Compound *20* separated as an oil, which resisted all attempts at crystallization. It was therefore taken up in ether and characterized as the hydrochloride, m.p. 208–210.°

IR spectra: all compounds exhibited a carbonyl absorption band in the 5.92–5.95 μ region.

3-Substituted 1,5-Diphenylhydantoins (Table III) —*A: Bromination of the 4-Imidazolin-2-ones*—To a solution of the appropriate 4-imidazolinone (0.01 mole) in chloroform (50 ml.) was slowly added, at room temperature, a solution of bromine (1.9 g., 0.012 mole) in chloroform (10 ml.). The solvent was then distilled (evolution of hydrogen bromide) and the oily residue was crystallized from 95% ethanol to afford the hydantoin.

Compound *14* (R = allyl) absorbed two molar equivalents of bromine to afford in 45% yield 3-(2,3-dibromo-1-propyl)1,5-diphenylhydantoin (XI), m.p. 131–133° after crystallization from benzene–petroleum ether. The same compound was obtained on treatment of the allylhydantoin *25* with one molar equivalent of bromine, in 65% yield.

Anal.—Calcd. for $C_{18}H_{16}Br_2N_2O_2$: C, 47.81; H, 3.56; N, 6.19. Found: C, 47.83; H, 3.73; N, 6.00.

Treatment of the 4-imidazolinones *19*, *20* (as the oily base), *21*, and *22* with bromine, followed by crystallization of the oily reaction product from ethanol, afforded the hydrobromides of the hydantoins *30* (m.p. 224–226°; N% Calcd. 10.39. Found: 10.30.); *31* (m.p. 189–191°; N% Calcd. 9.72. Found: 9.56.); *32* (m.p. 258–261° dec.; N% Calcd. 9.72. Found: 9.61)., and *33* (m.p. 287–288° dec.; N% Calcd. 9.41. Found: 9.38.). The salts were converted into the free bases by treatment with 10% sodium carbonate.

B: Treatment of 5-Bromo-3,4-diphenyl-4-oxazolin-2-one (V, R = Ph) with Amines—Mixtures containing 3.16 g. (0.01 mole) of the bromooxazolone (1) and 0.015 mole of the appropriate amine were heated 6 hr. at 100°. Mixtures containing low-boiling amines (*n*-propyl, *n*-butyl, isobutyl, and allylamine) were heated at the reflux temperature of the amine for 8–10 hr. The excess amine was then distilled off at reduced pressure and the crude product was crystallized from 95% ethanol.

IR spectra: all compounds exhibited a typical hydantoin carbonyl absorption (6) (two bands in the regions 5.68–5.69 μ and 5.87–5.89 μ).

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Keyphrases

3, 4 - Diphenyl - 4 - oxazolin - 2 - one derivatives—synthesis
Pharmacological screening—3,4-diphenyl-4-oxazolin-2-one derivatives
IR spectrophotometry—structure

Antibacterial and Antifungal Activity of Certain β-Aminoketones

By RAJENDRA S. VARMA* and W. LEWIS NOBLES

Preliminary biological evaluation for 17 compounds is provided. Eleven compounds in this study exhibited some degree of activity.

UNDER THE CONDITIONS of the Mannich reaction, a series of β-aminoketones dihydrochlorides was synthesized utilizing 1-(*N*-β-hydroxyethyl-4-piperidyl)-3-(4-piperidyl)-propane (I) and several aromatic ketones (1). In this report, preliminary screening results for antibacterial and antifungal activities are described.

Several techniques are available to test for antimicrobial activity. Among the *in vitro* methods are dilution or agar diffusion techniques. The former methods are suitable for assay procedures, but the methods are time consuming for screening of a large number of compounds, and many of them are not satisfactory to determine antifungal activity when filamentous fungi are used as test organisms. This is particularly true if partial inhibition is studied because it is difficult to determine the amount of growth of these fungi (2). Diffusion methods such as those represented by the use of filter paper disks on an agar plate were chosen because of their suitability for water-soluble compounds and their simplicity of operation.

