The Synthesis of Azahomotryptophane Derivatives. The Transformation of *N*-Trifluoroacetyl-5-bromo-4-oxonorvaline Methyl Ester into 4-(Imidazo[1,2-*a*]azinyl-3)-4-oxohomoalanine Derivatives

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Azatryptophane homologues, 4-(imidazo[1,2-*a*]pyridinyl-3)- **9a-9f** and 4-(imidazo[1,2-*a*]pyrimidinyl-3)-4-oxohomoalanine derivatives **9g-9i**, were prepared from *N,N*-dimethyl-*N'*-(pyridinyl-2)- **6a-6f** and *N,N*-dimethyl-*N'*-(pyrimidinyl-2)formamidines **6g-6i**, and *(S)*-*N*-trifluoroacetyl-5-bromo-4-oxonorvaline methyl ester (**2**) and its *(R,S)*-isomer.

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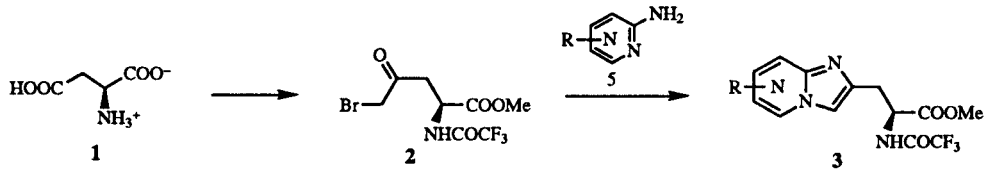
Since nonproteinogenic amino acids play an important role in pharmaceutical applications [1-3], we decided to focus our efforts to the synthesis of heteroaryl- and heteroarylamino substituted α-amino acids [4].

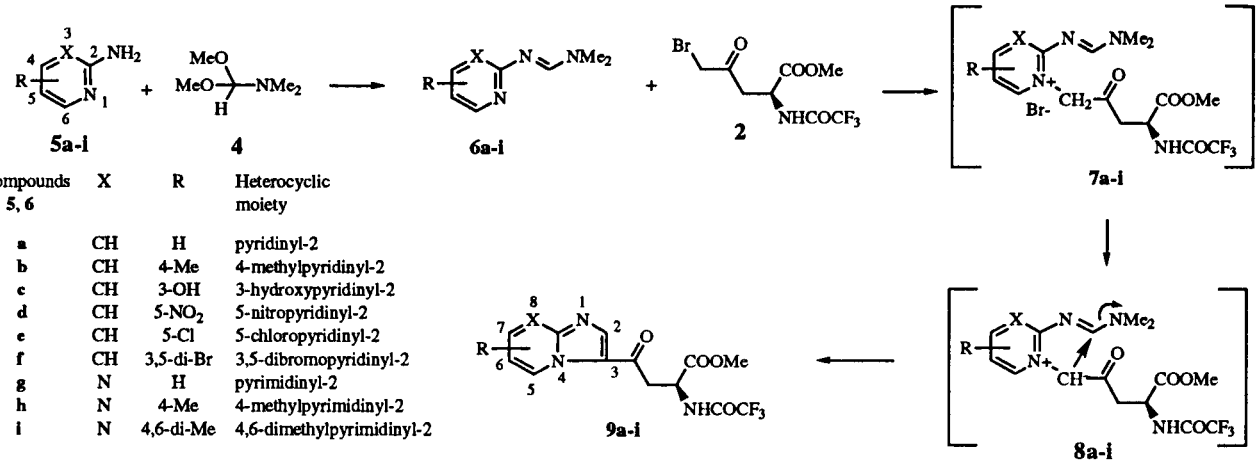
In our previous paper [5], we reported the transformation of optically active and racemic isomers of aspartic acid (**1**) into the corresponding isomers of *N*-trifluoroacetyl-5-bromo-4-oxonorvaline methyl ester (**2**) which served as the starting material in the synthesis of 2-substituted imidazo[1,2-*x*]azines **3** with the amino acid residue attached at the position 2 of the imidazole part of the molecule [5] (Scheme 1).

