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A New Route to 4-Ethynyl-*N*-hydroxy-2-imidazolidinones via Oxime Addition

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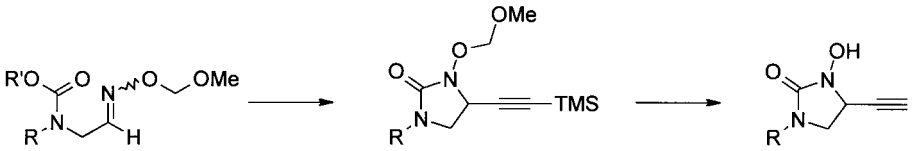
Abstract—A rapid route was developed to afford ethynyl-substituted imidazole derivatives which served as key compounds for aryl–alkynyl-coupling reactions. Addition of mono-silylated acetylene to O-protected oximes was carried out in the absence of Lewis acids, directly affording the title compounds **3a**–**c** in a one-pot reaction. Limitations and dependence of the feasibility on N_1-substituents are discussed.

In the course of our studies on novel NSAIDs (non-steroidal anti-inflammatory drugs), we developed a synthetic route to ethynyl-substituted cyclic *N*-hydroxyureas **3a**–**c** in few steps, starting from cheap commercial materials and providing unlimited variety of N_1-substituents (alkyl and aryl). The key reaction represents a nucleophilic addition of TMS-protected lithium acetylide to an isomeric mixture of the appropriate oxime ethers **1a**–**c** which were obtained through routine chemistry in three steps and high yields, followed by double deprotection of compounds **2a**–**c** (Schemes 1 and 2). Acetals **4a**–**c** were synthesized according to the literature,[1] acylated and hydrolyzed to aldehydes **5a**–**c**, and reacted with O-methoxymethyl(MOM)-protected hydroxylamine derived from phthalimide **6**[2] with methylhydrazine.

NMR spectroscopic analysis of **1a**–**c** revealed *E*/*Z* isomers ranging from 60:40 to 40:60, thus affecting yields of the following addition reaction, as the (*Z*)-isomers of similar, α-hydrogen containing oxime ethers are known to react preferentially in addition reactions with organometallic compounds.[3]

Often, poor conversions have been observed for this reaction type. Uno et al. reported formation of hydroxylamines in moderate to good yields by adding various nucleophiles across C–N double bonds of (*Z*)-oximes in toluene and in the presence of BF_3 as precomplexating agent and anion scavenger in this solvent.[4] We found that addition of our nucleophilic agent, (trimethylsilyl)ethynyl lithium salt,[5] in the absence of any Lewis acid, led to immediate cyclization when treated with the isomeric mixture of oxime ethers **1a**–**c**, probably via formation of a reactive, negative-charged hydroxylamino species **I** that underwent intramolecular reaction with the carbon atom of the carbamic ester group (Scheme 3). The (*E*)-isomer remained inert to the chosen conditions.

This step was optimized by variation of solvent and temperature. Diethyl ether was preferable to other solvents such as toluene or THF, as the formed lithium salt (LiOMe; LiOPh) precipitated from the solution. Low temperatures promoted the selectivity of the reaction but also reduced solubility of the reactants. Best results were achieved at 15°C and afforded 49–72% referred to the (*Z*)-oxime



1a, R = Me, R' = Ph
1b, R = Ph, R' =Me
1c, R = 4-MeOPh, R' = Me

2a-c

3a-c

Scheme 1.

