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A multi-component synthesis of 3-aryl-1-(arylmethylideneamino) pyrrolidine-2,5-diones

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ABSTRACT

A multi-component synthesis of 3-aryl-1-(arylmethylideneamino)pyrrolidine-2,5-diones is described. A mixture of *N*-isocyaniminotriphenylphosphorane, an aldehyde, and Meldrum's acid undergo a 1:2:1 addition reaction under mild conditions to afford the title compounds in good to excellent yields.

1. Introduction

Multi-component reactions (MCRs) have become a significant part of today's arsenal of methods in combinatorial chemistry due to their valued features, such as atom economy, straightforward reaction design, and the opportunity to construct target compounds by the introduction of several diversity elements in a single chemical event. Typically, purification of products resulting from MCRs is also simple since all the organic reagents employed are consumed and are incorporated into the target compound.[1] MCRs, leading to interesting heterocyclic scaffolds, are particularly useful for the construction of diverse chemical libraries of 'drug-like' molecules. The isocyanide-based MCRs are especially important in this area.[1d,e]

Succinimides (pyrrolidine-2,5-diones) are an important class of heterocyclic compounds with numerous applications in different fields.[2] In medicine, they have been used for the treatment of arthritis, tuberculosis, convulsion, and epilepsy. They are considered as bioisosteres of hydantoins,[3] a heterocycle widely exploited in the synthesis of combinatorial libraries.[4,5] In organic synthesis they have been used as valuable reagents and intermediates for the synthesis of natural and non-natural compounds.[6] Recently, succinimide-based pseudopeptides have been shown to stabilize β-turn conformations.[7] It has also been shown that they can be used as irreversible protease inhibitors.[8] The bioactive natural product andrimid (Fig. 1) was found to exhibit potent in vitro antibacterial activity against methicillin resistant *Staphylococcus aureus* and a range of other antibiotic resistant human pathogens.[9,10] The cytotoxic labdane alkaloid haterumaimide A (Fig. 1) has been used as a protein synthesis inhibitor[11] and antitumor drug.[12]

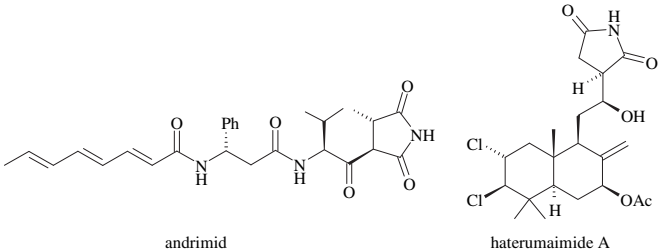

Figure 1. Examples of succinimide subunit containing natural products.

There are several reports on the use of *N*-isocyanimino triphenylphosphorane **1** in the synthesis of metal complexes.[13,14] However, applications of **1** in organic synthesis are rare. Recently, a synthesis of 1,3,4-oxadiazepines via a three-component reaction between **1**, dialkyl acetylenedicarboxylates, and 1,3-diphenyl-1,3-propanedione[15] and a synthesis of 2-aryl-1,3,4-oxadiazoles

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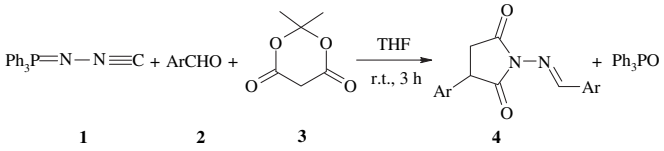
from **1** and benzoic acids[16] were reported. Very recently, we have described a new synthesis of 2-aryl-5-hydroxyalkyl-1,3,4-oxadiazoles via a three-component reaction between **1**, aldehydes, and carboxylic acids.[17]

