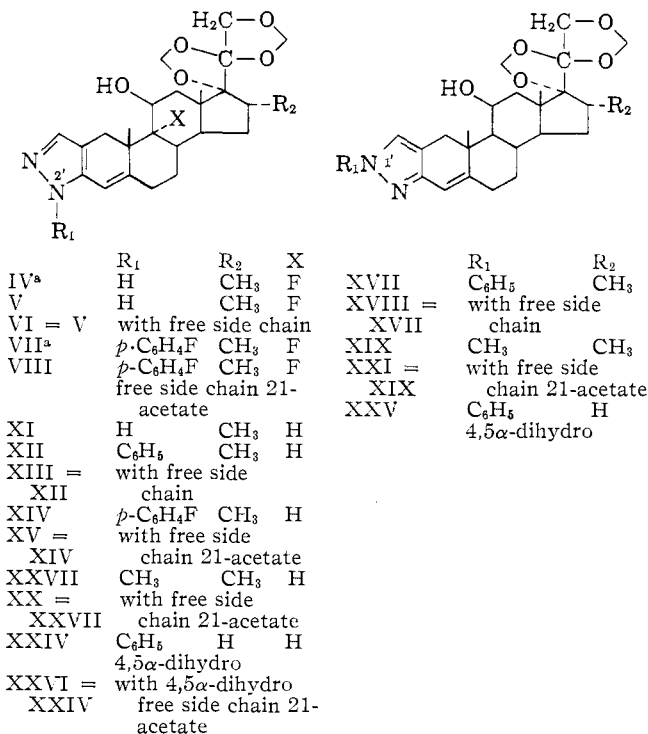


times cortisol. The isomeric 1'- and 2'-methylpyrazoles XXI and XX were, however, of more comparable potency (1.5 and 5.9 times cortisol, respectively). Thus the 2'-*p*-fluorophenylpyrazole function is the most powerful activity enhancing group yet reported in the anti-inflammatory field. The application of these findings to the 6-dehydro-6-methylcortisol series is described in a separate communication.^{17,18}



11-keto rather than 11- β -hydroxyl.

(17) J. H. Fried, H. Mrozik, G. E. Arth, T. S. Bry, N. G. Steinberg, M. Tishler, R. Hirschmann and S. L. Steelman, *J. Am. Chem. Soc.*, **85**, Jan. 20 (1963).

(18) It is noteworthy that in the androgen series, the 6 α -methyl and the 9 α -F-substituents decrease the activity of the pyrazoles.^{6b}

MERCK SHARP & DOHME
RESEARCH LABORATORIES
DIVISION OF MERCK & CO., INC.
RAHWAY, NEW JERSEY

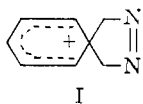
RALPH HIRSCHMANN
N. G. STEINBERG
PAUL BUCHSCHACHER
J. H. FRIED
G. J. KENT
MAX TISHLER

MERCK INSTITUTE FOR THERAPEUTIC RESEARCH
RAHWAY, NEW JERSEY
S. L. STEELMAN
RECEIVED NOVEMBER 30, 1962

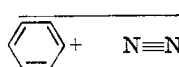
A TRACER DEMONSTRATION OF A REVERSIBLE STEP IN DIAZONIUM SALT DECOMPOSITION

Sir:

A study of the effect of thiocyanate ion concentration on the rate of decomposition of benzenediazonium ion led to the conclusion that an intermediate could revert to the diazonium ion.¹ Among the tentatively considered structures for this intermediate were some, I for example, in which the two nitrogen atoms are indistinguishable, and others, such as the caged pair II, with non-equivalent nitrogens.



I

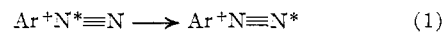


II

A consequence of any structure (such as I) with equivalent nitrogens, or any structure in which the

(1) E. S. Lewis and J. E. Cooper, *J. Am. Chem. Soc.*, **84**, 3847 (1962).

nitrogens are readily interconvertible, is that the isotopic rearrangement, reaction (1), should accompany the solvolysis of a labelled diazonium salt. We now show evidence for this reaction.

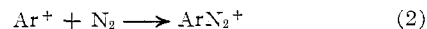


Benzenediazonium- α -N¹⁵ fluoroborate was prepared from aniline-N¹⁵ (99% N¹⁵) by diazotization with normal sodium nitrite. Decomposition in water at 35° to the extent of 80% (assuming the rate to be the same as that of normal diazonium salt²) left a solution of residual diazonium salt which was degassed and then degraded by treatment with sodium azide.³ The "primary nitrogen" derived only from the azide ion, was discarded, except in one experiment in which it was shown to have normal isotopic abundance of N¹⁵. The "secondary nitrogen," 1/4 of which is derived *via* phenylpentazole from the β -nitrogen of the diazonium salt, was collected for analysis. A second sample of nitrogen was obtained by arsenite reduction of the total phenyl azide; this contained the remainder of the β -nitrogen and none of the α -nitrogen. Mass spectrometric analysis of these samples then gives the N¹⁵ content of the β -nitrogen: it was found to have 2.6% N¹⁵ (natural abundance 0.36%). The value calculated from the phenyl azide nitrogen agreed with that from the "secondary nitrogen" if the literature value³ for the relative amounts of reaction by the two routes (which we confirm more roughly) was used.

The quantitative specificity of labelling and the degradation were both checked by repeating the same process omitting only the prior 80% decomposition. All samples had only natural abundance of N¹⁵, showing that N¹⁵ appears in the β position only after extensive decomposition. Reaction (1) therefore occurs during the solvolysis reaction.

If reaction (1) follows a first-order course, with the rate constant k_1 , accompanying the solvolysis with rate constant k_s , it can be shown that $k_1 = 0.014k_s$. This result is consistent with the existence of an intermediate which can return to diazonium ion, as well as going on to phenol; in this intermediate the initial C-N bond is nearly or totally broken.

The reaction (2) is a possible return reaction of interest in connection with nitrogen fixation. Although



rigorous evidence is not available, we lean toward an incompletely separated intermediate, both for the reasons previously cited,¹ and because carbon monoxide at 700 p.s.i. is not detectably incorporated into decomposing benzenediazonium ion (to give benzoic acid), even though it is more nucleophilic than the isoelectronic nitrogen molecule.

Acknowledgment.—We gratefully acknowledge support from the Robert A. Welch Foundation. The work would not have been done without the skillful and willing cooperation of Dr. E. G. Carlson and his co-workers at the Shell Oil Company, who did the mass spectrometry.

CHEMISTRY DEPARTMENT
WILLIAM MARSH RICE UNIVERSITY
HOUSTON, TEXAS

JOAN M. INSOLE
EDWARD S. LEWIS

RECEIVED NOVEMBER 14, 1962

(2) E. A. Moelwyn-Hughes and P. Johnson, *Trans. Faraday Soc.*, **36**, 948 (1940); D. F. DeTar and A. R. Ballentine, *J. Am. Chem. Soc.*, **76**, 3916 (1954).

(3) K. Clusius and H. Hurler, *Helv. Chim. Acta*, **37**, 798 (1954); R. Huisgen and I. Ugi, *Chem. Ber.*, **90**, 2914 (1957).