Highly Stereoselective Synthesis of Cyclopropyl Heterocycles *via* Cyclopropanation of Olefin with Arsonium Salt

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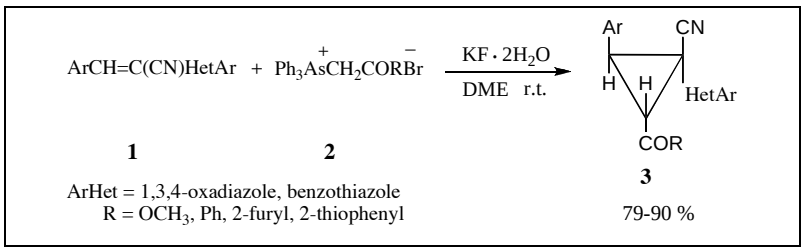

An efficient and highly stereoselective approach for the preparation of highly functionalized cyclopropyl heterocycles *via* the cyclopropanation of olefines with arsonium salts in the presence of $KF{\cdot}2H_2O$ has been developed.

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INTRODUCTION

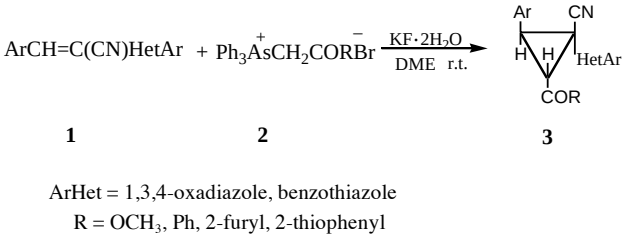
Cyclopropyl heterocyclic compounds now occupy an important place in bioorganic and pharmaceutical research due to their biological properties [1], natural occurrence [2] and synthetic utility [3]. Moreover, the introduction of cyclopropyl group into pharmaceuticals has proved to be a very efficient strategy for the improvement and enhancement of their biological activity [4]. These results stimulated synthetic chemists to develop new and efficient methods for synthesis of cyclopropyl heterocycles in order to test their biological activity [5].

In general, the most efficient methods for preparing the cyclopropyl heterocycles are (1) halomethylmetal-mediated cyclopropanation, (2) transition metal-catalyzed decomposition of diazoalkanes and (3) Michael-initiated ring closure [6]. Although these methods are efficient for the synthesis of cyclopropyl heterocyclic compounds, they are often not highly stereoselective, therefore, a mixture of *cis*/*trans* isomers is generally obtained [7-9]. Thus a new efficient and stereoselective approach is still strongly required.

In recent years, the concept of privileged structure, repeatedly occurring in biologically active molecules, has become important for the design and synthesis of drug candidates. The 1,3,4-oxadiazole [10] and benzothiazole [11] have been employed as a core structural feature of many drug candidates due to their wide range of biological activity. And cyclopropanes, bearing the appropriate functional groups, have been widely used for biological and pharmaceutical studies.

Based on the facts mentioned above, we hope to construct the cyclopropanes possessing carbonyl, cyano, aryl and heteroaryl groups in order to test their biological and pharmaceutical activities. To our knowledge, relatively little attention has been paid to the stereoselective synthesis of tetra-substituted cyclopropane, so it is a significant subject. Here we report an approach for highly stereoselective synthesis of functionalized cyclopropyl heterocycles from olefins and arsonium salts in the presence of $KF{\cdot}2H_2O$. (Scheme 1)

Scheme 1



The needed olefins incorporating the heterocyclic ring system are easily prepared *via* Knoevenagel condensation of aryl aldehydes with active methylene compounds possessing heteroaryl and cyano groups. The common way of generating arsonium ylide is the deprotonation of arsonium salt with a suitable base [12]. We first test some inorganic bases, such as K_2CO_3, $NaHCO_3$, $KF{\cdot}2H_2O$ [13]. In model experiment, a mixture of olefin **1a** (1 equiv), arsonium salt **2a** (1 equiv) and base (3 equiv) in dimethoxyethane (DME) was stirred at room temperature. The results showed that $KF{\cdot}2H_2O$ as base provided the best yield (Table 1 entry 2). Further, the screening for a suitable solvent was performed in the presence of $KF{\cdot}2H_2O$ at room temperature. It was found that DME was the best solvent for this reaction (Table 1 entry 5).

Table 1

The results of the optimization of base and solvent

entry	Base	Solvent	Time (h)	Yield (%)	entry	Base	Solvent	Time (h)	Yield (%)
1	K_2CO_3	DME	24	69	4	$KF{\cdot}2H_2O$	THF	24	77
2	$KF{\cdot}2H_2O$	DME	24	88	5	$KF{\cdot}2H_2O$	$CHCl_3$	24	86
3	$NaHCO_3$	DME	24	78					

To determine the generality of this approach, a variety of olefins and arsonium salts were employed in the reaction under the optimized condition. In all case, the cyclopropanation reactions proceeded smoothly to afford the desired cyclopropyl heterocyclic compounds with high stereoselectivity in high to excellent yields. The results are summarized in Table 2.

The structures of cyclopropyl heterocycles (**3a-s**) were confirmed by ^{1}H NMR, MS, IR, elemental analysis and X-ray (**3a** and **3h**).

A plausible mechanism for this process may involve following key steps (Scheme 2).