Keywords: cyclization; addition; oximes; cyclic hydroxyurea; imidazole; protective groups.
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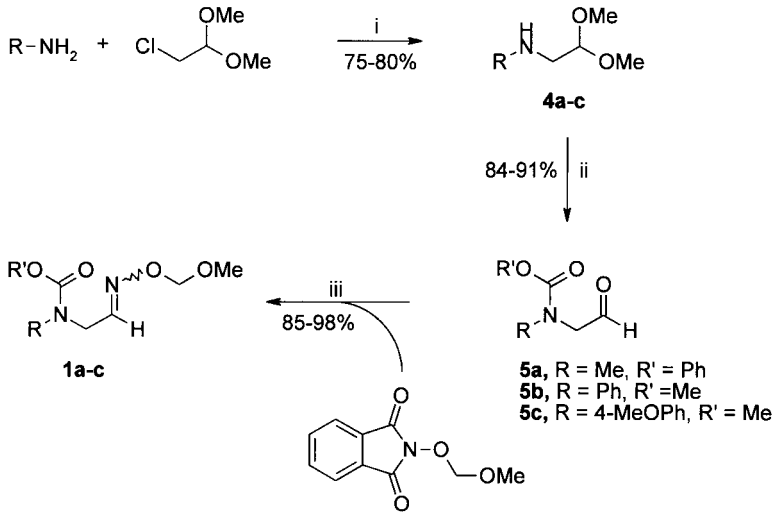
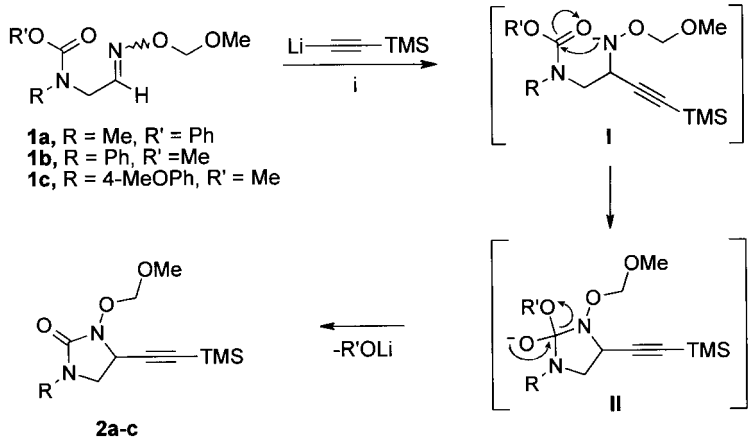


Scheme 2. Reagents: (i) K_2CO_3, DMF, 60°C; (ii) (a) Cl-COOR′, $NaHCO_3$(aq.), THF, rt; (b) 2N HCl, 55°C; (iii) CH_3NHNH_2, Et_2O, 0°C.



Scheme 3. Reagents: (i) THF, 15°C.

(Table 1). No improvement could be accomplished by varying other conditions such as molar ratios of reactants. Modest yields of this reaction were mainly contributed to a competing elimination process (structures **I** and **III**) which resulted in the corresponding carbamate **IV** and methyloxime **V** as side products (30–40%), as deduced from ^{1}H NMR analysis (Scheme 4). The by-products and unchanged (*E*)-oxime could be removed by flash chromatography.

The choice of the carbamic ester residue R′ played an important role, as deterioration of the conversion was observed for increasing +I effects exhibited by the N-substituent R. For the cyclization of the methyl derivative **2a** it was essential to use R′=Ph due to its better leaving group properties. R′=Me gave no considerable conversion in this case. For both aryl compounds **2b** and **2c** change of R′ did not affect yields. Table 1 summarizes yields obtained for each of the substituents.

