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Synthesis of 5-Phenylproline Derivatives with Antibacterial Activity

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Abstract—Methyl esters of 5-phenylprolines with the vinylsulfonyl or cyano group in the 4-position of the pyrrolidine ring have been synthesized. X-ray crystallography shows that all substituents in the vinylsulfonyl derivatives are *cis* to each other. All compounds are inhibitors of *Staphylococcus aureus* sortase SrtA.

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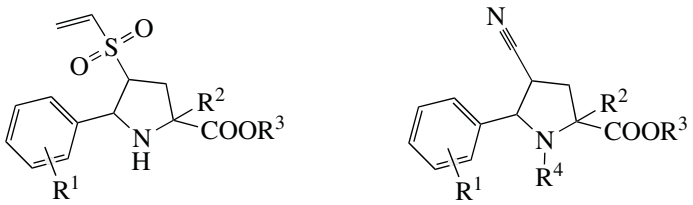
Gram-positive bacteria produce surface proteins that mediate bacterial cell attachment to the host organism and hinder phagocytosis. Surface proteins are sorted at the bacterial cell wall envelope, and this process is catalyzed by the sortase enzyme [1]. *S. aureus* sortase SrtA catalyzes the transpeptidation reaction in which the surface protein containing the LPXTG motif undergoes cleavage at the bond between the threonine (T) and glycine (G) residues. Then, the threonine carboxyl group is attached to the amino group of the peptidoglycan pentaglycine cross-bridge of the bacterial cell membrane. As a result of this reaction, surface proteins are covalently anchored to the bacterial cell wall. There is experimental evidence that SrtA sortase plays a significant role in the surface functionality of a bacterial cell expressing virulent factors and in pathogenesis of many *S. aureus* infections. Deactivation of SrtA genes in *S. aureus* and other gram-positive microorganisms inhibits the adherence of surface proteins and decreases the virulence of a bacterium [2]. Thus, the inhibition of sortase activity can be considered as a new approach to treatment of gram-positive bacterial infections, which is supplementary to routine methods using traditional antibiotics.

Several classes of *S. aureus* SrtA inhibitors are currently known: peptides [3, 4], plant extracts [5, 6], and small organic molecules [6–8]. The latter are regarded by pharmaceutical companies as the most promising compounds for development of drugs. Based on syntheses of different derivatives of 2-pyrrolidinecarboxylic acids [9, 10] and the knowledge of pharmacophores of known inhibitors (vinylsulfonyl moiety [7] and nitrile group [8]), the virtual design and synthesis of 5-phenylprolines **A** and **B** (Fig. 1) have been carried out and their *S. aureus* SrtA inhibiting properties have been studied.

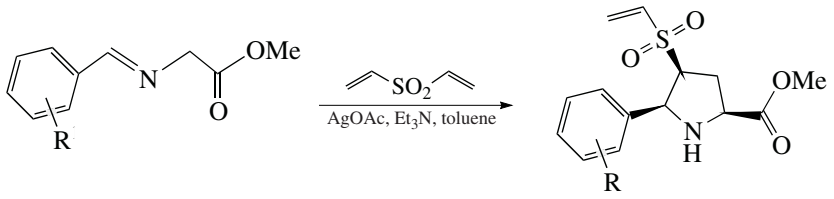
Synthesis of compounds **A** and **B** is based on 1,3-dipolar cycloaddition of dipolarophiles to azomethine ylides produced from α-amino acid imino esters. The reaction of divinylsulfone with imino esters **1**, synthesized from glycine methyl ester and benzaldehydes, in the presence of silver(I) acetate gives 4-vinylsulfonyl-5-phenylprolines **2a**–**2c** in yields not exceeding 30% (Scheme 1), which differs from the reaction of dimethyl 2-benzylideneaminopentanedioate with divinylsulfone [9].