(1) The arsonium ylide **A** is formed from arsonium salt with $KF{\cdot}2H_2O$ used as base. (2) The arsonium ylide **A** nucleophilically attacks the olefin **B** to provide two of intermediates **D** or **E**. Apparently the **E** should be favored over the **D**, due to the steric repulsion between bulky COR and Ar groups in the conformation of **D**. (3) The intramolecular ring closure *via* intermediate E takes place to afford the cyclopropane **F**.

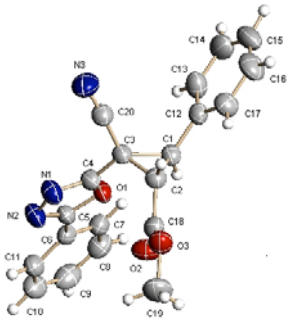


Figure. 1 X-ray structure of compound **3a**.

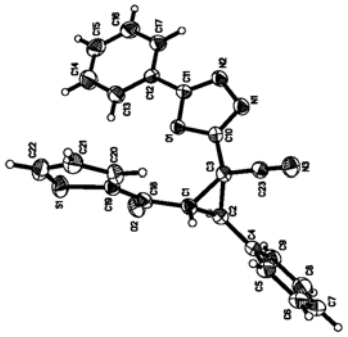
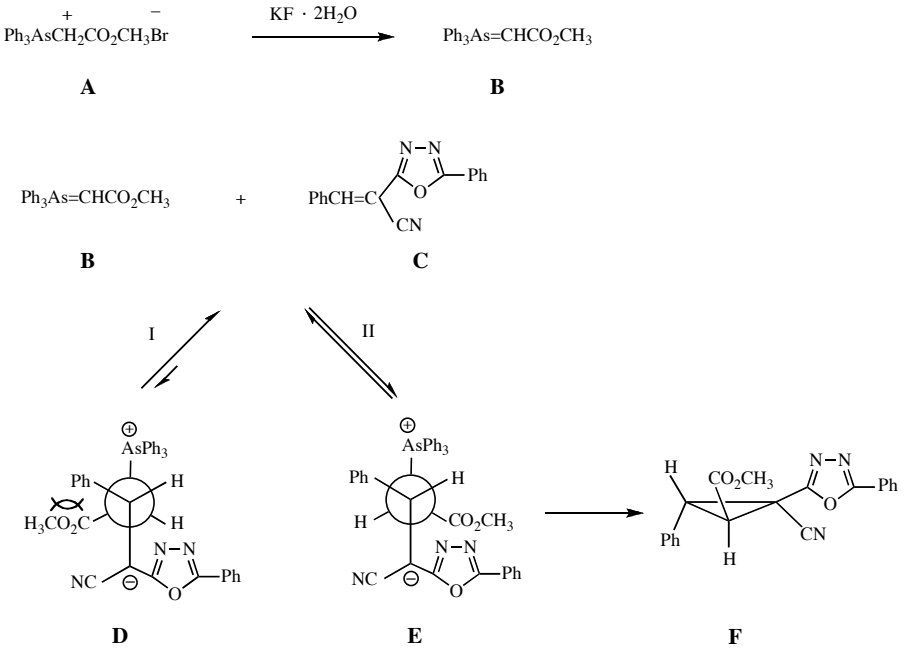


Figure 2. X-ray structure of compound **3h**.

Scheme 2



According to the present mechanism, in the structure of product **F** the COR and heteroaryl groups are situated on the same side of the ring. It is obvious that the repulsion interaction of these groups becomes serious and is unfavorable for the construction of the structure of cyclopropane **F** when R is a bulky heteroaryl (furan or thiophene) or phenyl group. It is unclear whether this steric hindrance results in a different configuration of cyclopropane. The determination of their structures is useful for understanding the reaction pathway. The structure of product **3h** was determined by X-ray analysis. The result showed that the configuration of **3h** (Fig. 2) was the same as that of **3a** (Fig. 1). It clearly demonstrated that the stereoselectivity of the reactions was general. In addition, it confirmed that the intermediate E played crucial role for stereoselectively controlling pathway.

In summary, we have developed an approach for the synthesis of highly functionalized cyclopropyl heterocycles from olefins and arsonium salts in the presence of $KF{\cdot}2H_2O$. Its advantages are mild reaction, high yield and stereoselectivity.

Table 2

Synthesis of Heterosubstituted Cyclopropanes

entry	product	Heterosubstituted	Ar	R	Time (h)	Yield %[a]
1	**3a**	oxadiazole	C_6H_5	OCH_3	24	88
2	**3b**	oxadiazole	*p*-ClC_6H_4	OCH_3	24	90
3	**3c**	oxadiazole	*p*-$CH_3OC_6H_4$	OCH_3	24	86
4	**3d**	oxadiazole	*p*-$NO_2C_6H_4$	OCH_3	24	81
5	**3e**	oxadiazole	*o*-ClC_6H_4	OCH_3	24	83
6	**3f**	oxadiazole	C_6H_5	Ph	24	87
7	**3g**	oxadiazole	*p*-$NO_2C_6H_4$	Ph	24	79
8	**3h**	oxadiazole	C_6H_5	2-furyl	24	87
9	**3i**	oxadiazole	C_6H_5	2-thiophenyl	24	83
10	**3j**	benzothiazole	C_6H_5	Ph	24	88
11	**3k**	benzothiazole	*p*-ClC_6H_4	Ph	24	89
12	**3l**	benzothiazole	*p*-$CH_3OC_6H_4$	Ph	24	76
13	**3m**	benzothiazole	*p*-$CH_3C_6H_4$	Ph	24	84
14	**3n**	benzothiazole	*m*-$NO_2C_6H_4$	Ph	24	81
15	**3o**	benzothiazole	*o*-ClC_6H_4	Ph	24	80
16	**3p**	benzothiazole	*m*-ClC_6H_4	Ph	24	87
17	**3q**	benzothiazole	C_6H_5	2-furyl	24	86
18	**3r**	benzothiazole	*p*-ClC_6H_4	2-furyl	24	90
19	**3s**	benzothiazole	*p*-ClC_6H_4	2-thiophenyl	24	87

