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Diastereoselective Synthesis of Structurally and Stereochemically Diversified 2-Oxa-7-azabicyclo[4.1.0]hept-3-enyl Carboxylates and Their Potential Application toward the Synthesis of Functionalized Pyranooxazolone and Pyrrole Derivatives through Skeletal Transformations

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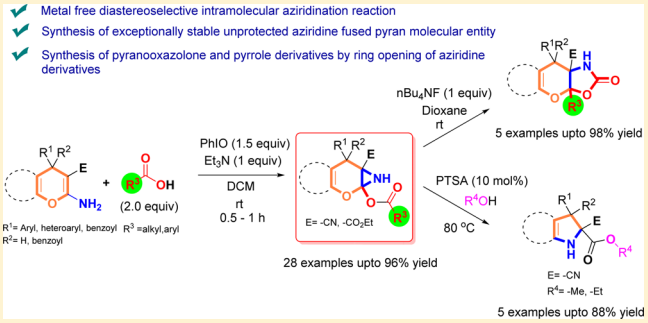
Supporting Information

ABSTRACT: An advanced protocol for the diastereoselective intramolecular aziridination reaction has been developed to synthesize 2-oxa-7-azabicyclo[4.1.0]hept-3-en-1-yl carboxylates from their corresponding 4-*H*-pyrans and spiropyrans analogues employing iodosylbenzene as the exclusive oxidant in the presence of carboxylic acid and triethylamine. High structural and stereochemical diversity of these pyran fused NH-azridine scaffolds makes them useful in evaluating their biological and pharmacological activities by SAR studies. Additionally, their potential synthetic application has been uncovered by efficient transformation into biologically relevant novel pyranooxazolone and pyrrole derivatives.



INTRODUCTION

A fused heterocyclic moiety is one of the fundamental structural requirements for numerous natural products and synthetic compounds to exhibit their extensive variety of biological activities.[1] Fused heterocycles, being essentially the hybrid of two or more bioactive heterocyclic fragments, possess versatile biological and pharmacological activities originated due to the presence of multiple pharmacophores in a single molecular entity. Further, carefully designed synthetic hybrid molecules, possessing high skeletal and stereochemical diversity, with bioactivity can be used as protein function modulators and key leads in drug development of the medicinal field.[2] Thus, development of an efficient and direct synthetic route to synthesize fused heterocyclic compounds bearing multiple chiral centers has taken a great deal of attention over the past decades.[3]

The pyran framework is a privileged pharmacophore embedded as the structural core in numerous biologically relevant natural products and synthetic compounds.[4] On the other hand, aziridine is the key constituent of several bioactive natural products[5] regardless of its high affinity toward countless ring-opening reactions due to the ring strain.[6] Although various literature reports concerning bioactivities of pyran and aziridine derivatives intensely justify the construction of hybrid molecular entities having an aziridine fused pyran scaffold as the structural motif, much less effort has been specified to develop the synthetic methodologies to achieve them.[7] Availability of a handful of literature data regarding the synthesis of pyran fused aziridine molecular entities may be due to their inherent instability, which prevents their isolation as a stable molecular entity. In this context, it is noteworthy to mention that some previous reports enlighten the in situ synthesis of pyran fused aziridine molecular scaffolds which then induced immediate chemical transformations without isolating them as stable compounds.[8] Consequently, their preparation and isolation still remain challenging as well as important synthetic targets to the organic chemists.

Plentiful synthetic methods have been developed over the past decades to synthesize aziridine derivatives in their protected and unprotected form.[9] Most of them consist of intramolecular substitution reactions within the amine derivatives, reaction of carbenes with imines, and reaction of nitrenes with olefins. Recently, Zhao et al. have established a synthetic route to construct 2*H*-azirines from several enamine derivatives using iodobenzene diacetate (Scheme 1, entry 1).[10] In our previous work,[7d] we have demonstrated an intramolecular aziridination reaction to construct a pyran fused 2-acetoxy-NH-aziridine molecular scaffold by exploiting the enamine fragment of 2-amino-4*H*-pyrans and 2-amino-spiropyrans employing iodobenzene diacetate (Scheme 1, entry 2). It was indeed the first report of the synthesis and isolation of highly stable pyran fused 2-acetoxy-NH-aziridines. The use of hypervalent iodine as the sole reagent for aziridination is beneficial since it offers a

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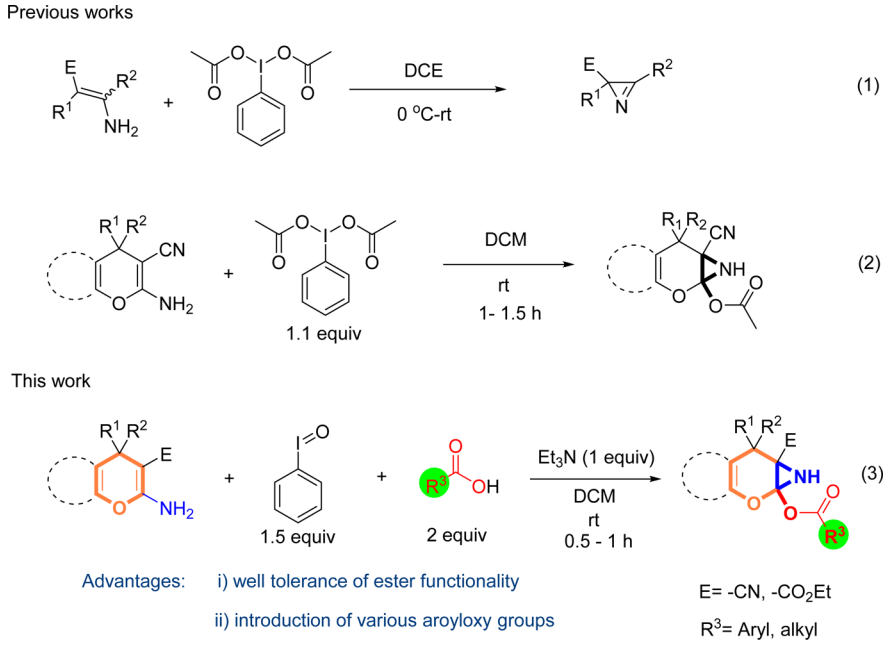
Scheme 1. Synthesis of 2-Oxa-7-azabicyclo[4.1.0]hept-3-en-1-yl Carboxylates by Intramolecular Aziridination



Scheme 2. Acid and Fluoride Ion Catalyzed Ring-Opening of 2-Oxa-7-azabicyclo[4.1.0]hept-3-enyl Carboxylates

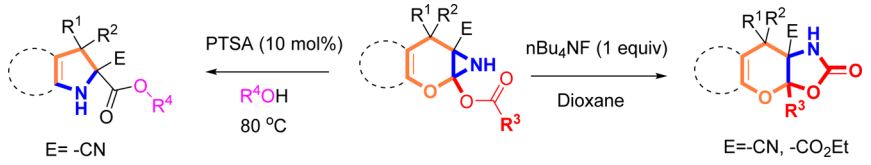
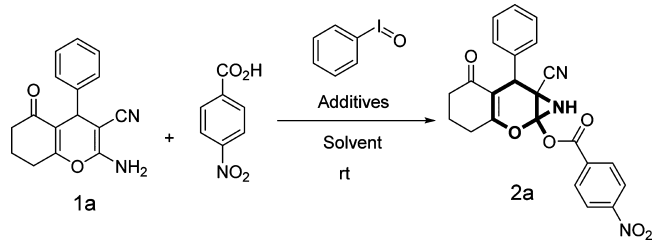


Table 1. Optimization of Reaction Conditions[a]



entry	PhIO (mmol)	carboxylic acid (mmol)	additive (1 mmol)	solvent	time (min)	yield[b](%)
1	1.0	1		DCM	60	10
2	1.0	1	Et_3N	DCM	40	40
3	1.2	1	Et_3N	DCM	35	45
4	1.5	1	Et_3N	DCM	30	55
5	1.6	1	Et_3N	DCM	30	50
6	1.5	1.5	Et_3N	DCM	30	70
7	1.5	1.8	Et_3N	DCM	30	90
8	**1.5**	**2.0**	**Et_3N**	**DCM**	**30**	**92**
9	1.5	2.1	Et_3N	DCM	30	91
10	1.5	2.0	Cs_2CO_3	DCM	45	15
11	1.5	2.0	NaOAc	DCM	55	12
12	1.5	2.0	Et_3N	DCE	50	74
13	1.5	2.0	Et_3N	EtOAc	50	62
14	1.5	2.0	Et_3N	toluene	45	60
15	1.5	2.0	Et_3N	dioxane	55	65
16	1.5	2.0	Et_3N	THF	52	70
17	1.5	2.0	Et_3N	acetonitrile	55	72

[a]1 mmol of **1a** was taken in 5 mL of solvent in all the cases. [b]Yield of the isolated product.

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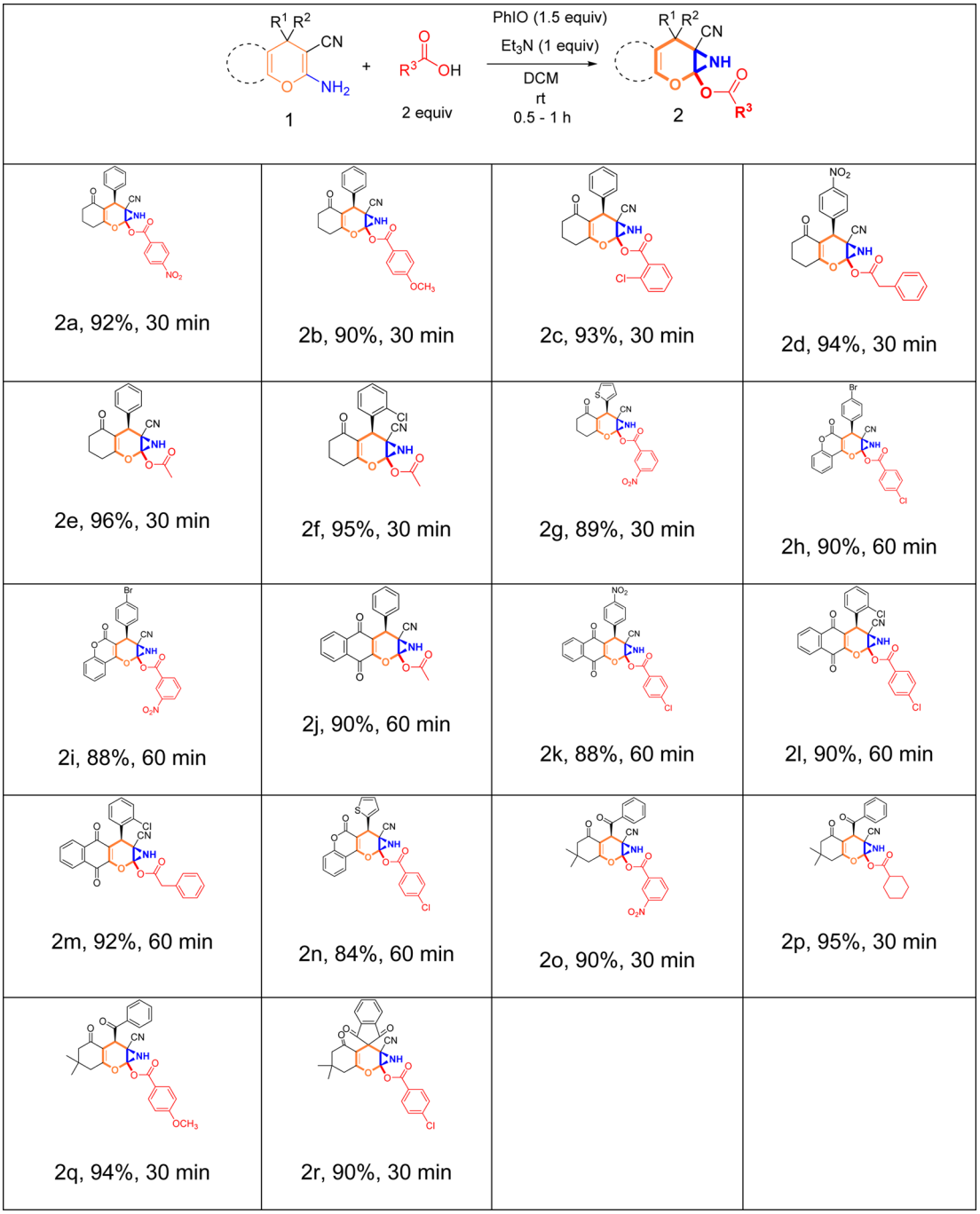
Table 2. Substrate Scope to Synthesize 3-Cyano-2-oxa-7-azabicyclo[4.1.0]hept-3-enyl Carboxylates[a,b]



[a]Reaction conditions: **1** (1 mmol), PhIO (1.5 mmol), carboxylic acids (2 mmol), Et_3N (1 mmol), DCM (5 mL), rt. [b]Isolated yield and reaction time.

metal-free mild reaction condition. In addition, hypervalent iodine reagents are easily available, less toxic, and easy to handle. Despite of the success, our previous protocol suffers from generalized functionalization of the target molecule, since only the acetoxy group can be introduced in the angular position of the 2-oxa-7-azabicyclo[4.1.0]hept-3-ene framework. Also, the protocol has the limitation to be unproductive when the −CN group is replaced by the $-CO_2Et$ group in the starting pyran derivatives. Thus, development of a comprehensive methodology with broader substrate scope and higher functional group tolerance, and suitable for introducing a higher degree of diversity in the resulting pyran fused NH-aziridines, is still challenging and of course in demand.

