Preparation of Heterocycle-Masked β-Enamino Acids

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The preparation of masked *N*-substituted β-enamino acid derivatives **3a**−**n** by reaction of 2-alkyl-oxa(thia)zolines **2a**,**b** with imidoylbenzotriazoles **1a**−**g** in the presence of LDA was described.

β-Amino acid units are important components of, and synthetic building blocks for, natural products[1a−c] and are widely used in other stereoselective syntheses,[2a,b] for example, of β-lactam antibiotics,[3a−c] and other heterocycles.[4a,b] The study of the synthesis and reactivity of β-amino acids has recently intensified,[2b,5] in part because many of them are natural product metabolites.[6a,b]

New synthetic methodologies recently developed for β-amino acids include (i) Michael additions of amines or lithium amides to α,β-unsaturated esters;[7a−d] (ii) nucleophilic additions to imines;[8a−e] and (iii) chemoselective reduction of β-enamino esters.[9a−h]

Strategy iii is a convenient and promising approach due to the simplicity of the procedure and the availability of the starting materials. Difficulties in selective reduction caused by the high reactivity of the ester functionality toward many reducing agents were solved by Fustero and co-workers by introducing a masked carboxylic acid into the β-position of an enamine function.[9c,d,10a,b] β-Enamino acid derivatives were prepared from 2-alkyl-2-oxazolines and 2-alkyl-2-thiazolines by reaction with imidoyl chlorides as electrophiles.[10a] Imidoyl chlorides are generally prepared in situ by treatment of the corresponding amides and cyanohydrins/ureas with phosgene, thiophosgene, oxalyl chloride, phosphorus *penta*- and trihalides, thionyl chloride, sulfuryl chloride, and halogens.[11] They also can be prepared from isocyanides, nitriles, isocyanates, imines, and amines.[11] Although the preparation of imidoyl chlorides normally provides good yields, side-reactions such as self-condensation have been reported at elevated temperatures if α-CH groups are present in the imidoyl chloride.[12] A major disadvantage in the use of imidoyl chlorides is their extreme lability toward hydrolysis. Therefore, imidoyl chlorides are sel-

Scheme 1

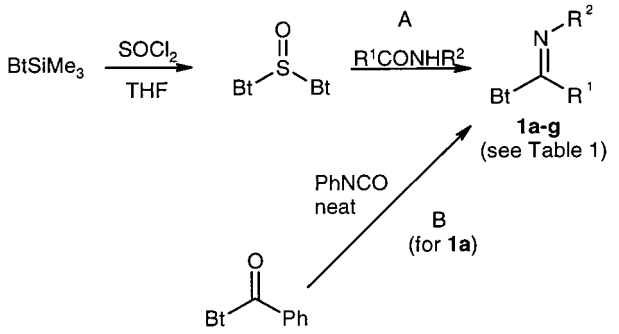

Table 1. Preparation of Imidoylbenzotriazoles 1a−g

product	R^1	R^2	method	yield (%)
1a	Ph	Ph	B	97
1b	Ph	*p*-Cl-C_6H_4	A	40
1c	Ph	*p*-Br-C_6H_4	A	50
1d	*p*-Me-C_6H_4	Ph	A	57
1e	*p*-Me-C_6H_4	*p*-Br-C_6H_4	A	39
1f	Ph	*p*-MeO-C_6H_4	A	60
1g	*p*-Me-C_6H_4	*p*-MeO-C_6H_4	A	40

