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A novel protocol for the facile construction of tetrahydroquinoline fused tricyclic frame works via an intramolecular 1, 3 - dipolar nitrile oxide cycloaddition reaction

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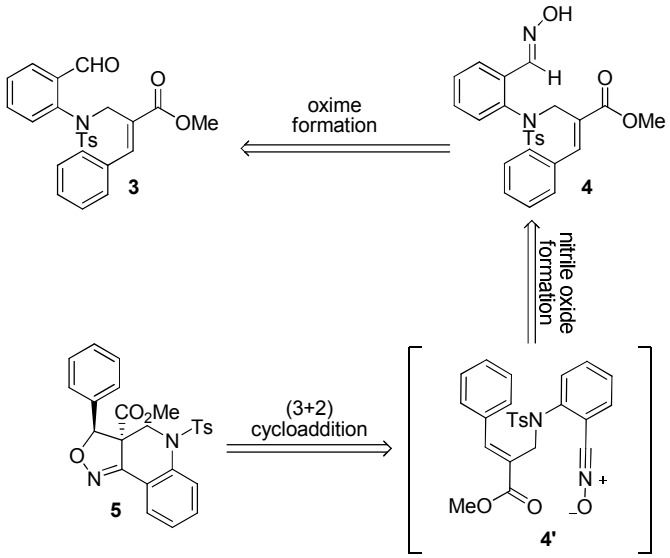
An efficient method towards the synthesis of quinoline fused tricyclic compounds involving an intramolecular 1, 3–dipolar nitrile oxide cycloaddition reaction utilizing Baylis–Hillman derivatives in good yields have been described for the first time. A highly functionalized tricyclic frameworks created by forming two rings and two adjacent stereocentres through the formation of two N–C, one C–C and one O–C bonds in high regio and diastereoselective manner.

Introduction

The development of efficient synthetic strategies in the direction of bioactive compounds such as natural products, analogs, drugs, diagnostics, and agrochemicals remains to be challenging objectives in modern organic synthesis.[1] Heterocyclic compounds, particularly nitrogen containing heterocycles are the very essential type of compounds in the pharmaceutical and agrochemical sectors.[2] Among various heterocycles, the quinoline ring system is a very common structural motif and is found in several biologically active natural products and pharmacologically relevant therapeutic agents.[3] Due to the significance of these structural units in drug discovery and medicinal chemistry, the development of new methodologies for the synthesis of quinoline derivatives remains to be a very active field of research.[4]

In the domain of cycloaddition,[5,6] intramolecular 1,3-dipolar nitrile oxide cycloaddition is one of the versatile methods for the construction of functionalized poly heterocyclic frameworks. The application of intramolecular nitrile oxide cycloaddition[7,8e] in *O*- and *N*-allyl / alkynyl derivatives is an emerging field focused on the synthesis of variety of cyclic frameworks including cyclic ethers and amines.

In continuation of our interest in the field of heterocyclic chemistry,[8] herein we describe the construction of tricyclic tetrahydroisoxazoloquinoline scaffolds with angular substitution via in situ formation of nitrile oxide and later intramolecular 1, 3–dipolar nitrile oxide cycloaddition reaction sequence. The synthesis of tricyclic tetrahydroisoxazolo quinoline (**5**) involves the formation of nitrile oxide precursor (**4'**) which would be derived from aldoxime derivative (**4**). The aldoxime derivative (**4**) can be prepared from *N*-allylated aminoaldehyde derivative (**3**) and $NH_2OH.HCl$ as per the retrosynthetic strategy depicted in Scheme 1.



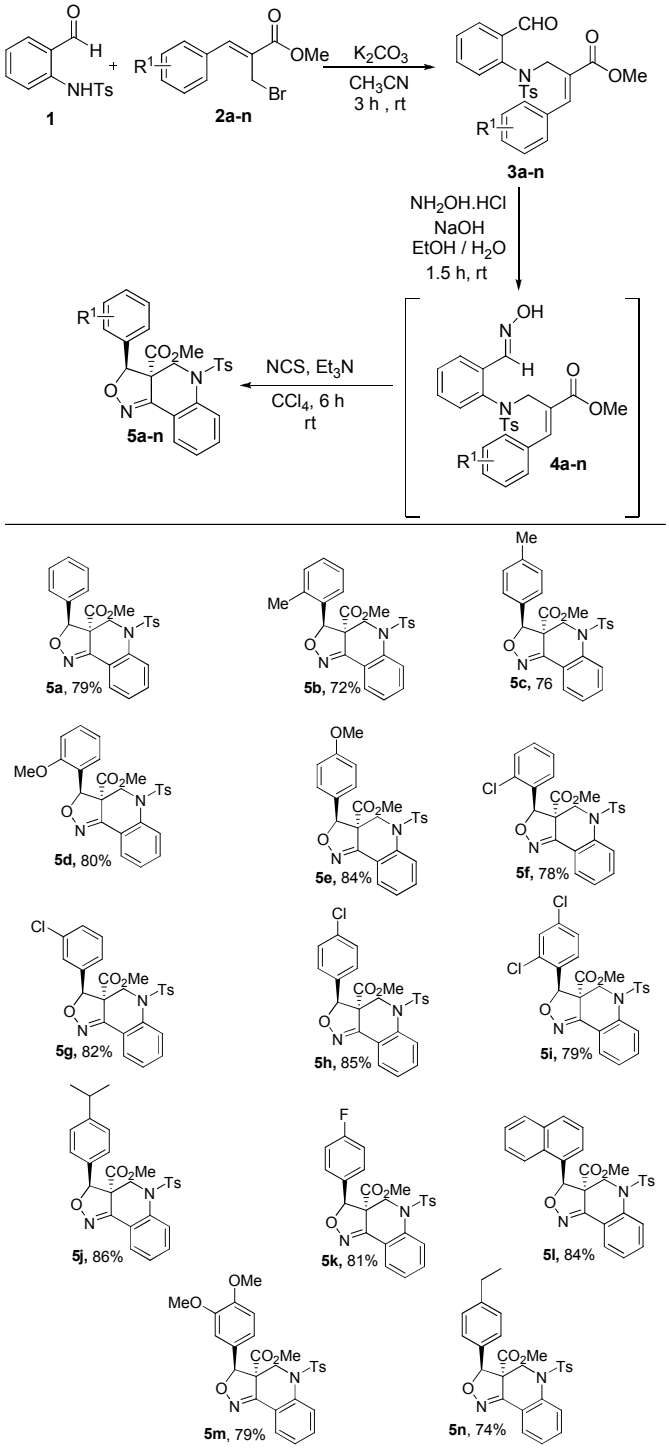
Scheme 1. Retrosynthetic strategy for the synthesis of tricyclic frameworks

The requisite substrate molecules which is required for the execution of our objectives was prepared starting from *N*-tosylated benzyl alcohol from the reaction of *O*-aminobenzyl alcohol and tosyl chloride with the aid of pyridine as a base.[9g]

The *N*-tosylated benzyl alcohol was subsequently oxidized into corresponding aldehyde using MnO_2 which smoothly led to the *N*-tosylated aldehyde (**1**) in good yield.[9g] Further reaction of bromo derivatives of the Baylis–Hillman adducts with N-tosylated aldehyde under basic (K_2CO_3) condition in acetonitrile led to the required precursors (**3**). To execute our idea, we treated *N*-allylated aminoaldehyde (**3a**) with $NH_2OH.HCl$ in the presence of 50% sodium hydroxide which lead to the required aldoxime **4a** and further treatment of aldoxime derivative (without isolation) with NCS and Et_3N in CCl_4 at room temperature over a period of 6 h successfully

provided the anticipated tricyclic tetrahydroisoxazoloquinoline **5a** in 79% yield with regio and diasteroseletive manner.

