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REACTION OF 2-METHYL-2-AMINO-1,3-PROPAN-DIOL WITH ALDEHYDES AND KETONES SYNTHESIS OF OXAZOLIDINE AND IMIDAZOLINE DERIVATIVES AS ANTIMICROBIAL AGENTS

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Aromatic aldehydes as well as ketones reacted with 2-methyl-2-amino-1,3-propandiol to give monoxazolidine or di-oxazolidine derivatives according to molar ratio. Aromatic amines, hydrazine hydrate and ammonium hydroxide, reacted with oxazolidines to give the corresponding imidazolidines, triazines and pentazines. The antimicrobial character of the prepared products was studied.

Key words: Methyl, Amino, Aromatic addehydes Ketones, Antimicrobial Character.

INTRODUCTION

The dihydric alcohol, propane-1,3-diol, and its 2-amino derivatives are reactive intermediates and have wide applications [1,2,4,5,7,8]. Badr *et. al.* [11], and Pierce [6] reported that the condensation of 2-amino-2-methylol-1,3-propane-diol with aldehydes afforded oxazolidines by loss of one mole of water between molar quantity of an aldehyde and amino alcohol, and two moles of water from condensation of two moles of aldehydes and one mole of 2-amino-propan-triol to form dioxazolidines. In continuation of the work on the chemistry of azalactone [16,17], imidazoline [9,10] and in oxazolidine [6,11], 2-amino-2-methyl-1, 3-propane-diol was subjected to reactions for the preparation of these derivatives.

EXPERIMENTAL

Melting points were determined on an open capillary tube on a thermal electric melting point apparatus Galenkamp, and are uncorrected. The infrared spectra were determined in a solid KBr disc with a Beckman infrared spectrophotometer 1180 and a 390-90 MHZ spectrometer was used for ^{1}H.N.M.R. determinations.

2.1. Synthesis of mono-oxazolidines II_{a-f}. A mixture of amino alcohol (1) (0.01 mol) and appropriate aldehyde or ketone (0.01 mol) was heated on a water bath till complete fusion (cap.20 min). After cooling, the monooxazolidines so formed (II_{a-f}) were extracted with ethanol and isolated (cf. Table 1).

I.R. spectrum of II_a, showed absorption bands at 2950 cm^{-1} (ν -CH_2), 1595 cm^{-1} (ν -NH) bending in plane, 3435 cm^{-1} (ν -NH) stretching, 3660 cm^{-1} (ν -OH) and at 2350 cm^{-1} (ν -CH_3), I.R. spectrum of II_f showed characteristic peaks at 1590 cm^{-1} (ν -NH) bending in plane, at 3450 cm^{-1} (ν -NH) stretching, at 2340 cm^{-1} (ν -CH_3), 2925 cm^{-1} (ν -CH_2) and at 3580 cm^{-1} (ν-free OH). ^{1}H.N.M.R. spectrum of II_f showed doublet signals at δ 2.65 (S, 3H.C$\underline{H}_3$), and overlapped double signals at δ 3.35 (S, 4H, 2-CH_2). One of the CH_2 groups is in the cyclic-CH_2-O-form, besides a multiplet signals at δ 7.4-7.6 (m, 4H, C_6H_4 of biphenyl) and the other multiplet signals at δ 7.7-7.9 (S, 5H, $C_6\underline{H}_5$) of biphenyl) and finally a singlet signal at δ 8.1 (S, 1H, N$\underline{H}$).

2.2 Synthesis of di-oxazolidines (III_{a-f}). Method A. Aminodialcohol (I), (0.01 mol), and the appropriate aldehyde or ketone (0.021 mol) were heated on a steam bath till complete fusion and the reaction is completed as in procedure 1.

Method B. Monoxazolidine derivatives (II_{a-f}) (0.01 mol) and an appropriate aldehyde or ketone (0.01 mol) were heated on a steam bath till complete fusion; then the procedure was completed as in 1.

