SYNTHESIS AND BIOACTIVITIES OF FUSED PERIMIDINE DERIVATIVES

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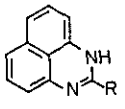
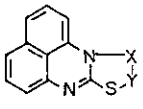
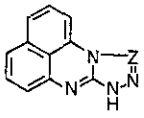
As a part of continuing study of bridgehead nitrogen heterocycles, a series of ring-fused perimidine derivatives were synthesized. The synthetic reactions were performed starting from 2-mercaptoperimidine (Ia), which was obtained from 1,8-diaminonaphthalene by treating with carbon disulfide under the action of alkali[1]. Cyclocondensation of Ia with some bifunctional electrophiles, such as dimethyl acetylenedicarboxylate, ethyl chloroacetate, oxalyl chloride, α,ω-dihaloalkanes or dihaloalkenes afforded the expected fused perimidine derivatives IIa-f. Hydrolysis of Ia or its S-methylated derivative Ib with hydazine hydrate gave another key intermediate, 2-hydrazinoperimidine (Ic). Ic was then condensed with some orthoesters, benzoyl chloride, carbon disulfide in alkaline solution or diazotized to the corresponding 1,2,4-triazolo- or 1,2,4-tetrazolo-(4,3-a)perimidines (IIIa-f).



I	R
a	SH
b	SCH_3
c	$NH-NH_2$



II	X	Y
a	C=O	$C=CHCO_2CH_3$
b	C=O	C=O
c	C=O	CH_2
d	$-CH=CH-$	
e	$-CH_2-CH_2-$	
f	$-CH_2CH_2CH_2-$	



III	Z
a	CH
b	$C-CH_3$
c	$C-C_2H_5$
d	$C-C_6H_5$
e	C-SH
f	N

A preliminary pharmacological investigation on animals showed that all synthetic products possess no central nervous system depressant effects in mice and no distinct hypotensive action in normotensive rats. However, at a p.o. dose of 50 mg/kg, most compounds exhibited the moderate anorectic activity in mice with the T/C values of 31-85% in comparision with the psychotonic standard, D-amphetamine (100%).

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1) K.C. Liu, J.Y. Tuan and B.J. Shih, Arch. Pharm. (Weinheim), 309, 928 (1976).