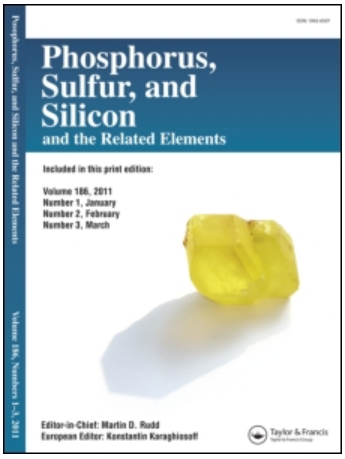

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SOME REACTIONS OF 2-MERCAPTO-3,5,7-TRIPHENYLPYRIDO[2,3-d]PYRIMIDINE-4(3H)-ONE SYNTHESIS OF PYRIDOTRIAZOLO AND PYRIDOTETRAZOLOPYRIMIDINE DERIVATIVES

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SOME REACTIONS OF 2-MERCAPTO-3,5,7-TRIPHENYLPYRIDO[2,3-d]PYRIMIDINE-4(3H)-ONE SYNTHESIS OF PYRIDOTRIAZOLO AND PYRIDOTETRAZOLOPYRIMIDINE DERIVATIVES

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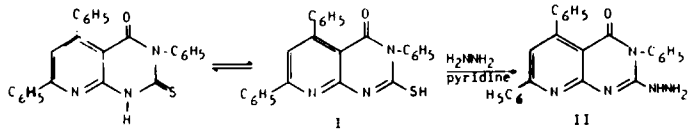
Treatment of 2-Mercapto-3,5,7-triphenylpyrido[2,3-d]pyrimidine-4(3H)-one (**I**) with hydrazine hydrate afforded 2-hydrazino derivative **II**. Compound **II** underwent ring closure with formic acid and/or triethyl orthoformate, acetic anhydride and/or acetyl chloride and other different reagents to give the title compounds.

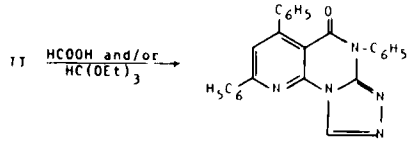
Key words: Mercaptopyridopyrimidine; pyridotriazolo; pyridotetrazolopyrimidine.

The importance of some pyridopyrimidine thiones as analgesic, antiinflammatory and central nervous system depressing agents[1,2] led us to examine the chemistry of 2-mercapto-3,5,7-triphenylpyrido[2,3-d]pyrimidine-4(3H)-one (**I**)[3] to be used as a starting material for the synthesis of pyridotriazolo and pyridotetrazolopyrimidine derivatives.



I II

2-Hydrazino 3,5,7-triphenylpyrido[2,3-d]pyrimidine-4(3H)-one (**II**) readily underwent ring closure with formic acid and/or triethyl orthorformate to give 2,4,6-triphenylpyrido[3,2-e][1,2,4]triazolo[4,3-a]pyrimidine-5(6H)-one (**III**)

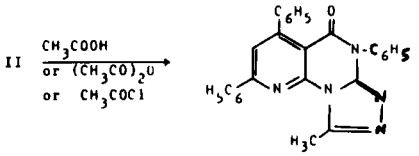


III

The structure of **III** was established on the basis of elemental analysis as well as spectroscopic data.

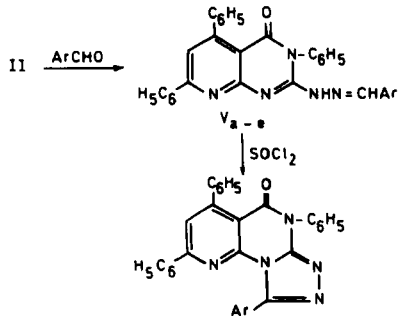
Reaction of **II** with acetic acid at reflux temperature afforded 9-methyl-2,4,6-triphenylpyrido[3,2-e][1,2,4]triazolo[4,3-a]pyrimidine-5(6H)-one (**IV**). The elucidation of the structure of **IV** was based on elemental analysis and spectroscopic data or by its unequivocal synthesis via interaction of **II** with acetic anhydride[4]

and/or acetyl chloride.



IV

The reaction of hydrazino derivative **II** with aromatic aldehydes gave easily the corresponding condensation products **Va–e** (cf. Table I) which also cyclized easily on treatment with excess thionyl chloride to give 9-aryl-2,4,6-triphenyl pyrido[3,2-e][1,2,4]-triazolo[4,3-a]pyrimidine-5(6H)-ones VIa-e.

