A Highly Efficient and Stereoselective Cycloaddition of Nitrones to *N*-Vinylpyrroles

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Abstract: 1,3-Dipolar cycloadditions of a number of *C*-aryl, *C*-carbamoyl-, and *C*,*C*-bis(methoxycarbonyl)nitrones and substituted *N*-vinylpyrroles proceed with high efficiency and regioselectivity with the formation of only one isomeric substituted 5-(1*H*-pyrrol-1-yl)isoxazolidine cycloadduct.

Key words: pyrroles, nitrones, isoxazolidines, cycloaddition, stereoselectivity

1,3-Dipolar cycloaddition is as one of the most powerful tools to create five-membered *N*,*O*-heterocycles. In particular, dipolar cycloaddition of nitrones as 1,3-dipoles to C=C bonds of different alkenes allows access to a variety of isoxazolidines. These cycloadducts have attracted considerable attention due to the potential biological activity of isoxazolidines, and as promising precursors for the synthesis of such natural products as β-lactam antibiotics and alkaloids through reductive cleavage of the N–O bond.[1] Earlier, it was shown that the regio- and stereoselectivity of the reaction of nitrones with cyclopropenes and methylenecyclopropanes substantially depends on substitution on the double bond.[2]

Pyrroles and its derivatives are amongst the most important fundamental structural units of biologically and physiologically active molecules such as chlorophyll, porphyrins, hemoglobin, vitamin B_{12} and others.[3] The development of synthetic strategies for the preparation of pyrrolyl- or indolyl-triazoles, as well as pyrrolyl-imidazole ensembles, remains the subject of a steadily growing number of investigations.[4,5]

Herein, we disclose an efficient method for the synthesis of isoxazolidines, containing a pyrrolyl substituent at position 5. The method comprises the 1,3-dipolar cycloaddition of nitrones to the double bond of 2-phenyl-1-vinyl-1*H*-pyrrole (**1**), 2-(thien-2-yl)-1-vinyl-1*H*-pyrrole (**2**), and 1-vinyl-4,5,6,7-tetrahydro-1*H*-indole (**3**), easily available via the Trofimov reaction.[6] It was found that *C*,*N*-diarylnitrones **4a**–**d** and *N*-aryl-*C*-carbamoylnitrones **5a**–**d** reacted with vinylpyrroles **1**–**3** in toluene at reflux (110 °C) for 9–15 hours with high regio- and stereoselectivity to give *cis*- and *trans*-5-(pyrrol-1-yl)isoxazolidines **6** and **7** only (Table 1 and Table 2).

Stereoselectivity of the reaction of *C*,*N*-diarylnitrone **4a** with pyrrole **2** is lower and diastereomers **6i** and **6i′** are obtained in a ratio of 10:1.5. Reactions of *N*-methylnitrone **4e** with pyrroles **1**–**3** require prolonged heating (30–100 h) and they afford modest yields of products, in these cases the starting *N*-vinylpyrroles were recovered (30–40%); the ratio of diastereomers **6j**–**l** and **6j′**–**l′** is close to unity. Analysis of the reaction mixture of *N*-methylnitrone **4e** and pyrrole **1** after 40, 100, and 140 hours of heating shows that the ratio of diastereomers does not change. The structure of products **6a**–**l** and **6j′**–**l′** were established on the basis of their spectral data. The *cis* orientation of substituents in adducts **6a**–**j** was established on the basis of the comparison of chemical shifts and coupling constants between isoxazolidine protons and confirmed by X-ray crystal structure analysis of compound **6d** (Figure 1).[7]

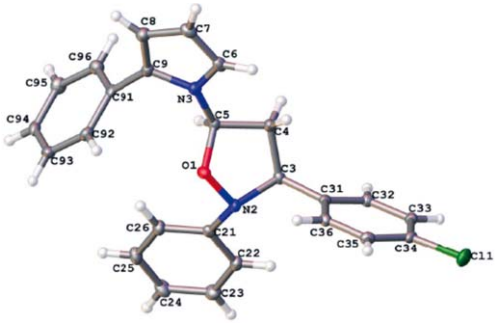

Figure 1 X-ray crystal structure of **6d**

The reactions of pyrroles **1**–**3** with *C*-carbamoylnitrones **5a**–**d** require significantly shorter reaction times (6 h) compared with nitrones **4a**–**e** and usually give better yields of cycloadducts (Table 2).

The reaction of nitrones **5a** and **5d** with 2-(thien-2-yl)pyrrole **2** afford two diastereomers **7i**,**j** and **7i′**,**j′** in a 10:1 ratio. The structure of products **7a**–**j** was established on the basis of their spectral data and X-ray crystal structure data for compound **7g** (Figure 2).[7] From the data obtained, the main isomers of the products **7a**–**j** have a *cis* relationship

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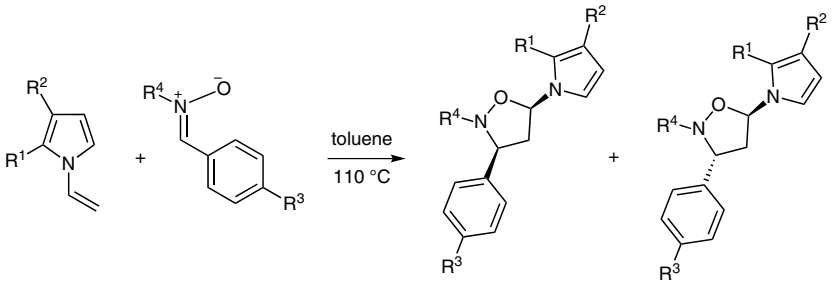
Table 1 Cycloaddition between Nitrones **4a–e** and *N*-Vinylpyrroles **1–3**



1–3 **4a–e** **6a–l** **6i′–l′**

Pyrrole	Nitrone	R^1	R^2	R^3	R^4	Time (h)	Product	Yield (%)	Ratio[a] (*cis*/*trans*)
1	**4a**	Ph	H	H	Ph	15	**6a**	81	>20:1
1	**4b**	Ph	H	Me	Ph	15	**6b**	90	>20:1
1	**4c**	Ph	H	OMe	Ph	15	**6c**	85	>20:1
1	**4d**	Ph	H	Cl	Ph	15	**6d**	80	>20:1
3	**4a**	$(CH_2)_4$		H	Ph	11	**6e**	95	>20:1
3	**4b**	$(CH_2)_4$		Me	Ph	15	**6f**	78	>20:1
3	**4c**	$(CH_2)_4$		OMe	Ph	11	**6g**	79	>20:1
3	**4d**	$(CH_2)_4$		Cl	Ph	9	**6h**	59	>20:1
2	**4a**	2-thienyl	H	H	Ph	9	**6i**/**6i′**	87 (57[b])	10:1.5
1	**4e**	Ph	H	Cl	Me	30	**6j**/**6j′**	30[b]	10:7
3	**4e**	$(CH_2)_4$		Cl	Me	100	**6k**/**6k′**	57[b]	10:6
2	**4e**	2-thienyl	H	Cl	Me	35	**6l**, **6l′**	28[b]	10:8

[a] From ^{1}H NMR analysis of the crude reaction mixture.
[b] Isolated yield of pure *cis* isomer.

between the substituents in the 3- and 5-positions on the isoxazolidine ring.

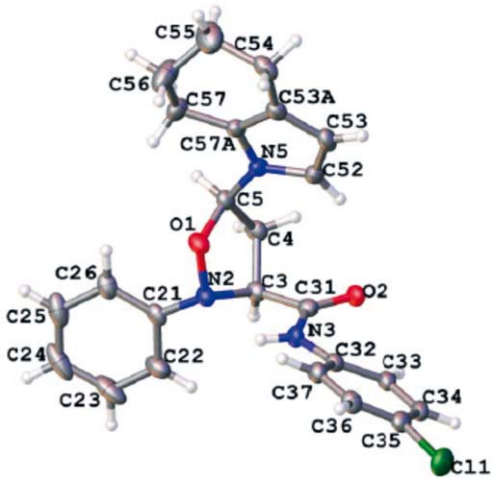


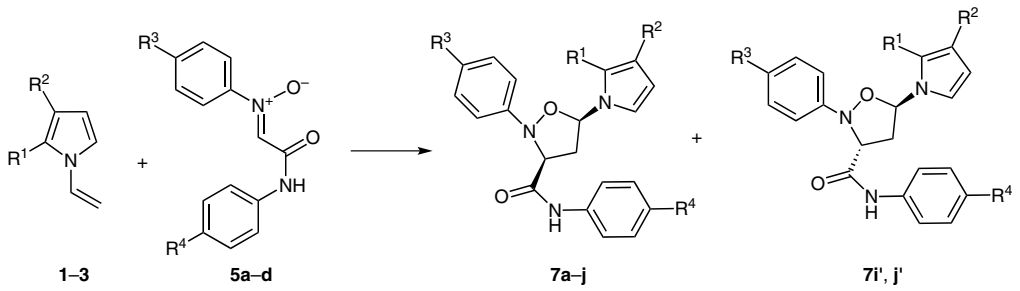
Figure 2 X-ray crystal structure of **7g**

The reaction of nitrones **5a–d** with pyrroles **1–3** under microwave heating requires substantially shorter time and gives the same ratio of diastereomers. The increased steric hindrance of N,C,C-trisubstituted nitrones may cause inversion of the regioselectivity of the 1,3-dipolar cycloaddition reaction,[8] but in our case the reaction of pyrroles **1–3** with *N*-aryl-*C*,*C*-bis(methoxycarbonyl)nitrones **8a–c** affords only 5-(pyrrol-1-yl)isoxazolidines **9a–g** in high yields (Table 3).

Cleavage of the N–O bond is the most synthetically useful reaction for the modification of the obtained cycloadducts, which can be done by a variety of methods, including hydrogenation over Raney nickel, Pd/C, or $Pd(OH)_2$,[9–13] reaction with Zn/H^+,[9,10,14] $Mo(CO)_6/H_2O$,[15] $Zn/Cu(OAc)_2$/AcOH,[16] and SmI_2.[17] As an illustration, in our studies (Scheme 1), adducts **6c** and **7c** were hydrogenated on $Pd/CaCO_3$ to give 1,3-amino alcohols **10a**,**b** in good isolated yields (~66–95%).

