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Synthesis of 4-(1*H*-Azol-1-ylmethyl)benzohydrazides and Their Acyclic and Heterocyclic Derivatives

V. A. Osyanin, P. P. Purygin, and Z. P. Belousova

Samara State University, Samara, Russia

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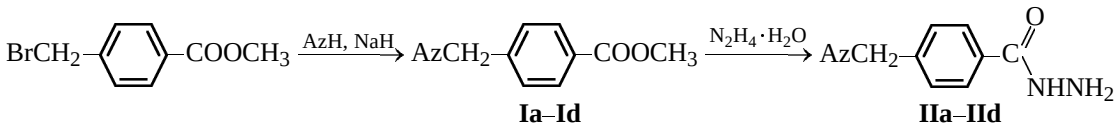
Abstract — 4-(1*H*-Azol-1-ylmethyl)benzohydrazides were prepared from methyl 4-(bromomethyl)benzoate, azoles, and hydrazine hydrate. Reactions of 4-(1*H*-imidazol-1-ylmethyl)benzohydrazide with carbonyl compounds gave hydrazones whose tautomerism was studied. From the hydrazides, 1,3,4-oxadiazoles, 1,2,4-triazole-5-thione, and *N*-benzoyl-*N*'-alkyl(aryl)sulfonylhydrazines were synthesized.

Hydrazides and their functional derivatives were used to prepare a series of antitubercular and antibacterial preparations [1, 2]. Many heterocyclic compounds directly prepared from hydrazides, too, possess valuable biological and physicochemical properties. Azole substitution in such compounds strongly affects their properties [3]. Aimed at the synthesis of azole-substituted hydrazides, we developed a method for preparing 4-(1*H*-azol-1-ylmethyl)-benzohydrazides and a series of their acyclic and heterocyclic derivatives.

Methyl 4-(1*H*-azol-1-ylmethyl)benzoates **Ia**–**Id** were synthesized from methyl (4-bromomethyl)benzoate and azoles AzH in the presence of sodium hydride in anhydrous DMF. Subsequent boiling of methyl benzoates **Ia**–**Id** with hydrazine hydrate for 3–4 h gave hydrazides **IIa**–**IId**.



Ia–**Id** **IIa**–**IId**

Az = imidazol-1-yl (**Ia, IIa**), benzimidazol-1-yl (**Ib, IIb**), 1,2,4-triazol-1-yl (**Ic, IIc**), benzotriazol-1-yl (**Id, IId**).

After purification, the yields of the hydrazides were 79–86%. The IR spectra contain C=O and NH absorption bands at 1672–1622 and 3339–3165 cm^{-1}, respectively. In the spectra measured in D_2O, the NH proton signals disappear because of fast exchange.

The hydrazides were reacted with various carbonyl compounds to obtain 4-(1*H*-azol-1-ylmethyl)benzoylhydrazones **IIIa**–**IIIh**. The reactions with aromatic aldehydes proceed rather fast without catalysts at 1 : 1 reagent molar ratios in 95% ethanol.

With isatin, too, compound **IIIi** was obtained by simply boiling equimolar reagent amounts for 4 h in ethanol.

By TCL it was established that in the presence of traces of water cyclohexanone acylhydrazone is hydrolyzed to the starting compounds. It is known that formation of benzoylhydrazones can be catalyzed by acids. However, we failed to prepare ketone acylhydrazones in the presence of sulfuric or *p*-toluenesulfonic acid, probably because the preferred protonation center was the nitrogen atom of the heterocyclic fragments, and the use of much catalysts shifted the equilibrium to the starting compounds.

The IR spectra of acylhydrazones **III** contain a broad band at 3200–3100 cm^{-1}, belonging to a hydrogen-bonded NH group. In the spectra of compounds **IIIf** and **IIIh**, an additional band is present near 3340 cm^{-1}, assignable to free NH group. The carbonyl group appears at 1680–1637 cm^{-1}.

