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Synthesis of new derivatives of the 1*H*-1,2,3-triazole ring using 1-aryl-5-phenyl-1*H*-1,2,3-triazole-4-carbohydrazides as precursors

Bakr F. Abdel-Wahab,[a] Benson M. Kariuki,[b] Hanan A. Mohamed,[a] Mohamed S. Bekheit,[c] and Gamal A. El-Hiti[d,*]

[a]Applied Organic Chemistry Department, National Research Centre, Dokki, Giza 12622, Egypt. [b]School of Chemistry, Cardiff University, Main Building, Park Place, Cardiff CF10 3AT, UK. [c]Department of Pesticide Chemistry, National Research Centre, Dokki, Giza 12622, Egypt. [d]Department of Optometry, College of Applied Medical Sciences, King Saud University, Riyadh 11433, Saudi Arabia
Email: gelhiti@ksu.edu.sa

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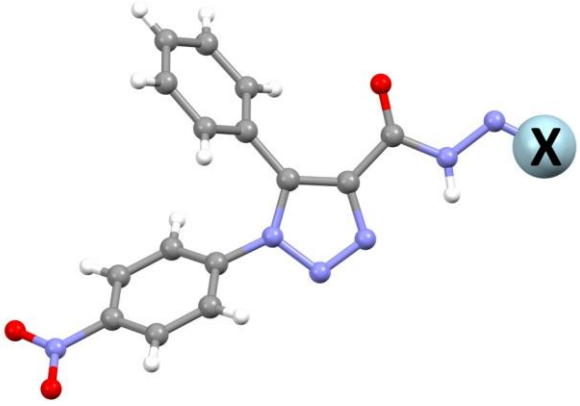
Abstract

Condensation of 1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole-4-carbohydrazide and phenyl isothiocyanate in ethanol in the presence of a catalytic quantity of triethylamine under reflux gave 5-(1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)-*N*-phenyl-1,3,4-oxadiazol-2-amine in 84% yield. 2-(2-(5-Phenyl-1*H*-1,2,3-triazole-4-carbonyl)hydrazineylidene)-*N*-propanehydrazonoyl chlorides were synthesized, in 87–90% yields, by the condensation of 1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole-4-carbohydrazide and hydrazonoyl chlorides. In a similar manner, condensation of 1*H*-1,2,3-triazole-4-carbohydrazides and carbonyl compounds in boiling ethanol under acidic conditions gave the corresponding hydrazones in 88–92% yield. The structures of the new heterocycles were confirmed by nuclear magnetic resonance spectral data and X-ray crystallography.



Keywords: Acid hydrazides; 1,2,3-Triazoles; Hydrazonoyl chlorides; Hydrazones; X-Ray diffraction

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Introduction

Acid hydrazides are frequently incorporated in the design of bioactive molecules and therefore are of interest to both chemists and biologists. Hydrazone-containing compounds act as valuable intermediates in the synthesis of compounds displaying biological activity.[1] Hydrazides are often involved in the manufacture of medications, glues, polymers, herbicides, dyes, and numerous other industrial products. Thus, for example, isonicotinic acid hydrazide, commercially known as isoniazid, has been applied in the treatment of tuberculosis.[2–6] Hydrazides act as antibacterial, antifungal, and antiviral reagents.[7–11] In addition, they are useful in the production of many heterocycles, with different ring sizes, through cyclization with various reagents.[12–17] Hydrazides act as bidentate ligands and react with both nucleophilic and electrophilic reagents. The most common types of hydrazides include carbohydrazides, phosphoryl hydrazides, and sulfonohydrazides based on the substituents attached to the nitrogen atom (Figure 1). The simple procedures for the synthesis of hydrazides involve reactions of substituted hydrazine or hydrazides and carbonyl compounds (e.g., aldehydes, ketones, esters, acyl halides, and anhydrides).[18,19] In addition, compounds containing both hydrazides and hydrazone moieties have been found to be biologically active.[20–22]

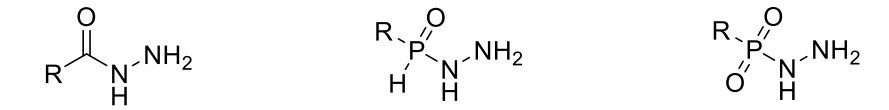
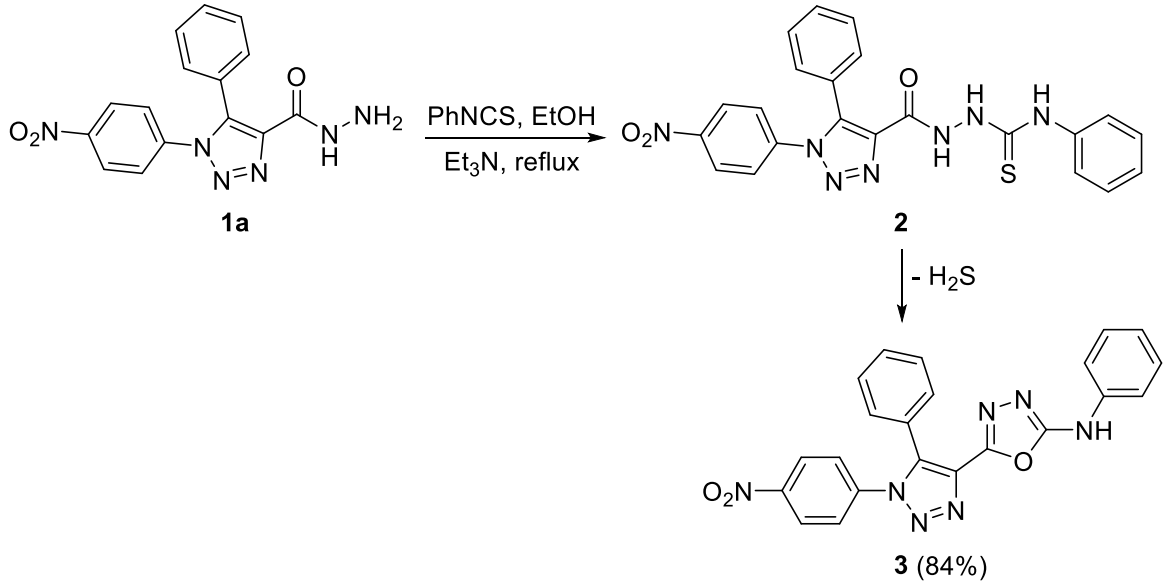


Figure 1. Common types of hydrazides.

Heterocycles containing triazole moieties show a wide range of biological activities. They act as antibacterial, antifungal, antiviral, analgesic, antitubercular, anticonvulsant, anti-inflammatory, and antidepressant agents and others.[23–29] In addition, they are used in agriculture as insecticides and fungicides.[30,31] Therefore, the current research deals with the synthesis and structure elucidation of several heterocycles containing 1,2,3-triazole moieties in continuation of our long-term interest in the synthesis of novel heterocycles.[32–35] Simple and efficient procedures are utilized to provide new heterocycles in high yields.