I.R. spectrum of III_a and III_e showed characteristic bands of -CH_2 and CH_3 groups at 2960 cm^{-1} (III_a ν -CH_2), 2945 cm^{-1} (III_e ν -CH_2) and at 2365 cm^{-1} (III_a ν -CH_3), 2350 cm^{-1} (III_e, ν CH_3). ^{1}H.N.M.R. spectrum of III_d showed a doublet signals at δ 1.1.-1.2 (S, 6H-2-C$\underline{H}_3$-C-O- of ketone), singlet signal at δ 2.45 (m, 3H, -CH_3-C-), besides doublet signals at δ 3.3 and at δ 3.5 (m, 4H, 2-C$\underline{H}_2$ of -C-CH_2-O-) and multiplet signals at δ 6.55-6.7 (S, 4H, $C_6\underline{H}_4$) and at δ 7.65-7.8 (S, 4H, $C_6\underline{H}_4$).

2.3. Action of phthaldehyde: synthesis of IV. Equimoles of (I) and phthaldehyde were heated on a steam bath till complete fusion (cap. 2 hr), the product obtained was extracted with benzene. Excess benzene was distilled off completely and the separated yellow oil was left overnight

to solidify and on recrystallization from ethanol gave with crystals of m.p. 64-50° in 86 % yield.

Analysis for $C_{12}H_{13}NO_2$ (203)

Calc. C, 70.93 % ; H, 6.40 % ; N, 6.89

Found C, 70.82 ; H, 6.36 % ; N, 6.78

2.4. Action of aromatic amines on II_a and III_{a-c}

(A) *Synthesis of imidazoline derivative VI_a.* Equimoles of aromatic amine (*p*-aminoacetophenone) and II_B were refluxed in absolute ethanol (Riedel) for 5 hr. After cooling, the reaction mixture was poured into ice-cold water and the separated solid product was filtered, washed with water and then ethanol till it become colourless. Compound VI was crystallised from methanol as orange cyrstals m.p. 67.8° in 66 % yield.

Analysis for $C_{21}H_{27}N_3O_2$ (353)

Calc. C, 71.38 % ; H, 7.64 % ; N, 11.89 %

Found C, 71.41 ; H, 7.56 % ; N, 12.02 %

H^1.N.M.R. of IV showed singlet signal at δ 2.55 (3H, $C\underline{H}_3$ of $-CH_3-C-$), singlet signal at δ 3.1(V.S. 9H, -6H, $N\lessgtr^{CH_3}_{CH_3}$ and 3H for $-\overset{O}{\overset{\|}{C}}-C\underline{H}_3$), singlet signal at δ 3.4 (S, 2H, $-C-C\underline{H}_2-N-$) besides a singlet signal at δ 3.6 (m, 2H, $-C\underline{H}_2$), also a doublet signals at δ 6.7-6.9 (4H, $C_6\underline{H}_4$), multiplet signals at δ 7.6-8.1 (S, 5H, $C_6\underline{H}_4$ of $C_6H_4-N\lessgtr^{CH_3}_{CH_3}$ and 1H of $C\underline{H}$ of imidazoline ring) and finally a weak signal at δ 8.5 (1H, $N\underline{H}$).

(B) Synthesis of 1,3,5-triazine-derivatives VII_{a-c}: III_{a-c} (0.01 mole) and aromatic amines (0.022 mole) (*p*-aminodiphenylamine, *p*-aminoacetophenone) were refluxed in absolute ethanol (Riedel, 50 ml) for 6 hrs. After cooling and pouring into ice-cold water the separated solid products were recrystallized from benzene (VII_a) and from methanol (VII_c). For physical data, see Table 3.

Synthesis of VII_b. Furfurylamine (.022 mol) and III_b (0.02 mol) in absolute ethanol (Riedel), (50 ml) were refluxed for 4 hr. After cooling and acidification by dilute hydrochloric acid till complete solubility, filtration was resorted to remove any impurities. Neutralization of the filtrate with Na_2CO_3 solution gave a solid product in 58 % yield. On crystallization from ethanol buff briliant crystals were obtained, m.p. 66.67°

Analysis for $C_{32}H_{39}N_5O_2$ (525)

Calc. C, 73.14 % ; H, 7.42 % ; N, 13.33 %

Found C, 73.26 % ; H, 7.31 % ; N, 13.28 %

(iii) *Action of hydrazine hydrate: synthesis of X_{a-b}, XI_{a-e}.* Oxazolidine derivatives (II_{b-f}) (III_{a-e}) (0.01 mol) and hydrazine hydrate (1 ml) in absolute ethanol (Riedel) (25 ml) were refluxed untill the reaction mixture was clear (cap. 3.5 hr). After cooling and pouring into ice-cold water, the separated solid products were recrystallized from ethanol.