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Scheme 2

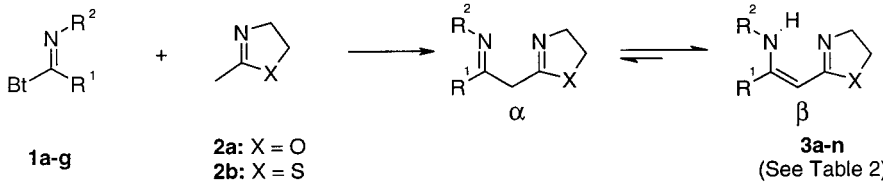

Table 2. Preparation of *β*-Enamino Acid Derivatives 3a−n

compd	sm **1**	imine **2**	X	R^1	R^2	yield (%)
3a	**1a**	**2a**	O	Ph	Ph	85
3b	**1a**	**2b**	S	Ph	Ph	79
3c	**1b**	**2a**	O	Ph	*p*-Cl-C_6H_4	87
3d	**1b**	**2b**	S	Ph	*p*-Cl-C_6H_4	88
3e	**1c**	**2a**	O	Ph	*p*-Br-C_6H_4	89
3f	**1c**	**2b**	S	Ph	*p*-Br-C_6H_4	98
3g	**1d**	**2a**	O	*p*-Me-C_6H_4	Ph	82
3h	**1d**	**2b**	S	*p*-Me-C_6H_4	Ph	91
3i	**1e**	**2a**	O	*p*-Me-C_6H_4	*p*-Br-C_6H_4	96
3j	**1e**	**2b**	S	*p*-Me-C_6H_4	*p*-Br-C_6H_4	89
3k	**1f**	**2a**	O	Ph	*p*-MeO-C_6H_4	84
3l	**1f**	**2b**	S	Ph	*p*-MeO-C_6H_4	85
3m	**1g**	**2a**	O	*p*-Me-C_6H_4	*p*-MeO-C_6H_4	85
3n	**1g**	**2b**	S	*p*-Me-C_6H_4	*p*-MeO-C_6H_4	84

dom isolated or purified. Fustero's method was also limited because strong bases such as *n*-butyllithium could not be used in this reaction due to the high reactivity of the imidoyl halides toward nucleophiles.[9d,10a]

Our success in benzotriazole-mediated syntheses of enaminones[13] prompted a study of the preparation of *β*-enamino acid derivatives by imidoylation of metalated heterocyclic imines using imidoylbenzotriazoles as stable analogues[14] of imidoyl chlorides.[11]

Preparation of Imidoylbenzotriazoles 1a−g. Two routes were used to prepare imidoylbenzotriazoles **1a−g** as shown in Scheme 1. In method A, secondary amides were reacted with dibenzotriazolyl sulfoxide following a literature procedure to give **1b−g** in 39−60% yields (Table 1).[14] Alternatively, phenyl isocyanate was reacted with benzoylbenzotriazole in a sealed tube according to a general procedure reported previously[15] to give **1a** in 97% yield. Other routes to imidoylbenzotriazoles are also known and include (i) reactions of amides with benzotriazole and phosphoryl chloride[16] and (ii) from oximes by reaction with BtTs via a Beckmann rearrangement.[17]

Preparation of *β*-Enamino Acid Derivatives 3a−n. Treatment of 2-methyl-2-oxazoline **2a** or 2-methyl-2-thiazoline **2b** (1.0 equiv) with LDA (2.0 equiv) or *n*-BuLi (2.0 equiv) at −78 °C in THF for 10−15 min generated a bright yellow solution of the corresponding azaallylic anion. THF solutions of imidoylbenzotriazoles **1a−g** were added dropwise at −78 °C, and the resulting solution was allowed to warm to room-temperature overnight. After standard workup, the desired products **3a−n** were obtained in good to excellent yields (Scheme 2, Table 2). Both LDA and *n*-BuLi give essentially the same yields, implying that both of these reagents could be used. The structural assignment of compounds **3a−n** was made on the basis of their spectral and analytical data. Compounds **3a−n** were all isolated as enamine tautomers *β*, as confirmed by their NMR spectra. The oxazolines (**3a**,**c**,**e**,**g**,**i**,**k**,**m**) all show a singlet around 5.00 ppm corresponding to the vinyl proton in the HC=C group. For the thiazolines (**3b**,**d**,**f**,**h**,**j**,**l**,**n**) this singlet is around 5.20 ppm. A broad singlet around 10.50−11.20 ppm is assigned to the NH proton, such a low-field chemical shift being consistent with the formation of the intramolecular hydrogen bond between the amino group and the sp^2 nitrogen atom of the oxazoline or thiazoline ring in the *β* tautomer. For thiazoline compounds, this is the only possible conformer in which intramolecular hydrogen bond can be formed. By analogy, we also designate the oxazoline analogues as existing in the similar tautomeric form. These results are consistent with those reported by Fustero.[10a]

In conclusion, heterocycle masked *β*-enamino acids were prepared in high yields by a modification of Fustero's method[9c,d,10a] starting from imidoylbenzotriazoles, which shows advantages in stability and ease of preparation as compared to the corresponding imidoyl halides. Hence, the present method extends those previously reported for the synthesis of *β*-enamino acid derivatives and provides an experimentally convenient general procedure for the preparation for these compounds.