It is known that acylhydrazones **III** can exist as tautomers **A**–**C** [4–6]. Analysis of the ^1H NMR and IR spectra show that the acylhydrazones in crystal and in DMSO solutions are present in form **A**. The absorp-

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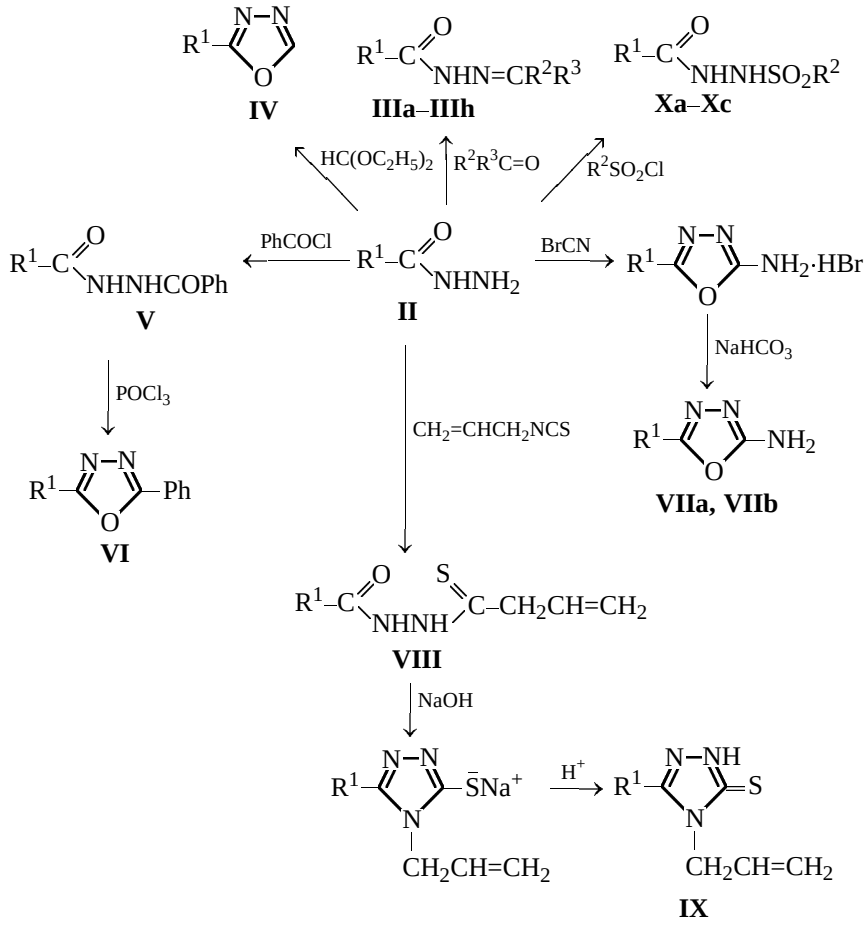
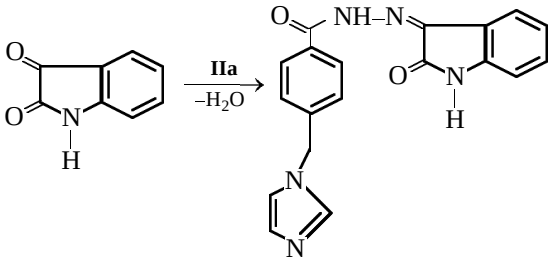


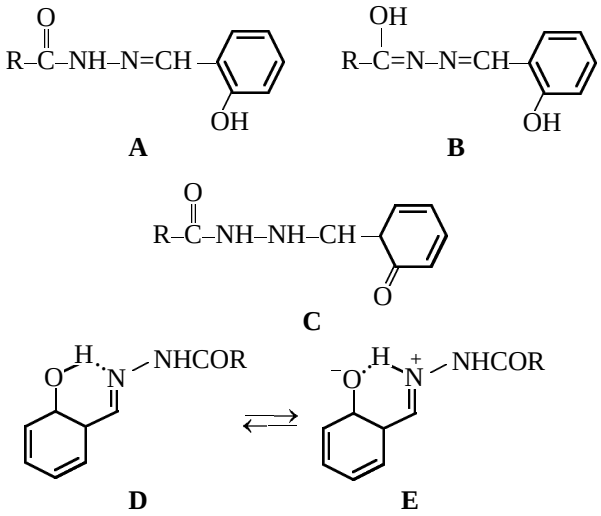
R^1 = *p*-$C_6H_4CH_2Az$; R^2 = H, R^3 = C_6H_5 (**IIIa**); R^2 = H, R^3 = 2-HOC_6H_4 (**IIIb**); R^2 = H, R^3 = 4-HOC_6H_4 (**IIIc**), R^2 = H, R^3 = 4-HO-3-$CH_3OC_6H_3$ (**IIId**); R^2 = H, R^3 = $(CH_3)_2NC_6H_4$ (**IIIe**); R^2R^3 = $(CH_2)_4$ (**IIIf**); R^2 = CH_3, R^3 = 4-HOC_6H_4 (**IIIg**), R^2R^3 = $(CH_2)_5$ (**IIIh**); R^2 = CH_3 (**Xa**); R^2 = C_6H_5 (**Xb**); R^2 = 4-$CH_3C_6H_4$ (**Xc**); Az = imidazol-1-yl (**IIIa**–**IIIg, IV, V, VI, VIIa, VIII, IX, Xa**–**Xc**), 1,2,4-triazol-1-yl (**IIIh**), benzimidazol-1-yl (**VIIb**).