Action of ammonium hydroxide; synthesis of imidazoline derivatives, $(XIII)_{a,b}$). Oxazolidine derivatives (II_a, $III_{a,b}$), (0.01 mol) and excess ammonium hydroxide (10 ml) in ethanol (50 ml) were refluxed for 3 hr, then an additional quantity of ammonium hydroxide (10 ml) was added, and refluxing continued for further 3 hr. After cooling and leaving overnight in an ice-chest, the separated solid product was filtered and washed with water XII, pale yellow crystals from an aqueous ethanol in 52 % yield, m.p. 81.82°.

Table 1. Physical data

Comp. No.	R	Ar.	M.P°C	Yield %	Molecular formula		Analysis % C	H
II_a	H	C_6H_5	Yellow oil	68	$C_{11}H_{15}NO_2$	Calc.	66.30	8.28
						Found	66.22	8.51
II_b	H	$C_6H_4-N\lessgtr^{CH_3}_{CH_3}$	Yellow oil	85	$C_{13}H_{20}O_2$	Calc.	66.10	8.47
						Found	66.28	8.32
II_c	H	C_6H_4-Br (p)	87-8	89	$C_{11}H_{15}BrNO_2$	Calc.	48.35	5.49
						Found	48.26	5.52
II_d	CH_3	$C_6H_4NH_2$ (p)	100-1	85	$C_{12}H_{18}N_2O_2$	Calc.	64.68	8.10
						Found	64.51	7.92
II_e	CH_3	$C_6H_4NO_2$ (p)	75-6	77	$C_{12}H_{16}N_2O_4$	Calc.	57.14	6.35
						Found	57.27	6.17
II_f	CH_3	$C_6H_4-C_6H_5$ (p)	115	88	$C_{18}H_{21}NO_2$	Calc.	75.79	7.42
						Found	75.96	7.56

Table 2. Physical data

Comp. No.	R	Ar.	M.P°C	Yield %	Molecular formula		Analysis % C	H
III_a	H	C_6H_5	120-1	52	$C_{18}H_{19}NO_2$	Calc.	76.86	6.76
						Found	76.88	6.88
III_b	H	C_6H_4-N$<^{CH_3}_{CH_3}$	Yellow viscous Oil	81	$C_{22}H_{29}N_3O_2$	Calc.	71.93	7.90
						Found	72.04	7.78
III_c	H	C_6H_4-Br (p)	178-9	55	$C_{18}H_{9\,17}Br_2NO_2$	Calc.	49.20	3.87
						Found	48.98	3.82
III_d	$-CH_3$	$C_6H_4NH_2$ (p)	88-9	69	$C_{20}H_{25}N_3O_2$	Calc.	70.79	7.37
						Found	70.89	7.32
III_e	$-CH_3$	$C_6H_4NO_2$ (p)	69-70	55	$C_{20}H_{21}N_3O_6$	Calc.	60.15	5.26
						Found	60/27	5.19
III_f	$-CH_3$	C_6H_4-C_6H_5 (p)	110	62	$C_{32}H_{31}NO_2$	Calc.	83.29	6.72
						Found	83.21	6.64

Table 3. Physical data

Comp. No.	Colour	M.P. (°C)	Yield %	Molecular formula	R	Analysis % Calc.	Found
VII_a	Green Yellow	188-9	62	$C_{46}H_{49}N_7$	$-NHC_6H_5$	C, 78.97	78.91
						H, 7.01	7.01
						N, 14.02	13.96
VII_c	Orange	175-6	68	$C_{38}H_{43}N_5O_2$	$-\overset{O}{\overset{\|}{C}}-CH_3$	C, 75.87	75.92
						H, 7.15	7.09
						N, 11.64	11.70

Analysis for $C_{13}H_{21}N_3O$
Calc. C, 66.38 % ; H, 8.93 ; N, 10.21 %
Found C, 66.50 % ; H, 8.75 ; N, 10.42 %

$(XII)_a$, white crystals from ethanol, in 55 % yield, m.p. 93-4°,
Analysis for $C_{18}H_{21}N_3$
Calc. C, 77.42 % ; H, 7.52 % ; N, 15.05 %
Found C, 77.46 % ; N, 7.41 % ; N, 14.98 %

