ISSN: 0974 - 7516 Volume 10 Issue 9

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 10(9), 2014 [337-350]

Synthesis of new biologically active 4-isobutylhydrotropoyl (Ibuprofen) derivatives

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ABSTRACT

The synthesis of 4-isobutylhydrotropoylamino acids **(12-17)**, dipeptide methyl ester **(18-71)**, dipeptide **(72-125)** and their corresponding hydrazides **(126-179)** is described. All the synthesized compounds were found to be active against some of the tested micro organisms and fungi.

INTRODUCTION

Recently the synthesis of many substituted nitro, amino and halophthaloylamino acid and peptide Derivatives was reported[1-4]. All these compounds were found to possess specific antimicrobial activity[1-4]. This promoted me to synthesis some 4-isobutylhydrotropoylamino acids, dipeptide methyl ester, dipeptide and hydrazides.

EXPERIMENTAL

Melting points are uncorrected and determined using electrothermal melting point apparatus "SMPI". Purity of compounds was checked by Thin layer chromatography "TLC" on plastic sheets silica gel-60-"Merek" and developed with benzene-ethyl acetate (3:1) using iodine-KI (20%) solution as spraying agent. Benzidine, ninhydrin, hydroxamate, and silver nitrate tests were used for detection reactions. The infrared "IR" Spectra were taken in KBr on Berkin elmar IR 5300 spectrometer. UV and visible spectra were measured on Shimadzu UV160 spectrometer. The mass spectra were taken on GC MS-QP 1000 mass spectrometer at 70 ev. Elemental analysies were carried out in microanalytical Research Center, Faculty of Science, Cairo University. Optical rotations $[\alpha]_D^{20}$ were measured in Bellingham-Stanley polarimeter with 1 dm tube, C=5 in DMF.

Biological activities were measured in Botany and Microbiology department.

General procedure for synthesisof 4-isobutylhydrotropoylaminoAcid derivatives (12-17)

The amino acid (0.001 mole) was dissolved in 1N-NaOH, and the solution cooled to (10 °C) (solution A). 4-isobutylhydrotropoyl acid chloride **(11)** [0.01mole] was dissolved in benzene (solution B). Solution (A) was gradually added during 75 mins. with stirring to solution (B). The temperature of the reaction mixture was kept at (10 °C) until complete addition, and the reaction mixture stirred for further three hrs. at room temperature. The benzene layer was separated out, and the aqueous layer acidified with 2N-HCl to pH =5. The crude compound **(12-17)** was filtered, washed with cold water and recrystallized from –water.

The IR spectrum of compounds **(12-17)** in KBr

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Compd. No.	X	Yield %	M.P. °C	R_F	$[\alpha]_D^{20}$ *	Molecular Formula (MW)	Elemental analysis % Calculated/Found		
							C	H	N
12	GLy	90	85-87	0.50	-	$C_{15}H_{21}NO_3$	68.44	7.98	5.32
						(263)	68.49	7.99	5.38
13	β-Ala	95	80-82	0.66	-	$C_{16}H_{23}NO_3$	69.31	8.30	5.05
						(277)	69.35	8.38	5.10
14	DL-Val	88	89-91	0.86	-	$C_{18}H_{27}NO_3$	70.81	8.85	4.58
						(305)	70.86	5.90	4.65
15	DL-Leu	75	95-97	0.66	-	$C_{19}H_{29}NO_3$	71.47	9.10	4.38
						(319)	71.55	9.15	4.42
16	DL-Phe	90	67-69	0.75	-	$C_{22}H_{27}NO_3$	74.78	7.64	3.96
						(353)	74.82	7.70	4.02
17	DL-Met	90	72-74	0.85	-	$C_{18}H_{27}NO_3S$	64.09	8.01	4.15
						(337)	64.13	8.06	4.20
18	Gly-Gly-OMe	80	108-10	0.27	-	$C_{18}H_{26}N_2O_4$	64.76	7.78	8.38
						(334)	64.80	7.82	9.49
19	GLy-β-Ala-OMe	75	113-15	0.74	-	$C_{19}H_{28}N_2O_4$	65.51	8.04	8.04
						(348)	65.66	8.10	8.10
20	GLy-DL-Ala-OMe	53	110-12	0.80	-	$C_{19}H_{28}N_2O_4$	65.51	8.04	8.04
						(348)	65.66	8.10	8.10
21	GLy- L-Val-OMe	65	118-20	0.71	+158	$C_{21}H_{32}N_2O_4$	67.02	8.51	7.44
						(376)	67.10	8.58	7.50
22	Gly-DL-Val-OMe	70	115-17	0.75	-	$C_{18}H_{28}N_2O_4$	67.02	8.51	7.44
						(376)	67.10	8.58	7.50
23	Gly-DL-Leu-OMe	80	125-27	O.70	-	$C_{22}H_{34}N_2O_4$ (390)	67.69 67.75	8.71 8.75	7.17 7.25
24	GLy-DL-Phe-OMe	60	135-37	0.58	-	$C_{25}H_{32}N_2O_4$	70.75	7.54	6.60
						(424)	70.83	7.62	6.65
25	GLy-DL-Ser-OMe	55	136-38	0.75	-	$C_{19}H_{28}N_2O_4$	62.63	7.69	7.69
						(364)	62.70	7.74	7.75
26	GLy-DL-Met-OMe	63	126-28	0.66	-	$C_{21}H_{32}N_2O_4S$	61.76	7.65	6.86
						(408)	61.78	7.68	6.99
27	β-Ala-GLy-OMe	80	139-41	0.50	-	$C_{19}H_{28}N_2O_4$	65..51	8.04	8.04
						(348)	65.58	8.10	8.10
28	β-Ala- β -ALa-OMe	80	140-42	0.75	-	$C_{20}H_{30}N_2O_4$	66.29	8.28	7.73
						(362)	66.35	8.32	7.85
29	β -Ala- DL-ALa-OMe	80	136-38	0.59	-	$C_{20}H_{30}N_2O_4$	66.29	8.28	7.73
						(362)	66.35	8.32	7.85
30	β- Ala -L-Val -OMe	52	128-30	0.50	+210	$C_{22}H_{34}N_2O_4$	62.68	6.46	6.96
						(390)	62.79	6.58	7.10
31	β -Ala- DL-Val -OMe	74	212-14	0.93	-	$C_{22}H_{34}N_2O_4$	62.68	6.46	6.96
						(390)	62.79	6.58	7.10
32	β -Ala-DL-Leu -OMe	60	152-54	0.95	-	$C_{23}H_{36}N_2O_4$	68.31	8.91	6.93
						(404)	68.38	8.95	6.99
33	β-Ala-DL-Phe -OMe	83	156-58	0.82	-	$C_{26}H_{34}N_2O_4$	71.23	7.93	6.39
						(438)	71.30	8.00	6.45