Table 1. Yields of one-pot addition/cyclization in dependence of substituents

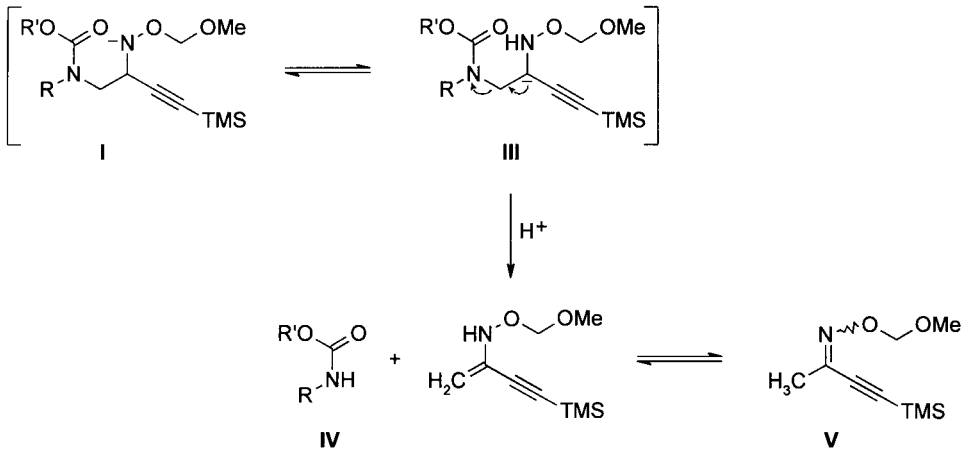
Product	R	R′	Yield (%)
2a	Me	Ph	49
2b	Ph	Me	72
2c	4-MeOPh	Me	63

Cleavage of the MOM group in compounds **2a**–**c** was performed with 4*N* methanolic HCl[6] and subsequent treatment with K_2CO_3 for alkaline cleavage of TMS[7] (Scheme 5). The obtained title compounds **3a**–**c** could be easily purified by recrystallization.

The presence of the unprotected *N*-hydroxyurea group did not adversely affect the desired aryl–alkynyl *Stille*-type coupling reaction, using 5-[(4-fluorophenyl)methyl)]-2-iodothiophene **7** as a well-known lipid binding template[8] that we employed in our studies. This reaction was carried out in dry THF and excess diisopropylamine, with $Pd(PPh_3)_4$ and copper(I)iodide as catalysts[9] (Scheme 6). Products **8a**–**c** were purely obtained in 50–60% yield after work-up and recrystallization.

Conclusions

Although the one-pot addition/cyclization was overshadowed by lack of selectivity, the method described

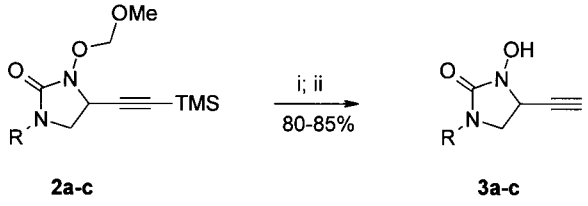


Scheme 4.

represents a new synthetic route which is quick, cheap and easy to handle. The obtained alkynyl-substituted *N*-hydroxy-imidazolidinones served as substrates for aryl–alkynyl coupling, thus proving their usefulness as synthons. Due to the facile synthesis of the precursor compounds, a reasonable overall yield could be achieved.

Experimental

Unless otherwise indicated, all reagents were purchased from commercial suppliers and used without further purification. TLC analyses were carried out on precoated silica gel plates (Merck 60 F_{254}), and spots were visualized with UV light. Chromatography refers to flash chromatography using Fluka silica gel 60, 220–240 mesh. Melting points were measured on a Kofler bank and are uncorrected. ^{1}H NMR spectra were recorded on a Bruker 200FS FT-NMR-spectrometer and are reported as ppm downfield from Me_4Si with multiplicity, number of protons, and coupling constant(s) in Hertz indicated parenthetically. Ambiguous assignments are pointed out (*). The following abbreviations are used to indicate spin multiplicities: s (singlet), bs (broad singlet), d (doublet), dd (doublet of doublets), t (triplet) or m (multiplet). Elemental analyses (C, H, and N) were performed by the Microanalytical Laboratory, Institute of Physical Chemistry at Vienna University, Austria.

