

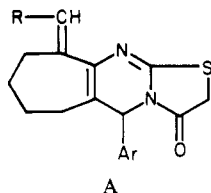
# Synthesis and Reactions of 2,3-Dihydro-7H-6-styryl-7,7-dimethylthiazolo[3,2-a]pyrimidin-3-ones

Abou-El Fotooh G. Hamman\* and Mohamed I. All

National Research Centre, Dokki, Giza, and Department of Chemistry, Faculty of Science,  
University of Cairo, Giza, Arab Republic of Egypt

The pyrimidinethione I reacted with chloroacetic acid and an aromatic aldehyde to give the 2-(arylmethylene)trimethylthiazolo[3,2-a]pyrimidin-3-ones II. Also the pyrimidinethione I reacted with aromatic aldehydes in the presence of KOH to give the styrylpyrimidinethione III, which condensed with chloroacetic acid to give the title compounds. The title compounds reacted with aromatic aldehydes to give the 2-arylmethylene derivatives V. The styrylpyrimidinethione III also reacted with 3-bromopropionic acid to give 2,3-dihydro-2H,8H-8,8-dimethyl-6-styryl(1,3)thiazin[3,2-a]pyrimidin-4-ones VI.

Recently, it has been found that among a series of tricyclic thiazolopyrimidine, compound A showed borderline carcinostatic



activity (1, 2). Now we wish to report on the synthesis of some pyrimidinethion derivatives.

## Experimental Section

**2-(Arylmethylene)-2,3-dihydro-7H-5,7,7-trimethylthiazolo[3,2-a]pyrimidin-3-ones (II).** A mixture of 1.0 g (0.01 mol) of I (3, 4, 6), 1 g of chloroacetic acid, 0.01 mol of the appropriate aldehyde, and 2 g of fused sodium acetate in 10 mL of acetic acid and 4 mL of acetic anhydride was refluxed for 1 h (see Scheme I). The reaction mixture was allowed to cool and then poured into cold water gradually while stirring with a glass rod. The solid that separated was dissolved in ether and dried over anhydrous sodium sulfate. The ethereal solution was treated with petroleum ether 40-60 to give a yellow solid, which was filtered off and crystallized from the proper solvent. Compounds II show CO absorption at ca. 1695  $\text{cm}^{-1}$  (see Table I).

**3,4-Dihydro-4,4-dimethyl-6-styryl-2(1H)-pyrimidinethione (III).** Compound IIIa was prepared by Zigeuner (7) in ~70% yield. In this work, we could prepare the styrylpyrimidinethiones III in ~90% yield as follows.

A mixture of 10 g of I and 15 mL of the appropriate aromatic aldehyde in 10 mL of ethanol (75%) was heated at 70 °C with stirring until a clear solution was obtained. To this solution was added 50 mL of ethanolic potassium hydroxide (15 g of KOH in 50 mL of 50% ethanol). Heating and stirring were continued at 70 °C for 15 min; then the mixture was allowed to stand at room temperature for 5 h. The yellow crystals formed were filtered off and washed with dilute methanol to give III. The IR spectra of compounds I showed absorption at ca. 1704  $\text{cm}^{-1}$ . This peak was shifted to lower frequencies at ca. 1650  $\text{cm}^{-1}$  in compounds III. Most likely this absorption has to be attributed to the methyl-substituted ethylenic moiety (5) (see Table II).

Scheme I

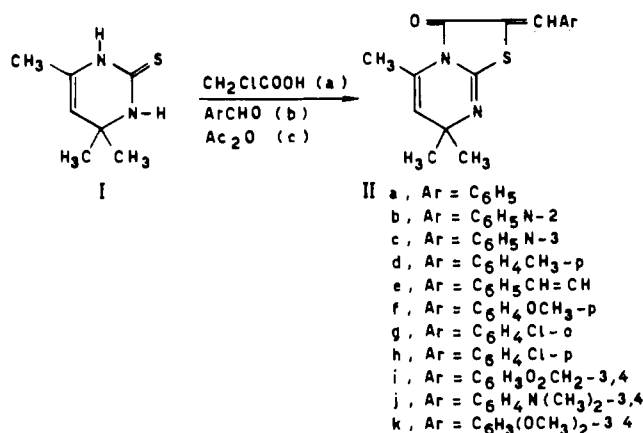


Table I. 2-(Arylmethylene)-2,3-dihydro-7H-5,7,7-trimethylthiazolo[3,2-a]pyrimidin-3-ones (II)<sup>b</sup>