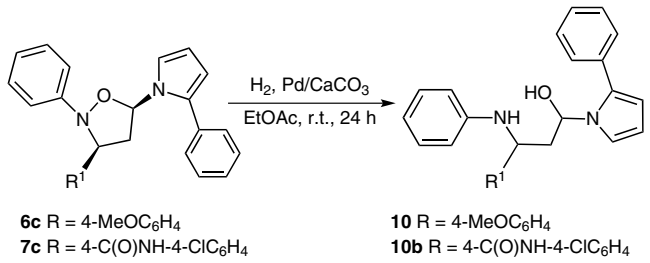
The basic treatment of isoxazolidines suitably activated at the 3-position of the ring has been exploited for a synthetic approach to 3-(alkylamino)furan-2(5*H*)-ones, versatile synthons for β-lactams[18,19] and (or) β-enaminones.[20] Treatment of isoxazolidines **7c**,**d** with sodium hydride or tetrabutylammonium fluoride led to the formation of com-

Table 2 Cycloaddition between Nitrones **5a–d** and *N*-Vinylpyrroles **1–3**

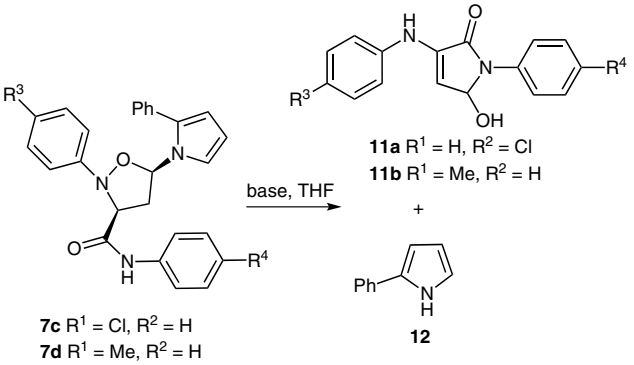


Pyrrole	Nitrone	R^1	R^2	R^3	R^4	Product	Yield (%) Conventional heating[a]	MW[b]	Ratio[c] *cis*/*trans*
1	**5a**	Ph	H	H	H	**7a**	82	89[d]	>20:1
1	**5b**	Ph	H	H	Me	**7b**	84	97[d]	>20:1
1	**5c**	Ph	H	H	Cl	**7c**	91	93[e]	>20:1
1	**5d**	Ph	H	Me	H	**7d**	85	94[d]	>20:1
3	**5a**	$(CH_2)_4$		H	H	**7e**	82	97[e]	>20:1
3	**5b**	$(CH_2)_4$		H	Me	**7f**	80	83[e]	>20:1
3	**5c**	$(CH_2)_4$		H	Cl	**7g**	85	93[d]	>20:1
3	**5d**	$(CH_2)_4$		Me	H	**7h**	87	93[e]	>20:1
2	**5a**	2-thienyl	H	H	H	**7i**/**7i′**	92 (55[d])	–	10:1
2	**5d**	2-thienyl	H	Me	H	**7j**/**7j′**	84 (72[d])	–	10:1

[a] Toluene, 110 °C, 6 h.
[b] Microwave, toluene–chlorobenzene (3:1), 100 °C, 40 min.
[c] From ^{1}H NMR analysis of the crude reaction mixture.
[d] Isolated yield of pure *cis* isomer.
[e] Spectroscopic (NMR) yield.



Scheme 1 Hydrogenation of isoxazolidines **6c** and **7c**



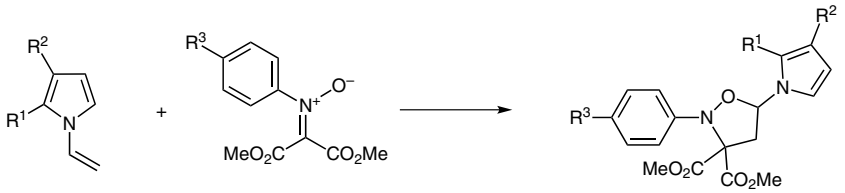
Scheme 2 The treatment of isoxazolidines **7c**,**d** with base

pounds **11a**,**b** (55–75% yield) and 2-phenyl-1*H*-pyrrole (**12**) (Scheme 2).[21]

In summary, we have demonstrated that the reaction between *C*,*N*-diaryl-, *N*-aryl-*C*-carbamoyl-, and *C*,*C*-bis(methoxycarbonyl)nitrones with 2-phenyl-1-vinyl-1*H*-pyrrole, 2-(thien-2-yl)-1-vinyl-1*H*-pyrrole, and 1-vinyl-4,5,6,7-tetrahydro-1*H*-indole proceeds as a normal 1,3-dipolar cycloaddition with high regioselectivity to give only 5-(pyrrol-1-yl)isoxazolidines in good yields. The hydrogenation of the obtained cycloadducts led to 1,3-amino alcohols and the treatment of the isoxazolidines by a base afforded 3-(arylamino)-5-hydroxy-1,5-dihydro-2*H*-pyrrol-2-ones.

All reactions were performed in anhydrous solvents under an argon atmosphere. Toluene was distilled from Na metal/benzophenone. Reaction progress was monitoring using TLC on precoated Silufol UV–254 plates. The IR spectra were measured on a Bruker Tensor 27 spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using a Bruker DPX-300 spectrometer or Bruker Avance

Table 3 Cycloaddition between Nitrones **8a–c** and *N*-Vinylpyrroles **1–3**



1–3 **8a–c** **9a–g**

Pyrrole	Nitrone	R^1	R^2	R^3	Time (h)	Product	Yield (%) Conventional heating[a]	MW[b]
1	**8a**	Ph	H	H	7	**9a**	78	91[c]
1	**8b**	Ph	H	Me	7	**9b**	80	88[d]
1	**8c**	Ph	H	Cl	7	**9c**	90	89[c]
3	**8a**	$(CH_2)_4$		H	15	**9d**	92	91[d]
3	**8b**	$(CH_2)_4$		Me	7	**9e**	87	95[c]
3	**8c**	$(CH_2)_4$		Cl	7	**9f**	87	95[c]
2	**8a**	2-thienyl	H	H	5	**9g**	94	–

[a] Toluene, 110 °C.
[b] Microwave, toluene–chlorobenzene (3:1), 100 °C, 40 min.
[c] Spectroscopic (NMR) yield.
[d] Isolated yield of pure *cis* isomer.

400. HRMS spectra were obtained with a Bruker-microTOF and Bruker-maXis (QTOF). In microwave experiments used the Discover SP DC7299 apparatus. Nitrones were prepared using known procedures.[22]

Cycloaddition Reactions; General Procedure
A mixture of nitrone (1.0 mmol) and *N*-vinylpyrrole (1.3 mmol) in toluene (5 mL) was heated at reflux until TLC showed complete consumption of the nitrone (see Tables 1–3). The solvent was evaporated under reduced pressure, and the residue was subjected to column chromatography (silica gel, petroleum ether–EtOAc) followed by crystallization (EtOH) to give the product. In some cases (MW irradiation), the product was not isolated, and the yield was calculated on the basis of ^{1}H NMR spectra of the reaction mixture using 1,1,2,2-tetrachloroethane as an internal standard.

2,3-Diphenyl-5-(2-phenyl-1*H*-pyrrol-1-yl)isoxazolidine (6a)
Prepared from nitrone **4a** and pyrrole **1** as a white solid; yield: 296 mg (81%); mp 142–143 °C; R_f = 0.50 (9% EtOAc–hexane).

IR (KBr): 3140, 3104, 3060, 3032, 2989, 2951, 1597, 1486, 1464, 1442, 1411, 1296, 1241, 762, 698 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.85 (ddd, *J* = 13.0, 6.7, 6.3 Hz, 1 H), 3.23 (ddd, *J* = 13.0, 7.8, 7.4 Hz, 1 H), 4.83 (dd, *J* = 7.8, 6.7 Hz, 1 H), 6.20 (dd, *J* = 7.4, 6.3 Hz, 1 H), 6.23–6.30 (m, 2 $H_{pyrrole}$), 6.95–7.04 (m, 4 H_{arom}), 7.18–7.30 (m, 2 H_{arom}), 7.35–7.68 (m, 10 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.9 (CH_2), 70.3 (CH), 84.0 (CH), 109.9 (CH), 110.2 (CH), 116.5 (2 CH), 119.5 (CH), 123.2 (CH), 127.0 (2 CH), 127.9 (CH), 128.2 (CH), 128.9 (2 CH), 129.2 (2 CH), 129.4 (2 CH), 129.9 (2 CH), 133.2 (C), 135.8 (C), 141.0 (C), 150.0 (C).

Anal. Calcd for $C_{25}H_{22}N_2O$: C, 81.94; H, 6.05; N, 7.64. Found: C, 81.83; H, 6.10; N, 7.57.

2-Phenyl-5-(2-phenyl-1*H*-pyrrol-1-yl)-3-(*p*-tolyl)isoxazolidine (6b)
Prepared from nitrone **4b** and pyrrole **1** as a white solid; yield: 342 mg (90%); mp 132–133 °C; R_f = 0.53 (9% EtOAc–hexane).

IR (KBr): 3138, 3097, 3050, 3024, 2968, 2951, 2921, 2876, 1597, 1489, 1464, 1405, 1294, 1237, 762, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.42 (s, 3 H, CH_3), 2.84 (ddd, *J* = 13.0, 6.7, 6.3 Hz, 1 H), 3.20 (ddd, *J* = 13.0, 7.8, 7.4 Hz, 1 H), 4.76 (dd, *J* = 7.8, 6.7 Hz, 1 H), 6.18 (dd, *J* = 7.4, 6.3 Hz, 1 H), 6.22–6.32 (m, 2 $H_{pyrrole}$), 6.90–7.05 (m, 4 H_{arom}), 7.15–7.25 (m, 4 H_{arom}), 7.35–7.55 (m, 7 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.6 (CH_3), 46.1 (CH_2), 70.2 (CH), 83.9 (CH), 109.9 (CH), 110.1 (CH), 116.7 (2 CH), 119.6 (CH), 123.2 (CH), 127.0 (2 CH), 127.8 (CH), 128.9 (2 CH), 129.1 (2 CH), 129.9 (2 CH), 130.1 (2 CH), 133.2 (C), 135.8 (C), 137.9 (2 C), 150.7 (C).