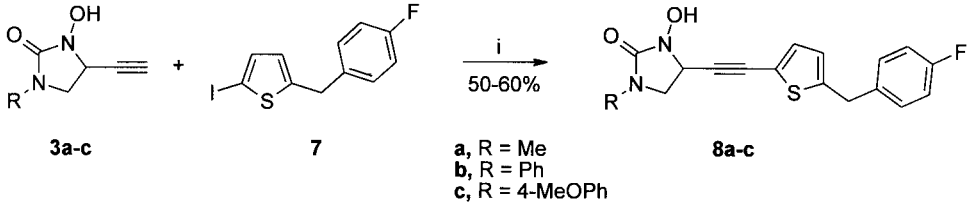


Scheme 5. Reagents: (i) 4N methanolic HCl, 40°C; (ii) K_2CO_3, 25°C.

General procedure for the formation of aldehydes 5a–c

To a stirred, saturated solution of $NaHCO_3$ (1100 ml) was added dropwise a solution of the appropriate acetal **4a–c** (0.619 mol) in THF (1100 ml), followed by addition of methyl chloroformiate (1.36 mol) at room temperature. After stirring for 15 h, the organic layer was separated and evaporated, and the aqueous phase was extracted with ether. The combined organic layers were dried (Na_2SO_4), evaporated and short-path distilled in vacuo for purification. The distillate was taken up in excess 6*N* hydrochloric acid and vigorously stirred at 55°C for 30 min. After cooling down to room temperature, the organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were dried (Na_2SO_4), evaporated and short-path distilled to yield **5b** and **5c** in 84 and 91% yield, respectively. **5a** was obtained by reaction with phenyl chloroformiate and passed on to the subsequent step immediately after hydrolysis without work-up.

(2-Oxoethyl)phenylcarbamic acid methyl ester (5b). This compound was obtained as a bright yellow liquid, bp 105°C (0.5 mbar); R_f (PE/EtOAc 2:1) 0.3; ^{1}H NMR ($CDCl_3$): δ 3.72 (s, 3H, O–CH_3), 4.39 (s, 2H, CH_2); 7.19–7.30 (m, 3H, phenyl), 7.31–7.41 (m, 2H, phenyl), 9.69 (s, 1H,



Scheme 6. Reagents: (i) $Pd(PPh_3)_4$, CuI, $(iPr)_2NH$, THF, 25°C.

CHO). Anal. Calcd for $C_{10}H_{11}NO_3$: C, 62.17; H, 5.74; N, 7.25. Found: C, 62.00; H, 5.73; N, 7.28.

(2-Oxoethyl)(4-methoxyphenyl)carbamic acid methyl ester (5c). This compound was obtained as a brownish oil, bp 95°C (0.1 mbar); R_f (PE/EtOAc 3:1) 0.2; ^{1}H NMR ($CDCl_3$): δ 3.72 (s, 3H, O–CH_3), 3.80 (s, 3H, OCH_3), 4.37 (s, 2H, CH_2); 6.88 (d, 2H, phenyl, J=8 Hz), 7.18 (d, 2H, phenyl, J=8 Hz), 9.70 (s, 1H, CHO). Anal. Calcd for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27. Found: C, 59.49; H, 6.06; N, 6.06.

General procedure for the formation of oxime ethers 1a–c

2-[(Methoxy)methoxy]-2*H*-isoindol-1(3*H*),3-dione **6** (23.0 g, 111 mmol) was suspended in dry ether (250 ml) under a nitrogen atmosphere. To the vigorously stirred mixture was added dropwise methylhydrazine (4.97 g, 108 mmol) at 0°C, followed by warming to room temperature and stirring for 4 h. The precipitate was filtered off, and the filtrate containing free *O*-(methoxymethyl)hydroxylamine (103 mmol) was dropped to a solution of the appropriate aldehyde **5a–c** (82 mmol) in dry ether. After stirring for 1 h under nitrogen, the mixture was washed with 2*N* HCl, and the aqueous layer re-extracted three times with ether. The combined organic layers were dried (Na_2SO_4) and evaporated. The oily residue was purified by flash chromatography (silica gel—toluene/EtOAc 3:1) to give **1a–c** in 98, 85 and 95% yield, respectively.