[a] Isolated yield

Table 3

Selected bond lengths and bond angels for compounds **3a** and **3h**

Compound **3a**	Lengths (A)	Angels (deg)	Compound **3h**	Lengths (A)	Angels (deg)
C(1)-C(2)	1.488 (2)		C(1)-C(2)	1.480 (3)	
C(1)-C(12)	1.495 (2)		C(1)-C(18)	1.519 (3)	
C(1)-C(3)	1.5189 (18)		C(1)-C(3)	1.535 (3)	
C(2)-C(18)	1.487 (2)		C(2)-C(4)	1.486 (3)	
C(2)-C(3)	1.543 (2)		C(2)-C(3)	1.552 (3)	
C(3)-C(20)	1.448 (2)		C(3)-C(23)	1.452 (3)	
C(3)-C(4)	1.4775 (9)		C(3)-C(10)	1.467 (3)	
C(2)-C(1)-C(12)		122.79 (13)	C(2)-C(1)-C(18)		117.34 (18)
C(2)-C(1)-C(3)		61.73 (9)	C(2)-C(1)-C(3)		61.95 (14)
C(12)-C(1)-C(3)		121.22 (12)	C(18)-C(1)-C(3)		122.14 (17)
C(18)-C(2)-C(1)		119.61 (13)	C(1)-C(2)-C(4)		125.28 (19)
C(18)-C(2)-C(3)		116.78 (12)	C(1)-C(2)-C(3)		60.76 (13)
C(1)-C(2)-C(3)		60.12 (9)	C(4)-C(2)-C(3)		121.73 (18)
C(20)-C(3)-C(4)		112.79 (11)	C(23)-C(3)-C(10)		111.35 (19)
C(20)-C(3)-C(1)		120.16 (12)	C(23)-C(3)-C(1)		117.98 (17)
C(4)-C(3)-C(1)		119.65 (11)	C(10)-C(3)-C(1)		123.48 (18)
C(20)-C(3)-C(2)		115.36 (12)	C(23)-C(3)-C(2)		115.03 (17)
C(4)-C(3)-C(2)		120.37 (12)	C(10)-C(3)-C(2)		121.81 (17)
C(1)-C(3)-C(2)		58.15 (9)	C(1)-C(3)-C(2)		57.28 (13)

EXPERIMENTAL

General Experimental Conditions. All reagents and solvents were obtained from commercial source and used without purification. The 2-arylidenecyanomethyl-1,3,4-oxadiazole was prepared according to the literature [14]. The 2-arylidenecyanomethyl-benzothiazoles was prepared according to the literature [15]. All melting points were uncorrected. Melting points were determined on WRS-1 digital melting point apparatus made by Shanghai physical instrument factory (SPOIF), China. IR spectra were measured in KBr on a PE-580B spectrometer. ^{1}H NMR spectra were recorded on a Bruker AM-300 or Bruker AV-500, using $CDCl_3$ as solvent and TMS as internal reference. Mass spectra were taken with a HP5989A mass spectrometer at an ionizing voltage of 70 eV. Elemental analyses were measured on the elementar vario EL III. X-Ray crystal data were collected with Smart Apex CCD or Bruker Smart Apex2 CCD.

General procedure for preparing heterosubstituted cyclopropanes (3a-s). The general process for synthesis of heterosubstituted cyclopropanes (**3a-s**) is as follows: a mixture of olefin (**1**) (1 mmole), arsonium salt (**2**) (1 mmole) and $KF{\cdot}2H_2O$ (0.284 g, 3 mmoles) was stirred at room temperature in dimethoxyethane (DME) (5 ml). Completion of the reaction was determined by TLC. The DME was removed under reduced pressure and the residue was run on a silica gel chromatographic column (petroleum ether-ethyl acetate, 8:1). Triphenylarsine can be recovered and the desired products (**3**) obtained respectively.

Methyl (1*R*,2*R*,3*S*)-2-cyano-3-phenyl-2-(5-phenyl-1,3,4-oxadiazol-2-yl)cyclopropanecarboxylate (3a). This compound was obtained as a white solid, mp 173-174 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (300 MHz, deuteriochloroform): δ 3.27 (d, J=7.9 Hz, 1H), 3.71 (s, 3H), 4.07 (d, J=7.9 Hz, 1H), 7.43-7.50 (m, 5H), 7.64-7.67 (m, 3H), 8.08-8.11 (m, 2H); ^{13}C nmr (75 MHz, deuteriochloroform): δ 21.1, 34.0, 36.0, 53.2, 76.6, 77.0, 77.4, 114.2, 123.1, 127.1, 128.3, 129.1, 129.2, 130.7, 132.3, 158.4, 166.1, 166.4; ir (potassium bromide): 2245 (CN), 1731 (CO), 1608, 1549 cm^{-1}; ms (m/z) (%): 345 (2) (M^+), 286 (59) [M-CO_2CH_3]$^+$, 77 (100) [Ph-H]$^+$. *Anal.* calcd. for $C_{20}H_{15}N_3O_3$: C, 69.56; H, 4.38; N, 12.17. Found: C, 69.56; H, 4.21; N, 11.91.

