μg/ml. The medium was poured into petri dishes and left to harden overnight at room temp. The surface of the agar was then inoculated with the test organisms (0.02 ml of standard suspension). The inoculated plates together with the appropriate organism controls were incubated for 3 days at 37° in the case of *P. ovale* and up to 5 days in the case of *P. orbiculare*. MIC's were detd by observing the lowest concn which inhibited growth under the prescribed condns.

Suspension Technique. Each test compd (0.1 g) was dissolved or suspended in Tween 40 (2 ml) and the vol made up to 100 ml with sterile dist H_2O. A sample was inoculated with *P. ovale* (0.1 ml of standard suspension contg 10^6 organisms/ml) and stored at room temp for 1 hr. The test samples and appropriate controls were plated out on petri dishes of Dixon's medium[2] and incubated at 37° for 3 days. Activity of the compds was assessed on the growth observed.

References

(1) J. Lodder, "The Yeasts; A taxonomic study," North Holland Publishing Co., Amsterdam, 1970, pp. 1166–1186.
(2) N. J. Van Abbé, *J. Soc. Cosmet. Chem.*, **15**, 609 (1964).
(3) T. H. Sternberg and F. M. Keddie, *Arch. Dermatol.*, 84, 999 (1961).
(4) R. C. Burke, *J. Invest. Dermatol.*, **36**, 389 (1961).
(5) J. E. Hogan, Ph.D. Thesis, University of London, 1970.
(6) J. K. Sugden, Ph.D. Thesis, University of London, 1964.
(7) C. Caldo, *Chim. Ind. (Milan)*, 44, 753 (1962).

New Compounds

A Rapid, Convenient Preparative Procedure for Phenethylamines

Edgar F. Kiefer

Department of Chemistry, University of Hawaii, Honolulu, Hawaii 96822. *Received August 6, 1971*

In view of the very broad pharmacological utility of substituted 2-phenylethylamines, we wish to contribute a synthetic procedure which, because of its versatility and convenience, may find considerable use. Although based entirely on standard synthetic methods, the overall scheme is specifically tailored to the properties of the benzylic intermediates involved, and eliminates the need for isolation of intermediates and other time-consuming operations. The procedure is described for the *p*-methoxy derivative; it is also applicable without substantive modification to other ring alkoxy-, alkyl-, and halogen-substituted phenethylamines.

Experimental Section

4-Methoxyphenylethylamine Hydrochloride. *p*-Anisyl alcohol (100 g, 0.725 mole) was shaken with 500 ml of concd HCl for 2 min. The org phase was washed with H_2O, 5% $NaHCO_3$, and H_2O, then added over 40 min to a stirred slurry of 49 g (1.0 mole) of NaCN in 400 ml of DMSO,[1] with ice-water cooling to maintain the temp at 35–40°. After addn was complete, the cooling bath was removed, the mixt was stirred for 90 min and then added to 300 ml of H_2O, and the small upper phase sepd. The aq DMSO layer was extd with two 100-ml portions of Et_2O, which were combined with the product layer, and the whole was washed once with H_2O and dried ($MgSO_4$).

A dry flask was charged with *ca.* 600 ml of abs Et_2O and chilled in ice as 80 g (0.6 mole) of anhyd $AlCl_3$ was added portionwise, followed by 23 g (0.6 mole) of LAH.[2]† The dried Et_2O soln of crude *p*-methoxyphenylacetonitrile was added at such a rate as to maintain gentle reflux without external heat (*ca.* 1 hr). The mixt was stirred for 2 hr, then chilled in ice, and treated dropwise with 25 ml of H_2O followed by 250 ml of 20% of aq NaOH, with periodic addn of Et_2O through the condenser to replenish losses and facilitate stirring. The resulting voluminous, granular ppt of NaCl and LiCl and aluminate was removed by filtration, washed well with Et_2O, and discarded. The filtrate was mixed with one-third its vol of abs EtOH and 60 ml of concd HCl was added slowly with continuous swirling and ice cooling. After chilling to 0°, the cryst amine hydrochloride was collected, 101 g, mp 212–214°, identified by mass spectroscopy [*m/e* 122, 30, 121, 28, 151 (M^+)]. The overall yield was 75% from anisyl alcohol. The hydrochloride may be recrystd from Et_2O–EtOH or *i*-PrOH.

†LAH alone and other metal hydride reagents are unsatisfactory for the reduction of benzylic nitriles to amines.

***N*-Methyl-*p*-methoxyphenylethylamine Hydrochloride.** *p*-Methoxyphenethylamine, generated from 100 g (0.536 mole) of the hydrochloride by stirring with concd aq NaOH, was treated with 100 ml of PhH and 70 g (0.66 mole) of PhCHO. A mildly exothermic reaction began at once. The mixt was heated under reflux until no more H_2O was present in the condensate (*ca.* 1 hr), then, without cooling, an attached Dean-Stark trap was removed and a soln of 82 g (0.65 mole) of Me_2SO_4[3] in 200 ml of PhH was added through the condenser at such a rate as to maintain reflux (15 min). The 2-phase mixt was heated for 90 min on the steam bath, cooled slightly, treated with 200 ml of H_2O, and heated for an addl 20 min. After cooling in ice, the aq layer was washed twice with Et_2O to remove unreacted PhCHO and made strongly basic with 50% aq NaOH. Two Et_2O exts of the basic aq phase were added to the amine layer which sepd, and the resulting soln was evacd at the aspirator for 30 min, leaving 90 g (102%) of crude *N*-methyl-*p*-methoxyphenethylamine. This material was dissolved in 500 ml of 20% abs EtOH–Et_2O and treated with 50 ml of concd HCl with swirling and cooling to yield the white, cryst hydrochloride, which was washed thoroughly with ice-cold 20% EtOH–Et_2O and dried, mp 185.5–186.5°, identified by mass spectroscopy [*m/e* 121, 44, 165 (M^+)]. The yield was 83 g (77%).

References

(1) R. A. Smiley and C. Arnold, *J. Org. Chem.*, **25**, 257 (1960).
(2) R. F. Nystrom, *J. Amer. Chem. Soc.*, 77, 2544 (1955).
(3) J. J. Lucier, A. D. Harris, and P. S. Korosec, *Org. Syn.*, 44, 72 (1964).

Synthesis of 2-Fluoro-9-β-D-ribofuranosylpurine (2-Fluoronebularine)

Masajiro Kawana, Robert J. Rousseau,* and Roland K. Robins

ICN Nucleic Acid Research Institute, Irvine, California 92664. *Received August 16, 1971*

The antibiotic nebularine (9-β-D-ribofuranosylpurine) has shown tuberculostatic,[1] antimitotic,[2] and anticancer activity.[2,3] The mode of action has been proposed to be in the purine biosynthetic pathway.[4,5] It has limited usefulness because of its high toxicity.[2,6,7]

We wish to report the synthesis of 2-fluoronebularine (2a). Synthesis of the title compound 2a was accomplished by removal of the benzylthio group from 6-benzylthio-2-fluoronebularine (1)[8] with Raney Ni.