Concentrating on the efforts in the development of innovative and efficient methodologies toward the synthesis of biologically relevant compounds,[11] herein we wish to reveal a simple and robust diastereoselective protocol to construct a stable, highly functionalized, and stereochemically diversified pyran fused NH-aziridine scaffold by reacting 2-amino-4*H*-pyran and 2-aminospiropyran derivatives with iodosylbenzene as the exclusive oxidant in the presence of triethylamine and carboxylic acids (1:2) at room temperature, avoiding metal catalysts (Scheme 1, entry 3).

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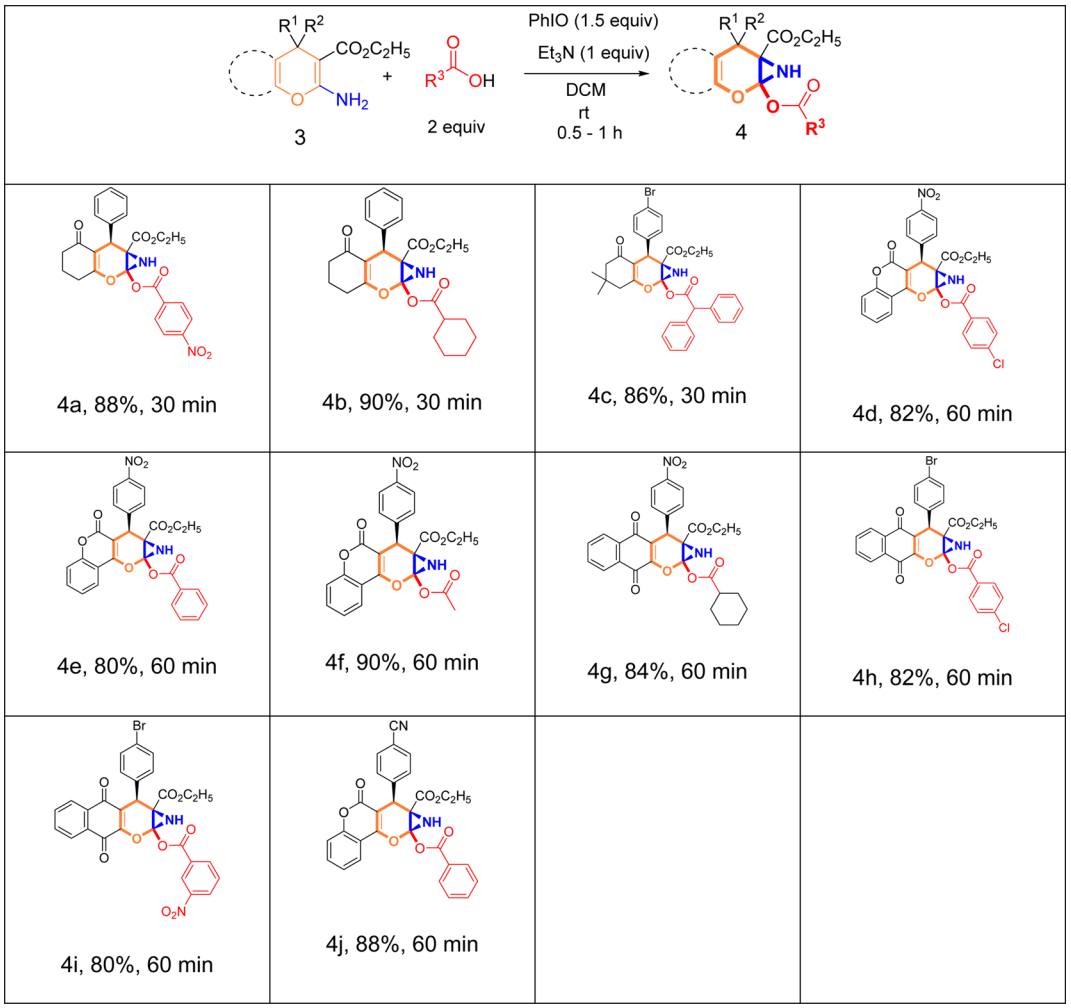
Table 3. Substrate Scope to Synthesize Ethyl 1-(Carbethoxy)-2-oxa-7-azabicyclo[4.1.0]hept-3-ene-6-carboxylates[a,b]



[a]Reaction conditions: **3** (1 mmol), PhIO (1.5 mmol), carboxylic acids (2 mmol), Et_3N (1 mmol), DCM (5 mL), rt. [b]Isolated yield and reaction time.

Additionally, synthetic applications of these synthesized NH-aziridine derivatives was also explored by carrying out their ring-opening transformations under different reaction conditions. Interestingly, they have been found to be the key precursor in synthesizing densely functionalized novel pyranooxazolone molecular scaffolds when treated with tetrabutylammonium fluoride. In addition, acid catalyzed ring-opening of these NH-aziridines leads to the formation of biologically privileged highly functionalized pyrrole derivatives (Scheme 2). To the best of our knowledge, this is the first report revealing the synthesis of these particular functionalized pyranooxazolone and pyrrole molecular scaffolds originating from pyran fused aziridine derivatives upon simple and efficient ring transformation conditions.

RESULTS AND DISCUSSION

To investigate the feasibility of this strategic approach for intramolecular aziridination reaction, 2-amino-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4*H*-chromene-3-carbonitrile **1a** was synthesized using a known method[12a] and employed as a model substrate in this reaction. When **1a** was treated with iodosylbenzene (1 mmol) in the presence of 4-nitrobenzoic acid (1 mmol) in DCM (5 mL) at room temperature, after 60 min, **2a** was obtained in very low yield (Table 1, entry 1). Interestingly, use of triethylamine (1 mmol) as an additive increased the product yield to 40% in a comparatively shorter reaction time (Table 1, entry 2). The use of a higher amount of oxidant was found to be effective for improving the product yield within a shorter reaction time (Table 1, entries 3 and 4). However, further enhancement of product yield was not observed when more than 1.5 mmol of iodosylbenzene was used (Table 1, entry 5). When carboxylic acid loading was increased, the yield of **2a** was greatly elevated and the isolated yield was 92% (applying 2 mmol of carboxylic acid) (Table 1, entries 6−8). A further increase of the carboxylic acid amount did not afford any better result (Table 1, entry 9). Furthermore, to improve the reaction time and product yield, the reaction was performed in the presence of different additives and different solvents. Bases such as Cs_2CO_3 and NaOAc were found to be inefficient compared to triethylamine (Table 1, entries 10 and 11), and **2a** was isolated in low yield when solvents such as dichloroethane, ethyl acetate, toluene, dioxane, tetrahydrofuran, and acetonitrile were used replacing DCM (Table 1, entries 12−17).

With these optimized reaction conditions (Table 1, entry 8), we then focused our attention to explore the feasibility of this intramolecular aziridination reaction. Several known 2-amino-3cyano-4*H*-pyran derivatives[12a−j] with high functionalization

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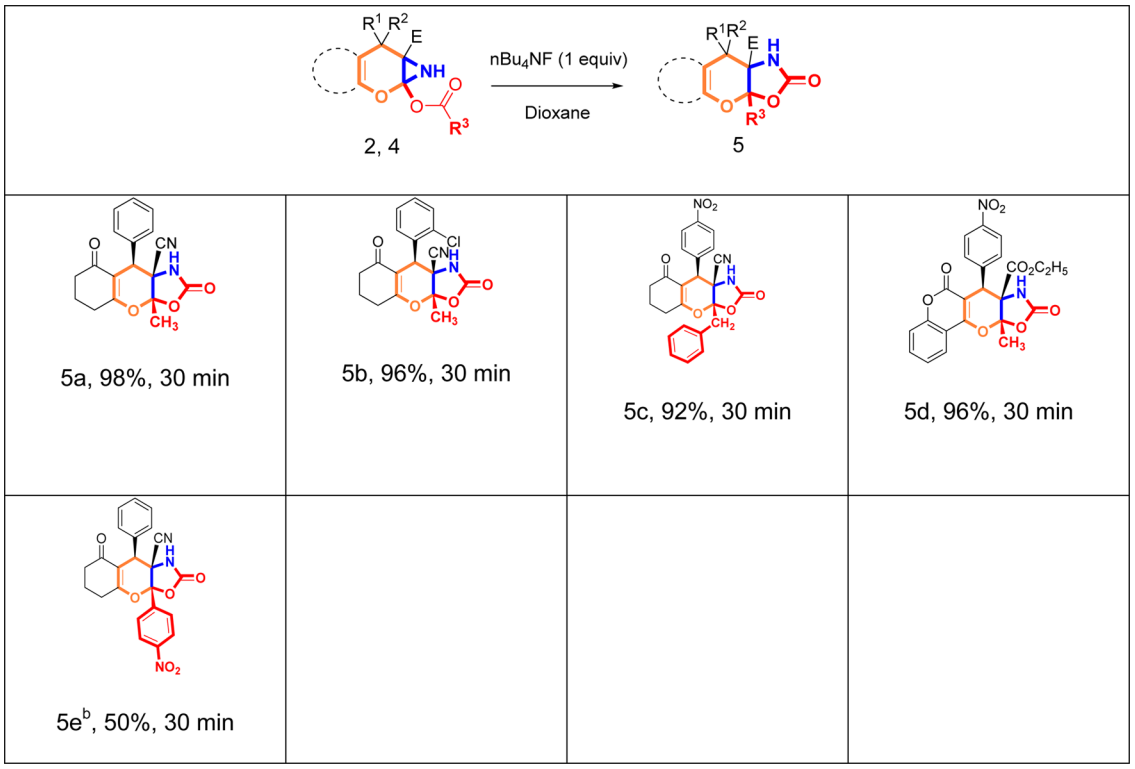
Table 4. Synthesis of Pyranooxazolones[a,c]



[a]Reaction conditions: **2** or **4** (1 mmol), **n**Bu_4NF (1 mmol), dioxane (2 mL), rt. [b]Heated at 60 °C. [c]Isolated yield and reaction time.

