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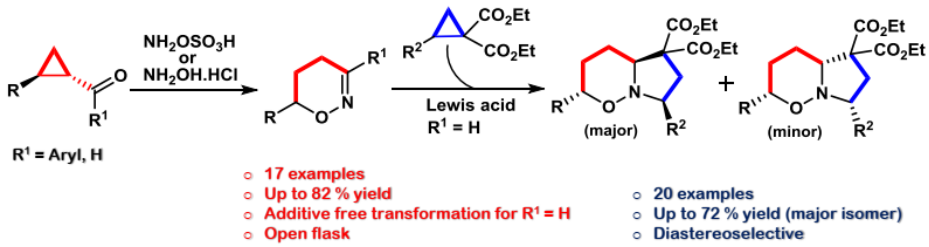
Accessing Dihydro-1,2-oxazine *via* Cloke-Wilson type Annulation of Cyclopropyl Carbonyls: Application towards the Diastereoselective Synthesis of Pyrrolo[1,2-*b*][1,2]oxazine

Pankaj Kumar, Rakesh Kumar, and Prabal Banerjee*

Department of Chemistry, Indian Institute of Technology Ropar, Nangal Road, Rupnagar, Punjab, India, 140001

Fax: (+91)-1881-223395; e-mail: prabal@iitrpr.ac.in

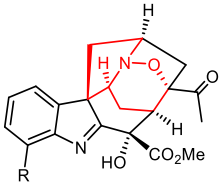
ABSTRACT



A convenient additive-free synthesis of dihydro-4*H*-1,2-oxazines *via* a Cloke-Wilson type ring expansion of the aryl substituted cyclopropane carbaldehydes (ACC) with the hydroxylamine salt is introduced. Comparatively less active cyclopropyl ketones also follow a similar protocol if supplemented by catalytic *p*TSA.H_2O. The transformation is performed in an open-to-air flask as it shows negligible sensitivity towards air/moisture. Dihydro-4*H*-1,2-oxazines when subjected to cycloaddition with the cyclopropane diester, affords a trouble-free formulation of the valued hexahydro-2*H*-pyrrolo[1,2-*b*][1,2]oxazine derivatives. Cascade one-pot variant of this two-step strategy offers a comparable overall yield of the final product.

INTRODUCTION

Cyclic oxime ethers[1a] and their bicyclic derivatives are an interesting class of compounds for their potential application in the synthesis of naturally occurring as well as biologically important target molecules. With unique functionalities, these cyclic oxime ethers contribute to the basic structure of many bioactive molecules and at the same time, offer as intermediates for the synthesis of pyrroles, pyrrolidines, amino alcohols and various furan derivatives. In this regard, isoxazoles, isoxazolines and hexahydropyrrolo[1,2-*b*]isoxazole have been studied thoroughly for the synthesis of various alkaloids, steroids, prostaglandins and many other natural products.[1] Although, the pyrrolo[1,2-*b*][1,2]oxazine moiety does serve as the key structural core of the two novel alkaloids alsmaphorazine A and alsmaphorazine B, isolated from the alstonia plant (Figure 1),[2] the study of six-membered cyclic oxime-ethers and especially their bicyclic derivative hexahydro-2*H*-pyrrolo[1,2-*b*][1,2]oxazine is very limited due to the lack of convenient methods of their preparation. At this point, there lies an obvious urge to standardize a straight-forward route for the synthesis of these potential cyclic as well as bicyclic oxime ether derivatives from readily available substrates and so their further exploration.

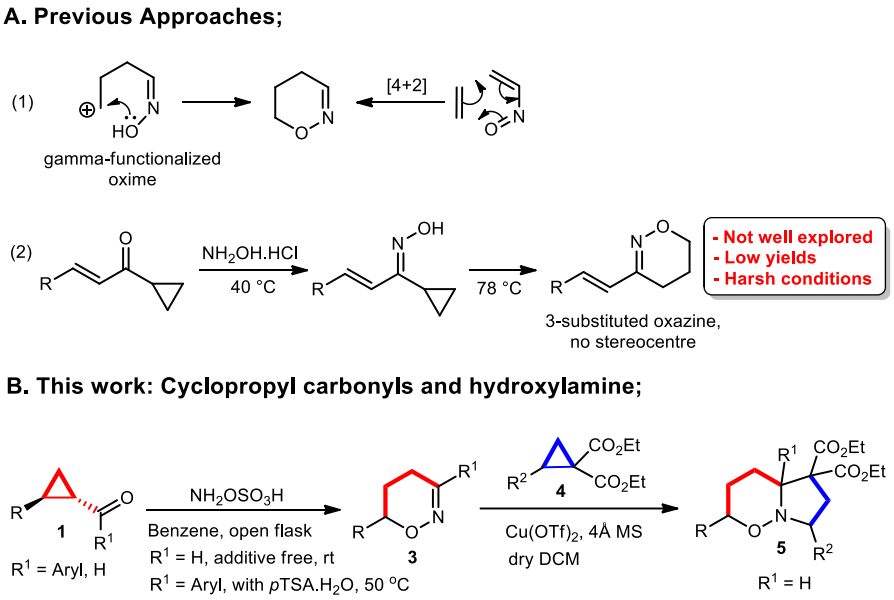


alsmaphorazine A: R=OH
alsmaphorazine B: R=H

Figure 1: Alkaloids having pyrrolo[1,2-*b*][1,2]oxazine as their core structure.

Most of the reports on the synthesis of 5,6-dihydro-4*H*-1,2-oxazine are based on [4+2] cycloaddition of nitrosoalkenes to olefins and intramolecular cyclization of the γ-

functionalized oxime derivatives (Scheme 1, A), most of which require harsh reaction conditions and sensitive reaction setups.[1a, 3] Surprisingly, the involvement of strain driven reactivity of donor-acceptor cyclopropanes[4] for the facile synthesis of six membered oxime ethers has been overlooked for years. The only report considering the intramolecular cyclopropane ring opening by the oxygen atom of the oximino group was back in 1981 by C. N. Rentzea using cyclopropyl styryl ketone and hydroxylammonium chloride constructing 3-vinyl- substituted dihydrooxazines (Scheme 1, A).[5] However, the strategy suffered low yields (29-50%) even under reflux conditions. Remarkably, for the last four decades, no attempts were reported utilizing the activated donor-acceptor cyclopropane analogues for a relatively simplified route for 6-substituted dihydrooxazines and their potential application towards the cycloaddition reactions. Undoubtedly, the participation of cyclopropyl aldoximes in a possible Cloke-Wilson type ring expansion reaction[6] could serve as an intriguing technique for the convenient synthesis of dihydrooxazines.



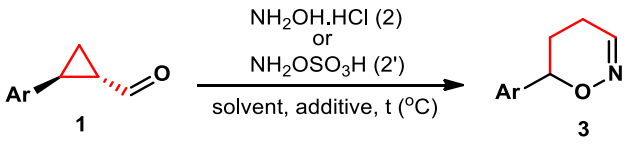
Scheme 1. Available synthetic routes to oxazine derivatives and this work.

To seize this opportunity, we intended to use the aryl substituted cyclopropane carbaldehyde (ACC, **1**) and the hydroxylamine salt as precursors of cyclopropyl aldoximes that would undergo the much anticipated Cloke-Wilson type rearrangement for an effortless construction of 6-aryl-5,6-dihydro-4*H*-1,2-oxazine (**3**, Scheme 1, B). The idea worked smoothly in an open flask at room temperature, without any additive or a catalytic reagent. So, to carry out the transformation, we have to just stir the two substrates in an appropriate solvent. Further, the electronegativity of oxygen atom in the cyclic oxime ether is expected to enhance polarization of the carbon-nitrogen double bond, and we thought it might serve as an interesting dipolarophile for a possible cycloaddition process with a dipolar species like the well-known donor-acceptor cyclopropane our group has been working on. Consequently, we tried this proposal with the aryl substituted cyclopropane diester (**4**) in the presence of various Lewis acids to successfully construct 2,7-diarylhexahydro-2*H*-pyrrolo[1,2-*b*][1,2]oxazine (**5**, Scheme 1, B). We also attempted this two-step strategy for a tandem one-pot synthesis of **5** and conveniently managed to capitalize a promising one-pot approach for the synthesis of 2,7-diarylhexahydro-2*H*-pyrrolo[1,2-*b*][1,2]oxazine with a comparative yield to that of the step-wise process.

RESULTS AND DISCUSSION

A recent report on the reactivity of cyclopropyl diketones with the hydroxylamine hydrochloride[7] and our earlier work on ACCs[8] assisted us to start our trials with *trans*-2-(4-methoxyphenyl)cyclopropane-1-carbaldehyde (**1a**). We attempted the expected transformation with hydroxylammine hydrochloride (**2**) in dimethylsulfoxide (DMSO) solvent, but this ended up to an isomeric mixture of cyclopropyl oximes and the cyclopropane ring remained intact. In order to make the hydroxyl group of the cyclopropyl oxime attack on aryl end of the ACC, we used bases like K_2CO_3 and NaH

Table 1. Optimization of the reaction conditions[a]



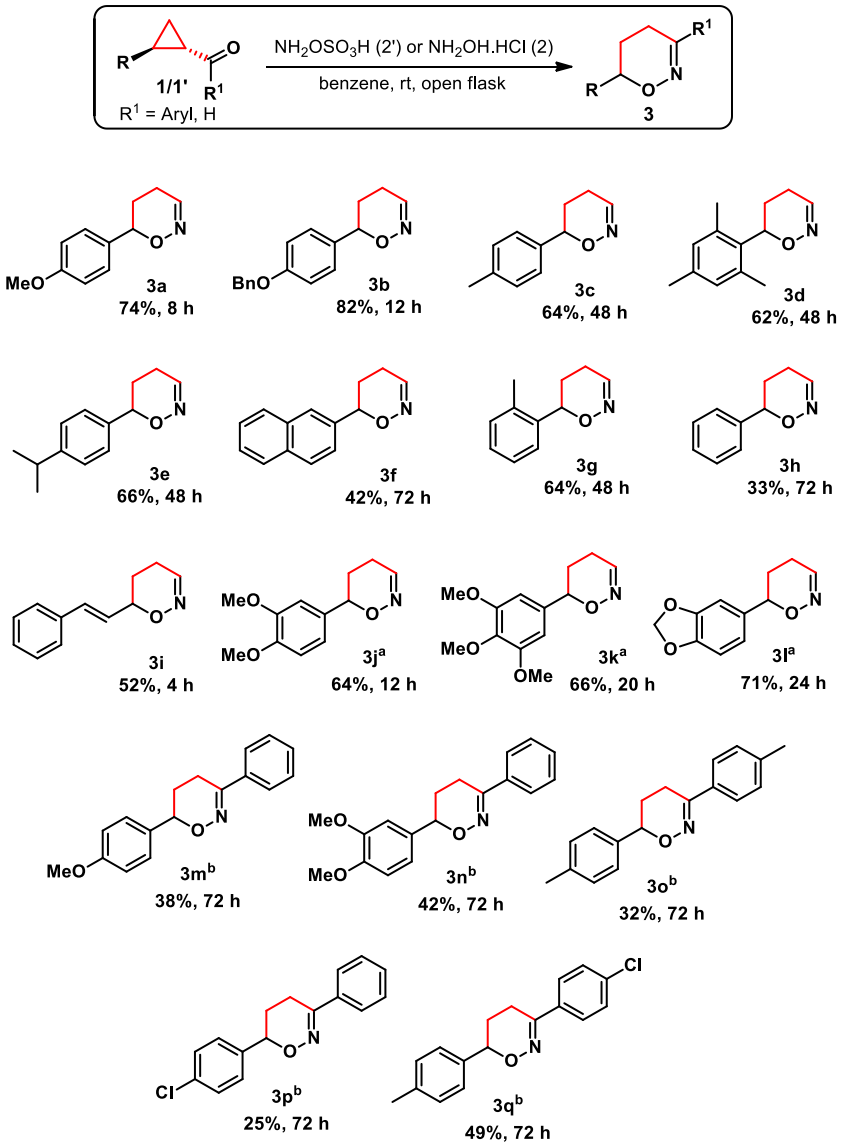
entry	ACC	**2/2´**	solvent	additive	T (°C)	yield (%)[b]
1	**1a**	**2**	DMSO	-	rt	m.o.[c]
2	**1a**	**2**	DMSO	K_2CO_3/NaH	rt	m.o.[c]
3	**1a**	**2**	DMSO	$InCl_3$/MgI_2/$TiCl_4$	rt	c.m.[d]
4	**1a**	**2**	DMSO	*p*-TSA/CSA	rt	c.m.[d]
5	**1a**	**2**	DMSO	-	80 °C/ reflux	c.m.[d]
6	**1j**	**2**	DMSO	-	rt	m.o.[c]
7	**1k**	**2**	DMSO	-	rt	m.o.[c]
8	**1a**	**2**	CH_2Cl_2	-	rt	m.o.[c]
9	**1a**	**2**	THF	-	rt	38
10	**1a**	**2**	C_6H_6	-	rt	52
11	**1a**	**2**	toluene	-	rt	48
12	**1a**	**2´**	C_6H_6	-	rt	74
13	**1a**	**2´**	toluene	-	rt	66

[a]Reactions were carried out with 1 equiv. of **1** and 1.5 equiv. of **2/2´**. [b]Isolated % yields of **3**. [c]m.o. = mixture of oximes. [d]c.m. = complex mixture.

that might increase the nucleophilicity of oxygen, but was all in vain (entry 2, Table 1). Further, we longed that the activation of cyclopropane ring might have been the problem. So, we used more activated ACCs like the *trans*-2-(3,4,5-trimethoxyphenyl)cyclopropane-1- carbaldehyde (**1k**), and also added various Lewis as well as Brønsted acids like $InCl_3$, MgI_2, $TiCl_4$, *p*-toluene sulfonic acid (*p*-TSA) and camphorsulfonic acid (CSA), but again none of them could help (entry 3-4, Table 1). Later on, we attempted the reaction in different solvents like diethyl ether, tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), methanol, dimethylformamide (DMF), benzene (C_6H_6) and toluene, where we finally thrived in isolating the expected product (**3a**) from THF, benzene and toluene solvents with 38, 52 and 48% of respective yields. To enhance the yield of this transformation we tried to perform the reaction at high temperatures under reflux conditions, but the cyclopropane got decomposed under such harsh conditions. However, when we switched hydroxylamine hydrochloride (**2**) with hydroxylamine-*O*-sulfonic (**2´**) acid in benzene solvent, a huge increase in the isolated yield was observed, and we got **3a** in 74% yield (entry 12, Table 1). Finally, we performed the optimized reaction in an open-to-air flask, in reagent grade benzene solvent to find out how the resulting yield is altered in open atmosphere. Remarkably, the isolated yield was almost consistent with that obtained in an inert setup, and so, all the reactions that followed were performed in open-flasks.