HRMS (ESI): *m*/*z* $[M + K]^+$ calcd for $C_{26}H_{24}KN_2O$: 419.1520; found: 419.1503.

3-(4-Methoxyphenyl)-2-phenyl-5-(2-phenyl-1*H*-pyrrol-1-yl)isoxazolidine (6c)
Prepared from nitrone **4c** and pyrrole **1** as a white solid; yield: 336 mg (85%); mp 117–118 °C; R_f = 0.35 (9% EtOAc–hexane).

IR (KBr): 3095, 3073, 3022, 2976, 2939, 2874, 2843, 1598, 1510, 1491, 1465, 1294, 1244, 1172, 756, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.84 (ddd, *J* = 13.0, 6.7, 6.3 Hz, 1 H), 3.19 (ddd, *J* = 13.0, 7.8, 7.4 Hz, 1 H), 3.88 (s, 3 H, OCH_3), 4.74 (dd, *J* = 7.8, 6.7 Hz, 1 H), 6.19 (dd, *J* = 7.4, 6.3 Hz, 1 H), 6.25–6.32 (m, 2 $H_{pyrrole}$), 6.85–7.05 (m, 6 H_{arom}), 7.20–7.30 (m, 2 H_{arom}), 7.35–7.55 (m, 7 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.1 (CH_2), 55.8 (OCH_3), 70.1 (CH), 83.9 (CH), 109.9 (CH), 110.1 (CH), 114.8 (2 CH), 116.8 (2 CH), 119.6 (CH), 123.3 (CH), 127.8 (CH), 128.3 (2 CH), 128.9 (2

CH), 129.1 (2 CH), 129.9 (2 CH), 132.8 (C), 133.3 (C), 135.8 (C), 150.6 (C), 159.6 (C).

Anal. Calcd for $C_{26}H_{24}N_2O_2$: C, 78.76; H, 6.10; N, 7.07. Found: C, 78.58; H, 6.14; N, 7.06.

3-(4-Chlorophenyl)-2-phenyl-5-(2-phenyl-1*H*-pyrrol-1-yl)isoxazolidine (6d)

Prepared from nitrone **4d** and pyrrole **1** as a white solid; yield: 320 mg (80%); mp 152–153 °C; R_f = 0.48 (9% EtOAc–hexane).

IR (KBr): 3140, 3063, 3043, 2990, 2952, 1597, 1488, 1463, 1347, 1296, 1240, 762, 693 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.79 (ddd, *J* = 13.0, 6.7, 6.3 Hz, 1 H), 3.21 (ddd, *J* = 13.0, 7.8, 7.4 Hz, 1 H), 4.81 (dd, *J* = 7.8, 6.7 Hz, 1 H), 6.19 (dd, *J* = 7.4, 6.3 Hz, 1 H), 6.22–6.32 (m, 2 $H_{pyrrole}$), 6.90 (s, 1 $H_{pyrrole}$), 6.95–7.05 (m, 3 H_{arom}), 7.20–7.30 (m, 2 H_{arom}), 7.40–7.55 (m, 9 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.9 (CH_2), 69.6 (CH), 84.1 (CH), 110.0 (CH), 110.3 (CH), 116.4 (2 CH), 119.4 (CH), 123.5 (CH), 127.9 (CH), 128.4 (2 CH), 129.0 (2 CH), 129.3 (2 CH), 129.6 (2 CH), 129.9 (2 CH), 133.1 (C), 134.0 (C), 135.9 (C), 139.7 (C), 150.4 (C).

Anal. Calcd for $C_{25}H_{21}ClN_2O$: C, 74.90; H, 5.28; N, 6.99. Found: C, 74.97; H, 5.35; N, 6.97.

1-(2,3-Diphenylisoxazolidin-5-yl)-4,5,6,7-tetrahydro-1*H*-indole (6e)

Prepared from nitrone **4a** and pyrrole **3** as a white solid; yield: 326 mg (95%); mp 98–99 °C; R_f = 0.39 (9% EtOAc–hexane).

IR (KBr): 3127, 3089, 3059, 3028, 3001, 2923, 2844, 1598, 1483, 1446, 1372, 1294, 1019, 891, 739, 692 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.72–1.84 (m, 2 H, CH_2), 1.85–1.99 (m, 2 H, CH_2), 2.48–2.69 (m, 3 H), 2.71–2.88 (m, 2 H, CH_2), 3.18–3.29 (m, 1 H), 4.84–4.95 (m, 1 H), 5.94 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.02–6.09 (m, 1 H), 6.67 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.98–7.11 (m, 3 H_{arom}), 7.23–7.51 (m, 5 H_{arom}), 7.60 (d, *J* = 7.0 Hz, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.9 (CH_2), 23.1 (CH_2), 23.2 (CH_2), 23.5 (CH_2), 44.4 (CH_2), 69.9 (CH), 83.0 (CH), 108.7 (CH), 115.2 (2 CH), 116.2 (CH), 118.8 (C), 122.3 (CH), 126.5 (2 CH), 127.7 (CH), 128.5 (C), 128.9 (2 CH), 129.0 (2 CH), 141.3 (C), 151.0 (C).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{25}N_2O$: 345.1961; found: 345.1956.

1-[2-Phenyl-3-(*p*-tolyl)isoxazolidin-5-yl]-4,5,6,7-tetrahydro-1*H*-indole (6f)

Prepared from nitrone **4b** and pyrrole **3** as a white solid; yield: 279 mg (78%); mp 96–97 °C; R_f = 0.54 (9% EtOAc–hexane).

IR (KBr): 3122, 3096, 3070, 3035, 2999, 2928, 2849, 2832, 1597, 1485, 1437, 1293, 1206, 793, 759 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.71–1.83 (m, 2 H, CH_2), 1.84–1.97 (m, 2 H, CH_2), 2.41 (s, 3 H, CH_3), 2.49–2.59 (m, 2 H, CH_2), 2.59–2.69 (m, 1 H), 2.70–2.87 (m, 2 H, CH_2), 3.20 (ddd, *J* = 13.4, 7.8, 7.4 Hz, 1 H), 4.84 (t, *J* = 7.8 Hz, 1 H), 5.97–6.08 (m, 2 H, H + $H_{pyrrole}$), 6.71 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.96–7.05 (m, 1 H_{arom}), 7.06 (d, *J* = 7.8 Hz, 2 H_{arom}), 7.20–7.31 (m, 4 H_{arom}), 7.47 (d, *J* = 7.8 Hz, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.1 (CH_3), 21.9 (CH_2), 23.0 (CH_2), 23.2 (CH_2), 23.5 (CH_2), 44.6 (CH_2), 69.8 (CH), 82.9 (CH), 108.6 (CH), 115.2 (2 CH), 116.3 (CH), 118.7 (C), 122.2 (CH), 126.4 (2 CH), 128.5 (C), 128.8 (2 CH), 129.6 (2 CH), 137.3 (C), 138.2 (C), 151.0 (C).

Anal. Calcd for $C_{24}H_{26}N_2O$: C, 80.41; H, 7.31; N, 7.81. Found: C, 80.20; H, 7.34; N, 7.66.

1-[3-(4-Methoxyphenyl)-2-phenylisoxazolidin-5-yl]-4,5,6,7-tetrahydro-1*H*-indole (6g)

Prepared from nitrone **4c** and pyrrole **3** as a yellowish solid; yield: 295 mg (79%); mp 114–117 °C; R_f = 0.22 (9% EtOAc–hexane).

IR (KBr): 3073, 3040, 2997, 2938, 2833, 1597, 1513, 1485, 1440, 1304, 1246, 1177, 1036, 798, 760 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.72–1.88 (m, 2 H, CH_2), 1.85–1.99 (m, 2 H, CH_2), 2.51–2.69 (m, 3 H), 2.73–2.86 (m, 2 H, CH_2), 3.19 (ddd, *J* = 13.0, 7.8, 7.4 Hz, 1 H), 3.87 (s, 3 H, OCH_3), 4.79–4.88 (m, 1 H), 6.02 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.02–6.09 (m, 1 H), 6.72 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.98 (d, *J* = 8.5 Hz, 2 H_{arom}), 6.98–7.10 (m, 3 H_{arom}), 7.24–7.32 (m, 2 H_{arom}), 7.50 (d, *J* = 8.5 Hz, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.9 (CH_2), 23.1 (CH_2), 23.2 (CH_2), 23.5 (CH_2), 44.6 (CH_2), 55.3 (CH_3), 69.6 (CH), 82.9 (CH), 108.6 (CH), 114.3 (2 CH), 115.4 (2 CH), 116.2 (CH), 118.7 (C), 122.3 (CH), 127.7 (2 CH), 128.5 (C), 128.8 (2 CH), 133.1 (C), 150.9 (C), 159.1 (C).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{27}N_2O_2$: 413.1626; found: 413.1618.

1-[3-(4-Chlorophenyl)-2-phenylisoxazolidin-5-yl]-4,5,6,7-tetrahydro-1*H*-indole (6h)

Prepared from nitrone **4d** and pyrrole **3**; grey solid; yield: 223 mg (59%); mp 152–154 °C; R_f = 0.34 (9% EtOAc–hexane).

IR (KBr): 3059, 2996, 2936, 2835, 1597, 1488, 1440, 1370, 1296, 1205, 796, 760 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.75–1.84 (m, 2 H, CH_2), 1.84–1.93 (m, 2 H, CH_2), 2.50–2.69 (m, 3 H, CH_2 + $CHCH_2CH$), 2.71–2.80 (m, 2 H, CH_2), 3.22 (ddd, *J* = 13.4, 8.2, 7.4 Hz, 1 H, $CHCH_2CH$), 4.89 (t, *J* = 7.4 Hz, 1 H, $CHCH_2CH$), 6.02 (d, *J* = 2.6 Hz, 1 $H_{pyrrole}$,), 6.02–6.09 (m, 1 H, $CHCH_2CH$), 6.61 (d, *J* = 2.6 Hz, 1 $H_{pyrrole}$), 7.00–7.07 (m, 3 H_{arom}), 7.26–7.32 (m, 2 H_{arom}), 7.42 (d, *J* = 8.5 Hz, 2 H_{arom}), 7.53 (d, *J* = 8.5 Hz, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8 (CH_2), 23.0 (CH_2), 23.2 (CH_2), 23.5 (CH_2), 44.1 (CH_2), 69.2 (CH), 83.0 (CH), 108.9 (CH), 115.1 (2 CH), 116.1 (CH), 118.9 (C), 122.5 (CH), 127.9 (2 CH), 128.6 (C), 129.0 (2 CH), 129.1 (2 CH), 133.4 (C), 139.8 (C), 150.8 (C).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{24}ClN_2O$: 379.1572; found: 379.1575.

