Synthesis and Spectroscopy of Novel-α- Pyrazolylglycine Derivatives

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Summary: The synthesis of α-pyrazolylglycine derivatives (**7a-j**) with different substituents, starting from glycine have been prepared. The spectroscopy of intermediate compounds and the final amino acids has been discussed.

Introduction

The number of naturally occurring α-amino acids has grown substantially beyond roughly 20-amino acids normally found in proteins to over 500 which are now known [1]. In addition, there has been a tremendous surge of interest in preparation of relatively inaccessible unnatural amino acids whose potential biological properties and general synthetic utility are just beginning to be realized. Of the methods presently available, those derived from electrophilic glycine equivalents [2,3] are worth mentioning.

In the course of our studies on cyclization reactions of different β-diketones with hydrazine derivatives, hydroxylamine, aliphatic 1,2-diamines, phenylenediamine and o-aminothiophenols to give pyrazoles, isoxazoles, diazepines, benzodiazepines and benzothiazepines respectively, we have been able to prepare α-pyrazolyl-α-amino acids via scheme 1. In this paper we report the synthesis and spectroscopy of these amino acids and the intermediate compounds.

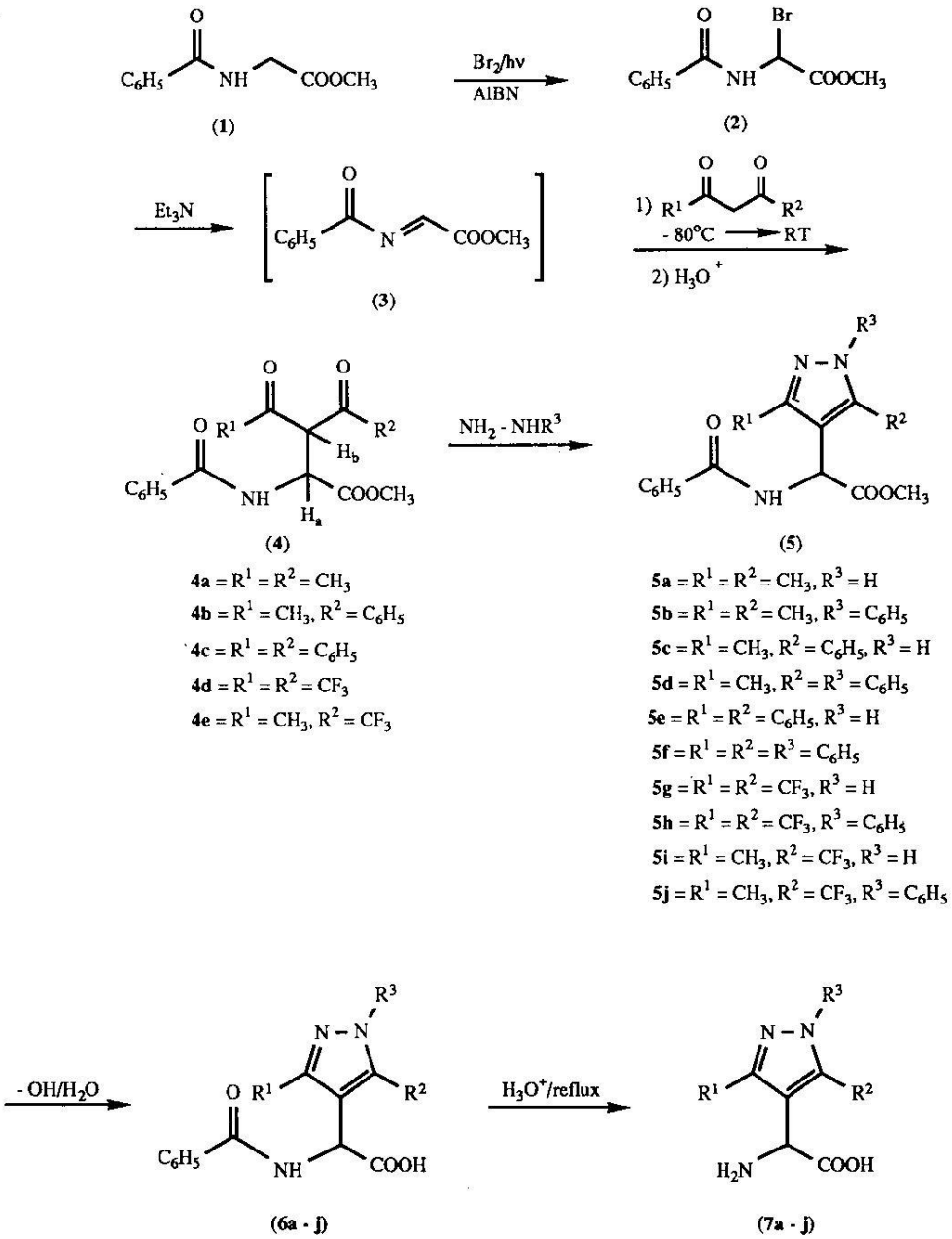
Results and Discussion

Esterification of hippuric acid with $SOCl_2$/CH_3OH, a method already reported [4], gave (**1**) in good yield. Photolytic bromination of ester in the presence of AIBN (azobisiso butyronitrile) a radical initiator resulted in the formation of α-bromo-ester (**2**) [5]. On treatment of (**2**) with tertiary amine, highly reactive α-acyliminoacetate (**3**) was formed *in situ* which on reaction with β-diketones gave (**4**) in reasonably good yield. This 1,3-diketoderivative on cyclization with hydrazine derivatives afforded N-protected α-pyrazolylglycine esters (**5**). Further cleavage of acid and amino protected groups leds to free amino acids (**7**). The physical data of compounds (**7a-j**) is tabulated in Table 1.