Experimental Section

General Comments. Melting points were determined on a hot stage apparatus and are uncorrected. ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded in $CDCl_3$ with TMS or $CDCl_3$, respectively, as the internal reference. Elemental analyses were performed on a Carlo Erba-1106 instrument. High resolution mass spectra were measured on a Kratos/AE1-MS 30 mass spectrometer. THF was distilled from sodium/benzophenone under nitrogen immediately prior to use. All reactions with air-sensitive compounds were carried out under argon atmosphere.

***N*-Phenylbenzenecarboximidoyl-1-benzotriazole (1a):** yield 97%, yellow needles (from EtOH), mp 132−133 °C, [lit.[14] mp 130−132 °C]; ^1H NMR *δ* 6.90 (d, *J* = 7.8 Hz, 2H), 7.02 (t, *J* = 7.1 Hz, 1H), 7.24 (t, *J* = 7.8 Hz, 2H), 7.27−7.52 (m, 5H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.76 (t, *J* = 7.5 Hz, 1H), 8.24 (d, *J* = 8.4 Hz, 1H), 8.45 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR *δ* 115.1, 119.7, 121.0, 123.9, 125.9, 127.9, 128.7, 129.6, 129.9, 130.0, 130.4, 131.3, 145.7, 146.9, 153.8.

***N*-[(*Z*)-1*H*-1,2,3-Benzotriazol-1-yl(phenyl)methylidene]-4-chloroaniline (1b):** yield 40%, orange needles (from EtOH/CH_2Cl_2), mp 134−136 °C; ^1H NMR *δ* 6.82 (d, *J* = 8.1 Hz, 2H), 7.06 (t, *J* = 7.2 Hz, 1H), 7.20−7.40 (m, 6H), 7.52 (t, *J* = 8.1 Hz, 1H), 7.65 (t, *J* = 7.2 Hz, 1H), 8.15 (d, *J* = 8.4 Hz, 1H), 8.48 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR *δ* 115.3, 120.0, 121.3, 124.3, 125.6, 128.5, 128.9, 129.3, 131.5, 131.8, 136.4, 146.3, 146.6, 152.5. HRMS (CI) *m*/*z* Calcd for $C_{19}H_{14}N_4Cl$ (M + 1): 333.0907. Found: 333.0925.

***N*-[(*Z*)-1*H*-1,2,3-Benzotriazol-1-yl(phenyl)methylidene]-4-bromoaniline (1c):** yield 50%, orange needles (from EtOAc/hexanes), mp 131−133 °C; ^1H NMR *δ* 6.71 (d, *J* = 8.4 Hz, 2H),

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7.32−7.64 (m, 9H), 8.14 (d, J = 8.1 Hz, 1H), 8.42 (d, J = 8.1 Hz, 1H); ^{13}C NMR δ 115.3, 117.4, 120.1, 123.3, 125.7, 128.4, 129.4, 129.9, 130.1, 130.6, 131.7, 131.9, 146.0, 146.4, 154.2. HRMS (CI) m/z Calcd for $C_{19}H_{14}N_4Br$ (M + 1): 377.0402. Found: 377.0429.

***N*-[(*Z*)-1*H*-1,2,3-Benzotriazol-1-yl(4-methylphenyl)-methylidene]aniline (1d):** yield 57%, yellow needles (from Et_2O), mp 102−103 °C, [lit.[14] mp 100−101 °C]; ^{1}H NMR δ 2.35 (s, 3H), 6.85 (d, J = 7.5 Hz, 2H), 7.03 (t, J = 7.1 Hz, 1H), 7.14 (d, J = 8.1 Hz, 2H), 7.23−7.36 (m, 4H), 7.49 (t, J = 7.8 Hz, 1H), 7.61 (t, J = 7.8 Hz, 1H), 8.15 (d, J = 8.1 Hz, 1H), 8.44 (d, J = 8.3 Hz, 1H); ^{13}C NMR δ 21.6, 115.3, 120.0, 121.5, 124.1, 125.5, 127.3, 128.9, 129.0, 129.2, 130.2, 132.1, 140.7, 146.4, 147.2, 153.9.

