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Synthesis, Anti-Cancer and Anti-HIV Activities of Some New Formazans

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A series of 1-phenyl-3-(2-methoxy-4-N,N′-bis-2-cyanoethyl-aminophenyl) 2-hydroxy-5-bromobenzoformazan have been synthesised by reacting 2-methoxy-4-N,N′-bis-2′-cyanoethyl aminobenzaldehyde with 5-bromosalicyl-hydrazide which gave respective acid hydrazone. The acid hydrazone on reaction with diazotized aromatic amines furnished formazans in good yield.

INTRODUCTION

Acid hydrazones have been found to possess antimicrobial properties.[1] Certain compounds bearing cyanoethyl group have shown promising anticancer activity.[2] Some hydrazones of benzaldehyde and salicylaldehyde have been screened for their activity against a large number of micro-organisms.[3] Formazans are used as dyes[4] and as chelating agents.[5] Formazans have been found to possess antiviral[6], antimicrobial[7, 8] and anti-inflammatory[9] activities. Some products from 2-methyl-4-N,N′-bis-2′-cyanoethylaminobenzaldehyde have shown anticancer activity which prompted the use of these aldehydes for synthesis of new formazans. Products of farmazans such as imidazolones, Schiff bases have claimed to possess high degree of anticancer and anti-HIV and antimicrobial activities. Recently a number of new formazans have been synthesised for assessing their antiviral activity, Hongo[12] and co-workers have referred to the activity of certain formazans against cancer cells. The present study records the reaction of 2-(methoxy-4-NN′-bis-2′-cyanoethylaminobenzaldehyde) (I) and 5-bromosalicyl hydrazide(II) which gave the acid hydrazone(III). The acid hydrazone on treatment with diazotised aromatic amines in pyridine medium furnished formazans(IV) (Table-1). The reaction sequence has been outlined in Scheme-I.

EXPERIMENTAL

5-Bromosalicylhydrazide and 2-methoxy-4-NN′-bis-2-cyanoethylamino-benzaldehyde were prepared by procedures given in the literature.

*Synthesis of 5-bromosalicylhydrazone of 2-methoxy-4-*NN′*-bis-2-cyanoethyl- aminobenzaldehyde:*

2-methoxy-4-NN′-bis-2′-cyanoethylaminobenzaldehyde (2.41 g, 0.01 Mole) and 5-bromosalicylhydrazide (2.31 g, 0.01 mole) were dissolved separately in