IIIi

tion bands at 1530 cm^{-1}, that would appear if structure **B** [ν(N=CO)] or quinoid structure **C** had been formed in the presence in the benzene ring of *ortho*- or *para*-hydroxy group [ν(NHCH=CC=O)] [4, 5] are lacking.

In the ^{1}H NMR spectra, the NH proton appears at 9.31–11.80 ppm. The strong deshielding can be explained by hydrogen bonding [7]. The chemical shifts of the NH protons in the ^{1}H NMR spectra of compounds **IIIf** and **IIIh** whose IR spectra contain a broad absorption band of free NH group are the lowest, implying that here the hydrogen bonds involving the NH protons are the weakest. The signals of phenolic hydroxyls in the spectra of compounds **IIIc**, **IIId**, and **IIIg** are at 9.51–9.89 ppm, whereas the respective signal in the spectrum of compound **IIIb** is at 12.05 ppm. This result provides evidence in favor of intramolecular hydrogen bonding (form **D**). The



lack in the ^{1}H NMR spectrum of splitting from the methine proton points to lack of intramolecular proton transfer and formation of structure **E**. The lack of the HOC=N proton signal rules out presence of structure **B** in DMSO.

Hydrazides are used in organic synthesis for preparing a great variety of heterocyclic systems. Of particular interest is synthesis of 1,3,4-oxadiazoles and triazole-1,2,4-triones [8–10]. To prepare a 5-unsubstituted 1,3,4-oxadiazole, we made use of the reaction of orthoformic ester with 4-(1*H*-imidazol-1-ylmethyl)benzohydrazide. 2-[4-(1*H*-Imidazol-1-ylmethyl)phenyl]-5-phenyl-1,3,4-oxadiazole (**VI**) was synthesized by cyclization of diacylhydrazine **V** under the action of $POCl_3$. 5-Amino-substituted 1,3,4-oxadiazoles **VIIa** and **VIIb** were obtained by the reactions of cyanogen bromide with hydrazides in absolute ethanol under stirring for 10 h at room temperature. Attempted synthesis of 2-[4-(1*H*-imidazol-1-ylmethyl)phenyl]-5-methyl-1,3,4-oxadiazole from the corresponding hydrazide and ethyl acetimidate hydrochloride failed.

The IR spectra of 1,3,4-oxadiazoles **IV**, **VI**, **VIIa**, and **VIIb** display very strong absorption maxima at 1622–1600 and 1502–1460 cm^{-1}, characteristic of stretching vibrations of the oxadiazole ring. The presence of this ring is confirmed by the observation of absorption bands at 1245–1227 and 1028–1022 cm^{-1}, assignable to stretching vibrations of the =COC= fragment [11].

N'-(Allylthiocarbonyl)-4-(1*H*-imidazol-1-ylmethyl)-benzohydrazide (**VIII**) was synthesized from allyl isothiocyanate and hydrazide **IIa**. When heated with alkali for 1 h, the product undergoes cyclization into 4-allyl-3-[4-(1*H*-imidazol-1-ylmethyl)phenyl]-4,5-dihydro-1*H*-1,2,4-triazole-5-thione (**IX**). Its IR spectrum contains absorption bands at 2600–2500 and 900–850 cm^{-1} [ν(SH)] and a strong band at 1507 cm^{-1} assignable to the thioamide group, which provides evidence for the thione structure. The absorption maximum near 1345 cm^{-1} due to C=S vibrations in triazole-1,2,4-thiones, too, is supportive of the proposed structure.

Hydrazides fairly readily react with sulfonyl chlorides in pyridine. In the IR spectra of the reaction products, there are absorption bands due to asymmetric and symmetric vibrations of the SO_2 group (1340 and 1180 cm^{-1}, respectively) [12].

The yields, melting points, and IR and ^{1}H NMR spectra of the synthesized compounds are listed in the table.

EXPERIMENTAL

The IR spectra were obtained on an IKS-29 instrument in mineral oil. The ^{1}H NMR spectra were obtained on a Bruker instrument at 400 MHz, solvents $(CD_3)_2SO$, CD_3CN, or D_2O, internal reference HMDS.

