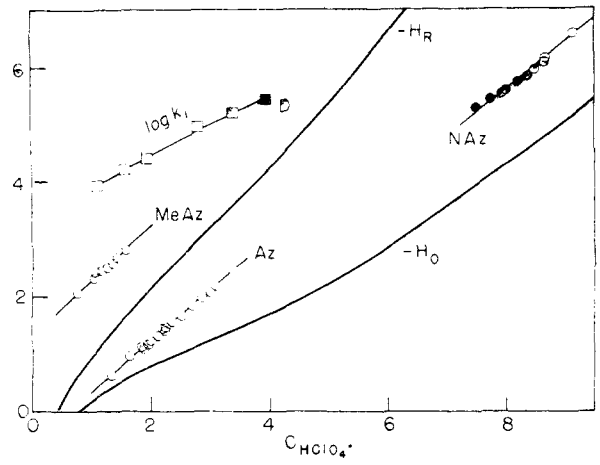

Fig. 1.—Curve MeAz is log I + 2.5 for 1-methylazulene; curve Az is log I + 1.5 for azulene; curve NAz is log I + 6 for 1-nitroazulene; curve D is log k_1 + 9 (in sec.$^{-1}$) for detritiation of 1-nitroazulene-t_1(3) All data are for 25°.

(log I)/dH_0 are: 1.6 for 1-methylazulene; 1.9 for azulene; 1.0$_5$ for 1-nitroazulene. As an indication of relative basicities, the H_0 values at which I is unity are −0.36, −0.92 and −4.68 for the above three compounds respectively, values which are in reasonable accord with the expected effects of the substituents involved.

In a limited sense these equilibrium results confirm and extend those of Kresge and Chiang in that for two of the azulenes, for which monoprotonation on carbon is assured, log I is more nearly proportional to $-H_R$ than to $-H_0$. However, for nitroazulene this is not true, even though the evidence from ultraviolet spectra, infrared spectra and proton exchange are all consistent with the proposal that protonation is on the 3-carbon for this molecule also. Figure 1 suggests that perhaps the most significant feature of azulene and methylazulene is their greater basicity a consequence being that their protonation reaction occurs in an acidity region where $-H_0$ is only a slowly increasing function of C_{H^+}. Clearly one cannot yet conclude that correlation of log I with H_R is a general feature of protonation on the carbon of aromatics.

The rate coefficients in sec.$^{-1}$ for detritiation of azulene in aqueous solution by solvated protons are given by $k_1 = 0.19C_{H^+}$.[4,7] Since these data result from measurements in the pH range of from two to four, a region where the functions C_{H^+}, h_0 and h_R are virtually identical, no significant comparisons of acidity function dependence are possible. The situation with nitroazulene (Fig. 1) is, however, more favorable. For this substrate the rate of aqueous detritiation is almost linear in h_0, the observed first order rate coefficients being well fitted by the equation $k_1 = 5.3 \times 10^{-6} h_0^{1.05}$ sec.$^{-1}$. The acidity dependence for forming the transition state for hydrogen exchange is thus within experimental error the same as the dependence for forming the equilibrium conjugate acid. This different behavior from that reported for trimethoxybenzene cannot be rationalized by considerations of base strength since nitroazulene is slightly the weaker base. We conclude that there is considerable specificity in the interactions of these systems with acid, a not surprising conclusion in view of the high electrolyte concentrations of the media involved and the consequent large and doubtless somewhat specific medium effects on the activity coefficients of the various species.

(7) B. Challis and J. Schulze, unpublished work.

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DEHYDROBUFOTENINE, A NOVEL TYPE OF TRICYCLIC SEROTONIN METABOLITE FROM *Bufo Marinus*

Sir:

Dehydrobufotenine,[1] the principal indole constituent isolable from the parotid glands of the South American toad (*Bufo marinus*), has now become easily available by a simplified ion exchange column procedure.[2] From 100 toads 600 mg. of the crystalline hydrochloride has been obtained. The original assignment of structure I to dehydrobufotenine has been in doubt since the close similarity of its ultraviolet spectrum with that of serotonin was noticed.[3] The novel tricyclic structure III now has been found to be the correct expression.

Dehydrobufotenine (III) with sodium in liquid ammonia undergoes the Emde-type fission typical of quaternary anilinium bases[4] and almost quantitatively opens up to bufotenine (II). The ultraviolet spectrum of dehydrobufotenine (λ_{max} 293 mμ) on oxidation in aqueous solution with NBS[5] changed to λ_{max} 265 mμ characteristic of an oxindole.[3] Final confirmation of the tricyclic structure III, rather than the isomer IV,[1] came from a detailed study of the n.m.r. spectra[6] of III and II

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(2) F. Märki and B. Witkop, to be published.
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(4) *Cf.* G. F. Smith and J. T. Wrobel, *J. Chem. Soc.*, 1463 (1960).
(5) *Cf.* W. B. Lawson, A. Patchornik and B. Witkop, *J. Am. Chem. Soc.*, **82**, 5918 (1960).
(6) We thank Mr. Robert Bradley for taking the n.m.r. spectra on a Varian DP-60 instrument.

in CD_3OD at 60 Mc./sec τ-Values relative to internal tetramethylsilane are shown on the formulas. As required for a tricyclic indole derivative the n.m.r. signals show the presence of three aromatic protons, one of which is typical for the singlet of a proton in the α-position of 3-substituted indoles and tryptamines.[7] The other two aromatic protons form an AB quartet characteristic of 2 *ortho* protons($J_{6,7}$, 9 cps.).[8] Position 4 of the indole ring must therefore be substituted and formula IV is excluded.