For the study of generality, we carried out this transformation with a variety of substitutions on the cyclopropane ring (Scheme 2). It was noted that the approach is fairly compatible with both highly activated as well as less activated ACCs, however, the best yield (82%) was obtained for the benzyloxyphenyl derivative (**3b**, scheme 2). The electron donating groups on the aryl ring enhances the activation of the

cyclopropane ring and so, reduced the reaction time to a few hours (**3a**, **3b**, **3j**-**3l**), whereas the less activated ACCs like those substituted with phenyl, naphthyl or tolyl groups took longer time for the conversion to complete (**3c**-**3h**). On the other hand, negligibly activating or deactivating substitutes like *p*-bromophenyl, *p*-chlorophenyl or the alkyl groups on cyclopropane carbaldehyde, could only afford the isomeric mixture

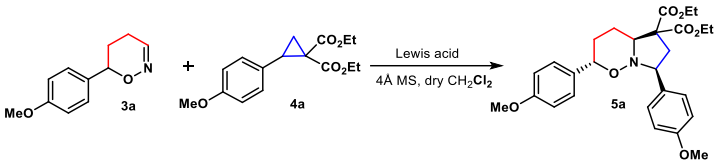


Scheme 2: Substrate scope for Cloke-Wilson type rearrangement of cyclopropyl carbonyls with hydroxylamine salts. Unless otherwise mentioned, all reactions were carried out with 1 equiv. of **1**/**1´** and 1.5 equiv. of **2´**. [a]Reactions were carried out with 1.5 equiv. of **2**. [b]Reactions were carried out with 2 equiv. of **2** in the presence of *p*TSA.H_2O (0.2 equiv.) at 50 ºC.

of oxime and not the oxazine derivatives. Formulation of (*E*)-6-styryl-5,6-dihydro-4*H*-1,2-oxazine (**3i**) from *trans*-2-((*E*)-styryl)cyclopropane-1-carbaldehyde (**1i**) with an isolated yield of 52% was the fastest of all under normal reaction conditions (Scheme 2). The single-crystal X-ray structure[16] of **3b** confirmed that the oxazine ring is in half-chair conformation with an exo orientation of the substituent. To check whether the reaction is feasible with aryl substituted cyclopropyl ketones, we tried the standard protocol with (trans-2-(4-methoxyphenyl)cyclopropyl)(phenyl)methnone (**1a´**), but it did not show any conversion. After a few changes in the reaction conditions, the transformation did work out, however, under comparatively harsh circumstances. The transformation was optimized with hydroxylamine hydrochloride and in the presence of catalytic amount of *p*-toluene sulfonic acid monohydrate (*p*TSA.H_2O) at 50 ºC (**3m-3q**, Scheme 2). The conversion rates were found to be very low as were the percentage yields, and it was understandable as ketones are less reactive as compared to the aldehydes. We also tried to increase the reactivity of the cyclopropane by having more electron releasing 3,4-dimethoxy phenyl group on the vicinal position of the cyclopropane but no noticeable change was observed in the percentage yield (**3n**). Having an electron withdrawing group like the 4-chlorophenyl, on the keto group did raised the yield to 49% (**3q**), but it was the highest we could get with the aryl substituted cyclopropyl ketones.

With the library of dihydro-4*H*-1,2-oxazine derivatives in hand, we projected a promising cycloaddition on the carbon-nitrogen double bond of these cyclic oxime ethers. Driven by our previous experience on the donor-acceptor cyclopropanes (DACs),[9] Lewis acid catalysed aryl substituted cyclopropane diester appeared to be a good precursor for our proposal. We started our trials with diethyl 2-(4-methoxyphenyl)cyclopropane-1,1-dicarboxylate (**4a**) as the standard substrate. Its

Table 2. Optimization of the reaction conditions for the cycloaddition process[a]

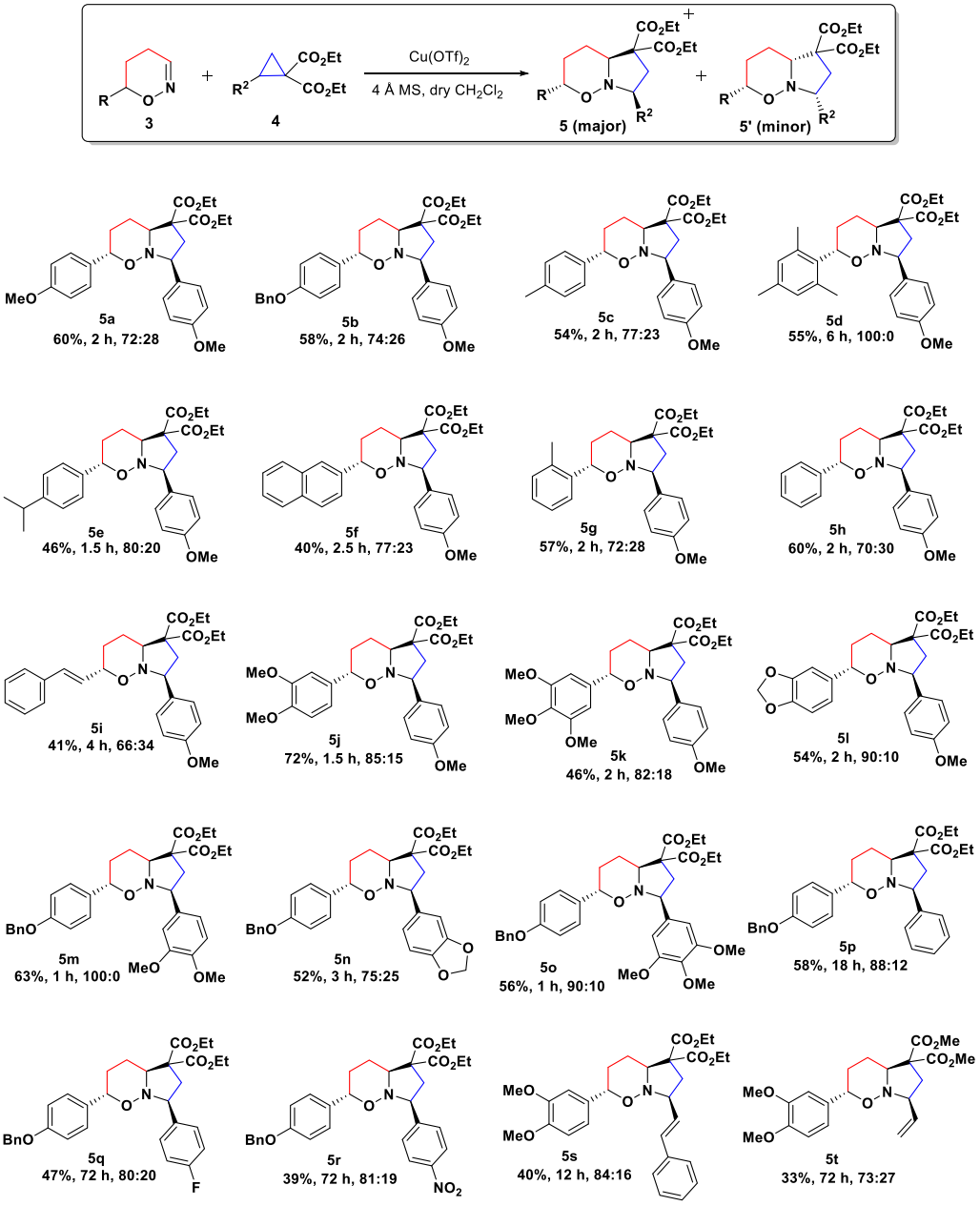


entry	Lewis acid	equiv.	t (h)	Yield (%)[b]
1	$InCl_3$	0.2	5	54
2	MgI_2	0.2	2	44
3	$MgBr_2$	0.2	12	28
4	TMSOTf	0.2	24	12
5	$TiCl_4$	0.2	0.5	c.m.[c]
6	$SnCl_4$	0.2	0.5	c.m.[c]
7	$BF_3.OEt_2$	0.2	0.5	c.m.[c]
8	$Sc(OTf)_3$	0.2	4	53
9	$Yb(OTf)_3$	0.2	6	42
10	$In(OTf)_3$	0.2	6	38
11	$Cu(OTf)_2$	0.1	4	55
12	$Cu(OTf)_2$	0.2	2	60
13	$Cu(OTf)_2$	0.4	2	52
14	$Cu(OTf)_2$	0.5	1.5	46

[a]Reactions were carried out in dry CH_2Cl_2 with 1 equiv. of **3a** and 1 equiv. of **4a**. [b]Isolated yield of the major isomer **5a**. [c]c.m. = complex mixture.

reaction with **3a** in the presence of 0.2 equivalent $InCl_3$, constructed diethyl 2,7-bis(4-methoxyphenyl)hexahydro-5*H*-pyrrolo[1,2-*b*][1,2]oxazine-5,5-dicarboxylate (**5a**, major isomer) in 54% isolated yield. To capitalize the process, trials were carried out with varying concentrations of different Lewis acids like $MgBr_2$, MgI_2, TMSOTf, $Yb(OTf)_3$, $Sc(OTf)_3$, $In(OTf)_3$, $Cu(OTf)_2$, $BF_3.OEt_2$, $SnCl_4$ and $TiCl_4$, which recommended 0.2 equivalent of $Cu(OTf)_2$ in anhydrous dichloromethane solvent to be the pre-eminent reaction condition for this strategy (entry 12, Table 2).

Using the optimized conditions, we moved further to check the substrate scope of this cycloaddition process in terms of differently substituted dihydro-4*H*-1,2-oxazine derivatives and also with various cyclopropane diesters. Here we successfully synthesized a series of 20 examples with moderate to excellent yields, advocating the broad generality of this strategy (Scheme 3). To have an overview on the reactivity of differently substituted dihydro-4*H*-1,2-oxazine derivatives, we subjected them to the cycloaddition reaction. All the dihydrooxazine derivatives derived from various ACCs easily underwent the expected transformation within a few hours, and thus supported the fact that the substitution on 6th position does not have a major role in the reaction kinetics (**5a**-**5l**, Scheme 3). However, the steric bulk of this substituent is found to actually affect the diastereoselectivity of the transformation. A big mesityl group at the 6th position of dihydro-4*H*-1,2-oxazine afforded exclusively a single isomer (**5d**, Scheme 3), whereas, the less bulky styryl substituent induced the worst diastereoselectivity (66:34, **5i**:**5i´**). In most of the cases, we could isolate only the major isomers in pure form, but for **5i**/**5i´** we managed to isolate both the isomers and their relative configuration was established by analysing the 2D NMR spectra (Figure 2). From the 2D NMR elucidations of the two isomers, it was clear that the protons H_d and H_f were in close proximity and the fused pyrrolidine rings in both **5i** and **5i´** were having



Scheme 3: Substrate scope for the cycloaddition process. Unless otherwise mentioned, all reactions were carried out in dry CH_2Cl_2 with 1 equiv. of **3**, 1 equiv. of **4** and 0.2 equiv. of $Cu(OTf)_2$. Isolated yields of the major isomers (**5**) are reported. Diastereomeric ratios (**5**:**5´**) of major (**5**) and minor isomers (**5´**) are reported.

the thermodynamically stable *cis* configuration of its substituents.[10] Diastereomers **5i** and **5i´** differ only in their relative configuration of the proton H_a with respect to that of H_d and H_f. In the minor isomer **5i´**, protons H_a, H_d and H_f are in the *cis* configuration while in the major isomer **5i**, H_a is *trans* to both H_d and H_f (Figure 2). We generalized

this stereochemical model of the diastereomers to all other examples also because the respective ^{1}H NMR patterns were exactly the same except for the relatively upfield shift of the proton H_a in case of **5i**/**5i´**, which was anticipated for the styryl substitution here. The diastereomeric ratios for all the products were calculated by examining their crude ^{1}H NMR spectrum. We also carried out the cycloaddition reaction with differently substituted cyclopropane diesters and found that the reaction kinetics was directly affected by the reactivity of DAC. Electron releasing substituents like the 3,4-dimethoxyphenyl and 3,4,5-trimethoxyphenyl on vicinal position of the cyclopropane increases the reactivity of DAC and so reduced the reaction time (**5m** and **5o**, Scheme 3). On the other hand, with electron withdrawing substituents like the 4-fluorophenyl and 4-nitrophenyl on vicinal position of the cyclopropane, the reaction time increased up to 3 days (**5p**-**5r**). With 3,4-dimethoxyphenyl substituted cyclopropane diester (**4b**), exclusive formation of the major isomer **5m** was observed. Styryl and vinyl substituted cyclopropane diesters also underwent the proposed cycloaddition reaction, however, their reaction time and percentage yields were disappointing (**5s**, **5t**, Scheme 3).

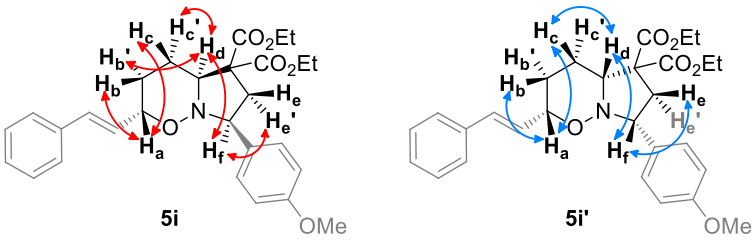
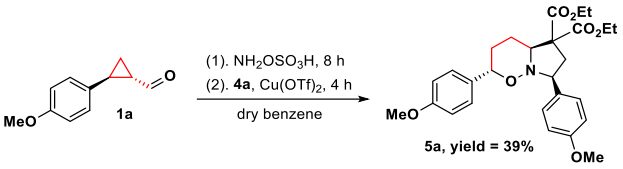


Figure 2: 2D NOE correlations determining the diastereomeric structures of **5i**:**5i´**.

Once we standardized this stepwise strategy for a number of hexahydro-5*H*-pyrrolo[1,2-*b*][1,2]oxazine derivatives, we were motivated to attempt a cascade one-pot route to the final product (**5**). Accordingly, we carried out the reaction of **1a** with hydroxylamine-*O*-sulfonic acid (**2´**) in dry benzene and after 8 hours, confirming the formation of **3a** on TLC, added a benzene solution of **4a** and $Cu(OTf)_2$ into the reaction

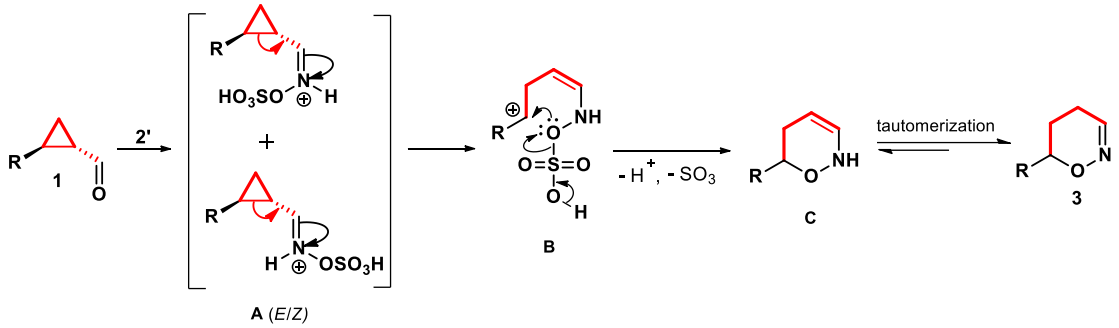
mixture. The procedure worked really well and the major isomer of the final product (**5a**) was isolated in 39% overall yield which was comparable to the 44.4% overall yield of **5a** obtained in a stepwise process (Scheme 4).