Methyl 4-(1*H*-azol-1-ylmethyl)benzoates Ia–Id. Azole, 0.04 mol, was added in portions to a suspension of 0.04 mol of NaH (89% suspension in Paraffin) in 30 ml of anhydrous DMF. The mixture was stirred until hydrogen no longer evolved, after which a solution of 0.04 mol of (4-bromomethyl)benzoate in 20 ml of DMF was added over the course of 15 min at 5–10°C, and the mixture was stirred for 4 h. The solvent was removed in a vacuum, the residue was dissolved in benzene with heating, undissolved residue was filtered off, the filtrate was evaporated in a vacuum, and the residue was recrystallized from a benzene–cyclohexane mixture.

Yields, melting points, and IR and ^{1}H NMR spectra of the synthesized compounds

Comp. no	Yield, %	mp, °C	IR spectrum, cm^{-1}	^{1}H NMR spectrum, δ, ppm (solvent)
Ia	74	76–77	1709, 1612, 1500, 1456, 1436, 1302, 1278, 1231, 1190, 1081, 731	3.85 s (3H, CH_3), 5.35 s (2H, CH_2), 7.06 s (1H, azole H^4), 7.29 s (1H, azole H^5), 7.37 d (2H, arom. H^3), 7.69 d (2H, arom. H^2), 7.77 s (azole H^2)
Ib	72	102–103	1721, 1710, 1612, 1495, 1443, 1426, 1365, 1282, 1261, 741, 732	[CD_3CN] 3.85 s (3H, CH_3), 5.51 s (2H, CH_2), 7.24 m (2H, azole H), 7.32 d (2H, arom. H^3), 7.35 m (1H, azole H), 7.71 m (1H, azole H), 7.95 d (2H, arom. H^2, $J_{2,3}$ 8.1 Hz), 8.11 s (1H, azole H^2) [CD_3CN]
Ic	77	111–112	2967, 1713, 1611, 1576, 1506, 1451, 1341, 1312, 1287, 1110	3.87 s (3H, CH_3), 5.44 s (2H, CH_2), 7.37 d (2H, arom. H^3), 7.90 s (1H, azole H^3), 7.99 d (2H, arom. H^2, $J_{2,3}$ 8.4 Hz), 8.32 s (1H, azole H^5) [CD_3CN]
Id	68	130–131	1728, 1613, 1454, 1436, 1283, 1223, 1088, 744, 737	3.85 s (3H, CH_3), 5.82 s (2H, CH_2), 7.37 d (2H, arom. H^3), 7.41–7.57 m (2H, azole $H^{5,6}$), 7.83 d (2H, arom. H^2), 7.86 d, 8.12 d (2H, azole $H^{4,7}$) [CD_3CN]
IIa	84	154–155	3317, 3285, 3180, 1622, 1569, 1570, 1541, 1504, 1387, 1337, 1275, 1229	5.25 s (2H, CH_2), 7.09 s (1H, azole H^4), 7.14 s (1H, azole H^5), 7.33 d (2H, arom. H^3), 7.70 d (2H, arom. H^2, $J_{2,3}$ 8.1 Hz), 7.79 s (1H, azole H^2) [D_2O]
