SYNTHESIS OF NOVEL THIAZOLO[5,4-f]MORPHANS

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Synthesis of novel analgesics, thiazolo[5,4-f]morphans, are described. Thiazolization of 4,4-dimethyl-1,3-cyclohexanedione gave 2-aminothiazole (I). Deamination of I afforded II, which was converted into thiazolo[5,4-f]morphan skeleton in the following manner. Cyanomethylation of II afforded III. Compound (III) was treated with $LiAlH_4$ and the resulting amino alcohol was converted into IV by Wagner-Meerwein rearrangement. Reaction of IV and bromine followed by treatment with K_2CO_3 gave the bridged aziridine (V). Compound (V) was cleaved into thiazolo[5,4-f]morphan derivative (VI) by the action of benzoyl bromide. Dehydrobromination of VI and subsequent hydrolysis afforded VII. Synthesis of thiazolo[5,4-f]morphans (VIII-IX) was completed by hydrogenation and Eschweiler-Clarke N-methylation of VII.