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FACILE SYNTHESIS OF FLUORINE CONTAINING IMIDAZO [1,2-b][1,2,4] TRIAZINES THROUGH α-OXO-N-ARYL-α ARYLETHANEHYDRAZONOYL BROMIDES

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SUMMARY

Treatment of fluorine containing arylglyoxals with aminoguanidine bicarbonate in aqueous ethanol formed fluorinated 3-amino-5-aryltriazines which in turn on treatment with α-oxo-N-aryl-α-arylethanehydrazonoyl bromides afforded 3,6-diaryl-7-arylazoimidazo[1,2-b][1,2,4] triazines in 75-80% yield. All the compounds were characterized by their analytical and spectral (IR, PMR and Mass) data. Mass fragmentation patterns of these compounds have also been discussed. The screening of biological activities are in progress.

INTRODUCTION

Recently, we have undertaken a comprehensive study of fluorinated N-aryl-α-oxo-α-arylethanehydrazonoyl bromides and have reported electrophilic substitution reactions of new fluorine containing N-aryl-α-oxo-α-arylethanehydrazones[1]. Subsequently the facile synthesis of fluorine-containing 2,6-diaryl-3-arylazo-1H-pyrazolo[5,1-a]imidazoles, 3-aryl-2-arylazoimidazo[1,2-a] pyridine, 4-aryl-5-arylazo-2-iminothiazoles[2], [4-aryl 4,5-dihydro 5-imino-1,3,4-thiadiazole-2yl-aryl] methanones, 2-amino-4-aryl-5-

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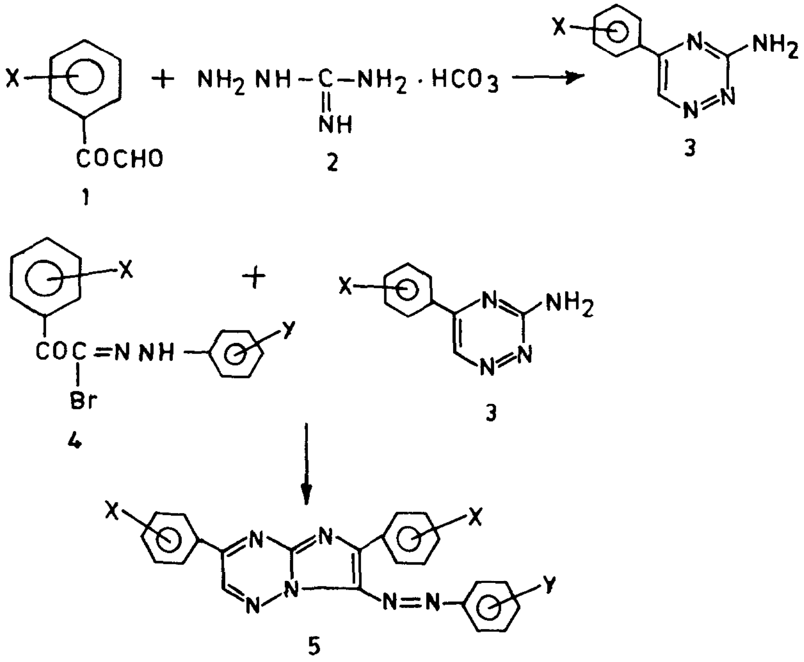
arylazothiazoles and 3-aryl-4-acetyl/benzoyl-5-methyl-7-phenylpyrazoles [3] have been reported by us via N-aryl-∝oxo-∝-arylethanehydrazonoyl bromides.

The synthetic application of hydrazidoyl bromides as reaction intermediates for synthesis of various heterocyclic systems viz: 1,4-dihydro-1,2,4,5-tetrazine, 4,5-dihydro-1H-pyrazoles, pyrazoles and 1,3,4-oxodiazolidenes[4-7] has aroused great interest during the last decade. These reactions take place through 1,3-dipolar cycloaddition or nucleophilic substitution reactions.

As a part of our comprehensive programme for developing fluorine containing bioactive heterocycles, we now wish to report the synthesis and mass spectral studies of ten new fluorine containing 3,6-diaryl-7-arylazoimidazo[1,2-b][1,2,4]-triazines.