IIb	79	164–165	3334, 3277, 3188, 3164, 3087, 1626, 1573, 1626, 1495, 1433, 1366, 1349, 1319, 1282, 1265	4.50 br.s (2H, NH_2), 5.55 s (2H, CH_2), 7.20 m (2H, azole H), 7.35 d (2H, arom. H^3), 7.49 m (1H, azole H), 7.66 m (1H, azole H), 7.77 d (2H, arom. H^2, $J_{2,3}$ 8.1 Hz), 8.41 s (1H, azole H^2), 9.69 s (1H, NH) [$(CD_3)_2SO$]
IIc	86	170–171	3332, 3283, 3189, 1625, 1573, 1539, 1507, 1457, 1374, 1349, 1321, 1273, 1137, 1014, 958	5.53 s (2H, CH_2), 7.41 d (2H, arom. H^3), 7.75 d (arom. H^2, $J_{2,3}$ 8.1 Hz), 8.13 s (1H, azole H^3), 8.62 s (1H, azole H^5) [D_2O]
IId	81	161–162	3336, 3256, 1661, 1631, 1613, 1573, 1548, 1504, 1495, 1454, 1442, 1340, 1304, 1278, 1221	5.85 s (2H, CH_2), 6.75 t, 6.86 d, 7.04 d, 7.14 t, 7.37 t, 7.50 t, 7.76 d, 8.02 (8H, arom. H, azole H), 9.87 s (1H, NH) [$(CD_3)_2SO$]
IIIa	87	189–190	3165, 3117, 1665, 1618, 1563, 1510, 1437, 1352, 1277, 1231	5.29 s (2H, CH_2), 6.94 s (2H, azole H^4), 7.21 s (2H, azole H^5), 7.38 d (2H, arom. H, *J* 7.8 Hz), 7.45 m (3H, arom. H), 7.72 m (2H, arom. H), 7.89 d (2H, arom. H, *J* 7.2 Hz), 7.79 s (1H, azole H^2), 8.45 s (1H, CH=N), 11.80 s (1H, NH) [$(CD_3)_2SO$]
IIIb	79	225–227	3149, 3098, 1662, 1651, 1610, 1347, 1285, 1261	5.30 s (2H, CH_2), 6.93 m (3H, ald. $H^{3,5}$, azole H^4), 7.21 s (1H, azole H^5), 7.30 t (1H, ald. H^4), 7.39 d (2H, arom. H^3), 7.54 d (1H, ald. H^6), 7.79 s (1H, azole H^2), 7.92 d (2H, arom. H^2), 8.63 s (1H, CH=N), 11.25 s (1H, NH), 12.05 s (1H, OH) [$(CD_3)_2SO$]
IIIc	74	260–261	3225, 3117, 1651, 1613, 1598, 1550, 1508, 1455, 1284, 1272, 1163	5.28 s (2H, CH_2), 6.84 d (2H, ald. H^3), 6.94 s (1H, azole H^4), 7.20 s (1H, azole H^5), 7.36 d (2H, arom. H^3), 7.55 d (2H, ald. H^2, $J_{2,3}$ 7.5 Hz), 7.79 s (1H, azole H^2), 7.87 d (2H, arom. H^2, $J_{2,3}$ 7.8 Hz), 8.33 s (1H, CH=N), 9.89 s (1H, OH), 11.57 s (1H, NH) [$(CD_3)_2SO$]
IIId	68	240–241	3246, 3173, 3112, 1657, 1627, 1585, 1558, 1502, 1426, 1292, 1269	3.83 s (3H, CH_3), 5.29 s (2H, CH_2), 6.84 d (1H, ald. H^5), 6.94 s (1H, azole H^4), 7.09 d (1H, ald. H^6), 7.21 s (1H, azole H^5), 7.31 s (1H, ald. H^2), 7.37 d (2H, arom. H^3), 7.79 s (1H, azole H^2), 7.87 d (2H, arom. H^2, $J_{2,3}$ 7.8 Hz), 8.33 s (1H, CH=N), 9.51 s (1H, OH), 11.60 s (1H, NH) [$(CD_3)_2SO$]