2. Results and discussion

Due to the unique properties of succinimides, the development of synthetic methods, which enable facile access to these useful entities are desirable. As part of our current studies on the development of efficient methods for the preparation of biologically active heterocyclic compounds,[18] herein we describe a novel, one-pot, and multi-component synthesis of 3-aryl-1-(arylmethylideneamino)pyrrolidine-2,5-diones. Thus a mixture of *N*-isocyaniminotriphenylphosphorane **1**, an aldehyde **2**, and Meldrum's acid **3** undergo a 1:2:1 addition reaction in THF at ambient temperature to afford the corresponding 3-aryl-1-(arylmethylideneamino)pyrrolidine-2,5-diones **4a–j** in 81–92% yields (Scheme 1, Table 1). All the reactions went to completion within 3 h. ^{1}H NMR spectroscopic analysis of the reaction mixtures clearly indicated formation of the corresponding pyrrolidine-2,5-diones **4** in good to excellent yields.



Scheme 1. One-pot synthesis of 3-aryl-1-(arylmethylideneamino)-pyrrolidine-2,5-diones **4a–j**.

Table 1
Synthesis of 3-aryl-1-(arylmethylidene amino)-pyrrolidine-2,5-diones **4a–j**

4	Ar	Yield[a] (%)
a	4-$O_2NC_6H_4$	92
b	C_6H_5	90
c	4-BrC_6H_4	91
d	4-ClC_6H_4	92
e	4-$CH_3C_6H_4$	89
f	3-$CH_3OC_6H_4$	81
g	3-FC_6H_4	83
h	4-FC_6H_4	91
i	2-Furyl	86
j	2-Thienyl	88

[a] Isolated yield.

The structures of the isolated products **4a–j** were deduced on the basis of IR, ^{1}H and, ^{13}C NMR spectroscopy, mass spectrometry, and elemental analysis. The mass spectrum of **4a** displayed the molecular ion (M^+) peak at m/z=368, which was consistent with the product structure. The ^{1}H NMR spectrum of **4a** exhibited a sharp singlet at δ=9.36 ppm due to the aldimine H atom. An *ABX* system ($CH_AH_BCH_X$) was observed for the two diastereotopic H atoms of the methylene group (δ_A=3.02 ppm, dd, ^2J=17.9 Hz, ^3J=5.8 Hz; δ_B=3.34 ppm, dd, ^2J=17.9 Hz, ^3J=9.5 Hz) and the adjacent methine H atom (δ_X=4.55 ppm, dd, ^3J=5.8 Hz, ^3J=9.5 Hz). The characteristic signals for the eight H atoms of the two aryl substituents were seen with appropriate chemical shifts and coupling constants. The ^{1}H decoupled ^{13}C NMR spectrum of **4a** showed characteristic signals at δ=35.0 ppm (due to CH_2), 43.8 ppm (arising from CH), 159.3 ppm (for the aldimine, N=CH) as well as two deshielded resonances at δ=171.7 and 173.0 ppm (due to the two carbonyl groups) along with other eight distinct resonances for the two aryl substituents in agreement with the proposed structure. Partial assignments of these resonances are given in the Experimental section.

Single-crystal X-ray analysis of **4c** conclusively confirmed its structure, and by analogy those of **4a**,**b**,**d–j**. An ORTEP diagram of **4c** is shown in Figure 2.[19]

A plausible mechanism for the formation of the pyrrolidine-2,5-diones **4** is provided in Scheme 2. On the basis of the chemistry of isocyanides,[1d,e,20–22] it is reasonable to assume that the 5-arylmethylidene Meldrum's acid **5** formed from the initial condensation of the aldehyde **2** and Meldrum's acid **3** could undergo nucleophilic attack of *N*-isocyaniminotriphenylphosphorane **1** leading to the intermediate **6** by removal of an acetone molecule. Then, this intermediate may be attacked by a water molecule to form adduct **7**, which may undergo intramolecular addition of nitrogen atom to the adjacent ketene moiety to produce the *N*-iminotriphenylphosphorane pyrrolidine-2,5-dione intermediate **8**. Aza Wittig reaction of this intermediate with another aldehyde molecule would afford the isolated 3-aryl-1-(arylmethylideneamino)-pyrrolidine-2,5-dione **4** by removal of a triphenylphosphine oxide molecule and decarboxylation.