[[(Methoxy)methoxyimino]ethyl]methylcarbamic acid phenyl ester (1a). This compound was obtained as a yellowish oil; R_f (PE/ether 1:1) 0.1; ^{1}H NMR ($CDCl_3$): δ 2.99–3.17 (m, 3H, N–CH_3), 3.44 (s, 3H, O–CH_3), 4.18 (d, 2H, N–CH_2, J=6 Hz), 4.32 (d, 2H, N–CH_2^*, J=4 Hz), 5.09 (s, 2H, O–CH_2), 5.13 (s, 2H, O–CH_2^*), 6.90 (t, 1H, CH*, J=4 Hz), 7.09–7.28 (m, 3H, phenyl), 7.29–7.41 (m, 2H, phenyl), 7.54 (t, 1H, CH, J=6 Hz). Anal. Calcd for $C_{12}H_{16}N_2O_4$: C, 57.13; H, 6.39; N, 11.10. Found: C, 57.38; H, 6.66; N, 11.09.

[[(Methoxy)methoxyimino]ethyl]phenylcarbamic acid methyl ester (1b). This compound was obtained as a colorless oil; R_f (toluene/EtOAc 3:1) 0.5; ^{1}H NMR ($CDCl_3$): δ 3.37 (s, 3H, O–CH_3), 3.38 (s, 3H, O–CH_3^*), 3.71 (s, 3H, O–CH_3), 3.73 (s, 3H, O–CH_3^*), 4.40 (d, 2H, N–CH_2, J=5 Hz), 4.61 (d, 2H, N–CH_2*, J=3 Hz), 5.03 (s, 2H, O–CH_2), 5.09 (s, 2H, O–CH_2^*), 6.95 (t, 1H, CH*, J=3 Hz), 7.13–7.42 (m, 5H, phenyl), 7.59 (t, 1H, CH, J=5 Hz). Anal. Calcd for $C_{12}H_{16}N_2O_4$: C, 57.13; H, 6.39; N, 11.10. Found: C, 57.35; H, 6.21; N, 10.98.

[[(Methoxy)methoxyimino]ethyl]-(4-methoxyphenyl)carbamic acid methyl ester (1c). This compound was obtained as a yellowish oil; R_f (PE/EtOAc 3:1) 0.4; ^{1}H NMR ($CDCl_3$): δ 3.37 (s, 3H, O–CH_3), 3.38 (s, 3H, O–CH_3^*), 3.69 (s, 3H, O–CH_3), 3.71 (s, 3H, O–CH_3^*), 3.78 (s, 3H, O–CH_3), 3.80 (s, 3H, O–CH_3^*), 4.37 (d, 2H, N–CH_2, J=5 Hz), 4.63 (d, 2H, N–CH_2^*, J=3 Hz), 5.02 (s, 2H, O–CH_2), 5.07 (s, 2H, O–CH_2^*), 6.83 (d, 2H, phenyl, J=6 Hz), 6.89 (d, 2H, phenyl*, J=6 Hz), 7.09 (t, 1H, CH*, J=3 Hz), 7.10 (d, 2H, phenyl, J=6 Hz), 7.14 (d, 2H, phenyl, J=6 Hz), 7.56 (t, 1H, CH, J=5 Hz). Anal. Calcd for $C_{13}H_{18}N_2O_5$: C, 55.31; H, 6.43; N, 9.92. Found: C, 55.19; H, 6.26; N, 10.08.

General procedure for the one-pot addition/cyclization

A solution of freshly prepared (trimethylsilyl)acetylene lithium salt (178 mmol) in dry ether (200 ml) was added to a solution of the appropriate oxime ether **1a–c** (60.6 mmol) under a nitrogen atmosphere at 15°C. After stirring for 25 min at room temperature, the mixture was quenched with aqueous $NaHCO_3$, and the organic layer was separated. The aqueous layer was extracted with ether, and the combined organic phases were washed with brine, dried (Na_2SO_4) and evaporated to an oily residue.

