

Pyrimidine Antagonists. Part-IV. Synthesis and Anticancer Screening of Substituted Pyrimidines

(Miss) MAITREYEE DEBI*

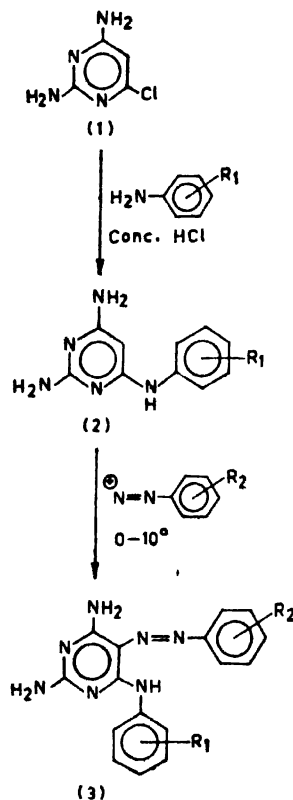
Department of Chemical Technology,
University Colleges of Science and Technology,
92, Acharya Prafulla Chandra Road, Calcutt-700 009

Manuscript received 10 April 1989, revised 9 August 1991,
accepted 3 September 1991

THE antagonistic activity of purines and pyrimidines on nucleic acid metabolism^{1,2} was well-known. The effect of the presence of hydroxyl and/or amino groups in C-2 and C-4 positions of the pyrimidine ring on their biological activities³ have already been documented.

In the present work a number of new 2,4-diamino-6-substituted-phenylamino-5-substituted-phenylazopyrimidines (3) have been prepared by diazocoupling of 2,4-diamino-6-substitutedaminopyrimidines⁴ (2). The structures of the compounds have been established based on their elemental analysis, uv and ir spectral data (Table 1).

Some of the compounds have been screened for their anticancer activity against mouse Leukemia P 388.



* Present address: Civil Engineering Department, National Test House, 11/1 Judges Court Road, Alipore, Calcutta-700 027.

NOTES

TABLE 1—PHYSICAL, ANALYTICAL, AND SPECTRAL DATA OF COMPOUNDS 2 AND 3*

Compd. no.	R ₁	R ₂	M.p.** °C	Yield %	Colour/nature	λ_{\max} nm	ν_{\max} cm ⁻¹
2a	<i>o</i> -NO ₂	—	200 ^a	98	Yellow shining crystal	205, 240, 315	1 350(NO ₂), 1 520
2b	<i>m</i> -NO ₂	—	200 ^a	98	Lemmon yellow crystal	305, 330, 370	1 360(NO ₂), 1 530
3a	<i>p</i> -Br	<i>m</i> -SO ₃ H	225d ^b	82	Orange shining needle	205s, 290 356	520(Br), 640(SO ₃ H), 1 060, 1 185
3b	<i>p</i> -COOH	<i>m</i> -SO ₃ H	163 ^a	80	Orange plate	305s, 420br, 435s	640, 1 050, 1 200, 1 660(CO), 2 650(COOH)
3c	<i>p</i> -NO ₂	<i>m</i> -SO ₃ H	340d ^a	80	Chocolate crystal	205, 305, 420	650, 1 050, 1 210, 1 355, 1 540
3d*	<i>p</i> -OC ₂ H ₅	<i>m</i> -SO ₃ H	270d ^a	75	Brick red plate	278s, 312, 375, 405s	660, 1 040, 1 060(OC ₂ H ₅), 1 170
3e	<i>p</i> -SO ₃ H	<i>m</i> -SO ₃ H	240d ^a	75	Lemmon yellow shining crystal	205, 300, 410	640, 1 030, 1 165
3f	<i>p</i> -SO ₃ NH ₂	<i>m</i> -SO ₃ H	250d ^a	80	Orange crystal	209s, 256, 288, 421s	640, 1 060, 1 130, 1 150, 1 320(SO ₃ NH ₂)
3g	<i>o</i> -NO ₂	<i>o</i> -NO ₂	310d ^a	80	Blood red crystal	205s, 240, 315s, 415	1 350, 1 500, 1 520

*All the compounds gave satisfactory C, N and H analysis. **Solvent for crystallisation: ^aethanol, ^bethyl acetate, ^cdilute HCl; 3c decomposed without melting; 3d turned green when kept in air.

Experimental

Melting points were determined in open capillary tubes and are uncorrected.

The compounds were crystallised from aqueous 95% ethanol. Uv spectra of the compounds were determined on a Shimadzu 210A spectrophotometer and ir spectra (KBr) on a Hitachi 270–30 spectrophotometer.

Trisubstituted-pyrimidine (2) were prepared from 2,4-diamino-6-chloropyrimidine⁵ following earlier procedure⁴. Compound 2a was washed with ethanol and water to remove *o*-nitroaniline and 2b with ethanol and hot water to remove *m*-nitroaniline.

5-Phenylazopyrimidines (3) were prepared from 2 by coupling with substituted-phenyldiazonium salts as reported earlier⁴.

Leukemia P 388 screening: Anticancer activity was determined against Leukemia P 388 following the procedure as adopted earlier⁴. The compounds were tested at doses of 50 (3f), 100 (2b, 3b, 3c), 200 (3a, 3b, 3d) and 400 (2a, 2b, 3b, 3e, 3g) mg/kg. Compound 2b was found to be toxic and all others were found to be inactive at the doses tested.

Acknowledgement

The author is grateful to Dr. A. Basu and Dr. T. K. Bhattacharjya of this department for facilities and ir spectra and to Dr. S. Roy, Indian Association

for the Cultivation of Science, Calcutta, for uv spectra. Leukemia screening was performed under the auspices of Therapeutics Program, Division of Cancer Treatment, National Cancer Institute, Bethesda, U.S.A.

References

1. N. R. LONAX and V. L. NARAYANAN, "Chemical Structures of Interest to the Division of Cancer Treatment", National Cancer Institute, U. S. A., 1988, Vol. VI.
2. M. DEBI, *J. Indian Chem. Soc.*, 1989, **66**, 418
3. D. SEN, A. DASGUPTA and P. SENGUPTA *Indian J. Chem., Sect. B*, 1985, **24**, 952; DE O'BRIEN and C. C. CHENG, *J. Med. Chem.*, 1966, **9**, 575.
4. M. DEBI, *J. Indian Chem. Soc.*, 1987, **64**, 612; 1989, **66**, 489.
5. B. ROTH, J. M. SMITH, and M. E. HULTQVIST, *J. Am. Chem. Soc.*, 1950, **72**, 1915.