2,3-Diphenyl-5-[2-(thiophen-2-yl)-1*H*-pyrrol-1-yl]isoxazolidine (6i/6i′)

Prepared from nitrone **4a** and pyrrole **2**; yield: 301 mg (87%). Crystallization (EtOH) gave *cis*-isomer **6i** as a grey solid; yield: 212 mg (57%); mp 114–115 °C; R_f = 0.51 (20% EtOAc–hexane).

IR (KBr): 3142, 3064, 3033, 2986, 2950, 1597, 1486, 1465, 1411, 1290, 764, 702 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ (major isomer) = 2.85 (ddd, *J* = 13.3, 7.0, 5.5 Hz, 1 H), 3.29 (dt, *J* = 13.3, 8.1 Hz, 1 H), 4.75–4.84 (m, 1 H), 6.26 (t, *J* = 3.3 Hz, 1 H_{arom}), 6.31–6.36 (m, 2 H, H + H_{arom}), 6.99–7.07 (m, 4 H_{arom}), 7.12–7.20 (m, 2 H_{arom}), 7.21–7.27 (m, 2 H_{arom}), 7.35–7.41 (m, 2 H_{arom}), 7.41–7.47 (m, 2 H_{arom}), 7.56–7.61 (m, 2 H_{arom}).

^1H NMR (400 MHz, $CDCl_3$): δ (minor isomer) = 2.91 (dt, *J* = 13.6, 7.3 Hz, 1 H), 3.26–3.33 (m, 1 H), 4.99–5.08 (m, 1 H), 6.16 (t, *J* = 3.3 Hz, 1 H_{arom}), 6.37 (dd, *J* = 3.5, 1.7 Hz, 1 H_{arom}), 6.41 (dd, *J* = 7.3, 3.4 Hz, 1 H), 6.86–6.95 (m, 4 H_{arom}), 7.12–7.20 (m, 2 H_{arom}), 7.32–7.35 (m, 2 H_{arom}), 7.35–7.41 (m, 2 H_{arom}), 7.41–7.47 (m, 2 H_{arom}), 7.51–7.55 (m, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ (major isomer) = 45.6 (CH_2), 69.7 (CH), 83.3 (CH), 109.6 (CH), 111.4 (CH), 116.3 (2 CH), 119.8 (CH), 122.9 (CH), 125.8 (CH), 126.6 (2 CH), 127.0 (CH), 127.1

(C), 127.4 (CH), 127.8 (CH), 128.7 (2 CH), 129.0 (2 CH), 133.8 (C), 140.4 (C), 150.1 (C).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{21}N_2OS$: 373.1369; found: 373.1372.

3-(4-Chlorophenyl)-2-methyl-5-(2-phenyl-1*H*-pyrrol-1-yl)isoxazolidine (6j)

Prepared from nitrone **4e** and pyrrole **1** as a white solid; yield: 100 mg (30%); mp 102–103 °C; R_f = 0.47 (9% EtOAc–hexane).

IR (KBr): 3104, 3062, 2992, 2958, 2865, 2847, 1600, 1491, 1467, 1400, 1287, 1234, 700 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.65 (s, 3 H, CH_3), 2.67–2.79 (m, 1 H), 3.16 (dt, *J* = 13.7, 8.0 Hz, 1 H), 3.63 (dd, *J* = 10.0, 8.0 Hz, 1 H), 6.07 (dd, *J* = 8.0, 4.8 Hz, 1 H), 6.22–6.30 (m, 1 $H_{pyrrole}$), 6.33–6.39 (m, 1 $H_{pyrrole}$), 7.22–7.47 (m, 10 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 43.4 (CH_3), 48.0 (CH_2), 73.3 (CH), 82.7 (CH), 109.5 (CH), 109.9 (CH), 119.5 (CH), 127.5 (CH), 128.9 (2 CH), 129.3 (2 CH), 129.6 (2 CH), 129.8 (2 CH), 133.4 (C), 134.4 (C), 135.3 (C), 136.6 (C).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{20}H_{20}ClN_2O$: 339.1259; found: 339.1261.

1-[3-(4-Chlorophenyl)-2-methylisoxazolidin-5-yl]-4,5,6,7-tetrahydro-1*H*-indole (6k, 6k′)

Prepared from nitrone **4e** and pyrrole **3** as an oil, mixture of diastereomers; yield: 180 mg (57%); R_f = 0.28 (17% EtOAc–hexane).

IR (KBr): 3093, 2991, 2927, 2865, 2847, 1492, 1458, 1367, 1293, 1090, 1014, 829 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ (mixture of isomers) = 1.70–1.82 (m, 3.2 H, major + minor), 1.82–1.95 (m, 3.2 H, major + minor), 2.48–2.57 (m, 3.2 H, major + minor), 2.57–2.76 (m, 4.8 H, major + minor), 2.61 (s, 3 H, CH_3, major), 2.64 (s, 1.8 H, CH_3, minor), 2.86–2.96 (m, 0.6 H, minor), 3.15 (dt, *J* = 13.6, 7.9 Hz, 1 H, major), 3.64 (dd, *J* = 9.6, 7.9 Hz, 1 H, major), 3.80–3.90 (m, 0.6 H, minor), 5.93 (dd, *J* = 7.9, 5.0 Hz, 1 H, major), 5.98 (dd, *J* = 8.3, 4.2 Hz, 0.6 H, minor), 6.06 (d, *J* = 3.0 Hz 1 $H_{pyrrole}$, major), 6.08 (d, *J* = 2.9 Hz, 0.6 $H_{pyrrole}$, minor), 6.85 (д, *J* = 2.9 Hz, 0.6 $H_{pyrrole}$, minor), 7.04 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$, major), 7.34–7.45 (m, 6.4 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ (major isomer) = 21.9 (CH_2), 23.1 (CH_2), 23.2 (CH_2), 23.5 (CH_2), 43.0 (CH_3), 46.3 (CH_2), 72.8 (CH), 81.4 (CH), 108.2 (CH), 116.2 (CH), 118.3 (C), 128.0 (C), 128.8 (2 CH), 129.1 (2 CH), 133.9 (C), 136.5 (C).

^{13}C NMR (100 MHz, $CDCl_3$): δ (minor isomer) = 21.9 (CH_2), 23.1 (CH_2), 23.2 (CH_2), 23.5 (CH_2), 43.0 (CH_3), 45.1 (CH_2), 72.1 (CH), 82.0 (CH), 108.8 (CH), 115.5 (CH), 118.7 (C), 128.4 (C), 129.0 (2 CH), 129.0 (2 CH), 134.0 (C), 136.8 (C).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{22}ClN_2O$: 317.1415; found: 317.1406.

3-(4-Chlorophenyl)-2-methyl-5-[2-(thiophen-2-yl)-1*H*-pyrrol-1-yl]isoxazolidine (6l)

Prepared from nitrone **4e** and pyrrole **2** as an oil; yield: 96 mg (28%); R_f = 0.42 (9% EtOAc–hexane).

IR (KBr): 3102, 2992, 2960, 2916, 2872, 2849, 1492, 1463, 1433, 1411, 1282, 1014, 701 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.65 (s, 3 H), 2.65–2.74 (m, 1 H), 3.18 (dt, *J* = 13.6, 7.9 Hz, 1 H), 3.64 (dd, *J* = 9.8, 7.9 Hz, 1 H), 6.19 (dd, *J* = 7.9, 4.7 Hz, 1 H), 6.30–6.34 (m, 2 $H_{pyrrole}$), 7.03–7.08 (m, 1 H_{arom}), 7.08–7.13 (m, 1 H_{arom}), 7.31–7.35 (m, 1 H_{arom}), 7.38–7.47 (m, 5 H_{arom}).

^{1}H NMR (400 MHz, $CDCl_3$): δ (minor isomer **6l′**) = 2.66 (s, 3 H), 2.68–2.81 (m, 1 H), 2.91 (ddd, *J* = 13.5, 7.2, 3.6 Hz, 1 H), 3.85–4.05 (s, 1 H), 6.23 (dd, *J* = 8.4, 3.6 Hz, 1 H), 6.34–6.37 (m, 2 $H_{pyrrole}$), 7.09–7.15 (m, 1 H_{arom}), 7.16–7.21 (m, 2 H_{arom}), 7.33–7.44 (m, 5 H_{arom}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 43.0 (CH_3), 47.5 (CH_2), 72.8 (CH), 82.2 (CH), 109.4 (CH), 110.9 (CH), 119.6 (CH), 125.6 (CH), 126.6 (CH), 126.7 (C), 127.4 (CH), 128.8 (2 CH), 129.1 (2 CH), 134.0 (C), 134.2 (C), 136.2 (C).

^{13}C NMR (100 MHz, $CDCl_3$): δ (minor isomer **6l′**) = 43.1 (CH_3), 72.8 (CH), 82.5 (CH), 109.9 (CH), 111.2 (CH), 118.6 (CH), 125.6 (CH), 126.6 (CH), 127.5 (CH), 129.0 (2 CH), 129.0 (2 CH), 133.6 (C), 134.0 (C), 136.4 (C). Some signals overlapped with signals of major isomer **6l**.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{18}ClN_2OS$: 345.0823; found: 345.0826.

***N*,2-Diphenyl-5-(2-phenyl-1*H*-pyrrol-1-yl)isoxazolidine-3-carboxamide (7a)**

Prepared from nitrone **5a** and pyrrole **1** as a white solid; yield: 350 mg (82%); mp 138–139 °C; R_f = 0.45 (20% EtOAc–hexane).