In this paper, we report a novel synthesis of 3-substituted imidazo[1,2-*a*]azines, the azahomotryptophane derivatives **9**. The synthesis is based on our earlier observation, that *N,N*-dimethyl-*N'*-heteroarylformamidines **6** react with simple α-haloketones to give 3-acyl substituted imidazo[1,2-*x*]-azines [6-7]. Therefore, utilisation of *N*-trifluoroacetyl-5-bromo-4-oxonorvaline methyl ester (**2**) as an α-bromo ketone gives with **6** 3-substituted imidazo[1,2-*x*]azines, with the amino acid residue attached at position 3 of the heterocyclic system, *i.e.* *N*-trifluoroacetyl-4-(imidazo[1,2-*a*]azinyl-3)-4-oxohomoalanine methyl esters **9**. The following 2-aminoazine derivatives, 2-aminopyridine (**5a**), 2-amino-4-

Scheme 1



Scheme 2



Compounds 5, 6	X	R	Heterocyclic moiety
a	CH	H	pyridinyl-2
b	CH	4-Me	4-methylpyridinyl-2
c	CH	3-OH	3-hydroxypyridinyl-2
d	CH	5-NO_2	5-nitropyridinyl-2
e	CH	5-Cl	5-chloropyridinyl-2
f	CH	3,5-di-Br	3,5-dibromopyridinyl-2
g	N	H	pyrimidinyl-2
h	N	4-Me	4-methylpyrimidinyl-2
i	N	4,6-di-Me	4,6-dimethylpyrimidinyl-2

Compounds 9	X	R	Heterocyclic moiety
a	CH	H	imidazo[1,2-*a*]pyridinyl-3
b	CH	7-Me	7-methylimidazo[1,2-*a*]pyridinyl-3
c	CH	8-OH	8-hydroxyimidazo[1,2-*a*]pyridinyl-3
d	CH	6-NO_2	6-nitroimidazo[1,2-*a*]pyridinyl-3
e	CH	6-Cl	6-chloroimidazo[1,2-*a*]pyridinyl-3
f	CH	6,8-di-Br	6,8-dibromoimidazo[1,2-*a*]pyridinyl-3
g	N	H	imidazo[1,2-*a*]pyrimidinyl-3
h	N	7-Me	7-methylimidazo[1,2-*a*]pyrimidinyl-3
i	N	5,7-di-Me	5,7-dimethylimidazo[1,2-*a*]pyrimidinyl-3