RESULTS AND DISCUSSION

The reaction of arylglyoxals (1) with aminoguanidine bicarbonate (2) in aqueous ethanol gave the compounds (3). In the IR spectra of compounds (3a-c), the appearance of the NH_2 absorption bands at 3300 cm^{-1} confirms the formation of the desired compound. In the ^1H NMR spectra, the appearance of a resonance signal at δ 5.7 ppm (NH_2) confirms the formation of the compound (3a-c). Further support was obtained by mass spectral data as the molecular ion peak M^+ at m/z 190 (3a), corresponds to the molecular mass.

Compound (3a) under electron impact gave its molecular ion (I) at m/z 190 (96%). This molecular ion is further fragmented by two pathways. In pathway A, it is decomposed to a neutral $NCNH_2$ molecule and a cation radical II (m/z 148, 8.3%). Cation radical II eliminates a neutral nitrogen molecule to give cation radical III (m/z 120, 100%) which in turn eliminates an acetylide radical to afford cation IV (m/z 95, 66.4%).

In pathway B, molecular ion (I) fragments into a cation radical V (m/z 121, 70%) and a cation VI (m/z 69, 55%). Cation VI eliminates a neutral N≡N molecule and affords cation VII (m/z 41, 14.9%) which in turn eliminates two hydrogen radicals successively to give VIII (m/z 40, 18.2%) and IX (m/z 39, 19.9%) cation and cation radical respectively. Cation VI eliminates a radical $\dot{C}{\equiv}N$ to afford cation radical X (m/z 43, 16.6%).

The reaction of an N-aryl-α-oxo-α-arylethanhydrazonoyl bromide (4) [1] with a 3-amino-5-aryltriazine (3) in ethanol gave the compound (5). In the IR spectra of compounds (5a-g) the disappearance of the >NH band from 3200 cm^{-1} and >C=O from 1640 cm^{-1} confirms the formation of the compound (5). In the ^1H NMR spectra the >NH signal disappears from δ 11.2 ppm. All aromatic proton resonance signals appear as multiplets in the region δ 7.0-8.5 ppm. Additional support was obtained by mass spectra as molecular ion peaks M^+ at m/z 412 (5a), and 426 (5b) correspond to their molecular masses.

Compound (5) under electron impact provides a molecular ion peak I (m/z 412, 42.0%). This molecular ion is further fragmented by two pathways. In pathway A, it is decomposed to cation radical II and III (m/z 28, 100%; m/z 384, 15.3%). Cation radical III eliminates a phenyl radical and gives a cation IV (m/z 307, 24.6%) which in turn eliminates a neutral $FC_6H_4C{\equiv}N$ moiety to