Methyl (1*R*,2*R*,3*S*)-3-(4-chlorophenyl)-2-cyano-2-(5-phenyl-1,3,4-oxadiazol-2-yl)cyclopropanecarboxylate (3b). This compound was obtained as a white solid, mp 221-222 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (300 MHz, deuteriochloroform): δ 3.23 (d, J=8.0 Hz, 1H), 3.72 (s, 3H), 4.04 (d, J=8.0 Hz, 1H), 7.39 (d, J=8.5 Hz, 2H), 7.45 (d, J=8.5 Hz, 2H), 7.54-7.60 (m, 3H), 8.07-8.12 (s, 2H); ^{13}C nmr (75 MHz, deuteriochloroform): δ 21.1, 34.0, 35.3, 53.3, 76.6, 77.0, 77.4, 114.0, 123.0, 127.1, 129.1, 129.3, 129.4, 129.7, 132.4, 135.3, 158.2, 166.1; ir (potassium bromide): 2249 (CN), 1729 (CO), 1605, 1548 cm^{-1}; ms (m/z) (%): 381 (1) (M^++1), 380 (5) (M^+), 321 (35) [M-CO_2CH_3]$^+$, 77 (75) [Ph-H]$^+$. *Anal.* calcd. for $C_{20}H_{14}ClN_3O_3$: C, 63.25; H, 3.72; N, 11.06. Found: C, 63.46; H, 3.57; N, 11.04.

Methyl (1*R*,2*R*,3*S*)-2-cyano-3-(4-methoxyphenyl)-2-(5-phenyl-1,3,4-oxadiazol-2-yl)cyclopropanecarboxylate (3c). This compound was obtained as a white solid, mp 196-197 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (300 MHz, deuteriochloroform): δ 3.23 (d, J=8.0 Hz, 1H), 3.71 (s, 3H), 3.84, (s, 3H), 4.02 (d, J=8.0 Hz, 1H), 6.98 (d, J=8.8 Hz, 2H), 7.37 (d. J=8.8 Hz, 2H), 7.51-7.58 (m, 3H), 8.07-8.09 (m, 2H); ^{13}C nmr (75 MHz, deuteriochloroform): δ 21.1, 34.0, 35.6, 53.1, 55.2, 76.6, 77.0, 77.4, 114.4, 122.5, 123.0, 127.0, 129.1, 129.4, 132.2, 158.5, 160.1, 165.9, 166.4; ir (potassium bromide): 2246 (CN), 1731 (CO), 1611, 1549 cm^{-1}; ms (m/z) (%): 375 (4) (M^+), 316 (36) [M-CO_2CH_3]$^+$, 77 (77) [Ph-H]$^+$. *Anal.* calcd. for $C_{21}H_{17}N_3O_4$: C, 67.19; H, 4.56; N, 11.19. Found: C, 67.25; H, 4.31; N, 11.09.

Methyl (1*R*,2*R*,3*S*)-2-cyano-3-(4-nitrophenyl)-2-(5-phenyl-1,3,4-oxadiazol-2-yl)cyclopropanecarboxylate (3d). This compound was obtained as a white solid, mp 188-189 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (300 MHz, deuteriochloroform): δ 3.34 (d, J=8.0 Hz, 1H), 3.76 (s, 3H), 4.16 (d, J= 8.0 Hz, 1H), 7.53-7.59 (m, 3H), 7.66 (d, J=8.8 Hz, 2H), 8.07-8.10 (m, 2H), 8.34 (d, J=8.8 Hz, 2H); ^{13}C nmr (75 MHz, deuteriochloroform): δ 21.2, 34.0, 35.0, 53.5, 76.6, 77.0, 77.4, 113.7, 122.8, 124.3, 127.1, 129.1, 129.5, 132.5, 137.9, 148.3, 157.7, 165.7, 166.3; ir (potassium bromide): 2253 (CN), 1731 (CO), 1607, 1546 cm^{-1}; ms (m/z) (%): 390 (3) (M^+), 331 (22) [M-CO_2CH_3]$^+$, 77 (77) [Ph-H]$^+$. *Anal.* calcd. for $C_{20}H_{14}N_4O_5$: C, 61.54; H, 3.61; N, 14.35. Found: C, 61.43; H, 3.23; N, 14.29.

Methyl (1*R*,2*R*,3*S*)- 3-(2-chlorophenyl)-2-cyano-2-(5-phenyl-1,3,4-oxadiazol-2-yl)cyclopropanecarboxylate (3e). This compound was obtained as a white solid, mp 121-122 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (300 MHz, deuteriochloroform): δ 3.29 (d, J=8.0 Hz, 1H), 3.76 (s, 3H), 4.12 (d, J=8.0 Hz, 1H), 7.35-7.42 (m, 3H), 7.51-7.59 (m, 4H), 8.08-8.11 (m, 2H); ^{13}C nmr (75 MHz, deuteriochloroform): δ 20.8, 34.4, 53.2, 76.6, 77.0, 77.4, 114.0, 123.0, 126.9, 127.2, 129.0, 129.3, 130.0, 130.5, 132.2, 135.8, 158.2, 165.8, 166.0; ir (potassium bromide): 2248 (CN), 1738 (CO), 1608, 1549 cm^{-1}; ms (m/z) (%): 381 (2) (M^++1), 380 (5) (M^+), 321 (30) [M-CO_2CH_3]$^+$, 77 (99) [Ph-H]$^+$. *Anal.* calcd. for $C_{20}H_{14}ClN_3O_3$: C, 63.25; H, 3.72; N, 11.06. Found: C, 63.25; H, 3.59; N, 11.00.