were synthesized via the above-mentioned three-component reaction[12a] in which a variety of aromatic and heteroaromatic aldehydes along with phenylglyoxal were reacted with malononitrile and ethyl cyanoacetate in the presence of various 1,3-dicarbonyls such as dimedone, cyclohexane-1,3-dione, 4-hydroxycoumarin, and 2-hydroxy-1,4-naphthoquinone. These pyran derivatives were then treated with iodosylbenzene (1.5 mmol) in the presence of carboxylic acid (2 mmol) and triethylamine (1 mmol) in 5 mL of DCM to synthesize 2-oxa-7-azabicyclo[4.1.0]hept-3-enes. In this purpose, a large variety of aromatic as well as aliphatic carboxylic acids were employed to amplify this developed protocol. Astonishingly, this protocol was found to be really efficient in affording diversified 2-oxa-7-azabicyclo[4.1.0]hept-3-enes in good to excellent yields (Tables 2 and 3). A wide range of aromatic carboxylic acids containing electron-donating as well as electron-withdrawing groups at different positions of the ring along with aliphatic acids such as acetic acid, phenylacetic acid, and sterically bulky diphenyl acetic acid were successfully introduced at the angular position of the 2-oxa-7-azabicyclo[4.1.0]hept-3-ene framework. This protocol offers an absolutely clean reaction as no other side products were obtained after completion of the reaction. It may be due to the high reactivity of the oxidant toward the enamine fragment of the starting material while the alternative double bond of the pyran ring and other functional groups during the reaction remained nonreactive. Notably, the reaction was found to proceed with the same efficiency in the case of ethyl 2-amino-4*H*-pyran-3-carboxylate derivatives, which broadens the scope of this protocol further (Table 3, entries **4a**−**4i**). Compounds **4a**−**i** were obtained at slightly lower yield compared to **2a**−**r**, which seem to be probably due to the greater electron-withdrawing ability of nitrile than that of the ethoxycarbonyl group. Apart from their role in protecting the enamine tautomeric form in starting materials, −CN and $-CO_2Et$ groups also induce nucleophilic property of the carbon center to which they are stitched, since the pyran oxygen atom and amine group are in conjugation with them through the intervening double bond. To test the viability of the reaction in the case of the spiropyran system, a known spiropyran derivative[12k] was synthesized using the same procedure which was used to synthesize 4*H*-pyrans.[12a] The reaction was also found to be convenient in transforming the spiropyran into the corresponding pyran fused NH-aziridine with excellent product yield (Table 2, entry **2r**). The starting materials which possess coumarin or naphthoquinone fused pyran substructures were found to take a longer reaction time for this transformation, however, not affecting the yield of their corresponding products (Table 2, entries **2i**−**o** and Table 3, entries **4d**−**i**). The reaction proceeded with almost equal efficiency in the presence of several aromatic and aliphatic acids (Table 2, entries **2a**−**r** and Table 3, entries **4a**−**i**). All the synthesized 2-oxa-7-azabicyclo-[4.1.0]hept-3-en-1-yl carboxylates are significantly stable, and they remain unaffected during column chromatographic separation of the reaction mixture (silica gel mesh size 100−200). All products are well characterized through ^{1}H NMR, ^{13}C NMR, IR, HRMS, and elemental analysis data, and finally, the structural motif of the synthesized compounds were established through X-ray crystallographic analysis of one representative compound **4g** (CCDC 1472710). The information about the relative stereochemistry obtained from the X-ray crystallographic analysis of compound **4g** (see the Supporting Information) enables us to assign the relative configuration of C^2, C^3, and C^4 centers of the pyran ring as *R*, *R*, and *S*, respectively.

In this present endeavor, we have also successfully evaluated the synthetic application of these synthesized 2-oxa-7-

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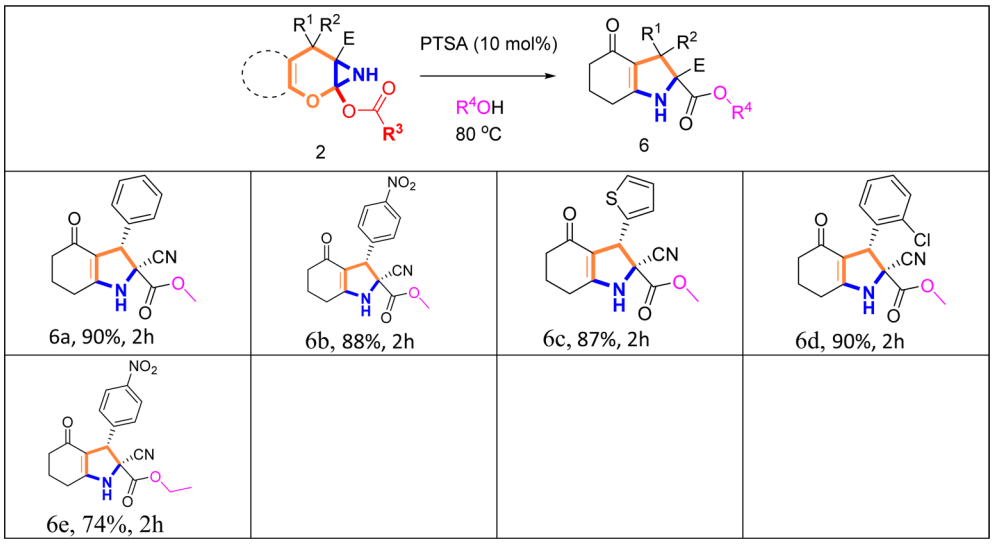
Table 5. Synthesis of Pyrroles[a,b]



[a]Reaction conditions: **2** (1 mmol), PTSA (10 mol %), alcohol (3 mL), 80 °C. [b]Isolated yield and reaction time.

azabicyclo[4.1.0]hept-3-enyl carboxylates by converting them into highly functionalized pyranooxazolone and pyrrole derivatives by devising fluoride ion and acid catalyzed ring-opening of the aziridine moiety. For the fluoride ion catalyzed transformation, tetrabutylammonium fluoride was employed as suitable reagent owing to its solubility in organic solvents. Further strong hydrogen bonding affinity of the fluoride ion and its specialty in providing a clean reaction by maintaining neutral reaction environment make it a better choice of reagent for this purpose. Some selective 2-oxa-7-azabicyclo[4.1.0]hept-3-enyl carboxylates were transformed into pyranooxazolones in the presence of 1 equiv of tetrabutylammonium fluoride in dioxane medium at room temperature. The transformation was very fast (~30 min) (when R^3 = methyl, benzyl) and almost quantitatively afforded a well decorated pyranooxazolone scaffold bearing an angular functionality (Table 4, entries **5a**–**d**). Applying this method, **2e**, **2f**, **2d**, **4f**, and **2a** were successfully transformed into **5a**–**e**, respectively. The transformation is equally efficient for both the ester and the nitrile derivatives of 2-oxa-7-azabicyclo[4.1.0]hept-3-enyl carboxylates (Table 4, entries **5a**–**e**). They were (**5a**–**e**) well characterized by ^{1}H NMR, ^{13}C NMR, IR, HRMS, and elemental analysis data, and their structural motif was fully confirmed through X-ray crystallographic analysis of a single crystal of compound **5c** (CCDC 1472711). One very interesting structural feature (see the Supporting Information) of this pyranooxazolone molecular scaffold is that the *p*-nitrophenyl, nitrile, and benzyl groups are in a syn relationship to each other. Literature reviews suggest that both this type of pyranooxazolones and their synthetic route are new.

Furthermore, when some selective 2-oxa-7-azabicyclo[4.1.0]-hept-3-enyl carboxylates were treated with *p*-toluenesulfonic acid (10 mol %) in refluxing methanol, they were transformed into well functionalized pyrrole derivatives. In all cases, the conversion took place in a short reaction time (~2 h) and the products are obtained in excellent yields (Table 5, **6a**–**d**). **2a**, **2d**, **2f**, and **2g** were converted to **6a**–**d**, respectively, by applying this protocol, and when compound **2d** was subjected to the same *p*-TsOH catalyzed reaction in ethanol medium, pyrrole **6e** was obtained in good yield. However, this conversion is very efficient only for cyano derivatives of 2-oxa-7-azabicyclo[4.1.0]hept-3-enyl carboxylates which possess a cyclohexanone fragment fused with the pyran moiety.

Compounds **6a**–**e** are also fully characterized by ^{1}H NMR, ^{13}C NMR, IR, HRMS, and elemental analysis data, and confirmation of the structural motif was done by single-crystal X-ray crystallographic analysis of compound **6a** (CCDC 1472712). Interestingly, product pyrroles evolved via acid catalyzed transformation, which features a quaternary carbon atom, attached with both a nitrile and a methoxy carbonyl group at the same time, and the −CN group is in a syn relationship with the aryl group of the C^3 atom. In the case of compound **6a**, the relative configuration of C^2 and C^3 centers of the pyrrole ring can be assigned as *R* and *S*, respectively, from the X-ray crystal structure of it (see the Supporting Information).

A mechanism for the formation of 2-oxa-7-azabicyclo[4.1.0]-hept-3-enyl carboxylates is depicted in Scheme 3. On the basis of the fact that iodobenzene diacetate undergoes ligand exchange in the presence of carboxylic acids,[13] we tentatively assume that the initial reaction between iodosyl benzene and carboxylic acid has produced the species $PhI(OCOR)_2$ (**I**), which then acted as the actual reagent in this reaction. Initially, **I** attacks the amino group of the starting material (**1**), leading to the formation of *N*-iodo intermediate **II**. The carboxylic acid released in this step is consumed by triethylamine to produce an ion pair which could serve as a source of carboxylate ion. Attack by the double bond, assisted by the pyran oxygen atom, to the electrophilic nitrogen center generates the intermediate **III** by releasing iodobenzene and carboxylate ion. The attachment of the pyran oxygen atom with the enamine moiety is crucial for the formation of 2-oxa-7-azabicyclo[4.1.0]hept-3-enyl carboxylates since it assists in the formation and stabilization of the intermediate **III**. Subsequently, attack by the carboxylate ion to the C^2 center of the pyran ring of **III** takes place, which ultimately generates 2-oxa-7-azabicyclo-[4.1.0]hept-3-enyl carboxylate **2**. The X-ray crystal structure of compound **4g** (see the Supporting Information) explains the relative stereochemistry in the pyran fused NH-aziridine scaffold and clearly displays the syn relationship between the aziridine ring and the 4-nitrophenyl substituent of the C^4 center of the pyran ring. This syn orientation in the product aziridine

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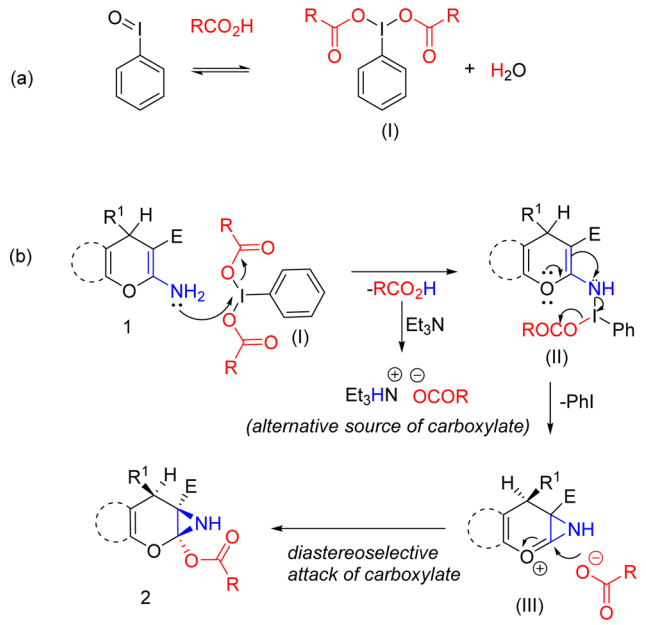
Scheme 3. Mechanism for the Synthesis of 2-Oxa-7-azabicyclo[4.1.0]hept-3-enyl Carboxylates