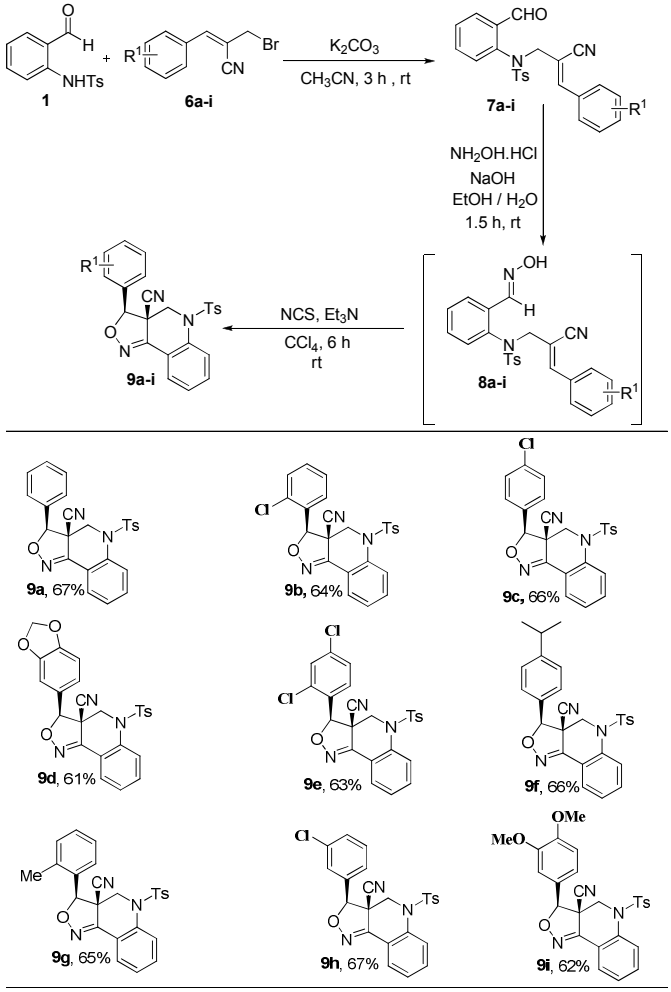
Table 1. Synthesis of tricyclic tetrahydroisoxazoloquinoline scaffolds (**5a-n**)



[a]All the reactions were carried out using 2 mmol of *N*-allylated derivatives (**3**) and $NH_2OH.HCl$ (6 mmol) with 5 mmol of NCS in the presence of Et_3N (4 mmol). [b]Yields of the pure products (**5**) obtained after column chromatography (silica gel 60-120 mesh 10% EtOAc in hexanes).

Delighted by this result, we generated an array of aldoxime derivatives and treated with NCS and Et_3N in CCl_4 at room temperature for 6 h, which successfully led to the desired tetrahydroisoxazolo quinolines (**5b-n)** in 72-86 % yields (Table 1). It is important to mention here that this is the first report for the regio and stereoselective synthesis of tricyclic isoxazoloquinolines containing diverse functionalities using Baylis-Hillman derivatives via intramolecular 1,3-dipolar nitrile oxide cycloaddition.

Table 2. Synthesis of tricyclic tetrahydroisoxazoloquinoline scaffolds (**9a-i**)



[a]All the reactions were carried out using 2 mmol of *N*-allylated derivatives (**6**) and $NH_2OH.HCl$ (6 mmol) with 5 mmol of NCS in the presence of Et_3N (4 mmol). [c]Yields of the pure products (**9**) obtained after column chromatography (silica gel 60-120 mesh 10% EtOAc in hexanes).

In order to extend the generality and of this protocol, we have utilized various Baylis–Hillman derivatives (**7a-i**) derived from acrylonitrile and transformed them into their corresponding aldoxime derivatives (**8a-i**). Further reaction of the aldoxime derivatives (**8a-i**) (without isolation) with NCS and Et_3N in CCl_4 at room temperature for 6 h, successfully afforded the desired tricyclic tetrahydroisoxazoloquinolines (**9a-i**) containing nitrile moiety at the ring junction in 62-67% yields (Table 2).

Based on the ORTEP diagram[10] of the tetrahydro isoxazoloquinoline **5a**, shown in Figure 1, the relative stereochemistry of the phenyl group and the adjacent ester moiety are in *trans* orientation. It is observed that the *trans*

product was formed, when olefin **3**, having a *trans* geometry (aryl and ester groups present in the *vicinal* positions of compound **3**). In the same manner, olefin **7b**, having a cis geometry (nitrile and aryl functionalities present in the vicinal positions of compound **9b**), led to the construction of cis product in a stereospecific fashion.

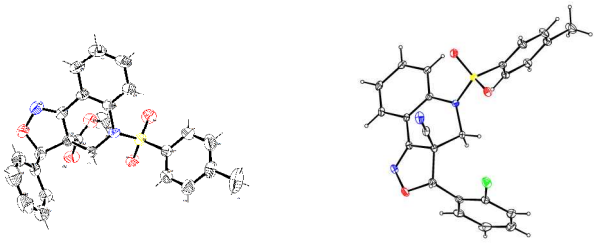


Figure 1. ORTEP diagram of compounds[9] **5a** and **9b**

Conclusions

In conclusion, the successful development of a facile and general protocol for the construction of fused tricyclic tetrahydroisoxazoloquinoline scaffolds in good yields via an intramolecular 1,3–dipolar nitrile oxide cycloaddition strategy was achieved. This protocol leads to the formation of highly functionalized tricyclic tetrahydroisoxazoloquinolines containing two new rings, two contiguous stereocenters, one of them being an all carbon quaternary center in a highly regio and diastereoselective manner.

Experimental section

General information and materials

^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ with TMS as an internal standard (300 MHz ^{1}H, 75 MHz ^{13}C) at room temperature. All commercially available reagents and chemicals were purchased from chemical suppliers and used as received without further purification. Column chromatography was performed on silica gel (60–120 mesh). Mass analyses and HRMS were obtained by ESI on a TOF mass analyzer.

Typical experimental procedure for the synthesis of compound (3a):

A solution of N-(2-formylphenyl)-4-methylbenzene-1-sulfonamide (**1**) (1 mmol, 0.28 g) and potassium carbonate (2 mmol, 0.28 g) in acetonitrile solvent was stirred for 15 minutes at room temperature. To this solution, (Z)-methyl 2-(bromomethyl)-3-phenylacrylate (**2a**) (1.2 mmol, 0.31 g) was added drop wise till the addition is complete. After the completion of the reaction as indicated by TLC, the reaction mixture was concentrated and extracted with ethylacetate (2x15 mL). The organic layer thus obtained was washed with water (2x10 mL), followed by brine solution (2x 10 mL) and dried over anhydrous sodium sulphate. The crude product obtained was purified by a pad of silica gel (100-200 mesh) column chromatography using ethylacetate and Hexane (1:9) to afford the compound (**3a**) as a colourless solid (0.44 g, 98% yield).