Results and Discussion

The condensation of 1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole-4-carbohydrazide (**1a**) and phenyl isothiocyanate in EtOH containing a catalytic amount of Et_3N, under reflux, gave 5-(1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl)-*N*-phenyl-1,3,4-oxadiazol-2-amine (**3**, Scheme 1). The reaction of hydrazide **1a** and phenyl isothiocyanate at room temperature leads to the formation of intermediate **2** (Scheme 1). Elimination of H_2S from **2** then leads to ring closure and formation of the 1,3,4-oxadiazole moiety.



Scheme 1. Synthesis of **3**.

The structure of **3** was confirmed by the NMR spectral data and single crystal X-ray diffraction (Figure 2). The ^{1}H NMR spectrum of **3** showed an exchangeable singlet at 10.74 ppm due to the NH proton. In addition, it showed the presence of 14 aromatic protons corresponding to the two phenyl and aryl groups. The ^{13}C NMR spectrum of **3** showed the two carbons of the newly formed 1,3,4-oxadiazole ring at 151.8 and 160.5 ppm (See the Supplementary Materials for details).

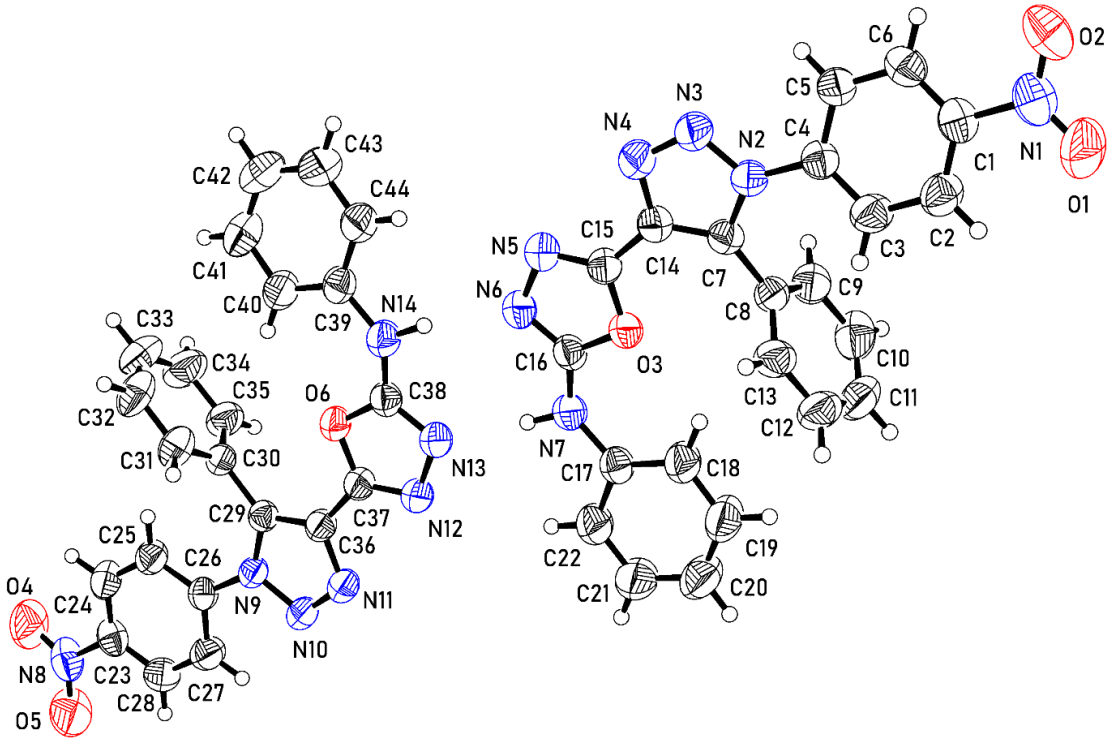
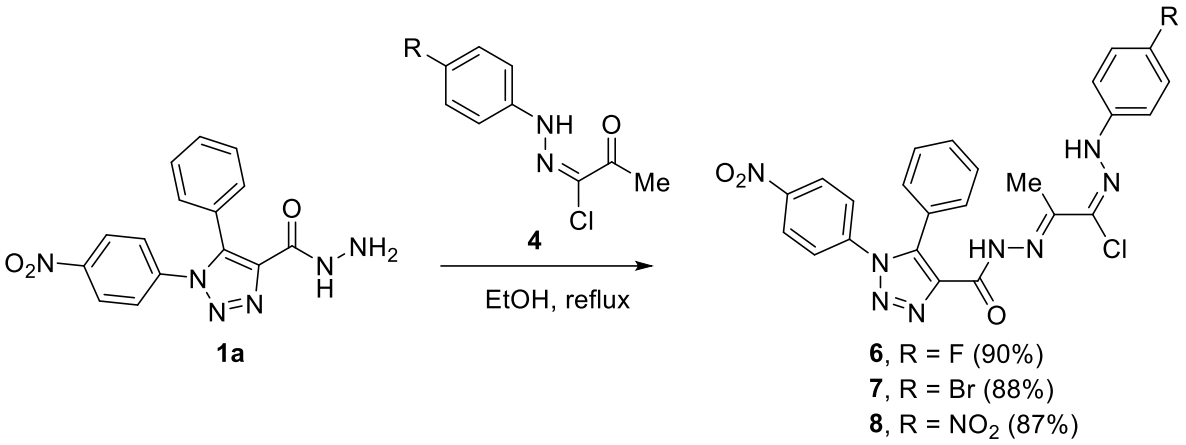


Figure 2. An ORTEP representation of the two independent molecules in the crystal structure of **3**.

The crystal structure of **3** has two independent molecules M_1 and M_2 (Figure 2). Each molecule of **3** comprises nitrobenzene (M_1**A**: C1–C6, N1, O1, O2 & M_2**A**: C23–C28, N8, O4, O4), triazole (M_1**B**: C7, C14, N2–N4 & M_2**B**: C29, C30, N9–N11), oxadiazole (M_1**C**: C15, C16, N5, N6, O3 & M_2**C**: C37, C38, N12, N13, O6), aniline (M_1**D**: C17–C22, N7 & M_2**D**: C39–C44, N14) and phenyl (M_1**E**: C8–C13 & M_2**E**: C30–C35) groups. Apart from the phenyl group (M_1**E** and M_2**E**), the molecule is essentially planar. This is indicated by twist angles M_1**A**/M_1**B**, M_1**B**/M_1**C**, M_1**C**/M_1**D** of 20.3 (1)°, 6.1(1)° and 9.3(1)°, respectively for molecule M_1 and M_2**A**/M_2**B**, M_2**B**/M_2**C**, M_2**C**/M_2**D** angles of 1.8(1)°, 5.8(1)° and 12.0(1)°, respectively for molecule M_2. The phenyl groups are almost perpendicular to the plane of the rest of the molecule with twist angles M_1**B**/M_1**E** of 80.5(1)° for molecule M_1 and M_2**B**/M_2**E** of 81.3(1)° for molecule M_2. In the crystal, the two independent molecules are linked by a pair of N–H…N hydrogen bonds (with geometry N14-H14…N6 =167.6(19)°, N14…N6 = 2.940(2)Å and N7-H7…N13 = 174.4(19)°, N7…N13 = 2.864(2)°)Å.