(1*R*,2*R*,3*S*)-2-Benzoyl-3-phenyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)cyclopropanecarbonitrile (3f). This compound was obtained as a white solid, mp >300 °C (decomp.) (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (300 MHz, deuteriochloroform): δ 4.11 (d, J=8.0 Hz, 1H), 4.28 (d, J= 8.0 Hz, 1H), 7.45-7.57 (m, 10 H), 7.64-7.66 (m, 1H), 7.97-8.05 (m, 4H); ^{13}C nmr (75 MHz, deuteriochloroform): δ 22.6, 36.2, 37.5, 76.6, 77.0, 77.4, 114.7, 123.0, 127.0, 128.2, 128.4, 128.9 129.0, 129.1, 131.2, 132.1, 134.5, 135.7, 158.6, 165.8, 190.2; ir (potassium bromide): 2244 (CN), 1673 (CO), 1597, 1551 cm^{-1}; ms (m/z) (%): 286 (5) [M- COPh]$^+$, 105 (100) [COPh]$^+$, 77 (99) [Ph-H]$^+$. *Anal.* calcd. for $C_{25}H_{17}N_3O_2$: C, 76.71; H, 4.38; N, 10.74. Found: C, 76.74; H, 4.28; N, 10.72.

(1*R*,2*R*,3*S*)-2-Benzoyl-3-(4-nitrophenyl)-1-(5-phenyl-1,3,4-oxadiazol-2-yl)cyclopropanecarbonitrile (3g). This compound was obtained as a white solid, mp 174-175 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (300 MHz, deuteriochloroform): δ 4.17 (d, J=8.0 Hz, 1H), 4.38 (d, J=8.0 Hz, 1H), 7.47-7.59 (m, 5H), 7.66-7.75 (m, 3H), 7.96 (d, *J*= 8.8 Hz, 2H), 8.03-8.05 (m, 2H), 8.37 (d, *J*= 8.8 HZ, 2H); ^{13}C nmr (75 MHz, deuteriochloroform): δ 22.7, 35.1, 37.5, 76.6, 77.0, 77.4, 114.1, 122.8, 124.2, 127.0, 128.5, 129.1, 129.4, 129.5, 132.3, 134.8, 135.4, 138.5, 148.2, 157.9, 166.1, 189.3; ir (potassium bromide): 2245 (CN), 1678 (CO), 1598, 1548 cm^{-1}; ms (m/z) (%): 436 (1) (M^+), 331 (4) [M-COPh]$^+$, 105 (100) [COPh]$^+$, 77 (43) [Ph-H]$^+$. *Anal.* calcd. for $C_{25}H_{16}N_4O_4$: C, 68.80; H, 3.70; N, 12.84. Found: C, 68.89; H, 3.55; N, 12.73.

(1*R*,2*R*,3*S*)-2-(Furan-2-carbonyl)-3-phenyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)cyclopropanecarbonitrile (**3h**). This

compound was obtained as a white solid, mp 150-151 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (300 MHz, deuteriochloroform): δ 4.13 (d, J=8.0 Hz, 1H), 4.24 (d, J=8.0 Hz, 1H), 6.64-6.67 (m, 1H), 7.35-7.37 (m, 1H), 7.44-7.56 (m, 8H), 7.73-7.74 (m, 1H), 8.02-8.06 (m, 2H); ^{13}C nmr (75 MHz, deuteriochloroform): δ 22.4, 36.0, 36.4, 76.6, 77.0, 77.4, 113.2, 114.5, 119.2, 123.0, 126.9, 128.3, 128.9, 131.1, 132.0, 148.0, 151.9, 158.4, 165.8, 178.6; ir (potassium bromide): 2243 (CN), 1655 (CO), 1609, 1566 cm^{-1}; ms (m/z) (%): 381 (1) (M^+), 286 (27) $[M-C_5H_3O_2]^+$, 95 (100) $[C_5H_3O_2]^+$, 77 (15) $[Ph-H]^+$. *Anal.* calcd. for $C_{23}H_{15}N_3O_3$: C, 72.43; H, 3.96; N, 11.02. Found: C, 72.36; H, 3.69; N, 11.04.