Compd. No.	X	Yield %	M.P. °C	R_F	$[\alpha]_D^{20}$ *	Molecular Formula (MW)	Elemental analysis % Calculated/Found		
							C	H	N
34	β-Ala-DL-Ser -OMe	65	148-50	0.67	-	$C_{20}H_{30}N_2O_5$	66.66	7.93	7.40
						(378)	63.49	7.99	7.45
35	β-Ala-DL-Met -OMe	55	160-62	0.70	-	$C_{22}H_{34}N_2O_4S$	62.55	8.05	6.63
						(422)	62.60	8.10	6.70
36	DL-Val-Gly-OMe	80	149-51	0.82	-	$C_{21}H_{32}N_2O_4$	67. 02	8.51	7.44
						(376)	67.10	8.60	7.50
37	DL-Val-β-Ala-OMe	85	155-57	0.56	-	$C_{22}H_{34}N_2O_4$	67.69	8.71	7.17
						(390)	67.75	8.75	7.25
38	DL-Val-DL- Ala-OMe	70	150-52	0.94	-	$C_{22}H_{34}N_2O_4$	67.69	8.71	7.17
						(390)	67.75	8.75	7.25
39	DL-Val-L-Val-OMe	68	125-27	0.50	+215	$C_{24}H_{38}N_2O_4$	68.89	9.09	6.69
						(418)	68.95	9.15	6.75
40	DL-Val-DL-Val-OMe	72	129-31	0.92	-	$C_{24}H_{38}N_2O_4$	68.89	9.09	6.69
						(418)	68.95	9.15	6.75
41	DL-Val-DL-Leu-OMe	80	134-36	.800	-	$C_{25}H_{40}N_2O_4$	69.44	9.25	6.48
						(432)	69.50	9.30	6.54
42	DL-Val-DL-Phe-OMe	75	128-30	0.36	-	$C_{28}H_{38}N_2O_4$	72.10	8.15	6.00
						(466)	72.15	8.20	6.10
43	DL-Val-DL-Ser-OMe	72	132-34	0.93	-	$C_{22}H_{34}N_2O_4$	65.02	6.89	6.89
						(406)	65.10	6.95	6.95
44	DL-Val-DL-Met-OMe	82	154-56	0.87	-	$C_{24}H_{38}N_2O_4$	64.0	8.44	6.22
						(450)	64.10	8.49	6.28
45	DL-Leu-Gly-OMe	75	160-62	0.75	-	$C_{22}H_{34}N_2O_4$	67.69	8.71	7.17
						(390)	67.75	8.75	7.25
46	DL-Leu- β –Ala-OMe	80	158-60	0.66	-	$C_{23}H_{36}N_2O_4$	68.31	8.91	6.93
						(404)	68.38	8.99	6.99
47	DL-Leu-DL-Ala-OMe	7075	166-68	0.84	-	$C_{23}H_{36}N_2O_4$	68.31	8.91	6.93
						(404)	68.38	8.99	6.99
48	DL-Leu L-Val-OMe	60	142-44	0.60	+310	$C_{25}H_{40}N_2O_4$	69.44	9..25	6.48
						(432)	69.50	9.30	6.55
49	DL-Leu-DL-Val-OMe	75	154-56	0.82	-	$C_{25}H_{40}N_2O_4$	69.44	9..25	6.48
						(432)	69.50	9.30	6.55
50	DL-Leu-DL-Leu-OMe	82	148-50	0.46	-	$C_{26}H_{39}N_2O_4$	70.42	8.80	6.48
						(443)	70.48	8.85	6.54
51	DL-Leu-DL-Phe-OMe	68	160-62	083	-	$C_{29}H_{40}N_2O_4$	72.50	8.33	5.83
						(480)	72.55	8.40	5.90
52	DL-Leu-DL-Ser-OMe	74	195-97	0.92	-	$C_{23}H_{35}N_2O_4$	65.87	8.35	5.83
						(419)	65.93	8.40	5.90
53	DL-Leu-DL-Met-OMe	65	180-82	0.78	-	$C_{25}H_{40}N_2O_4S$	64.65	8.62	6.03
						(464)	64.70	8.67	6.09
54	DL-Phe-Gly -OMe	58	157-59	0.65	-	$C_{25}H_{32}N_2O_4$	70.75	7.54	6.60
						(424)	70.85	7.60	6.65
55	DL-Phe-β-Ala -OMe	70	158-60	0.70	-	$C_{26}H_{34}N_2O_4$	71.23	7.76	6.39
						(438)	71.30	7.80	6.45
56	DL-Phe-DL-Ala -OMe	75	160-62	0.64	-	$C_{26}H_{34}N_2O_4$	71.23	7.76	6.39
						(438)	71.30	7.80	6.45
57	DL-Phe-L-Val -OMe	68	175-77	0.65	+250	$C_{28}H_{38}N_2O_4$	72.10	8.15	6.00
						(466)	72.15	8.20	6.10