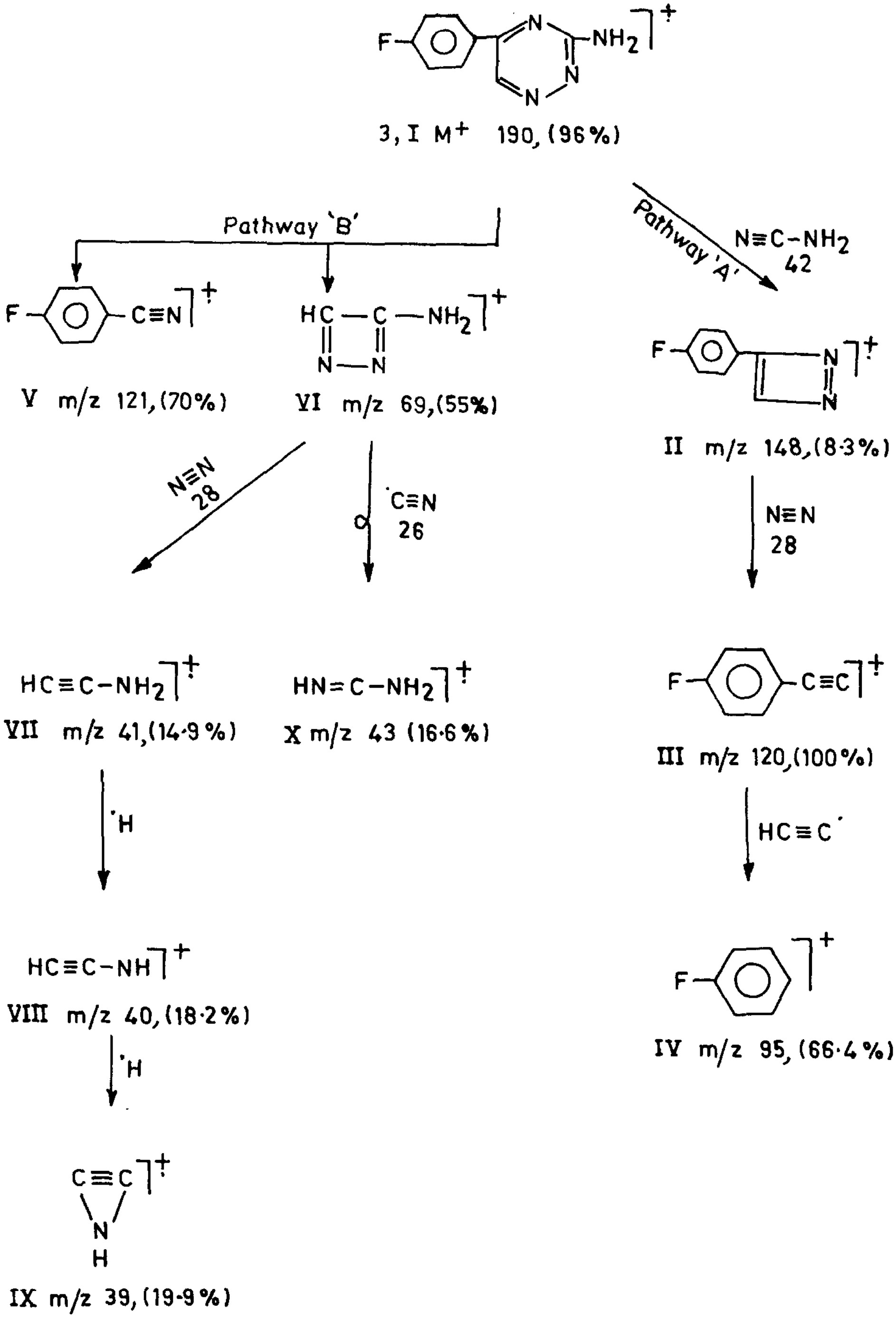

F
NH2
3, I M+ 190, (96%)
Pathway 'B'
Pathway 'A'
N≡C–NH2
42
F–C≡N
V m/z 121, (70%)
HC—C—NH2
N—N
VI m/z 69, (55%)
II m/z 148, (8·3%)
N≡N
28
α
·C≡N
26
N≡N
28
HC≡C–NH2
VII m/z 41, (14·9%)
HN=C–NH2
X m/z 43 (16·6%)
F–C≡C
III m/z 120, (100%)
·H
HC≡C·
HC≡C–NH
VIII m/z 40, (18·2%)
·H
F
IV m/z 95, (66·4%)
C≡C
N
H
IX m/z 39, (19·9%)

TABLE I

Analytical data of new compounds prepared

Compound No.	X	M.P. °C	Yield (%)	Molecular formula	Elemental analysis Calc/Found			IR (cm^{-1})					^{1}H NMR (δ ppm)	
					C	H	N	NH_2	ArC–F (vs)	C=N (s)	C–N (w)	N=N (vw)	$-NH_2$	$-CH_3$
3a	4-F	195	70	$C_9H_7FN_4$	56.7 56.7	3.6 3.6	29.4 29.3	3300	1400–1000	1620	1240	1605	5.7	-
3b	4-F, 2-CH_3	180	65	$C_{11}H_9FN_4$	64.7 64.7	4.4 4.4	27.4 27.4	3290	1400–1000	1610	1230	1600	5.6	2.1
3c	2-Cl, 4-F	210	60	$C_9H_6ClFN_4$	48.1 48.0	2.6 2.6	24.9 24.8	3295	1400–1000	1620	1240	1610	5.7	-