***N*-[(*Z*)-1*H*-1,2,3-Benzotriazol-1-yl(4-methylphenyl)-methylidene]-4-bromoaniline (1e):** yield 39%, orange prisms (EtOAc/hexanes), mp 118−120 °C; ^{1}H NMR δ 2.38 (s, 3H), 6.73 (d, J = 8.4 Hz, 2H), 7.16−7.25 (m, 4H), 7.32 (d, J = 8.7 Hz, 2H), 7.50 (t, J = 7.5 Hz, 1H), 7.60 (t, J = 7.8 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 8.39 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 21.6, 115.2, 117.3, 120.0, 123.3, 125.6, 126.9, 129.1, 129.3, 130.1, 131.9, 132.0, 141.1, 146.2, 146.4, 154.4. HRMS (CI) m/z Calcd for $C_{20}H_{16}N_4Br$ (M + 1): 391.0558. Found: 391.0551.

***N*-[(*Z*)-1*H*-1,2,3-Benzotriazol-1-yl(phenyl)methylidene]-4-methoxyaniline (1f):** yield 60%, orange platelets (from EtOAc/hexanes), mp 104−105 °C; ^{1}H NMR δ 3.76 (s, 3H), 6.74−6.81 (m, 4H), 7.37−7.52 (m, 6H), 7.62 (t, J = 7.2 Hz, 1H), 8.14 (d, J = 8.4 Hz, 1H), 8.47 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 55.3, 114.1, 115.3, 120.0, 123.1, 125.4, 128.4, 129.1, 130.1, 130.3, 132.1, 139.8, 146.4, 153.2, 156.6. HRMS (CI) m/z Calcd for $C_{20}H_{16}N_4O$: 328.1324. Found: 328.1325.

***N*-[(*Z*)-1*H*-1,2,3-Benzotriazol-1-yl(4-methylphenyl)-methylidene]-4-methoxyaniline (1g):** yield 40%, orange prisms (from EtOAc/hexanes), mp 56−58 °C; ^{1}H NMR δ 2.35 (s, 3H), 3.73 (s, 3H), 6.76 (q, J = 8.4 Hz, 4H) 7.15 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 7.47 (t, J = 7.5 Hz, 1H), 7.54 (q, J = 7.2 Hz, 1H), 8.10 (d, J = 8.1 Hz, 1H), 8.41 (d, J = 8.4 Hz, 1H); ^{13}C NMR δ 21.4, 55.2, 113.9, 115.2, 119.7, 122.3, 122.9, 125.2, 127.5, 128.9, 130.0, 132.0, 139.9, 140.4, 146.2, 153.1, 156.4. HRMS (CI) m/z Calcd for $C_{21}H_{18}N_4O$: 342.1481. Found: 342.1485.