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Compd. No.	X	Yield %	M.P. °C	R_F	$[\alpha]_D^{20}$ *	Molecular Formula (MW)	Elemental analysis % Calculated/Found		
							C	H	N
58	DL-Phe-DL_Val -OMe	84	175-77	0.85	-	$C_{28}H_{38}N_2O_4$	72.10	8.15	6.00
						(466)	72.15	8.20	6.10
59	DL-Phe-DL-Leu -OMe	65	190-92	0.90	-	$C_{29}H_{40}N_2O_4$	72.50	8.33	5.83
						(480)	72.55	8.40	5.90
60	DL-Phe-DL-Phe -OMe	90	204-06	0.75	-	$C_{32}H_{38}N_2O_4$	74.70	7.39	5.44
						(514)	74.75	5.75	549
61	DL-Phe-DL-Ser -OMe	68	212-14	0.72	-	$C_{26}H_{34}N_2O_4$	68.72	7.48	6.16
						(454)	68.75	7.54	6.22
62	DL-Phe-DL-Met- OMe	58	213-15	0.65	-	$C_{28}H_{38}N_2O_4S$	72.10	8.15	6.00
						(466)	72.15	8.20	6.08
63	DL-Met-Gly-OMe	48	162-64	0.40	-	$C_{21}H_{32}N_2O_4S$	61.76	7.84	6.86
						(408)	61.80	7.94	6.94
64	DL-Met -β-Ala-OMe	67	147-49	0.65	-	$C_{22}H_{34}N_2O_4S$	60.00	5.55	6.63
						(422)	62.55	8.05	6.68
65	DL-Met-DL-Ala-OMe	70	149-51	0.49	-	$C_{22}H_{34}N_2O_4S$	60.00	5.55	6.63
						(422)	62.55	8.05	6.68
66	DL-Met-L-Val-OMe	42	201-03	0.40	+280	$C_{24}H_{38}N_2O_4S$	64.00	8.44	6.22
						(450)	64.05	8.50	6.30
67	DL-Met-DL-Val-OMe	64	203-05	0.83	-	$C_{24}H_{38}N_2O_4S$	64.00	8.44	6.22
						(450)	64.05	8.50	6.30
68	DL-Met-DL-Leu-OMe	50	137-39	0.85	-	$C_{25}H_{40}N_2O_4S_1$	64.65	8.62	6.03
						(464)	63.55	8.68	6.10
69	DL-Met-DL-Phe-OMe	73	223-25	0.72	-	$C_{28}H_{38}N_2O_4S$	67.46	7.63	5.62
						(498)	67.55	7.70	5.70
70	DL-Met-DL-Ser-OMe	55	202-04	0.57	-	$C_{22}H_{34}N_2O_5S$	60.27	7.76	6.39
						(438)	60.35	7.80	6.45
71	DL-Met-Met -OMe	45	222-24	0.60	-	$C_{24}H_{38}N_2O_4S$	59.75	7.88	5.80
						(482)	59.85	7.94	5.95
72	Gly-Gly	65	156-58	0.59	-	$C_{17}H_{24}N_2O_4$	63.75	7.50	8.75
						(320)	63.80	7.55	8.80
73	GLy-β-Ala	80	163-65	0.84	-	$C_{18}H_{26}N_2O_4$	64.67	7.78	8.38
						(334)	64.75	7.85	8.45
74	GLy-DL-Ala	85	162-64	0.68	-	$C_{18}H_{26}N_2O_4$	64.67	7.78	8.38
						(334)	64.75	7.85	8.45
75	GLy- L-Val	68	174-76	0.50	+160	$C_{20}H_{30}N_2O_4$	66.29	8.28	7.73
						(362)	66.35	8.35	7.80
76	GLy-DL-Val	78	175-77	0.84	-	$C_{20}H_{30}N_2O_4$	66.29	8.28	7.73
						(362)	66.35	8.35	7.80
77	Gly-DL-Leu	65	140-42	0.86	-	$C_{21}H_{32}N_2O_4$	67.02	8.51	7.44
						(376)	76.10	8.59	7.50
78	GLy-DL-Phe	85	182-84	0.73	-	$C_{24}H_{30}N_2O_4$	70.24	7.31	6.82
						(410)	70.30	7.38	6.90

Compd. No.	X	Yield %	M.P. °C	R_F	$[\alpha]_D^{20}$ *	Molecular Formula (MW)	Elemental analysis % Calculated/Found		
							C	H	N
79	GLy-DL-Ser	70	176-78	0.76	-	$C_{18}H_{26}N_2O_4$	61.71	7.42	8.00
						(350)	61.79	7.49	8.07
80	GLy-DL-Met	60	195-97	0.79	-	$C_{20}H_{30}N_2O_4$	60.91	7.61	7.10
						(394)	60.96	7.69	7.15
81	β-Ala-GLy	53	164-66	0.55	-	$C_{18}H_{26}N_2O_4$	64.67	7.78	8.38
						(334)	64.73	7.83	8.43
82	β-Ala- β -ALa	72	192-95	0.65	-	$C_{19}H_{28}N_2O_4$	65.51	8.04	8.04
						(348)	65.56	8.10	8.10
83	β -Ala- DL-ALa	75	194-96	0.54	-	$C_{19}H_{28}N_2O_4$	65.51	8.04	8.04
						(348)	65.56	8.10	8.10
84	β- Ala- L-Val	47	215-17	0.55	+340	$C_{21}H_{32}N_2O_4$	67.02	8.51	6.96
						(376)	67.10	8.60	7.44
85	β -Ala- DL-Val	69	212-14	0.80	-	$C_{21}H_{32}N_2O_4$	67.02	8.51	6.96
						(376)	67.10	8.60	7.44
86	β -Ala-DL-Leu	55	149-51	0.85	-	$C_{22}H_{34}N_2O_4$	67.69	8.71	7.17
						(390)	67.75	8.76	7.20
87	β-Ala-DL-Phe	78	221-23	0.60	-	$C_{25}H_{32}N_2O_4$	70.75	7.54	6.60
						(424)	70.81	7.60	6.68
88	β-Ala-DL-Ser	60	154-56	0.67	-	$C_{19}H_{28}N_2O_5$	62.63	7.69	7.69
						(364)	62.68	7.75	7.76
89	β-Ala-DL-Met	53	184-86	0.50	-	$C_{21}H_{32}N_2O_4$	61.76	7.84	6.86
						(408)	61.85	7.90	6.90
90	DL-Val-Gly	73	158-60	0.75	-	$C_{20}H_{30}N_2O_4$	66.29	8.28	7.73
						(362)	66.35	8.35	7.88
91	DL-Val-β-Ala	76	222-24	0.60	-	$C_{21}H_{32}N_2O_4$	67.02	8.51	7.44
						(376)	67.10	8.60	7.50
92	DL-Val-DL- Ala	48	215-17	0.52	-	$C_{21}H_{32}N_2O_4$	67.02	8.51	7.44
						(376)	67.10	8.60	7.50
93	DL-Val-L-Val	70	135-37	0.93	+230	$C_{23}H_{36}N_2O_4$	68.31	8.91	6.93
						(404)	68.38	8.99	7.10
94	DL-Val-DL-Val	60	134-36	0.94	-	$C_{23}H_{36}N_2O_4$	68.31	8.91	6.93
						(404)	68.38	8.99	7.10
95	DL-Val-DL-Leu	79	138-40	0.83	-	$C_{24}H_{38}N_2O_4$	68.89	9.09	6.93
						(418)	68.95	9.15	7.10
96	DL-Val-DL-Phe	61	155-57	0.78	-	$C_{27}H_{36}N_2O_4$	71.68	7.96	6.19
						(452)	71.75	8.05	6.25
97	DL-Val-DL-Ser	51	200-02	0.72	-	$C_{21}H_{32}N_2O_5$	64.28	8.16	7.14
						(392)	64.35	8.22	7.20
98	DL-Val-DL-Met	54	203-05	0.54	-	$C_{23}H_{36}N_2O_4S$	63.30	8.25	6.42
						(436)	63.38	8.34	6.48
99	DL-Leu-Gly	85	160-62	0.70	-	$C_{21}H_{32}N_2O_4$	67.02	8.71	7.44
						(376)	67.08	8.79	7.55