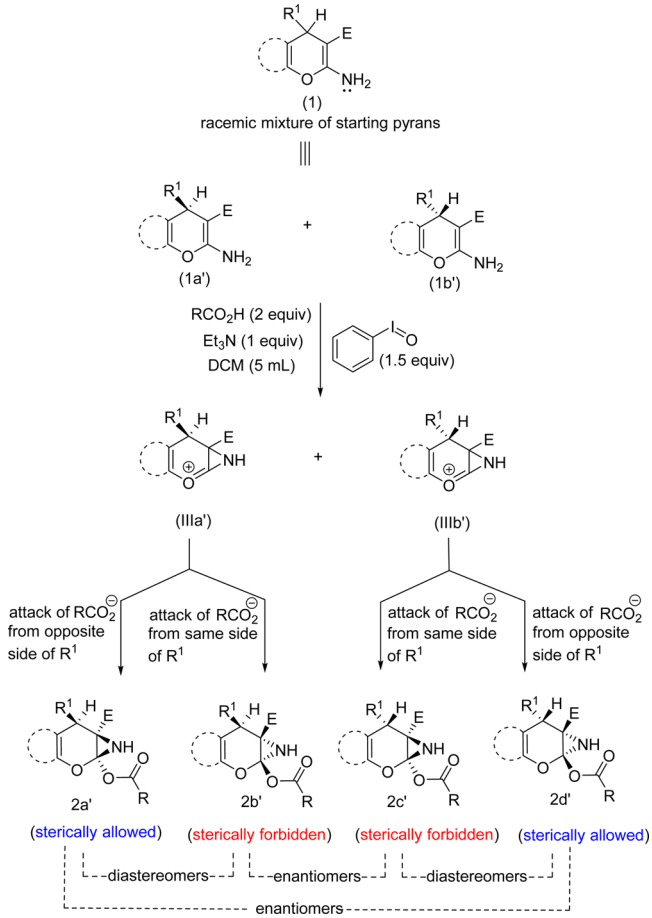


molecules undoubtedly indicates that the attacking carboxylate ion has approached from the opposite side of the 4-nitrophenyl group. This, in turn, establishes the diastereoselective nature of this particular reaction. During the nucleophilic attack (carboxylate ion), the large group (R^1) of the C^4 carbon atom controls the facial selectivity. The carboxylate ion prefers the α attack, i.e., the attack from the opposite side of R^1, hence leading to the formation of **2** as the exclusive diastereomer. The β attack, which is sterically hindered, does not take place at all under the imposed experimental condition.

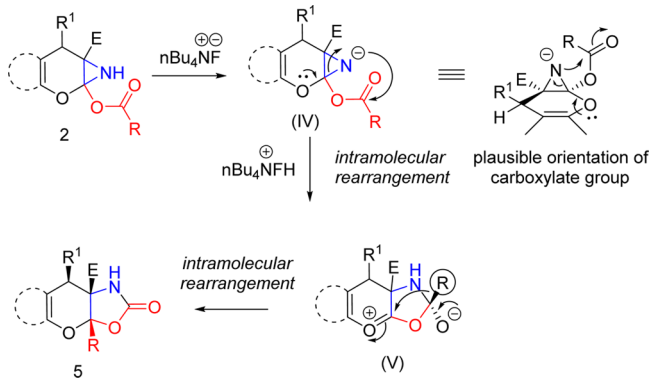
The stereochemical course of this aziridination reaction is described in Scheme 4. The starting pyran compounds are racemates since they have been synthesized applying achiral methodology. When a starting pyran derivative **1** is treated with 1.5 equiv of iodosylbenzene in the presence of 2 equiv of a carboxylic acid and 1 equiv of triethylamine, its corresponding enantiomers **1a′** and **1b′** result in the formation of the intermediates **IIIa′** and **IIIb′** following the same mechanistic pathway as proposed in Scheme 3. In the next step, subsequent attack by the carboxylate ion to the C^2 center of the pyran ring of both **IIIa′** and **IIIb′** takes place to generate the final aziridine product. Now, during the nucleophilic attack of the carboxylate ion, the preferred approach is controlled by a steric factor and takes place from the opposite side of the R^1 group. Consequently, the intermediates **IIIa′** and **IIIb′** rapidly transformed into the products **2a′** and **2d′**, respectively. The formation of **2b′** and **2c′** is sterically forbidden, and they have not formed at all during the course of reaction. Now, **2a′** and **2d′** possess an enantiomeric relationship to each other. On the other hand, **2a′** and **2d′** possess a diastereomeric relationship with **2b′** and **2c′**, respectively. Thus, the reaction follows the diastereoselective pathway and eventually transforms the racemic pyran compound to the corresponding pyran fused NH-aziridine racemate (**2a−r** and **4a−j**) in a diastereoselective manner.

Plausible mechanisms for the fluoride ion and acid catalyzed transformations of the 2-oxa-7-azabicyclo[4.1.0]hept-3-enyl carboxylates are also depicted in Schemes 5 and 6, respectively.

Scheme 4. Stereochemical Course of the Aziridination Reaction



Scheme 5. Mechanism for the Synthesis of Pyranooxazole



The acidic nature of the H of the aziridine ring in **2** facilitates its abstraction by the fluoride ion to generate intermediate **IV**. This negatively charged species **IV** then immediately undergoes intramolecular rearrangement with concomitant proton abstraction to generate **V**. During this step, the plausible orientation of the carboxylate group in intermediate **IV** is depicted in Scheme 3. **V** then follows a second intramolecular rearrangement pathway in which migration of the R group takes place to the α-position of the positively charged oxygen atom, which ultimately affords the compound **5**.

In the case of acid catalyzed ring-opening reaction (Scheme 6), the aziridine ring of **2** is first opened up in the presence of

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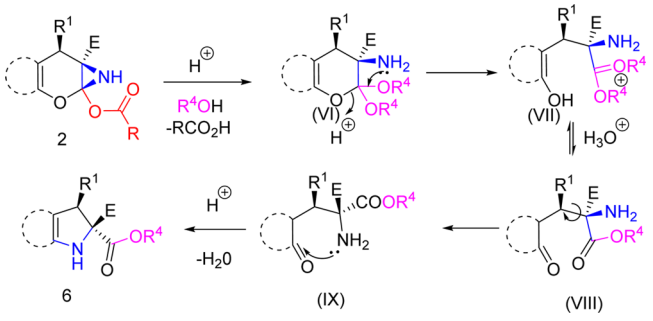
Scheme 6. Mechanism for the Synthesis of Pyrroles



H^+ ion, resulting in the formation of intermediate **VI**, which then undergoes acid catalyzed ring-opening and generates **VII**. **VII**, on tautomerization, changes into its keto form **VIII**, which then transformed into **IX** in the presence of acid. Finally, **IX** undergoes acid catalyzed cyclization to assume the product **6**, i.e., the fused pyrrole derivative.

CONCLUSION

In conclusion, an advanced protocol of intramolecular aziridination reaction has been developed to synthesize 2-oxa-7-azabicyclo[4.1.0]hept-3-en-1-yl carboxylates from their corresponding 4-*H*-pyrans and spiropyrans using iodosylbenznene as the exclusive oxidant in the presence of various aromatic as well as aliphatic carboxylic acids and triethylamine. Regardless of its broader substrate scope, this methodology offers a very simple, robust, and diastereoselective route to construct pyran fused NH-aziridine molecular scaffolds. Good functional group tolerance of the oxidant makes this protocol suitable to introduce high skeletal and stereochemical diversity in the product NH-azridines. Their potent synthetic efficacy has been discovered by efficiently transforming them into biologically relevant novel pyranooxazolone and pyrrole derivatives under mild reaction conditions.

EXPERIMENTAL SECTION

General Procedure for the Synthesis of 4-*H*-Pyrans.[12a] Triethylamine (1 drop) was added to a solution of aromatic aldehydes (2 mmol), malononitrile (or ethyl 2-cyanoacetate) (2 mmol), and 1,3-diketones (2 mmol) in EtOH (5 mL), and the reaction mixture was refluxed for 15 min. The precipitate thus appeared was filtered off, washed with water (5 × 10 mL) and EtOH (3 × 5 mL), and finally recrystallized from EtOH. The crystallized pure compounds[12a−j] were then subjected for the synthesis of 2-oxa-7-azabicyclo[4.1.0]hept-3-en-1-yl carboxylates.

General Procedure for the Synthesis of Spiropyran.[12a] Triethylamine (1 drop) was added to a solution of ninhydrin (2 mmol), malononitrile (2 mmol), and dimedone (2 mmol) in EtOH (5 mL), and the reaction mixture was refluxed for 15 min. The precipitate thus formed was filtered off, washed with water (5 × 10 mL) and EtOH (3 × 5 mL), and finally recrystallized from EtOH. The crystallized pure compound[12k]was then subjected for the synthesis of 2-oxa-7-azabicyclo[4.1.0]hept-3-en-1-yl carboxylates.

General Procedure for the Synthesis of 2-Oxa-7-azabicyclo-[4.1.0]hept-3-en-1-yl Carboxylates 2a−r and 4a−j. To a stirring suspension of iodosylbenzene (1.5 mmol) in 5 mL of DCM was added carboxylic acid (2 mmol), and the mixture was stirred for 5 min at rt, followed by addition of triethylamine (1 mmol), and stirred for another 2 min. Finally, 2-amino-4-*H*-pyrans (1 mmol) were added in the reaction mixture and stirred for the stipulated time (Tables 2 and 3) until the total consumption of the starting material (monitored by TLC) was observed. After completion of the reaction, the mixture was diluted with DCM (10 mL) and washed with saturated sodium bicarbonate solution (10 mL × 3 times). The combined organic layers were dried over sodium sulfate and subjected to column chromatographic separation (20−50% ethyl acetate in petroleum ether) to get the pure products. The same procedure was applied in the case of 2-amino spiropyran. All the synthesized compounds were characterized by spectral (^{1}H NMR, ^{13}C NMR, IR, HRMS, and elemental analysis) data, and X-ray crystallographic analysis (**4g**).

7a-Cyano-6-oxo-7-phenyl-3,4,5,6,7,7a-hexahydrochromeno[2,3-b]azirin-1a(1H)-yl 4-Nitrobenzoate ***2a***. Yield: 396 mg, 92%; white solid; Mp: 208−210 °C; IR (KBr): 3214, 2956, 2832, 2245, 1750, 1710, 1680, 1632, 1530, 1350, 1091, 987 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 2.07 (d, J = 4.8 Hz, 2H), 2.30−2.41 (m, 3H), 2.60 (d, J = 4.8 Hz, 2H), 4.61 (s, 1H), 7.21−7.25 (m, 2H), 7.30−7.36 (m, 3H), 8.26−8.35 (m, 4H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 20.2, 27.9, 36.8, 36.9, 38.9, 88.8, 110.2, 116.0, 123.9, 127.4, 128.1, 129.0, 131.6, 132.5, 136.3, 151.5, 161.6, 165.4, 195.7; HRMS (ESI-TOF) m/z Calcd for $[C_{23}H_{17}N_3O_6 + H]^+$: 432.1190, found: 432.1215 and $[C_{23}H_{17}N_3O_6 + Na]^+$: 454.1010, found: 454.1016.

7a-Cyano-6-oxo-7-phenyl-3,4,5,6,7,7a-hexahydrochromeno[2,3-b]azirin-1a(1H)-yl 4-Methoxybenzoate ***2b***. Yield: 374 mg, 90%; white solid; Mp: 190−200 °C; IR (KBr): 3254, 2938, 2844, 2243, 1726, 1675, 1630, 1605, 1166, 1100, 937, 606 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 1.91 (s, 2H), 2.26 (d, J = 3.9 Hz, 2H), 2.53 (s, 2H), 3.85 (s, 3H), 4.33 (s, 1H), 5.84 (s, 1H), 7.13 (d, J = 8.7 Hz, 2H), 7.20−7.32 (m, 5H), 8.02 (d, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 24.9, 32.6, 40.7, 41.7, 60.8, 84.2, 93.4, 114.5, 118.8, 119.7, 121.4, 123.9, 132.1, 132.8, 133.2, 133.4, 133.9, 136.4, 137.3, 143.1, 167.4, 169.6, 170.7, 200.6; Anal. Calcd for $C_{24}H_{20}N_2O_5$: C 69.22; H 4.84; N 6.73%. Found: C 69.20; H 4.86; N 6.70%.