compd	mp, °C	solvent <sup>a</sup>	yield, %
IIa	125	L	90
b	160	E	85
c	150	E	88
d	170	E	90
e	185	L	90
f	110	C	90
g	215	L	95
h	200	L	95
i	150	L	90
j	200	C	85
k	135	L	90

<sup>a</sup> Solvent key: A = acetic acid; E = ethanol; M = methanol; L = petroleum ether 60/80. <sup>b</sup> Elemental analyses in agreement with theoretical values were obtained.

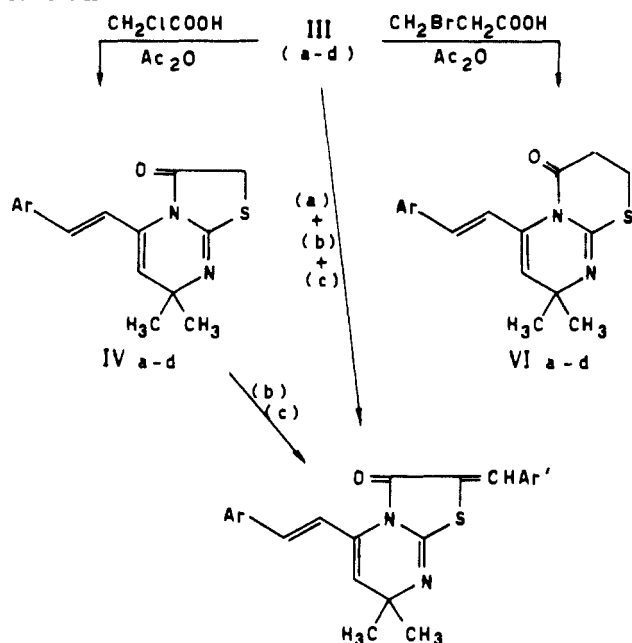
Table II. 3,4-Dihydro-4,4-dimethyl-6-styryl-2(1H)-pyrimidinethiones (III)<sup>a</sup>

compd	mp, °C	solvent	yield, %
IIIa	218	E	88
b	228	E	85
c	210	E	90
d	195	E	88

<sup>a</sup> Refer to footnotes of Table I.

**2,3-Dihydro-7H-5-styryl-7,7-dimethylthiazolo[3,2-a]pyrimidin-3-ones (IV).** A mixture of 2 g of III, 1 g of chloroacetic acid, and 3 g of fused sodium acetate in 10 mL of acetic acid and 7 mL of acetic anhydride was refluxed for 2 h, allowed

Scheme II



Ar	Ar'
V a, $\text{C}_6\text{H}_5$	$\text{C}_6\text{H}_5$
b, $\text{C}_6\text{H}_5$	$\text{C}_6\text{H}_4\text{CH}=\text{CH}$
c, $\text{C}_6\text{H}_5$	$\text{C}_6\text{H}_3\text{O}_2\text{CH}_2-3,4$
d, $\text{C}_6\text{H}_4\text{CH}_3-p$	$\text{C}_6\text{H}_4\text{CH}_3-p$
e, $\text{C}_6\text{H}_4\text{CH}_3-p$	$\text{C}_6\text{H}_4\text{Cl}-o$
f, $\text{C}_6\text{H}_4\text{OCH}_3-p$	$\text{C}_6\text{H}_5\text{N}-3$
g, $\text{C}_6\text{H}_4\text{OCH}_3-p$	$\text{C}_6\text{H}_4\text{CH}_3-p$
h, $\text{C}_6\text{H}_4\text{Cl}-o$	$\text{C}_6\text{H}_4\text{Cl}-o$
i, $\text{C}_6\text{H}_4\text{Cl}-o$	$\text{C}_6\text{H}_3\text{O}_2\text{CH}_2-3,4$
j, $\text{C}_6\text{H}_4\text{Cl}-o$	$\text{C}_6\text{H}_3(\text{OCH}_3)_2-3,4$

