Facile Synthesis of Fluorine-containing [4-Aryl-4,5-dihydro-5-imino-1,3,4-thiadiazol-2-ylaryl]methanone, 2-Amino-4-aryl-5-arylazothiazoles and 3-Aroyl-4-acetyl/benzoyl-5-methyl-1-phenylpyrazoles through *N*-Aryl-α-oxo-α-arylethanehydrazonoyl Bromide

Krishna C. Joshi*, Vijai N. Pathak and Sharda Sharma

Department of Chemistry, University of Rajasthan,
Jaipur-302004, India

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N-Aryl-α-oxo-α-arylethanehydrazonoyl bromides **2** react with potassium thiocyanate in ethanol leading to the formation of [4-aryl-4,5-dihydro-5-imino-1,3,4-thiadiazol-2-ylaryl]methanone **5** in quantitative yield. Treatment of **2** with thiourea and β-diketones affords 2-amino-4-aryl-5-arylazothiazoles **4** and 3-aroyl-4-acetyl/benzoyl-5-methyl-1-phenylpyrazoles **6** in 65-70 and 60-70% yields respectively. Compound **5** has also been subjected to acetylation and chloroacetylation. All the compounds are characterized by their analytical and spectral (ir, ^{1}H-nmr and ms) data. Mass fragmentation patterns of these compounds are discussed.

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Recently, we have undertaken a comprehensive study of fluorinated *N*-aryl-α-oxo-α-arylethanehydrazonoyl bromides and related compounds and have reported the synthesis of new fluorinated *N*-aryl-α-oxo-α-arylethanehydrazones and their electrophilic substitution reactions [1] including consequent facile synthesis of 2,6-diaryl-3-arylazo-1*H*-pyrazolo[5,1-*a*]imidazoles, 3-aryl-2-arylazoimidazo-[1,2-*a*]pyridine and 4-aryl-5-arylazo-2-iminothiazoles *via* *N*-aryl-α-oxo-α-arylethanehydrazonoyl bromides [2].

The synthetic applications of hydrazidoyl bromides as reaction intermediate for the synthesis of a variety of heterocyclic systems *viz:* 1,4-dihydro-1,2,4,5-tetrazine, 4,5-dihydro-1*H*-pyrazoles, pyrazoles and 1,3,4-oxadiazolones [3-6] has aroused considerable interest during the last decade. Further studies on *N*-aryl-α-oxo-α-arylethanehydrazonoyl bromide systems were therefore undertaken leading to new fluorine containing [4-aryl-4,5-dihydro-5-imino-1,3,4-thiadiazole-2-ylaryl]methanone, 2-amino-4-aryl-5-arylazothiazoles and 3-aroyl-4-acetyl/benzoyl-5-methyl-1-phenylpyrazoles. A number of acylated and chloro-acylated derivatives have also been synthesized (Scheme 1). The mass fragmentation patterns of such heterocyclic systems are not available in the literature [7,8] and have now been studied.

The reaction of *N*-aryl-α-oxo-α-arylethanehydrazonoyl bromide (**2**) with potassium thiocyanate in ethanol gave the compound **5**. Some successful reactions of **5** *viz:* acetylation and chloroacetylation were carried out. Compound