The low yield of target products of 1,3-dipolar cycloaddition of **2** is due to the bifunctionality of the dipolarophile used and the possibility of competing conjugated addition of divinylsulfone to the α position of imino ester **1** (Scheme 2) [11]. Metal dipole **C** is able to act as the Michael donor and to react with divinylsulfone to give azomethine ylide **D**. The latter enters the intramolecular reaction to produce bicyclic product **3**.



A **B**

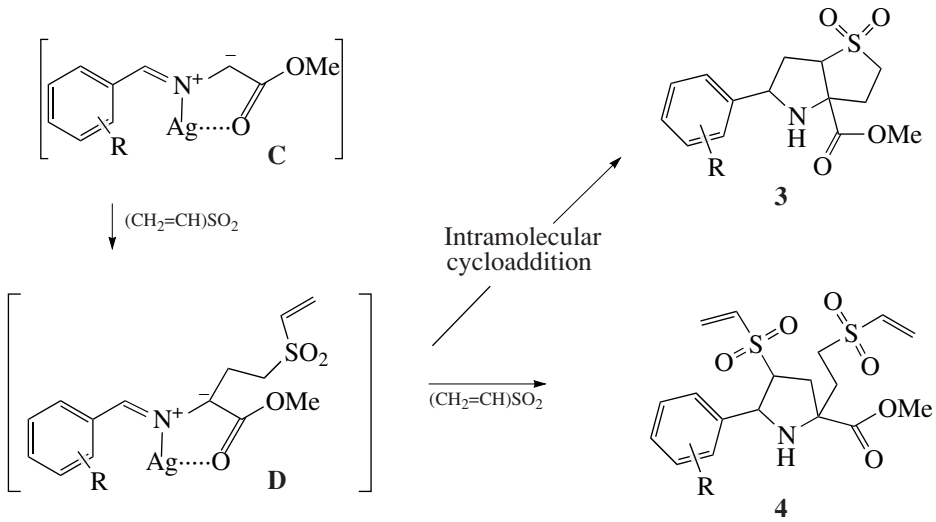
Fig. 1. 5-Phenylprolines **A** and **B**.



1a–1c (±)-**2a**–**2c**, 13–26%

R = H (**a**), 2-F (**b**), 3-F (**c**)

Scheme 1.



Scheme 2.

The addition of the second divinylsulfone molecule gives substituted 5-phenylproline **4** with two vinylsulfonyl groups. Compounds spectrally corresponding to structures **3** and **4** were obtained by the reaction of imino esters **1** with divinylsulfone but were not studied in detail.

X-ray crystallography showed that all the three substituents in pyrrolidinevinylsulfone **2c** are *cis* to each other (Fig. 2). Selected bond lengths and bond angles in **2c** are listed in the table. The basic geometric parameters of molecule **2c** have common values [12].

The ^{1}H NMR chemical shifts and spin coupling constants for the protons of the pyrrolidine ring of prolines **2a**–**2c** are the same (see Experimental), which allows us to conclude that the three compounds have the same spatial structure. Pyrrolidinylvinylsulfones **2a**–**2c** are stable for one year when kept at +4°C notwithstanding the fact that the same molecule contains the Michael acceptor (vinylsulfonyl group) and donor (secondary amine).

The cyano group was introduced into the pyrrolidine ring by the reaction of imino esters **1**, obtained from

Selected bond lengths (d, Å) and bond angles (ω, deg) in molecule **2c**

Bond	d, Å	Bond	d, Å	Angle	ω, deg
S(1)–O(1)	1.378(10)	N(1)–C(1)	1.472(14)	O(1)–S(1)–O(2)	117.6(6)
S(1)–O(2)	1.455(8)	O(3)–C(5)	1.235(17)	O(1)–S(1)–C(7)	109.7(7)
S(1)–C(7)	1.764(13)	O(4)–C(5)	1.259(16)	O(1)–S(1)–C(2)	106.6(6)
S(1)–C(2)	1.812(12)	O(4)–C(6)	1.401(16)	O(2)–S(1)–C(2)	110.5(6)
F(1)–C(11)	1.351(18)	C(7)–C(8)	1.31(2)	C(7)–S(1)–C(2)	104.9(6)
N(1)–C(4)	1.453(15)	–	–	C(4)–N(1)–C(1)	105.9(9)