IR (KBr): 3341, 3135, 3059, 3032, 2963, 1685, 1599, 1524, 1490, 1442, 1307, 1243, 758 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.91 (ddd, *J* = 13.7, 9.0, 8.5 Hz, 1 H), 3.26 (ddd, *J* = 13.7, 5.2, 2.6 Hz, 1 H), 4.67 (dd, *J* = 9.0, 2.6 Hz, 1 H), 6.17 (dd, *J* = 8.5, 5.2 Hz, 1 H), 6.27 (m, 1 $H_{pyrrole}$), 6.30 (m, 1 $H_{pyrrole}$), 7.05–7.12 (m, 4 H_{arom}), 7.14–7.20 (m, 1 H_{arom}), 7.30–7.60 (m, 9 H_{arom}), 7.72 (d, *J* = 8.0 Hz, 2 H_{arom}), 9.16 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 36.6 (CH_2), 70.3 (CH), 85.3 (CH), 110.4 (CH), 111.1 (CH), 115.0 (CH), 119.0 (CH), 120.5 (2 CH), 124.1 (CH), 125.3 (CH), 128.2 (CH), 128.9 (2 CH), 129.2 (2 CH), 129.5 (2 CH), 129.9 (2 CH), 130.0 (CH), 132.9 (C), 136.2 (C), 137.5 (C), 149.4 (C), 169.1 (CO).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{23}N_3O_2$: 410.1863; found: 410.1865.

2-Phenyl-5-(2-phenyl-1*H*-pyrrol-1-yl)-*N*-(*p*-tolyl)isoxazolidine-3-carboxamide (7b)

Prepared from nitrone **5b** and pyrrole **1** as a white solid; yield: 368 mg (84%); mp 81–82 °C; R_f = 0.46 (20% EtOAc–hexane).

IR (KBr): 3371, 3336, 3137, 3105, 3060, 3033, 2968, 2918, 2863, 1681, 1592, 1520, 1489, 1306, 1243, 764, 701 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.37 (s, 3 H, CH_3), 2.90 (ddd, *J* = 13.7, 9.3, 8.5 Hz, 1 H), 3.26 (ddd, *J* = 13.7, 5.2, 2.5 Hz, 1 H), 4.65 (dd, *J* = 9.3, 2.5 Hz, 1 H), 6.16 (dd, *J* = 8.5, 5.2 Hz, 1 H), 6.20–6.24 (m, 1 $H_{pyrrole}$), 6.25–6.32 (m, 1 $H_{pyrrole}$), 7.00–7.10 (m, 4 H_{arom}), 7.12–7.15 (m, 2 H_{arom}), 7.20–7.35 (m, 2 H_{arom}), 7.40–7.62 (m, 7 H_{arom}), 9.20 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3 (CH_3), 36.6 (CH_2), 70.2 (CH), 85.3 (CH), 110.4 (CH), 111.0 (CH), 115.0 (2 CH), 119.1 (CH), 120.5 (2 CH), 124.0 (CH), 128.1 (CH), 128.9 (2 CH), 129.8 (2 CH), 130.0 (2 CH), 130.4 (2 CH), 132.9 (C), 134.9, 135.0 (C), 136.2 (C), 149.5 (C), 168.9 (CO).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{25}N_3NaO_2$: 446.1839; found: 446.1841.

***N*-(4-Chlorophenyl)-2-phenyl-5-(2-phenyl-1*H*-pyrrol-1-yl)isoxazolidine-3-carboxamide (7c)**

Prepared from nitrone **5c** and pyrrole **1** as a white solid; yield: 418 mg (91%); mp 113–114 °C; R_f = 0.55 (20% EtOAc–hexane).

IR (KBr): 3338, 3135, 3102, 3060, 3034, 2964, 1687, 1590, 1519, 1491, 1400, 1305, 1241, 762, 700 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.83–2.95 (m, 1 H), 3.20–3.32 (m, 1 H), 4.68 (d, *J* = 8.8 Hz, 1 H), 6.17 (dd, *J* = 8.2, 5.6 Hz, 1 H), 6.27–6.30 (m, 1 $H_{pyrrole}$), 6.31–6.34 (m, 1 $H_{pyrrole}$), 6.97–7.00 (m, 1 $H_{pyrrole}$), 7.02–7.15 (m, 3 H_{arom}), 7.25–7.60 (m, 9 H_{arom}), 7.64 (d, *J* = 8.0 Hz, 2 H_{arom}), 9.29 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 36.5 (CH_2), 70.2 (CH), 85.3 (CH), 110.5 (CH), 111.1 (CH), 115.0 (2 CH), 118.8 (CH), 121.7 (2 CH), 124.2 (CH), 128.2 (CH), 128.9 (2 CH), 129.5 (2 CH), 129.9 (2 CH),

130.0 (2 CH), 130.3 (C), 132.8 (C), 136.1 (C), 136.3 (C), 149.2 (C), 169.2 (CO).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{26}H_{22}ClN_3NaO_2$: 466.1293; found: 466.1293.

_N_-Phenyl-5-(2-phenyl-1*H*-pyrrol-1-yl)-2-(*p*-tolyl)isoxazolidine-3-carboxamide (7d)

Prepared from nitrone **5d** and pyrrole **1** as a white solid; yield: 370 mg (85%); mp 161–162 °C; R_f = 0.49 (20% EtOAc–hexane).

IR (KBr): 3335, 3140, 3051, 3011, 2985, 2921, 2860, 1687, 1599, 1520, 1505, 1442, 1413, 1307, 1290, 1245, 814, 762, 752, 695 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.33 (s, 3 H), 2.89 (ddd, *J* = 13.7, 9.3, 8.6 Hz, 1 H), 3.26 (ddd, *J* = 13.7, 5.2, 2.6 Hz, 1 H), 4.63 (dd, *J* = 9.3, 2.6 Hz, 1 H), 6.17 (dd, *J* = 8.6, 5.2 Hz, 1 H), 6.27 (m, 1 $H_{pyrrole}$), 6.29 (m, 1 $H_{pyrrole}$), 6.95–7.05 (m, 3 H_{arom}), 7.10–7.20 (m, 3 H_{arom}), 7.37–7.60 (m, 7 H_{arom}), 7.70 (d, *J* = 8.0 Hz, 2 H_{arom}), 9.30 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0 (CH_3), 36.5 (CH_2), 70.3 (CH), 85.3 (CH), 110.3 (CH), 111.0 (CH), 115.1 (2 CH), 119.1 (CH), 120.4 (2 CH), 125.3 (CH), 128.1 (CH), 128.9 (2 CH), 129.5 (2 CH), 130.0 (2 CH), 130.4 (2 CH), 132.9 (C), 133.8 (C), 136.2 (C), 137.6 (C), 147.0 (C), 169.2 (CO).

Anal. Calcd for $C_{27}H_{25}N_3O_2$: C, 76.57; H, 5.95; N, 9.92. Found: C, 76.41; H, 6.03; N, 9.82.

_N_,2-Diphenyl-5-(4,5,6,7-tetrahydro-1*H*-indol-1-yl)isoxazolidine-3-carboxamide (7e)

Prepared from nitrone **5a** and pyrrole **3** as a white solid; yield: 317 mg (82%); mp 109–110 °C; R_f = 0.49 (20% EtOAc–hexane).

IR (KBr): 3277, 3132, 3092, 3057, 2928, 2843, 1675, 1597, 1526, 1488, 1442, 1298, 757, 693 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.70–1.80 (m, 2 H), 1.82–1.92 (m, 2 H), 2.45–2.52 (m, 2 H), 2.53–2.67 (m, 1 H), 2.68–2.80 (m, 1 H), 3.01 (ddd, *J* = 13.7, 9.3, 8.2 Hz, 1 H), 3.22 (ddd, *J* = 13.7, 6.1, 3.3 Hz, 1 H), 4.69 (dd, *J* = 9.3, 3.3 Hz, 1 H), 6.02 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.09 (dd, *J* = 8.2, 6.1 Hz, 1 H), 6.76 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 7.10–7.12 (m, 4 H_{arom}), 7.32–7.60 (m, 4 H_{arom}), 7.63 (d, *J* = 7.8 Hz, 2 H_{arom}), 9.28 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 22.2 (CH_2), 23.4 (CH_2), 23.6 (CH_2), 23.8 (CH_2), 36.4 (CH_2), 69.9 (CH), 84.3 (CH), 110.2 (CH), 114.8 (2 CH), 116.5 (CH), 119.9 (CH), 120.5 (2 CH), 123.9 (CH), 125.2 (C), 129.1 (C), 129.5 (2 CH), 130.0 (2 CH), 137.5 (C), 150.0 (C), 169.2 (CO).

HRMS (ESI): *m*/*z* $[M + K]^+$ calcd for $C_{24}H_{25}KN_3O_2$: 426.1578; found: 426.1578.

2-Phenyl-5-(4,5,6,7-tetrahydro-1*H*-indol-1-yl)-*N*-(*p*-tolyl)isoxazolidine-3-carboxamide (7f)

Prepared from nitrone **5b** and pyrrole **3** as a white solid; yield: 320 mg (80%); mp 118–119 °C; R_f = 0.40 (20% EtOAc–hexane).

IR (KBr): 3269, 3138, 3092, 3033, 2927, 2843, 1673, 1593, 1524, 1486, 1298, 759, 693 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.69–1.81 (m, 2 H), 1.82–1.98 (m, 2 H), 2.36 (s, 3 H), 2.45–2.53 (m, 2 H), 2.54–2.80 (m, 2 H), 2.93–3.08 (m, 1 H), 3.22 (ddd, *J* = 13.7, 5.9, 3.3 Hz, 1 H), 4.67 (dd, *J* = 9.3, 3.3 Hz, 1 H), 6.01 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.05–6.16 (m, 1 H), 6.75 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 7.18 (d, *J* = 8.2 Hz, 2 H_{arom}), 7.09–7.21 (m, 3 H_{arom}), 7.41 (t, *J* = 7.8 Hz, 2 H_{arom}), 7.51 (d, *J* = 8.2 Hz, 2 H_{arom}), 9.12 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9 (CH_3), 21.7 (CH_2), 23.0 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 36.0 (CH_2), 69.4 (CH), 84.0 (CH), 109.7 (CH), 114.3 (2 CH), 116.0 (CH), 119.4 (C), 120.1 (2 CH), 123.4 (CH), 128.7 (C), 129.5 (2 CH), 129.5 (2 CH), 134.4 (C), 134.5 (C), 149.4 (C), 168.5 (CO).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{25}H_{28}N_3O_2$: 402.2176; found: 402.2179.