Scheme 1

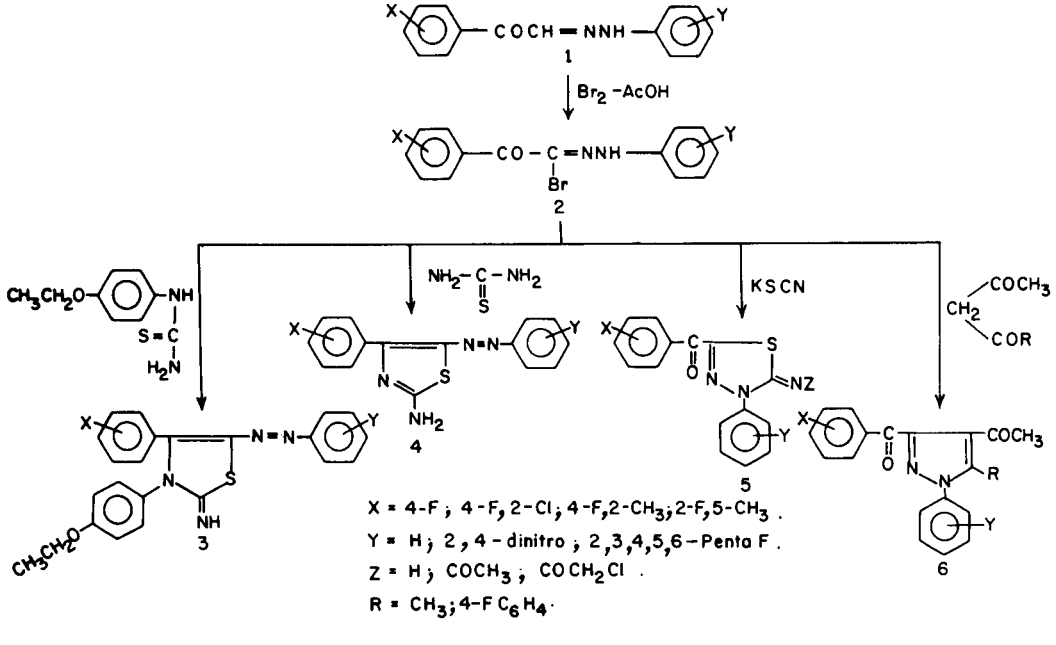


Table I

[4-Aryl-4,5-dihydro-5-imino-1,3,4-thiadiazol-2-yl-aryl]methanones **5**

Compound No.	X	Y	Z	MP °C	Yield %	Molecular Formula	Analysis % C (Calcd.)	H (Calcd.)	N (Calcd.)	C (Found)	H (Found)	N (Found)
5a	4-F	H	H	120	75	$C_{15}H_{10}FN_3OS$	60.2	3.3	14.0	60.1	3.2	14.0
5b	4-F 2-CH_3	H	H	125	70	$C_{16}H_{12}FN_3OS$	61.3	3.6	13.4	61.4	3.8	13.4
5c	2-Cl, 4-F	H	H	115	68	$C_{15}H_9ClFN_3OS$	53.9	2.6	13.3	54.0	2.5	13.3
5d	4-F, 2-CH_3	2,3,4,5,6 -Penta F	H	325	70	$C_{16}H_7F_6N_3OS$	47.6	1.7	10.4	47.5	1.8	10.4
5e	4-F	2,3,4,5,6 -Penta F	H	305	73	$C_{15}H_5F_6N_3OS$	46.2	1.2	10.7	46.1	1.2	10.8
5f	4-F, 2-CH_3	2,3-dinitro	H	205	65	$C_{16}H_{10}FN_5O_5S$	47.6	2.4	17.3	47.7	2.5	17.3
5g	2-F, 5-CH_3	2,4-dinitro	H	195	66	$C_{16}H_{10}FN_5O_5S$	47.6	2.4	17.3	47.5	2.4	17.4
5h	2-Cl, 4-F	2,4-dinitro	H	178	69	$C_{15}H_7ClFN_5O_5S$	42.5	1.6	15.4	42.5	1.6	15.4
5i	4-F	H	$COCH_3$	170	70	$C_{17}H_{12}FN_3O_2S$	59.8	3.5	12.3	59.9	3.6	12.3
5j	4-F, 2-CH_3	H	$COCH_3$	190	72	$C_{17}H_{14}FN_3O_2S$	61.2	4.2	12.2	61.3	4.1	12.2
5k	2-Cl, 4-F	H	$COCH_3$	135	69	$C_{17}H_{11}ClN_3O_2S$	57.2	3.8	11.5	57.4	3.9	11.5
5l	4-F	H	$COCH_2Cl$	195	70	$C_{17}H_{14}FN_3O_2S$	59.4	4.0	11.1	59.3	4.0	11.2

5 showed characteristic ir absorption bands at 3300 (=NH), 1650 (>C=O) and 1610 cm^{-1} (>C=N), which are in favour of complete cyclization of bromide **2** into **5**. The ^1H nmr spectra of **5** showed multiplet at δ 7.0-9.0 (aromatic and imino protons). Further support was obtained by mass spectral data as molecular ion peaks M^+ at m/z 299 (**5a**), 313 (**5b**) correspond to their molecular masses.