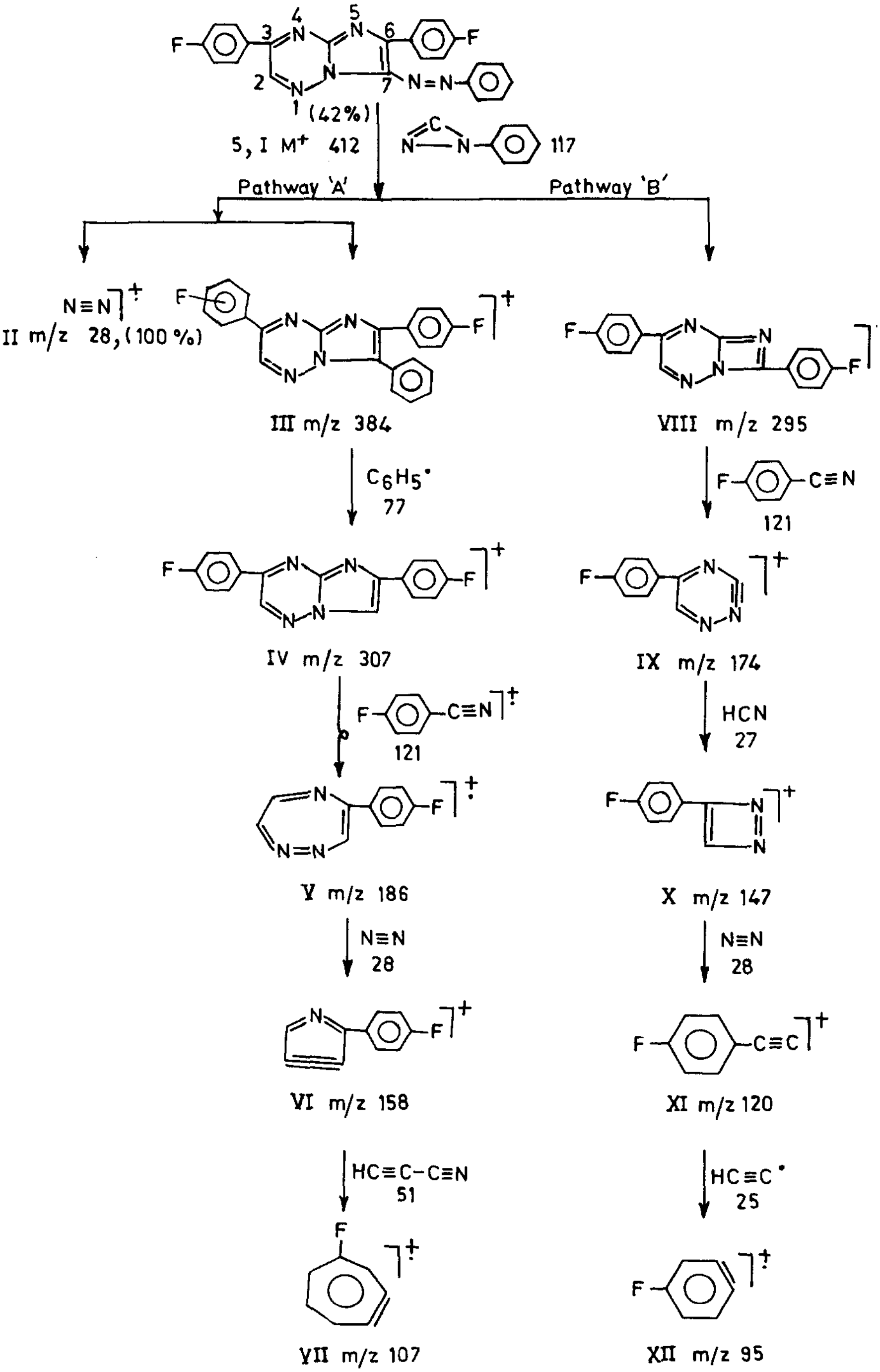
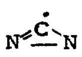

1 2 3 4 5 6 7
(42%)
5, I M+ 412
117
Pathway 'A'
Pathway 'B'
II m/z 28, (100 %)
III m/z 384
VIII m/z 295
C6H5• 77
F–C6H4–C≡N 121
IV m/z 307
IX m/z 174
F–C6H4–C≡N 121
HCN 27
V m/z 186
X m/z 147
N≡N 28
N≡N 28
VI m/z 158
XI m/z 120
HC≡C–C≡N 51
HC≡C• 25
VII m/z 107
XII m/z 95

