SYNTHESES OF APOGALANTHAMINE ANALOGS AS α-ADRENERGIC BLOCKING AGENTS

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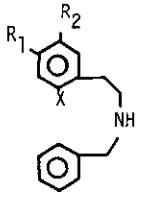
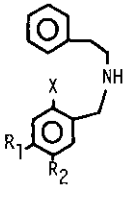
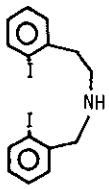
The apogalanthamine analogs 5,6,7,8-tetrahydrodibenz[c,e]azocine (1), 10,11-methylenedioxy-, and 10,11-dimethoxy-5,6,7,8-tetrahydrodibenz[c,e]azocines (2 and 3, respectively) having α-adrenergic blocking activities, and the related compounds 2,3-methylenedioxy-, 2,3-dimethoxy-, 9-iodo-, and 4-iodo-5,6,7,8-tetrahydrodibenz[c,e]azocines (4-7, respectively) were synthesized by photochemical methods: photolysis of 2-, 2'-halogeno-, or 2,2'-diiodo-N-benzyl-β-phenethylamine derivatives (8-14) gave the corresponding compounds (1-7, respectively), which seemed to be formed via the corresponding arylcyclohexadienyl radicals.



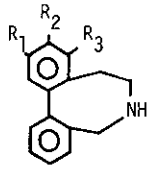
8: X=I, R_1=R_2=H
9: X=I or Br, R_1=R_2=OCH_2O
10: X=I or Br, R_1=R_2=OMe



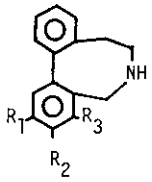
11: X=I, R_1=R_2=H
12: X=I or Br, R_1=R_2=OCH_2O
13: X=I or Br, R_1=R_2=OMe



14

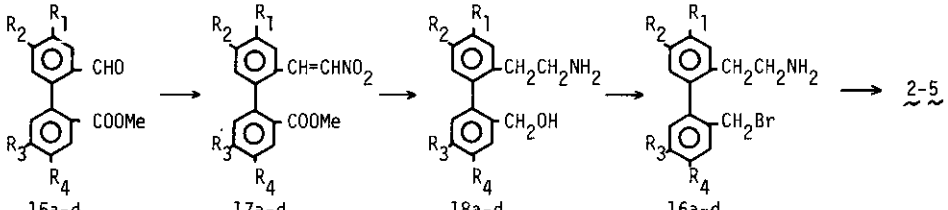


1: R_1=R_2=R_3=H
2: R_1, R_2=OCH_2O, R_3=H
3: R_1=R_2=OMe, R_3=H
6: R_1=R_2=H, R_3=I



4: R_1, R_2=OCH_2O, R_3=H
5: R_1=R_2=OMe, R_3=H
7: R_1=R_2=H, R_3=I

An alternative synthesis of compounds 2-5 has also been realized by the following sequence of chemical reactions. Methyl 2'-formyl-2-biphenylcarboxylates (15a-d) as starting materials were converted to the corresponding 2'-aminoethyl-2-bromomethylbiphenyls (16a-d) via the nitrostyrene derivatives (17a-d) and the amino-alcohols (18a-d). Intramolecular cyclization of the bromides (16a-d) by alkali gave 2-5, respectively. Only compound 1 was prepared from diphenide by 5 steps. The half-tub conformation of the apogalanthamine analogs was discussed on the basis of studies on nuclear magnetic double resonance spectra.



15a-d → 17a-d → 18a-d → 16a-d → 2-5

a: R_1, R_2=OCH_2O, R_3=R_4=H
b: R_1=R_2=OMe, R_3=R_4=H
c: R_1=R_2=H, R_3, R_4=OCH_2O
d: R_1=R_2=H, R_3=R_4=OMe