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Compd. No.	X	Yield %	M.P. °C	R_F	$[\alpha]_D^{20}$ *	Molecular Formula (MW)	Elemental analysis % Calculated/Found		
							C	H	N
100	DL-Leu- β –Ala	89	178-80	0.54	-	$C_{22}H_{34}N_2O_4$	67.69	8.71	7.17
						(390)	67.75	8.80	7.25
101	DL-Leu-DL-Ala	50	180-82	0.45	-	$C_{22}H_{34}N_2O_4$	67.69	8.71	7.17
						(390)	67.75	8.80	7.25
102	DL-Leu L-Val	70	146-48	0.88	+180	$C_{24}H_{38}N_2O_4$	68.89	9.09	6.69
						(418)	68.95	9.15	6.75
103	DL-Leu-DL-Val	54	148-50	0.90	-	$C_{24}H_{38}N_2O_4$	68.89	9.09	6.69
						(418)	68.95	9.15	6.75
104	DL-Leu-DL-Leu	76	157-59	0.77	-	$C_{25}H_{37}N_2O_4$	69.93	8.62	6.52
						(429)	69.99	8.69	6.62
105	DL-Leu-DL-Phe	60	207-09	0.62	-	$C_{28}H_{38}N_2O_4$	72.10	8.15	6.00
						(466)	72.15	8.20	6.10
106	DL-Leu-DL-Ser	53	200-02	0.65	-	$C_{22}H_{33}N_2O_4$	65.18	8.14	6.91
						(405)	65.25	8.20	7.03
107	DL-Leu-DL-Met	70	201-03	0.76	-	$C_{24}H_{38}N_4O_4S$	64.00	8.44	6.22
						(450)	64.05	8.50	6.28
108	DL-Phe-Gly	65	145-47	0.77	-	$C_{24}H_{30}N_2O_4$	70.24	7.31	6.82
						(410)	70.30	7.38	6.88
109	DL-Phe-β-Ala	75	165-67	0.61	-	$C_{25}H_{32}N_2O_4$	70.75	7.54	6.60
						(424)	70.80	7.60	6.66
110	DL-Phe-DL-Ala	80	168-70	048	-	$C_{25}H_{32}N_2O_4$	70.75	7.54	6.60
						(424)	70.80	7.60	6.66
111	DL-Phe-L-Val	85	180-82	0.90	+270	$C_{27}H_{36}N_2O_4$	71.68	7.96	6.19
						(452)	71.75	7.99	6.25
112	DL-Phe-DL_Val	65	180-82	0.51	-	$C_{27}H_{36}N_2O_4$	71.68	7.96	6.19
						(452)	71.75	7.99	6.25
113	DL-Phe-DL-Leu	75	210-12	0.31	-	$C_{28}H_{38}N_2O_4$	72.10	5.55	15.55
						(466)	72.15	8.15	6.00
114	DL-Phe-DL-Phe	75	212-14	0.31	-	$C_{31}H_{36}N_2O_4$	74.40	7.20	5.60
						(500)	74.50	7.30	5.65
115	DL-Phe-DL-Ser	70	205-07	0.42	-	$C_{25}H_{32}N_2O_5$	74.40	7.27	6.36
						(440)	74.45	7.32	6.40
116	DL-Phe-DL-Met	73	220-22	0.66	-	$C_{27}H_{36}N_2O_4$	71.68	7.96	6.19
						(452)	71.75	8.01	6.25
117	DL-Met-Gly	73	182-84	0.71	-	$C_{20}H_{30}N_2O_4S$	61.91	7.61	7.10
						(394)	61.99	7.66	7.15
118	DL-Met -β-Ala	67	215-17	0.71	-	$C_{21}H_{32}N_2O_4S$	61.76	7.84	6.86
						(408)	61.80	7.90	6.90
119	DL-Met-DL-Ala	77	229-31	0.55	-	$C_{21}H_{32}N_2O_4S$	61.76	7.84	6.86
						(408)	61.80	7.90	6.90
120	DL-Met-L-Val	82	217-19	0.42	+160	$C_{23}H_{36}N_2O_4S$	63.30	8.25	6.42
						(436)	63.35	8.30	6.50
121	DL-Met-DL-Val	87	224-26	0.84	-	$C_{23}H_{36}N_2O_4S$	63.30	8.25	6.42
						(436)	63.35	8.30	6.50