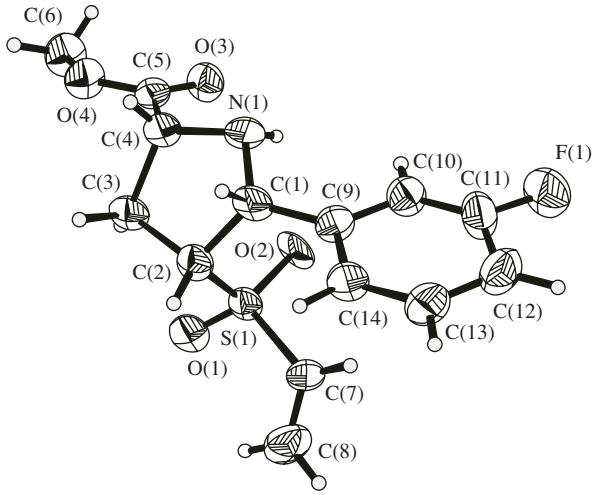


Fig. 2. Molecular structure of **2c**.

glycine and alanine methyl esters and benzaldehydes with acrylonitrile in the presence of lithium bromide (Scheme 3). Cycloaddition in this case is characterized by low selectivity and leads to the formation of *exo* products **5** and *endo* products **6** [13]. Isomeric 4-cyano-5-phenylprolinates **5** and **6** are separated chromatographically or by fractional recrystallization.

The structures of potential inhibitors were further modified by methylation of the secondary amine nitrogen in compounds **5** (Scheme 4).

All 4-substituted 5-phenylprolinates **2**, **5**, **6**, and **7** taken in 5 mM concentration in vitro inhibit *S. aureus* sortase SrtA. Details of these tests will be reported in a separate paper.

EXPERIMENTAL

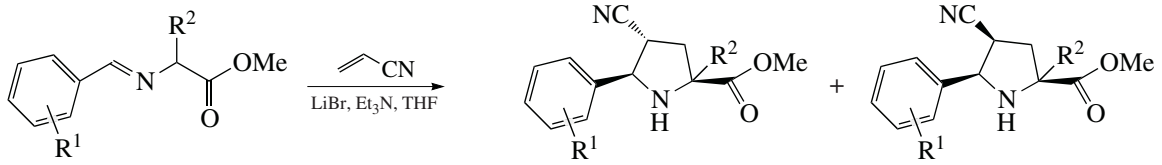
The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 spectrometer (400 MHz (^{1}H), 100 MHz (^{13}C)) at 303 K in solutions in DMSO-d_6 or $CDCl_3$. Residual signals of the solvents were used as internal references. Spin coupling constants (J) are in Hz. Compound **2c** was studied by X-ray crystallography on an Enraf-Nonius CAD4 automated diffractometer at 293 K. Compounds **2**, **5**, **6**, and **7** were synthesized by the methods described in [9, 10].

Methyl (2*S,4*S**,5*S**)-4-ethylenesulfonyl-5-phenylpyrrolidine-2-carboxylate (2a).** Yield, 13%; colorless crystals with mp 111–112°C. ^{1}H NMR ($CDCl_3$), δ, ppm: 2.66–2.80 (m, 2H, H-3), 3.09 (br s, 1H, NH), 3.76 (ddd, 1H, H-4, J = 8.3, 6.3, 6.3), 3.84 (s, 3H, COOC$\underline{H}_3$), 4.02 (dd, 1H, H-2, J = 8.3, 8.3), 4.57 (d, 1H, H-5, J = 6.3), 5.39 (dd, 1H, CH_2=C$\underline{H}$, J = 16.4, 9.9), 5.61 (d, 1H, C$\underline{H}_2$=CH, J = 9.9), 5.92 (d, 1H, C$\underline{H}_2$=CH, J = 16.4), 7.31–7.39 (m, 3H, Ar), 7.42–7.46 (m, 2H, Ar). ^{13}C NMR ($CDCl_3$), δ, ppm: 30.74, 52.54, 58.46, 64.26, 67.27, 128.25 (2C), 128.33 (2C), 128.40, 129.53, 134.97, 136.10. 172.35.