Compound **5a** under electron impact gave its molecular ion (I) at m/z 299 (84%). The molecular ion (I) decomposes **via** a retro Diels-Alder process to yield a neutral HCNS moiety and a cation radical II; II fragments into cation III and cation radical V. Cation III eliminates a neutral CO molecule to yield cation IV (m/z 95, 100%). The high intensity peaks corresponding to cation III and IV are ascribed due to presence of high degree of resonance in these species. Cation radical V eliminates a N≡N molecule to yield a stable tropylium cation radical VI (m/z 89, 23%).

In the ir spectra of compounds **5i-l** disappearance of =NH band from 3300 cm^{-1} and appearance of a new carbonyl absorption band at 1640 cm^{-1} confirms the formation of the desired compounds. In the ^1H-nmr spectra, appearance of a resonance signal at δ 2.3 ppm (-$COCH_3$) confirms the formation of the compounds **5i-k**. The compound **5l** is confirmed by the appearance of a resonance signal at δ 4.2 ppm due to $COCH_2Cl$ protons. All the aromatic proton resonance signals appear as multiplet in the region of δ 7.0-8.5 ppm.

The reaction of **2** with thiourea in ethanol afforded 2-amino-4-aryl-5-arylazothiazoles **4**, which agrees with analytical and spectral data. The ir spectra of compound **4** exhibits a broad absorption band between 3300-3450 (NH_2)

Scheme 2

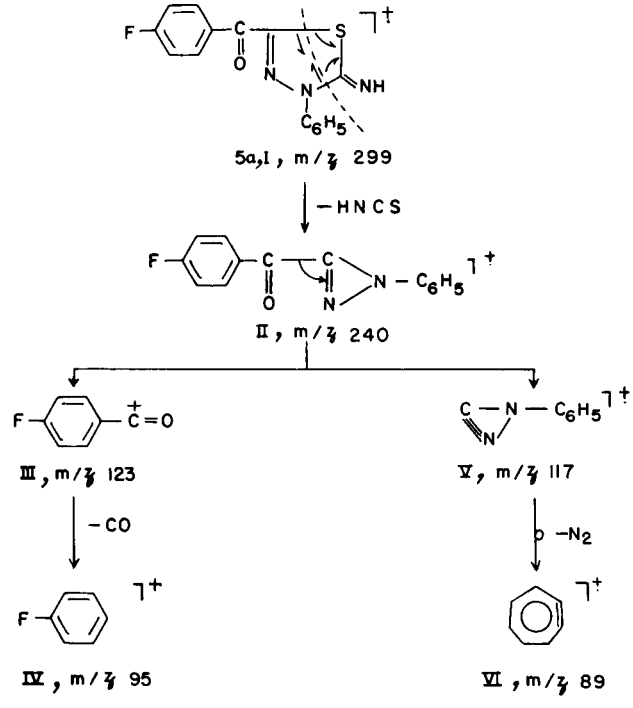


Table II

2-Amino-4-aryl-5-arylazothiazoles **4**

Compound No.	X		Y	MP °C	Yield %	Molecular Formula	Analysis % C (Calcd.)	H (Calcd.)	N (Calcd.)	C (Found)	H (Found)	N (Found)
4a	4-F		H	225	70	$C_{15}H_{11}FN_4S$	60.4	3.6	18.8	60.4	3.5	18.4
4b	4-F,	2-CH_3	H	200	65	$C_{16}H_{13}FN_4S$	61.5	4.1	17.9	61.4	4.0	17.9
4c	2-Cl,	4-F	H	180	68	$C_{15}H_{10}ClFN_4S$	54.1	3.0	16.8	54.0	3.0	16.8
4d	4-F,	2-CH_3	2,4-dinitro	108	65	$C_{16}H_{11}FN_6O_4S$	46.1	2.8	21.9	46.1	2.9	21.8
4e	2-Cl,	4-F	2,4-dinitro	140	65	$C_{15}H_8ClFN_6O_4S$	42.6	1.8	14.9	42.5	1.8	14.9

Table III

3-Aroyl-4-acetyl/benzoyl-5-methyl-1-Phenylpyrazoles **6**

Compound No.	X		R	MP °C	Yield %	Molecular Formula	Analysis % C (Calcd.)	H (Calcd.)	N (Calcd.)	C (Found)	H (Found)	N (Found)
6a	4-F		CH_3	120	60	$C_{19}H_{15}FN_2O_2$	70.8	4.6	8.6	70.9	4.5	8.6
6b	4-F,	2-CH_3	CH_3	135	70	$C_{20}H_{17}FN_2O_2$	71.4	5.0	8.3	71.4	5.0	8.4
6c	4-F		4-FC_6H_4	158	65	$C_{24}H_{16}F_2N_2O_2$	71.6	3.9	6.8	71.5	4.0	6.7