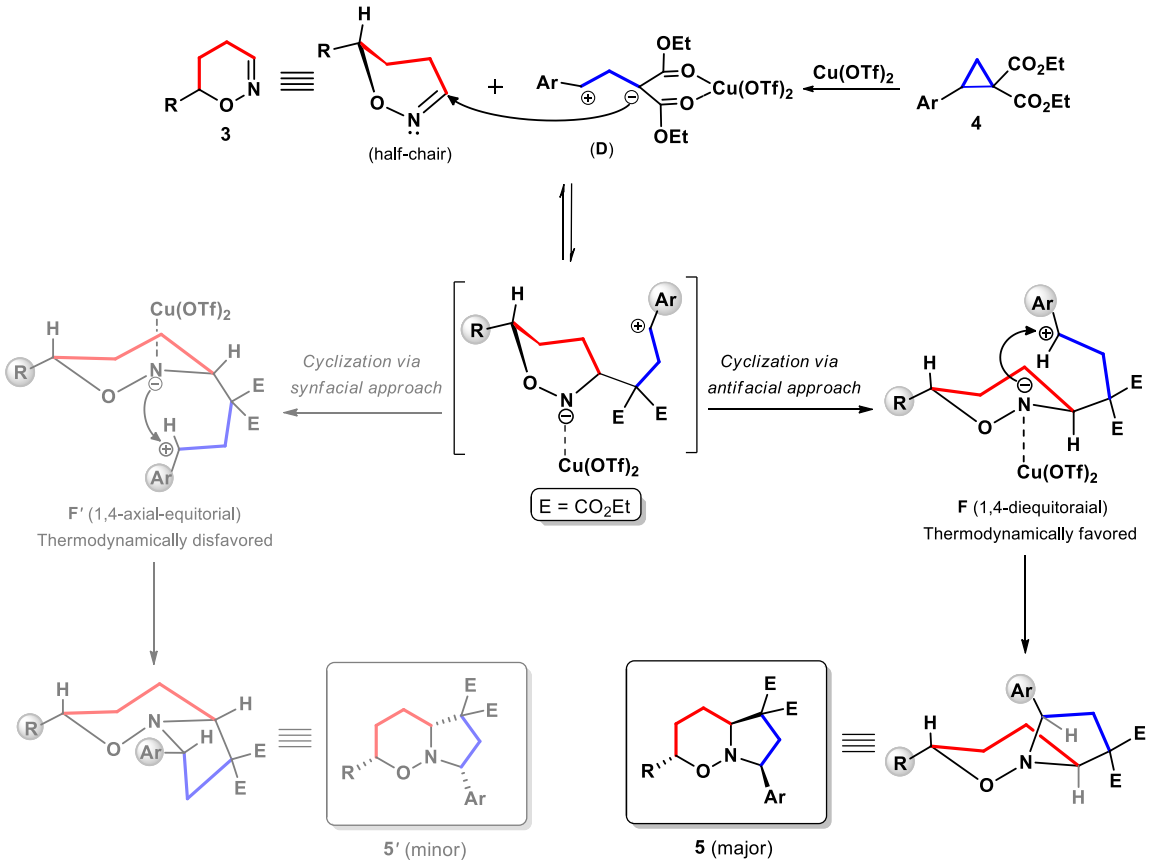
Scheme 4: Towards one-pot synthesis of **5a**.

The probable mechanistic pathway this process follows is in agreement with the general reactivity of its precursors[4,5,11] involving condensation of the ACC (**1**) with the hydroxylamine-*O*-sulfonic acid (**2´**) and formation of cyclopropyl oxime-*O*-sulfonic acid (**A**, Scheme 5). Here, the iminium ion formation and subsequent activation of the cyclopropane ring is attributable to the presence of acidic proton in the substrate **2´** and thus, no additional activator or reagent is required. Conventionally, a mixture of *E* and *Z* oximes will form (**A**), however, the geometry of *E* oxime would restrict it from taking part in the direct cyclization. Even with the *Z* oxime, the direct cyclization would be a *6-endo-tet* process which is disfavored according to the Baldwin's rule for ring closure reactions.[12] To confront both these issues, we propose that the cyclopropane undergoes ring opening prior to the cyclization and generate a benzyl cation/enamine intermediate **B**. The carbon-nitrogen bond in intermediate **B** is free to rotate and can easily assume the desired geometry for cyclization. Consequently, through a nucleophilic attack of oxygen on the carbocation, intermediate **B** undergoes cyclization and with loss of sulphur trioxide furnishes a six membered cyclic enamine derivative **C**. Intermediate **C** then undergoes tautomerization to afford the half-chair conformer of dihydro-4*H*-1,2-oxazine (**3**) i.e., the first product of this protocol. In the second step, product **3** behave as a dipolarophile when subjected to the cycloaddition reaction with

Step 1: Cloke-Wilson type annulation reaction



Step 2: Cycloaddition reaction

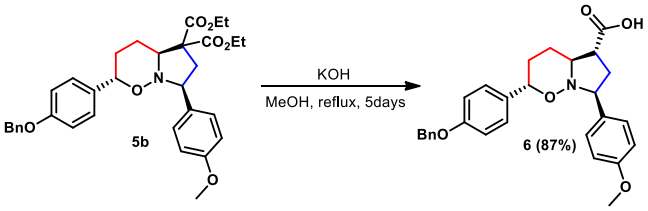


Scheme 5: Plausible mechanism.

4 in the presence of $Cu(OTf)_2$. The carbon-carbon bond of the DAC is activated by the co-ordinate interactions of its diester group with $Cu(OTf)_2$ and it ultimately undergoes heterolytic cleavage to give a 1,3-zwitterionic species **D**.[13] Shortly, the imine bond in product **3** (in half-chair conformation) encounters a nucleophilic attack by the enolate

group of intermediate **D**. This reversible carbon-carbon bond formation would ease the half-chair conformation of the dihydrooxazine ring to a chair conformation which finally participates in a carbon-nitrogen bond formation between the dihydrooxazine nitrogen and the benzylic carbocation to complete the cyclization process. The final cyclization can take place through an approach which is either *synfacial* or *antifacial* to substituent R of the dihyrooxazine ring. In the *synfacial* approach, the reaction proceeds *via* a thermodynamically disfavored 1,4-axial-equitorial transition state **F´**, leading to the minor diastereomer **5´** of the final product. On the other hand, the *antifacial* approach instigates a thermodynamically favored transition state **F** with both the bulky substituents on equitorial positions. This stable 1,4-diequitorial transition state leads to the formation of major diastereomer **5** of the hexahydro-5*H*-pyrrolo[1,2-*b*][1,2]oxazine derivative (Scheme 5).

After we established the strategy well for a number of substrates, we were curious to see what further scope can we have for the designed molecules. The diester group in **5b** when subjected to hydrolysis with KOH in methanol under reflux conditions underwent monodecarboxylation to afford the monocarboxylic acid **6** with the generation of a new stereocentre in the molecule (Scheme 6).[14] The geometry of **6** was established by its single-crystal X-ray structure[16] which further helped us to ascertain the relative stereochemistry of the major diastereomer **5b**.



Scheme 6: Monodecarboxylation of **5b**.

CONCLUSIONS

To sum up, an additive-free technique has been developed for the synthesis of 5,6-dihydro-4*H*-1,2-oxazine that works perfectly well in open flask and at ambient temperatures. Cyclopropyl ketones, though with *p*TSA.H_2O as mediator, does follow the same course at higher temperatures. This approach might serve as a good synthetic tool for industrial purpose also as it eliminates the sophisticated reaction setup requirements. Lewis acid catalysed cycloaddition of the dihydrooxazine derivative with the donor-acceptor cyclopropane, to afford the distinctive hexahydro-5*H*-pyrrolo[1,2-*b*][1,2]oxazine and its one-pot variant, offers an effortless protocol for the synthesis of selectively functionalized pyrrolo[1,2-*b*][1,2]oxazines from simple and readily available precursors. Monodecarboxylation of the diester functionality in the final product supplements another stereocentre to the molecule and substantiate it for further functionalizations as well. This protocol is believed to serve as a convenient tool for the development of 5,6-dihydro-4*H*-1,2-oxazine as well as hexahydro-5*H*-pyrrolo[1,2-*b*][1,2]oxazine based chemistry, both for the research and industrial purposes.

EXPERIMENTAL SECTION

General Information

All solvents and reagents were obtained from commercial sources and were purified following the standard procedure prior to use (unless otherwise mentioned). Powdered molecular sieves (4 Å MS) were dried at 200 °C under vacuum prior to use. The developed chromatogram was analysed by UV lamp (254 nm) or using the *p*-anisaldehyde charring solution. Products were purified by flash chromatography on silica gel (mesh size 230–400). Melting points were determined using a Stuart SMP30 advanced digital melting point apparatus. Infrared (FTIR) spectra were recorded for

the neat samples and reported in wavenumber (cm^{-1}). Mass spectral data (HRMS) were obtained using XEVO G2-XS QTOF instrument. The ^{1}H NMR and $^{13}C\{^{1}H\}$ NMR spectra were recorded at 400 MHz and 100 MHz respectively on 400 MHz JEOL JNM ECS400 instrument in $CDCl_3$ solvent (unless otherwise mentioned). Chemical shifts of ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra are expressed in parts per million (ppm). All coupling constants (*J*) are absolute values and are expressed in hertz (Hz). The description of the signals includes the following: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, dt = doublet of triplet, q = quartet, dq = doublet of quartet, br = broad, and m = multiplet.

General procedure for the synthesis of *trans*-2-arylcyclopropane-1-carbaldehydes (ACCs, 1)[8]: Following the established literature, synthesis of **1** was carried out by following the known procedures as mentioned below. For the reaction scheme, see Scheme S1 in the Supporting Information.

1) To a mixture of triethyl phosphonoacetate (1.1 equiv.), DBU (0.035 equiv.), and finely ground K_2CO_3 (2 equiv.) was added ArCHO (1 equiv.) and the resulting mixture was stirred using a magnetic stirrer for 4 h at room temperature under argon atmosphere. Ethyl acetate was added to the crude mixture and the solid was filtered off. The solid was rinsed with ethyl acetate and the combined filtrate was concentrated. The resulting oil was distilled under reduced pressure using a bulb-to-bulb apparatus (10 mm Hg/240 °C) to give corresponding alkene (yield 84%) (*E*:*Z* = 99:1).

2) A suspension of TMSOI (2.5 equiv.) and NaH (2.5 equiv.) in anhydrous DMSO (25 mL) was stirred at ambient temperature for 30 minutes. A DMSO solution (14 mL) of alkene (14 mmol, 1 equiv) was added at 0 °C. The reaction mixture was stirred at 55 °C (on silicone oil bath) for another 48 h. On completion (monitored by TLC), the

reaction mixture was poured into a brine solution and extracted 3 times with ethyl acetate. The combined organic layer was washed with water and brine, dried over Na_2SO_4, concentrated and purified by silica gel column using ethyl acetate/hexane as eluent to afford corresponding cyclopropane derivative (60-80% yield).

3) To a stirred solution of LAH (1.5 equiv.) in 7 mL diethyl ether was added dropwise a solution of cyclopropane ester (0.90 mmol, 1equiv.) in 3 mL diethyl ether under N_2 atmosphere. After addition was completed the reaction mixture was stirred at room temperature for another 2 to 6 h. On completion (monitored by TLC), the excess LAH was destroyed by ice cold water. 15 mL of 10% H_2SO_4 and 8 mL of ether was added and the aqueous layer was extracted several times with diethyl ether. The combined organic layer was washed with water and 5% $NaHCO_3$, dried over $MgSO_4$ and concentrated in a rotary evaporator (90-95% yield). Without any further purification, the crude material (a colorless oil) was used for next step.

4) To a solution of cyclopropane alcohol (6.8 mmol, 1 equiv.) in dry DCM (14 mL), PCC (1.5 equiv.) was added in a portion-wise manner through a solid addition tube under N_2 atmosphere. After 3 h reaction mixture was filtered through a small plug of celite and concentrated in vacuo. The crude mixture was purified by silica gel column chromatography using ethyl acetate/hexane as eluent. Starting from aryl aldehyde the 2-arylcyclopropanecarbaldehydes was obtained in 40-55% overall yield.

trans-2-(4-methoxyphenyl)cyclopropane-1-carbaldehyde (**1a**). 4-methoxybenzaldehyde (1.0 g, 7.35 mmol), **1a** (0.62 g, 3.53 mmol), 48% overall yield, white solid, ^{1}H NMR (400 MHz): δ 9.30 (d, *J* = 4.9 Hz, 1H), 7.05 (d, *J* = 8.7 Hz, 2H), 6.83 (d, *J* = 8.7 Hz, 2H), 3.79 (s, 3H) 2.63-2.56 (m, 1H), 2.13-2.06 (m, 1H), 1.73-1.67 (m, 1H), 1.51-1.45 (m, 1H)

trans-2-(4-(benzyloxy)phenyl)cyclopropane-1-carbaldehyde (**1b**). 4-(benzyloxy)benzaldehyde (1.0 g, 4.71 mmol), **1b** (0.55 g, 2.16 mmol), 46% overall yield, yellow solid, ^{1}H NMR (400 MHz): δ 9.30 (d, *J* = 4.5 Hz, 1H), 7.44-7.31 (m, 5H), 7.04 (d, *J* = 8.5 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 5.04 (s, 2H), 2.62-2.55 (m, 1H), 2.13-2.06 (m, 1H), 1.72-1.67 (m, 1H), 1.51-1.45 (m, 1H)

trans-2-(p-tolyl)cyclopropane-1-carbaldehyde (**1c**). 4-methylbenzaldehyde (1.0 g, 8.32 mmol), **1c** (0.69 g, 4.32 mmol), 52% overall yield, colorless liquid, ^{1}H NMR (400 MHz): δ 9.30 (d, *J* = 4.5 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.2 Hz, 2H), 2.63-257 (m, 1H), 2.32 (s, 3H), 2.16-2.10 (m, 1H), 1.74-1.68 (m, 1H), 1.54-1.48 (m, 1H)

trans-2-mesitylcyclopropane-1-carbaldehyde (**1d**). 2,4,6-trimethylbenzaldehyde (1.0 g, 6.75 mmol), **1d** (0.53 g, 2.84 mmol), 42% overall yield, pale yellow liquid, ^{1}H NMR (400 MHz): δ 9.28 (d, *J* = 5.4 Hz, 1H), 6.85 (s, 2H), 2.45-2.39 (m, 1H), 2.33 (s, 6H), 2.25 (s, 3H), 1.98-1.91 (m, 1H), 1.82-1.76 (m, 1H), 1.40-1.34 (m, 1H)

trans-2-(4-isopropylphenyl)cyclopropane-1-carbaldehyde (**1e**). 4-isopropylbenzaldehyde (1.0 g, 6.75 mmol), **1e** (0.63 g, 3.37 mmol), 50% overall yield, yellow liquid, ^{1}H NMR (400 MHz): δ 9.31 (d, *J* = 4.5 Hz, 1H), 7.17 (d. *J* = 8.2 Hz, 2H), 7.06 (d, *J* = 8.2 Hz, 2H), 2.95-2.84 (m, 1H), 2.65-2.58 (m, 1H), 2.19-2.13 (m, 1H), 1.75-1.69 (m, 1H), 1.56-1.49 (m, 1H), 1.24 (d, *J* = 6.8 Hz, 6H)