(1*R*,2*R*,3*S*)-2-Phenyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)-3-(thiophene-2-carbonyl)cyclopropanecarbonitrile (3i). This compound was obtained as a white solid, mp 156-157 °C (CH_2Cl_2/petroleum ether; v:v=1:1). ^{1}H nmr (300 MHz, deuteriochloroform): δ 3.99 (d, J=8.0 Hz, 1H), 4.27 (d, J=8.0 Hz, 1H), 7.23-7.26 (m, 2H), 7.47-7.56 (m, 7H), 7.78-7.80 (m, 1H), 8.01-8.04 (m, 3H); ^{13}C nmr (75 MHz, deuteriochloroform): δ 22.5, 36.3, 37.9, 76.6, 77.0, 77.4, 114.6, 123.1, 127.1, 128.2, 128.7, 129.0, 129.1, 131.1, 132.1, 133.7, 136.1, 142.8, 158.5, 165.9, 182.5; ir (potassium bromide): 2248 (CN), 1650 (CO), 1608, 1546 cm^{-1}; ms (m/z) (%): 397 (1) (M^+), 286 (20) $[M-C_5H_3OS]^+$, 111 (100) $[C_5H_3OS]^+$, 77 (14) $[Ph-H]^+$. *Anal.* calcd. for $C_{23}H_{15}N_3O_2S$: C, 69.50; H, 3.81; N, 10.57. Found: C, 69.56; H, 3.43; N, 10.54.

(1*R*,2*R*,3*S*)-1-(Benzo[*d*]thiazol-2-yl)-2-benzoyl-3-phenylcyclopropanecarbonitrile (3j). This compound was obtained as a white solid, mp 144-145 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (500 MHz, deuteriochloroform): δ 4.09 (d, J=8.0 Hz, 1H), 4.42 (d, J= 8.0 Hz, 1H), 7.33-7.51 (m, 9H), 7.56-7.59 (m, 1H), 7.77 (d, J=7.5 Hz, 1H), 7.94 (d, J=7.5 Hz, 1H), 7.99-8.01 (m, 2H); ^{13}C nmr (125 MHz, deuteriochloroform): δ= 30.6, 36.9, 40.3, 117.2, 121.7, 123.9, 126.1, 126.7, 128.5, 128.6, 128.9, 129.1, 129.2, 132.6, 134.2, 135.6, 135.5, 152.6, 160.3, 190.3; ir (potassium bromide): 2243 (CN), 1680 (CO), 1596, 1513 cm^{-1}; ms (m/z) (%): 275 (28) $[M-COPh]^+$, 105 (100) $[COPh]^+$, 77 (66) $[Ph-H]^+$. *Anal.* calcd. for $C_{24}H_{16}N_2OS$: C, 75.77; H, 4.24; N, 7.36. Found: C, 75.93; H, 4.04; N, 7.36.

(1*R*,2*R*,3*S*)-1-(Benzo[*d*]thiazol-2-yl)-2-benzoyl-3-(4-chlorophenyl)cyclopropanecarbonitrile (3k). This compound was obtained as a white solid, mp 177-178 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (500 MHz, deuteriochloroform): δ 4.02 (d, J=8.0 Hz, 1H), 4.38 (d, J=8.0 Hz, 1H), 7.32-7.35 (m, 1H), 7.43-7.47 (m, 7H), 7.56-7.58 (m, 1H), 7.74 (d, J=8.0 Hz,1H), 7.92 (d, J=8.0 Hz, 1H), 7.96-7.98 (m, 2H); ^{13}C nmr (125 MHz, deuteriochloroform): δ 30.5, 36.0, 40.4, 117.0, 121.7, 123.9, 126.2, 126.8, 128.6, 129.2, 129.4, 129.9, 131.2, 134.4, 135.0, 135.5, 136.4, 152.6, 159.9, 189.9; ir (potassium bromide): 2240 (CN), 1679 (CO), 1597, 1498 cm^{-1}; ms (m/z) (%): 105 (100) $[COPh]^+$, 77 (62) $[Ph-H]^+$. *Anal.* calcd. for $C_{24}H_{15}ClN_2OS$: C, 69.48; H, 3.64; N, 6.75. Found: C, 69.62; H, 3.46; N, 6.59.

(1*R*,2*R*,3*S*)-1-(Benzo[*d*]thiazol-2-yl)-2-benzoyl-3-(4-methoxyphenyl)cyclopropanecarbonitrile (3l). This compound was obtained as a white solid, mp 165-166 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (500 MHz, deuteriochloroform): δ 3.83 (s, 3H), 4.04 (d, J=8.0 Hz, 1H)), 4.37 (d, J=8.0Hz, 1H), 6.98 (d, J=8.5 Hz, 2H), 7.34-7.37 (m, 1H), 7.43 (d, J=8.5 Hz, 2H), 7.45-7.49 (m, 3H), 7.57-7.61 (m, 1H), 7.78 (d, J=8.0Hz, 1H), 7.94 (d, J=8.0 Hz, 1H), 7.99-8.02 (m, 2H); ^{13}C nmr (125 MHz, deuteriochloroform): δ 30.7, 36.6, 40.1, 55.5, 114.6, 117.4, 121.7, 123.8, 124.5, 126.0, 126.7, 128.6, 129.1, 129.7, 134.2, 135.5, 136.6, 152.7, 160.1, 160.5, 190.4; ir (potassium bromide): 2244 (CN), 1680 (CO), 1611, 1515 cm^{-1}; ms (m/z) (%): 410 (14) (M^+), 305 (11) $[M-COPh]^+$, 105 (100) $[COPh]^+$, 77 (77) $[Ph-H]^+$. *Anal.* calcd. for $C_{25}H_{18}N_2O_2S$: C, 73.15; H, 4.42; N, 6.82. Found: C, 73.11; H, 4.24; N, 6.77.