Table III. 2,3-Dihydro-7H-5-styryl-7,7-dimethylthiazolo[3,2-a]pyrimidin-3-ones (IV)<sup>a</sup>

compd	mp, °C	solvent	yield, %
IVa	225	M	68
b	200	E	65
c	160	E	63
d	195	E	64

<sup>a</sup> Refer to footnotes of Table I.

to cool, and then poured gradually while stirring into cold water (see Scheme II). The solid obtained was filtered off and crystallized from the proper solvent. The IR spectra of IV show CO absorption at ca.  $1710\text{ cm}^{-1}$ . The UV spectrum of compound IVd shows absorption at  $\lambda = 280\text{ nm}$  ( $\epsilon = 10000$ ) (see Table III).

**2-(Arylmethylene)-2,3-dihydro-7H-6-styryl-7,7-dimethylthiazolo[3,2-a]pyrimidin-3-ones (V).** Compounds V

Table IV. 2-(Arylmethylene)-2,3-dihydro-7H-6-styryl-7,7-dimethylthiazolo[3,2-a]pyrimidin-3-ones (V)<sup>a</sup>

compd	mp, °C	solvent	yield, %
Va	180	M	90
b	195	L	88
c	170	M	93
d	170	E	90
e	190	E	88
f	140	L	75
g	175	E	80
h	225	A	90
i	155	E	93
j	220	A	90

<sup>a</sup> Refer to footnotes of Table I.Table V. 2,3-Dihydro-2H,8H-8,8-dimethyl-6-styryl(1,3)thiazin[3,2-a]pyrimidin-4-ones (VI)<sup>a</sup>

compd	mp, °C	solvent	yield, %
VIa	210	M	64
b	200	E	67
c	170	E	65
d	220	E	65

<sup>a</sup> Refer to footnotes of Table I.

were prepared by the same method used for compounds II, but by using compounds III instead of I. Compound Vh also was prepared from IVd as follows. A mixture of 1 g of IVd and 1 mL of *o*-chlorobenzaldehyde in 5 mL of acetic acid and 7 mL of acetic anhydride was refluxed for 1 h, allowed to cool, and then poured into cold water. The solid obtained was crystallized from acetic acid (mp and mixed mp,  $225\text{ }^\circ\text{C}$ ). Compounds V show CO absorption at ca.  $1695\text{ cm}^{-1}$ . The UV spectrum of compound Vh shows absorption at  $\lambda = 320\text{ nm}$  ( $\epsilon = 14000$ ) (see Table IV).

**2,3-Dihydro-2H,8H-8,8-dimethyl-6-styryl(1,3)thiazin[3,2-a]pyrimidin-4-ones (VI).** Compounds VI were prepared by the same method used for compounds IV, but by using 3-bromopropionic acid instead of chloroacetic acid. Compounds VI show CO absorption at ca.  $1680\text{ cm}^{-1}$  (see Table V).

#### Literature Cited

- (1) Ali, M. I.; El Kaschef, M. A. F.; Hammam, A. G.; Khalaf, S. A. *J. Chem. Eng. Data* **1979**, *24*, 377.
- (2) Ali, M. I.; Hammam, A. G. *J. Chem. Eng. Data* **1978**, *23*, 351.
- (3) Mathes, R. A.; Stewart, F. D. *J. Am. Chem. Soc.* **1950**, *72*, 1879.
- (4) Mathes, R. A. *J. Am. Chem. Soc.* **1953**, *75*, 1747.
- (5) Silverstein, R. M.; Bassler, C. G.; Morrill, R. C. "Spectrometric Identification of Organic Compounds", 3rd ed.; Wiley: New York, 1974; Table IV, p 145.
- (6) Takeshima, T.; Imamoto, T.; Tokoyama, M.; Yamamoto, K.; Akano, M. *J. Org. Chem.* **1968**, *33*, 2877.
- (7) Zlignuner, G.; Frank, A.; Dujmovits, H.; Adam, W. *Monatsh. Chem.* **1970**, *101*, 1415.

Received for review June 12, 1980. Accepted August 22, 1980.