The condensation of **1a** and hydrazonoyl chlorides (**4a–4c**, R = F, Br, NO_2) in EtOH under reflux conditions gave the corresponding 2-(2-(5-phenyl-1*H*-1,2,3-triazole-4-carbonyl)hydrazineylidene)-*N*-propanehydrazonoyl chlorides **6–8** in 87–90% yields (Scheme 2). The formation of **6–8** involves the elimination of water from the condensation of **1a** and **4**. None of the expected 1,3,4-oxadiazine was obtained indicating that no cyclization step has taken place.



Scheme 2. Synthesis of **6–8**.

The ^{1}H NMR spectra of **6–8** showed the presence of two exchangeable singlets that appeared downfield in the 10.21–10.32 and 10.81–10.90 ppm regions due to the two NH protons. The methyl protons appeared as a singlet in the 2.31–2.46 ppm region. The ^{13}C NMR spectra of **6–8** showed the carbonyl carbons at high field at 162.8 ppm, while the methyl carbons appeared at high field at 13.8 ppm. The ^{13}C NMR spectrum of heterocycle **6** showed the coupling between the fluorine and the carbon atoms of the aryl ring. The C2/C6, C3/C5, and C4 of the 4-fluorophenyl group appeared at 116.0, 116.2, and 158.2 ppm as doublets with coupling constants of 8.5, 22.7, and 249.5 Hz, respectively (See the Supplementary Materials for details). The structures of **6** and **7** were also confirmed by the single crystal X-ray diffraction.

The molecule of compound **6** obtained from the crystal structure is shown in Figure 3. The structure also contains DMF solvent molecules located on two sites, one of which is disordered. The molecule of **6** consists of nitrobenzene (**A**: C1–C6, N1, O1, O2), triazole (**B**: C7, C14, N2–N4), (formylhydrazinylidene)propanehydrazonoyl chloride (**C**: C15–C18, N5-N8, O3, Cl1), fluorobenzene (**D**: C19–C24, Br1) and phenyl (**E**: C8–C13) groups. The triazole, (formylhydrazinylidene)propanehydrazonoyl chloride

and fluorobenzene groups are coplanar with twist angles **B**/**C** and **C**/**D** of 5.4(2)°, and 12.4(1)°, respectively. The nitrobenzene and phenyl groups are rotated from this **BCD** plane, as indicated by **A**/**B** and **B**/**E** twist angles of 47.1(1)° and 49.9(2)°, respectively. One DMF solvent molecule accepts an N–H…O hydrogen bond from a molecule of **6** (with geometry N8–H8…O4 = 155.1°, N8…O4 = 2.941(5)Å).

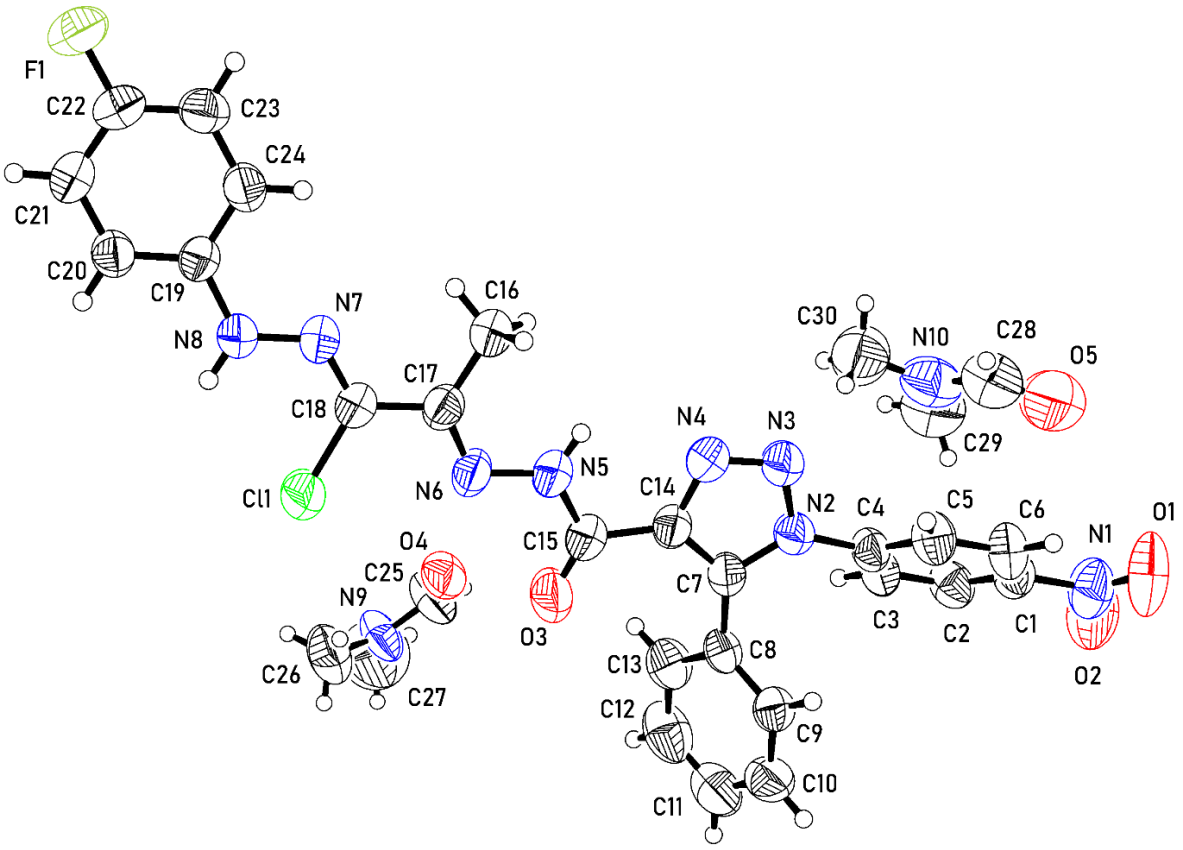


Figure 3. ORTEP representation of the asymmetric unit of compound **6**.

The molecule from the crystal structure of compound **7** is shown in Figure 4. The molecule consists of nitrobenzene (**A**: C1–C6, N1, O1, O2), triazole (**B**: C7, C14, N2–N4), (formylhydrazinylidene)propanehydrazonoyl chloride (**C**: C15–C18, N5–N8, O3, Cl1), bromobenzene (**D**: C19–C24, Br1) and phenyl (**E**: C8–C13) groups. The triazole, (formylhydrazinylidene)propanehydrazonoyl chloride and bromobenzene groups are coplanar with twist angles **B**/**C** and **C**/**D** of 12.7(2)°, and 15.8(1)°, respectively. The nitrobenzene and phenyl groups are twisted from this plane as indicated by twist angles **A**/**B** and **B**/**E** of 44.2(1)° and 54.1(1)°, respectively.