3-[(Methoxy)methoxy]-1-methyl-4-[2-(trimethylsilyl)-ethynyl]-2-imidazolidinone (2a). The crude product was purified by flash chromatography (silica gel—PE/EtOAc 5:2) to give a yellow oil (49%); R_f (PE/EtOAc 2:1) 0.4; ^{1}H NMR ($CDCl_3$): δ 0.18 (s, 9H, Si–CH_3), 2.82 (s, 3H, N–CH_3), 3.25 (dd, 1H, CH_{2a}, J=8 Hz, 8), 3.48 (dd, 1H, CH_{2b}, J=8, 8 Hz), 3.58 (s, 3H, O–CH_3), 4.28 (dd, 1H, CH, J=8, 8 Hz), 4.94 (d, 1H, O–CH_{2a}, J=7 Hz), 5.03 (d, 1H, O–CH_{2b}, J=7 Hz). Anal. Calcd for $C_{11}H_{20}N_2O_3Si$: C, 51.53; H, 7.86; N, 10.93. Found: C, 52.01; H, 7.68; N, 10.47.

3-[(Methoxy)methoxy]-1-phenyl-4-[2-(trimethylsilyl)-ethynyl]-2-imidazolidinone (2b). The crude product was recrystallized from *n*-hexane to give colorless crystals (72%); mp 75–76°C;) R_f (PE/ether 2:1 0.3; ^{1}H NMR ($CDCl_3$): δ 0.18 (s, 9H, Si–CH_3), 3.63 (s, 3H, O–CH_3), 3.76 (dd, 1H, CH_{2a}, J=8, 8 Hz), 3.92 (dd, 1H, CH_{2b}, J=8, 8 Hz), 4.46 (dd, 1H, CH, J=8, 8 Hz), 5.01 (d, 1H, O–CH_{2a}, J=7 Hz), 5.11 (d, 1H, O–CH_{2b}, J=7 Hz), 7.12 (t, 1H, phenyl, J=8 Hz), 7.35 (t, 2H, phenyl, J=8 Hz), 7.52 (d, 2H, phenyl, J=8 Hz). Anal. Calcd for $C_{16}H_{22}N_2O_3Si$: C, 60.35; H, 6.96; N, 8.80. Found: C, 60.62; H, 6.85; N, 8.85.

3-[(Methoxy)methoxy]-1-(4-methoxyphenyl)-4-[2-(trimethylsilyl)ethynyl]-2-imidazolidinone (2c). The crude product was purified by flash chromatography (silica gel—PE/EtOAc 4:1) and obtained as colorless crystals (63%), mp 107–108°C; R_f (PE/EtOAc 3:1) 0.7; ^{1}H NMR ($CDCl_3$): δ 0.15 (s, 9H, Si–CH_3), 3.63 (s, 3H, O–CH_3), 3.74 (s, 3H, O–CH_3), 3.88 (dd, 1H, CH_{2a}, J=8, 8 Hz), 4.12 (dd, 1H, CH_{2b}, J=8, 8 Hz), 4.46 (dd, 1H, CH, J=8, 8 Hz), 5.01 (d, 1H, O–CH_{2a}, J=7 Hz), 5.09 (d, 1H, O–CH_{2b}, J=7 Hz), 6.87 (d, 2H, phenyl, J=8 Hz), 7.41 (d, 2H, phenyl, J=8 Hz). Anal. Calcd for $C_{17}H_{24}N_2O_4Si$: C, 58.59; H, 6.94; N, 8.04. Found: C, 58.88; H, 7.05; N, 8.13.