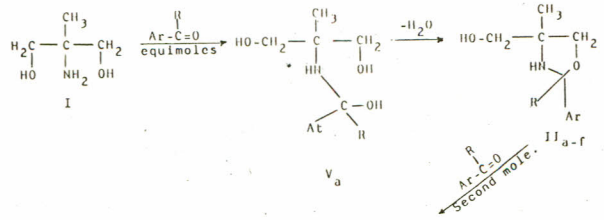
$XIII_b$, Brilliant white needles from ethanol/acetone mixture (3:2) in 59 % yield ; m.p. 67.8°
Analysis for $C_{22}H_{31}N_5$
Calc. C, 72.73 % ; H, 8.49 % ; N, 19.17
Found C, 72.71 % ; H, 8.51 % ; N, 19.10 %

I.R ; 1365 cm^{-1} (ν-gem-dimethyl), 1595 cm^{-1} (ν-C-NH), 1630 cm^{-1} (ν-Sec. NH) bending, 3400 cm^{-1} (ν-NH) stretching.

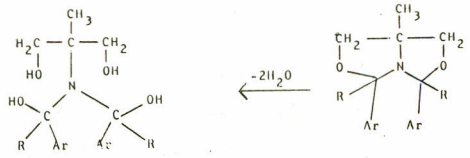
H^1.N.M.R., δ 3.1 (V.S., 12H, 2-N$<^{CH_3}_{CH_3}$), δ 3.3 (S, 4H. 2-CH_2), δ 6.8 (V.S., 4H, C_6H_4), δ 7.7 (V.S., 4H, C_6H4).

DISCUSSION

2-Amino-2-methyl propane-1, 3-diol (I) condenses with aromatic aldehydes or ketones under mild conditions to give either mono-(II_{a-f}) or dioxazolidines (III_{a-f}) according to the molar ratio of the carbonyl derivative used. Equimolar ratio from the reactants favours the formation of monoxazolidines (II_{a-f}), 3-methyl-3-methylol-1-oxa-4-azaspiro-5-substituted phenyl 4,5 decan (II_{a-c}) and 3-methyl-3-methylol-1-oxa-4-azaspiro-5-methyl-5-substituted phenyl 4,5 decan (II_{d-f}).



I $\quad$ V_a $\quad$ II_{a-f}



V_b $\quad$ III_{a-f}

III_a, Ar; C_6H_5-R=H

b, Ar; C_6H_4-N(CH$_3$)$_2$ (p), R=H

c, Ar; C_6H_4-Br (p), R=H

d, Ar; C_6H_4-NH_2(p), R=-CH_3

e, Ar; C_6H_4-NO_2(p), R=-CH_3

f, Ar; C_6H_4-C_6H_5(p), R=-CH_3

II_a, Ar, a; C_6H_5, R=H

b, Ar=C_6H_4-N(CH$_3$)$_2$ (p), R=H

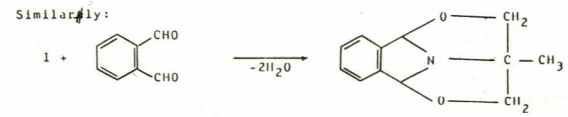
c, Ar=C_6H_4-Br (p), R=H

d, Ar=C_6H_4-NH_2(p), R=-CH_3

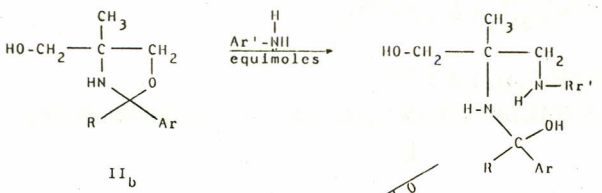
e, Ar=C_6H_4-NO_2(p), R=-CH_3

f, Ar=C_6H_4-C_6H_5(p), R=-CH_3

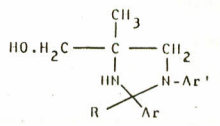
Similarly:



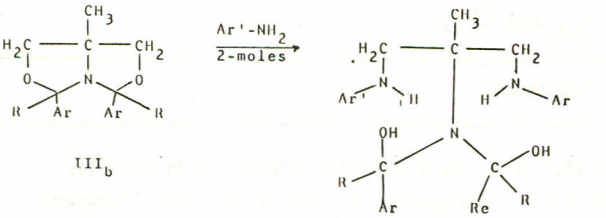
Scheme $\quad$ IV



II_b $\quad$ VIII



VI



III_b $\quad$ IX $\quad$ VII_{a-c}

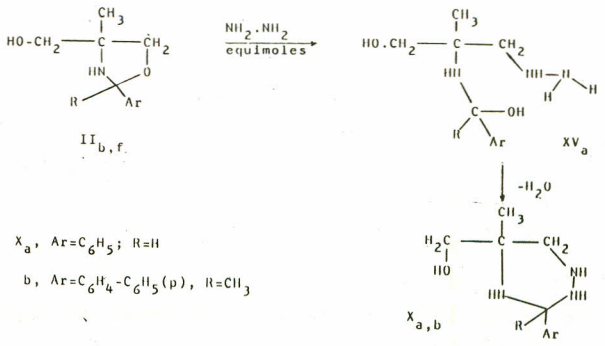
VI, a, Ar' =-C_6H_4-CO-CH_3 (p), R=H

VIII, a, Ar' = C_6H_4-NH.C_6H_5, R=H

b, Ar' =-CH_2- , R=H

c, Ar' = C_6H_4-CO-CH_3 (p), R=H

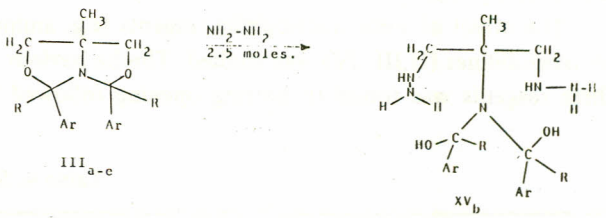
Scheme 2



$II_{b,f}$ $\quad$ XV_a $\quad$ $X_{a,b}$

X_a, Ar=C_6H_5; R=H

b, Ar=C_6H_4-C_6H_5(p), R=CH_3



III_{a-e} $\quad$ XV_b $\quad$ XI_{a-f}

XI_a, Ar=C_6H_5; R=H

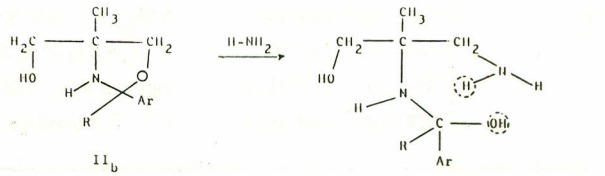
b, Ar=C_6H_4-N(CH$_3$)$_2$ (p); R=H

c, Ar=C_6H_4-Br (p); R=H

d, Ar=C_6H_4-NH_2(p); CH_3

e, Ar=C_6H_4-NO_2(p); R=-CH_3

Scheme 3

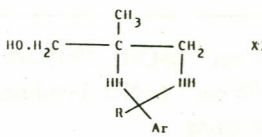


II_b $\quad$ XVI_a

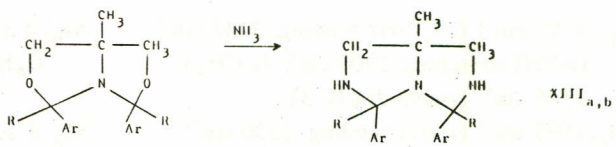
XII, Ar=C H -N(CH$_3$)$_2$ (p), R=-H

Dehydration

$-H_2O$



XII



$XIII_{a,b}$

$XIII_a$, Ar=C_6H_5; R=H

b, Ar=C_6H_5-N(CH$_3$)$_2$ (p); R=-H.

Scheme 4

Condensation of two moles of the carbonyl derivatives with one mole of the amino alcohol (I) gave di-oxazolidines (III_{a-f}), namely, the 3-methyl-6,8-disubstituted phenyl-7-aza-1,5-dioxa-bicyclo (3,7) octanes (III_{a-c}), and the 3-methyl-6,8-dimethyl-6,8-disubstituted phenyl-7-azaspiro-1,5-dioxa-bicyclo (3,7) decanes (III_{d-f})-o-Dioldehydes, e.g. phthalaldehyde reacted with the aminodialcohol (I) in equimolar ratio with the loss of two moles of water and gave 3-methyl-1,5-dioxa, 7-azaspiro-bicyclo [3,7], 1,8-5,6-benzpyrrolidine (IV).