Methyl (2E)-2-{[N-(2-formylphenyl)(4-methylbenzene) sulfo namido]methyl}-3-phenylprop-2-enoate (3a)

Colourless solid; Yield: 98% mp: 98-100 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) :δ 2.43 (s, 3H), 3.68 (s, 3H), 4.53 (d, 1H, J = 13.5 Hz), 5.06 (d, 1H, J = 13.5 Hz), 6.42 - 7.91 (m, 14H), 9.89 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 46.4, 52.3, 126.3, 127.6, 127.9, 128.3, 128.3, 128.7, 129.5, 129.5, 129.63, 132.9, 133.4, 133.9, 136.1, 141.4, 144.3, 167.5, 189.9; MS (m/z): 451 (M^++1).

Methyl (2E)-2-{[N-(2-formylphenyl)(2-methylbenzene) sulfo namido]methyl}-3-(4-methylphenyl)prop-2-enoate (3b)

Colourless solid; Yield: 87%; mp: 100-102ºC;^{1}H NMR ($CDCl_3$, 300 MHz) : δ 1.96 (s, 3H), 2.39 (s, 3H), 3.76 (s, 3H), 4.35 (d, 1H, J = 13.8Hz), 4.91 (d, 1H, J = 13.5 Hz), 6.25-7.94 (m, 13H), 10.01 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 19.6, 21.6, 46.8, 52.3, 125.6, 127, 127.6, 127.8, 128.1, 128.2, 128.9, 129.1, 129.5, 130.2, 132.9, 133.5, 133.6, 135.9, 137.5, 142.2, 143.6, 144.2, 167.1, 190.1; MS (m/z): 465 (M^++1).

Methyl (2E)-2-{[N-(2-formylphenyl)(4-methylbenzene) sulfo namido]methyl}-3-(4-methylphenyl)prop-2-enoate (3c)

Colourless solid; Yield: 87%; mp: 103-105 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.42 (s, 3H), 2.44 (s, 3H), 3.64 (s, 3H), 4.57 (d, 1H, J = 13.5 Hz), 5.08 (d, 1H, J = 13.5 Hz), 6.48-7.90 (m, 13H), 9.87 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.5, 21.6, 46.4, 52.2, 124.9, 127.7, 127.9, 128.3, 128.7, 129.5, 129.5, 129.9, 131.1, 132.9, 133.3, 136.2, 140.2, 141.2, 144.3, 144.6, 167.7, 189.9; MS (m/z): 465 (M^++1).

Methyl (2E)-2-{[N-(2-formylphenyl)(4-methylbenzene)sulfo namido]methyl}-3-(2-methoxy phenyl)prop-2-enoate (3d)

Colourless solid; Yield: 97%; mp: 110-112 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.41 (s, 3H), 3.69 (s, 3H), 3.70 (s, 3H), 4.45 (d, 1H, J = 13.5 Hz), 5.01 (d, 1H, J = 13.8 Hz), 6.38 - 7.87 (m, 13H), 9.85 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 46.7, 52.2, 55.3, 110.7, 120.3, 123.1, 126.3, 127.5, 127.8, 128, 128.3, 129.5, 130, 130.9, 133.3 (m/z): 481 (M^++1).

Methyl (2E)-2-{[N-(2-formylphenyl)(4-methylbenzene)sulfo namido]methyl}-3-(4-methoxyphenyl)prop-2-enoat(3e)

Colourless solid; Yield : 97%; mp:110-112 ºC; 1H NMR (CDCl3, 300 MHz): δ 2.40 (s, 3H), 3.68 (s, 6H), 4.40 (d, 1H, J = 13.5Hz), 5.01 (d, 1H, J = 13.8Hz), 6.37 - 7.89 (m, 13H), 9.85 (s, 1H);13C NMR (CDCl3, 75 MHz): δ 21.6, 46.7, 52.2, 55.3, 110.7, 120.3, 123.1, 126.4, 127.4, 127.7, 128., 128.2, 129.5, 129.9, 130.9, 133.2, 133.3, 136.1, 140.9, 141.5, 144.1, 157.4, 167.4, 190;MS (m/z): 481 (M^++1).

Methyl (2E)-2-{[N-(2-formylphenyl)(4-methylbenzene)sulfo namido]methyl}-3-(2-chlorophenyl)prop-2-enoate (3f)

Colourless solid; Yield : 90%; mp: 142-144 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.43 (s, 3H), 3.65 (s, 3H), 4.49 (d, 1H, J = 13.5 Hz), 5.01 (d, 1H, J = 13.8 Hz), 6.44-7.91 (m, 13H), 9.98 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) : δ 21.6, 46.5, 52.4, 117.7, 123, 127.3, 128, 128.3, 128.5, 128.9, 129.6, 129.8, 130.9, 132.4, 133.5, 135.6, 136.1, 136.2, 141.3, 142.9, 144.5, 167.2, 189.8; MS(m/z): 485 (M^++1).

Methyl (2E)-2-{[N-(2-formylphenyl)(4-methylbenzene)sulfo namido]methyl}-3-(3-chlorophenyl)prop-2-enoate (3g)

Colourless solid; Yield: 90% ;mp: 142-144 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.43 (s, 3H), 3.65 (s, 3H), 4.49 (d, 1H, J = 13.5 Hz), 5.00 (d, 1H, J = 13.5 Hz), 6.44-7.91 (m, 13H), 9.97 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 46.4, 52.3, 126.9, 127.7, 128, 128.3, 128.5, 128.9, 129.6, 130.9, 132.4, 132.9, 133.50, 135.61, 136.07, 141.32, 142.87, 144.52, 167.22, 189.76; MS (m/z): 485 (M^++1).

Methyl (2E)-2-{[N-(2-formylphenyl)(4-methylbenzene)sulfo namido]methyl}-3-(4-chlorophenyl)prop-2-enoate (3h)

Colourless solid; Yield : 79%; mp:145-147ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.43 (s, 3H), 3.64 (s, 3H), 4.49 (d, 1H, *J* = 13.2 Hz), 5.00 (d, 1H, J = 12.9 Hz), 6.44-7.90 (m, 13H), 9.98 (s, 1H);^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.6, 46.5, 52.3, 126.9, 127.7, 128, 128.3, 128.5, 128.9, 129.6, 130.9, 132.4, 132.9, 133.5, 135.6, 136.1, 141.3, 142.9, 144.5, 167.2, 189.8; MS (m/z): 485 (M^++1).

(E)-methyl 3-(2,4-dichlorophenyl)-2-((N-(2-formylphenyl)-4-methylphenylsulfonamido)methyl)acrylate(3i)
Colourless solid; Yield : 80%, mp: 98-100ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) : δ 2.48 (s, 3H), 3.72 (s, 3H), 4.34 (d, 1H, J = 13.5Hz), 4.89 (d, 1H, J = 13.8Hz), 6.36-7.95 (m, 12H), 10.02 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) :δ 21.6, 46.8, 52.5, 117.7, 122.9, 127, 127.3, 128.1, 128.3, 128.6, 129.6, 129.8, 130.1, 131.1, 133.7, 134.9, 135.8, 136.1, 139.7, 141.4, 144.2, 189.7, 195; MS (m/z): 516 (M^++1).