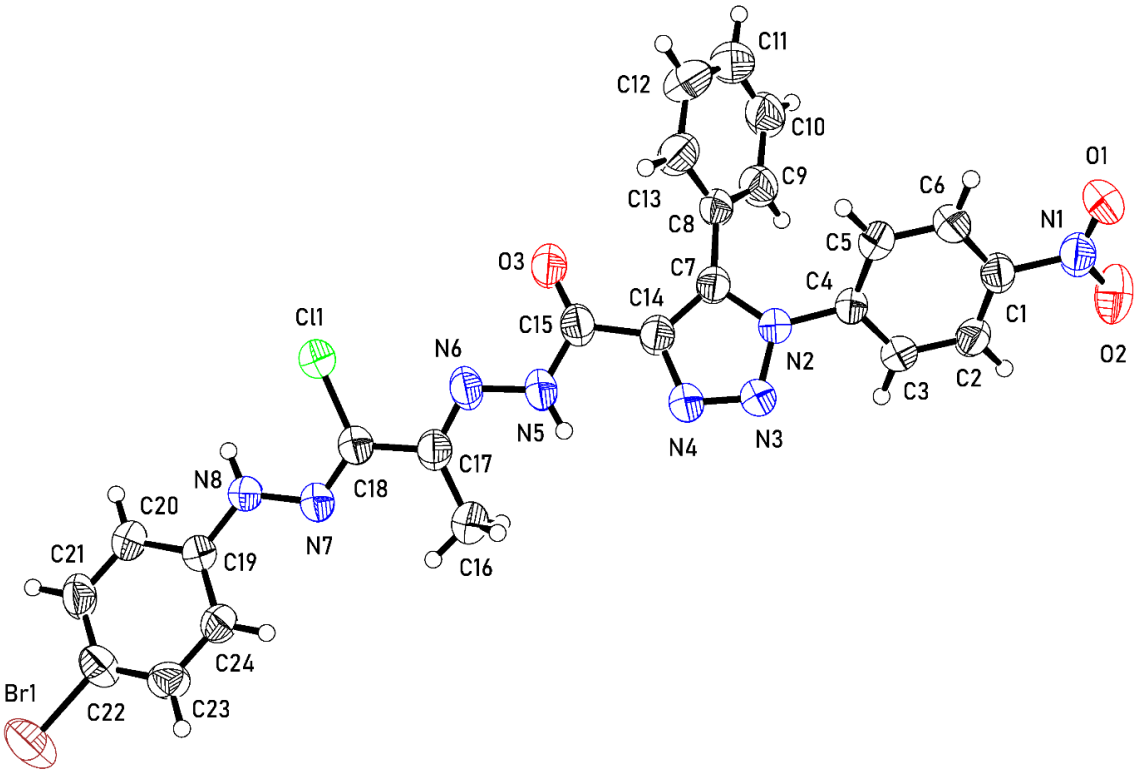
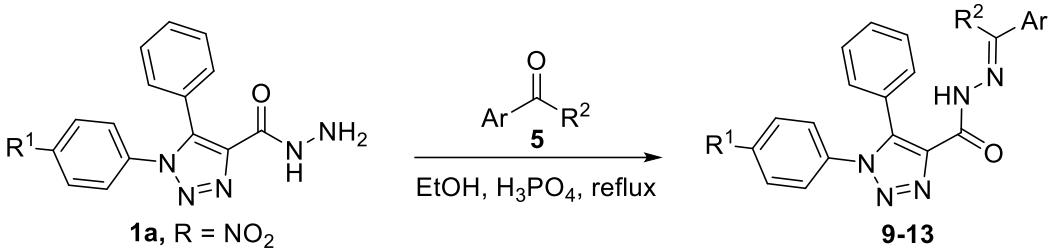


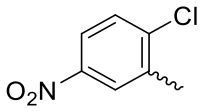
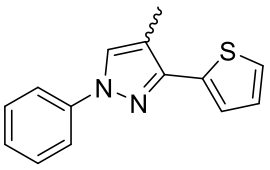
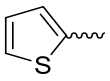
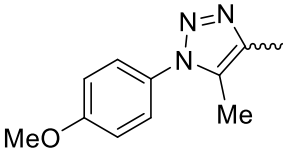
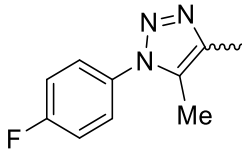
Figure 4. An ORTEP representation of **7**.

The condensation of hydrazide **1a,b** (R^1 = NO_2, H) and carbonyl compounds **5a–5e** (aldehydes or methyl ketones) in the presence of H_3PO_4 as a catalyst in boiling EtOH gave the corresponding hydrazones **9–13** (Scheme 3) in 88–92% yields (Table 1). No cyclization took place, only condensation to give compounds **9–13**.



Scheme 3. Synthesis of heterocycles **9–13**.

Table 1. Synthesis of heterocycles **9–13** according to Scheme 3

Heterocycle	R^1	R^2	Ar	MP (°C)	Yield (%)
9	H	H		230–231	92
10	H	H		240–241	90
11	NO_2	Me		240–242	88
12	NO_2	Me		16–162	88
13	NO_2	F		230–231	92

The structures of **9–13** were confirmed by NMR spectroscopy. The ^{1}H NMR spectra of hydrazones **9–13** showed an exchangeable singlet due to the NH protons that appeared in the 10.80–12.34 ppm region. The carbonyl carbons in **12** and **13** appeared at 160.5 and 163.9 ppm, respectively in their ^{13}C NMR spectra. For heterocycle **13**, the ^{13}C NMR spectrum showed the C3/C5 (117.2 ppm), C2/C6 (128.4 ppm), and C4 (162.0 ppm) signals of the 4-fluorophenyl group as three doublets with coupling constants of 22.7, 8.3, and 245.6 Hz, respectively (See the Supplementary Materials for details). It was not possible to record the ^{13}C NMR spectra for compounds **9** and **11** due to poor solubility in deuterated solvents. Their structures were confirmed by the X-ray diffraction, however, as shown in Figures 5 and 6, respectively, as was the chemical structure of **12** (Figure 7).

Figure 5 shows the molecule of **9** extracted from the crystal structure. The crystal also contains disordered DMF solvent molecules. The molecule of **9** consists of chloronitrobenzene (**A**: C1–C6, N1, O1, O2, Cl1), methylideneformohydrazide (**B**: C7, C8, N2, N3, O3), triazole (**C**: C9, C10, N4–N6), and two phenyl (**D**: C11–C16, **E**: C17–C22) groups. The chloronitrobenzene, methylideneformohydrazide and triazole groups are coplanar with twist angles **A**/**B** and **B**/**C** of 5.4(2)° and 14.2(2)°, respectively. The two phenyl groups deviate from the plane of the rest of the atoms (**ABC**) by **C**/**D** and **C**/**E** twists of 55.9(1)° and 60.3(1)°, respectively. The crystals also contain DMF solvent molecules which accept N–H…O hydrogen bonding from the molecule of **9** (with geometry N3-H3A…O4 = 143.0°, N3…O4 = 2.823(10)Å for one solvent component and N3–H3A…O4A = 150.0°, N3…O4A = 3.055(13)Å for the other component).