Compd. No.	X	Yield %	M.P. °C	R_F	$[\alpha]_D^{20}$ *	Molecular Formula (MW)	Elemental analysis % Calculated/Found		
							C	H	N
122	DL-Met-DL-Leu	67	229-31	0.45	-	$C_{24}H_{38}N_2O_4S$	64.00	8.44	6.22
						(450)	64.08	8.50	6.28
123	DL-Met-DL-Phe	57	218-20	0.44	-	$C_{27}H_{36}N_2O_4S$	66.94	7.43	5.78
						(484)	66.99	7.48	5.83
124	DL-Met-DL-Ser	77	226-28	0.45	-	$C_{21}H_{32}N_2O_5S$	59.43	7.54	6.60
						(424)	59.48	7.60	6.65
125	DL-Met–DL-Met	72	205-07	0.56	-	$C_{23}H_{36}N_2O_4S_2$	58.97	7.69	5.98
						(468)	58.99	7.75	6.09
126	Gly-Gly-N_2H_3	80	182-84	0.60	-	$C_{17}H_{26}N_4O_3$	61.07	7.78	16.76
						(334)	61.15	7.85	16.80
127	GLy-β-Ala-N_2H_3	74	215-17	0.60	-	$C_{18}H_{28}N_4O_3$	62.06	8.04	16.09
						(348)	62.10	8.10	16.15
128	GLy-DL-Ala-N_2H_3	76	219-21	0.55	-	$C_{18}H_{28}N_4O_3$	62.06	8.04	16.09
						(348)	62.10	8.10	16.15
129	GLy- L-Val-N_2H_3	81	217-19	0.54	+320	$C_{20}H_{32}N_4O_3$	63.82	8.51	14.89
						(376)	63.89	8.59	14.95
130	GLy-DL-Val-N_2H_3	80	219-21	0.83	-	$C_{20}H_{32}N_4O_3$	63.82	8.51	14.89
						(376)	63.89	8.59	14.95
131	Gly-DL-Leu-N_2H_3	55	229-31	0.54	-	$C_{21}H_{34}N_4O_3$	64.61	8.71	14.35
						(390)	64.68	8.75	14.40
132	GLy-DL-Phe-N_2H_3	54	215-17	0.35	-	$C_{24}H_{32}N_4O_3$	67.92	7.69	13.20
						(424)	67.99	7.75	13.30
133	GLy-DL-Ser-N_2H_3	50	222-24	0.40	-	$C_{18}H_{28}N_4O_5$	59.34	7.69	15.38
						(364)	59.40	7.76	15.45
134	GLy-DL-Met-N_2H_3	79	208-10	0.48	-	$C_{20}H_{32}N_4O_3S$	58.82	7.84	13.72
						(408)	58.94	7.93	13.78
135	β –Ala-Gly-N_2H_3	64	186-88	0.61	-	$C_{18}H_{28}N_4O_3$	62.06	8.04	16.09
						(348)	62.10	8.10	16.15
136	β-Ala- β -ALa-N_2H_3	58	227-29	0.61	-	$C_{19}H_{30}N_4O_3$	62.98	8.28	15.46
						(362)	62.99	8.35	15.55
137	β –Ala- DL-ALa-N_2H_3	68	228-30	0.45	-	$C_{19}H_{30}N_4O_3$	62.98	8.28	15.46
						(362)	62.99	8.35	15.55
138	β- Ala- L-Val -N_2H_3	63	226-28	0.32	+250	$C_{21}H_{34}N_4O_3$	64.61	8.71	14.35
						(390)	64.70	8.80	14.40
139	β –Ala -DL-Val -N_2H_3	68	224-26	0.74	-	$C_{21}H_{34}N_4O_3$	64.61	8.71	14.35
						(390)	64.70	8.80	14.40
140	β -Ala-DL-Leu -N_2H_3	58	229-31	0.35	-	$C_{22}H_{36}N_4O_4$	65.34	8.91	13.86
						(404)	65.40	9.99	13.90
141	β-Ala-DL-Phe -N_2H_3	48	218-20	0.35	-	$C_{25}H_{34}N_4O_3$	68.49	7.76	12.78
						(438)	68.55	7.80	12.83
142	β-Ala-DL-Ser -N_2H_3	67	226-28	0.55	-	$C_{19}H_{30}N_4O_4$	60.31	7.93	14.81
						(378)	60.38	7.99	14.89
143	β-Ala-DL-Met -N_2H_3	63	205-07	0.66	-	$C_{21}H_{34}N_4O_3S$	59.71	8.05	13.27
						(422)	59.86	8.14	13.35

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Compd. No.	X	Yield %	M.P. °C	R_F	$*[\alpha]_D^{20}$	Molecular Formula (MW)	Elemental analysis % Calculated/Found		
							C	H	N
144	DL-Val-Gly-N_2H_3	56	190-92	0.61	-	$C_{20}H_{32}N_4O_3$	63.82	8.51	14.89
						(376)	63.88	8.60	14.95
145	DL-Val-β-Ala-N_2H_3	50	219-21	0.72	-	$C_{21}H_{34}N_4O_3$	64.61	8.71	14.35
						(391)	64.70	8.78	14.40
146	DL-Val-DL- Ala-N_2H_3	60	221-23	0.60	-	$C_{21}H_{34}N_4O_3$	64.61	8.71	14.35
						(391)	64.70	8.78	14.40
147	DL-Val-L-Val-N_2H_3	65	227-29	0.42	+180	$C_{23}H_{38}N_4O_3$	66.02	9.09	13.39
						(418)	66.10	9.15	13.45
148	DL-Val-DL-Val-N_2H_3	70	229-31	0.80	-	$C_{23}H_{38}N_4O_3$	66.02	9.09	13.39
						(418)	66.10	9.15	13.45
149	DL-Val-DL-Leu-N_2H_3	50	233-35	0.63	-	$C_{24}H_{40}N_4O_3$	66.66	9.25	12.96
						(432)	66.70	9.30	13.05
150	DL-Val-DL-Phe-N_2H_3	40	228-30	0.35	-	$C_{27}H_{38}N_4O_3$	69.52	8.15	12.01
						(466)	69.58	8.20	12.10
151	DL-Val-DL-Ser-N_2H_3	60	235-37	0.42	-	$C_{21}H_{34}N_4O_4$	62.06	8.37	13.29
						(406)	62.15	8.45	13.35
152	DL-Val-DL-Meth-N_2H_3	55	213-15	0.33	-	$C_{23}H_{38}N_4O_3S$	61.33	8.44	12.44
						(450)	61.38	8.50	12.50
153	DL-Leu-Gly-N_2H_3	64	194-96	0.70	-	$C_{21}H_{34}N_4O_3$	64.61	8.71	14.35
						(390)	64.70	8.80	14.40
154	DL-Leu- β –Ala-N_2H_3	50	210-12	0.72	-	$C_{22}H_{36}N_4O_3$	65.34	8.91	13.86
						(404)	65.40	8.99	13.95
155	DL-Leu-DL-Ala-N_2H_3	55	213-15	0.54	-	$C_{22}H_{36}N_4O_3$	65.34	8.91	13.86
						(404)	65.40	8.99	13.95
156	DL-Leu L-Val-N_2H_3	65	221-23	0.41	+218	$C_{24}H_{40}N_4O_3$	66.66	9.25	12.96
						(432)	66.70	9.35	13.05
157	DL-Leu-DL-Val-N_2H_3	73	224-26	0.84	-	$C_{24}H_{40}N_4O_3$	66.66	9.25	12.96
						(432)	66.70	9.35	13.05
158	DL-Leu-DL-Leu-N_2H_3	54	235-37	0.44	-	$C_{25}H_{39}N_4O_3$	67.72	8.80	12.64
						(443)	67.79	8.89	12.70
159	DL-Leu-DL-Phe-N_2H_3	45	240-42	0.43	-	$C_{28}H_{40}N_4O_3$	70.00	8.33	11.66
						(480)	70.05	8.40	11.70
160	DL-Leu-DL-Ser-N_2H_3	65	238-40	0.24	-	$C_{22}H_{35}N_4O_4$	63.00	8.35	13.36
						(419)	63.10	8.43	13.45
161	DL-Leu-DL-Met- N_2H_3	58	219-21	0.35	-	$C_{24}H_{40}N_4O_3S$	62.06	8.62	12.06
						(464	62.10	8.70	12.10
162	DL-Phe-Gly -N_2H_3	43	195-97	0.48	-	$C_{24}H_{32}N_4O_3$	67.92	7.54	13.20
						(424)	67.99	7.60	13.28
163	DL-Phe-β-Ala -N_2H_3	37	226-28	0.48	-	$C_{25}H_{34}N_4O_3$	68.49	7.76	12.78
						(438)	68.55	7.85	12.85
164	DL-Phe-DL-Ala -N_2H_3	47	229-31	0.82	-	$C_{25}H_{34}N_4O_3$	68.49	7.76	12.78
						(438)	68.55	7.85	12.85