Infrared spectra of (**4a-e**) showed -C-NH- stretching from 3364 to 3280 cm^{-1}. The carbonyl stretching of amide group from 1688-1638 cm^{-1}. The carbonyl group of ester ranges from 1788-1743 cm^{-1}. The C-O-C stretching of ester groups are in the region 1280-1215 cm^{-1}. The aromatic protons showed stretching vibration in the region from 1536-1530 cm^{-1}. The NMR spectra of (**4**) showed singlet for -C-O-CH_3 group in the region 3.75-2.8 ppm. Aromatic protons exhibited a multiplet at 7.6-7.7 ppm. The two methine protons (Ha and Hb) showed a doublet of doublet and a doublet at 5.3-5.8 ppm and 4.1-6.3 ppm respectively.

The infrared spectra of (**5a-j**) showed -C-NH- stretching from 3376-3274 cm^{-1}. The carbonyl stretching of amide group from 1680-1635 cm^{-1}. The carbonyl stretching of ester group from 1785-1728 cm^{-1}. The C-O-C stretching of ester groups were in the region 1257-1140 cm^{-1}. The aromatic protons showed their stretching vibration in the region from 1539-1504 cm^{-1}. In the NMR spectra of (**5**), protons of esters showed singlet at 3.70-3.80 ppm. The methine protons showed coupling with the proton of NH and showed a doublet at 5.5-5.8 ppm. Aromatic protons showed multiplet at 7.8 ppm. The methyl protons attached to pyrazole ring showed singlet at 2.1-2.4 ppm. In N-phenyl derivative, these methyl groups showed separate singlets due to unequal environmental conditions.

Compounds (**6a-j**) obtained by saponification of the esters (**5a-j**) were identified only by IR spectra where the C=O vibrations were observed at 1734-1720 cm^{-1} in place of carbonyl stretching of



Scheme 1

ester group at 1785-1728 cm^{-1}. Moreover C-O-C stretching of ester groups at 1257-1140 cm^{-1} were also absent in these compounds. The purity of acids was confirmed by elemental analysis.

The IR spectra of (**7a-j**) showed NH stretching in the region 2908 cm^{-1} to 3148 cm^{-1}, C=O stretching in the region 1605-1635 cm^{-1}, NH deformation in the region 1503-1527 cm^{-1}. In the NMR spectrum of (**7**), the methine proton appeared as singlet at 5.2 ppm. Aromatic protons appeared as singlet at 7.4-7.5 ppm. Methyl protons of pyrazole ring were seen at 2.12-2.25 ppm.

The IR and NMR spectroscopic data of compounds (**7a-j**) is summarized in Table 2. The mass

Table 1: Physical data of compounds (7 a-j).

Compound	R^1	R^2	R^3	mp°C	Mole formula (Mol. wt.)	Analysis calculated found C	H	N
(7a)	CH_3	CH_3	H	233 dec	$C_7H_{11}N_3O_2$	49.7	6.5	24.8
					(169)	49.43	6.4	23.19
(7b)	CH_3	CH_3	C_8H_5	220 dec	$C_{13}H_{15}N_3O_2$	63.67	6.12	17.14
					(245)	63.48	6.58	17.04
(7c)	CH_3	C_8H_5	H	230 dec	$C_{12}H_{13}N_3O_2$	62.33	5.62	18.18
					(231)	61.87	5.51	17.95
(7d)	CH_3	C_6H_5	C_6H_5	216 dec	$C_{18}H_{17}N_3O_2$	70.35	5.59	13.68
					(307)	69.12	5.51	13.29
(7e)	C_6H_5	C_6H_5	H	264 dec	$C_{17}H_{15}N_3O_2$	69.62	5.11	14.33
					(293)	69.01	5.01	13.99
(7f)	C_6H_5	C_6H_5	C_6H_5	202 dec	$C_{23}H_{19}N_3O_2$	74.79	5.14	11.38
					(369)	74.11	4.93	11.07
(7g)	CF_3	CF_3	H	223 dec	$C_7H_5N_3O_2F_8$	30.32	1.8	15.6
					(277)	29.96	1.79	15.21
(7h)	CF_3	CF_3	C_6H_5	212 dec	$C_{13}H_9N_3O_2F_6$	44.3	2.55	11.93
					(353)	44.12	2.51	11.87
(7i)	CH_3	CF_3	H	215 dec	$C_7H_8N_3O_2F_3$	37.66	3.58	18.83
					(223)	37.56	3.09	18.05
(7j)	CH_3	CF_3	C_6H_5	204 dec	$C_{13}H_{12}N_3O_2F_3$	52.17	4.01	14.04
					(299)	52.11	3.75	14.00