3. Conclusion

In conclusion, we have developed a one-pot and multi-component reaction between *N*-isocyaniminotriphenylphosphorane, aldehydes, and Meldrum's acid for the preparation of 3-aryl-1-(arylmethylideneamino)pyrrolidine-2,5-diones, which are of potential chemical, synthetic and pharmacological interest. Good to excellent yields of the products and mild reaction conditions are the main advantages of this method.

4. Experimental

4.1. General

All the reagents and solvents were obtained from Merck (Germany) and were used without further purification. *N*-Isocyaniminotriphenylphosphorane **1** was prepared according to the literature procedure.[13] Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H, and N were

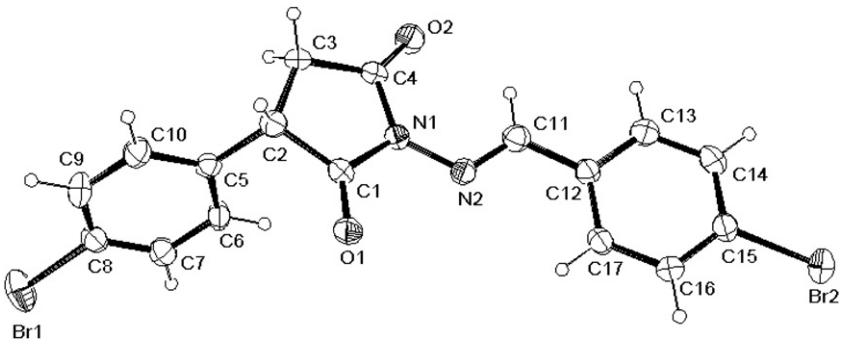
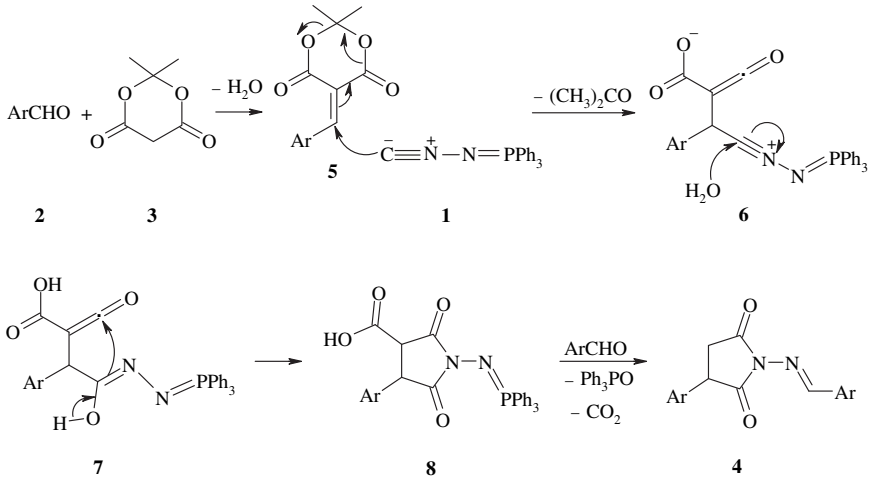


Figure 2. ORTEP diagram of the molecular structure of **4c**.



Scheme 2. Proposed mechanism for the reaction.

performed using a Heraeus CHN-O-Rapid analyzer. Mass spectrometry was performed on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 20 eV. ^{1}H NMR and ^{13}C NMR spectra (DMSO-d_6 solution) were recorded using a Bruker DRX-500 AVANCE spectrometer at 500.1 and 125.8 MHz, respectively. Infrared spectra were recorded on a Shimadzu IR-460 spectrometer. X-ray crystallography was performed on a Bruker SMART diffractometer equipped with a CCD area detector with graphite monochromatized Mo Kα radiation. Chromatography columns were prepared from Merck silica gel 60 mesh.