For $C_{14}H_{17}NO_4S$ anal. calcd. (%): C, 56.93; H, 5.80; N, 4.74.

Found (%): C, 56.81; H, 5.87; N, 4.48.

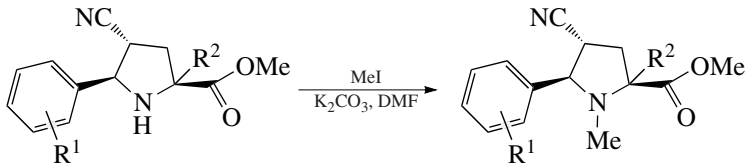
Methyl (2*S,4*S**,5*S**)-4-ethylenesulfonyl-5-(2-fluorophenyl)pyrrolidine-2-carboxylate (2b).** Yield, 26%; colorless crystals with mp 97–99°C. ^{1}H NMR ($CDCl_3$), δ, ppm: 2.73–289 (m, 2H, H-3), 3.20 (br s,



1a, 1b, 1d–1g (±)-**5**, 41–70% (±)-**6**, 20–21%

R^1 = H, R^2 = H (**a**); R^1 = 2-F, R^2 = H (**b**); R^1 = 3-Cl, R^2 = H (**d**); R^1 = 2-Cl, R^2 = Me (**e**); R^1 = 4-Cl, R^2 = Me (**f**); R^1 = 2-Me, R^2 = Me (**g**)

Scheme 3.



(±)-**5b, 5e, 5g** (±)-**7b,** 7**e, 7g,** 81–97%

Scheme 4.

1H, NH), 3.85 (s, 3H, COOC$\underline{H}_3$), 3.87–3.92 (m, 1H, H-4), 3.99 (dd, 1H, H-2, J = 9.1, 7.6), 4.61 (d, 1H, H-5, J = 6.1), 5.65 (m, 1H, CH_2=C$\underline{H}$), 5.81–5.85 (m, 2H, C$\underline{H}_2$=CH), 6.99–7.06 (m, 1H, Ar), 7.21 (t, 1H, Ar, J = 7.6), 7.30–7.37 (m, 1H, Ar); 7.56 (t, 1H, Ar, J = 7.3). ^{13}C NMR ($CDCl_3$), δ, ppm: 30.97, 52.54, 58.11, 58.70, 64.39, 114.63 (d, J_{CF} = 21.2), 123.25 (d, J_{CF} = 13.9), 124.22, 128.36 (d, J_{CF} = 3.7), 129.75 (d, J_{CF} = 8.7), 129.80, 135.08, 160.77 (d, J_{CF} = 245.9), 171.99.

For $C_{14}H_{16}FNO_4S$ anal. calcd. (%): C, 53.66; H, 5.15, N, 4.47.

Found (%): C, 53.87; H, 5.07; N, 4.68.