Table 1
Experimental Data

Compound	Solvent Time Yield	mp °C	Molecular Formula Analyses
9a *(S)*-isomer	dichloromethane 4 hours [8] 43%	130.5-132.5 (washed with water)	$C_{14}H_{12}F_3N_3O_4$ Calcd. C, 48.97; H, 3.53; N, 12.24. Found C, 48.87; H, 3.43; N, 12.13
9a *(R,S)*-isomer	ethanol 2.5 hours 29%	196-199 (from 50% ethanol)	$C_{14}H_{12}F_3N_3O_4$ Calcd. C, 48.97; H, 3.53; N, 12.24 Found C, 48.74; H, 3.32; N, 12.31
9b *(S)*-isomer	dichloromethane 3 hours 43%	147-150 (from ethanol/water)	$C_{15}H_{14}F_3N_3O_4$ Calcd. C, 50.41; H, 3.95; N, 11.76 Found C, 50.52; H, 4.09; N, 12.07.
9b *(R,S)*-isomer	dichloromethane 2.5 hours 25%	157-158.5 (from 50% ethanol)	$C_{15}H_{14}F_3N_3O_4$ Calcd. C, 50.41; H, 3.95; N, 11.76 Found C, 50.30; H, 3.78; N, 11.49
9c *(S)*-isomer	ethanol 80 hours [9] 33%	226-228 (from 50% ethanol)	$C_{14}H_{12}F_3N_3O_5$ Calcd. C, 46.79; H, 3.37; N, 11.70 Found C, 46.54; H, 3.18; N, 11.83
9c *(R,S)*-isomer	ethanol 4 hours 25%	254-256 (from 50% ethanol)	$C_{14}H_{12}F_3N_3O_5$ Calcd. C, 46.79; H, 3.37; N, 11.70 Found C, 46.63; H, 3.25; N, 11.60
9d *(R,S)*-isomer	ethanol 4 hours [10] 21%	169.5-171 (from 50% ethanol)	$C_{14}H_{11}F_3N_4O_6$ Calcd. C, 43.29; H, 2.86; N, 14.43 Found C, 43.20; H, 2.77; N, 14.28
9e *(S)*-isomer	chloroform 4.5 hours 12%	166-169 (from etanol/water)	$C_{14}H_{11}ClF_3N_3O_4$ Calcd. C, 44.56; H, 2.94; N, 11.14 Found C, 44.27; H, 2.78; N, 10.90
9e *(R)*-isomer	chloroform 4.5 hours 67%	170-171 (from etanol/water)	$C_{14}H_{11}ClF_3N_3O_4$ Calcd. C, 44.56; H, 2.94; N, 11.14 Found C, 44.23; H, 2.86; N, 10.98
9e *(R,S)*-isomer	chloroform 3 hours 44%	140-146 (from 50% ethanol)	$C_{14}H_{11}ClF_3N_3O_4$ Calcd. C, 44.56; H, 2.94; N, 11.14 Found C, 44.31; H, 2.77; N, 11.05
9f *(R,S)*-isomerO_4	ethanol 3 hours 15%	206-209 (from 50% ethanol)	$C_{14}H_{10}Br_2F_3N_3O_4$ Calcd. C, 33.67; H, 2.02; N, 8.42 Found C, 33.71; H, 1.77; N, 8.50
9g *(S)*-isomer$_4$	dichloromethane 2 hours 41%	136-138 (from 50% ethanol)	$C_{13}H_{11}F_3N_4O_4$ Calcd. C, 45.34; H, 3.22; N, 16.28 Found C, 44.95; H, 3.28; N, 16.20
9g *(R)*-isomer	dichloromethane 2 hours 62%	135-137 (from 50% ethanol)	$C_{13}H_{11}F_3N_4O_4$ Calcd. C, 45.34; H, 3.22; N, 16.28 Found C, 45.22; H, 3.02; N, 16.18
9g *(R,S)*-isomer	dichloromethane 3 hours 26%	208-210 (from 50% ethanol)	$C_{13}H_{11}F_3N_4O_4$ Calcd. C, 45.34; H, 3.22; N, 16.28 Found C, 45.06; H, 3.00; N, 16.35
9h *(S)*-isomer	dichloromethane 3 hours 53%	168-171 (from 50% ethanol)	$C_{14}H_{13}F_3N_4O_4$ Calcd. C, 46.92; H, 3.66; N, 15.64 FoundC, 46.58; H, 3.48; N, 15.45
9h *(R,S)*-isomer	dichloromethane 3 hours 21%	186-189 (from ethanol/water)	$C_{14}H_{13}F_3N_4O_4$ Calcd. C, 46.92; H, 3.66; N, 15.64 Found C, 46.75; H, 3.52; N, 15.64
9i *(S)*-isomer	dichloromethane 3 hours 46%	192-193.5 (from ethanol/water)	$C_{15}H_{15}F_3N_4O_4$ Calcd. C, 48.37; H, 4.06; N, 15.05 Found C, 48.45; H, 3.91; N, 14.91
9i *(R,S)*-isomer	dichloromethane 3 hours 35%	176-178 (from 50% ethanol)	$C_{15}H_{15}F_3N_4O_4$ Calcd. C, 48.37; H, 4.06; N, 15.05 Found C, 48.00; H, 3.85; N, 15.10

