New Compounds

Synthesis of Thiocarbamate S-Ester Derivatives

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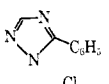
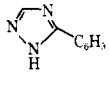
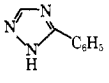
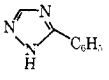
We have synthesized a number of substituted thiocarbamates of the general formula $R_1SCONHR_2$ (see Table I). Our attempt was to generate a thiocarbamate derivative of a tolnaftate-like compound having both antifungal and antibacterial[1] activity. The compounds were evaluated[2] in a primary *in vitro* screen (agar strip) against bacteria and fungi. None of them demonstrated a zone of inhibition equal to tolnaftate when evaluated at the equiv concn.

TABLE I

No.	R_1	R_2	Mp, °C	Procedure	Reaction solvent	Formulas[b]
1	C_6H_5		151–154	A	THF	$C_9H_8N_4S$[c]
2	C_6H_5		209–210	A	THF	$C_{15}H_{12}N_4OS$
3	C_6H_5		180–182	A	THF	$C_{14}H_9ClN_2OS_2$
4	C_6H_5	2-Naphthyl	145–147	A	THF	$C_{17}H_{13}NOS$
5	C_6H_5	C_6H_4OH	148–150	A	THF	$C_{13}H_{11}NO_2S$
6	C_6H_5	$CH_2C_6H_4Cl$	127–129	A	THF	$C_{14}H_{12}ClNOS$
7	C_6H_5	*i*-Pr_2[a]	104–107	B	THF	$C_{13}H_{19}NOS$
8	Et		127–130	A	THF	$C_5H_8N_4OS$[c]
9	*n*-Pr		103–105	A	THF	$C_7H_{10}N_2OS_2$
10	*i*-Pr		142–143	A	THF	$C_7H_{10}N_2OS_2$
11	Et		160–162	B	D[d]	$C_{11}H_{12}N_4OS$
12	*n*-Pr		148–150	A	D	$C_{12}H_{14}N_4OS$
13	*i*-Pr		189–191	A	D	$C_{12}H_{14}N_4OS$
14	Et	$CH_2C_6H_5$	61–62	A	D	$C_{10}H_{13}NOS$

[a] Disubstituted amide resulted as shown by elemental analysis and spectral data. [b] All compds were analyzed for C, H, N unless otherwise noted. [c] Also S anal. [d] D, dioxane.

Experimental Section

Thiocarbamates. Method A.—To a soln of the amine in the reaction solvent (see Table I) was added dropwise 0.5 equiv of the appropriate chlorothioformate dissolved in the reaction solvent. The mixt was allowed to stir for 18 hr. The amine salt was isolated by filtration and the thiocarbamate by evapn of the filtrate under reduced pressure. The product was recrystd from EtOH or PhH–Et_2O.

Method B.[3]—To a soln of amine in the reaction solvent (see Table I) was added dropwise 0.5 equiv of the appropriate chlorothioformate dissolved in the reaction solvent. After stirring overnight the mixt was poured into ice water. The solid thiocarbamate was collected by filtration, washed successively with 2 *N* HCl and H_2O, and recrystd from H_2O or Me_2CO–H_2O.

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Potential Folic Acid Antagonists. 6. Potential Irreversible Folate Reductase Inhibitors Derived from 2,4-Diamino-5-arylazopyrimidines

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Previous studies[1,2] have described the irreversible inhibition of folate reductase produced by 5-arylazopyrimidines bearing an alkylating function at the 6 position (I). It appeared of interest in the light of our previous[1,3,4] rationalizations of the structure-activity relationships of 5-arylazopyrimidines to prepare and examine the activities of related compounds in which the alkylating function is attached to the 5-aryl group (II). In view of the pronounced lack of activity of the compounds listed in Table III $(I)/(S)_{0.5} > 5.0$) the corresponding alkylating analogs (X = Cl) were not prepared.

Experimental Section[5]

2-Nitro-ω-bromoalkylbenzenes (IV, *n* = 2–5).—These compds were prepared by nitration and fractional distillation of 2-bromo-

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(5) Melting points were recorded on a Thomas-Kofler hot stage and are corrected. Analyses were performed by Dr. A. E. Bernhardt and, where indicated only by symbols of the elements, were within 0.4% of the theoretical values.