_N_-(4-Chlorophenyl)-2-phenyl-5-(4,5,6,7-tetrahydro-1*H*-indol-1-yl)isoxazolidine-3-carboxamide (7g)

Prepared from **5c** and **1** as a white solid; yield: 359 mg (85%); mp 183–184 °C; R_f = 0.48 (20% EtOAc–hexane).

IR (KBr): 3263, 3136, 3093, 3054, 3034, 2957, 2930, 2849, 1676, 1588, 1522, 1489, 1401, 1304, 763, 693 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.69–1.82 (m, 2 H), 1.83–1.98 (m, 2 H), 2.45–2.53 (m, 2 H), 2.54–2.82 (m, 2 H), 2.92–3.08 (m, 1 H), 3.21 (ddd, *J* = 13.7, 5.6, 3.0 Hz, 1 H), 4.68 (dd, *J* = 9.6, 3.0 Hz, 1 H), 6.02 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.03–6.12 (m, 1 H), 6.71 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 7.10–7.24 (m, 3 H_{arom}), 7.34 (d, *J* = 8.9 Hz, 2 H_{arom}), 7.38–7.46 (m, 2 H_{arom}), 7.59 (d, *J* = 8.9 Hz, 2 H_{arom}), 9.19 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.7 (CH_2), 23.0 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 35.8 (CH_2), 69.4 (CH), 84.0 (CH), 109.8 (CH), 114.3 (2 CH), 115.9 (CH), 119.5 (C), 121.2 (2 CH), 123.6 (CH), 128.7 (C), 129.0 (2 CH), 129.6 (2 CH), 129.8 (C), 135.7 (C), 149.1 (C), 168.8 (CO).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{24}H_{25}ClN_3O_2$: 422.1630; found: 422.1627.

_N_-Phenyl-5-(4,5,6,7-tetrahydro-1*H*-indol-1-yl)-2-(*p*-tolyl)isoxazolidine-3-carboxamide (7h)

Prepared from nitrone **5d** and pyrrole **3** as a white solid; yield: 349 mg (87%); mp 164–165 °C; R_f = 0.55 (20% EtOAc–hexane).

IR (KBr): 3269, 3130, 3097, 3031, 3016, 2962, 2928, 2848, 1669, 1593, 1507, 1448, 1306, 712 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.69–1.82 (m, 2 H), 1.83–1.98 (m, 2 H), 2.37 (s, 3 H), 2.45–2.54 (m, 2 H), 2.55–2.80 (m, 2 H), 2.92–3.08 (m, 1 H), 3.20 (ddd, *J* = 13.7, 5.8, 3.0 Hz, 1 H), 4.65 (dd, *J* = 9.5, 3.0 Hz, 1 H), 6.01 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.02–6.12 (m, 1 H), 6.74 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 7.08 (d, *J* = 8.5 Hz, 2 H_{arom}), 7.15–7.24 (m, 1 H_{arom}), 7.22 (d, *J* = 8.5 Hz, 2 H_{arom}), 7.32–7.46 (m, 2 H_{arom}), 7.63 (d, *J* = 7.8 Hz, 2 H_{arom}), 9.20 (s, 1 H, NH).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6 (CH_3), 21.7 (CH_2), 23.0 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 35.8 (CH_2), 69.4 (CH), 84.0 (CH), 109.7 (CH), 114.4 (2 CH), 116.0 (CH), 119.3 (C), 120.0 (2 CH), 124.7 (CH), 128.8 (C), 129.0 (2 CH), 130.0 (2 CH), 133.1 (C), 137.1 (C), 146.9 (C), 168.8 (CO).

Anal. Calcd for $C_{25}H_{27}N_3O_2$: C, 74.79; H, 6.78; N, 10.47. Found: C, 74.62; H, 6.61; N, 10.32.

_N_,2-Diphenyl-5-(2-(thiophen-2-yl)-1*H*-pyrrol-1-yl)isoxazolidine-3-carboxamide (7i/7i′)

Prepared from nitrone **5a** and pyrrole **2** to give a mixture of isomers; yield: 382 mg (92%). Pure *cis*-isomer was separated by crystallization from EtOH as a white solid; yield: 228 mg (55%); mp 160–162 °C; R_f = 0.32 (20% EtOAc–hexane).

IR (KBr): 3341, 3260, 3105, 3057, 3032, 2971, 1676, 1596, 1527, 1490, 1443, 1320, 1294, 760, 694 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ (major isomer) = 2.96 (ddd, *J* = 14.0, 9.1, 9.0 Hz, 1 H), 3.28 (ddd, *J* = 14.0, 5.0, 2.5 Hz, 1 H), 4.67 (dd, *J* = 9.1, 2.5 Hz, 1 H, $CHCH_2CH$), 6.27 (t, *J* = 3.2 Hz, 1 $H_{pyrrole}$), 6.29–6.36 (m, 2 H, H + H_{arom}), 7.04–7.07 (m, 1 H_{arom}), 7.08–7.27 (m, 6 H_{arom}), 7.30–7.48 (m, 5 H_{arom}), 7.60–7.71 (m, 2 H_{arom}), 9.24 (s, 1 H, NH).

^1H NMR (400 MHz, $CDCl_3$): δ (minor isomer) = 3.22 (ddd, *J* = 14.0, 7.2, 5.8 Hz, 1 H), 3.36 (ddd, *J* = 14.0, 9.1, 3.5 Hz, 1 H, $CHCH_2CH$), 4.84 (dd, *J* = 9.1, 5.8 Hz, 1 H), 5.92 (t, *J* = 3.2 Hz, 1 $H_{pyrrole}$), 6.38 (dd, *J* = 7.2, 3.5 Hz, 1 H), 6.49–6.53 (m, 1 $H_{pyrrole}$), 6.87 (d, *J* = 7.8 Hz, 2 H_{arom}), 6.95–7.01 (m, 1 H_{arom}), 7.08–7.27 (m, 6 H_{arom}), 7.30–7.48 (m, 5 H_{arom}), 9.08 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ (major isomer) = 36.1 (CH_2), 69.8 (CH), 84.6 (CH), 110.6 (CH), 112.1 (CH), 114.7 (2 CH), 119.3 (CH), 120.0 (2 CH), 123.7 (CH), 124.8 (CH), 126.3 (CH), 127.3 (CH), 127.5 (CH), 127.5 (C), 129.0 (2 CH), 129.4 (2 CH), 133.2 (C), 137.0 (C), 149.0 (C), 168.5 (CO).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{22}N_3O_2S$: 416.1427; found: 416.1431.

_N_-Phenyl-5-(2-(thiophen-2-yl)-1_H_-pyrrol-1-yl)-2-(_p_-tolyl)isoxazolidine-3-carboxamide (7j/7j′)

Prepared from nitrone **5d** and pyrrole **2** as a mixture of isomers; yield: 360 mg (84%). Crystallization (EtOH) gave *cis*-isomer **7j** as a white solid; yield: 309 mg (72%); mp 159–160 °C; R_f = 0.43 (20% EtOAc–hexane).

IR (KBr): 3256, 3137, 3012, 2952, 1668, 1593, 1528, 1505, 1449, 1419, 1320, 1282, 723, 696 cm^{-1}.

Major Isomer 7j

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.35 (s, 3 H), 2.95 (dt, *J* = 14.0, 9.2 Hz, 1 H), 3.26 (ddd, *J* = 14.0, 5.0, 2.6 Hz, 1 H), 4.63 (dd, *J* = 9.2, 2.6 Hz, 1 H), 6.22–6.28 (m, 1 $H_{pyrrole}$), 6.29–6.40 (m, 2 H), 6.96–7.07 (m, 3 H_{arom}), 7.11–7.18 (m, 3 H_{arom}), 7.18–7.23 (m, 2 H_{arom}), 7.38–7.48 (m, 3 H_{arom}), 7.66 (d, *J* = 7.6 Hz, 2 H_{arom}), 9.27 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.5 (CH_3), 36.0 (CH_2), 69.8 (CH), 84.6 (CH), 110.6 (CH), 112.0 (CH), 114.8 (2 CH), 119.3 (CH), 120.0 (2 CH), 124.8 (CH), 126.3 (CH), 127.3 (CH), 127.4 (CH), 127.5 (C), 129.0 (2 CH), 129.9 (2 CH), 133.2 (C), 133.4 (C), 137.1 (C), 146.6 (C), 168.6 (CO).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{24}N_3O_2S$: 430.1584; found: 430.1587.

Minor Isomer 7j′

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 3.21 (ddd, *J* = 13.9, 7.2, 5.5 Hz, 1 H), 3.32 (ddd, *J* = 13.8, 8.8, 4.0 Hz, 1 H), 4.79 (dd, *J* = 8.8, 5.5 Hz, 1 H), 5.99–6.06 (m, 1 $H_{pyrrole}$), 6.30–6.40 (m, 2 H), 6.51–6.56 (m, 1 H_{arom}), 6.78 (d, *J* = 8.5 Hz, 2 H_{arom}), 6.97–7.07 (m, 2 H_{arom}), 7.11–7.22 (m, 2 H_{arom}), 7.29–7.33 (m, 1 H_{arom}), 7.34–7.48 (m, 3 H_{arom}), 7.64 (d, *J* = 7.6 Hz, 2 H_{arom}), 9.12 (s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.5 (CH_3), 37.8 (CH_2), 69.0 (CH), 85.4 (CH), 109.6 (CH), 112.0 (CH), 114.0 (2 CH), 119.1 (CH), 119.8 (2 CH), 124.8 (CH), 125.8 (CH), 126.6 (CH), 127.6 (CH), 128.0 (C), 129.0 (2 CH), 129.5 (2 CH), 132.2 (C), 133.7 (C), 137.0 (C), 147.8 (C), 168.6 (CO).