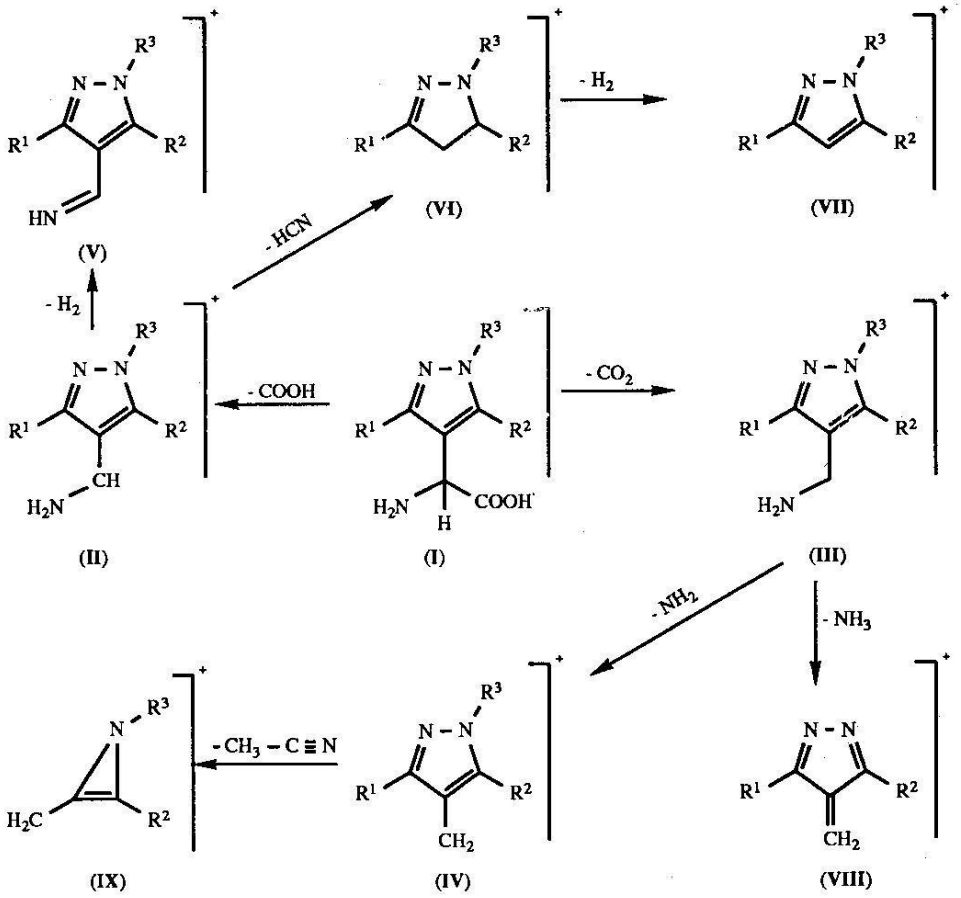
Table 2: IR and ^{1}H-NMR spectroscopic data of compounds (7 a-j).

Compound	R^1	R^2	R^3	CO_2(St.) cm^{-1}	$-NH_3$(St.) cm^{-1}	-NH(def.) cm^{-1}	$-CH_3$ ppm	Methine H ppm	Phenyl ppm
(7a)	CH_3	CH_3	H	1614	2908	1518	2.25 (s, 6H)	5.20 (s, 1H)	--
(7b)	CH_3	CH_3	C_6H_5	1635	3064	1503	2.12 (s, 3H) 2.18 (s, 3H)	5.2 (s, 1H)	7.4 (s, 5H)
(7c)	CH_3	C_6H_5	H	1605	3148	1527	2.25 (s, 3H)	5.2 (s, 1H)	7.5 (s, 5H)
(7d)	CH_3	C_6H_5	C_6H_5	1617	3046	1506	2.24 (s, 3H)	4.07 (s, 1H)	7.25 (s, 10H)
(7e)	C_6H_5	C_6H_5	H	1620	3045	1511	--	5.9 (s, 1H)	7.5 (s, 10H)
(7f)	C_6H_5	C_6H_5	C_6H_5	1629	3051	1510	--	5.93 (s, 1H)	7.6 (s, 15H)
(7g)	CF_3	CF_3	H	1601	3142	1547	--	6.01 (s, 1H)	--
(7h)	CF_3	CF_3	C_6H_5	1619	3055	1521	--	5.9 (s, 1H)	7.8 (s, 5H)
(7i)	CH_3	CF_3	H	1628	3061	1533	2.27 (s, 3H)	5.6 (s, 1H)	--
(7j)	CH_3	CF_3	C_6H_5	1631	3073	1523	2.28 (s, 3H)	5.63 (s, 1H)	7.8 (s, 5H)

spectra of (7) showed base peak due to the loss of -COOH group. The primary fragmentation consistent in all of the compounds was characterized by the presence of m/z M^+ - 44] and M^+ -45] due to the loss of CO_2 and -COOH from the molecular ion respectively. The detailed mass fragmentation pattern of these compounds is shown in Scheme 2 and the prominent mass peaks are tabulated in Table 3.