trans-2-(naphthalen-2-yl)cyclopropane-1-carbaldehyde (**1f**). 2-naphthaldehyde (1.0 g, 6.41 mmol), **1f** (0.53 g, 2.69 mmol), 42% overall yield, off white solid, ^{1}H NMR (400 MHz): δ 9.37 (d, *J* = 4.5 Hz, 1H), 7.82-7.74 (m, 3H), 7.58 (s, 1H), 7.49-7.41 (m, 2H), 7.20 (dd, *J* = 8.4, 1.8 Hz, 1H), 2.82-2.76 (m, 1H), 2.30-2.23 (m, 1H), 1.83-1.77 (m, 1H), 1.69-1.62 (m, 1H)

trans-2-(o-tolyl)cyclopropanecarbaldehyde (**1g**). 2-methylbenzaldehyde (1.0 g, 8.32 mmol), **1g** (0.60 g, 3.75 mmol), 45% overall yield, colourless liquid, ^{1}H NMR (400 MHz): δ 9.35 (d, *J* = 4.6 Hz, 1H), 7.18-7.11 (m, 3H), 7.03-6.99 (m, 2H), 2.65-2.59 (m, 1H), 2.35 (s, 3H), 2.05-1.99 (m, 1H), 1.73-1.67 (m, 1H), 1.58-1.52 (m, 1H)

trans-2-phenylcyclopropane-1-carbaldehyde (**1h**). Benzaldehyde (1.0 g, 9.43 mmol), **1h** (0.69 g, 4.72 mmol), 50% overall yield, white solid, ^{1}H NMR (400 MHz): δ 9.32 (d, *J* = 4.5 Hz, 1H), 7.33-7.27 (m, 2H), 7.25-7.20 (m, 1H), 7.13-7.09 (m, 2H), 2.66-2.60 (m, 1H), 2.21-2.14 (m, 1H), 1.76-1.71 (m, 1H), 1.57-1.51 (m, 1H)

trans-2-styrylcyclopropanecarbaldehyde (**1i**). *trans*-cinnamaldehyde (1.0 g, 7.56 mmol), **1i** (0.52 g, 3.02 mmol), 40% overall yield, viscous yellow liquid, ^{1}H NMR (400 MHz): δ 9.25 (d, *J* = 4.9 Hz, 1H), 7.32-7.29 (m, 4H), 7.24-7.19 (m, 1H), 6.56 (d, *J* = 16.0 Hz, 1H), 5.76 (dd, *J* = 16.0, 8.6 Hz, 1H), 2.33-2.25 (m, 1H), 2.08-2.01 (m, 1H), 1.66-1.60 (m, 1H), 1.34-1.28 (m, 1H)

trans-2-(3,4-dimethoxyphenyl)cyclopropanecarbaldehyde (**1j**). 3,4-dimethoxybenzaldehyde (1.0 g, 6.02 mmol), **1j** (0.53 g, 2.59 mmol), 43% overall yield, off white solid, ^{1}H NMR (400 MHz): δ 9.31 (d, *J* = 4.4 Hz, 1H), 6.79 (d, *J* = 7.9 Hz, 1H), 6.69-6.64 (m, 2H), 3.87 (s, 3H), 3.86 (s, 3H), 2.64-2.58 (m, 1H), 2.15-2.08 (m, 1H), 1.73-1.67 (m, 1H), 1.53-1.47 (m, 1H)

trans-2-(3,4,5-trimethoxyphenyl)cyclopropanecarbaldehyde (**1k**)**.** 3,4,5-trimethoxybenzaldehyde (1.0 g, 5.09 mmol), **1k** (0.58 g, 2.45 mmol), 48% overall yield, white solid, ^{1}H NMR (400 MHz): δ 9.31 (d, *J* = 4.5 Hz, 1H), 6.33 (s, 2H), 3.84 (s, 6H), 3.81 (s, 3H), 2.62-2.56 (m, 1H), 2.18-2.11 (m, 1H), 1.73-1.67 (m, 1H), 1.53-1.47 (m, 1H)

trans-2-(benzo[d][1,3]dioxol-5-yl)cyclopropanecarbaldehyde (**1l**). benzo[*d*][1,3]dioxole-5-carbaldehyde (1.0 g, 6.66 mmol), **1k** (0.56 g, 2.93 mmol), 44% overall yield, off white solid, ^{1}H NMR (400 MHz): δ 9.30 (d, *J* = 4.6 Hz, 1H), 6.72 (d, *J* = 8.1 Hz, 1H), 6.61 (dd, *J* = 8.0, 1.8 Hz, 1H), 6.56 (d, *J* = 1.8 Hz, 1H), 5.93 (s, 2H), 2.60-2.54 (m, 1H), 2.12-2.05 (m, 1H), 1.71-1.64 (m, 1H), 1.48-1.41 (m, 1H)

General procedure for the synthesis of (*trans*-2-arylcyclopropyl)(aryl)methnone (1′): For the reaction scheme, see Scheme S2 in the Supporting Information.

1) To a mixture of Ar′$COCH_3$ (1 g, 1 equiv.) and benzaldehyde (1.1 equiv.) in ethanol (10 mL), pellets of KOH (1.2 equiv) were added. Reaction was stirred at ambient temperature for 4 h then reaction was carefully neutralized with 3 N HCl and extracted 3 times with CH_2Cl_2. The combine organic layer was dried over Na_2SO_4, concentrated and purified by silica gel column chromatography using ethyl acetate/hexane as eluent to afford pure chalcone (55-75% yield).

2) A suspension of TMSOI (2 equiv.) and NaH (2 equiv.) in anhydrous DMSO (10 mL) was stirred at ambient temperature for 30 minutes. A DMSO solution (5 mL) of chalcone (1 g, 1 equiv) was added at 0 °C. The reaction mixture was stirred at room temperature for 2 h and on completion (monitored by TLC), reaction mixture was poured into a brine solution and extracted 3 times with ethyl acetate. The combined organic layer was washed with water and brine, dried over Na_2SO_4, concentrated and purified by silica gel column using ethyl acetate/hexane as eluent to afford the corresponding cyclopropane derivative (50-70% yield).

(trans-2-(4-methoxyphenyl)cyclopropyl)(phenyl)methnone (**1a′**). acetophenone (1.0 g, 8.32 mmol), **1a′** (1.05 g, 4.16 mmol), 50% overall yield, light yellow liquid, ^{1}H NMR (400 MHz): δ 7.99 (d, *J* = 7.9 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 2H),

7.11 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 2.86-2.80 (m, 1H), 2.69-2.63 (m, 1H), 1.93-1.87 (m, 1H), 1.54-1.49 (m, 1H)

(trans-2-(3,4-dimethoxyphenyl)cyclopropyl)(phenyl)methnone (**1b′**). acetophenone (1.0 g, 8.32 mmol), **1b′** (1.15 g, 4.08 mmol), 49% overall yield, yellow liquid, ^{1}H NMR (400 MHz): δ 7.99 (d, *J* = 7.4 Hz, 2H), 7.56 (t, *J* = 7.3 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 1H), 6.74-6.69 (m, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 2.87-2.80 (m, 1H), 2.70-2.63 (m, 1H), 1.92-1.85 (m, 1H), 1.57-1.50 (m, 1H)

p-tolyl(trans-2-(p-tolyl)cyclopropyl)methnone (**1c′**). 1-(*p*-tolyl)ethan-1-one (1.0 g, 7.45 mmol), **1c′** (0.97 g, 3.88 mmol), 52% overall yield, white solid, ^{1}H NMR (400 MHz): δ 7.89 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 2.87-2.81 (m, 1H), 2.68-2.61 (m, 1H), 2.40 (s, 3H), 2.33(s, 3H), 1.91-1.85 (m, 1H), 1.54-1.47 (m, 1H)

(trans-2-(4-chlorophenyl)cyclopropyl)(phenyl)methnone (**1d′**). acetophenone (1.0 g, 8.32 mmol), **1d′** (0.75 g, 2.91 mmol), 35% overall yield, off white solid, ^{1}H NMR (400 MHz): δ 7.98 (d, *J* = 7.8 Hz, 2H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 2.89-2.83 (m, 1H), 2.70-2.64 (m, 1H), 1.95-1.89 (m, 1H), 1.55-1.49 (m, 1H)

(4-chlorophenyl)(trans-2-(p-tolyl)cyclopropyl)methnone (**1e′**). 1-(4-chlorophenyl)ethan-1-one (1.0 g, 6.47 mmol), **1e′** (0.79 g, 2.92 mmol), 45% overall yield, colourless oil, ^{1}H NMR (400 MHz): δ 7.88 (d, *J* = 8.5 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 7.7 Hz, 2H), 7.02 (d, *J* = 7.7 Hz, 2H), 2.78-2.73 (m, 1H), 2.66-2.60 (m, 1H), 2.30 (s, 3H), 1.90-1.84 (m, 1H), 1.55-1.49 (m, 1H)

General procedure for the synthesis of donor-acceptor cyclopropanes (DACs, 4)[9]: Following the established literature, synthesis of **4** was carried out by following the

known procedures as mentioned below. For the reaction scheme, see Scheme S3 in the Supporting Information.

Sodium hydride (1.5 equiv) was taken in two-neck round bottom flask, washed 3 to 4 times with dry hexane under N_2 atmosphere DMSO and added anhydrous DMSO. The solution of trimethyl sulfoxonium iodide (1.5 equiv.) in anhydrous DMSO was added to the reaction mixture at 0 ºC. After 30 minutes a solution of diethylbenzylidenemalonate (1 equiv.) in anhydrous DMSO was added to the stirred solution at 0 ºC, and the reaction mixture was allowed to stir for 2 h at room temperature. Upon Completion of the reaction (as monitored by TLC), the reaction mixture was quenched with ice cold water, and the aqueous layer was extracted 3 times with diethyl ether. The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated in *vacuo*. The crude mixture was further purified by silica gel column chromatography using ethyl acetate/hexane as eluent.

Diethyl 2-(4-methoxyphenyl)cyclopropane-1,1-dicarboxylate (**4a**). diethyl 2-(4-methoxybenzylidene)malonate (1.0 g, 3.59 mmol), **4a** (0.77 g, 2.64 mmol), 74% yield, colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 4.26-4.17 (m, 2H), 3.87-3.79 (m, 2H), 3.75 (s, 3H), 3.15 (t, *J* = 8.3 Hz, 1H), 2.13-2.08 (m, 1H), 1.69-1.63 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 0.90 (t, *J* = 7.1 Hz, 3H)

Diethyl 2-(3,4-dimethoxyphenyl)cyclopropane-1,1-dicarboxylate (**4b**). diethyl 2-(3,4-dimethoxybenzylidene)malonate (1.0 g, 3.24 mmol), **4b** (0.76 g, 2.36 mmol), 73% yield, colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$): 1H-NMR (400 MHz, CDCl3): δ 6.76-6.72 (m, 3H), 4.26-4.20 (m, 2H), 3.87-3.82 (m, 8H), 3.17 (t, *J* = 7.1 Hz, 1H), 2.14-2.10 (m, 1H), 1.70-1.65 (m, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 0.92 (t, *J* = 7.1 Hz, 3H)

Diethyl 2-(benzo[d][1,3]dioxol-5-yl)cyclopropane-1,1-dicarboxylate (**4c**). diethyl 2-(benzo[*d*][1,3]dioxol-5-ylmethylene)malonate (1.0 g, 3.42 mmol), **4c** (0.82 g, 2.67 mmol), 78% yield, colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.72–6.64 (m, 3 H), 5.91 (s, 2 H), 4.28-4.17 (m, 2 H), 3.95-3.88 (m, 2 H), 3.14 (t, *J* = 7.5 Hz, 1 H), 2.09-2.07 (m, 1 H), 1.67-1.65 (m, 1 H), 1.29 (t, *J* = 7.1 Hz, 3 H), 0.97 (t, *J* = 7.1 Hz, 3 H)

Diethyl 2-(3,4,5-trimethoxyphenyl)cyclopropane-1,1-dicarboxylate (**4d**). diethyl 2-(3,4,5-trimethoxybenzylidene)malonate (1.0 g, 2.96 mmol), **4d** (0.74 g, 2.10 mmol), 71% yield, light yellow crystalline solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.42 (s, 2H), 4.31-4.16 (m, 2H), 3.95-3.86 (m, 2H), 3.83 (s, 6H), 3.79 (s, 3H), 3.17 (t, *J* = 8.6 Hz, 1H), 2.11 (dd, *J* = 8.1, 5.0 Hz, 1H), 1.68 (dd, *J* = 8.8, 4.0 Hz, 1H), 1.29 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 3H)

Diethyl 2-phenylcyclopropane-1,1-dicarboxylate (**4e**). diethyl 2-benzylidenemalonate (1.0 g, 4.03 mmol), **4e** (0.71 g, 2.71 mmol), 67% yield, colorless oil, ^{1}H NMR (400 MHz): δ 7.27-7.17 (m, 5H), 4.30-4.15 (m, 2H), 3.81 (q, *J* = 14.3, 7.1 Hz, 2H), 3.20 (t, *J* = 8.7 Hz, 1H), 2.17 (dd, *J* = 7.8, 5.0 Hz, 1H), 1.69 (dd, *J* = 9.2, 5.1 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 0.84 (t, *J* = 7.3 Hz, 3H)

Diethyl 2-(4-fluorophenyl)cyclopropane-1,1-dicarboxylate (**4f**). diethyl 2-(4-fluorobenzylidene)malonate (1.0 g, 3.75 mmol), **4f** (0.73 g, 2.60 mmol), 69% yield, colorless oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.17-7.12 (m, 2H), 6.93 (t, *J* = 8.7 Hz, 2H), 4.29-4.14 (m, 2H), 3.90-3.79 (m, 2H), 3.16 (t, *J* = 8.6 Hz, 1H), 2.11 (dd, *J* = 5.0, 3.6 Hz, 1H), 1.68 (dd, *J* = 5.3, 3.7 Hz, 1H), 1.27 (t, *J* = 7.0 Hz, 3H), 0.89 (t, *J* = 7.1 Hz, 3H)

Diethyl 2-(4-nitrophenyl)cyclopropane-1,1-dicarboxylate (**4g**). diethyl 2-(4-nitrobenzylidene)malonate (1.0 g, 3.41 mmol), **4g** (0.66 g, 2.15 mmol), 63% yield, cream coloured solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, *J* = 8.6 Hz, 2H), 7.37 (d,

J = 8.6 Hz, 2H), 4.36-4.17 (m, 2H), 3.96-3.79 (m, 2H), 3.26 (t, *J* = 8.5 Hz, 1H), 2.20 (dd, *J* = 8.1, 5.6 Hz, 1H), 1.79 (dd, *J* = 8.9, 5.4 Hz, 1H), 1.30 (t, *J* = 7.0 Hz, 3H), 0.92 (t, *J* = 7.0 Hz, 3H)

Diethyl (E)-2-styrylcyclopropane-1,1-dicarboxylate (**4h**). diethyl (*E*)-2-(3-phenylallylidene)malonate (1.0 g, 3.64 mmol), **4h** (0.71 g, 2.47 mmol), 68% yield, yellow liquid, ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.31-7.26 (m, 4H), 7.24-7.17 (m, 1H), 6.63 (d, *J* = 15.6 Hz, 1H), 5.81 (dd, *J* = 15.6, 8.4 Hz, 1H), 4.29-4.11 (m, 4H), 2.73 (q, *J* = 8.4 Hz, 1H), 1.81 (dd, *J* = 7.4, 5.0 Hz, 1H), 1.65 (dd, *J* = 9.0, 5.0 Hz, 1H), 1.28 (t, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.0 Hz, 3H)

General procedure for the preparation of dimethyl 2-vinylcyclopropane-1,1-dicarboxylate (4i)[15]: Following the established literature, synthesis of **4i** was carried out by following the known procedures as mentioned below. For the reaction scheme, see Scheme S4 in the Supporting Information.