General procedure for deprotection

The protected imidazolidinone **2a–c** (2.92 mmol) was dissolved in a 4 N solution of HCl in dry MeOH(40 ml) and stirred at 40°C for 3 h. Water (50 ml) was added, and the solution was extracted with EtOAc. The combined organic layers were dried (Na_2SO_4) and evaporated. The residue was dissolved in dry MeOH (30 ml), and anhydrous K_2CO_3 (560 mg, 4.05 mmol) was added. After stirring for 4 h at room temperature, the suspension was taken up in

water (30 ml) and extracted with EtOAc. The combined organic layers were dried (Na_2SO_4) and evaporated.

4-Ethynyl-3-hydroxy-1-methyl-2-imidazolidinone (3a). The crude product was digested with ether to give colorless crystals (80%), mp 149–151°C; R_f (PE/EtOAc 1:1) 0.5; ^{1}H NMR (dmso-d_6): δ 2.69 (s, 3H, N–CH_3), 3.12 (dd, 1H, CH_{2a}, J=8, 8 Hz), 3.41 (d, 1H, ethyne-H, J=2 Hz), 3.52 (dd, 1H, CH_{2b}, J=8, 8 Hz), 4.14 (dd, 1H, CH, J=8, 8 Hz), 9.32 (br s, 1H, OH). Anal. Calcd for $C_6H_8N_2O_2$: C, 51.42; H, 5.75; N, 19.99. Found: C, 51.46; H, 5.73, N, 19.74.

4-Ethynyl-3-hydroxy-1-phenyl-2-imidazolidinone (3b). The crude product was recrystallized from toluene to give colorless crystals (85%), mp 157–160°C. R_f (PE/ether 1:2) 0.5; ^{1}H NMR (dmso-d_6): δ 3.49 (d, 1H, ethyne-H, J=2 Hz), 3.62 (dd, 1H, CH_{2a}, J=8, 8 Hz), 4.03 (dd, 1H, CH_{2b}, J=8, 8 Hz), 4.43 (dd, 1H, CH, J=8, 8 Hz), 7.12 (t, 1H, phenyl, J=8 Hz), 7.36 (t, 2H, phenyl, J=8 Hz), 7.55 (d, 2H, phenyl, J=8 Hz), 9.69 (s, 1H, OH). Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.34; H, 4.98; N, 13.85. Found: C, 65.46; H, 5.11, N, 13.73.

4-Ethynyl-3-hydroxy-1-(4-methoxyphenyl)-2-imidazolidinone (3c). The crude product was digested with acetone to give colorless crystals (81%), mp 143–145°C (decomp.); R_f (PE/EtOAc 1:1) 0.4; ^{1}H NMR (dmso-d_6): δ 3.50 (d, 1H, ethyne-H, J=2 Hz), 3.63 (dd, 1H, CH_{2a}, J=8, 8 Hz), 3.72 (s, 3H, O–CH_3), 4.01 (dd, 1H, CH_{2b}, J=8, 8 Hz), 4.42 (dd, 1H, CH, J=8, 8 Hz), 6.95 (d, 2H, phenyl, J=8 Hz), 7.48 (d, 2H, phenyl, 6, J=8 Hz), 9.63 (br s, 1H, OH). Anal. Calcd for $C_{15}H_{20}N_2O_3$: C, 62.06; H, 5.21; N, 12.06. Found: C, 61.88; H, 5.43, N, 11.96.

General procedure for aryl–alkynyl coupling

The deprotected imidazolidinone **3a**–**c** (2.47 mmol), palladium tetrakis(triphenylphosphine) (64 mg, 0.060 mmol) and copper(I)iodide (23 mg, 0.120 mmol) were suspended in dry THF (30 ml) and stirred for 5 min at room temperature. 5-[(4-fluorophenyl)methyl]-2-iodothiophene **7** (788 mg, 2.47 mmol) was added to the mixture, followed by another 5 min of stirring and addition of diisopropylamine (3.5 ml, 34.6 mmol). After 2 h of stirring, the mixture was quenched with 2 N HCl (100 ml), and the organic layer was separated. The aqueous phase was extracted with ether, and the combined organic layers were washed with a $NaHCO_3$ solution, dried (Na_2SO_4) and evaporated to give a solid, which was triturated with cold diisopropyl ether and purified by flash chromatography (silica gel—toluene/EtOAc 3:1).