Compd. No.	X	Yield %	M.P. °C	R_F	$[\alpha]_D^{20}$ *	Molecular Formula (MW)	Elemental analysis % Calculated/Found C	H	N
165	DL-Phe-L-Val -N_2H_3	57	215-17	0.60	+240	$C_{27}H_{38}N_4O_3$	69.52	8.15	12.01
						(466)	69.60	8.23	12.10
166	DL-Phe-DL_Val -N_2H_3	64	218-20	0.61	-	$C_{27}H_{38}N_4O_3$	69.52	8.15	12.01
						(466)	69.60	8.23	12.10
167	DL-Phe-DL-Leu -N_2H_3	52	229-31	0.58	-	$C_{28}H_{40}N_4O_4$	70.00	8.33	11.66
						(480)	70.10	8.38	11.73
168	DL-Phe-DL-Phe -N_2H_3	55	218-20	0.64	-	$C_{31}H_{38}N_4O_3$	72.37	7.59	10.89
						(514)	72.45	7.65	10.95
169	DL-PheD-L-Ser -N_2H_3	60	216-18	0.68	-	$C_{25}H_{34}N_4O_4$	60.07	7.48	12.33
						(454)	60.15	7.55	12.38
170	DL-Phe-DL-Met-N_2H_3	63	238-40	0.58	--	$C_{27}H_{38}N_4O_3S$	69.52	8.15	12.01
						(466)	69.59	8.21	12.10
171	DL-Met-Gly-N_2H_3	54	210-12	0.65	-	$C_{20}H_{32}N_4O_3S$	58.82	7.84	13.72
						(408)	58.89	7.92	1379
172	DL-Met -β-Ala-N_2H_3	58	227-29	0.64	-	$C_{21}H_{34}N_4O_3S$	59.71	8.05	13.27
						422)	59.78	8.12	13.35
173	DL-Met-DL-Ala-N_2H_3	68	229-31	0.55	-	$C_{21}H_{34}N_4O_3S$	59.71	8.05	13.27
						422)	59.78	8.12	12.44
174	DL-Met-L-Val-N_2H_3	63	225-27	0.46	+310	$C_{23}H_{38}N_4O_3S$	61.33	8.44	12.44
						(450)	61.38	8.52	12.53
175	DL-Met-DL-Val-N_2H_3	54	128-30	0.60	-	$C_{23}H_{38}N_4O_3S$	61.33	8.44	12.44
						(450)	61.38	8.52	12.53
176	DL-Met-DL-Leu-N_2H_3	58	234-36	0.60	-	$C_{24}H_{40}N_4O_3S$	62.06	8.62	12.06
						(464)	62.12	8.70	12.10
177	DL-Met-DL-Phe-N_2H_3	58	235-37	0.54	-	$C_{27}H_{38}N_4O_3S$	65.06	7.75	11.24
						(498)	65.12	7.83	11.32
178	DL-Met-DL-Ser-N_2H_3	63	230-32	0.42	-	$C_{21}H_{34}N_4O_4S$	57.53	7.76	12.78
						(438)	57.62	7.85	12.86
179	DL-Met–DL-Met-N_2H_3	68	234-36	0.83	-	$C_{23}H_{38}N_4O_3S_2$	57.26	7.88	11.61
						(482)	57.35	7.95	1172

showed a characteristic bands at: 3379, 3272 cm^{-1} (NH); 3092 cm^{-1} (CH-aromatic), 2955, 2872 cm^{-1} (CH_3-valine); 1717cm^{-1} (C=O) and another bands characteristic for the remaining part of the molecule. ^{1}Hn.m.r spectrum of compounds **(12-17)** in dimethyl sulfoxide-d_6 exhibited the following signals at δ : 0.8 (s, 6H, $2CH_3$-alanine); 1.808 (m, 6H, $CH(CH3)_2$- alanine); 3.6 (m, 1H, CH valine), 7.08-7.199 (m, isobutylhydrotropoyl protons), 8.14,8.13 (d, 1H,NH), 12.19 (b, 1H, OH-carboxylic), which confirmed its structure.

General procedure for synthesisof 4-isobutylhydrotropoyldipeptide methyl esters (18-71)

4-isobutylhydrotropoyl amino acid **(12-17)**; 0.001 mole) was dissolved in (15 ml.) tetrahydrofuran (THF) [Solution A]. Amino acid methyl ester hydrochloride (1-9; 0.001mole) was suspended in (THF; 20 ml.) containing triethylamine (0.5 ml.). The mixture was stirred for 30 min; then cooled to (0°C). The precipitated triethylamine hydrochloride was filtered off {the filtrate contains free amino acid methyl ester [Solutaion B]}. Solution (A) was added to solution (B), and the mixture cooled to 0°C, then N,N'-dicyclohexylcarbodiamide [DCC; 0,206 g; 0.001 mole]

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TABLE 1 : Antimicrobial activities of the synthesized compounds (12-179)