The assignment of the upfield pair of the quartet to the signal from the C-6 proton follows from the shielding influence of the adjacent oxygen, and from the corresponding peaks in bufotenine which show both *ortho* ($J_{6,7}$, 9 cps.) and *meta* ($J_{4,6}$, 2 cps.) coupling.[9] The position of the singlet for two equivalent N-methyl groups changes from τ 7.70 in bufotenine (*cf.* $N_{(b)}$-methyltryptamines[7]) to 6.30 in dehydrobufotenine, a shift which agrees with their attachment to an anilinium-type nitrogen in III. Chemical shifts for methylene hydrogens are given at the center of bands in which the fine structure is obscured because of overlapping either with each other or with solvent and N-Me peaks. The comparative evaluation of the n.m.r. data of bufotenine with those of dehydrobufotenine fully support structure III, whose synthesis and biosynthesis are under investigation.

(7) L. A. Cohen, J. W. Daly, H. Kny and B. Witkop, *J. Am. Chem. Soc.*, **82**, 2184 (1960).

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(9) *para* coupling ($J_{4,7}$, 0.5 cps.) also was resolved in the signals from the protons on C-4 and C-7 in bufotenine.

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THE RELATIVE REACTIVITY OF THIOACYL AND SELENOACYL ANALOGS[1]

Sir:

The high reactivity of acyl derivatives of coenzyme A and of thiol esters in general has been attributed to polarization of the type R-C(=O)-SR[1] activating the carbon of the carbonyl group to attack by nucleophilic reagents.[2]

Since polarization increases in passing from carbamyl to thiocarbamyl to selenocarbamyl analogs,[3,4,5] it seemed likely that selenoacyl compounds should be more highly polarized and more reactive than their thioacyl analogs.

(1) This work was supported, in part, by a grant (CY-3937) from the United States Public Health Service.

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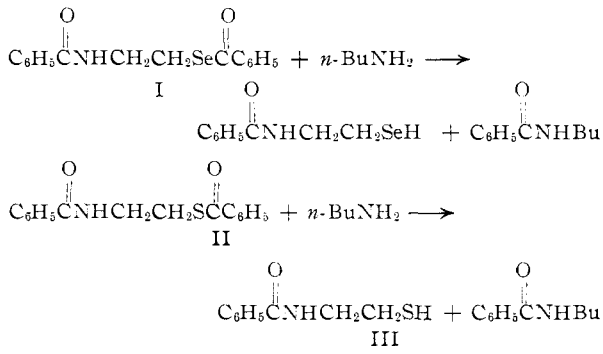
(3) H. G. Mautner and W. D. Kumler, *J. Am. Chem. Soc.*, **78**, 97 (1956).

(4) H. G. Mautner, *ibid.*, **78**, 5292 (1956).

(5) H. G. Mautner and E. M. Clayton, *ibid.*, **81**, 6270 (1959).

It was found that selenopantethine[6] could fully replace its sulfur analog in *Lactobacillus helveticus*,[7] a microörganism requiring preformed pantethine for growth. On the other hand, selenopantethine inhibits the utilization of pantethine[8] as a precursor of coenzyme A in a pigeon liver system.[9,10] These observations coupled with the recent finding that for certain animals selenium is an essential trace element,[11,12] and the claim[13] that selenocoenzyme A is formed when selenite is administered to rats, raised further interest in the relative reactivity of thioacyl and selenoacyl analogs.

To study transacylation rates this test system was used



N,Se-Dibenzoylselenocysteamine (I) was prepared by the reaction of benzoyl chloride with selenocysteamine and then recrystallized from 50% methanol. A yield of 90% of analytically pure, crystalline product melting at 99–100° was obtained.

Ultraviolet Spectrum.—Absolute ethanol: λ_{max} 240, 285, 305 mμ (inflect.); E_{max} 21,630, 5,520, 4,390.

The corresponding sulfur analog (II) was prepared by the method of Fry.[14] When N,Se-dibenzoylselenocysteamine (I) and N,S-dibenzoylcysteamine (II) were permitted to react with an excess of *n*-butylamine in ethanol, the selenium compound was found to react much more rapidly than its sulfur analog:

	Concn. acyl compound, M	Concn. amine, M	$k_{obs.}$, sec.$^{-1}$	Temp., °C.
Compd. I	8.76×10^{-5}	3.38×10^{-1}	2.73×10^{-3}	29.8
Compd. II	8.76×10^{-5}	3.38×10^{-1}	2.31×10^{-5}	29.8

The reaction rates were followed by observing the disappearance of the ultraviolet thiobenzoyl peak at 264 mμ or the selenobenzoyl peak at 285 mμ.

(6) W. H. H. Günther and H. G. Mautner, *ibid.*, **82**, 6270 (1960).

(7) H. G. Mautner and W. H. H. Günther, *Biochim. Biophys. Acta*, **36**, 561 (1959).

(8) H. G. Mautner and W. H. H. Günther, unpublished data.

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