4.2. General procedure

A mixture of *N*-isocyaniminotriphenylphosphorane (0.5 mmol) and the appropriate aldehyde (1 mmol) was dissolved in hot THF (5 mL). Then, Meldrum's acid (0.5 mmol) was added to the reaction mixture, which was stirred at ambient temperature for 3 h. Then, the solvent was removed under the reduced pressure and the residue was purified by column chromatography using *n*-hexane–EtOAc (4:1) as eluent. The solvent was removed, and the product was obtained as colorless crystals.

*4.2.1. 1-(4-Nitrobenzylideneamino)-3-(4-nitrophenyl)pyrrolidine-2,5-dione (**4a**).* Colorless crystals, mp 275 °C, yield: 0.17 g, 92%. IR (KBr) (ν_{max}/cm^{-1}): 1712, 1596, 1511, 1334, 1179, 1104, 1046, 965, 845, 737, 692. MS, *m*/*z* (%): 368 (M$^+$, <1), 220 (13), 178 (13), 165 (5), 152 (15), 151 (100), 150 (87), 119 (9), 105 (23), 104 (20), 92 (12), 77 (63), 65 (13), 51 (42). Anal. Calcd for $C_{17}H_{12}N_4O_6$ (368.30): C, 55.44; H, 3.28; N, 15.21. Found: C, 55.4; H, 3.4; N, 15.1%. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ 3.02 (1H, dd, *J*=5.8, 17.9 Hz, CH), 3.34 (1H, dd, *J*=9.5, 17.9 Hz, CH), 4.55 (1H, dd, *J*=5.8, 9.5 Hz, CH), 7.75 (2H, d, *J*=8.8 Hz, 2CH), 8.14 (2H, d, *J*=8.8 Hz, 2CH), 8.23 (2H, d, *J*=8.8 Hz, 2CH), 8.34 (2H, d, *J*=8.8 Hz, 2CH), 9.36 (1H, s, CH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 35.0 (CH_2), 43.8 (CH), 123.7, 124.2, 129.3, and 129.9 (4CH), 138.9, 144.9, 146.9, and 149.3 (4C), 159.3 (CH), 171.7, and 173.0 (2C=O).

*4.2.2. 1-(Benzylideneamino)-3-phenylpyrrolidine-2,5-dione (**4b**).* Colorless crystals, mp 158–159 °C, yield: 0.12 g, 90%. IR (KBr) (ν_{max}/cm^{-1}): 1703, 1602, 1570, 1492, 1450, 1378, 1319, 1162, 1072, 1033, 975, 943, 912, 753, 691. MS, *m*/*z* (%): 278 (M$^+$, 2), 227 (9), 192 (3), 175 (18), 167 (7), 149 (17), 104 (100), 90 (16), 77 (13), 70 (3), 63 (4). Anal. Calcd for $C_{17}H_{14}N_2O_2$ (278.31): C, 73.37; H, 5.07; N, 10.07. Found: C, 73.3; H, 5.0; N, 9.8%. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ 2.89 (1H, dd, *J*=5.3, 17.9 Hz, CH), 3.29 (1H, dd, *J*=9.5, 17.9 Hz, CH), 4.28 (1H, dd, *J*=5.3, 9.5 Hz, CH), 7.32 (1H, dd, *J*=6.4, 6.5 Hz, CH), 7.36–7.43 (4H, m, 4CH), 7.51–7.60 (3H, m, 3CH), 7.87 (2H, d, *J*=7.0 Hz, 2CH), 9.04 (1H, s, CH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 35.5 (CH_2), 44.1 (CH), 127.5, 128.2, 128.3, 128.7, 129.1, and 132.3 (6CH), 132.8, and 137.7 (2C), 163.6 (CH), 172.1, and 173.8 (2C=O).