(E)-methyl 2-((N-(2-formylphenyl)-4-methylphenylsulfonamido)methyl)-3-(4-isopropylphenyl)acrylate(3j)
Colourless solid; Yield: 88%; mp: 101-103 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz,): δ 1.29 (s, 3H), 1.31 (s, 3H), 2.43 (s, 3H), 2.96 (sep, 1H, J = 6.9 Hz), 3.62 (s, 3H), 4.58 (d, 1H, J = 13.2 Hz), 5.06 (d, 1H, J = 13.5 Hz), 6.49 - 7.88 (m, 13H), 9.85 (s, 1H); ^{13C} NMR ($CDCl_3$, 75 MHz): δ 21.6, 23.8, 23.9, 34.1, 46.5, 52.2, 124.9, 126.9, 127.8, 127.9, 128.3, 128.4, 129.5, 130.1, 131.4, 132.9, 133.3, 136.2, 141, 144.3, 144.6, 151.1, 167.8, 189.8; MS (m/z) : 492 (M^++1).

Methyl (2E)-2-{[N-(2-formylphenyl)(4-methylbenzene)sulfonamido]methyl}-3-(4-fluorophenyl)prop-2-enoate (3k)
Colourless solid; Yield: 79%; mp:132-134ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.43 (s, 3H), 3.63 (s, 3H), 4.53 (d, 1H, J = 13.2 Hz), 5.03 (d, 1H, J = 13.5 Hz), 6.46-7.90 (m, 13H), 9.93 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.5, 45.2, 51.2, 114.7, 114.9, 124.8, 126.5, 126.9, 127.2, 127.3, 128.5, 128.9, 128.9, 130.7, 130.8, 131.8, 132.3, 135, 140.1, 142, 143.4, 160.5, 166.7, 188.6; MS (m/z): 469 (M^++1).

Methyl (2E)-2-{[N-(2-formylphenyl)(4-methylbenzene)sulfonamido]methyl}-3-(naphthalen-1-yl)prop-2-enoate) (3l)
Colourless solid; Yield: 97%; mp:139-141ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.36 (s, 3H), 3.85 (s, 3H), 4.43 (d, 1H, J = 13.5 Hz), 5.00 (d, 1H, J = 13.8 Hz), 6.03 - 8.22 (m, 15H), 10.08 (s, 1H);^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.5, 46.9, 52.5, 124.6, 124.9, 126.4, 126.6, 126.7, 127.3, 127.9, 128, 128, 128.3, 129, 129.4, 131.3, 131.4, 133.2, 133.4, 135.8, 141.4, 142.9, 144, 166.9, 189.9; MS (m/z): 501 (M^++1).

Methyl (2E)-2-{[N-(2-formylphenyl)(4-methylbenzene)sulfonamido]methyl}-3-(3,4-dimethoxyphenyl)prop-2-enoate (3m)
Colourless solid; Yield:92%; mp:123-125ºC; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.45 (s, 3H), 3.59 (s, 3H), 3.95 (s, 3H), 3.96(s, 3H), 4.67 (d, 1H, J = 13.2 Hz), 5.13 (d, 1H, J = 13.2 Hz), 6.51-7.89 (m, 12H), 9.89 (s, 1H);^{13}C NMR ($CDCl_3$, 75MHz): δ 21.6, 46.2, 52.2, 56.1, 56.3, 111.1, 112.9, 122.7, 124.6, 126.5, 127.91, 128.4, 128.4, 128.6, 129.6, 133.1, 133.3, 136.4, 140.76, 141.8, 144.4, 144.8, 150.9, 168.1, 189.8; MS (m/z) : 511 (M^++1).

Methyl (2E)-2-{[N-(2-formylphenyl)(4-methylbenzene)sulfonamido]methyl}-3-(4-methylphenyl)prop-2-enoate (3n)
Colourless solid; Yield:87%: mp:110-112 ºC; ^{1}H NMR ($CDCl_3$, 300 MHz) : δ 1.29 (t, 3H, J = 7.5 Hz), 2.46 (s, 3H), 2.71 (q, 2H, J = 7.5 Hz), 3.60 (s, 3H), 4.46 (d, 1H, J = 12.9 Hz), 4.97 (d, 1H, J = 12.9 Hz), 6.25-7.52 (m, 13H), 9.89 (s, 1H);^{13}C NMR ($CDCl_3$, 75 MHz) : δ 15.4, 21.6, 28.8, 47.2, 52.1, 125.5, 127.55, 127.8, 128.2, 128.5, 128. 9, 129.5, 130, 130.8, 131.4, 133.6, 136.5, 142.7, 144.1, 144.2, 146.1, 168.1, 189.5; MS (m/z) 465 (M^++1).

General experimental procedures

Representative procedure for the synthesis of Methyl 3-phenyl-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate (5a):
To a solution of 2 mmol of N-allylated derivative (**3a**) in ethanol, $NH_2OH.HCl$ (6 mmol) was added and stirred well at room temperature for 1 h. After the completion of the reaction as evidenced by the tlc, ethanol was removed under reduced pressure and the crude thus obtained was further treated with 10 mL CCl_4 and NCS (5 mmol) and Et_3N (4 mmol) and the reaction mixture and stirred well at room temperature for 1 h. After completion of the reaction, reaction mixture was evaporated under reduced pressure and the resulting crude mass was diluted with water (15 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layer was washed with brine (2 × 10 mL) and dried over anhydrous Na2SO4. The organic layer was evaporated and the crude mass was purified by column chromatography (silica gel 60-120 mesh 5% EtOAc in hexanes) to provide the desired pure product **5a (**0.36 g, 79% yield).

Methyl 3-phenyl-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carboxylate (5a):
Colourless solid; mp 163 – 165 ˚C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.38 (s, 3H), 2.66 (d, 1H, J = 12.9 Hz), 3.80 (s, 3H), 4.74 (d, 1H, J = 12.9 Hz), 6.11 (s, 1H), 7.10 – 8.10 (m, 13H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 50.1, 53.6, 62.6, 88.2, 117.0, 119.8, 124.0, 125.4, 126.3, 126.7, 128.9, 129.0, 129.9, 131.1, 135.0, 136.6, 137.5, 144.2, 150.6, 170.6; IR (neat) : ν 1240, 1361, 1600 (medium), 1736 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{25}H_{22}N_2O_5S$ $[M + H]^+$ 463.1249, Found 463.1308.

Methyl 3-o-tolyl-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a- carboxylate (5b):
Colourless solid; Yield: 72%; mp 168 – 170ºC ; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.35 (s, 3H), 2.50(s, 3H), 2.77 (d, 1H, J = 12.9 Hz), 3.86 (s, 3H), 4.75 (d, 1H, J = 12.9 Hz) 6.30 (s, 1H), 7.11 – 8.10 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.4, 20.6, 23.7, 48.6, 52.7, 61.7, 115.7, 116.0, 118.5, 119.3, 123.0, 124.6, 125.6, 127.5, 128.0, 128.9, 130.0, 130.1, 133.2, 135.7, 136.5, 143.2, 149.4, 169.8; IR (neat): ν 1252, 1458, 1598 (medium), 1735 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{26}H_{24}N_2O_5S$ $[M + H]^+$ 477.1342, Found 477.1474.

