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NOTE

Synthesis and Biological Activity of Some Substituted Phenyl Ureas

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Synthesis and anti-AIDS, anti-cancer, fungicidal, anti-bacterial activities of some new substituted α(2′-chloro-5′-nitro) benzamido-4-N,N-bis-2′-cyano-ethylaminocinnamo substituted phenylureas are reported.

Oxazolones and their derivatives have been shown to exhibit various types of biological activities.[1] In view of the effectiveness of drugs with cyanoethyl moiety[2], some new substituted α-(2′-chloro-5′-nitro)benzamido-4-N,N-bis-2′-cyanoethylaminocinnamo substituted phenylureas were synthesised by reacting 2-(2′-chloro-5′-nitro)phenyl-4-(*p*-N,N - bis - 2′ - cyanoethylaminobenzylidene) - 5-oxazolone[3] with hydrazine which furnished α-(2′-chloro-5′-nitro)benzamido-4-N,N-bis-2′-cyanoethylaminocinnamo hydrazide (1) which on treatment with nitrous acid gave α-(2′-chloro-5′-nitro)benzamido-4-N,N-bis-2′-cyanoethyl-aminocinnamoazide (2) which later on treatment with aromatic amines furnished α-(2′-chloro-5′-nitro)benzamido-4-N,N-bis-2′-cyanoethylaminocinnamo substituted phenylureas (3a–j). (Scheme-1). Structures of new products were confirmed by elemental analysis and by spectral studies.

Biological activities

Anti-HIV activity: The compounds 1, 2, 3f and 3h were screened for antiviral activity for AIDS which involved susceptible human host cells. The response of the compound on the infected plates was 21.77, 25.09, 12.93 and 13.88% respectively as compared to the standard AZT.

Anti-tubercular activity: The compounds (1, 2, 3a and 3i) were incorporated into Lowenstin-Jension egg medium having concentrations of 10 and 100 μg mL^{-1} and were inoculated with *Mycobacterium tuberculosis* H_{37} RV strain incubated at 37°C and observed weekly for the growth of organism for eight weeks. The compounds were found to be inactive at the concentraion used.

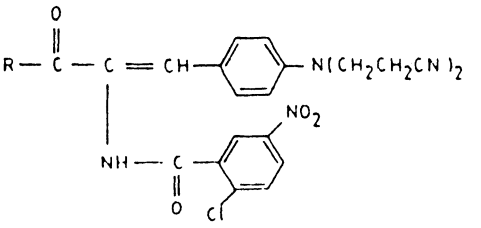
Fungicidal activity: Compounds 1, 2, 3a, 3c, 3e, 3g and 3h were evaluated by Agar plate food poisoning method[4] in 500, 750 and 1000 ppm concentrations. All compounds were found active (19–55%) against *Alternaria alternata*, *Rihizopus arrhizus* and *Aspergillus niger* at the concentrations tested.

Antibacterial activity: All compounds were tested for their antibacterial activity against the gram positive *S. aureus* and gram-negative *E. coli* using cup-plate method.[5] The control was found in the range of 30–45%.

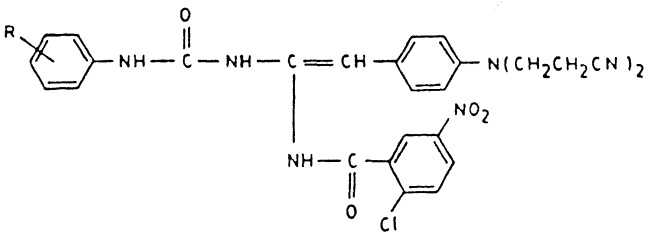
Anticancer activity: The compounds were tested for anticancer activity which involved different cell lines (lung, colon, malonoma, ovarian, renal). The compounds did not show significant anticancer activity.

The melting points of all the compounds were uncorrected. The IR spectra were taken on the Perkin-Elmer-577 model spectrophotometer, PMR on FX-100 model and elemental analysis were carried out by CEST 110 Model.