*4.2.3. 1-(4-Bromobenzylideneamino)-3-(4-bromophenyl)pyrrolidine-2,5-dione (**4c**).* Colorless crystals, mp 208–209 °C, yield: 0.20 g, 91%. IR (KBr) (ν_{max}/cm^{-1}): 1701, 1582, 1480, 1375, 1320, 1224, 1170, 1059, 1002, 945, 858, 817, 721, 658. MS, *m*/*z* (%): 438 (M$^+$ ^{81}Br$_2$, 1), 436 (M$^+$ ^{81}Br^{79}Br, 2), 434 (M$^+$ ^{79}Br$_2$, 1), 312 (6), 254 (35), 226 (25), 210 (21), 182 (67), 173 (100), 145 (13), 129 (12), 101 (39), 89 (23), 75 (28). Anal. Calcd for $C_{17}H_{12}Br_2N_2O_2$ (436.10): C, 46.82; H, 2.77; N, 6.42. Found: C, 46.8; H, 2.8; N, 6.4%. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ 2.90 (1H, dd, *J*=5.5, 17.9 Hz, CH), 3.27 (1H, dd, *J*=9.5, 17.9 Hz, CH), 4.30 (1H, dd, *J*=5.5, 9.5 Hz, CH), 7.38 (2H, d, *J*=8.4 Hz, 2CH), 7.56 (2H, d, *J*=8.4 Hz, 2CH), 7.73 (2H, d, *J*=8.4 Hz, 2CH), 7.81 (2H, d, *J*=8.4 Hz, 2CH), 9.36 (1H, s, CH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 35.2 (CH_2), 43.5 (CH), 120.7, and 125.8 (2C), 130.1, 130.5, and 131.5 (3CH), 132.1 (C), 132.2 (CH), 136.9 (C), 161.7 (CH), 171.9, and 173.4 (2C=O).

*4.2.4. 1-(4-Chlorobenzylideneamino)-3-(4-chlorophenyl)pyrrolidine-2,5-dione (**4d**).* Colorless crystals, mp 201 °C, yield: 0.16 g, 92%. IR (KBr) (ν_{max}/cm^{-1}): 1708, 1586, 1560, 1490, 1378, 1329, 1233, 1178, 1167, 1088, 1069, 1049, 1012, 975, 947, 827. MS, *m*/*z* (%): 347 (M$^+$, <1), 322 (27), 279 (19), 266 (66), 238 (13), 220 (12), 205 (15), 167 (40), 149 (100), 138 (33), 122 (39), 97 (19), 83 (27), 69 (53). Anal. Calcd for $C_{17}H_{12}Cl_2N_2O_2$ (347.20): C, 58.81; H, 3.48; N, 8.07. Found: C, 58.7; H, 3.6; N, 7.9%. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ 2.90 (1H, dd, *J*=5.5, 17.9 Hz, CH), 3.27 (1H, dd, *J*=9.5, 17.9 Hz, CH), 4.32 (1H, dd, *J*=5.5, 9.5 Hz, CH), 7.41–7.48 (4H, m, 4CH), 7.59 (2H, d, *J*=8.5 Hz, 2CH), 7.89 (2H, d, *J*=8.5 Hz, 2CH), 9.09 (1H, s, CH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 35.2 (CH_2), 43.4 (CH), 128.6, 129.2, 129.9, and 130.2 (4CH), 131.7, 132.2, 136.4, and 136.8 (4C), 161.6 (CH), 171.9, and 173.5 (2C=O).

*4.2.5. 1-(4-Methylbenzylideneamino)-3-(4-methylphenyl)pyrrolidine-2,5-dione (**4e**).* Colorless crystals, mp 175–176 °C, yield: 0.13 g, 89%. IR (KBr) (ν_{max}/cm^{-1}): 1704, 1599, 1564, 1512, 1376, 1325, 1167, 1062, 977, 944, 811, 700. MS, *m*/*z* (%): 306 (M$^+$, 9), 279 (8), 189 (27), 167 (18), 149 (45), 118 (100), 105 (18), 91 (16), 78 (12). Anal. Calcd for $C_{19}H_{18}N_2O_2$ (306.36): C, 47.05; H, 5.92; N, 9.14. Found: C, 46.9; H, 6.0; N, 9.1%. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ 2.29 and 2.37 (6H, 2s, 2CH_3), 2.83 (1H, dd, *J*=5.2, 17.9 Hz, CH),