Methyl 3-p-tolyl-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carboxylate (5c):
Colourless solid; Yield: 76%; mp 170-172 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.26 (s, 3H), 2.31(s, 3H), 2.63 (d, 1H, J = 12.9 Hz), 3.70 (s, 3H), 4.66 (d, 1H, J = 12.9.1 Hz), 5.99 (s, 1H), 7.01 – 8.01 (m, 12H);^{13}C NMR (75 MHz $CDCl_3$): δ 21.1, 21.5, 50.1, 53.6, 62.5, 88.2, 117.0, 119.8, 124.0, 125.3, 126.8, 126.8, 129.7,129.9, 131.1, 132.0, 136.6, 137.6, 138.8, 144.2, 150.6, 170.7; IR (neat): ν 1244, 1464, 1636 (medium), 1740 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{26}H_{24}N_2O_5S$ $[M + H]^+$ 477.1362, Found 477.1478.

Methyl 3-(2-methoxyphenyl)-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate (5d): Colourless solid; Yield: 80%; mp 132-134 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3H), 2.81 (d, 1H, J = 12.9 Hz), 3.80 (s, 6H), 5.10 (d, 1H, J = 12.9 Hz), 6.51 (s, 1H), 7.09 – 8.05 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 48.8, 53.6, 63.0, 85.8, 116.6, 120.0, 124.0, 126.3, 126.8, 127.5, 128.0, 129.9, 130.0, 130.1, 131.3, 131.4, 131.5, 132.9, 136.9, 137.5, 144.2, 150.9, 169.6; IR (neat):ν 1224, 1461, 1622 (medium), 1736 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{26}H_{24}N_2O_6S$ $[M + H]^+$ 493.1433, Found; 493.1533.

Methyl 3-(4-methoxyphenyl)-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate (5e): Colourless solid; Yield: 84%; mp 140-142 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3H), 2.72 (d, 1H, J = 12.6 Hz), 3.78 (s, 3H), 3.80 (s, 3H), 4.72 (d, 1H, J = 12.9 Hz), 6.06 (s, 1H), 6.88 – 8.09 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 50.1, 53.6, 55.3, 62.5, 88.1, 114.4, 117.1, 119.8, 124.0, 126.3, 126.7, 126.8,

127.1, 129.9, 131.2, 136.6, 137.6, 144.2, 150.6, 160.0, 170.7; IR (neat):ν 1287, 1513, 1613 (medium), 1740 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{26}H_{24}N_2O_6S$ $[M + H]^+$ 493.1344, Found 493.1433.

Methyl 3-(2-chlorophenyl)-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate (5f): Colourless solid; Yield: 78%; mp 155-157 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3H), 2.81 (d, 1H, J = 12.9 Hz), 3.80 (s, 3H), 5.10 (d, 1H, J = 12.9 Hz), 6.51 (s, 1H), 7.09 – 8.08 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 48.6, 53.6, 62.9, 85.8, 116.6, 120.0, 124.4, 126.8, 127.5, 128.0, 129.4, 129.9, 130.0, 130.1, 131.3, 131.4, 132.9.136.9, 137.5, 144.2, 150.7, 169.6; IR (neat): ν 1241, 1461, 1601 (medium), 1736 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{25}H_{21}ClN_2O_5S$ $[M + H]^+$ 497.0816, Found 497.0932.

Methyl 3-(3-chlorophenyl)-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate (5g): Colourless solid; Yield: 82%; mp 160-162 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3H), 2.67 (d, 1H, J = 12.9 Hz), 3.79 (s, 3H), 4.72 (d, 1H. J = 12.9 Hz), 6.09 (s, 1H), 7.10 – 8.08 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 50.1, 53.7, 62.6, 87.4, 116.8, 120.0, 124.2, 126.3, 126.7, 126.9, 126.9, 129.2, 129.3, 130.0, 131.3, 133.6, 134.9, 136.6, 137.5, 144.4, 150.7, 170.4; IR (neat):ν 1246, 1479, 1636 (medium), 1732 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{25}H_{21}ClN_2OS$ $[M + H]^+$ 497.0812, Found 497.0930.

Methyl 3-(4-chlorophenyl)-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate(5h): Colourless solid; Yield: 85%; mp 159-161 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.40 (s, 3H), 2.66 (d, 1H, J = 12.6 Hz), 3.80 (s, 3H), 4.72 (d, 1H, J = 12.9 Hz), 6.09 (s, 1H), 7.11 – 8.08 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 50.1, 53.7, 62.6, 87.4, 116.8, 120.0, 124.2, 126.3, 126.7, 126.9, 129.3, 130.0, 131.3, 133.6, 134.9, 136.6, 137.6, 144.3, 150.7, 170.7; IR (neat): ν 1243, 1490, 1616 (medium), 1740 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{25}H_{21}ClN_2O_5S$ $[M + H]^+$ 497.0924, Found 497.0932.

Methyl 3-(2,4-dichlorophenyl)-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate (5i): Colourless solid; Yield: 79%; mp 157-159 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.40 (s, 3H), 2.81 (d, 1H, J = 12.9 Hz), 3.80 (s, 3H), 5.06 (d, 1H, J = 12.6 Hz), 6.46 (s, 1H), 7.10 – 8.07 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$) : δ 21.6, 48.8, 53.7, 63.0, 85.4, 116.5, 120.1, 124.1, 126.3, 126.8, 127.9, 129.1, 129.8, 130.0, 131.5, 131.6, 132.1, 135.4, 137.0, 137.5, 144.3, 151.1, 169.5; IR (neat): ν 1244, 1463, 1636 (medium), 1737 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{25}H_{20}Cl_2N_2O_5S$ $[M + H]^+$ 531.0436, Found 531.0549.

Methyl 3-(4-isopropylphenyl)-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate (5j): Colourless solid; Yield: 86%; mp 152-154 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.16 (d, 6H, J = 6.9 Hz), 2.31 (s, 3H), 2.83 (sep, 1H, J = 6.9 Hz), 2.61 (d, 1H, J = 12.9 Hz), 3.71 (s, 3H), 4.68 (d, 1H, J = 12.9 Hz), 5.99 (s, 1H), 7.02 – 8.02 (m, 12H).^{13}C NMR (75 MHz $CDCl_3$): δ 21.5, 23.8, 23.9, 33.8, 50.1, 53.6, 62.5, 88.3, 117.0, 119.7, 124.0, 125.4, 126.3, 126.8, 127.0, 129.9, 131.1, 132.3, 136.6, 137.4, 144.2, 149.7, 150.63, 170.7; IR (neat): ν 1260, 1461, 1606 (medium), 1742 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{28}H_{28}N_2O_5S$ $[M + H]^+$ 505.1674, Found 505.1795.