7a-Cyano-6-oxo-7-phenyl-3,4,5,6,7,7a-hexahydrochromeno[2,3-b]azirin-1a(1H)-yl 2-Chlorobenzoate ***2c***. Yield: 391 mg, 93%; white solid; Mp: 182−184 °C; IR (KBr): 3277, 2922, 2890, 2243, 1751, 1672, 1632, 1369, 1188, 1099, 1088, 1025, 918, 743 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.91−2.07 (m, 2H), 2.19−2.36 (m, 2H), 2.40 (s, 1H), 2.45−2.60 (m, 2H), 4.50 (s, 1H), 7.14−7.33 (m, 6H), 7.45−7.46 (d, J = 3.6 Hz, 2H), 7.92−7.95 (d, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz; CDCl3; Me_4Si): δ 19.8, 27.7, 36.6, 38.7, 88.3, 109.8, 115.8, 126.0, 126.7, 127.1, 127.14, 127.2, 127.6, 128.6, 131.4, 132.1, 134.2, 135.1, 136.3, 161.2, 165.3, 195.6; HRMS (ESI-TOF) m/z Calcd for $[C_{23}H_{17}ClN_2O_4 + H]^+$: 421.0950, found: 421.0931 and $[C_{23}H_{17}ClN_2O_4 + Na]^+$: 443.0769, found: 443.0748.

7a-Cyano-7-(4-nitrophenyl)-6-oxo-3,4,5,6,7,7a-hexahydrochromeno[2,3-b]azirin-1a(1H)-yl 2-Phenylacetate ***2d***.[7d] Yield: 419 mg, 94%; white solid; Mp: 204−206 °C; IR (KBr): 3114, 2956, 2826, 2243, 1788, 1653, 1632, 1515, 1347, 1236, 1091, 995 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 2.02 (s, 2H), 2.27−2.55 (m, 5H), 3.83 (s, 2H), 4.41 (s, 1H), 7.30−7.39 (m, 7H), 8.16−8.18 (d, J = 8.7 Hz, 2H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 15.3, 23.2, 31.5, 32.0, 34.5, 35.6, 83.3, 104.8, 110.6, 119.1, 123.1, 124.05, 124.1, 124.6, 126.6, 139.5, 142.7, 161.4, 163.4, 191.0; Anal. Calcd for $C_{24}H_{19}N_3O_6$: C 64.72; H 4.30; N 9.43%. Found: C 64.74; H 4.32; N 9.40%.

7a-Cyano-6-oxo-7-phenyl-3,4,5,6,7,7a-hexahydrochromeno[2,3-b]azirin-1a(1H)-yl Acetate ***2e***.[7d] Yield: 311 mg, 96%; off-white solid; Mp: 132−134 °C; IR (KBr): 3175, 2963, 2238, 1791, 1631, 1238, 1229, 1152, 1100, 1063, 936 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 1.90 (s, 2H), 2.24 (s, 5H), 2.50 (s, 2H), 4.26 (s, 1H), 5.67 (s, 1H), 7.17−7.33 (m, 5H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 20.3, 20.7, 28.0, 36.0, 37.1, 88.5, 109.8, 116.8, 127.5, 128.2, 128.6, 138.5, 166.0, 168.1, 196.0; HRMS (ESI-TOF) m/z Calcd for $[C_{18}H_{16}N_2O_4 + H]^+$: 325.1183, found: 325.1188.

7-(2-Chlorophenyl)-7a-cyano-6-oxo-3,4,5,6,7,7a-hexahydrochromeno[2,3-b]azirin-1a(1H)-yl Acetate ***2f***.[7d] Yield: 341 mg, 95%; white solid; Mp 142−144 °C; IR (KBr):cm^{-1}; 3217, 2956, 2937, 2244, 1788, 1668, 1626, 1234, 1175, 1102, 1064, 768 cm^{-1}; ^{1}H NMR (300 MHz; CDCl3; Me_4Si): δ 1.90−1.98 (m, 2H), 2.18 (s, 3H), 2.22−2.26 (t, J = 6.2 Hz, 2H), 2.36 (s, 1H), 2.48−2.51 (t, J = 5.3 Hz, 2H), 5.06 (s, 1H), 6.85−6.88 (d, J = 7.5 Hz, 1H), 7.04−7.16 (m, 2H), 7.36−7.39 (d, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz; CDCl3; Me_4Si): δ 19.8, 20.1, 27.5, 34.4, 35.2, 36.5, 87.8, 110.6, 115.6, 126.2, 128.5, 128.8, 129.4,

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133.7, 134.3, 165.5, 166.9, 195.1; HRMS (ESITOF) m/z Calcd for $[C_{18}H_{15}ClN_2O_4 + H]^+$: 359.0793, found: 359.0799.

7a-Cyano-6-oxo-7-(thiophen-2-yl)-3,4,5,6,7,7a-hexahydrochromeno[2,3-b]azirin-1a(1H)-yl 3-Nitrobenzoate ***2g***. Yield: 389 mg, 89%; pale yellow solid; Mp: 180−182 °C; IR (KBr):cm^{-1}; 3188, 2954, 2840, 2246, 1786, 1688, 1632, 1528, 1352, 1234, 1091, 930 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 1.80 (s, 2H), 2.19 (s, 2H), 2.43 (s, 2H), 4.65 (s, 1H), 6.20 (s, 1H), 6.91 (s, 2H), 7.30 (s, 1H), 7.83 (s, 1H), 8.37 (d, J = 6 Hz, 1H), 8.52 (d, J = 6 Hz, 1H), 8.64 (s, 1H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 19.8, 27.6, 35.0, 35.2, 36.7, 88.9, 110.0, 116.0, 124.4, 125.2, 126.0, 126.6, 128.5, 129.6, 131.4, 135.9, 140.4, 148.2, 161.4, 164.7, 195.5; Anal. Calcd for $C_{21}H_{15}N_3O_6S$: C 57.66; H 3.46; N 9.61%. Found: C 57.64; H 3.44; N 9.64%.

7-(4-Bromophenyl)-7a-cyano-6-oxo-7a,8-dihydro-6H-chromeno-[3′,4′:5,6]pyrano[2,3-b]azirin-8a(7H)-yl 4-Chlorobenzoate ***2h***. Yield: 495 mg, 90%; off-white solid; Mp: 220−222 °C; IR (KBr): 3310, 2241, 1768, 1712, 1645, 1489, 1384, 1241, 1108, 701, 564 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 4.76 (s, 1H), 6.43 (s, 1H), 7.23 (d, J = 8.4 Hz, 2H), 7.29−7.38 (m, 2H), 7.49 (d, J = 8.1 Hz, 2H), 7.60−7.68 (m, 3H), 7.78 (d, J = 6.9 Hz, 1H), 8.04 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 35.9, 90.0, 100.4, 113.7, 115.9, 116.9, 121.5, 123.3, 125.2, 126.1, 130.1, 130.8, 131.8, 132.3, 133.6, 136.9, 140.8, 152.4, 155.2, 159.9, 162.6; Anal. Calcd for $C_{26}H_{14}BrClN_2O_5$: C 56.80; H 2.57; N 5.10%. Found: C 56.78; H 2.59; N 5.12%.

7-(4-Bromophenyl)-7a-cyano-6-oxo-7a,8-dihydro-6H-chromeno-[3′,4′:5,6]pyrano[2,3-b]azirin-8a(7H)-yl 3-Nitrobenzoate ***2i***. Yield: 493 mg, 88%; pale yellow solid; Mp: 230−232 °C; IR (KBr): 3320, 2241, 1768, 1720, 1645, 1530, 1489, 1384, 1330, 1241, 762 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 4.87 (s, 1H), 6.60 (s, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.39−7.52 (m, 2H), 7.58 (d, J = 8.4 Hz, 2H), 7.72 (t, J = 7.8 Hz, 1H), 7.89 (d, J = 8.1 Hz, 1H), 7.97 (t, J = 8.1 Hz, 1H), 8.52 (d, J = 7.8 Hz, 1H), 8.66 (d, J = 8.4 Hz, 1H), 8.80 (s, 1H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 35.9, 90.1, 100.5, 115.9, 116.9, 121.5, 123.3, 124.9, 125.2, 128.9, 130.1, 130.8, 131.8, 133.7, 136.4, 136.8, 148.6, 152.4, 155.1, 161.8; HRMS (ESI-TOF) m/z Calcd for $[C_{26}H_{14}BrN_3O_7 + H]^+$: 560.0088, found: 560.0113.

7a-Cyano-7-(4-nitrophenyl)-6-oxo-7a,8-dihydro-6H-chromeno-[3′,4′:5,6]pyrano[2,3-b]azirin-8a(7H)-yl 4-Chlorobenzoate ***2j***. Yield: 348 mg, 90%; off-white solid; Mp: 216−218 °C; IR (KBr): 3291, 2244, 1752, 1720, 1678, 1661, 1636, 1239, 1118, 949 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 2.24 (s, 3H), 4.77 (s, 1H), 6.01 (s, 1H), 7.25 (s, 5H), 7.75 (d, J = 7.2 Hz, 3H), 7.94−7.97 (m, 1H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 20.7, 35.8, 89.3, 116.3, 119.6, 126.3, 126.5, 128.0, 128.7, 128.9, 130.8, 131.7, 134.5 135.2, 137.8, 150.2, 168.1, 177.6, 182.7; Anal. Calcd for $C_{22}H_{14}N_2O_5$: C 68.39; H 3.65; N 7.25%. Found: C 68.37; H 3.63; N 7.28%.

9a-Cyano-9-(4-nitrophenyl)-3,8-dioxo-3,8,9,9a-tetrahydrobenzo-[6,7]chromeno[2,3-b]azirin-1a(1H)-yl 4-Chlorobenzoate ***2k***. Yield: 465 mg, 88%; yellow solid; Mp: 222−224 °C; IR (KBr): 3298, 2246, 1756, 1722, 1678, 1661, 1636, 1534, 1350, 1295, 1101, 701 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$ and DMSO-d_6; Me_4Si): δ 4.80 (s, 1H), 5.26 (s, 1H), 7.42 (d, J = 8.4 Hz, 2H), 7.51 (d, J = 8.1 Hz, 2H), 7.66−7.68 (m, 2H), 7.82 (d, J = 2.4 Hz,1H), 7.99−8.05 (m, 3H), 8.16 (d, J = 8.4 Hz, 2H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 35.1, 89.8, 115.7, 118.8, 124.0, 126.0, 126.4, 126.6, 130.2, 130.9, 131.5, 132.3, 134.7, 135.2, 140.9, 145.3, 147.5, 150.5, 162.4, 177.4, 182.7; HRMS (ESI-TOF) m/z Calcd for $[C_{27}H_{14}ClN_3O_7 + Na]^+$: 550.0412, found: 550.0428.

9-(2-Chlorophenyl)-9a-cyano-3,8-dioxo-3,8,9,9a-tetrahydrobenzo[6,7]chromeno[2,3-b]azirin-1a(1H)-yl 4-Chlorobenzoate ***2l***. Yield: 466 mg, 90%; yellow solid; Mp: 212−214 °C; IR (KBr): 3291, 2242, 1752, 1720, 1678, 1661, 1636, 1239, 1094, 714 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 2.87 (s, 1H), 5.62 (s, 1H), 7.10 (s, 1H), 7.19 (d, J = 7.2 Hz, 1H), 7.28 (d, J = 3 Hz, 1H), 7.48−7.57 (m, 3H), 7.73 (d, J = 3.3 Hz, 2H), 7.94 (d, J = 3.9 Hz, 1H), 8.04−8.08 (m, 2H), 8.13 (d, J = 2.7 Hz, 1H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 35.8, 36.0, 89.2, 115.3, 120.0, 125.3, 126.7, 127.0, 129.3, 129.5, 129.9, 130.1, 130.4, 131.5, 131.9, 133.8, 134.0, 134.8, 141.8, 150.1, 162.3, 182.2; Anal. Calcd for $C_{27}H_{14}Cl_2N_2O_5$: C 62.69; H 2.73; N 5.42%. Found: C 62.66; H 2.75; N 5.40%.