General Procedure for the Preparation of Masked β-Enamino Acids 3a−n. A three-necked flask equipped with an argon inlet adapter, rubber septum, and a magnetic stirring bar was flame dried. Diisopropylamine (2.2 mmol) was added to the flask with THF (5 mL) and cooled to 0 °C at stirring under argon. *n*-Butyllithium (2.0 mmol, hexanes solution) was then added dropwise. After being stirred for 10 min, the resulting solution was cooled to −78 °C and **2a**,**b** (1.0 mmol) in THF (5 mL) was added. The resulting bright yellow mixture was allowed to stir for 10−15 min at this temperature and then the solution of imidoylbenzotriazole derivative **1a**−**g** (1.0 mmol) in THF (5 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature while stirring overnight. The reaction was quenched with saturated ammonium chloride solution and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine and dried over Na_2SO_4. After filtration the solvent was removed in vacuo, and the residue was subjected to column chromatography purification with hexanes/EtOAc to give **3a**−**n**.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-phenylethenyl]-aniline (3a):** yield 85%, colorless needles (from CH_2Cl_2), mp 82−84 °C, [lit.[9a] mp 86−88 °C]; ^{1}H NMR δ 4.01 (t, J = 9.0 Hz, 2H), 4.22 (t, J = 9.0 Hz, 2H), 5.00 (s, 1H), 6.65 (d, J = 7.8 Hz, 2H), 6.85 (t, J = 7.5 Hz, 1H), 7.06 (t, J = 7.5 Hz, 2H), 7.25−7.31 (m, 3H), 7.36 (d, J = 6.0 Hz, 2H), 10.68 (br s, 1H); ^{13}C NMR δ 54.4, 65.7, 88.6, 121.7, 122.1, 128.1, 128.4, 128.5, 128.9, 136.6, 141.2, 154.0, 166.2.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-phenylethenyl]-aniline (3b):** yield 79%, yellow platelets (from EtOAc/CH_2Cl_2), mp 83−85 °C; ^{1}H NMR δ 3.25 (t, J = 9.0 Hz, 2H), 4.37 (t, J = 9.0 Hz, 2H), 5.19 (s, 1H), 6.65 (d, J = 7.5 Hz, 2H), 6.86 (t, J = 8.7 Hz, 1H), 7.06 (t, J = 8.1 Hz, 2H), 7.25−7.31 (m, 5H), 11.21 (br s, 1H); ^{13}C NMR δ 32.7, 64.3, 95.4, 121.8, 122.2, 128.2, 128.3, 128.5, 128.9, 136.4, 151.8, 166.8. HRMS (CI) m/z Calcd for $C_{17}H_{17}N_2S$ (M + 1): 281.1112. Found: 281.1128.

***N*-(4-Chlorophenyl)-*N*-[(*Z*)-2-(4,5-dihydro-1,3-oxazol-2-yl)-1-phenylethenyl]amine (3c):** yield 87%, yellow platelets (from EtOAc/CH_2Cl_2), mp 124−126 °C; ^{1}H NMR δ 4.00 (t, J = 9.0 Hz, 2H), 4.21 (t, J = 9.0 Hz, 2H), 4.98 (s, 1H), 6.65 (d, J = 7.5 Hz, 2H), 6.88 (t, J = 7.2 Hz, 1H), 7.08 (t, J = 8.1 Hz, 2H), 7.23−7.32 (m, 4H), 10.65 (br s, 1H); ^{13}C NMR δ 54.4, 65.8, 89.0, 121.8, 122.4, 128.6, 129.4, 134.8, 135.0, 141.0, 152.7, 166.0. Anal. Calcd for $C_{17}H_{15}N_2OCl$: C, 68.34; H, 5.06; N, 9.38. Found: C, 68.19; H, 5.39; N, 9.36.