Experimental

The melting points are uncorrected, for recording IR, ^{1}H-NMR and mass spectra, Hitachi 270-50, Jeol Model JNM_FX 900 and Varian Mat CH-5 were used respectively. The elemental analysis was carried out on Carlo Erba model DP 200. The NMR spectra of all the compounds were



Scheme 2

Table 3

Prominent mass spectral data of compounds 7(a-j)

	COMPOUND NO.	7a		7b		7c		7d		7e		7f		7g		7h		7i		7j	
Peak No.	Peak	m/z	%	m/z	%	m/z	%	m/z	%	m/z	%	m/z	%	m/z	%	m/z	%	m/z	%	m/z	%
I	$M^{+\cdot}]$	169	1-15	245	2	231	1-5	307	1-5	293	1-1	369	1-2	277	1-4	353	1-21	223	1-2	299	1-1
II	$M-COOH]^{+}$	124	100	200	100	186	100	262	100	248	100	324	100	232	100	308	100	178	100	254	100
III	$M-CO_2]^{+\cdot}$	125	17-34	201	21-9	187	26	263	30-05	249	15-01	325	17-1	233	25	309	21	179	19	255	12-5
IV	$III-NH_2]^{+}$	109	34-10	185	35-8	171	23	247	13-29	233	12-4	309	22-1	217	19-5	293	15-9	163	11-11	233	9-8
V	$II-H_2]^{+\cdot}$	122	34-10	198	5-2	184	13-2	260	7-5	246	3-4	322	2-3	230	3-7	306	2-1	176	1-2	252	1-8
VI	$II-HCN]^{+}$	97	38-7	173	16-7	159	15	235	4-04	221	2-2	297	2-1	205	5-2	281	6-1	151	7-3	227	6-1
VII	$VI-H_2]^{+}$	95	7-5	171	1-7	157	2	233	2-04	219	2-5	295	2-4	203	4-6	279	7-3	149	10-5	225	9-2
VIII	$III-NH_3]^{+\cdot}$	108	37-5	-	-	170	15	-	-	232	11-3	-	-	216	8-7	-	-	162	13-6	-	-
IX	$IV-C_2H_3N]^{+}$	68	9-8	144	3-4	130	6-3	206	3-5	-	-	-	-	-	-	-	-	122	2-4	192	3-9

recorded in $CDCl_3$ except the final amino acids (**7a-j**) where D_2O was used as solvent.

General procedure for the reaction of methyl 2-acylamino-2- bromoacetate with β-dicarbonyl compound

The acyliminoester (**3**) use generated by addition of triethylamine (0.75 ml, 5.5 m mol) to bromoester (**2**) in dry THF at -78°C. After 30 minutes the β-dicarbonyl compound (6 m.mole), stirred with triethylamine (6 m. mole) in dry THF at room temperature for 30 minutes, was added slowly to the acyliminoester. After warming up, the mixture was stirred for 12 hours at room temperature. Then aqueous 20% citric acid (5 ml) was added and the solution was neutrilized with aq. sodium hydrogen carbonate. The product was extracted with ethylacetate (3x) and the dried organic phase was evaporated *in vacuo*. Purification was possible by recrystallization from ethylacetate/pet.ether or by column chromatography using ethylacetate/pet. ether as eluent.

*Methyl-2-benzoylamino-4-oxo-3-(1-oxoethyl)pentanoate (**4a**)*

(60%), m.p. 119°C: ν_{max} (KBr) 3292, 3016, 2956, 1749, 1731, 1704, 1647, 1581, 1536, 1494, 1458, 1422, 1365, 1323, 1290, 1242, 1167, 1149, 1104, 1056, 999, 960, 642, 849, 801, 777, 726, 690, 558, 462, 375 cm^{-1}. δ_H 2.28 (3H, s), 2.37 (3H, s), 3.75 (3H, s, $COOCH_3$) 4.58 (1H, d, J 2Hz), 6.52 (1H, dd, 6.5 Hz), 7.6 (6H, m).

*Methyl-2-benzoylamino-4-oxo-3(1-oxophenylmethyl)pentanoate (**4b**)*

(65%), m.p. 87°C: ν_{max} (KBr) 3280, 3000, 2950, 1751, 1712, 1677, 1640, 1520, 1442, 1375, 1290, 1220, 1164, 981, 760, 713, 671 cm^{-1}. δ_H 2.42 (3H, s), 2.7 (3H, s), 5.75-5.34 (2H, m, 2 CH), 7.6 (11 H, m).

*Methyl-2-benzoylamino-4-oxo-4-phenyl-3-(1-oxophenylmethyl) butanoate (**4c**)*

(85%), m.p. 154-157°C: ν_{max} (KBr) 3382, 3064, 2962, 2848, 1989, 1818, 1743, 1689, 1665, 1599, 1581, 1530, 1491, 1452, 1341, 1323, 1278, 1182, 1092, 1074, 1050, 1026, 996, 960, 945, 867, 792, 773, 717, 690, 618, 591,,552, 525, 477, 405 cm^{-1}. δ_H 3.74 (3H, s), 5.8 (1H, dd, J 7Hz), 6.3 (1H, d, 2.5 Hz) 7.7 (16 H, m).