3.26 (1H, dd, J=9.4, 17.9 Hz, CH), 4.21 (1H, dd, J=5.2, 9.4 Hz, CH), 7.17 (2H, d, J=7.9 Hz, 2CH), 7.26 (2H, d, J=8.0 Hz, 2CH), 7.33 (2H, d, J=7.9 Hz, 2CH), 7.75 (2H, d, J=8.0 Hz, 2CH), 8.94 (1H, s, CH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 20. 6 and 21.1 ($2CH_3$), 35.5 (CH_2), 43.7 (CH), 127.9, 128.3, 129.2, and 129.6 (4CH), 130.1, 134.7, 136.6, and 142.4 (4C), 163.6 (CH), 172.1, and 173.9 (2C=O).

*4.2.6. 1-(3-Methoxybenzylideneamino)-3-(3-methoxyphenyl)pyrrolidine-2,5-dione (**4f**).* Colorless crystals, mp 172 °C, yield: 0.13 g, 81%. IR (KBr) (ν_{max}/cm^{-1}): 1701, 1595, 1492, 1455, 1382, 1321, 1251, 1174, 1092, 1033, 970, 882, 782, 689. MS, m/z (%): 338 (M^+, 6), 279 (18), 205 (18), 167 (39), 149 (100), 134 (31), 122 (9), 113 (9), 104 (11), 91 (11), 71 (18). Anal. Calcd for $C_{19}H_{18}N_2O_4$ (338.36): C, 67.44; H, 5.36; N, 8.28. Found: C, 67.6; H, 5.5; N, 8.1%. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ 2.89 (1H, dd, J=5.3, 17.9 Hz, CH), 3.27 (1H, dd, J=9.5, 17.9 Hz, CH), 3.76 and 3.81 (6H, 2s, $2OCH_3$), 4.25 (1H, dd, J=5.3, 9.5 Hz, CH), 6.88 (1H, dd, J=2.2, 8.0 Hz, CH), 6.94 (1H, d, J=7.6 Hz, CH), 6.98 (1H, d, J=1.9 Hz, CH), 7.14–7.16 (1H, m, CH), 7.28 (1H, t, J=7.9 Hz, CH), 7.42 (1H, d, J=2.2 Hz, CH), 7.44 (2H, d, J=5.0 Hz, 2CH), 9.00 (1H, s, CH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 35.5 (CH_2), 44.1 (CH), 55.1, and 55.2 ($2OCH_3$), 112.3, 113.0, 113.9, 118.4, 120.3, 121.1, 129.7, and 130.2 (8CH), 134.2, 139.1, 159.5, and 159.6 (4C), 163.3 (CH), 172.1, and 173.7 (2C=O).