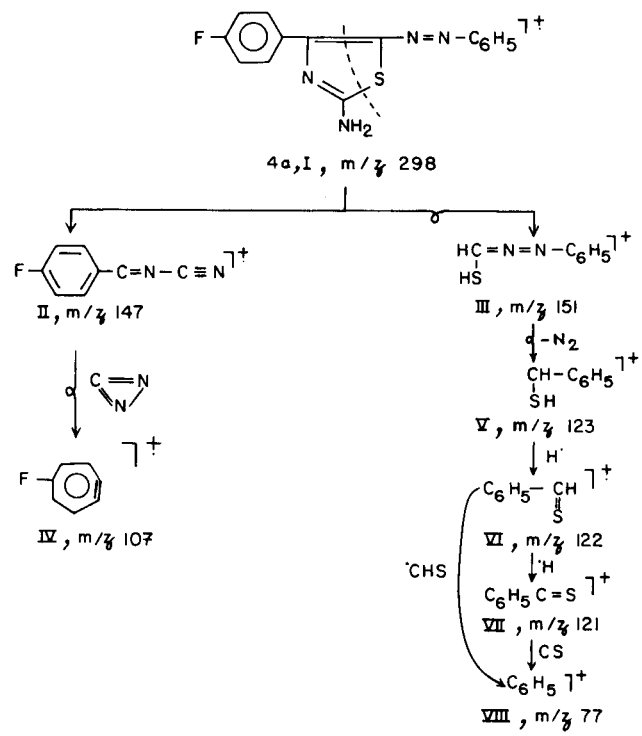
and a strong absorption at 1650 cm^{-1} (-N=N- and >C=N). In the ^1H nmr a broad resonance signal between δ 5.5-6.6 ppm (NH_2) which disappeared on deuterium oxide exchange. In **4b**, a sharp singlet at δ 2.5 ppm (CH_3) is present. In all compounds, aromatic protons appear as a multiplet in the region of δ 6.5-8.0 ppm. Additional support was obtained by the mass spectra as molecular ion peak M^+ at m/z 321 (**4b**) and 298 (**4a**) corresponds to their molecular masses.

Molecular ion (I) of compound **4a** (m/z 298, 40%) eliminates cation radical II (m/z 147, 10%) *via* a retro Diels-Alder process to yield a cation III (m/z 151, 100%). Cation III eliminates a N≡N molecule to yield cation radical V (m/z 123, 85%) which in turn eliminates two hydrogen radicals successively to yield cation VII. This eliminates a neutral CS moiety to afford cation VIII (m/z 77, 25%).