methylpyridine (**5b**), 2-amino-3-hydroxypyridine (**5c**), 2-amino-5-nitropyridine (**5d**), 2-amino-5-chloropyridine (**5e**), 2-amino-3,5-dibromopyridine (**5f**), 2-aminopyrimidine (**5g**), 2-amino-4-methylpyrimidine (**5h**), and 2-amino-4,6-dimethylpyrimidine (**5i**), were transformed with *N,N*-dimethylformamide dimethyl acetal (**4**) into the corresponding *N,N*-dimethyl-*N'*-azinylformamidines **6a-i** according to the procedure we described earlier [6]. Reaction

Table 2

^{1}H NMR Data

Compound	MHz Solvent	δ (TMS)
9a *(S)*-isomer	60 DMSO-d_6	3.24 (2H, d, CH_2CH), 3.36 (3H, s, OMe), 4.32-4.68 (1H, m, *CH*COOMe), 6.62 (1H, dd, $H_{6'}$), 6.78-7.23 (2H, m, $H_{7'}$ and $H_{8'}$), 7.83 (1H, s, $H_{2'}$), 8.49-8.70 (1H, m, $H_{5'}$), 8.85-9.06 (1H, m, NH), J_{CH_2CH} =7 Hz J_{NHCH} = 7 Hz, $J_{H5'H6'}$ = 7 Hz, $J_{H6'H7'}$ = 7 Hz, $J_{H6'H8'}$ = 2 Hz
9a *(R,S)*-isomer	300 $CDCl_3$	3.56 (1H, dd, CH_2CH), 3.81 (3H, s, OMe), 3.84 (1H, dd, CH_2CH), 4.99 (1H, ddd, *CH*COOMe), 7.13 (1H, dt, $H_{6'}$), 7.56 (1H, ddd, $H_{7'}$), 7.65 (1H, br d, NH), 7.81 (1H, td, $H_{8'}$), 8.39 (1H, s, $H_{2'}$), 9.55 (1H, td, $H_{5'}$), J_{CH_2CH} = 4.2 Hz, J_{CH_2} (gem) = 17.5 Hz, J_{NHCH} = 8.1 Hz, $J_{H5'H6'}$ = $J_{H6'H7'}$ = 6.9 Hz, $J_{H5'H7'}$ = $J_{H6'H8'}$ = 1.1 Hz, $J_{H7'H8'}$ = 9.0 Hz
9b *(S)*-isomer	60 DMSO-d_6	2.07 (3H, s, 7'-Me), 2.88 (2H, d, CH_2), 3.30 (3H, s, OMe), 4.05-4.44 (1H, m, *CH*COOMe), 6.00 (1H, dd, $H_{6'}$), 6.51 (1H, s, $H_{8'}$), 6.87 (1H, s, $H_{2'}$), 7.56 (1H, d, $H_{5'}$), 8.97-9.12 (1H, broad peak, NH), J_{CH_2CH} = 7 Hz, J_{NHCH} = 8 Hz, $J_{H5'H6'}$ = 7 Hz, $J_{H6'H8'}$ = 1.5 Hz
9b *(R,S)*-isomer	60 DMSO-d_6	2.07 (3H, s, 7'-Me), 2.88 (2H, d, CH_2), 3.30 (3H, s, OMe), 4.05-4.44 (1H, m, *CH*COOMe), 6.00 (1H, dd, $H_{6'}$), 6.51 (1H, br s, $H_{8'}$), 6.87 (1H, s, $H_{2'}$), 7.56 (1H, d, $H_{5'}$), 8.97-9.12 (1H, broad peak, NH), J_{CH_2CH} = 7 Hz, $J_{H5'H6'}$ = 6.5 Hz, $J_{H6'H8'}$ = 1.5 Hz
9c *(S)*-isomer	60 DMSO-d_6	3.24 (2H, d, CH_2), 3.36 (3H, s, OMe), 2.49-3.81 (1H, broad peak, OH), 4.29-4.59 (1H, m, *CH*COOMe), 6.12-6.57 (2H, m, $H_{6'}$ and $H_{7'}$), 7.59 (1H, s, $H_{2'}$), 8.16 (1H, dd, $H_{5'}$), 8.97-9.12 (1H, broad peak, NH), J_{CH_2CH} = 7 Hz, J_{NHCH} = 7 Hz, $J_{H5'H6'}$ = 7 Hz, $J_{H6'H7'}$ = 7 Hz, $J_{H5'H7'}$ = 1 Hz