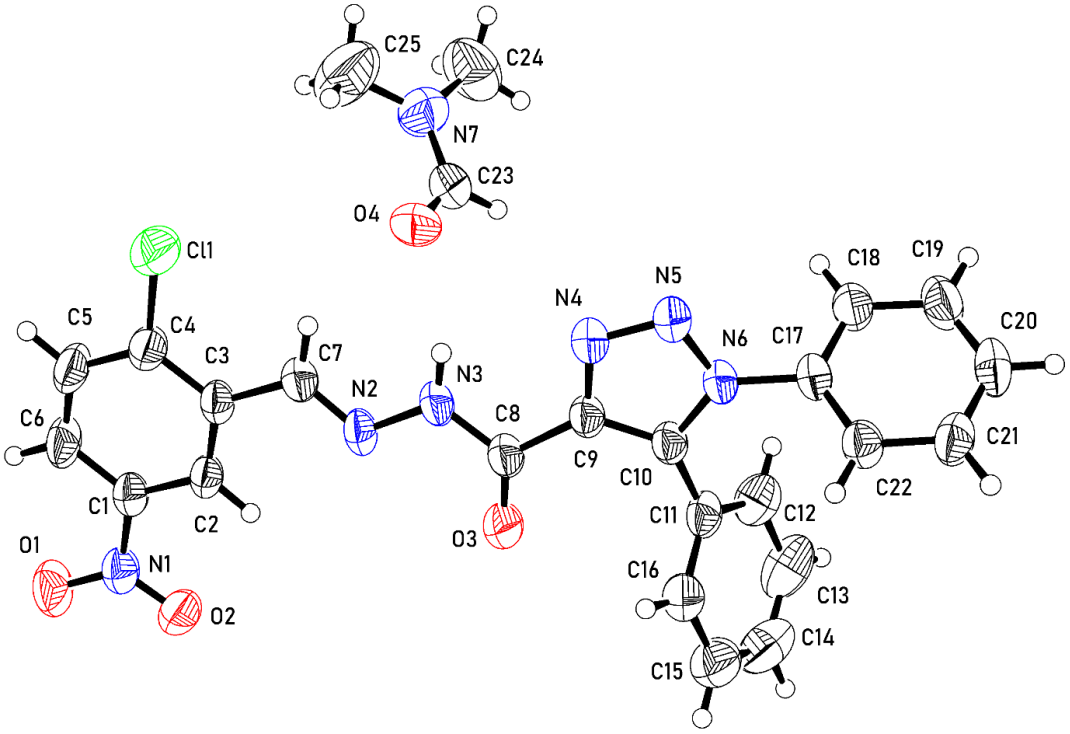


Figure 5. An ORTEP representation of asymmetric unit of the crystal structure of compound **9**.

There are two independent molecules of **11** (M_1 and M_2) in asymmetric unit of the crystal structure (Figure 6). Each molecule of **11** is composed of a nitro group (M_1**A**: N1, O1,O2 & M_2**A**: N7, O4, O5), the benzene ring linked to the nitro group (M_1**B**: C1–C6 & M_2**B**: C22–C27), triazole (M_1**C**: C7, C14, N2–N4 & M_2**C**: C28, C35, N8–N10), phenyl (M_1**D**: C8–C13 & M_2**D**: C29–C34), methylformohydrazide (M_1**E**: C15–C17, N5, N6, O3 & M_2**E**: C36–C38, N11, N12, O6), and thiophene (M_1**F**: C18–C21, M_2**F**: C39–C42, S2) groups.

In molecule M_1, nitro group is disordered with two components related by a twist of 31.5(8)°. The nitro groups in the structure deviate from the plane of the rings they are attached to by M_1**A**/M_1**B** and M_2**A**/M_2**B** twist angles in the range 8 - 24°. For molecule M_1, the triazole, methylformohydrazide and thiophene groups are coplanar with twist angles M_1**C**/M_1**E** and M_1**E**/M_1**F**, of 7.3(1)° and 5.6(1)°, respectively. The corresponding angles M_2**C**/M_1**E** and M_2**E**/M_1**F** for molecule M_2 are 16.2(1)° and 9.1(3)°, respectively. The orientations of the aryl groups of the nitrophenyl and the phenyl ring deviate significantly from the coplanar fragments of the molecule as indicated by twist angles, M_1**B**/M_1**C,** and M_1**C**/M_1**D** of 50.3(1)° and 54.5(1)° for molecule M_1. The corresponding twist angles for molecule M_2 areM_2**B**/M_2**C,** and M_2**C**/M_2**D** are 41.5(1)° and 65.5(1)°.

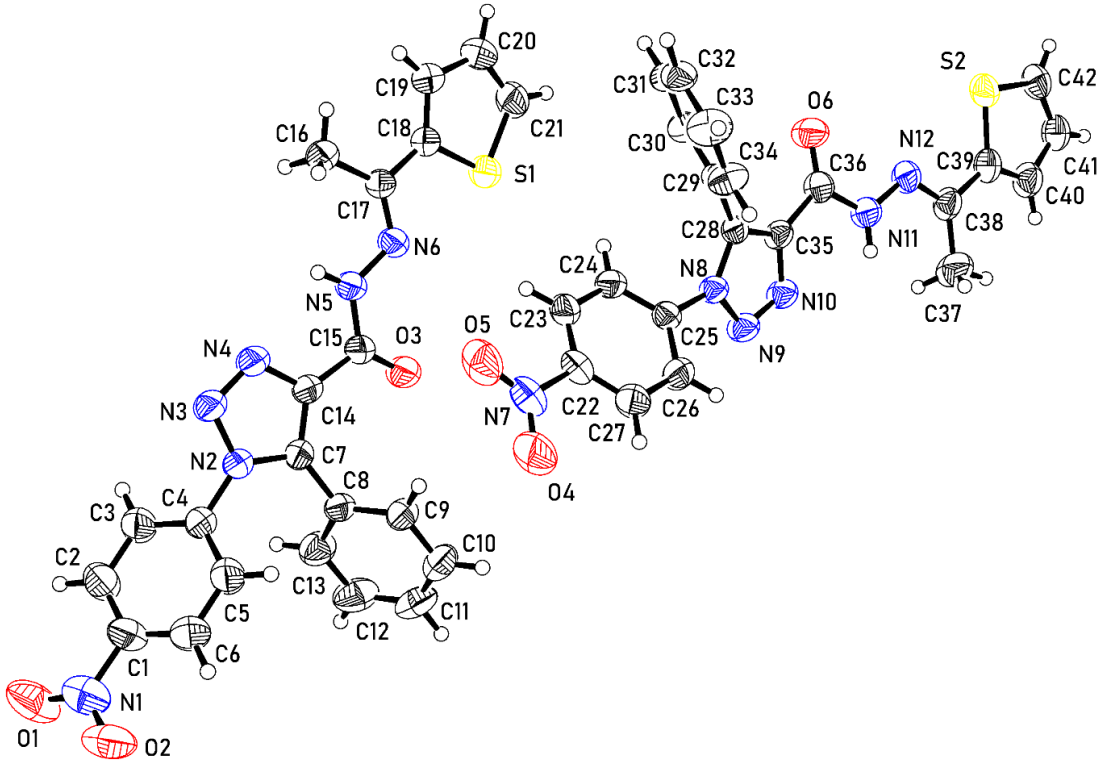


Figure 6. An ORTEP representation of the asymmetric unit of the crystal structure of compound **11**.

