SYNTHESES AND STEREOISOMERS OF 1-(1,3-DIOXOLAN-4-YLMETHYL)PIPERIDINOL DERIVATIVES

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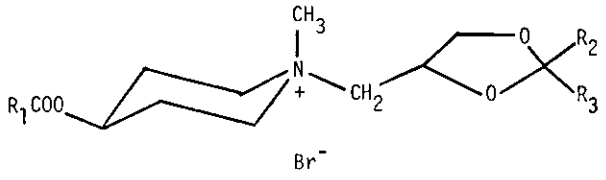
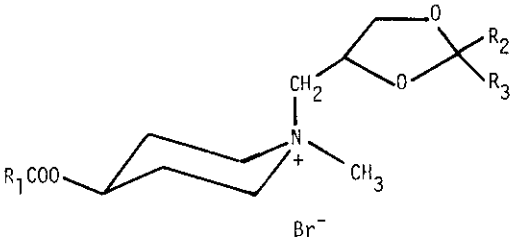
3(And 4)-acyloxy-1-(1,3-dioxolan-4-ylmethyl)piperidines (I and II) and their quaternary salts (III and IV) were synthesized for the purpose of testing pharmacological actions. Structures of the quaternary salts were assigned by means of nuclear magnetic resonance spectroscopy.

Quaternization of II (R_1=benzhydryl, 9-xanthenyl, benzyl, diphenylmethyl, and 9-fluorenyl) with methyl bromide caused the formation of two epimers, IVa and IVe, in almost same proportions. This result differs from the reports in which quaternization of 1,4-disubstituted piperidines occurs predominantly with axial attack of alkylating agent. In this experiment, we concluded that the bulky and flexible 4-acyloxy substituent having at least one phenyl group hinders axial attack of methyl moiety to II, and hence formation of equatorial methyl epimer increases.

These quaternary salts showed an anti- cholinergic action. It was found that axial methl epimers (IVa) exhibited more intense activity than equatorial ones (IVe).



IVa



IVe