SCHEME-1



1. R = —NH—NH_2
2. R = —N=N^{+}=N^{-}



3a. R = H
3b. R = CH_3 (2)
3c. R = CH_3 (3)
3d. R = CH_3 (4)
3e. R = OCH_3 (2)
3f. R = OCH_3 (3)
3g. R = OCH_3 (4)
3h. R = Cl (2)
3i. R = Cl (3)
3j. R = Cl (4)

α-(2′-*Chloro*-5′-*nitro*) *benzamido*-4-*N*,*N* - *bis* - 2′ - *cyanoethylaminocinnamo-hydrazide*(1): The oxazolone (1.0 g) and diethylether (8 mL) were taken in a porcelain dish and a solution of hydrazine hydrate (1 mL, 85%) was added dropwise with constant stirring. The deep orange colour of the oxazolone faded after some time and the solid separated. The contents were allowed to remain at room temperature for ten minutes, the solid was filtered under suction, washed with water and recrystallised from ethanol as light orange crystals: (62.24%); m.p. 160°C (Found: C, 54.69; H, 4.09; N, 20.27; Cl, 7.41%; $C_{22}H_{20}N_7O_4Cl$ requires: C, 54.77; H, 4.14; N, 20.33; Cl, 7.46%); ν_{max} (KBr) 725 (disubstituted phenyl), 822 (—Cl), 1335 (—N<), 1515 (—NO_2), 1600 (phenyl), 1760 (>C=O), 2220 (—CN), 2900 (>CH_2) and 3300 cm^{-1} (—NH).

α-(2′-*Chloro*-5′-*nitro*)*benzamido*-4-*N*,*N*-*bis*-2′-*cyanoethylaminocinnamo-hydrazide* (2): Solution of the hydrazide (1) (1.0 g) in acetic acid (8 mL) was cooled and treated with a solution of sodium nitrite (0.4 g) in water (2 mL). The contents were left in an ice bath maintaining low temperature (0–5°C) and after a few minutes a red precipitate separated out. It was filtered under suction, washed with cold water and recrystallized from ethanol. (70.99%); m.p. 180°C

(Found: C, 53.45; H, 3.39; N, 22.66; Cl, 7.35 %; $C_{22}H_{17}N_8O_4Cl$ requires: C, 53.54; H, 3.44; N, 22.71; Cl, 7.30%); ν_{max} (KBr) 730 (disubstituted phenyl), 820 (—Cl), 1340 (—N<), 1510 (—NO_2), 1600 (phenyl), 1760 (>C=O), 2220 (—CN), 2900 (>CH_2) and 3300 cm^{-1} (—NH).

α-(2′-Chloro-5′-nitro)benzamido - 4- N,N - bis - 2′-cyanoethylaminocinnamophenyl urea (3a): A mixture of azide (2) (0.493 g, 0.001 mol.) and aniline (0.093 g, 0.001 mol.) was heated on a water bath till the evolution of nitrogen ceased. On cooling and acidification with aqueous hydrochloric acid a brown product separated. It was filtered under suction and recrystallised from ethanol as brown needles: (44.8%), m.p. 105°C (found: C, 60.19; H, 4.29; N, 17.49; Cl, 6.49%; $C_{28}H_{24}N_7O_4Cl$ requires: C, 60.21; H, 4.30; N, 17.56; Cl, 6.45%); ν_{max} (KBr) 750 (disubstituted phenyl), 810 (—Cl), 1350 (—N<),.1510 (NO_2), 1590 (Phenyl), 1650 (>C=O), 2240 (—CN) and 3300 cm^{-1} (—NH). PMR ($CDCl_3$) δ 9.84 (S due to —NH), 7.1–7.2 (m, due to Ar—H). 6.75 (S due to Ph CH=), 3.91 and 2.73 (2t, due to CH_3).

The other substituted ureas were prepared by following a similar procedure.

3b,	$C_{29}H_{26}O_4N_7Cl$,	yield 40%,	m.p. 154°C;
3c,	$C_{29}H_{26}O_4N_7Cl$,	yield 37%,	m.p. 145°C;
3d ,	$C_{29}H_{26}O_4N_7Cl$,	yield 47%,	m.p. 165°C;
3e,	$C_{29}H_{26}O_5H_7Cl$,	yield 37%,	m.p. 225°C;
3f,	$C_{29}H_{26}O_5N_7Cl$,	yield 34%,	m.p. 115°C;
3g,	$C_{29}H_{26}O_5N_7Cl$,	yield 49%,	m.p. 110°C;
3h,	$C_{28}H_{23}O_4N_7Cl_2$,	yield 28%,	m.p. 190°C;
3i,	$C_{29}H_{23}O_4N_7Cl_2$,	yield 22%	m.p. 125°C;
3j,	$C_{28}H_{23}O_4N_7Cl_2$,	yield 30%,	m.p. 130°C.

All these compounds also gave satisfactory elemental analyses.

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