Dimethyl 2-Phenyl-5-(2-phenyl-1_H_-pyrrol-1-yl)isoxazolidine-3,3-dicarboxylate (9a)

Prepared from nitrone **8a** and pyrrole **1** as a white solid; yield: 317 mg (78%); mp 83–85 °C; R_f = 0.39 (20% EtOAc–hexane).

IR (KBr): 3116, 3056, 3026, 2956, 1760, 1737, 1491, 1432, 1294, 1268, 1204, 1082, 767, 696 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.33 (dd, *J* = 13.7, 5.2 Hz, 1 H), 3.53 (s, 3 H), 3.54 (dd, *J* = 13.7, 7.4 Hz, 1 H), 3.75 (s, 3 H), 6.22–6.25 (m, 1 $H_{pyrrole}$), 6.25 (dd, *J* = 7.4, 5.2 Hz, 1 H), 6.33–6.35 (m, 1 $H_{pyrrole}$), 7.10–7.16 (m, 1 H_{arom}), 7.26–7.32 (m, 2 H_{arom}), 7.36–7.42 (m, 3 H_{arom}), 7.43–7.46 (m, 5 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.6 (CH_2), 52.7 (CH_3), 53.1 (CH_3), 77.8 (C), 81.3 (CH), 109.5 (CH), 110.0 (CH), 119.6 (CH), 119.7 (2 CH), 125.2 (CH), 127.3 (CH), 128.3 (2 CH), 128.6 (2 CH), 129.4 (2 CH), 132.5 (C), 135.4 (C), 145.9 (C), 167.4 (CO), 168.0 (CO).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{23}N_2O_5$: 407.1601; found: 407.1601.

Dimethyl 5-(2-Phenyl-1_H_-pyrrol-1-yl)-2-(_p_-tolyl)isoxazolidine-3,3-dicarboxylate (9b)

Prepared from nitrone **8b** and pyrrole **1** as a white solid; yield: 336 mg (80%); mp 140–141 °C; R_f = 0.43 (20% EtOAc–hexane).

IR (KBr): 3117, 3061, 3031, 3006, 2954, 2926, 2842, 1758, 1738, 1508, 1467, 1433, 1290, 1271, 1202, 1079, 800, 708 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3 H, CH_3), 3.31 (dd, *J* = 13.8, 5.0 Hz, 1 H), 3.51 (dd, *J* = 13.8, 7.4 Hz, 1 H), 3.55 (s, 3 H), 3.71 (s, 3 H), 6.20–6.25 (m, 2 H), 6.31–6.35 (m, 1 $H_{pyrrole}$), 7.10 (d, *J* = 8.1 Hz, 2 H_{arom}), 7.28–7.33 (m, 2 H_{arom}), 7.34–7.39 (m, 1 H_{arom}), 7.41–7.48 (m, 5 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.3 (CH_3), 45.0 (CH_2), 53.1 (CH_3), 53.4 (CH_3), 78.2 (C), 81.7 (CH), 110.3 (CH), 110.8 (CH), 120.1 (CH), 120.6 (2 CH), 127.7 (CH), 129.0 (2 CH), 129.3 (2 CH), 129.8 (2 CH), 133.0 (C), 135.5 (C), 135.8 (C), 143.7 (C), 167.9 (CO), 168.4 (CO).

Anal. Calcd for $C_{24}H_{24}N_2O_5$: C, 68.56; H, 5.75; N, 6.66. Found: C, 68.43; H, 5.84; N, 6.59.

Dimethyl 2-(4-Chlorophenyl)-5-(2-phenyl-1_H_-pyrrol-1-yl)isoxazolidine-3,3-dicarboxylate (9c)

Prepared from nitrone **8c** and pyrrole **1** as a white solid; yield: 396 mg (90%); mp 132–133 °C; R_f = 0.45 (20% EtOAc–hexane).

IR (KBr): 3118, 3060, 3044, 3009, 2954, 2842, 1758, 1737, 1483, 1467, 1432, 1296, 1276, 1205, 1080, 836, 770, 722 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.33 (dd, *J* = 13.8, 5.0 Hz, 1 H), 3.48–3.55 (m, 1 H), 3.56 (s, 3 H), 3.78 (s, 3 H), 6.21–6.27 (m, 2 H), 6.32–6.36 (m, 1 $H_{pyrrole}$), 7.26 (d, *J* = 8.5 Hz, 2 H_{arom}), 7.34 (d, *J* = 8.5 Hz, 2 H_{arom}), 7.39–7.42 (m, 1 H_{arom}), 7.43–7.47 (m, 5 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 45.9 (CH_2), 53.3 (CH_3), 53.6 (CH_3), 78.1 (C), 81.8 (CH), 110.0 (CH), 110.5 (CH), 119.9 (CH), 121.5 (2 CH), 127.9 (CH), 128.7 (2 CH), 129.0 (2 CH), 129.8 (2 CH), 130.8 (C), 132.9 (C), 135.9 (C), 144.9 (C), 167.6 (CO), 168.2 (CO).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{22}ClN_2O_5$: 441.1212; found: 441.1211.

Dimethyl 2-Phenyl-5-(4,5,6,7-tetrahydro-1_H_-indol-1-yl)isoxazolidine-3,3-dicarboxylate (9d)

Prepared from nitrone **8a** and pyrrole **3** as a white solid; yield: 353 mg (92%); mp 96–98 °C; R_f = 0.43 (20% EtOAc–hexane).

IR (KBr): 2946, 2846, 1761, 1733, 1488, 1437, 1305, 1279, 1197, 1172, 1081, 959, 695 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.70–1.80 (m, 2 H), 1.80–1.91 (m, 2 H), 2.48–2.58 (m, 2 H), 2.58–2.73 (m, 2 H), 3.33 (dd, *J* = 13.7, 5.9 Hz, 1 H), 3.46 (dd, *J* = 13.7, 7.1 Hz, 1 H), 3.59 (s, 3 H), 3.71 (s, 3 H), 6.05 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.12 (t, *J* 6.5 Hz, 1 H), 7.05 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 7.05–7.12 (m, 1 H_{arom}), 7.21–7.30 (m, 2 H_{arom}), 7.35 (d, *J* = 7.8 Hz, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8 (CH_2), 23.0 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 44.6 (CH_2), 52.8 (OCH_3), 53.0 (OCH_3), 77.8 (C), 80.8 (CH), 109.0 (CH), 116.6 (CH), 118.6 (C), 119.4 (2 CH), 124.9 (CH), 128.2 (2 CH), 128.4 (C), 146.1 (C), 167.8 (CO), 167.9 (CO).

Anal. Calcd for $C_{21}H_{24}N_2O_5$: C, 65.61; H, 6.29; N, 7.29. Found: C, 65.41; H, 6.30; N, 7.15.

Dimethyl 5-(4,5,6,7-Tetrahydro-1_H_-indol-1-yl)-2-(_p_-tolyl)isoxazolidine-3,3-dicarboxylate (9e)

Prepared from nitrone **8b** and pyrrole **3** as a white solid; yield: 346 mg (87%); mp 86–89 °C; R_f = 0.48 (20% EtOAc–hexane).

IR (KBr): 2935, 2843, 1767, 1739, 1505, 1435, 1273, 1270, 1068, 832 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.70–1.80 (m, 2 H), 1.80–1.90 (m, 2 H), 2.30 (s, 3 H), 2.48–2.55 (m, 2 H), 2.55–2.72 (m, 2 H), 3.31 (dd, *J* = 13.7, 5.9 Hz, 1 H), 3.43 (dd, *J* = 13.7, 7.4 Hz, 1 H), 3.61 (s, 3 H), 3.70 (s, 3 H), 6.05 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.09 (dd, *J* = 7.4, 5.9 Hz, 1 H), 7.02–7.08 (m, 1 $H_{pyrrole}$), 7.07 (d, *J* = 8.5 Hz, 2 H_{arom}), 7.25 (d, *J* = 8.5 Hz, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.8 (CH_3), 21.8 (CH_2), 23.0 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 44.5 (CH_2), 52.8 (OCH_3), 52.9 (OCH_3), 77.8 (C), 80.8 (CH), 108.9 (CH), 116.6 (CH), 118.6 (C), 119.9 (2 CH), 128.4 (C), 128.8 (2 CH), 134.8 (C), 143.5 (C), 167.8 (CO), 167.9 (CO).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{22}H_{27}N_2O_5$: 399.1914; found: 399.1917.

Dimethyl 2-(4-Chlorophenyl)-5-(4,5,6,7-tetrahydro-1*H*-indol-1-yl)isoxazolidine-3,3-dicarboxylate (9f)

Prepared from nitrone **8c** and pyrrole **3** as a white solid; yield: 364 mg (87%); mp 90–92 °C; R_f = 0.50 (20% EtOAc–hexane).

IR (KBr): 2950, 2930, 2842, 1765, 1738, 1484, 1437, 1298, 1268, 1068, 842 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.69–1.81 (m, 2 H), 1.81–1.91 (m, 2 H), 2.47–2.55 (m, 2 H), 2.55–2.72 (m, 2 H), 3.32 (dd, *J* = 13.7, 5.9 Hz, 1 H), 3.47 (dd, *J* = 13.7, 7.4 Hz, 1 H), 3.62 (s, 3 H), 3.74 (s, 3 H), 6.05 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 6.09 (dd, *J* = 7.4, 5.9 Hz, 1 H), 7.01 (d, *J* = 3.0 Hz, 1 $H_{pyrrole}$), 7.23 (d, *J* = 8.9 Hz, 2 H_{arom}), 7.30 (d, *J* = 8.9 Hz, 2 H_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.8 (CH_2), 23.0 (CH_2), 23.1 (CH_2), 23.4 (CH_2), 44.5 (CH_2), 52.9 (OCH_3), 53.1 (OCH_3), 77.7 (C), 80.8 (CH), 109.1 (CH), 116.5 (CH), 118.8 (C), 120.8 (2 CH), 128.2 (2 CH), 128.5 (C), 130.1 (C), 144.6 (C), 167.5 (CO), 167.6 (CO).

Anal. Calcd for $C_{21}H_{23}N_2O_5Cl$: C, 60.22; H, 5.53; N, 6.69. Found: C, 60.03; H, 5.51; N, 6.48.