Table (Contd.)

Comp. no	Yield, %	mp, °C	IR spectrum, cm^{-1}	^1H NMR spectrum, δ, ppm (solvent)
IIIe	53	232–233	3175, 1655, 1609, 1592, 1502, 1290, 1275	3.32 s (6H, CH_3), 5.28 s (2H, CH_2), 6.76 d (2H, ald. H^3), 6.93 s (1H, azole H^4), 7.20 s (1H, azole H^5), 7.36 d (2H, arom. H^3), 7.54 d (2H, ald. H^2, $J_{2,3}$ 8.4 Hz), 7.78 s (1H, azole H^2), 7.87 d (2H, arom. H^2, $J_{2,3}$ 7.8 Hz), 8.30 s (1H, CH=N), 11.48 s (1H, NH) [$(CD_3)_2SO$]
IIIf	62	141–142	3335, 3015, 1680, 1537, 1471, 1310, 1269, 1221, 1105, 1076	1.71 m (4H, $CH_2CH_2CH_2$), 2.37 m (4H, $=CCH_2$), 5.29 s (2H, CH_2), 6.94 s (1H, azole H^4), 7.21 s (1H, azole H^5), 7.36 d (2H, arom. H^3), 7.76 s (1H, azole H^2), 7.86 d (2H, arom. H^2, $J_{2,3}$ 7.8 Hz), 9.38 s (1H, NH) [CD_3CN]
IIIg	67	249–251	3395, 3190, 1673, 1628, 1532, 1277, 1245, 1167, 1087, 1012	2.27 s (3H, CH_3), 5.28 s (2H, CH_2), 6.80 d (2H, ald. H^3), 6.93 s (1H, azole H^4), 7.21 s (1H, azole H^5), 7.36 d (2H, arom. H^3, *J* 7.2 Hz), 7.70 br.s (2H, ald. H^2), 7.79 s (1H, azole H^2), 7.84 br.s (2H, arom. H^2), 9.75 s (1H, OH), 10.59 s (1H, NH) [$(CD_3)_2SO$]
IIIh	70	150–151	3342, 3285, 3122, 1637, 1618, 1504, 1476, 1403, 1242	1.69 m (6H, $CH_2CH_2CH_2$), 2.36 m (4H, $=CCH_2$), 5.42 s (2H, CH_2), 7.35 d (2H, arom. H^3), 7.80 d (2H, arom. H^2), 7.89 s (1H, azole H^3), 8.32 s (1H, azole H^5), 9.31 br.s (1H, NH) [CD_3CN]
IIIi	64	295–296 (decomp.)	3124, 1694, 1673, 1621, 1556, 1347, 1301, 1262, 1212, 1191, 1152, 1120, 1105, 1078	5.33 s (2H, CH_2), 6.95 s (1H, azole H^4), 6.97 d (1H, isatin H^7), 7.12 t (1H, isatin H^5), 7.23 s (1H, azole H^5), 7.40 t (1H, isatin H^6), 7.44 d (2H, arom. H^3), 7.60 d (1H, isatin H^4), 7.81 s (1H, azole H^2), 7.88 d (2H, arom. H^2, $J_{2,3}$ 8.1 Hz), 11.34 s (1H, NH), 13.88 s (1H, isatin NH) [$(CD_3)_2SO$]
IV	79	139–140	1659, 1614, 1585, 1555, 1502, 1438, 1229, 1116, 1026	5.32 s (1H, CH_2), 6.94 s (1H, azole H^4), 7.22 s (1H, azole H^5), 7.44 d (2H, arom. H^3), 7.79 s (1H, azole H^2), 8.02 d (2H, arom. H^2, $J_{2,3}$ 8.1 Hz), 9.32 s (1H, oxadiazole H) [$(CD_3)_2SO$]
V	75	238–239	3258, 3125, 1679, 1650, 1512, 1279, 1229	5.30 s (2H, CH_2), 6.94 s (1H, azole H^4), 7.22 s (1H, azole H^5), 7.37 d (2H, arom. H^3, *J* 8.1 Hz), 7.55 m (3H, arom. $H^{3',4'}$), 7.79 s (1H, azole H^2), 7.92 m (4H, arom. $H^{2,2'}$), 10.47 s (2H, NH) [$(CD_3)_2SO$]
VI	74	173–174	1622, 1585, 1460, 1245, 1025	5.34 s (2H, CH_2), 6.97 s (1H, azole H^4), 7.25 s (1H, azole H^5), 7.48 d (2H, arom. H^3), 7.65 m (3H, arom. H), 7.84 s (1H, azole H^2), 8.13 d (4H, arom. H) [$(CD_3)_2SO$]
VIIa	69	224–225	3328, 3118, 1642, 1584, 1545, 1411, 1280, 1227, 1074, 1028	5.27 s (2H, CH_2), 6.93 s (1H, azole H^4), 7.21 m (3H, azole H^5, NH_2), 7.37 d (2H, arom. H^3, 7.77 d (2H, arom. H^2), 7.78 s (1H, azole H^2) [$(CD_3)_2SO$]
VIIb	65	225–227 (decomp.)	3350–2900, 1664, 1600, 1579, 1495, 1289, 1275	5.50 s (4H, CH_2, NH_2), 7.25 m (2H, azole H), 7.35 d (2H, arom. H^3), 7.39 m (1H, azole H), 7.71 m (1H, azole H), 7.83 d (2H, arom. H^2, $J_{2,3}$ 8.4 Hz), 8.12 s (1H, azole H^2) [CD_3CN]
VIII	82	164–165	3274, 3174, 1672, 1612, 1567, 1534, 1504, 1290, 1229	4.10 s (2H, $CH_2CH=CH_2$), 5.03 d (1H, *trans*-$CH=CH_2$), 5.12 d (1H, *cis*-$CH=CH_2$), 5.27 s (2H, CH_2), 5.82 m (1H, CH=), 6.92 s (1H, azole H^4), 7.18 s (1H, azole H^5), 7.35 d (2H, arom. H^3), 7.77 s (1H, azole H^2), 7.90 d (2H, arom. H^2, $J_{2,3}$ 8.1 Hz), 8.22 br.s (1H, $NHCH_2$), 9.33 s (1H, NH), 10.32 br.s (1H, CONH) [$(CD_3)_2SO$]

Table (Contd.)