The molecule from the crystal structure of **12** is shown in Figure 7. The molecule consists of nitrobenzene (**A**: C1–C6, N1, O1, O2), triazole (**B**: C7, C14, N2–N4), [ethylidene]formohydrazide (**C**: C15–C17, N5, N6), methyl triazole (**D**: C18–C20, N7–N9), methoxybenzene (**E**:C21–C27, O4) and phenyl (**F**: C8–C13) groups. The backbone of the molecule, comprising the triazole, [ethylidene]formohydrazide and methyl triazole groups, is planar with twist angles **B**/**C** and **C**/**D** of 11.1 (1)° and 3.9(1)°, respectively. The nitrobenzene, methoxybenzene and phenyl groups deviate from the plane of the backbone with twist angles **A**/**B**, **D**/**E** and **B**/**F** of 53.9(2)°, 50.5(1)° and 39.7(1)°, respectively.

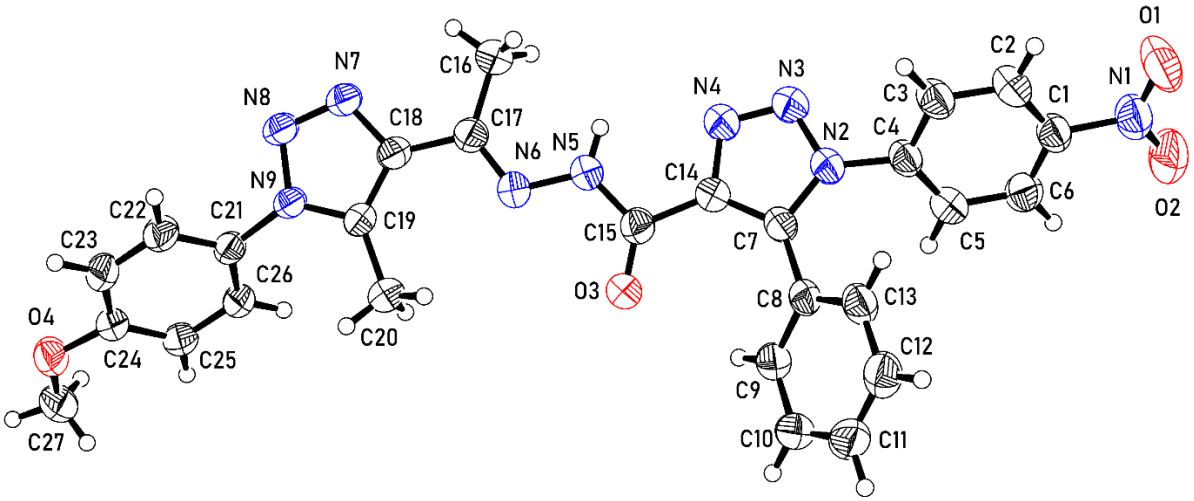


Figure 7. An ORTEP representation of **12**.

Conclusions

Several new derivatives of the 1*H*-1,2,3-triazole ring system have been synthesized. The synthesized heterocycles were obtained in high yields using simple procedures. Nuclear magnetic resonance and X-ray diffraction have been used to establish the structures of the newly synthesized heterocycles.

Experimental Section

General. Chemicals, solvents, and reagents were purchased from Merck Gillingham, UK). An Electrothermal melting point apparatus (Cole-Parmer, Illinois, IL, USA) was used to determine the melting points. The synthesized heterocycles were dissolved in deuterated dimethyl sulfoxide (DMSO-d_6) and a JEOL NMR 500 MHz spectrometer (Tokyo, Japan) was used to record the NMR spectra (δ in ppm and *J* in Hz) at 500 MHz for the ^{1}H and 125 MHz for the ^{13}C NMR measurements. A CHNS-932 (LECO) Vario elemental analyzer was used for elemental analyses. Compounds **1**,[36] **4a–c**,[37] **5b**,[38] **5d**,[39] and **5e**[39] were prepared according to literature procedures.

Synthesis of 5-[1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazol-4-yl]-*N*-phenyl-1,3,4-oxadiazol-2-amine (3). A mixture of **1a** (5.0 mmol, 1.62 g) and phenyl isothiocyanate (5.0 mmol, 0.67 g) in EtOH (20 mL) containing Et_3N (0.1 mL) was refluxed for 2 h. On cooling to rt, the resultant solid was filtered off, washed with EtOH, dried, and crystallized from DMF giving **3** in 84% yield. MP 237–238 °C. ^{1}H NMR (ppm; Hz): 6.96 (t, *J* 7.6, 1H, Ph), 7.29 (t, *J* 7.6 Hz, 2H, Ph), 7.42–7.50 (m, 7H, Ph), 7.68 (d, *J* 9.1 Hz, 2H, Ar), 8.30 (d, *J* 9.1 Hz, 2H, Ar), 10.74 (s, exch., 1H, NH). ^{13}C NMR (ppm): 117.6 (C2/C6 of Ph), 122.6 (C4 of Ph), 125.0(C2/C6 of Ar), 125.4 (C3/C5 of Ar), 127.0 (C2/C6 of Ph), 127.4 (C4 of Ph), 129.2 (C3/C5 of Ph), 129.6 (C3/C5 of Ph), 130.9 (C1 of Ph), 131.0 (C5 of triazolyl), 132.2 (C4 of triazolyl), 138.9 (C1 of Ph), 140.7 (C1 of Ar), 148.1 (C4 of Ar), 151.8 5 (C2 of oxadiazolyl), 160.5 (C5 of oxadiazolyl). Anal. Calcd. for $C_{22}H_{15}N_7O_3$ (425.41): C, 62.11; H, 3.55; N, 23.05. Found: C, 62.37; H, 3.68; N, 23.13%.

General synthesis of heterocycles 6–8. A mixture of **1a** (2.0 mmol, 0.65 g) and hydrazonoyl chloride **4a–4c** (2.0 mmol) was refluxed for 2 h in EtOH (15 mL). On cooling to rt, the solid was filtered off, washed with EtOH, dried, and crystallized from DMF yielding the corresponding heterocycles **6–8**.

***N*-(4-Fluorophenyl)-2-2-[1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole-4-carbonyl)hydrazineylidene]propanehydrazonoyl chloride (6).** Yield: 90%. MP 190–191 °C. ^{1}H NMR (ppm; Hz): 2.31 (s, 3H, Me), 7.10 (t, *J* 8.6 Hz, 2H, Ph), 7.30–7.43 (m, 7H, Ph and Ar), 7.66 (d, *J* 9.1 Hz, 2H, Ar), 8.31 (d, *J* 9.1 Hz, 2H, Ar), 10.21 (s, exch., 1H, NH), 10.81 (s, exch., 1H, NH). ^{13}C NMR (ppm): 13.8 (Me), 116.0 (d, *J* 8.5 Hz, C2/C6 of Ar), 116.2 (d, *J* 22.7 Hz, C3/C5 of Ar), 117.2 (C3/C5 of Ar), 123.9 (C2/C6 of Ar), 125.4 (C4 of Ph), 127.0 (C2/C6 of Ph), 127.4 (C3/C5 of Ph), 129.0 (C1 of Ph), 130.6 0 (C5 of triazolyl), 130.9 0 (C4 of triazolyl), 140.6 (C1 of Ar), 140.8 (C1 of Ar), 148.3 (C4 of Ar), 150.5 (C–Me), 150.2 (C–Cl), 158.2 (d, 249.5 Hz, C4 of Ar), 162.8 (C=O). Anal. Calcd. for $C_{24}H_{18}ClFN_8O_3$ (520.91): C, 55.34; H, 3.48; N, 21.51. Found: C, 55.49; H, 3.55; N, 21.62%.