Structure assignment of oxazolidines II_{a-f},and IV was based on similarity to the work of Badr *et. als.* [11] in the current literature, and from elemental and spectral analysis [3,12,15].

The effect of some nucleophilie reagents (e.g. amines) on oxazolidines (II,III, IV) was studied. The be haviour of these reagents was found to be ring opening followed by recyclization to give the corresponding mono- or di-imidazolidines (VI) and (VII) respectively. The reaction mechanism can be represented by scheme 2.

As a confirmation of this reaction mechanism we were able to synthesise the 1,3,4-triazine derivatives (X) and pentazines ($XI_{a,c}$) by the interaction of hydrazine hydrate with oxazolidine derivatives ($II_{b,f}$) and (III_{a-e}) which can be represented by scheme 3).

Amines as nucleophilic reagents attack the oxazolidine ring to form imidazolidine. This is done by ring opening followed by recyclisation by water elimination as indicated in the scheme.

Similar to oxazolon-4-ones [10b], oxazolidine derivatives (II_b), and ($III_{a,b}$) reacted with ammonium hydroxide to give imidazoline derivatives XII_a and $XIII_{a,b}$[9] probably through the formation of intermediates $XVI_{a,b}$ (c.f. scheme 4).

Table 4. Spectral data of VII_{a-c}.

Comp. No.	I.R.	^{1}H.N.M.R./in DMSO
VII_a	– 1485 cm^{-1} (ν-CH), – 1595 cm^{-1} (ν-C-N), – 2350 cm^{-1} (ν-CH_3), – 2900 cm^{-1} (ν-CH_2),	δ 3.1 (V.S, 12H, 4-C$\underline{H}_3$ of 2.N$\langle^{CH_3}_{CH_3}$), δ 2.5 (3H), -CH_3, CH_3-C-), δ 6.7-6.8 (S,4H,$C_6\underline{H}_4$), δ 7.7-7.8 (S,4H,$C_6\underline{H}_4$), δ 7.0-7.5 (N,S,20H,18($C_6\underline{H}_4$-N.$C_6\underline{H}_5$) and 2-CH of imidazole ring. H
VII_c	– 1595 cm^{-1} (ν-C-N), – 1660 cm^{-1} (ν-C-O), – 2350 cm^{-1} (ν-CH_3), – 2900 cm^{-1} (ν-CH_2),	VII_b, δ 2.2(V.S,12H + 2- N($C\underline{H}_3$)$_2$, δ 2.5 (S,3H, -$C\underline{H}_3$-CH_3-C-), δ 3.3 (S,4H, 2-$C\underline{H}_2$), δ 6.8-doublet signal (V.S., 10H,2-$C_6\underline{H}_4$, -2-C$\underline{H}$ of imidazoline), δ 7.-7.5 doublet signals, (V.S.6H,2(3-C$\underline{H}$) furan).

Table 5. Spectral data of $X_{a,b}$ and XI_{a-e}.

I.R. Spectrum	^{1}H.N.M.R. Spectrum
X_a, 366 cm^{-1} (ν-OH), 2900 cm^{-1} (ν-CH_2), 1595 cm^{-1} (ν-NH) bending, 3425 cm^{-1} stretching.	X_b, δ -2.0(6H, 2-C$\underline{H}_3$), δ 3.3 (V.S, 4H-C-C$\underline{H}_2$-N-, and 2-H for -C$\underline{H}_2$ δ 6.3 (W.1H, O$\underline{H}$), δ 7.3-7.5 (triplet) (3H,3N$\underline{H}$) and δ 7.6-7.9 (triplet). (S,9H, $C_6\underline{H}_4$-C_6H4-$C_6\underline{H}_5$).
X_b, 1595 cm^{-1} (ν-C-NH) bending, 3445 cm^{-1} (ν-NH) stretching, 2900 cm^{-1} (ν-CH_2) 1365 cm^{-1} (ν-gem-di-CH 3).	XI_b, δ 3.1 (V.S, 12H, 2N$\langle^{CH_3}_{CH_3}$), δ 3.25 (S, 4H, 2-C$\underline{H}_2$), δ 6.8 (S,4H, C_6H_4), δ 8.55 (V.S, 2H, 2-C$\underline{H}$).
XI_c,1595 cm^{-1} (νNH) bending, 2350 cm^{-1} (ν- CH_3), 2920 cm^{-1} (ν-CH_2) stretching, 1485 cm^{-1} (ν-CH 2) bending.	XI_e, δ 2.15 (V.S. 6H,2-C$\underline{H}_3$), δ 3.4 (S,4H, 2-C$\underline{H}_2$), δ 7.9 (S,4H,$C_6\underline{H}_4$), δ 8.2 (S,4H, C_6H_4).