Comp No.	*pseudo*		*E-coli*		*B-sutlas*		*staph*		*Aspero.n*		*Aspero.fl*	
	A	M.I.C	A	M.I.C	A	M.I.C	A	M.I.C	A	M.I.C	A	M.I.C
16	-		+	500	–		+	500	–		–	
17	-		+	500			+	500				
18	-		+	500	–		+	500	–		–	
19	-		++	250	–		+	500	–		–	
20	-		-		–		++	250	–		–	
21	-		-		–		+	500	–		–	
22	-		-		–		+	500	–		–	
32	-		-		–		+	500	–		–	
33	-		+	500	–		+	500	–		–	
34	-		+	500	–		+	500	–		–	
35	-		++	250	–		+	500	–		–	
36	-		+	500	–		++	250	–		–	
37	-		+	500	–		+	500	–		–	
38	-		+	500	–		-		–		–	
39	-		+	500	–		+	500	–		–	
40	-		+	500	–		-		–		–	
41	-		+	500	–		-		–		–	
42	-		++	250	–		-		–		–	
43	-		+	500	–		+	500	–		–	
44	-		+	500	–		+	500	–		–	
45	-		+	500	–		++	250	–		–	
46	-		+	500	–		+	500	–		–	
47	-		+	500	–		-		–		–	
48	-		+	500	–		-		–		–	
49	-		++	250	–		-		–		–	
50	-		+	500	–		-		–		–	
51	-		+	500	–		-		–		–	
52	-		+	500	–		-		–		–	
53	-		+	500	–		-		–		–	
54	-		+	500	–		+	500	–		–	
55	-		+	500	–		++	250	–		–	
56	-		+	500	–		+	500	–		–	
57	-		+	500	–		+	500	–		–	
58	-		++	250	-		-		–		–	
59	-		+	250	-		-					
60	-		+	500	-		-		–		–	
61	-		+	500	-		-		–		–	
62	-		++	250	-		-		–		–	
63	-		+	500	-		-		–		–	
64	-		+	500	-		-		–		–	
65	-		+	500	-		-		–		–	
66	+	500	-		-		-		–		–	

Comp No.	*pseudo*		*E-coli*		*B-sutilis*		*staph*		*Aspero.n*		*Aspero.fl*	
	A	**M.I.C**	**A**	**M.I.C**	**A**	**M.I.C**	**A**	**M.I.C**	**A**	**M.I.C**	**A**	**M.I.C**
67	-		-		-		-		–		–	
68	-		-		+	500	-		–		–	
69	-		-		+	500	-		–		–	
77	-		-		-		-		–		–	
78	-		-		++	250	-		–		–	
79	-		-		+	500	-		–		–	
80	-		-		+	500	-		–		–	
101	-		-		+	500	+	500	–		–	
116	-		-		-		+	500	–		–	
117	++	250	-		-		++	250	–		–	
118	++	250	-		-		+	500	–		–	
119	-		-		-		+	500	–		–	
120	+	500	-		-		+	500	–		–	
121	-		-		-		-		–		–	
122	-		-		-		-		–		–	
123	+	500	-		+	500	-		–		–	
124	+	500	+	500	+	500	-		–		–	
132	+	500	+	500	-		-		–		–	
133	+	500	+	500	-		+	500	–		–	
134	+	500	-		-		+	500	–		–	
135	+	500	-		-		+	500	–		–	
136	+	250	-		-		+	500	–		–	
137	+	500	-		-		+	500	–		–	
138	+	500	-		-		+	500	–		–	
139	+	500	-		-		+	500	–		–	
140	+	500	-		-		+	500				
141	-		-		-		-		–		–	
142	-		-		-		+	500	–		–	
143	-		-		-		+	500	–		–	
144	-		-		-		+	500	–		–	
145	-				-		+	500	–		–	
146	+	500	+	500	-		+	500	–		–	
147	++	250	+	500	-		+	500	–		–	
148	+	500	+	500	-		+	500	–		–	
149	+	500	++	250	-		+	500	–		–	
150	+	500	+	500	-		-		–		–	
151	+	500	-		-		+	500	–		–	
152	+	500	-		-		+	500	–		–	
153	+	500	-		-		+	500	–		–	
154	+	500	-		-		+	500	–		–	
155	+	500	-		-		+	500	–		–	
156	-		-		-		-		–		–	
157	-		+	500	-		-		–		–	
158	-		-		-		-		–		–	

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Comp No.	*pseudo*		*E-coli*		*B-sutilis*		*staph*		*Aspero.n*		*Aspero.fl*	
	A	M.I.C	A	M.I.C	A	M.I.C	A	M.I.C	A	M.I.C	A	M.I.C
159	-		-		-		-		–		–	
160	-		-		-		+	500	–		–	
161	-		-		-		+	500	–		–	
162	-		-		-		+	500	–		–	
163	-		-		-		+	500	–		–	
164	-		-		-		-		–		–	
165	-		-		-		-		–		–	
166	-		+	500	-		-		–		–	
167	-		-		-		-		–		–	
168	-		-		-		-		–		–	
169	+	500	+	500	-		+	500	–		–	
170	+	500	+	500	-		+	500	–		–	
171	+	500	++	250	-		+	500	–		–	

MIC: Minimal inhibtory concentration; A: Antimicrobial activities; -: Inactive compound or its MIC>500 µ/ml; +: Weak activity; ++: Moderate activity; +++: High activity

was added. The reaction mixture was stirred for 4-6 hrs. at (0°C), and left over night. The precipitated dicyclohexylurea (DCC) was filtered off. The filtrate evaporated in vacuo and the residual material was purified by recrystallization from ethanol-water to give compounds **(18-71)**.

The synthesized compounds **(18-71)** were chromato- graphically homogeneous when developed with benzidine, iodine solution, and gave positive hydroxamate reaction and negative ninhydrin test. The IR spectrum of compounds **(18-71)** in KBr showed the characteristic bands at: 3325, 3296 cm^{-1} (NH, CONH); 2928, 2856 cm^{-1} (CH_3); 1657cm^{-1} (C=O); 1601 cm^{-1} ($COOCH_3$); and other frequencies for the remaining part of the molecule which confirmed its structure. ^{1}Hn.m.r spectrum of compounds **(18-71)** in dimethylsulfoxide-d_6 exhibited the following signals at δ : 1.02 (s,6H, $2CH_3$-Methionine); 1.52(m,1H,CH-serine); 2.5(s, 2H, CH_2 methionine); 3.2 (d, 1H, CH-CH serine); 3.8(s, 1H, CH methionine); 7.26-7.75 (m, aromatic protons), 8.34,8.35 (d, 1H,NH-serine), 11.26 (b, 1H, OH-carboxylic) which confirmed its structure.

General procedure for synthesis of 4-isobutylhydrotropoyldipeptides (72-125)

4-isobutylhydrotropoyldipeptide methyl ester **(18-71)**; 0.001mole) was added to a solution of 0.5-N NaOH. The mixture was refluxed with continuous stirring for 1 hour at (100 °C) on water bath. The reaction mixture was allowed to cool, then acidified with 1N-HCl to pH=5. The crude product **(72-125)** was separated, filtered and purified by recrystallization from DMF.