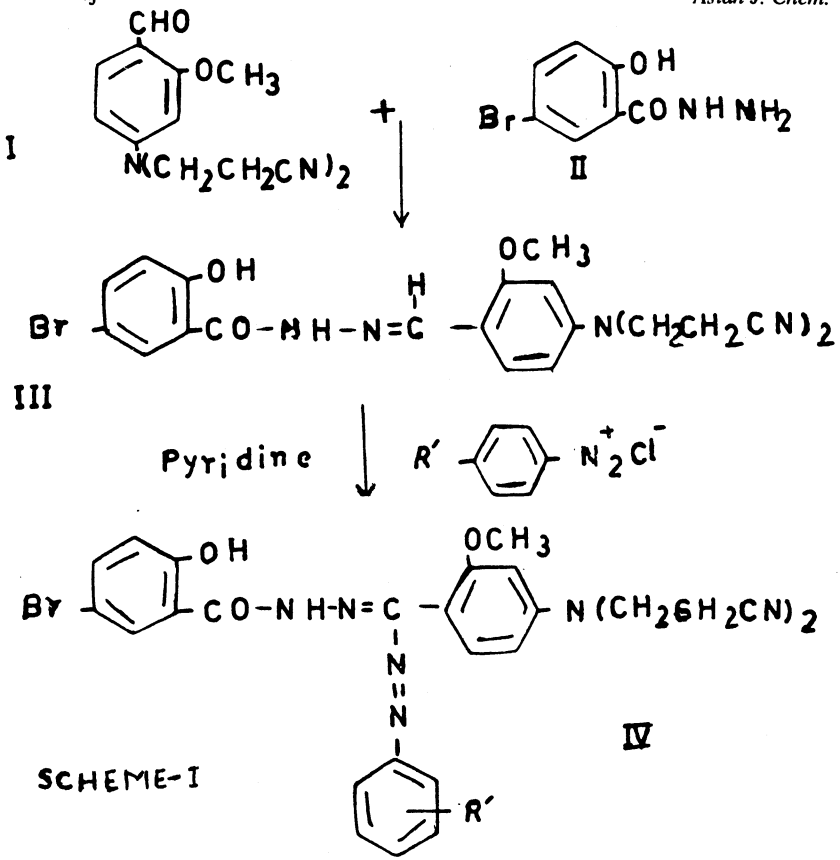

TABLE-1
PHYSICAL DATA OF FORMAZANS

S. No.	R^1	Yield (%)	m.p. (°C)	Colour
1.	H	50	138	light yellow
2.	$CH_3(o)$	50	142	light yellow
3.	$CH_3(m)$	50	130	yellow
4.	$CH_3(p)$	50	145	brown
5.	Cl(*o*)	90	104	dark brown
6.	Cl(*m*)	50	98	brown
7.	Cl(*p*)	60	118	light yellow
8.	$OCH_3(o)$	50	200	light yellow
9.	$OCH_3(m)$	70	135	dark brown
10.	$OCH_3(p)$	60	130	dark brown
11.	$NO_2(o)$	50	98	dark brown
12.	$NO_2(m)$	60	108	dark brown
13.	$NO_2(p)$	40	106	orange yellow
14.	COOH(*o*)	50	204	light yellow
15.	COOH(*p*)	40	124	light yellow

1. All compounds gave satisfactory elemental analysis.
2. Solvent for crystallisation—ethanol.

ethanol (10 mL). The solutions were mixed and refluxed for 15 min. On cooling, the separated solid was filtered under suction and recrystallised from rectified spirit; m.p. 210°C, yield 80%. Analysis: found (%) C 51.2, H 5.1, N 16.0, Br 16.0; required(%) C 53.6, H 4.3, N 14.9, Br 17.0.

IR ν_{max} (cm^{-1}) ν(N—H) 3325–3320 cm^{-1}, ν(OCH_3) 2820–2810 cm^{-1}, ν(C=O) 1670–1660 cm^{-1}, ν(C—N) 1380–135 cm^{-1}, ν(C=N) 1610–1600 cm^{-1}, ν(C—OH) 3500 cm^{-1}, (halogen Br) 725 cm^{-1}.

Synthesis of 1-phenyl-3-(2--methoxy-4-NN'-bis-2-cyanoethylaminophenyl)-5-(2-hydroxy-5-bromobenzoformazan):

Aniline (0.46 g, 0.01 mole) was dissolved in aqueous hydrochloric acid (4 mL 1 : 1); the contents were cooled and aqueous sodium nitrite (0.3 g in 2 mL water) was slowly added.

2-Methoxy-4-NN'-bis-2'-cyanoethylaminobenzalidene-5-bromosalicylhydrazone (0.57 g) was dissolved in dry pyridine (10 mL) and sodium acetate (0.3 g) was added. The contents were cooled in ice bath and stirred. Clear and cold solution of benzene diazonium chloride was added drop by drop for 30 min maintaining low temperature (0°C). The reaction mixture was kept in the ice bath for 4 h and then poured with stirring in water. The resulting dark coloured mass was washed with water till free from pyridine, filtered under suction and dried. The product was crystallised from ethanol, m.p. 138°C, yield 50%. Analysis: found (%) C 57.1, H3.9, N 16.8, Br 12.2; required(%) C 56.4, H 4.4, H 17.0, Br 13.8 mol. formula $C_{21}H_{20}N_5O_3Br$. IR spectra were recorded on Perkin-Elmer Model 1720 x FT IR infracord spectrophotometer. The product shows IR bands. ν (C—OH) 3500 cm^{-1}, ν (N—H) 3325–3320 cm^{-1}, ν(C=O) 1680–1670 cm^{-1}, ν(C=N) 1610–1600 cm^{-1}, ν(N=N) 1570–1560 cm^{-1}, ν (C—N) 1350–1330 cm^{-1} (halogen—Br) 738 cm^{-1}.

Most of the compounds are low melting solids of light to dark brown and yellow colour. Formazans are highly soluble in acetone and ethanol.

*Anticancer Activity** Seven formazans (Nos. 1, 4, 7, 9, 10, 13, 15) were tested for their anticancer activity. The compounds did not show significant anti-cancer activity.

*Anti-HIV activity**: Seven formazans (Nos. 1, 4, 7, 9, 10, 13, 15) were tested for anti-HIV activity. The compounds did not show significant HIV activity.

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