Methyl (2*S,4*S**,5*S**)-4-ethylenesulfonyl-5-(3-fluorophenyl)pyrrolidine-2-carboxylate (2c).** Yield, 19%; colorless crystals with mp = 99–100°C. ^{1}H NMR ($CDCl_3$), δ, ppm: 2.64–2.78 (m, 2H, H-3), 3.00 (br s, 1H, NH), 3.77 (ddd, 1H, H-4, J = 7.8, 6.6, 6.6), 3.84 (s, 3H, COOC$\underline{H}_3$), 4.01 (t, 1H, H-2, J = 8.3), 4.58 (d, 1H, H-5, J = 6.6), 5.60–5.75 (m, 2H, C$\underline{H}_2$=C$\underline{H}$), 5.98 (d, 1H, C$\underline{H}_2$=CH, J = 16.2), 7.03 (td, 1H, Ar, J = 8.3, 1.5), 7.18–7.27 (m, 2H, Ar), 7.34 (ddd, 1H, Ar, J = 7.8, 7.8, 6.1). ^{13}C NMR($CDCl_3$), δ, ppm: 30.61, 52.57, 58.28, 63.56, 66.76, 115.25 (d, J_{CF} = 21.2). 115.40 (d, J_{CF} = 22.7), 124.03, 129.77 (d, J_{CF} = 8.1), 219.86, 134.90, 139.01 (d, J_{CF} = 7.3), 162.65 (d, J_{CF} = 247.4), 172.25.

For $C_{14}H_{16}FNO_4S$ anal. calcd. (%): C, 53.66; H, 5.15; N, 4.47.

Found (%): C, 53.52; H, 5.05; N, 4.28.

Methyl (2*S,4*R**,5*R**)-4-cyano-5-phenylpyrrolidine-2-carboxylate (5a).** Yield, 41%; colorless crystals with mp 90°C (lit.: mp 93–94°C [13]). ^{1}H NMR ($CDCl_3$), δ, ppm: 2.46–2.55 (m, 1H, H-3), 2.57–2.64 (m, 1H, H-3), 2.69 (br s, 1H, NH), 3.26–3.32 (m, 1H, H-4), 3.83 (s, 3H, COOC$\underline{H}_3$), 3.99 (dd, 1H, H-2, J = 8.5, 6.7), 4.42 (d, 1H, H-5, J = 6.3), 7.32–7.38 (m, 1H, Ar), 7.41 (t, 2H, Ar, J = 7.3), 7.49 (d, 2H, Ar, J = 7.6). ^{13}C NMR ($CDCl_3$), δ, ppm: 34.15, 35.94, 52.29, 58.55, 64.70, 119.28, 127.04 (2C), 128.54, 128.67 (2C), 137.72, 172.96.

For $C_{13}H_{14}N_2O_2$ anal. calcd. (%): C, 67.81; H, 6.13; N, 12.17.

Found (%): C, 67.99; H, 6.03; N, 12.28.

Methyl (2*S,4*R**,5*R**)-4-cyano-5-(2-fluorophenyl)pyrrolidine-2-carboxylate (5b).** Yield, 41%; colorless crystals with mp 51°C. ^{1}H NMR ($CDCl_3$), δ, ppm: 2.44–2.52 (m, 1H, H-3), 2.59 (m, 2H, H-3, NH), 3.42–3.49 (m, 1H, H-4), 3.82 (s, 3H, COOC$\underline{H}_3$), 3.97 (dd, 1H, H-2, J = 8.8, 6.8), 4.67 (d, 1H, H-5, J = 6.6), 7.04–7.12 (m, 1H, Ar), 7.22 (td, 1H, Ar, J = 7.6, 0.8), 7.30–7.37 (m, 1H, Ar), 7.73 (td, 1H, Ar, J = 7.6, 1.0). ^{13}C NMR ($CDCl_3$), δ, ppm: 34.01, 34.62, 52.56, 58.03, 58.23, 115.14 (d, J_{CF} = 22.0), 119.12, 124.50 (d, J_{CF} = 2.9), 125.16 (d, J_{CF} = 13.2), 127.87 (d, J_{CF} = 3.7), 129.92 (d, J_{CF} = 8.8), 160.22 (d, J_{CF} = 245.9), 172.72.

For $C_{13}H_{13}FN_2O_2$ anal. calcd. (%): C, 62.90; H, 5.28; N, 11.28.

Found (%): C, 62.72; H, 5.29; N, 11.18.