To a freshly prepared solution of NaOMe (prepared by stirring sodium metal (2 equiv.) in 10 mL methanol for 5 minutes) in a round bottom flask, was added dimethyl malonate (3 equiv.). The reaction mixture was stirred at room temperature for 5 minutes and added dropwise, a methanol (10 mL) solution of (*E*)-1,4-Dibromobut-2-ene (1g, 1 equiv.). The reaction mixture was then stirred under reflux conditions (on silicone oil bath) for 3 h. On completion, the reaction mixture was concentrated on rotary evaporator, added ice cold water and extracted 3 times with ethyl acetate. The combined organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The crude mixture was further purified by silica gel column chromatography using ethyl acetate/hexane as eluent.

Dimethyl 2-vinylcyclopropane-1,1-dicarboxylate (**4i**). (*E*)-1,4-dibromobut-2-ene (1.0 g, 4.68 mmol), **4i** (0.78 g, 4.23 mmol), 90% yield, light yellow liquid, ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.47-5.35 (m, 1H), 5.29 (d, *J* = 16.8 Hz, 1H), 5.13 (d, *J* = 10.5 Hz, 1H), 3.73 (s, 6H), 2.58 (q, *J* = 8.3 Hz, 1H), 1.71 (dd, *J* = 7.8, 4.9 Hz, 1H), 1.58 (dd, *J* = 9.1, 5.1 Hz, 1H)

Representative procedure for synthesis of 6-aryl-5,6-dihydro-4*H*-1,2-oxazine (3) *via* additive free annulation of *trans*-2-arylcyclopropane-1-carbaldehyde (1) with hydroxylamine-O-sulfonic acid (*2′*): For the reaction scheme, see Scheme S5 in the Supporting Information.

An open round-bottom flask, equipped with magnetic stir bar was charged with cyclopropanecarbaldehyde (**1**), hydroxylamine-O-sulfonic acid (***2′***) (or hydroxylammonium chloride (**2**)) and benzene (reagent grade). The reaction mixture was stirred open-to-air at ambient temperatures. Upon completion, as monitored by TLC, the solvent was evaporated in rotary evaporator and the crude mixture was further purified by column chromatography on silica gel with ethyl acetate/hexane as eluent.

6-(4-methoxyphenyl)-5,6-dihydro-4H-1,2-oxazine (**3a**). Reaction time: 8 h, **1a** (0.050 g, 0.28 mmol), ***2′*** (0.047 g, 0.42 mmol), **3a** (0.040 g, 0.21 mmol), Yield: 74%, orange sticky solid, mp 89-91 °C, R_f = 0.35 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, *J* = 8.6 Hz, 3H), 6.91 (d, *J* = 8.6 Hz, 2H), 4.71 (dd, *J* = 8.5, 4.7 Hz, 1H), 3.81 (s, 3H), 2.46-2.24 (m, 2H), 2.11-2.04 (m, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 159.6, 148.6, 132.0, 128.0, 113.9, 77.3, 55.3, 25.2, 22.6 IR (neat): 2930, 2836, 1692, 1605, 1512, 1457, 1245, 1174, 1029, 827, 537 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{11}H_{14}NO_2$ 192.1025, found 192.1035

6-(4-(benzyloxy)phenyl)-5,6-dihydro-4H-1,2-oxazine (**3b**). Reaction time: 12 h, **1b** (0.050 g, 0.20 mmol), ***2′*** (0.034 g, 0.30 mmol), **3b** (0.044 g, 0.16 mmol), Yield: 82%, off white solid, mp 84-86 °C, R_f = 0.40 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.27 (m, 5H), 7.27 (d, *J* = 8.5 Hz, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 5.02 (s, 2H), 4.66 (dd, *J* = 8.7, 4.6 Hz, 1H), 2.39-2.28 (m, 1H), 2.26-2.17 (m, 1H), 2.08-1.96 (m, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 158.7, 148.5, 136.8, 132.2, 128.5, 128.0, 127.9, 127.4, 114.8, 77.1, 69.9, 25.0, 22.4 IR (neat): 2908, 2852, 1609, 1510, 1468, 1376, 1243, 1179, 998, 798, 735, 696, 504 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{18}NO_2$ 268.1338, found 268.1333

6-(p-tolyl)-5,6-dihydro-4H-1,2-oxazine (**3c**). Reaction time: 48 h, **1c** (0.050 g, 0.31 mmol), ***2′*** (0.053 g, 0.46 mmol), **3c** (0.035 g, 0.20 mmol), Yield: 64%, off white solid, mp 50-52 °C, R_f = 0.48 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.28 (m, 1H), 7.27 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 4.74 (dd, *J* = 9.6, 3.5 Hz, 1H), 2.45-2.32 (m, 1H), 2.35 (s, 3H), 2.32-2.22 (m, 1H), 2.11-2.00 (m, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.6, 138.0, 136.9, 129.2, 126.5, 77.4, 25.2, 22.3, 21.2 IR (neat): 2922, 2853, 1725, 1612, 1511, 1461, 1210, 903, 811, 758, 516 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{11}H_{14}NO$ 176.1075, found 176.1053

6-mesityl-5,6-dihydro-4H-1,2-oxazine (**3d**). Reaction time: 48 h, **1d** (0.050 g, 0.26 mmol), ***2′*** (0.044 g, 0.39 mmol), **3d** (0.032 g, 0.16 mmol), Yield: 62%, colourless viscous liquid, R_f = 0.44 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.31 (m, 1H), 6.84 (s, 2H), 5.09 (dd, *J* = 12.4, 2.7 Hz, 1H), 2.48-2.38 (m, 1H), 2.37 (s, 6H), 2.36-2.27 (m, 2H), 2.26 (s, 3H), 1.92-1.83 (m, 1H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.1, 137.3, 136.3, 132.7, 130.1, 75.5, 22.7, 22.2, 20.8, 20.6 IR (neat): 2921, 2853, 1718, 1611, 1450, 1181, 1077, 1005, 894, 850, 822, 734, 572 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{18}NO$ 204.1388, found 204.1401

6-(4-isopropylphenyl)-5,6-dihydro-4H-1,2-oxazine (**3e**). Reaction time: 48 h, **1e** (0.050 g, 0.26 mmol), ***2′*** (0.044 g, 0.39 mmol), **3e** (0.035 g, 0.17 mmol), Yield: 66%, pale yellow liquid, R_f = 0.45 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, *J* = 8.2 Hz, 3H), 7.23 (d, *J* = 8.1 Hz, 2H), 4.74 (dd, *J* = 9.2, 3.7 Hz, 1H), 2.97-2.85 (m, 1H), 2.45-2.34 (m, 1H), 2.32-2.23 (m, 1H), 2.15-1.99 (m, 2H), 1.24 (d, *J* = 6.8 Hz, 6H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 149.0, 148.5, 137.2, 126.6, 77.4, 33.9, 25.1, 24.0, 22.4 IR (neat): 2957, 2923, 2852, 1702, 1513, 1459, 1054, 1008, 900, 822, 561 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{18}NO$ 204.1388, found 204.1406

6-(naphthalen-2-yl)-5,6-dihydro-4H-1,2-oxazine (**3f**). Reaction time: 72 h, **1f** (0.050 g, 0.25 mmol), ***2′*** (0.043 g, 0.38 mmol), **3f** (0.023 g, 0.11 mmol), Yield: 42%, sticky brown solid, mp 84-86 °C, R_f = 0.60 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88-7.81 (m, 4H), 7.51-7.46 (m, 3H), 7.37-7.35 (m, 1H), 4.97 (dd, *J* = 9.7, 3.2 Hz, 1H), 2.50-2.39 (m, 1H), 2.35-2.25 (m, 1H), 2.24-2.11 (m, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.7, 137.3, 133.3, 133.2, 128.4, 128.1, 127.7, 126.3, 126.2, 125.6, 124.3, 77.5, 25.4, 22.1 IR (neat): 3053, 2922, 2851, 1691, 1600, 1300, 1003, 905, 856, 805, 742, 475 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{14}H_{14}NO$ 212.1075, found 212.1073

6-(o-tolyl)-5,6-dihydro-4H-1,2-oxazine (**3g**). Reaction time: 48 h, **1g** (0.050 g, 0.31 mmol), ***2′*** (0.053 g, 0.47 mmol), **3g** (0.035 g, 0.20 mmol). In this case, the reaction could not be capitalized for an exclusively pure 6-(*o*-tolyl)-5,6-dihydro-4*H*-1,2-oxazine (**3g**), even on heating or addition of *p*TSA. Thus, traces of cyclopropyl oxime can be seen in its ^{1}H NMR spectrum along with **3g** in major amount as both the compounds have exactly the same R_f. However, one can see the NMR signals corresponding to the major product **3g** quite clearly. Yield: 64%, orange liquid, R_f = 0.55 (ethyl

acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41-7.38 (m, 1H), 7.36-7.33 (m, 1H), 7.25-7.12 (m, 3H), 4.92 (dd, *J* = 8.4, 5.0 Hz, 1H), 2.51-2.40 (m, 1H), 2.38 (s, 3H), 2.36-2.29 (m, 1H), 2.11-2.03 (m, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.6, 130.5, 128.1, 126.3, 126.0, 74.6, 24.5, 22.9, 19.1 IR (neat): 2920, 2851, 1695, 1460, 1007, 898, 833, 753, 453 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: [M + H]$^{+}$ Calcd for $C_{11}H_{14}NO$ 176.1075, found 176.1082

6-phenyl-5,6-dihydro-4H-1,2-oxazine (**3h**). Reaction time: 72 h, **1l** (0.050 g, 0.34 mmol), ***2′*** (0.058 g, 0.51 mmol), **3l** (0.018 g, 0.11 mmol), Yield: 33%, pale yellow liquid, R_f = 0.55 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.30 (m, 6H), 4.78 (dd, *J* = 9.8, 3.1 Hz, 1H), 2.46-2.35 (m, 1H), 2.32-2.23 (m, 1H), 2.17-2.01 (m, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.6, 139.9, 128.6, 128.3, 126.5, 77.5, 25.3, 22.2 IR (neat): 2924, 2853, 1700, 1452, 1291, 1008, 897, 827, 753, 697, 530 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: [M + H]$^{+}$ Calcd for $C_{10}H_{12}NO$ 162.0919, found 162.0915

(E)-6-styryl-5,6-dihydro-4H-1,2-oxazine (**3i**). Reaction time: 4 h, **1h** (0.050 g, 0.29 mmol), ***2′*** (0.050 g, 0.44 mmol), **3h** (0.028 g, 0.15 mmol), Yield: 52%, yellow liquid, R_f = 0.52 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 7.3 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 7.29-7.26 (m, 1H), 6.69 (d, *J* = 16.1 Hz, 1H), 6.21 (dd, *J* = 16.1, 6.3 Hz, 1H), 4.46 (t, *J* = 8.3 Hz, 1H), 2.36-2.18 (m, 2H), 2.10-2.02 (m, 1H), 1.94-1.83 (m, 1H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.5, 136.3, 132.9, 128.6, 128.0, 127.0, 126.6, 75.8, 23.9, 21.1 IR (neat): 2923, 2852, 1677, 1493, 1448, 1176, 964, 747, 693 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: [M + H]$^{+}$ Calcd for $C_{12}H_{14}NO$ 188.1075, found 188.1070

6-(3,4-dimethoxyphenyl)-5,6-dihydro-4H-1,2-oxazine (**3j**). Reaction time: 12 h, **1i** (0.050 g, 0.24 mmol), **2** (0.023 g, 0.36 mmol), **3i** (0.034 g, 0.15 mmol), Yield: 64%,

viscous yellow liquid, R_f = 0.25 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33-7.29 (m, 1H), 6.94-6.80 (m, 3H), 4.70 (dd, *J* = 9.7, 3.3 Hz, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 2.46-2.35 (m, 1H), 2.33-2.23 (m, 1H), 2.14-2.00 (m, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.6, 132.5, 118.9, 111.0, 109.9, 77.4, 55.9, 25.3, 22.5 IR (neat): 3000, 2935, 2836, 1679, 1591, 1515, 1462, 1258, 1234, 1137, 1024, 860, 803, 760, 731, 632 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{12}H_{16}NO_3$ 222.1130, found 222.1134

6-(3,4,5-trimethoxyphenyl)-5,6-dihydro-4H-1,2-oxazine (**3k**). Reaction time: 20 h, **1k** (0.050 g, 0.21 mmol), **2** (0.021 g, 0.32 mmol), **3k** (0.035 g, 0.14 mmol), Yield: 66%, off white solid, mp 53-55 °C, R_f = 0.14 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.31 (m, 1H), 6.60 (s, 2H), 4.70 (dd, *J* = 10.3, 2.6 Hz, 1H), 3.87 (s, 6H), 3.84 (s, 3H), 2.47-2.36 (m, 1H), 2.34-2.25 (m, 1H), 2.17-1.99 (m, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 153.3, 148.7, 137.8, 135.6, 103.5, 77.6, 60.9, 56.1, 25.5, 22.4 IR (neat): 2935, 2836, 1587, 1507, 1460, 1419, 1328, 1234, 1120, 995, 889, 816, 690 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{13}H_{18}NO_4$ 252.1236, found 252.1227

6-(benzo[d][1,3]dioxol-5-yl)-5,6-dihydro-4H-1,2-oxazine (**3l**). Reaction time: 24 h, **1j** (0.050 g, 0.26 mmol), **2** (0.025 g, 0.39 mmol), **3j** (0.038 g, 0.18 mmol), Yield: 71%, viscous brown liquid, R_f = 0.36 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.28 (m, 1H), 6.88-6.77 (m, 3H), 5.96 (s, 2H), 4.67 (dd, *J* = 10.0, 3.0 Hz, 1H), 2.45-2.34 (m, 1H), 2.32-2.23 (m, 1H), 2.09-1.96 (m, 2H) ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 148.5, 147.8, 147.5, 133.8, 120.3, 108.2, 107.2, 101.1, 77.4, 25.3, 22.4 IR (neat): 2896, 1684, 1487, 1442, 1240, 1034, 925, 863, 801 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{11}H_{12}NO_3$ 206.0817, found 206.0811

Representative procedure for synthesis of 3,6-diaryl-5,6-dihydro-4*H*-1,2-oxazine (3) *via* annulation of (*trans*-2-arylcyclopropyl)(aryl)methnone (1′) with hydroxylamine hydrochloride (2): For the reaction scheme, see Scheme S6 in the Supporting Information.