*4.2.7. 1-(3-Flurobenzylideneamino)-3-(3-fluophenyl)pyrrolidine-2,5-dione (**4g**).* Colorless crystals, mp 143 °C, yield: 0.13 g, 83%. IR (KBr) (ν_{max}/cm^{-1}): 1702, 1581, 1487, 1445, 1377, 1310, 1250, 1148, 1071, 976, 899, 866, 780, 688. MS, m/z (%): 314 (M^+, 3), 193 (27), 167 (8), 149 (24), 122 (100), 108 (23), 96 (15), 75 (9), 69 (8). Anal. Calcd for $C_{17}H_{12}F_2N_2O_2$ (314.29): C, 64.97; H, 3.85; N, 8.91. Found: C, 65.0; H, 3.8; N, 8.9%. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ 2.93 (1H, dd, J=5.6, 17.9 Hz, CH), 3.28 (1H, dd, J=9.5, 17.9 Hz, CH), 4.35 (1H, dd, J=5.6, 9.5 Hz, CH), 7.15 (1H, ddd, J=2.1, 8.4, 8.8 Hz, CH), 7.25 (1H, d, J=7.7 Hz, CH), 7.34 (1H, ddd, J=1.8, 2.1, 10.2 Hz, CH), 7.39–7.44 (2H, m, 2CH), 7.58 (1H, ddd, J=2.0, 6.0, 8.0 Hz, CH), 7.66–7.69 (1H, m, CH), 7.72 (1H, d, J=7.7 Hz, CH), 9.13 (1H, s, CH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 35.1 (CH_2), 43.7 (d, $^4J_{FC}$=1.2 Hz, CH), 114.1 (d, $^2J_{FC}$=22.6 Hz, CH), 114.3 (d, $^2J_{FC}$=21.0 Hz, CH), 115.1 (d, $^2J_{FC}$=22.2 Hz, CH), 119.0 (d, $^2J_{FC}$=21.3 Hz, CH), 124.6 (d, $^4J_{FC}$=1.2 Hz, CH), 124.7 (d, $^4J_{FC}$=2.6 Hz, CH), 130.5 (d, $^3J_{FC}$=8.4 Hz, CH), 131.2 (d, $^3J_{FC}$=8.0 Hz, CH), 135.3 (d, $^3J_{FC}$=7.9 Hz, C), 140.1 (d, $^3J_{FC}$=7.8 Hz, C), 161.4 (d, $^4J_{FC}$=2.7 Hz, CH), 162.2 (d, $^1J_{FC}$=243.7 Hz, C), 162.3 (d, $^1J_{FC}$=245.1 Hz, C), 171.8, and 173.3 (2C=O).

*4.2.8. 1-(4-Flurobenzylideneamino)-3-(4-fluophenyl)pyrrolidine-2,5-dione (**4h**).* Colorless crystals, mp 135 °C, yield: 0.14 g, 91%. IR (KBr) (ν_{max}/cm^{-1}): 1703, 1596, 1504, 1376, 1314, 1225, 1152, 1017, 943, 835, 702. MS, m/z (%): 314 (M^+, 4), 279 (7), 193 (13), 167 (14), 149 (39), 122 (100), 108 (21), 96 (7), 69 (14). Anal. Calcd for $C_{17}H_{12}F_2N_2O_2$ (314.29): C, 64.97; H, 3.85; N, 8.91. Found: C, 65.1; H, 3.9; N, 8.7%. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ 2.88 (1H, dd, J=5.5, 17.9 Hz, CH), 3.27 (1H, dd, J=9.5, 17.9 Hz, CH), 4.31 (1H, dd, J=5.5, 9.5 Hz, CH), 7.19 (2H, dd, $^3J_{FH}$=8.8 Hz, $^3J_{HH}$=8.8 Hz, 2CH), 7.37 (2H, dd, $^3J_{FH}$=8.8 Hz, $^3J_{HH}$=8.8 Hz, 2CH), 7.45 (2H, dd, $^4J_{FH}$=5.5 Hz, $^3J_{HH}$=8.8 Hz, 2CH), 7.94 (2H, dd, $^4J_{FH}$=5.6 Hz, $^3J_{HH}$=8.8 Hz, 2CH), 9.04 (1H, s, CH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 35.4 (CH_2), 43.3 (CH), 115.4 (d, $^2J_{FC}$=21.6 Hz, CH), 116.2 (d, $^2J_{FC}$=22.1 Hz, CH), 129.4 (d, $^4J_{FC}$=2.8 Hz, C), 130.2 (d, $^3J_{FC}$=8.3 Hz, CH), 130.7 (d, $^3J_{FC}$=9.0 Hz, CH), 133.7 (d, $^4J_{FC}$=2.9 Hz, C), 161.5 (d, $^1J_{FC}$=243.7 Hz, C), 162.2 (CH), 164.4 (d, $^1J_{FC}$=250.5 Hz, C), 171.9, and 173.7 (2C=O).