Methyl (2*S,4*R**,5*R**)-5-(3-chlorophenyl)-4-cyanopyrrolidine-2-carboxylate (5d).** Yield, 50%; colorless crystals with mp 97–99°C. ^{1}H NMR (DMSO-d_6), δ, ppm: 2.20–2.27 (m, 1H, H-3), 2.52–2.58 (m, 1H, H-3), 3.62–3.67 (m, 1H, NH), 3.70 (s, 3H, COOC$\underline{H}_3$), 3.71–3.76 (m, 1H, H-4), 3.90–3.96 (m, 1H, H-2), 4.43 (dd, 1H, H-5, J = 6.1, 6.1), 7.32–7.44 (m, 3H, Ar), 7.55–7.58 (m, 1H, Ar).

For $C_{13}H_{13}ClN_2O_2$ anal. calcd. (%): C, 58.99; H, 4.95; N, 10.58.

Found (%): C, 59.15; H, 5.01; N, 10.69.

Methyl (2*S,4*R**,5*R**)-5-(2-chlorophenyl)-4-cyano-2-methylpyrrolidine-2-carboxylate (5e).** Yield, 58%; colorless crystals with mp 95°C. ^{1}H NMR (DMSO-d_6), δ, ppm: 1.42 (s, 3H, CH_3), 2.24 (dd, 1H, H-3, J = 13.2, 8.1), 2.64 (dd, 1H, H-3, J = 13.2, 4.1), 3.38–3.44 (m, 1H, NH), 3.70 (s, 3H, COOC$\underline{H}_3$), 3.86 (ddd, 1H, H-4, J = 8.1, 6.0, 4.1), 4.87 (dd, 1H, H-5, J = 6.0), 7.32 (td, 1H, Ar, J = 7.5, 1.8), 7.39 (td, 1H, Ar, J = 7.5, 1.3), 7.49 (dd, 1H, Ar, J = 7.8, 1.3), 7.84 (dd, 1H, Ar, J = 7.8, 1.8).

For $C_{14}H_{15}ClN_2O_2$ anal. calcd. (%): C, 60.33; H, 5.42; N, 10.05.

Found (%): C, 60.15; H, 5.31; N, 10.19.

Methyl (2*S,4*R**,5*R**)-5-(4-chlorophenyl)-4-cyano-2-methylpyrrolidine-2-carboxylate (5f).** Yield, 70%; colorless crystals with mp 101–102°C. ^{1}H NMR (DMSO-d_6), δ, ppm: 1.40 (s, 3H, CH_3), 2.16 (dd, 1H, H-3, J = 7.8, 13.2), 2.65 (dd, 1H, H-3, J = 3.7, 13.2), 3.38 (d, 1H, NH, J = 6.1), 3.70 (s, 3H, COOC$\underline{H}_3$), 3.65–3.69 (m, 1H, H-4), 4.60 (dd, 1H, H-5, J = 6.1, 6.1), 7.39–7.50 (m, 4H, Ar).

For $C_{14}H_{15}ClN_2O_2$ anal. calcd. (%): C, 60.33; H, 5.42; N, 10.05.

Found (%): C, 60.45; H, 5.55; N, 10.29.

Methyl (2*S,4*R**,5*R**)-4-cyano-2-methyl-5-(*o*-tolyl)pyrrolidine-2-carboxylate (5g).** Yield, 46%; oily substance. ^{1}H NMR (DMSO-d_6), δ, ppm: 1.42 (s, 3H, CH_3), 2.23 (dd, 1H, H-3, J = 7.8, 13.2), 2.30 (s, 3H, ArC$\underline{H}_3$), 2.64 (dd, 1H, H-3, J = 3.9, 13.2), 3.18 (d, 1H, NH, J = 6.1), 3.71 (s, 3H, COOC$\underline{H}_3$), 3.76 (ddd, 1H, H-4, J = 3.9, 6.1, 7.8), 4.72 (dd, 1H, H-5, J = 6.1, 6.1), 7.12–7.23 (m, 3H, Ar), 7.68 (dd, 1H, Ar, J = 1.5, 8.5).