*Methyl-2-benzoylamino-4-oxo-5,5,5-trifluoro-3-(1-oxo-2,2,2- trifluoroethyl) pentanoate (**4d**)*

(51%) m.p. 205°C: ν_{max} (KBr) 3316, 3058, 2950, 2842, 2344, 2152, 1989, 1755, 1638, 1581, 1530, 1488, 1443, 1377, 1338, 1272, 1215, 1185, 1158, 1104, 1074, 1038, 999, 954, 924, 843, 801, 771, 723, 696, 666, 621, 606, 588, 537 cm^{-1}. δ_H 3.81 (3H, s), 5.73 (2H, m, 2 CH), 7.4 (6H, m, Ar) (Found: C, 44.98; H, 2.62; N, 3.40, $C_{15}H_{11}NO_5F_6$ required: C, 45.11; H, 2.75; N, 3.50%).

*Methyl-2-benzoylamino-4-oxo-5,5,5-trifluoro-3(1-oxo-ethyl) pentanoate (**4e**)*

(69%), m.p. 146°C: ν_{max} (KBr) 3976, 3880, 3682, 3622, 3562, 3472, 3364, 3170, 3070, 2920, 2854, 2728, 2686, 2638, 2602, 2452, 2326, 2170, 1965, 1908, 1788, 1680, 1647, 1605, 1584, 1530, 1494, 1449, 1371, 1332, 1305, 1275, 1236, 1146, 1086, 1026, 987, 882, 867, 705, 687, 633, 603 cm^{-1}. δ_H 2.38 (3H, s), 3.78 (3H,s), 5.69 (2H, m), 7.5 (6H, m), (Found: C, 52.03; H, 4.01; N, 3.99, $C_{15}H_{14}NO_5F_3$ required C, 52.17; H, 4.05; N, 4.05%).

*General procedure for cyclization of (**4**)*

(**4a-e**), (5 m. mole) dissolved in ethanol (50 ml) and after addition of hydrazine hydrate (100%) or phenyl hydrazine (5 m. mole), this mixture was refluxed for 2-3 hours. After evaporation to dryness the product was purified by recrystallization from ethyl acetate/pet.ether or by column chromatography.

*Methyl-2-benzoylamino-2 (3,5-dimethyl pyrazol-4-yl) acetate (**5a**)*

(95%), m.p. 223-226°C: ν_{max} (KBr) 3340, 3196, 3064, 2926, 1728, 1635, 1578, 1539, 1494, 1446, 1385, 1344, 1257, 1152, 1083, 1044, 1002, 939, 819, 768, 693 cm^{-1}. δ_H 2.31 (6H, s), 3.76 (3H, s, $COOCH_3$), 5.81 (1H, d, J 3.75 Hz), 7.7 (6H, m).

*Methyl-2-benzoylamino-2 (3,5-dimethyl-1-phenylpyrazol-4-yl) acetate (**5b**)*

(68.57%), m.p. 159-160.2°C: ν_{max} (KBr) 3352, 3064, 3010, 2950, 1755, 1638, 1599, 1584, 1530, 1506, 1488, 1434, 1383, 1344, 1317, 1257, 1209, 1179, 1149, 1092, 1077, 1032, 984, 906, 810, 762, 717, 693 $cm.^{-1}$ δ_H 2.32 (3H, s), 2.38 (3H, s), 3.78 (3H, s, $COOCH_3$), 5.7 (1H, d, J 3.75 Hz), 7.58 (11H, m).

*Methyl-2-benzoylamino-2(3-methyl 5-phenyl pyrazol-4-yl) acetate (**5c**)*

(54%), m.p. 182-183°C: ν_{max} (KBr) 3884, 3612, 3380, 3224, 3140, 2244, 2092, 1646, 1600, 1504, 1482, 1446, 1382, 1326, 1296, 1206, 1146, 1076, 1054, 1028, 1000, 966, 926, 840, 772, 740, 702, cm^{-1}. δ_H 2.44 (3H, s), 2.72 (3H, s), 5.76 (1H, d, J 4Hz), 7.72 (1H, m).

*Methyl-2-benzoylamino-2(3-methyl-1,5-diphenyl pyrazol-4-yl) acetate (**5d**)*

(58%), m.p. 138-139°C: ν_{max} (KBr) 3784, 3688, 3292, 3060, 2956, 2916, 1756, 1662, 1600, 1582, 1506, 1486, 1448, 1370, 1336, 1282, 1218, 1200, 1164, 1138, 1088, 1072, 1026, 1004, 980, 912, 798, 764, 740, 692 cm^{-1}. δ_H, 2.55 (3H, s) 2.73 (3H, s), 5.73 (1H, d, J 3.7 Hz), 7.74 (16H, m).

*Methyl-2-benzoylamino-2 (3,5 diphenyl pyrazol-4-yl) acetate (**5e**)*

(63.12%), m.p. 236-239.6°C: ν_{max} (KBr) 3358, 3256, 3058, 1641, 1518, 1485, 1449, 1374, 1332, 1140, 1080, 1026, 966, 936, 891, 879, 780, 747, 696 cm^{-1}. δ_H, 3.71 (3H, s), 6.4 (1H, d, J 3.7 Hz), 7.9 (16H, m).