Methyl 3-(4-fluorophenyl)-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate (5k): Colourless solid; Yield: 81%; mp 139-141 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3H), 2.66 (d, 1H, J = 12.6 Hz), 3.79 (s, 3H), 4.72 (d, 1H, J = 12.9 Hz), 6.09 (s, 1H), 7.05 – 8.08 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.5, 50.1, 53.7, 62.6, 87.5, 115.9, 116.2, 116.8, 119.9, 124.1, 126.3, 126.7, 127.3, 127.4, 130.0, 130.9, 131.2, 136.6, 137.5, 144.4, 150.7, 170.5; IR (neat): ν 1240, 1508, 1603 (medium), 1746 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{25}H_{21}FN_2O_5S$ $[M + H]^+$ 481.1124, Found 481.1235.

Methyl 3-(naphthalen-2-yl)-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate (5l): Colourless solid; Yield: 84%; mp 155-157 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.34 (s, 3H), 2.62 (d, 1H, J = 12.9 Hz), 3.87 (s, 3H), 4.69 (d, 1H, J = 12.9 Hz), 6.96 (s, 1H), 7.11 – 7.93 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.4, 50.2, 53.8, 63.3, 86.2, 117.4, 120.2, 122.5, 124.0, 124.2, 125.5, 126.2, 126.0, 126.5, 127.4, 129.0, 129.2, 129.7, 129.8, 130.2, 131.0, 133.6, 136.9, 137.6, 144.1, 150.6, 171.1; IR (neat): ν 1240, 1486, 1600 (medium), 1738 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{29}H_{24}N_2O_5S$ $[M + H]^+$ 513.1370, Found 513.1488.

Methyl 3-(3,4-dimethoxyphenyl)-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate (5m): Colourless solid; Yield: 79%; mp 156-158 ºC; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.39 (s, 3H), 2.73 (d, 1H, J = 12.9 Hz), 3.79 (s, 3H), 3.87 (d, 6H, J = 4.8 Hz), 4. 73 (d, 1H, J = 12.9 Hz), 6.06 (s, 1H), 6.75 – 8.08 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.5, 28.6, 49.1, 52.6, 54.9, 55.1, 61.5, 87.1, 107.3, 110.5, 116.0, 116.8, 118.9, 123.0, 125.2, 127.7, 126.5, 129.0, 130.1, 135.6, 136.6, 143.3, 148.4, 149.7, 169.7; IR (neat):ν 1237, 1512, 1623 (medium), 1737 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{27}H_{26}N_2O_7S$ $[M + H]^+$ 523.1422, Found 523.1534.

Methyl 3-(4-ethylphenyl)-5-tosyl-3,3a,4,5-tetrahydro isoxazolo[4,3-c]quinoline-3a-carboxylate(5n): Colourless solid; Yield: 74%; mp 163-165 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.24 (t, 3H, J = 7.5 Hz), 2.38 (s, 3H), 2.67 (q, 3H, J = 7.5 Hz), 3.78 (s, 3H), 4.75 (d, 1H, J = 12.9 Hz), 6.07 (s, 1H), 7.11 – 8.09 (m, 12H); ^{13}CNMR (75 MHz, $CDCl_3$): δ 15.4, 21.5, 28.5, 50.1, 53.6, 62.5, 88.3, 117.0, 119.8, 122.4, 124.0, 125.4, 126.3, 126.8, 128.5, 129.9, 131.1, 132.2, 136.6, 137.5, 144.2, 145.1, 170.7; IR (KBr): ν 1245, 1486, 1606 (medium), 1737 (strong) cm^{-1} ; HRMS (m/z) Calcd for $C_{27}H_{26}N_2O_5S$ $[M + H]^+$491.1523, Found 491.1639.

Typical experimental procedure for the synthesis of (Z)-N-(2-cyano-3-phenylallyl)-N-(2-formylphenyl)-4-methylbenzenesulfonamide (7a): A solution of N-Ts aminobenzaldehyde (**1**) (1 mmol, 0.28g) and potassium carbonate (2 mmol, 0.29 g) in acetonitrile solvent was stirred for 15 min at room temperature. To this solution, (E)-2-(bromomethyl)-3-arylacrylonitrile (**6a**) (1.2 mmol, 0.27 g) was added drop wise till the addition is complete. After the completion of the reaction as indicated by TLC, the reaction mixture was concentrated and extracted with ethylacetate (2x15 mL). The organic layer thus obtained was washed with water (2x10 mL), followed by brine solution (2x 10 mL) and dried over anhydrous sodium sulphate. Then the crude sample was purified by a pad of silica gel (100-200 mesh) column chromatography using ethylacetate and Hexane (1:9) to afford the pure product (**7a**) as a colourless solid (0.38 g, 92% yield).

(Z)-N-(2-cyano-3-phenylallyl)-N-(2-formylphenyl)-4-methylbenzenesulfonamide (7a)

Colorless solid; Yield:92%; mp:126-128°C; 1H NMR (300 MHz, CDCl3): δ 2.44 (s, 3H), 4.27 (d, 1H, J = 14.4Hz), 4.82 (d, 1H, J = 13.8Hz), 6.85–8.03 (m, 14H), 10.46 (s, 1H); 13C NMR (CDCl3, 75 MHz): δ 21.7, 55.8, 105.5, 117.5, 128.1, 128.3, 128.9, 129, 129.3, 129.4, 129.9, 131.2, 132.4, 134, 134.3, 135.9, 140.3, 144.8, 147.9, 189,6; MS (m/z):417 (M^++1).

(2Z)-2-{[N-(2-Formylphenyl)(4-methylbenzene)sulfonamido]methyl}-3-(2-chlorophenyl) prop-2-enenitrile (7b)
Colorless solid; Yield :92%; mp: 134-136°C; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 2.46 (s, 3H), 4.30 (d, 1H, J = 13.1 Hz), 4.87 (d, 1H, J = 13.8 Hz), 6.86–8.03 (m, 13H), 10.46 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) : δ 21.7, 55.3, 109.1, 116.6, 127.3, 128.1, 129.2, 129.3, 129.5, 129.8, 129.9, 130.8, 131.9, 133.9, 134.2, 134.3, 135.9, 140.1, 144.5, 144.8, 189.5; MS (m/z): 452 (M^++1).

(2Z)-2-{[N-(2-Formylphenyl)(4-methylbenzene)sulfonamido]methyl}-3-(4-chlorophenyl) prop-2-enenitrile (7c)
Colorless solid; Yield: 92%; mp: 131-133°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.45 (s, 3H), 4.30 (d, 1H, J = 13.1 Hz), 4.87 (d, 1H, J = 13.8 Hz), 6.86–8.03 (m, 13H), 10.42 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.7, 55.8, 106.3, 117.2, 128, 128.4, 129.3, 129.3, 129.5, 129.9, 130.3, 130.8, 133.9, 134.4, 135.8, 137.2, 140.3, 144.9, 146.3, 189.5; MS (m/z) :452 (M^++1).

(2Z)-3-(2H-1,3-Benzodioxol-5-yl)-2-{[N-(2-formylphenyl)(4-methylbenzene)sulfonamido| methyl}prop-2-enenitrile (7d)
Colorless solid; Yield :92%; mp:136-138°C; ^{1}HNMR (300 MHz, $CDCl_3$) : δ 2.45 (s, 3H), 4.24 (d, 1H, J = 13.5 Hz), 4.77 (d, 1H, J = 13.5 Hz), 5.99 (s, 2H), 6.75-8.00 (m, 12H), 10.40 (s, 1H);^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.7, 55.9, 101.8, 102.5, 107.8, 108.6, 117.8, 125.9, 126.6, 127.3, 128, 128.4, 129.3, 129.4, 129.8, 134.2, 135.9, 140.3, 144.7, 147.5, 148.3, 150.3, 189.6; MS (m/z) : 462 (M^++1).