9c *(R,S)*-isomer	60 DMSO-d_6	3.24 (2H, d, CH_2), 3.36 (3H, s, OMe), 2.49-3.81 (1H, broad peak, OH), 4.29-4.59 (1H, m, *CH*COOMe), 6.12-6.57 (2H, m, $H_{6'}$ and $H_{7'}$), 7.59 (1H, s, $H_{2'}$), 8.16 (1H, d, $H_{5'}$), 8.97-9.12 (1H, broad peak, NH), J_{CH_2CH} = 7 Hz, J_{NHCH} = 7 Hz, $J_{H5'H6'}$ = 7 Hz, $J_{H6'H7'}$ = 7 Hz, $J_{H5'H7'}$ = 1 Hz
9d *(R,S)*-isomer	300 $CDCl_3$	3.66 (1H, dd, CH_2), 3.85 (3H, s, OMe), 3.87 (1H, dd, CH_2), 5.00 (1H, ddd, *CH*COOMe), 7.54 (1H, br d, NH), 7.89 (1H, dd, $H_{8'}$), 8.31 (1H, dd, $H_{7'}$), 8.53 (1H, s, $H_{2'}$), 10.57 (1H, d, $H_{5'}$), J_{CH_2CH} = 4.2 Hz, J_{CH_2} (gem)= 17.8 Hz, J_{NHCH} = 7.4 Hz, $J_{H7'H8'}$ = 9.8 Hz, $J_{H5'H7'}$ = 2.3 Hz, $J_{H5'H8'}$ = 0.5 Hz
9e *(S)*-isomer	300 $CDCl_3$	3.58 (1H, dd, CH_2CH), 3.82 (3H, s, OMe), 3.83 (1H, dd, CH_2CH), 4.98 (1H, dt, *CH*COOMe), 7.52 (1H, dd, $H_{7'}$), 7.59 (1H, br d, NH), 7.74 (1H, dd, $H_{8'}$), 8.38 (1H, s, $H_{2'}$), 9.64 (1H, dd, $H_{5'}$), J_{CH_2CH} = 4.2 Hz, J_{CH_2} (gem) = 17.7 Hz, J_{NHCH} = 7.9 Hz, $J_{H5'H7'}$ = 2.0 Hz, $J_{H5'H8'}$ = 0.6 Hz, $J_{H7'H8}$ = 9.5 Hz
9e *(R)*-isomer	300 $CDCl_3$	3.58 (1H, dd, CH_2CH), 3.82 (3H, s, OMe), 3.83 (1H, dd, CH_2CH), 4.98 (1H, dt, *CH*COOMe), 7.53 (1H, dd, $H_{7'}$), 7.59 (1H, br d, NH), 7.74 (1H, dd, $H_{8'}$), 8.38 (1H, s, $H_{2'}$), 9.64 (1H, dd, $H_{5'}$), J_{CH_2CH} = 4.2 Hz, J_{CH_2} (gem) = 17.6 Hz, J_{NHCH} = 7.9 Hz, $J_{H5'H7'}$ = 1.9 Hz, $J_{H5'H8'}$ = 0.6 Hz, $J_{H7'H8}$ = 9.5 Hz
9e *(R,S)*-isomer	300 $CDCl_3$	3.58 (1H, dd, CH_2CH), 3.82 (3H, s, OMe), 3.83 (1H, dd, CH_2CH), 4.98 (1H, dt, *CH*COOMe), 7.53 (1H, dd, $H_{7'}$), 7.59 (1H, br d, NH), 7.74 (1H, dd, $H_{8'}$), 8.38 (1H, s, $H_{2'}$), 9.64 (1H, dd, $H_{5'}$), J_{CH_2CH} = 4.2 Hz, J_{CH_2} (gem) = 17.6 Hz, J_{NHCH} = 7.9 Hz, $J_{H5'H7'}$ = 2.0 Hz, $J_{H5'H8'}$ = 0.6 Hz, $J_{H7'H8}$ = 9.5 Hz
9f *(R,S)*-isomer	60 DMSO-d_6	3.30 (2H, d, CH_2), 3.36 (3H, s, OMe), 4.38-4.74 (1H, m, *CH*COOMe), 7.56 (1H, d, $H_{7'}$), 7.98 (1H, s, $H_{2'}$), 8.79 (1H, s, $H_{5'}$), 9.00-9.27 (1H, broad peak, NH), J_{CH_2CH} = 7Hz, J_{NHCH} = 8 Hz, $J_{H5'H7'}$ = 2 Hz
