Grignard reagents by oxygen.[5]

(4) H. E. Zimmerman and D. H. Paskovich, *J. Am. Chem. Soc.*, **86**, 2149 (1964), footnote 12.
(5) C. Walling and S. A. Buckler, *ibid.*, **75**, 4372 (1953).

The interesting possibilities suggested by this novel reaction are under active investigation in our laboratories.

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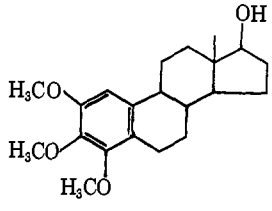
Additions and Corrections

A Steroidal Analgesic [*J. Am. Chem. Soc.*, **88,** 856 (1966)]. By LEONARD R. AXELROD and P. NARASIMHA RAO, Southwest Foundation for Research and Education, San Antonio, Texas, and DAVID H. BAEDER, Mallinckrodt Chemical Works, St. Louis, Missouri.

In the above publication, the synthesis of a new class of compounds having poly(lower alkoxy)estrane structures was reported. In a subsequent publication [L. R. Axelrod and D. H. Baeder, *Proc. Soc. Exptl. Biol. Med.*, **121,** 1184 (1966)], analgesic activity of one of these compounds was compared with that of some clinically active standard analgesics. Based on the findings of this investigation, the compound, MP-2001, *d*-2,3,4-trimethoxyestra-1,3,5(10)-trien-17β-ol



was reported to be more potent than morphine. More recently, laboratory testing of poly(alkoxy)estratrienes yielded results which indicated that the compounds were devoid of pharmacologic activity [D. R. Van Deripe, G. B. Hoey, W. R. Teeters, and T. W. Tusing, *J. Am. Chem. Soc.*, **88,** 5365 (1966)].

Since the pharmacologic evaluation of these compounds for the above-cited studies was not conducted in our laboratories, it was decided to reevaluate MP-2001 for analgesic activity using morphine and meperidine as comparison standards.

The procedures used were the tail-flick test in rats [F. E. D'Amour and D. L. Smith, *J. Pharmacol.*, **72,** 74 (1941)] and a variation of the titration method [B. Weiss and V. G. Laties, *Science*, **125,** 1575 (1958)] in a cynomolgous monkey. Our experience with the tail-flick technique revealed the necessity for rigid control of several critical variables to prevent false positives in the use of this test. We have discussed this elsewhere in detail [I. Geller and L. R. Axelrod, presented at the International Symposium on Pain, Paris, France, April 11–13, 1967]. These variables include ambient temperature, pretraining of animals, and sudden changes in exteroceptive stimuli. The titration method involves the periodic delivery to an animal of electric shocks of successively increasing intensities. In our procedure, the monkey was able to reduce the shock intensity to zero by pressing a lever. After a period of training, resets to zero generally occurred at the same shock level throughout a 6-hr experimental session.

Morphine and meperidine were prepared in water and MP-2001 was prepared in propylene glycol. The drugs were administered intraabdominally to the rats and intravenously to the monkey. Morphine and meperidine were both active in the tail-flick test, yielding AD_{50} values of 3.5 and 10.6 mg/kg, respectively. MP-2001, in a dose range of 1.0 and 16.0 mg/kg, showed no activity in this test. In the titration test, following intravenous administrations of morphine at 2.0 and 3.0 mg/kg and meperidine at 12.5 mg/kg, resets of shock levels to zero occurred at intensities above control values. The monkey tolerated higher shock intensities under morphine and meperidine. Intravenous administrations of MP-2001 at 5 and 10 mg/kg were ineffective in this test.

Electron Spin Resonance Studies of Substituent Effects. Correlations with σ Constants [*J. Am. Chem. Soc.*, **88,** 2065 (1966)]. By E. THOMAS STROM, Mobil Research and Development Corp., Field Research Laboratory, Dallas, Texas 75221.

In calculating the ρ values given in the communication, the coordinates were inadvertently reversed so the values cited are really the reciprocals of the slopes. Even if the ρ values had been calculated correctly, they would have units of gauss and would be meaningless in comparing the sensitivity of the hyperfine splitting constants to substituent. If the ratio $A^{H}_{sub}/A^{H}_{unsub}$ is plotted *vs.* σ, however, the slope will be unitless and its value will be a measure of the sensitivity of the system