An open round-bottom flask, equipped with magnetic stir bar was charged with cyclopropyl ketone (**1′**, 1 equiv.), hydroxylamine hydrochloride (**2**, 2 equiv.) and benzene (reagent grade). The reaction mixture was stirred open-to-air at room temperature for 1 h and added *p*-toluene sulfonic acid monohydrate (*p*TSA.H_2O, 0.2 equiv.). The reaction mixture was then stirred at about 50 ºC (on silicone oil bath). Upon completion, as monitored by TLC, the solvent was evaporated in rotary evaporator and the crude mixture was further purified by column chromatography on silica gel with ethyl acetate/hexane as eluent.

6-(4-methoxyphenyl)-3-phenyl-5,6-dihydro-4H-1,2-oxazine (**3m**). Reaction time: 72 h, **1a′** (0.050 g, 0.198 mmol), **2** (0.026 g, 0.396 mmol), **3m** (0.020 g, 0.075 mmol), Yield: 38%, brown viscous liquid, R_f = 0.33 (ethyl acetate/hexane 20:80), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (d, *J* = 8.2 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.30 (d, *J* = 8.6 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 4.78 (t, *J* = 6.4 Hz, 1H), 3.80 (s, 3H), 3.10 (t, *J* = 6. 8 Hz, 2H), 2.19 (q, *J* = 6.8 Hz, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 200.5, 159.1, 136.8, 136.5, 133.1, 128.6, 128.1, 127.0, 113.9, 73.3, 55.3, 34.9, 33.0 IR (neat): 2930, 2835, 1679, 1598, 1510, 1447, 1244, 1173, 1030, 831, 749, 689, 551 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{18}NO_2$ 268.1338, found 268.1322

6-(3,4-dimethoxyphenyl)-3-phenyl-5,6-dihydro-4H-1,2-oxazine (**3n**). Reaction time: 72 h, **1b′** (0.050 g, 0.177 mmol), **2** (0.023 g, 0.354 mmol), **3n** (0.022 g, 0.074 mmol), Yield:

42%, off white solid, mp 84-86 °C, R_f = 0.25 (ethyl acetate/hexane 20:80), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76-7.70 (m, 2H), 7.43-7.35 (m, 3H), 7.01 (s, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 6.87 (d, *J* = 8.2 Hz, 1H), 4.79 (dd, *J* = 10.5, 2.2 Hz, 1H), 3.90 (s, 3H), 3.89 (s, 3H), 2.78 (dd, *J* = 8.2, 5.2 Hz, 2H), 2.35-2.14 (m, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 154.4, 149.0, 148.9, 135.7, 132.2, 129.5, 128.4, 125.3, 118.8, 110.9, 109.7, 76.9, 55.9, 25.9, 22.6 IR (neat): 2923, 2848, 1703, 1592, 1517, 1445, 1310, 1258, 1234, 1139, 1026, 902, 762, 695, 674, 557 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{18}H_{20}NO_3$ 298.1443, found 298.1441

3,6-di-p-tolyl-5,6-dihydro-4H-1,2-oxazine (**3o**). Reaction time: 72 h, **1c′** (0.050 g, 0.199 mmol), **2** (0.026 g, 0.399 mmol), **3o** (0.017 g, 0.064 mmol), Yield: 32%, brown viscous liquid, R_f = 0.38 (ethyl acetate/hexane 20:80), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (d, *J* = 8.1 Hz, 2H), 7.30-7.21 (m, 4H), 7.16 (d, *J* = 8.1 Hz, 2H), 4.80 (t, *J* = 6.4 Hz, 1H), 3.08 (t, *J* = 6.9 Hz, 2H), 2.41 (s, 3H), 2.35 (s, 3H), 2.19 (q, *J* = 6.7 Hz, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 200.3, 143.9, 141.4, 137.2, 134.3, 129.3, 129.2, 128.2, 125.7, 73.5, 34.7, 33.1, 21.7, 21.1 IR (neat): 2921, 2853, 1676, 1605, 1512, 1408, 1260, 1179, 1038, 1017, 815, 542 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{18}H_{20}NO$ 266.1545, found 266.1536

6-(4-chlorophenyl)-3-phenyl-5,6-dihydro-4H-1,2-oxazine (**3p**). Reaction time: 72 h, **1d′** (0.050 g, 0.195 mmol), **2** (0.025 g, 0.389 mmol), **3p** (0.013 g, 0.048 mmol), Yield: 25%, light brown solid, mp 74-76 °C, R_f = 0.35 (ethyl acetate/hexane 20:80), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.1 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 2H), 7.32 (d, *J* = 0.9 Hz, 4H), 4.83 (dd, *J* = 7.8, 4.8 Hz, 1H), 3.12 (dt, *J* = 6.9, 2.4 Hz, 2H), 2.25-2.09 (m, 2H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 200.5, 142.8, 136.6, 133.3, 133.1, 128.6, 128.1, 127.1, 72.9, 34.6, 33.0 IR (neat): 3492, 2922, 2851, 1679, 1593,

1488, 1406, 1362, 1211, 1073, 978, 828, 741, 686, 535, 448 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{16}H_{15}NOCl$ 272.0842, found 272.0827

3-(4-chlorophenyl)-6-(p-tolyl)-5,6-dihydro-4H-1,2-oxazine (**3q**). Reaction time: 72 h, **1e′** (0.050 g, 0.184 mmol), **2** (0.024 g, 0.369 mmol), **3q** (0.026 g, 0.091 mmol), Yield: 49%, off white solid, mp 70-72 °C, R_f = 0.36 (ethyl acetate/hexane 20:80), ^1H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.6 Hz, 2H), 7.42 (d, *J* = 8.3 Hz, 2H), 7.26 (d, *J* = 7.8 Hz, 2H), 7.16 (d, *J* = 7.5 Hz, 2H), 4.78 (t, *J* = 6.2 Hz, 1H), 3.06 (t, *J* = 7.0 Hz, 2H), 2.34 (s, 3H), 2.18 (q, *J* = 7.0 Hz, 2H) $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 199.2, 141.2, 139.5, 137.4, 135.1, 129.5, 129.3, 128.9, 125.7, 73.4, 34.8, 32.9, 21.1 IR (neat): 3316, 2917, 2858, 1682, 1586, 1484, 1398, 1237, 1203, 1090, 960, 922, 815, 799, 523, 505 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{17}H_{17}NOCl$ 286.0999, found 286.0984

Representative procedure for Lewis acid catalysed cycloaddition of 6-aryl-5,6-dihydro-4*H*-1,2-oxazine (3) with donor-acceptor cyclopropanes (4): For the reaction scheme, see Scheme S7 in the Supporting Information.

An oven dried round-bottom flask, equipped with magnetic stir bar was charged with 6-aryl-5,6-dihydro-4*H*-1,2-oxazine (**3**), donor-acceptor cyclopropane (**4**), $Cu(OTf)_2$, 4 Å molecular sieves (200 wt%) and dry CH_2Cl_2 under inert atmosphere. The reaction mixture was stirred at ambient temperatures. Upon completion, as monitored by TLC, the reaction mixture was filtered through a celite plug and concentrated *in vacuo.* The crude mixture was then purified by column chromatography on silica gel with diethyl ether/hexane as eluent.

Here, two diastereomers were obtained as is clear by the crude ^1H NMR data. But even after our continuous efforts, we were not successful in separating the second isomer (minor, **5′**) in most of the cases with publishable purity. However in case of

5i/**5i´**, we did succeed in separating both the diastereomers and the relative stereochemistries were established on the basis of their 2D NMR analysis. So, for other examples, we isolated only the major isomer and the diastereomeric ratios were calculated by comparing their characteristic signals in the crude ^{1}H NMR spectrum. Yields reported are that of the major isomer (**5´**) only.

Diethyl-2,7-bis(4-methoxyphenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5a**). Reaction time: 2 h, **3a** (0.050 g, 0.26 mmol), **4a** (0.076 g, 0.26 mmol), **5a** (0.075 g, 0.16 mmol), Yield: 60%, colourless viscous liquid, R_f = 0.50 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.6 Hz, 2H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.79 (d, *J* = 8.6 Hz, 2H), 4.72 (dd, *J* = 10.3, 2.1 Hz, 1H), 4.33-4.16 (m, 4H), 3.85 (t, *J* = 9.3 Hz, 1H), 3.78 (s, 3H), 3.74 (s, 3H), 3.41 (dd, *J* = 11.1, 2.5 Hz, 1H), 2.64 (dd, *J* = 14.5, 9.7 Hz, 1H), 2.49 (dd, *J* = 14.1, 9.1 Hz, 1H), 2.27-2.20 (m, 1H), 2.00-1.93 (m, 1H), 1.82-1.64 (m, 2H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.9, 169.7, 159.0, 158.8, 132.9, 132.7, 128.5, 127.8, 113.6, 113.5, 80.2, 68.3, 66.4, 61.7, 61.6, 57.5, 55.2, 37.5, 31.6, 27.1, 14.2, 14.0 IR (neat): 2926, 2852, 1728, 1612, 1513, 1243, 1175, 1033, 829, 539 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{34}NO_7$ 484.2335, found 484.2343

Diethyl-2-(4-(benzyloxy)phenyl)-7-(4-methoxyphenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5b**). Reaction time: 2 h, **3b** (0.050 g, 0.19 mmol), **4a** (0.055 g, 0.19 mmol), **5b** (0.062 g, 0.11 mmol), Yield: 58%, off white solid, mp 60-62 °C, R_f = 0.52 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.27 (m, 7H), 7.16 (d, *J* = 8.7 Hz, 2H), 6.89-6.81 (m, 4H), 5.01 (s, 2H), 4.71 (d, *J* = 10.3 Hz, 1H), 4.33-4.16 (m, 4H), 3.85 (t, *J* = 9.4 Hz, 1H), 3.78 (s, 3H), 3.40 (dd, *J* = 11.2, 2.5 Hz, 1H), 2.64 (dd, *J* = 14.0, 9.1 Hz, 1H), 2.49 (dd, *J* = 14.0, 9.0 Hz, 1H), 2.27-2.19 (m,

1H), 2.01-1.93 (m, 1H), 1.82-1.64 (m, 2H), 1.33-1.23 (m, 6H) $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.8, 169.7, 158.8, 158.2, 137.0, 132.9, 128.5, 128.4, 127.9, 127.8, 127.4, 114.5, 113.6, 80.2, 69.9, 68.3, 66.4, 61.7, 61.6, 57.4, 55.2, 37.5, 31.6, 27.1, 14.2, 14.0 IR (neat): 2923, 2853, 1728, 1612, 1512, 1367, 1241, 1174, 1002, 828, 735, 696, 540 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{33}H_{38}NO_7$ 560.2648, found 560.2653

Diethyl-7-(4-methoxyphenyl)-2-(p-tolyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5c**). Reaction time: 2 h, **3c** (0.050 g, 0.28 mmol), **4a** (0.083 g, 0.28 mmol), **5c** (0.072 g, 0.15 mmol), Yield: 54%, yellow viscous liquid, R_f = 0.60 (diethyl ether/hexane 40:60), ^1H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.7 Hz, 2H), 7.14 (d, *J* = 8.3 Hz, 2H), 7.07 (d, *J* = 7.9 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 4.74 (dd, *J* = 10.8, 2.1 Hz, 1H), 4.34-4.17 (m, 4H), 3.87 (t, *J* = 9.3 Hz, 1H), 3.77 (s, 3H), 3.42 (dd, *J* = 11.2, 2.3 Hz, 1H), 2.66 (dd, *J* = 13.7, 9.5 Hz, 1H), 2.50 (dd, *J* = 13.8, 8.8 Hz, 1H), 2,28 (s, 3H), 2.26-2.20 (m, 1H), 2.02-1.92 (m, 1H), 1.81-1.66 (m, 2H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H) $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.9, 169.7, 158.8, 137.6, 137.3, 132.9, 128.8, 128.5, 126.4, 113.6, 80.5, 68.3, 66.4, 61.7, 61.6, 57.5, 55.2, 37.5, 31.9, 27.1, 21.1, 14.2, 14.0 IR (neat): 2922, 2854, 1729, 1513, 1444, 1366, 1243, 1178, 1002, 947, 808, 537 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{34}NO_6$ 468.2386, found 468.2380

Diethyl-2-mesityl-7-(4-methoxyphenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5d**). Reaction time: 6 h, **3d** (0.050 g, 0.24 mmol), **4a** (0.072 g, 0.24 mmol), **5d** (0.065 g, 0.13 mmol), Yield: 55%, off white solid, mp 90-92 °C, R_f = 0.65 (diethyl ether/hexane 40:60), ^1H NMR (400 MHz, $CDCl_3$): δ 7.35 (d, *J* = 8.6 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 6.74 (s, 2H), 5.12 (dd, *J* = 11.8, 2.4 Hz, 1H), 4.35-4.17 (m, 4H), 3.89 (t, *J* = 9.3 Hz, 1H), 3.75 (s, 3H), 3.49 (dd, *J* = 11.2, 2.7 Hz, 1H), 2.66 (dd, *J*

= 14.3, 9.6 Hz, 1H), 2.48 (dd, *J* = 14.4, 9.0 Hz, 1H), 2.34 (s, 6H), 2.27-2.20 (m, 1H), 2.18 (s, 3H), 2.06-1.93 (m, 1H), 1.76-1.64 (m, 2H), 1.30 (t, *J* = 7.3 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H) $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 170.9, 169.8, 158.8, 136.5, 136.0, 133.9, 133.0, 129.8, 128.5, 113.7, 78.9, 68.4, 66.8, 61.7, 61.6, 57.6, 55.2, 37.5, 28.5, 27.5, 21.4, 20.7, 14.2, 14.0 IR (neat): 2916, 2849, 1721, 1613, 1511, 1447, 1364, 1271, 1245, 1177, 1084, 997, 832, 569, 547 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{29}H_{38}NO_6$ 496.2699, found 496.2698

Diethyl-2-(4-isopropylphenyl)-7-(4-methoxyphenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5e**). Reaction time: 1.5 h, **3e** (0.050 g, 0.25 mmol), **4a** (0.072 g, 0.25 mmol), **5e** (0.056 g, 0.11 mmol), Yield: 46%, colourless liquid, R_f = 0.62 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.7 Hz, 2H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 4.74 (d, *J* = 11.1 Hz, 1H), 4.33-4.16 (m, 4H), 3.86 (t, *J* = 9.2 Hz, 1H), 3.77 (s, 3H), 3.41 (dd, *J* = 11.1, 2.4 Hz, 1H), 2.89-2.77 (m, 1H), 2.64 (dd, *J* = 14.2, 9.4 Hz, 1H), 2.49 (dd, *J* = 14.1, 9.0 Hz, 1H), 2.26-2.20 (m, 1H), 2.02-1.96 (m, 1H), 1.82-1.65 (m, 2H), 1.32-1.25 (m, 6H), 1.18 (d, *J* = 7.0 Hz, 6H) $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 170.9, 169.7, 158.8, 148.3, 137.9, 133.0, 128.4, 126.5, 126.2, 113.6, 80.5, 68.3, 66.4, 61.7, 61.6, 57.5, 55.2, 37.6, 33.8, 31.7, 27.1, 24.0, 14.2, 14.0 IR (neat): 2957, 2923, 2852, 1730, 1513, 1461, 1366, 1244, 1179, 1048, 828, 578 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{29}H_{38}NO_6$ 496.2699, found 496.2715