(1*R*,2*R*,3*S*)-1-(Benzo[*d*]thiazol-2-yl)-2-benzoyl-3-(4-methylphenyl)cyclopropanecarbonitrile (3m). This compound was obtained as a white solid, mp 150-151 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (500 MHz, deuteriochloroform): δ 2.38 (s, 3H), 4.07 (d, J=8.0 Hz, 1H), 4.39 (d, J=8.0 Hz, 1H), 7.26 (d, J=8.0 Hz, 2H), 7.35-7.39 (m, 1H), 7.42 (d, J=8.0 Hz, 2H), 7.46-7.58 (m, 3H), 7.56-7.59 (m, 1H), 7.70 (d, J=8,5 Hz, 1H), 7.94 (d, J=8.5 Hz, 1H), 8.00-8.02 (m, 2H); ^{13}C nmr (125 MHz, deuteriochloroform): δ 21.4, 30.7, 36.8, 40.4, 117.3, 121.7, 123.8, 126.o, 126.7, 129.1, 129.5, 135.5, 136.6, 138.8, 152.6, 160.5, 183.5, 190.4; ir (potassium bromide): 2240 (CN), 1680 (CO), 1596, 1518 cm^{-1}; ms (m/z) (%): 393 $(M-H)^+$, 289 (29) $[M-COPh]^+$, 105 (100) $[COPh]^+$, 77 (59) $[Ph-H]^+$. *Anal.* calcd. for $C_{25}H_{18}N_2OS$: C, 76.12; H, 4.60; N, 7.10. Found: C, 76.17; H, 4.30; N, 6.96

(1*R*,2*R*,3*S*)-1-(Benzo[*d*]thiazol-2-yl)-2-benzoyl-3-(3-nitrophenyl)cyclopropanecarbonitrile (3n). This compound was obtained as a white solid, mp 184-185 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (500 MHz, deuteriochloroform): δ 4.17 (d, J=8.0 Hz, 1H), 4.57 (d, J=8.0 Hz, 1H), 7.37-7.40 (m, 1H), 7.45-7.52 (m, 3H), 7.60-7.68 (m, 2H), 7.78 (d, J=8.0 Hz, 1H), 7.88 (m, 1H), 7.97 (d, J=8.0 Hz, 1H), 8.02 (m, 2H), 8.27-8.29 (m, 1H), 8.37 (s, 1H); ^{13}C nmr (125 MHz, deuteriochloroform): δ 30.5, 35.5, 40.2, 116.7, 121.8, 123.7, 124.0, 126.3, 126.9, 128.7, 129.2, 130.4, 134.6, 134.9, 135.0, 135.6, 136.1, 148.7, 152.5, 159.1, 189.3; ir (potassium bromide): 2242 (CN), 1677 (CO), 1594, 1530 cm^{-1}; ms (m/z) (%): 426 (2) $(M+1)^+$, 320 (18) $[M-COPh]^+$, 105 (100) $[COPh]^+$, 77 (69) $[Ph-H]^+$. *Anal.* calcd. for $C_{24}H_{15}N_3O_3S$: C, 67.75; H, 3.55; N, 9.88. Found: C, 67.66; H, 3.28; N, 9.76.

(1*R*,2*R*,3*S*)-1-(Benzo[*d*]thiazol-2-yl)-2-benzoyl-3-(2-chlorophenyl)cyclopropanecarbonitrile (3o). This compound was obtained as a white solid, mp 145-146 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (500 MHz, deuteriochloroform): δ 4.10 (d, J=8.0 Hz, 1H), 4.38 (d, J=8.0 Hz, 1H), 7.35-7.44 (m, 5H), 7.47-7.53 (m, 2H), 7.53-7.55 (m, 1H), 7.58-7.61 (m, 1H), 7.81 (d, *J*=8.5 Hz, 1H), 7.92 (d, *J*=8.5 Hz, 1H), 8.02-8.04 (m, 2H); ^{13}C nmr (125 MHz, deuteriochloroform): δ 30.4, 35.7, 40.4, 117.0, 121.7, 123.9, 126.1, 126.6, 127.4, 128.7, 129.1, 129.6, 130.2, 130.4, 131.3, 134.3, 135.5, 136.4, 136.5, 152.7, 160.2, 190.2; ir (potassium bromide): 2239 (CN), 1668 (CO), 1598, 1493 cm^{-1}; ms (m/z) (%): 310 (5) $[M-COPh]^+$, 105 (100) $[COPh]^+$, 77 (65) $[Ph-H]^+$. *Anal.* calcd. for $C_{24}H_{15}ClN_2OS$: C, 69.48; H, 3.64; N, 6.75. Found: C, 69.60; H, 3.54; N, 6.72.

(1*R*,2*R*,3*S*)-1-(Benzo[*d*]thiazol-2-yl)-2-benzoyl-3-(3-chlorophenyl)cyclopropanecarbonitrile (3p). This compound was obtained as a white solid, mp 174-175 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (300 MHz, deuteriochloroform): δ 4.07 (d, J=8.0 Hz, 1H), 4.43 (d, J=8.0 Hz, 1H), 7.35-7.40 (m, 4H), 7.43-7.50 (m, 4H), 7.59-7.62 (m, 1H), 7.78 (d, J=8.0 Hz, 1H), 7.96 (d, J=8.0 Hz, 1H), 8.00-8.02 (m, 2H); ^{13}C nmr (Hz, deuteriochloroform): δ 30.5, 36.0, 40.2, 116.9, 121.8, 123.9, 126.2, 126.7, 126.8, 128.6, 128.9, 129.1, 129.2, 130.5, 134.2, 134.7, 135.1, 135.6, 136.4, 152.6, 1259.8, 189.8; ir (potassium bromide): 2239 (CN), 1669 (CO), 1598, 1570 cm^{-1};

ms (m/z) (%): 415 (1) (M^+), 310 (4) [M-COPh]$^+$, 105 (100) [COPh]$^+$, 77 (68) [Ph-H]$^+$. *Anal*. calcd. for $C_{24}H_{15}ClN_2OS$: C, 69.48; H, 3.64; N, 6.75. Found: C, 69.47; H, 3.34; N, 6.58.