4-[[5-[(4-Fluorophenyl)methyl]-2-thienyl]ethynyl]-3-hydroxy-1-methyl-2-imidazolidinone (8a). The product was triturated with cold acetone to give colorless crystals (52%), mp 143–144°C; R_f (PE/EtOAc 2:5) 0.4; ^{1}H NMR ($CDCl_3$): δ 2.69 (s, 3H, N–CH_3), 3.18 (dd, 1H, CH_{2a}, J=8, 8 Hz), 3.58 (dd, 1H, CH_{2b}, J=8, 8 Hz), 4.13 (s, 2H, thienyl-CH_2), 4.42 (dd, 1H, CH, J=8, 8 Hz), 6.85 (d, 1H, thienyl, J=4 Hz), 7.06–7.23 (m, 2H, phenyl), 7.23–7.35 (m, 3H, thienyl, phenyl), 9.38 (br s, 1H, OH). Anal. Calcd for $C_{17}H_{15}FN_2O_2S$: C, 61.80; H, 4.58; N, 8.48. Found: C, 61.94; H, 4.78, N, 8.39.

4-[[5-(4-Fluorophenyl)methyl]-2-thienyl]ethynyl]-3-hydroxy-1-phenyl-2-imidazolidinone (8b). The product was recrystallized from toluene to give colorless crystals (60%); mp 119–120°C; R_f (toluene/EtOAc 3:1) 0.4; ^{1}H NMR ($CDCl_3$): δ 3.77 (dd, 1H, CH_{2a}, J=8, 8 Hz), 4.10 (dd, 1H, CH_{2b}, J=8, 8 Hz), 4.15 (s, 2H, thienyl-CH_2), 4.71 (dd, 1H, CH, J=8, 8 Hz), 6.85 (d, 1H, thienyl, J=4 Hz), 7.12 (dd, 2H, phenyl, J=9, 1 Hz), 7.20 (d, 1H, thienyl, J=4 Hz), 7.31–7.25 (m, 3H, fluorophenyl, phenyl), 7.36 (dd, 2H, phenyl, J=9, 1 Hz), 7.67 (dd, 2H, fluorophenyl, J=8, 1 Hz), 9.63 (br s, 1H, OH). Anal. Calcd for $C_{22}H_{17}FN_2O_2S$: C, 67.33; H, 4.37; N, 7.14. Found: C, 67.40; H, 4.51, N, 7.07.

4-[[5-[(4-Fluorophenyl)methyl]-2-thienyl]ethynyl]-3-hydroxy-1-(4-methoxyphenyl)-2-imidazolidinone (8c). The product was triturated with methyl *t*-butyl ether to give colorless crystals (56%), mp 134–135°C; R_f (toluene/EtOAc 3:1) 0.35; ^{1}H NMR ($CDCl_3$): δ 3.75 (dd, 1H, CH_{2a}, J=8, 8 Hz), 3.78 (s, 3H, O–CH_3), 3.94 (dd, 1H, CH_{2b}, J=8, 8 Hz), 4.08 (s, 2H, thienyl-CH_2), 4.62 (dd, 1H, CH, J=8, 8 Hz), 6.63 (d, 1H, thienyl, J=4 Hz), 6.87 (d, 2H, phenyl, J=8 Hz), 7.00–7.18 (m, 2H, fluorophenyl), 7.19 (d, 1H, thienyl, J=4 Hz), 7.20 (dd, 2H, fluorophenyl, J=8, 8 Hz), 7.42 (d, 2H, phenyl, J=8 Hz), 9.71 (br s, 1H, OH). Anal. Calcd for $C_{23}H_{19}FN_2O_3S$: C, 65.39; H, 4.55; N, 6.63. Found: C, 65.65; H, 4.85, N, 6.61.

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