For $C_{15}H_{18}N_2O_2$ anal. calcd. (%): C, 69.74; H, 7.02; N, 10.84.

Found (%): C, 69.55; H, 7.05; N, 10.69.

Methyl (2*S,4*S**,5*R**)-4-cyano-5-phenylpyrrolidine-2-carboxylate (6a).** Yield, 20%; colorless crystals with mp 77°C (lit.: colorless liquid [13]). ^{1}H NMR ($CDCl_3$), δ, ppm: 2.48–2.61 (m, 3H, H-3, NH), 2.83 (q, 1H, H-4, J = 9.0), 3.80 (s, 3H, COOC$\underline{H}_3$), 4.08 (dd, 1H, H-2, J = 8.8, 5.3), 4.37 (d, 1H, H-5, J = 9.0), 7.33–7.42 (m, 3H, Ar), 7.48–7.52 (m, 2H, Ar). ^{13}C NMR ($CDCl_3$), δ, ppm: 34.31, 36.42, 52.54, 58.54, 67.27, 119.76, 126.63 (2C), 128.65, 128.95 (2C), 138.81, 173.68.

For $C_{13}H_{14}N_2O_2$ anal. calcd. (%): C, 67.81; H, 6.13; N, 12.17.

Found (%): C, 67.70; H, 6.18; N, 12.10.

Methyl (2*S,4*S**,5*R**)-4-cyano-5-(2-fluorophenyl)pyrrolidine-2-carboxylate (6b).** Yield, 21%; oily substance. ^{1}H NMR ($CDCl_3$), δ, ppm: 2.49–2.54 (m, 2H, H-3), 2.61 (br s, 1H, NH), 3.01 (q, 1H, H-4, J = 8.1), 3.80 (s, 3H, COOC$\underline{H}_3$), 4.12 (t, 1H, H-2, J = 7.3), 4.71 (d, 1H, H-5, J = 8.1), 7.09 (ddd, 1H, Ar, J = 10.6, 8.3, 0.8), 7.18 (td, 1H, Ar, J = 7.6, 0.8), 7.29–7.36 (m, 1H, Ar), 7.59 (td, 1H, Ar, J = 7.6, 1.5). ^{13}C NMR ($CDCl_3$), δ, ppm: 34.11, 35.11, 52.54, 58.70, 61.05, 115.84 (d, J_{CF} = 21.22), 119.64, 124.68 (d, J_{CF} = 3.7), 125.95 (d, J_{CF} = 12.4), 128.43 (d, J_{CF} = 3.7), 130.12 (d, J_{CF} = 8.1), 160.73 (d, J_{CF} = 246.6), 173.33.

For $C_{13}H_{13}FN_2O_2$ anal. calcd. (%): C, 62.90; H, 5.28; N, 11.28.

Found (%): C, 63.15; H, 5.39; N, 11.18.

Methyl (2*S,4*R**,5*R**)-4-cyano-5-(2-fluorophenyl)-1-methylpyrrolidine-2-carboxylate (7b).** Yield, 97%; colorless crystals with mp 66–68°C. ^{1}H NMR (DMSO-d_6), δ, ppm: 2.16–2.23 (m, 1H, H-3), 2.23 (s, 3H, N–C$\underline{H}_3$), 2.66 (dt, 1H, H-3, J = 13.2., 8.8), 3.39 (dd, 1H, H-4, J = 8.8, 7.1), 3.72 (s, 3H, COOC$\underline{H}_3$), 3.72–3.77 (m, 1H, H-2), 4.09 (d, 1H, H-5, J = 7.1), 7.22 (ddd, 1H, Ar, J = 10.7, 8.1, 1.1), 7.29 (ddd, 1H, Ar, J = 7.6, 1.1, 1.1), 7.36–7.42 (m, 1H, Ar), 7.62 (ddd, 1H, Ar, J = 7.6, 1.7, 1.7).

