staying together of electron and sodium $t_{Na} \geq 3 \times 10^{-7}$ second.

WASHINGTON UNIVERSITY F. C. ADAM
SAINT LOUIS, MISSOURI S. I. WEISSMAN

RECEIVED FEBRUARY 10, 1958

EFFECT OF 1-PHENYL-2-HYDRAZINOPROPANE, A POTENT MONOAMINE OXIDASE (MAO) INHIBITOR, ON BRAIN LEVELS OF NOREPINEPHRINE AND SEROTONIN

Sir:

We have synthesized certain hydrazine analogs,[1] in the hope of obtaining sympathomimetic substances with greater affinity for the cell receptor sites and increased stability toward metabolic degradation. One such compound, α-methylphen-

—$CH_2CH(CH_3)$—NH—$NH_2 \cdot HCl$ (JB-516)

ethylhydrazine hydrochloride exhibited amphetamine-like activity. In addition, it was demonstrated by Horita[2] to be an MAO inhibitor, many times more potent than iproniazid.

The therapeutic significance of the MAO inhibitor iproniazid in the treatment of depressed mental conditions[3] prompted us to report on the preparation, preliminary pharmacological and biochemical effects of this new hydrazine derivative. Phenyl-2-propanone was treated with methanolic hydrazine hydrate to form phenyl-2-propanone hydrazone in 80% yield, b.p. 101–103° (0.30 mm); found: N, 18.46; $n^{20}D$ 1.5613. The hydrazone was reduced to α-methylphenethylhydrazine with platinum oxide in ethanol–acetic acid solution, b.p. 82–86° (0.50 mm.); yield 55–60% (found: N, 18.71; $n^{20}D$ 1.5401). The monohydrochloride melted at 122–124° (found: Cl, 18.97; C, 57.95; H, 8.10; N, 15.01.)

Five mg./kg. of JB-516 produced marked central stimulatory effects in rabbits similar to those of amphetamine. Lower doses (1 mg./kg.) exerted no obvious effects. However, this dose appeared to inhibit brain monoamine oxidase activity,[4,5] since rabbits pretreated with 1 mg./kg. of JB-516 and then given 5 mg./kg. reserpine exhibited excitation instead of depression.

Monoamine oxidase has been shown to have a major role in the physiologic inactivation of both serotonin and norepinephrine in brain.[6]

Since these substances may be involved in the regulation of certain brain functions,[7,8] it was of interest to investigate the effect of JB-516 in low dosage on serotonin and norepinephrine levels in brain. JB-516 (1 mg./kg.) and iproniazid (10 mg./kg.) were administered daily (s.c.) to rabbits for five days. The levels of the amines, in brain stem, measured by methods previously described[9,10] rose slowly and reached two to three times the normal value within five days. By the third or fourth day central stimulation was evident. The administration of 5 mg./kg. of iproniazid and 50 mg./kg. of isoniazid daily for 5 days elicited neither excitation nor an increase in the levels of the brain amines. The effects of the various drugs on brain levels of norepinephrine and serotonin are summarized in Table I. Each value represents the average of three animals.

Mg./kg.				
JB-516	Iproniazid		Isoniazid	
1.0	10	5	50	Controls
Norepinephrine levels (γ/g. tissue)				
0.95	1.1	0.43	0.40	0.40
Serotonin levels (γ/g. of tissue)				
1.6	0.92	0.60	0.58	0.58

These results suggest that JB-516 is at least ten times as active as iproniazid in eliciting central excitation and a rise in brain levels of nor-epinephrine and serotonin. The increase in nor-epinephrine may be related to central action of JB-516; in this regard it is noteworthy that large doses of 3,4-dihydroxyphenylalanine, a norepinephrine precursor, cause central excitation which is enhanced by pretreatment with iproniazid.[11]

In summary, the replacement of an amino group by a hydrazino moiety in amphetamine has yielded a compound which embodies the effects of amphetamine but is in addition a very potent MAO inhibitor. The compound is now undergoing extensive clinical investigation for treatment of depressed mental conditions.

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CHEMISTRY DIVISION JOHN H. BIEL
LAKESIDE LABORATORIES, INC.
MILWAUKEE 1, WISCONSIN ALEXANDER E. DRUKKER
LABORATORY OF CHEMICAL PARKHURST A. SHORE
PHARMACOLOGY SYDNEY SPECTOR
NATIONAL HEART INSTITUTE BERNARD B. BRODIE
BETHESDA, MARYLAND

RECEIVED JANUARY 28, 1958

INTERCONVERSION OF VOLATILE BORANES BY BASIC REAGENTS

Sir:

All of the known effective methods of converting one volatile boron hydride to another have been adjustments of physical conditions governing decomposition-type reactions—as in the conversion of diborane mostly to pentaborane-9 by fast-flow methods at elevated temperatures,[1] or mostly to pentaborane-11 by flow at higher pressures and lower temperatures,[2,3] or to tetraborane by a partial reversal of the process.[2] We now report that some borane interconversions can be done efficiently by the action of appropriately chosen chemical reagents, well below room temperature and

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