TABLE I.—INFRARED ABSORPTION FREQUENCIES OF INDOLE COMPOUNDS

Indole	609 cm.$^{-1}$	587 cm.$^{-1}$
N-Methylindole	608	572
2-Methylindole	609	575
3-Methylindole	610	572
5-Methylindole	618	589
7-Methylindole	617	575
4-Methoxyindole	620, 635	600
5-Methoxyindole	615	599
7-Methoxyindole	615, 605	594
4-Methoxytryptamine	611	589
6-Methoxytryptamine	610	593
7-Methoxytryptamine	605, 615	572
Ibogaine	621, 631	575
Harmane	634	569, 581
Ajmalicine	606, 618	587
Tetraphyllicine	603, 627, 637	541, 572, 591
Tetraphylline	625, 637	581
Ibogamine	602	550, 581
Bufotenine	606, 644	594
Gramine	635	572, 587
3-Formylindole	638	597, 537
Harmine	598, 637	550
3-Indoleacetic acid	598, 622	581

for the second. It would seem apparent then that these two absorptions could be used as a diagnostic tool to determine the presence or absence of the indole system.

620 cm.$^{-1}$ Region.—All indoles have at least one band in this region. In some cases more than one band is observed, but this may be due to splitting of a single broad band. The consistency and persistence of the occurrence of this absorption throughout the series permits assignment of the absorption to the indole ring system. This assignment is also in agreement with previously published Raman data (5). The spectral data presented here further suggest that this absorption is due to that portion of the indole ring not containing the nitrogen atom. If we examine the data reported for the methyl- and methoxyindole series, we find that the frequency of the 620 cm.$^{-1}$ band increases relative to indole itself when the substituent is in the 4, 5, 6, or 7 position. Presence of the substituent in the 2 or 3 position has no perceptible effect on the frequency. This would indicate the further possibility and utility of this band as an indicator of the substitution position of indoles.

575 cm.$^{-1}$ Region.—The second characteristic absorption of this series of compounds is located at 575 ± 25 cm.$^{-1}$, and this is also assigned to the indole ring system. This assignment is also in agreement with previously published Raman data (6). This absorption, like the one at 620 cm.$^{-1}$, is remarkably consistent and found in every member of the series. The nature of the substituent on the ring appears to have little effect on the position or intensity of the two absorptions. The position of the substituent does involve small shifts in the frequency of the absorption but, other than that, these two absorptions are independent of the type of substituent.

SUMMARY

Data have been presented to show that indole ring compounds possess two characteristic absorptions in the range 700–400 cm.$^{-1}$. The absorptions are consistent in location and independent of the substituent on the ring.

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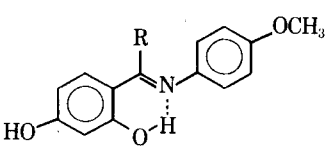
Synthesis and Pharmacology of Some Azomethines

By E. O. MAGARIAN*, ALTA RAY GAULT, and W. LEWIS NOBLES

Three azomethines were prepared and evaluated for estrogenic activity according to the Allen-Doisy method. They demonstrated weak estrus exciting properties.

THE THERAPEUTIC usefulness of the estrogens in the treatment of prostatic and breast carcinomas is well known (1). Hormones are essential for the growth and functional development of certain normal tissues, and there seems to be little doubt that these hormones may also be involved in the development of malignancies of these tissues. Perhaps the hormonal imbalances induced by the administration of estrogens result in the temporary regression of these tumors.

Several azomethines have been prepared and tested for estrogenic activity (2). Nomura (3) prepared and evaluated compounds of the following type:



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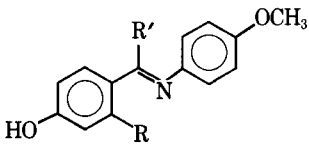
* Present address: Department of Pharmaceutical Chemistry, College of Pharmacy, University of Rhode Island, Kingston.

TABLE I.—AZOMETHINES



R	R'	Yield, %	M.p., °C.[a]	Formula	Anal., % Calcd.	Found
H	CH_3	11	168.5–169.5[b]	$C_{15}H_{15}NO_2$	C, 74.66	74.53
					H, 6.27	6.36
					N, 5.80	6.12
CH_3	CH_3	12	210 dec.[b, c]	$C_{16}H_{17}NO_2$	C, 75.26	74.89
					H, 6.71	6.56
H	C_2H_5	20	204 dec.[b, c]	$C_{16}H_{17}NO_2$	C, 75.26	75.48
					H, 6.71	6.73
					N, 5.49	5.59

[a] Melting points are uncorrected. [b] Recrystallized from ethanol. [c] This is the temperature at which the compound had completely melted.

The compound in which R was ethyl was most active. The hydroxyl group, *ortho* to the azomethine linkage, was introduced with the expectation that intramolecular hydrogen bonding would confer some rigidity upon the molecule, a condition considered by many as essential for estrogenic activity. Grundy (2) indicated, however, that it would be difficult to relate the activity of this compound to molecular rigidity, since rigidity might be expected to be important only when it affects the relative orientation of the hydrogen bonding groups. In fact, the results reported by Oki and Urushibara (4) indicate that rigidity would be an undesirable feature. They concluded from the spectroscopic data that diethylstilbestrol is not absolutely planar, and that the resulting molecular thickness is important for its estrogenic activity. In addition, others have observed that alkyl groups in both *ortho* positions enhanced the potency of these compounds, which perhaps may be attributed to an increase in lipid solubility and/or an increase in molecular thickness.

In view of the foregoing, it seemed reasonable to prepare compounds represented by the general formula in Table I. It was hoped that the increased lipid solubility and molecular thickness would augment the estrogenic potency of these compounds. The results of the vaginal cornification test in spayed rats, as first described by Allen and Doisy, were disappointing, since only weak estrus exciting properties were observed.

It is anticipated that future studies will involve the preparation of compounds possessing substantially larger alkyl groups at positions designated as R and R' on the formula in Table I.

EXPERIMENTAL

The preparative procedure was essentially that of Nomura (3); it involved the condensation of the appropriate ketone with *p*-anisidine under the catalytic influence of anhydrous zinc chloride. The compounds and pertinent data are listed in Table I.

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