SYNTHESIS AND ANTIHYPERTENSIVE ACTIVITY OF SOME FUSED QUINAZOLINE DERIVATIVES

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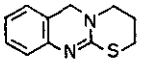
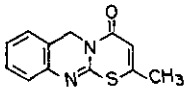
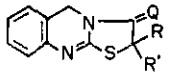
In continuing the study of the biological activity of pseudothiourea-fused heterocycles[1], some 1,3-thiazino(2,3-b)- and thizolo(2,3-b)quinazoline derivatives were synthesized. The synthetic experiments were worked out starting from 3,4-dihydro-2(H)-quinazolinethione, which was obtained from 2-aminobenzylamine by treating with carbon disulfide in alkaline solution. This key intermediate was then reacted with α,ω-dihaloalkanes, ethyl 3-chlorocrotonate, ethyl chloroacetate, maleic anhydride, N-phenylmaleimide, or dimethyl acetylenedicarboxylate in suitable solvents to give the title compounds Ia,b, IIa-e in satisfactory yields (42-96%).



Ia



Ib



II	Q	R	R'
a	H_2	H	H
b	O	H	H
c	O	H	CH_2CO_2H
d	O	H	$CH_2CONHC_6H_5$
e	O	$=CH-CO_2CH_3$	

Linear fusion system for all products was assigned according to spectral analyses and further verified by an unequivocal synthesis. A preliminary antihypertensive evaluation of the products in anesthetic cats at the usual i.v. dose level showed that the built-in pseudothiourea unit as well as the thialactam structure feature is essential for the hypotensive activity. However, it may be negatively influenced by the steric or electronic effects of the substituent present on the heterocyclic ring.

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1) K.C. Liu, L.C. Lee, B.J. Shih, C.F. Chen and T.M. Tao, Arch. Pharm. (Weinheim) 315, 872 (1982).