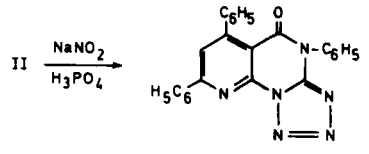


VI

Ar = C_6H_5, *p*-ClC_6H_4-, *p*-$H_3COC_6H_4$-, *p*-$O_2NC_6H_4$-, *o*-HO-C_6H_4-

The structural assignments of **Va–e** were based on elemental and spectroscopic data (Results are depicted in Table I). The cyclization of **Va–e** to **VIA–e** using thionyl chloride proceeded according to the reported mechanism.[5] Also the elucidation of the structures of compounds **VIa–e** was based on their elemental and spectroscopic analyses (cf. Table II).

Further structural assignments of 9-phenyl-2,4,6-triphenyl-pyrido[3,2-e][1,2,4]triazolo[4,3-a]pyrimidine-5(6H)-one **VIa** was carried out by its synthesis using another route via heating of **II** with benzoyl chloride under reflux. The two routes gave the same compound. Treatment of **II** with sodium nitrite in concentrated phosphoric acid gave 4,6,8-triphenylpyrido[3,2-e][1,2,4]tetrazolo-[1,5-a]pyrimidine-5(4H)-one (**VII**).



VII

Reaction of **II** with diethyl malonate and/or acetylacetone gave ethyl-5,6-dihydro-5-oxo-2,4,6-triphenylpyrido[3,2-e][1,2,4]-triazolo[4,3-a]pyrimidine-9-acetate (**VIII**) and 2-(3,5-Dimethyl-1H-pyrazol-1-yl)-3,5,7-triphenylpyrido[2,3-

TABLE I

Aromatic aldehyde-(3,4-dihydro-4-oxo-3,5,7-triphenylpyrido[2,3-d]pyrimidin-2-yl) hydra

Compound No.[a]	Ar	Mp (°C)	Yield (%)	Molecular formula	Analysi Calcd./(Foun C	H	
Va	C_6H_5	290–292	75	$C_{32}H_{23}N_5O$	77.89	4.67	
					(77.75)	(4.56)	(
b	C_6H_4Cl-p	298–300	80	$C_{32}H_{22}N_5OCl$	72.80	4.17	
					(72.71)	(4.09)	(
c	$C_6H_4OCH_3$-p	282–285	70	$C_{33}H_{25}N_5O_2$	75.72	4.78	
					(75.57)	(4.70)	(
d	$C_6H_4NO_2$-p	297–300	75	$C_{32}H_{22}N_6O_3$	71.38	4.09	
					(71.40)	(4.10)	(
e	C_6H_4OH-o	312–314	78	$C_{32}H_{23}N_5O_2$	75.45	4.52	
					(75.55)	(4.56)	(

[a] Solvent of crystallization: **Va**, Benzene + Pet. ether (1:1); **Vb**, Dioxane; **Vc**, **d**, Benzene

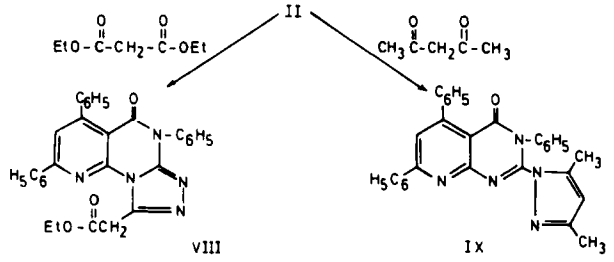
TABLE II

9-Aryl-2,4,6-triphenylpyrido[3,2-e][1,2,4]-triazolo[4,3-a]pyrimidine-5(6H)-ones (V

Compound No.[a]	Ar	Mp (°C)	Yield (%)	Molecular formula	Analysi Calcd./(Foun C	H	
VIa	C_6H_5	315	68	$C_{32}H_{21}N_5O$	78.21	4.28	
					(78.33)	(4.30)	(
b	C_6H_4Cl-p	310–312	70	$C_{32}H_{20}N_5OCl$	73.07	3.81	
					(73.10)	(3.77)	(
c	$C_6H_4OCH_3$-p	268–270	55	$C_{33}H_{23}N_5O_2$	76.01	4.41	
					(76.11)	(4.39)	(
d	$C_6H_4NO_2$-p	198–200	60	$C_{32}H_{20}H_{20}N_6O_3$	71.64	3.73	
					(71.60)	(3.75)	(
e	C_6H_4OH-o	305–307	45	$C_{32}H_{21}N_5O_2$	75.74	4.14	
					(75.76)	(4.09)	(

[a] Solvent of crystallization: **VIa**, Dioxane; **VIb**,**e**, Benzene; **VIc**, Dil. dioxane; **VId**, Eth

d]pyrimidine-4(3H)-one (**IX**) respectively.