***N*-(4-Bromophenyl)-2-[2-(1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole-4-carbonyl)hydrazineylidene]propanehydrazonoyl chloride (7).** Yield: 88%. MP 250–252 °C. ^{1}H NMR (ppm; Hz): 2.31 (s, 3H, Me), 7.24–7.45 (m, 9H, Ar), 7.65 (d, *J* 9.1 Hz, 2H, Ar), 8.31 (d, *J* 9.1 Hz, 2H, Ar), 10.32 (s, exch., 1H, NH), 10.81 (s, exch., 1H, NH). ^{13}C NMR (ppm): 13.8 (Me), 113.1 (C4 of Ar), 114.8 (C3/C5 of Ar), 116.4 (C2/C6 of Ar), 117.4 (C2/C6 of Ar), 125.4 (C3/C5 of Ar), 127.4 (C3/C5 of Ph), 129.0 (C4 of Ph), 130.6 (C2/C6 of Ph), 131.0 (C1 of Ph), 132.3 (C5 of triazolyl), 140.1 (C4 of triazolyl), 140.8 (C1 of Ar), 143.3 (C1 of Ar), 148.3 (C4 of Ar),

150.0 (C–Me), 156.6 (C–Cl), 162.8 (C=O). Anal. Calcd. for $C_{24}H_{18}BrClN_8O_3$ (581.81): C, 49.55; H, 3.12; N, 19.26. Found: C, 49.67; H, 3.26; N, 19.39%.

***N*-(4-Nitrophenyl)-2-[2-(1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole-4-carbonyl)hydrazineylidene]propanehydrazonoyl chloride (8).** Yield: 87%. MP 205–206 °C. ^{1}H NMR (ppm; Hz): 2.34 (s, 3H, Me), 7.36–7.47 (m, 7H, Ar), 7.66 (d, 9.1 Hz, 2H, Ar), 8.15 (d, *J* 9.1 Hz, 2H, Ar), 8.32 (d, *J* 9.1 Hz, 2H, Ar), 10.12 (s, exch., 1H, NH), 10.90 (s, exch., 1H, NH). ^{13}C NMR (ppm): 13.8 (Me), 114.1 (C2/C6 of Ar), 125.4 (C2/C6 of Ar), 126.2 (C3/C5 of Ar), 127.4 (C3/C5 of Ar), 128.3 (C2/C6 of Ph), 129.0 (C4 of Ph), 129.7 (C3/C5 of Ph), 130.2 (C1 of Ph), 130.6 (C5 of triazolyl), 130.9 (C4 of triazolyl), 131.0 (C4 of Ar), 139.9 (C1 of Ar), 140.8 (C–Me), 141.1 (C4 of Ar), 148.3 (C1 of Ar), 149.6 (C–Cl), 162.8 (C=O). Anal. Calcd. for $C_{24}H_{18}ClN_9O5$ (547.92): C, 52.61; H, 3.31; N, 23.01. Found: C, 52.78; H, 3.45; N, 23.28%.

Synthesis of hydrazones 9–13. A mixture of **1a,b** (2.0 mmol) and carbonyl compounds **5** (2.0 mmol) was refluxed for 2 h in EtOH (15 mL) containing H_3PO_4 (0.2 mL). The ensuing solid was filtered off, washed with EtOH, dried, and crystallized from DMF giving the corresponding heterocycles **9–13** in high yields (Table 1).

(*E*)-*N*′-(2-Chloro-5-nitrobenzylidene)-1,5-diphenyl-1*H*-1,2,3-triazole-4-carbohydrazide (9). ^{1}H NMR (ppm; Hz): 7.36–7.47 (m, 10H, 2 Ph), 7.77 (d, *J* 8.6 Hz, 1H, H3 of Ar), 8.17 (dd, *J* 8.6, 2.2 Hz, 1H, H4 of Ar), 8.65 (s, 1H, H6 of Ar), 9.03 (s, 1H, CH=N), 12.75 (s, exch., 1H, NH). Anal. Calcd. for $C_{22}H_{15}ClN_6O_3$ (446.85): C, 59.13; H, 3.38; N, 18.81. Found: C, 59.27; H, 3.49; N, 18.98%.

1,5-Diphenyl-*N*′-[(1-phenyl-3-(thiophen-2-yl)-1*H*-pyrazol-4-yl)methylene]-1*H*-1,2,3-triazole-4-carbohydrazide (10). ^{1}H NMR (ppm; Hz): 7.17 (t, *J* 4.0 Hz, 1H, H4 of thiophenyl), 7.33–7.46 (m, 7H, Ar), 7.51 (t, *J* 7.7 Hz, 2H, H3/H5 of Ph), 7.62 (d, *J* 4.0 Hz, 1H, H5 of thiophenyl), 7.66 (d, *J* 8.6 Hz, 2H, H2/H6 of Ph), 7.93 (m, 2H, Ar), 7.97 (d, *J* 4.0 Hz, 1H, H3 of thiophenyl), 7.30 (d, *J* 8.6 Hz, 2H, H2/H6 of Ph), 8.87 (s, 1H, pyrazolyl), 8.91 (s, 1H, CH=N), 12.35 (s, exch., 1H, NH). ^{13}C NMR (ppm): 117.0 (C4 of pyrazolyl), 119.3 (C2/C6 of Ph), 125.3 (C2/C6 of Ph), 125.7 (C4 of Ph), 127.5 (C3/C5 of Ph), 127.6 (C3/C5 of Ph), 128.2 (C4 of Ph), 128.5 (C3 of thiophenyl), 128.8 (C3/C5 of Ph), 129.2 (C4 of thiophenyl), 130.2 (C2/C6 of Ph), 130.5 (C4 of Ph), 131.1 (C5 of thiophenyl), 134.8 (C1 of Ph), 139.2 (C1 of Ph), 139.3 (C4 of triazolyl), 140.4 (C5 of triazolyl), 140.9 (C3 of pyrazolyl), 141.6 (C1 of Ph), 146.4 (C5 of pyrazolyl), 148.3 (C2 of thiophenyl), 156.4 (CH=N), 162.8 (C=O). Anal. Calcd. for $C_{29}H_{21}N_7OS$ (515.60): C, 67.56; H, 4.11; N, 19.02. Found: C, 67.66; H, 4.33; N, 19.25%.

1-(4-Nitrophenyl)-5-phenyl-*N*′-1-(thiophen-2-yl)ethylidene)-1*H*-1,2,3-triazole-4-carbohydrazide (11). ^{1}H NMR (ppm; Hz): 2.33 (s, 3H, Me), 7.07 (br t, 1H, H4 of thiophenyl), 7.36–7.42 (m, 5H, Ar), 7.51 (br, 1H, H3 of thiophenyl), 7.58 (br d, 1H, H5 of thiophenyl) 7.66 (d, 2H, *J* 8.8 Hz, Ar), 8.31 (d, 8.8 Hz, 2H, Ar), 10.80 (s, exch., 1H, NH). Anal. Calcd. for $C_{21}H_{16}N_6O_3S$ (432.46): C, 58.32; H, 3.73; N, 19.43. Found: C, 58.45; H, 3.87; N, 19.61%.