*4.2.9. 1-((Furan-2-yl)methyleneamino)-3-(furan-2-yl)pyrrolidine-2,5-dione (**4i**).* Colorless crystals, mp 139 °C, yield: 0.11 g, 86%. IR (KBr) (ν_{max}/cm^{-1}): 1722, 1595, 1468, 1388, 1353, 1293, 1161, 1968, 1008, 936, 885, 820, 756, 678. MS, m/z (%): 258 (M^+, 42), 165 (19), 149 (23), 94 (100), 81 (10), 71 (7), 66 (19). Anal. Calcd for $C_{13}H_{10}N_2O_4$ (258.23): C, 60.47; H, 3.90; N, 10.85. Found: C, 60.5; H, 3.9; N, 10.8%. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ 2.93 (1H, dd, J=5.3, 17.8 Hz, CH), 3.19 (1H, dd, J=9.5, 17.8 Hz, CH), 4.42 (1H, dd, J=5.3, 9.5 Hz, CH), 6.45 (1H, dd, J=2.1, 2.3 Hz, CH), 6.49 (1H, d, J=3.1 Hz, CH), 6.73 (1H, dd, J=1.0, 1.8 Hz, CH), 7.25 (1H, d, J=3.4 Hz, CH), 7.64 (1H, dd, J=0.6, 0.8 Hz, CH), 8.01 (1H, s, CH), 8.87 (1H, s, CH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 32.8 (CH_2), 38.1 (CH), 108.1, 110.7, 112.7, 119.3, 143.0, and 147.5 (6CH), 148.9, and 149.4 (2C), 151.5 (CH), 171.4, and 171.7 (2C=O).

*4.2.10. 1-((Thiophen-2-yl)methyleneamino)-3-(thiophen-2-yl)pyrrolidine-2,5-dione (**4j**).* Colorless crystals, mp 135–136 °C, yield: 0.12 g, 88%. IR (KBr) (ν_{max}/cm^{-1}): 1700, 1592, 1426, 1381, 1340, 1183, 1091, 1043, 977, 928, 701. MS, m/z (%): 290 (M^+, 20), 181 (22), 167 (20), 149 (57), 138 (16), 110 (100), 96 (19), 69 (31). Anal. Calcd for $C_{13}H_{10}N_2O_2S_2$ (290.36): C, 53.77; H, 3.47; N, 9.64. Found: C, 53.5; H, 3.7; N, 9.5%. ^{1}H NMR (500.1 MHz, DMSO-d_6): δ 3.00 (1H, dd, J=5.5, 17.8 Hz, CH), 3.32 (1H, dd, J=9.3, 17.8 Hz, CH), 4.55 (1H, dd, J=5.5, 9.3 Hz, CH), 7.03 (1H, dd, J=4.7, 5.0 Hz, CH), 7.15 (1H, d, J=3.2 Hz, CH), 7.23 (1H, dd, J=3.8, 4.7 Hz, CH), 7.49 (1H, d, J=5.1 Hz, CH), 7.74 (1H, d, J=3.6 Hz, CH), 7.88 (1H, d, J=5.0 Hz, CH), 9.17 (1H, s, CH). ^{13}C NMR (125.8 MHz, DMSO-d_6): δ 35.5 (CH_2), 39.2 (CH), 125.7, 126.0, 127.0, 128.3, 132.2, and 135.3 (6CH), 137.1, and 138.6 (2C), 157.7 (CH), 171.5, and 172.5 (2C=O).

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19. Selected X-ray crystallographic data for compound **4c**: $C_{17}H_{12}N_2O_2Br_2$, triclinic, space group=P-1, a=5.6060(12) Å, b=8.6946(19) Å, c=16.922(4) Å, α=100.217(3)°, β=92.498(3)°, γ=91.331(3)°, V=810.6(3) Å^3, T=295(2) K, Z=2, D_{calcd}=1.787 g cm^{-3}, μ=5.01 mm^{-1}, 1865 observed reflections, final R_1=0.045, wR_2=0.108 and for all data R_1=0.082, wR_2=0.126. CCDC 746984 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.
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