Structure of products **VII VIII** and **IX** was confirmed by elemental and spectroscopic analyses.

EXPERIMENTAL

Melting points are uncorrected. Infrared spectra were measured on a Perkin–Elmer 599 B Spectrophotometer. Nuclear magnetic resonance spectra were measured on EM-360 (90 MHz) NMR Spectrophotometer. The mass spectra were carried out at the Department of Chemistry, University College, Cardiff CFI IXL, U.K.

2-Mercapto-3,5,7-triphenylpyrido[2,3-d]pyrimidin-4(3H)-one (**I**) and 2-hydrazino-3,5,7-triphenylpyrido[2,3-d]pyrimidin-4(3H)-one (**II**) were prepared according to our previous work.[3]

2,4,6-Triphenylpyrido[3,2-e][1,2,4]triazolo[4,3-a]pyrimidine-5(6H)-one (**III**). Compound II (0.7 g, 0.017 mole) was refluxed with formic acid or triethyl orthoformate (10 ml) for 5 hours. On cooling the reaction mixture a white precipitate was formed. The product was crystallized from benzene to give III as colourless crystals in 70% yield, mp 315–17°C; ir (KBr): 1685 cm^{-1} (C=O), 3020 cm^{-1} (CH aliphatic), 1600 cm^{-1} (C=N); pmr ($CDCl_3$): δ7.7 (s, 1H, pyridine), 9.2 (s, 1H, CH=N), 7.3–7.6 and 8.1–8.3 (m, 15H, aromatic). Anal. Calcd. for $C_{26}H_{17}N_5O$: C, 75.18; H, 4.10; N, 16.87. Found: C, 75.35; H, 4.24; N, 16.59.

9-Methyl-2,4,6-triphenylpyrido[3,2-e][1,2,4]triazolo[4,3-a]-pyrimidine-5(6H)-one (*IV*). 0.8 g (0.0019 mole) of compound **II** was refluxed with excess acetic acid or acetic anhydride and/or acetyl chloride for 5 hours. The reaction mixture was cooled to room temperature whereby a pale yellow precipitate was formed. The product was crystallized from dioxane or benzene to give IV as colourless crystals in 65% yield, mp 313–315°C; ir (KBR): 1685 cm^{-1} (C=O), 1600 cm^{-1} (C=N), 3020 cm^{-1} (CH aliphatic); pmr ($CDCl_3$): δ3.3 (s, 3H, CH_3), 7.85 (s, 1H, pyridine), 7.4–7.7 and 8.1–8.3 (m, 15H, aromatic); ms (FD): m/z (% rel. int.) 429 (100). Anal. Calcd. for $C_{27}H_{19}N_5O$: C, 75.52; H, 4.43; N, 16.32. Found: C, 75.72; H, 4.51; N, 16.77.

Aromatic aldehyde-(3,4-dihydro-4-oxo-3,5,7-triphenylpyrido-[2,3-d]pyrimidine-2-yl)hydrazone (**Va–e**). General Procedure: A mixture of **II** (0.001 mole) and the required aromatic aldehyde (0.001 mole) was refluxed in absolute ethanol in the presence of a few drops of piperidine for 3 hours. The solid product were filtered off and crystallized from the proper solvents (cf. Table I); ir (KBr): 3320 cm^{-1} (NH), 1690 (C=O), 1615 cm^{-1} (C=N); pmr for V ($CDCl_3$): δ7.15 (s, 1H, pyridine), 7.2–7.8 (m, 20H, aromatic), 8.0–8.2 (s, 1H, NHN=CH); ms for Va (FD); m/z (% rel. int.) 493 (100).

9-Aryl-2,4,6-triphenylpyrido[3,2-e][1,2,4]triazolo[4,3-a]pyrimidine-5(6H)-one (**VIa–e**). General Procedure: A mixture of **Va–e** (0.5 g) and thionyl chloride (10 ml) was heated on a water bath for 3 hours. The excess thionyl chloride was removed under reduced pressure and the residue was triturated with petroleum ether (60–80°C). The products were crystallized from the suitable solvents to give **VIa–e** (cf. Table II); ir (KBr) showed bands at: 1700 cm^{-1} (C=O), 1600 (C=N) and no characteristic band for Nh group; pmr for **VIa** (DMSO-d_6): δ7.0–7.7 (m, 20H, aromatic), 7.8 (s, 1H, pyridine); ms for VIa: m/z (% rel. int.) 491 (100), 490 (50), 463 (33), 414 (19), 388 (40), 387 (53), 382 (14), 360 (19), 332 (38).