(Z)-N-(2-cyano-3-(2,4-dichlorophenyl)allyl)-N-(2-formylphenyl)-4-methylbenzenesulfonamide (7e)
Colorless solid; Yield:92%; mp:126-132°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.46 (s, 3H), 4.30 (d, 1H, J = 14.4Hz), 4.80 (d, 1H, J = 14.7Hz), 6.87–8.01 (m, 12H), 10.42 (s, 1H);^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.7, 55.8, 106.2, 117.2, 125.6, 127.4, 128, 128.4, 129.1, 129.3, 129.4, 129.5, 129.7, 129. 9, 130.3, 130.8, 130.9, 134.4, 135.8, 137.2, 140.3. 144.9, 146.3, 189.6; MS (m/z): 483 (M^++1).

((Z)-N-(2-cyano-3-(4-isopropylphenyl)allyl)-N-(2-formylphenyl)-4-methylbenzenesulfonamide(7f)
Colorless solid; Yield: 88%; mp:132-136 ºC ^{1}H NMR ($CDCl_3$, 300 MHz,): δ 1.29 (s, 6H), 2.46 (s, 3H), 2.42 (sep, J = 6.3 Hz, 1H), 4.27 (d, 1H, J = 14.1Hz), 4.84 (d, 1H, J = 13.8Hz), 6.86 - 8.01 (m, 13H), 10.45 (s, 1H).^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.7, 23.7, 23.8, 34.1, 55.8, 103.9, 117.7, 127.1, 128.1, 128.3, 129.3, 129.3, 129.6, 129.8, 129.9, 129.9, 134.1, 134.3, 135.9, 140.3, 144.7, 147.9, 152.7, 189.6; MS (m/z); 457 (M^++1).

(2Z)-2-{[N-(2-Formylphenyl)(4-methylbenzene)sulfonamido]methyl}-3-(2-methylphenyl) prop-2-enenitrile (7g)
Colorless solid; Yield: 92%; mp:121-123°C; ^{1}H NMR (300 MHz, $CDCl_3$) : δ 2.06 (s, 3H), 2.46 (s, 3H), 4.30 (s, 1H), 4.88 (d, 1H, J = 11.7 Hz), 6.87–8.03 (m, 13H), 10.49 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) : δ 19.5, 21.7, 55.4, 107.7, 117.1, 126.4, 127.8, 128.1, 129.2, 129.3, 129.9, 130.5, 130.7, 131.8, 133.8, 134.3, 136, 137.1, 140.2, 144.9, 147.3, 189.6; MS (m/z); 432 (M^++1).

(2Z)-2-{[N-(2-formylphenyl)(4-methylbenzene)sulfonamido]methyl}-3-(3-chlorophenyl) prop-2-enenitrile(7h)
Colorless solid; Yield: 92%; mp: 124-228°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.45 (s, 3H), 4.29 (d, 1H, J = 14.1Hz), 4.81 (d, 1H, J = 14.1Hz), 6.87–8.01 (m, 13H), 10.43 (s, 1H); ^{13}C NMR (CDCl3, 75 MHz): δ 21.7, 55.8, 105.5, 117.5, 127.3, 128.1, 128.4, 128.9, 129, 129.3, 129.5, 129.9, 131.2, 132.3, 134.1, 134.3, 135.8, 140.3, 144.8, 147.9, 189.6; MS (m/z); 452 (M^++1).

(2Z)-2-{[N-(2-Formylphenyl)(4-methylbenzene)sulfonamido]methyl}-3-(3,4-dimethoxyphenyl)prop-2-enenitrile (7i)
Colorless; solid; Yield: 92%; mp: 139-141°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.45 (s, 3H), 3.86 (s, 3H), 3.88 (s, 3H), 4.23 (d, 1H, J = 14.4 Hz), 4.83 (d, 1H, J = 13.1 Hz), 6.80–8.01 (m, 12H), 10.47 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) : δ 21.6, 55.9, 55.9, 55.9, 60.9, 101.9, 110.5, 110.8, 118.2, 124.4, 125.3, 128, 128.2, 129.2, 129.8, 129.9, 134.1, 134.3, 135.9, 140.4, 144.7, 147.8, 149, 151.7, 189.7; MS (m/z): 478 (M^++1).

Representative procedure for the synthesis of 3-Phenyl-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carbonitrile (9a):
To a solution of 2 mmol of N-allylated derivative (**7a**) in ethanol, $NH_2OH.HCl$ (6 mmol) was added and stirred well at room temperature for 1 h. After the completion of the reaction as evidenced by the tlc, ethanol was removed under reduced pressure and the crude thus obtained was further treated with 10 mL CCl_4 and NCS (5 mmol) and Et_3N (4 mmol) and the reaction mixture and stirred well at room temperature for 1 h. After completion of the reaction, reaction mixture was evaporated under reduced pressure and the resulting crude mass was diluted with water (15 mL) and extracted with ethyl acetate (3 × 15 mL). The combined organic layer was washed with brine (2 × 10 mL) and dried over anhydrous Na_2SO_4. The organic layer was evaporated and the crude mass was purified by column chromatography (silica gel 60-120 mesh 5% EtOAc in hexanes) to provide the desired pure product **9a (**0.29 g, 67% yield).

3-Phenyl-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carbonitrile(9a):
Colourless solid; Yield: 67%; mp 136 - 138 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.38, (s, 3H), 3.90 (d, 1H, J = 12.6 Hz), 5.30 (d, 1H, J = 12.9 Hz), 5.49 (s, 1H), 7.12 – 7.95 (m, 13H); ^{13}CNMR (75 MHz, $CDCl_3$): δ 21.6, 51.0, 54.2, 89.4, 113.8, 114.0, 119.7, 124.5, 126.7, 126.8, 128.8, 129.1, 130.2, 131.5, 132.7, 135.5, 136.7, 145.5, 151.6; IR (KBr): ν1262, 1444, 1603, 2837 (medium) cm^{-1} ; HRMS (m/z) Calcd for $C_{24}H_{19}N_3O_3S$ $[M + H]^+$ 430.1168, Found 430.1203.

3-(2-Chlorophenyl)-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carbonitrile (9b):
Colourless solid; Yield: 64%; mp 160-162 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.32 (s, 3H), 2.76 (d, 1H, J = 13.2 Hz), 5.10 (d, 1H, J = 12.9 Hz), 6.49 (s, 1H), 7.02 – 7.93 (m, 12H); ^{13}CNMR (75 MHz, $CDCl_3$): δ 21.6, 43.7, 48.5, 50.9, 86.3, 113.7, 116.6, 119.4, 124.2, 127.1, 127.8, 128.1, 129.9, 130.9, 131.1, 131.4, 131.1, 132.4, 135.7, 136.5, 145.0, 148.0; IR (KBr): ν 1261, 1523, 1633, 2057 (medium) cm^{-1}; HRMS (m/z) Calcd for $C_{24}H_{18}ClN_3O_3S$ $[M + H]^+$ 464.0767, Found 464.0842.