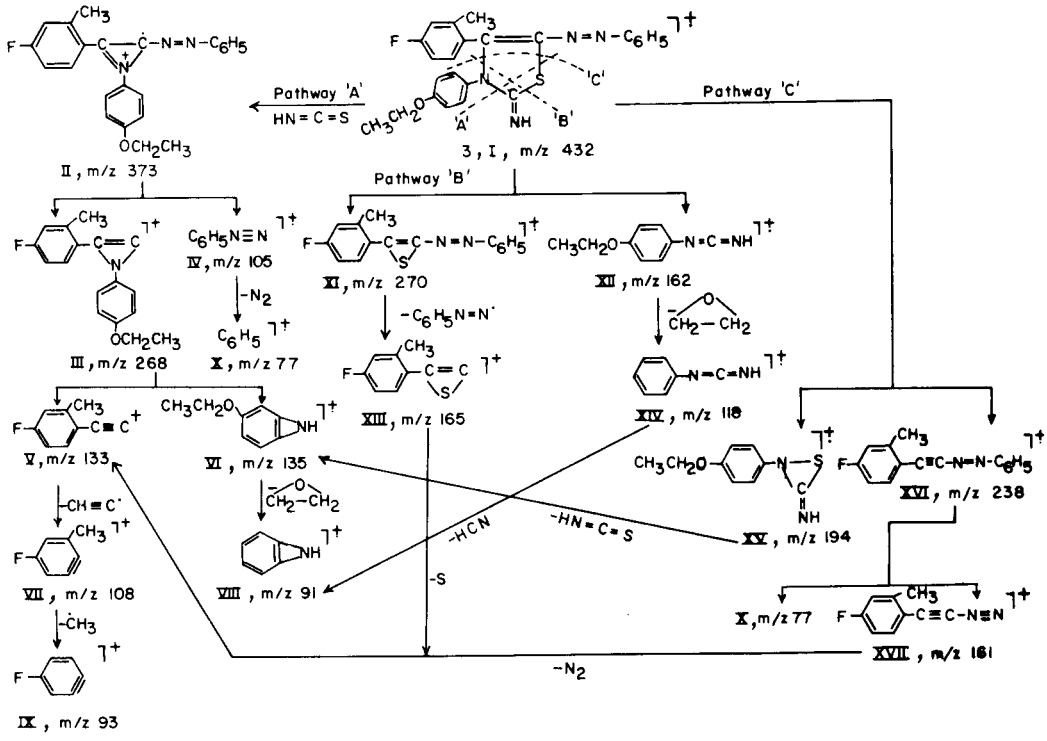
In contrast to this, condensation of **2** with 4-ethoxyphenylthiourea affords 4-aryl-5-arylazo-2-aminothiazoles **3**, having an imino function in place of an amino function as position 2. Compound **3** exhibits a characteristic =NH absorption peak at 3200 cm^{-1} in the ir spectra and in the ^1H nmr spectrum it shows a triplet at δ 1.5, a quartet centred at δ 4.1 and aromatic protons plus imino proton at δ 6.5-8.5 ppm. Further its structure has been supported by its mass spectral study (as shown in Scheme 4).

Compound **3** under electron impact provides a molecular ion (I) peak (m/z 432, 50%). This molecular ion is further fragmented by three pathways. In pathway a, it is decomposed by a retro Diels-Alder process to a neutral HNCS molecule and a cation radical II (m/z 373, 8%). This in turn fragmented into cation III (m/z 268, 30%) and cation radical IV (m/z 105, 10%). Cation III further frag-

Scheme 3



Scheme 4



mented into cation V and cation radical VI (m/z 133, 42% and m/z 135, 15%). Loss of an acetylide radical from V yielded cation VII which, in turn eliminates a methyl radical to afford cation IX. Cation radical VI eliminates a neutral ethylene oxide moiety to give cation radical VIII. Cation radical IV eliminates a N≡N molecule to yield X (m/z 77, 100%). The high degree of relative intensity may be associated with large number of resonating structures of X.

In pathway B, molecular ion (I) fragments into sulfur containing cation radical XI (m/z 270, 5%) and cation radical XII (m/z 162, 20%). Cation radical XI eliminates a phenyldiazonium radical to give cation XIII (m/z 165, 70%) which eliminates sulfur acetylide and methyl radicals successively to yield cation radical IX (m/z 93, 35%). Similarly XII eliminates neutral ethylene oxide and HCN molecules successively to afford VIII (m/z 91, 34%).

In pathway C, molecular ion (I) first fragments into cation radical XV and XVI as shown in the Scheme 4. Cation radical XV eliminates neutral HNCS and ethylene oxide moieties successively to yield VIII. Cation radical XVI fragments into cation radical X and cation radical XVII (m/z 161, 10%). Further fragmentation of XVII is similar to that of the Scheme 4 given in the pathway A.

Treatment of **2** with an ethanolic solution of sodium enolate of the β-diketones yielded 3-aroyl-4-acetyl/benzoyl-5-methyl-1-phenylpyrazoles **6** in 60-70% yield. The structure of the product was established by elemental analyses and by study of their spectra. Thus, the ir of **6** (potassium bromide) revealed in each case, the existence of acetyl >C=O (1680 cm^{-1}), benzoyl >C=O (1660 cm^{-1}) and >C=N (1610 cm^{-1}) bands. The ^1H nmr spectra of **6** showed, in addition to an aromatic proton multiplet at δ 7.0-8.5 ppm, three singlets centred at δ 2.5 (3H, CH_3CO), 2.45 (3H, CH_3) and 2.4 (3H, Ar-CH_3) ppm are partially coalesced. Further support was obtained by mass spectra as molecular ion peak M^+ at 336 (**6b**) corresponds to its molecular mass.