Table 6. Physical data of $X_{a,b}$, XI_{a-e}

Comp.	R	Ar.	M.P. (°C)	Yield %	Molecular formula		Analysis (%) C	H	N
X_a	H	C_6H_4-N CH_3 CH_3 (p)	256-7	62	$C_{13}H_{22}N_4O$	Calc.	62.40	8.80	22.4
						Found	62.28	8.84	22.5
X_b	CH_3	C_6H_4-C_6H_5 (p)	130-1	58	$C_{18}H_{23}N_3O$	Calc.	72.72	7.74	14.14
						Found	72.69	7.77	14.32
XI_a	H	C_6H_5	133-4	65	$C_{18}H_{23}N_5$	Calc.	69.90	7.44	22.65
						Found	69.92	7.32	22.61
XI_b	H	C_6H_4-N CH_3 CH_3 (p)	239-40	58	$C_{22}H_{33}N_7$	Calc.	66.83	8.35	24.81
						Found	66.88	8.28	24.66
XI_c	H	C_6H_4-Br (p)	172-3	61	$C_{18}H_{21}Br_2N_5$	Calc.	46.25	4.49	14.98
						Found	46.49	4.44	14.86
XI_b	-CH_3	C_6H_4NH 2 (p)		52	$C_{20}H_{29}N_7$	Calc.	65.39	7.90	26.70
						Found	65.51	7.64	26.77
XI_e	-CH_3	C_6H_4-NO)p)	137-8	59	$C_{20}H_{25}N_7O_4$	Calc.	56.20	5.85	22.95
						Found	56.21	6.12	23.06

Table 7. Antimicrobial activity study.

	Micro-organism Inhibition zone/m.m. at conc. 1 x 10^{-2}					Micro-organism Inhibition zone/m.m. at conc. 1 x 10^{-2}				
Tested Comp.	B.cereus.	Sar. lat.	E.coli I	Serr. sp.	Candida albic.	B.cereus	Sar. lat.	E.coli I	Serr. sp.	Candida alibic.
II_b	–	10	–	14	–	–	–	–	10	–
II_d	–	12	–	18	–	–	–	–	14	–
III_d	–	13	–	15	–	–	10	–	10	–
III_d	–	10	14	22	–	–	–	10	20	–
VI_a	15	14	12	22	–	12	–	–	18	–
VII_a	13	–	–	–	–	10	–	–	–	–
VII_b	–	–	–	12	–	–	–	–	8	–
XI_b	–	–	–	13	–	–	–	–	10	–
XI_e	–	–	–	-	–	–	–	–	--	–
XII_a	–	16	12	12	–	–	10	8	–	–
$XIII_a$	30	18	29	15	–	22	12	24	10	–
XII_b	29	16	30	14	–	24	10	22	10	–

4. *Biological studies*

The antimicrobial activity of compounds II_b, II_d, III_b, III_d, VI_a, VII_a, VII_b, $VIII_b$, XI_b, XI_e, XII_a, $XIII_a$, $XIII_b$ was examined by the agar diffusion method [18] using different bacterial species in addition to one speciecs of yeast. These species were represented by *Bacillus cereus, Sarcina lateus, Escherichia coli, Serraitia sp.* and *Candia albicans.* Bacteria were incubated at 370 for 24 hr. yeast at 28° for 2 days. Biological activities of tested compounds were measured in 1 x 10^{-2} and 1 x 10^{-3} concentration.

The activities of the tested products were determined at the Microorganisms Department at the National Organisation for Drug Research and Control, Cairo, Egypt. Results are tabulated in table 6.

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