***N*-(4-Chlorophenyl)-*N*-[(*Z*)-2-(4,5-dihydro-1,3-thiazol-2-yl)-1-phenylethenyl]amine (3d):** yield 88%, yellow prisms (from EtOAc/CH_2Cl_2), mp 138−140 °C. ^{1}H NMR δ 3.24 (t, J = 9.0 Hz, 2H), 4.36 (t, J = 9.0 Hz, 2H), 5.16 (s, 1H), 6.65 (d, J = 7.8 Hz, 2H), 6.88 (t, J = 7.2 Hz, 1H), 7.08 (t, J = 8.1 Hz, 2H), 7.22−7.31 (m, 4H), 11.21 (br s, 1H); ^{13}C NMR δ 32.8, 64.3, 95.7, 122.0, 122.5, 128.6, 128.7, 129.5, 134.7, 134.8, 140.8, 150.5, 166.7. Anal. Calcd for $C_{17}H_{15}N_2ClS$: C, 64.85; H, 4.80; N, 8.90. Found: C, 64.82; H, 4.67; N, 8.63.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-phenylethenyl]-4-bromoaniline (3e):** yield 89%, yellow needles (from EtOAc/CH_2Cl_2), mp 93−94 °C; ^{1}H NMR δ 4.00 (t, J = 9.0 Hz, 2H), 4.22 (t, J = 9.0 Hz, 2H), 5.03 (s, 1H), 6.52 (d, J = 8.7 Hz, 2H), 7.15 (d, J = 8.7 Hz, 2H), 7.28−7.35 (m, 5H), 10.69 (br s, 1H); ^{13}C NMR δ 54.3, 65.8, 89.5, 114.7, 123.0, 128.0, 128.5, 129.1, 131.4, 136.1, 140.4, 153.4, 166.1. Anal. Calcd for $C_{17}H_{15}N_2OBr$: C, 59.49; H, 4.40; N, 8.16. Found: C, 59.53; H, 4.53; N, 8.00.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-phenylethenyl]-4-bromoaniline (3f):** yield 98%, orange needles (from EtOAc/CH_2Cl_2), mp 139−141 °C; ^{1}H NMR δ 3.26 (t, J = 8.1 Hz, 2H), 4.37 (t, J = 8.1 Hz, 2H), 5.21 (s, 1H), 6.50 (d, J = 8.7 Hz, 2H), 7.15 (d, J = 8.7 Hz, 2H), 7.26−7.32 (m, 5H), 11.21 (br s, 1H); ^{13}C NMR δ 32.7, 64.3, 96.1, 114.8, 123.1, 128.1, 128.5, 129.1, 131.5, 135.9, 140.3, 151.3, 167.0. Anal. Calcd for $C_{17}H_{15}N_2BrS$: C, 56.83; H, 4.21; N, 7.80. Found: C, 56.75; H, 3.77; N, 7.65.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methylphenyl)ethenyl]aniline (3g):** yield 82%, orange needles (from CH_2Cl_2), mp 118−119 °C; ^{1}H NMR δ 2.33 (s, 3H), 4.00 (t, J = 9.0 Hz, 2H), 4.18 (t, J = 9.0 Hz, 2H), 4.99 (s, 1H), 6.67 (d, J = 7.5 Hz, 2H), 6.86 (t, J = 9.0 Hz, 1H), 7.04−7.09 (m, 3H), 7.26−7.27 (m, 3H), 10.63 (br s, 1H); ^{13}C NMR δ 21.3, 54.4, 65.7, 88.2, 121.7, 122.0, 128.0, 128.5, 129.1, 133.6, 139.0, 141.4, 154.1, 166.2. HRMS (CI) m/z Calcd for $C_{18}H_{19}N_2O$ (M + 1): 279.1497. Found: 279.1503.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-(4-methylphenyl)ethenyl]aniline (3h):** yield 91%, yellow needles (from EtOAc/CH_2Cl_2), mp 113−114 °C, ^{1}H NMR δ 2.33 (s, 3H), 3.24 (t, J = 9.0 Hz, 2H), 4.36 (t, J = 9.0 Hz, 2H), 5.17 (s, 1H), 6.66 (d, J = 7.8 Hz, 2H), 6.86 (t, J = 9.0 Hz, 1H), 7.07−7.09 (m, 3H), 7.24−7.26 (m, 3H), 11.18 (br s, 1H); ^{13}C NMR δ 21.6, 33.1, 64.6, 95.4, 122.1, 122.4, 128.4, 128.8, 129.4, 133.7, 139.2, 141.6, 152.2, 167.2. HRMS (CI) m/z Calcd for $C_{18}H_{19}N_2S$ (M + 1): 295.1269. Found: 295.1291.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methylphenyl)ethenyl]-4-bromoaniline (3i):** yield 96%, pale yellow needles (from CH_2Cl_2), mp 136−138 °C; ^{1}H NMR δ 2.34 (s, 3H), 3.99 (t, J = 9.0 Hz, 2H), 4.21 (t, J = 8.7 Hz, 2H), 5.01 (s, 1H), 6.52 (d, J = 8.7 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 7.16 (d, J = 8.7 Hz, 2H), 7.23 (d, J = 8.1 Hz, 2H), 10.66 (br s, 1H); ^{13}C NMR δ 21.3, 54.3, 65.7, 88.9, 114.5, 123.0, 128.0, 129.4, 131.3, 131.6, 133.1, 139.2, 140.5, 153.5, 166.1. Anal. Calcd for $C_{18}H_{17}N_2OBr$: C, 60.52; H, 4.80; N, 7.84. Found: C, 60.53; H, 4.83; N, 7.74.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-(4-methylphenyl)ethenyl]-4-bromoaniline (3j):** yield 89%, pale yellow needles (from EtOAc/CH_2Cl_2), mp 156−157 °C; ^{1}H NMR δ 2.34 (s, 3H), 3.25 (t, J = 8.1 Hz, 2H), 4.36 (t, J = 8.1 Hz, 2H), 5.19 (s, 1H), 6.51 (d, J = 8.7 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 7.15 (d, J = 8.7 Hz, 2H), 7.25 (t, J = 8.1 Hz, 2H), 11.19 (br s, 1H); ^{13}C NMR δ 21.3, 32.7, 64.3, 95.8, 114.7, 123.1, 128.0, 129.2, 131.4, 133.0, 139.2, 140.4, 151.4, 167.0. Anal. Calcd for