***N*′-[1-(1-(4-Methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)ethylidene]-1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole-4-carbohydrazide (12).** ^{1}H NMR (ppm; Hz): 2.47 (s, 3H, Me), 2.50 (s, 3H, Me), 3.82 (s, 3H, OMe), 7.12 (d, *J* 8.6 Hz, 2H, H3/H5 of Ar), 7.38–7.44 (m, 5H, Ph), 7.50 (d, *J* 8.6 Hz, 2H, H2/H6 of Ar), 7.65 (d, *J* 8.9 Hz, 2H, H2/H6 of Ar), 8.31 (d, *J* 8.9 Hz, 2H, H3/H5 of Ar), 10.84 (s, exch., 1H, NH). ^{13}C NMR (ppm): 10.8 (Me), 14.4 (Me), 56.1 (OMe), 115.3 (C3/C5 of Ar), 125.4 (C2/C6 of Ar), 125.6 (C3/C5 of Ar), 127.4 (C2/C6 of Ar), 127.5 (C2/C6 of Ph), 127.9 (C1 of Ar), 130.6 (C4 of Ph), 131.0 (C3/C5 of Ph), 131.2 (C1 of Ph), 134.0 (C5 of triazolyl), 139.4 (C4 of triazolyl), 139.9 (C5 of triazolyl), 140.8 (C5 of triazolyl), 142.3 (C1 of Ar), 148.2 (CH=N), 151.2 (C4 of Ar), 156.4 (C=O), 160.6 (C4 of Ar). Anal. Calcd. for $C_{27}H_{23}N_9O_4$ (537.54): C, 60.33; H, 4.31; N, 23.45. Found: C, 60.57; H, 4.61; N, 23.61%.

***N*′-[1-(1-(4-Fluorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl)ethylidene]-1-(4-nitrophenyl)-5-phenyl-1*H*-1,2,3-triazole-4-carbohydrazide (13).** ^{1}H NMR (ppm; Hz): 2.42 (s, 3H, Me), 2.47 (s, 3H, Me), 7.41–7.45 (m, 7H, Ar), 7.64–7.66 (m, 4H, Ar), 8.30 (d, *J* 8.6 Hz, 2H, H3/H5 of Ar), 10.85 (s, exch., 1H, NH). ^{13}C NMR (ppm): 10.9 (Me), 14.4 (Me), 117.2 (d, *J* 22.7 Hz, H3/H5 of Ar), 125.5 (C2/C6 of Ar), 125.6 (C1 of Ar), 127.4 (C3/C5 of Ar), 127.6

(C4 of Ph), 128.4 (d, *J* 8.3 Hz, C2/C6 of Ar)), 129.0 (C2/C6 of Ph), 130.6 (C1 of Ph), 131.0 (C3/C5 of Ph), 132.5 (C4 of triazolyl), 134.2 (C5 of triazolyl), 139.3 (C4 of triazolyl), 140.0 (C5 of triazolyl), 140.8 (C1 of Ar), 142.5 (C4 of Ar), 148.3 (CH=N), 156.6 (C=O), 162.0 (d, 245.6 Hz, C4 of Ar). Anal. Calcd. for $C_{26}H_{20}FN_9O_3$ (525.50): C, 59.43; H, 3.84; N, 23.99. Found: C, 59.60; H, 3.98; N, 24.10%.

Crystal structure determination. An Agilent SuperNova Dual Atlas diffractometer, equipped with mirror monochromated Cu or Mo radiation, was used to collect single-crystal x-ray diffraction data at RT. Solution and refinement of the crystal structures was by SHELXT[40] and SHELXL,[41] respectively. Non-hydrogen atoms were refined with anisotropic displacement parameters and idealized geometry was used for hydrogen atoms. The Uiso(H) were set to 1.2- or 1.5-times isotropic displacement values of the bonded atoms. The crystals of compounds **6** and **9** contain sites with disordered solvent molecules. One nitro group in **11** is disordered with two components of occupancy 0.55(2)/0.45(2) and the thiophene ring is disordered with two components of occupancy 0.81(1)/0.19(1). The nitrobenzene group in **12** is disordered with two components of occupancy 0.76(3)/0.24(3). Table 2 summarizes the crystal, data collection, and structure refinement information. The crystal structures have been assigned CCDC Numbers 2240731–2240736 in the Cambridge Structural Database.

Table 2. Crystal and structure refinement data of heterocycles **3**, **6**, **7**, **9**, **11** and **12**

	3	**6**	**7**	**9**	**11**	**12**
MF	$C_{22}H_{15}N_7O_3$	$C_{30}H_{32}ClFN_{10}O_5$	$C_{24}H_{18}BrClN_8O_3$	$C_{25}H_{22}ClN_7O_4$	$C_{42}H_{32}N_{12}O_6S_2$	$C_{27}H_{23}N_9O_4$
FW	425.41	667.10	581.82	519.94	864.91	537.54
T (K)	296(2)	293(2)	296(2)	293(2)	296(2)	293(2)
λ (Å)	1.54184	0.71073	0.71073	0.71073	0.71073	0.71073
System	Monoclinic	Triclinic	Monoclinic	Monoclinic	Triclinic	Monoclinic
Space group	$P2_1/c$	$P\bar{1}$	$P2_1/c$	$P2_1/n$	$P\bar{1}$	$P2_1/n$
a (Å)	10.4072(2)	11.1482(4)	8.7527(5)	7.7509(4)	9.5194(4)	19.6288(10)
b (Å)	21.4613(4)	11.9859(5)	12.1953(5)	15.5184(7)	11.1689(6)	6.5259(2)
c (Å)	18.2283(3)	12.7336(7)	23.6770(14)	21.2712(12)	21.6211(8)	20.7651(13)
α (°)	90.	102.064(4)	90	90	93.961(4)	90
β (°)	103.757(2)	92.876(4)	97.015(5)	94.173(5)	96.523(3)	108.008(6)
γ (°)	90.	96.725(3)	90	90	112.489(4)	90
V (Å^3)	3954.53(13)	1647.56(13)	2508.4(2)	2551.8(2)	2094.30(17)	2529.6(2)
Z	8	2	4	4	2	4
D (Mg/m^3)	1.429	1.345	1.54	1.353	1.372	1.411
Size (mm^3)	0.31 × 0.09 × 0.05	0.27 × 0.20 × 0.09	0.46 × 0.40 × 0.19	0.44 × 0.09 × 0.08	0.36 × 0.32 × 0.19	0.42 × 0.22 × 0.05
Refractions	29716	14664	21627	25556	20227	24895
Ind. refs	7791	7797	6242	6273	9967	6388
Goodness-of-fit	1.018	1.035	1.042	1.033	1.044	1.098
R1 [I>2σ(I)]	0.0474	0.0866	0.0579	0.0543	0.0614	0.0602
wR2 [I>2σ(I)]	0.1265	0.2168	0.1353	0.1308	0.1459	0.1276
Largest diff. peak and hole (e.Å^{-3})	0.176 and –0.236	0.838 and –0.479	0.729 and –0.743	0.201 and –0.340	0.405 and –0.328	0.216 and –0.184

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Supplementary Material

The Supporting Information is available free of charge and contains NMR spectra of the synthesized heterocycles.

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