Dimethyl 2-Phenyl-5-[2-(thiophen-2-yl)-1*H*-pyrrol-1-yl]isoxazolidine-3,3-dicarboxylate (9g)

Prepared from **8a** and **2** as a pink solid; yield: 381 mg (93%); mp 105–106 °C; R_f = 0.35 (20% EtOAc–hexane).

IR (KBr): 3139, 3099, 3085, 3015, 2953, 2842, 1758, 1740, 1595, 1488, 1434, 1293, 1286, 1247, 1211, 1078, 697 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.31 (dd, *J* = 14.0, 4.6 Hz, 1 H), 3.52 (s, 3 H), 3.59 (dd, *J* = 14.0, 7.8 Hz, 1 H), 3.78 (s, 3 H), 6.29–6.32 (m, 1 H_{arom}), 6.33 (dd, *J* = 3.5, 1.8 Hz, 1 H_{arom}), 6.38 (dd, *J* = 7.8, 4.6 Hz, 1 H), 7.07–7.16 (m, 3 H_{arom}), 7.25–7.34 (m, 2 H_{arom}), 7.35–7.42 (m, 3 H_{arom}), 7.43–7.47 (m, 1 H_{arom}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.5 (CH_2), 52.7 (OCH_3), 53.1 (OCH_3), 77.7 (C), 81.2 (CH), 109.2 (CH), 111.2 (CH), 119.6 (2 CH), 120.2 (CH), 125.2 (CH), 125.8 (CH), 126.9 (CH), 127.2 (C), 127.5 (CH), 128.3 (2 CH), 133.6 (C), 145.8 (C), 167.3 (CO), 168.0 (CO).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{21}N_2O_5S$: 413.1166; found: 413.1169.

3-(4-Methoxyphenyl)-3-(phenylamino)-1-(2-phenyl-1*H*-pyrrol-1-yl)propan-1-ol (10a); Typical Procedure

To a solution of isoxazolidine **6c** (0.5 mmol) in EtOAc (4 mL) was added 5% $Pd/CaCO_3$ (150 mg) and the mixture was stirred under an atmosphere of H_2 at r.t. for 24 h. The mixture was filtered and concentrated. The product was purified using column chromatography (silica gel, petroleum ether–EtOAc) followed by crystallization (CH_2Cl_2–hexane) to give **10a** as a white solid; yield: 189 mg (95%); mp 114–116 °C; R_f = 0.26 (20% EtOAc–hexane).

IR (KBr): 3471, 3382, 2948, 2920, 2838, 1765, 1603, 1508, 1282, 1232, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.29 (ddd, *J* = 14.1, 6.3, 4.0 Hz, 1 H), 2.57 (ddd, *J* = 14.1, 8.0, 7.6 Hz, 1 H), 3.80 (s, 3 H), 3.40–4.00 (m, 2 H, NH, OH, exchange), 4.40 (dd, *J* = 7.6, 6.3 Hz, 1 H), 5.74 (dd, *J* = 8.0, 4.0 Hz, 1 H), 6.21 (s, 1 $H_{pyrrole}$), 6.34 (t, *J* = 2.9 Hz, 1 $H_{pyrrole}$), 6.53 (d, *J* = 7.9 Hz, 2 H_{arom}), 6.67–6.74 (m, 1 H_{arom}), 6.83 (d, *J* = 8.4 Hz, 2 H_{arom}), 7.12 (d, *J* = 8.4 Hz, 2 H_{arom}), 7.06–7.13 (m, 1 H_{arom}), 7.14–7.23 (m, 4 H_{arom}), 7.23–7.35 (m, 3 H_{arom}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 45.5 (CH_2), 55.2 (OCH_3), 55.3 (CH), 77.7 (CH), 109.3 (CH), 109.7 (CH), 114.1 (2 CH), 114.2 (2 CH), 117.7 (CH), 118.0 (CH), 127.1 (CH), 127.2 (2 CH), 128.4 (2 CH), 129.0 (2 CH), 129.1 (2 CH), 132.6 (C), 134.1 (C), 134.6 (C), 146.7 (C), 158.8 (C).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{27}N_2O_2$: 399.2067; found: 399.2068.

***N*-(4-Chlorophenyl)-4-hydroxy-2-(phenylamino)-4-(2-phenyl-1*H*-pyrrol-1-yl)butanamide (10b)**

Prepared from isoxazolidine **7c** as a white solid; yield: 147 mg (66%); mp 140–145 °C; R_f = 0.24 (20% EtOAc–hexane).

IR (KBr): 3440, 3402, 3370, 3314, 3285, 3102, 2892, 1666, 1604, 1512, 1494, 1401, 1286, 1090, 1053, 757 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.48 (ddd, *J* = 14.5, 8.1, 8.0 Hz, 1 H), 2.58 (ddd, *J* = 14.5, 4.2, 3.9 Hz, 1 H), 3.55 (d, *J* = 3.8 Hz, 1 H, NH), 3.78 (ddd, *J* = 8.0, 3.9, 3.8 Hz, 1 H), 4.53 (d, *J* = 3.2 Hz, 1 H, OH), 5.90 (ddd, *J* = 8.1, 4.2, 3.2 Hz, 1 H), 6.22 (dd, *J* = 1.7, 3.3 Hz, 1 $H_{pyrrole}$), 6.35 (t, *J* = 3.3 Hz, 1 $H_{pyrrole}$), 6.55 (d, *J* = 7.8 Hz, 2 H_{arom}), 6.80–6.90 (t, *J* = 7.4 Hz, 1 H_{arom}), 7.08–7.12 (m, 1 $H_{pyrrole}$), 7.15–7.25 (m, 2 H_{arom}), 7.26–7.38 (m, 6 H_{arom}), 7.40 (d, *J* = 8.8 Hz, 2 H_{arom}), 8.73 (s, 1 H, C(O)NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 39.6 (CH_2), 58.5 (CH), 78.2 (CH), 109.8 (CH), 110.0 (CH), 114.4 (2 CH), 117.9 (CH), 120.1 (CH), 121.2 (2 CH), 127.4 (CH), 128.7 (2 CH), 128.9 (2 CH), 129.0 (2 CH), 129.5 (2 CH), 129.7 (C), 132.4 (C), 133.8 (C), 135.5 (C), 146.0 (C), 171.2 (CO).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{26}H_{25}ClN_3O_2$: 446.1630; found: 446.1634.

1-(4-Chlorophenyl)-5-hydroxy-3-(phenylamino)-1,5-dihydro-2*H*-pyrrol-2-one (11a)

To a solution of isoxazolidine **7c** (0.66 mmol) in anhydrous THF (6 mL) was added TBAF·$3H_2O$ (1 mmol) and the mixture was stirred for 4 h at r.t. The mixture was quenched with H_2O (3 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL), and the combined organic extracts were dried (Na_2SO_4) and concentrated. The product was purified by column chromatography (silica gel, petroleum ether–EtOAc) followed by crystallization (EtOH) to give a yellowish solid; yield: 138 mg (75%); mp 170–175 °C (dec); R_f = 0.30 (17% EtOAc–hexane).

IR (KBr): 3296, 3219, 3122, 3057, 1680, 1658, 1594, 1477, 1428, 1402, 1070 cm^{-1}.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 6.07 (dd, *J* = 10.1, 2.3 Hz, 1 H), 6.12 (d, *J* = 2.3 Hz, 1 H, OH), 6.32 (d, *J* = 10.1 Hz, 1 H), 6.92–6.96 (m, 1 H_{arom}), 7.25–7.38 (m, 4 H_{arom}), 7.49 (d, *J* = 8.8 Hz, 2 H_{arom}), 7.80 (d, *J* = 8.8 Hz, 2 H_{arom}), 8.16 (s, 1 H, NH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 81.7 (CH), 106.2 (CH), 117.6 (2 CH), 121.2 (CH), 122.6 (2 CH), 128.5 (C), 129.1 (2 CH), 129.5 (2 CH), 133.9 (C), 136.6 (C), 142.2 (C), 165.6 (CO).

HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{14}ClN_2O_2$: 301.0738; found: 301.0733.

5-Hydroxy-1-phenyl-3-(*p*-tolylamino)-1,5-dihydro-2*H*-pyrrol-2-one (11b)

To a solution of isoxazolidine **7d** (281 mg, 0.66 mmol) in anhydrous THF (6 mL) was added NaH (35 mg, 60%, 0.88 mmol) and the mixture was stirred for 4 h at r.t. The mixture was quenched with H_2O (3 mL), and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 5 mL), and the combined organic extracts were dried (Na_2SO_4) and concentrated. The product was puri-

fied by column chromatography (silica gel, petroleum ether–EtOAc) followed by crystallization (EtOH) to give a grey solid; yield: 103 mg (55%); mp 155–157 °C; R_f = 0.44 (11% EtOAc–hexane).

IR (KBr): 3289, 3131, 3063, 3030, 2915, 1680, 1659, 1503, 1435, 1404, 1061 cm^{-1}.

^1H NMR (400 MHz, DMSO-d_6): δ = 2.25 (s, 3 H), 6.02 (d, J = 2.3 Hz, 1 H, OH), 6.06 (dd, J = 9.9, 2.3 Hz, 1 H), 6.24 (d, J = 9.9 Hz, 1 H), 7.11 (d, J = 8.4 Hz, 2 H_{arom}), 7.15–7.21 (m, 1 H_{arom}), 7.23 (d, J = 8.4 Hz, 2 H_{arom}), 7.39–7.49 (m, 2 H_{arom}), 7.75 (d, J = 7.6 Hz, 2 H_{arom}), 8.02 (s, 1 H, NH).

^{13}C NMR (75 MHz, DMSO-d_6): δ = 20.8 (CH_3), 81.7 (CH), 105.2 (CH), 117.7 (2 CH), 121.3 (2 CH), 124.6 (CH), 129.1 (2 CH), 129.9 (2 CH), 130.0 (C), 134.2 (C), 137.7 (C), 139.8 (C), 165.6 (CO).

HRMS (ESI): m/z $[M + H]^+$ calcd for $C_{17}H_{17}N_2O_2$: 281.1285; found: 281.1295.

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