3-(4-Chlorophenyl)-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carbonitrile (9c):
Colourless solid; Yield: 66%; mp 158-160°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.31 (s, 3H), 3.81 (d, 1H, J = 12.9 Hz), 5.21 (d, 1H, J = 12.6 Hz), 5.40 (s, 1H), 7.05 – 7.98 (m, 12H); ^{13}CNMR (75 MHz, $CDCl_3$): δ 20.5, 28.6, 49.9, 53.2, 87.6, 112.6, 112.9, 118.7, 123.6, 125.8, 127.0, 127.2, 128.4, 128.9, 131.8, 134.5, 135.3, 135.7, 144.2, 150.6; IR (KBr): ν 1284, 1491, 1636, 2925 (medium) cm^{-1} ; HRMS (m/z) Calcd for $C_{24}H_{18}ClN_3O_3S$ $[M + H]^+$ 464.0756, Found 464.0833.

3-(Benzo[d][1,3]dioxol-5-yl)-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carbonitrile (9d):
Colourless solid; Yield: 61%; mp 175-177 °C; ^{1}H NMR (300

MHz, $CDCl_3$): δ 2.39 (s, 3H), 3.84 (d, 1H, J = 12.9 Hz), 5.27 (d, 1H, J = 12.9 Hz), 5.40 (s, 1H), 6.05 (s, 2H), 6.90 – 7.96 (m, 11H); ^{13}CNMR (75 MHz, $CDCl_3$): δ 21.6, 51.0, 54.0, 57.2, 89.3, 101.6, 107.2, 108.7, 113.8, 119.7, 121.0, 124.5, 124.8, 126.7, 128.1, 129.9, 132.7, 135.5, 136.7, 145.1, 148.3, 149.2, 151.6; IR (KBr): ν 1024, 1362, 1605, 2830 (medium) cm^{-1} ; HRMS (m/z) Calcd for $C_{25}H_{19}N_3O_5S$ $[M + H]^+$ 474.1045, Found 474.1125.

3-(2,4-dichlorophenyl)-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carbonitrile (9e): Colourless solid; Yield: 63%; mp 152-154 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.38 (d, 3H), 3.87 (d, 1H, J = 12.9 Hz), 5.28 (d, 1H, J = 12.9 Hz), 5.46 (s, 1H), 7.11 – 7.96 (m, 11H); ^{13}CNMR (75 MHz, $CDCl_3$): δ 15.3, 21.6, 28.7, 51.0, 54.1, 89.5, 113.9, 114.2, 119.7, 124.5, 126.7, 126.9, 128.0, 128.5, 128.6, 129.9, 132.6, 135.6, 136.7, 145.1, 146.5, 151.6; IR (KBr): ν 1286, 1462, 1604, 2963 (medium) cm^{-1} ; HRMS (m/z) Calcd for $C_{24}H_{17}Cl_2N_3O_3S$ $[M + H]^+$ 498.0346, Found 498.0460.

3-(4-Isopropylphenyl)-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carbonitrile(9f): Colourless solid; Yield: 66%; mp 183-185 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.30 (d, 6H, J = 15.0 Hz), 2.38 (s, 3H), 2.83 (sep, 1H, J = 6.6 Hz), 3.87 (d, 1H, J = 11.7 Hz), 5.26 (d, 1H, J = 9.9 Hz), 5.40 (s, 1H), 7.13 – 7.96 (m, 12H); ^{13}CNMR (75 MHz, $CDCl_3$): δ 21.6, 23.8, 23.9, 34.0, 51.0, 54.0, 89.5, 113.9, 114.2, 119.7, 124.5, 126.7, 127.0, 128.5, 129.9, 132.6, 135.6, 136.7, 145.1, 151.6; IR (KBr): ν 1269, 1463, 1637, 2398 (medium) cm^{-1} ; HRMS (m/z) Calcd for $C_{27}H_{25}N_3O_3S$ $[M + H]^+$ 472.1578, Found 472.1694.

3-o-Tolyl-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carbonitrile (9g): Colourless solid; Yield: 65%; mp 190-192 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.30 (s, 3H), 2.31 (s, 3H), 3.85 (d, 1H, J = 12.6 Hz), 5.28 (d, 1H, J = 12.9 Hz), 5.75 (s, 1H), 7.03 – 7.8 (m, 12H); ^{13}CMR (75 MHz, $CDCl_3$): δ 14.1, 19.7, 21.6, 29.7, 51.1, 54.3, 86.5, 113.8, 119.6, 124.5, 126.7, 127.5, 128.1, 129.7, 130.9, 132.6, 135.4, 135.5, 136.5, 145.1, 151.1; IR (KBr): ν 1287, 1489, 1633, 2852 (medium) cm^{-1} ; HRMS (m/z) Calcd for $C_{25}H_{21}N_3O_3S$ $[M + H]^+$ 444.1254, Found 444.1379.

3-(3-Chlorophenyl)-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carbonitrile (9h): Colourless solid; Yield: 67%; mp 155-157 °C; 1H NMR (300 MHz, CDCl3): δ 2.30 (s, 3H), 3.83 (d, 1H, J = 5.1 Hz), 5.23 (d, 1H, J = 5.1 Hz), 5.43 (s, 1H), 7.02 – 7.86 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.6, 28.6, 50.0, 53.2, 88.3, 112.8, 118.7, 123.5, 125.8, 127.0, 128.1, 128.8, 128.9, 129.2, 130.6, 130.5, 131.7, 134.5, 135.7, 144.1, 150.6; IR (KBr): ν 1260, 1521, 1635, 2923 (medium) cm^{-1} ; HRMS (m/z) Calcd for $C_{24}H_{18}ClN_3O_3S$ $[M + H]^+$ 464.0746 Found 464.0829.

3-(3,4-Dimethoxyphenyl)-5-tosyl-3,3a,4,5-tetrahydroisoxazolo[4,3-c]quinoline-3a-carbonitrile (9i): Colourless solid; Yield: 62%; mp 180-182 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.33 (s, 3H), 3.94 (d, 1H, J = 21.6 Hz), 3.95 (s, 6H), 5.54 (d, 1H, J = 13.2 Hz), 5.95 (s, 1H), 7.10 – 7.97 (m, 11H); ^{13}CNMR (75 MHz, $CDCl_3$): δ 21.5, 51.4, 54.5, 56.3, 88.2, 111.5, 112.9, 113.7, 114.1, 115.4, 119.8, 122.9, 124.5, 126.6, 128.0, 129.9, 132.7, 135.8, 136.8, 145.0, 148.9, 150.8, 151.6; IR (KBr): ν 1268, 1461, 1637, 2925 (medium) cm-^{1} ; HRMS (m/z) Calcd for $C_{26}H_{23}N_3O_5S$ $[M + H]^+$ 490.1324, Found 490.1431.

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Electronic Supplementary Information (ESI) available: Representative experimental procedures, with all spectral data of **3a-n, 5a-n, 7a-i, 9a-i**, crystal data, ORTEP diagram and the CCDC number for **5a, 9b** is **1060438** and **1406080**. For ESI and crystallographic data]. See DOI: 10.1039/c000000x/

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9. Structure was cofirmed by single-crystal X-ray data. CCDC number for compound **5a, 9b** is **1060438** and **1406080** respectively.