Diethyl-7-(4-methoxyphenyl)-2-(naphthalen-2-yl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5f**). Reaction time: 2.5 h, **3f** (0.050 g, 0.24 mmol), **4a** (0.069 g, 0.24 mmol), **5f** (0.048 g, 0.095 mmol), Yield: 40%, sticky colourless solid, mp 48-50 °C, R_f = 0.50 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.67 (m, 4H), 7.45-7.38 (m, 4H), 7.36 (d, *J* = 8.6 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 2H), 4.93

(d, *J* = 10.5 Hz, 1H), 4.35-4.18 (m, 4H), 3.92 (t, *J* = 9.2 Hz, 1H), 3.77 (s, 3H), 3.48 (dd, *J* = 11.2, 2.2 Hz, 1H), 2.69 (dd, *J* = 14.4, 9.5 Hz, 1H), 2.53 (dd, *J* = 14.4, 9.0 Hz, 1H), 2.32-2.25 (m, 1H), 2.13-2.05 (m, 1H), 1.92-1.72 (m, 2H), 1.35-1.24 (m, 6H) $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 170.9, 169.7, 158.9, 138.1, 133.1, 132.9, 128.5, 128.0, 127.8, 127.6, 125.9, 125.8, 124.9, 124.8, 113.7, 80.8, 68.4, 66.5, 61.8, 61.7, 57.5, 55.2, 37.6, 32.1, 27.2, 14.2, 14.0 IR (neat): 2923, 2851, 1728, 1512, 1443, 1366, 1243, 1174, 1004, 857, 818, 745, 477 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{30}H_{34}NO_6$ 504.2386, found 504.2400

Diethyl-7-(4-methoxyphenyl)-2-(o-tolyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5g**). Reaction time: 2 h, **3g** (0.050 g, 0.28 mmol), **4a** (0.083 g, 0.28 mmol), **5g** (0.073 g, 0.16 mmol), Yield: 57%, white solid, mp 68-70 °C, R_f = 0.62 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.7 Hz, 2H), 7.33-7.29 (m, 1H), 7.14-7.09 (m, 2H), 7.06-7.01 (m, 1H), 6.84 (d, *J* = 8.7 Hz, 2H), 4.89 (dd, *J* = 11.0, 2.2 Hz, 1H), 4.35-4.17 (m, 4H), 3.81 (t, *J* = 9.2 Hz, 1H), 3.78 (s, 3H), 3.42 (dd, *J* = 11.4, 2.3 Hz, 1H), 2.67 (dd, *J* = 14.1, 9.7 Hz, 1H), 2.49 (dd, *J* = 14.1, 8.9 Hz, 1H), 2.32-2.25 (m, 1H), 2.05 (s, 3H), 2.02-1.83 (m, 2H), 1.78-1.67 (m, 1H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.28 (t, *J* = 7.3 Hz, 3H) $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 170.9, 169.8, 158.9, 137.8, 137.0, 133.0, 130.3, 128.8, 127.7, 125.7, 125.6, 113.5, 77.8, 68.4, 66.6, 61.7, 61.6, 57.5, 55.3, 37.7, 29.6, 27.3, 18.9, 14.2, 14.0 IR (neat): 2924, 2853, 1729,1512, 1367, 1243, 1176, 1001, 949, 830, 752, 543 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{34}NO_6$ 468.2386, found 468.2405

Diethyl-7-(4-methoxyphenyl)-2-phenylhexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5h**). Reaction time: 2 h, **3h** (0.050 g, 0.31 mmol), **4a** (0.091 g, 0.31 mmol), **5h** (0.084 g, 0.186 mmol), Yield: 60%, colourless viscous liquid, R_f = 0.62 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (d, *J* = 8.3 Hz, 2H),

7.31-7.19 (m, 5H), 6.86 (d, *J* = 8.2 Hz, 2H), 4.78 (dd, *J* = 9.2, 2.2 Hz, 1H), 4.35-4.18 (m, 4H), 3.89 (t, *J* = 9.2 Hz, 1H), 3.79 (s, 3H), 3.44 (dd, *J* = 9.4, 2.2 Hz, 1H), 2.67 (dd, *J* = 14.2, 9.5 Hz, 1H), 2.52 (dd, *J* = 14.2, 9.2 Hz, 1H), 2.26 (d, *J* = 8.0 Hz, 1H), 2.02 (d, *J* = 9.5 Hz, 1H), 1.82-1.67 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H) $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 170.9, 169.7, 158.8, 140.6, 132.9, 128.5, 128.2, 127.6, 126.4, 113.7, 80.6, 68.3, 66.4, 61.7, 61.6, 57.5, 55.2, 37.5, 32.0, 27.1, 14.2, 14.0 IR (neat): 2980, 2934, 1725, 1612, 1514, 1444, 1369, 1246, 1128, 1031, 832, 759, 699, 531 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{26}H_{32}NO_6$ 454.2230, found 454.2248

Diethyl-(E)-7-(4-methoxyphenyl)-2-styrylhexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5i**). Reaction time: 4 h, **3i** (0.050 g, 0.27 mmol), **4a** (0.078 g, 0.27 mmol), **5i** (0.052 g, 0.11 mmol), Yield: 41%, colourless liquid, R_f = 0.58 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.6 Hz, 2H), 7.32-7.16 (m, 5H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.46 (d, *J* = 16.0 Hz, 1H), 6.08 (dd, *J* = 16.0, 6.3 Hz, 1H), 4.43-4.37 (m, 1H), 4.32-4.15 (m, 4H), 3.82 (t, *J* = 9.2 Hz, 1H), 3.79 (s, 3H), 3.34 (dd, *J* = 11.0, 2.3 Hz, 1H), 2.62 (dd, *J* = 14.1, 9.6 Hz, 1H), 2.48 (dd, *J* = 14.3, 9.1 Hz, 1H), 2.22-2.16 (m, 1H), 1.90-1.83 (m, 1H), 1.71-1.54 (m, 2H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 7.0 Hz, 3H) $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 170.8, 169.7, 158.9, 136.7, 132.9, 131.4, 128.5, 128.4, 128.0, 127.6, 126.5, 113.7, 79.3, 68.3, 66.5, 61.7, 61.6, 57.5, 55.3, 37.6, 30.8, 26.8, 14.2, 14.0 IR (neat): 2924, 2852, 1728, 1513, 1446, 1367, 1243, 1176, 1034, 830, 746, 693 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{28}H_{34}NO_6$ 480.2386, found 480.2401

Diethyl-(E)-7-(4-methoxyphenyl)-2-styrylhexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5i´**). Reaction time: 4 h, **3i** (0.050 g, 0.27 mmol), **4a** (0.078 g, 0.27 mmol), **5i´** (0.026 g, 0.054 mmol), Yield: 20%, colourless liquid, R_f = 0.56 (diethyl

ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 (d, *J* = 8.5 Hz, 2H), 7.35-7.19 (m, 5H), 6.85 (d, *J* = 8.5 Hz, 2H), 6.60 (dd, *J* = 16.4, 5.5 Hz, 1H), 6.32 (d, *J* = 16.5 Hz, 1H), 4.57 (t, *J* = 5.2 Hz, 1H), 4.30-4.10 (m, 4H), 3.78 (s, 3H), 3.74 (t, *J* = 9.4 Hz, 1H), 3.37 (dd, *J* = 11.5, 2.4 Hz, 1H), 2.58-2.43 (m, 2H), 2.06-1.97 (m, 2H), 1.91-1.84 (m, 1H), 1.80-1.67 (m, 1H), 1.26 (t, *J* = 7.0 Hz, 3H), 1.22 (t, *J* = 7.1 Hz, 3H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.8, 169.6, 159.0, 137.3, 132.9, 130.5, 130.3, 128.6, 128.5, 127.3, 126.3, 113.8, 76.9, 68.5, 66.9, 61.7, 61.6, 58.1, 55.3, 37.6, 28.8, 23.6, 14.1, 14.0 IR (neat): 2929, 2853, 1728, 1512, 1445, 1244, 1173, 1030, 829, 748, 693, 554 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{28}H_{34}NO_6$ 480.2386, found 480.2400

Diethyl-2-(3,4-dimethoxyphenyl)-7-(4-methoxyphenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5j**). Reaction time: 1.5 h, **3j** (0.050 g, 0.23 mmol), **4a** (0.066 g, 0.23 mmol), **5j** (0.085 g, 0.16 mmol), Yield: 72%, viscous peach coloured liquid, R_f = 0.35 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 6.81-6.73 (m, 3H), 4.70 (dd, *J* = 11.0, 2.1 Hz, 1H), 4.33-4.17 (m, 4H), 3.87 (t, *J* = 9.3 Hz, 1H), 3.81 (s, 3H), 3.80 (s, 3H), 3.77 (s, 3H), 3.42 (dd, *J* = 11.0, 2.3 Hz, 1H), 2.66 (dd, *J* = 14.2, 9.6 Hz, 1H), 2.49 (dd, *J* = 14.3, 9.1 Hz, 1H), 2.27-2.20 (m, 1H), 2.01-1.94 (m, 1H), 1.83-1.65 (m, 2H), 1.30 (t, *J* = 7.3 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, 3H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.9, 169.7, 158.9, 148.7, 148.5, 133.2, 132.9, 128.6, 118.8, 116.1, 113.6, 110.7, 109.9, 80.5, 68.3, 66.4, 61.8, 61.7, 57.5, 55.9, 55.8, 55.3, 37.5, 31.7, 27.1, 14.2, 14.1 IR (neat): 2932, 2836, 1727, 1611, 1513, 1462, 1242, 1156, 1026, 830 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{28}H_{36}NO_8$ 514.2441, found 514.2462

Diethyl-7-(4-methoxyphenyl)-2-(3,4,5-trimethoxyphenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5k**). Reaction time: 2 h, **3k** (0.050 g, 0.199 mmol),

4a (0.058 g, 0.199 mmol), **5k** (0.050 g, 0.092 mmol), Yield: 46%, viscous yellow liquid, R_f = 0.45 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 (d, *J* = 8.4 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 2H), 6.46 (s, 2H), 4.69 (dd, *J* = 9.8, 1.6 Hz, 1H), 4.33-4.17 (m, 4H), 3.88 (t, *J* = 9.2 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 6H), 3.43 (dd, *J* = 9.8, 2.2 Hz, 1H), 2.67 (dd, *J* = 14.4, 9.6 Hz, 1H), 2.50 (dd, *J* = 14.4, 9.0 Hz, 1H), 2.24 (d, *J* = 9.2 Hz, 1H), 1.98 (d, *J* = 10.0 Hz, 1H), 1.81-1.64 (m, 2H), 1.30 (t, *J* = 7.2 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.9, 169.7, 158.9, 152.9, 137.3, 136.3, 132.8, 128.5, 116.1, 113.6, 103.5, 80.9, 68.3, 66.4, 61.8, 61.7, 60.8, 57.4, 56.0, 55.3, 37.4, 32.0, 27.1, 14.2, 14.0 IR (neat): 2938, 2838, 1727, 1590, 1511, 1459, 1241, 1183, 1124, 1005, 828, 759, 712, 562, 520 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{29}H_{38}NO_9$ 544.2547, found 544.2537

Diethyl-2-(benzo[d][1,3]dioxol-5-yl)-7-(4-methoxyphenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5l**). Reaction time: 2 h, **3l** (0.050 g, 0.244 mmol), **4a** (0.071 g, 0.244 mmol), **5l** (0.066 g, 0.132 mmol), Yield: 54%, viscous yellow liquid, R_f = 0.50 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.5 Hz, 2H), 6.84 (d, *J* = 8.5 Hz, 2H), 6.74 (s, 1H), 6.69 (s, 2H), 5.88 (s, 2H), 4.68 (dd, *J* = 11.0, 2.1 Hz, 1H), 4.33-4.16 (m, 4H), 3.85 (t, *J* = 9.3 Hz, 1H), 3.78 (s, 3H), 3.39 (dd, *J* = 11.0, 2.2 Hz, 1H), 2.64 (dd, *J* = 14.1, 9.6 Hz, 1H), 2.49 (dd, *J* = 14.1, 9.2 Hz, 1H), 2.23 (d, *J* = 8.5 Hz, 1H), 1.95 (d, *J* = 9.3 Hz, 1H), 1.79-1.62 (m, 2H), 1.30 (t, *J* = 6.8 Hz, 3H), 1.27 (t, *J* = 6.8 Hz, 3H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.8, 169.7, 158.8, 147.4, 146.9, 134.5, 132.8, 128.5, 119.9, 113.7, 107.9, 107.3, 100.9, 80.4, 68.3, 66.4, 61.7, 61.6, 57.4, 55.2, 37.5, 31.8, 27.0, 14.2, 14.0 IR (neat): 2916, 2850, 1727, 1612, 1511, 1441, 1367, 1241, 1181, 1036, 910, 809, 729, 565 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{27}H_{32}NO_8$ 498.2128, found 498.2123

Diethyl-2-(4-(benzyloxy)phenyl)-7-(3,4-dimethoxyphenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5m**). Reaction time: 1 h, **3b** (0.050 g, 0.19 mmol), **4b** (0.060 g, 0.19 mmol), **5m** (0.068 g, 0.12 mmol), Yield: 63%, yellow liquid, R_f = 0.35 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43-7.26 (m, 5H), 7.17 (d, *J* = 8.8 Hz, 2H), 7.08 (d, *J* = 1.9 Hz, 1H), 6.98 (dd, *J* = 8.4, 1.9 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 2H), 6.79 (d, *J* = 8.3 Hz, 1H), 5.01 (s, 2H), 4.73 (dd, *J* = 10.8, 1.9 Hz, 1H), 4.33-4.16 (m, 4H), 3.89-3.81 (m, 1H), 3.88 (s, 3H), 3.85 (s, 3H), 3.42 (dd, *J* = 10.8, 2.3 Hz, 1H), 2.66 (dd, *J* = 14.4, 9.6 Hz, 1H), 2.50 (dd, *J* = 14.5, 9.1 Hz, 1H), 2.27-2.21 (m, 1H), 2.02-1.95 (m, 1H), 1.84-1.66 (m, 2H), 1.32-1.24 (m, 6H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.8, 169.6, 158.3, 148.8, 148.1, 137.0, 133.4, 132.8, 128.6, 127.9, 127.8, 127.4, 119.5, 114.5, 110.8, 110.4, 80.3, 69.9, 68.3, 66.6, 61.6, 57.5, 55.9, 55.8, 37.5, 31.4, 27.1, 14.2, 14.0 IR (neat): 2928, 2853, 1727, 1610, 1512, 1454, 1367, 1235, 1175, 1025, 808, 735, 697 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: [M + H]$^+$ Calcd for $C_{34}H_{40}NO_8$ 590.2754, found 590.2755