All the synthesized compounds **(72-125)** were chromato-graphically homogeneous when developed with iodine solution, benzidine and gave negative ninhydrin test, and hydroxmate reaction. The IR spectrum of compounds **(72-125)** in KBr showed the characteristic bands at: 3394, 3055cm^{-1} (NH, CONH); 2925, 2871 cm^{-1} (CH aliphatic); 1718 cm^{-1} (C=O); and other frequencies for the remaining part of the molecule which confirmed its structure. ^{1}Hn.m.r spectrum of compounds **(72-125)** in dimethylsulfoxide-d_6 exhibited the following signals at δ : 2.2(s, 2H, CH_2 glycine); 3.3 (s,2H,CH_2-glycine); 7.1-7,3 (m, aromatic protons), 12.19 (s,1H,OH-carboxilic) which confirmed its structure.

General procedure for synthesis of 4-isobutylhydrotropoyl dipeptide hydrazides (126-179)

4-isobutylhydrotropoyl dipeptide methyl ester (**(18-71)**; 0.001mole) was dissolved in (30 ml) of 1M alcoholic hydrazine hydrate (prepared from 6.6 ml hydrazine hydrate in 93.4 ml of abs. ethanol). The reaction mixture was heated on water bath for ½ hr. and kept 24 hrs in the refrigerator. The hydrazide was separated out and recrystallized from ethanol-water.

All compounds **(126-179)** were chromatographically homogenous when developed with iodine solu-

tion, benzidine, and gave positive silver nitrate test and negative hydroxamate, and ninhydrin tests.

The IR spectrum of compounds **(126-179)** in KBr showed the characteristic bands at: 3480,3099 cm^{-1} (NH,NH_2); 2871, 2756 cm^{-1} (CH_2 aliphatic); 1619, 1588 cm^{-1} (amide I, amide II)and other frequencies for the remaining part of the molecule which confirmed its structure. ^{1}Hn.m.r spectrum of compounds **(126-179)** in dimethylsulfoxide-d_6 exhibited the following signals at δ : 2.49 (m, 1H, CH_2 alanine); 3.3 (s,2H,CH_2-Leucine); 3.6 (s, 3H, $COOCH_3$); 3.8(t,2H,CH2-alanine); 5.51,5.54 (d, 1H,NH- Leucine); 7.04-7.18 (m, aromatic protons), 8.2 (d, 1H,NH-alanine), 8.24 (1H,NH Leucine) which confirmed its structure.

RESULT AND DISCUSSION

Chemistry

4-isobutylhydrotropoyl amino acids **(12-17)**: were easily synthesized by coupling of 4-isobutylhydrotropoyl (Ibuprofen) acid chloride **(11)** with amino acids in sodium hydroxide-benzene medium. First, amino acids were dissolved in 1N-NaOH solution and cooled to 10 °C solution (A), 4-isobutylhydrotropoyl (Ibuprofen) acid chloride **(11)** was dissolved in benzene (solution B). Solution (A) added gradually with stirring to solution (B) during 75 mins. After complete addition, the stirring was continued for 3 additional hrs. at room temperature. The aqueous layer was separated, and acidified with 2N-HCl to pH=5 to give the desired compounds **(12-17)**. The crude products **(12-17)** were purified by recrystallization from ethanol–water and obtained in yields (75-95 %).

4-isobutylhydrotropoyl dipeptide methyl esters (18-71): were prepared by carbodiimide method[5] which considered the most suitable method for the preparation of these compounds and no side reactions observed. Many scientists confirmed that in peptide synthesis[6-10].

4-isobutylhydrotropoyl amino acid **(12-17)** was coupled with amino acid methyl ester hydrochlorides [1-9; 1:1 molar ratio] by carbodiimide technique[5]. First, 4-isobutyl-hydrotropoyl amino acid **(12-17)** was dissolved in tetrahydrofuran and cooled to 0 °C (Solution A). The amino acid methyl ester hydrochlorides **(1-9)** were suspended in THF and triethylamine, and then the mixture stirred for 30 min. at (0 °C), the triethylamine hydrochloride was filtered off (Solution B). (Solution A) was added to (solution B) and N,N\-dicyclohexyl carbodiimide (DCC) was added (as the same ratio of amino acid methyl ester hydrochlorides) at (0 °C). The mixture was stirred at (0 °C) for 4-6 hrs., and left over night and the time of the reaction was controlled by TLC. The precipitated dicyclohexylurea (DCC) was filtered off, and the filtrate evaporated in vacuo. The residual material was purified from ethanol-water. The compounds **(18-71)** were obtained in yields (52-83%).

4-isobutyl-hydrotropoyl dipeptides (72-125)

Were prepared by adding 4-isobutylhydrotropoyl dipeptide methyl ester **(18-71)**; 0.001mole) was added to a solution of 0.5-N NaOH. and refluxed the mixture with continuous stirring for 1 hour ON water bath. The reaction mixture was allowed to cool, then acidified with 1N-HCl to pH=5. The crude compounds **(72-125)** were separated, filtered, recrystallized from ethanol-water, and obtained in (52-86%) yields.

4-isobutylhydrotropoyl dipeptides hydrazides (126-179)

The titled compounds **(126-179)** were synthesized by the action of hydrazine hydrate in presence of ethyl alcohol on the corresponding 4-isobutylhydrotropoyl dipeptide methyl ester **(18-71)**. The reaction mixture was heated on water bath for ½ hr. and left 24 hrs at °C. The crude hydrazides **(126-179)** were separated out, recrystallized from ethanol-water, and obtained in good yields (55-85%).

THE BIOLOGICAL ACTIVITIES OF THE SYNTHESIZED COMPOUNDS

The biological activities of the synthesized compounds **(12-179)** were tested using the hole plate and filter paper disk methods[11-14]. All the compounds **(12-179)** were tested against different types of bactria (Gram-positive and Gram-negative bacteria) as follow :

A. Pseudomonas aeruginosa.
B. E.Coli.
C. Bacillus Subtilis.
D. Staphyococus.

And, Ampicillin was used as a reference compound (c.f.TABLE 1).

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Also, all the synthesized compounds **(12-179)** were tested against different types of fungi as follow :

A. Asprigillus flavus.

B. Asprigillus niger.

And, Claforan was used as a reference compound (c.f.TABLE1).

From TABLE 1, we found the following:-

1) The starting materials **(13& 14)** were found to possess a inactivities against pseud, B. Subtilis. (c.f.TABLE1).
2) The compounds **(31-51)** were found to be Moderate active or have a very weak activity against all tested microorganisms, at MIC >500 μg/ml (c.f.TABLE 1).

From the above results, we concluded that the combination of Ibuprofen moiety with different amino acids or peptides residues gave Moderate active compounds against all tested.

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