4,6,8-Triphenylpyrido[3,2-e]tetrazolo[1,5-a]pyrimidine-5(4H)-one (**VII**). To **II** (0.7 g; 0.0017 mole) in concentrated phosphoric acid (10 ml), sodium nitrite solution (1.0 g in 10 ml cold H_2O; 0.01 mole) was added at zero degree during 15 minutes with stirring. The mixture was stirred for a further 3

hours. and the precipitate was filtered off and dried. The solid product was crystallized from benzene to give VII as colourless crystals in 90% yield, mp > 360°; ir (KBr) showed band at 1260 cm^{-1} (tetrazole ring)[12], no absorption band at 2120–2150 cm^{-1} characteristic for azido group, 1705 cm^{-1} (C=O); pmr ($CDCl_3$): δ7.9 (s, 1H, pyridine), 7.4–7.7 and 8.23–8.35 (m, 15H, aromatic). Anal. Calcd. for $C_{25}H_{16}N_6O$: 72.12; H, 3.85; N, 20.19. Found: C, 72.30; H, 3.77; N, 19.99.

Ethyl-5,6-dihydro-5-oxo-2,4,6-triphenylpyrido[3,2-e][1,2,4]-triazole[4,3-c]pyrimidine-9-acetate (**VIII**). **II** (0.0019 mole) was heated with 5 ml of diethylmalonate for 6 hours. The product was crystallized from benzene to give **VIII** as a pale brown product in 60% yield, mp 245°; ir (KBr): 1725 cm^{-1} (C=O, ester), 1200 cm^{-1} (C=O, ester), 3020 cm^{-1} (CH aliphatic), 1605 (cm^{-1} (C=N), 1690 cm^{-1} (C=O); pmr (DMSO): δ0.8–1.0 (t, 3H, CH_3), 3.7–3.95 (q, 2H, CH_2), 4.5 (s, 2H, CH_2), 7.8 (s, 1H, pyridine), 7.2–7.5 and 8.0–8.2 (m, 15H, aromatic). Anal. Calcd. for $C_{30}H_{23}N_5O_3$: C, 89.78; H, 5.74; N, 17.46. Found: C, 89.59; H, 5.59; N, 17.66.

2-(3,5-Dimethyl-1H-pyrazol-1-yl)-3,5,7-triphenylpyrido[2,3-d]-pyrimidine-4(3H)-one (**IX**). A mixture of **II** (0.6 g, 0.0015 mole) and (0.2 ml, 0.002 mole) of acetylacetone was refluxed for 5 hours. The reaction mixture was cooled whereby yellow product separated out, fillered, collected and dried. It was crystallized from benzene as yellow crystals in 50% yield, mp 307°; ir (KBr): 1720 cm^{-1} (C=O), 1660 cm^{-1} (C=N), 3000 $^{-1}$ (CH aliphatic); pmr (DMSO); δ3.0 (s, 6H, $2CH_3$), 6.9–7.3 (m, 15H, aromatic), 7.9–8.05 (2H, 1H pyridine, 1H pyrazole). Anal. Calcd. for $C_{30}H_{23}N_5O$: C, 76.76; H, 4.90; N, 14.93. Found: C, 76.66; H, 4.63: N, 14.81.

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REFERENCES

1. E. Wiedemann, M. Thiel, K. Stack, E. Doesch and K. Hardebech, *Ger. Offen*, I, 962, 057 (1971); *Chem. Abstr.*, **75,** 63811 (1971).
2. K. Noda, A. Nakagwa, T. Motomura, S. Yamazaki, S. Migata and K. Yamagata, Japan Patent, 76, 82, 297 (1976); *Chem. Abstr.*, **86,** 554781.
3. Kh. M. Hassan, M. S. K. Youssef, M. F. El-Zohry and R. Abo El-Wafa *Phosphorous and Sulfur,* **36,** 1988 (Proof).
4. N. P. Peet and S. Sunder, Heterocycles Vol. 24, No. 11 Page 3213–3221 (1986).
5. M. S. K. Youssef, Kh. M. Hassan, F. M. Atta and M. S. Abbady, *J. Heterocyclic Chem.*, **21,** 1565 (1984).