Diethyl-7-(benzo[d][1,3]dioxol-5-yl)-2-(4-(benzyloxy)phenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5n**). Reaction time: 3 h, **3b** (0.050 g, 0.19 mmol), **4c** (0.058 g, 0.19 mmol), **5n** (0.055 g, 0.10 mmol), Yield: 52%, colourless solid, mp 104-106 °C, R_f = 0.56 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.27 (m, 5H), 7.18 (d, *J* = 8.7 Hz, 2H), 7.05 (d, *J* = 1.4 Hz, 1H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.84 (dd, *J* = 8.2, 1.6 Hz, 1H), 6.71 (d, *J* = 8.2 Hz, 1H), 5.91 (s, 2H), 5.01 (s, 2H), 4.72 (dd, *J* = 11.2, 1.8 Hz, 1H), 4.33-4.16 (m, 4H), 3.82 (t, *J* = 9.1 Hz, 1H), 3.39 (dd, *J* = 11.4, 2.4 Hz, 1H), 2.59 (dd, *J* = 14.3, 9.4 Hz, 1H), 2.48 (dd, *J* = 14.1, 9.1 Hz, 1H), 2.26-2.19 (m, 1H), 1.99-1.92 (m, 1H), 1.82-1.61 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H), 1.27 (t, *J* = 7.0 Hz, 3H) ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 170.8, 169.6, 158.3, 147.6, 146.7, 137.0, 134.9, 132.9, 128.6, 127.9, 127.8, 127.4, 120.7, 114.5, 107.9, 107.7,

100.8, 80.4, 69.9, 68.2, 66.7, 61.7, 61.6, 57.5, 37.7, 31.7, 27.1, 14.2, 14.0 IR (neat): 2919, 2852, 1719, 1611, 1510, 1449, 1385, 1241, 1177, 1035, 927, 834, 731, 697, 551 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{33}H_{36}NO_8$ 574.2441, found 574.2452

Diethyl-2-(4-(benzyloxy)phenyl)-7-(3,4,5-trimethoxyphenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5o**). Reaction time: 1 h, **3b** (0.050 g, 0.19 mmol), **4d** (0.067 g, 0.19 mmol), **5o** (0.066 g, 0.11 mmol), Yield: 56%, colourless viscous liquid, R_f = 0.30 (diethyl ether/hexane 40:60), ^1H NMR (400 MHz, $CDCl_3$): δ 7.43-7.26 (m, 5H), 7.19 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.9 Hz, 2H), 6.71 (s, 2H), 5.02 (s, 2H), 4.76 (dd, *J* = 11.0, 2.2 Hz, 1H), 4.33-4.17 (m, 4H), 3.89-3.77 (m, 1H), 3.85 (s, 6H), 3.82 (s, 3H), 3.43 (dd, *J* = 10.9, 2.4 Hz, 1H), 2.64 (dd, *J* = 13.8, 9.6 Hz, 1H), 2.52 (dd, *J* = 13.8, 8.7 Hz, 1H), 2.28-2.21 (m, 1H), 2.02-1.95 (m, 1H), 1.86-1.67 (m, 2H), 1.34-1.22 (m, 6H) $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.8, 169.5, 158.4, 153.0, 137.0, 136.9, 136.6, 132.7, 128.6, 127.9, 127.4, 114.6, 104.0, 80.5, 69.9, 68.2, 66.9, 61.7, 61.6, 60.8, 57.4, 56.0, 37.5, 31.5, 27.0, 14.2, 14.0 IR (neat): 2935, 2851, 1728, 1590, 1510, 1459, 1234, 1175, 1122, 1003, 829, 735, 697 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{35}H_{42}NO_9$ 620.2860, found 620.2858

Diethyl-2-(4-(benzyloxy)phenyl)-7-phenylhexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5p**). Reaction time: 18 h, **3b** (0.050 g, 0.19 mmol), **4e** (0.050 g, 0.19 mmol), **5p** (0.058 g, 0.11 mmol), Yield: 58%, off white solid, mp 90-92 °C, R_f = 0.50 (diethyl ether/hexane 40:60), ^1H NMR (400 MHz, $CDCl_3$): δ 7.46 (dd, *J* = 8.2, 1.4 Hz, 2H), 7.41-7.20 (m, 8H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.01 (s, 2H), 4.75 (dd, *J* = 11.1, 2.2 Hz, 1H), 4.33-4.17 (m, 4H), 3.91 (t, *J* = 9.2 Hz, 1H), 3.43 (dd, *J* = 11.1, 2.7 Hz, 1H), 2.66 (dd, *J* = 13.9, 9.7 Hz, 1H), 2.54 (dd, *J* = 13.8, 8.9 Hz, 1H), 2.28-2.21 (m, 1H), 2.02-1.94 (m, 1H), 1.84-1.67 (m, 2H), 1.33-1.24 (m, 6H) $^{13}C\{^1H\}$

NMR (100 MHz, $CDCl_3$): δ 170.8, 169.6, 158.3, 140.9, 137.0, 132.9, 128.6, 128.2, 127.9, 127.8, 127.4, 127.3, 127.2, 114.5, 80.3, 69.9, 68.3, 66.9, 61.7, 61.6, 57.6, 37.6, 31.6, 27.1, 14.2, 14.0 IR (neat): 2920, 2852, 1724, 1512, 1457, 1369, 1240, 1174, 1057, 1005, 857, 736, 699, 528 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{32}H_{36}NO_6$ 530.2543, found 530.2538

Diethyl-2-(4-(benzyloxy)phenyl)-7-(4-fluorophenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5q**). Reaction time: 72 h, **3b** (0.050 g, 0.19 mmol), **4f** (0.053 g, 0.19 mmol), **5q** (0.049 g, 0.09 mmol), Yield: 47%, off white solid, mp 78-80 °C, R_f = 0.55 (diethyl ether/hexane 40:60), ^1H NMR (400 MHz, $CDCl_3$): δ 7.45-7.27 (m, 7H), 7.16 (d, *J* = 8.6 Hz, 2H), 6.98 (t, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.01(s, 2H), 4.72 (d, *J* = 10.3 Hz, 1H), 4.33-4.17 (m, 4H), 3.88 (t, *J* = 9.2 Hz, 1H), 3.42 (dd, *J* = 11.3, 2.3 Hz, 1H), 2.65-2.48 (m, 2H), 2.25 (dd, *J* = 11.7, 2.2 Hz, 1H), 1.97 (dd, *J* = 11.6, 2.3 Hz, 1H), 1.84-1.64 (m, 2H), 1.33-1.24 (m, 6H) $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 170.7, 169.6, 163.3, 160.9, 158.4, 137.0, 136.7, 136.6, 132.8, 128.9, 128.8, 128.6, 127.9, 127.8, 127.4, 115.1, 114.9, 114.6, 80.4, 69.9, 68.2, 66.2, 61.8, 61.7, 57.5, 37.6, 31.5, 27.1, 14.2, 14.0 IR (neat): 2915, 2850, 1722, 1609, 1509, 1463, 1261, 1240, 1184, 1049, 835, 740, 698, 663, 552, 536, 503 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{32}H_{35}FNO_6$ 548.2448, found 548.2446

Diethyl-2-(4-(benzyloxy)phenyl)-7-(4-nitrophenyl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5r**). Reaction time: 72 h, **3b** (0.050 g, 0.19 mmol), **4g** (0.058 g, 0.19 mmol), **5r** (0.043 g, 0.07 mmol), Yield: 39%, yellow viscous liquid, R_f = 0.58 (diethyl ether/hexane 40:60), ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, *J* = 8.8 Hz, 2H), 7.62 (d, *J* = 8.8 Hz, 2H), 7.40-7.27 (m, 5H), 7.16 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.01 (s, 2H), 4.74 (dd, *J* = 11.2, 2.4 Hz, 1H), 4.33-4.17 (m, 4H), 4.00 (t, *J* = 9.4 Hz, 1H), 3.45 (dd, *J* = 11.2, 2.6 Hz, 1H), 2.58 (d, *J* = 9.3 Hz, 2H), 2.31-2.24

(m, 1H), 2.01-1.95 (m, 1H), 1.86-1.65 (m, 2H), 1.32- 1.25 (m, 6H) $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 170.3, 169.4, 158.5, 148.8, 147.3, 136.9, 132.3, 128.6, 128.1, 128.0, 127.9, 127.4, 123.7, 114.6, 80.8, 69.9, 68.1, 66.1, 61.9, 61.8, 57.6, 37.2, 31.3, 27.1, 14.2, 14.0 IR (neat): 2924, 2855, 1728, 1606, 1514, 1345, 1241, 1175, 1051, 1002, 850, 736, 696, 532 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{32}H_{35}N_2O_8$ 575.2393, found 575.2416

Diethyl-2-(3,4-dimethoxyphenyl)-7-((E)-styryl)hexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5s**). Reaction time: 12 h, **3j** (0.050 g, 0.226 mmol), **4h** (0.065 g, 0.226 mmol), **5s** (0.046 g, 0.090 mmol), Yield: 40%, off white solid, mp 84-86 °C, R_f = 0.45 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.7 Hz, 2H), 7.30-7.16 (m, 3H), 6.91-6.84 (m, 2H), 6.79 (d, *J* = 8.7 Hz, 1H), 6.55 (d, *J* = 16.0 Hz, 1H), 6.30 (dd, *J* = 16.0, 7.3 Hz, 1H), 4.75 (dd, *J* = 11.6, 2.0 Hz, 1H), 4.34-4.12 (m, 4H), 3.94-3.84 (m, 1H), 3.83 (s, 3H), 3.80 (s, 3H), 3.53 (q, *J* = 7.4 Hz, 1H), 3.34 (dd, *J* = 11.3, 2.0 Hz, 1H), 2.64 (dd, *J* = 14.0, 9.6 Hz, 1H), 2.38 (dd, *J* = 14.0, 8.6 Hz, 1H), 2.23 (d, *J* = 12.0 Hz, 1H), 1.98 (d, *J* = 13.5 Hz, 1H), 1.80 (dq, *J* = 12.4, 3.8 Hz, 1H), 1.66 (dq, *J* = 12.4, 3.8 Hz, 1H), 1.34-1.22 (m, 6H) $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 170.7, 169.6, 148.7, 148.6, 136.9, 132.8, 132.5, 128.9, 128.4, 127.4, 126.5, 119.0, 116.1, 110.8, 110.1, 80.5, 68.5, 65.6, 61.8, 61.7, 57.4, 55.9, 55.7, 34.9, 31.3, 27.0, 14.2, 14.0 IR (neat): 2928, 2852, 1726, 1516, 1451, 1249, 1162, 1101, 1025, 964, 866, 819, 755, 696, 547 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{29}H_{36}NO_7$ 510.2492, found 510.2487

Dimethyl-2-(3,4-dimethoxyphenyl)-7-vinylhexahydro-5H-pyrrolo[1,2-b][1,2]oxazine-5,5-dicarboxylate (**5t**). Reaction time: 72 h, **3j** (0.050 g, 0.226 mmol), **4i** (0.042 g, 0.226 mmol), **5t** (0.030 g, 0.074 mmol), Yield: 33%, mustard yellow solid, mp 78-80 °C, R_f = 0.40 (diethyl ether/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.90-6.85 (m, 2H),

6.83-6.77 (m, 1H), 5.99-5.88 (m, 1H), 5.24 (d, *J* = 17.0 Hz, 1H), 5.15 (d, *J* = 10.1 Hz, 1H), 4.73 (dd, *J* = 11.5, 2.0 Hz, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.77 (s, 6H), 3.36 (q, *J* = 7.2 Hz, 1H), 3.29 (dd, *J* = 11.5, 2.2 Hz, 1H), 2.54 (dd, *J* = 14.0, 9.6 Hz, 1H), 2.33 (dd, *J* = 14.0, 8.6 Hz, 1H), 2.22-2.14 (m, 1H), 1.99-1.91 (m, 1H), 1.77 (dq, *J* = 12.6, 4.0 Hz, 1H), 1.64-1.52 (m, 1H) $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 171.0, 169.8, 148.5, 148.4, 137.0, 132.6, 118.8, 117.3, 115.9, 110.6, 109.8, 80.3, 68.3, 65.6, 57.2, 55.7, 55.6, 52.7, 52.5, 34.2, 31.2, 26.7 IR (neat): 2950, 2920, 2837, 1725, 1591, 1514, 1437, 1238, 1203, 1159, 1018, 990, 868, 817, 764, 656, 621, 491, 415 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{21}H_{28}NO_7$ 406.1866, found 406.1876

General procedure for the monodecarboxylation of 5b[14]: For the reaction scheme, see Scheme S8 in the Supporting Information.

Compound **5b** and KOH (4 equiv) were dissolved in methanol and stirred under reflux conditions (on silicone oil bath) for 5 days. Upon completion (monitored by TLC), the reaction mixture was cooled down to room temperature and after acidification by 1N HCl solution, it was extracted three times with CH_2Cl_2. The combined organic layer was then concentrated in *vacuo* and the product (**6**) was purified by silica gel column chromatography using ethyl acetate/hexane as eluent.

2-(4-(benzyloxy)phenyl)-7-(4-methoxyphenyl)hexahydro-2*H*-pyrrolo[1,2-*b*][1,2]oxazine-5-carboxylic acid (**6**). Reaction time: 5 days, **5b** (0.050 g, 0.09 mmol), **6** (0.036 g, 0.08 mmol), Yield: 87%, brown solid, mp 153-155 °C, R_f = 0.35 (ethyl acetate/hexane 40:60), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43-7.27 (m, 7H), 7.20 (d, *J* = 8.6 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.02 (s, 2H), 4.82 (dd, *J* = 11.2, 1.8 Hz, 1H), 3.98 (t, *J* = 9.0 Hz, 1H), 3.78 (s, 3H), 2.96 (dt, *J* = 10.7, 1.9 Hz, 1H), 2.83-2.74 (m, 1H), 2.63-2.54 (m, 1H), 2.31 (d, *J* = 11.6 Hz, 1H), 2.05-1.67 (m, 4H)

$^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 179.0, 158.6, 158.3, 137.0, 133.5, 133.0, 128.6, 128.0, 127.9, 127.8, 127.4, 114.6, 113.7, 80.6, 69.9, 66.8, 66.4, 55.3, 43.2, 32.8, 31.5, 29.4 IR (neat): 2922, 2852, 1704, 1608, 1511, 1456, 1242, 1173, 1033, 828, 735, 696, 594 cm^{-1} HRMS (ESI, Q-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{28}H_{30}NO_5$ 460.2124, found 460.2132

ASSOCIATED CONTENT

Supporting Information

^{1}H NMR, ^{13}C NMR, HRMS data and IR spectra of all new compounds; evaluation of stereospecificity (PDF)

Single-crystal X-ray data and images for **3b** (CIF)

Single-crystal X-ray data and images for **6** (CIF)

AUTHOR INFORMATION

Corresponding Author

Prabal Banerjee - *Department of Chemistry, Indian Institute of Technology Ropar, Rupnagar, Punjab 140001, India;*

orcid.org/0000-0002-3569-7624; Email: prabal@iitrpr.ac.in

Authors

Pankaj Kumar - *Department of Chemistry, Indian Institute of Technology Ropar, Rupnagar, Punjab 140001, India*

Rakesh Kumar - *Department of Chemistry, Indian Institute of Technology Ropar, Rupnagar, Punjab 140001, India*

Notes

The authors declare no competing financial interest.

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