9-(2-Chlorophenyl)-9a-cyano-3,8-dioxo-3,8,9,9a-tetrahydrobenzo[6,7]chromeno[2,3-b]azirin-1a(1H)-yl 2-Phenylacetate ***2m***. Yield: 457 mg, 92%; yellow solid; Mp: 208−210 °C; IR (KBr): 3180, 2244, 1754, 1735, 1670, 1661, 1636, 1350, 1295, 1239, 1094, 949, 701 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 3.97−4.13 (m, 2H), 5.29 (s, 1H), 6.45 (s, 1H), 7.23 (s, 2H), 7.36 (s, 6H), 7.59 (d, J = 7.2 Hz, 1H), 7.82 (s, 3H), 8.03 (d, J = 5.7 Hz, 1H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 34.2, 36.5, 89.4, 119.6, 126.3, 126.5, 127.7, 127.8, 128.7, 129.0, 129.7, 130.0, 130.8, 131.3, 131.5, 132.9, 134.6, 135.2, 150.5, 169.2, 177.4, 182.6; Anal. Calcd for $C_{28}H_{17}ClN_2O_5$: C 67.68; H 3.45; N 5.64%. Found: C 67.66; H 3.48; N 5.62%.

7a-Cyano-6-oxo-7-(thiophen-2-yl)-7a,8-dihydro-6H-chromeno-[3′,4′:5,6]pyrano[2,3-b]azirin-8a(7H)-yl 4-Chlorobenzoate ***2n***. Yield: 401 mg, 84%; off-white solid; Mp: 214−216 °C; IR (KBr): 3235, 2254, 1755, 1729, 1638, 1379, 1228, 1090, 755, 708 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 2.86 (s, 1H), 5.04 (s, 1H), 6.96 (t, J = 4.4 Hz, 1H), 7.09 (d, J = 3.3 Hz, 1H), 7.17−7.26 (m, 3H), 7.43 (d, J = 8.1 Hz, 2H), 7.51 (t, J = 7.8 Hz, 1H), 7.73 (d, J = 7.5 Hz, 1H), 8.00 (d, J = 8.1 Hz, 2H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 36.5, 37.1, 89.4, 100.4, 113.4, 115.2, 116.8, 123.1, 124.5, 125.2, 125.9, 127.1, 127.2, 129.4, 131.9, 133.1, 137.5, 141.9, 152.6, 159.9, 162.2; Anal. Calcd for $C_{24}H_{13}ClN_2O_5S$: C 60.45; H 2.75; N 5.87%. Found: C 60.43; H 2.77; N 5.85%.

7-Benzoyl-7a-cyano-4,4-dimethyl-6-oxo-3,4,5,6,7,7a-hexahydrochromeno[2,3-b]azirin-1a(1H)-yl 3-Nitrobenzoate ***2o***. Yield: 439 mg, 90%; white solid; Mp: 188−190 °C; IR (KBr): 3240, 2959, 2840, 2244, 1743, 1660, 1605, 1533, 1350, 1260, 1200, 1168, 1094, 934 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.05 (s, 6H), 2.22 (s, 2H), 2.29−2.47 (m, 2H), 3.20 (s, 1H), 5.19 (s, 1H), 7.49 (t, J = 7.4 Hz, 2H), 7.58−7.68 (m, 2H), 8.09 (d, J = 7.5 Hz, 2H), 8.35 (d, J = 7.5 Hz, 1H), 8.44 (d, J = 8.1 Hz, 1H), 8.86 (s, 1H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 27.8, 28.4, 32.6, 34.1, 38.1, 41.2, 50.0, 88.1, 108.3, 115.2, 125.4, 129.0, 129.1, 129.2, 130.2, 134.6, 135.3, 135.8, 148.5, 161.6, 164.4, 196.0, 196.1; HRMS (ESI-TOF) m/z Calcd for $[C_{26}H_{21}N_3O_7 + Na]^+$: 510.1272, found: 510.1251.

7-Benzoyl-7a-cyano-4,4-dimethyl-6-oxo-3,4,5,6,7,7a-hexahydrochromeno[2,3-b]azirin-1a(1H)-yl Cyclohexanecarboxylate ***2p***. Yield: 426 mg, 95%; white solid; Mp: 136−138 °C; IR (KBr): 3272, 2966, 2928, 2840, 2242, 1740, 1668, 1605, 1250, 1208, 1168, 1094, 934 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.11 (s, 6H), 1.24−1.32 (m, 3H), 1.52 (d, J = 10.8 Hz, 2H), 1.77 (s, 2H), 1.99 (d, J = 12.6 Hz, 2H), 2.25 (s, 2H), 2.32−2.52 (m, 3H), 2.97 (s, 1H), 5.16 (s, 1H), 7.55 (t, J = 7.7 Hz, 2H), 7.66 (d, J = 7.5 Hz, 1H), 8.15 (d, J = 7.8 Hz, 2H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 25.1, 25.5, 27.7, 28.3, 28.5, 32.5, 34.1, 38.3, 41.2, 42.4, 50.0, 87.1, 108.0, 115.5, 129.1, 134.4, 135.4, 164.6, 172.9, 195.9, 196.2; HRMS (ESI-TOF) m/z Calcd for $[C_{26}H_{28}N_2O_5 + H]^+$: 449.2071, found: 449.2068, and $[C_{26}H_{28}N_2O_5 + Na]^+$: 471.1890, found: 471.1869.

7-Benzoyl-7a-cyano-4,4-dimethyl-6-oxo-3,4,5,6,7,7a-hexahydrochromeno[2,3-b]azirin-1a(1H)-yl 4-Methoxybenzoate ***2q***. Yield: 444 mg, 94%; white solid; Mp: 184−186 °C; IR (KBr): 3272, 2959, 2932, 2864, 2244, 1743, 1660, 1605, 1373, 1260, 1200, 1168, 1094, 934, 767, 612 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.03 (s, 6H), 2.20 (s, 2H), 2.26−2.46 (m, 2H), 3.02 (s, 1H), 3.79 (s, 3H), 5.16 (s, 1H), 6.87 (d, J = 9.0 Hz, 2H), 7.48 (t, J = 7.7 Hz, 2H), 7.58 (t, J = 7.4 Hz, 1H), 7.98 (d, J = 9.0 Hz, 2H), 8.09 (d, J = 7.8 Hz, 2H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 27.7, 28.5, 32.5, 34.2, 38.4, 41.2, 50.0, 55.6, 87.7, 108.1, 114.2, 115.5, 119.4, 129.1, 129.1, 132.7, 134.4, 135.5, 163.0, 164.7, 164.8, 196.0, 196.2; HRMS (ESI-TOF) m/z Calcd for $[C_{27}H_{24}N_2O_6 + Na]^+$: 495.1527, found: 495.1529.

7a-Cyano-4,4-dimethyl-1′,3′,6-trioxo-1,1′,3,3′,4,5,6,7a-octahydro-1aH-spiro[chromeno[2,3-b]azirine-7,2′-inden]-1a-yl 4-Chlorobenzoate ***2r***. Yield: 453 mg, 90%; off-white solid; Mp: 220−222 °C; IR (KBr): 3247, 2967, 2939, 2833, 2249, 1790, 1752, 1713, 1665, 1644, 1369, 1249, 1214, 942, 720 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me4Si): δ 0.98 (d, J = 5.4 Hz, 3H), 1.04 (s, 3H), 1.98−2.50 (m, 3H), 2.58−2.74 (m, 1H), 6.86 (d, J = 6.0 Hz, 1H), 7.69−7.74

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(m, 2H), 8.05−8.10 (m, 6H); ^{13}C NMR (75 MHz; DMSO-d_6; Me4Si): δ 26.4, 28.8, 32.8, 35.6, 49.4, 54.8, 87.9, 109.3, 113.8, 124.2, 125.9, 130.1, 132.3, 137.3, 137.8, 140.8, 141.1, 161.9, 169.0, 193.9, 196.6, 196.8; HRMS (ESI-TOF) m/z Calcd for $[C_{27}H_{19}ClN_2O_6 + H]^+$: 503.1004, found: 503.1033.

Ethyl 1a-((4-Nitrobenzoyl)oxy)-6-oxo-7-phenyl-1,1a,3,5,6,7-hexahydrochromeno[2,3-b]azirine-7a(4H)-carboxylate ***4a***. Yield: 421 mg, 88%; off-white solid; Mp: 202−204 °C; IR (KBr): 3290, 2967, 2833, 1740, 1713, 1642, 1611, 1530, 1350, 1200, 1093, 941 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.27 (t, J = 7.1 Hz, 3H), 2.05 (s, 2H), 2.34−2.46 (m, 2H), 2.58 (d, J = 4.2 Hz, 2H), 4.21−4.26 (m, 2H), 5.07 (s, 1H), 7.25 (s, 5H), 8.23 (d, J = 7.8 Hz, 2H), 8.33 (d, J = 6.6 Hz, 2H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 14.1, 20.3, 28.1, 35.9, 37.2, 48.4, 63.4, 90.0, 112.1, 123.9, 127.0, 128.1, 128.2, 131.4, 133.0, 138.8, 151.3, 161.9, 165.2, 167.2, 196.5; HRMS (ESI-TOF) m/z Calcd for $[C_{25}H_{22}N_2O_8 + H]^+$: 479.1449, found: 479.1441 and $[C_{25}H_{22}N_2O_8 + Na]^+$: 501.1268, found: 501.1255.

Ethyl 1a-((Cyclohexanecarbonyl)oxy)-6-oxo-7-phenyl-1,1a,3,5,6,7-hexahydrochromeno[2,3-b]azirine-7a(4H)-carboxylate ***4b***. Yield: 396 mg, 90%; white solid; Mp: 120−122 °C; IR (KBr): 3280, 2980, 2940, 2826, 1740, 1715, 1642, 1611, 1200, 1093, 950 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 1.20−1.34 (m, 8H), 1.57 (s, 1H), 1.64 (s, 2H), 1.78 (s, 2H), 1.90 (t, J = 5.9 Hz, 2H), 2.24 (s, 2H), 2.39 (s, 1H), 4.10 (s, 1H), 4.13−4.21 (m, 2H), 4.73 (s, 1H), 7.07 (d, J = 7.5 Hz, 2H), 7.12−7.24 (m, 3H); ^{13}C NMR (75 MHz; DMSO-d_6; Me4Si): δ 19.0, 25.0, 29.4, 30.1, 32.6, 33.0, 33.1, 41.0, 41.7, 46.4, 52.5, 67.5, 93.9, 115.6, 131.4, 132.8, 132.9, 144.6, 170.6, 171.7, 177.2, 201.0; Anal. Calcd for $C_{25}H_{29}NO_6$: C 68.32; H 6.65; N 3.19%. Found: C 68.30; H 6.63; N 3.21%.

Ethyl 7-(4-Bromophenyl)-1a-(2,2-diphenylacetoxy)-4,4-dimethyl-6-oxo-1,1a,3,5,6,7-hexahydrochromeno[2,3-b]azirine-7a(4H)-carboxylate ***4c***. Yield: 542 mg, 86%; off-white solid; Mp: 140−142 °C; IR (KBr): 3330, 2967, 2939, 2833, 1735, 1720, 1642, 1243, 1093, 1051, 1029, 950, 744, 668 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 0.99−1.06 (m, 9H), 2.11 (s, 2H), 2.30 (s, 2H), 2.64 (s, 1H), 3.85−3.92 (m, 2H), 4.77 (s, 1H), 4.96 (s, 1H), 7.00 (d, J = 7.8 Hz, 2H), 7.16−7.29 (m, 12H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 13.9, 28.0, 28.4, 31.7, 35.6, 41.6, 48.2, 50.9, 56.0, 63.1, 89.5, 110.4, 120.8, 127.6, 128.2, 128.3, 128.4, 128.5, 128.6, 128.7, 128.8, 129.9, 131.1, 136.9, 137.1, 138.0, 163.8, 166.6, 169.6, 196.4; Anal. Calcd for $C_{34}H_{32}BrNO_6$: C 64.77; H 5.12; N 2.22%. Found: C 64.75; H 5.10; N 2.25%.