(1*R*,2*R*,3*S*)-1-(Benzo[*d*]thiazol-2-yl)-2-(furan-2-carbonyl)-3-phenylcyclopropanecarbonitrile (3q). This compound was obtained as a white solid, mp 154-155 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (500 MHz, deuteriochloroform): δ 4.10 (d, J=8.0 Hz, 1H), 4.38 (d, J=8.0 Hz, 1H), 6.59-6.60 (m, 1H), 7.29-7.30 (m, 1H), 7.40-7.52 (m, 7H), 7.68 (s, 1H), 7.83 (d, J=8.0 Hz, 1H), 8.01 (d, J=8.0 Hz, 1H); ^{13}C nmr (125 MHz, deuteriochloroform): δ= 30.6, 31.1, 36.5, 39.2, 113.2, 117.0, 118.9, 121.8, 124.0, 126.2, 126.8, 128.6, 129.0, 129.3, 132.5, 135.8, 147.8, 152.7, 160.2, 178.7; ir (potassium bromide): 2245 (CN), 1671 (CO), 1562, 1513 cm^{-1}; ms (m/z) (%): 275 (7) [M-$C_5H_3O_2$]$^+$, 95 (100) [$C_5H_3O_2$]$^+$, 77 (8) [Ph-H]$^+$. *Anal*. calcd. for $C_{22}H_{14}N_2O_2S$: C, 71.33; H, 3.81; N, 7.56. Found: C, 71.03; H, 3.64; N, 7.50.

(1*R*,2*R*,3*S*)-1-(Benzo[*d*]thiazol-2-yl)-3-(4-chlorophenyl)-2-(furan-2-carbonyl)cyclopropanecarbonitrile (3r). This compound was obtained as a white solid, mp 179-180 °C (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (500 MHz, deuteriochloroform): δ 4.06 (d, J= 8.0 Hz, 1H), 4.36 (d, J=8.0 Hz, 1H), 6.60-6.61 (m, 1H), 7.28-7.31 (m, 1H), 7.40-7.50 (m, 6H), 7.69 (s, 1H), 7.93 (d, J= 8.0 Hz, 1H), 8.01 (d, J= 8.0 Hz, 1H); ^{13}C nmr (125 MHz, deuteriochloroform): δ 30.5, 35.7, 39.2, 113.3, 119.0, 121.8, 124.0, 126.3, 126.8, 129.5, 130.0, 131.0, 135.0, 135.8, 147.9, 152.6, 159.7, 178.4; ir (potassium bromide): 2244 (CN), 1669 (CO), 1561, 1512 cm^{-1}; ms (m/z) (%): 310 (6) [M-$C_5H_3O_2$]$^+$, 95 (70) [$C_5H_3O_2$]$^+$, 77 (12) [Ph-H]$^+$. *Anal*. calcd. for $C_{22}H_{13}ClN_2O_2S$: C, 65.27; H, 3.24; N, 6.92. Found: C, 65.40; H, 2.93; N, 6.74.

(1*R*,2*R*,3*S*)-1-(Benzo[*d*]thiazol-2-yl)-2-(4-chlorophenyl)-3-(thiophene-2-carbonyl)cyclopropanecarbonitrile (3s). This compound was obtained as a white solid, mp >300 °C (decomp.) (CH_2Cl_2/petroleum ether; v:v=1:1); ^{1}H nmr (500 MHz, deuteriochloroform): δ 3.97 (d, J=8.0 Hz, 1H), 4.39 (d, J=8.0 Hz 1H), 7.19 (dd, J=4.0, 4.5 Hz, 1H), 7.38-7.49 (m, 6H), 7.71 (d, J= 4.5 Hz, 1H), 7.81 (d, J=8.0 Hz, 1H), 7.94 (d, J=4.0 Hz, 1H), 7.99 (d, J=8.0 Hz, 1H); ^{13}C nmr (125 MHz, deuteriochloroform): δ 30.4, 36.1, 40.6, 116.9, 121.8, 124.0, 126.2, 126.8, 128.9, 129.5, 130.0, 131.1, 133.6, 135.1, 135.6, 135.8, 143.5, 152.6, 159.8, 182.2; ir (potassium bromide): 2246 (CN), 1656 (CO), 1557, 1514 cm^{-1}; ms (m/z) (%): 421 (1) (M^+) 310 (11) [M-C_5H_3OS]$^+$, 111 (100) [C_5H_3OS]$^+$, 77 (15) [Ph-H]$^+$. *Anal*. calcd. for $C_{22}H_{13}ClN_2OS_2$: C, 62.78; H, 3.11; N, 6.66. Found: C, 62.69; H, 2.83; N, 6.42.

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