$C_{18}H_{17}N_2BrS$: C, 57.91; H, 4.59; N, 7.50. Found: C, 57.83; H, 4.57; N, 7.35.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-phenylethenyl]-4-methoxyaniline (3k):** yield 84%, yellow gum; ^{1}H NMR δ 3.24 (t, J = 9.0 Hz, 2H), 3.69 (s, 3H), 4.36 (t, J = 8.1 Hz, 2H), 5.12 (s, 1H), 6.62 (s, 4H), 7.25−7.35 (m, 5H), 11.13 (br s, 1H); ^{13}C NMR δ 32.8, 55.3, 64.3, 94.0, 113.8, 123.9, 128.2, 128.4, 128.7, 134.3, 136.4, 152.7, 155.6, 166.9. HRMS (CI) *m*/*z* Calcd for $C_{18}H_{19}N_2O_2$ (M + 1): 295.1447. Found: 295.1415.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-phenylethenyl]-4-methoxyaniline (3l):** yield 85%, orange gum; ^{1}H NMR δ 3.25 (t, J = 9.0 Hz, 2H), 3.70 (s, 3H), 4.36 (t, J = 8.1 Hz, 2H), 5.12 (s, 1H), 6.63 (s, 4H), 7.26−7.35 (m, 5H), 11.13 (br s, 1H); ^{13}C NMR δ 32.8, 55.3, 64.3, 94.0, 113.8, 123.9, 128.2, 128.4, 128.7, 134.2, 136.4, 152.7, 155.3, 166.9. HRMS (CI) *m*/*z* Calcd for $C_{18}H_{19}N_2OS$ (M + 1): 311.1218. Found: 311.1215.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-oxazol-2-yl)-1-(4-methylphenyl)ethenyl]-4-methoxyaniline (3m):** yield 85%, orange needles (from EtOAc/CH_2Cl_2), mp 108−110 °C; ^{1}H NMR δ 2.32 (s, 3H), 3.70 (s, 3H), 3.99 (t, J = 9.0 Hz, 2H), 4.18 (t, J = 9.0 Hz, 2H), 4.92 (s, 1H), 6.64 (s, 4H), 7.06 (d, J = 8.1 Hz, 2H), 7.25 (t, J = 8.1 Hz, 2H), 10.53 (br s, 1H); ^{13}C NMR δ 21.3, 29.7, 55.3, 65.7, 86.5, 113.8, 123.7, 128.1, 128.9, 133.7, 134.6, 138.8, 154.9, 155.2, 166.6. HRMS (CI) *m*/*z* Calcd for $C_{19}H_{21}N_2O_2$ (M + 1): 309.1603. Found: 309.1583.

***N*-[(*Z*)-2-(4,5-Dihydro-1,3-thiazol-2-yl)-1-(4-methylphenyl)ethenyl]-4-methoxyaniline (3n):** yield 84%, pale yellow needles (from EtOAc/CH_2Cl_2), mp 133−135 °C; ^{1}H NMR δ 2.31 (s, 3H), 3.23 (t, J = 9.0 Hz, 2H), 3.69 (s, 3H), 4.34 (t, J = 9.0 Hz, 2H), 5.11 (s, 1H), 6.63 (s, 4H), 7.04 (d, J = 8.1 Hz, 2 H), 7.24 (d, J = 8.1 Hz, 2H), 11.10 (br s, 1H); ^{13}C NMR δ 21.3, 32.7, 55.3, 64.2, 93.6, 113.8, 123.8, 128.2, 128.9, 133.4, 134.4, 138.7, 152.8, 155.3, 166.9. Anal. Calcd for $C_{19}H_{20}N_2OS$: C, 70.34; H, 6.21; N, 8.63. Found: C, 69.97; H, 6.41; N, 8.47.

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