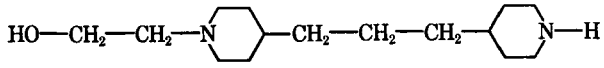

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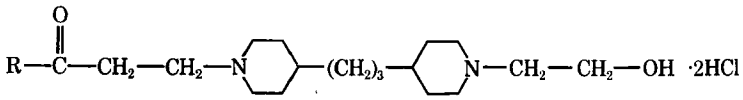
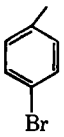
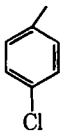
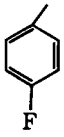
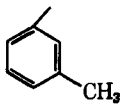
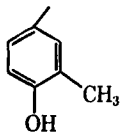
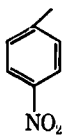
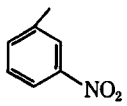
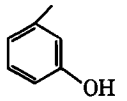
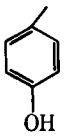
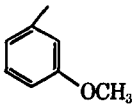
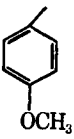
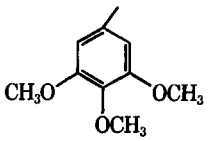
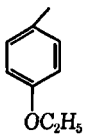
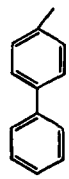
TABLE I—ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY OF β-AMINOKETONES



R	Microbial Spectrum[a]											
	1	2	3	4	5	6	7	8	9	10	11	12
	−	−	−	−	−	−	−	+	−	−	−	−
	−	−	−	−	−	+	+	−	−	−	−	−
	+	−	+	+	+	−	+	+	+	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	+	−	−	+	−	+	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−
	+	−	+	+	+	−	+	+	+	+	−	+
	−	−	−	−	+	+	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−

(*Continued on next page.*)

TABLE I (*Continued.*)

R	Microbial Spectrum[a] 1	2	3	4	5	6	7	8	9	10	11	12
	−	−	−	−	−	−	+	−	−	−	−	−
	−	−	−	−	+	−	−	+	−	−	−	−
	−	−	−	−	−	−	−	−	−	−	−	−
	−	−	+	+	−	−	+	−	+	+	−	−
	−	−	−	−	−	−	+	+	+	+	−	+
	+	−	+	+	+	+	+	+	−	+	+	−

[a] Microbial spectrum: Gram-positive—1, *Staphylococcus aureus* K257; 2, *Mycobacterium smegmatis*. Gram-negative—3, *E. coli* ATCC 4157; 4, *Pseudomonas aeruginosa*; 5, *Klebsiella pneumoniae* ATCC 8052; 6, *Proteus vulgaris* LBa 155; 7, *Neisseria catarrhalis*; 8, *Saccharomyces sp.*; 9, *Candida albicans* ATCC 10231; 10, *S. epidermidis*; 11, *Aspergillus niger*; 12, *Trichophyton mentagrophytes* ATCC 9129.

EXPERIMENTAL

Materials and Methods—The test organisms included Gram-positive *Staphylococcus aureus* K257, *Mycobacterium smegmatis*; Gram-negative *E. coli* ATCC 4157, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* ATCC 8052, *Proteus vulgaris* Lba 155, *Neisseria catarrhalis*; *Saccharomyces sp.*, *S. epidermidis*, *A. niger*, *Candida albicans* ATCC 10231, and *Trichophyton mentagrophytes* ATCC 9129. The agar medium was inoculated heavily with the test organism and then filter paper disks (6.35 mm.) saturated with two drops of the solution of the test compound (20 mg./ml. in aqueous ethanol or water) were placed on the agar. After 48 hr. of incubation period, the zones of inhibition around the disks were measured. Zone sizes smaller than 6.35 mm. were considered minus activity.

DISCUSSION

Seventeen β-aminoketones substituted at various positions in the aromatic ring were subjected to preliminary antibacterial and antifungal screening procedures. The substituents consisted of 4-fluoro, 4-chloro, 4-bromo, 4-nitro, 4-methyl, 4-phenyl, 4-hydroxy, 4-methoxy, 4-ethoxy, 3-nitro, 3-methoxy, 3-methyl, and 3-hydroxy. The activity against various organisms of these compounds is described in Table I. Hydroxy, fluoro, 4-methyl, 3,4,5-trimethoxy substituted β-amino ketones were completely inactive, whereas compounds with substituents such as chloro, bromo, and 4-nitro demonstrated the highest activity.

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Keyphrases

β-Amino ketones
Antibacterial activity—β-amino ketones
Antifungal activity—β-amino ketones
Paper disk method—analysis