For $C_{14}H_{15}FN_2O_2$ anal. calcd. (%): C, 64.11; H, 5.76; N, 10.68.

Found (%): C, 64.25; H, 5.79; N, 10.88.

Methyl (2*S,4*R**,5*R**)-5-(2-chlorophenyl)-4-cyano-1,2-dimethylpyrrolidine-2-carboxylate (7e).** Yield, 82%; colorless crystals with mp 95°C. ^{1}H NMR (DMSO-d_6), δ, ppm: 1.32 (s, 3H, CH_3), 2.15 (s, 3H, N-C$\underline{H}_3$), 2.32 (dd, 1H, H-3, J = 12.7, 8.3), 2.47–2.55 (m, 1H, H-3), 3.72 (s, 3H, COOC$\underline{H}_3$), 3.90–3.97 (m, 1H, H–4), 4.35 (d, 1H, H-5, J = 8.1), 7.36 (td, 1H, Ar, J = 7.6, 1.8), 7.41–7.50 (m, 2H, Ar), 7.68 (dd, 1H, Ar, J = 7.6, 1.8).

For $C_{15}H_{17}ClN_2O_2$ anal. calcd. (%): C, 61.54; H, 5.85; N, 9.57.

Found (%): C, 61.36; H, 5.81; N, 9.75.

Methyl (2*S,4*R**,5*R**)-4-cyano-1,2-dimethyl-5-(*o*-tolyl)pyrrolidine-2-carboxylate (7g).** Yield, 81%; colorless crystals with mp 115–117°C. ^{1}H NMR (DMSO-d_6), δ, ppm: 1.31 (s, 3H, CH_3), 2.11 (s, 3H, N–C$\underline{H}_3$), 2.26 (dd, 1H, H-3, J = 8.1, 12.7), 2.31 (s, 3H, ArC$\underline{H}_3$), 2.55 (dd, 1H, H-3, J = 6.1, 12.7), 3.72 (s, 3H, COOC$\underline{H}_3$), 3.81–3.89 (m, 1H, H-4), 4.17 (d, 1H, H-5, J = 7.6), 7.15–7.28 (m, 3H, Ar), 7.56 (d, 1H, Ar, J = 7.6).

For $C_{16}H_{20}N_2O_2$ anal. calcd. (%): C, 70.56; H, 7.40; N, 10.29.

Found (%): C, 70.75; H, 7.35; N, 10.59.

X-ray crystallographic study of 2c. Crystals of **2c** ($C_{14}H_{16}F_1N_1O_4S_1$), FW = 313.35) are monoclinic, space group Cc, a = 14.985(9) Å, b = 10.398(7) Å, c = 10.610(5) Å, β = 117.57(4)°, V = 1465.5(15) Å^3, Z = 4, D_{calc} = 1.420 g/cm^3, CuK_α radiation (λ = 1.54178 Å, graphite monochromator); μ(CuK_α) = 2.218 mm^{-1}, F(000) = 656. The intensities of 2229 reflections (1684 unique reflections, R_{int} = 0.0582) were measured using the ω scan mode in the range 5.40° < θ < 64.93° (–17 ≤ h ≤ 17, –3 ≤ k ≤ 12, –3 ≤ l ≤ 12). The experimental data were corrected for polarization and Lorentz factors [14]. Absorption correction was applied using the azimuthal scan method. The structure was solved by direct methods (SHELX86 [15]). All non-hydrogen atoms were refined by full-matrix anisotropic least-squares calculations on F^2 (SHELXL97 [16]). The H(1) amine atom (Fig. 2) was located from a difference synthesis, and the other hydrogen atoms were placed in calculated positions. All hydrogen atoms were refined as riding on their bonded non-hydrogen atoms. The final residual values were R_1 = 0.1162 and wR_2 = 0.2532 for 976 reflections with $I > 2\sigma(I)$ and 191 refined parameters. The Flack parameters was –0.03(8), $\Delta\rho_{min/max}$ = –1.253/0.631 e/Å^3.

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