9g *(S)*-isomer	300 $CDCl_3$	3.60 (1H, dd, CH_2), 3.81 (3H, s, OMe), 3.84 (1H, dd, CH_2), 5.01 (1H, ddd, *CH*COOMe), 7.20 (1H, dd, $H_{6'}$), 7.57 (1H, br d, NH), 8.56 (1H, s, $H_{2'}$), 8.83 (1H, dd, $H_{7'}$), 9.79 (1H, dd, $H_{5'}$), , J_{CH_2CH} = 4.2 Hz, J_{CH_2} (gem) = 17.6 Hz, J_{NHCH} = 7.9 Hz, $J_{H5'H6'}$ = 6.9 Hz, $J_{H6'H7'}$ = 4.3 Hz, $J_{H5'H7'}$ = 2.1 Hz
9g *(R)*-isomer	300 $CDCl_3$	3.60 (1H, dd, CH_2), 3.81 (3H, s, OMe), 3.84 (1H, dd, CH_2), 5.01 (1H, ddd, *CH*COOMe), 7.20 (1H, dd, $H_{6'}$), 7.57 (1H, br d, NH), 8.56 (1H, s, $H_{2'}$), 8.83 (1H, dd, $H_{7'}$), 9.79 (1H, dd, $H_{5'}$), J_{CH_2CH} = 4.2 Hz, J_{CH_2} (gem) = 17.6 Hz, J_{NHCH} = 7.9 Hz, $J_{H5'H6'}$ = 6.9 Hz, $J_{H6'H7'}$ = 4.3 Hz, $J_{H5'H7'}$ = 2.1 Hz
9g *(R,S)*-isomer	300 $CDCl_3$	3.60 (1H, dd, CH_2), 3.82 (3H, s, OMe), 3.84 (1H, dd, CH_2), 5.00 (1H, ddd, *CH*COOMe), 7.20 (1H, dd, $H_{6'}$), 7.55 (1H, br d, NH), 8.56 (1H, s, $H_{2'}$), 8.83 (1H, dd, $H_{7'}$), 9.79 (1H, dd, $H_{5'}$), J_{CH_2CH} = 4.2 Hz, J_{CH_2} (gem) = 17.6 Hz, J_{NHCH} = 7.9 Hz, $J_{H5'H6'}$ = 6.9 Hz, $J_{H6'H7'}$ = 4.3 Hz, $J_{H5'H7'}$ = 2.1 Hz
9h *(S)*-isomer	60 DMSO-d_6	2.37 (3H, s, 7'-Me), 3.21 (2H, d, CH_2), 3.36 (3H, s, OMe), 4.29-4.62 (1H, m, *CH*COOMe), 6.57 (1H, d, $H_{6'}$), 7.86 (1H, s, $H_{2'}$), 8.64 (1H, d, $H_{5'}$), 8.85-9.06 (1H, broad peak, NH), J_{CH_2CH} = 7 Hz, $J_{H5'H6'}$ = 7 Hz
9h *(R,S)*-isomer	60 DMSO-d_6	2.37 (3H, s, 7'-Me), 3.21 (2H, d, CH_2), 3.36 (3H, s, OMe), 4.29-4.62 (1H, m, *CH*COOMe), 6.57 (1H, d, $H_{6'}$), 7.86 (1H, s, $H_{2'}$), 8.64 (1H, d, $H_{5'}$), 8.85-9.06 (1H, broad peak, NH), J_{CH_2CH} = 7 Hz, $J_{H5'H6'}$ = 7 Hz
9i *(S)*-isomer	60 DMSO-d_6	2.25 (3H, s, 5'-Me), 2.37 (3H, s, 7'-Me), 3.24 (2H, d, CH_2), 3.33 (3H, s, OMe), 4.29-4.62 (1H, m, *CH*COOMe), 6.42 (1H, d, $H_{6'}$), 7.80 (1H, s, $H_{2'}$), 8.82-9.06 (1H, broad peak, NH), J_{CH_2CH} = 7 Hz, J_{NHCH} = 8 Hz
9i *(R,S)*-isomer	60 DMSO-d_6	2.25 (3H, s, 5'-Me), 2.37 (3H, s, 7'-Me), 3.24 (2H, d, CH_2), 3.33 (3H, s, OMe), 4.29-4.62 (1H, m, *CH*COOMe), 6.42 (1H, d, $H_{6'}$), 7.80 (1H, s, $H_{2'}$), 8.82-9.06 (1H, broad peak, NH), J_{CH_2CH} = 7 Hz