Comp. no	Yield, %	mp, °C	IR spectrum, cm^{-1}	^1H NMR spectrum, δ, ppm (solvent)
IX	70	217–218	3135, 3117, 1535, 1510, 1492, 1438, 1415, 1405, 1363, 1348, 1300, 1272	4.67 d.t (2H, $CH_2CH=CH_2$, *J* 4.8 Hz), 4.95 d.d (1H, *trans*-CH=CH_2, *J* 17.1 Hz), 5.17 d.d (1H, *cis*-CH=CH_2, *J* 10.6, $J_{cis,trans}$ 0.9 Hz), 5.25 s (2H, CH_2), 5.88 m (1H, CH=), 6.99 s (1H, azole H^4), 7.06 s (1H, azole H^5), 7.35 d (2H, arom. H^3), 7.62 s (1H, azole H^2), 7.64 d (2H, arom. H^2, $J_{2,3}$ 8.4 Hz) [CD_3CN]
Xa	72	154–155	3182, 1660, 1505, 1362, 1285	3.12 s (3H, CH_3), 5.25 s (2H, CH_2), 6.92 s (1H, azole H^4), 7.20 s (1H, azole H^5), 7.31 d (2H, arom. H^3), 7.65 d (2H, arom. H^2, $J_{2,3}$ 7.5 Hz), 7.79 s (1H, azole H^2), 9.74 s (1H, SO_2NH), 10.58 s (1H, CONH) [$(CD_3)_2SO$]
Xb	75	178–179 (decomp.)	3204, 1663, 1616, 1574, 1506, 1451, 1422, 1337, 1290, 1185	5.24 s (2H, CH_2), 6.93 s (1H, azole H^4), 7.19 s (1H, azole H^5), 7.28 d (2H, arom. H^3), 7.52 m, 7.61 m (3H, arom. $H^{3',4'}$), 7.66 d (2H, arom. H^2, $J_{2,3}$ 7.5 Hz), 7.78 s (1H, azole H^2), 7.82 d (2H, arom. H^2, $J_{2',3'}$ 8 Hz), 9.95 s (1H, SO_2NH), 10.65 s (1H, CONH) [$(CD_3)_2SO$]
Xc	68	203–205 (decomp.)	3144, 1664, 1566, 1506, 1347, 1294, 1229	2.42 s (3H, CH_3), 5.25 s (2H, CH_2), 6.94 s (1H, azole H^4), 7.19 s (1H, azole H^5), 7.27 d (2H, arom. H^3), 7.60 d (2H, arom. $H^{3'}$), 7.68 d (2H, arom. H^2, $J_{2,3}$ 7.5 Hz), 7.79 s (1H, azole H^2), 7.82 d (2H, arom. H^2, $J_{2',3'}$ 6.8 Hz), 9.96 s (1H, SO_2NH), 10.63 s (1H, CONH) [$(CD_3)_2SO$]

4-(1*H*-Azol-1-ylmethyl)benzohydrazides IIa–IId. A mixture of 0.07 mol of methyl 4-(1*H*-azol-1-ylmethyl)benzoate and 30 ml of 99% hydrazine hydrate was refluxed for 4 h. After cooling, a precipitate formed and was filtered off and recrystallized from a benzene–ethanol mixture.

***N*'-(Phenylmethylidene)-, *N*'-[(2-hydroxypheny)methylidene]-, *N*'-[(4-hydroxypheny)methylidene]-, *N*'-[(4-hydroxy-3-methoxypheny)methylidene]-, and *N*'-[(4-dimethylaminopheny)methylidene]-4-(1*H*-imidazol-1-ylmethyl)benzohydrazides (IIIa–IIIe).** A mixture of 1.5 mmol of 4-(1*H*-imidazol-1-ylmethyl)-benzohydrazide (**IIa**) and 1.5 mmol of aromatic aldehyde in 7 ml of 95% ethanol was heated under reflux for 3 h. After cooling, a precipitate formed and was filtered off and recrystallized from an ethanol–DMF mixture.

***N*'-(Cyclopentylidene)-4-(1*H*-imidazol-1-ylmethyl)benzohydrazide (IIIf), *N*'-[1-(4-hydroxyphenyl)ethylidene]-4-(1*H*-imidazol-1-ylmethyl)-benzohydrazide (IIIg), and *N*'-(cyclohexylidene)-4-(1*H*-1,2,4-triazol-1-ylmethyl)benzohydrazide (IIIh).** Two drops of triethylamine was added to 1.5 mmol of hydrazide **IIa** and 1.5 mmol of ketone in 50 ml of a mixture of benzene and absolute ethanol, and the mixture was refluxed for 8 h with a Dean–Stark trap. After cooling, crystals formed and were filtered off and recrystallized from an ethanol–ethyl acetate mixture.