EXPERIMENTAL

Melting points are uncorrected. The ir spectra were recorded on Perkin Elmer 157 G in potassium bromide. The ^1H nmr spectra were recorded on Bruker HX-90 using deuteriochloroform as solvent and TMS as internal standard mass spectra were recorded on Kratos 30 and 50. All compounds are homogeneous on tlc in the various solvent systems.

N-Aryl-α-oxo-α-arylethanehydrazonoyl Bromides **2**.

The hydrazonoyl bromides **2** 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 (1.6 g, 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.

[4-Aryl-4,5-dihydro-5-imino-1,3,4-thiadiazol-2-ylaryl]methanone (**5**).

To a suspension of the *N*-aryl-α-oxo-α-arylethanehydrazonoyl bromide (0.01 mole) in ethanol (50 ml), a solution of potassium thiocyanate (0.01 mole) in water (10 ml) was added and the mixture was stirred for 5 hours at room temperature. The resultant solid material was filtered, washed with water and purified by recrystallization from ethanol. Compounds were obtained in 70-80% yield. The physical and analytical properties of compounds **5a-h** are listed in Table I.

[4-Aryl-4,5-dihydro-5-iminoacetyl-1,3,4-thiadiazol-2-ylaryl]methanone (**5i-k**).

[4-Aryl-4,5-dihydro-5-imino-1,3,4-thiadiazol-2-ylaryl]methanone (1.0 g) was refluxed in acetic anhydride (20 ml) for 30 minutes, cooled and poured on crushed ice and left overnight at room temperature. The crude product, thus obtained, was filtered, washed with water and recrystallized from ethanol, yield 80%. The physical properties of the compounds are listed in Table I.

[4,5-Dihydro-5-iminochloroacetyl-4-phenyl-1,3,4-thiadiazol-2-yl-(4-fluorophenyl)]methanone (**5l**).

[4,5-Dihydro-5-imino-4-phenyl-1,3,4-thiadiazol-2-yl-(4-fluorophenyl)]-methanone (1.0 g) was treated with chloroacetyl chloride (20 ml) and refluxed for 1-2 hours. It was cooled and poured on crushed ice, left overnight at room temperature. The crude solid, which precipitated, was collected and recrystallized from ethanol yield 70%.

2-Amino-4-aryl-5-arylazothiazole (**4**).

A mixture of *N*-aryl-α-oxo-α-arylethanehydrazonoyl bromide (0.005 mole) and thiourea (0.01 mole) in ethanol (40 ml) was refluxed for 5 hours, then poured on crushed ice, and neutralized with few drops of ammonium hydroxide. The solid thus obtained was collected, washed with water and recrystallized from ethanol. The compounds were obtained in 65-70% yield. Physical properties of the compounds are listed in Table II.

3-Aroyl-4-acetyl/benzoyl-5-methyl-1-phenylpyrazole (**6**).

The appropriate β-diketones (0.01 mole) was added to an ethanolic sodium ethoxide solution prepared from sodium metal (0.23 g, 0.01 g-atom) and 50 ml of absolute ethanol. After stirring for 30 minutes, *N*-aryl-α-oxo-α-arylethanehydrazonoyl bromide (0.01 mole) was added and stirring was continued for 1 hour. The reaction mixture was left overnight at room temperature. The product was collected by filtration or dilution of the reaction mixture with water followed by filtration. It was then washed with water, dried and purified by recrystallization from ethanol. The physical and analytical properties of compounds are listed in Table III.

3-(4-Ethoxyphenyl)-4-(4-fluoro-2-methylphenyl)-2-imino-5-phenylazothiazole (**3**).

Compound **3** was prepared by the method of Joshi *et al.* [2]). A mixture of α-oxo-*N*-phenyl-α-(4-fluoro-2-methylphenyl)ethanehydrazonoyl bromide (1.67 g, 0.005 mole) and 4-ethoxyphenylthiourea (1.78 g, 0.01 mole) in ethanol (50 ml) was refluxed for 3 hours, poured on crushed ice and neutralized with a few drops of ammonium hydroxide. The solid formed was collected, washed with water and purified by column chromatography using benzene as mobile phase, mp 181°, yield 60%.

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