*Methyl-2-benzoylamino-2(1,3,5-triphenyl-pyrazol-4-yl) acetate (**5f**)*

(62.3%), m.p. 170-172°C: ν_{max} (KBr) 3356, 2370, 3051, 1654, 1518, 1480, 1453, 1404, 1381, 1330, 1211, 1079, 1026, 926, 902, 779, 690 cm^{-1}. δ_H, 3.70 (3H, s), 6.2 (1H, d, J 4.1 Hz), 7.8 (21 H, m).

*Methyl-2-benzoylamino-2[3,5-di(trifluoromethyl)-pyrazol-4- yl) acetate (**5g**)*

(65.2%), m.p. 203-204°C: ν_{max} (KBr) 3274, 3246, 1773, 1644, 1581, 1533, 1506, 1485, 1446, 1371, 1344, 1290, 1269, 1203, 1131, 1107, 1071, 1026, 750, 696 cm^{-1}. δ_H 3.86 (3H, s), 5.8 (1H, d, J 3.5 Hz), 7.7 (6H, m).

*Methyl-2-benzoylamino-2[1-phenyl-3,5-di(tri-fluoromethyl)- pyrazol-4-yl) acetate (**5h**)*

(60.5%) m.p. 168-172°C: ν_{max} (KBr) 3316, 3064, 2956, 2848, 1899, 1788, 1758, 1680, 1644, 1605, 1581, 1533, 1491, 1443, 1416, 1371, 1335, 1275, 1257, 1218, 1158, 1104, 1074, 1044, 1026, 1002, 954, 924, 861, 843, 801, 774, 726, 693, 666, 624, 588, 546, 507, 474, 408, 366 $cm.^{-1}$ δ_H, 382 (3H, s), 5.91 (1H, d, J 3.7 Hz), 7.8 (11H, m).

*Methyl-2-benzoylamino-2 (3-methyl, 5-tri-flouromethyl-pyrazol-4-yl) acetate (**5i**)*

(61%), m.p. 195°C: ν_{max} (KBr) 3286, 1962, 1704, 1644, 1605, 1581, 1530, 1491, 1449, 1362, 1299, 1272, 1170, 1137, 1098, 1020, 963, 921, 852, 696, 618 cm^{-1}. δ_H, 2.73 (3H, s), 3.84 (3H, s), 6.01 (1H, d, J 4 Hz), 7.6 (6H, m).

*Methyl-2-benzoylamino-2-(1-phenyl,3-methyl-5-tri-fluoromethyl- pyrazol-4-yl)acetate (**5j**)*

(59.2%), m.p. 150-153°C: ν_{max} (KBr) 3940, 3850, 3796, 3736, 3562, 3364, 3130, 3070, 2962, 2920, 2596, 2326, 2266, 2170, 1965, 1887, 1785, 1688, 1647, 1605, 1587, 1530, 1494, 1371, 1329, 1305, 1278, 1242, 1146, 1086, 1026, 999, 867, 798, 705, 687, 633, 603, cm^{-1}. δ_H, 2.74 (3H, s), 3.86 (3H, s), 6.12 (1H, d, 3.7 Hz), 7.7 (11H, m).

General procedure for the cleavage of protective groups

A. Basic cleavage of methyl ester

The N-benzoylamino acid methyl ester (1 m mole) was refluxed for one hour with a mixture of ethanol (20 ml) and 1N KOH (1.5 ml). Then the solvent was evaporated under reduced pressure, the residue dissolved in water (20 ml), acidified with 1N HCl (2 ml) and extracted with ethyl acetate (3 x 20 ml). The organic layer was dried with $MgSO_4$ anhydrous and evaporated to dryness. The crude acid was purified by recrystallization from ethyl acetate/pet. ether.

B. Benzoyl cleavage

The suspension of N-benzoylamino acid (1 m. mole) in 20 ml of 10% HCl was refluxed for 50 hours. Cold mixture was extracted with ethylacetate and aqueous phase was applied to an ion exchange column (Amberlite CG 120, 20 ml of resin bed). The column was eluted with water followed by 2% NH_3 solution. The aqueous ammonia fraction was evaporated *in vacuo*. The crude products were recrystallized from ethanol/acetone.

2-Benzoylamino-(3,5-dimethyl pyrazol-4-yl)acetic acid **(6a)**

(70%), m.p. 225-228°C: ν_{max} (KBr), 3220, 2930, 1730, 1649, 1510, 1370, 1211, 1077, cm^{-1}. (Found C, 60.87; H, 5.03; N, 14.91, $C_{14}H_{15}N_3O_3$ required C, 61.53; H, 5.49; N, 15.38%).

2-Benzoylamino-2(3,5-dimethyl 1-phenylpyrazol-4-yl) acetic acid **(6b)**

(74%), m.p. 198°C: ν_{max} (KBr) 3262, 2932, 1734, 1617, 1569, 1533, 1506, 1498, 1431, 1377, 1332, 1251, 1212, 1182, 1140, 1077, 1047, 894, 810, 765, $cm.^{-1}$ (Found: C, 68.10; H, 5.06; N, 11.71, $C_{20}H_{19}N_3O_3$ required C, 68.76; H, 5.44; N, 12.03%).