of *(S)*- and *(R,S)*-*N*-trifluoroacetyl-5-bromo-4-oxonorvaline methyl ester (**2**) with formamidines **6** afforded *(S)*- and *(R,S)*-*N*-trifluoroacetyl-4-(imidazo[1,2-*a*]azinyl-3)-4-oxohomoalanine methyl esters **9a-i**, respectively (Scheme 2).

The structure of the compounds **9** was determined by elemental analyses for C, H, and N, and ^{1}H nmr spectra. The ^{1}H nmr spectral characteristics for imidazo[1,2-*a*]-azinyl part are in agreement with those found for other 3-acyl derivatives [7].

Optical purity of azahomotryptophane derivatives **9**, examined by ^{1}H nmr spectral characterisation of *(R,S)*-*N*-trifluoroacetyl-4-(6-chloroimidazo[1,2-*a*]pyridinyl-3)-4-oxohomoalanine methyl ester (**9e**) and *(R,S)*-*N*-trifluoroacetyl-4-(imidazo[1,2-*a*]pyrimidinyl-3)-4-oxohomo-

Table 3

Optical Rotation Data

Compound	Configuration	Specific Rotation
9a	*(S)*-	$[\alpha]_D^{24}$ = +10.6° (c = 0.971, methanol)
9b	*(S)*-	$[\alpha]_D^{24}$ = -7.0° (c = 1.104, methanol)
9c	*(S)*-	$[\alpha]_D^{25}$ = +15.3° (c = 1.228, methanol)
9e	*(S)*-	$[\alpha]_D^{25}$ = +8.0° (c = 0.960, methanol)
9e	*(R)*-	$[\alpha]_D^{24}$ = -9.1° (c = 1.136, methanol)
9g	*(S)*-	$[\alpha]_D^{20}$ = +8.7° (c = 0.841, methanol)
9g	*(R)*-	$[\alpha]_D^{24}$ = -9.2° (c = 1.782, methanol)
9h	*(S)*-	$[\alpha]_D^{25}$ = +9.1° (c = 0.701, methanol)
9i	*(S)*-	$[\alpha]_D^{25}$ = -0.8° (c = 0.745, methanol)