Ethyl 8a-((4-Chlorobenzoyl)oxy)-7-(4-nitrophenyl)-6-oxo-8,8a-dihydro-6H-chromeno[3′,4′:5,6]pyrano[2,3-b]azirine-7a(7H)-carboxylate ***4d***. Yield: 462 mg, 82%; off-white solid; Mp: 180−182 °C; IR (KBr): 3315, 1740, 1642, 1529, 1349, 1200, 1093, 1051, 1029, 941, 746 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.29 (t, J = 7.1 Hz, 3H), 3.12 (s, 1H), 4.19−4.36 (m, 2H), 5.36 (s, 1H), 7.27−7.33 (m, 2H), 7.45−7.60 (m, 4H), 7.69−7.75(m, 1H), 7.87 (d, J = 7.8 Hz, 1H), 8.02 (d, J = 8.4 Hz, 2H), 8.13 (d, J = 8.4 Hz, 1H), 8.25 (s, 1H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 14.1, 37.5, 48.4, 63.9, 90.4, 101.0, 113.9, 116.7, 122.7, 123.1, 123.7, 124.4, 125.6, 129.2, 129.4, 131.7, 132.7, 135.0, 140.0, 141.5, 148.3, 152.6, 155.8, 160.8, 162.6, 166.1; Anal. Calcd for $C_{28}H_{19}ClN_2O_9$: C 59.74; H 3.40; N 4.98%. Found: C 59.72; H 3.42; N 4.96%.

Ethyl 8a-(Benzoyloxy)-7-(4-nitrophenyl)-6-oxo-8,8a-dihydro-6H-chromeno[3′,4′:5,6]pyrano[2,3-b]azirine-7a(7H)-carboxylate ***4e***. Yield: 423 mg, 80%; off-white solid; Mp: 170−172 °C; IR (KBr): 3350, 1745, 1640, 1540, 1350, 1190, 1093, 1050, 1029, 941, 745 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.25−1.33 (m, 3H), 3.00 (d, J = 9.3 Hz, 1H), 4.18−4.30 (m, 2H), 5.30 (d, J = 9.6 Hz, 1H), 7.17−7.65 (m, 8H), 7.82 (t, J = 8.4 Hz, 1H), 7.93 (t, J = 8.4 Hz, 1H), 8.07 (t, J = 8.4 Hz, 1H), 8.18 (d, J = 10.5 Hz, 1H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 14.1, 37.4, 48.4, 64.1, 90.3, 101.0, 113.9, 116.7, 122.7, 123.1, 123.7, 124.4, 126.3, 127.0, 129.2, 131.7, 132.3, 132.7, 134.5, 134.9, 135.3, 139.9, 148.3, 152.6, 155.8, 160.8, 161.6, 166.3; Anal. Calcd for $C_{28}H_{20}N_2O_9$: C 63.64; H 3.81; N 5.30%. Found: C 63.66; H 3.83; N 5.28%.

Ethyl 8a-Acetoxy-7-(4-nitrophenyl)-6-oxo-8,8a-dihydro-6H-chromeno[3′,4′:5,6]pyrano[2,3-b]azirine-7a(7H)-carboxylate ***4f***. Yield: 420 mg, 90%; off-white solid; Mp: 196−198 °C; IR (KBr): 3328, 1750, 1638, 1535, 1350, 1190, 1093, 1050, 1025, 941, 740 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.26 (t, J = 6.3 Hz, 3H), 2.08 (s, 3H), 2.79 (s, 1H), 4.21 (t, J = 7.2 Hz, 2H), 5.14 (s, 1H), 7.21 (t, J = 8.0 Hz, 2H), 7.37 (d, J = 7.5 Hz, 2H), 7.46 (t, J = 7.8 Hz, 1H), 7.75 (d, J = 7.8 Hz, 1H), 8.03 (d, J = 7.2 Hz, 2H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 14.2, 20.3, 37.5, 48.0, 63.8, 89.7, 101.0, 113.9, 116.7, 123.0, 123.6, 124.4, 129.5, 132.7, 145.3, 147.4, 152.6, 155.6, 160.8, 166.2, 167.5; Anal. Calcd for $C_{23}H_{18}N_2O_9$: C 59.23; H 3.89; N 6.01%. Found: C 59.21; H 3.87; N 6.04%.

Ethyl 1a-((Cyclohexanecarbonyl)oxy)-9-(4-nitrophenyl)-3,8-dioxo-1,1a,3,9-tetrahydrobenzo[6,7]chromeno[2,3-b]azirine-9a-(8H)-carboxylate ***4g***. Yield: 459 mg, 84%; yellow solid; Mp: 180−182 °C; IR (KBr): 3291, 3103, 2967, 2833, 1752, 1720, 1678, 1661, 1636, 1530, 1350, 1295, 1239, 1216, 1200, 1118, 1101, 1054, 949 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.12−1.39 (m, 8H), 1.59 (s, 2H), 1.68 (s, 2H), 1.84 (s, 1H), 2.35 (t, J = 10.8 Hz, 1H), 2.79 (s, 1H), 4.18−4.29 (m, 2H), 5.30 (s, 1H), 7.43 (d, J = 7.8 Hz, 2H), 7.59−7.67 (m, 2H), 7.79−7.82 (m, 1H), 8.04−8.10 (m, 2H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 14.2, 25.0, 25.1, 25.5, 28.3, 28.6, 37.5, 42.3, 48.0, 63.7, 89.5, 120.1, 123.6, 126.4, 126.6, 129.4, 129.6, 130.6, 130.7, 131.6, 133.8, 134.5, 145.4, 147.3, 150.5, 166.1, 172.8, 177.5, 183.1; HRMS (ESI-TOF) m/z Calcd for $[C_{29}H_{26}N_2O_9 + Na]^+$: 569.1531, found: 569.1530.

Ethyl 9-(4-Bromophenyl)-1a-((4-chlorobenzoyl)oxy)-3,8-dioxo-1,1a,3,9-tetrahydrobenzo[6,7]chromeno[2,3-b]azirine-9a(8H)-carboxylate ***4h***. Yield: 499 mg, 82%; yellow solid; Mp: 172−174 °C; IR (KBr): 3300, 3113, 1750, 1722, 1675, 1668, 1632, 1294, 1236, 1216, 1200, 1120, 1106, 1055, 945, 724, 663 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.14 (t, J = 7.2 Hz, 3H), 2.96 (s, 1H), 4.08−4.20 (m, 2H), 5.28 (s, 1H), 7.15−7.19 (m, 2H), 7.37 (t, J = 8.4 Hz, 4H), 7.61−7.7.73 (m, 2H), 7.83−7.86 (m, 1H), 7.91 (d, J = 8.4 Hz, 2H), 8.02−8.05 (m, 1H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 14.1, 37.1, 48.3, 63.6, 90.3, 120.9, 121.6, 125.8, 126.5, 127.0, 129.2, 130.4, 131.0, 131.6, 131.7, 133.7, 134.5, 137.0, 141.3, 150.2, 162.7, 166.3, 177.8, 183.1; Anal. Calcd for $C_{29}H_{19}BrClNO_7$: C 57.21; H 3.15; N 2.30%. Found: C 57.23; H 3.12; N 2.28%.

Ethyl 9-(4-Bromophenyl)-1a-((3-nitrobenzoyl)oxy)-3,8-dioxo-1,1a,3,9-tetrahydrobenzo[6,7]chromeno[2,3-b]azirine-9a(8H)-carboxylate ***4i***. Yield: 496 mg, 80%; yellow solid; Mp: 184−186 °C; IR (KBr): 3291, 3103, 1752, 1720, 1678, 1661, 1536, 1350, 1239, 1216, 1200, 1118, 1054, 949, 714 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.19 (t, J = 7.1 Hz, 3H), 3.03 (s, 1H), 4.17 (t, J = 7.8 Hz, 2H), 5.29 (s, 1H), 7.17 (d, J = 8.1 Hz, 2H), 7.36 (d, J = 8.1 Hz, 2H), 7.66 (d, J = 7.8 Hz, 3H), 7.86 (s, 1H), 8.05 (s, 1H), 8.31 (d, J = 7.2 Hz, 1H), 8.44 (d, J = 8.1 Hz, 1H), 8.80 (s, 1H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 14.2, 37.2, 48.2, 63.9, 90.6, 121.1, 121.8, 125.4, 126.7, 129.0, 129.3, 130.3, 130.5, 130.6, 131.7, 131.9, 133.8, 134.7, 135.9, 136.9, 148.5, 150.2, 161.7, 166.4, 177.8, 183.2; Anal. Calcd for $C_{29}H_{19}BrN_2O_9$: C 56.24; H 3.09; N 4.52%. Found: C 56.22; H 3.07; N 4.54%.

Ethyl (7R,7aR)-8a-(Benzoyloxy)-7-(4-cyanophenyl)-6-oxo-8,8a-dihydro-6H-chromeno[3′,4′:5,6]pyrano[2,3-b]azirine-7a(7H)-carboxylate ***4j***. Yield: 447 mg, 88%; white solid; Mp: 170−172 °C; IR (KBr): 3350, 2244, 1745, 1640, 1615, 1385, 1295, 1243, 1190, 1093, 1050, 1029, 941, 745 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.14−1.21 (m, 3H), 3.02 (s, 1H), 4.13−4.23 (m, 2H), 5.25 (s, 1H), 7.19−7.55 (m, 8H), 7.61 (t, J = 8.1 Hz, 2H), 7.70 (d, J = 7.8 Hz, 1H), 7.79 (d, J = 7.8 Hz, 2H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 13.7, 37.4, 48.0, 63.4, 89.9, 100.7, 111.1, 113.6, 116.4, 117.1, 118.5, 122.8, 124.0, 126.8, 127.8, 128.6, 129.1, 130.0, 131.9, 132.3, 133.0, 133.8, 134.5, 143.0, 152.3, 155.4, 160.5, 163.0, 165.8; HRMS (ESI-TOF) m/z Calcd for $[C_{29}H_{20}N_2O_7 + Na]^+$: 531.1163, found: 531.1153.

General Procedure for the Synthesis of Pyranooxazolones (5a−e). In a dry 25 mL r.b. flask having a calcium chloride guard tube, 1 mmol of 2-oxa-7-azabicyclo[4.1.0]hept-3-en-1-yl carboxylates and 3 mL of dry dioxane were taken. Then, to it was added 1 mmol of tetrabutylammonium fluoride, and the reaction mixture was stirred at rt for the stipulated time. After completion of the reaction (monitored by TLC), dioxane was removed under reduced pressure and the resulting mass was then immediately subjected for column chromatographic separation (30−50% ethyl acetate in petroleum ether) to get

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the pure products. The same procedure was applied to get **5e**, except the reaction mixture was stirred at 60 °C. All the synthesized compounds were characterized through analysis of spectral (^{1}H NMR, ^{13}C NMR, IR, HRMS, and elemental analysis) data, and X-ray crystallography (**5c**).

3a-Methyl-2,8-dioxo-9-phenyl-1,2,5,7,8,9-hexahydro-6H-chromeno[3,2-d]oxazole-9a(3aH)-carbonitrile ***5a***. Yield: 318 mg, 98%; white solid; Mp: 200−202 °C; IR (KBr): 3317, 2962, 2925, 2853, 1790, 1646, 1379, 1070, 961, 917, 719 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 1.75 (s, 3H), 1.92−2.10 (m, 2H), 2.37−2.46 (m, 2H), 2.62 (t, J = 5.6 Hz, 2H), 4.50 (s, 1H), 7.16−7.19 (m, 2H), 7.26−7.31 (m, 3H), 7.49 (s, 1H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 20.1, 24.7, 28.3, 36.3, 41.3, 64.6, 104.2, 113.2, 115.6, 129.1, 129.2, 129.3, 134.1, 153.8, 170.9, 197.1; HRMS (ESI-TOF) m/z Calcd for $[C_{18}H_{16}N_2O_4 + H]^+$: 325.1183, found: 325.1191.