2-Benzoylamino-2 (3-methyl,5-phenyl pyrazol-4-yl) acetic acid **(6c)**

(71%), m.p. 201-202°C: ν_{max} (KBr) 3202, 1896, 1725, 1644, 1578, 1515, 1482, 1302, 1071, 918, 837, 699 cm^{-1}. (Found: C, 67.52: H, 4.59; N, 11.93, $C_{19}H_{17}N_3O_3$ requires C, 68.05; H, 5.07; N, 12.53%).

2-Benzoylamino-2(3-methyl-1, 5-diphenylpyrazol-4-yl) acetic acid **(6d)**

(78%), m.p. 187°C: ν_{max} (KBr) 3940, 3412, 3046, 2920, 2542, 1953, 1722, 1668, 1602, 1581, 1554, 1503, 1482, 1446, 1431, 1374, 1311, 1254, 1194, 1074, 1026, 978, 765, 732, 693, cm^{-1}. (Found: C 72.23; H, 4.79; N, 9.55, $C_{25}H_{11}N_3O_3$ required C, 72.99; H, 5.10; N, 10.21%).

2-Benzoylamino-2(3,5-diphenyl pyrazol-4-yl) acetic acid **(6e)**

(69%), m.p. 241-242°C: ν_{max} (KBr) 3778, 3430, 3220, 3052, 2920, 2578, 2146, 1941, 1899, 1722, 1656, 1605, 1581, 1515, 1485, 1452, 1335, 1308, 1260, 1212, 1158, 1080, 1026, 999, 783, 738, 720, 699 $cm.^{-1}$ (Found: C, 71.81; H, 4.09, N, 9.97; $C_{24}H_{19}N_3O_3$ requires C, 72.54; H, 4.78; N, 10.57).

2-Benzoylamino-2(1,3,5-triphenyl-pyrazol-4-yl) acetic acid **(6f)**

(81%), m.p. 186-188°C: ν_{max} (KBr) 3760, 3440, 3202, 2914, 2611, 2577, 2140, 1944, 1880, 1720, 1655, 1601, 1579, 1480, 1467, 1330, 1020, 696 $cm.^{-1}$ (Found: C, 75.85; H, 4.13; N, 8.19; $C_{30}H_{23}N_3O_3$ required C, 76.10; H, 4.86; N, 8.87%).

2-Benzoylamino-2(3,5-di(trifluoromethyl) pyrazol-4-yl) acetic acid **(6g)**

(62%), m.p. 211-213°C: ν_{max}: (KBr) 3772, 3500, 3452, 3219, 2909, 2551, 1725, 1660, 1609, 1471, 1313, 650 cm^{-1}. (Found: C, 43.47; H, 1.81; N, 10.38, $C_{14}H_9N_3O_3F_6$ required C, 44.09; H, 2.36; N, 11.02%).

2-Benzoylamino-2-(1-phenyl-3,5-di(trifluoromethyl) pyrazol-4-yl) acetic acid **(6h)**

(64%), m.p. 191-193°C: ν_{max} (KBr) 3640, 3549, 3411, 3401, 3331, 2961, 2539, 1721, 1661, 1617, 1298, 1225, 1173, 711, 629 cm^{-1}. (Found: C, 51.89; H, 2.27; N, 8.88; $C_{20}H_{13}N_3O_3F_6$ required C, 52.51; H, 2.84; N, 9.19%).

2-Benzoylamino-2 (3-methyl-5-trifluoromethyl-pyrazol-4-yl) acetic acid **(6i)**

(52%), m.p. 203-205°C: ν_{max} (KBr) 3621, 3474, 3402, 3399, 3157, 1730, 1652, 1613, 1466, 1019, 771, 627 cm^{-1}. (Found: C, 50.90; H, 3.07; N, 12.13, $C_{14}H_{12}N_3O_3F_3$ required C, 51.37; H, 3.66; N, 12.84%).

2-benzoylyamino-2-(1-phenyl-3-methyl-5-trifluoromethyl pyrazol-4-yl) acetic acid **(6j)**

(58%), m.p. 169-171°C: ν_{max} (KBr) 3939, 3041, 2939, 1723, 1671, 1619, 1512, 1444, 1431, 1374, 1251, 1025, 766, 692 cm^{-1}. (Found: C, 58.99; H, 3.09; N, 9.81, $C_{20}H_{16}N_3O_3F_3$ required C, 59.55, H, 3.97; N, 10.42%).

(3-5-Dimethylpyrazol-4-yl)-glycine **(7a)**

(69%) m.p. 233°C dec: ν_{max} (KBr) 2908, 1614, 1518, 1446, 1377, 1344, 1287, 1212, 1149, 1044, 999, 894, 825, 738, 696 cm^{-1}. δ_H (D_2O) 2.25 (s, 6H, CH_3), 5.20 (s, 1H) m/z : 169 (1.15% M^+), 168 (6.3), 167 (9.2), 152 (1.73), 125 (17.34), 124 (100), 122 (34.1), 109 (26.01), 108 (37.5), 97 (38.7), 95 (7.5), 56 (17.34), 52 (10.4).