Table 4

Optical Purity Data [a]

Compound	Configuration	^{1}H Chemical Shift(s) for OMe Group δ (ppm)	Area (%)
9e	*(R,S)*-	3.4756	55
		3.4828	45
9e	*(S)*-	3.4846	100
9e	*(R)*-	3.4287	100
9g	*(R,S)*-	3.4681	49
		3.5593	51
9g	*(S)*-	3.650	100
9g	*(R)*-	3.648	98
		3.686	2

[a] The following instrumentation and conditions apply: nmr spectrometer: Bruker AVANCE DPX 300 (300 MHz); solvent: deuteriochloroform; internal standard: TMS; shift reagent: tris [3-heptafluoropropylhydroxymethylene)-d-camphorato]praseodymium(III).

alanine methyl ester (**9g**) and their *(R)*- and *(S)*-isomers, was found to be very high (ee >95%). Apparently, no significant racemisation took place in the preparation of *(S)*-*N*-trifluoroacetyl-4-(imidazo[1,2-*a*]azinyl-3)-4-oxohomoalanine methyl esters **9** and their *(R)*-isomers (Table 4).

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage and on a Büchi 535 melting point apparatus. Unless otherwise stated, the ^{1}H nmr spectra were obtained on a Varian EM60L (60 MHz) spectrometer and on a Bruker AVANCE DPX 300 (300 MHz) spectrometer with DMSO-d_6 and deuteriochloroform ($CDCl_3$) as solvents and TMS as internal standard. The elemental analyses for C, H, and N were obtained on a Perkin-Elmer CHN Analyser 2400. The optical rotations were measured on a Perkin-Elmer 241 MC Polarimeter.

N-Trifluoroacetyl-5-bromo-4-oxonorvaline Methyl Ester (**2**).

(S)- And *(R,S)*-isomers of **2** were prepared according to the procedure described in the literature [5].

N,N-Dimethyl-*N'*-heteroarylformamidines **6a-i**.

These compounds were prepared from the corresponding aminoazines **5** and *N,N*-dimethylformamide dimethyl acetal (**4**) according to the procedure described in the literature [6]. Thus, a mixture of aminoazine **5** (0.003 mole), toluene (3 ml) and **4** (95%, 0.45 ml, 0.0032 mole) was heated at reflux temperature for one hour. Volatile components were evaporated *in vacuo* to give a crude formamidine **6** which was used without purification in further transformations.

Preparation of *N*-Trifluoroacetyl-4-(imidazo[1,2-*a*]pyridinyl-3)-4-oxohomoalanine Methyl Esters **9a-9f** and *N*-Trifluoroacetyl-4-(imidazo[1,2-*a*]pyrimidinyl-3)-4-oxohomoalanine Methyl Esters **9g-9i**. General Procedure.

A mixture of *N*-trifluoroacetyl-5-bromo-4-oxonorvaline methyl ester **2** (0.003 mole) and *N,N*-dimethyl-*N'*-heteroarylformamidine **6** (0.003 mole) in an appropriate solvent (20 ml, see Table 1) was heated under reflux for several hours. Volatile components were evaporated *in vacuo*, water (15 ml) was added to the residue and stirred for 2 hours. The precipitate was collected by filtration to give **9**. Experimental details and analytical data are given in Tables 1-4.

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[8] Before trituration with water (see general procedure), the residue was first purified by flash chromatography (silica gel-Kieselgel 60, ethyl acetate as eluent).

[9] Reaction was carried out at room temperature (see general procedure).

[10] Hot water (20 ml, approximately 80°) was added to the residue which was obtained after evaporation of volatile components (see general procedure). While stirring, this mixture was allowed to cool to room temperature. The precipitate was collected by filtration to give **9**.