TABLE II

Analytical data of new compounds prepared

Compound No.	X	Y	Z	M.P. °C	Yield (%)	Molecular formula	Elemental analysis Calc/Found C	H	N	IR (cm^{-1}) C=N (s)	-N=N- (vw)	ArC–F (vs)	C–N (w)	^{1}H NMR (δ ppm) CH$_3$	Ar–H
5a	4–F	4–F	H	300	70	$C_{23}H_{14}F_2N_6$	66.9 67.0	3.3 3.3	20.3 20.3	1620	1605	1400–1000	1240	–	7.0–8.5
5b	4–F, 2–CH$_3$	4–F	H	295	75	$C_{24}H_{10}F_2N_6$	67.6 67.5	3.7 3.7	19.9 20.0	1620	1605	1400–1000	1230	2.1	7.0–8.5
5c	4–F	4–F 2–CH$_3$	H	305	75	$C_{24}H_{16}F_2N_6$	67.6 67.6	3.7 3.7	19.9 20.0	1620	–	1400–1000	1230	2.1	7.0–8.5
5d	4–F 2–CH$_3$	4–F 2–CH$_3$	H	280	70	$C_{25}H_{18}F_2N_6$	68.1 68.2	4.0 4.0	19.2 19.2	1620	1605	1400–1000	1240	2.2	6.5–8.5
5e	4–F 2–Cl	4–F	H	310	65	$C_{23}H_{14}ClF_2N_6$	61.8 61.8	3.1 3.1	18.8 18.7	1620	1600	1400–1000	1240	–	7.0–8.5
5f	4–F 2–Cl	4–F 2–CH$_3$	H	320	65	$C_{24}H_{16}ClF_2N_6$	60.2 60.1	3.4 3.4	18.2 18.1	1620	–	1400–1000	1235	2.1	7.0–8.5
5g	4–F	4–F	2, 3, 4, 5, 6–PentaF	292	70	$C_{23}H_9F_7N_6$	35.0 35.0	1.7 1.7	16.7 16.7	1620	1605	1400–1000	1240	–	7.0–8.5
5h	4–F 2–CH$_3$	4–F	2, 3, 4, 5, 6–PentaF	280	65	$C_{24}H_{17}F_7N_6$	55.6 55.6	2.1 2.1	16.2 16.1	1620	1605	1400–1000	1240	2.3	7.0–8.5

yield cation V (m/z 186, 4.6%). Loss of a neutral nitrogen molecule from cation V yielded cation VI (m/z 158, 27.6%). Cation VI eliminates a neutral HC≡C-C≡N molecule to afford a more stable fluorinated tropylium cation VII (m/z 108, 23.0%) with retention of the C-F bond and aromaticity.

In pathway B the cation radical I eliminates a radical  - C_6H_5 to give cation VIII (m/z 295, 12.3%). The cation VIII further eliminates the neutral molecule $FC_6H_4C{\equiv}N$ to yield cation IX (m/z 174, 7.6%). Cation IX eliminates a neutral HCN molecule to afford cation X (m/z 147, 26.1%) which in turns eliminates a neutral nitrogen (N≡N) molecule to give cation XI (m/z 120, 30.1%). Loss of an acetylide radical from XI yielded cation radical XII (m/z 95, 26.0%) with retention of the C-F bond and aromaticity.

EXPERIMENTAL

Melting points are uncorrected. IR spectra were recorded on a Perkin Elmer 157 G machine in KBr. ^1H NMR spectra were recorded on a Bruker HX 90 instrument using $CDCl_3$ as solvent and TMS as internal standard. Mass spectra were recorded on Kratos 30 and 50 machines. All compounds are homogeneous on TLC in various solvent systems.

N-aryl-α-oxo-α-arylethanhydrazonoyl bromides (4)

The hydrazonoyl bromides were prepared by the method of Joshi et al. [1]. N-aryl-α-oxo-α-arylethanehydrazone (0.01 mole) was rapidly stirred in glacial acetic acid (70 ml) at room temperature while a solution of bromine (0.01 mole) in acetic acid (20 ml) was added dropwise during 30 minutes. The bromo derivative was collected after 5 hours, washed thoroughly with water and recrystallized from acetic acid.

3-Amino-5-(4-fluorophenyl)triazine (3)

Treatment of 4-fluorophenylglyoxal (1) (1.52 g, 0.01 mole) with aminoguanidine bicarbonate (2) (1.02 g, 0.01 mole) in aqueous ethanol at 25°. The reaction was slow at first but carbon dioxide began gradually to be evolved. After standing for 22 hours at 25° the mixture was warmed to 50° for an hour then chilled and filtered yielding white solid, which was recrystallized from ethanol-toluene (3:1). The physical properties of the compound are listed in Table I.

3,6-Di(4-fluorophenyl)-7-phenylazoimidazo[1,2-b][1,2,4] triazine (5)

A mixture of α-oxo-N-(4-fluorophenyl) α-arylethanehydrazonoyl bromide (4) (3.35 g; 0.01 mole) and 3-amino-5-(4-fluorophenyl) triazine(3) (1.40 g, 0.01 mole) was refluxed in ethanol for 3 to 4 hours cooled and the crude product was collected and recrystallized from ethanol. The physical properties of the compounds are listed in Table II.

Acknowledgement

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