(3,5-Dimethyl-1-phenyl pyrazol-4-yl) glycine **(7b)**

(72%) m.p. 220°C dec: ν_{max} (KBr) 3064, 1635, 1503, 1431, 1380, 1206, 1116, 1017, 693, 759 cm^{-1}. δ_H (D_2O), 2.12 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 5.2 (s, 1H, CH), 7.4 (s, 5H, Ar) m/z : 245 (2%, M^+) 201,

(21.9), 200 (100), 198 (5.2), 185 (35.8), 184 (40.46), 173 (16.7), 171 (1.7), 132 (1.7), 77 (59.5).

(3-Methyl-5-phenyl-pyrazol-4-yl)glycine **(7c)**

(58%) m.p. 230°C dec: ν_{max} (KBr) 3148, 2866, 1605, 1527, 1488, 1452, 1368, 1344, 1296, 1263, 1215, 1155, 1098, 999, 969, 792, 771, 729, 693 cm^{-1}. δ_H (D_2O) 2.25 (s, 3H, CH_3), 5.2 (s, 1H, CH), 7.5 (s, 5H, Ar) m/z : 231 (1.5% M^+), 187 (26), 186 (100), 184 (13.2), 171 (23.12), 170. (14.45), 159 (15), 118 (5.2), 117 (5.7), 77 (32.3).

(3-Methyl-1,5-diphenyl-pyrazol-4-yl)glycine **(7d)**

(63%), m.p. 216°C dec: ν_{max} (KBr) 3364, 3160, 3046, 2716, 2548, 1617, 1506, 1449, 1431, 1371, 1323, 1296, 1263, 1107, 1074, 1011, 969, 912, 825, 792, 762, 696 $cm.^{-1}$ δ_H (D_2O) 2.24 (s, 3H), 4.07 (s, 1H), 7.25 (s, 10H, Ar). m/z : 307 (1.5%, M^+) 307 (1.5), 290 (0.9), 263 (30.05), 262 (100), 260 (7.5), 235 (4.04), 233 (2.04), 246 (19.07), 247 (12.7), 185 (3.46), 169 (1.2), 132 (5.7), 131 (10.4), 194 (2.89), 117 (6.35), 108 (5.78), 92 (1.7), 91 (1.7), 77 (59.53).

(3-5-Diphenyl pyrazol-4-yl) glycine **(7e)**

(77%), m.p. 264°C dec: ν_{max} (KBr), 3362, 3045, 2556, 1620, 1511, 1429, 1368, 1266, 1107, 955, 760 cm^{-1}. δ_H (D_2O), 5.9 (s, 1H), 7.5 (s, 10H), m/z: 293 (1.1% M^+), 276 (0.7), 249 (15.01), 248 (100), 246 (3.4), 232 (11.3), 221 (2.2), 118 (17.2).

(1,3,5-Triphenyl pyrazol-4-yl) glycine **(7f)**

(48%), m.p. 202°C dec: ν_{max} (KBr) 3331, 3051, 2545, 1629, 1510, 1370, 1120, 774, cm^{-1} δ_H (D_2O), 5.93 (s, 1H), 7.6 (s, 15H), m/z: = 369 (1.2% M^+), 324 (100), 352 (0.8), 325 (17.1), 308 (13.2), 194 (16.1), 322 (2.3), 297 (2.1), 295 (2.4).

[3,5-Di(trifluoromethyl)pyrazolyl-4-yl]glycine (7g)

(54%), m.p. 223°C dec: ν_{max} (KBr) 3760, 3342, 1631, 1601, 1547, 1377, 1109, 693, $cm.^{-1}$ δ_H (D_2O), 6.01 (1H, CH), m/z: 277 (1.4%, M^+), 232 (100), 260 (1.1), 233 (25), 216 (8.7), 110 (7.2), 230 (3.7), 205 (5.2), 203 (4.6).

[1-phenyl-3,5-di(trifluoromethyl)pyrazol-4-yl]glycine (7h)

(47%), m.p. 212°C dec. ν_{max} (KBr) 3055, 1619, 1521, 1463, 1202 cm^{-1}. δ_H (D_2O), 5.9 (s, 1H), 7.8 (s, 5H), m/z: 353 (1.31%, M^+), 308 (100), 336 (1.3), 309 (21), 292 (11.1), 186 (6.6), 306 (2.1), 281 (6.1), 279 (7.3).

(3-Methyl, 5-triflouromethyl pyrazol-4-yl) glycine **(7i)**

(43%) 215°C dec: ν_{max} (KBr) 3061, 1628, 1533, 1441, 1197, 932, $cm.^{-1}$ δ_H (D_2O), 2.27 (s, 3H), 5.6 (s, 1H), m/z : 223 (1.2%, M^+), 178 (100), 206 (0.9), 179 (19), 163 (11.7), 162 (12.6), 110 (2.4), 176 (1.2), 151 (7.3), 149 (10.5).

[3,Methyl-5-trifluoromethyl-1-phenylpyrazol-4-yl) glycine (7j)

(41%), m.p. 204°C ν_{max} (KBr) 3073, 1631, 1523, 1455, 902 cm^{-1}. δ_H (D_2O), 2.28 (s, 3H), 5.63 (s, 1H), 7.8 (s, 5H), m/z: 299 (1.1% M^+), 254 (100), 282 (1.2), 255 (12.5), 239 (9.3), 238 (13.1), 186 (3.5), 252 (1.8), 227 (6.1), 225 (9.2).

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