***N*'-(2-Oxo-2,3-dihydro-1*H*-3-indolylidene)-4-(1*H*-imidazol-1-ylmethyl)benzohydrazide (IIIi).** Isatin, 3.4 mmol, and 3.4 mmol of hydrazide **IIa** in 20 ml of absolute ethanol was refluxed for 4 h. An orange precipitate formed and was filtered off and recrystallized from an ethanol–DMF mixture.

2-[4-(1*H*-Imidazol-1-ylmethyl)phenyl]-1,3,4-oxadiazole (IV). Hydrazide **IIa**, 2.3 mmol, was refluxed with 20 ml of orthoformic ester for 8 h. The ester was removed in a vacuum, and the residue was recrystallized from ethanol.

***N*-Benzoyl-*N*'-[4-(1*H*-imidazol-1-ylmethyl)]benzoylhydrazine (V).** A solution of 2.3 mmol of benzoyl chloride in 3 ml of dioxane was added over the course of 20 min to a stirred solution of hydrazide **IIa** and 2.3 mmol of $NaHCO_3$ in a mixture of 4 ml of dioxane and 2 ml of water. The mixture was stirred at room temperature for 15 h. The solvent was removed in a vacuum, and the residue was washed with water and recrystallized from an ethanol–dioxane mixture.

2-[4-(1*H*-Imidazol-1-ylmethyl)phenyl]-5-phenyl-1,3,4-oxadiazole (VI). A mixture of 0.63 mmol of hydrazine **V** and 2.5 ml of $POCl_3$ was heated for 2 h. After cooling, the solution was poured into ice water, neutralized to pH 7 with NaOH. The precipitate that formed was thoroughly stirred with water, dissolved in ethanol with heating, the hot solution was filtered, the filtrate was evaporated, and the residue was recrystallized from a dioxane–ethyl acetate mixture.

5-Amino-2-[4-(1*H*-imidazol-1-ylmethyl)phenyl]-1,3,4-oxadiazole (VIIa). A solution of 1.64 of cyanogen bromide in 3 ml of absolute ethanol was added to a solution of 1.64 mmol of hydrazide **IIa** in 10 ml of absolute ethanol, and the nixture was stirred at room temperature for 10 h. To the colorless precipitate, 1.64 mmol of $NaHCO_3$ in 4 mlof water was added. The resulting solution was stirred for 2 h, the solvent was removed in a vacuum, and the residue was washed with water and recrystallized from ethanol.

5-Amino-2-[4-(1*H*-benzimidazol-1-ylmethyl)-phenyl]-1,3,4-oxadiazole (VIIb) was synthesized like compound **VIIa** from compound **IIb** and cyanogen bromide.

***N*'-(Allylthiocarbonyl)-4-(1*H*-imidazol-1-ylmethyl)benzohydrazide (VIII).** A mixture 4.6 mmol of hydrazide **IIa** and 0.46 ml of allyl isothiocyanate in 5 ml of ethanol was refluxed for 2 h. After cooling, colorless crystals formed and were filtered off and recrystallized from ethanol.

4-Allyl-3-[4-(1*H*-imidazol-1-ylmethyl)phenyl]-4,5-dihydro-1*H*-1,2,4-triazole-5-thione (IX). A solution of 1.43 mmol of NaOH in 10 ml of water was added to 0.95 mmol of compound **VIII**, and the mixture was refluxed for 1 h. The solution was cooled and acidified with acetic acid to pH 4. The precipitate that formed was filtered off and recrystallized from ethanol.

***N*-[4-(1*H*-Imidazol-1-ylmethyl)benzoyl]-*N*'-(4-methylsulfonyl)hydrazine (Xa).** A solution of 1.85 mmol of hydrazide **IIa** in 6 ml of pyridine was added to a solution of 1.85 mmol of mesyl chloride in 5 ml of absolute pyridine. The mixture was stirred for 4 h, pyridine was removed in a vacuum, and the residue was washed with water and recrystallized from ethanol.

***N*-[4-(1*H*-Imidazol-1-ylmethyl)benzoyl]-*N*'-(4-phenylsulfonyl)hydrazine (Xb) and *N*-[4-(1*H*-imidazol-1-ylmethyl)benzoyl]-*N*'-(4-tosyl)hydrazine (Xc)** were prepared like compound **Œa** by treatment of compound **IIa** with benzenesulfonyl chloride and tosyl chloride, respectively.

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