9-(2-Chlorophenyl)-3a-methyl-2,8-dioxo-1,2,5,7,8,9-hexahydro-6H-chromeno[3,2-d]oxazole-9a(3aH)-carbonitrile ***5b***. Yield: 344 mg, 96%; off-white solid; Mp: 268−270 °C; IR (KBr): 3330, 2962, 2935, 2846, 1790, 1646, 1314, 1281, 1070, 945 729 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 1.76 (s, 3H), 1.94 (s, 2H), 2.28−2.33 (m, 2H), 2.65 (s, 2H), 4.95 (s, 1H), 7.18 (d, J = 7.5 Hz, 1H), 7.35 (t, J = 6.6 Hz, 2H), 7.56 (d, J = 7.2 Hz, 1H), 9.96 (s, 1H); ^{13}C NMR (75 MHz; $CDCl_3$ and DMSO-d_6; Me_4Si): δ 20.0, 24.6, 28.0, 36.1, 37.0, 63.0, 103.3, 112.7, 115.4, 126.9, 128.4, 129.8, 130.4, 132.9, 135.9, 153.9, 169.5, 194.9; Anal. Calcd for $C_{18}H_{15}ClN_2O_4$: C 60.26; H 4.21; N 7.81%. Found: C 60.24; H 4.19; N 7.84%.

3a-Benzyl-9-(4-nitrophenyl)-2,8-dioxo-1,2,5,7,8,9-hexahydro-6H-chromeno[3,2-d]oxazole-9a(3aH)-carbonitrile ***5c***. Yield: 410 mg, 92%; pale yello solid; Mp: 236−238 °C; IR (KBr): 3349, 2924, 2852, 1796, 1637, 1526, 1384, 1120, 938, 698 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 1.88 (t, J = 5.4 Hz, 2H), 2.24−2.31 (m, 2H), 2.46 (s, 2H), 2.94 (d, J = 14.4 Hz, 1H), 3.35 (s, 1H), 4.45 (s, 1H), 7.23−7.29 (m, 5H), 7.57 (d, J = 8.4 Hz, 2H), 8.16 (d, J = 8.1 Hz, 2H), 9.64 (s, 1H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 19.9, 27.8, 36.0, 40.9, 42.5, 64.0, 102.6, 110.8, 116.0, 124.1, 127.6, 128.1, 131.0, 131.4, 132.1, 142.8, 147.7, 153.3, 170.1, 195.5; Anal. Calcd for $C_{24}H_{19}N_3O_6$: C 64.72; H 4.30; N 9.43%. Found: C 64.70; H 4.32; N 9.41%.

Ethyl 10a-Methyl-7-(4-nitrophenyl)-6,9-dioxo-8,9-dihydro-6H,7H-chromeno[3′,4′:5,6]pyrano[3,2-d]oxazole-7a(10aH)-carboxylate ***5d***. Yield: 448 mg, 96%; white solid; Mp: 210−212 °C; IR (KBr): 3317, 1790, 1750, 1646, 1530, 1412, 1379, 1350, 1314, 961, 719 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 1.21 (t, J = 7.1 Hz, 3H), 1.70 (s, 3H), 4.21−4.33 (m, 2H), 5.09 (s, 1H), 7.31−7.39 (m, 4H), 7.63 (t, J = 7.2 Hz, 1H), 7.79 (d, J = 7.2 Hz, 1H), 8.05 (d, J = 8.7 Hz, 2H), 8.17 (s, 1H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 14.2, 19.8, 64.2, 70.1, 101.1, 105.3, 114.5, 116.8, 123.1, 124.2, 125.0, 130.4, 133.3, 144.8, 147.4, 152.7, 156.5, 157.0, 160.1, 169.3; HRMS (ESI-TOF) m/z Calcd for $[C_{23}H_{18}N_2O_9 + H]^+$: 467.1085, found: 467.1077.

3a-(4-Nitrophenyl)-2,8-dioxo-9-phenyl-1,2,5,7,8,9-hexahydro-6H-chromeno[3,2-d]oxazole-9a(3aH)-carbonitrile ***5e***. Yield: 216 mg, 50%; pale yellow solid; Mp: 152−154 °C; IR (KBr): 3400, 2925, 2852, 1810, 1644, 1527, 1384, 1354, 1089, 994, 854 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me4Si): δ 2.12 (d, J = 15 Hz, 2H), 2.52 (s, 2H), 2.77 (s, 2H), 3.63 (bs, 1H), 4.68 (s, 1H), 7.18−7.29 (m, 5H), 7.50 (d, J = 7.8 Hz, 2H), 8.08 (d, J = 7.5 Hz, 2H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 20.1, 28.5, 36.4, 42.7, 67.8, 105.3, 114.9, 116.1, 123.7, 128.0, 129.1, 129.4, 129.5, 132.5, 140.3, 149.1, 153.1, 171.5, 197.0; Anal. Calcd for $C_{23}H_{17}N_3O_6$: C 64.04; H 3.97; N 9.74%. Found: C 64.06; H 3.99; N 9.76%.

General Procedure for the Synthesis of Pyrroles (6a−e). 1 mmol of 2-oxa-7-azabicyclo[4.1.0]hept-3-en-1-yl carboxylates was taken in 3 mL of alcohol. Then, to it was added 10 mol % of PTSA (0.019 g), and the reaction mixture was heated at 80 °C for the stipulated time. After completion of the reaction (monitored by TLC), alcohol was removed and the mixture was immediately subjected for column chromatographic separation (50−70% ethyl acetate in petroleum ether) to get the pure products. All the synthesized compounds were characterized through spectral (^{1}H NMR, ^{13}C NMR, IR, HRMS, and elemental analysis) data, and X-ray crystallographic analysis (**6a**).

Methyl (3R)-2-Cyano-4-oxo-3-phenyl-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylate ***6a***. Yield: 267 mg, 90%; white solid; Mp: 180−182 °C; IR (KBr): 3433, 3197, 2950, 2861, 1770, 1740, 1579, 1495, 1231, 1181, 700 cm^{-1}; ^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si): δ 2.02 (t, J = 6 Hz, 2H), 2.30 (d, J = 5.4 Hz, 4H), 3.89 (d, J = 1.5 Hz, 3H), 4.71 (s, 1H), 6.52 (s, 1H), 7.23−7.42 (m, 5H); ^{13}C NMR (75 MHz; $CDCl_3$; Me_4Si): δ 21.9, 23.1, 36.1, 54.4, 54.9, 68.1, 111.1, 114.4, 127.9, 128.2, 128.5, 136.6, 167.0, 167.5, 192.2; HRMS (ESI-TOF) m/z Calcd for $[C_{17}H_{16}N_2O_3 + H]^+$: 297.1234, found: 297.1232.

Methyl (3R)-2-Cyano-3-(4-nitrophenyl)-4-oxo-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylate ***6b***. Yield: 300 mg, 88%; pale yellow solid; Mp: 200−202 °C; IR (KBr): 3132, 2957, 2854, 1758, 1597, 1516, 1473, 1349, 1231, 703 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me_4Si): δ 1.85−1.91 (m, 2H), 2.03 (s, 2H), 2.36−2.53 (m, 2H), 3.76 (s, 3H), 4.76 (s, 1H), 7.37 (d, J = 7.8 Hz, 2H), 8.09 (d, J = 7.5 Hz, 2H), 8.64 (s, 1H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 22.4, 23.4, 36.6, 54.6, 55.1, 68.3, 109.0, 123.9, 130.4, 146.2, 190.6; Anal. Calcd for $C_{17}H_{15}N_3O_5$: C 59.82; H 4.43; N 12.31%. Found: C 59.84; H 4.44; N 12.28%.

Methyl (3R)-2-Cyano-4-oxo-3-(thiophen-2-yl)-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylate ***6c***. Yield: 263 mg, 87%; off-white solid; Mp: 160−162 °C; IR (KBr): 3125, 2949, 2861, 2767, 1766, 1582, 1496, 1182, 1140, 1140, 701 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me4Si): δ 6.53 (t, J = 6.53 Hz, 2H), 2.10 (t, J = 6.3 Hz, 2H), 2.38−2.56 (m, 2H), 3.82 (s, 3H), 4.89 (s, 1H), 6.95 (d, J = 3.6 Hz, 2H), 7.38 (t, J = 3.3 Hz, 1H), 8.66 (s, 1H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 21.9, 22.9, 36.2, 49.8, 54.5, 68.5, 109.7, 114.9, 125.8, 126.5, 127.0, 141.9, 166.5, 167.6, 189.9; HRMS (ESI-TOF) m/z Calcd for $[C_{15}H_{14}N_2O_3S + H]^+$: 303.0798, found: 303.0790.

Methyl (3S)-3-(2-Chlorophenyl)-2-cyano-4-oxo-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylate ***6d***. Yield: 298 mg, 90%; off-white solid; Mp: 170−172 °C; IR (KBr): 3123, 2951, 2857, 1754, 1602, 1585, 1476, 1447, 1277, 1243, 1189, 1120, 923, 742, 673 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me4Si): δ 1.98−2.10 (m, 2H), 2.18 (d, J = 4.2 Hz, 2H), 2.49 (s, 1H), 2.59 (s, 1H), 3.88 (s, 1H), 5.04 (s, 1H), 7.13−7.16 (m, 1H), 7.31−7.34 (m, 2H), 7.503 (t, J = 4.4 Hz, 1H), 8.76 (s, 1H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 22.4, 23.5, 36.6, 51.9, 55.0, 68.2, 108.7, 115.3, 127.9, 129.8, 130.2, 130.3, 133.9, 135.5, 167.2, 168.9, 190.7; Anal. Calcd for $C_{17}H_{15}ClN_2O_3$: C 61.73; H 4.57; N 8.47%. Found: C 61.71; H 4.55; N 8.50%.

Ethyl (3R)-2-Cyano-3-(4-nitrophenyl)-4-oxo-2,3,4,5,6,7-hexahydro-1H-indole-2-carboxylate ***6e***. Yield: 263 mg, 74%; off-white solid; Mp: 128−130 °C; IR (KBr): 3213, 2946, 2862, 1759, 1607, 1579, 1521, 1493, 1349, 1238, 1111, 962, 700 cm^{-1}; ^{1}H NMR (300 MHz; DMSO-d_6; Me4Si): δ 1.31 (d, J = 6.6 Hz, 3H), 1.98 (d, J = 5.1 Hz, 2H), 2.16 (s, 2H), 2.50 (s, 2H), 4.36 (s, 2H), 4.83 (s, 1H), 7.51 (s, 2H), 8.22 (d, J = 6.3 Hz, 2H), 8.78 (s, 1H); ^{13}C NMR (75 MHz; DMSO-d_6; Me_4Si): δ 14.2, 22.3, 23.4, 36.5, 54.7, 63.5, 64.3, 68.4, 108.9, 123.9, 130.3, 146.1, 147.6, 166.2, 169.0, 190.6; HRMS (ESI-TOF) m/z Calcd for $[C_{18}H_{17}N_3O_5 + H]^+$: 356.1241, found: 356.1247.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00849.

Materials and method, ORTEP diagrams of compounds **4g**, **5c**, and **6a**, X-ray crystallography data of compounds **4g**, **5c**, and **6a**, and ^{1}H and ^{13}C NMR spectra of all compounds (PDF)

X-ray data of compound **4g** (CIF)

X-ray data of compound **5c** (CIF)

X-ray data of compound **6a** (CIF)

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Notes

The authors declare no competing financial interest.

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